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# Annals of the Rheumatic Diseases

The EULAR Journal






## Annual European Congress of RHEUMATOLOGY

**EULAR 2016**

London, UK, 8–11 June 2016

Abstracts

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Annals of the Rheumatic Diseases

# Annual European Congress of Rheumatology

8 – 11 June, 2016

London, United Kingdom

## Abstracts

The EULAR Journal

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# Welcome Message

Dear Colleagues,

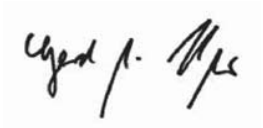
Welcome to this EULAR Annual European Congress of Rheumatology in London!

The annual EULAR congresses which began in 2000 are today a major event in the calendar of world rheumatology. This meeting will again provide a unique occasion for the exchange of scientific and clinical information. It will facilitate interaction between patients, medical doctors, scientists, health professionals and professionals representing the pharmaceutical industry both from Europe and from around the world. You are certainly aware that participating in the congress is just one element of the annual educational package provided by EULAR. Thus in addition, the participants will have the opportunity to watch virtually all oral presentations through electronic capture and will be provided with a complimentary one-year access to the newest developments and publications in the field of RMDs.

EULAR has grown rapidly in terms of the number of participants and the quality of the submissions. Thus, more than 4'000 abstracts have been submitted to this congress in London and 199 sessions and poster tours are offered. This enormous success reflects the ever increasing interest in rheumatic and musculoskeletal diseases (RMDs) which has been seen in most societies and is now recognized also by the EU. It also reflects the availability of increased information on the size, burden and cost of these diseases for society, and a significantly improved ability to diagnose and treat them. The incorporation of health professional and patient organisations within EULAR has been a considerable stimulus for these advances.

The EULAR Congress 2016 in London will once again provide a wide range of topics including clinical innovations, clinical translational and basic science. In addition there will be significant contributions made by People with Arthritis and Rheumatism (PARE), by Health Professionals in Rheumatology (HPR) and by the health care industry. The core science and central activity of the congress will be the poster presentations and poster tours with their highly interactive exchanges between participants. The London meeting will further promote the reputation of the EULAR Congress as the most innovative and informative venue for clinical research for the practising physician. The EULAR EMEUNET organisation of young rheumatologists also hopes to attract young colleagues to the meeting and will disseminate the message that rheumatology is one of the most attractive and successful disciplines of medicine.

The city of London needs little introduction. "Tired of London, tired of life" is a quotation previously used for the 2011 EULAR congress in London, and it is even more reinforced by the recent accolade of "world city", and indicates how ideal a venue this is for an international meeting such as the EULAR Congress which has truly become a world congress. The elegance of London with its architecture, galleries, theatres and ambience should again provide an excellent background for clinical exchanges, international collaborations and renewal of friendships. It is our great pleasure and a real joy in welcoming medical doctors, patients, health professionals and representatives of the pharmaceutical industry and hope their stay in London will be delightful, informative, and educational.



GERD R. BURMESTER
*President of EULAR*

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# Speakers Abstracts

# Speaker Presentations

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## WIN session 1

### SP0001 WHAT IS NEW IN VASCULITIS?

C.G. Kallenberg. *Dept. of Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, Netherlands*

The vasculitides comprise a heterogeneous group of disorders characterized by inflammation of blood vessels. Definitions of these conditions have been provided by the Chapel Hill Consensus Conference (updated in 2012). A large prospective study defining and validating diagnostic and classification criteria for the vasculitides (DCVAS, ClinicalTrials.gov NCT01066208) is underway.
In the ANCA-associated vasculitides morbidity and mortality is still very high, in the initial phase due to disease activity and infections, in the late phase due to cardiovascular disease and malignancies. Use of high dose corticosteroids and cyclophosphamide (CYC) plays a major role in morbidity and mortality. Recent studies have shown that CYC can be replaced by rituximab (RTX), both for induction and maintenance treatment. Phase 2 data suggests that prednisone can be replaced by an oral complement C5a-receptor inhibitor. Defining risk factors for relapse is important in order to select patients for long-term maintenance treatment. Some biomarkers for relapsing disease have been defined, such as PR3-ANCA vs. MPO-ANCA, rises in PR3-ANCA in renal disease and pulmonary hemorrhage, HLA-DPB1, and others, but prospective studies should demonstrate their clinical value with respect to level and duration of maintenance treatment.
In giant cell arteritis (GCA) aortitis has been recognized to occur in one out of three patients although being less severe in GCA than in isolated aortitis. Color duplex ultrasonography is valuable for a diagnosis of GCA, is comparable to MRI, but its use for selecting the site of biopsy did not improve the sensitivity of a temporal artery biopsy for a diagnosis of GCA. FDG-PET is useful as well for assessing active vascular inflammation in GCA and Takayasu arteritis but objective cut-off values for activity should still be defined. Levels of BAFF and Il-6 in serum are biomarkers for disease activity in GCA and PMR. In this respect, a phase 2 trial with tocilizumab in GCA has been succesful in showing that tocilizumab together with prednisone resulted in a higher rate of complete remission at a dose of 0.1 mg/kg/d at 12 weeks and a higher rate of relapse free remission at 52 weeks compared to prednisone alone. EULAR/ACR recommendations for the management of PMR have been established last year.
New developments in the other vasculitides will be discussed as well.
**Disclosure of Interest:** None declared
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### SP0002 SYSTEMIC SCLEROSIS

J. Varga. *Northwestern Scleroderma Program, Feinberg School of Medicine, Evanston, United States*

Scleroderma remains a challenging disease with no effective therapy. Obstacles to development of effective therapies include the complex, multifactorial pathogenesis, lack of clear etiologic agent, uncertain role of genetic risks; patient-to-patient variability in clinical manifestations and disease outcomes; variable rates of disease progression in different organs in the same individual; lack of validated biomarkers, and lack of consensus regarding optimal clinical trial design. Each of these obstacles is being addressed by current research, and significant progress is being achieved. A large number of plausible drug targets have been identified and are being validated in preclinical models. Innovative clinical trial designs and increasingly more robust outcome measures allow more effective drug testing. Molecular omics approaches further facilitate patient stratification, and matching drugs to patients in an increasingly personalized precision approach to management.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## Catastrophizing pain in RA

### SP0003 THREE RA PATIENTS WITH PAIN CATASTROPHIZING

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Rheumatoid arthritis (RA) is a chronic inflammatory joint disease causing pain and disability. Discordance between inflammatory activity and pain in RA has earlier been reported, and one important psychosocial factor that influences the experience of pain is *catastrophizing*. Pain catastrophizing involves both cognitive and emotional components of pain perception, and leads the patient to expect the worst. Several studies have shown that pain catastrophizing is important for the pain experience in RA, with no clear correlation to objective clinical parameters.
Patients' perspective, including pain, patient global assessment and fatigue, has increasingly been recognized as an outcome measure for therapies. Catastrophizing may therefor influence disease activity scores in RA and also measurements of response to biologic disease modifying drugs (bDMARD).
Three patients with RA starting bDMARD will we presented through one-year follow-up data from the ULRABIT cohort. The patients reveal different pain catastrophizing levels during the study, and we will explore the impact of catastrophizing on subjective and composite scores, in contrast to objective inflammatory variables such as CRP, swollen joint count or ultrasound synovitis. Further, we will discuss the impact of pain catastrophizing on DAS28 remission, demonstrating the difficulties in reaching remission according to composite scores if there are increased levels of pain catastrophizing.
Patient 1: high level of pain catastrophizing both at baseline and at 12 months.
Patient 2: pain catastrophizer at baseline, but not at 12 months.
Patient 3: neither pain catastrophizer at baseline nor at 12 months.
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### SP0004 THE IMPACT OF CATASTROPHIZING IN OBTAINING REMISSION IN RA

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Pain catastrophizing is conceptualized as a negative cognitive–affective response to anticipated or actual pain and has been associated with a number of important pain-related outcomes. Catastrophizing is defined as a tendency to magnify or exaggerate the threat value or seriousness of pain sensations, and tendency to pain-related worry and fear, coupled with an inability to divert attention away from pain.
A Coping Strategies Questionnaire (CSQ) was developed and later a Pain Catastrophizing Scale (PCS). Factor analytic work indicated that the PCS yielded the three second-order factors helplessness, rumination and magnification. Thus pain catastrophizing evaluated by the questionnaires is characterized by the tendency to magnify the threat value of pain stimulus and to feel helpless in the context of pain, and by a relative inability to inhibit pain-related thoughts in anticipation of, during or following a painful encounter [1].
Pain catastrophizing has most typically been conceptualized and assessed as a dispositional variable. However, maladaptive thoughts are latent and in need of a cue to become manifest. Enough evidence has accumulated to suggest that high levels of catastrophizing about pain should be considered a "risk marker" for adverse immediate and long-term pain-related outcomes. Moreover, the apparent role of catastrophizing in contributing to the effectiveness of a variety of pain treatments suggests that it may become a key target of many chronic pain management programs.
Pain is the most common and disabling symptom of rheumatoid arthritis (RA). Although physicians often assume that inflammation is the stimulus for pain, many RA patients continue to have pain despite adequately suppressed inflammation. A review on pain catastrophizing [2] found that it is positively related, in both cross-sectional and prospective studies across different musculoskeletal conditions, to the reported severity of pain, affective distress, muscle and joint tenderness, pain-related disability, poor outcomes of pain treatment, and, potentially, to inflammatory disease activity. Moreover, these associations generally persist after controlling for symptoms of depression. There appear to be multiple mechanisms by which catastrophizing exerts its harmful effects, from maladaptive influences on the social environment to direct amplification of the central nervous system's processing of pain.
Several prospective studies have illustrated the longitudinal association of catastrophizing with pain in RA. In daily diary studies, patients with RA who exhibited greater catastrophizing reported more day-to-day pain and attention to pain than low catastrophizers. Findings from another prospective study suggested that baseline catastrophizing scores predicted enhanced pain and depression in patients with RA at 1-year follow-up. Catastrophizing may also influence the success of pain-related treatments in patients with musculoskeletal disease.
Our group found the level of pain catastrophizing to be highly associated to all patient's reported outcomes (joint pain VAS, patient's global VAS, MHAQ, tender joints) as well as composite scores (DAS28, SDAI, CDAI) in contrast to no associations with the more objective assessments (swollen joints, laboratory and ultrasound assessments) in established RA patients starting bDMARD [3]. This may have important consequences regarding the evaluation of disease activity of patients with established.
We also found that the level of pain catastrophizing decreased during the one-year study, indicating that pain catastrophizing may be influenced by the clinical

treatment including both psychosocial and medical factors. In addition, patients shifting from being pain catastrophizers to not being pain catastrophizers after one year, showed significantly lower levels of patient's reported outcomes than patients staying pain catastrophizers, in spite of no differences in objective measures of disease activity.
Thus, pain catastrophizing is a critically important variable in understanding the experience of pain in rheumatologic disorders as well as other chronic pain conditions. It is important to be aware of the level of pain catastrophizing in the evaluation of medical treatment of patients with different inflammatory rheumatic diseases.
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### SP0005 THE PAINDETECT QUESTIONNAIRE USED AS A CLINICAL TOOL IN PATIENTS WITH ARTHRITIS

K. Amris on behalf of S. Rifbjerg-Madsen. *The Parker Institute, Copenhagen University Hospital Bispebjerg and Frederiksberg, Frederiksberg, Denmark*

Emerging evidence suggests that pain might be more effectively classified and treated according to the mechanisms underlying the onset and/or the maintenance of pain. Multiple mechanisms that can produce pain have been identified, including tissue injury and inflammation (inflammatory pain), damage to the nervous system (neuropathic pain), and abnormal responsiveness or function of the central nervous system (central sensitization, dysfunction of descending pain modulating systems). Central pain mechanisms may play an important role in rheumatic diseases, traditionally considered peripheral inflammatory entities. Inflammation sensitizes polymodal nociceptors. This peripheral sensitization induces hyperexcitability of nociceptive neurons in the central nervous system (central sensitization) and the two together generate the features of pathological pain, allodynia and hyperalgesia, confined to the inflamed tissues. Increased responsiveness of peripheral and central neurons (pain hypersensitivity) in the presence of tissue injury and inflammation is a normal response (neuroplasticity). As a rule, these sensitization phenomena extinguish themselves as the tissue heals and inflammation subsides. However, persistent pain is common in patients with inflammatory joint disorders and the key question is whether these neuroplastic changes persists in subsets of patients and leads to chronic pain states in which pain is no longer coupled to the presence of ongoing peripheral inflammation. If central pain mechanisms do play a significant role in pain processing and persistence of pain in subgroups of patients, strategies for managing pain in addition to inflammatory disease suppression may be required. Furthermore, in these patients, persistent pain hypersensitivity may lead to continuous high reports of tender joints and poor global health and pain leaving the physician with the clinical dilemma that patient reported outcomes and composite disease activity scores do not correspond to the objective level of inflammatory activity.
Simple methods assisting identification of underlying pain mechanisms in the clinical care of rheumatologic patients are therefore needed. The painDETECT Questionnaire (PDQ) is a patient administered screening questionnaire originally developed to determine the likelihood of a predominant neuropathic pain component being present. The questionnaire comprises 7 weighted somatosensory symptom and sign items and 2 items relating to the spatial (radiating) and temporal characteristics of the individual pain pattern. Although developed as a screening questionnaire for neuropathic pain, the PDQ has increasingly been used to assess neuropathic pain features as a proxy of central pain mechanisms in, for example, patients with osteoarthritis and fibromyalgia. Recently, the PDQ has also been introduced in studies assessing pain mechanisms in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA).
The clinical utility of the PDQ in patients with arthritis will be covered based on patient cases, registry data and clinical studies. The prevalence and description of PDQ-derived pain phenotypes and the prognostic value thereof will be discussed.
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**WEDNESDAY, 8 JUNE 2016**

## Axial spondyloarthritis and psoriatic arthritis: emerging pathways

### SP0006 THE IL-17 PATHWAY IN THE PATHOGENESIS OF SPA: FOCUS ON STRUCTURAL DAMAGE

D. Baeten. *Clinical Immunology and Rheumatology, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands*

The IL-17 pathway is now firmly established to play a central role in the pathogenesis of axial and peripheral SpA. The evidence from genetics, functional studies, experimental models, and human expression analysis has been confirmed by phase III clinical trials with anti-IL17A antibodies in ankylosing spondylitis (AS) and psoriatic arthritis (PsA) showing a profound suppression of signs and symptoms of inflammation. Interestingly, these trials also showed a suppression of articular destruction in PsA and low mSASSS progression rates in AS. A key scientific and clinical question is thus how and to what extend the IL-17 pathway contributes to structural damage in SpA.
The role of IL-17A in driving osteoclast maturation and activation is well understood. Its potential role in new bone formation, however, remains much more controversial. Recent animal experiments indicate that IL-17A may suppress osteoblast activity and new bone formation by inhibition of Wnt signaling. In contrast, however, work in the HLA-B27 tg rat model showed that IL-17A inhibition halts pathological axial and peripheral osteoproliferation. Albeit this may be an indirect effect related to suppression of inflammation, bone formation experiments with human cells indicate a direct osteoblast-promoting effect of IL-17A. This concept is further supported by recent studies in bone fracture models.
The differential effects of IL-17 family members on bone formation illustrates well that the functional outcome of cytokine signaling is highly dependent on the exact cellular and immunological context in which it is occurring, with important difference between mice and humans. Further translational studies in human patients are needed to establish whether IL-17 blockade may not only suppress inflammation but also halt both catabolic and anabolic aspects of structural damage in human SpA.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## HOT session 1

### SP0007 IMAGING IN DIAGNOSIS: HOW TO DO

M. Østergaard. *Copenhagen Center for Arthritis Research, Copenhagen University Hospital Rigshospitalet, Glostrup, Denmark*

This talk reviews the current knowledge on how to use imaging in clinical practice in the diagnostic process, when peripheral or axial inflammatory diseases, such as rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis or gout, are suspected. Conventional radiography, magnetic resonance imaging (MRI), ultrasonography, computed tomography (CT), dual-energy CT and optical imaging will be addressed, as will international recommendations and criteria published by European League of Rheumatology (EULAR), American College of Rheumatology (ACR), The Assessment of SpondyloArthritis international Society (ASAS).
The main focus will be how to do in current clinical practice. However, the talk will also briefly address recent and upcoming advances, which are likely to improve our routine clinical practice with the coming few years.
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**WEDNESDAY, 8 JUNE 2016**

## Balancing benefits and risk of glucocorticoids; a challenge for implementation

### SP0008 UNDER WHAT CONDITIONS MAY LONG-TERM GLUCOCORTICOIDS HAVE A GOOD BENEFIT-RISK RATIO?

F. Buttgereit. *Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, Berlin, Germany*

Although there is convincing evidence for the beneficial effects of glucocorticoids at low dosages to treat rheumatoid arthritis and other rheumatic diseases, the potential harms lead patients and physicians to be grouped as glucocorticoid "supporters", "opponents" or "neutrals" (i.e. people not favouring any pro or con position, perhaps the majority). In detail, patients are usually aware of both benefits and risks of glucocorticoid therapy. There is, however, sometimes even a certain imbalance favouring the risks over the benefits. This may be reflected in serious concerns about adverse effects and sometimes even refusal to take

glucocorticoid treatment which hinders optimal treatment. Also with regard to medical doctors, nobody really questions the efficacy of these drugs, but the splitting up into the mentioned groups is primarily driven by safety concerns. And indeed, every group has their good arguments.
To approach this problem, a EULAR Task Force was convened in order to achieve consensus on specific conditions where long-term glucocorticoid therapy has an acceptably low risk of harm in the treatment of chronic inflammatory rheumatic diseases (Strehl et al., Ann Rheum Dis, 2016). After a systematic literature search, the evidence on the four most worrisome adverse effects of glucocorticoid therapy (osteoporosis, hyperglycaemia/diabetes mellitus, cardiovascular diseases, and infections) was critically reviewed. Robust evidence on the risk of harm of long-term glucocorticoid therapy was often lacking since relevant study results were often either missing, contradictory, or at a high risk of bias. The group agreed that the risk of harm is low for the majority of patients at long-term dosages of $\leq$5mg prednisone equivalent per day, whereas at dosages of $>$10mg/d the risk of harm is elevated. At dosages between $>$5 and $\leq$10mg/d, patient-specific characteristics including protective and/or risk factors need consideration when estimating the risk of harm.
In conclusion, the level of harm of glucocorticoids depends on both dose and patient-specific parameters. General, disease and glucocorticoid associated risk factors but also protective factors like a healthy lifestyle should be taken into account when evaluating the actual and future risk.
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## SP0009 PATIENTS' VIEW ON THE EULAR RECOMMENDATIONS

N. Caeyers. *ReumaNet vzw, Mol, Belgium*

The use of glucocorticoids has always had a negative connotation among patients. Within the general public the beliefs still stand that the side effects cause more harm than that this medication is helping the patient. Pressure from the environment also keeps people away from the treatment with GC, as well as confrontation with visible side effects.
But not only patients, also some health professionals tend to believe GC are more harmful than good. They are especially reluctant to prescribe high doses, although for some conditions this could be lifesaving.
Patients often do a Google search on the internet when prescribed new medication. Reading these awful stories, having doubtful information and the pressure from their peers and consulting a doctor who is not convinced of the benefits of GC, might make them refuse to start treatment.
The EULAR recommendations on the use of GC can help change this perception among patients' and clinicians' communities. These recommendations are now available in a lay version which means also people with a non-medical background can read and understand the important messages. To change the view of patients, but also GP's and other health care professionals, it would be worthwhile to spread this information. Patient and scientific organisations can play an important role in the implementation.
In Flanders, we have already made the translation and put the lay version on the website, together with the original manuscript. Some quotes of people who have read the recommendations show these guidelines are also valuable for patients.
*"Finally, this is medical information that I can understand! This is useful for me"*
*"These recommendations give information in a clear and comprehensive way. They allow me to contribute in the process to get the best possible care for me. I can now make well-informed decisions and can ask more direct questions to my rheumatologist."*
*"It is nice to know patients were involved in developing these recommendations. This means also our concerns were heard."*
This lecture will feature results of a survey among Flemish and Dutch patients about their view on GC as well as their ideas to use lay versions of scientific publications.
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## SP0010 CAN WE CHANGE PERCEPTIONS ON THE USE OF GLUCOCORTICOIDS?

M. de Wit[1,2]. [1]*Standing Committee of People with Arthritis/Rheumatism in Europe (PARE), EULAR, Zurich, Switzerland;* [2]*Medical Humanities, VU University Medical Centre, Amsterdam, Netherlands*

Glucocorticoids have a bad reputation. not only among patients but also among health professionals and the general public. It makes that the same scientific data can be interpreted differently and leads to recommendations that are seen as arbitrary. The lack of consensus confuses patients who receive different messages when prednisolon is prescribed and it hampers an effective implementation of recommendations in clinical practice. The result is that patients are not optimally informed and educated about the real benefits and risks of the treatment. It can lead to non-adherence, under-treatment, over-treatment, the use of expensive medicines and ultimately to suboptimal disease outcomes.
With the new EULAR consensus document the first hurdle of controversial recommendations has been tackled. This document paves the way to a better education of patients, health professionals and general public. However, the key messages are difficult to understand and require an effort of all involved to develop an innovative approach to communicate the complex interplay between disease activity and the benefits and risks of glucocorticoid use to patients. The first step is to disseminate the recommendations in a tailored manner to the different audiences. Patients require other kinds of information and provided in other formats than health professionals or the general public. Examples will be presented during this session.
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## SP0011 LONG-TERM GLUCOCORTICOID USE AND THE SKIN

J.W. Jacobs. *University Medical Center Utrecht, Utrecht, Netherlands*

Glucocorticoids (GCs) are frequently and often chronically used for the treatment of rheumatoid arthritis (RA) and other immune diseases and vasculitis. An estimated 0.8–1.2% of the population in developed countries at any moment in time uses GCs.[1,2] EULAR guidelines state that the adverse effects (AEs) of GC therapy should be considered and discussed with the patient before treatment is initiated.[3] However, reliable quantitative data on cutaneous AEs are lacking.[4]
**Methods:** We performed a study to assess the occurrence of cutaneous AEs of GCs and its association with current and cumulative GC-doses. This cross-sectional study was performed at the outpatient departments of the Charité University Medicine Berlin and the University Medical Center Utrecht; 381 RA-patients were included. Patients were classed into 4 groups, according their mean daily dose during the past 12 months: 0 mg (n=87), $<$5mg (n=108), 5–7.5 mg (n=130), and $>$7.5 mg (n=56) of prednisolone equivalent.
Cushingoid appearance, ecchymosis, stretch marks, steroid acne, perioral dermatitis, hirsutism, and scalp hair loss were assessed by physical examination using a predefined scoring system, and by patients' self-assessments. Easy bruising, skin atrophy, and impaired wound healing were patients' self-assessed reports. Data were analyzed according GC dose categories and cumulative doses.
**Results:** Of the 381 patients, 76% was female; 67% was rheumatoid factor positive and 55% had erosive joint disease. The median (quartiles) disease duration was 9 (4–17) years. The mean number of lifetime conventional synthetic DMARDs used was 2.6 and for biological DMARDs it was 1.0. The median (quartiles) total duration of GC use was 4.0 (1.5–10) years, and the mean (sd) cumulative dose was 14 (17) g.
Cushingoid habitus, easy bruising, skin atrophy, and impaired wound healing as reported by patients occurred significantly more frequent in those using GC the past 12 months, compared to those not using GC, see figure. At physicians' assessments, only Cushingoid habitus and ecchymosis were more prevalent in GC-users, see figure. The prevalence of these AEs was statistically significantly positively associated with current and cumulative GC dose.

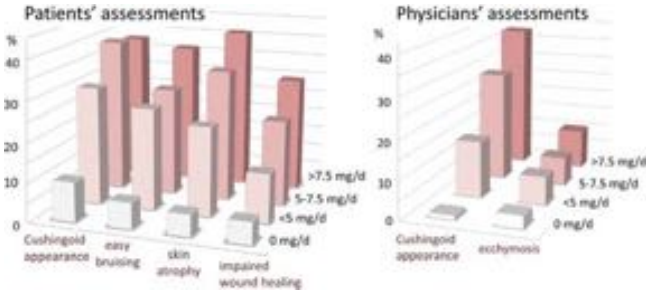



Figure 1

There was a low occurrence of abnormal stretch marks, acne, perioral dermatitis, alopecia, and hirsutism in our study, and there were no correlations between these AEs and GC therapy.
**Conclusion:** Cushingoid habitus, easy bruising, skin atrophy, impairment of wound healing, and ecchymosis are AEs of GC which can be observed relatively frequently in clinical daily practice. They are GC dose-dependent (current and cumulative dose). At the lower GC doses used in RA, abnormal stretch marks, acne, perioral dermatitis, alopecia, and hirsutism are rare AEs of GC.
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treatment in rheumatoid arthritis: published evidence and prospective trial data. Ann Rheum Dis 2006; 65: 285–93.
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**WEDNESDAY, 8 JUNE 2016**

## What CVD outcomes to use in clinical rheumatological practice?

### SP0012 HOW TO ASSESS THE CVD RISK IN THE INDIVIDUAL PATIENT?

N. Sattar. *BHF Centre, University of Glasgow, Glasgow, United Kingdom*

This talk will overview the methods of assessing CVD risk in patients with Rheumatoid arthritis. It will give a rationale for why CVD risk screening in RA can be done using risk scores developed for the general population and also give two examples of scores which include RA as a risk stratifier. The talk will highlight that i) CVD risk scoring is easy to do in routine clinical practice, ii) requires simple additional of non-fasting lipids and blood pressure, iii) can be intergrated to existing RA clinics and iv) can be repeated at intervals of time which is pragmatic. The talk will further emphasise that consideration of usual CVD risk factors is critically important in determing who should be recommended statins and that having RA alone does not mean individuals are necessarily at high CVD risk. A case history will be used to highlight main points discussed in the talk. Finally, the talk will also discuss the pros and cons of additional tests and discuss the recommendations from recent guidelines which will fit in with the talks conclusions.
**Disclosure of Interest:** N. Sattar Consultant for: Roche, Astrazeneca, Amgen, Sanofi, Merck, Speakers bureau: Roche
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### SP0013 IS IT ENOUGH JUST TO TREAT INFLAMMATION TO REDUCE CARDIOVASCULAR RISK?

M.T. Nurmohamed. *Amsterdam Rheumatology immunology Center (ARC) | VU University Medical Center & Reade, Center for Rheumatology and Rehabilitation, Amsterdam, Netherlands*

The risk of cardiovascular disease (CVD) is up to twofold increased in patients with inflammatory joint disorders (IJD). This increased CVD risk is due to both traditional risk CVD risk factors such as hypertension, smoking and dyslipidemia as well as the underlying chronic systemic inflammation in IJD. Traditional CV risk factors are more often present in IJD and partially a consequence of changes in physical function related to the underlying IJD. Approximately 50% of the increased CV risk is due to traditional CV risk factors and 50% due to the inflammatory process. Inflammation may have a negative impact on CV risk factors, but this effect only marginally explains the increased prevalences of CV risk factors.
CV risk management should thus not only target the inflammation but also CV risk factors. It has three main principles: non-pharmacological interventions, pharmacological management of CV risk factors, and control of disease activity.
**Non-pharmacological strategies:** Life style management should include counselling for smoking cessation (albeit that the favorable cardiovascular effects of smoking cessation might be less than in the general population) as well as increasing physical activity, and healthy (Mediterranean) diet.
**Treatment of CV-risk factors:** Thus far, adequate CV endpoint trials with statins and or antihypertensive agents have not been published. However, population and databases investigations indicate that antihypertensive agents and statins do not work less than in the general population. Indeed, statins have additional anti-inflammatory effects, that might be important from a CV point of view.
**Disease activity:** There is mounting evidence that cumulative disease activity as well as the number and duration of flares over time do contribute to the cardiovascular risk.
Hence, inflammation reduction is important for CVD risk reduction, but it appears that the type of treatment is less important. Nowadays, tapering of biologicals is becoming more and more standard of care and has several benefits, but one of the drawbacks might be the possible negative effect on thrombotic markers. As thrombotic markers normalize with biologicals therapy, this favorable effect might be reversed and thus exposing our patients to an increased CV-risk.
Furthermore, it is important to realize that it cannot be excluded some biologic agents as well as targeted synthetic DMARDs might have adverse cardiovascular effects. Finally, NSAIDs/COXIBs and steroids might have a negative impact on the cardiovascular risk profile.
**Conclusions:** The increased CV risk in IJD is widely acknowledged for about a decade. Nonetheless, CV mortality has hardly improved, despite major improvements in antirheumatic therapy. Hence, targeting disease activity only is just NOT enough to reduce the CV risk of our patients. In line of this, most (recent) studies indicate poor CV risk management in daily clinical practice and thus the CV challenge for the future is optimizing CV risk management and its implementation.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6265

**WEDNESDAY, 8 JUNE 2016**

## Different perspectives on pain in osteoarthritis

### SP0014 PERIPHERAL AND CENTRAL PAIN SENSITIVITY IN OSTEOARTHRITIS

L. Arendt-Nielsen. *Center for Sensory-Motor Interaction (SMI), School of Medicine, Aalborg University, Aalborg E, Denmark*

Today's management of osteoarthritis (OA) consists mainly of symptomatic treatment of pain although traditional analgesics such as NSAIDs may offer only weak pain relief and risk serious adverse reactions. New safe and more efficient treatment regimes are needed for OA, but such a development requires a solid fundamental understanding of the peripheral and central pain mechanisms involved in OA.
OA is characterized by a progressive erosion of articular cartilage and bone remodelling which can be accompanied by pain, local inflammation, and joint degeneration. The main biological factors thought to be responsible for cartilage degradation are the matrix metalloproteinases (MMP) and aggrecanases. Biochemical markers of OA pathophysiology have received increasing attention due to their superior sensitivity in comparison with conventional structural (e.g. radiological) endpoints.
In the individual patient, little association is found between joint damage, local inflammation, and pain. Recently cytokine levels, degree of sensitization (local and spreading), descending pain control, comorbidities, and pain duration are some of the individual factors playing a role for pain severity. With the expected demographic and lifestyle changes, the incidence of joint pain will continue to increase. Better understanding of the individual fundamental pain mechanisms may improve patient profiling, help individualizing management, suggest new treatment options and thereby advance the development of new therapies.
The sources pain in OA and mechanisms responsible are not well understood. Joint nociception can lead to peripheral and central sensitization. It has consistently been shown that pain intensity, pain durations, and the number of OA locations are important drivers for sensitization in OA.
Various animal models of OA have been established to investigate the consequences of experimental OA on pain processing and various pain mechanisms, but they do not translate well into humans. As a consequence, data derived from these models for drug development programs are not always predictive of efficacy, and new strategies are needed for developing translational pain biomarkers. In clinical OA conditions, the poor relationship between joint pathology and pain is found, and better understanding and characterization of the underlying mechanisms of pain are important. Techniques for assessing pain mechanisms in OA patients provide biomarkers capable of quantifying pain mechanisms such as temporal summation, descending inhibition, spreading sensitisation, and primary and secondary hyperalgesia. Such pain biomarkers can help to phenotype OA patients based on the contribution of peripheral and central pain sensitization. Biomarkers are currently being explored as tools to facilitate better understanding of pain mechanisms and to predict pain outcomes after e.g. total knee replacement surgery. Preoperative pain intensity, acute postoperative pain, and pain sensitization have been shown to be predictors for the development of chronic postoperative pain after knee joint replacement.
Relating clinical benefit of a given therapy with quantitative assessment of the pain mechanisms involved provides new opportunities for tailored and individualized management regimes. The use of biological biomarkers in combination with techniques such as comprehensive quantitative sensory testing that explore OA pain mechanisms has increased the understanding of dynamic pathological events that lead to patients' symptoms.
**Disclosure of Interest:** None declared
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### SP0015 PAIN TRAJECTORY GROUPS IN PERSONS WITH OSTEOARTHRITIS

G.M. Peat. *Arthritis Research UK Primary Care Centre, Research Institute for Primary Care & Health Sciences, Keele University, Keele, United Kingdom*

Pain in persons with osteoarthritis does not follow a simple, single, immutable 'natural history'. In recent years several prospective cohorts using repeated measures of patient-reported health states have matured and there has been a flurry of publications on the existence of discrete developmental trajectories of reported pain severity and other states. What does it all add up to? And what

does it teach us about concepts of time, heterogeneity, and prognosis in OA? This presentation will (i) briefly introduce the rationale and assumptions underlying these methods, (ii) review published findings when applied to pain and other patient-reported health states in osteoarthritis, (iii) discuss implications of these findings for research and clinical practice, (iv) contemplate productive directions for future investigation in this field.
**Disclosure of Interest:** None declared
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### SP0016 EXERCISE THERAPY TO REDUCE PAIN IN KNEE OSTEOARTHRITIS: MECHANISMS AND TREATMENT OPTIMIZATION

M. Van Der Leeden. *Rehabilitation Research, Reade, Amsterdam, Netherlands*

Exercise is effective in reducing pain in knee osteoarthritis (moderate effect size)[1]. The working mechanisms of the positive effects of exercise therapy in knee OA are not fully elucidated. Improvement in physiological factors such as upper leg muscle strength, joint range of motion and proprioception have been found to be related to improvement in pain and activity limitations[2], but also psychosocial and general health related mechanism might be involved. Additionally, reduction in local as well as systemic inflammation seems to be a working mechanism of exercise therapy, although evidence is still limited.
Severe knee pain hampers the ability to participate in exercise therapy. Patients with knee OA who experience severe knee pain form a substantial group of patients with knee OA. These patients may benefit insufficiently from exercise therapy. Recently, an intervention protocol which combines standardized analgesic prescription and exercise therapy has been developed[3]. The purpose of this intervention protocol was to reduce pain by optimization of analgesics, thereby allowing the patient to participate in exercise therapy. The feasibility and outcome of this combined intervention will be presented.
**References:**
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### SP0017 THE EFFECT OF NON-PHARMACOLOGICAL INTERVENTIONS FOR HAND OA

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The hand is a common site of peripheral osteoarthritis (OA). The most common sites for hand OA are distal and proximal interphalangeal joints and the base of the thumb. Because the natural history of hand OA is poorly understood and there is no preventive treatment or cure after the onset of development, the goal of OA treatment is the management and alleviation of pain as well as the maintenance and improvement of functional capacity. Many non-pharmacological treatments, including patient education, assistive technology, splinting, therapeutic exercises and physical therapies, has been used to treat patients with hand OA. This presentation will provide an overview the principles of these treatment methods and the scientific evidence supporting the efficacy of these treatments in relieving pain and improving function.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## Epigenetics solving the OA puzzle

### SP0018 DNA METHYLATION AND OSTEOARTHRITIS

L.N. Reynard. *Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom*

One mechanism of epigenetic gene regulation is DNA methylation, which involves the addition of a methyl group to a cytosine base by DNA methyltransferase enzymes and occurs predominantly at CpG dinucleotides in mammalian cells. DNA methylation within the gene promoter regions is associated with gene repression through effects on transcription factor binding and recruitment of chromatin remodelling complexes. In contrast, gene body methylation positively correlates with gene expression and has been implicated in transcription from alternative promoters as well as alternative splicing.
DNA methylation changes occur during aging and in response to environmental factors including diet and smoking. Furthermore, aberrant DNA methylation patterns have been implicated in the aetiology of many common human disease including cancer, RA and SLE. Over the last 10 years, there has been increasing interest in the potential contribution of DNA methylation in the molecular mechanisms underlying OA pathogenesis, which will be the focus of this talk. I will begin by examining candidate gene studies that have focused on the relationship between cartilage promoter methylation, transcription factor binding and mRNA expression of genes implicated in OA, including the OA susceptibility gene *GDF5*, the chondrogenic transcription factor SOX9 and the matrix degrading enzyme MMP13. I will then review the key findings from genome-wide DNA methylation studies of osteoarthritic cartilage and bone. These DNA methylome studies have shown that hip and knee cartilage are epigenetically distinct, and have highlighted the potential importance of cartilage inflammation and TGFβ signalling in OA pathogenesis. I will finish by discussing areas for future DNA methylation studies in OA research and, given that OA is a disease of the whole joint, the potential to extend these analyses to other tissue compartments.
**Disclosure of Interest:** None declared
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### SP0019 HISTONE MODIFICATION AND OSTEOARTHRITIS

S. Monteagudo. *Skeletal Biology and Engineering Research Center, KU Leuven, Leuven, Belgium*

Epigenetic mechanisms, processes that alter gene expression without changes in DNA sequence, precisely regulate gene expression by dynamic remodeling of chromatin. Eukaryotic DNA is wrapped around a histone octamer (H3/H4 heterotetramer and two H2A/H2B dimers) to form the nucleosome, the fundamental building block of chromatin. Histone proteins are subject to covalent modifications that modulate the local structure of chromatin and influence gene expression by regulating the accessibility of gene loci to transcriptional machinery. The dynamic remodeling of chromatin through histone modifications by nuclear proteins including histone acetyltransferases, deacetylases, and methyltransferases, as well as by demethylases, modulate spatiotemporal gene expression during cartilage development, homeostasis and disease.
Disruptor of telomeric silencing 1-like (DOT1L) is the main histone-modifying enzyme that catalyzes the methylation on lysine-79 of histone 3 (H3K79). The human protein DOT1L contains 1537 aminoacids, with its N-terminal part responsible for the methyltransferase activity. The remaining C-terminal part is involved in physical interactions with many transcription relevant proteins. The general function of DOT1L is to methylate H3K79 as a member of a large protein complex, which can influence the transcriptional state. DOT1L's histone methyltransferase activity has been linked to active transcription, and plays a role in many biological processes including the DNA damage response, the cell cycle, embryonic development and cell reprogramming. In cancer biology, DOT1L is involved in MLL-rearranged leukemia and in other tumors. We reported a strong genetic association between polymorphisms in the human *DOT1L* gene and hip cartilage thickness as well as osteoarthritis (OA). Variations in the *DOT1L* gene are also associated with human height. Furthermore, we earlier demonstrated that silencing of *Dot1L* inhibited chondrogenic differentiation of murine progenitor cells. Interestingly, DOT1L-associated H3K79 methylation has been linked to the Wingless-type (Wnt) cascade. Gain and loss of function studies for Wnt signaling mediator beta-catenin or Wnt antagonists such as Frizzled related protein have demonstrated that tight regulation of this pathway is key to joint health. This could specifically identify DOT1L as an attractive target for joint diseases, more particularly for OA. DOT1L is an enzyme and, thus, can be pharmacologically modulated.
We therefore hypothesized that DOT1L plays a major role in cartilage homeostasis by tightly regulating gene expression patterns of key signaling pathways, such as the Wnt cascade. New insights into the transcriptional mechanisms may contribute to the development of new epigenetics-based strategies for the treatment of joint diseases, adding a new way to modulate fundamental signaling pathways in joint disease and repair.
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### SP0020 THE ROLE OF MICRORNAS IN THE PATHOGENESIS OF OSTEOARTHRITIS

I. Clark on behalf of Tracey E Swingler, Linh TT Le, Natalie Crowe, Matt J Barter, Guy Wheeler, Tamas Dalmay, David A Young. *School of Biological Sciences, University of East Anglia, Norwich, United Kingdom*

Small non-coding RNAs known as microRNAs (miRs) have recently been recognised as important regulators of gene expression in human cells. Whilst originally mooted to fine-tune gene expression, it is now clear that they can have profound effects on physiology and disease.
A role for microRNAs in chondrogenesis and osteoarthritis has become clear over the last decade. Deletion of the machinery for microRNA biogenesis specifically in the cartilage of mice has shown that, as a class, microRNAs influence the development of the skeleton and homeostasis of articular cartilage. Identifying roles for individual microRNAs has been more difficult, with the main in vivo data coming from miR-140.
This session will review the role of microRNAs in the molecular pathogenesis of osteoarthritis (OA). It will present data on the regulation of microRNAs by relevant factors and their impact on intracellular signalling. Key targets of microRNAs in OA will also be explored. It will touch upon the use of microRNAs as circulating biomarkers of disease and the potential for microRNA-based therapy.

The focus of the Clark lab has been on the role and function of microRNAs in cartilage, particularly miR-455, the miR-29 family, miR-140 and miR-3085.
MicroRNA-455 is genomically located within an intron of COL27A1. Collagen XXVII is expressed in cartilage, suggesting function of the miR in this tissue. We initially described a role for miR-455 in TGFbeta signalling, but have more recently uncovered function in Wnt signalling and in the regulation of Sirt1.
The miR-29 family have been well-researched and are known e.g. to regulate collagen gene expression, giving them a role in fibroses. We identified miR-29b as one of only two miRs which was regulated at an early time point after surgery in the murine DMM ("destabilisation of the medial meniscus") model of OA. Potential targets of miR-29 were regulated in the opposite direction to the miR, suggesting function. The miR-29 family were regulated in many models of chondrocyte differentiation and in human end-stage OA. In chondrocytes we have shown that miR-29 is negatively regulated by Sox9 and negatively regulates a number of key intracellular signalling pathways in OA. We have identified novel direct targets in the Wnt pathway and we have also shown that miR-29 directly targets a number of ADAMTS protease genes.
We used RNA-Seq to explore the full range of miRs expressed by human articular chondrocytes from OA patients. This showed that the so-called passenger strand of miR-140, miR-140-3p was more highly expressed than the guide strand, miR-140-5p in newly isolated osteoarthritic chondrocytes. We have now shown that miR-140-3p directly targets a number of enzymes in the heparan sulphate proteoglycan synthesis pathway. These studies also identified miR-3085 in human chondrocytes. This miR had only previously been annotated in rodents where it was presumed intergenic. However, in man it is located in the final intron of the CRTAC1 gene, which codes for cartilage acidic protein 1. We have shown it to directly target ITGA5, the integrin alpha5 gene, but it also strongly induces interleukin-1 signalling in chondrocytes.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## Muscle biology & inflammation

### SP0021 FREE RADICAL SIGNALING BEHIND THE MUSCLE WEAKNESS ASSOCIATED WITH RHEUMATOID ARTHRITIS

J. Lanner. *Department of Physiology & Pharmacology, Karolinska Institutet, Stockholm, Sweden*

In addition to the primary symptoms arising from inflammatory processes in the joints, muscle weakness and impaired work capacity are commonly reported by patients with rheumatoid arthritis (RA). Reduced muscle strength has always been more or less synonymous with decreased muscle mass. However, our data show that muscle weakness associated with RA is not only a result of atrophic muscles. Instead, intracellular (intrinsic) muscle dysfunction appears as important factors behind arthritis-induced muscle weakness. Our data suggests that the impaired capacity to produce force is the result of free radical (reactive oxygen/nitrogen species (ROS/RNS)) signaling altering the intracellular Ca2+ release and contractile proteins (myosin and actin) inside the skeletal muscle fibers. Here our latest data on the mechanisms behind arthritis-induced skeletal muscle weakness from animal studies and patients with RA will be presented. Altered contractile function induced by the RNS peroxynitrite (ONOO-) and the prospective of using antioxidant treatment to counteract muscle weakness in inflammatory conditions will be discussed.
**Disclosure of Interest:** None declared
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### SP0022 INFLAMMATORY MEDIATORS IN INFLAMMATORY MYOPATHIES

B. De Paepe. *Neuromuscular Reference Center & Lab Neuropathology, Ghent University Hospital, Ghent, Belgium*

Idiopathic inflammatory myopathies (IM) constitute a heterogeneous group of chronic disorders which include dermatomyositis (DM), polymyositis (PM), sporadic inclusion body myositis (IBM) and necrotizing autoimmune myopathy (NAM). These diseases represent distinct pathological entities but, most often, share predominant inflammation in muscle tissue. Many of the immunopathogenic processes behind the IM remain poorly understood until today, however, the role played by various inflammatory mediators becomes more and more clear. Induction of major histocompatibility complexes on the membranes, makes that IM muscle fibers actively participate to the immune processes by becoming antigen presenters. Several myositis-specific autoantibodies have been recognized, typing different subgroups of patients with distinct clinical phenotype. Cytokines, the master regulators of leukocyte activation and migration, have especially been recognized as crucial factors. The IM are characterized by strong expression of subsets of Tumor Necrosis Factors (TNF$\alpha$, LT$\beta$, BAFF), Interferons (IFN$\alpha/\beta/\gamma$), Interleukins (IL-1/6/12/15/18/23) and Chemokines (CXCL9/10/11/13, CCL2/3/4/8/19/21) in the muscle tissue. The latter are important for attracting distinct subsets of T-cells, B-cells, macrophages and dendritic cells, and for their intra-muscular organization. The complex inflammatory network in IM pinpoints targets for neutralization through a selective therapeutic approach as a necessary alternative for patients that do not respond to conventional immune-suppressants. Results so far are promising, but have also shown the necessity for further subtyping of patients to develop future precision therapies and predict treatment outcome.
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## Lessons from the children (monogenic causes of autoimmunity)

### SP0023 MONOGENIC LUPUS AND PROTEIN KINASE C DELTA DEFICIENCY

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Next generation sequencing (NGS) represents a revolution in the field of molecular medicine, and offers a new approach to deciphering the pathogenesis of complex diseases. Paediatric-onset SLE (pSLE) is considered as a paradigm of early-onset autoimmunity and is a very rare and more severe disease than its adult-onset counterpart. These differences are possibly associated with a greater contribution of genetic aetiological factors.
Others and we have identified the deficiency of Protein Kinase C-delta (PKC-delta) as a new cause of monogenic autoimmunity. To date, six patients in four kindred have been reported. The phenotype is broad and ranges from lymphoproliferative disease to lupus-like autoimmunity.
In mouse, PKC-delta deficiency is associated to systemic autoimmunity and is B cell autonomous. We have shown that BCR- or Thapsigargin-dependent apoptosis is impaired in patient's B cells. PKC-delta is crucial in regulating B cell negative selection.
PKC-delta is widely expressed and mutations may impact on additional immune cells. One out of our three patients has developed late-onset papillomatosis suggestive for NK cell deficiency but the underlying mechanisms remain unclear. As described in other apoptosis deficiencies, PKC-delta deficiency may occur in a context of somatic mutation. As part of an exome sequencing panel project on SLE-related genes, we have recently screened 130 additional patients with early-onset SLE but we did not identified any homozygous or heterozygous variants suggesting *PRKCD* mutations remain extremely rare in juvenile SLE.
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### SP0024 TYPE I INTERFERONOPATHIES

Y. Crow[1,2]. *[1]Neurogenetics, Imagine, Paris, France; [2]Genetic Medicine, University of Manchester, Manchester, United Kingdom*

Dissection of the genetic basis of Aicardi-Goutières syndrome has highlighted a fundamental link between nucleic acid metabolism and type I interferon induction, leading to the concept of the human interferonopathies, a broader set of Mendelian disorders where disease pathology relates to a primary upregulation of type I interferon activity. Here we discuss the clinical phenotypes associated with these novel inborn errors of immunity, their pathological basis, and strategies for their treatment.
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### SP0025 COMPLEMENT DEFICIENCIES AND RHEUMATIC DISEASES

L. Trouw. *Rheumatology, LUMC, Leiden, Netherlands*

The complement system is an integral part of both the innate and adaptive immune responses. Although a wealth of insight into the function of the different complement proteins has been obtained by biochemical studies, real insight into the overall role of complement and specific complement proteins has been obtained by studying the rare cases of complete genetic deficiency observed in the human population. The detailed analyses of the clinical manifestations of persons genetically deficient for complement proteins identified some obvious aspects, but also several rather remarkable ones. For example the genetic deficiency of circulating C3 led to increased risk for several types of bacterial infections, but deficiency in C9, an essential component of the membrane attack complex (MAC) required for lysis did only predispose to one particular type of infections; with *Neisseria*. These data indicate that complement is involved in the immune defence against infections via C3, but that lysis by the MAC is except for *Neisseria* not so relevant.
One other remarkable observations was the association between genetic deficiency for classical pathway complement proteins with autoimmunity, especially systemic lupus erythematosus (SLE). Sspecially striking is the observation that there is a hierarchy, within the pathway, with C1q being the strongest associated with SLE, followed by C4 and C2 with almost no association with C3 deficiency. How deficiency of classical pathway proteins contributes is not yet clear but

seems to be the result of an interplay between decreased clearance of dead cells and an altered adaptive immune activation threshold.
Recently we identified a new case of complete C1q deficiency and this child did not display signs of SLE (yet). We were struck by the absence of reports on follow-up data of the cases with reported C1q deficiency and conducted a questionnaire based study. From this study we could conclude that there is enormous variation in the severity of clinical symptoms between persons, with some being very affected leading to premature death and other individuals, sometimes from the same family, seemingly completely unaffected. These findings are relevant also in view of the developments of therapy as now haematopoietic stem cell transplantation (HSCT) has become a feasible option to treat such individuals. In this context we argue for a well-balanced evaluation of the pro's and con's of such treatment modalities in view of the variation in clinical symptoms and severity observed in these individuals.
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**WEDNESDAY, 8 JUNE 2016**

## ABC of statistics

### SP0026 THE BASICS OF A REGRESSION ANALYSIS

S. Norton. *King's College London, London, United Kingdom*

The aim of this presentation is to provide a brief introduction to the basics of the regression model. This model provides the foundation of modern statistical modelling and allows us to assess whether a variable, or range of variables, is associated with an outcome variable. Extrapolating from the model we can develop predictions about the level of an outcome variable, such as disease outcome, based on the values of predictive variables. The underlying equation, meaning of key terms and basic diagnostics to determine the robustness of inference from a regression model will be explained.
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### SP0027 CONFOUNDING - FRIEND OR FOE? HOW TO HANDLE?

L. Carmona. *Instituto de Salud Musculoesquelética, Madrid, Spain*

Confounding is a major issue in observational studies, and it is a bias that needs to be corrected, controlled or adjusted for whatever your research question is. In this lecture we will review the definition of confounding and ways to tackle it. We will discuss two specific biases related to confounding in drug studies: confounding by indication and channelling bias. In addition, we will explain how to handle confounding in the different phases of research: 1) design phase, with an overview, among other issues, of what causal diagrams (directed acyclic graphs, DAG) are; 2) data collection and mining; 3) and finally analysis and reporting. In this latter part, we will explain how confounding is explored in datasets and the difference between confounding and modification. We will end with an overview of propensity scores, as a ways to tackle confusion in an efficient way, and a list of recommendations.
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**WEDNESDAY, 8 JUNE 2016**

## Capillaroscopy I

### SP0028 HOW TO DIFFERENTIATE NORMAL FROM ABNORMAL CAPILLAROSCOPIC PATTERNS: ROLE OF IN EARLY DIAGNOSIS

V. Smith on behalf of the EULAR Study Group on Microcirculation in Rheumatic Diseases. *Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium*

The difference between a normal capillaroscopy and an "abnormal" capillaroscopy is important in the differential diagnosis between a primary Raynaud's phenomenon (=not linked to any condition) from a secondary RP.
A normal capillaroscopic pattern, by qualitative assessment, is characterized by a homogeneous distribution of hairpin shaped capillaries as a "comb-like structure", with a density of between 9–14 capillaries per mm. Yet, there exists a wide intra- and inter-individual variety in a normal population (non-specific variations) which will be discussed during the workshop.
An abnormal capillaroscopic image due to systemic sclerosis (SSc) is characterized by (a combination) of specific changes (giants, capillary loss, hemorrhages and abnormal shapes (ramifications)). Depending on their relative prevalence three SSc-patterns are described by Cutolo et al. with a 200 magnification videocapillaroscope: the "early", "active" and "late" scleroderma pattern. The combination of the presence of a scleroderma pattern on capillaroscopy with the presence of an SSc-specific antibody in a patient with Raynaud's phenomenon allows the "early" diagnosis of SSc. When the patient also has "puffy" fingers he/she meets the VEDOSS criteria for very early diagnosis of SSc.
In patients with connective tissue diseases "other than" SSc and diseases of the scleroderma spectrum there are no "unique" capillary patterns. A variety of capillary abnormalities (change in morphology, dimension, presence of hemorrhages) have been observed. These abnormalities by themselves are not predictive of any defined condition and may be referred to as non-specific abnormalities.
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### SP0029 COUNTING AND SCORING THE CAPILLARIES: MANUAL VERSUS SEMI-AUTOMATIC SYSTEMS

A. Sulli. *Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy*

Microangiopathy is a primary clinical feature of systemic sclerosis (SSc), and nailfold videocapillaroscopy (NVC) is the standard tool to detect morphological capillary abnormalities. NVC may discover the "Early" pattern of microangiopathy, monitor its progression, inform on disease status, and also predict future organ involvement. NVC has been proposed as possible biomarker in SSc, correlating the capillary damage extent with the internal organ involvement (1–3).
SSc patients show pathognomonic capillary abnormalities, which characterize the scleroderma-pattern of microangiopathy (2,4,5). Among these, giant capillaries (dilation of both capillary branches >50 microns), microhaemorrhages, reduction of capillary number (below 9 per linear millimetre), ramified (neoangiogenic) capillaries and disorganization of the vascular array are the major capillary abnormalities. These abnormalities do not occur all together at the same time, but sequentially, and three different patterns of nailfold microvascular damage ("Early", "Active" and "Late" scleroderma-patterns) have been proposed and validated in SSc patients (4–8). As a matter of fact, in some patients the capillary pattern remain unchanged for several years, whereas other patients show a fast evolution of the microangiopathy in a few months or years, along with progressive internal organ involvement (8,9). The factors influencing the time of evolution of the microangiopathy from the "Early" to the "Late" stage have not yet been determined.
To score SSc capillary abnormalities by NVC qualitative and quantitative assessments may be adopted (9).
The qualitative assessment include the classification of the nailfold microangiopathy into one of the three patterns above reported, and to correctly identify them the following criteria may be used (7–8). "Early" NVC pattern: few (<33%) enlarged/giant capillaries, few (<33%) capillary haemorrhages, relatively well-preserved capillary distribution, absent or mild (<33%) loss of capillaries. "Active" NVC pattern: frequent (>33%) giant capillaries, frequent (>33%) capillary haemorrhages, moderate (<66%) loss of capillaries, moderate (<66%) disorganisation of the capillary architecture, absent or few (<33%) ramified capillaries. "Late" NVC pattern: irregular enlargement of the capillaries, few (<33%) or absent giant capillaries and haemorrhages, severe (>66%) loss of capillaries with avascular areas, disorganisation of the normal capillary array, ramified/bushy capillaries.
The quantitative assessment is performed by adopting a simple rating scale to score each capillary abnormalities (score 0–3) (score 0 = no changes; score 1 = less than 33% of capillary alterations/reduction; score 2 = 33–66% of capillary alterations/reduction; score 3 = more than 67% of capillary alterations/reduction, per linear millimetre. Reduction = capillary number per linear millimetre <9). The mean score value for each capillaroscopic parameter is calculated from the analysis of at least two millimetres in the centre of the nailfold, by evaluating the first row of capillaries in each finger from 2nd to 5$^{th}$ (8). Also the microangiopathy evolution score (MES) may be calculated, by summing the scores of capillary loss, capillary ramifications and capillary disorganization (score 0–9) (8).
Alternative to MES calculation, the simple capillary number per linear millimetre may be adopted to monitor SSc microangiopathy and estimate the risk of digital ulcer appearance (10).
To decrease time of assessment and intra- and inter-operator variability, and increase NVC performance and reliability, automated calculation software are under development to score nailfold capillary number (11–14). Actually, even if enough feasible in counting capillaries in healthy subjects, the performance of these software is strongly reduced when working in the capillary alteration mosaic of scleroderma microangiopathy (e.g. haemorrhages, ramifications, giant capillaries, reduced transparency of nailfold bed).
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### SP0030 CAPILLAROSCOPIC VERSUS LASER DOPPLER ANALYSIS OF THE MICROCIRCULATION

A.L. Herrick. *University of Manchester, Manchester, United Kingdom*

Nailfold capillaroscopy is used primarily to study microvascular *structure,* and in patients with Raynaud's phenomenon (RP) helps to differentiate between primary (idiopathic) RP and RP secondary to an underlying systemic sclerosis-spectrum disorder. In contrast, laser Doppler techniques measure microcirculatory blood flow, and therefore assess microvascular *function.* Capillaroscopy and laser Doppler are therefore complementary. There are different laser Doppler techniques: flowmetry (using a single probe), laser Doppler imaging (LDI), and laser speckle contrast imaging (LSCI). LDI and LCSI both measure blood flow over an area rather than at a single site. Laser Doppler techniques have been applied in research studies in patients with RP and systemic sclerosis, including as outcome measures in clinical trials: protocols often involve dynamic imaging, measuring blood flow response to (for example) a standard temperature stimulus. This lecture will describe the main applications of capillaroscopy and laser Doppler techniques in clinical practice and research, relevant to the rheumatologist, and the rationale underpinning these.
Upon completion of the session, participants should be able to:
1. Discuss applications of capillaroscopy and different laser Doppler methods in patients with RP and systemic sclerosis
2. Discuss similarities and differences between the techniques.

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### SP0031 HOW TO SELECT THE MOST APPROPRIATE CAPILLAROSCOPIC DEVICE: PROS AND CONS

W. Hermann. *Department of Rheumatology and Clincial Immunology, Kerckhoff-Klinik, Bad Nauheim, Germany*

One of the most important indications for performing capillaroscopy is to differentiate between primary and secondary Raynaud's syndrome. Different kinds of microscopes are at hand and generally vary in terms of picture quality or price. Before purchasing a microscope and capillaroscopy software, several considerations about the required standards of examination should be made; some of which are summarized as follows:
– The region of interest (ROI). Normal capillaries have a mean diameter of about 8 μm. For an accurate assessment a magnification of 100–200x is recommended, for an overview the magnification of 50x is sufficient.
– Measurement. Beside qualitative measures like changes in vessel architecture, there should be the possibility of quantifying the number of capillaries/mm or vessel diameters.
– Documentation. All parts of the examination have to be stored and assigned to patient and case.
– Practical aspects and handling of the device.
– Different kinds of microscopes are on the market of which three will be discussed in detail. Briefly summarized:
– Stereo microscopes.
Advantages: Very good image quality, zooming in and out without problems, relatively easy to use.
Disadvantages: device is not mobile, in patients with finger contractures examinations are difficult to perform, relatively high costs.
– Videocapillaroscopes:
Advantages: Very good image quality, easy to use, "gold standard" for capillaroscopy.
Disadvantages: No overview, zooming in and out not applicable (change of lenses required), relatively high costs.
– USB microscopes:
Advantages: low costs, zooming in and out without problems, easy to use.
Disadvantages: limited picture quality, documentation laborious.
Selecting a capillaroscopic device depends on the conditions of use ("quick look" vs. "academic evaluation and follow up"), which should be clarified before buying a device. The price range is significant and usually differs between 100€ for USB microscopes and up to 10,000€ for stereo and videocapillaroscopes.

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**WEDNESDAY, 8 JUNE 2016**

## Optimizing treatment and patient care through precision medicine: a threat or an opportunity for patients and patient organisations?

### SP0032 COLLABORATION BETWEEN RESEARCH AND PATIENT ORGANISATIONS: IMPROVING PATIENT CARE THROUGH THE DANISH RHEUMATOLOGIC BIOBANK

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Within the field of rheumatology, the number of available medical treatments is steadily increasing. During the last decades the biological disease modifying drugs (bDMARDs) have significantly improved outcomes for patients otherwise refractory to treatment. However, adverse effects, insufficient drug response and subsequent switching from one drug to another remain a significant problem for numerous patients in daily clinical practice. Within the field of oncology, personalized treatment strategies have come a long way. But for patients with inflammatory rheumatic diseases, the ability to choose the right drug for the right patient is still limited or non-existing. International treatment guidelines all follow a "one-size-fits-all" or "trial-and-error" strategy.
The nationwide Danish Rheumatologic Biobank was established in year 2015 and is funded by the patient organization The Danish Rheumatism Association and the public hospital owners (Danish Regions). The aim of the Danish Rheumatologic Biobank is to promote the identification of new biomarkers for personalised treatment of patients with inflammatory rheumatic diseases. Biological samples (blood, synovial fluid etc.) are collected after written informed patient consent for specific research projects. Corresponding high-quality clinical data are registered prospectively in the nationwide quality and research registry, DANBIO. The treating physician registers patient demographics, previous and current treatment (DMARDs) including reasons for withdrawal, and physician-reported outcomes (clinical characteristics, treatment response, imaging) whereas the patient provides patient-reported outcomes (functional status, pain/fatigue/global scores).
Danish Rheumatologic Biobank exemplifies a unique collaboration between patients and researchers, patient organisations and hospital owners aiming to pave the road for personalized treatment of patients with inflammatory rheumatic diseases. We expect the Danish Rheumatologic Biobank to facilitate high quality research and improved patient care within the field of rheumatology.
During this lecture the rationale, infrastructure and status for DRB will be discussed.
Acknowledgements: The Danish Rheumatism Association and the Danish Regions for funding. The DANBIO registry for hosting clinical data. The Danish Departments of Rheumatology and Biochemistry for participating in DRB sample collection. Thanks to professor Merete Lund Hetland, the main initiator of DRB and the working group behind DRB: Estrid Høgdall, Tina Kringelbach and Julia Sidenius Johansen.
**Disclosure of Interest:** None declared
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### SP0033 IMPROVING THE SCREENING AND MANAGEMENT OF COMORBIDITIES IN RHEUMATIC DISEASES

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Research has shown that comorbidities, one or more additional disorders (or diseases) co-occurring with the primary disease, occur more frequently in patients with chronic inflammatory rheumatic diseases than in the general population, and are sub-optimally prevented, screened for and managed. In order to contribute to improvement, a EULAR task force has developed points to consider for reporting, screening and preventing selected comorbidities in daily practice. The points to consider and the results from the literature that supported their development have been presented at the EULAR conference in Rome in 2015 and have recently been accepted for publication in ARD.
In accordance with the EULAR Standardized Operating Procedures, a multidisciplinary task force from 12 different countries selected six comorbidities (ischemic cardiovascular diseases, malignancies, infections, peptic ulcer, osteoporosis, depression), based on their frequency and severity (e.g. their impact on mortality and disease outcomes) in a first meeting. Results from a systematic literature review of existing recommendations or guidelines on the reporting, screening, or prevention for each of the selected comorbidities guided the second meeting of the task force. In this consensus meeting a reporting form, an extensive list of variables to be collected in order to report history/occurrence of the comorbidity and current treatments, risk factors and screening, or prevention, was decided on. Standardization of the screening for and reporting of comorbidities will enhance implementation across Europe.
The role of patients in the management of their own disease, including the screening for comorbidities, is increasing. Facilitating patients' involvement in their own care requires various activities. Regarding comorbidities, awareness about

the points to consider by developing and disseminating a lay version is necessary but is not sufficient.
Tools such as self-administered questionnaires and supporting information can help strategic implementation of the points to consider, particularly if they are supported with further explanation to the patient whilst empowering them to become more actively engaged in comorbidity self-management. Tools however, also need to make sense to the patient, and should be easily administered and results should be easily interpreted. Also, follow-up of results should be clear.
In what way such a tool can be integrated in daily care, what educational materials for patients are necessary, and how concerns for comorbidities can be reduced needs further exploration.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## EULAR projects in Musculoskeletal Imaging

### SP0034 DEVELOPMENT OF THE EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN OSTEOARTHRITIS CLINICAL PRACTICE

A. Iagnocco on behalf of G. Sakellariou, W. Zhang, J.W.J. Bijlsma, P. Boyesen, M.A. D'Agostino, M. Doherty, D. Fodor, M. Kloppenburg, J. Maeder, F. Miese, E. Naredo, M. Porcheret, P.G. Conaghan. *Sapienza Università di Roma, Rome, Italy*

In the last few years the application of musculoskeletal imaging in rheumatology clinical practicehas become more widespread. However recommendations on its use in osteoarthritis (OA) are lacking.
**Objective:** To develop evidence-based recommendations for the use of imaging in OA clinical practice
**Methods:** After the project was approved by the EULAR Executive Committee, a task force of experts in the field of OA and imaging met in order to plan the strategy for a systematic literature review (SLR), subsequently conducted by a research fellow under the supervision of the conveners and the methodologist of the group. The task force identified areas of application of imaging in OA clinical practice and developed the research questions to drive the SLR. The imaging modalities (conventional radiography, ultrasound, magnetic resonance imaging, computed tomography, radioisotope scan) and joints (knee, hip, hand and foot) were first identified. Second, the role of imaging in the diagnosis of OA, identification of OA characteristics, detection of other diseases, managing OA, defining its prognosis, monitoring the disease progression as well asguiding treatment was addressed. A systematic search was performed separately for each question and site using PubMed and Embase.
**Results:** From an initial SLR, 6858 references were found, 1317 papers were reviewed in detail and 380 of them were included. Furthermore, to investigate evidence not addressed by the first SLR,the task force required additional SLRs to evaluate the accuracy and efficacy of imaging-guided compared to blind injections and the comparison of different radiographic projections. For the first SLR, 25 papers out of 5379 abstracts were assessed and 8 included, while for the comparison of different projections 53 papers out of 4774 abstracts were reviewed, with the inclusion of 31 papers. After analysing the results of the SLRs and giving their expert opinion, the task force developed consensus recommendations. These covered different areas such as the lack of need for diagnostic imaging in patients with typical symptoms, the role of imaging in differential diagnosis, the use of imaging in monitoring OA when no significant therapeutic modification isrelated, the first choice imaging modality, how to acquire images, the influence of different joints on selecting the type and use of imaging modalities, and the role of imaging in guiding local injections. Future research recommendations were developed based on areas where there was a paucity of literature.
**Conclusions:** EULAR recommendations for the use of imaging in osteoarthritis clinical practice have been developed thus filling a knowledge gap in the field.
**Key messages:**
– Recommendations on the use of imaging in OA clinical practice are lacking.
– Based on the results of a SLR and expert opinion, recommendations on the use of imaging in the clinical management of OA were developed.
**Disclosure of Interest:** None declared
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### SP0035 DEVELOPMENT OF EULAR STANDARDISED PROCEDURES FOR RHEUMATOLOGY ULTRASOUND IMAGING (RHUS)

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The objectives of this EULAR Project are:
To update the technical requirements for performing musculoskeletal ultrasound (MSUS) of the essential lesions present in rheumatic diseases accessible by MSUS including patient position, initial probe placement, scanning method and US landmarks.
To develop procedures for additional MSUS assessment of additional musculoskeletal lesions/ abnormalities related to rheumatic diseases accessible to ultrasound evaluation.
To develop procedures for ultrasound scanning of non-musculoskeletal anatomic regions of importance in rheumatologic practice that are readily accessible to ultrasound evaluation (i.e. large vessels, salivary glands, ligaments, and peripheral nerves).
The creation of a concise illustrated manual of these procedures including internet access to video-clips accessible to all with interest in incorporating RHUS in their practice.
**Disclosure of Interest:** None declared
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### SP0036 THE ROLE AND TRAINING NEEDS OF NON-MEDICAL HEALTH PROFESSIONALS USING MUSCULOSKELETAL ULTRASOUND FOR THE MANAGEMENT OF PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

H. Siddle on behalf of EULAR Task Force for Health Professionals undertaking Musculoskeletal Ultrasound. *Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*

The role of the non-medical health professional has advanced with many health professionals undertaking training and using musculoskeletal ultrasound (MSUS) to extend their scope of practice. Guidelines to support training for rheumatologists have been identified but currently there are not any recommendations to support the education and training needs of non-medical health professionals using MSUS.
A EULAR Task Force was established to reach a consensus on the role and education and training needs of non-medical health professionals undertaking MSUS for the management of patients with rheumatic and musculoskeletal diseases (RMDs).
Based on an extensive search of the literature and expert consensus seven points to consider were formulated encompassing the role and scope of health professionals using MSUS, including the application, feasibility and added value in daily practice, and the training and competency required by health professionals. The seven points to consider are intended to support the education and training needs for health professionals using MSUS to improve the management of patients with RMDs across Europe, in conjunction with local and national regulations.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## Difficult osteoporosis

### SP0037 WHAT TO DO WHEN A FRACTURE OCCURS AFTER 3 YEARS TREATMENT WITH AN ORAL BISPHOSPHONATE?

B. Langdahl. *Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus C, Denmark*

Osteoporosis is characterised by reduced bone mass, deteriorated bone architecture and increased risk of fractures. A fracture in a patient with osteoporosis is therefore not uncommon, not even in treated patients as none of the available treatments can prevent fractures completely. Despite this knowledge a fracture is a disturbing event for the patient and should prompt the treating physician to consider the situation. First of all, compliance with the treatment including supplementation with calcium and vitamin D should be checked. Secondly, competing diseases and treatments and other risk factors may have emerged since the patient was diagnosed and started on treatment, and these conditions may attenuate the anti-fracture efficacy of the treatment (thyrotoxicosis, prednisolone, aromatase inhibitors etc). If compliance is good and no new risk factors have emerged, treatment failure should be considered.
Treatment failure can be assessed by new fractures, changes in BMD or bone turnover markers. Treatment failure is suggested if treatment has been ongoing for more than 12 months with good compliance and 2 or more new fractures occur or 1 new fracture in combination with declining BMD or non-suppressed bone turnover markers or BMD declines in combination with non-suppressed bone turnover markers.
If treatment failure is demonstrated then the treatment should be reconsidered. The absorption of oral bisphosphonates is 1–2% under optimal conditions, so the first alternative would be intravenous zoledronic acid or alternatively denosumab. Both are strong antiresorptives which have been proven to be able to increase BMD and suppress bone turnover in patients previously treated with oral bisphosphonates. If the incident fracture is a vertebral fracture, it could also be considered to change to teriparatide, a bone forming treatment with very prominent effects on spine BMD and vertebral fractures.
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**WEDNESDAY, 8 JUNE 2016**

## Clinical relevance of immunogenicity and therapeutic drug monitoring

### SP0038 HOW CAN THE PROLIFERATION OF BIOSIMILARS IMPACT ON R&D AND QUALITY?

R. Van Vollenhoven. *Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands*

Almost twenty years ago, the advent of biological therapies changed the world of rheumatology in three ways: clinical results became dramatically better; treating patients became more complicated but also much more rewarding; and the price of antirheumatic therapy skyrocketed. The advent of biosimilars that has started recently is viewed by many as an important correction of the third aspect; it will also add a little to the complexity of treating patients; but by definition, it will not make clinical results any better at the individual patient level: "bio-*similar*".

Certainly, making antirheumatic therapy sustainable at the societal level is a laudable goal, if not for the individual physician, then at least for the health care system as a whole. But are there any downsides to the introduction in practice of biosimilars?

Part of the answer to that question can be understood if one asks another question: *why* are biosimilars less expensive than the originator products? An important part of the answer to that question is that the manufacturer of biosimilars can avoid the very large investments in research and development (R&D) that are needed for developing originator products. But this is then also the answer to the first question: the savings generated by biosimilars are to a significant extent taken from the R&D budgets in pharmaceutical industry. For those who are concerned about the long-term perspectives of health care from the societal point of view this should be a sobering thought.

A second concern is generated by the increasing number of biological products on the market, including both originator and biosimilar products. These medications are by their nature complex mixtures of proteins, the quality control of which is an extremely demanding task. The agencies charged with overseeing these processes will have to adjust to a reality where, for the treatment of RA alone, nine approved originator products will co-exist with easily as many biosimilar products, some of which are manufactured in several different places around the globe and transported across continents under varying physical conditions. To maintain the highest possible level of quality under these circumstances will be a daunting task for these agencies.

Biosimilars are now a fact of rheumatological life. Neither of the two concerns described here should be a reason not to use biosimilars when it would be medically appropriate to do so. But for those who are charged with setting health-care priorities, enthusiasm over the shorter-term financial gains with biosimilars should be balanced with prudence in view of the longer-term perspectives for future generations of patients.

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**WEDNESDAY, 8 JUNE 2016**

## Hepatitis C and rheumatology: the impact of new therapies

### SP0039 NEW STRATEGIES FOR THE TREATMENT OF HEPATITIS C

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An average of 150 millions people are chronically infected by Hepatitis C virus (HCV) worldwide resulting in significant morbidity and mortality (1.4 millions yearly), related to hepatic and extra-hepatic manifestations. The virologic sustained virologic response (SVR) which is allowed by antiviral treatments significantly reduces both morbidity (hepatocellular carcinoma, liver transplantation) and hepatic as well as extra-hepatic mortality. The overall mortality in those patients achieving SVR was reduced by 75%, especially in cirrhotic patients but also in HIV/HCV co-infected patients and the occurrence of hepatocellular carcinoma at 5 years of follow-up dropped from 15 to 5% and need of liver transplantation from 10 to 1.2%, respectively in a recent meta-analysis of patients receiving interferon-including regimen. In a prospective study of more than 1300 HCV-infected patients with biopsy-proven cirrhosis in the Cirvir ANRS CO12 cohort, a significant decrease in the occurrence of hepatocellular carcinoma, of bacterial spontaneous peritoneal infection or other cirrhosis complications has been reported in cirrhotic patients with vs. without SVR at 3 or 5 years of follow-up but also a decrease in the occurrence of vascular disease (cardio- or cerebro-vascular disease). All these data underline the need of achieving SVR in most of HCV-infected patients which means a large screening, an improvement of access to care of infected patients.

The combination of pegylated interferon alfa and ribavirin) which led to a sustained virologic response (or SVR which corresponds to a complete recovery) in around 45% of patients with HCV genotype 1, 65% with HCV genotype 4, 70% with HCV genotype 3 and around 85% with HCV genotype 2 which was the standard of care for two decades has been replaced from 2011 to 2013 by a combination with first generation NS3/4A protease inhibitors (Telaprevir or Boceprevir) in genotype 1-infected patients, allowing around 70% of SVR with a reduction of the duration of therapy from 48 to 24 weeks in half of treated patients (23). These first-generation regimens unexpectedly disappeared in 2014 with the rapid availability of interferon-free regimens combining different direct-acting antiviral drugs (DAAs). These DAAs target the main viral proteins involved in the replication cycle of HCV and combine NS3/4A protease inhibitors (Simeprevir or Paritaprevir boosted by ritonavir), NS5B nucleos(t)idic (Sofosbuvir) and non nucleos(t)idic (Dasabuvir) polymerase inhibitors, NS5A replication complex inhibitors (Dacalatasvir, Ledipasvir, Elbasvir, Velpatasvir). This therapeutic revolution combines 2 or 3 second wave DAAs, with or without ribavirin but without interferon. The combinations are given (for 8 to 24 weeks) according to baseline factors including fibrosis stage, genotype and subtype, baseline viral load, prior therapeutic history of the patient (naïve or experienced) and pre-existing resistance-associated variants, result in a SVR rate greater than 90% with a good tolerance. The SVR rates (and the safety) are similar in the clinical trials and in the real-life, usually higher than 95% in per-protocol analysis.

Despite these great achievements, new treatments are about to be launched (Grazoprevir/elbasvir: Zepatier) and next generation are finalizing their phase III (Sofbuvir/velpatasvir in the Polaris program or the Abbvie 2nd gen with Endurance). To be competitive, these new combinations need to prove an added value regarding the pill burden (a single tablet regimen STR appears to be a pre-requisite), the reduced duration of treatment (6 or 8 weeks instead of 12 weeks) and/or a ribavirin-free regimen with drugs with a low drug-drug interaction profile and a fair safety/tolerance.

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### SP0040 NEW ANTIVIRALS FOR EXTRAHEPATIC MANIFESTATIONS OF HEPATITIS C VIRUS: THE MODEL OF MIXED CRYOGLOBULINEMIA VASCULITIS

P. Cacoub. *Internal Medicine & Clinical Immunology, Hôpital Ia Pitié Salpêtrière, Paris, France*

Mixed cryoglobulinemia vasculitis (Cryovas) is a small vessel vasculitis involving mainly the skin, the joints, the peripheral nerve system and the kidneys. Hepatitis C virus (HCV) infection is the cause of Cryovas in about 80% of cases. The disease expression is variable, ranging from mild symptoms (purpura, arthralgia) to fulminant life-threatening complications (glomerulonephritis, widespread vasculitis). Most HCV-Cryovas manifestations respond to clearance of HCV during antiviral therapy. Patients who relapse for HCV infection after responding to antiviral therapy usually relapse for the Cryovas with the return of viremia.

Interferon alpha-based therapy has long been the cornerstone of HCV-Cryovas treatment. In the early 2010's, use of triple HCV therapy with pegylated-interferon/ribavirin and a direct antiviral agent (DAA, boceprevir or telaprevir) led to improved rates of sustained virological response and Cryovas remission. However, frequent side effects limited the use of such combinations. During the last two years, all oral interferon-free, DAA regimens have been used in HCV-Cryovas, associated with very high rates of sustained virological response and clinical remission of the Cryovas, and few toxicities. In daily practice, HCV-Cryovas patients with mild to moderate disease should be given an optimal all oral, interferon-free, DAA regimen. For patients with severe vasculitis control of disease with rituximab, with or without plasmapheresis, is required while starting optimal antiviral therapy. Other immunosuppressants should be given only in case of refractory forms of HCV-Cryovas.

**Disclosure of Interest:** P. Cacoub Shareholder of: ILTOO pharma, Speakers bureau: Abbvie, Astra Zeneca, Bayer, Boehringer Ingelheim, Gilead, Glaxo Smith Kline, Janssen, Merck Sharp Dohme, Pfizer, Roche, Servier, Vifor.

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**WEDNESDAY, 8 JUNE 2016**

## Outcome measures in clinical practice in gout and CPPD. The use of the new EULAR guidelines

### SP0041 GOUT-THE COMING EPIDEMIC. THE IMPACT ON THE HEALTH CARE SYSTEM AND THE SOCIETY

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Gout is worldwide the most common non-degenerative inflammatory joint disease, exemplified by a prevalence of 3.9% in the US and 1.7–2.5% in Europe.

The incidence increase with increasing age and BMI, is influenced by genetic, dietary factors and other life style factors as well the occurrence of comorbidity. Of the latter decreasing kidney function is by far the most important.
Several studies have pointed out that the age-adjusted incidence is rising worldwide, partly due to an increase in age and BMI, and we therefore face an upcoming epidemic.
Comorbidity outcomes: Gout identified in registers, thus reflecting the whole spectrum of the disease, has repeatedly been shown to be strongly associated with an increased morbidity in cardiovascular outcomes, deteriorating kidney function and overall mortality. To what extent this is related to hyperurecemia or systemic inflammation as reflected by clinical gout has not been completely disentangled. Very low serum-urate levels have on the other hand been suggested to increase the risk for dementia and Parkinsons disease, although this would need be confirmed.
Health related Quality of Life (HQoL): Whereas it is clinically obvious that very severe gout can have severe impact on HQoL, there is limited data to what extent early disease or more limited gout manifestations reduces HQoL
Societal costs: Once considered a disease of the wealthy, gout has recently been shown to be associated with lower income and socioeconomic class as is the case for most chronic diseases. It is difficult to disentangle the effects of joint manifestations and associated comorbidities on the incremental costs that some studies have demonstrated in groups of gout and this would need to be furthers studied.
What can we do to stop this epidemic? Apparently there are still large opportunities for improvements with regard to early detection and initiation of urate lowering therapy. In addition, improvements in life style are likely to be highly protective. Since gout is an increasing problem, there is also a high need for studies describing the effects on HQoL and costs over the whole range of the disease.
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### SP0042 THE ROLE OF IMAGING IN THE MANAGEMENT OF GOUT

M. Doherty. *University of Nottingham, Nottingham, United Kingdom*

Identification of monosodium urate (MSU) crystals by microscopy remains the accepted gold standard for definitive diagnosis of gout. However, caveats include: suboptimal inter-observer agreement, lack of quantification of the extent of crystal deposition, and the impracticality of this method for diagnosis in primary care. In this presentation the pros and cons of different imaging methods for diagnosis, assessment and monitoring of gout will be discussed.
Plain radiography is readily available and can show the extent of joint damage from gout, but changes usually occur late, are largely non-specific and sensitivity of detection is low. Computed tomography (CT) and helical CT allow detection and quantification of tophi and bone erosions and dual energy CT (DECT) allows detection (with high specificity) and quantification of size and number of subclinical tophi – these techniques may also be useful in diagnosing atypical gout syndromes (e.g. radiculopathy from axial tophi). MRI can also demonstrate tophi, joint damage and associated inflammation, though specificity is low and aspirate confirmation is usually required. Ultrasound (US) can demonstrate bone erosions, tophi and the double-contour sign and although the specificity of these findings has been questioned US is a widely available imaging technique in clinical practice. DECT and US show promise in being able to monitor reduction in tophus size on urate lowering therapy in clinical trials. Raman spectroscopy is an interesting newly applied technique that currently being explored.
An important caveat to all imaging techniques is that they remain impractical in primary care where most gout patients are diagnosed and treated. Developing diagnostic methods that could be applied easily in this setting remains a priority.
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### SP0043 CLINICAL OUTCOMES FOR GOUT PATIENTS IN RHEUMATOLOGICAL CARE

T. Uhlig. *Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*

With increased interest in gout and the advent of better management opportunities more attention has been paid to defining relevant outcomes in gout, also for use in clinical practice.
International guidelines advocate treatment to below a threshold of 360 μmol/l (6 mg/dl) and below 300 μmol/l (5 mg/dl) if a patient has tophi. While this is the target for treatment, other outcome domains have been developed as part of OMERACT work.
Identified outcomes for acute gout include mandatory core outcomes: pain, joint swelling, joint tenderness, patient global assessment of disease activity, and activity limitations. In addition there are additional domains for assessment which include: an acute phase marker of inflammation, work disability, joint impairment, joint erythema, and physician global assessment of disease activity.
Many different instruments have been used to assess the acute gout core domains. In order to reduce existing variation, standardisation of measuring the most important domains of gout is recommended.
In clinical practice flares indicate a failure of ongoing treatment of gout. On the other hand the development of a responder index is an area of investigation as is the definition of remission in gout. Ongoing research tries to define a time period in which a flare needs to be absent so the patient can be defined as in remission.
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**WEDNESDAY, 8 JUNE 2016**

## Hand osteoarthritis: state of the art and future perspectives

### SP0044 FUNCTIONAL CONSEQUENCES OF HAND OSTEOARTHRITIS

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Hand osteoarthritis (OA) is not a single disease but a group of complex conditions ranging from a syndrome of joint pain accompanied by functional limitation to highly characterised subsets of radiographic hand OA. Whilst hand OA is one of the commonest forms of osteoarthritis there is a "knowledge-to-practice" gap in recognising and addressing functional consequences of hand OA across the clinical pathway.
This presentation will consider functional consequences of hand OA at four levels: societal (population level); health care delivery (organisational level); health care professional level; and the impact on the person living with hand OA (individual level). It will draw on findings from three large cohorts of adults 50 years and over studied in North West Midlands, UK (n=30,000) (1–3) to describe the functional consequences of hand OA at a population level. Findings from a randomised controlled trial (3), an implementation study (4) and qualitative data (5) will be used to illustrate health care (e.g. primary care; occupational therapy) for the functional consequences of hand OA. The impact on the individual will be described using qualitative data of participant experiences of living with hand OA (6).
Proposals for closing the "knowledge-to-practice" gap for the functional consequences of hand OA will be discussed.
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### SP0045 ASSESSING HAND OSTEOARTHRITIS IN CLINICAL CARE AND RESEARCH

C.H.E. Van Den Ende. *Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands*

Assessment of hand osteoarthritis (OA) is a challenge due to the involvement of multiple joints in the disease process and the complex interplay between thumb, fingers, wrists and hands. Symptoms of hand OA, commonly addressed by non-pharmacological interventions are pain, stiffness, reduced joint mobility, instability and reduced muscle function. Treatment of hand OA focuses on the relief of symptoms, improvement of dexterity, and the improvement of hand activities. In clinical research standardization of assessment is necessary to estimate the clinical burden of the disease and to evaluate the efficacy of (novel) treatment modalities. The OMERACT (Outcome Measures in Rheumatology) identified four core domains for clinical research in OA: pain, physical function and patient global assessment for symptom modifying trials and, in addition, imaging for structure modifying trials. Recently, a working group of the OMERACT proposed a preliminary set of core (sub) domains with preliminary instruments.[1]
In clinical practice assessment of hand OA guides setting of treatment goals and the treatment plan. In addition, structured assessment of OA can be used to monitor progress and to evaluate treatment results. In general, structured assessment in clinical practice comprises a combination of self-reported, objective and performance-based measures. The choice for a specific measurement instrument should be based on the purpose of assessment (for instance to

provide information about possible targets for treatment) and on the psychometric qualities of measurement instruments. An overview of measures to assess hand OA in clinical practice and research will be presented and discussed.
**References:**
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**WEDNESDAY, 8 JUNE 2016**

## Chronobiology of the immune reponse

### SP0046 SLEEP AS A MODULATOR AND ADJUVANT IN IMMUNITY

T. Lange. *Clinic for Rheumatology, University of Luebeck, Luebeck, Germany*

Sleep and immunity are linked by bidirectional interactions. On the one hand, immune activation induces fatigue, sleepiness and non-rapid eye movement (NREM) sleep, whereas REM sleep is suppressed. On the other hand, sleep, in particular NREM sleep, regulates immune functions in an overall immunosupportive manner. Thus, NREM sleep drives the release of pro-inflammatory hormones such as growth hormone, prolactin and aldosterone at a time when anti-inflammatory hormones such as cortisol and catecholamines reach lowest levels. In healthy subjects this unique endocrine pattern during NREM sleep seems to facilitate T cell homing to lymph nodes, pro-inflammatory cytokine production by stimulated monocytes and dendritic cell precursors and vaccine-driven T and B cell responses. However, in addition to this adjuvant-like action, sleep also exerts anti-inflammatory, regulatory functions. Thus, sleep presumably counteracts sterile, low-grade systemic inflammation, shifts anti-inflammatory cytokine production of stimulated monocytes to the daytime period and supports regulatory T cell functions. In autoimmune diseases these fine-tuned interactions between sleep and immunity are distorted. Potential causes, consequences and therapeutic implications of this dysregulation will be outlined exemplarily for patients with rheumatoid arthritis, systemic lupus erythematosus and systemic sclerosis.
**Disclosure of Interest:** None declared
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### SP0047 CIRCADIAN CLOCKS AND INFLAMMATION: THE CLOCK AS A PHARMACOLOGICAL TARGET FOR INFLAMMATORY DISEASE

J.E. Gibbs. *Faculty of Medical and Human Sciences, University of Manchester, Manchester, United Kingdom*

The circadian clock is a biological timing mechanism that allows organisms to align their physiology with the external daily environment. 24h rhythms are generated within every cell by a transcriptional-translational feedback loop, the cellular clock. It is now evident that the cellular clock operates within the immune system, and this explains how responses to inflammatory stimuli show circadian variation. A prime example of this is the macrophage, which is capable of generating 24h rhythms *in vivo*, but also *ex vivo* in the absence of entraining signals. Macrophage responses (pro-inflammatory cytokine release) to inflammatory stimuli are significantly greater if the provocation occurs at dusk compared to dawn. Genetic ablation of the clock, by deletion of *bmal1*, in macrophages, renders them arrhythmic, and results in loss of this time of day variation in response. The cellular clock transmits timing information through REV-ERB alpha, a nuclear hormone receptor and transcriptional repressor. From this we discovered REV-ERB alpha is a tractable pharmacological target for inflammatory disease.
Other cell types involved in the pathogenesis of inflammatory arthritis are also intrinsically rhythmic, including T cells, dendritic cells and synovial fibroblasts. Indeed, using mouse collagen-induced arthritis we have shown that levels of inflammatory markers within inflamed joints show robust 24h rhythmicity. Transcript levels of *il1b* and *il6* peak at dawn, which is remarkably consistent with clinical observations, showing a rise in circulating levels of cytokines in the early morning. Further analysis revealed that the negative arm of the molecular clock (specifically CRYPTOCHROME) suppresses arthritis during the night. Furthermore, small molecule CRYPTOCHROME activators were found to have anti-inflammatory actions in both murine and human synovial fibroblasts – re-affirming the notion that the circadian clock is a therapeutic target for inflammatory disorders.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## Nanomedicine in rheumatology

### SP0048 WHAT ARE NANOPARTICLES: PHYSICS FOR MEDICAL DOCTORS

A. Shah. *Duke University, Duham, United States*

Nanotechnology has improved the medical world broadly rheumatology specifically through a number of innovative applications used to enhance diagnostics through imaging and therapeutics through enhanced drug delivery. In order to have a better understanding of nanomedicine, however it is helpful to review the basic chemistry and quantum physics that serve as the basic fundamental science of this technology. The building blocks of the nanoworld are atoms as well as the electromagnetic forces between them are the basic forces that give nanomaterials their properties These atoms, in particular carbon, are then shaped into a variety of structures including buckyballs, carbon nanotubes and nanowires that comprise much of todays nanotechnology. In addition thermal agitation as well as cohesion between atoms and molecules serve critical roles in contributing to unique nanomaterial characteristics. Finally, light, namely viewed as a stream of particles called photons, plays a critical role in nanomedicine. Electron microscopy and scanning tunneling microscopy are only two examples of exploiting photons at the nanoscale in order to enhance the role of nanomedicine in medical imaging.
**Disclosure of Interest:** None declared
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### SP0049 NANOPARTICLES AND THE IMMUNE SYSTEM

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An individually tailored diagnosis and therapy (theragnostic) could be beneficial in chronic, systemic, inflammatory autoimmune diseases like rheumatoid arthritis. The destructive nature of the disease, resulting in irreversible damages of cartilage and bone, demonstrates the urgent need for a very early diagnosis. Promising candidates for such a tool are represented by nanoparticles which have been intensively investigated over the last 20 years for various *in vitro* and *in vivo* biomedical applications. For example, nanoparticles are already in use as contrast enhancer for magnetic resonance imaging due to their favorable physicochemical properties and their biocompatibility. Further developments like surface modifications are ongoing. In order to permit the medical application of nanoparticles safety aspects need consideration.
The collaborative project NanoDiaRA was funded by the European Union and focused on the “Development of novel nanotechnology based diagnostic systems for Rheumatoid Arthritis and Osteoarthritis”. Within the project, a novel generation of superparamagnetic iron oxide nanoparticles (SPION) was developed and their effect on human immune cell survival and activity was analyzed. The nanoparticles were modified stepwise until there was no negative influence of the improved type of SPION on human immune cells. Finally, the resulting generation of nanoparticles has been demonstrated to be suitable within the human system and, therefore, represent a promising tool for theragnostic in rheumatic diseases.
**Disclosure of Interest:** None declared
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### SP0050 NANOMEDICINE APPROACHES IN RHEUMATOLOGY

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Rheumatoid arthritis (RA) is one of the most common and severe autoimmune diseases related to joints [1, 2]. Regrettably, RA inflammatory process remains puzzling, and finding effective therapies for the disease as well as new means for its early diagnosis have been daunting tasks. As a response to RA inflammation, the synovial tissue shows synovial lining hyperplasia as a result of Fibroblast-Like Synoviocyte (FLS) and Macrophage-Like Synoviocyte (MLS) accumulation. In fact, the synovial intimal lining in RA, instead of one or two cells deep, is frequently up to five-fold deeper. Consequently, more macrophages, lymphocytes, and fibroblasts are activated and the RA inflammatory process remains [2–4]. Thus, macrophages play a pivotal role in the features and progress of RA, and effective diagnosis and therapy may encompass the ability to target these cells.
Currently, the main target of RA therapy is to control the inherent inflammatory response and alleviate pain. Several therapeutic options have been used to manage and slow down the progression of the disease, which include the use of sulfasalazine, hydroxychloroquine or methotrexate – a first line disease modifying anti-rheumatic drug (DMARD) [5, 6]. Methotrexate (MTX), is being widely used due to its satisfactory safety profile, efficacy and low cost. It is an analogue of folic acid as it disrupts cellular folate metabolism by inhibiting its target enzyme, dihydrofolate reductase [6–8]. Still, there is a lack of specificity for MTX and/or other similar drugs.
Nanomedicine has thrived and is now providing new possibilities for the use of nanomaterials in medical applications for drug delivery and tissue regeneration [9–11]. Recent developments in the understanding of inflammation have led to an increased interest in the use of nanomedicine in the treatment of rheumatoid arthritis. Nanomedicine may also offer new opportunities to combine diagnosis and therapy in a single approach. Improved theranostics processes are being studied in order to develop new means to diagnose, fight and follow disease. The release and action of anti-rheumatic drug may be enhanced and controlled, and potentially without injuring healthy tissues and organs, while simultaneously providing a non-invasive and specific imaging tool for RA.
This presentation aims at explaining the major applications of nanomedicine in rheumatoid arthritis treatment and diagnosis. Commercial successes of RA active targeting of nanomedicine and products under development will be revised. Insights on multifunctional anti-CD64 mAb-modified nanoparticles for the combined delivery of MTX and iron oxide nanoparticles (SPIONs) proposed by

our group will be presented [12, 13]. Proposed nanoparticles have the potential to provide a new theranostic approach for RA management.

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**WEDNESDAY, 8 JUNE 2016**

## HOT session 2

SP0051 **PAIN MANAGEMENT**

E. Choy. *Department of Rheumatology, Cardiff University School of Medicine, Cardiff, United Kingdom*

Musculoskeletal conditions are the most common causes of chronic pain leading to consultation in primary care. The most common conditions are osteoarthritis, inflammatory arthritis, chronic regional pain (e.g. back pain) and chronic widespread pain (fibromyalgia). Since musculoskeletal conditions are prevalent, it is not uncommon for a patient to suffer from more than one chronic painful musculoskeletal condition. Functional neuroimaging studies have shown that all types of pain are processed within a common human pain matrix in the brain. Inflammation causes pain in many musculoskeletal conditions. Typically, inflammation is caused by activation of the leucocytes, which release cytokines and convert arachidonic acid into prostaglandins by cyclo-oxygenase II (COX-II) enzyme. At the site of inflammation, prostaglandin E2 (PGE2) increases the responsiveness of peripheral nocioceptors and contributes to the development of peripheral sensitisation. In animal model of inflammatory arthritis, COX-2 is also upregulated in the dorsal horn of the spinal cord and contributes to the development of central sensitization. Furthermore, cytokine receptors are also expressed by sensory nocioceptive neurones, which are activated by cytokines. Therefore inflammation has direct and indirect roles in the development of chronic pain in many musculoskeletal diseases. This review will focus on treatments that could be applied to most musculoskeletal conditions rather than disease specific treatment such as disease modifying drugs for inflammatory arthritis.

The aims of treatment of chronic musculoskeletal pain are to educate patient on diagnosis, reduce severity of symptom, improve function and empower patients to self-manage. Treatment of chronic musculoskeletal pain should be tailored to the individual, addressing their particular needs and minimising the risk of side effects from treatment. The best strategy is to use a multidisciplinary holistic approach combining non-pharmacological and pharmacological interventions. National bodies such as the British Society for Rheumatology and IASP Musculoskeletal Taskforce have published management recommendations based on systematic reviews. Patient education and graded exercise are important in all patients with chronic musculoskeletal pain. Topical treatment such as ice, heat, transcutaneous nerve stimulator and manual therapies may provide symptomatic relief although the strength of evidence is weak, the risk of side effect is small. Cognitive behavioural therapy has been shown to improve pain and function. It should be considered especially in patients with difficulty in cope with pain and have significant functional impairment.

Pharmacological intervention should starts with simply analgesia such as paracetamol. Codeine phosphate or nefopam can be added if necessary. Topical and oral non-steroidal anti-inflammatory drugs (NSAIDs) or cyclo-oxygenase (COX-2) inhibitors may be added to simple analgesics for treating acute exacerbation. NSAIDs and COX2 agents should be used with caution in patients with cardiovascular diseases. Short courses of tramadol, a weak opioid analgesic with serotonergic and adrenergic activities can be used for treating moderate to severe pain. For patients with moderate to severe chronic musculoskeletal pain, satisfactory analgesia may be achieved by using a non-escalating dose of opioids with minimal risk of addiction. Depression is common in patients with chronic musculoskeletal pain. Serotonin and nor-adrenaline are important neurotransmitters involved in the pain pathway, hence many anti-depressants have pain modification property and can be used as adjunctive treatment. However, patients with severe depression should be referred for management by mental health team. All patients should be given advice for self-management and dealing with exacerbation of symptoms. For patients with persistent distress or increasing disability referral to secondary care physician, psychologist or multidisciplinary pain clinic is recommended.

**Disclosure of Interest:** None declared
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SP0052 **HOW TO TREAT/MANAGE FIBROMYALGIA**

D.A. Williams. *Anesthesiology, University of Michigan, Ann Arbor, United States*

Fibromyalgia (FM) is often associated with profound suffering on the part of patients and can be quite challenging to the clinician to treat/manage. This talk will provide demographic information about FM as well as a brief summary of current research supporting putative peripheral and central nervous system mechanisms underpinning this condition. Multiple approaches have been used to diagnose FM and these methods will be reviewed and clarified for a clinical audience. Multi-modal treatment is considered optimal for the long-term management of FM and a variety of pharmacological as well as non-pharmacological options are available. This talk will review some of the evidence supporting these options and will describe how best to craft a logical treatment plan taking into account the needs of the individual patient.

**Disclosure of Interest:** D. Williams Consultant for: Health Focus, Inc.
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**WEDNESDAY, 8 JUNE 2016**

## Beyond EMEUNET: development of a European-wide network of young clinicians from different specialties focusing on inflammatory diseases

SP0053 **EXPERIENCES FROM YOUNG RHEUMATOLOGISTS INTO EMEUNET**

A. Moltó on behalf of EMEUNET. *Rheumatology Department, Hopital Cochin, Paris, France*

EMEUNET, the Emerging EUlar NETwork, is a network of young clinicians and researchers in the field of rheumatology in Europe. The principal objectives of EMEUNET are:

(1) To enhance the quality of education among emerging rheumatologists and researchers by, among others:
- Dedicated content on the EMEUNET Website, facebook and Twitter and regular Newsletters
- A network of Country Liaisons responsible for communicating EMEUNET projects/activities and documents to the national societies, and particularly to young trainees and researchers in EULAR member countries
- EMEUNET initiated courses and mentoring projects
- EMEUNET Observers, recruited yearly from among EMEUNET Working Group Members on the Standing Committees of EULAR
- Participation in EULAR task forces for the development of EULAR recommendations
- Sessions proposals for "The Young Rheumatologist" track at the EULAR Annual Congress under the umbrella of the EULAR Standing Committee for Education and Training (ESCET)

(2) To promote research and create collaborations among emerging rheumatologists and researchers by, among others:
- Establishing a database of young rheumatologists involved in research and of researchers working in the field of rheumatology
- Supporting exchange of methodologies, technical data and knowledge as well as dissemination of documents between emerging researchers, through the EMEUNET Website, Facebook, and Twitter
- Organizing together with Annals of the Rheumatic Diseases the peer-review mentoring program
- Promoting networking at social events held at the EULAR and ACR Annual Congress

– Organizing mentor/mentee meetings between EMEUNET members and leaders in the field at the EULAR and ACR Annual Congress

None of these objectives could be fulfilled without the work and enthusiasm of the people involved in the 7 subgroups that form the Working Group of EMEUNET: Education, Peer Mentoring, Newsletters, Social Media, Visibility, Country Liaisons and Global Affairs.

EMEUNET subgroups are enthusiastically engaged in several activities, and the list of current and upcoming projects has quickly expanded over the past few months.

With all these initiatives and activities we hope that EMEUNET will continue to be embraced by the young rheumatology community and more and more young clinicians and researchers in rheumatology will become involved in rheumatology education, research and EULAR, making EMEUNET a successful and influential resource that fosters new and long-term collaborative endeavours and ensures that excellence in European Rheumatology and EULAR is maintained.

**Disclosure of Interest:** None declared

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## SP0054 EXPERIENCES FROM YOUNG GASTROENTEROLOGISTS INTO Y-ECCO

P. Hindryckx on behalf of Young-ECCO. *Gastroenterology, University Hospital of Ghent, Ghent, Belgium*

The European Crohn's and Colitis Organisation (ECCO) is an association that aims to improve the care of patients with inflammatory bowel disease through education, research and collaboration. ECCO was founded in 2001 and has been rapidly growing over the past years. The last ECCO congress had almost 7000 attendees. The operational board of ECCO consists of the chairs of the different ECCO committees. Among these ECCO committees is Young-ECCO (Y-ECCO), which was founded in 2007 as a platform for young IBD physicians and scientists that are below 35 years of age or still in training, in order to promote friendship and collaboration between them. Y-ECCO has initiated numerous activities within ECCO (for example, a workshop on career development, literature reviews, a basic science workshop, ...) and closely collaborates with the other ECCO committees to fulfill the mission of ECCO.

**Disclosure of Interest:** None declared

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## SP0055 EXPERIENCES FROM YOUNG REPRESENTATIVE OF PAEDIATRIC RHEUMATOLOGY EUROPEAN SOCIETY

E. Smith. *Institute of Translational Medicine, University of Liverpool, Liverpool, United Kingdom*

The Paediatric Rheumatology European Society (PRES) is a European scientific society for healthcare professionals in the field of paediatric rheumatology. The societies missions are to promote knowledge of paediatric rheumatic diseases, stimulate research in this field, disseminate knowledge through scientific meetings and publications, provide guidelines and standards for good clinical practice. Importantly PRES provides guidelines and standards for the training of doctors and allied health professionals in the practice of paediatric rheumatology. As the young/trainee representative on the PRES council I am involved in representing the views of trainees at council meetings. PRES holds a scientific congress each year which is preceded by an annual Young Investigators Meeting (YIM), which I organize along with a local trainee(s). This is a very popular meeting which is increasing in size and currently brings together approximately 150 young investigators (clinicians and scientists) from across Europe but also America, Australia, India, Africa. It is a good opportunity for young investigators to have their first international presentation and network with senior faculty to discuss and develop research ideas. As the trainee representative I am also involved in organising and promoting PRES funded training courses and gaining opinion from trainees about the type or course they would like. PRES plans to run summer/winter schools on certain conditions in the near future. I have recently assisted the PRES Education and Training Committee in updating the European Paediatric Rheumatology syllabus which will be launched in summer 2016.

**Disclosure of Interest:** None declared

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## SP0056 BEYOND EMEUNET: DEVELOPMENT OF A EUROPEAN-WIDE NETWORK OF YOUNG CLINICIANS FROM DIFFERENT SPECIALTIES FOCUSING ON INFLAMMATORY DISEASES: EXPERIENCES FROM THE YOUNG NEPHROLOGISTS' PLATFORM

A.C. Ferreira on behalf of Young Nephrologists' Platform. *Department of Nephrology, Centro Hospitalar de Lisboa Central - Hospital de Curry Cabral, Lisbon, Portugal*

The Young Nephrologists' Platform (YNP) was developed in 2012 and started its formal activity in 2013. It aims to involve all young professionals with interest in nephrology in all *European Renal Association - European Dialysis and Transplant Association* (ERA EDTA) activities. It is composed of 9 Board Members: 6 elected members from the ERA EDTA plus 3 ex-officio members, winners of the annual *Young Investigator* award.

All young (<40 years old) ERA EDTA members can apply to became Ordinary Members, and those are the ones who benefit from YNP activities.

The communication among the members is performed by electronic means, as blast emails, surveys, and using the YNP blog. In these last three years, YNP developed two programs (free membership program and the advisory program), annually prepares the annual session at the European congress and annual CME Courses, and developed a new educational tool – the hot topics.

The Free Membership Program offers 50 ERA EDTA memberships to YNP Ordinary Members, based on two types of accomplishments: the abstract-based type (30 free memberships to the 30 best abstracts submitted to annual ERA EDTA Congress) and the paper-based type (20 free memberships for manuscripts published on ERA EDTA journals by YNP members as 1st or last author).

The Advisory Program is a 9 to 12 month length unique opportunity to exchange experiences and knowledge between two participants, the advisor (an experienced nephrologist, member of ERA EDTA) and the advisee (a young professional, member of YNP).

The YNP sessions at the ERA EDTA annual congress are organized to provide an opportunity for young recognized researchers to show their experiments and results. Every year the Young Investigator Awardee is also invited to lecture during the YNP session.

The YNP CME Courses are focusing different topics each year.

The *Hot Topics* is seen as a new tool of study, and was developed to help young physicians to gather the latest information on certain topics, but also to interact with renowned experts. On each topic, YNP invites an expert to discuss a recent and relevant paper about the topic, and all YNP members can participate and communicate with the expert, via blog, adding questions or comments. Additionally, YNP members can test their knowledge with the YNP quizzes we provide on each topic.

**Disclosure of Interest:** A. C. Ferreira Grant/research support from: From the Portuguese Society of Nephrology.

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**WEDNESDAY, 8 JUNE 2016**

# Data visualisation: tables and graphs for publication and presentation I

## SP0057 DATA VISUALISATION: TABLES AND GRAPHS FOR PUBLICATION AND PRESENTATION

M. Boers. *Epidemiology & Biostatistics; Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands*

This workshop (repeated on Friday, 15:30, Capital Suite 06) is an introduction to the principles of good graph and table design as pioneered by Cleveland[1] and Tufte[2] and updated by Few[3] so that the participant can better answer the following questions:

*Which of the messages in my research results requires a graph or table?*

Recognizing how graphs improve on simple statistics and convey much more information. Knowing when a table is better, or keeping the data in the body text.

*How can I best convey the message?*

Striving for clear vision by choice of graph, scaling, discrimination of data series, minimizing non-data ink, avoiding chart junk.Striving for clear understanding through a balance between data and explanation. Using order, subheadings, formatting and rules to guide your reader through your table data.

*Is my graph/table truthful?*

Creating a direct proportion between graph and data quantities, avoiding forms prone to misinterpretation, labels to prevent ambiguity; keeping data in context, avoiding more dimensions in the graph than in the data.

This year's course will extend introductory material available via YouTube clips on the ARD website (ard.com)! Direct link: https://www.youtube.com/playlist?list=PLXU14EQbU_V9JpmolAKsaCC0VjJzbxzAN

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[1] USA; 2004.

**Disclosure of Interest:** None declared

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**WEDNESDAY, 8 JUNE 2016**

## Ultrasound basic I

### SP0058 SCORING OSTEOARTHRITIS (OA)

I. Möller. *Instituto Poal de Reumatologia, Barcelona, Spain*

Musculoskeletal ultrasound (US) is an imaging tool applicable in the detection and scoring of elementary lesions in patients with knee and hand OA. After defining and reaching a consensus on the US detected elementary lesions in patients with hand and knee OA, the reliability of the agreed scoring system has been tested. In both cases, using semi-quantitative and/or dichotomous scales, the results showed moderate to good reliability. The results vary depending on the elementary lesion tested. For example, there was good reliability for osteophyte scoring in hand OA but fair to moderate for cartilage with intermediate degrees of damage according to the proposed scoring systems. Other joints will be tested in the future with the purpose of assessing reliability of the scoring these elementary OA lesions.

**Disclosure of Interest:** None declared

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### SP0059 SCORING LARGE VESSEL VASCULITIS

A.P. Diamantopoulos. *Rheumatology, Hospital of Southern Norway Trust, Kristiansand S, Norway*

Giant cell arteritis (GCA) and Takayasu's arteritis are the two main forms of large vessel vasculitides (LVV) predominantly affecting the large and medium vessels. GCA is the most common form of systemic vasculitis.

Studies have shown that ultrasound yields a high sensitivity and specificity in the diagnostics of GCA, and that it could also be useful as follow up tool. In coronary syndromes, the presence of increased carotid intima–media thickness (IMT) and plaques in the carotid or femoral arteries have been correlated with classic risk factors and coronary risk. Yet, in LVV, no studies exist regarding increased IMT due to vasculitis and its influence on disease activity and prognosis. Possible explanations include the lack of definitions on angiopathology, technique standardization and of a widely acknowledged scoring system. Recently, an OMERACT group on ultrasound in LVV introduced definitions on both vasculitic lesions and atherosclerosis.

This session aims to present: 1. An overview and demonstration of the ultrasonographic definitions of vasculitis, 2. Considerations around potential scoring systems.

**Disclosure of Interest:** None declared

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### SP0060 IMPACT ON SCORING - MACHINE AND EXPERIENCE

G. Tamborrini. *Rheumatology, UltrasoundCenter, Basel, Switzerland*

In this practical ultrasound session we discuss exemplary studies demonstrating the feasibility and reproducibility of scoring systems for e.g. Rheumatoid Arthritis. We emphasis the importance of the quality of ultrasound machines, the correct settings and the training of sonographers for the implementation of ultrasound scoring in the routine daily care of RA patients. We promote consensus guidelines and high quality training to improve musculoskeletal ultrasound reliability.

**Literature:**

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**WEDNESDAY, 8 JUNE 2016**

## Patient organisations in action

### SP0061 THE ROLE OF PATIENT ORGANISATIONS IN HEALTH TECHNOLOGY ASSESSMENT

K. Facey. *Patient Involvement Methods and Impact Working Group, HTAi, Drymen, United Kingdom*

Health Technology Assessment (HTA) is defined as a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to use of a health technology (medicines, devices, vaccines, rehabilitation etc) in a systematic, transparent, unbiased, robust manner. Its aim is to inform health policy at local or national level including decisions about reimbursement and access.

Principles of good practice for HTA were published in 2008 and these included "stakeholder involvement", recognising that policy initiatives should include a democratic right for involvement. Patients and their representatives are clearly key stakeholders, but questions arise about how they should be involved in the complex processes of HTA without compromising scientific integrity.

The Health Technology Assessment International (HTAi) Interest Group for Patient/Citizen Involvement in HTA believes that patients and their representatives can provide valuable input to HTA by sharing their experiences of living with a condition, use of current health technologies and experiences and expectations of new health technologies. This unique knowledge can add value to every stage of the HTA process, but in many countries there is no involvement of patients and no transparency about how patients can be involved in HTA. So, the HTAi Interest Group works with all stakeholders to develop tools and initiatives to support HTA bodies to involve patients and patient organisations in a meaningful manner and to support patient organisations to get involved in HTA.

Any patient group's approach to HTA must be specific to their own setting, but can draw on the international recommendations made by HTAi – such as their Values and Quality Standards for Patient Involvement in HTA. Furthermore, patient groups can help support capacity building through better collaboration about their experiences in HTA and development of generic information about their condition and its unmet needs that can be shared internationally. Finally they have a crucial role in evaluating HTA processes to ensure that they are fair and transparent.

**Disclosure of Interest:** K. Facey Consultant for: A range of health technology companies, HTA bodies and patient organsiations

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**WEDNESDAY, 8 JUNE 2016**

## Hot topics in paediatric rheumatology

### SP0062 SHARE RECOMMENDATIONS ON CONNECTIVE TISSUE DISEASES

M.W. Beresford[1,2]. [1]*Institute of Translational Medicine, University of Liverpool;* [2]*Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom*

**Introduction:** The paediatric connective tissue disorders and paediatric systemic vasculitides are rare, complex and can lead to significant associated morbidity and mortality. Evidence-based guidelines are sparse and management is mostly based on physician experience. Consequently, treatment regimens differ widely throughout Europe.

In 2013, a European initiative called SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) was launched to optimize and disseminate guidelines for diagnosis and management for children and young adults with paediatric rheumatic diseases (PRD) within Europe including the connective tissue disorders and vasculitides.

**Objectives:** To provide evidence-based recommendations for diagnosis and treatment of paediatric connective tissue disorders and systemic vasculitides.

**Methods:** Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. International expert committees were instituted, consisting of paediatric rheumatologists with relevant expertise along with experts from other related disciplines. A detailed systematic literature review was undertaken, articles scored for validity and level of evidence. Recommendations derived from the literature were evaluated using an online survey, reformulated and discussed at a consensus meeting using the nominal group technique. Recommendations were accepted if more than 80% agreement is reached.

**Results:** Summary results of the systematic literature reviews overview of the final consensus SHARE recommendations will be presented. These provide evidence based, internationally agreed standards of minimal care for PRDs including the paediatric connective tissue disorders, rare as well as more common vasculitides. Specific detail will focus on childhood-onset systemic lupus erythematosus and the vasculitides.

**Conclusion:** The SHARE initiative provides recommendations for diagnosis and management treatment and thereby facilitates improvement and uniformity of care for patients throughout Europe.

**Disclosure of Interest:** None declared

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### SP0063 CLINICAL TRIAL DESIGN IN PEDIATRIC RHEUMATOLOGY

N. Ruperto on behalf of the Paediatric Rheumatology International Trials Organisation (PRINTO). *Pediatria II, Reumatologia, PRINTO, Istituto Giannina Gaslini, Genova, Italy*

This lecture will present a general overview, with pros and cons, of the different study design that could be employed for drug evaluation in pediatric rheumatic diseases.

Among the multitude of study designs that could be considered in pediatric rheumatology, the major trial designs are the classic parallel randomized clinical trial (RCT) with placebo or active comparator and the randomized withdrawal design. While the parallel design still remain the gold standard for establishing the efficacy and short-term safety of an experimental agent, disadvantages include ethical concerns due to the use of placebo in children with chronic condition for

which alternative treatments are available. The option of using an active control is not feasible due to the high sample size that are required by these kind of trial. The double-blind, controlled, randomized withdrawal design was proposed for the first time by Dr Lovell and Dr Giannini for use in pediatric rheumatology studies in particular for juvenile idiopathic arthritis. Eligible children are treated in an open label fashion with the experimental therapy to be tested in the trial for a few months after which responders (typically defined as those demonstrating an ACR Pediatric 30 response) are randomized in a double-blind fashion either to continue the experimental therapy or to switch to placebo. In this segment of the study, called the double-blind withdrawal phase, patients who demonstrate a pre-defined definition of disease worsening (e.g. "flare") are withdrawn from the double-blind withdrawal phase and usually re-treated with the experimental therapy in an open label fashion. The withdrawal design has proven to be very effective design and has been used in nearly all recent trials of biologic agents in children with JIA. Data gathered by use of this design led to the approval of biologic agents for children with JIA by both the FDA and EMA.

**Disclosure of Interest:** N. Ruperto Grant/research support from: The Gaslini Hospital, which is the public Hospital where I work as full time public employee, has received contributions from the following industries: Abbott, BMS, "Francesco Angelini", GlaxoSmithKline (GSK), Hoffman-La Roche, Italfarmaco, Janssen, Novartis, Pfizer, Sanofi Aventis, Schwarz Biosciences, Sobi, Xoma, Wyeth. This money has been reinvested for the research activities of the hospital in a fully independent manners besides any committment with third parties., Speakers bureau: The undersigned Dr Nicolino Ruperto received honoraria for consultancy or speaker's bureau from the following pharmaceutical companies: Abbott, AbbVie, Amgen, Biogenidec, Astellas, Alter, AstraZeneca, Boehringer, BMS, CD-Pharma,Celgene, CrescendoBio, EMD Serono,Hoffman-La Roche, Italfarmaco, Janssen, MedImmune, Medac, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, Servier, Takeda, Vertex.
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**THURSDAY, 9 JUNE 2016**

## Plasma cells as key players and therapeutic target in rheumatic diseases

### SP0064 PATHOGENIC MEMORY PLASMA CELLS IN RHEUMATIC DISEASES - A CRITICAL TARGET OF THERAPY

A. Radbruch. *Cell Biology, Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), Berlin, Germany*

Plasma cells can contribute to rheumatic inflammation through the secretion of pathogenic (auto)antibodies. While autoreactive plasma blasts are short-lived products of the chronic inflammation, autoreactive memory plasma cells can be generated already early on, in the preclinical phase, and continuously thereafter. They are refractory to conventional immunosuppressive therapy, such as glucocorticoids, anti-TNF or anti-CD20 antibodies, aiming at the termination of ongoing immune reactions. Memory plasma cells secreting pathogenic antibodies thus can provide the memory for chronic inflammation. In diagnostic terms, titers of (auto)antibodies maintained in spite of immunosuppressive therapy, in a given patient, indicate the presence of memory plasma cells secreting them: A therapeutic challenge. Memory plasma cells reside in special survival niches within the bone marrow, but also in the inflamed tissue itself, resting in terms of proliferation and mobility. They do not express CD20. They are not long-lived intrinsically, but kept alive by survival factors, such as VCAM1 and APRIL, provided by stroma cells and accessory cells of their survival niche. Understanding the lifestyle of memory plasma cells has provided strategic options to target them, but so far almost all therapeutic options do not discriminate between pathogenic and protective plasma cells, and thus imply loss of humoral memory and increased risk of infections. The therapeutic challenge is to ablate pathogenic plasma cells selectively and maintain protective humoral memory as much as possible, and to prevent regeneration of memory plasma cells from their precursors.

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### SP0065 IMMUNOSUPPRESSIVE ACTIVITIES OF B CELLS AND PLASMA CELLS

S. Fillatreau. *Team Immunity in Health and Disease, INEM, Paris, France*

B cells can contribute to immunity through production of antibodies, presentation of antigen to T cells, and secretion of cytokines. Through these mechanisms, B cells can act both as drivers and as regulators of immunity, and these two antagonistic activities seem to be at play during the majority of immune responses. Understanding how these opposite functions are mediated shall stimulate the elaboration of novel approaches for monitoring and manipulating the immune system. Here, we will discuss specifically about how B cells negatively regulate immunity through provision of cytokines. The presentation will discuss the suppressive roles of B cells during autoimmune disorders, and infectious diseases. The signals controlling the acquisition of suppressive functions by B cells (BCR, TLR, CD40), the mediators of suppression (production of IL-10 and IL-35), and the mechanisms of suppression (effects on innate cells, effector and regulatory T cells) will be presented. Moreover, we will discuss the phenotype of the B cells providing these regulatory functions *in vivo*, emphasizing the concept that specific subsets of plasma cells/plasmablasts are the major B cell source of regulatory IL-10 and IL-35 *in vivo*.

**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

## Global year against joint pain

### SP0066 PERIPHERAL PROCESSING AND CENTRAL MODULATION OF PAIN

S. Sikandar. *Wolfson Institute of Biomedical Research, University College London, London, United Kingdom*

The ability to perceive pain from cutaneous to deeper tissues and organs is part of the normal sensory repertoire of many animal species. Nonetheless, ongoing chronic pain substantially reduces the quality of life of suffering patients, often accompanied with co-morbidities that further add to the socioeconomic burden of chronic pain. Pain harnesses many neuronal systems from the periphery along the central neuraxis to higher centres of the brain. Following tissue or nerve injury, sustained activity in peripheral afferents can significantly increase the excitability of spinal cord neurones and higher centres in the brain, producing central sensitisation with ensuing pain and altered sensory function.

This talk will outline our current understanding of pain pathways in the peripheral and central nervous system. The significant role of supraspinal influences and changes in spinal excitability in the development and maintenance of abnormal sensitivity in chronic pain states will be discussed. Indeed, descending projections from the brain to the spinal cord can protect again persistent pain, e.g. in placebo analgesia, and central sensitization can occur in the absence of peripheral pathology, e.g. after opioid-induced hyperalgesia. This talk will cover the pro-nociceptive changes that occur in peripheral, spinal and supraspinal centres in chronic pain states and relate this to potential improvement of targeted analgesic therapies.

**Disclosure of Interest:** None declared
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### SP0067 SENSITIZATION AND PAIN IN OA

T. Neogi. *Clinical Epidemiology Unit, Boston University School of Medicine, Boston, United States*

Osteoarthritis (OA) is the most common form of arthritis, with the hand, knee and hip being the most prevalent joints affected. Pain is the primary clinical symptoms of knee OA and knee OA itself is a leading cause of disability among older adults worldwide. Yet there are limited management options for the symptoms of knee OA, and no proven therapies that can alter its progression. An improved understanding of pain etiology in knee OA is critical to improving OA outcomes by identifying rational therapeutic targets.

While there are data to support the importance of structural pathology as contributing to pain in knee OA, such structural lesions do not fully account for the pain experience in OA. Whereas knee OA pain is typically activity-related earlier in the course of disease, pain can be come chronic later in the disease course, suggesting the possibility of altered neurobiological pathways playing a role in OA pain. Peripheral and central sensitization, which reflect alterations in the ascending nociceptive signals in the peripheral and central nervous systems, respectively, and inadequate descending inhibition can lead to heightened pain sensitivity.

Sensitization can be assessed in clinical studies with pressure pain threshold and temporal summation, and assessment of conditioned pain modulation provides insights into efficiency of the descending inhibitory pathways. Conditioned pain modulation has been demonstrated to be abnormal in patients awaiting joint replacement surgery, and to improve post-replacement, raising in the intriguing possibility that certain abnormalities of pain processing can be altered by removing the pathologic tissue. In terms of sensitization, pressure pain threshold is lower (i.e., more pain sensitive and/or sensitized) in subjects with knee OA than in healthy controls around the knee and other anatomic sites on both the ipsilateral and contralateral sides. Lower pressure pain threshold and temporal summation are also associated with higher likelihood of pain presence and severity both at the knee and distant to the knee, but have no clear relation to radiographic severity or duration of disease. However, synovitis and effusion, which are inflammatory lesions in knee OA, are associated with both pressure pain threshold and temporal summation. In contrast, bone marrow lesions, which are largely mechanically-driven lesions in knee OA, are not associated with these measures of sensitization. These results suggest that certain features of knee OA may result in sensitization, and offer a potential avenue for targeted therapy to reduce the occurrence of sensitization, and thereby reduce pain severity in knee OA.

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### SP0068 LINKS BETWEEN ANGIOGENESIS, INFLAMMATION AND PAIN IN OA

D.A. Walsh. *Arthritis Research UK Pain Centre, Academic Rheumatology, University of Nottingham, Nottingham, United Kingdom*

Pain is the most troublesome symptom for people with arthritis, and yet the relationships between pathological change within the joint and symptoms are often weak. Key progress on understanding which specific pathological processes contribute to the generation of pain signals from the arthritic joint have pointed to new blood vessel growth (angiogenesis). Angiogenesis is a component of normal tissue growth and even pathological angiogenesis need not of itself cause pain, for example in diabetic retinopathy. However, angiogenesis is also characteristic of chronic inflammation, and the various growth factors and cytokines that stimulate blood vessel growth can also induce sensitisation of peripheral sensory nerves. Furthermore, vascular growth factors can also stimulate neuronal growth and, reciprocally, nerve growth factors might be angiogenic. This close interplay between vascular and neuronal growth is reflected in the normal sequence by which angiogenesis is followed by the extension of sensory nerve terminals, often into diseased tissues that would not normally receive innervation nor be a source of pain. Examples of tissues that might be sources of pain from arthritic, but not normal joints include the non-calcified articular cartilage and inner two thirds of knee menisci. Angiogenesis might also facilitate inflammation, permitting increased cellular recruitment, concomitant release of other neuronal sensitising factors and exacerbation of structural change. Furthermore, blood vessel growth is a prerequisite for endochondral ossification, contributing directly to structural change and altered biomechanics within the joint. Angiogenesis might be a marker for other pathological processes associated with pain. For example, vascular breaching of the osteochondral junction in OA is associated with subchondral marrow replacement by fibrovascular tissues that is characteristic of some bone marrow lesions observed by MRI scanning. Angiogenesis inhibitors have potential to prevent or relieve arthritis pain, but their application to human arthritis has been limited by potential toxicity that might result from inhibition of physiological angiogenesis (e.g. during the menstrual cycle or pregnancy) or tissue repair. Reduction of pain by angiogenesis inhibitors might result from indirect effects on inflammation that could be achieved by other strategies. However, more recent research into the plurality of effects of vascular endothelial growth factor and its isoforms suggests that inhibition of angiogenic factors might also directly influence pain transmission in the central nervous system, independent of effects on blood vessel growth. Continuing research into angiogenesis in arthritis is revealing previously unexpected insights into the relationship between joint structure and patient symptoms, particularly pain.

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**THURSDAY, 9 JUNE 2016**

## HOT session 4

### SP0069 JIA AND OTHER PAEDIATRIC RHEUMATIC DISEASES

N. Ruperto on behalf of the Paediatric Rheumatology International Trials Organisation (PRINTO). *Pediatria II, Reumatologia, PRINTO, Istituto Giannina Gaslini, Genova, Italy*

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disorder in children and is also a major cause of acquired disability and quality of life impairment in childhood. Children with oligoarticular JIA are usually treated with NSADS and intraarticular steroid injections. For children with polyarticular course JIA, methotrexate (MTX) is the drug of first choice since it provides significant clinical benefits, with an acceptable toxicity profile. For children not responding to MTX, the introduction of the biologic agents has determined a substantial advantage for the therapy of JIA since for the first time we have now drugs able to selectively block key components of the inflammation cascade.

Biologic agents can be globally divided into 2 categories: drugs able to block the tumor necrosis factor (TNF) (etanercept, infliximab, adalimumab and others) and drugs with different mechanism of action (eg abatacept, tocilizumab, anakinra, canakinumab ecc). In general biologic agents, also for their elevated cost, have to administered in children with severe arthritis non responsive to conventional therapies, primarily MTX.

The real novelty in these last years, has been the availability of biologic agents to be specifically used for the treatment of systemic JIA where, along with arthritis, children have systemic manifestations such as fever, rash, serositis, lymphadenopathy etc. These new drugs are indeed able to block selectively molecules that has been shown to be pivotal in the inflammatory process such as IL6 (tocilizumab) and IL 1 (anakinra, canakinumab and others)

Most of the biologic agents have been tested (or are currently under study) thanks to the involvement of the Pediatric Rheumatology International Trials Organisation (PRINTO at www.printo.it) and of the Paediatric Rheumatology Collaborative Study Group (PRCSG at www.prcsg.org).

This review will present a practically orientated overview of the “state of the art” for the treatment of JIA and the other major paediatric rheumatic disases including an overview on safety aspects.

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### SP0070 HOW TO TREAT IGG4-RELATED DISEASE

J.H. Stone. *Rheumatology, Massachusetts General Hospital, Boston, United States*

IgG4-related disease (IgG4-RD) is an emerging condition highly relevant to rheumatologists because of its immune-mediated nature, its propensity to cause multi-organ disease, and its ability to mimic multiple classic rheumatologic conditions. IgG4-RD readily mimics Sjogren’s syndrome, lupus nephritis, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, sarcoidosis, large-vessel vasculitis (e.g., giant cell arteritis) and others. Despite its only recent recognition approximately a dozen years ago, we have learned much about the pathophysiology of this condition. Our understanding of disease mechanisms informs both current and future approaches to treatment. I will discuss the practical, hands-on management of IgG4-RD and also consider ways in which our mechanistic understanding is driving current treatment trials.

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**THURSDAY, 9 JUNE 2016**

## Designing solutions to support young people to address the challenges of living with a rheumatic or musculoskeletal disease

### SP0071 THE ROLE OF YOUNG PARE IN GETTING ORGANISED: THE VIRTUAL KNOWLEDGE CENTRE

P. Balazova[1,2]. [1]*Young PARE, EULAR, Zurich, Switzerland;* [2]*Slovak League Against Rheumatism, Piestany, Slovakia*

**Background:** The EULAR Young PARE working group launched the Virtual Knowledge Centre (VKC) in March 2016. The VKC is an online toolbox exclusively for the Young PARE network of liaison persons. Liaison persons are representatives of European national organisations, with particular interests in supporting young people with rheumatic and musculoskeletal diseases (RMDs). The VKC can be found on www.youngpare.org.

**Objectives:** The objectives of the VKC were to: (1) establish a database with information about national youth organisations; (2) create the European network of RMD youth groups to exchange best practices; (3) provide support to national youth organisations; and (4) ensure that national youth organisations, via liaison persons stay in contact with each other to share knowledge and experiences.

**Methods:** The VKC interface offers the possibility to see the members of EULAR Young PARE, upload and download best practices and interact with other members via a moderated forum. The VKC is secure, and requires users to login, once approved by a moderator. When logged in members are able to send private messages to each other.

**Results:** The VKC has been designed to help patient organisations to collaborate and share knowledge about their work. It provides support to the network through interaction and gives the opportunity to communicate with each other in a secure and safe environment.

**Conclusions:** EULAR Young PARE is continuing to improve the VKC through gathering best practices and feedback from its members. EULAR Young PARE will also work on more effective management strategies of the forum, to ensure the VKC becomes a lively environment.

**Acknowledgement:** Simon Stones, Linda Van Nieuwkoop, Jeanette Andersen, Theodora Papastavrou, Nele Caeyers, Florian Klett

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**Disclosure of Interest:** None declared

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SP0072 **THE ROLE OF HEALTH PROFESSIONALS IN IMPROVING SHARED DECISION MAKING WITH YOUNG PEOPLE WITH RMDS**

A. Alunno. *Department of Medicine, Rheumatology Unit, University of Perugia, Perugia, Italy*

In the past, physician-patient relationship was mostly unilateral and disease-centered as the physician made all the disease-related decisions on behalf of the patients. Nowadays, based on different cultural and legal aspects, the physician-patient relationship relies on the shared decision making (SDM) process. SDM is the approach where health professionals and patients decide the best approach on disease-related decisions. In this process, patients receive from clinicians and health professionals other than medical doctors the support and all relevant information to analyze the different available options and to identify their preferences in terms of tests, treatments and daily management of the disease. In this context, SDM has a positive impact in clinical practice allowing the integration of the physician's point of view with the patients' perspective. The main target of SDM is to achieve the most effective, most satisfactory and best tolerated approach to optimize diagnostic, therapeutic and overall management strategies through: i. patients' awareness and attitude towards the disease, ii. patients' self-confidence, iii. tailored therapy, iv. therapy adherence, v. informed decision regarding disease-related daily life issues. In the field of rheumatic and musculoskeletal diseases (RMDs), the SDM process requires a multidisciplinary team involving not only rheumatologists but also other specialists and health care professionals, other than medical doctors, specialized in rheumatology. However, the multidisciplinary team pursuing this patient-centered approach, should be guided by the rheumatologist that has the widest point of view regarding all possible aspects of the disease. Such multidisciplinary approach ensures that patients are fully aware of all aspects of the disease, of how their life may be affected and, most importantly, of how to manage different situations. Patients with distinct RMDs suffer from different complaints and require different treaments according to the diagnosis. Moreover, it is well established that young people with RMDs have different priorities and needs compared to adult patients. Finally, subjects included in different age ranges within young patients are further different from each other. This requires an additional effort of the multidisciplinary team to tailor the support to specific circumstances. Self-confidence, working disability as well as social life, family life and intimacy represent some of the domains mostly affected in young patients with RMDs. Therefore, the interaction of rheumatologists, other specialists, and health professionals specialized in rheumatology is compelling to optimize the management as well as the SDM process with young patients with RMDs. In conclusion, empowering young patients with RMDs to know and manage their own condition is crucial for long-term improvement of their quality of life and should be thoroughly applied in clinical practice.

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SP0073 **EMPOWERING YOUNG PEOPLE WITH RMD TO FIND THEIR VOICE AND CLAIM THEIR SPACE**

I.A. Murphy. *Galway Branch of Arthritis Ireland, Galway, Ireland*

The presentation will focus on empowering young people in relation to their condition and through participation in local, national and international structures. The importance of empowering young people to self manage their condition and navigate transitions in their lives will be explored in the context of their holistic development. The second element of the presentation will focus on participation of young people in RMD related organisations. The key model of participation will be that of Professor Laura Lundy: SPACE, VOICE, AUDIENCE and INFLUENCE and how this can be facilitated in existing organisations. Practice examples will be included. The presenter contends that the engagement of young people in RMD structures will lead to better individual outcomes and enrich existing organisations.

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**THURSDAY, 9 JUNE 2016**

## WIN session 3

SP0074 **WHAT IS NEW: EARLY ARTHRITIS**

K. Raza. *Rheumatology, University of Birmingham, Birmingham, United Kingdom*

New onset inflammatory sounding joint pain (or clinically suspect arthralgia) and new onset inflammatory arthritis are both common. In some cases patients develop rheumatoid arthritis (RA) and in others symptoms and signs resolve spontaneously. This WIN session will highlight important recent developments in the areas of (a) disease mechanisms, (b) outcome prediction, (c) care pathways and (d) therapeutic approaches, for patients with, or at risk of, new onset synovial swelling.

**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

## Advancements in the imaging of PsA

SP0075 **LINKING HISTOLOGY AND IMAGING IN THE PATHOGENESIS OF PSA**

E. Filippucci. *Rheumatology Department, Università Politecnica delle Marche, Jesi, Italy*

Psoriatic arthritis (PsA) is a chronic inflammatory disease with a wide and heterogeneous spectrum of pathologic conditions including intra-articular and peri-tendinous synovitis, enthesitis, psoriatic plaque and onycopathy (1). Since angiogenesis plays a key role in the pathogenesis of both synovial tissue and skin involvement, the term "psoriatic disease" has been introduced to underline that the disease has the potential to affect different tissues (2). Technological advances are constantly improving the diagnostic ability of the imaging modalities, especially of ultrasound and magnetic resonance imaging, opening new sceneries in the research field (3–11). The recent availability of an ultrasound probe with a B-mode frequency reaching 22 MHz allows for a detailed morpho-structural assessment together with a highly sensitive detection of blood flow in small vessels of superficial tissues. This is of particular interest, considering that most of the PsA targets are superficial tissues. The main aims of this presentation are to discuss the most relevant investigations aiming at assessing the role of histology and imaging in PsA, and to show the diagnostic ability of the last generation imaging modalities in the evaluation of the main PsA targets (i.e. joint, tendon, enthesis, skin, and nail).

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SP0076 **PROGNOSTIC VALUE OF IMAGING MARKERS IN PSORIATIC ARTHRITIS**

M. Østergaard. *Copenhagen Center for Arthritis Research, Copenhagen University Hospital Rigshospitalet, Glostrup, Denmark*

Psoriatic arthritis (PsA) is an inflammatory joint disease characterised by arthritis and often enthesitis in patients with psoriasis, but presenting a wide range of disease manifestations in various patterns. Imaging procedures used in PsA are primarily conventional radiography, ultrasonography (US) and magnetic resonance imaging (MRI), whereas other modalities such as computed tomography are not routinely used. Imaging is an integral part of management of psoriatic arthritis for multiple reasons including establishing or confirming the diagnosis, determining

extent of disease, monitoring change in disease e.g. activity and damage, assessing therapeutic efficacy, prognostication and identifying complications of disease or treatment, in the setting of clinical practise or clinical studies. These entirely different contexts may favour different imaging approaches. This talk will focus on the available data of different imaging modalities, particularly MRI and US, for predicting 1) the development of psoriatic arthritis in patients with psoriasis, 2) the response to therapy in patients with PsA and 3) the disease course in patients with PsA.
**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

## When and how to treat Raynaud's phenomenon and related complications

### SP0077 DIFFERENTIAL DIAGNOSIS BETWEEN PRIMARY AND SECONDARY RAYNAUD'S PHENOMENON

V. Smith on behalf of the EULAR Study Group on Microcirculation in Rheumatic Diseases. *Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium*

Clinical rheumatologists frequently get patients with Raynaud's phenomenon (discoloration of extremities upon exposure to cold or stress) referred. The challenge is to distinguish patients with a primary Raynaud's phenomenon (not connected to any connective tissue disease) from patients with a secondary Raynaud's phenomenon (due to a connective tissue disease).
A large 20-year follow-up study (Koenig Arthritis Rheum 2008) of patients presenting at baseline with merely the Raynaud's phenomenon and no sign of a connective tissue disease has taught the scientific community that if a CTD is to develop in such a population then it is systemic sclerosis. Subsequently it makes sense to screen for SSc in a Raynaud's phenomenon population.
In 1992 LeRoy and Medsger proposed criteria to distinguish primary from secondary Raynaud's phenomenon. Retrospective validation of these criteria allow correct classification of a patient in one clinical consultation in 89%. Amongst other criteria, a "normal" capillaroscopy is obligatory to be able to speak of a "primary" Raynaud's phenomenon. Conversely patients with a secondary RP due to SSc have the combination of a SSc-specific antibody and a scleroderma pattern on capillaroscopy.
These criteria have prospectively been validated. The triade of RP, SSc-specific antibody and scleroderma pattern on capillaroscopy has a high positive predictive value for the development of SSc, whilst the absence of SSc-specific antibodies and a scleroderma pattern has a high negative predictive value for the non-occurrence of SSc.
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### SP0078 WHEN AND HOW TO MANAGE PRIMARY RAYNAUD'S PHENOMENON

J.-L. Cracowski. *Clinical Pharmacology Department, Université Grenoble Alpes, Grenoble, France*

Primary Raynaud's phenomenon (PRP) is a common condition characterized by transient ischemia in the extremities in response to cold or emotions, which does not progress to digital ulcerations. The pathophysiology of PRP is multifactorial and complex, and while PRP is considered as a benign condition, it can be associated with significant disability during the cold season. The objective of this talk is to further clarify how a diagnosis of PRP can be performed, and to review the different pharmacological and non pharmacological treatments currently used in the management of RP, from their mechanism of action to the available evidence regarding their efficacy. We will also address the issue of drug-induced RP.
**Disclosure of Interest:** J.-L. Cracowski Grant/research support from: Pfizer; Bioprojet
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### SP0079 WHEN AND HOW TO MANAGE THE SECONDARY RAYNAUD'S PHENOMENON AND RELATED CONDITIONS

A.L. Herrick. *University of Manchester, Manchester, United Kingdom*

When Raynaud's phenomenon (RP) occurs secondary to an underlying condition (most importantly to rheumatologists to connective tissue disease), it can be very severe and progress to tissue injury, for example digital ulceration.
Most work on secondary RP has been in systemic sclerosis (SSc)-related RP and this will be the focus of this lecture, in order to exemplify the key principles of management. The main aims are to reduce symptoms and to prevent progression to digital ulceration and/or critical ischaemia. The first step in management is to establish the diagnosis, and decide whether there are any aggravating or triggering factors (e.g. smoking) amenable to intervention. Non-drug therapy, drug therapy and surgical options will all be discussed, with a focus on recent advances. Although calcium channel blockers remain first-line drug therapy for RP, phosphodiesterase inhibitors are being increasingly used. In those patients who progress to digital ulceration and/or critical ischaemia, intravenous prostanoids and (for patients with recurrent digital ulcers) endothelin receptor antagonism should be considered. For those patients refractory to medical management, surgical debridement of ulcers and/or digital sympathectomy may be beneficial. Botulinum toxin (Botox) injections are given in some centres, but further research is required to establish their efficacy. Studies are ongoing investigating new approaches to therapy.
Upon completion of the session, participants should be able to:
1. Describe the general approach to management of secondary RP, including of digital ulceration and critical ischaemia.
2. Discuss the indications for "advanced therapies" (intravenous prostanoids, endothelin receptor antagonism, surgery).
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**THURSDAY, 9 JUNE 2016**

## Role of new imaging techniques as RMD outcomes

### SP0080 IMAGING IN EARLY DETECTION OF RA JOINT DAMAGE. WHAT TECHNIQUE AND HOW TO USE?

S. Finzel. *Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, Freiburg, Germany*

Bone erosion is a characteristic of rheumatoid arthritis. Commonly, erosion is not only used to monitor radiographic progression over time as well as therapy efficaciousness, it also helps to correctly diagnose the disease. However, there are further signs of pathological bone alterations and inflammation such as periarticular loss of bone structure, and bone marrow edema. Nowadays, treatment and diagnostic strategies do not only aim at tight disease control and treat to remission, but to diagnose rheumatoid arthritis already at a very early stage of the disease and to detect alterations in bone even before erosion have occurred.
The session will give an overview of the available modern imaging techniques, and of their strengths and weaknesses; after the session, the participant will have a clearer impression of when to use which imaging modality.
**Disclosure of Interest:** None declared
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### SP0081 IMAGING IN THE MANAGEMENT OF GOUT. CLINICAL TOOL OR ENDPOINT?

N. Dalbeth. *Department of Medicine, University of Auckland, Auckland, New Zealand*

Imaging techniques can identify the core features of disease in gout: urate crystal deposition, joint inflammation and structural damage. Clinical applications include detection and measurement of urate crystal deposition using high resolution ultrasonography (US) and dual energy computed tomography (DECT), assessment of disease severity to guide treatment decisions, and detection of disease complications (eg. structural damage, tendon disease, concomitant infection). Although imaging modalities such as US and DECT are increasingly used for gout diagnosis in clinical practice, there are uncertainties about interpretation of results in asymptomatic hyperuricaemia, the sensitivity of these methods in early disease, artefact issues, and reliability. Imaging techniques also have potential to assess response to treatment, both in clinical practice and in research settings. Key questions remain about the sensitivity to change of urate crystal deposition, inflammation and joint damage using imaging techniques. Imaging techniques that allow visualisation of urate crystal deposition may play a particularly important role in patient understanding of disease and promoting engagement with long-term urate-lowering treatments.
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**THURSDAY, 9 JUNE 2016**

## "Fewer words - more action" - tailored care for men with rheumatic diseases?

### SP0082 DISABILITY IN MEN AND WOMEN WITH RA. DOES IT DIFFER AND DOES IT MATTER?

M. Björk. *Department of social and welfare studies, Linköping University, Norrköping, Sweden*

With pharmacological advancements, early diagnosis and multi-professional treatment, many patients with RA today, have high expectations of being able to participate in valued life activities and to experience a high quality of life.

It is an on going discussion if and how RA affects women and men differently. For example, in the Swedish TIRA-project (Early Interventions in Rheumatoid Arthritis), women report higher pain intensity and more participation restrictions than men. This raises the question if men and women also have different needs of rehabilitation and if rehabilitation should be tailored differently for men and women.
This session will present an overview of impairments and participation restrictions of today's women and men with RA, and how men and women express their disabilities. The session will also focus on differences between women and men and discuss how this may be expressed as different rehabilitation needs.
**Disclosure of Interest:** None declared
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### SP0083 BALANCING WORK AND LIFE: "WHEN IS A MAN A MAN ?"

F. Demtröder. *ÜBAG MVZ Dr. Eberhard & Partner und Klinikum Dortmund, Zentrum für Endokrinologie, Diabetologie, Rheumatologie, Dortmund, Germany*

Working is a very important part of our life.
There are lots of problems and barriers for people with chronic rheumatic diseases in starting a professional career. Furthermore it is a challenge to stay in the working process for many years.
Great and never ending efforts are needed to get over multiple obstacles. But are there special aspects for men? And (why) is working so important especially for men?
What is the meaning of working? What are the goals of working for our life and living? And what does it mean with respect to any "treat to target"?
How can we be successful and what is success? Do we have to accept limits? And what strategies are available to manage a successful working life being a man with a chronic rheumatic disease?
Even if we do not find any answers let us shed some light on these important questions from a patient's view.
**Conclusion:** To be successful for men with rheumatic diseases in balancing work and life the following strategies might be helpful:
Ability to work must be kept in mind when thinking of "treat to target" in people with chronic rheumatic diseases.
Obstacles can be overcome and problems can be solved by multiple different solutions.
Goals should be looked at from different points of view – particularly from the patient's perspective. The aims should be tailored in an individual way to achieve personally defined success and happiness.
Life is what you make it – especially in RHEUMATISM!
Right Help Empowers Us – More Action Towards Independent Self-Management.
**Disclosure of Interest:** None declared
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### SP0084 BEING PHYSICAL ACTIVE IS A SALVATION? MEN'S PREFERENCES FOR PHYSICAL ACTIVITY

B.A. Esbensen[1,2]. *[1]Rigshospitalet - Glostrup, COPECARE, Centre for Rheumatology and Spine Diseases & Research Unit, Glostrup; [2]University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*

Physical activity (PA) has been recommended as an essential part of the non-pharmacological management of inflammatory arthritis (IA). Among others, positive health effects of PA in IA have been demonstrated as improved cardiorespiratory fitness, muscle strength, mobility, physical functioning and quality of life. Also a reduction in disease activity, pain, fatigue and stiffness has been proved. While studies reveal inconsistent results on whether persons with IA are more or less physically active than their healthy counterparts, it has repeatedly been argued that people with IA engage in less PA at the higher intensities (moderate and vigorous) compared to healthy populations.
Through previous qualitative research it has been suggested that men with IA, besides describing PA as an important strategy to manage their arthritis, also view engagement in PA an essential part of being a man. Thus, it could be argued that interventions or offers based on PA could be received as a legitimate form of health promoting activity responding to meet masculinity in needs and preferences among male patients with IA. Data from two qualitative studies focusing on men with IA will be presented as well as data from a cross-sectional study investigating physical activity behaviour, motivations, barriers and preferences for PA in men with IA.
**Disclosure of Interest:** None declared
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### SP0085 DESIGN OF A SELF-MANAGEMENT INTERVENTION FOR MEN WITH RA

C.A. Flurey. *Faculty of Health & Life Sciences, University of the West of England, Bristol, United Kingdom*

Rheumatoid arthritis affects more women than men (30% male) and current research reflects this difference. Evidence from several long term conditions suggests disease impacts differently on men compared to women, leading to the proposal that men need their own health strategy (White et al 2011). However, the coping styles and support needs of men with RA has not previously been the focus of discussion within rheumatology.
If men experience and cope with RA differently to women then the support required is likely to be different. However, current self-management interventions in RA have been designed and tested mainly in women.
This talk will address the experiences and coping styles of men with RA and their preferences for the design and delivery style of a self-management intervention. This talk will discuss the potential designs for a self-management intervention and potential solutions for engaging men in taking part in such an intervention.
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**THURSDAY, 9 JUNE 2016**

## Recent advances in our understanding of macrophage biology

### SP0086 TISSUE SPECIFIC DIFFERENTIATION OF INTESTINAL MACROPHAGES

A. Mowat. *University of Glasgow, Glasgow, United Kingdom*

Resident macrophages (møs) from different tissues are highly heterogeneous in terms of their functions and origins. Intestinal møs are one of the largest populations in the body and have several characteristic features, including expression of high levels of MHCII and CX3CR1, constitutive production of IL10 and TNFa and avid phagocytic activity. However they are refractory to stimuli such as TLR ligands. We have shown that adult intestinal møs are derived from circulating Ly6Chi monocytes that acquire the properties of the resident cells in the mucosa. However the mechanisms responsible for this local differentiation process are unknown. By comparing their transcriptome with monocyte- and embryonically derived møs from other tissues, here we identify a genetic signature of resident intestinal møs and validated it by Q-PCR and FACS. Soon after entry into the intestine, maturing møs become genetically distinct, even from møs in other tissues that are replenished by monocytes, such as the dermis. Many of the selectively expressed molecules are involved in tissue remodeling and in uptake of apoptotic cells, including avβ5 integrin, metalloproteases 2, 9 & 14, C1Q and CD36. Several are TGFβ inducible genes and although intestinal møs numbers are normal in CD11c-cre-TGFβR1fl/fl mice, their gene signature is altered and they show reduced expression of IL10 and CX3CR1. In parallel, chimeric mice lacking TGFβR signaling only on møs show evidence of increased inflammatory monocyte recruitment. Thus TGFβR signaling is critical for tissue specific adaptation of intestinal møs, driving the differentiation of monocytes into møs with homeostatic and anti-inflammatory functions.
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**THURSDAY, 9 JUNE 2016**

## Lubricants: potential as osteoarthritis treatment?

### SP0087 NATURAL OCCURRING LUBRICANTS TO MAINTAIN JOINT HOMEOSTASIS

J. Klein. *Weizmann Institute of Science, Rehovot, Israel*

Cartilage surfaces sliding past each other in the major joints (such as hips and knees) exhibit extremely low levels of friction under physiologically-high pressures, a lubricity which is essential for their healthy perfomance. A detailed molecular-level understanding of this could benefit treatments of osteoarthritis (OA), as well as improved prosthetic joint implants. Any insight must, first and foremost, be able to account for the low friction (coefficient of friction (CoF) down to ca. 0.001) at the high pressures (which can reach 100 atm or higher) of the joints. However, the main molecular "suspects" thought to constitute the lubricating boundary layer on cartilage, namely hyaluronic acid, lubricin or phospholipids, do not, individually, provide especially good lubrication. Recently[1] we discovered that hyaluronan (HA) which is attached to a surface – to resemble its configuration at the outer cartilage surface – may complex with phosphatidylcholines (PCs), lipids that are ubiquitous in synovial joints, to form robust boundary layers. These layers act synergistically to provide the very low friction (CoF $\approx$ 0.001) characteristic of cartilage, at the highest physiological pressures, and contrast with surface-attached HA on its own, which leads to considerably higher friction. The very low friction is ultimately due to the phosphocholine groups exposed by the HA/PC surface complexes; these groups are known to be strongly and highly-hydrated, and they lubricate via the recently elucidated hydration-lubrication mechanism[2]. Our results thus point to a scenario[3] where HA, PCs and lubricin, each with a very different role, act together synergistically to reduce friction of cartilage in articulating joints. Hyaluronan, anchored at the outer surface of articular cartilage by lubricin molecules (which are known to be present in the outer superficial zone), complexes with joint phosphatidylcholines to provide

the extreme boundary lubrication of synovial joints via the hydration-lubrication mechanism.
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### SP0088 HYDROGELS FOR OSTEOARTHRITIS TREATMENT

S.J. Bryant. *Chemical and Biological Engineering, University of Colorado, Boulder, United States*

Osteoarthritis is a debilitating disease that affects cartilage and bone in joints. Cartilage injuries, if left untreated, are one of the leading risk factors for developing osteoarthritis. Thus, treating cartilage injuries early may help prevent progression of osteoarthritis. There are however no clinical solutions that are capable of repairing damaged cartilage and replacing it with healthy functional articular cartilage. Thus, the focus of our research program is to develop novel hydrogels that support regeneration leading to full restoration of joint tissue and its function. Towards this goal, we focus on developing hydrogels that support differentiation and tissue growth and have begun to translate our materials *in vivo* towards the long-term goal of creating a viable clinical solution for cartilage regeneration.
Synthetically-derived hydrogels offer a highly tunable platform to create biomimetic environments that support repair of damaged or diseased cartilage. Our group has worked extensively to identify and create biomimetic, biodegradable, and photopolymerizable hydrogels. Photopolymerization offers the ability to form hydrogels directly in the defect and control gelation time (e.g., $\sim$ 10 seconds). In developing the chemistry of the biomimetic hydrogel, our research has pointed to the importance of physiochemical cues in directing stem cell differentiation for chondrogenesis and cartilage regeneration. The incorporation of cartilage specific extracellular matrix (ECM) analogs into a synthetic hydrogel combined with dynamic mechanical loading results in a synergistic response that produces a robust differentiation and improves tissue growth. These physiochemical cues appear to be more potent than either chemical or mechanical cues alone. For example, we have incorporated chondroitin sulfate, the main sulfated glycosaminoglycans found in cartilage, into a synthetic hydrogel to mimic cartilage's high fixed charge density. Upon dynamic loading, this creates an environment that induces oscillations in ion flow and leads to dynamic changes in local osmolarity and streaming potentials, both of which can regulate ion channels on the cell membrane. We have also incorporated cell adhesion peptides that enable integrins on encapsulated cells to interact with the hydrogel and which can act as mechanoreceptors. We have found that combining both ECM analogs into a cartilage biomimetic hydrogel improves ECM synthesis capabilities in chondrocytes, but only under dynamic loading. This cartilage biomimetic hydrogel enhances chondrogenesis of mesenchymal stem cells, but under dynamic loading is able to inhibit RunX2, collagen X, and MMP13 activity, which are characteristic markers of a hypertrophic phenotype in cartilage. Thus, this novel cartilage biomimetic hydrogel holds promise for maintaining a stable chondrogenic phenotype and regenerating cartilage within the joint where dynamic mechanical forces are prevalent.
In addition to identifying a local hydrogel environment that supports chondrogenesis and cartilage tissue regeneration, the success of such a therapy requires the translation *in vivo*. Towards this goal, we have created an *in vitro* model of a cartilage defect in an osteochondral plug that is subjected to physiological and dynamic compressive loading. When left untreated, the cartilage surrounding the defect undergoes rapid remodeling in four weeks, leading to loss of proteoglycans, increased collagen degradation, and a decrease in mechanical properties; signs of cartilage degeneration and a precursor to osteoarthritis. However, if the defect is filled with a mechanically supportive hydrogel that distributes the loads across the osteochondral plug degeneration could be arrested. Specifically, there was no evidence of proteoglycan loss, minimal collagen degradation, and no change in mechanical properties. Using this novel defect model, we have shown that mechanical loading can have detrimental effects on cartilage injuries if left untreated, but that a mechanically supportive hydrogel can protect the surrounding tissue from further damage.
While our research is still on going, we have identified novel cartilage biomimetic hydrogels that support differentiation and tissue growth. We are currently testing this novel biomimetic, biodegradable, and photopolymerizable hydrogel in a skeletally mature (8 month old) rabbit model with an osteochondral defect. Additionally, we are developing advanced strategies to combine our novel cartilage biomimetic hydrogel with stiff structural features to create mechanically supportive environments the enable tissue growth and protect the surrounding tissue from further degeneration. Our long-term goal is to develop clinically useful technologies that help prevent the onset of osteoarthritis by treating cartilage injuries early and restoring normal function.
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**THURSDAY, 9 JUNE 2016**

## Extraarticular complications of JIA

### SP0089 OSTEOPOROSIS IN JUVENILE IDIOPATHIC ARTHRITIS

R. Cimaz. *AOU Meyer, Firenze, Italy*

In children with rheumatic disorders the physiological development of bone strength in response to mechanical loads (the mechanostat model) is frequently impaired. In this population the prolonged inflammatory process and systemic treatment with glucocorticoids (GC) represent the two main risk factors which interfere with the bone remodelling process.
Up to 6% of children with GC-treated rheumatic disorders develop a vertebral fracture in the first 12 months of therapy; children with more severe inflammation and more systemic involvement, such as those with systemic-onset JIA or connective tissue diseases, appear to be at higher risk.
Inflammation exerts a direct and detrimental effect on bone, as generalized bone loss can occur independently from GC exposure. Although cytokines are considered to be the final executors of chronic inflammation on bone, the role of immune cells (e.g. Th17) has recently been highlighted. GC therapy, often at high doses and for prolonged periods, is associated with detrimental effects on bone mass and growth by means of multiple pathogenic mechanisms. By exerting a direct effect on bone cells, GC-induced osteoporosis is characterized by a decreased bone turnover with a disproportionate reduction in bone formation over bone resorption.
The most important clinical outcome arising from lack of bone strength development in childhood rheumatic disorders is represented by fragility fractures. In order to diagnose osteoporosis in children, fracture history should be considered the base of the definition, with additional consideration for the risk factors (sun avoidance, vitamin D deficiency, reduced physical activity), and the overall BMD Z-score trajectory. Several techniques can be used to evaluated bone health in children (e.g. Dual-energy x-ray absorptiometry, peripheral quantitative computerized tomography, and quantitative ultrasound). Dual-energy x-ray absorptiometry (DXA) is the technique currently considered the most appropriate for children because of low radiation, speed, and accuracy.
In rheumatic diseases, a reduction of disease activity represent the mainstay of the treatment, and an anti-inflammatory action of medications such as methotrexate and b*iological* response *modifiers* has been associated to an improved bone health. The effect of bone-targeted therapy such as bisphosphonates on a developing skeleton has also been explored in pediatric rheumatology. In addition to correct vitamin D deficiency and encourage physical activity, oral or i.v. bisphosphonates can therefore be useful in selected patients, but caution should be used since their long-term effects on a growing skeleton are still unknown.
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**THURSDAY, 9 JUNE 2016**

## The elephant in the room: how to avoid biases in research?

### SP0090 RISK OF BIAS WHEN REPORTING A TRIAL

H. Yazici. *Academic Hospital, Istanbul, Turkey*

While it is given that some or all of the biases involved in the design and the implementation of a trial are carried to the reporting, our concern in this talk is a list of biases more specific for this stage. I propose that the common denominator in this list is the "urge to prove" (1). One important outcome of this urge is the relative reluctance of the authors to acknowledge the limitations of their work. It is interesting to note that this reluctance is more pronounced in basic science (2) while it has even been said that the main purpose of the discussion sections should be authors discussing limitations of their work, naturally best known to them (3). Another manifestation of the same urge has to do with the pervasive mistaken or ill-use of the p values. As yet again brought up recently (4), the medical literature, for decades, has been replete with articles about this misconception. Physicians and investigators, with no apparent differences between the clinicians and the basic scientists, have singularly been reluctant to correctly understand and use the p value. The main elements of the said misconception seem to be a. Inadequacy in formal probabilistic thinking, the most common being that a p value represents the probability of our trial results being false positive while it actually represents the probability of obtaining the actual trial results had it been they were only due to chance; b. The power of a test is not only important in avoiding a Type II but also a Type I error; c. The information we get from any one p value much depends on the pre-test probabilities of what we try to measure in the study design in which we do this, i.e., an observational or a cross sectional study versus a placebo controlled randomized clinical trial (5). Publication bias traditionally referred to as the athors' and journal editors' propensity to publish positive or otherwise *striking* results. Recently this has been re-considered (6) and the proposal has been that a myriad of other biases, perhaps even including almost all items related to the "urge to prove" might also be included under this broader definition of a publication bias, and again perhaps now better called a

'dissemination bias'. Although much discussed this bias remains rather difficult to accurately identify and quantitate. Finally it has to be remembered, like all biases, the biases involved when reporting a trial can either be unintentional or intentional and this is equally difficult to differentiate and quantify.

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**THURSDAY, 9 JUNE 2016**

## Digital applications for the benefit of the patient

### SP0091 CAN INDIVIDUAL PATIENTS BENEFIT FROM REGISTRIES?

S. Ernestam. *Rheumatology, Karolinska Institutet, Stockholm, Sweden*

SRQ, the Swedish Rheumatology Quality Care Register, has more than 60 000 registered patients with different inflammatory conditions, mainly arthritis diseases. Approximately 20 000 patients are on treatment with biologic drugs and a total of 35 000 patients have ever been treated with biological drugs. All rheumatology units in Sweden are part of the register.

The variables registered are mainly patient reported outcomes such as global health on a visual analogue scale, pain on a visual analoge scale, fatigue, HAQ and number of swollen and tender joints registered by both patient and provider. The patient may register their data before the consultation at a secure web page or at a computer in the waiting room. During the consultation the results of the patient reported outcome measurements are visualised to both the patient and provider and a shared decision of treatment are agreed on together. A treatment plan may be made on both medications and life style factors.

Patients may themselves take part of their individual results over time from home. During the session a short film about the way of working with SRQ will be shown.

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### SP0092 DIGITAL INTERVENTIONS TO IMPROVE SELF-CARE FOR LONG TERM CONDITIONS

E. Murray. *Research Department of Primary Care and Population Health, University College London, London, United Kingdom*

People living with a long term condition (LTC), such as diabetes or rheumatoid arthritis have to learn to live with their health problem and to manage the consequences. Not managing is not an option – what varies is the degree to which self-management improves or harms overall health and wellbeing. Corbin and Strauss have defined three tasks for patients with an LTC: medical management; emotional management; and role management. Medical management includes adopting healthy behaviours such as healthy eating, physical activity, working with health care professionals and taking medication as prescribed. Less well recognised, but equally challenging, are managing the emotional reactions of having a long term condition, including anger, despair, shame and guilt; and the changes to one's role, or biographical narrative. For many people a diagnosis of a serious illness fundamentally alters their perceptions of their essential self, and their role in life.

Digital health interventions (DHI) have significant potential for helping people undertake these three tasks. DHI are interventions which are delivered digitally, e.g. over the web to a PC, tablet or phone, or via an app. They can combine information with interactive components such as decision support, emotional support and behaviour change support, and often deliver treatments that have previously been offered face to face, such as cognitive behavioural therapy, mindfulness training, or medication changes according to pre-defined algorithms responding to self-monitoring data entered by patients. The use of video, audio and graphics can make complex information accessible and comprehensible to people with low literacy, or poor language skills. Software programming allows information and responses to be tailored to each individual, reflecting specific needs.

In this talk I will explain how DHI can help patients with the complex tasks of self-management, providing examples of available interventions. I will also summarise the research evidence on their uptake, acceptability and effectiveness.

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### SP0093 HOW INNOVATIVE TECHNOLOGIES CAN SUPPORT INDIVIDUALS TO BETTER SELF-MANAGE THEIR CONDITIONS

S.R. Stones[1,2,3]. *[1]Faculty of Life Sciences, The University of Manchester, Manchester; [2]Paediatric Rheumatology CSG, NIHR CRN:Children/Arthritis Research UK, Liverpool, United Kingdom; [3]Young PARE, EULAR, Zurich, Switzerland*

We live in a technologically-driven society; however, the acceptance of technology in the health and social care landscape has been slow and poorly acknowledged, largely due to complex health policies and frameworks in place. As highlighted in a recent industry article, technological innovations are driving forward new diagnostics, treatments, techniques, and medical monitoring [1]. Smartphones have become central to our daily lives, and are now used by 66% of adults in the United Kingdom (UK) [2]. Therefore, it appears evident to utilise the technology at the end of our fingertips to transform the way that individuals manage their health, wellbeing and relationships with healthcare professionals and peers.

The Food and Drug Administration (FDA) in the United States has now approved over 100 health apps, and in the UK, accredited apps are shown in the NHS Health Apps Library. These apps have undergone rigorous approval processes, contrary to the wealth of apps available on the internet that are widely available. In a recent international systematic review, mobile and tablet apps were considered feasible health interventions [3]; however, more studies involving larger samples, patient and professional input were deemed necessary, in order to determine the acceptability of apps, and their effectiveness in supporting disease self-management and health outcomes.

Apps and web platforms can help individuals to track their health, by recording symptoms, treatments, and other health-related aspects. However, it is equally important to connect individuals with their peers, as social interactions play an indispensable role in physical and psychological wellbeing. One of the leading platforms that has transformed the way that patients track their health is PatientsLikeMe [4]. The platform enables individuals to monitor their health, interact with other people living with similar conditions, and "donate" their data for research. In practice, patient health data is collected by medical professionals, during consultations, investigations and in-hospital admissions; however, this likely accounts for less than 10% of time. For the remaining 90% of time spent outside of the clinical setting, patients live with their conditions without effective monitoring.

Symptoms are often unpredictable for those living with rheumatic and musculoskeletal diseases (RMDs). Therefore, a clinician's understanding of how their patients are responding is based upon on memory recall, with no objective measure available to measure disease severity and quality of life in between follow-up consultations. The long-term aim of apps should therefore meet this demand, by manipulating technology that will improve communication and relationships between patients and healthcare professionals. In turn, this can empower those living with RMDs to become partners in the treatment of their disease, through better quality information and efficient shared decision making.

Aside from helping patients to track and report their symptoms, data is being generated to transform tomorrow's healthcare. The use of innovative technologies has the potential to revolutionise the way that individuals are treated and monitored in the future, as long as patients, carers, healthcare professionals and industry colleagues are involved in the development, evaluation and implementation of such technologies as equal partners.

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**THURSDAY, 9 JUNE 2016**

## EULAR projects in Clinical Affairs

### SP0094 EULAR/EFORT RECOMMENDATIONS FOR PREVENTION AND MANAGEMENT OF OSTEOPOROTIC FRACTURES

W.F. Lems. *Amsterdam Rheumatology and immunology Centre, Amsterdam, Netherlands*

Fragility fractures in women and men older than 50 years are among the most frequent musculoskeletal manifestations for which patients consult healthcare workers from more than one medical specialty. Immediately following a fracture, the patient needs acute fracture care, supplied by an orthopaedic or trauma surgeon. This is followed in a later phase by subsequent fracture prevention

in patients identified at high risk for a subsequent fracture, usually under the responsibility of rheumatologists or other bone disease experts. Thus, at a local level, a close collaboration between these specialities is necessary. Both the European League Against Rheumatism (EULAR) and the European Federation of National Associations of Orthopaedics and Traumatology (EFORT) have recognised the importance of optimal fracture care and prevention of subsequent fractures in high-risk patients and have therefore collaboratively initiated this recommendation.

The recommendations will be discussed during the meeting. Some overarching principles that play a crucial role in the recommendations are:

– especially in the frail elderly with a major fracture, an orthogeriatric and multidisciplinairy approach in an in-hospital setting is warranted, to avoid complications, delirium, and prevent increased morbidity and mortality
– optimal care in the preoperative, operative and postoperative phase has an important effect on clinical outcome. As a consequence, it is very likely that limited mobility and a low quality of life in the postoperative phase may have an elevated risk of future fractures.
– for prevention of subsequent fractures, it is important that in all patients fracture risk will be investigated systematically, including DXA, imaging of the spine, fall risk evaluation and screening for secondary osteoporosis.
– for subsequent prevention of fractures in high risk patients, not only effective and safe drugs should be prescribed, but non-pharmacological treatment options and patient education are also crucial.

**Disclosure of Interest:** None declared

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### SP0095 EULAR/ERA-EDTA RECOMMENDATIONS FOR THE MANAGEMENT OF ANCA-ASSOCIATED VASCULITIS

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We published the EULAR recommendations for the management of systemic vasculitis in 2009. We proposed and received a mandate from EULAR to revise the recommendations for the management of ANCA associated vasculitis. This project was done in partnership with the ERA-EDTA.

A team of 22 experts representing rheumatology, renal medicine, chest medicine, clinical immunology, internal medicine, ENT medicine, ophthalmology, vasculitis nursing and patient support group was formed. There was representation from 11 European countries and the USA. EULAR standardised operating procedures were followed throughout. 10 items for update and 5 new items for consideration were identified via a Delphic process. Search strings were created to identify 1347 papers. Quality scoring of manuscripts was performed using the Critical Appraisals Skills Programme. 44 papers were identified to inform the recommendations. Level of evidence was ascertained as per EULAR SOP. Statements were formed and graded for strength by the task force and by the membership of the European vasculitis society for ascertaining further validity. The level of evidence for EGPA was poor and is reflected by the low grade of recommendations.

Patients with AAV should have expert involvement in their care. A biopsy remains the gold standard for diagnosis and should be performed whenever clinically feasible. Cyclophosphamide or rituximab are the mainstay of remission induction but methotrexate and mycophenolate mofetil may be appropriate for a small number of cases. Major relapses should be treated as new – but rituximab maybe favoured over cyclophosphamide in this category. Consideration should be given to strengthening immunosuppression even for patients with minor relapses. Patients with severe renal disease or diffuse alveolar haemorrhage should be considered for plasma exchange. Remission can be maintained with either azathioprine or rituximab. In a small number of patients, methotrexate of mycophenolate mofetil may be appropriate. Remission maintenance should be continued for a minimum of 24 months after which tapering should be considered. Refractory disease should be managed at an expert centre. The role of follow-up monitoring, urological assessment, immunoglobulin monitoring, cardiovascular risk, educational needs & comorbidity assessment has also been discussed.

**Disclosure of Interest:** None declared

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**THURSDAY, 9 JUNE 2016**

## Optimization of MTX in RA treatment

### SP0096 OPTIMIZATION OF MTX IN RA TREATMENT

M. Schiff. *University of Colorado, Colorado, United States*

EULAR and ACR guidelines agree that Methotrexate (MTX) should be the first part of Rheumatoid Arthritis therapy if there is no contraindication As stated in the EULAR guidelines "*MTX should be part of the first treatment strategy in patients with active RA...* and thus continues to serve as an anchor drug in RA."

After decades of successful use of MTX the ideal way to optimize MTX is still being discussed.

This presentation will address MTX as the current anchor drug in RA and how to better optimize its dosing for best patient care. Recent EULAR, ACR presentations will be highlighted.

The pharmokinetics will be illustrated from recent Annals of Rheumatic disease papers to help clinicians optimize MTX. Genetic concerns will be addressed and how they might impact the clinical utility and future dosing of MTX.

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### SP0097 INTRACELLULAR MTX POLYGLUTAMATES AND CLINICAL RESPONSE

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Low-dose methotrexate is the cornerstone disease-modifying anti-rheumatic drug in the treatment of patients with rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA). Although MTX levels can be measured easily in plasma, low-dose MTX is rapidly cleared from plasma and is therefore not routinely measured. In contrast, MTX is transported into and retained in cells long after it has been eliminated from plasma. We have developed an LC-MS/MS assay to measure MTX-polyglutamates (MTX-PG) in erythrocytes and measured drug concentrations in three prospective cohort studies in RA and JIA patients. Erythrocyte MTX-PG levels were related to clinical response in all cohorts and hence, could be used for therapeutic drug monitoring of low-dose MTX therapy. Moreover, higher baseline erythrocyte folate was associated with higher erythrocyte MTX-PG accumulation and improved clinical response. Determinants of MTX-PG concentrations were age, polymorphisms in ABC transporters, erythrocyte folate and dosing.

**Disclosure of Interest:** None declared

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**THURSDAY, 9 JUNE 2016**

## Joint replacement in OA: friend or foe?

### SP0098 FOR WHOM ARE JOINT REPLACEMENTS MOST SUCCESSFUL? AN OVERVIEW OF THE CURRENT LITERATURE

L. Mandl. *Medicine, Hospital for Special Surgery, Weill Cornell Medicine, New York City, United States*

Total hip and knee replacements are are some of modern medicine's biggest success stories. They are, in general, extremely successful procedures, providing patients witih end stage arthritis significant improvements in pain, function and qualify of life. However, these procedures are not universal panaceas; in fact, it is estimated that up to 25% of total knee replacement patients may have residual chronic pain years after their original surgery. As aging babyboomers-who expect to continue an active lifestyle at higher rates than previous generations-increase the demand for joint replacements, it will become even more important to understand the risks and benefits of arthroplasty. This lecture will discuss outcomes of hip and knee replacements, with an emphasis on which patients are most likely to derive benefit.

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**THURSDAY, 9 JUNE 2016**

## Physical activity assessment - what do we know, what do we do, how does it work?

### SP0099 AWARENESS AND USE OF OBJECTIVE AND SUBJECTIVE ASSESSMENTS OF PHYSICAL ACTIVITY AMONG HEALTH PROFESSIONALS AND BARRIERS FOR IMPLEMENTATION

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It is widely acknowledged that regular physical activity confers multiple health benefits in people with inflammatory rheumatic diseases. Participation in physical activity should therefore be encouraged by health professionals. Despite recognising the importance of physical activity, health professionals frequently fail to provide advice on promoting same. As advice alone is not always translated into behavior, subjective and objective measures of both physical activity and sedentary behaviour are important in order to motivate change in behaviour. Questionnaires, diaries, pedometers, accelerometers and multi-sensor devices are example of useful tools for assessing and monitoring progress of physical activity in clinic and research trials. However, health professionals awareness and use of such instruments in a clinical setting, in addition to barriers for not using same to date, has been scarcely described, and will be highlighted during this session. Data from an international cross-sectional study, describing the awareness and use of objective and subjective measures of physical activity, as well as barriers for implementation of such methods in health professionals working with patients with inflammatory arthritis in Sweden, Ireland, Denmark and Belgium, will be presented.

**Disclosure of Interest:** None declared
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### SP0100 AWARENESS AND USE AMONG PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASE OF OBJECTIVE AND SUBJECTIVE ASSESSMENTS OF PHYSICAL ACTIVITY

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People with inflammatory arthritis (IA) are more physical inactive and sedentary than the general population, which can have serious health consequences such as increased risk of cardiovascular diseases and diabetes. Increasing physical activity levels (PA) (even light intensity) and reduction of sedentary behaviour (SB) have been proved in intervention studies to be feasible for patients and also found to be associated with improvements in health outcomes, such as quality of life, fatigue, pain, physical function and self-efficacy.

Different tools can be used to measure PA. Subjective and objective measures have been used in both clinical practice and in research to assess PA and SB including questionnaires, diaries, pedometry, accelerometry, multi-sensor and observational methods. However, knowledge about patients' perspective, awareness and use of different tools to measure own level of PA and SB is still scarce. Anyhow, it is crucial for health professionals to gain insight in patients' attention to both objective and subjective assessments of PA to give advises to patients about such tools. Behavioural approaches such as making use of self-monitoring has been integrated in studies targeting both increasing PA and reduction of SB in people with IA, showing positive effects. These positive effects might be an issue for health professionals to take advantage of and e.g. teach patients about being physically active and how to make different tools be a part of own self-management.

Data from an international cross-sectional study will be presented investigating the awareness and use of objective and subjective measures of physical activity for patients with IA in Sweden, Ireland, Belgium and Denmark.

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### SP0101 WHEN TO USE OBJECTIVE AND SUBJECTIVE ASSESSMENT OF PHYSICAL ACTIVITY? ISSUES OF RELIABILITY, VALIDITY AND USABILITY

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Over the last decade, physical activity has become a key outcome domain in the assessment of rheumatic and musculoskeletal diseases (RMDs). Physical activity can be defined as any bodily movement produced by skeletal muscle that results in energy expenditure. Both physical and mental aspects of health in RMDs have been associated with optimal levels and patterns of physical activity. Also, intervention studies promoting physical activity in people with RMDs have largely confirmed these health benefits. Although there is consensus on its importance, the assessment of physical activity is complex and research in this area is rapidly growing. This lecture will therefore give a narrative overview of the state-of-the-art assessment of physical activity in RMDs considering the perspective of a researcher, a clinician, a patient and (to a lesser extent) the general population.

In a first part, this lecture will discuss the relationship between physical activity and energy expenditure. More specifically, we will explain how total energy expenditure can be partitioned in obligatory energy expenditure to support basal metabolism (basal/resting metabolic rate), diet-induced energy expenditure and activity-induced energy expenditure (physical activity). A quick overview of gold standard tools to assess each component will be discussed in non-technical way. We will focus on the assessment of activity-induced energy expenditure (physical activity) using patient-reported (e-)questionnaires and (e-)diaries, observer-based and technology-based outcomes in RMDs. Often used single-sensor devices e.g. pedometer but also trends in more complex-sensor devices e.g. wearables combined with apps will be discussed.

In a second part, we will shortly present the OMERACT framework to evaluate the measurement properties (i.e. how good is it?) of physical activity assessment tools. We will present the latest findings in this area for people with RMDs. Reliability and validity of commonly used outcomes e.g. steps, physical activity level or bouts of moderate to vigorous activities in RMDs and beyond will be presented.

In a last part, we will formulate guiding principles in selecting the right physical activity assessment tool for your clinical or research question taking into account cost, measurement properties and feasibility (usability) for both clinicians and patients.

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### SP0102 PHYSICAL ACTIVITY ASSESSMENT – WHAT DO WE KNOW, WHAT DO WE DO, HOW DOES IT WORK? PERSPECTIVES FROM A PATIENT WITH ARTHRITIS

C. Kinneavy. *Arthritis Ireland, Newbridge, Ireland*

This speaker's experience spans thirty three years living with severe Rheumatoid Arthritis and had treatments and care to deal with a myriad of very difficult challenges involving multiple surgeries. Her medications included gold injections when she was first diagnosed to life changing biologic therapies for the past fifteen years. She will speak about her experiences and reflections of engaging with and monitoring and reviewing physical activity strategies and share her insights of new experiences using IT solutions to support this. Her exercise habits have been influenced by a fear of increased disability and serious co morbidity along with a desire for enjoyment and camraderie.

Alongside medication her favourite ally has been exercise and she self referred for physiotherapy advice and treatment, an experience which liberated her and provided new coping skills. Therapeutic exercises were prescribed and only performed intermittently for various reasons e.g. as there was not much fun involved! Through the Stanford self management programme and support from her physiotherapist she learned to experiment with gym and pool exercises, gaining confidence and enjoying the social aspect of leisure club membership. Monitoring her exercise programmes was limited initially to simple talk tests and increasing frequency, distance and duration of exercise.

The ongoing severity and nature of the disease continued to drive her and she has since become a self management educator, facilitating workshops in the community. This rewarding opportunity has helped her and many others to allay fears about exercise, monitor exercise activities, set new goals, review techniques and develop new pain management strategies. An opportunity arose to participate in a controlled gym based exercise study in 2009 which improved her fitness and increased her capacity for exercise. This motivated the speaker to organise some community based exercise groups for people with arthritis. Currently she exercises regularly by Aqua jogging in an Aqua Aerobics class, Nordic walking and gym based exercises all of which have increased her quality of life.

In 2015 she cautiously joined a modern gym with state of the art equipment to help improve cardiovascular health, maintain bone density and monitor her physical activity more closely. A longstanding trust in physiotherapy professionals has always prompted her to crosscheck her exercise regime. Perhaps there is a need for physiotherapy professionals to work more closely with community based exercise instructors so that patients with chronic disease can learn how to monitor and adjust their exercise habits for optimum effect and enjoyment?

For the past year she has been using a smartphone pedometer and it has motivated her to increase the frequency of walking. Choosing electronic monitoring devices has become very difficult as there are so many products and accuracy varies – patients with arthritis need accurate information from health professionals and exercise instructors. Monitoring exercise is not just important for individual patients. Patient organisations, family, carers, health providers, town planners, designers and community organisations can play a key role by promoting accessible facilities and exercise monitoring tools in their cultures and values. On reflection, she noted a number of concerns namely, affordability, accuracy, reliability, usability, information quality and potential inequality for patients.

During the past twenty years many advances have been made in the fields of medicine and allied care for rheumatology patients. As the field develops further, how important will exercise monitoring become? Will it change the way patients

interact with health professionals and services? Will we see monitoring devices and state of the art gym equipment in hospital settings, health centres and outdoor parks to support personalised patient exercise compliance?
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**THURSDAY, 9 JUNE 2016**

## How cell death shapes immunity and tolerance

### SP0103 APOPTOTIC CELL ENGULFMENT MACHINERY AND RHEUMATOID ARTHRITIS

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Specific recognition and removal of apoptotic cells is a process that occurs throughout life in all tissues, as part of homeostasis and during pathological conditions. In active rheumatoid arthritis, apoptotic cells are seen in the synovial fluid of human patients and in mice with experimental arthritis, but their contribution to disease severity is not well understood. Recently, many components of apoptotic cell clearance machinery have been identified. Using global and conditional knockout mouse strains and primary cell cultures, we have addressed specific components of the engulfment machinery for their role in rheumatoid arthritis. We observe that molecules linked to apoptotic cell clearance can affect both the extent of inflammation and bone erosion seen during arthritis in mouse models. These data suggest that targeting the components of the engulfment machinery might be a viable therapeutic approach.
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### SP0104 NEUTROPHILS IN THE RESOLUTION OF INFLAMMATION

M. Herrmann. *Department for Internal Medicine 3, University Hospital Erlangen, Erlangen, Germany*

Neutrophils are often considered being just cells of the first line defense against pathogens. They are endowed with an arsenal of deadly weapons like reactive oxygen species, proteases and anti-microbial peptides. In a cellular process referred to as degranulation neutrophils secrete preformed chemokines and cytokine that recruit and activate further neutrophils as well as other leukocytes. Neutrophils are phagocytes that vigorously ingest and kill bacteria. In addition, they take up several kinds of particular matter including monosodium urate crystals. After strong activation neutrophils eject their chromatin to form pro-inflammatory, chemo-attractive and bactericidal extracellular traps (NETs). These immobilize and kill pathogens and attract further leukocytes. IL8 secretion, neutrophil attraction and NETosis form a self-stimulating feed back loop that initiates and perpetuates inflammation. Important questions are (Q1) How is this potential dangerous vicious circle controlled? (Q2) Which mechanisms are responsible for the resolution of inflammation?
When the density of the neutrophils reaches a certain threshold the NETs tend to aggregate (aggNET) and form extended clumps of chromatin that are decorated with proteolytically active serine proteases. The clumps and the proteases sequester and proteolytically inactivate the neutrophil-derived cytokines and chemokines. Thus NETosis and aggNET formation play important roles for the initiation and resolution of neutrophil-driven inflammation, respectively.
Christine Schauer, Markus Hoffmann, Luis Munoz & Martin Herrmann
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**THURSDAY, 9 JUNE 2016**

## "Smoke a joint to protect the joint". Cannabidoids & neuropeptides in pain and inflammation

### SP0105 BIOCHEMISTRY AND PHARMACOLOGY OF THE ENDOCANNABINOID SYSTEM

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Nearly 30 years after the discovery of the psychoactive ingredient of *Cannabis sativa*, $\Delta^9$-tetrahydrocannabinol (THC) in 1964, the endogenous counterparts of THC were discovered and were collectively termed endocannabinoids (eCBs). To date, among several members of the eCB family *N*-arachidonoylethanolamine (anandamide, AEA) and 2-arachidonoylglycerol (2-AG) are widely recognized as the most bioactive substances, able to bind to and activate G protein-coupled type-1 ($CB_1$) and type-2 ($CB_2$) cannabinoid receptors, as well as other non-$CB_1$/non-$CB_2$ receptor targets. In addition, an ensemble of proteins that synthesize, transport and degrade eCBs have been identified in the last 20 years, altogether forming the so-called eCB system. eCBs control basic biological processes spanning from cell choice between survival and death, progenitor/stem cell proliferation and differentiation, and neurotransmission to reproductive events, energy balance and immune response. Unsurprisingly, in the last two decades eCBs have emerged as key regulators of human pathophysiology at multiple levels. Here, a modern view of the biochemistry and pharmacology of the eCB system will be presented, in order to put in a better perspective the impact of eCB signaling on human health and disease, both centrally and peripherally. In particular, it will be shown that eCBs regulate bone elongation and remodeling, as well as inflammation and adaptive/innate immunity. Moreover, unprecedented results on AEA and 2-AG alterations in human patients with systemic lupus erythematosus will be presented, that may help to better understand the role of lipid signaling in this disease.
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### SP0106 NEUROPEPTIDES, TRPS AND INFLAMMATION: FOCUS ON THE JOINT

S. Brain. *Cardiovascular Div, King's College London, London, United Kingdom*

Arthritis is a debilitating condition characterised by chronic pain in and around the joint. Sensory nerves that contain and release neuropeptides innervate the joint and play a major role in mediating pain. We are interested in the role of the transient receptor potential (TRP) channels, that are calcium-permeable cation channels in mediating the pain and inflammation that occur in the joint during arthritis. We have used TNF and CFA murine models of joint inflammation to elucidate mechanisms. Our early work investigated the role of TRPV1, a channel that is localised to sensory nerves and best known for its activation by the chilli pepper extract capsaicin, noxious heat as well as certain lipids. Studies in TRPV1 knockout mice revealed that CFA thermal pain was alleviated, but TNF levels remained high. TRPA1 is a second TRP channel localised to TPRV1-containing sensory nerves. TRPA1 is activated, amongst other things, by noxious cold and reactive oxygen species. TRPA1 mediates pain in arthritis, as demonstrated by studies including from our laboratory, in a number of species. We have shown that TRPA1 is a vascular cold sensor, also that mice demonstrate exacerbated CFA-induced joint pain after environmental cold exposure. Finally we have now discovered evidence of a regulatory role for the TRPC5 receptor, in that TRPC5KO mice exhibit an enhanced inflammation that is mirrored in WT mice treated with a TRPC5 antagonist.
Thus there is compelling evidence that TRP receptors have potential roles in mediating pain, and in some cases the inflammation, in arthritis. They can act via pro-inflammatory and anti-inflammatory mechanisms, depending on subtype. These effects appear to depend on the TRP channels, with some evidence that the neuropeptides are also involved in pain processing.
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### SP0107 CANNABINOIDS AND INFLAMMATION: FOCUS ON THE JOINT

T. Biro. *Department of Immunology, University of Debrecen, Hungary, Debrecen, Hungary*

The emerging endocannabinoid system (ECS; comprising the endogenous lipid mediators endocannabinoids [eCBs], produced in virtually all tissues; their metabotropic and ionotropic cannabinoid receptors; biosynthetic pathways and metabolizing enzymes) has been implicated in multiple regulatory functions of the human body. Namely, the ECS and its "tone", defined by the local levels of eCBs, were shown to control major functions of the central nervous system as well as of multiple peripheral organs (e.g. liver and other metabolic tissues, skin, cardiovascular and pulmonary systems, etc.). Recent studies have intriguingly suggested the existence of a functional ECS in the immune system. Indeed, most immune cells functionally express the bioactive eCBs and the ECS where their activities chiefly exert immune-suppressive and anti-inflammatory actions.
The ECS is functionally active in the joints as well. Importantly, the "eCB tone" was shown to modulate various symptoms and pathogenetic steps of rheumatoid arthritis (RA) and osteoarthritis (OA) in several models of the diseases. Indeed, activation of type-2 cannabinoid receptors (CB2) suppresses cytokine release, inhibits functions of various cells of innate and adaptive immunity, and conveys anti-inflammatory actions. Moreover, stimulation of CB1/CB2 receptors results in analgesic, anti-proliferative, and osteogenetic effects. Interestingly, with respect to fibroblast functions, CB2-coupled signaling exerts anti-fibrotic action whereas, conversely, engagement of CB1 mostly leads to augmentation of fibroblast proliferation.
This presentation reviews the current state-of-the-art of the role of the ECS in the biology of the joints. Moreover, it delineates novel, promising ECS-targeted therapeutic possibilities where synthetic, semi-synthetic or naturally occurring (e.g. from the Cannabis sativa plant) modulators of the "ECS-tone" could be successfully employed in the future clinical management of RA and OA.
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**THURSDAY, 9 JUNE 2016**

## EULAR - EMA session

SP0108 **DIFFERENT APPROACHES TO DRUG APPROVAL BY EMA AND FDA – THE EXAMPLE OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS**

J. Sieper. *Charite, University Medicine Berlin, Berlin, Germany*

Recently new classification criteria have been developed for axial spondyloarthritis (SpA) covering both patients who already show radiographic evidence of structrual damage in the sacroilac joints (or spine), termed radiographic axila SpA (or using the older term: ankylosing spondylitis (AS)) and patients in the earlier phase without radiographic evidence of structural damage in the bone, termed non-radiographic (nr) axial SpA. There is general agreement that these two stages represent a continuum of the same disease and that preferentially the term axial SpA should be used. Both EMA and FDA have raised questions about the natural course of the earlier stage (nr-axSpA), the potential rate of spontaneous remission and the possibilty of overtreatment with biologcs in these patients. However, the EMA has accepted that there was an unmet need for treatment with TNF-blockers of these patients if they fail conventional therapy, which resulted in an approval for TNF-blockers for nr-axSpA - in addition to patients with AS - in the EU, if they have objective signs of inflammation such as positive CRP and/or active bone inflammation on MRI, and many other countries but not the US. The EMA has demanded post-approval studies from the TNF-blocker companies investigating what happens if the drug is stopped (or the dosage reduced) in patients who are reaching remission. These studies are ongoing and will deliver sufficient informations whether overtreatment might occur in these patients. In contrast, the FDA is asking for further phase 3 trials which include a placebo-controlled phase over 12 months. Such a study design would be very difficult to be conducted in EU countries – withholding an effective drug up to 12 months from active patients. But the different apporaches used by the two agencies also reflect that European rheumatologists have been much more familiar over the last decades with this early phase of axSpA compared to US rheumatologists. It is hoped that the results of the ongoing trials - in Europe, US and other parts oft he world – will result in a worldwide acceptance of the axial SpA concept and of the need to offer adaequate treatment to all axial SpA patients in their active phase.

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**THURSDAY, 9 JUNE 2016**

## Teaching clinical skills

SP0109 **HOW TO PERFORM CLINICAL HISTORY AND PHYSICAL EXAMINATION?**

M. Doherty. *University of Nottingham, Nottingham, United Kingdom*

The GALS (gait, arms, legs, spine) screen is useful to detect musculoskeletal (MSK) abnormality as part of a general assessment (1). However, for a person with MSK complaints a more detailed assessment is required to determine the diagnosis and impact on the patient. A thorough history alone usually suggests the single most likely cause for the patient's problem(s). The examination that follows should be a targeted assessment in which the practitioner selects the required skills from a range of competencies according to specific elements in the history (i.e. not a uniform set of identical procedures in each patient). The overall assessment needs to be holistic and individualised as the enquiry proceeds, since the impact of any condition is person specific and influenced by many factors (e.g. psychosocial factors, illness perceptions, sleep, comorbidity etc.).

This presentation will cover key principles and considerations related both to the history and examination (2). Examples include:

(1) in the *history:* determination of pain localisation and features that associate with radiated pain; important pain and stiffness characteristics that differentiate mechanical usage-related pain, inflammatory pain, acute crystal synovitis pain, destructive bone pain and neurogenic pain; non-specific symptoms of inflammation

(2) in the *examination:* usual order of inspection at rest, inspection during movement, then palpation at rest and during movement; contrasting clinical findings that differentiate joint and peri-articular problems; detection of "stress pain" (pain worse in tight-pack positions but reduced/absent in loose-pack positions - the most sensitive sign of inflammation); examination for effusion, soft-tissue and firm swelling; use of resisted active movements and stress tests for peri-articular lesions.

With experience, following a thorough history and examination the combined aspects of the history and examination which differentiate between major categories of MSK conditions permit pattern recognition and a confident clinical diagnosis in the majority of cases. A simple way of assembling the clinical findings to enable them increasingly to point to a likely single diagnosis will be presented.

EULAR learning resources available at http://www.eular.org/edu_training_dvd.cfm include: (1) The "GALS" screen and (2) Principles of the musculoskeletal history and examination.

**Disclosure of Interest:** None declared
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SP0110 **WHAT MAKES AN EFFECTIVE MENTOR AND AN EFFECTIVE MENTEE?**

J. Hafler. *Yale University, New Haven, United States*

Mentoring is a key teaching skill that is considered to be a core component of the duties of all medical school faculty. Effective mentoring requires understanding the needs of the mentee. How do we learn how to be an effective mentor? How we we learn how to be an effective mentee? As Daloz (1986) said "I resolved to look more closely at what good teachers and mentors actually do as they guide their charges along on their transformational journeys." In this session I will explore what good mentors and good mentees can do toward achieving successful outcomes and address specific characteristics of effective mentors. This session will be of interest to mentors and mentees in research and clinical areas.

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**THURSDAY, 9 JUNE 2016**

## Local procedures including aspirations, injections and biopsies I

SP0111 **SONOGRAPHIC-GUIDED JOINT AND PERIARTICULAR ASPIRATIONS AND INJECTIONS**

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For more than 60 years intra-articular an peri-articular injection are part of the standard treatment of arthritis. In vast majority of interventions needles used to be guided by anatomical landmarks as orientation ("blind" join injection). However, studies of the accuracy of "blind" injections into various joints showed that about two thirds of knee and ankle injections and only half of the wrist injections were intra-articular. The accuracy of blind corticosteroid injections into the glenohumeral joint is also questionable. Tobola et al. found the accuracy of an anterior approach glenohumeral injection was 64.7%, regardless of clinician experience. Utilizing the additional measure of ultrasound or another image modality to guide injections improves accuracy. In comparison to a blind posterior injection technique, ultrasound guided injections had a greater success rate of reaching of the glenohumeral joint (72.5% vs. 92.5%. Musculoskeletal ultrasound (MSUS) allows the possibility of reliable guidance of needle during diagnostic (e.g. needle aspiration of synovial liquid for analysis) and treatment interventions (e.g., intra-articular injections of drugs). Ultrasound guidance enables the exact placement of the needle into the structure of interest and accurate injection of medication. Moreover, it helps in establishing more precise diagnosis and in confirmation of the indication for injection. Ability of ultrasound guided injections to improve clinical outcomes compared to that of palpation guided injections however remains unclear. Lee et al. compared ultrasound-guided injections of triamcinolone with blind injections. At 6 weeks, the ultrasound guided injection group did not have statistically superior improvements than blind injections in flexion, abduction, external rotation or internal rotation, although improvements from baseline were significant within both groups ($p<0.001$). The ultrasound guided injection group also did not have significantly better VAS score improvements after 3 weeks. On the contrary, one study showed that US guidance significantly improved the outcome of intra-articular steroid injections compared with anatomical palpation guidance. For successful implementation of ultrasound-guided injection technique appropriate training is required. After successful training, guidance of needle allows precise and successful diagnostic and/or treatment intervention. Moreover, ultrasound examination can visualize different tissues which could be damaged by the needle during the "blind" injection. Ultrasound visualization allows examiner to minimize possible damage of blood vessels, nerves, tendons, ligaments, cartilage and other tissues by the needle. Two main advantages of ultrasound-guided injections are increased accuracy and minimal risk of adverse events during and after the intervention.

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SP0112 **MINIMALLY INVASIVE ULTRASOUND-GUIDED SYNOVIAL BIOPSY**

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Ultrasound-guided biopsy of synovial tissue is an increasingly performed procedure for diagnostic and research purposes.

In clinical practice, synovial tissue analysis may assist in the diagnostic work-up in selected (rare) joint diseases, including neoplastic or granulomatous diseases, deposition diseases including crystal-associated arthritis or infection, when synovial fluid analysis and culture are not conclusive.

As demonstrated by several studies, including the 1987 ACR classification criteria for rheumatoid arthritis (RA) study, synovial tissue analysis helps in distinguishing inflammatory from non-inflammatory arthritis and between different forms of immune-mediated inflammatory arthritis (IA). Despite morphological

and immunohistochemistry analyses are accurate in differentiating RA from spondyloarthritis, at this moment the usefulness of these tests to establish the diagnosis in clinical practice is not justified.
Further applications of synovial tissue analysis include disease activity assessment at joint and patient level, as well as prognostic stratification, but no specific prognostic biomarkers are enough specific and predictive to be included in a standard patient assessment. However, in the setting of drug development, the evaluation of biological activity of experimental drugs at the site where the disease process takes place is now a well-recognized approach, and evaluation of serial synovial biopsies assists in screening for potential efficacy of novel compounds provides insights into the mechanism of therapy.
Form a technical point of view, needle biopsy is simple, cheap and minimally invasive, while arthroscopic biopsy is regarded as the gold standard sampling method, since it provides adequate synovial tissue samples selected under direct vision from both large and small joints even from clinically uninvolved joints. The availability of more recent office-based mini-invasive ultrasound-guided techniques are increasing the diffusion of the synovial tissue analysis in inflammatory arthritis research and clinical practice.
Depending on the indication for the biopsy procedure, the tissue needs to be handled substantially differ. Under the assumption that inflammation in one inflamed joint is generally comparable to that in other inflamed joints, in order to minimize sampling error, multiple sampling (typically at least six samples from different areas throughout the joint) need to be applied. As recently demonstrated in validation studies on US-guided derived synovial samples, both at large and small joints: good quality tissue collection is feasible; quantification of digital synovial inflammation by image analysis is a valid, sensitive and time efficient; and quantitative PCR and different microarray analysis techniques can be used to analyze US synovial tissue samples for research purposes.
Future advances in the field of minimally invasive ultrasound-guided synovial biopsy will include new technical developments, identification of novel biomarkers, able to improve diagnostic/prognostic characterization of individuals at the onset of the disease, and even more importantly, to personalize treatment based on potential treatment selection biomarkers.
**Disclosure of Interest:** None declared
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### SP0113 MINIMALLY INVASIVE BIOPSY OF SALIVARY GLANDS

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**Background:** Salivary gland disorders include disorder of immune system, inflammatory, bacterial, viral, and neoplastic etiologies. Diagnosis is made by radiological examinations (ultrasonography, magnetic resonance imaging, computed tomography) and biopsy of salivary glands. Minimally invasive biopsy, such as Fine-needle aspiration (FNA), are commonly used in the diagnosis of salivary gland disorders. Submucosal minor salivary gland biopsy should be done if the diagnosis of Sjögren syndrome (SS) cannot be made by history and serologic testing. Fine-needle aspiration is widely applied in the preoperative diagnosis of salivary gland lesions. Distinguishing neoplastic from non-neoplastic lesions and benign from malignant tumors of the salivary glands is extremely important for medical and surgical management of salivary gland disorders.
**Aims:** The aim of this study was to provide a systematic review of the literature to analyze the role and several aspects of minimally invasive biopsy of salivary gland disorders.
**Methods:** A systematic bibliographic search of the medical literature between January 2011 and January 2016 was conducted using electronic databases of National Library of Medicine (Medline). The bibliographic search was carried out with combination of this medical subject heading terms and text words: salivary gland, biopsy, minimal invasive biopsy, histological findings and fine-needle aspiration. For the inclusion on this review, studies had to evaluate several aspect of biopsy of salivary glands. The authors to determine the eligibility on this study performed an independent review of the finding data.
**Results:** The PubMed search identified 161 items. After a first evaluation, 57 full-text articles were finally selected for further evaluation. Of these 57 articles, 38 were excluded because they did not completely meet the inclusion criteria, whereas 19 were considered eligible for this review study.
**Conclusions:** The advantages of minimally invasive biopsy of salivary glands include decreased tissue damage, no need for anesthesia, and repeated sampling when specimens are insufficient after immediate assessment at the examination site. A biopsy of salivary glands offers valuable information for planning of subsequent therapeutic management. Fine-needle aspiration is a safe diagnostic technique that has a high specificity and sensitivity for the assessment of salivary gland disorders. The sensitivity and specificity reported is high for infective, immunological and benign lesions, whereas it decreases in cases of malignant tumors for the great variety of morphological patterns found in malignant salivary gland tumors.
**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

## MRI I

### SP0114 HOW TO DEFINE AND ASSESS INFLAMMATORY AND DESTRUCTIVE CHANGES IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS? INCLUDING QUIZ CASES

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Compared to conventional clinical, biochemical and radiographical examinations, magnetic resonance imaging (MRI) offers improved sensitivity to early inflammatory and destructive changes in peripheral joints in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and other inflammatory joint diseases. Furthermore, MRI measures provide high sensitivity to change and prognostic value.
Accurate and reproducible assessment requires strict definitions and validated assessment methods. Such methods can be qualitative, semiquantitative or quantitative. The present talk will outline currently available definitions and assessment systems of inflammatory and destructive changes in RA and PsA. The most used methods, i.e the RAMRIS (RA MRI scoring system) and PsAMRIS (PsA MRI scoring system), both developed by the OMERACT group, will be described, as will recent alternative approaches including whole-body MRI, dynamic contrast-enhanced MRI and volume quantification.
At the end of the talk, quiz cases for audience participation will be presented.
**Disclosure of Interest:** None declared
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### SP0115 MRI OF INFLAMMATORY DISEASES OF VESSELS AND MUSCLES – HOW TO APPLY, INCLUDING CASE STORIES

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A variety of diagnostic imaging techniques have made the non-invasive evaluation of skeletal muscles and vessels in inflammatory diseases possible. The standard imaging methods for muscle evaluation are US, MRI and scintigraphy while for vessel imaging conventional angiography as well as CT angiography and PET-CT play an important role.
Magnetic resonance imaging (MRI) is especially sensitive in the diagnosis of muscle disorders and injury and has proved to be useful in determining the extent of inflammatory disease, in directing interventions, and in monitoring the response to therapies. Thus, the current imaging indications for muscles include: diagnosis, assessment of disease burden (localization) and biopsy site selection. Several experimental techniques are used nowadays for further muscle evaluation including spectroscopy (metabolic imaging), BOLD imaging (perfusion and oxygenation) and diffusion tensor imaging DTI (DTI; muscle function-structure relationship).
In vessel imaging, CT, MRI and conventional angiography help in the anatomic evaluation of disease including the evaluation of disease distribution, vessel stenosis, wall thickening (CT and MRI only) and end organ damage. MRI and FDG-PET-CT add valuable information regarding active inflammation including detection of wall edema, delayed wall enhancement and high glucose metabolic activity.
The basics of MR muscle and vessel imaging as well as the more advanced imaging techniques will be presented along with some case stories.
**Disclosure of Interest:** None declared
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### SP0116 HOW TO USE MRI TO DIFFERENTIATE SPA FROM ITS DIFFERENTIAL DIAGNOSES?

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Magnetic resonance imaging (MRI) in axial spondyloarthritis has an increasing importance, especially in patients without or with equivocal changes in radiography. However, radiologists are often uncomfortable with imaging of rheumatic diseases and reports consequently sometimes confusing. Therefore, rheumatologists are increasingly confronted with the need to receive their own impression of radiography and MR images.
The aim of this talk is to give basic ideas on interpretation of MRI sequences with a focus on the sacroiliac joints in a case-based manner. The participants will learn to easily differentiate common MR sequences and to decide, which information can be derived of an image. They will discover to detect common differential diagnoses (such as condensing osteitis, osteoarthritis and anatomical variants) and to differentiate them from inflammatory changes. In a comparison of radiography, MRI and computed tomography they will experience the strengths and weaknesses of the different imaging methods and learn to decide, in which patients further imaging – additional to MRI – may be useful.
This talk will also provide a perspective of future innovations in MRI and what additional advantages might go along with them. In the end, the experience might encourage an intensified communication between rheumatologists and radiologists in daily practice with a better understanding of the thinking and needs within the respective medical field.

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SP0117 **WHEN AND HOW TO USE MRI IN CLINICAL PRACTICE**

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MRI is very popular among clinicians and patients are referred to a large extent to radiological facilities to help establishing diagnoses. However, despite MRI is one of the more expensive imaging tests its not automatically the one solving all clinical problems.
The lecture will highlight the value of MRI for early diagnosis of both axial and appendicular arthritides. On the other hand, certain diagnostic problems will be outlined that did benefit from additional imaging modalities or from a carefully obtained medical history.
Learning objectives:
- Learn how to use MRI for establishing a diagnosis.
- Learn how early detection differs from differentiation of arthritides.
- Identify diseases that do not benefit from MR imaging.

**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

## The Health Professionals' approach to pain management in inflammatory arthritis and osteoarthritis

SP0118 **THE ONGOING SHIFT OF PARADIGMS WITHIN PHYSIOTHERAPY AND PAIN MANAGEMENT**

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During the past three decades the search for effective non-pharmacological pain management methods in chronic non-cancer pain conditions has been intensified. However, despite a growing body of scientific studies, there is still no cure for chronic pain, and treatments targeting pain per se do not report sufficient effects in terms or pain relief. This lecture presents some important changes in foci regarding pain management in general and physiotherapy in particular. These are: (1) *From* problem-identification *to* goal attainment, (2) *From* pain intensity *to* activity interference, (3) *From* pain relief *to* behavioural skills training. The perspectives will be described and illustrated by scientific studies underpinning this development. Implications for pain management in inflammatory diseases and physiotherapy will be discussed with the audience.
**Disclosure of Interest:** None declared
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SP0119 **SYSTEMATIC REVIEWS AND META-ANALYSES FOR DUMMIES: A TUTORIAL ON HOW, WHEN, AND WHY TO GET STARTED**

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The world today is overflowing with results from trials to the point where anyone can be overwhelmed. Being able to sort out the good systematic reviews and meta-analyses from the bad ones and then be confident in the ability to judge the quality of the evidence is critical. Systematic reviews (i.e., the process of systematically locating and synthesizing data from completed studies) and meta-analyses (i.e., the statistical component of a systematic review) are the procedures that make it possible to synthesize data from a series of studies (i.e., evidence synthesis); these are essential to summarise evidence relating to efficacy and safety of health care interventions accurately and reliably.
The process begins with a pre-specified protocol [1] asking an explicit question, in terms of the populations, alternative management strategies (an intervention, sometimes experimental and a comparator, sometimes standard care), and all patient-important outcomes [2]. After the evidence is collected, summarised, and reported [3], a good systematic review will help determine the quality of evidence based on study design, risk of bias, imprecision, inconsistency, indirectness, and magnitude of effect [4]. Quality of the evidence (QoE) reflects our confidence that the estimates of the effect are correct. High QoE: "*We are very confident that the true effect lies close to that of the estimate of the effect*" (no more research needed); Very low QoE: "*The true effect is likely to be substantially different from the estimate of effect*" [5].
Following this, guideline panels might conclude with either a strong or conditional recommendation, either for or against an intervention - indicating whether patients should receive the specific course of action {6}.
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SP0120 **RECOMMENDATIONS FOR PROMPT PAIN MANAGEMENT IN INFLAMMATORY ARTHRITIS AND OSTEOARTHRITIS**

R. Geenen on behalf of EULAR HP Pain Mangement Task Force. *Psychology, Utrecht University, Utrecht, Netherlands*

Pain is a predominant symptom for people with inflammatory arthritis (IA) and osteoarthritis (OA). Health professionals should have knowledge and skills to offer the first principles of assessment and management of pain to people with IA and OA. Aim of the EULAR project was to provide "recommendations" (advice with sufficient evidence) and "points to consider" (advice that cannot be substantiated by data) that enable HPs to provide prompt and knowledgeable pain management support for people with IA or OA. A task force of health professionals, patients and rheumatologists from Europe and the United States considered recommendations and points to consider with respect to 1) background knowledge 2) assessment of the patient and the pain, and 3) management options including core prompt and general pain management that virtually any HP should be able to give and referral to specialized pain management. The detailed recommendations and points to consider will be presented and discussed.
**Disclosure of Interest:** None declared
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SP0121 **THE BENEFITS OF PROMPT PAIN MANAGEMENT IN INFLAMMATORY ARTHRITIS AND OSTEOARTHRITIS. A SYSTEMATIC LITERATURE REVIEW**

C.L. Overman on behalf of Task force "The Health Professionals' approach to pain management in inflammatory arthritis and osteoarthritis". *Social, Health and Organizational Psychology, Utrecht University, Utrecht, Netherlands*

**Objective:** To identify the scientific evidence associated with the benefits of the health professional's (HPs) approach to pain management for people with inflammatory arthritis (IA) and osteoarthritis (OA), serving as a basis for the the first "recommendations" and "points to consider" that enable HPs to provide prompt and knowledgeable support for pain in people with IA or OA.
**Methods:** A systematic literature search was undertaken. Cochrane, Embase, PsycINFo, PubMed, Scopus, and Web of Science were searched for records of systematic reviews, meta-analyses, (practice) guidelines and recommendation articles containing results of studies evaluating management strategies for IA and OA and their effect on pain. Quality of the body of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.
**Results:** Of 1569 papers, 184 papers were included. Papers reviewed effects of interventions on pain for OA (141 papers), RA (42 papers), and axial spondyloarthropathies (7 papers); for psoriatic arthritis no relevant papers were found. Interventions covered by this overview of reviews were: exercise interventions (87 papers), non-exercise physiotherapy interventions such as acupuncture, transcutaneous electrical nerve stimulation, electromagnetic fields, laser, diathermy, thermotherapy, and balneotherapy (77 papers), orthotics and assistive devices (41 papers), education (21 papers), weight reduction (14 papers), and psychological interventions (10 papers).
**Conclusion:** During the conference the effects on pain and quality of the evidence will be presented per disease by type of intervention. A necessary research agenda is proposed. For IA, but also some types of OA, well-designed randomized controlled trials assessing the effect of non-pharmacological interventions on pain, are still needed. Evidence for prompt types of pain management is even more necessary.
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**FRIDAY, 10 JUNE 2016**

## News from kinase inhibitors

SP0122 **KINASE INHIBITORS: CLINICAL ASPECTS**

G.S. Firestein. *USCD, San Diego, United States*

Kinases play a critical role in inflammatory disease and immune regulation. They

are critical molecules that transduce signals from the environment, including cytokines and toxic exposures. Their participation in human rheumatic disease has been confirmed through the testing and introduction of kinase inhibitors to treat various immune-mediated diseases. Janus kinase inhibitors, for example, are effective in rheumatoid arthritis, psoriasis and many others. These observations create opportunities for targeting other pathways and kinases that play a role in B cell activation and differentiation, stress responses, and cytokine signaling. Our experience with kinase inhibitors also demonstrates that the specific kinase and its inhibitor must be carefully matched to the pathogenic process. Several unsuccessful clinical development programs, such as p38 MAP kinase or Syk, show that the balance between efficacy, clinical indication, and toxicity need to be carefully considered. The future, however, is bright because there is an abundance of potential targets. Carefully designed clinical trials, use of biomarkers to stratify patients, and patience will pay off we new and creative ways to treat our patients.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Crystal arthritis

### SP0123 GOUT: A VARIABLE INFLAMMATORY DISEASE

R. Terkeltaub Md. *San Diego VAMC Rheumatology Section Chief. Professor of Medicine, UCSD., San Diego, United States*

In patients with tissue deposits of urate crystals, acute flares of gout develop more frequently after certain dietary triggers and in early uric acid lowering therapy (ULT). However, most acute flares of gout develop and recur variably and unpredictably. New gout inflammation biomarkers, and novel, rational, lab discovery-based therapeutics targeted to them, would advance care. Elevation of serum urate, though a biomarker for long-term prognosis in gout, has no clear role in assessing the inflammatory state in gout. Moreover, the only serum biomarker of inflammation in both acute and intercritical gout appears to be elevation of IL-8. Increasing the number of options for anti-inflammatory treatment for gout also is a central unmet need. Gouty inflammation is driven by innate immune responses to urate crystals, with "first signal" priming of the NLRP3 inflammasome in macrophage lineage cells by C5a, NF-kB transcription factor activation and a variety toll-like receptor 2 and 4 (TLR2, 4) ligands, and coupled "second signals" via NLRP3 inflammasome activation driving secretion of mature IL-1beta. Sources of variability in the capacity of urate crystals to cause inflammation will be reviewed in this talk. They include not simply exogenous dietary factors, but also constitutive "master" regulation of host inflammatory responses to urate crystals. I will discuss, in depth, AMP-activated protein kinase (AMPK), a druggable master regulator of urate crystal-induced inflammation and mediator of comorbidity. AMPK is one of several biosensors of changes in nutrition and cellular energy processes (eg, glycolysis, oxidative phosphorylation) that are emerging as therapy targets for controlling adaptive and innate immune inflammatory responses, exemplified by suppression of SLE using metformin. Last, I will summarize how metabolic regulation of innate inflammation is directly relevant to gout, since both hyperuricemia and clinical expression of gouty arthritis are influenced by highly prevalent metabolic co-morbidities and dietary factors, such as the linked co-morbidities obesity, metabolic syndrome and type II diabetes, and related caloric excesses.
**Disclosure of Interest:** R. Terkeltaub Md Consultant for: Sobi, AZ, REVIVE, Relburn
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### SP0124 SYSTEMIC PREDISPOSITION TO CPPD AND INTERACTION WITH OSTEOARTHRITIS

A. Abhishek. *Academic Rheumatology, Nottingham University, Nottingham, United Kingdom*

Calcium pyrophosphate deposition (CPPD) is generally regarded as a local joint specific phenomenon with a few reported instances of widespread polyarticular CPPD attributed to inherited disorders, severe generalised structural arthropathy, or uncommon to rare metabolic disorders like haemochromatosis, hyperparathyroidism, hypomagnesemia and hypophosphatasia. Recent research by our group has demonstrated that chondrocalcinosis (a surrogate for CPPD) occurs due to a systemic predisposition. We have also demontrated that the association between chondrocalcinosis and osteoarthirtis is joint specific and that chondrocalcinosis at both index and distant joints modifies the radiographic phenotype of lower limb large joint osteoarthritis. For instance knee chondrocalcinosis and chondrocalcinosis at distant joints (in the absence of any knee chondrocalcinosis) associate with attrition in knees with osteoarthritis. In this lecture I will describe the pathogenesis of CPPD, review the research which demonstrates that there is a systemic predisposition to CPPD, and that its interactions with osteoarthritis are joint specific.
**Disclosure of Interest:** None declared
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### SP0125 RENAL HANDLING OF URATE AND GOUT

H.-J. Anders. *Medizinische Klinik IV, LMU Munich, Muenchen, Germany*

Humans, birds, reptiles have (dinosaurs had) a tendency to develop gout because they lack sufficient uricase expression. Elimination of uric acid largely depends on excretion in the urine. A number of factors can limit this process such as genetic variants of uric acid transporters, drug-related inhibition of uric acid excretion, urine pH or loss of GFR. Visceral gout is a common phenomenon on birds, poultry, and reptiles with renal failure.
Excreting large amounts of uric acid crystals is no problem for birds and reptiles (birds droppings are white for this reason), because urine concentration takes place in the cloacae close to the external orifice. In humans urine concentration takes place in the collecting ducts, which implies that hyperuricosuria imposes a risk for urolithiasis. By contrast, uric acid retention is a common cause for hyperuricemia together with increased purine load from metabolism and diet. Conceptually, a visit is a beer garden is dangerous for two reasons, the intake of purine rich food and drinks (beer) and the intake of fructose-rich soft drinks that blocks certain urate transporters that facilitate urate excretion. A number of well-known triggers for gout relate to renal function. For example, saturnine gout, the gout of the whine-drinking romans or of noblemen of the 17$^{th}$ century related to the cups made of lead or other nephrotoxic metals used at that time that caused chronic kidney disease (CKD)-related hyperuricemia. Also the prevalence of gout and CKD increase both with age. The lecture discusses the role of hyperuricemia and gout in CKD and the role of different therapeutic options in CKD patients.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## HOT session 7

### SP0126 HOW TO TREAT/MANAGE (HOT) MYOSITIS

I.E. Lundberg[1,2]. *[1]Department of Rheumatology, University of Southern Denmark, Odense, Denmark; [2]Department of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden*

The idiopathic inflammatory myopathies (IIM) or briefly myositis is a heterogenous group of disorders where muscle weakness and inflammation in skeletal muscle tissue are predominating features but other organ involvement is common, such as skin, joints, lungs, gastrointestinal tract and heart. Treatment is based on a combination of pharmacological treatment in combination with physical exercise. However, treatment effect varies and may often be disappointing with persisting muscle weakness, muscle fatigue and low health related quality of life. Thus there is a high unmet need for new therapies and for this we need a better understanding on the molecular pathogenesis and this is likely to be different in different subsets.
Based on differences in clinical and histopathological features IIM has since long been subdivided into polymyositis, dermatomyositis and inclusion body myositis. This subclassification has several limitations as treatment response and prognosis varies within these subgroups. Furthermore, the varying treatment response suggests that there may be different pathogenic mechanisms in these different subgroups. During recent years several new myositis specific autoantibodies have been identified and they are associated with distinct clinical phenotypes and thus may be associated with differences in molecular pathways. Autoantibody profile is important in the clinic to alert for organ involvement such as interstitial lung disease (ILD) and malignancy. Autoantibodies may also predict treatment response.
Pharmacological treatment is based on high doses of glucocorticoids in combination with another immunosuppressive agent to improve the immunosuppressive effect and reduce the need of glucocorticoids. Most experts recommend methotrexate or azathioprine as first line treatment together with glucocorticoids, but other agents are also used with varying effect. New biologics such as anti-TNF therapies have had limited effect and even worsened inflammation in some cases. Treatment with the B- cell blocking agent rituximab has been more successful, but still with varying results. Presence of anti-Jo-1 or anti-Mi-2 antibodies seems to predict response. Interstitial lung disease (ILD) is a major risk factor for morbidity and mortality. Careful monitoring of pulmonary function is required in these patients As first line treatment for myositis associated ILD most experts recommend high doses of glucocorticoids in combination with pulse cyclophosphamide but controlled trials are lacking. Beneficial effect of rituximab on pulmonary function has been reported in case series but needs to be evaluated under controlled conditions.
Physical exercise in combination with immunosuppressive treatment is safe and has beneficial effects on muscle performance and health related quality of life. In addition, exercise has beneficial effects on muscle metabolism and may restore a disturbed mitochondrial function and may even have anti-inflammatory effects.
To learn more about which treatment should be preferred for a specific patient we need more knowledge on predictive markers. To achieve this an international collaboration where we collect validated clinical outcome data in a standardized way on a large number of patients will be important. This will be essential to analyze treatment effects in large enough homogenous subgroups. One such initiative is the Euromyositis register, www.euromyositis.eu. In addition, we need

to perform controlled clinical trials in well-defined patient subgroups in large multi-center trials and we need to learn more about the pathogenesis of these diseases to develop new therapies.
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**FRIDAY, 10 JUNE 2016**

## WIN session 6

SP0127 **YEAR IN REVIEW - OSTEOARTHRITIS**

M. Doherty. *University of Nottingham, Nottingham, United Kingdom*

This talk will highlight, and place into perspective, new research published on osteoarthritis (OA) in the past year. The focus is on studies that significantly contribute to our better understanding of OA or which may influence management of people with OA. Topics with recent key publications that will be included to date are: new genetic data on OA; correlation between symptoms and structural changes of OA; the role of inflammation in OA, including early OA; relationship between calcium crystal deposition and OA; inter-relationships between sleep, fatigue and pain in OA; the use of network meta-analysis to compare different effects sizes of available treatments; the high proportion of contextual effect of OA treatments; and ways to present results of RCTs that may reduce the efficacy paradox. Additional topics may be included depending on publications in Q2 2016.
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**FRIDAY, 10 JUNE 2016**

## Difficult to treat rheumatoid arthritis

SP0128 **A CASE OF DIFFICULT TO MANAGE RHEUMATOID ARTHRITIS**

L. Schoneveld. *Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands*

Rheumatoid arthritis (RA) is a chronic inflammatory disease that requires early treatment to prevent articular damage. Treatment with first line conventional DMARDs may be accompanied by side effects. Approximately 20 percent of patients with RA fail to respond to conventional DMARDs within 5 years and require biological DMARDs. However, a significant portion of the patients on tumor necrosis factor inhibitors, lose response over time or are unable to tolerate treatment. Furthermore, treatment with biological DMARDs may result in serious infectious complications. We will discuss a case of a 76 year old man with seropositive RA whose arthritis treatment was hampered by multiple problems during the course of his disease.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Biomarkers: powerful or powderpuff?

SP0129 **BIOMARKERS ARE CRITICAL FOR OUR FUTURE**

R. Van Vollenhoven. *Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands*

Even the best therapies do not work if given to the wrong patient. In practice we assess the activity or severity of the disease using history, physical examination and various additional tests when making a decision as to which therapy to recommend. Such tests can be called biomarkers.
For many decades, there were only a few therapeutic agents in rheumatology and the choices among them were mostly based on "hit-or-miss". As more and more effective therapies have been developed these choices are becoming more difficult and at the same time more critical, considering the impact that failure to control disease has on patient quality-of-life and long-term prognosis. But while therapy has become more sophisticated, our assessment tools have not kept pace: diagnostics rely on some biomarkers (RF, ACPA) and activity assessment on others (ESR, CRP) but clinical assessments and trial-and-error continue to play a major role.
The advent of next-generation biomarkers and biomarker panels are going to enable clinicians to become much more proactive and evidence-based in their daily practice. Data from recently published and ongoing studies show that biomarkers and biomarker panels help identify patients likely to respond to first-line or second-line therapy, patients at risk for radiographic progression, and patients more or less likely to respond to various biologics. Thus, the presence in serum of survivin, a tumor-associated cytokine found in around 1/3rd of patients with RA, was associated with poor response to MTX[1]. The multi-biomarker disease activity (MBDA) panel identified patients at risk for radiographic progression[2], and was also shown to identify which patients could benefit more from triple therapy and which ones from anti-TNF[3]. And a low interferon-α signature in RA associated with higher likelihood to respond to rituximab[4].
As rheumatology specialists, we must embrace these development in order to be able to provide our patients with the best possible treatment at cost levels that are sustainable for societies. Biomarkers are an indispensable part of our future.
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**Disclosure of Interest:** R. Van Vollenhoven Grant/research support from: AbbVie, Amgen, BMS, GSK, Pfizer, Roche, UCB, Consultant for: AbbVie, Biotest, BMS, Celgene, Crescendo, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, Vertex
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**FRIDAY, 10 JUNE 2016**

## HOT session 8

SP0130 **COMORBIDITIES IN RHEUMATOID ARTHRITIS: CAUSE OR EFFECT?**

D. Solomon. *Rheumatology, Harvard Medical School, Boston, United States*

Dr. Solomon will discuss several areas in his presentation:
1. The concept of morbidities in rheumatoid arthritis;
2. Specific morbidities including cardiovascular disease, diabetes, and hyperlipidemia; and
3. Whether morbidities should be viewed as cause or effect with respect to rheumatoid arthritis.
The discussion will focus on current scientific developments and how they pertain to rheumatology practice.
**Disclosure of Interest:** D. Solomon Grant/research support from: Amgen, Lilly, Pfizer, Genentech, Bristol Myers Squibb
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**FRIDAY, 10 JUNE 2016**

## The role of nuclear medicine in rheumatology

SP0131 **FDG-PET FOR IMAGING JOINT INFLAMMATION IN CHRONIC JOINT DISEASE**

C.J. Van Der Laken. *Rheumatology, Amsterdam Rheumatology & immunology Center, location VU University Medical Center, Amsterdam, Netherlands*

As the spectrum of diagnosis of inflammatory joint diseases is shifting towards very early diagnosis and individualised treatment strategies are required to optimize treatment outcomes, there is a need for sensitive imaging techniques to detect and monitor joint inflammation. FDG-PET(-CT) allows highly sensitive imaging of (subclinical) arthritis at a molecular level. The technique provides non-invasive information of the whole body in one scan session. Both visual and quantitative analyses can be applied, the latter in particular useful for therapy monitoring. Pattern of FDG uptake in (peri-)articular tissues can aid in the diagnostic work-up of the individual patient. Most recently, hybrid PET-MRI has been introduced on the market, which enables investigation of both inflammatory and anatomical signs of arthritis, at a reduced radiation level as compared to PET-CT. The lecture will provide an overview of the current status of FDG-PET for imaging in joint inflammation in chronic joint diseases and will include comparison with other advanced imaging techniques as ultrasound and MRI.
**Disclosure of Interest:** None declared
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SP0132 **60 YEARS OF RADIOSYNOVIORTHESIS - STATE OF THE ART**

W.U. Kampen. *Nuklearmedizin Spitalerhof, Hamburg, Germany*

Since its first description in 1952, radiosynoviorthesis (RSO) is performed as a local treatment of synovitis in patients with inflammatory joint disease by intraarticular injection of beta-emitting radiocolloides. The radioactive particles are phagocytized by the superficial type-A synoviocytes and the local high-energy beta radiation with a therapeutic range of only a few millimetres results in a coagulation necrosis of the superficial synovial layers. The necrotic tissue is then repelled, the respective area is demarcated by a pronounced inflammatory reaction and finally a new synovial membrane is regenerated. Clinically, a

significant reduction of both joint effusion and articular pain is noted with a consecutive improved mobility. Apart from its classical indication Rheumatoid Arthritis, RSO can be used to treat each kind of synovitis, regardless of the underlying pathology. The indication for RSO should be discussed in line with an interdisciplinary treatment regimen in cooperation between the nuclear medicine physician and a clinician experienced in rheumatology or orthopaedics, dependant on the respective patient.
Clinical results with significant pain reduction and improved joint motion are achieved in approx. 60–80% of all joints treated are published in several randomized, controlled studies on evidence level Ib in patients with rheumatoid Arthritis. The treatment is cost-effective and safe, assuming a proper patient selection and a skilful injection technique. Local complications are very rare with an overall rate of 1‰ and less.
This presentation will give an overview of the different indications for RSO, the pretherapeutic examinations and prerequisites necessary for patient selection, the procedure of the treatment itself with special aspects of radiation protection and imaging. Finally, possible side effects and complications with treatment strategies will be discussed.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## PROMs/PROs in rheumatological research - time for a critical appraisal?

### SP0133 DO WE NEED NEW PROMS OR CAN WE REUSE THEM?

S. Hewlett. *Nursing and Midwifery, University of the West of England, Bristol, Bristol, United Kingdom*

The re-use of validated PROMs from one condition into a different condition is common. However, this is often done without understanding the conceptual model of the particular health issue that the PROM attempts to capture in the first population, nor its formulation in the new target population (face and content validity). Furthermore, there is often no attempt to explore psychometric evidence for validity in the new patient population (construct, criterion, sensitivity and reliability). Second, once a PROM has been developed in the initial language, there are instances when researchers simply translate the words, without considering cultural issues in the new population. The original PROM developers may not be involved in ensuring conceptual equivalence of the health issue between the old and new populations, let alone cultural transferability. These new translations need evaluating fot only for cultural and conceptual equivalence, but also psychometric validity. Such work has implications for cost and time, but there are good examples of robust and well-thought through translation protocols by either researchers or PROM translation companies. This presentation will explore these re-use issues and provide examples of good practice (or otherwise).
**Disclosure of Interest:** S. Hewlett Grant/research support from: Unrestricted educational grant from GSK towards PhD student to develop a questionnaire, Consultant for: Institution received funding to support translation of questionnaire, from UCB and Bristol Myers Squibb
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### SP0134 PATIENT'S PERCEPTIONS OF REMISSION AND THE ART OF CONCILIATION

M. de Wit[1,2]. [1]*Standing Committee of People with Arthritis/Rheumatism in Europe (PARE), EULAR, Zurich, Switzerland;* [2]*Medical Humanities, VU University Medical Centre, Amsterdam, Netherlands*

Untill recently definitions of remission have been developed on the basis of pragmatic arguments and with the purpose to create a treatment target that is achievable in a significant number of patients. Definitions were designed using statistical analysis of existing trial data sets. Patients were not involved in this exercise. Since EULAR/ACR agreed on a preliminary definition of remission in rheumatoid arthritis (RA), it was suggested to explore whether this definition, formulated in a rather artificial algorithm, also reflects the perspective of patients. Qualitative research, carried out by members of Outcome Measures in Rheumatology (OMERACT), demonstrated that patients' view on remission is quite straight forward. In RA main characteristics are the absence of any signs and symptoms of disease activity, reduction of disease impact and going back to "normality", a state similar to before diagnosis. The discordance between the patients' definition of remission derived from the ideal world and the researchers' pragmatic definition of remission as an achievable target is seen in other disease areas as well.
The widely accepted quantitative approaches to defining cutoffs for disease activity/remission are based on data that are limited to what has been collected in clinical trial datasets and hamper a serious dialogue between patients and physicians/researchers. Exclusively quantitative approaches can bring us to a set of variables that are most associated with change in disease status but cannot expand our understanding of remission. Patients' and physicians' perceptions of disease often do not align and there is great need to explicitly seek the patient perspective regarding the real life experience of remission. Even when the patients' perspective is available, efforts to reconcile physican and patient perspectives during consensus meetings may result in patients adjusting their views and agreeing on a definition of remission that is in accordance with contemporary treatment outcome expectations.
In this presentation we will present original data from an international qualitative research project in psoriatic arthritis. We will discuss the impact of disease duration on the opinions of patients and the value of the concept of Patient Acceptable State of Symptoms (PASS), and review evidence on patient definitions of remission in other rheumatic diseases.
**Results from the international qualitative project**.There were 90 participants in 16 focus groups in 6 countries. Remission was one of the themes we explored in the focus groups. There was a nuanced perception of remission of disease activity with people seeming to expect slightly different benefits from their treatment. For some remission meant the absence of symptoms, or the absence of flare, while for others remission meant complete return to normality, similar to health before diagnosis. There was even differentiation for a participant between controlled/acceptable disease status versus remission. Remission was described by patients, in its most stringent definition as complete absence of symptoms as well as any type of limitation/life impact including emotional and social life. The differences observed may be explained by personal experiences with treatment results, disease severity and access to medications.
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**FRIDAY, 10 JUNE 2016**

## Collaboration for success. User-centred design for improvement of health services

### SP0135 CO-DESIGNING A MOBILE INTERNET SERVICE FOR SELF-MANAGEMENT OF PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS

Å. Revenäs. *Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden*

**Background:** Co-design denotes involvement of lead users, i.e. potential users of the future service, who collaborate with researchers and/or clinicians and other stakeholders in the development of health care services. This project describes the process and outcome of co-designing a mobile internet service for self-management of physical activity in rheumatoid arthritis (RA).
**Objectives:** Our aims were to describe the iterative process of deciding what features to include in a self-management service for physical activity, the challenges of co-design and the results from the evaluation of the test version of the service.
**Methods:** Principles of experience-based co-design were used to study the process and outome of the project. In the *needs inventory and idea generation phase* six focus group interviews were performed with lead users (n=26). In the *requirements specification phase* four workshops were conducted including lead users, clinical and research physiotherapists, an eHealth strategist and an officer from the Swedish Rheumatism Association (n=10). In the *system evaluation phase*, the first test version of the service was evaluated during six weeks (n=28). Qualitative methods were mainly applied except for the evaluation phase where mixed methods were used.
**Results:** Four core aspects important to consider in the development of the service were identified: features, customized options, user interface, and access and implementation (1). The core challenge of co-design was the merging of participants' different perspectives (2). The merging resulted in "tRAppen", a mHealth service for maintenance of physical activity. tRAppen included two key components: 1) "My self-regulation features" and 2) "My peer support features" (3). The evaluation demonstrated that most participants registered physical activity, sent likes and made exercise plans. tRAppen was generally rated as easy and fun



to use. The experiences of using tRAppen seemed to be influenced by physical and mental state and personal preferences.
**Conclusions:** The use of co-design in the development of the physical activity self-management service tRAppen was successful. The first test version was perceived as feasible and to have the potential to support a physically active lifestyle. Co-design in collaborative workshops involved an extensive decision-making process that put high demands on the participants' ability to find solutions, negotiate, come to agreements, and reach final decisions.
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**Disclosure of Interest:** None declared
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### SP0136 USER INVOLVEMENT IN THE DEVELOPMENT OF EHEALTH PRODUCTS

S. Van Der Weegen[1,2]. [1]*CAPHRI, Maastricht University, Maastricht;* [2]*Innovation & Research, Vilans, Utrecht, Netherlands*

Technology has the potential to improve quality and efficiency of healthcare. It is important to involve end users in the design process of new technologies and interventions at an early stage to enhance the fit between the user, technology, and the organization of care. It improves usability, prevents the inclusion of unnecessary features and maximizes the likelihood of a successful adoption. This presentation gives an example of user involvement during the development of an eHealth intervention to stimulate physical activity in people with type 2 diabetes or COPD and will try to inspire you to co-create with end users by providing different methods for user involvement.
**Disclosure of Interest:** None declared
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### SP0137 A USERS' PERSPECTIVE AND EXPERIENCE OF CO-DESIGN

K. Hakansson. *Private, Stocksund, Sweden*

**Background:** I developed RA (rheumatoid arthritis) when I was 27 years old. Soon after meeting my rheumatologist (in Stockholm), I was asked to participate in a research study. The study was to develop an internet-based programme on physical activity/exercise designed specifically to assist RA patients. The study was run by researchers at Karolinska Institutet and Uppsala University, Sweden.
I was a member of one of the six focus groups consisting of five people (all with RA).The focus groups met and discussed various ideas on important content in the future internet-based programme (1). The next step was to specify and create an application (app). To do this, one of the researchers appointed five researchers and specialists to work together with five RA patients (of which I was one) to specify the requirements of (co-design) the app. For this second phase of the study we met on 4 occasions. Each meeting was 4 to 8 hours. The objective of these meetings was for us to cooperate and decide everything about the app from the graphics and name to the content and what kind of RA-patient we wanted to reach with this app (2,3).
**Objectives:** Sharing my experience of co-designing an internet based health service.
**Methods:** Analyzing my perspective of my participation in co-design.
**Result:** In the first phase (the focus groups) I found it fun and rewarding to meet other people with RA, sharing our experiences and learning how different we are in sickness and in attitudes to physical activity. Phase 2 (the cooperative meetings) provided me with the opportunity to learn from professionals about statistics and to share our different views. As a group we were reflective and engaged. It was very enjoyable. It was extremely difficult to solve the issue/address the fact that all people with RA are different and require customized programmes for physical activity and exercise. How to resolve this and still provide an app that would be useful for as many people with RA as possible was very challenging.
**Conclusion:** Co-design is a powerful instrument to make sure patients are involved in their own healthcare. For future co-designing of applications for RA-patients I would suggest to specify the target group of RA individuals based of their physical condition and interest in physical activity to reduce all compromises and time.
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**Disclosure of Interest:** None declared
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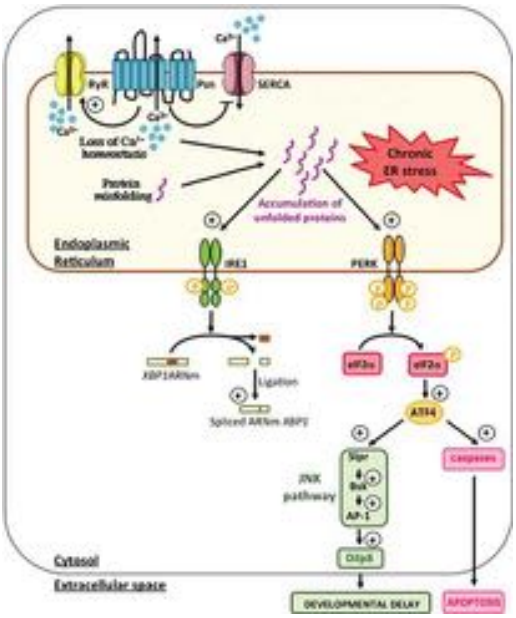
**FRIDAY, 10 JUNE 2016**

## ER stress & rheumatic disease

### SP0138 THE FRUIT FLY, AS A TOOL TO STUDY ER STRESS

S. Gaumer[1,2]. [1]*Laboratoire de Génétique et Biologie Cellulaire, Université Versailles-St-Quentin-en-Yvelines;* [2]*Laboratoire Génétique Moléculaire et Physiologique, EPHE, Montigny-le-Bretonneux, France*

Endoplasmic Reticulum (ER) stress is a cellular event found misregulated in numerous diseases including osteoporosis, osteoarthritis and inflammatory pathologies. ER stress is also involved in physiological events such as fibroblast differentiation after injuries. Numerous proteins transit through the ER in which they are folded and glycosylated. This organelle is also responsible for the synthesis of lipids and calcium homeostasis. If any of these missions fails, aggregating proteins accumulate and become cytotoxic, leading to devastating pathologies. An adaptive response, known as the Unfolded Protein Response (UPR), normally prevents such accumulation by resolving the stress or ultimately eliminating the cell.




*Drosophila* is a powerful model organism to study ER stress. Indeed, the UPR is largely conserved between insects and humans. We show how *Drosophila* genetics and its numerous tools can be easily used to show that both protein aggregation and calcium dyshomeostasis activate the same PERK/ATF4 branch of the UPR to induce both caspase-dependent apoptosis and a JNK-dependent hormonal response that allows tissue homeostasis. Interestingly, this response is tissue-specific.
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**FRIDAY, 10 JUNE 2016**

## Role of imaging in childhood-onset rheumatic diseases

### SP0139 THE ROLE OF ULTRASOUND IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

J. Vojinovic. *Clinical Centre, Medical Faculty, University of Nis, Nis, Serbia*

Juvenile idiopathic arthritis (JIA) is a potentially debilitating disease of early

childhood that may carry with it significant physical, psychological, and financial costs. At this time, pediatric rheumatologists rely on physical examination to diagnose JIA. There is an increased interest in the use of musculoskeletal ultrasound (MSUS) to evaluate JIA. MSUS has several advantages over other imaging techniques for use in pediatric subjects, which include non-invasiveness, rapidity of performance, ease of repeatability, high patient acceptability and lack of exposure to ionizing radiation. In addition, it does not require sedation for scanning in younger children. MSUS allow precise and thorough visualization of inflammatory and destructive joint abnormalities, including synovial hyperplasia, joint effusion, cartilage damage, bone erosion, tenosynovitis and enthesopathy. MSUS is more sensitive than physical examination and may detect early disease that is not evident on physical examination. Recent studies in children with JIA have also shown that remission defined by clinical criteria does not always equate to the complete absence of inflammation as measured by MSUS. A high prevalence of US-detected subclinical synovitis was found in joints that were recorded as normal on clinical examination. Thus early detection and treatment may prevent and/or delay adverse outcomes such as joint damage and disability in JIA.

OMERACT definitions are not applicable to pediatric patients, owing to the unique features of the growing skeleton and the changes in joint morphology during development. Thus, Pediatric Ultrasound subtask force of the OMERACT Ultrasound Group was created to develop definitions and standards for MSUS assessment in children. This group has done a great deal of effort and activity to standardize and validate the method for performing MSUS and detecting and scoring MSUS abnormalities in children through several steps: a) Development of definitions for MSUS findings in healthy children by a Delphi consensus process[1] and amendment of definitions for the MSUS features in healthy children (manuscript in preparation); b) Development of a standardized MSUS scanning method in children of different age groups and collection of images showing the physiological vascularization in several joints.[2]; c) Development of definitions for synovitis through a Delphi consensus process and validation of these definitions in a still image exercise (publication in preparation); d) Development of EULAR/PReS recommendations for usage of different imaging modalities in JIA[3]; e) Evaluation of the multiobserver and intraobserver reliability of the physiological blood vessels present in different age groups of healthy children and new scoring system to graduate maturation of ossification nuclei in healthy children (publication in preparation) and f) Development and validation of a semiqantitative scoring system for synovitis on grey-scale (GS) and Power Doppler (PD) modes. All novel knowledge is presented in details.

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**Disclosure of Interest:** None declared

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### SP0140 IMAGING TECHNIQUES IN PEDIATRIC CONNECTIVE TISSUE DISEASE – WHICH AND WHEN?

P. Collado. *Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain*

**Systemic lupus erythematosus:** Renal disease and haematological involvement are common in Juvenile SLE, but musculoskeletal symptoms are often present and can cause substantial morbidity. Several studies have demonstrated that ultrasonography might be convenient in visualizing the involvement of peri- and intraarticular soft tissues in JSLE as well as in adults. Osteonecrosis occurs in 10–20% of JSLE. Plain films and MRI should be considered for the diagnosis of avascular necrosis (AVN) in a JSLE patient with painful hip/limp who had been treated with steroids for long periods. Nailfold capillaroscopy (NFC) is a useful technique to differentiate primary from secondary Raynaud's phenomenon associated to several connective tissue diseases, particularly in girls with JSLE.

**Idiopathic inflammatory myopathy in childhood:** JDM is the commonest inflammatory myopathy of childhood. Diagnostic criteria continue to be based on those of Bohan and Peter, but an international survey in 2006 proposed adding items such as MRI and NFC.

Historically, MRI techniques used to evaluate muscle disorders in children have included T1-weighted images (T1WI) and water-sensitive sequences (i.e., short-tau inversion recovery (STIR) or T2-weighted images (T2WI), with or without fat suppression). These latter sequences are very sensitive to the presence of intramuscular oedema reflecting inflammation, whereas fatty infiltration and muscle atrophy can be detected on T1WI in chronically affected muscles. Whole-body MRI is useful in the assessment of disease activity in JDM as well as guiding muscle biopsy. Recent MR techniques have expanded the use of MR imaging to include quantitative analysis. Ultrasound may be a cost-effective alternative to MRI, with contrast-enhanced ultrasound (CEUS) also permitting the assessment of muscle vascularization. With ultrasound elastography, the relative tissue stiffness can be visualised. In Raynaud's phenomenon (RF), NFC can early demonstrate some typical capillary changes in patients with inflammatory myopathy that it has been called "scleroderma-like pattern".

**Sclerodermas:** Scleroderma is a rare condition in children. There are 2 main distinctive categories: juvenile systemic sclerosis (SSc) and juvenile localized scleroderma. *Localized Scleroderma* is more frequent than SSc in children but still an uncommon condition. US can demonstrate changes in dermal thickness and level of echogenicity that seems to correlate with disease activity. NFC shows typical capillary changes in RF. Unlike adults, in juvenile-onset SSc the overall capillaroscopic pattern is called "scleroderma pattern" and the classification in "early", "active" and "late" pattern has not common been applied.

During the last years, various new technologies (infrared thermography [IT], laser doppler flowmetry [LDF], high-frequency Gray Scale-ultrasound, elastography, MRI and high-resolution computed tomography thorax) have been developed for better identifying and managing of disease. Because active disease can persist for years and can involved systemic structures, recommendations for screening for cardiopulmonary involvement in JSS have recently been discussing by PRES Scleroderma Working Group.

**S. Sjögren and mixed connective tissue disease:** Primary Sjögren's syndrome (pSjS) is a systemic autoimmune disease uncommon in children. Secondary SjS has a more frequent occurrence in childhood, most commonly accompanies SLE, or less often accompanies another Connective Tissue Disease (CTD). Since salivary gland (GS) biopsy is considered as an invasive technique for children, ultrasonography could be a kind tool to provide information about parotid and major salivary glands morphology. In US assessment of SjS, parotid echogenecity is compared to thyroid echogenecity. Some studies on adult pSjS have described a typical pattern on SGUS characterised by lost of the homogeneous internal echogenicity and echotexture, with multiple oval hypoechoic areas of different size. Similar SGUS changes have been reported in juvenile pSjS.

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**FRIDAY, 10 JUNE 2016**

## Physician-patient relationship in the era of interactive media

### SP0141 THE POINT OF VIEW OF PHYSICIAN. SOCIAL MEDIA: PROS AND CONS OF SHARING PATIENT AND PHYSICIAN PERSONAL EXPERIENCE

E. Nikiphorou. *Rheumatology, Whittington Hospital, London, United Kingdom*

The world of social media (SM) is rapidly evolving and we are experiencing a new era of online communication and social interaction. Aside from SM platforms being used for recreational/leisure purposes, in more recent years, they are being increasingly used for professional communication and for sharing knowledge and information. SM platforms like Twitter and Facebook are commonly used at conferences and other educational events, eliminating geographical barriers and enabling rapid dissemination of information. Educational activities on SM platforms like Twitter include journal clubs, participation in clinical/research quizzes and problem-solving. Communication between physicians and other health care professionals and patients on SM is becoming increasingly popular. SM allows for patients and physicians to connect on a different level; yet, this kind of interaction has both advantages and disadvantages. If, however, SM is used appropriately, it can be an incredibly powerful means of good communication, learning and development.

**Disclosure of Interest:** None declared

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**FRIDAY, 10 JUNE 2016**

## Capillaroscopy II

### SP0142 HOW TO SELECT THE MOST APPROPRIATE CAPILLAROSCOPIC DEVICE: PROS AND CONS

F. Ingegnoli. *Dept of Clinical Sciences & Community Health, ASST G. Pini, University of Milano, Italy, Milano, Italy*

Nailfold capillaroscopy is a noninvasive technique that allows direct observation of capillaries using a magnification lens for the two-dimensional projection of the three-dimensional capillary network. After application of a drop of immersion oil, capillaries can be observed with a magnification lens because they run parallel to the epidermis at the nailfold area.
A number of different instruments are available to perform the exam. They have different characteristics in terms of their cost, quality of images, magnifications, training period, software for image analysis and storage.
Some of these instruments can be used both in clinical and research settings such as the stereomicroscope and the videocapillaroscope. The stereomicroscope allows the widefield visualization of the nailfold with low magnifications, the training is relatively short, but the examination is difficult to perform in patients with digital contractures.
There appears to be consensus regarding the use of videocapillaroscopy that allows a detailed visualisation of capillary morphology using higher magnifications (100–300x). Contact probe with polarized light microscopy permits easier observation of the skin surface, and the training period is briefer. Specific softwares are available for images analysis, storage, and complete medical reports (text + images) can be produced.
By contrast, in a clinical setting, nailfold capillaries can generally be visualised using more simple but also efficient tools such as a dermatoscope, USB microscope, ophtamloscope or smartphone device. The quality of images can be quite good, although the lower magnification means that some details are unlikely to be seen, and they often lack the possibility of image storage and measurement.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Ultrasound advanced I

### SP0143 ULTRASOUND FOR DIAGNOSING INFLAMMATORY VERSUS MECHANICAL MIDFOOT PAIN AND RELEVANT GUIDED INTERVENTIONS WITH DEMONSTRATION

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The midfoot is a relatively unknown entity and difficult to examine clinically. Recent inflammatory arthritis studies have demonstrated that patients in disease remission may still have active disease in those residual joints not included in commonly used disease activity assessments.
Osteoarthritis (OA) of the midfoot has previously been reported as being relatively uncommon (prevalence of 3.8%) however recent studies have highlighted that medial midfoot OA is more prevalent than previously described. Halstead et al (2015) reported changes most frequently in the cuneiform-second metatarsal joint (73%), followed by the naviculo-medial cuneiform joint (51%), the cuneiform-first metatarsal joint (46%) and the talo-navicular joint (24%), with patients indicating pain to the dorsal midfoot area.
The midfoot is a complex structure and frequently undertreated. Differentiating between inflammatory and mechanical disease in the midfoot will enable the clinician to direct their treatment strategies more appropriately. Ultrasound imaging offers the clinician the opportunity to differentiate between joints that require treatment with mechanical interventions such as orthoses and footwear, and those that may also require local treatment of inflammatory disease which may include a guided steroid injection to improve the clinical outcome.
**Disclosure of Interest:** None declared
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### SP0144 ULTRASOUND OF THE NAIL; WHY USE IT IN RHEUMATOLOGY?

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Nail psoriasis represents an important feature of psoriasis and psoriatic arthritis patients. In psoriasis patients, nail involvement represents a risk factor for psoriatic arthritis. Moreover, nail psoriasis was associated with distal interphalangeal joint arthritis. It is also one of the CASPAR classification criteria for psoriatic arthritis.
The complex anatomy of the nail, including the enthesis complex, makes the clinical assessment difficult, as well as the accurate description of the pathology for each structure.
Studies have shown a link between nail, extensor tendon enthesis and DIP joints involvement in psoriatic and psoriatic arthritis patients.
Ultrasound of the nail includes the evaluation of nail plate, nail bed, and extensor tendon enthesis.
Ultrasound of the normal nail plate shows a trilaminar structure: two hyperechoic lines, the ventral and dorsal, separated by a hypoechoic line. The nail bed appears like a hypoechoic band, between the ventral plate and the bone. Some Doppler signals may be seen in the normal nail bed.
In early nail involvement, irregularities and loss of sharpness of the dorsal plate can be seen. As the disease progresses, loss of sharpness of ventral plate and loss of trilaminar structure can be seen.
In the nail bed involvement, the distance between the ventral plate and the bone can be increased. Also, an increase of Doppler signal has been reported.
Compared to rheumatoid arthritis patients, different patterns of both nail plate and nail bed involvement have been seen in psoriatic arthritis patients.
**Disclosure of Interest:** None declared
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### SP0145 HOW TO DIFFERENTIATE EROSIONS AND VESSEL CHANNELS

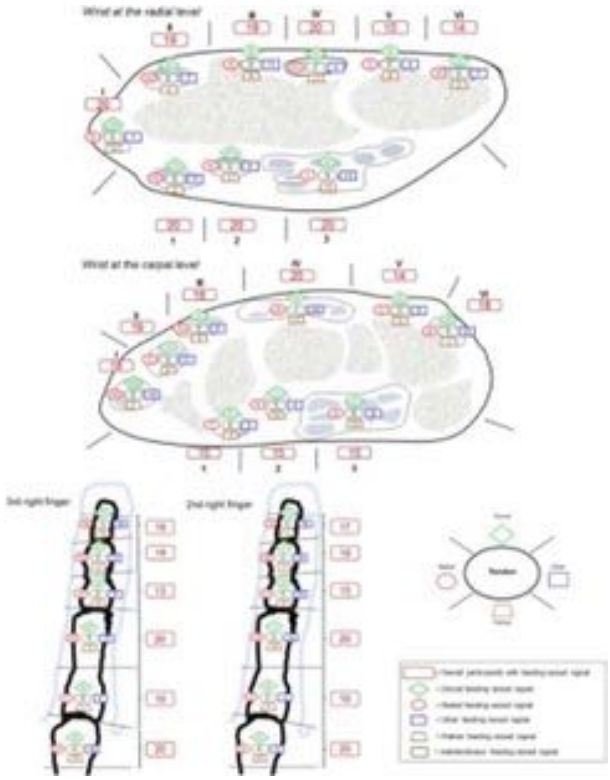
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Cortical breaks are a common feature in periarticular bone, even in healthy individuals. The true nature of a cortical break sometimes is difficult to determine. Therefore, high-resolution imaging techniques (such as musculoskeletal ultrasound) as well as well profound knowledge of the anatomy are needed in order to not overestimate the amount of pathological cortical breaks (i.e. erosions) and correctly discern them from nutritive vascular channels.
The session focusses on pathological and physiological cortical breaks in healthy elderly individuals as well as patients with inflammatory joint diseases such as rheumatoid arthritis and psoriatic arthritis. After the lecture and demonstration the participant should be able to better understand and categorize cortical breaks.
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### SP0146 3D DOPPLER ULTRASOUND FINDINGS IN HEALTHY WRIST AND FINGER TENDON SHEATHS – CAN FEEDING VESSELS LEAD TO MISINTERPRETATION IN DOPPLER-DETECTED TENOSYNOVITIS?

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**Introduction:** To investigate the presence of feeding vessels in or in close proximity to extensor and flexor tendon sheaths at the wrists level and in finger flexor tendon sheaths in healthy controls, using 3D ultrasound (US), which may



cause pitfalls in order to ensure correct interpretation of Doppler signals when diagnosing tenosynovitis.
**Method:** Forty healthy participants (20 women and 20 men in the age 23–67 years) without prior history of arthritis, tendon diseases or present pain in their hands were included. Twenty participants had 3D Doppler US of the 2nd and 3rd finger and twenty of the right wrist. US was carried out using a GE Logiq E9 unit with a 3D US probe. The colour Doppler settings were according to published recommendation.
**Results:** The feeding vessels in or in close proximity to the tendon sheaths were found in the flexor and extensor tendons sheaths at least once in each participant. No significant difference in feeding vessels was seen between the radial and carpal level in the wrist (p=0.06) or between the 2nd and 3rd flexor tendon sheath (p=0.84).
**Conclusion:** Doppler findings in or in close proximity to the tendon sheaths were common in wrists and fingers in healthy participants. These feeding vessels can be a source of error, not only due to their presence but also because they may be interpreted as being inside the tendon sheath due to blooming and reverberations artefacts. These vessels should be taken into consideration when diagnosing Doppler tenosynovitis.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## It's in your hands

### SP0147 A SELF-DETERMINED LIFE WITH A RHEUMATIC DISEASE? HOW CAN SOCIAL PARTICIPATION BE PRESERVED OR OBTAINED AND HOW CAN BARRIERS BE OVERCOME?

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Health care professionals are increasingly aware of the multifaceted burden of rheumatic and musculoskeletal diseases (RMDs). Aside from typical symptoms such as pain and limited range of motion of the affected joints or other body parts the patients frequently suffer as much from limited social participation and even isolation. Reduced participation in the labor force associated with high indirect costs for society and potential effects of expensive medications have gained increasing attention among researchers and health care insurances.
However, other affected social roles concerning family, friends, and leisure activities have been less focused, even though they may be more prominent for individuals with RMDs than working life. The experience of limited social participation depends on medical factors such as disease severity and treatment but also on mostly neglected non-medical environmental and personal factors (i.e., social network and services, individual skills and preferences). Low communication skills may be significant barriers to social participation. In a nationwide project funded by the German League against Rheumatism (GLR) persons with RMDs reported difficulties in disease-related conversations across various situations. Significant factors of RMD-related everyday communication were identified. Based on the results, a training to enhance the communication skills of persons with RMDs in various situations significant for social participation is underway. The GLR offers various other services that facilitate social participation of individuals with RMDs. These services were evaluated by different RMD groups in order to identify the potential for further adjustment according the patients' preferences.
**Disclosure of Interest:** None declared
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### SP0148 LEARNING TO CONTROL – THE POWER OVER THE DAY-TO-DAY SETBACKS IS ... OURS!

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Mental training is a powerful tool to give back the control of the patient's sensations, in pain relief and in emotional influence over the setbacks of the day. Being always complementary to medical treatment, mental training gives the patient the knowledge to manipulate the perceptions of pain and frustration, anger and sadness, contributing to reduce pain and to think differently about the difficulties in each patient's life. Knowing how to deal with the day-to-day setbacks is very empowering, for the patient takes back the control of his feelings, well-being and self-awareness.
There are several techniques that can be used in pain control – distraction, moving the pain from one spot to another, increasing and decreasing its perception, putting it in another platform (for example, out of our mind). These techniques can be chosen and adapted to each patient and to each pain in particular. Every time the patient uses mental training, he will also gain in relaxation, well-being and self-confidence, so important is this constant struggle.
On the other hand, when the patient gains control of his thoughts, so many times depressive, frustrated, angry or desperate, he can then decide what to do, how to feel, how to act. The way we live and give power to suffering is a choice, not a burden. It has been already proved how our thoughts modify the body chemistry – now it's time to do it regularly and get relief more quickly.
The description of this suffering or rejection of the illness is also a good help and often shows exactly what it has been doing to the patient feelings. Writing about these sensations (of pain or frustration) and its part in day-to-day routine can show to each one how to deal with it and exactly how much damage are we prepared to let it do to our lives. Words written (where our eyes can read them, observing rather than feeling) will let our minds think about them and decide what to do next. Emotional writing, when used as a technique to relieve the patient from his suffering, is a wonderful tool. Doing this in a group session can be the beginning of a different way of feeling. Most people live alone with their suffering. Hearing what others say and write about this, and how each one copes with their illness, can make this loneliness disappear, giving space to a new way to live beyond this illness.
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## The EULAR School of Rheumatology - a new era of education

### SP0149 EULAR EDUCATION: WHAT IS IN IT FOR YOU?

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By 2017, EULAR will be a pre-eminent provider and facilitator of high-quality education for physicians, health professionals in rheumatology, and people with rheumatic and musculoskeletal diseases. In addition to educational sessions at the annual congress and the EULAR symposia at AFLAR, PANLAR, APLAR, currently available educational offers cover different fields and are represented by online and live courses, exchange programmes, bursaries, grantsand awards, publications and other materials.
In terms of online courses, in recent years, EULAR has put substantial effort and investment into developing e-learning opportunities. All EULAR courses, as electronic ways of continuous medical education in rheumatology, are managed by a scientific course committee responsible for the structure and content of the courses and for ensuring quality control. EULAR teams of expert authors regularly review and update courses to keep up with the newest developments in the field. While the 2-year Online Course on Rheumatic Diseases offers a comprehensive introduction to and update on all aspects of rheumatology, a number of shorter online courses (i.e. US introductory, Paediatric, Health Professionals, Systemic Sclerosis) offer flexible learning for the specialist.
Live courses are currently planned and developed with the objective of making a targeted contribution to training and further education to rheumatologists and health professionals, complementing the standard range of opportunities provided by universities, hospitals and other institutions. To this end EULAR offers a number of its own branded courses and, in addition, grants "EULAR scientific endorsement" as a mark of scientific quality to selected courses and meetings run by established providers in Europe. In this context, EULAR invites other courses and scientific meetings in the field of rheumatology to apply for endorsement. EULAR views scientific endorsement as an opportunity to positively influence the quality of rheumatology training in Europe, which is in line with EULAR longer-term goals. Quality control associated with EULAR scientific endorsement focuses on the proposed content and faculty as well as on evaluation of these courses or meetings.
The purpose of the EULAR/ACR Exchange Program is to promote the international exchange of clinical and research skills, expertise and knowledge within rheumatology. The program recognizes outstanding rheumatology faculty and provides exposure to the exciting work being done by colleagues overseas. This exchange program allows participants to share knowledge and experience, and creates opportunities for collaboration.
Another EULAR objective is the use of bursaries to contribute to the personal and professional development of rheumatologists, health professionals as well as people with rheumatic diseases. To this end, EULAR facilitates attendance at the annual EULAR congress in the form of travel bursaries, also provides bursaries to attend EULAR courses in rheumatology. EULAR is committed to helping individuals develop their skills, expertise and network of contacts and therefore offers a range of educational grants tailored to the needs of researchers and clinicians, health professionals and patient organisations. Educational grants are offered at regular intervals.
In terms of publications, in addition to the two EULAR journals (ARD and RMDopen), and next to the EULAR Textbook on Rheumatic Diseases, EULAR has published the Textbook on Systemic Sclerosis, and also endorsed several books which are relevant to the EULAR live and online courses. The new EULAR Texbook on Ultrasound will be launched at the annual Congress in London, on June 2016.
Additional opportunities are represented by educational activities such as a network of imaging centres, videos which offer an insight into some EULAR courses and international events, practical DVDs with video production on undergraduate training in history and physical examination of the musculoskeletal system. New activities that will be launched in 2016 are a medical student primer, student webinars on "case of the month" and webinar monthly lecture given by experts.

**Key messages:**
– By 2017, EULAR will be a pre-eminent provider and facilitator of high-quality education for physicians, health professionals in rheumatology, and people with rheumatic and musculoskeletal diseases.
– Currently available educational offers cover different fields with online and live courses, exchange programmes, bursaries, grants and awards, publications and other materials.

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## Vaccination in rheumatic patients: a two-edged sword

### SP0150 "ASIA" – AUTOIMMUNE (AUTO-INFLAMMATORY) SYNDROMES INDUCED BY ADJUVANTS

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Vaccines, administered to animal and humans, are clearly one of the best achievements of modern medicine and are commonly and safely inoculated to the vast majority of subjects. However in rare occasions vaccines may induce autoimmune or auto-inflammatory conditions both in animals and in humans [1]. These conditions, either defined diseases such as Gullian Barre syndrome or enigmatic ones, have been reported following different vaccines and vaccination protocols. The susceptibility factors and the temporal association between vaccines and these rare immune mediated reactions are yet to be defined, however the similarities between vaccines and infections and the addition of an adjuvant (i.e. alum, squalene etc.) to almost every vaccine are considered major contributors to such adverse events. Perhaps the most evaluated condition is MMF, in which a cause was clearly delineated. MMF is a rare condition caused by deposition of alum, used to adjuvant different vaccines, which bring about an immune mediated muscles disease [2]. The discrepancy between the wide application of aluminum hydroxide and the rarity of MMF was resolved by the observations that alum may trigger MMF in genetically susceptible subjects carrying the HLA–DRB1*01 [3]. Thus, in only a minority of genetically prone patients alum may induce this syndrome.
A common denominator to each of these four syndromes as well as to various infectious agents is the trigger entailing adjuvant activity. Adjuvants are commonly used in medicine to augment an immune response to treatments such as the protective response induced by vaccines and were considered to be inert. Nalp3 inflammasome system. Moreover adjuvants enhance adaptive immune responses *via* inducing Th2 cell activation as well as chemokines and cytokines secretion thus helping the recruitment of B and T cells [4–6]. as well as inducing the secretion of Il-17 [7]. Alas, studies of animal models and humans demonstrated the ability of some of these adjuvants to inflict an immune mediated disease and even autoimmunity by themselves [8].
Thus, herein we will describe the syndrome entitled the "Autoimmune (Auto-inflammatory) Syndrome induced by adjuvants" (ASIA) [9]. We will also delineate who is at risk of developing autoimmune conditions upon exposure to adjuvants [10].

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**FRIDAY, 10 JUNE 2016**

## Advances in large vessel vasculitis

### SP0151 CLINICAL DIAGNOSIS OF LARGE VESSEL VASCULITIS

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Defining the clinical features of large vessel vasculitiS (LVV) is not easy because their boundaries are not completely clear, their symptoms are very often unspecific, and the correlation between clinical features and imaging, the gold standard of diagnosis, is unpredictable. LVV include giant cell arteritis (GCA), Takayasu's arteritis (TA), isolated ascending aortitis, PMR-associated LVV, retroperitoneal fibrosis, periaortitis, inflammatory abdominal aneurisms, relapsing polychondritis, and IgG4-related diseases.
The organs/tissues affected are various, as in most vasculitides, resulting in symptoms and signs localized to the joints, muscles, eye, brain, kidney, skin and lungs. An interplay between autoimmune and atherosclerosis-associated inflammation is probably at work. Systemic symptoms, including fever, weight loss, malaise, fatigue, night sweats, and depression are often present and may represent the only signs of the disease. At clinical examination, bruits may be present on auscultation. Acute phase reactants are generally unreliable especially for follow-up. Diagnosis relies on imaging, including CE-CT, CE-MRI, and PET/CT or PET/MRI. Vessel biopsy is fundamental to confirm the diagnosis although rarely performed in non-temporal arteritis LVV. Although it is commonly believed that GCA and TA cannot be distinguished by histology, adventitia is relatively spared in TA and commonly damaged in GCA. As in most other rheumatic conditions, the clinician should consider disease activity and damage, although in this case the two entities are not easy to separate. There are no outcome measures specifically developed for LVV, although disease activity has been measured by BVAS, ITAS 2010, and DEI-Tak, each showing some weakness. Damage consists mainly in stenotic or aneurismatic lesions of the vessels, which can appear also long intervals after inflammation has subsided. For this reason, follow-up of patients should continue long-term even if the disease has been apparently cured.
LVV are highly detrimental to the patients, who cannot understand the origin of their symptoms, a situation sometimes shared with the attending clinician since the diagnostic delay may be very long. In addition, long periods of asymptomatic disease, with on-going damage, are not rare. Disease-specific patients reported outcomes have not been developed in these conditions, and are a field open to research.

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### SP0152 ROLE OF IMAGING IN THE DIAGNOSIS AND TREATMENT OF LARGE VESSEL VASCULITIS

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Over the past years imaging techniques such as Color-Coded Duplex Sonongraphy (CCDS), Magnetic Resonance Imaging (MRI), Magnetic Resonance Angiography (MRA) and Positron Emission Computed Tomography (PET CT) have greatly improved their diagnostic accuracy for the diagnosis of large vessel vasculitis. This presentation summarises the specific advantages and limitations of CCDS, MRI/MRA and PET CT.
CCDS is the diagnostic procedure of first choice in the hands of an experienced observer. CCDS is readily available and may display the so called "halo-sign" of an inflamed vessel wall of the superficial temporal, axillary, carotid, vertebral and subclavian artery.
PET CT is thougt to be the most sensitive imaging modality, especially for the assessment of extracranial large artery involvement. PET CT is not as widely available, rather costly and applies radiation.
MRI and MRA are noninvasive imaging modalities that display mural inflammatory changes of intracranial, extracranial and large artery involvement. MRI and MRA do not use radiation. In relation to costs and availability MRI and MRA lie somewhere between CCDS and PET CT. Image acquisition in PET CT and MRI/MRA is standardized and largely independent of the operator.
Mural inflammatory signs depicted by CCDS, PET CT and MRI/MRA vanish over time under sufficient therapy. However, interpretation of persistant mural changes and imaging of relapsing disease is not yet fully understood.

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SP0153 **EMERGING THERAPIES IN LARGE VESSEL VASCULITIS**

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**Background:** Giant Cell Arteritis (GCA) and Takayasu arteritis (TAK) are the two main forms of large vessel vasculitis. Because of parallels in clinical, radiographic and histologic features, the therapeutic approach to GCA and TAK has generally been similar. In both conditions, glucocorticoids (GC) are effective for remission induction. However relapses frequently occur during tapering of GC, and adverse effects commonly occur. The use of conventional immunosuppressive agents has not shown consistent benefit in maintaining disease remission or reducing GC-associated adverse events.
**Emerging therapies:** Several biologic agents have been studied in observational and randomized trials for both GCA and TAK. Tumor necrosis factor-alpha inhibitors appear to be effective in the treatment of TAK based on observational study data. In clinical trials of patients with GCA, TNF inhibitors have failed to show significant therapeutic efficacy and their use is not recommended. Interleukin-6 inhibition has gained particular focus in the treatment of GCA and TAK. Observational evidence supports the use of interleukin-6 inhibitors in TAK. Several retrospective studies and a recent randomized placebo-controlled trial has demonstrated efficacy of tocilizumab in GCA. Preliminary clinical trial data also suggests that abatacept may reduce the risk of relapse in GCA. Based on a small open-label study, ustekinumab appears safe and potentially effective for refractory GCA. A possible role of B cell dysregulation may contribute to pathogenic mechanisms in large vessel vasculitis, and B cell depleting therapy may also be an emerging treatment option. Ongoing clinical trials will yield vital information on the efficacy of biologic agents for GCA and TAK within the next year.
**Summary:** Interleukin-6 inhibitors appear efficacious in the treatment of refractory cases of large vessel vasculitis. Abatacept and ustekinumab are promising targets for therapy in large vessel vasculitis but further investigation is needed before routine use is considered.
**Disclosure of Interest:** None declared
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## HOT session 9

SP0154 **COMORBIDITIES OF PSORIATIC ARTHRITIS AND OTHER RHEUMATIC DISEASES**

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Over the past several decades it has become clear that many rheumatologic conditions are complicated by a number of comorbidities. Comorbidities are distinct from extra-articular features of a rheumatologic disorder. These are other conditions that occur in individuals with either inflammatory or non-inflammatory rheumatologic disorders, but are not directly related to the underlying condition.
Many rheumatology patients have co-existent diabetes. This is particular true among patients with psoriatic arthritis (PsA). Recent data demonstrate that diabetes occurs with higher prevalence among PsA patients, and its prevalence has increased over the past few decades. Another important comorbidity is cardiovascular disease. Cardiovascular disease occurs more commonly among patients with rheumatoid arthritis, systemic lupus erythematosus, PsA and ankylosing spondylitis, than in the general population. Moreover, cardiovascular events occur at an earlier age in patients with these inflammatory conditions. Hypertension also occurs more frequently among patients with rheumatologic conditions, partly related to the therapy provided. In each of these conditions it seems that the underlying inflammatory condition predisposes to the comorbidity, and in several studies the degree of inflammation is related to both the frequency and severity of the underlying disease. More recently it has become clear that the metabolic syndrome which incorporates obesity, diabetes, hyperlipidemia, and hypertension is increase among patients with PsA, AS and SLE, thus predisposing them to cardiovascular disease.
Another comorbidity which affects patients with rheumatologic disorders is depression. This is particularly noticeable among patients with PsA, who also suffer from psoriasis, a condition also known to be associated with depression. The depression may also be related to the inflammatory burden of both skin and joint disease.
The management of these comorbidities requires firstly screening for them. Studies have shown that we do not do a good job screening for and treating hypertension, hyperglycemia and hyperlipidemia in rheumatology patients. One issue to consider is who should be doing this, is it the rheumatologist or the family physician, and how it should be done.
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## When and how to diagnose and treat vitamin D deficiency?

SP0155 **VITAMIN D AND SYSTEMIC LUPUS ERYTHEMATOSUS: WHEN AND HOW TO TREAT VITAMIN D INSUFFICIENCY/DEFICIENCY**

L. Andreoli. *Clinical and Experimental Sciences, University of Brescia, Brescia, Italy*

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disorder with a complex pathogenesis including genetic, immunologic, hormonal and environmental factors. Among environmental modulators of SLE, vitamin D has been increasingly investigated over the years. Such interest derived from several observations: 1) SLE patients are particularly prone to vitamin D insufficiency due to the avoidance of sun exposure, but in some cases also because of the renal involvement of the disease or medications; 2) *in vitro* studies have demonstrated that vitamin D is able to modulate several different cell types (dendritic cells, T and B cells) with effects that may be beneficial in autoimmune diseases; 3) animal models of SLE have shown disease amelioration upon supplementation with vitamin D.
Recent review papers and meta-analyses confirmed that vitamin D insufficiency is widespread in SLE, affecting 38–96% of the patients. What needs to be still clarified is the relationship between low levels of vitamin D and disease activity/severity and whether vitamin D supplementation can be useful to positively influence the course of the disease. There is trend toward an inverse relationship between vitamin D insufficiency and higher disease activity, although many studies failed to describe it. In addition, vitamin D insufficiency seems to be related to cardiovascular events in SLE patients, although this association may be mediated by "traditional" cardiovascular risk factors. Interventional studies are still limited in number and did not reach definite conclusions in terms of optimal vitamin D supplementation to be applied in SLE patients.
It should be acknowledged that different results across studies may be due to methodological issues. In fact, the outcomes of a study investigating the role of vitamin D can be affected by many variables: demographic factors (age, ethnicity, body mass index, nutritional intake), sample size of the cohort and study design, compound used for supplementation (cholecalciferol vs. ergocalciferol), dosage and timing (low vs. high dose; daily/weekly/monthly schedule), outcomes of the study (variations in indices of SLE disease activity, cytokines and lymphocyte populations, inflammatory and hemostatic markers, or IFNalfa signature). By measuring 25-OH vitamin D levels, clinical studies do not get a direct picture of the actual activity of the vitamin D system. Additional relevant information may come from the evaluation of the active form 1,25-OH vitamin D and from the analysis of the polymorphisms of the vitamin D receptor.
In the clinical setting, every SLE patient should be assessed for circulating levels of 25-OH vitamin D. Supplementation should be tailored upon the individual vitamin D status and other characteristics (obesity, renal failure, etc.). Especially in those patients taking steroids and at a higher risk of osteoporosis, vitamin D levels should be kept in the range of sufficiency (above 30 ng/ml). The fascinating immunomodulatory role of vitamin D needs to be confirmed in the clinical setting in order to support a more intensive treatment with vitamin D in SLE patients. Nonetheless, it should be considered that vitamin D is a cheap intervention with an excellent safety profile, so the routine use of moderate doses of cholecalciferol (1000–2000 UI/day) in SLE patients should not raise any major concern.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6346

**FRIDAY, 10 JUNE 2016**

## Data harmonization across (rheumatoid arthritis) clinical cohorts and registers

SP0156 **HOW TO COLLECT COMORBIDITIES**

E. Nikiphorou. *Department of Rheumatology, Whittington Hospital, London, United Kingdom*

The need to better understand and quantify the impact of comorbidity on patients and survival is well-recognised and forms an important area both for routine clinical practice and also for future research. However, there remain several challenges to overcome, a key one being the identification of optimal ways to accurately and consistently collect and measure comorbidity. To date, effective, simple and validated instruments to collect and aggregate comorbidity data are lacking. As a result, standard assessment and care for comorbidity varies considerably in rheumatology departments. Standardised ways for capturing data are therefore necessary for good quality research but more importantly for optimising patient care, quality of life, outcomes and prognosis. This talk reviews ways of collecting

comorbidities in rheumatoid arthritis based on the existing literature, discussing general and disease-specific "indices" for quantifying comorbidity burden.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Telemedicine and e-health in community care

### SP0157 DELIVERING TECHNOLOGY ENABLED CARE SERVICES IN PRIMARY CARE

R. Chambers[1,2,3,4]. *[1]Chair, Stoke-on-Trent CCG, Stoke-on-Trent; [2]Long Term Conditions Priority Lead, WMAHSN, Birmingham; [3]Honorary Professor, Keele University, Keele; [4]Honorary professor, Staffordshire University, Stoke-on-Trent, United Kingdom*

**Background:** there are many pilots of various types of technology enabled care in general practice settings in the UK. The challenge is to integrate such technology as a natural option for delivery of care in specific pathways or for particular patient groups, across and between healthcare settings.
**Project:** Adoption of technology enabled care in Staffordshire and beyond in general practice settings, and interacting with clinicians in acute care, mental health and community settings, and pharmacies. Modes of technology included locally evolved apps, Flo telehealth, skype and videoconsultations with encrypted mode, social media (eg Facebook); foci included patients with asthma, COPD, heart failure, hypertension, AF and other conditions. The presentation will capture challenges and how these have been overcome.
**Discussion:** How do we in the NHS match patients' needs and preferences for technology enabled care? How do we prove to the commissioners of care and frontline practitioners that technology enabled care is worth doing?
**Disclosure of Interest:** None declared
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### SP0158 TECHNOLOGICAL CHALLENGES IN IMPLEMENTING E-HEALTH

T. Dawson. *Rescon Technologies, Crondall, United Kingdom*

This presentation will focus on the story of a UK SME, Rescon Technologies, that started with an idea to harness history at source in 2011. This involved developing a tool to allow patients to capture their own medical history in real-time, in an accessible easy to use format. It will cover the journey from idea generation to co-development pilots through to going to market in the UK. This will include examples of how opportunities need to be embraced to allow obstacles to be overcome in getting a product to market in a fragmented health and social care ecosystem.
Specific topics that will be addressed are:

1. The issues around contemporary history taking;
2. The rise of patient reported outcome measures;
3. History as a diagnostic and prognostic tool;
4. How history relates to new outcome commissioning models;
5. Accessibility;
6. User interfaces and user experience;
7. Segmentation, quantification and digitisation;
8. Co-production;
9. System and workflow integration;
10. Competition, interoperability, and collaboration;
11. Health economics;
12. Advantages of an integrated information technology approach.

The presentation will conclude with recommended considerations before embarking on the journey of turning an idea or aspiration into a sustainable product that will improve health or social care.
**Disclosure of Interest:** T. Dawson Shareholder of: Rescon Technologies
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### SP0159 ETHICAL IMPLICATIONS OF EMPLOYING E-HEALTH SOLUTIONS TO PROMOTE HEALTHY LIFESTYLES

M. Niezen. *Tilburg Institute for Law, Technology and Society, Tilburg University, Tilburg, Netherlands*

Increasingly e-health solutions and specifically eHealth applications (health apps) combine interactive persuasive technologies [1,2] with behaviour change systems [3]. Within the field of mobile health (mHealth) these technologies can be used for influencing human behaviour and empowering users to gain or maintain a healthy lifestyle. However, such health apps are relatively new emerging technologies and also come with expectations and worries with respect to their unknown and unintended effects and related ethical issues that might arise from their design or distribution. In this presentation I will discuss how health apps can raise issues on matters such as privacy, autonomy, liability and division of responsibilities among stakeholders. In addition, I will discuss potential ways of developing e-Health applications in a more responsible manner, taking into account ethical, legal and social preconditions for e-Health's acceptance.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6428

**FRIDAY, 10 JUNE 2016**

## Inflammasome as therapeutic target in inflammatory diseases

### SP0160 PROTECTIVE AND DETRIMENTAL ROLES OF INFLAMMASOMES

M. Lamkanfi[1,2]. *[1]VIB; [2]Ghent University, Zwijnaarde, Belgium*

Inflammasomes are multi-protein platforms that assemble in the cytosol of immune cells to cope with pathogens and cellular stress. The pattern-recognition receptors NLRP1, NLRP3, NLRC4, AIM2 and Pyrin all assemble canonical platforms for caspase-1 activation, and the related inflammatory caspases 4, 5 and 11 respond to cytosolic detection of the Gram-negative lipopolysaccharides. Inflammasomes contributes importantly to controlling pathogen replication through their roles in maturation and secretion of the inflammatory cytokines interleukin-(IL)1β and IL18, and they also induce pyroptosis. Contrasting to their beneficial roles in these host defense responses, deregulated inflammasome activation is thought to be detrimental in the context of chronic inflammatory arthritis and autoinflammatory diseases such as cryopyrin-associated periodic fever syndromes (CAPS) and Familial Mediterranean Fever (FMF).
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## What's new: latest advances in treatment and management of systemic sclerosis and fibromyalgia

### SP0161 LATEST ADVANCES IN THE TREATMENT AND MANAGEMENT OF SYSTEMIC SCLEROSIS

U. Müller-Ladner on behalf of Otylia Kowal-Bielecka, for the EUSTAR/EULAR Recommendation Group. *Rheumatology and Clinical Immunology, Justus-Liebig University Giessen, Kerckhoff Klinik Bad Nauheim, Bad Nauheim, Germany*

Based on the 2009 EULAR recommendations for the treatment of systemic sclerosis (SSc), a complete set with attention to new therapeutic approaches was analysed and verified for clinical use. This update of the previous treatment recommendations was performed according to EULAR standard operating procedures. The task force consisted of 32 SSc clinical experts from Europe and USA, two patients nominated by the pan-European patient association for SSc (FESCA), a clinical epidemiologist and 2 research fellows. All centers from the EULAR Scleroderma Trials and Research (EUSTAR) group were invited to submit and select clinical questions concerning SSc treatment using a Delphi approach. Accordingly, 46 clinical questions addressing 26 different interventions were selected for systematic literature review. The new recommendations were based on the available evidence and developed in a consensus meeting with clinical experts and patients. The procedure resulted in sixteen recommendations being developed (instead of 14 in 2009) that address treatment of several SSc-related organ complications: Raynaud's phenomenon (RP), digital ulcers (DUs), pulmonary arterial hypertension (PAH), skin and lung disease, scleroderma renal crisis, and gastrointestinal involvement. Compared with the 2009 recommendations, the 2015 recommendations include phosphodiesterase type 5 (PDE-5) inhibitors for the treatment of SSc-related RP and DUs, riociguat, new aspects for endothelin receptor antagonists, prostacyclin analogues, and PDE-5 inhibitors for SSc-related PAH. New recommendations regarding the use of fluoxetine for SSc-related RP and haematopoietic stem cell transplantation for selected patients with rapidly progressing SSc were also added. In addition, several comments regarding other treatments addressed in clinical questions and suggestions for the SSc research agenda were formulated. Taken together, these updated data- and consensus-derived recommendations will help rheumatologists to manage patients with SSc in an evidence-based way. These recommendations also give directions for future clinical research in SSc and add to the emerging novel therapies for the different aspects of SSc.
**Disclosure of Interest:** U. Müller-Ladner Grant/research support from: EULAR, EUSTAR, WSF

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**FRIDAY, 10 JUNE 2016**

## EULAR projects in Investigative Rheumatology

### SP0162 BECOMING A BOOKMAKER: THE ODDS OF RHEUMATOID ARTHRITIS

D. Van Der Woude. *Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

"Doctor, what exactly is my risk of getting rheumatoid arthritis?"
Despite all our knowledge about rheumatoid arthritis (RA), this question is often difficult to answer.
This presentation will review familial risk in RA and the underlying genetic risk factors, as well as environmental risk factors for disease. Autoantibodies are a potent prognostic marker when it comes to the risk of developing RA, and play a key role in current pathophysiological hypotheses. The latest concepts of how the various risk factors contribute to disease onset will be discussed, along with strategies to easily communicate the concept and extent of RA-risk to our patients.
**Disclosure of Interest:** None declared
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**SATURDAY, 11 JUNE 2016**

## WIN session 8

### SP0163 WHAT IS NEW: IDIOPATHIC INFLAMMATORY MYOPATHIES

J. Vencovsky. *Institute of Rheumatology, Praha, Czech Republic*

Myositis or Idiopathic inflammatory myopathies (IIMs) are acquired, heterogeneous autoimmune disorders characterized by immune-mediated skeletal muscle inflammation leading to muscle weakness and to damage to muscle tissue. Traditionally IIMs include dermatomyositis, polymyositis, cancer associated dermatomyositis, juvenile dermatomyositis and myositis as part of the overlap syndromes. Immune mediated necrotizing myopathy (IMNM) is newly recognized myositis subgroup with a majority of patients having anti-SRP or anti-HMGCR antibody in their serum. The data shows that anti-HMGCR+ IMNM is associated with previous use of statins that presumably induce autoimmune reaction towards the 3-hydroxy-3-methyl glutaryl-coenzyme A reductase (HMGCR). The incidence of this form of IMNM is increasing, probably due to the growing use of statins in the population. Patients with anti-HMGCR+ IMNM tend to respond to immunosuppressive treatments and if resistant to this, then usually favourably react to intravenous immunoglobulins, even without concomitant glucocorticoids. Anti-SRP+ patients, on the other hand, are notoriously difficult to treat. Recent studies showed that some of these patients may respond to rituximab.
Inclusion body myositis (IBM) is a late onset myositis leading to progressive muscle wasting. It is still debated whether IBM is a primary autoimmune disease or a degenerative myopathy. Recent discovery of antibodies to cytosolic 5'-nucleotidase 1A (anti-cN1A) that are present in a certain proportion of IBM patients points to immune pathogenesis. This is supported by the fact that anti-cN1A may be seen also in some other autoimmune diseases. IBM is usually resistant to immunosuppressive treatment. Several new directions in the treatment are being explored in the early phases of clinical trials, e.g. with ariclomol (increases expression of cytoprotective heat shock proteins in muscle), bimagrumab (monoclonal antibody that blocks the activin IIA and IIB receptors that bind myostatin) or follistatin (gene therapy inhibiting myostatin expression).
Patients with IIMs may have several myositis specific autoantibodies (MSA) which are associated with particular clinical manifestations. The most recent addition to this rule is the antibody to muscle-specific protein FHL1. Presence of anti-FHL1 is predictive for muscle atrophy, dysphagia, pronounced muscle fibre damage, and vasculitis. Interestingly, mutations of the gene encoding four-and-a-half LIM domain 1 (FHL1) are the causative factor of several X-linked hereditary myopathies, suggesting that antibodies to this protein may have pathogenic properties.
Most of the recent treatment studies performed in patients with IIMs did not meet primary endpoints, with the exception of the trial in juvenile DM, in which combination of prednisone with either cyclosporine or methotrexate was more effective than prednisone alone. The safety profile and steroid-sparing effect favoured the combination of prednisone plus methotrexate.
Newly developed criteria for clinical response quantitatively assess the improvement on the 0–100 scale and use thresholds for minimal, moderate, and major improvement. They provide a sensitive and specific tool for longitudinal patient follow-up and hopefully will perform better in proving efficacy of new treatments in the future.
**Disclosure of Interest:** J. Vencovsky Consultant for: Servier
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**SATURDAY, 11 JUNE 2016**

## The elderly patient with osteoarthritis

### SP0164 PROBLEMS IN CONVENTIONAL THERAPY IN OSTEOARTHRITIS: A CASE PRESENTATION

W.-Y. Kwok. *Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

In this case presentation a 57-year old male patient is illustrated, who suffers from non-inflammatory arthralgia due to osteoarthritis. He visits the outpatient clinic with the specific question for advice with respect to pain management, especially for his hand pain since he is a technician in a dental laboratory. However, non-steroidal anti-inflammatory drugs (NSAIDS) are contra-indicated by his ischemic cardiomyopathy, cerebral vascular accident, hypertension and ulcus duodeni in the past.
**Disclosure of Interest:** None declared
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### SP0165 BALNEOTHERAPY:EFFICACY AND SAFETY IN OSTEOARTHRITIS

T. Bender. *Physical Therapy, Hospitaller Brother of St. John of God, Budapest, Hungary*

**Background:** The scientific field dealing with balneotherapy is called balneology.Balneotherapy means the use of natural mineral waters, natural peloids and muds, natural sources of different gases for medical purposes.
**Objectives:** A growing number of evidence is available about the beneficial effect of balneotherapy for patients suffering from Osteoarthritis. The lecture would like to give a survey about the efficacy and safety of balneotherapy in Osteoarthritis
**Methods:** We searched in the medical database (Pubmed, Scopus, Pedro, Web of Sciences, Sciences Direct) and took into consideration articles only published in the English language. We focused on the clinical studies, but we paid attention on the possible side effects,risks and harmful effects of balneotherapy. We overviewed not only the RTC studies, but also the reviews,meteaanalysis and guidelines.
**Results:** Untill now more than 50 RTC single or double blind studies had been published on the effect of balneotherapy in OA(this number continually increased).The majorities of the studies dealing with the role of the balneotherapy on the knee arthrosis, but there are studies involved with the shoulder,neck,hand,hip and lumbar regions too. On the basis of the available evidence, balneotherapy has a beneficial effect on pain and quality of life for OA patients. As for as the safety of balneotherapy,the side effects during the treatment are negligible. On account of the latest OARSI guideline, balneotherapy is an appropriate treatment in case of multi- joint type OA with comorbidities.
**Conclusion:** On the basis of the available evidence balneotherapy is effective and safe, non-pharmacological therapy in the treatment of OA, but further multicentric studies are necesseray to prove its efficacy.
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**SATURDAY, 11 JUNE 2016**

## SLE: what will it be and how will it be treated 5 years from now

### SP0166 THE INTERFERON PATHWAY IN SLE: FROM IMMUNOLOGY TO NEW INSIGHTS AND NEW TREATMENT

L. Rönnblom. *Department of Medical Sciences, Uppsala University, Uppsala, Sweden*

The interferons (IFNs) consist of a large family of proteins classified as type I-III IFNs and originally defined by their capacity to interfere with viral replication. Subsequent studies revealed that IFNs also have many immunomodulatory effects and can act as immune adjuvant. Among the immunostimulatory effects by type

I IFN are maturation and differentiation of dendritic cells, activation of T cells and enhanced antibody production by B cells. There are several observations suggesting an important role for the type I IFN system in the etiopathogenesis of SLE. Among these are the reported development of autoimmune diseases, including SLE, during treatment with IFN and a prominent increase in the expression of type I IFN regulated genes (an IFN signature) in cells from SLE patients. Recent data also show that the regulation of the type I IFN system is abnormal in SLE, which all together suggests that inhibition of the type I IFN system could be beneficial in SLE. Many different therapeutic targets exists and several studies are in progress aiming to block, or down-regulate, the activated type I IFN system in SLE. A number of studies with monoclonal anti-IFN-alpha antibodies have been reported, and a small study investigating vaccination with an interferon-alpha-kinoid against IFN-alpha has been published. Trials targeting the type I IFN receptor are also under way, and preliminary data was recently reported. Other possibilities include elimination of endogenous IFN inducers and inhibition of key molecules in the type I IFN signaling pathway. The results so far show that it's possible to partially suppress the IFN signature, improve several biomarkers and reduce disease activity in a subset of SLE patients. No major safety problems have been observed so far, but complete inhibition of the type I IFN system will automatically increase the risk for severe infections.
**Disclosure of Interest:** L. Rönnblom Grant/research support from: Astra/Zeneca
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### SP0167 OUTCOME ASSESSMENT IN SLE

R. Fischer-Betz. *Rheumatology, Heinrich-Heine-University, Duesseldorf, Germany*

Outcome is defined as "something that follows as a result or consequence of an activity or process". Although the outcome of patients with SLE has improved within the last decades (e.g. considering mortality rates), the disease is a condition still associated with considerable burden and increased morbidity. In routine care the assessment of SLE patients is biased by the experience of the treating physician which leads to significant variability. This may impact quality of care offered to patients and ultimately influence outcomes. Almost five years ago, a 'core set' of minimal variables for the assessment and monitoring of patients with SLE in clinical practice was developed which includes e.g. disease activity, damage and co-morbidities. More recently, targets have been defined in order to improve the long-term outcome. In this context, consensus definitions of "low disease activity state" (LLDAS) and of "remission" in SLE were generated. First retrospective studies showed that e.g. achievement of LLDAS was associated with significantly reduced organ damage accrual. Therefore in 5 years from now, outcome assessment will hopefully change from a "passive approach" to an active process leading to targeted treatment decisions.
**Disclosure of Interest:** None declared
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### SP0168 HOW NEW TREATMENTS IN LUPUS ARE CHANGING THE LANDSCAPE

A. Voskuyl. *rheumatology, VU University Medical Center, Amsterdam, Netherlands*

For decades patients with systemic lupus erythematosus have been been treated with classical immunosuppressive drugs, either as single use or in combination, with or without low-medium- high dose corticosteroids. The ultimate goal of treatment is cure, although low disease activity and preferably remission are the primary goals of treatment, yet. Prevention of lupus flares and reduction of corticosteroids dose are in line with these goals. An overview will be given on the current use (indication, efficacy, side effects) of biologicals (i.e. rituximab, belimumab) in lupus, in particular in daily clinical practice. Also, the following questions will be discussed: Do the use of biologicals add to the former mentioned goals of treatment? What can be expected from the use of biologicals in lupus in the future? Which new treatments, including biologicals, are currently being investigated in clinical trials?
**Disclosure of Interest:** None declared
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**SATURDAY, 11 JUNE 2016**

## HOT session 10

### SP0169 PHARMACOLOGICAL MANAGEMENT OF OSTEOPOROSIS

S. Papapoulos. *Center for Bone Quality, Leiden University Medical Center, Leiden, Netherlands*

The aim of any intervention for osteoporosis is the prevention of fractures at all skeletal sites in patients who have not yet fractured or of the progression of the disease in patients who have already sustained a fragility fracture. Correction of deficiencies/insufficiencies in vitamin D (and calcium) should be the first step in management. The effects of pharmacological interventions are above those obtained with calcium and vitamin D, as in clinical trials these are usually given to placebo-treated patients. The evidence of the antifracture efficacy of pharmacological interventions varies among approved agents and for treatment decisions the highest level of available evidence should be selected. Consistent with the pathophysiology of osteoporosis, pharmacological interventions are distinguished into inhibitors of bone resorption, stimulators of bone formation and compounds whose action on bone remodeling has not yet been fully elucidated, such as strontium ralenate. Of those, only the bisphosphonates alendronate, risedronate and zoledronate and the RANKL-inhibitor denosumab have been shown to reduce the risk of all osteoporotic fractures with variable efficacy up to 5 years of treatment. Despite the fact that the primary action of all four agents is the reduction of bone resorption and turnover, there are also considerable differences between bisphosphonates and denosumab that can be considered in clinical practice. In the absence of head-to-head studies with fracture endpoints these data together with the safety profile should be considered in therapeutic choices for individuals at risk. Cathepsin K inhibitors that decrease bone resorption while maintaining bone formation are not yet available for clinical use. Reduction of bone resorption, though essential for the maintenance or improvement of bone strength, cannot replace already lost bone. For this, specific stimulation of bone formation is required. The teriparatide paradigm illustrated the possibility of stimulating bone formation in osteoporotic patients and opened the way for the development of novel forms of PTH or PTHrP are at different stages of clinical development but a synthetic analog of PTHrP (abaloparatide) given for 18 months was recently shown to decrease the incidence of vertebral and nonvertebral fractures in women with osteoporosis. However, optimal pharmacological management of osteoporosis should aim at concurrently decreasing bone resorption and stimulating bone formation at all skeletal envelopes. Such approach will not only prevent the structural decay of bone tissue but will also substantially increase bone mass leading to enhanced reduction of the risk of fractures particularly at sites with predominantly cortical bone. The combination of teriparatide with denosumab that allows continuous stimulation of bone formation by teriparatide by blocking its concurrent stimulating effect on bone resorption by denosumab may be an interesting option in severely affected patients. The recognition of the central role of the Wnt signaling pathway in bone formation provided attractive targets, such as sclerostin, for the development of bone building pharmaceuticals that reduce also bone resorption. Neutrlizing antibodies to sclerostin (romosozumab, blosozumab) represents a very promising novel anabolic therapy for patients with osteoporosis, in whom 2-year data of phase II studies are available. These new developments may allow tailoring pharmacotherapy to the specific needs and pathophysiological profile of the individual patient. Because osteoporosis is a chronic disease, knowledge of the long-term efficacy and risk profile of every individual agent prescribed is essential for proper patient care.
**Disclosure of Interest:** S. Papapoulos Consultant for: Amgen, Axsome, Merck, Mereo, Novartis, UCB
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**SATURDAY, 11 JUNE 2016**

## "Time is joint": early recognition and treatment of arthritis

### SP0170 TIME TO JOINT: EARLY RECOGNITION AND TREATMENT OF ARTHRITIS – THE HEALTH PROFESSIONALS PERSPECTIVE

P.D. Kirwan[1,2]. [1]*School of Physiotherapy, Royal College of Surgeons in Ireland;* [2]*Physiotherapy Dept, Connolly Hospital, Dublin, Ireland*

Early recognition of inflammatory arthritis is of utmost importance, as failure to do so can delay appropriate treatment and result in permanent joint damage and disability. This presentation will set out to explore the role a Physiotherapist/Healthcare Professional can play in recognition of inflammatory joint disease. Healthcare Professionals/Physiotherapists are often the first point of contact for patients suffering from joint/musculoskeletal pain. They are therefore very well positioned to be the first to identify possible inflammatory sources of pain versus non-inflammatory sources. The question as to whether a physiotherapist can recognise inflammatory joint disease versus non-inflammatory joint conditions will be explored with the aim being to highlight the important role a physiotherapist can play in this important diagnostic challenge. With reference to ongoing clinical and research work in this field, this presentation will set out to ask whether or not a Healthcare Professional/Physiotherapist can acurately recognise/diagnose inflammatory arthritis and whether they miss inflammatory arthritis.
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**SATURDAY, 11 JUNE 2016**

## Clinical outcomes for PMR/GCA

### SP0171 EULAR/ACR GUIDELINES FOR PMR – THE UPDATED EVIDENCE

C. Dejaco. *Rheumatology, Medical University Graz, Graz, Austria*

Polymyalgia rheumatica (PMR) is the second most common inflammatory

rheumatic disease in older people after rheumatoid arthritis. According to the 2015 EULAR-ACR recommendations for the management of PMR, oral glucocorticoids (GC) are the first choice treatment for this condition. It is recommended to choose the minimum effective GC dose within a range of 12.5–25mg prednisone equivalent daily as the initial therapy and to gradually taper the dose, based on regular monitoring of patient disease activity, laboratory markers and adverse events. An early introduction of methotrexate (MTX) in addition to GCs may be considered, particularly in patients at high risk for relapse and/or prolonged therapy as well as in cases with risk factors, co-morbidities, and/or concomitant medications where GC related adverse events are more likely to occur. For other conventional disease modifying anti-rheumatic drugs (DMARDs), a specific recommendation was not possible due to the absence of good evidence. Among biological agents, infliximab and etanercept failed its primary endpoint in randomized controlled trials, and consequently, a strong recommendation against the use of TNF-a blocking agents was made.
Since the publication of 2015 EULAR-ACR recommendations, observational studies and small, randomized trials reported promising results about the effective use of interleukin (IL)-6 blocking agents in PMR. If these preliminary data are confirmed by larger randomized controlled trials, IL-6 blockade might become an important therapeutic option for PMR patients in future.
In this session, we will discuss current evidence on the role of steroid sparing agents in the treatment of PMR including the promising new results from studies on IL-6 blockade.
**Disclosure of Interest:** C. Dejaco Grant/research support from: Pfizer, MSD, Consultant for: MSD, Pfizer, UCB, AbbVie, Roche, GSK, Novartis, Lilly, BMS, Celgene, Speakers bureau: MSD, Pfizer, UCB, AbbVie, Roche, GSK, Novartis, Lilly, BMS, Celgene, Merck, Signatis Pharma
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### SP0172 GLUCOCORTICOID-INDUCED COMPLICATIONS IN PATIENTS WITH POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS

F. Buttgereit. *Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, Berlin, Germany*

With over 60 years of experience with glucocorticoids (GC), the number of patients treated and the range of clinical applications is more extensive than with other treatments. GC are still widely used in clinical medicine today, and they form a mainstay of therapy for polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) since they are cost-effective drugs which exert strong anti-inflammatory and immunosuppressive.
However, there is increasing awareness of the potential for these drugs to produce adverse effects. Especially if higher dosages have to be given over longer periods of time, cardiovascular, gastrointestinal, dermatological, ophthalmological, and metabolic adverse effects, an increased risk of infection, the incidence of a Cushingoid phenotype, and in particular GC-induced osteoporosis (GIOP) are to be mentioned. The available data describing frequency and severity of these adverse effects are fragmentary. For example, it is difficult to distinguish specific adverse effects of a GC therapy from other causations (e. g., the treated disease itself, other concomitant diseases or concomitant therapies).
Therefore, as a general rule, also in PMR and GCA as much GC as necessary, but as little as possible should be administered. Recommendations and guidelines have been developed describing in detail suggested approaches for using GC in induction therapy, during initial and further tapering until discontinuation, and flare management. It should be noted however, that these algorithms base upon expert opinion and assessment of the literature, but they have not been formally tested in randomized controlled trials.
Treatment of PMR and GCA is usually required for 1–3 years, but frequently also longer and often with daily GC doses around 5 mg prednisone equivalent. Therefore, a recent publication of a EULAR Task Force is important since it reports the risk of harm to be low for the majority of patients at long-term dosages of $\leq$5mg prednisone equivalent per day, whereas at dosages of $>$10mg/d the risk of harm is elevated. At dosages between $>$5 and $\leq$10mg/d, patient-specific characteristics including protective and/or risk factors need consideration when estimating the risk of harm.
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### SP0173 POLYMYALGIA RHEUMATICA: IMPROVING OUTCOMES FOR PATIENTS IN PRIMARY CARE

T. Helliwell. *Primary care sciences, Keele University, Institute of Primary Care and Health Sciences, Keele, United Kingdom*

Polymyalgia rheumatic (PMR) is the most common inflammatory arthritis managed in primary care settings. The majority of clinical care is typically provided by General Practitioners (GPs) with evidence suggesting that current management is suboptimal. This talk will highlight some of the key challenges faced by GPs highlighting areas where the diagnosis, monitoring and long term care can be improved.

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**SATURDAY, 11 JUNE 2016**

## Getting active against rheumatoid arthritis fatigue

### SP0174 HEALTH BEHAVIOUR CHANGE TECHNIQUES TO EFFECTIVELY PROMOTE PHYSICAL ACTIVITY IN PEOPLE WITH RHEUMATOID ARTHRITIS

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Engaging in sufficient levels of physical activity (PA) is of particular importance for patients with rheumatoid arthritis (RA), as it can help to maintain functional ability and reduce the risk of cardiovascular disease. While many healthcare professionals have the ability to effectively promote PA among patients with RA, some techniques common in clinical practice can actually be counterproductive. As consultations are becoming increasingly shorter, having a clear understanding of the evidence on how to best promote PA in practice can help healthcare providers' to improve the efficiency and effectiveness of their PA promotion efforts. This session will provide an overview of prominent behavioural determinants and theories, and outline how behaviour change typically unfolds among patients with rheumatoid arthritis. It will then present research which has identified behaviour change techniques associated with increased motivation and intention for PA and changes in PA behaviour itself. Finally, it will provide practical, evidence-based tips that can be implemented to help guide behaviour and lifestyle change efforts in clinical settings, even when time is short.
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### SP0175 ACTIVITY MONITORING TO SUPPORT PATIENT GOALS AND ASSESS PROGRESS

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Increasing participation in PA is important for everyone, including people with RA (1,2). The reported benefits of PA for the RA population include improved aerobic fitness and muscle strength, resulting in enhanced ability in activities of daily living and health-related quality of life and an improvement in disease related characteristics, such as pain and stiffness (2). However, studies have shown that physical activity is reduced in people with arthritis (1). Enhancing physical activity and reducing sedentary time are thus important goals for people with arthritis, however achieving long-term behaviour change relating to physical activity can be challenging. Monitoring of physical activity for patients with chronic disease can be valuable in supporting patients achieve their goals and to help with assessing progress. There are a number of considerations when using physical activity monitoring in this way including practical aspects of monitoring over long periods, patient preferences, type of monitors available and suitability of the device to match patient goals (3, 4). This presentation will consider these issues and will provide a context for the use of activity monitors and subjective monitoring to support goal setting and monitor progress in achieving activity goals. Numerous devices and subjective measures have been used, with some validated, to measure activity in people with arthritis (5, 6) - a review of these will be presented with consideration of how they can be used to monitor varying aspects of activity and physical fitness. The perspective of the person with arthritis will also be presented to allow consideration of how well activity monitoring matches patients' goals for activity. A key message from the talk will be the importance of matching the patient goals with the activity monitor. The importance of understanding what aspects of physical activity and/or sedantariness are to be measured will be emphasised to ensure that progress can be appropriately recorded.
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**SATURDAY, 11 JUNE 2016**

## Endothelial to mesenchymal transition and angiogenesis as driving mechanisms in systemic sclerosis

### SP0176 ROLE OF ENDOTHELIAL TO MESENCHYMAL TRANSITION IN THE PATHOGENESIS OF THE VASCULAR ALTERATIONS IN SYSTEMIC SCLEROSIS

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Systemic Sclerosis (SSc) is a systemic autoimmune disease characterized by progressive fibrosis of skin and multiple internal organs and severe fibroproliferative microvascular alterations. Despite currently available therapeutic approaches SSc has a high mortality rate. The high mortality of SSc is largely caused by severe, progressive and generalized vascular involvement resulting in the development of multiple organ alterations including SSc-associated interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH). These two complications have emerged as the most frequent causes of disability and mortality in SSc.
The pathogenesis of the fibrotic process and the progressive fibroproliferative vasculopathy in SSc is complex and despite extensive investigation the exact mechanisms have remained elusive. Myofibroblasts are the cells ultimately responsible for tissue fibrosis and fibroproliferative vasculopathy in SSc. Tissue myofibroblasts originate from several sources including expansion of quiescent tissue fibroblasts and transmigration and tissue accumulation of circulating CD34+ bone-marrow-derived fibrocytes. Besides these sources, myofibroblasts may result from the phenotypic conversion of epithelial cells, adipocytes or endothelial cells into activated myofibroblasts. The transdifferentiation of endothelial cells into myofibroblasts involves numerous and complex biochemical, molecular, and gene expression events collectively known as endothelial to mesenchymal transition or EndoMT.
Recently, it has been postulated that EndoMT may play a role in the development of tissue fibrosis and SSc-associated ILD and PAH. However, despite the demonstration of the occurrence of EndoMT in experimentally induced cardiac, renal, and pulmonary fibrosis and in several human disorders, the contribution of EndoMT to the pathogenesis of tissue fibrosis and fibroproliferative vasculopathy in SSc has not been generally accepted. Here, the experimental evidence supporting the concept that EndoMT plays a role in the pathogenesis of the vascular alterations in SSc and, more specifically, in the development of SSc-associated ILD and PAH will be critically reviewed.
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**SATURDAY, 11 JUNE 2016**

## Cell-cell interaction in joint inflammation

### SP0177 INHIBITORY PATHWAYS OF SYNOVIAL ANGIOGENESIS

E. Brahn on behalf of Cell-Cell Interaction in Joint Inflammation. *Division of Rheumatology, UCLA School of Medicine, Los Angeles, United States*

**Introduction:** Angiogenesis occurs in a variety of normal processes, such as wound healing, organ development and the menstrual cycle. However, angiogenesis is also associated with numerous disease processes, including tumor growth, proliferative retinopathy, atherosclerosis and proliferative synovitis. Consequently, these pathologic processes are attractive therapeutic targets. Healthy joint vasculature is maintained by an appropriate balance between proangiogenic and antiangiogenic molecules. However, in rheumatoid arthritis (RA), this balance is disrupted; the levels of VEGF, hypoxia-inducible factor (HIF) and basic FGF (b-FGF), all of which are proangiogenic, are elevated in the joints of both patients with RA and in adjuvant-induced arthritis. The elevation of these proangiogenic factors occurs in the absence of adequate counterbalancing antiangiogenic factors. The new vasculature permits synovial hyperplasia which ultimately contributes to joint inflammation and structural damage.
**Results:** In the United States, there are already at least 13 FDA approved anti-cancer therapies with recognized antiangiogenic properties in oncology that target the endothelial cell, pericyte, or tumor cell. These agents, which interrupt critical cell signaling pathways involved in tumor angiogenesis and growth, comprise three primary categories: 1) Monoclonal antibodies directed against specific proangiogenic growth factors and/or their receptors; 2) Small molecule tyrosine kinase inhibitors (TKIs) of multiple proangiogenic growth factor receptors; and 3) Inhibitors of mTOR (mammalian target of rapamycin). In addition there are other angiogenic agents whose mechanisms are not completely understood. A variety of angiogenesis inhibitors are being examined for their potential in treating RA, and although none of these compounds have advanced beyond phase II clinical trials, several angiogenesis inhibitors have demonstrated efficacy in preclinical RA models.
**Conclusions:** Angiogenesis is an attractive therapeutic target although blood vessel growth is complex with multiple mechanisms. Different diseases may utilize different dominant pathways but surrogate markers such as bFGF, VEGF, and vessel density, may be helpful as predictors of likely candidates for therapeutic intervention. Angiogenesis inhibitors warrant further studies in rheumatic diseases. They lend themselves to combination therapies 1) that target multiple vessel proangiogenic pathways or 2) that could be used with biologic response modifiers.
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**SATURDAY, 11 JUNE 2016**

## Transition of care

### SP0178 TRANSITION CARE PROGRAMMES: A EUROPEAN PERSPECTIVE

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The special health care needs of adolescents and young adults with chronic diseases and the inadequate state of services for them have been on the agenda for almost 30 years. But still too many young people, including those with inflmmatory rheumatic diseases, do not receive the care they expect and need. In fact, approximately half of young people are not satisfied with the experienced mode of transition. One in two wishes a better preparation for adult health care. For one third the transfer to adult care comes too early, unplanned or abruptly. Up to half of young people with rheumatic diseases do not make a successful transfer to adult rheumatology and are therefore at particular risk of unfavorable outcome. In response to this, there have been a number of guidelines and activities across Europe seeking to reduce the risks associated with moving to adult services and to implement developmentally focused adolescent care as normal part of a health-care plan.
This lecture will describe European initiatives, which aim at improving health care transition services, such as specific and generic transition care programmes or checklists, education programmes, recommended frameworks and pathways to implement and assess transition programmes.
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### SP0179 TRANSITION CARE PROGRAMMES: A NORTH AMERICAN PERSPECTIVE

L. Tucker. *Pediatrics, BC Childrens Hospital, Vancouver, Canada*

Adolescents with rheumatic diseases frequently continue to require rheumatologic care into adulthood, either due to continued active disease and requirement for treatment, or management of sequelae of disease. In addition, these vulnerable adolescents need to manage transition in schooling, work, living situation, health insurance coverage, and peer relationships. In the recent years, there has been increased focus on improving transition support to adolescents with chronic diseases, resulting in a variety of specialized programs and resources. Objectives for this talk are:

a) To describe North American transition guidelines and models for youth with rheumatic diseases, and how these are applied across different centres and regions.
b) To compare transition practices in pediatric rheumatic programs in North America.
c) To review new transition planning resources for use in the pediatric rheumatology setting.

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**SATURDAY, 11 JUNE 2016**

## New approaches to understanding and managing chronic musculoskeletal pain

### SP0180 ADVANCES IN THE GENETICS OF CHRONIC PAIN SYNDROMES: HOW TWIN STUDIES HELP

F.M. Williams. *Twin Research and Genetic Epidemiology, King's College London, London, United Kingdom*

Chronic widespread musculoskeletal pain and fibromyalgia are increasingly viewed as spectrum disorders, and they co-exist with many other pain syndromes within individuals and their families. Large scale epidemiological studies are superior to clinical collections for providing evidence of overlap in the chronic pain syndromes and allowing the genetic and environmental risk factors to be

determined. Twin registers are a special case of this and allow many different types of study, which provide answers to important questions in chronic pain.
In this talk I will introduce the following concepts:-
1. The chronic pain syndromes
2. The concept of heritability
3. TwinsUK – an NIHR BioResource at KCL
4. Twin study designs which help shed light on chronic pain mechanisms
**Disclosure of Interest:** None declared
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### SP0181 CHRONIC PAIN CONTROL - EXPERIENCE OF A PORTUGUESE PATIENT GROUP INITIATIVE

C.S. Marques. *Patient Group of Chronic Pain, LPCDR – Portuguese League Against Rheumatic Diseases, Lisbon, Portugal*

The Patient Group of Chronic Pain (Núcleo da Dor) of the LPCDR - Portuguese League Against Rheumatic Diseases (which also has Osteoarthritis, Sjögren Syndrome and Scleroderma patients' groups), was born in 2014 and is centred in the chronic pain associated to rheumatic diseases. Its primary mission is to make this health condition VISIBLE to other people and to support the improvement of quality of life of all patients suffering from this pathology (about 30% of Portuguese people).
The Patient Group of Chronic Pain (ND) is a participatory group that wants to share experiences, learn and implement coping strategies, with a positive, global, ecological and effective attitude.
Besides the central role of the rheumatologist (an ally in pain reduction, disease control and treatment compliance), the support of all health professionals, family and friends, we know that the main role belongs to the patient as an expert of his body, and he's also the first to be involved in adapting daily life to new needs, difficulties and constraints. Each day with chronic pain is an emotional, functional and behavioural challenge that requires enhanced skills. Therefore, we believe that we do not choose to be sick, but we can choose to live better - with well-being and dignity - and that is in our hands to act and control the impact of pain on daily life. That's why ND is committed to:
Sharing experiences and self-effective strategies; Learning to live with pain; Reducing disturbances associated to pain experience; Informing, raising public awareness and call to action; Being committed to an effective treatment, therapeutic and additional activities; Capitalizing positive synergies; Identifying scientific, therapeutic, recreational, behavioural approaches; Preserving the dignity and the patient's well-being; Taking responsibility in pain's self-control; Defining priorities and reset beliefs, values, attitudes, behavior and skills (coping) ... and believing in the social responsibility of patients for a sustainable health.
How? Among other activities and events already developed, we launched a National Photography Contest "Chronicles of Paint" which was one of our starting points. It was an opportunity to raise awareness on the invisibility of pain while generating artistic products with powerful visual messages. As a result, the selected photographs provided us material for exhibitions, enabling us to reach out to different audiences. The "Chronicles of Pain" were exhibited at FNAC Alfragide Shopping Centre, at the National Association of Pharmacies and at the Rectory of the New University of Lisbon. We have also presented a poster about this initiative at the Annual Conference of PARE in Zagreb (2014). In 2015, the selected photos were published in the book commemorating the 33rd anniversary of LPCDR, "Turn the Page", along with 33 texts received for Edgar Stene Prize (2005–2014).
We have analysed the submitted photographs and the underlying perceptions of pain and suffering traduced in the visual snapshot, since the goal of the contest was to associate an image to pain. We have also analysed the preferences of a specific public, more closely related with rheumatic and musculoskeletal diseases. The results provided us some guidance towards a communication strategy.
Our Thematic Sessions also provided us some unmet needs that we are addressing, by developing larger projects (like POSSO - Oriented Program for Overcoming RMDs and Optimize Health) for a better management of pain and chronic conditions.
We must do something to draw the attention, talk about it, and call to action to reduce this PAIN scourge. There is no time to loose ... don't you agree?
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**SATURDAY, 11 JUNE 2016**

## Seronegative inflammatory arthritis: diagnostic and management challenges

### SP0182 IS THIS REALLY RHEUMATOID ARTHRITIS?

M. Gaudé on behalf of Xavier Puéchal, MD, PhD, National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, Université Paris-Descartes, Paris, France. *Hôpital Edouard Herriot, Lyon, France*

**Background:** Whipple's disease is a chronic, systemic, curable bacterial infection, caused by *Tropheryma whipplei* and often mistaken for rheumatoid arthritis. Indeed, the classical form usually begins with intermittent joint involvement several years before the development of weight loss and diarrhea, associated with other diverse clinical manifestations.
**Objectives:**
- To know the main clinical presentations of Whipple's disease and *Tropheryma whipplei* localized infections.
- To consider a diagnosis of Whipple's disease in a middle-aged man presenting with isolated intermittent arthritis before the development of chronic persistent polyarthritis and of digestive signs and symptoms.
- To be able to diagnose Whipple's disease by performing *Tropheryma whipplei* polymerase chain reaction from stools, saliva and synovial fluid.
- To know how to interpret polymerase chain reaction tests and pathological examination results.
- To know the therapeutic options in Whipple's disease according to central nervous system involvement.

**Methods:** This presentation describes a patient with a 28-year history of isolated chronic severe bilateral destructive polyarthritis. Blood tests showed elevated acute phase reactants, persistent leukocytosis, but rheumatoid factor and antinuclear antibody tests were negative. He was treated for a presumed seronegative rheumatoid arthritis. He then presented with fever, weight loss, diarrhea and adenopathy.
**Results:** *Tropheryma whipplei* polymerase chain reaction was positive from synovial fluid, synovial tissue, and lymph node specimens. Duodenal biopsy confirmed periodic acid-Schiff-positive macrophages. Whipple's disease was diagnosed. *Tropheryma whipplei* was successfully cultivated from the synovial fluid. Antibiotic treatment was instituted in the patient, after which his symptoms remitted.
**Conclusions:** Particular attention to a diagnosis of *Tropheryma whipplei* infection is warranted in a middle-aged man presenting with unexplained isolated intermittent arthritis. *Tropheryma whipplei* polymerase chain reaction from stools and saliva should be performed. Antibiotic therapy usually ensures the full resolution of all manifestations, which can otherwise be fatal, in case of late diagnosis of extended systemic forms.
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**SATURDAY, 11 JUNE 2016**

## HOT session 11

### SP0183 2016 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF EARLY ARTHRITIS

B. Combe on behalf of the EULAR Task Force on Early Arthritis Management. *Département de Rhumatologie, Hopital Lapeyronie, Université de Montpellier, Montpellier, France*

**Objectives:** In 2007 the EULAR recommendations for the management of early arthritis have been published. In 2010 EULAR also published recommendations for the management of rheumatoid arthritis (RA) with synthetic and biological DMARDs, which were updated in 2013. These later recommendations focussed on the generic pharmacological treatment of RA including Early RA, whereas the 2007 recommendations on early arthritis covered the entire spectrum of the management of early arthritis including also recognition of arthritis, referral, diagnosis, prognosis, classification, information, education, non-pharmacological interventions, and monitoring of the disease process. Between January 2005, when the systematic literature research (SLR) was performed to develop the 2007 recommendations, and 2015 an abundant and rich literature has been published in the field of early arthritis. Taken these points together, it seems important to currently update the EULAR recommendations on early arthritis management.
**Methods:** In accordance with 2014 EULAR Standardised Operating Procedures, the task force pursued an evidence-based approach and an approach based on expert opinion. The task force involved 20 rheumatologists, two patients and one health professional representing 12 European countries. One of them (RL) served as an epidemiologist in order to control the scientific content of the process. The group defined the focus of the task force, the target population, formulated an operational definition of "management" and selected the research questions. A SLR was performed by two fellows (CD, CH) with the help of skilled librarian. A set of draft recommendations was proposed on the basis of the research questions and the results of the literature search. For each recommendation the categories of evidence were clearly identified then the strength of the recommendation was derived and level of agreement was determined after voting process.
**Results:** Fifteen research questions, covering the entire spectrum of "management of early arthritis" were formulated. The updated recommendations comprise 3 overarching principles and 12 recommendations for the management of early arthritis. The selected statements included recognition of arthritis, referral, diagnosis, prognostication, imaging, classification, treatment of early arthritis (information, education, non pharmacological interventions, pharmacological treatments, and monitoring of the disease process) as well as strategy. The

strength of each recommendation was provided. On the basis of expert opinion, 10 items were identified as being important for future research.
**Conclusion:** These recommendations provide Rheumatologists, General Practitioners, Health professionals, Patients, and other stakeholders with an updated EULAR consensus on the management of patients with early arthritis
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**SATURDAY, 11 JUNE 2016**

## Paget's and other rare bone diseases

### SP0184 PAGET'S DISEASE: NEW DEVELOPMENTS

S.H. Ralston. *Rheumatic Diseases Unit, University of Edinburgh, Edinburgh, United Kingdom*

Paget's disease of bone (PDB) is a common skeletal disorder characterised by increased and disorganised bone remodelling affecting one or bone skeletal sites. Although about 20% of patients that come to clinical attention are asymptomatic others develop complications including bone pain, deformity, nerve compression syndromes and fragility fractures. Genetic factors play an important role in the pathogenesis of PDB and there is strong evidence that susceptibility is determined by variants within or close to genes that regulate osteoclast function. At the present time eight predisposing genes and loci have been discovered. Environmental factors also play a key role but little is known about the nature of these triggers. Bisphosphonates are a highly effective treatment for the elevations in bone turnover that are characteristic of PDB and are effective in the treatment of bone pain associated with Paget's disease but current evidence sugegsts that they do not prevent complications at least when administered to patients with established disease. Studies are currently in progress to determine if prophylactic treatment of patients with early asymptomatic disease might yield benefits in preventing the development of new lesions and perventing long term complications.
**Disclosure of Interest:** None declared
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### SP0185 REFLEX DYSTROPHY: DIAGNOSIS AND TREATMENT

A. Giusti. *Bone Clinic, Department of Ortho-Geriatrics, Rehabilitation and Stabilization, Galliera Hospital, Genoa, Italy*

Complex Regional Pain Syndrome type I (CRPS-I), in the past called reflex dystrophy, is a disabling disorder affecting a peripheral limb, usually developing after a trauma to an extremity. Several different diagnostic criteria have been proposed, and recently updated "Budapest Criteria" have been widely accepted, to diagnose CRPS-I. The diagnosis is made using clinical criteria and is based on the sole clinical history and examination. CRPS-I is characterized by the presence of spontaneous or stimulus-induced pain, disproportionate to the inciting event, allodynia and hyperalgesia. These symptoms are associated to a wide variety of autonomic and motor disturbances, or trophic abnormalities. There are no specific laboratory or radiological diagnostic procedures for CRPS-I, but a variety of tests may be useful to exclude other clinical conditions. These include x-rays, three-phase bone scintigraphy and MRI.
At present, several pharmacological treatments (e.g., analgesics, anesthetics, anticonvulsants, antidepressants, oral muscle relaxants, corticosteroids, calcitonin, bisphosphonates, and calcium channel blockers) have been proposed to reduce pain and pain sensitization, and to improve functional status in patients presenting with CRPS-I. While most of these medications demonstrated poor or partial efficacy on the short-term, bisphosphonates (BPs) showed better long-term beneficial effects on pain reduction and functional recovery.
BPs are potent inhibitors of osteoclastic activity widely used for the management of osteoporosis and other metabolic bone diseases. Their primary pharmacological action is the reduction of bone turnover. An enhanced osteoclastic activity has never been clearly demonstrated in CRPS-I. Therefore, it is likely that the positive effects of BPs in this condition are not related to their anti-resorptive properties, but to a more complex interaction between these pharmacological agents and the pathophysiological mechanisms underlying CRPS-I.
Results of several clinical trials have suggested the potential beneficial effects of BPs in CRPS-I. In five randomized-controlled trials, oral and intravenous alendronate, and intravenous clodronate, pamidronate and neridronate demonstrated to be effective in reducing pain and improving physical function in patients presenting with CRPS-I, with a good profile of safety and tolerability. Although these trials have a number of limitations, including the small samples enrolled, there is sufficient evidence to support the use of BPs as agents of choice in the management of CRPS-I.
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### SP0186 GLUCOCORTICOID-INDUCED OSTEOPOROSIS

F. Buttgereit. *Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, Berlin, Germany*

Glucocorticoids remain to be among the most important and most frequently used anti-inflammatory and immunosuppressive or immune-modulatory acting drugs to treat rheumatic (and other) diseases. Unfortunately, glucocorticoids also exert undesired effects, especially if higher dosages have to be given over longer periods of time. In this regard, cardiovascular, gastro-intestinal, dermatological, ophthalmological, and metabolic adverse effects, the increased risk of infection, the incidence of a Cushingoid phenotype, and in particular glucocorticoid-induced osteoporosis (GIOP) are to be mentioned.
However, the available data describing frequency and severity of these adverse effects are fragmentary. For example, it is difficult to distinguish specific adverse effects of a glucocorticoid therapy from other causations (e. g., the treated disease itself, other concomitant diseases or concomitant therapies). This statement is especially true for GIOP in the context of chronic inflammatory rheumatic diseases, since GIOP is counted among the two most important adverse effects of glucocorticoid therapy, by both rheumatologists and patients. This top (negative) ranking of GIOP stands in sharp contrast to the state of knowledge and scientific data, being sparse, partly conflicting and often derived from over-aged projects or studies.
With regard to the pathophysiology of GIOP it seems clear, however, that glucocorticoids contribute to early and rapid bone loss and increased fracture risk which is mediated by direct effects on osteoblasts (decreased bone formation), osteoclasts (increased bone resorption) and osteocytes (increased apoptosis and sclerostin levels), and indirect effects through alterations in gonadal hormones and the neuromuscular system (Rizzoli & Biver, Nat Rev Rheum, 2015).
With regard to the management of GIOP, general preventive measures comprise using the lowest possible GC dose, good nutrition with sufficient intake of calcium, vitamin D, regular weight-bearing exercise, the avoidance of tobacco use and alcohol abuse and other recommendations.
The treatment of GIOP consists of an early introduction of anti-osteoporotic therapy for patients receiving glucocorticoid therapy who are at increased risk of fracture. This treatment should be continued as long as the glucocorticoid dose is above intervention thresholds or fracture risk is increased. (Rizzoli & Biver, Nat Rev Rheum, 2015).
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**SATURDAY, 11 JUNE 2016**

## Analytical issues of complex databases

### SP0187 WHY MISSING DATA IS A PROBLEM, AND WHAT YOU SHOULDN'T DO TO SOLVE IT

T. Frisell. *Karolinska Institutet, Stockholm, Sweden*

Missing data, where either entire observations or individual variable values are for some reason not available for analysis, is a common challenge to research using complex data bases. Although missing data clearly lead to a loss of information and hence reduced statistical power, a more insidious consequence is that this lack of data may introduce selection bias, which could potentially invalidate the entire study. Fortunately, many solutions to this problem has been put forth, based on different ways of filling out (imputing) values where there are none. Unfortunately, several of these solutions are inherently flawed and may introduce more bias then they remove.
This brief presentation will introduce central concepts in the literature on missing data, go through the circumstances when missing data may introduce selection bias, and show some flaws in several methods sometimes used to impute data.
**Disclosure of Interest:** None declared
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### SP0188 MULTIPLE IMPUTATION: A POSSIBLE SOLUTION TO THE PROBLEM OF MISSING DATA

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Multiple imputation (MI) is a statistical technique that can be used to handle the problem of missing data. MI enables the use of all the available data without throwing any away and can avoid the bias and unrealistic estimates of uncertainty associated with other methods for handling missing data. In MI, the missing values in the data are filled in or "imputed" by sampling from distributions observed in the available data. This sampling is done multiple times, resulting in multiple datasets. Each of the multiple datasets is analysed and the results are combined to give overall results which reflect the uncertainty about the values of the missing data.

This talk will explore what MI is, when it can be used and how to use it. The content will be accessible to a wide audience and illustrated with clear examples.
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### SP0189 WHY CHOOSE RANDOM EFFECTS MODELS FOR LONGITUDINAL DATASETS?

S. Norton. *King's College London, London, United Kingdom*

Longitudinal data, where there are multiple repeated observations of an outcome variable for each individual, requires appropriate analysis to account for the non-independence of observations within individuals. A variety of methods are available, including random-effects (aka multi-level or mixed) models and marginal (GEE) models. Random-effects models, the focus of this presentation, extend the standard regression model to allow for subject-specific estimates of the baseline level of the outcome variable (random intercepts) and its rate of change over time (random slopes). Under certain circumstances both random-effects and marginal model approaches give equivalent estimates. However, in many situations they will not and it can be difficult to decide whether one approach should be favoured over the other.
This presentation will provide an introduction to the random-effects model for longitudinal data using data from the Early Rheumatoid Arthritis Study. Particular strengths of random-effects models such as how missing data on outcome variables at some assessments are handled and the clustering of individuals within hospitals will be considered. Furthermore, differences in the interpretation of coefficients between random-effects and marginal models where the outcome variable is dichotomous will be discussed, with guidance on situations where each approach is more useful.
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**SATURDAY, 11 JUNE 2016**

## Intimate life and sexual relations in RA

### SP0190 LIVED EXPERIENCES OF INTIMATE LIFE IN MEN AND WOMEN WITH EARLY RA

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**Background:** Women and men with rheumatoid arthritis (RA) experience restrictions in everyday life in spite of the development of new medications. Recent research has described in detail how participation limitations are experienced in everyday life from a patient perspective. However, knowledge of how sex and intimate relationships are affected is still scarce.
**Objectives:** The aim of this study was to explore sex life experiences in relation to sexual function and sexual relationships in women and men with early RA.
**Methods:** This study is part of the Swedish TIRA-project (the Swedish acronym for the prospective multi centre early arthritis project). The data collection includes 45 interviews with 24 women and 21 men, aged 20–63, which were recorded and transcribed verbatim. Critical Incident Technique was used to collect data, and content analysis to categorize the results.
**Results:** Half the participants stated that RA affected their sex life. The general descriptions formed five categories: sex life and tiredness, sex life and aging, emotional consequences of impaired sexual function, facilitators of sexual function and sexual relationships, and strain on the sexual relationship.
**Conclusions:** Sex life is still affected in early RA despite new effective treatment strategies. New strategies of communication, assessment and self-managing interventions concerning the sex life of patients with RA need to be implemented multi-professionally in health car
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6215

### SP0191 SEXUAL HEALTH IN RHEUMATOID ARTHRITIS - THE ROLE OF THE PHYSIOTHERAPIST TO ENHANCE SEXUAL HEALTH

K. Areskoug Josefsson. *Jönköping University, Jönköping Academy for Health and Welfare, Jönköping, Sweden*

Sexual health is often negatively affected by rheumatoid arthritis (RA), but rarely discussed between patients and health care professionals. Experienced reasons for decreased sexual health vary among patients, but pain, stiffness, reduced mobility, fatigue and negative feelings towards one's own body are common factors. In addition to negative effects experienced to be due to RA, there are also negative influences on sexual health by other factors, such as insufficient physical activity, low self-esteem, depression and stressful influences in life.
Physiotherapy is a common intervention for patients with RA and patients have reported improved sexual health due to physiotherapy. Regular physiotherapy interventions for patients with RA often include coaching towards increasing physical activity levels, hydrotherapy, pain reductive treatment and mobility exercises, both individually and in groups. The physiotherapy interventions leading to improved sexual health (according to patients with RA) has been regular interventions for patients with RA and not specifically aimed at enhancing sexual health. The patients do seldom describe that the physiotherapist has informed them of how physiotherapy might enhance sexual health, but they have themselves experienced how physiotherapy has improved their sexual life.
Patients describe that they experience joy, increased self-esteem and a more positive approach to their body, when participating in physiotherapy and that this positive feeling is affecting their life, including their sexual life. They also describe how increased physical capacity reduces fatigue and increases their capacity to engage in valued life activities, including sexual activities.
The way that the physiotherapist can further enhance sexual health, is by informing the patient of how sexual health is linked to experienced symptoms of RA and how physiotherapy interventions, for example increasing physical activity, can enhance also sexual health.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1365

### SP0192 DISEASE IMPACT ON SEXUALITY AND ITS MANAGEMENT IN RHEUMATOLOGY CARE

S.J. Ryan. *Rheumatology, Haywood Hospital, Stoke on Trent, United Kingdom*

This presentation will identify how the symptoms of Inflammatory Arthritis, including joint pain, joint stiffness and fatigue, have the potential to impact on sexuality. Although the issue of sexuality is often neglected in rheumatology care, health professionals can offer advice and support to reduce the effect of the condition on sexuality. Guidance that can be provided within a clinical setting will be discussed.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6239

### SP0193 NINE YEARS OF MARRIAGE AND THREE IN BED - MYSELF, MY HUSBAND AND MY RA

C. Zabalan. *Romanian League Against Rheumatism, Bucharest, Romania*

The most difficult adjustment within a life-threatening chronic illnesses and disabilities involves sexual activities.
Communicating openly and directly with partners, doctors and other health care professionals is not always easy in this field. People often have trouble discussing sexual issues or simply feel lucky to manage on their own in the daily program, therefore, as if they don't have the right to "complain" about changes in sexual functioning.
Problems that we ran into everyday, problems like joint movement limitations, chronic pain, chronic fatigue, weakness, stiffness, decreased mobility, decreased libido, altered genital sensation, vaginal dryness, side effects from medications (for example, risk for infections, weight gain or bloating) they affect all aspects of our lives (personal, family, professional and social) - they all can affect our self-esteem, self-image and, of course, our sexuality. We have negative moods, we have feelings like resentment, anger, guilt, grief, blame, depression, fears of isolation and of being rejected sexually, worries about sexually satisfying one's partner...
Solutions like acceptance, 100% communication, an individualized physical activity, planning the intercourse, devoting plenty of time to foreplay, devising a communication code for pain and pleasure, comfortable and safe positions, alternate ways to enjoy sex, learning some of the 64 Kama Sutra techniques and mastering some of the ancient arts a courtesan used to know, using sex toys and sex toy adjustments ... are all here, presented in my personal view.



**Conclusion:** Arthritis can lead to various sexual problems that require constant adjustment on the part of the individual with arthritis and the couple. But keeping in mind that "*our most powerful sex organs, as they always say, are our minds" will make us feel self-worth and will reassure ourselves that we are deserving a strong, loving, committed emotional and physical relationship.*
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6241

**SATURDAY, 11 JUNE 2016**

## Bone and heart: common molecular mechanisms in osteoporosis and atherosclerosis

### SP0194 DO BONE EROSIONS RESULT FROM LOCAL SYNOVITIS OR BONE MARROW EDEMA?

P. Geusens. *Rheumatology, MUMC&UHasselt, Maastricht & Hasselt, Belgium*

Bone erosions are one of the hallmarks in the diagnosis, prediction and follow-up in RA and other inflammatory rheumatic diseases, such as SpA, erosive hand OA and gout.
Osteoclast activation is the final pathway leading to bone destruction. Why bone erosions in RA occur by preference at the peri-articular regions of finger joints is unclear. The cortex at the finger joints is extremely thin and is, in the bare area, not covered by cartilage or periost, and is therefore easily susceptible for developing erosions. The classical outside-in hypothesis considers synovitis as the primary trigger, which attracts osteoclasts from the circulation, resulting in bone erosions at the bare area and beneath articular cartilage and secondary bone marrow edema (BME). In contrast, the inside-out hypothesis considers bone marrow involvement as the primary trigger. A first argument is the role of ACPA antibodies produced by B-cells: they are able to directly stimulate osteoclasts, are present more than 10 years before clinical RA, and, in subjects with ACPA, bone erosions occur before the clinical onset of arthritis. Second, peri-articular bone loss precedes the occurrence of erosions. Third, BME precedes clinical RA, predicts future erosions and consists of lymphocytic inflammatory infiltrates. Other hypotheses include the role of mechanical stress, as erosions are mostly found at the radial and ulnar site of MCP's, the main location of peri-articular entheses.
However, bone erosions are also frequently found in healthy controls (HC), using conventional radiography (CR), MRI, ultrasound (US) and high-resolution peripheral quantitative computer tomography (HRpQCT). In normal conditions, the only well documented peri-articular cortical breaks are blood vessels that perforate bone from the periost toward the bone marrow at the epiphyses, proximal and distal to the growth plate. These vascular connections enable a direct local communication between bone marrow and synovium. In the context of the above hypotheses, pre-existing vascular connections and angiogenesis stimulated by inflammation could predestine the occurrence of erosions at these pre-existing vascular channels.
In SpA, bone erosions are preceded by BME in the SI joints and at the entheses of the vertebrae and peripheral joints. Here the hypothesis is that mechanical stress at the entheses is a predilection site for inflammation and bone destruction. Again, the predictive value of the presence of BME for developing erosions suggests that inflammation in the bone marrow could precede the occurrence of erosions.
Currently, CR of the hands and feet are the gold standard for imaging bone erosions in RA in research and clinical practice settings. However, CR is less sensitive in detecting bone erosions than MRI, US and HRpQCT. In order to better understand the occurrence of bone erosions, the availability of high-resolution 3D imaging, such as HRpQCT, and other techniques, such as PET-scan using specific inflammation markers, will allow more insights in the above hypotheses and should be studied in prospective studies in RA and in other rheumatic diseases with risk of bone destruction.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6420

### SP0195 OSTEOPOROSIS AND CARDIOVASCULAR DISEASE

W.F. Lems. *Amsterdam Rheumatology and immunology Centre, Amsterdam, Netherlands*

Both osteoporotic fractures and cardiovascular events can be devastating events, which are more commonly in the elderly. This could be related to some risk factors that play a role in the pathogenesis of both events: postmenopausal estrogen deficiency, smoking, immobility and low-grade inflammation. A systematic review on the association of cardiovascular diseases and osteoporosis in the general population will be mentioned. The relationship between osteoporotic fractures and cardiovascular events could be even stronger in patients with systemic inflammatory diseases such as RA or AS. Finally, it will be discussed whether in patients with a recent cardiovascular event, it is useful to screen for underlying osteoporosis, and whether in patients with a recent fracture, cardiovascular risk factors should be determined.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6307

**SATURDAY, 11 JUNE 2016**

## Adiposity as a driver of arthritis through inflammatory mechanisms

### SP0196 OBESITY AND DIET IN EXPERIMENTAL MODELS OF OA

T. Griffin. *Aging and Metabolism, Oklahoma Medical Research Foundation, Oklahoma City, United States*

Obesity is a significant modifiable risk factor for osteoarthritis in both weight bearing and non-weight bearing joints. Pre-clinical animal models of diet-induced obesity and genetic models of obesity provide new insight into the pathogenesis of obesity-induced osteoarthritis and the underlying cellular and molecular mechanisms involved in this process. Multiple mechanisms appear to be responsible for this increased risk, including biomechanical, inflammatory, post-traumatic, genetic, and metabolic factors. A central finding of many of these studies is that increased dietary lipids and adiposity promote osteoarthritis pathology, even independent of weight gain. Adipose tissue inflammation is considered a central mechanism by which obesity increases osteoarthritis risk, and I will present evidence from the literature and our recent findings that explore this link in obese animal models, focusing on systemic versus local sources (e.g., abdominal versus infra-patellar fat pad). These findings indicate that the infra-patellar fat pad is a source of inflammatory mediators but does not recapitulate the pathogenesis of inflammation that occurs with abdominal adiposity. Additional evidence suggests that obesity alters pathways regulating chondrocyte metabolism. I will discuss these findings and present a working model for how obesity-associated increases in chondrocyte lipid metabolism may impair the homeostatic response of chondrocytes to biomechanical and inflammatory stresses.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6291

**SATURDAY, 11 JUNE 2016**

## EULAR educational offer

### SP0197 EULAR EDUCATIONAL OFFER: WHERE ARE WE NOW?

E. Hachulla. *National Reference Centre for Rare Autoimmune and Systemic Diseases, University of Lille, Claude Huriez Hospital, Lille, France*

Education is one of the major commitments of EULAR. Over time EULAR has developed a broad educational program which today includes courses, both physical and online, rheumatology textbooks, DVDs demonstrating diagnostic and treatment practices, as well as workshops and young rheumatologist sessions scheduled at the annual EULAR congress. In addition, EULAR provides various forms of education and training grants to individuals.
Listed below is an overview of the current offers:
**EULAR Live Courses**
EULAR ultrasound course
EULAR ultrasound trainer course
EULAR epidemiology course
EULAR postgraduate course
EULAR capillaroscopy course
**EULAR Scientific Endorsement**
Course on systemic lupus erythematosus
European workshop for rheumatology research (ewrr)
**EULAR On-Line Courses**
EULAR on-line course on rheumatic diseases
EULAR on-line course on connective tissue diseases
EULAR on-line course on systemic sclerosis
EULAR on-line introductory ultrasound course
EULAR on-line course in paediatric rheumatology
EULAR on-line course for health professionals
Except for the rheumatic diseases on-line course, which lasted 2 years (with 42 Modules), all other courses correspond to a one-year training course (with 7 to 10 Modules each).
Each module consists of:
– a main review text including learning objectives, pictures, summary points and key references
– at least two in-depth discussions expanding on clinical problems
– two interactive clinical cases with questions and answers
– assessment questions at the end of each module
**The EULAR Bookshelf**
EULAR textbook on rheumatic diseases
EULAR textbook on systemic sclerosis
Coming soon: EULAR textbook on paediatric rheumatology
Musculoskeletal ultrasound in rheumatology
Atlas of capillaroscopy in rheumatic diseases
EULAR training DVDS: Principles of the musculoskeletal history and examination and a second one dedicated to the GALS examination (G = gait, A = arms, L = legs, S = spine)

**EULAR Educational Grants**
Training bursaries for young rheumatologists
Educational visits for health professionals in rheumatology
**EULAR Fellow Sessions During the Annual Congress**
**EULAR Awards presented at the Annual Congress**
**EMEUNET:** the Emerging EUlar NETwork, is a EULAR working group of young clinicians and researchers in rheumatology promoting education and research
Further information: http://www.eular.org/edu_publications.cfm
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6411

## SP0198 A MASTERCLASS ON ASSESSMENT QUESTIONS IN ONLINE COURSES

C. Haines. *The Medical School, The university of Nottingham, -Nottingham, United Kingdom*

The Educationalist for EULAR, Catherine Haines, will give a brief summary of the crucial importance of assessment in ensuring effective practice for newer entrants to the specialism. The session is suitable for all who are involved in the educational processes in EULAR, including trainees and will focus on:
- why skilled assessment is important
- golden rules for skilled assessment
- quick ways to generate skilled assessment questions

**Disclosure of Interest:** None declared
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## SP0199 DEVELOPMENTS IN EULAR EDUCATIONAL PROJECTS IN ULTRASOUND

E. Naredo. *Rheumatology, Hospital GU Gregorio Marañón, Madrid, Spain*

Over the last two decades, an increasing number of rheumatologists have progressively incorporated musculoskeletal ultrasound (MSUS) as a valuable diagnostic and monitoring tool in their clinical practice and research. US is also expanding its applications to new anatomic regions of importance in rheumatologic practice such as large vessels, salivary glands, ligaments, and peripheral nerves. In the first decade of the 21st century, the increasing utility of MSUS in rheumatology has led to a great demand for appropriate education in this imaging modality among rheumatologists worldwide. The European League Against Rheumatism (EULAR) has promoted for many years education in MSUS among rheumatologists in Europe and other continents. The EULAR has supported many educational projects in MSUS such as the development of the content and conduct of a high-quality multi-level MSUS training programme that culminates with a competency assessment systems for rheumatologic MSUS. In addition, EULAR qualifies European centres to become part of a network of Imaging training centres which includes MSUS. Currently EULAR is developing an Imaging Library that will offer images from the wide spectrum of imaging modalities used in rheumatology for the purpose of learning or teaching.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6207

## SP0200 COMPETENCY ASSESSMENT IN US: AN EXAMPLE OF QUALIFICATION OFFERED BY EULAR

A. Iagnocco. *Sapienza Università di Roma, Rome, Italy*

The use of musculoskeletal ultrasound in rheumatology clinical practice has become widespread with increasing demand from rheumatologists attending EULAR Sonography Courses and participating in educational activities in the field. However, musculoskeletal ultrasound is widely considered an operator dependent imaging technique for which high level training and appropriate competency assessment are crucial in order to ensure the quality of ultrasound examinations. EULAR offers a huge educational programme in musculoskeletal ultrasound, with a number of own branded multi-level live sonography courses and an online introductory course on ultrasound, of which high quality structure and content is ensured. In addition, EULAR grants “scientific endorsement” as a mark of scientific quality to selected courses organised by established experts. Moreover, EULAR guidelines and recommendations on how to perform musculoskeletal ultrasound in rheumatology, and for the content and conduct of ultrasound, including teach-the-teachers, courses have recently been published, thus filling a knowledge gap in the field.
There was however, still the need for assessing the level of competency of delegates attending these educational courses in order to improve and regulate the skills of rheumatologists performing ultrasound. As a result, the EULAR competency assessment in musculoskeletal ultrasound in rheumatology was launched in 2015 with this objective. This new system represents an example of certification offered by EULAR and is based on 2 levels of competency: 1) Level 1 (i.e. the minimum level required to independently perform full rheumatologic musculoskeletal ultrasound, the contents of which are included in the EULAR online, basic, intermediate and advanced courses). 2) Level 2 (i.e. the minimum level required to teach musculoskeletal ultrasound). The EULAR faculty, a group of highly qualified and experienced experts in the field, assess the attendees of the annual EULAR sonography and teach-the teachers courses in order to provide EULAR certification approving their level of competency. All these procedures are regulated by rules available on the EULAR web site (www.eular.org).
The competency assessment requirements are reported below:
**Level 1**
- To complete the EULAR online MSUS course successfully.
- To attend the Basic and Intermediate EULAR MSUS course, or equivalent EULAR scientifically endorsed MSUS course and the Advanced EULAR MSUS course with a maximum of 2 years in between each course.
- To perform and document a minimum of 10 standardized complete MSUS examinations of each joint region (i.e. shoulder, elbow, wrist&hand, hip, knee, ankle&foot) of different normal subjects, after having attended the Basic MSUS course (EULAR or EULAR endorsed).
- To perform a minimum of 200 documented MSUS examinations of different anatomic areas(i.e. shoulder, elbow, wrist&hand, hip, knee, ankle&foot) of different patients with rheumatologic diseases that covers the full range of conditions included in the basic and intermediate level, after having attended the Intermediate MSUS course.
- The latter requirement of performing normal and pathological ultrasound images can be replaced with the achievement of level 1,2 or 3 of MSUS competency in rheumatology as stated by EFSUMB (European Federation of Societies for Ultrasound in Medicine and Biology). (Ref. Terslev L, et al. Ultraschall in Med; published online May 21, 2013;www.efsumb.org/guidelines)
- To successfully pass a practical exam that takes place during the Advanced EULAR MSUS course.

**Level 2**
- To have achieved level 1 competency.
- To attend the annual EULAR MSUS Teach the Teacher course and successfully pass the theoretical and practical examination on MSUS teaching capability that takes place during said course.
- The level 2 competency certification can be delivered under particular circumstances (and after having verified the particular requirements, by the EULAR Faculty members) to MSUS experts who have been a teacher in a EULAR MSUS Teach the Teacher course within the previous 3 years or have been a teacher in three Intermediate/Advanced EULAR MSUS courses within the previous 5 years.

Key messages:
- Appropriate training and competency assessment are highly important to ensure an appropriate and skilled use of musculoskeletal ultrasound by rheumatologists
- The EULAR competency assessment in musculoskeletal ultrasound represents a unique opportunity to guarantee a high level of competency of rheumatologist ultrasonographers

**Disclosure of Interest:** None declared
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**SATURDAY, 11 JUNE 2016**

# There is more than drugs

## SP0201 SPORT AND EXERCISE FOR ARTHRITIS PATIENTS

K. Pfeifer. *Institute of Sport Science and Sport, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany*

The positive health enhancing effects of exercise, physical activity (PA), and sport for the general population as well as for persons with musculoskeletal diseases like osteoarthritis or rheumatoid arthritis are indisputable. High potential lies in activating biopsychosocial exercise interventions that target long-term changes of physical activity behavior, and thus think beyond short intervention periods with mostly short-term effects on physical functions. Those behavioral interventions are related to the framework of the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization (WHO) and consider – in addition to the classical target area of restoration of body functions and structures – relevant activities and aspects of participation as well as personal context factors. Based upon recent psychological health behavior change (HBC) theories and using the principles of intervention mapping we identified 28 exercise-related techniques that impact relevant modifiable personal factors of PA. Together with classical exercise components these techniques were integrated into an ICF-based concept of a “Behavioral Exercise Therapy” (BET). This concept serves as a theory-driven “tool box” for designing complex BET programs to promote PA and to build and strengthen individual movement-related health competence. In BET relevant contents and methods are didactically arranged on three intervention levels to enable the development of movement-related health competence: 1) physical exercise and training, 2) learning/education, and 3) experience. Movement-related health competence is composed of the three components movement competence, control competence and self-regulation competence. It is regarded as a personal resource for the movement and mobility demands in daily life, for autonomous health enhancing physical activity and sport, and for coping with or adjustment to health disorders and diseases.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6224

## SP0202 PSYCHONEUROIMMUNOLOGY: FROM PSYCHE TO IMMUNE ACTIVITY AND BACK

C. Schubert. *Clinic for Medical Psychology, Medical University Innsbruck, Innsbruck, Austria*

Current biomedical thinking is characterized by mind-body dualism and reductionism. Psychoneuroimmunology (PNI) is a modern research area of psychosomatic medicine which tries to overcome such paradigmatic engravings. PNI investigates the interrelationship between psychological factors and stress system activities. In normal individuals, chronic psychosocial stress is associated with increased releases in cortisol (hypercortisolism), lower levels in T helper type 1 (TH1) and higher levels in T helper type 2 (TH2) immune activity. Such stress-induced TH1/TH2 shift promotes diseases in which TH1 is protective (e.g. virus infection) and TH2 is damaging (e.g. allergy). In traumatized patients, stress system functioning is disturbed which is associated with blunted cortisol decreases (hypocortisolism) and inflammation increases under stressful conditions. Inflammation increases, on the other hand, trigger behavioral symptoms related to atypical depression (e.g. fatigue). Investigating bidirectional PNI effects (from psyche to immune, from immune to psyche) is not possible by applying biomedical research approaches (e.g. pre-post design). PNI findings from integrative single-case studies on lupus patients will be presented.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6433

## SP0203 HOW THE DANISH RHEUMATISM ASSOCIATION WORKS WITH COMPLEMENTARY AND ALTERNATIVE TREATMENT

D.J. Pedersen on behalf of Henriette Thorseng. *The Danish Rheumatism Association, Gentofte, Denmark*

In The Danish Rheumatism Association, complementary and alternative treatment, is a subject of great interest and demand among people affected by rheumatic and musculoskeletal diseases (RMDs).

We offer free information about complementary and alternative treatment on our website, and free counselling from our mailbox and hotline advice service. Our overall approach is open-minded; we neither recommend nor advice against the use of such treatments, as documentation often is insufficient.

In our conducted surveys, we have investigated the relationship between people with RMDs and complementary and alternative treatment, to learn more about the use and experience. From these surveys we know, that people with RMDs use such treatments more often than the general population.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6212

# Scientific Abstracts

# Oral Presentations

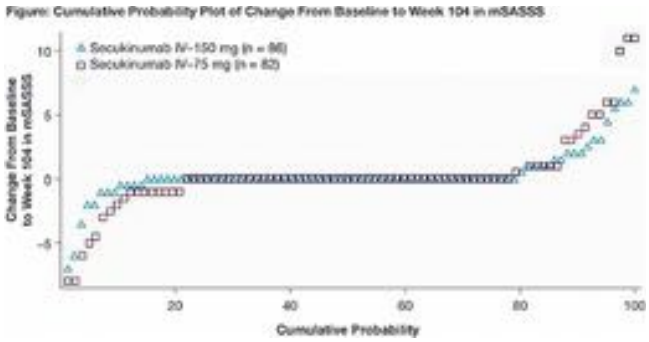
**WEDNESDAY, 8 JUNE 2016**

## Axial spondyloarthritis and psoriatic arthritis: emerging pathways

### OP0001 EFFECT OF SECUKINUMAB, AN INTERLEUKIN-17A INHIBITOR, ON SPINAL RADIOGRAPHIC CHANGES THROUGH 2 YEARS IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS OF THE PHASE 3 STUDY, MEASURE 1

J. Braun[1], X. Baraliakos[1], A. Deodhar[2], D. Baeten[3], J. Sieper[4], P. Emery[5], Z. Talloczy[6], R. Martin[6], H.B. Richards[7]. *[1]Rheumazentrum Ruhrgebiet, Herne, Germany; [2]Oregon Health & Science University, Portland, United States; [3]Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; [4]Charité University Medicine Berlin, Berlin, Germany; [5]Leeds Musculoskeletal Biomedical Research Unit/Institute Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [6]Novartis Pharmaceuticals Corporation, East Hanover, United States; [7]Novartis Pharma AG, Basel, Switzerland*

**Background:** Inhibition of radiographic spinal changes, which are primarily osteoproliferative in nature in active ankylosing spondylitis (AS), represents a main goal of therapy.
**Objectives:** To assess the effects of secukinumab on radiographic progression up to 104 weeks (wks) in the MEASURE 1 trial (NCT01358175).
**Methods:** In MEASURE 1, 371 patients (pts) with active AS were randomized to secukinumab or placebo (pbo). Pts on secukinumab received a 10 mg/kg intravenous (i.v.) loading dose at baseline (BL), Wks 2 and 4, and then 150 or 75 mg subcutaneously (s.c.) every 4 wks (q4w) from Wk 8. Pbo was given on the same schedule. Pbo pts were re-randomized to secukinumab 150 or 75 mg s.c. q4w based on ASAS20 response at Wk 16 (non-responders switched at Wk 16; responders at Wk 24). Lateral radiographs of the cervical and lumbar spine performed at BL and Wk 104 were read centrally applying the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Two independent readers, blinded to treatment arm and radiograph sequence, scored the images. Pts initially randomized to secukinumab, who had x-rays available at BL and Wk 104 (n=168), were included in this analysis. Observed data are shown.
**Results:** Secukinumab data were pooled for both the 150 mg and 75 mg doses as there were no major differences in radiographic results between the two doses. At BL, 104/168 (62%) pts had syndesmophytes, 105/168 (63%) had elevated (>5 mg/L) CRP levels, 42/168 (25%) were smokers, and 123/168 (73%) were male. The mean (±SD) mSASSS at BL was 10.22±16.62; mean change from BL at Wk 104 was 0.30±2.53. Approximately 80% of pts showed no radiographic progression (mSASSS change ≤0) from BL to Wk 104 (Figure). At Wk 104, new syndesmophytes were found in 3/64 (5%) pts who were without syndesmophytes at BL. Approximately 70% of pts with syndesmophytes at BL developed no additional syndesmophytes through Wk 104. Overall, BL mSASSS and mean mSASSS change at Wk 104 were higher in males (mean change 0.38±2.79 vs 0.08±1.58 in females), those with BL syndesmophytes (0.47±3.20 vs 0.02±0.26 in pts with no BL syndesmophytes), or elevated CRP levels at BL (0.47±2.66 vs 0.02±2.27 in pts with normal CRP levels). There were no major differences between the secukinumab only and pbo→secukinumab groups in terms of mSASSS change through Wk 104. Inter- and intra-reader agreement on mSASSS scores was 85% (Kappa 0.70) for both.




**Conclusions:** In secukinumab-treated pts, the mean change in mSASSS was low, with no major difference between doses. Changes were higher in pts who were male, had BL syndesmophytes, or elevated BL CRP. No radiographic progression was observed in ~80% of the pts receiving secukinumab over 104 wks. This is the first report of interleukin-17A inhibition on structural changes in patients with AS.
**Acknowledgement:** The study was sponsored by Novartis Pharma AG.
**Disclosure of Interest:** J. Braun Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Consultant for: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, X. Baraliakos Grant/research support from: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, Consultant for: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, Speakers bureau: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, A. Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer, UCB, D. Baeten Grant/research support from: Boehringer Ingelheim, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Boehringer Ingelheim, BMS, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, UCB, J. Sieper Grant/research support from: AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, Consultant for: AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, P. Emery Consultant for: AbbVie, BMS, Merck, Novartis, Pfizer, Roche, UCB, Z. Talloczy Shareholder of: Novartis, Employee of: Novartis, R. Martin Shareholder of: Novartis, Employee of: Novartis, H. Richards Shareholder of: Novartis, Employee of: Novartis
**DOI:** 10.1136/annrheumdis-2016-eular.3177

### OP0002 TOFACITINIB IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A PHASE 2, 16-WEEK, RANDOMISED, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

D. van der Heijde[1], A. Deodhar[2], J.C. Wei[3], E. Drescher[4], D. Fleishaker[5], T. Hendrikx[6], D. Li[6], S. Menon[5], K. Kanik[5]. *[1]Department of Rheumatology, Leiden University Medical Centre, Leiden, Netherlands; [2]Division of Arthritis & Rheumatic Diseases, Oregon Health & Science University, Portland, United States; [3]Division of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital, Taichung, Taiwan, Province of China; [4]Csolnoky Ferenc Hospital, Veszprém, Hungary; [5]Pfizer Inc, Groton; [6]Pfizer Inc, Collegeville, United States*

**Background:** Tofacitinib is an oral JAK inhibitor that has been investigated for the treatment of ankylosing spondylitis (AS).
**Objectives:** To investigate for the first time the effects of tofacitinib in adult patients (pts) with active AS.
**Methods:** This was a 16-week (wk), Phase 2, multicentre, randomised, double-blind, placebo (PBO)-controlled, dose-ranging study (NCT01786668) to investigate efficacy, safety and dose-response of tofacitinib in pts with AS. Pts fulfilling the modified New York criteria (central read) were randomised 1:1:1:1 to PBO or tofacitinib 2, 5 or 10 mg BID for 12 wks plus 4 wks follow-up. Primary efficacy endpoint was ASAS20 response rate at Wk 12 using a 3-parameter Bayesian $E^{max}$ model by assuming a monotonic response. Secondary endpoints included ASAS40 response rate, AS disease activity score using C-reactive protein (ASDAS), Bath AS disease activity index 50% (BASDAI50) response rate, Bath AS functional index, Bath AS metrology index (linear method), Spondyloarthritis Research Consortium of Canada (SPARCC) score of sacroiliac (SI) joints and spine. Safety endpoints included adverse events (AEs) and laboratory outcomes.
**Results:** 208 pts were randomised and 207 treated; 196 pts completed the study. 51 pts (PBO group) and 52 (each tofacitinib group) were included in analyses. Baseline demographics and disease characteristics were balanced between groups and typical of AS populations (87.4% HLA-B27 positive; 81.2% white; 69.1% male; mean age 42 years; mean disease duration 6.3 years; mean BASDAI 6.7).
The table summarises safety and efficacy results. The ASAS20 $E^{max}$ model showed tofacitinib 10 mg BID had a high response rate and its confidence bounds met a pre-specified efficacy decision rule. ASAS20 response rates by NRI were significantly greater with tofacitinib 5 mg BID vs PBO, compared with 2 or 10 mg BID. All tofacitinib groups had ASAS40, ASDAS and BASDAI50 improvements of similar magnitude vs PBO. Tofacitinib 2 mg BID did not differ vs PBO in remaining clinical efficacy measures or SPARCC scores. Tofacitinib 5 and 10 mg BID had greater clinical efficacy vs PBO, with minimal differences between doses, and significantly improved SPARCC SI joint and spine scores vs PBO.
No tofacitinib-related safety issues unique to the AS population or new safety concerns were identified. Two treatment-related herpes zoster cases were reported (1 each with tofacitinib 2 and 10 mg BID). No cases of tuberculosis,

malignancy, gastrointestinal perforation or death were reported. Dose-dependent changes in laboratory outcomes commonly reported in other tofacitinib studies were observed and returned to approximately baseline values by Wk 16.

**Table. Summary of efficacy and safety endpoints**

| | Placebo (n=51) | Tofacitinib 2 mg BID (n=52) | Tofacitinib 5 mg BID (n=52) | Tofacitinib 10 mg BID (n=52) |
|---|---|---|---|---|
| ***Primary endpoint ASAS20 $E_{max}$ model estimate[a]*** | | | | |
| ASAS20 response rate, % | 40.1 | 56.0 | 63.0 | 67.4 |
| ASAS20 response rate vs placebo, % | N/A | 15.8 | 22.9 | 27.3 |
| 50% credible interval | | (31.1, 39.9) | (17.8, 28.0) | (21.8, 33.0) |
| 60% credible interval | | (30.2, 21.2) | (16.5, 29.3) | (20.3, 34.4) |
| 95% credible intervals | | (5.0, 30.3) | (8.4, 37.7) | (10.7, 43.4) |
| ***Secondary efficacy endpoints at Week 12*** | | | | |
| ASAS20 response rate (%), by NRI[b] | 41.2 | 51.9 | 80.8*** | 55.8 |
| ASAS40 response rate (%), by NRI[b] | 19.6 | 42.3* | 46.2** | 38.5* |
| CfB in ASDAS, LS mean (SE) | -0.7 (0.1) | -1.2 (0.1)** | -1.4 (0.1)*** | -1.4 (0.1)*** |
| BASDAI50 response rate (%), by NRI[b] | 23.5 | 46.2* | 42.3* | 42.3* |
| CfB in BASFI, LS mean (SE) | -1.4 (0.3) | -1.9 (0.3) | -2.4 (0.3)* | -2.2 (0.3)* |
| CfB in BASMI, LS mean (SE) | -0.2 (0.1) | -0.3 (0.1) | -0.4 (0.1) | -0.6 (0.1)* |
| CfB in SPARCC MRI of the SI joints, LS mean (SE) | -0.8 (0.8) | -1.7 (0.8) | -3.2 (0.8)* | -3.6 (0.8)* |
| CfB in SPARCC MRI of the spine, LS mean (SE) | -0.1 (1.1) | -3.1 (1.1) | -5.5 (1.1)*** | -6.6 (1.1)*** |
| ***Safety endpoints*** | | | | |
| TEAEs, n (%) | 22 (43.1) | 23 (44.2) | 28 (53.8) | 27 (51.9) |
| Treatment related | 14 (27.5) | 14 (26.9) | 12 (23.1) | 14 (26.9) |
| Serious AEs, n (%) | 2 (3.9) | 0 | 1 (1.9) | 1 (1.9) |
| Treatment related | 1 (2.0)[c] | 0 | 0 | 0 |
| Discontinuations due to AEs, n (%) | 3 (5.9) | 0 | 1 (1.9) | 1 (1.9) |
| Treatment related | 2 (3.9)[d] | 0 | 1 (1.9)[e] | 1 (1.9)[f] |
| AST >3x ULN, n (%)[g] | 1 (2.0) | 0 | 3 (5.8) | 0 |
| ALT >3x ULN, n (%)[g] | 1 (2.0) | 0 | 2 (3.8) | 1 (2.0) |
| Week 12 CfB in serum creatinine, g/dL, mean (SD) | 0.0 (0.1) | 0.0 (0.1) | 0.0 (0.1) | 0.1 (0.1) |
| Week 12% CfB in LDL-C, mean (SD) | -1.2 (15.8) | 7.2 (13.5) | 9.6 (21.0) | 23.5 (28.3) |
| Week 12% CfB in HDL-C, mean (SD) | 1.0 (17.4) | 10.0 (15.1) | 11.0 (18.6) | 18.5 (17.0) |
| Week 12 CfB in ANC, cells $10^3$/mm$^3$, mean (SD) | -0.3 (1.2) | -0.3 (1.6) | -0.3 (1.4) | -0.9 (1.6) |
| Week 12 CfB in ALC, cells $10^3$/mm$^3$, mean (SD) | 0.0 (0.4) | 0.1 (0.4) | -0.1 (0.4) | 0.0 (0.4) |
| Week 12 CfB in Hb, g/dL, mean (SD) | -0.2 (0.6) | 0.1 (0.6) | 0.3 (0.7) | 0.1 (0.9) |

*p<0.05, **p<0.01, ***p<0.001

[a]NRI/LOCF [b]vertigo [c]spinal pain (placebo), hypertransaminasemia (placebo), peripheral swelling (tofacitinib 5 mg BID), herpes zoster (tofacitinib 10 mg BID) [d]50, 51, 52 and 50 patients receiving PBO, and tofacitinib 2, 5 and 10 mg BID, respectively were included in this analysis.

AE, adverse event; ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; ASAS, assessments in ankylosing spondylitis improvement; ASDAS, ankylosing spondylitis disease activity score using C-reactive protein; AST, aspartate aminotransferase; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; BASMI, Bath ankylosing spondylitis metrology index (linear method); BID, twice daily; CfB, change from baseline; Hb, haemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LOCF, last observation carried forward; LS, least squares; N/A, not applicable; NRI, non-responder imputation; SD, standard deviation; SE, standard error; SPARCC, Spondyloarthritis Research Consortium of Canada; TEAE, treatment-emergent AE; ULN, upper limit of normal.

**Conclusions:** Tofacitinib 5 and 10 mg BID demonstrated greater clinical and imaging efficacy vs PBO in reducing the signs and symptoms of AS in adults with active AS. Safety was similar to that reported for tofacitinib studies in other indications.

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**WEDNESDAY, 8 JUNE 2016**

## Balancing benefits and risk of glucocorticoids; a challenge for implementation

### OP0003 DEVELOPMENT OF A GLUCOCORTICOID TOXICITY INDEX USING MULTI-CRITERIA DECISION ANALYSIS

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**Background:** Glucocorticoids (GC) are associated with substantial treatment morbidity. New immunomodulatory agents offer the possibility of limiting GC exposure. To assess the comparative benefits of such agents, investigators must accurately measure their ability to prevent or reverse GC-related toxicity. No comprehensive instrument for measuring GC toxicity has previously been developed.

**Objectives:** We aimed to develop a GC Toxicity Index (GTI) to assess GC-related morbidity and GC-sparing ability of new agents. Intermediate aims were to 1) define toxicity items for inclusion in the GTI 2) assign relative weights to items and 3) begin the validation process.

**Methods:** 22 physician experts from 11 subspecialties with extensive experience in the clinical use, pharmacology, and toxicity of GCs were invited, and 19 participated. Ten investigators were from the United States and 9 were from Canada, Europe, or Australia. Group consensus methods and multi-criteria decision analysis using forced-choice technique (1000Minds platform) were utilized. The development process included ten 1-hour conference calls and a 12-hour face-to-face meeting.

*GTI components:* The GTI is composed of the Composite GTI (CGTI) and the Specific List. The CGTI reflects GC toxicity that is likely to change over the course of a trial and is designed to distinguish between low and high GC users. The toxicities included in the CGTI vary with GC exposure and are expected to occur in >5% of patients over the course of a clinical trial lasting 6 months to 3 years. The items in the CGTI are weighted and scored. The Specific List is designed to capture GC toxicity not included in the CGTI. Toxicities in the Specific List are comparatively less common and – although impactful for patients – are less likely to contribute to delineating between high and low dose GC regimens. Items of the Specific List are therefore tabulated but not weighted.

**Results:** *Item inclusion and definitions:* Thirty-one toxicity items derived from the literature and reviewed by the investigators were included in the CGTI, and 23 were included in the Specific List (Figure). The CGTI items reflect both improvement and worsening of GC toxicity and account for medication effects (e.g., anti-hypertensives) in scoring. The 31 mutually-exclusive CGTI items are organized in order of severity within nine domains. Only one item in each domain can be scored.

**Figure – Glucocorticoid Toxicity Index (GTI) composed of weighted CGTI and Specific List***

| Composite GTI | Item Weight | Specific List |
|---|---|---|
| **Body mass index** | | |
| Improvement in BMI | -8 | Major increase in BMI |
| No change in BMI | 0 | |
| Moderate increase in BMI | 21 | |
| Major increase in BMI | 36 | |
| **Glucose tolerance** | | |
| Improvement in glucose tolerance | -8 | Diabetic retinopathy |
| No change in glucose tolerance | 0 | Diabetic nephropathy |
| Worsening of glucose tolerance | 32 | Diabetic neuropathy |
| Worsening of glucose tolerance despite treatment | 44 | |
| **Blood pressure** | | |
| Improvement in blood pressure | -10 | Hypertensive emergency |
| No change in blood pressure | 0 | Posterior reversible encephalopathy syndrome |
| Worsening hypertension | 19 | |
| Worsening hypertension despite treatment | 44 | |
| **Lipids** | | |
| Improvement in lipids | -9 | |
| No change in lipids | 0 | |
| Worsening hyperlipidemia | 10 | |
| Worsening hyperlipidemia despite treatment | 30 | |
| **Bone density** | | |
| Improvement in bone density | -1 | Insufficiency fracture |
| No change in bone density | 0 | Major decrease in bone density |
| Decrease in bone density | 29 | |
| **Steroid myopathy** | | |
| No steroid myopathy | 0 | Severe steroid myopathy |
| Mild steroid myopathy | 9 | |
| Moderate steroid myopathy or greater | 63 | |
| **Skin toxicity** | | |
| No skin toxicity | 0 | Severe skin toxicity |
| Mild skin toxicity | 8 | |
| Moderate skin toxicity or greater | 26 | |
| **Neuropsychiatric toxicity** | | |
| No neuropsychiatric symptoms | 0 | Psychosis |
| Mild neuropsychiatric symptoms | 11 | GC-induced violence |
| Moderate neuropsychiatric symptoms or greater | 74 | Other severe neuropsychiatric symptoms |
| **Infection** | | |
| No significant infection | 0 | Grade 4 infection |
| Oral/vaginal candidiasis or uncomplicated zoster | 19 | Grade 5 infection |
| Grade 2 infection or greater | 93 | |
| **Endocrine** | | Adrenal insufficiency |
| **Gastrointestinal** | | Perforation |
| | | Peptic ulcer disease |
| **Musculoskeletal** | | Avascular necrosis |
| | | Tendon rupture |
| **Ocular** | | Central serous retinopathy |
| | | Intraocular pressure elevation |
| | | Posterior subcapsular cataract |
| **Total** | 36 to 439 | |

* Definitions for each item have been developed but are not shown.

*Weighting and evaluation of the CGTI:* Relative weights for each item in the CGTI were derived at a face-to-face meeting utilizing multi-criteria decision analysis (Figure). In order to assess reliability, all participants assigned toxicity items on the CGTI to 15 paper cases. Inter-rater agreement was high (kappa 0.89). To assess the degree to which the CGTI corresponds to expert clinical judgement, participants ranked 15 cases by clinical judgement in order of highest to lowest GC toxicity. Expert rankings were then compared to case ranking by the CGTI, yielding excellent agreement (weighted kappa 0.87).

**Conclusions:** We describe the development and initial evaluation of the GTI - a comprehensive instrument intended primarily for use in prospective, randomized clinical trials for the assessment of GC toxicity. The GTI can be used across clinical disciplines in trials that employ GCs to assess the comparative value of GC-sparing therapies, and to measure the impact of GC toxicity.

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**WEDNESDAY, 8 JUNE 2016**

## What CVD outcomes to use in clinical rheumatological practice?

### OP0004 COLLECTION AND MANAGEMENT OF SELECTED COMORBIDITIES AND THEIR RISK FACTORS IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES IN DAILY PRACTICE IN FRANCE

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**Background:** In chronic inflammatory rheumatic diseases including rheumatoid arthritis, spondyloarthritis and connective tissue diseases, comorbidities such as cardiovascular diseases and infections are sub-optimally prevented, screened and managed. EULAR recently developed points to consider to collect and report comorbidities but did not include the management phase. (ref)

**Objectives:** To develop a pragmatic form to collect, report and give management recommendations for selected comorbidities and risk factors, from a rheumatologist perspective.

**Methods:** Comorbidities were selected by an expert group of 18 persons, using the previous experience of the recent EULAR points to consider for comorbidities. (ref) The collection and reporting of these comorbidities and risk factors were adapted from the EULAR recommendations. (ref) To develop management recommendations, the process comprised (1) systematic literature reviews by 3 fellows and (2) a 2-day consensus process involving 110 experts (rheumatologists and health professionals). Votes of agreement (Likert 1–5 where 5 indicates full agreement) were obtained from the group.

**Results:** The six selected comorbidities were ischemic cardiovascular diseases, malignancies, infections, gastrointestinal diseases, osteoporosis and depression. The literature review retrieved 158 articles, mostly developed for the general population. The consensus process led to a pragmatic reporting form to collect the existence of a comorbidity (eg heart failure yes/no), current treatment (e.g. stent yes/no), risk factors (e.g. hypertension), screening (e.g. mammography) and prevention (e.g. vaccination). Furthermore, existing management recommendations were adapted to rheumatologists (or developed when unavailable) leading to 28 practical forms. These include physical examination elements such as blood pressure or lymph node examination, prescribing screening procedures, and interpreting results to refer in a timely manner to appropriate other health professionals. Agreement was high (mean, 4.37 ± 0.33 on a 1–5 scale).

**Conclusions:** Using an evidence-based approach followed by expert consensus, this initiative furthers the dissemination and the adaptation to a national context of the EULAR comorbidities initiative, and clearly defines what part of the management of comorbidities is potentially within the remit of rheumatologists. The pragmatic developed document should facilitate the periodical systematic review of patients suffering from chronic inflammatory rheumatic diseases. Next steps include dissemination and implementation of this document.

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[1] Baillet A, Gossec L, et al. EULAR points to consider for reporting, screening and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: A EULAR initiative. Annals of the Rheumatic diseases (submitted).

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**Disclosure of Interest:** None declared

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### OP0005 HOW TO IMPLEMENT CARDIOVASCULAR DISEASE RISK ASSESSMENT FOR PATIENTS WITH INFLAMMATORY JOINT DISEASES IN DAILY RHEUMATOLOGY PRACTICE: AN OVERWIEW OF THE NATIONWIDE NOCAR PROJECT

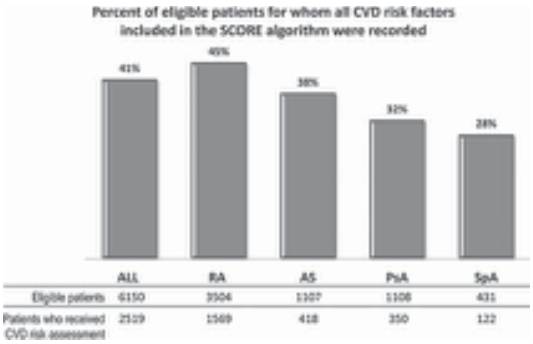
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**Background:** Patients with inflammatory joint diseases (IJD) have a high risk of cardiovascular disease (CVD). The EULAR recommendations for CVD risk management in patients with IJD states that CVD risk assessment should be considered annually in this patient population, and emphasizes that such assessment easily can be incorporated into a routine rheumatology visit. While other patient groups with high CVD risk often have structured programs to ensure adequate CVD prevention, these measures are rarely implemented for IJD patients.

**Objectives:** The aim of the NOrwegian Collaboration on Atherosclerosis in patients with Rheumatic joint diseases (NOCAR) was to design a program of annual CVD risk assessment for IJD patients that could be implemented into routine visits in rheumatology outpatient clinics.

**Methods:** NOCAR was started in April 2014 for quality assurance purposes, and comprises 11 rheumatology centres across Norway. All IJD patients >30 years registered in the electronic patient journal program GoTreatIt® Rheuma (GTI) are eligible. The CVD risk factors recorded in NOCAR are imputed directly into the GTI journal and are collected in a multidisciplinary manner: 1) Patients self-report CVD risk factors, 2) non-fasting lipids are ordered by health secretaries in addition to routine laboratory tests and 3) rheumatology nurses perform blood pressure measurement. Based on the Systematic COronary Risk Evaluation (SCORE) algorithm, GTI automatically calculates the patient's 10-year risk of a fatal CVD event. If the SCORE estimate is ≥5%, the rheumatologist forwards a note to the patient's primary physician to inform that there is indication for initiation of CVD-preventive measures (e.g. medication and lifestyle changes). Additionally, the rheumatologists and rheumatology nurses are instructed in how to deliver brief advice regarding smoking cessation and healthy diet. We report the initial capture rate in 3 NOCAR centres from which visit data was extracted in October 2015. We evaluated how many of the eligible patients who had received a CVD risk evaluation during these first 1.5 years of the NOCAR project. A CVD risk assessment was defined as having recoded all of the CVD risk factors included in the SCORE algorithm (total cholesterol, systolic blood pressure, smoking status, age and sex).

**Results:** Of the 6150 IJD patients (Rheumatoid arthritis [RA]: 3504, ankylosing spondylitis [AS]: 1107, psoriatic arthritis [PsA]: 1108, and other spondyloarthritides [SpA]: 431) who were eligible for the NOCAR project, 2519 (41%) patients received a CVD risk assessment during this 1.5 year interval (RA: 1569 [45%]), AS: 418 [38%], PsA: 350 [32%], SpA: 122 [28%]). The major obstacles to successful implementation encountered in NOCAR were time scarcity; defining a date for annual CVD risk assessment and making sure that lipids were measured before seeing the rheumatologist.




**Conclusions:** To our knowledge, this is the first multi-centre clinical project to show that incorporation of CVD risk assessment into routine rheumatology visits is feasible. Future studies are warranted to elucidate success criteria for optimal implementation of CVD preventive strategies in rheumatology.

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## Different perspectives on pain in osteoarthritis

OP0006-HPR **EVEN IN THE LONG RUN NORDIC WALKING IS SUPERIOR TO STRENGTH TRAINING AND HOME BASED EXERCISE FOR IMPROVING PHYSICAL FUNCTION IN OLDER PEOPLE WITH HIP OSTEOARTHRITIS - AN RCT**

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**Background:** Lack of regular physical activity is a risk factor for functional decline. In hip osteoarthritis, exercise therapy aims to improve patients' overall function. Systematic reviews have shown beneficial effects on pain and physical function from exercise therapy (1) but also that these positive effects are not sustained in the long term (2). The patients' self-efficacy and additional booster sessions offered after the treatment period are factors shown to positively influence physical activity maintenance (3) and beneficial posttreatment effects (2).
**Objectives:** In an observer-blinded, randomized trial to compare the long term effects of 4 months of supervised strength training (ST), supervised Nordic Walking (NW), and unsupervised home based exercise (HBE, control group) on functional performance.
**Methods:** 60+ years old people (n=152; 49 men, 103 women, age 70±6 years) with clinical hip osteoarthritis not on a waiting list for surgery were randomized to ST in a local fitness center (n=50), NW in a local park (n=50) or HBE (n=52). The ST- and NW-groups were offered individual counseling interviews, patient education and telephone-assisted counselling in order to improve adherence and maintenance of exercise/physical activity. Functional performance, i.e. 30s chair stand test (primary outcome), timed stair climbing and 6-minute walk test; and secondary self-reported outcomes, i.e. physical function, pain, physical activity level, self-efficacy and health related quality of life, were measured at baseline, 4- and 12 months.
**Results:** Intention-to-treat-analyses showed equal improvements (mean (95%CI)) after intervention in number of chair stands in all three groups at 4-months (ST: 0.9 (0.2–1.6), NW: 1.9 (0.8–3.0), HBE: 1.1 (0.1–2.0)), while a between-group difference in favor for the NW-group (1.4 (0.0–2.8)) compared to ST-group were present at 12 months. Significant between-group differences ($p<0.001$- $p<0.05$) in favor of NW compared to ST and HBE were found for functional performance at all follow-up time-points. Furthermore, NW was superior ($p<0.01$) to HBE for improving vigorous physical activity and to both ST and HBE for improving ($p<0.01$) mental health at all follow-up time-points, and ($p<0.05$) self-efficacy at 12 months.
**Conclusions:** Based on these results NW can be recommended compared with ST and HBE for older adults with hip osteoarthritis.
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**Disclosure of Interest:** None declared
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## Epigenetics solving the OA puzzle

OP0007 **DEEP RNA SEQUENCING REVEALS ARTHRITIS-SPECIFIC LNCRNA TRANSCRIPTOMES OF SYNOVIAL FIBROBLASTS AT DIFFERENT ANATOMIC LOCATIONS**

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**Background:** A number of susceptibility loci for rheumatoid arthritis (RA) map to noncoding genomic regions. Long noncoding RNA (lncRNA) represent the largest part of noncoding transcriptome and are key regulators of gene expression. We have recently shown that the expression pattern of noncoding RNA in synovial fibroblasts (SF) - one of the key local effector cells in arthritis – is largely determined by anatomic joint location.
**Objectives:** The aim of the present study was to identify arthritis-specific lncRNA transcriptomes of SF at different anatomic locations, focusing on RA and osteoarthritis (OA).
**Methods:** RNA was isolated from cultured SF, passages 5–8, obtained from hands, shoulders and knees of RA and OA patients and knees of non-arthritic patients experiencing joint pain (normal) (n=3 per each group). RNA sequencing (Illumina HiSeq2000) of SF was followed by read alignment to the reference genome and transcriptome (the Ensembl GRCh37, STAR version 2.3.0e_r291), identification of differentially expressed (DE) genes between diagnoses and locations (DESeq2, Bioconductor Version 3.0, log(foldchange) $>|0.5|$, $p<0.01$,) and pathway analysis (Metacore, Thomson Reuters) of DE protein-coding genes.
**Results:** RNA sequencing revealed that ~15.000 protein-coding RNA and 4000 lncRNA are expressed in SF at each joint location. Comparing different joints, 101, 182 and 155 of expressed lncRNA were DE between knee-hand, knee-shoulder and hand–shoulder SF, representing 2.4%, 4.1% and 3.5% of expressed lncRNA, respectively. Furthermore, comparing different diagnoses at each joint location 101 (2.4%) lncRNA were identified as DE between OA-RA hands (e.g. MALAT1, HOXA11-AS), 36 (0.8%) between OA-RA shoulders (e.g. DNAJC3-AS1, MIR29B1), 19 (0.5%) between OA-RA knees (e.g. TBX5-AS1, ITGB2-AS1), 136 (3.5%) between OA-normal knees (e.g. CTC-529P8.1) and 108 (2.6%) between RA-normal knees (e.g. IL21-AS1), respectively, with 51 lncRNA altered in OA and RA vs. normal knee SF. This showed that lncRNA transcriptional programmes of SF in particular differ between OA and RA hands with a difference comparable to that seen between healthy vs. arthritic knees and between anatomic locations. Only a minor number of joint-specific lncRNA were altered by arthritis. Pathway analysis revealed the enrichment of platelet-endothelial-leucocyte adhesion and ECM remodelling networks between RA and OA hands, inflammation – MIF signalling and cytoskeleton-intermediate filaments networks between OA and RA shoulders and chemotaxis and cadherin and integrin adhesion networks between OA and RA knees.
**Conclusions:** Our study identifies joint-specific alterations in stromal synovial lncRNA profiles in RA and OA and shows that in the same type of arthritis different disease pathways are activated at different joint locations. In particular in hands, stromal noncoding transcriptional programmes significantly differ between different types of arthritidis, emphasizing the central role of anatomic location when studying arthritis pathogenesis.
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OP0008 **SYNOVIAL FIBROBLAST PROLIFERATION IS ENHANCED BY MICRORNA-223 DELIVERY THROUGH MONOCYTE-DERIVED MICROPARTICLES**

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**Background:** Microparticles (MPs) have been described to function as extracellular vehicles that shuttle microRNAs (miR) from platelets to endothelial cells[1] and regulate recipient cell gene expression. Crosstalk of synovial monocytes (MC) with synovial fibroblasts (SF) is a key step to the inflammatory process in rheumatoid arthritis (RA).
**Objectives:** Herein, we investigated whether delivery of specific miRs by MC-derived MPs affects RASF behaviour.
**Methods:** Blood samples of healthy volunteers and RA patients were collected. MPs were obtained by differential centrifugation. $CD14^+$ cells were isolated from PBMCs by using positive selection and the cells were stimulated with 50 ng/ml recombinant human M-CSF for 6 days. Scanning electron microscopy, nanosight trafficking analysis and flow cytometry (FACS) have been applied to characterize MPs from human $CD14^+$MCs and THP-1 cells. Total and smallRNA sequencing were performed on macrophages (n=4) and RASFs (n=4) as well as on macrophage-derived MPs (n=4). (Pre-)miR-223 expression and copy number was quantified in cells or tissues via TLDA, qPCR & in situ hybridisation with specific primers and probes. Targeted pathways were identified using prediction algorithms (TargetScanHuman6.2). Transfer of miR-223 from MCs to SFs was determined by fluorescence microscopy, direct cell co-culture and FACS, as well as transwell co-culture. RASF proliferation assays with FGF-2 as positive control, as well as THP-1 derived MPs, miR-223 mimic, miR-223 inhibitor, control mimic and inhibitor were carried out.
**Results:** MPs from MCs & THP-1 cells are about 250nm in size (range 50–800nm). SmallRNA sequencing revealed high levels of miR-223 in macrophages as opposed to a lack of its expression in RASF. If co-cultured with MCs for 3d, RASF acquire miR-223 expression, but not pre-miR-223 to a significant extent (n=6, $C_t$ values $<30$) confirming transfer of mature miR-223 between cells. Prediction algorithms identified FBXW7 as a candidate target for miR-223

in RASF. FBXW7 acts as an ubiquitin ligase targeting cyclin E. Co-culture of RASF with THP-1 derived MPs increased RASF proliferation to a similar extent as FGF-2 (n=8, $p<0.01$). Transfection of RASF with miR-223 inhibitor prior to stimulation with THP-1 MPs abrogates their proliferative effect (n=5, $p<0.05$). miR-223 transfection (25nM & 50nM) itself led to an increase of RASF proliferation after 72 and 96h (n=6–8, $p<0.01$ for all).

**Conclusions:** miR-223 transport from MCs to SFs by MPs represents a novel intercellular mechanism that could stimulate SF proliferation during initiation or chronicity of synovial inflammation in RA.

**References:**

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**Acknowledgement:** We wish to thank Derek Baxter, Diane Vaughan, Margaret Mullin, Pawel Herzyk, Julie Galbraith, Russka Shumnalieva for their support and technical assistance.

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**WEDNESDAY, 8 JUNE 2016**

## Muscle biology & inflammation

### OP0009 DISTINCTIVE IMMUNOFLUORESCENCE PATTERN IN STATIN-ASSOCIATED AUTOIMMUNE MYOPATHY WITH ANTI-HMGCR AUTOANTIBODIES

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**Background:** A statin-associated autoimmune myopathy with anti-HMGCR antibodies has recently been described. Identification of these patients is of paramount importance because immunosuppressive therapy is usually needed for clinical improvement. Herein we report a new pattern of immunofluorescence (IIF) that could alert of the presence of this antibody in routine autoantibody screening on kidney, liver, stomach sections.

**Objectives:** Our objective was to study the concordance of this IIF pattern with anti-HMGCR in a series of patients with immune-mediated necrotizing myopathy (IMNM).

**Methods:** Seventeen patients diagnosed with IMNM positive for anti-HMGCR antibodies were tested for the presence of IIF pattern. As a control group, 90 patients diagnosed with systemic autoimmune diseases (SLE, autoimmune hepatitis, systemic sclerosis, rheumatoid arthritis, Sjögren syndrome, and dermatomyositis – 15 from each group), and 45 patients treated with statins (15 with familial severe dyslipidemia, 15 with a recent cerebrovascular event – treated high dose of atorvastatin, and 15 from the community) were also studied. Anti-HMGCR antibodies were measured by means of two ELISA assays: a in-house confirmed by blot using hidroxi-methil-glutharil-CoA (Sigma H7039) as antigen and commercial QUANTA Lite HMGCR ELISA Innova (San Diego). Indirect immunofluorescence studies on triple tissue (rat liver, kidney and stomach) was performed using Nova Lite assay (Innova Diagnostic, San Diego, USA). We used different commercial substrates (Innova, Euroimmune, ByoSistems, and Aeskulides) in order to confirm that the reactivity of the pattern do not depend on the commercial source. Indirect immunofluorescence on HEp-2 Slides (INOVA Diagnostics, Inc., San Diego Hep-2 ANA slides) was also performed. Immunoabsorption studies were performed using HMGCR human antigen (Sigma, St Louis, MO,USA) at different dilutions (PBS 10%) in those patients with a positive IIF pattern

**Results:** A cytoplasmatic pattern in scattered hepatocytes with perivascular distribution was observed in 15 out of 17 (88%) IMNM positive for anti-HMGCR antibodies. No patients from the autoimmune systemic disease group or those treated with statins disclosed this characteristic pattern. Consequently, the overall agreement between rat triple tissue IIF and ELISA confirmed by blot was 98.7% (kappa 0.93). Dispersed hepatocyte cytoplasmatic pattern (DHCP) was specifically absorbed by incubation with human purified antigen. A granular cytoplasmatic fluorescence pattern was observed in 6 out of 17 (35%) patients with human Hep cells.

**Conclusions:** A new distinctive IIF pattern on routine rat triple tissue is described in patients diagnosed with IMNM whit anti-HMGCR antibodies. It could be useful to alert of the presence of anti-HMGCR antibodies when performing a routine unexpensive autoantibody profile.

**Disclosure of Interest:** None declared

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### OP0010 THIGH MAGNETIC RESONANCE IMAGING REVEALS INCREASED ACTIVE AND CHRONIC MUSCLE DAMAGE IN NECROTIZING MYOSITIS COMPARED TO POLYMYOSITIS AND DERMATOMYOSITIS

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**Background:** The autoimmune myopathies include polymyositis (PM), dermatomyositis (DM), and necrotizing myositis (NM). Patients with clinically amyopathic dermatomyositis (CADM) have the cutaneous features of DM but with minimal or no muscle involvement. Muscle abnormalities can be assessed with magnetic resonance imaging (MRI), which detects edema (a feature of active muscle disease) and fatty replacement (a feature of chronic damage).

**Objectives:** To compare the prevalence of active and chronic muscle damage in patients with DM, PM, NM, CADM, and IBM using thigh MRI (tMRI).

**Methods:** All the patients of the Johns Hopkins Myositis Cohort with an available tMRI that fulfilled criteria for DM, PM, IBM, NM or CADM were included in the study. Fifteen muscles of the gluteal, lateral rotator, anterior, medial and posterior thigh compartments were studied bilaterally. In each muscle, the presence of edema, fatty replacement, and fascial thickening was recorded. We compared the tMRI features of clinical subsets using univariate and multivariate regression analysis. We also studied the effect on the tMRI, independently of the clinical subset, age at onset, sex, race and time from the onset to the tMRI.

**Results:** Six hundred and sixty-seven patients were included in the study (153 IBM, 101 NM, 176 PM, 220 DM and 17 CADM). The prevalence of edema, atrophy, and fatty replacement showed a gradient among different clinical subsets (IBM>NM>PM>DM>CADM). Similar to patients with IBM, tMRI of NM patients revealed more frequent edema (difference >22%), atrophy (difference >27%), and fatty replacement (difference >14%) than in PM or DM. Analysis of the different muscle compartments confirmed that, as previously described, IBM is characterized by fatty replacement and atrophy in the anterior compartment; in contrast, NM was associated with atrophy and fatty replacement in the lateral rotator compartment. Fascial thickening was the hallmark of DM (found in 51%; $p<0.001$) while PM was not associated with any specific pattern. Independent of the clinical subset, increased age at onset was associated with more muscle atrophy ($OR_{10\ years}$=1.2, 95%CI 1.01–1.3), fatty replacement ($OR_{10\ years}$=1.4, 95%CI 1.2–1.6), and muscle edema ($OR_{10\ years}$=1.3, 95%CI 1.2–1.5); the time from the onset of the disease to the tMRI was only associated with fatty replacement ($OR_{10\ years}$=1.7, 95%CI 1.2–2.5).

**Conclusions:** Patients with NM had more frequent edema, fatty replacement, and atrophy on tMRI compared to those with either DM or PM, suggesting that NM is often a more severe, and perhaps undertreated, form of myositis. In NM, fatty replacement occurred most frequently in the lateral rotators, whereas in IBM chronic damage was more frequent in the anterior compartment. As reported in other studies, increased fascial thickening was a hallmark feature of DM. In contrast, the lack of a consistent pattern of muscle involvement suggests that PM is a heterogeneous entity.

**Disclosure of Interest:** None declared

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## Lessons from the children (monogenic causes of autoimmunity)

### OP0011 INDUCED PLURIPOTENT STEM CELL-DERIVED MONOCYTIC CELL LINES FROM CONGENITAL IMMUNOLOGICAL DISORDERS SERVE A VERSATILE PLATFORM FOR PHENOTYPE-BASED COMPOUND SCREENING

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**Background:** One of the main players of immune system and immunological disorders is white blood cells, such as lymphocytes, monocytes, and neutrophils. Although the elucidation of their cellular pathophysiology has been largely based on *in vitro* studies using patient-derived primary hematopoietic cells, this approach has potential limitations. Patient-derived cells cannot be obtained in unlimited quantities, and their *in vitro* functions can be affected by *in vivo* conditions, such as the cytokine milieu or presence of therapeutic agents.

Due to their pluripotency and capacity for self-renewal, human induced pluripotent stem cells (iPSCs) are potential sources of cells for use in drug screening, toxicology testing and the investigation of disease mechanisms [1,2]. However, the phenotypic variance often hampers quantitative functional evaluation of iPS-derived progenies. Moreover, directed differentiation into immune cells financially prohibitive and labor-intensive. One of the solution of these issues is to immortalize iPSC-derived progenitor cells and use these cells as a source of

functional analysis. Here we took advantage of immortalization of iPSC-derived myeloid progenitors (iPS-MLs) that can differentiate into functional macrophages and dendritic cells.
**Objectives:** To overcome the limitations of iPSC-based study for immunological disorders, we are aiming at establishing a versatile and robust platform for disease modeling and high-throughput compound screening system by establishing iPS-MLs.
**Methods:** Generation of iPS cells from congenital immunological disorder patients was performed as described previously [1]. Hematopoietic cell differentiation was performed according to previously described protocols with some modifications [3,4]. For establishment of iPS-MLs, lentiviral constructs encoding *BMI1*, *cMYC* and *MDM2* floating hematopoietic cells differentiated into the monocytic lineage from iPSCs were collected on days 14 or 21. The cells were transfected with the lentiviral vectors encoding *BMI1*, *cMYC* and *MDM2* and subsequently cultured in the presence of M-CSF and. We differentiated the iPS-MLs into macrophages and used for subsequent analysis.
**Results:** We established iPSCs from patients with congenital immunological dysorders such as autoinflammatory syndrome and immunodeficiency. iPSCs were then immortalized immature monocytic progenitors by introducing three transgenes [5]. iPS-MLs expand rapidly and be able to differentiate both macrophages and dendritic cells. By taking advantage of iPS-ML, we constructed phenotypic screening system by evaluating cytokine production or morphological changes in intracellular granules.
**Conclusions:** Our system provides a large number of functional monocytic lineage cells and versatile platform for compound screening for modifying diseases-associated phenotypes. Therefore, it is useful for screening candidate compounds for treatment of congenital immunological disorders associated with monocytic lineage cells.
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## OP0012 MICRORNA ASSOCIATED WITH ACTIVE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS REGULATE CD163 EXPRESSION IN POLARIZED MACROPHAGES THROUGH TWO DISTINCT MECHANISMS

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**Background:** CD163 is a hemoglobin scavenger receptor and serves as a marker of activated monocytes and macrophages. It is also expressed on monocytes from children with active systemic juvenile idiopathic arthritis, and highly enriched on hemophagocytic macrophages that characterize the emergence of macrophage activation syndrome. However, the regulation of CD163 expression during monocyte and macrophage polarization is poorly understood. MicroRNA are small non-coding RNA that post-transcriptionally regulate gene expression, often serving as feedback loops to "fine tune" gene expression programs.
**Objectives:** Determine microRNA regulation of CD163 at the protein and mRNA levels using novel flow cytometry techniques.
**Methods:** Human THP-1 monocytic cells and primary monocytes and monocyte-derived macrophages (MDMs) from healthy donors were polarized with activating conditions including M1 (LPS and IFNg), M2a (IL-4), M2b (LPS and immune complexes) and M2c (TGFb or IL-10). CD163 expression was determined by quantitative RT-PCR or on a single-cell level using RNA flow cytometry. Transcripts were detected using the PrimeFlow kit, with probes specific for CD163 mRNA and other cell surface markers. Cells were also transfected with specific microRNA mimics.
**Results:** Significantly increased CD163 mRNA levels were detected only in monocytes and macrophages polarized towards M2c by IL-10 treatment. Similarly, single-cell RNA analysis showed markedly increased CD163 mRNA upon IL-10 treatment, with more modest increases in protein expression. Several candidate microRNA may regulate CD163. As such, our studies indicate that overexpression of miR-125a and miR-181c significantly reduced CD163 mRNA expression in IL-10 polarized macrophages. Notably, both of these microRNAs were significantly increased in monocytes from children with active systemic JIA. *In vitro*, miR-125a and miR-181c were both elevated in polarizing conditions that restrict CD163 expression. Interestingly, these microRNAs regulated CD163 expression through distinct mechanisms. Computationally, miR-181 is predicted to bind directly to CD163 mRNA. Indeed, using RNA immunoprecipitation (RIP) we found that overexpression of miR-181c significantly increased delivery of CD163 mRNA to the RNA-induced silencing complex. In contrast, CD163 does not have a predicted miR-125a binding site. Using whole transcriptome analysis of macrophages overexpressing miR-125a-5p, significantly reduced levels of mRNA encoding several macrophage receptors, including IL10RA and TGFbR2, was observed. This suggests that miR-125a-5p exerts more global effects to restrict M2c polarization.
**Conclusions:** These data show that microRNAs regulate the IL-10-induced expression of CD163 in human macrophages through distinct mechanisms, directly targeting of CD163 mRNA and indirectly inhibiting cytokine receptor expression. These findings illustrate how microRNA "fine-tune" innate immune activation during inflammatory responses, and expand the understanding of the phenotype of activated monocytes and macrophages in systemic JIA.
**Disclosure of Interest:** S. Thornton: None declared, T. Do: None declared, R. Tan: None declared, A. Sproles: None declared, M. Bennett: None declared, M. Medvedovic: None declared, M. DeLay: None declared, N. Shen: None declared, A. Grom Grant/research support from: Novartis, Novimmune, Consultant for: Novartis, Novimmune, G. Schulert: None declared
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# ABC of statistics

## OP0013 PREDICTION OF NON-RESPONSE TO METHOTREXATE THERAPY IN THE RHEUMATOID ARTHRITIS MEDICATION STUDY (RAMS)

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**Background:** Methotrexate (MTX) is the disease modifying drug of first choice in the treatment of rheumatoid arthritis (RA). However, response to MTX varies and the ability to predict likely non-response could enable earlier access to alternative drugs and the avoidance of disease progression for some patients.
**Objectives:** To predict non-response to MTX in the Rheumatoid Arthritis Medication Study (RAMS), a cohort of RA patients commencing MTX therapy for the first time.
**Methods:** RAMS is a national multi-centre observational study recruiting RA patients in the UK who are $\geq$18 years old and starting MTX for the first time. Data on potential predictors of response to MTX was acquired at baseline via questionnaires, case notes and blood samples and used to predict non-response to MTX at six months after commencement. Non-response to treatment was defined as failing to fulfil the EULAR criteria for good response: disease activity score-28 (DAS28) at six months $\leq$3.2 and reduction in DAS28 from baseline to six months $>$1.2. Potential predictors were chosen as candidate variables in a multivariable logistic regression model for non-response based on previous univariable analysis. The baseline measures included were body mass index (BMI), current smoking (yes/no), drinking of alcohol (yes/no), symptom duration, DAS28, functional disability (Health Assessment Questionnaire, HAQ), C-reactive protein (CRP), creatinine, anxiety and depression scores (Hospital Anxiety and Depression Scale, HADS) and beliefs about medicines necessity and concerns scores (Beliefs about Medicines Questionnaire, BMQ). All candidate predictors were initially included in a full model before backwards selection was used to remove non-significant terms ($p>0.05$) and produce a parsimonious final model. The ability of the models to discriminate between responders and non-responders was assessed using the area under the receiver operating characteristic curve (AUC).
**Results:** Data on baseline predictor values and response at six months was available on 781 participants: 546 (70%) female, median age 59 (IQR 48–68) years, median symptom duration 9 (IQR 4–28) months. 549 participants (70%) were non-responders. Multivariable age- and sex-adjusted odds ratios for the predictors in the full and final models are shown in Table 1. The full model had

Table 1. Multivariable age- and sex-adjusted logistic regression models for non-response to MTX at six months

| Predictor | Full model | | Final model | |
|---|---|---|---|---|
| | OR (95% CI) | p | OR (95% CI) | p |
| BMI (kg/m$^2$) | 1.05 (1.02, 1.09) | <0.01 | 1.06 (1.03, 1.09) | <0.01 |
| Current smoking (yes/no) | 1.57 (1.00, 2.47) | 0.05 | 1.59 (1.02, 2.48) | 0.04 |
| Drinking of alcohol (yes/no) | 0.72 (0.50, 1.04) | 0.08 | | |
| Symptom duration (months) | 1.00 (1.00, 1.00) | 0.27 | | |
| DAS28 | 0.65 (0.56, 0.76) | <0.01 | 0.68 (0.60, 0.78) | <0.01 |
| HAQ score | 1.27 (0.92, 1.75) | 0.15 | | |
| CRP (mg/l) | 1.00 (0.99, 1.00) | 0.24 | | |
| Creatinine (mg/dL) | 1.00 (0.99, 1.01) | 0.56 | | |
| HADS anxiety score | 1.09 (1.03, 1.15) | <0.01 | 1.11 (1.06, 1.15) | <0.01 |
| HADS depression score | 1.00 (0.94, 1.07) | 0.9 | | |
| BMQ necessity score | 1.01 (0.97, 1.06) | 0.67 | | |
| BMQ concerns score | 0.99 (0.94, 1.03) | 0.53 | | |

an AUC of 0.70. The final model, containing BMI, current smoking, DAS28 and HADS anxiety score, had an AUC of 0.69.
**Conclusions:** Baseline values of lifestyle, clinical and psychosocial predictors were used to predict non-response to MTX at six months. A model with a parsimonious set of core variables had similar discriminatory performance to a model with a full set of predictors. Of note is the role of participant anxiety on commencing treatment with MTX in predicting response, which may be related to subsequent adherence.
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**WEDNESDAY, 8 JUNE 2016**

## Optimizing treatment and patient care through precision medicine: a threat or an opportunity for patients and patient organisations?

### OP0014-PARE UPDATING THE PATIENT PARTNER EDUCATIONAL PROGRAM FOR RHEUMATOID ARTHRITIS IN BELGIUM: A SYSTEMATIC, SCIENTIFIC-BASED APPROACH LED BY PATIENT EXPERTS

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**Background:** Patient Partners (PP) are expert patients who train medical students, general practitioners and other healthcare providers about the clinical presentation of rheumatoid arthritis (RA). A direct objective is to improve musculoskeletal examination skills, facilitating appropriate referrals, fast diagnosis and early treatment initiation.
**Objectives:** We sought to critically review and update the PP Program for RA in Flanders because of changing needs based on new data about early intensive treatment strategies, patient beliefs and preferences in early RA, as well as about the hurdles to implement optimal care strategies.
**Methods:** We followed a structured plan of action, in which we aimed to make the course content more applicable to the new needs, and this for patients who are also more likely to present themselves without joint deformities, continuing their normal life as much as possible. Four content modules were developed by seven patient partners with RA who took the lead in this project. The other members of the project team were one rheumatologist, one nurse specialist and two doctoral researchers active in the field of early RA.
**Results:** After a brainstorm session by PP, a first team meeting was held to review their ideas and to add scientific input. They particularly indicated that the patient perspective (e.g., perceptions, impact of disease, general health advice) could be improved in the course content. Subsequently, the current content was reviewed and part of it was removed (focus on classical joint deformities), part of it was differently clustered. During this first debriefing, four content modules were proposed: aspects of treatment delay, treatment strategies and perceptions about medication (from a patient and healthcare provider perspective), the patient and his/her environment, and active participation. Next, the PP formed subgroups and worked out the modules. In a second debriefing, the modules were further refined and the new course structure was discussed including necessary adaptations to course material. We agreed on the implementation strategy. Thereafter, the updated program was presented to the entire group of PP during their annual meeting, and a credibility check was performed with a general practitioner and a medical student. Final changes were integrated based on their feedback. Lastly, during a two-day meeting, all PP were trained by the project team to implement the new content and structure in their lessons.
**Conclusions:** The update of the Belgian PP program for RA is an example of how expert patients can substantially be involved in updating educational programs. We strived to include new insights about RA and the patient perspective to a higher extent in the course content. Four content modules were implemented: aspects of treatment delay, perceptions about medication, the patient and his/her environment, and active participation. Making medical students and healthcare providers aware of the patient perspective is an important step towards optimal care in RA.
**Disclosure of Interest:** None declared
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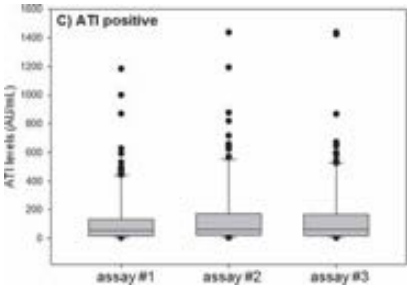
**WEDNESDAY, 8 JUNE 2016**

## Clinical relevance of immunogenicity and therapeutic drug monitoring

### OP0015 ANTIBODIES TO INFLIXIMAB IN REMICADE-TREATED RHEUMATIC PATIENTS SHOW IDENTICAL REACTIVITY TOWARDS BIOSIMILAR CT-P13

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**Background:** The first infliximab (IFX) biosimilar (CT-P13) in Europe is marketed as two brand names, Inflectra (IFT) and Remsima (RMS), that contain the same IFX molecule produced with the same manufacturing process. One of the main questions is whether patients treated with Remicade (RMC) can be effectively and safely switched to CT-P13.
**Objectives:** To determine if antibodies to infliximab (ATI) in RMC-treated patients cross-react with CT-P13.
**Methods:** Consecutive patients (250) with active rheumatoid arthritis (RA) and spondyloarthritis (SpA) under RMC treatment and never exposed to CT-P13, were retrospectively selected according to clinical information and anti-drug antibody (ADA) status. 37 IFX-naïve rheumatic patients, 19 IFX-naïve rheumatic patients with anti-adalimumab antibodies (AAA), and 21 healthy individuals were assayed as controls. ATI trough levels were measured in parallel with three different ELISA assays: #1 Promonitor-ANTI-IFX (Progenika, Spain) which uses RMC to crosslink patient ADA; #2 the same assay but using RMS, and #3 the same assay but using IFT.
**Results:** In total, 126 samples out of 250 Remicade-treated patient samples were tested positive with Promonitor-ANTI-IFX (50.4%, 131 patients). All were ATI-positive when either IFT or RMC bridging assays were used (Fig1). Positive and Negative Percent Agreements were 100%/100% for any comparison: RMC vs. IFT or RMC vs. RMS or IFT vs. RMS, respectively. Spearman's coefficients were determined to be 0.995, 0.996 and 0.998, for RMC vs. IFT, RMC vs. RMS, and IFT vs. RMS, respectively ($p<0.001$). No differences between RA and SpA, or between concomitant immunosuppressives, were observed. This is the first study that demonstrates cross-immunogenicity between RMC and a biosimilar molecule in patients with rheumatic diseases. Results are in agreement with previous data in patients with inflammatory bowel diseases[1].




**Conclusions:** ATI of RMC-treated patients cross-react with either IFT or RMS. Results suggest that the epitopes raising the immune response to the innovator drug are responsible for the same degree of reactivity when sera are confronted to the biosimilar molecule, although it must be noted that the biosimilar might present new epitopes due to different glycosylation pattern or impurities, and even conformational epitopes due to potential aggregations. ATI-positive patients treated with RMC should not be switched to a biosimilar treatment, since preexisting ATI will interact with the new drug, enhance clearance and potentially lead to loss of response and infusion-related reactions. Further studies with biosimilar-treated patients are warranted to increase our knowledge about potentially different immunogenic responses. Results also demonstrate that Promonitor-ANTI-IFX test can be used to monitor antibodies to CT-P13 in biosimilar-treated patients. This finding supports the utility for therapeutic drug monitoring before a switching strategy is considered.
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[1] Ben-Horin S et al Cross-immunogenicity: antibodies to infliximab in Remicade-treated patients with IBD similarly recognise the biosimilar Remsima. Gut 2015 [Epub ahead of print]
**Disclosure of Interest:** B. Ruiz-Argüello Employee of: Employee of Progenika Grifols, A. Maguregui Employee of: Employee of Progenika Grifols, A. Ruiz del Agua Employee of: Employee of Progenika Grifols, D. Pascual-Salcedo: None declared, A. Martínez: None declared, T. Jurado: None declared, C. Plasencia: None declared, A. Balsa: None declared, J. Rosas: None declared, F. Llinares-Tello: None declared, N. Torres Employee of: Employee of Progenika Grifols, A. Martínez Employee of: Employee of Progenika Grifols, D. Nagore Employee of: Employee of Progenika Grifols
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### OP0016 INCREASED FREQUENCY OF ANTI-DRUG ANTIBODIES IN PATIENTS CARRYING COMPATIBLE IGG1 ALLOTYPES AND TREATED WITH ANTI-TNF ANTIBODIES

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**Background:** One of the causes of insufficient response to biological drugs is the production of anti-drug antibodies (ADA) (1). These antibodies can decrease the effectiveness of treatment by altering bioavailability or by neutralizing the drug. In addition, they may contribute to hypersensitivity reactions. Some ADA are directed against IgG allotypes, which are protein polymorphisms able to induce an immune response in incompatible subjects. Infliximab (INX) and adalimumab (ADM) have the G1m17,1 allotypes, while about 50% of the Europeans are homozygous for the incompatible G1m3,n allotypes. Therefore, the allotypes could contribute to ADA and, in this way, explain the recently described loss of efficiency of INX in allotype-incompatible RA patients (2).
**Objectives:** We aimed to analyze the usefulness of IgG1 allotypes as biomarker of the development of ADA against INX and ADM.
**Methods:** The presence of ADA was determined in 252 consecutive patients with inflammatory arthritis in the Hospital La Paz (116 with rheumatoid arthritis (RA), 74 with ankylosing spondylitis (AS), 26 with psoriatic arthritis, 17 with non-radiographic spondylitis, 11 with spondylitis and inflammatory bowel disease, 3 with uveitis and 5 with other arthropathies). Patients were assessed during INX treatment (151), or with ADM (82), or sequentially during treatment with INX and ADM (19). ADA were determined by two-site bridging ELISA as described (1). Allotypes of IgG1 were determined by genotyping 2 SNPs, rs1071803 (for allotype G1m17/G1m3) and rs11621259 (for allotype G1m1/null) with the SNaPshot Multiplex kit (Applied Biosystems) as reported (2).
**Results:** Patients with compatible allotypes (carriers of G1m17,1) showed a larger frequency of ADA (33% *vs.* 20%, p=0.02) and a trend toward higher titers of these antibodies ($18.0x10^3$ *vs.* $8.3x10^3$ AU, ns) than patients with incompatible allotypes (homozygous for G1m3,n). This association was clearer in patients treated with INX (41% *vs.* 25%, p=0.03) than in those treated with ADM (18% *vs.* 12%, ns). ADA were more frequent in patients treated with INX than in those treated with ADM, as already known. Multivariate analysis showed that the frequency of ADA was increased in patients with RA compared to other diseases (OR =7.6, $p<0.0001$), and decreased in older patients (OR =0.65 per 10 years, $p<0.001$). Other factors, such as sex, having AS against other diseases, and treatment with methotrexate or corticosteroids, were not associated with ADA.
**Conclusions:** Patients with compatible allotypes showed more frequently ADA than patients with incompatible allotypes, showing for the first time this association in patients treated with INX and reinforcing the previously reported association for ADM (3). These results suggest a genetic factor in linkage with the allotype, but different from it, that will predispose to ADA.
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## Outcome measures in clinical practice in gout and CPPD. The use of the new EULAR guidelines

### OP0017 MEDICATION TAKING BEHAVIOUR OF ALLOPURINOL TREATMENT AMONG PATIENTS WITH GOUT: A RETROSPECTIVE COHORT STUDY IN THE CLINICAL PRACTICE RESEARCH DATALINK (CPRD)

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**Background:** Lowering serum uric acid concentrations is effective to control gout attack and prevent formation of tophi. Persistence with and adherence to uric acid lowering therapy are important to achieve benefit from medication. Therefore, insights into medication taking behaviour and factors influencing it, are extremely important.
**Objectives:** To describe patterns of persistence with and adherence to allopurinol treatment among gout patients in the UK, and explore determinants of non-persistence and non-adherence.
**Methods:** A retrospective cohort study using the UK Clinical Practice Research Datalink (CPRD) was conducted. Patients with a first ever diagnosing coding for gout between 1st January 1987 and 30th June 2014 were included. Start of follow-up was defined as the first prescription of allopurinol after the start of valid data collection. Patients were excluded if they were younger than 40 years, were (ever) users of febuxostat and probenecid, or had a follow-up of less than 90 days after completion of the first prescription. Determinants included patient characteristics (at baseline), medication use (6 months prior to index-date) and other comorbidities (ever before index-date). Medication taking behaviour was described by non-persistence (occurrence of a first gap of 30 or 90 days) and non-adherence (proportion of days covered [PDC] over observation period) to allopurinol treatment. Kaplan Meier survival and multivariable Cox- and logistic regression were used to estimate the median time until discontinuation, and the strength of the association between determinants with non-persistence (90-day gap) and non-adherence, respectively.
**Results:** A total of 47.744 gout patients (75.6% men; mean age 63.9 years) received allopurinol exclusively. After 5.3 years (SD 4.6) of follow-up 77% had a gap of 30-days and 54% had a gap of 90-days, and were non-persistence. Median survival time until discontinuation was 229 days (95% confidence interval [CI] 224 – 235) for a 30-day and 1059 days (CI 1012 – 1107) for a 90-day gap. The median PDC was 0.67 (IQR: 0.64). Over half of the patients (61%) were non-adherent ($PDC<0.80$) over the study period.
Females (HR 1.10; 95% CI 1.06–1.13; OR 1.21; CI 1.15–1.28) and current smokers (HR 1.15; CI 1.11–1.20; OR 1.17; CI 1.10–1.25) have an increased risk on non-persistence and non-adherence, while older age (ref: <50 years) (HR 0.77: CI, 0.74–0.80; OR 0.61; CI 0.58–0.65), overweight (HR 0.89; CI 0.86–0.92; OR 0.86; CI 0.82–0.91), receiving anti-hypertensive (HR 0.92; CI 0.89–0.96; OR: 0.64; CI 0.60–0.67), colchicine (OR 0.94; CI 0.89–0.98) and suffering from dementia (HR 0.58; CI 0.45–0.73; OR 0.59; CI 0.46–0.77), depression (HR 0.94; CI 0.89–0.99), diabetes (HR 0.86; CI 0.83–0.89; OR 0.90; CI 0.84–0.96) and dyslipidaemia (OR 0.81; CI 0.77–0.85) appear to decrease the risk of non-persistence and/or non-adherence.
**Conclusions:** This is the first large population based study in Europe which showed poor medication taking behaviour among gout patients initiating allopurinol. Females and current smokers have an increased risk, while an older age, overweight, receiving anti-hypertensives and suffering from certain comorbidities appear to decrease the risk of non-persistence and non-adherence.
**Disclosure of Interest:** None declared
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### OP0018 HYPERURICEMIA INCREASES MORTALITY ONLY IN PATIENTS WITH GOUT AND EXISTING CARDIOVASCULAR DISEASE. A PROSPECTIVE ANALYSIS FROM THE BUSSELTON HEALTH STUDY

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**Background:** Hyperuricemia is increasingly prevalent and associated with cardiovascular disease [1]. While hyperuricemia can induce endothelial dysfunction, oxidative stress and inflammation uncertainty remains regarding the association between hyperuricemia and vascular events [2,3].
**Objectives:** Investigate whether baseline and/or time averaged UA levels were associated with cardiovascular events and mortality in the Busselton Health Study (BHS) cohort.
**Methods:** Prospective study of the BHS cohort (n=4,171), using baseline serum UA measures and 15 year follow-up [4]. Outcomes included were cardiovascular events (CVE) and mortality, derived from State-wide registries. Hazard ratios (HR) for UA level as continuous and categorical (low, medium, high) predictor of outcomes, stratified for baseline cardiovascular disease and a history of gout were analysed by multivariate Cox regression.
**Results:** Hyperuricemia was present in 9.4% in participants free of CVE and 16.5% in those with CVE at baseline. In those free of CVE (n=3,475), a 0.1mmol/L rise in UA level was associated with increased mortality (HR 1.19, CI 1.04–1.36), cardiovascular mortality (HR 1.27, CI 1.03–1.57) and first CVE (HR 1.28, CI 1.13–1.44) after age & sex adjustment. Hyperuricemia significantly increased the risk of a first CVE (HR 1.52, CI 1.13–2.04). However, adjustment for a range of traditional cardiovascular risk factors attenuated these associations. Results were similar for the subset of 2,139 participants using multiple UA measures over time. In the fully adjusted model, gout was a significant independent predictor of mortality only in participants with a history of CVE at baseline (HR 1.75; CI 1.04–2.95).
**Conclusions:** Hyperuricemia is highly prevalent in the Busselton region of Western Australia and independently increased the risk CVE or mortality events in those with existing CVE and gout. UA lowering therapy for CVE prevention is advisable for patients with a history of gout and CVE, but clearly not warranted in those with asymptomatic hyperuricemia.
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## Hand osteoarthritis: state of the art and future perspectives

### OP0019-HPR EFFECTIVENESS OF A PROGRESSIVE RESISTANCE STRENGTH PROGRAM ON HAND OSTEOARTHRITIS: A RANDOMISED CONTROLLED TRIAL

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**Background:** Hand osteoarthritis is highly prevalent, affecting 55–70% of the population over 55 years with an age-related progressive increase. The OA of interphalangeal and carpometacarpal joints may have varying degrees of deformity associated with pain, decreased of grip and pinch strength, decreased range of motion and functional impairment. Effects of exercise in HOA in pain, function and strength is stiill unclear and based on experts opinions.
**Objectives:** To assess the effectiveness of progressive resistance strength training program on pain, function and strength in hand OA patients.
**Methods:** Diagnostic of hand OA according to ACR of at least 1year,over 50 years, both genders, pain in IF joints between 3–8 cm on NPS. Sixty patients who met the eligibility criteria were randomised into exercise group (EG) and control group (CG). Both groups performed a session regarding joint protection and energy conservation before randomisation. The EG performed a progressive resistance strength training program for intrinsic muscles of the hand for 12 weeks. The outcome measures were NPS, AUSCAN and COCHIN for hand function; grip and pinch strength using hydraulic hand dynamometers and patient satisfaction using a Likert scale. A blinded evaluator performed the evaluations at baseline, 6 and 12 weeks after treatment baseline.
**Results:** The groups were homogeneous at baseline except for the key pinch strength for nondominant hand and palmar pinch strength for both hands. The comparison between groups using repeated measures ANOVA shows an statistically difference between groups in AUSCAN (total score, p=0.005; pain, p=0.006 and function, p=0.047), COCHIN (p=0.042) and Likert scale (p=0.001) with better results for the EG. Results were presented in table 1.

Table 1 - Results of the study

| | T0 | | T6 | | T12 | | p ANOVA |
|---|---|---|---|---|---|---|---|
| | CG | EG | CG | EG | CG | EG | |
| NUMERICAL PAIN SCALE | | | | | | | |
| Dominant hand | 6,13 ± 1,63 | 6,10 ± 1,67 | 4,63 ± 2,71 | 4,40 ± 2,49 | 5,10 ± 2,68 | 3,80 ± 2,43 | 0.085 |
| Non-dominant hand | 5,93 ± 1,70 | 5,67 ± 1,89 | 4,73 ± 2,65 | 4,20 ± 2,47 | 5,10 ± 2,58 | 3,77 ± 2,53 | 0.295 |
| AUSCAN | | | | | | | |
| Pain | 6,47 ± 3,01 | 7,90 ± 4,49 | 8,93 ± 3,56 | 5,73 ± 4,24 | 8,23 ± 4,42 | 4,97 ± 4,07 | 0.006* |
| Stiffness | 2,30 ± 2,24 | 1,97 ± 1,90 | 2,33 ± 1,79 | 1,73 ± 1,91 | 2,13 ± 1,28 | 1,17 ± 1,15 | 0.386 |
| Function | 14,60 ± 7,05 | 12,67 ± 7,96 | 13,00 ± 7,08 | 11,77 ± 7,80 | 13,80 ± 7,42 | 8,77 ± 7,40 | 0.047* |
| Total score | 24,70 ± 9,68 | 22,50 ± 12,10 | 26,30 ± 10,02 | 19,20 ± 10,47 | 24,13 ± 12,02 | 14,23 ± 10,47 | 0.005* |
| COCHIN | 15,73 ± 10,37 | 14,53 ± 13,83 | 18,00 ± 12,26 | 12,30 ± 12,10 | 15,17 ± 11,71 | 8,90 ± 12,09 | 0.042* |
| GRIP STRENGTH | | | | | | | |
| Dominant hand | 15,13 ± 4,20 | 17,70 ± 5,2 | 14,90 ± 4,10 | 18,70 ± 5,10 | 15,60 ± 5,10 | 19,10 ± 4,70 | 0.052 |
| Non-dominant hand | 14,70 ± 4,20 | 16,50 ± 5,10 | 14,10 ± 3,80 | 16,90 ± 5,20 | 14,90 ± 4,50 | 17,80 ± 5,00 | 0.307 |
| PINCH STRENGTH | | | | | | | |
| Tip | | | | | | | |
| Dominant hand | 4,13 ± 1,28 | 4,51 ± 1,20 | 4,23 ± 0,95 | 4,44 ± 1,29 | 4,10 ± 1,16 | 4,54 ± 1,21 | 0.586 |
| Non-dominant hand | 3,87 ± 1,10 | 5,39 ± 5,71 | 3,93 ± 1,12 | 4,48 ± 1,21 | 3,76 ± 1,00 | 4,31 ± 1,15 | 0.372 |
| Key | | | | | | | |
| Dominant hand | 5,78 ± 1,27 | 6,36 ± 1,12 | 5,69 ± 1,32 | 6,50 ± 1,24 | 5,95 ± 1,52 | 6,54 ± 1,08 | 0.984 |
| Non-dominant hand | 5,18 ± 1,07 | 5,68 ± 1,00 | 5,26 ± 1,05 | 6,00 ± 0,98 | 5,53 ± 1,12 | 7,76 ± 8,98 | 0.308 |
| Palmar | | | | | | | |
| Dominant hand | 4,53 ± 1,24 | 5,18 ± 1,18 | 4,79 ± 1,18 | 5,18 ± 1,17 | 4,73 ± 1,18 | 5,12 ± 1,05 | 0.987 |
| Non-dominant hand | 4,16 ± 1,25 | 4,89 ± 1,12 | 4,42 ± 1,38 | 4,92 ± 0,97 | 4,40 ± 1,10 | 4,99 ± 1,01 | 0.910 |

T0 - baseline; T6 - after 6 weeks; T12 - after 12 weeks; CG - control group; EG - experimental group.

**Conclusions:** This progressive resistance strength training program was effective for pain, function, and treatment satisfaction for patients with hand OA.
**Disclosure of Interest:** None declared
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**WEDNESDAY, 8 JUNE 2016**

## Chronobiology of the immune reponse

### OP0020 THE ASSOCIATION OF GONADOTROPIN-RELEASING HORMONE AND CYTOKINES IN RHEUMATOID ARTHRITIS

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**Background:** Improvement of rheumatoid arthritis (RA) in pregnancy, and worsening postpartum is well known. This led to the finding that cortisone had anti-inflammatory effects. The hypothalamic proinflammatory hormone, gonadotropin-releasing hormone (GnRH), is the master regulator of the reproductive system, and also has a circadian rhythm. GnRH activity diminishes in pregnancy and increases postpartum. Prior to our AGRA (Antagonist to Gonadotropin Releasing Hormone in RA) trial, no research in RA had been performed on this principal hormone. GnRH can act like a cytokine in the periphery, being secreted by T cells (1). In the AGRA trial, GnRH antagonism showed anti-inflammatory effects including a significant reduction in TNF in RA patients. GnRH antagonists decrease inflammatory cytokine mRNA, and downregulate the NF-κB pathway. Conversely, GnRH agonists are associated with the onset and flares of autoimmune diseases.
**Objectives:** The purpose of this study was to investigate for the first time whether GnRH exists in the periphery in patients with an autoimmune disease. If GnRH exists in the periphery in patients with RA, is GnRH associated with cytokines?
**Methods:** Predefined endpoints from our proof-of-concept randomized, double-blind, Norwegian AGRA study (N=99, ITT population) with active RA have been reported earlier (ClinicalTrials.gov NCT00667758). Patients were randomized using computer-generated allocation (1:1) in dynamic blocks stratified for sex. Patients were assigned to cetrorelix, a GnRH antagonist (5mg days 1–2, 3mg days 3–5) or corresponding volumes of placebo. Blood sampling was at the same time of day and frozen to -80. We investigated serum GnRH baseline pretreatment levels using newly available ELISA assays according to the manufacturer's instructions, in duplicates, inter-assay CV<10% (USCN Life Science Inc.). Four serum cytokines were measured with multiplex technology (Luminex Inc.).
**Results:** Mean peripheral GnRH level at baseline was 241 pg/mL (s.d. ±83 pg/mL).

Table 1. Correlations of absolute levels of baseline cytokines, GnRH and confounding hormones in RA patients

| Variable | TNF | IL1 | IL10 | IL2 |
|---|---|---|---|---|
| GnRH (n=96) | 0.220 * | 0.396** | 0.239* | NS |
| Luteinizing Hormone (n=99) | NS | NS | NS | NS |
| Follicle-Stimulating Hormone (n=98) | NS | NS | NS | NS |
| Cortisol (n=99) | NS | NS | NS | NS |
| TNF (n=98) | – | 0.761** | 0.873** | 0.912** |
| IL1 (n=98) | 0.838** | – | 0.958** | 0.974** |
| IL10 (n=99) | 0.752** | 0.958** | – | 0.991** |
| IL2 (n=99) | 0.856** | 0.974** | 0.991** | – |

*p<0.05; **p≤0.001; NS, non-significant.

By day 5, TNF levels were significantly reduced by the GnRH antagonist vs. placebo (p=0.023). GnRH levels were not significantly changed by day 5.
**Conclusions:** Peripheral GnRH is presented for the first time in autoimmunity. Due to GnRH's potential association with cytokines, the existence of peripheral GnRH may be due to GnRH production by T cells (1). These results could support preexisiting literature on GnRH and the immune system, that GnRH stimulates the secretion of cytokines peripherally, and help to explain clinical observations. These results warrant confirmation.
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### OP0021-HPR SLEEP DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND RELATIONSHIP WITH DISEASE ACTIVITY

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**Background:** The rheumatoid arthritis (RA), as known, causes inability in various performance areas mostly in the musculoskeletal. Reduced physical activity, substantial disability and also sleep disorders have previously been described in people with RA.
**Objectives:** The aim of this study was to describe the socio-demographic profile and sleep disorders in RA patients from a specialized RA clinic in Colombia.
**Methods:** A descriptive cross-sectional study was performed in a specialized clinic dedicated to care patients with rheumatoid arthritis (RA). 1298 patients were included in the study, which were seen by the area of psychology, which information was collected through semi-structured interviews and non-probability sampling. Descriptive epidemiology was applied for continuous variables, using measures of central tendency and dispersion for categorical and qualitative variables by averages and percentages. We used chi2 test to study a possible relationship between the severity of disease activity and the sleep disorders.
**Results:** Total sample of patients was 1298, 1048 (80%) were women and 250 (19%) were men. Patients had a DAS28 2.6 in average ± 1.1; mean age was 55.1 ± 8.8 years; 846 (65%) were in remission, 205 (16%) were in low disease activity, 208 (16%) in moderate disease activity and 42 in severe disease activity (3%). Regarding education, 6% were illiterate, 44% had elementary school, 33% high school, 8% had a technical degree and only 7% had college level. 373 (28%) patients showed any sleep disorder, among type of sleep disorders were seen: primary insomnia 299 patients (80% of women and 20% of men), related sleep

disorder breathing (OSAS) 33 Patients (70% of women and 30% of men) and 20 patients with circadian rhythm disorder (74% of women and 26% of men), and hypersomnia 13 patients (92% of women and 8% men). It was established a relationship between having a sleep disorder and severity of disease activity statistically significant ($p<0.00$).
**Conclusions:** According to these findings sleep disorders are likely present in a great proportion patients with RA and in many cases linked with disease activity. Primary insomnia is the most prevalent.
**Disclosure of Interest:** None declared
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## Nanomedicine in rheumatology

### OP0022 TARGETING FIBROBLASTOID-LIKE CELLS BY DRUG LOADED ENGINEERED GOLD NANOPARTICLES AS A NOVEL APPROACH FOR ILD-SSC TREATMENT

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**Background:** Systemic Sclerosis (SSc) is an autoimmune fibrotic disorder characterised by collagen and extracellular matrix deposition in the skin and internal organs, such as the lung. Interstitial lung involvement (ILD) is frequent in SSc but effective therapies are lacking and ILD represents one of the most frequent causes of death. Gold nanoparticles (GNPs) have a great potential in biomedical applications among which drug-delivery. Previously, we proved that GNPs containing everolimus and functionalized with anti-CD44 antibody targeted to mesenchymal cells from patients with chronic lung allograft rejection (CLAD) specifically inhibited these cells. We proved that also fibroblastoid-like cells (FLCs) isolated from bronchoalveolar lavage (BAL) of ILD-SSc patients express CD44.
**Objectives:** we loaded GNPs with the drug imatinib (GNP-HCim) with the aim to specifically inhibit FLCs from ILD-SSc patients.
**Methods:** GNPs with imatinib and exposing an anti-CD44 antibody were engineered, as previously described (1).
GNP-HCim were incubated 2h with FLCs from three patients with ILD-SSc. Cell apoptosis (Annexin V) and proliferation (CFSE) were evaluated at different times by flow cytometry. Cell viability was assessed by MTT test. As control, functionalized GNPs without imatinib (GNP-HC) or imatinib alone (IM) were used. Fluorescent GNP-HC were generated to assess cell uptake by confocal microscopy and flow cytometry.
Statistical differences were evaluated using ANOVA by Graph Prism 5.0 program.
**Results:** Fluoresce experiments showed that only HC-functionalized nanoparticles entered FLCs within 1 h. The results showed that GNP-HCim inhibited cell proliferation without significant differences between the three cell lines. In particular, the effect of GNP-HCim was significant at 48 ($p<0.001$) and 72h ($p<0.01$). A significant inhibition was also observed in presence of GNP-HC both after 48 ($p<0.01$) and 72h ($p<0.05$). No changes were produced by IM alone (fig. 1). MTT assay confirmed the results obtained by CFSE since a significant reduction ($p<0.001$) of cell viability was observed with GNP-HCim and GNP-HC starting from 48 h. IM treatment affected the FLCs viability ($p<0.05$ at 48h; $p<0.001$ at 72h). Functionalized nanoparticles were able to significantly increase apoptosis after 8 ($p=0.0051$) and 24 h ($p<0.001$) compared to uFLCs. However, only drug-loaded nanoparticles still significantly increased apoptotic rate after 48 h ($p=0.004$).
**Conclusions:** We proved that specifically engineered GNPs significantly inhibit proliferation and induce apoptosis of FLCs from ILD-SSc patients, as already described for CLAD patients. FLCs treatment with imatinib alone was not effective as GNP-HCim demonstrating the superiority of the nanoparticles. Our results also suggest an unspecific effect of nanoparticles themselves which has to be further clarified before the possibility to use engineered nanoparticles to develop new pharmacological treatment for patients with pulmonary fibroproliferative disorders.
**References:**
[1] Cova E, Colombo M, Inghilleri S, et al. Nanomedicine 2015.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3957

### OP0023 TARGETED POLYMERIC NANOPARTICLES AS DIAGNOSTIC AND THERAPEUTIC TOOL FOR RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease affecting joints due to the persistent synovial tissue inflammation. RA treatment has dramatically evolved in the last 20 years due to the production of biological Disease Modifying Antirheumatic Drugs (bDMARDs). However, side effects and the high costs of biological drugs are holding back their widespread usage. Moreover, some patients fail to respond to bDMARDs, for all of these reasons, DMARDs remains the main desired strategy for the treatment of RA, and Methotrexate (MTX) is still the "anchor" drug to treat RA. A successful treatment depends also on the early diagnosis, treating patients as soon as possible to prevent the late stages of the pathology.
**Objectives:** The aim of this work is to develop targeted biodegradable nanoparticles (tBNPs) that could be used as a platform suitable to delivery drugs or diagnostic tracers specifically into the inflamed synovial tissue. This approach usually allows to enhance the efficacy and to reduce the side effects.
**Methods:** We used polymeric biodegradable nanoparticles, made of polylactic acid, polycaprolactone and polyethylene glycol and coated with a peptide characterized for its ability to target only inflamed synovial tissue. The tBNPs diameter was 170 nm with a low negative charge. Toxicity was studied in-vitro assay and in-vivo. Immunofluorescence technique was used to initially assess the ability of fluorescent-tBNPs to preferentially target inflamed synovial tissue. The biodistribution of the nanoparticles and the efficacy of the treatment with tBNPs loaded with MTX were studied in a rat model of antigen-induced arthritis (AIA). Finally, tBNPs efficacy was also studied in a mouse model of collagen-induced arthritis (CIA).
**Results:** Targeted BNPs evidenced the ability to specifically bind inflamed synovial tissue both in vitro and in vivo. The targeting is dependent on the inflammation degree and this highlights the potentiality of the tBNPs as an early diagnostics tools. A single injection of targeted BNPs loaded with MTX completely abrogated the inflammatory process in acute AIA rat model while the same dose of free-MTX was ineffective. Equivalent therapeutic effects were obtained comparing MTX-loaded tBNPs and the same dose of free-MTX in the mouse model of chronic CIA and no toxic effect was documented when MTX was loaded in nanoparticles in these animals.
**Conclusions:** Our results demonstrated that tBNPs can efficiently and selectively delivery drugs and diagnostic probes to inflamed synovial tissue, providing a new platform for an early detection and efficient chronic treatment of inflammatory arthritis, with minimal side effects.
**Disclosure of Interest:** F. Colombo: None declared, L. Nunez Employee of: Biotarget, P. Durigutto: None declared, S. Biffi: None declared, E. Rampazzo: None declared, B. Belmonte: None declared, D. Sblattero: None declared, A. Gulino: None declared, P. L. Meroni: None declared, F. Tedesco: None declared, P. Macor: None declared
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**WEDNESDAY, 8 JUNE 2016**

## Patient organisations in action

### OP0024-PARE DEVELOPMENT AND USE OF A CANADIAN ARTHRITIS PATIENT CHARTER

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**Background:** In 2001, the Arthritis Society in Canada created a Canadian Arthritis Patient Bill of Rights with multiple stakeholders[1]. In the subsequent 15 years, the landscape of arthritis and its care has changed dramatically. A patient-led and driven not for profit organization, the Canadian Arthritis Patient Alliance (CAPA), wished to provide patients and healthcare providers a new tool that reflected this evolution – a Canadian Arthritis Patient Charter (Charter)[2]. The Charter was created to enable conversation, better partnership, and improved patient outcomes. CAPA believes patients have both rights and responsibilities in the care and management of their disease, and as such, the Charter includes both.
**Objectives:** In 2014, CAPA led the creation of the Charter - a modernization of the Canadian Arthritis Patient Bill of Rights. We present the Charter's development and launch, its publicity, uses and perceived effect on patient care.
**Methods:** CAPA has driven this project with support from multiple arthritis stakeholders within Canada (including the Ontario Rheumatology Association, the Arthritis Society, the Arthritis Alliance of Canada, the Canadian Rheumatology Association, Arthritis Consumer Experts, Patient Partners, the Canadian Spondylitis Association, and individual patients). One Board member acted as

project manager and sought input from members of the arthritis community. Methods to achieve this included phone calls, in person meetings, emails, and online surveys.
**Results:** A Charter was created with input from all arthritis stakeholders, including patients, family and friends, health care professionals, not for profit, and industry. Through meetings over a year, the stakeholders outlined a draft Charter. Public feedback solicited through an online survey publicized by stakeholders through their own networks (including newsletters, social media, websites) led to over 730 survey responses. The Charter (postcard and poster versions in Canada's two official languages) permanently resides on CAPA's website and was mailed to all Canadian Rheumatology Association members. CAPA and its partners disseminated news about the Charter for September's Arthritis Month (newsletters, social media, articles online); these efforts continue. The Charter has been shared in blogs[3,4] and journals[5,6] and on Facebook and social media, and we will present the number of downloads and hits the CAPA website has had. Its limited use in rheumatology offices will be discussed and patients' perceptions on how it has impacted their care will be presented.
**Conclusions:** The Canadian Arthritis Patient Charter was created to support increased patient engagement in their rheumatology care. It was intended to help increase patients dialogue with their healthcare providers, help them understand rights and responsibilities associated with their care, and improve outcomes.
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[6] http://craj.ca/archives/2014/English/Winter/PDFs/CRAJ_Winter_2014.pdf.
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### OP0025-PARE INFORMATIVE AND PREVENTIVE CAMPAIGNS AT THE CITY COUNCILS IN THE GALICIAN REGION

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**Background:** There are more than 250 types of rheumatic diseases (RDs), in Galicia there are 1.065.841 persons affected (40% of the population), these cause 50% of the incapacities and 20% of the medical leaves. These diseases affect children and young adults and they become chronic in most of the cases.
**Objectives:** To prevent affected population without a diagnosis.
40% of the population is affected by RDs, many of these pathologies present themselves very quietly. There are many myths around RD patients like it only affects old people or that it does not have cure, because of this many of them do not go to the doctor or they wait too long to go. It is also very common to recognize indications of denial or selfdeception. The presence of these diseases increase exponentially with the increase of the population and the actual pace of life. In Galicia this fact is aggravated because of the aging of the population and it is heading to the early appereance in people in their 40s.
**Methods:** Our team is formed by:
1 psychologist who detects pychological indications, point out the denial signs and the conflict with the illness.
1 rheumatologist who informs about the nature of the RDs.
2 occupational therapists who inform about alert signals and preventive measures of the articular damage.
1 expert patient who transmit his experience on how it feels to be affected by a RD.
1 coordinator in charge of stablising the link between the city council and our organization through scedules and coordination of the activities.
We visit diferent city councils, setting up previously the dates for the general and specific informative sessions. During those sessions we detect possible profiles of denial, doubt, etc. And afterwards we do the data processing.
**Results:** Out of 100 persons that go to these informative campaigns 3 of them go to the Rheumatology Department in their Health Center and end up with a positive diagnosis. This does not mean that these are the only ones but at least we increase the consultations.
We have developed a standarized quiz for the doctors to questions their patients about how they got to decide about consulting a rheumatologist.
**Conclusions:** The Galician population presents an alarming lack of awarness on how to identify RDs and it is ignoranto to its consequences.
In many cases, the affected person does not go to the general practitioner and because of this he is not derivated to the rheumatologist, missing the key phase, meaning=Early diagnosis.
RDs are very serious pathologies that if not treated for a long time can derivate in incapacities, joint affections and irreversible vital organs malfunction.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5810

**THURSDAY, 9 JUNE 2016**

## Plasma cells as key players and therapeutic target in rheumatic disaeses

### OP0026 SYNOVIAL FLUID MONONUCLEAR CELLS PROVIDE AN ENVIRONMENT FOR LONG-TERM SURVIVAL OF ANTIBODY SECRETING CELLS AND PROMOTE THE SPONTANEOUS PRODUCTION OF ANTI-CITRULLINATED PROTEIN ANTIBODIES

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**Background:** Rheumatoid arthritis (RA) is characterized by the presence of antibodies against citrullinated protein antigens (ACPA). The striking efficacy of B cell-depleting interventions and an increasing number of experimental observations suggest that ACPA and/or ACPA-expressing B cells could be actively involved in initiating, aggravating and/or perpetuating the disease process. We recently demonstrated that ACPA-expressing B cells circulate in the peripheral blood of patients with ACPA-positive RA[1,2]. Next to ACPA-expressing memory B cells, we could identify a population of plasmablasts/-cells (PB/PC) that actively secrete ACPA in this compartment. To date, however, it is unknown whether these circulating PB/PC home to secondary lymphoid organs to compete for survival niches, or whether the synovial compartment of inflamed joints could be one of the tissues attracting these cells. As PC can produce excessive amounts of antibodies and survive in respective niches for years, they could be involved in driving and maintaining disease-specific pathogenic processes.
**Objectives:** To study whether cells from the synovial environment impact on the longevity of auto-reactive B cell responses against citrullinated antigens.
**Methods:** Synovial fluid and peripheral blood mononuclear cells (SFMC/PBMC) were obtained from patients with established RA and assessed for the presence of B cell subpopulations. Cells spontaneously secreting ACPA-IgG directly ex vivo were detected and enumerated by antigen-specific ELISpot. In addition, SFMC and PBMC were cultured without additional stimuli to assess the degree of spontaneous ACPA-IgG secretion. Cells surviving for several weeks in culture were characterized by CFSE-labelling and Ki-67 staining.
**Results:** Cells spontaneously secreting ACPA-IgG were readily detectable in peripheral blood and synovial fluid (SF) of ACPA-positive RA patients. SFMC showed an up to 200-fold increase in ex vivo ACPA-IgG secretion compared to PBMC despite lower numbers of B cells in SFMC. ELISpot confirmed the presence of spontaneously ACPA-IgG secreting cells, accounting for up to 50% (median 12%) of all IgG-secreting cells in SF. Spontaneous ACPA-IgG secretion was remarkably stable in SFMC cultures, maintained upon depletion of the $CD20^+$ B cell compartment prior to culture, and detectable for several months. CFSE labelling and Ki-67 staining confirmed the long-term survival of non-dividing plasma cells.
**Conclusions:** This study demonstrates a high frequency of differentiated, spontaneously ACPA-IgG secreting cells in SF. These cells are supported by SFMC for prolonged survival and autoantibody secretion, demonstrating that the synovial compartment is equipped to function as inflammatory niche for plasma cell survival.
**References:**
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OP0027 **ABNORMAL B CELL ACTIVATION THROUGH CELLULAR METABOLIC REPROGRAMMING AND ITS RELEVANCE TO THE PATHOGENESIS OF SLE**

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**Background:** B cells play a pivotal role in autoimmune diseases. In SLE, IFN signature is displayed and aberrant function of Toll-like receptors (TLR) for recognizing nucleic acids contributes to its pathology. Peripheral plasmablasts increase in active SLE, but the relevance of cellular metabolisms to B cell differentiation to plasmablasts remains unclear.
**Objectives:** To examine the mechanism by which cellular metabolic reprogramming regulates human B cell differentiation in vitro, and its involvement in pathological processes of SLE.
**Methods:** Human B cells were obtained from peripheral blood of healthy donors (HDs), and separated into 3 subsets; naïve ($IgD^+CD27^-$), IgM memory ($IgD^+CD27^+$) and class-switched (CS) memory B cells ($IgD^-CD27^+$). Each subset was cultured with CpG DNA (ligand of TLR9) and/or IFN-α. Plasmablast ($CD27^{hi}$) differentiation, immunoglobulin (IgM, IgG), and cytokine production (IL-6, IL-10), and cellular metabolism (mTORC1, AMPK, glycolysis) were assessed.
**Results:** When IgM memory B cells and CS memory B cells were stimulated with CpG, robust production of IL-6 and IL-10 as well as differentiation to plasmablasts were induced. The gene expression of IRF4, XBP1 and PRDM1 was increased by CpG, whereas that of BACH2 and BCL6 was decreased. These responses were amplified by IFN-α, which was abrogated by anti-IFNAR2 Abs. A JAK inhibitor tofacitinib did not attenuate CpG-induced B cell differentiation to plasmablasts, indicating that JAK-mediated signaling by autocrine IL-6 and IL-10 was not relevant to the differentiation. Next, we analyzed cellular metabolic reprogramming during B cell differentiation, which was recently highlighted for its involvement in T cell differentiation. CpG stimulation strongly induced p-mTORC1 and lactic acid production, indicating that there is a metabolic shift to glycolysis in B cells. IFN-α further augmented this pathway. However, a glycolysis inhibitor, 2-deoxy-D-glucose and an mTORC1 inhibitor, rapamycin significantly abrogated lactic acid production, cytokine production and plasmablast differentiation of B cells in a dose-dependent manner. AMPK activators, metformin and AICAR, which are known to indirectly inhibit mTORC1, not only suppressed plasmablast differentiation but also induced $IgD^-CD27^-$ memory B cells. These results indicate that CpG and IFN-α shifted mTORC1/AMPK balance toward mTORC1 activation and glycolysis, leading to plasmablast differentiation. Interestingly, p-mTORC1 was significantly enhanced in B cells of SLE patients, compared to HDs ($p<0.05$), and it positively correlated with percentage of peripheral plasmablasts ($r=0.709$, $p<0.01$) and SLEDAI score ($r=0.453$, $p<0.05$), and negatively correlated with CH50 ($r=-0.452$, $p<0.05$).
**Conclusions:** CpG and IFN-α shifted mTORC1/AMPK balance toward mTORC1 activation and glycolysis, resulting in plasmablast differentiation, especially in memory B cells. The metabolic shift to anabolism supplied sufficient proteins and nucleic acids for rapid cell proliferation, permitting efficient differentiation to plasmablasts. Abnormal B cell activation through cellular metabolic reprogramming could contribute to SLE pathology. Thus, we first propose the disturbance of "immunometabolism" in B cells, and the regulation of B cell metabolism can provide a new therapeutic strategy against SLE.
**Disclosure of Interest:** M. Torigoe: None declared, S. Iwata: None declared, K. Sakata Employee of: Mitsubishi Tanabe Pharma, S. Nakayamada: None declared, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-Kirin, Abbvie, Bristol-Myers, Consultant for: Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, Santen, Speakers bureau: Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, Santen
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**THURSDAY, 9 JUNE 2016**

## Global year against joint pain

OP0028 **ASSOCIATION OF DIFFERENTIAL SYNOVIAL EXPRESSION PATTERNS IN EARLY OSTEOARTHRITIS WITH PAIN AND PROGRESSION OF JOINT DAMAGE**

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**Background:** The cause for chronic pain in OA is largely unknown. Over 50% of osteoarthritis (OA) patients show synovial inflammation, even at early stages of the disease. However, if and how this synovial activation contributes to joint pathology and pain, is not known.
**Objectives:** To identify pathways that predict progression of cartilage damage and osteophyte (OP) formation in OA. In addition, we identified association between gene expression and pain in a cross-sectional approach.
**Methods:** From 25 patients with knee OA that entered the CHECK Cohort study (Cohort Hip and Cohort Knee) synovial biopsies were collected at baseline. CHECK is a prospective 10-year follow-up study on patients with early osteoarthritis-related complaints initiated by the Dutch Arthritis Foundation. Progression over 5 years was determined radiographically based on change of joint space width (JSW) and OP size in these radiographs. Pain was assessed at baseline by the WOMAC pain questionnaire. Synovial samples from baseline were studied using histology and microarray (affymetrix U133-plus-2.0), and Functional Annotation Clustering (FAC).
**Results:** We identified patients that were marked progressors or non-progressors, either based on JSW (respectively n=13 vs n=8) or OP size (respectively n=10 vs n=11) at these time points. Among the genes that were differentially expressed by OP progressors were MMP1, 2, 3, 9 and -14, whereas in JSW-progressors only MMP1 was differentially expressed. In the group of JSW-progressors, macrophage markers like CD14, S100A8, S100A9, MHC class II genes, and CXCR2 were positively associated with progression. This indicates that expression of these factors predict progression of cartilage damage in OA patients. The OP-progressors showed an increase of most of these markers, but to a far lesser extent. Using FAC we identified inflammatory response, macrophage differentiation, blood vessel formation, ossification and cell migration to be enriched in JSW-progressors. Blood vessel formation, wound healing, ossification and cell proliferation were enriched in OP-progressors. Histologically, in the JSW-progressors the lining layer was thicker and the cellularity was higher in the sublining compared to non-progressors, and compared to OP progressors. Both JSW-progressors and osteophyte-progressors showed increased vascularisation compared to non-progressors.
At baseline, FAC analysis pointed out that dendrite formation (p=0.036) response to heatshock/stress (p=0.015) and voltage gated ion transport (p=0.013) were annotation clusters that were related to pain. Surprisingly, no positive relation was found between inflammatory mediators and pain. In line with this, no relation between histological inflammation or lining thickness and pain was found.
**Conclusions:** We found evidence for a difference in underlying processes in the synovium regarding progression of cartilage damage and progression of osteophyte formation. The presence of macrophages, especially in the lining layer, is associated with progression of cartilage damage, whereas synovial expression of MMPs correlated to progression of osteophyte formation. Pain was associated with several nerve fiber related processes.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2912

OP0029 **PAIN SENSITIZATION AND RESPONSE TO PHYSIOTHERAPY TREATMENT IN PEOPLE WITH MODERATE TO SEVERE OSTEOARTHRITIS OF THE KNEE**

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**Background:** The clinical relevance of pain sensitization in knee osteoarthritis (OA) has been highlighted, whereby individuals with more severe knee pain demonstrate widespread hyperalgesia and increased temporal summation report. Physiotherapy is a frequently recommended conservative intervention for knee OA, however not all patients achieve clinically meaningful improvements in pain and function. To date the relationship between QST parameters and subsequent response to physiotherapy has not been prospectively investigated.
**Objectives:** The purpose of this prospective cohort study was to compare the somatosensory characteristics of people with knee OA who responded to physiotherapy with those who did not show a clinically meaningful response. We hypothesized that the non-responders to physiotherapy would demonstrate more evidence of pain sensitization at baseline.
**Methods:** A comprehensive battery of Quantitative Sensory Testing (QST) was conducted in 122 participants with knee OA referred for physiotherapy. QST measures included pressure pain thresholds (PPTs) measured at local, distal and remote sites, temporal summation (TS) at local and remore sites and conditioned pain modulation (CPM), in addition to measuring vibration threshold and mechanical detection thresholds.
Following physiotherapy participants were classified into responder and non-responder groups based on their change in WOMAC pain and function scores, and participants' global rating of change using the Outcome Measures in Rheumatology- Osteoarthritis Research Soceity International (OMERACT-OARSI) criteria.
A one-way between-groups multivariate analysis of variance (MANOVA) was performed to investigates effects of group (responder/non-responder) differences on QST parameters using a Bonferroni adjusted alpha level (p=.0083).
**Results:** 43 participants (35%) were responders to physiotherapy and 79 participants (65%) were non-responders. There were no significant differences in gender and age between the two groups. Likewise there were no significant differences between the groups with respect to sensory hypoesthesia (vibration and light touch).

The responder group demonstrated significantly higher PPTs at the arm (M =375kPa, SD =93.5) and tibia (M =378 kPa, SD =116) compared to the non-responder group (arm PPT, M =330 kPa, SD =85.2; tibia PPT, M =318.5, SD =96). Significantly lower temporal summation was also demonstrated in the responder group at the arm (M=1.1, SD=1.2) and at the knee (M =1.9, SD =1.6) compared to the non-responder group (TS arm M =1.9; SD =1.3; TS knee M =2.8, SD =1.46). The responder group also showed a more efficient CPM response (103% CPM change) compared to the non-responder group (99% CPM change), however these differences were not statistically significant (p=.056).

**Conclusions:** In knee OA non-responders to physiotherapy have a different somatosensory profile, showing increased hyperalgesia and enhanced temporal summation. While the results do not address predictors of treatment response, participants with greater indications of pain sensitization were more likely to be "non-responders" to physiotherapy. Patients identified at baseline as less likely to benefit from physiotherapy may warrant an alternate treatment approach.

**Disclosure of Interest:** None declared

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**THURSDAY, 9 JUNE 2016**

## Diagnosis and management of SSc

### OP0030 ASSOCIATED FACTORS WITH MORTALITY AND DERIVATION OF A SIMPLE 5-FACTORS TO PREDICT MORTALITY IN SSC-PATIENTS IN THE EUSTAR COHORT

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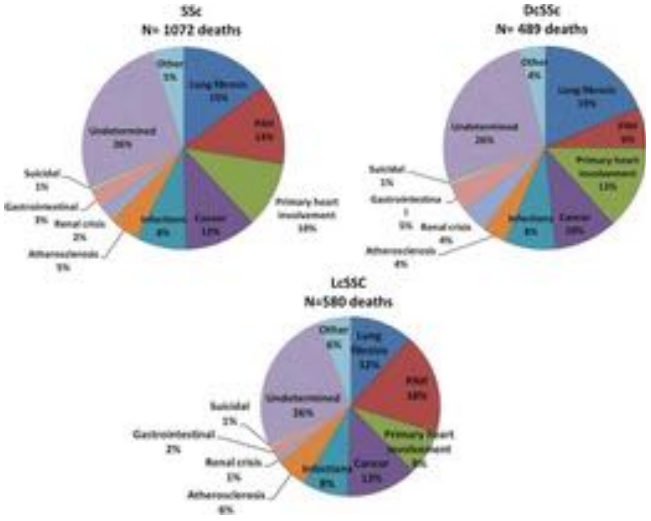
**Background:** Systemic sclerosis (SSc) remains a devastating condition associated with a high risk of mortality. However, the main causes of death and risk factors for mortality are only partially known.

**Objectives:** To investigate causes and independent predictors of death in a large European population of SSc-patients.

**Methods:** We performed a longitudinal observational study using the latest 2014 data extract from the EUSTAR cohort. We looked at (i) deaths and causes of death (SSc, non-SSc) and (ii) effect of demographics, disease characteristics and comorbidities on mortality. Investigators from each center were asked to indicate the single primary cause of death according to standardized definitions. Associated factors with mortality were analyzed first in univariate analysis using t-test, chi2 or fisher exact test as necessary, followed by multivariable Cox modeling. Based on cox multivariate analysis, a simple score was generated (SScore) by adding the integer of each hazard ratio of variables independently associated with mortality. The ability of the SScore was compared to the previous modified 5-factor score to predict overall and 5-years mortality, and SSc-related mortality during follow-up using C-statistics.

**Results:** A total of 11,194 SSc-patients were included: 86% of women, 31% of diffuse cutaneous forms, and mean disease duration: 5.9 [2.4–11.8] years. During mean follow-up of 27±33 months, 1072 (9.6%) patients died. Of these, 617 patients (58%) died from SSc-related cause, 270 from non-SSc cause (25%), whereas the cause of death remains unknown in 185 (17%). Main causes of death were lung fibrosis (14.7%) followed by PAH (12.9%), primary heart involvement (10.5%), cancer (11.5%), infections (8%) and atherosclerosis (4.8%).

The SScore comprised the following predictors: male gender (2 points), upper gastrointestinal involvement (2), proteinuria (5), LVEF<50% (3), DLCO<60% of predicted (2). Each increase of 1 point of the SScore was associated with a 35.9% [31.7–40.3] increase in mortality at 5 years. Areas under the ROC of the SScore to predict total mortality and SSc-related mortality were 0.70 (0.68–0.82) and 0.74 (0.72–0.76).




The accuracy of the previous 5-factor score was lower than the SScore to predict total mortality (p=0.005) and 5 years-mortality (p=0.003).

Further analyses looked at various subsets of SSc: by example, DcSSc patients had reduced survival as compared to LcSSc and causes of death were different: in DcSSc, the main causes of death were pulmonary fibrosis (18.6%), primary heart involvement (13.3%) and cancer (10.0%), whereas PAH (18.1%), cancer (12.8%) and pulmonary fibrosis (11.6%) were the leading causes in LcSSc (Figure).

**Conclusions:** Using the largest worldwide available cohort of SSc patients in which 1072 deaths have been recorded and characterized, we provide insight into the causes of deaths and emphasis on the contribution of the cardiopulmonary system.

In addition, we have established a new score to estimate the 5-year survival of SSc patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4285

### OP0031 RISK FACTORS FOR MALIGNANCIES SYNCHRONOUS TO THE ONSET OF SYSTEMIC SCLEROSIS IN PATIENTS POSITIVE FOR ANTI- RNA POLYMERASE III ANTIBODIES: A EUSTAR MULTICENTRE STUDY

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**Background:** Patients with anti-RNA polymerase III antibodies (anti-RNAP) have an increased risk of malignancies synchronous to the onset of Systemic Sclerosis (SSc). In a multicentre EUSTAR case-control study, however, only moderate odd ratio was observed (OR 3.85, 95%CI 1.3–10.9), except than for breast cancer (OR 20.2, 95%CI 1.4–355) (1). Defining clinical and demographic features characteristic of anti-RNAP+ SSc patients who suffer from simultaneous malignancy would be useful to individuate risk factors who can guide the clinicians in every-day practice to screen anti-RNAP+ SSc patients for cancer.

**Objectives:** To individuate risk factors for malignancies synchronous to the onset of SSc in anti-RNAP+ patients.

**Methods:** EUSTAR centers were asked to participate to this study, providing data on malignancy history of their anti-RNAP+ patients in a dedicated form.

**Results:** Among 158 anti-RNAP+ SSc patients collected from 13 EUSTAR centers, 14 cases of malignancies synchronous to the onset of SSc were identified. When compared with the other 144 anti-RNAP+ patients, patients with synchronous malignancies had an older mean age at SSc onset (65.3 yrs (SD 10.0) vs 49.3 (SD13.3); p<0.001) and an increased proportion of diffuse cutaneous subset (96% vs 56%; p:0.008; OR: 10.5 95%CI 1.33–82.6). A trend for increased proportion of males was also observed (43% vs 21%; p:0.06). In particular, the risk of non-breast cancer synchronous with SSc was greatly higher in male than in female patients (43% vs. 0.8%; p<0.001; OR 95.2 95%CI 10.2–890).

**Conclusions:** Anti-RNAP+ SSc patients of older age, and with diffuse cutaneous subset, are particularly at risk for malignancies synchronous to the onset of SSc. The risk of malignancies other than breast cancers is greatly increased in male patients. These risk factors may help in the screening for cancer in these patients.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.3171

## OP0032 GASTROINTESTINAL DISEASE AND MICROBIAL TRANSLOCATION IN PATIENTS WITH SYSTEMIC SCLEROSIS: AN OBSERVATIONAL STUDY ON THE EFFECT OF NUTRITIONAL INTERVENTION AND IMPLICATIONS FOR THE ROLE OF THE MICROBIOMA IN THE PATHOGENESIS OF THE DISEASE

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**Background:** Systemic Sclerosis (SSc) is an autoimmune disease characterized by progressive deposition of extracellular matrix components in the skin and visceral organs (1). Recently, it has been shown that microbial translocation plays an important role in immune system activation (2), and that dietary changes may affect gut microbiota, altering immune system activation and conditioning the development of several autoimmune diseases (3).
**Objectives:** The aims of the study were to investigate: a) which serum biomarkers could be used to evaluate and monitor GI disease in SSc patients and b) if nutritional intervention may reduce GI involvement, immune system activation and, finally, improve clinical symptoms and quality of life of SSc patients.
**Methods:** Thirty-eight SSc patients affected by GI involvement were enrolled in the study. At baseline. the following serum biomarkers were evaluated: intestinal-type fatty acid-binding protein (I-FABP), lipopolysaccharide (LPS), and soluble CD14 (sCD14) serum levels, markers of enterocyte damage, microbial translocation and immune system activation, respectively. Moreover, in each examination clinical symptoms and patient's reported outcomes (SF-36) were collected.
After six months from the assumption of a mediterranean diet with low introduction of meat and diary products (4), clinical symptoms and SF-36 were evaluated in all patients and sCD14, LPS and I-FABP in 14 SSc patients. Twenty-five normal subjects constituted the control group.
**Results:** At baseline, sCD14, LPS, and I-FABP resulted significantly higher in sera of SSc patients than healthy controls (Fig. 1A), and there was a strong correlation between sCD14/ I-FABP and LPS/I-FABP serum levels (Fig. 1B).

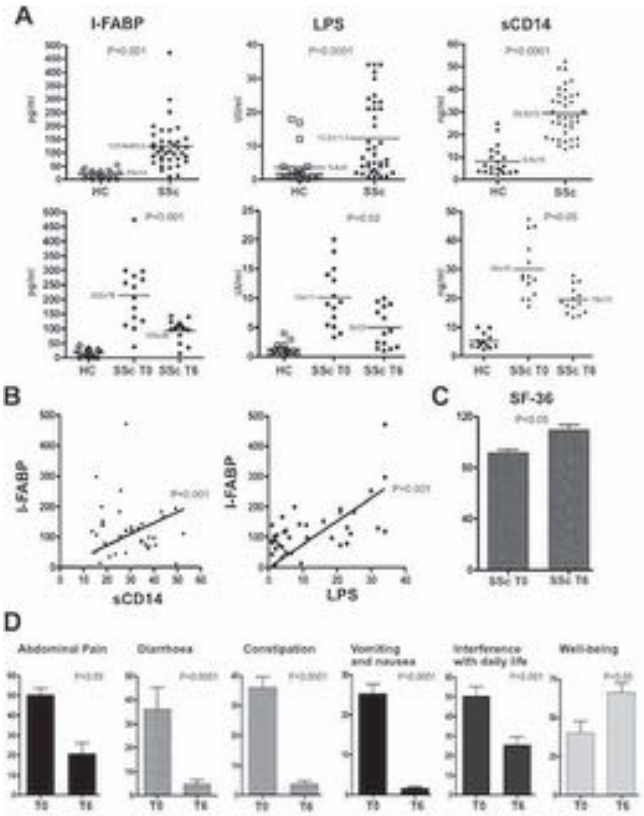



**Figure 1. Evaluation of gastrointestinal (GI) damage, microbial translocation, immune system activation and clinical symptoms before and after nutritional intervention in patients affected by Systemic Sclerosis (SSc). A.** Upper panel: Intestinal-type fatty acid-binding protein (I-FABP), lipopolysaccharide (LPS), and soluble CD14 (sCD14) serum levels, measured by ELISA, in SSc patients (SSc pts) and healthy controls (HC) at basal and, lower panel, after 6 months (T6) of mediterranean diet with low introduction of meat and diary products. **B.** Correlation between serum levels of I-FABP with sCD14 (left) and LPS (right) in sera of SSc patients. **C.** Evaluation of the quality of life in SSc pts before (T0) and after 6 months of semi-vegetarian and low-gluten nutritional intervention (T6). SF-36: Short Form (36) Health Survey questionnaire. **D.** Evaluation of GI symptoms and quality of life in SSc pts before (T0) and after 6 months of semi-vegetarian and low-gluten nutritional intervention (T6), carried out with the Visual Analogue Scale for Irritable Bowel Syndrome (VAS-IBS) questionnaire (Dengiavi M et al. BMC Gastroenterology 2007, 7:16). Horizontal bars: mean values ± SD. Statistical analysis has been carried out by the GraphPad Instat software. All the p-values have been calculated by Mann-Whitney unpaired test.

Higher LPS plasma levels (β=10.2, 95% CI (2.6, 17.9), p=0.01, $R^2$ =0.17), but not sCD14 and I-FABP, were associated with the presence of Small Intestine Bacterial Overgrowth (SIBO). There were no statistical differences between patients with and/or without elevated bowel transit time, as assessed by lactulose breath test.
After 6 months of diet, a significant decrease of sCD14, LPS and I-FABP was observed and patients reported a consistent improvement of GI symptoms as well as of the quality of life (Fig. 1A-D).
**Conclusions:** This work suggests that GI damage, and the consequent microbial translocation, triggers immune system activation and sustain clinical symptoms in SSc patients. Moreover, specific nutritional intervention significantly improves the clinical symptoms and the GI damage (I-FABP), thus reducing microbial translocation (LPS) and immune system activation (sCD14).
Gut microbioma and microbial translocation may play an important role in the activation of the immune system and, thus, in the pathogenesis of SSc disease.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4678

## OP0033 EUROPEAN SCLERODERMA STUDY GROUP ACTIVITY INDEX CAPTURES VARIATIONS IN DISEASE ACTIVITY OVER TIME AND PREDICTS ORGAN DAMAGE IN EARLY SYSTEMIC SCLEROSIS: DATA FROM THE CANADIAN SCLERODERMA RESEARCH GROUP

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**Background:** Endpoints in systemic sclerosis (SSc), such as modified Rodnan skin score (mRSS) and pulmonary function tests represent only parts of a multisystem disease. The European Scleroderma Study Group (EScSG) developed an SSc activity index, which captures involvement of multiple organs. The predictive validity of the SSc activity index is unclear.
**Objectives:** To estimate the effect of disease activity as measured by EScSG activity index, on the risk of subsequent organ damage in the Canadian Scleroderma Research Group (CSRG) cohort.
**Methods:** Of 421 SSc patients from the CSRG database with disease duration of ≤3 years, 197 who had no evidence of endstage organ damage initially and 3-year follow-up were included. Disease activity was assessed by EScSG activity index with two variability measures: 1. adjusted mean (am) EScSG activity score (the area under the curve of EScSG activity index over observation period), and 2. persistently active disease (PAD)/flare (EScSG score of ≥3 at follow-up visit). Internal organ involvement assessed over follow-up was based on Medsger severity scale and included accrual of a new severity score overall and by specific organ systems. Adjusted odds ratios (OR) for association between disease activity, severity and progression were calculated using regression analysis.
**Results:** After adjustment for covariates, amEScSG activity score was the most consistent predictor of risk at 3 year follow-up: disease progression as accrual of a new severity grade (Δ≥1) in any of the major internal organs (OR 1.42, 95%CI 1.14–2.25, p=0.007), lung disease (OR 1.86, 95%CI 1.31–2.64, p<0.0001), decline in FVC (OR 3.05, 95%CI 1.47–6.31, p=0.003) and DLCO (OR 1.61, 95%CI 1.06–2.46, p=0.026), ΔHAQ (OR 1.729, 95%CI 1.250–2.391, p<0.001), severity of visceral disease (Table). amEScSG predicted accrual of organ damage only in diffuse cutaneous SSc (dcSSc). In the multivariable analysis, progression of lung disease in dcSSc was predicted by amEScSG activity score (p=0.006), and severity of lung disease by amEScSG (p<0.0001), older age (p=0.023), mRSS (p<0.001) and initial severity of lung disease (p<0.0001). The best predictor of renal disease severity at 3-year was initial severity of kidney involvement (p<0.0001).

Table 1. Predictive value of EScSG activity index for a total severity score in cardiac, pulmonary and renal systems on Medsger's severity scale, at 1 and 3-year observation in regression analysis

| | 1-year FU | | | | | 3-year FU | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | B | Std. error | b | t | p | B | Std. error | b | t | P |
| EScSG activity index, baseline | | | | | | | | | | |
| Unadjusted | 0.177 | 0.056 | 0.252 | 3.152 | **0.002** | 0.159 | 0.066 | 0.202 | 2.385 | 0.018 |
| Adjusted | 0.100 | 0.049 | 0.143 | 2.042 | **0.043** | 0.106 | 0.059 | 0.135 | 1.799 | 0.074 |
| Active disease at baseline | | | | | | | | | | |
| Unadjusted | 0.441 | 0.177 | 0.202 | 2.491 | **0.014** | 0.429 | 0.208 | 0.176 | 2.067 | 0.041 |
| Adjusted | 0.223 | 0.151 | 0.102 | 1.471 | 0.144 | 0.271 | 0.182 | 0.111 | 1.491 | 0.138 |
| amEScSG activity score | | | | | | | | | | |
| Unadjusted | – | – | – | – | – | 0.364 | 0.077 | 0.401 | 4.739 | **<0.000** |
| Adjusted | | | | | | 0.274 | 0.072 | 0.303 | 3.826 | **<0.000** |
| PAD/Flare | | | | | | | | | | |
| Unadjusted | – | – | – | – | – | 0.893 | 0.256 | 0.293 | 3.493 | **0.001** |
| Adjusted | | | | | | 0.795 | 0.223 | 0.261 | 3.566 | **0.001** |

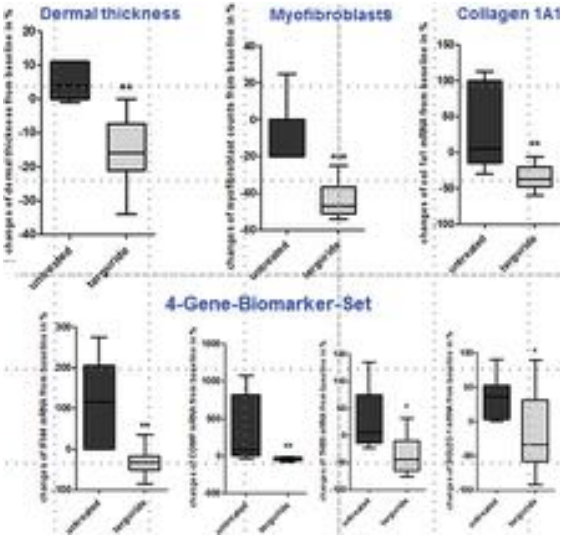
**Conclusions:** The mean adjusted EScSG reliably captured disease activity over time in individual patients and predicted the risk of deterioration in health status,

disease progression and development of severe internal organ involvement in diffuse SSc, after adjustment for key covariates.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4786

## OP0034 THE SEROTONIN RECEPTOR 2 INHIBITOR TERGURIDE HAS BENEFICIAL EFFECTS ON SKIN FIBROSIS: RESULTS FROM A PHASE 2 PROOF OF CONCEPT STUDY

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**Background:** Circumstantial evidence from preclinical studies indicates a key role of serotonin (5-HT) signaling via the 5-HT-2B receptor in the development of fibrosis. Terguride is an orally available 5-HT-2 receptor inhibitor that has shown beneficial effects in different animal models of systemic sclerosis (SSc).
**Objectives:** To evaluate the efficacy of Terguride for the treatment of fibrosis in patients with SSc in an investigator initiated phase 2 proof of concept study.
**Methods:** Main inclusion criteria were fulfillment of ACR classification criteria and diffuse cutaneous SSc (dcSSc). Patients with end-stage organ involvement and treatment with potentially disease modifying agents including immunosuppressives were excluded. Patients were treated with Terguride at up to 3 mg/d p.o. or standard of care (post hoc control) for three months. Primary efficacy endpoints were changes of pre-defined skin biopsy biomarkers over the three months treatment period. Secondary efficacy endpoints included change of mRSS and lung function parameters. Serious adverse events (SAEs) and AEs were coded using MedDRA. The study was externally monitored.
**Results:** Twelve patients were recruited into the Terguride group and 6 patients into the control group. The primary endpoints, skin biopsy biomarkers, showed a consistent and statistically significant down-regulation compared to the control group (Figure) for dermal thickness, myofibroblast counts and mRNA levels of col1a1, col1a2 as well as for the Lafyatis 4-gene biomarker set (COMP, THSP-1, SIGLEC-1, IFI-44). This was accompanied by a reduction in mRSS of - 32.3% versus baseline in the Terguride group versus stable values in the control group ($p<0.05$). Lung function parameters did not change significantly. Overall, 33 AEs (n=27 mild and n=6 moderate) and one SAE (pyelonephritis, not related) occurred in the Terguride group, most often consisting of nausea and vomiting (9% and 13% of patients respectively).Twelve patients were recruited into the Terguride group and 6 patients into the control group. The primary endpoints, skin biopsy biomarkers, showed a consistent and statistically significant down-regulation compared to the control group (Figure) for dermal thickness, myofibroblast counts and mRNA levels of col1a1, col1a2 as well as for the Lafyatis 4-gene biomarker set (COMP, THSP-1, SIGLEC-1, IFI-44). This was accompanied by a reduction in mRSS of - 32.3% versus baseline in the Terguride group versus stable values in the control group ($p<0.05$). Lung function parameters did not change significantly. Overall, 33 AEs (n=27 mild and n=6 moderate) and one SAE (pyelonephritis, not related) occurred in the Terguride group, most often consisting of nausea and vomiting (9% and 13% of patients respectively).




**Conclusions:** Terguride was well tolerated in patients with dcSSc. Strong and consistent effects on fibrosis related skin biopsy biomarkers could be observed in this open-label controlled phase 2 proof of concept study, which was further supported by a significant improvement of the mRSS over the control group. These data justify further investigation in an upcoming randomized placebo controlled phase 3 study.
**Disclosure of Interest:** O. Distler Grant/research support from: Bayer, Sanofi, Ergonex, Boehringer Ingelheim, Actelion, Pfizer, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, EpiPharm, Ergonex, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Pharmacyclics, Pfizer, Serodapharm, Sinoxa, B. Maurer: None declared, S. Vettori: None declared, S. Blumhardt: None declared, D. Frey: None declared, A. Distler: None declared, C. Beyer: None declared, J. H. Distler Shareholder of: 4 D Science, Consultant for: Actelion, BMS, Celgene, Bayer Pharma, Boehringer Ingelheim, JB Therapeutics, Sanofi-Aventis, Novartis, UCB, GSK, Array Biopharma and Active Biotech
**DOI:** 10.1136/annrheumdis-2016-eular.5587

## OP0035 CIRCULATING PLASMABLASTS LEVELS REFLECT INFLAMMATORY ACTIVITY IN IGG4-RELATED DISEASE LESIONS AS ASSESSED BY QUANTITATIVE POSITRON EMISSION TOMOGRAPHY

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**Background:** IgG4-Related Disease (IgG4-RD) is a systemic inflammatory condition characterized by fibrous swelling of affected organs, serum IgG4 elevation, and IgG4+ plasmacells tissue infiltration. 18-Fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) scan is emerging as a promising imaging technique to detect organs involved by IgG4-RD and to assess disease response to treatment. The relationship between FGD-PET findings and immunological perturbations occurring in IgG4-RD has never been evaluated.
**Objectives:** To correlate the intensity and distribution of FDG-PET uptake with clinical and immunological parameters in patients with active untreated IgG4-RD.
**Methods:** Patients with active, untreated, biopsy proven IgG4-RD were included in the study. Disease activity was assessed through clinical (IgG4-RD Responder Index (RI)) and immunological (erythrocyte sedimentation rate (ESR), C reactive protein (CRP), serum IgG4, and circulating plasmablasts) parameters. Plasmablasts, a recently characterized disease biomarker, were identified as CD19+CD20-CD27+CD38bright cells on flow cytometry. FDG-PET/CT was performed in all patients at diagnosis. Quantitative assessment of FDG uptake was measured using the mean Standardized Uptake Value corrected for the Partial Volume Effect (PVC-SUV). Lymph nodes <1 cm of diameter were excluded from the analysis because of the risk of PVC-SUV over/under-estimation. In patients with multiorgan involvement, the IgG4-RD lesion with the highest PVC-SUV was selected to correlate FGD uptake with clinical and serological parameters.
**Results:** We studied 15 patients (7 males, 8 females) with a mean age of 63 years (range, 30–77 years). Twelve (80%) patients had multiorgan IgG4-RD involving lymphnodes (7 patients); aorta (5 patients); parotids glands and pancreas (3 cases each); bones, skin, thyroid, lung, submandibular and lachrymal glands (2 cases each); meninges, nasal cavity, oropharynx, palate, liver, CNS, and retrorbital space (one case each). The median IgG4-RD RI was 9 (range 6–16; normal =0). The median levels of ESR, CRP, serum IgG4 and plasmablasts at baseline were 30 mm/h (range 6–121 mm/h, normal <20 mm/h), 11.0 mg/L (range 0.0–48.0 mg/L; normal <6mg/L), 284.0 mg/dL (range 45–2100 mg/dL, normal <121 mg/dL), and 3870 cells/mL (range 1000–10000 cells/mL, normal <690 cells/mL), respectively. The median PCV-SUV was 6.24 (range 2.48–16.39). Significant positive correlation was found between PVC-SUV and serum plasmablasts levels (r=.84, p=.004). No correlation was found between PVC-SUV and either CRP, ESR, serum IgG4 levels, number of organs involved, and IgG4-RD RI at baseline ($p>.05$).
**Conclusions:** Our study demonstrates for the first time a positive correlation between circulating plasmablasts and inflammatory activity in IgG4-RD lesions as assessed by PVC-SUV on FDG-PET. Our results further strengthen the utility of circulating plasmablasts as a biomarker of disease activity. Conventional inflammatory markers, serum IgG4 levels, and IgG4-RD RI do not appear to correlate with metabolic activity in IgG4-RD lesions.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6013

## OP0036 SCREENING FOR PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS: COMPARISON OF THE PREDICTIVE ACCURACY OF VARIOUS ALGORITHMS

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**Background:** Pulmonary arterial hypertension (PAH) is one of the leading causes of mortality in systemic sclerosis (SSc) and has a 3 year survival rate of approximately 50%. Early screening for PAH in SSc may improve survival.
**Objectives:** To compare the predictive accuracy of two SSc-PAH screening algorithms, DETECT and Australian Scleroderma Interest Group (ASIG), to the

2009 European Society of Cardiology/European Respiratory Society (ESC/ERS) screening recommendations in a well-defined North American cohort.
**Methods:** Consecutive SSc patients with suspected PAH according to the 2013 recommendations for screening PAH (1) undergoing right heart catheterization (RHC) were evaluated. Those patients with no pulmonary hypertension or PAH on RHC who also had clinical variables available for applying the various screening algorithms had DETECT (2), ASIG (3) and 2009 ESC/ERS (4) screening algorithms applied. For each model, contingency table analysis was used to determine sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively) for PAH [defined as mean pulmonary artery pressure (mPAP) > or =25, pulmonary capillary wedge pressure (PCWP) < or =15, and no/mild interstitial lung disease (ILD) on high-resolution CT scan of chest (HRCT), or FVC > or =70%].
**Results:** A total of 108 patients were screened for PAH, 77 of those patients met the recommendations for RHC, and 65 of those patients underwent RHC. The prevalence of PAH was 17%. Those patients with RHC values indicating no PH (N=35) or PAH (N=11) who also had biochemical markers available for review were identified and DETECT, ASIG, and ESC/ERS algorithms were applied to all of those patients. Those patients who met inclusion/exclusion criteria for DETECT and ASIG were also separately evaluated. DETECT and ASIG both had similar performances with sensitivity of 100% for those who met the respective inclusion/exclusion criteria. ESC/ERS had a sensitivity of 80% (Table 1).

Table 1. Summary of the predictive accuracies of screening algorithms for PAH in SSc

| | DETECT | | ASIG | | 2009 ESC/ERS |
|---|---|---|---|---|---|
| | All patients | Patients who met inclusion/ exclusion criteria* | All patients | Patients who met inclusion/ exclusion criteria** | All patients |
| Number of patients | 46 | 6 | 44 | 20 | 44 |
| Sensitivity | 1.00 | 1.00 | 0.90 | 1.00 | 0.80 |
| Specificity | 0.40 | 0.25 | 0.56 | 0.55 | 0.67 |
| Positive predictive value | 0.34 | 0.40 | 0.38 | 0.62 | 0.42 |
| Negative predictive value | 1.00 | 1.00 | 0.95 | 1.00 | 0.92 |

*Coghlan J et al. Ann Rheum Dis 2014; **Thakkar V et al. Arthritis Res Ther 2012.

**Conclusions:** In a well-defined North American cohort, DETECT and ASIG performed similarly and were superior to 2009 ESC/ERS screening recommendations in the detection of PAH in SSc patients. Many patients who are at-risk for PAH did not meet the inclusion/exclusion criteria for DETECT and ASIG in our cohort.
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## OP0037 FIRST PILOT STUDY OF AN IMPLANTABLE LOOP RECORDER (ILR) IN SYSTEMIC SCLEROSIS DETECTS SIGNIFICANT CARDIAC ARRHYTHMIAS WITH CMR ABNORMALITIES

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**Background:** SSc-cardiomyopathy associated conduction abnormalities carry a poor prognosis, but their pathogenesis is unclear. Early detection to prevent complications is essential. ILRs are well-established in cardiology practice.
**Objectives:** To determine the spectrum of cardiac conduction abnormalities (CCA) using the REVEAL® ILR & their association with CMR in patients (pts) with SSc with no known cardiac disease.
**Methods:** 20 pts with (ACR/EULAR criteria) SSc, with no diabetes &/or more than 1 cardiovascular (CV) risk factor, were assessed for SSc/CV profile & comprehensive CV assessment performed, inc. 3T delayed enhancement-CMR (reported by CMR-cardiologists) & ILR insertion. ILR data was downloaded 3 monthly +/– at pt request if indicated. One yr data is reported. CMR compared to 30 healthy controls.
**Results:** ILR data was available for 19 pts; 63% female, 84% Caucasian; mean (SD) age 53 (12)yrs, time from 1st non-RP symptom 9 (8)yrs; 32% dcSSc, 32% ACA+ve, 21% Scl70+ve, 54% palpitations hx, 42% known ILD, 11% DU hx, 0% pulmonary hypertension. Ten (52%) pts had ILR abnormalities; 4 with dcSSc, 3 ACA+ve, 3 Scl70+ve, 6 with palpitations hx, 4 known ILD, 3 DU hx. Subanalysis; 8 (42%) pts had supraventricular ectopics (SVE), 2 (11%) with ventricular ectopics (VE), 4 (21%) with arrhythmias of which 1 atrial flutter, 1 SVT, 1 VT & 1 complete heart block (CHB). Of the 4 pts with arrhythmias; 2 had dcSSc, 1 ACA+ve, 1 Scl70, 3 palpitations hx, 2 known ILD, 2 DU hx. Pt with CHB (dcSSc) had few SVE/VEs & 3 couplets on 24hr ECG 6 weeks previous. CMR data was available for 15 SSc pts (DE in 14; 1 pt claustrophobic, no IV access in 2, 1 CMR abandoned due to pacemaker insertion for CHB). Trend towards lower LVmass & distensibility (ie greater arterial stiffness) & higher extracellular volume (ECV, fibrosis marker) seen in pts with ILR abnormalities (p>0.05). Trend for higher ECV in those with SVE [unadj. mean difference (diff.) (95%CI) 1.1 (-2.5, 4.7)% p0.513], VE [0.7 (-4.9, 6.3)% p0.789] & arrhythmias [1.8 (-3.7, 7.3)% p0.486]. ECV was higher in SSc vs. controls; mean diff. 4.9 (3.2, 6.6)% p<0.001 $R^2$ 0.568, adj. for age/sex; with trend for lower LV mass & distensibility.

Table 1. CMR measures in SSc pts with/without ILR abnormalities

| CMR variable | ILR normal n (%) = 7 (47) | ILR abnormal n (%) = 8 (53) | Mean diff. [95% CI] p | Mean diff. [95% CI] p adj. age/sex |
|---|---|---|---|---|
| LVEF, % | 58.7 (3.5) | 61.3 (5.1) | 2.6 [–2.4, 7.5] 0.286 | 0.3 [–5.2, 5.8] 0.908 |
| LVmass/BSA, g/m$^2$ | 47.1 (13.7) | 42.9 (7.0) | –4.2 [–17.2, 8.9] 0.488 | –6.1 [–18.0, 5.7] 0.280 |
| LV mass/EDV, g/ml | 0.54 (0.07) | 0.54 (0.08) | –0.01 [–0.09, 0.08] 0.895 | 0.02 [–0.11, 0.11] 0.974 |
| Torsion, ° | 12.4 (4.1) n=6 | 13.5 (6.1) n=7 | 1.1 [–5.4, 7.6] 0.714 | –0.7 [–8.9, 7.5] 0.849 |
| Distensibility, $10^{-3}$mmHg$^{-1}$ | 4.6 (3.0) | 3.6 (2.6) n=7 | –1.0 [–4.3, 2.3] 0.510 | 0.3 [–3.5, 4.1] 0.863 |
| ECV, % | 29.1 (4.2) | 31.1 (1.7) n=7 | 2.0 [–2.0, 5.9] 0.278 | 1.7 [–3.1, 6.5] 0.444 |
| Late gad enhancement presence | 3 (42.9)* | 2 (28.6) n=7* | p=1.00 | p=0.784 |

Values = mean (SD) *n (%).

**Conclusions:** This first ILR in SSc study demonstrates its utility in the incidental detection of CCA, including serious cardiac arrhythmias & suggests associated CMR abnormalities. These data support the need for identification of pts at risk that would benefit from ILR & provide insights into the pathogenesis of SSc-cardiomyopathy
**Disclosure of Interest:** None declared
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## OP0038 IMPROVED SURVIVAL IN DERMATOMYOSITIS AND POLYMYOSITIS: A GENERAL POPULATION-BASE STUDY

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**Background:** Dermatomyositis (DM) and polymyositis (PM) are associated with significant mortality and morbidity. However, mortality trends for these two diseases are unknown, especially in the general population context.
**Objectives:** To address this knowledge gap, we assess mortality trends for individuals with PM and DM between January 1, 1997 and December 31, 2012 in the general population.
**Methods:** Using an administrative health database from province of British Columbia, Canada, we identified all incident cases of both PM and DM and up to 10 non-disease controls matched on sex-, age- and entry-time for each. Study cohorts for both PM and DM were divided into two subgroups based on the year of diagnosis (ie., 1997–2004 and 2005–2012).Mortality rates were calculated, as well as hazard ratios (HR) using a Cox proportional hazard model. HRs were adjusted for potential confounders (e.g., number of hospitalization and outpatient visits, Charlson's comorbidity index, glucocorticoid use, cardiovascular drugs, cox-2 inhibitors).
**Results:** Mortality rates (cases per 1000 person-years) in the early cohorts (ie.,1997–2004) for PM and DM patients were considerably higher than those in the later cohorts (ie., 2005–2012) (for PM: 226.1 vs 73.3; for DM: 287.0 vs 56.9). In contrast, smaller improvements were observed in the comparison groups (for PM: 28.9 vs 16.2; for DM: 31.0 vs 13.5). Corresponding to these two time periods, HRs for mortality for PM were 5.6 (95% CI, 3.2–9.9) and 3.1 (95%CI, 1.8–5.3), respectively, and 8.0 (95% CI, 4.0–16.0) and 2.9 (95%CI, 1.7–5.2) for DM, respectively. Testing for difference between incident cohorts via an interaction term were all significant (see table, p. 68).
**Conclusions:** This population-based study shows that the survival of PM and DM patients has improved in recent years, suggesting that new treatment strategies and improved management of PM and DM and its associated complications have led to significant improvements in PM- and DM-associated mortality.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5138

**Abstract OP0038** – Table 1. Incidence rates and hazard ratios (HR) for associations between PM/DM and death according to sub-group

| | Polymyositis | | | | Dermatomyositis | | | |
|---|---|---|---|---|---|---|---|---|
| | 1997–2004 | | 2005–2012 | | 1997–2004 | | 2005–2012 | |
| | PM Cohort | Non-PM Cohort | PM Cohort | Non-PM Cohort | DM Cohort | Non-DM Cohort | DM Cohort | Non-DM Cohort |
| **Overall** | 115.0 | 464.0 | 268.0 | 1072.0 | 79.0 | 324.0 | 250.0 | 1000.0 |
| Number of deaths | 56.0 | 51.0 | 50.0 | 55.0 | 42.0 | 36.0 | 40.0 | 46.0 |
| Mean follow-up time (person-years) | 2.2 | 3.8 | 2.5 | 3.2 | 1.9 | 3.6 | 2.8 | 3.4 |
| Death rate (deaths per 1000 person-years) | 226.1 | 28.9 | 73.3 | 16.2 | 287.0 | 31.0 | 56.9 | 13.5 |
| Fully adjusted HR (95% CI)* | 5.6 (3.2–9.9) | 1 (ref) | 3.1 (1.8–5.3) | 1 (ref) | 8.0 (4.0–16.0) | 1 (ref) | 2.9 (1.7- 5.2) | 1.0 (ref) |
| **Men** | 53.0 | 216.0 | 106.0 | 424.0 | 33.0 | 132.0 | 80.0 | 320.0 |
| Number of deaths | 25.0 | 35.0 | 23.0 | 23.0 | 19.0 | 21.0 | 20.0 | 25.0 |
| Mean follow-up time (person-years) | 2.1 | 3.8 | 2.4 | 3.1 | 1.7 | 3.7 | 2.8 | 3.6 |
| Death rate (deaths per 1000 person-years) | 228.2 | 42.3 | 89.0 | 17.3 | 329.1 | 42.8 | 90.8 | 21.8 |
| Fully adjusted HR (95% CI)* | 4.0 (1.8–9.0) | 1 (ref) | 2.9 (1.3–6.8) | 1 (ref) | 10.9 (3.7–31.8) | 1 (ref) | 3.7 (1.4–9.8) | 1 (ref) |
| **Women** | 62.0 | 248.0 | 162.0 | 648.0 | 46.0 | 192.0 | 170.0 | 680.0 |
| Number of deaths | 31.0 | 16.0 | 27.0 | 32.0 | 23.0 | 15.0 | 20.0 | 21.0 |
| Mean follow-up time (person-years) | 2.2 | 3.8 | 2.6 | 3.2 | 1.9 | 3.5 | 2.8 | 3.3 |
| Death rate (deaths per 1000 person-years) | 224.4 | 17.0 | 63.7 | 15.4 | 259.5 | 22.3 | 41.5 | 9.2 |
| Fully adjusted HR (95% CI)* | 9.6 (4.1–22.5) | 1 (ref) | 3.6 (1.8–7.4) | 1 (ref) | 7.4 (2.9–18.8) | 1 (ref) | 2.6 (1.3–5.3) | 1 (ref) |

**THURSDAY, 9 JUNE 2016**

## Advances in SLE therapeutics

### OP0039 IMPACT OF BELIMUMAB USE ON FLARES AMONG PATIENTS DIAGNOSED WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN A US COMMERCIALLY INSURED DATABASE: 2010-2014

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**Background:** Belimumab, a B-lymphocyte stimulator, was FDA-approved March 2011 for the treatment of adult patients with active, autoantibody-positive SLE receiving standard of care medications. There is a need to evaluate belimumab's effectiveness in real-world practice settings.
**Objectives:** To describe the effectiveness of initiating belimumab treatment on flare episodes.
**Methods:** Patients aged 18–64 years at first belimumab infusion (index date) between 01 Jan 2010 – 31 Dec 2014 were selected from the US Truven Health MarketScan® Commercial Database (study ID 204999). SLE diagnosis (ICD-9 code 710.0) was documented prior to/on index date. We included patients with complete medical and pharmacy benefits ≥6 months prior to index (baseline period). Moderate and severe SLE flare episodes were defined using previously published algorithms developed for claims data (Garris C, 2013). Incidence rates (IRs) and 95% CIs were calculated per subject for 3-month intervals, with two intervals in the baseline period and a variable number of intervals in the follow-up period. In primary "as treated" analyses, person-time spanned the duration of belimumab exposure including one month after last infusion. Sensitivity analyses were performed using "intention to treat" (ITT) analysis including all follow-up during each interval for person-time. To statistically compare the period before and after belimumab initiation, IRs were calculated in the total baseline and follow-up period per patient in both as-treated and ITT analyses, and compared using the Wilcoxon signed-rank test.

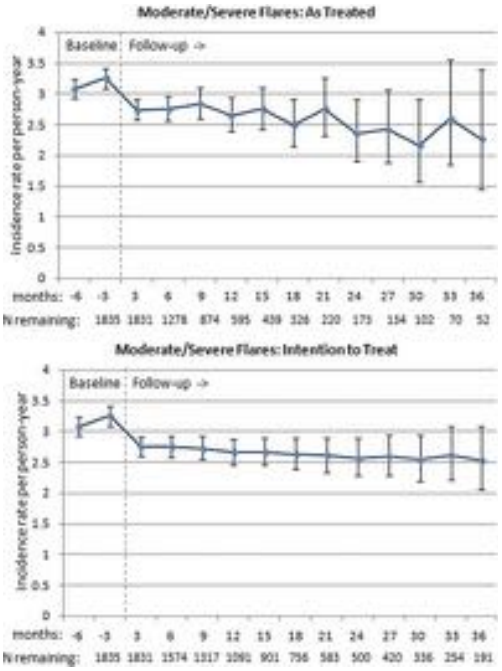



Figure 1. Incidence rates and 95% CIs for moderate and severe SLE flares among 1835 patients initiating belimumab: six month baseline period and follow-up.

**Results:** We identified 1835 belimumab initiators (mean age 43 years, SD 11; 94% female). SLE comorbidities in the baseline period included arthritis (46%), lupus nephritis (7%), anemia (20%), rash (27%), arthralgia (43%), and mood disorders (34%). Similarly, 15% were hospitalized and 27% had ER visits. Baseline medications included antimalarials (68%), oral corticosteroids (71%), immunosuppressants (59%), and NSAIDs (32%). Belimumab continuation rates were 81% at 6 months, 55% at year 1, 35% at year 2 and 27% at year 3 post index. There was a marked and sustained decrease in moderate/severe flare incidence following belimumab initiation (Figure 1). This pattern was similar in the ITT sensitivity analysis. The Wilcoxon signed-rank test yielded highly statistically significant results for both the primary as treated analysis and the ITT analysis ($p<0.001$).
**Conclusions:** In this large sample of SLE patients initiating belimumab, the rates of moderate/severe SLE flares during belimumab treatment were significantly lower compared with those in the pre-belimumab period. The comparative effectiveness of belimumab vs. standard of care immunosuppressants, as well as causes and effects of belimumab discontinuation should be further explored.
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### OP0040 PERIPHERAL BLOOD TRANSCRIPTIONAL CHANGES ELICITED BY TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS WITH DAPIROLIZUMAB PEGOL (A PEGYLATED ANTI-CD40L FAB')

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**Background:** CD40-CD40L is a critical costimulatory pathway necessary for normal immune function (including B cell differentiation, germinal center formation and antibody isotype switching) and strongly implicated in the pathogenesis of autoimmune disorders such as SLE. In a randomised, placebo-controlled, parallel group Phase 1 study, dapirolizumab pegol (DZP), a pegylated anti-CD40L Fab', was administered to patients with active SLE on stable background therapy (NCT01764594).
**Objectives:** To examine the effect of DZP on peripheral blood RNA transcripts associated with immune cell subsets and SLE disease activity as biomarkers for proof of biological activity.
**Methods:** Twenty-four subjects were randomised (2:1) to receive DZP or placebo and 22 subjects completed the study. Subjects randomised to DZP received a loading dose of 30 mg/kg followed by 15 mg/kg every 2 weeks for a total of 6 doses and were subsequently followed for 18 weeks. For transcriptional analyses, blood was collected in PAXgene tubes at Weeks 0, 2, 4, 8, 12, 20 and 28. A panel of 96 genes was selected for analysis by qPCR including genes expressed in plasma cells, B cells and other immune cells. Also included were transcripts associated with SLE disease activity, such as the Type I Interferon (IFN) signature. For the analysis, genes were grouped into functional domains (such as B cells, T

cells, IFN) and decision criteria were designed to identify consistent expression changes within a domain. At a gene level, a positive signal required a >2 fold up- or down-regulated change from baseline, and occurring on at least 2 successive visits. Differences in changes from baseline between DZP and placebo groups were considered significant at <0.0894 (to achieve a 5% false positive rate at a functional domain level).
**Results:** Changes in genes within the plasma cell and B cell domains had the greatest degree of statistical significance. Among the plasma cell genes, the DZP group exhibited rapid decreases in the expression of several immunoglobulin-associated genes (secretory IgA, IgG, Igk, Igl, J chain) starting at Week 2 and maintained over the treatment period. Among the B cell genes, the DZP group showed a transient increase in CD19 and CD20 RNA transcripts at Week 2 that was mirrored by flow cytometry data. Additionally, there were transient increases in membrane IgD, membrane IgM and TCL1A genes which are associated with naïve B cells. Several of the patients in the DZP group also exhibited a ≥2 fold reduction in the expression of IFN-responsive genes (MX1, OAS1, IFITM3, G1P2) for at least 2 time points. No other consistent changes in other functional group expression patterns were observed.
**Conclusions:** In summary, DZP treatment resulted in changes in peripheral blood RNA transcripts found in plasma cells and B cells consistent with the inhibition of CD40L:CD40 signaling. A trend in the reduction of the IFN signature was also observed with DZP. The utility of this approach to monitor biological activity, early clinical response and patient stratification will be further explored.
**Disclosure of Interest:** A. Ranger: None declared, N. Allaire Employee of: Biogen, P. Colman Employee of: Biogen, C. Wager Employee of: Biogen, H. Li Employee of: Biogen, A. Thai Employee of: Biogen, P. Cullen Employee of: Biogen, C. Otoul Employee of: UCB Pharma, J. Czerkowicz Employee of: Biogen, C. Roberts Employee of: Biogen, C. Chamberlain Shareholder of: UCB Pharma, Employee of: UCB Pharma, L. Burkly Employee of: Biogen, G. Johnston Shareholder of: UCB Pharma, Employee of: UCB Pharma
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## OP0041 JNJ-473 POTENTLY AND SPECIFICALLY DEPLETES PDCS IN SLE PATIENT BLOOD IN VITRO AND ABLATES TLR9-INDUCED INTERFERON ALPHA RESPONSES

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**Background:** Plasmacytoid dendritic cells (pDCs) are potent producers of IFNα and are thought to have a pathogenic role in Systemic Lupus Erythematosus (SLE). JNJ-473, previously known as CSL362, is an Fc engineered, neutralising anti-IL-3Rα (CD123) monoclonal antibody that depletes CD123 expressing cells, such as pDCs. CSL362 has recently completed a phase I clinical trial in acute myeloid leukemia.
**Objectives:** To investigate the *in vitro* depletion of pDCs with JNJ-473 in SLE patient blood and evaluate novel biomarkers of JNJ-473 efficacy.
**Methods:** Blood samples from 34 SLE patients (31 female and 3 male; mean age = 44.5; mean SLEDAI = 4, range 0–21) and 34 healthy controls (HC), matched for age and gender, were obtained. Whole blood (WB) was analysed by flow cytometry (FACS) for absolute cell counts of various cell subsets (pDC, myeloid DC, basophils, monocytes, T-cell subsets, B-cell subsets, neutrophils, eosinophils and natural killer (NK) cells) and for CD123 expression. Peripheral blood mononuclear cells (PBMC) from SLE patients and HC were cultured with JNJ-473 (0, 0.0041, 0.0123 or 1 μg/ml) for 20 h and depletion of cell subsets analysed by FACS. Serum was assayed for 117 analytes by Luminex and RNA was extracted for RNAseq. PBMC from 9 SLE patients and 9 HC were cultured with 1 μg/ml JNJ-473 or isotype control for 20 h before stimulation with 0.5 μM CpG for 24 h and culture supernatant analysed by Luminex for 87 analytes.
**Results:** pDCs expressed the highest level of CD123 and SLE patients had significantly higher CD123 expression than HC (49325 vs 44152 receptors per cell). JNJ-473 induced potent and specific *in vitro* depletion of pDCs via NK cell mediated ADCC in PBMC from SLE patients (mean 85.80% depleted) and HC (mean 93.79% depleted). Basophils, which also express high levels of CD123, were partially depleted in SLE (mean 33.07% depleted) and HC (mean 66.64% depleted). NK cells were functional as demonstrated by up-regulation of the degranulation marker CD107a, and down-regulation of CD16 after JNJ-473 treatment and by effective depletion of pDCs. In SLE sera, 27 analytes were significantly increased compared to HC, including IFN inducible proteins IP-10 and ITAC. RNAseq analysis showed that SLE patient samples had 605 up-regulated and 498 down-regulated transcripts when compared to HC. These included many secreted proteins, some of which (IP-10, ITAC, IGFBP2, MCP-2 and BAFF) were upregulated at both the RNA and protein level in SLE. Depletion of pDCs with JNJ-473 prevented TLR9 agonist (CpG)-induced production of IFNα and other proteins including IP-10, ITAC and MCP-2.
**Conclusions:** JNJ-473 potently and specifically depletes SLE patient peripheral blood pDCs *in vitro*. JNJ-473–mediated depletion of pDCs resulted in reduced TLR9-induced IFNα and IFN-regulated protein production. These JNJ-473 modulated proteins were significantly elevated at both the protein and RNA level in our SLE patient cohort. These findings suggest JNJ-473 could effectively deplete pDCs and inhibit TLR9-induced proteins in SLE.
**Disclosure of Interest:** K. Monaghan Shareholder of: CSL limited, Employee of: CSL limited, T. Tai Employee of: CSL limited, J. Benson Shareholder of: Janssen, Employee of: Janssen, B. Linggi Employee of: Janssen, S. Oon Grant/research support from: CSL Limited, M. Ng Employee of: CSL Limited, A. Hoi Grant/research support from: CSL Limited, E. Morand Grant/research support from: CSL Limited, N. Wilson Shareholder of: CSL limited, Employee of: CSL limited
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## OP0042 HUMANISED ANTI-CD20 ANTIBODIES IMPROVE DEPLETION AND RESPONSE IN SLE PATIENTS WITH RESISTANCE TO RITUXIMAB: RESULTS FROM THE FIRST 100 PATIENTS AT A SINGLE CENTRE

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**Background:** Rituximab (RTX) is effective for refractory SLE based on strong evidence for efficacy from open label evidence. We have observed cases of SLE patients who previously responded well to RTX developing anti-rituximab antibodies (HACA). We have therefore treated these patients with alternative, humanised anti-CD20 antibodies.
**Objectives:** To evaluate the incidence of secondary non-response to RTX and efficacy of switching to humanised anti-CD20 antibodies in SLE.
**Methods:** We conducted a retrospective observational study of the first 100 consecutive SLE patients treated with RTX at a single centre (total follow-up: 445 patient-years). Each cycle of RTX consisted of 2x1000mg infusions repeated on clinical relapse. Patients who demonstrated features of HACA, ie: infusion reaction >24 hours after the second infusion with <50% B cell depletion as analysed using HSFC were treated either with 2x1000mg ocrelizumab (OCR) or 2x700mg ofatumumab (OFT). Response was defined as improvement to ≤1 persistent BILAG B and no A/B flare.
**Results:** 94 patients with complete response data at 6 months were studied. In Cycle 1 (C1), 81/94 (86%) achieved a BILAG response. 1 patient with severe SLE whom B cell had not depleted and C1 non-responder was retreated with RTX but subsequently developed HACA. She was treated with OCR resulted in depletion and biological response ie: normalisation of anti-dsDNA but died 6 months later with multi-organ failure. Of the C1 responders, 63 patients received RTX on clinical relapse. Of this, 54/63 (86%) responded and 8/9 (13%) were non-responders due to HACA. Of the C2 non-responders, 3/9 patients were treated with OCR resulted in depletion in 2/3 and all responded. 1/9 was treated with OFT achieved depletion for the first time as well as stabilisation of renal function. In C3, 1 had HACA and was treated with OFT, resulted in depletion and response.

| Characteristic | Previous rituximab cycle | | Rituximab cycle with secondary non-response (n=5) | | 1st Alternative anti-CD20 antibody cycle | |
|---|---|---|---|---|---|---|
| | Before | After | Before | After | Before | After |
| BILAG domains | | | | | | |
| Mucocutaneous | 1/5 = A | 0/5 = A | 1/5 = A | 2/5 = A | 2/5 = A | 0/5 = A |
| | 1/5 = B | 0/5 = B | 1/5 = B | 0/5 = B | 0/5 = B | 0/5 = B |
| | 3/5 = C | 3/5 = C | 0/5 = C | 0/5 = C | 0/5 = C | 1/5 = C |
| Musculoskeletal | 0/5 = A | 0/5 = A | 0/5 = A | 1/5 = A | 1/5 = A | 0/5 = A |
| | 0/5 = B | 0/5 = B | 2/5 = B | 2/5 = B | 2/5 = B | 0/5 = B |
| | 3/5 = C | 0/5 = C | 1/5 = C | 0/5 = C | 0/5 = C | 1/5 = C |
| Neuropsychiatric | 2/5 = A | 0/5 = A | 0/5 = A | 0/5 = A | 0/5 = A | 0/5 = A |
| | 0/5 = B | 1/5 = B | 2/5 = B | 2/5 = B | 2/5 = B | 0/5 = B |
| | 0/5 = C | 0/5 = C | 0/5 = C | 0/5 = C | 0/5 = C | 0/5 = C |
| Renal | 2/5 = A | 0/5 = A | 3/5 = A | 3/5 = A | 3/5 = A | 0/5 = A |
| | 0/5 = B | 1/5 = B | 0/5 = B | 0/5 = B | 0/5 = B | 1/5 = B |
| | 1/5 = C | 1/5 = C | 0/5 = C | 0/5 = C | 0/5 = C | 0/5 = C |
| B cell numbers [$\times 10^9$ cells/L], median | | | | | | |
| Naïve B cells | 0.0570 | 0.0002 | 0.0423 | 0.0051 | 0.0184 | 0 |
| Memory B cells | 0.0068 | 0 | 0.0210 | 0.0054 | 0.0116 | 0 |
| Plasmablasts | 0.0203 | 0.0032 | 0.0103 | 0.0073 | 0.0029 | 0.0005 |
| Total B cells | 0.0722 | 0.0032 | 0.0946 | 0.0210 | 0.0383 | 0.0009 |

**Conclusions:** Following initial response to RTX, the incidence of secondary non-response was 15%, mostly due to HACA. Switching to alternative humanised anti-CD20 antibodies improves depletion and clinical response in rituximab-resistant patients in this largest case series to date. Humanised anti-CD20 may be more appropriate than RTX in SLE.
**Disclosure of Interest:** None declared
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## OP0043 CORTICOSTEROID USE OVER TIME IN THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS (SLICC) INCEPTION COHORT - A DESCRIPTIVE ANALYSIS

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**Background:** Corticosteroid (CS) use has been identified as a key factor associated with damage in SLE but detailed analyses of patterns of use in large international cohorts have not previously been reported.
**Objectives:** To describe oral (PO) and parenteral CS use in a large international SLE cohort.
**Methods:** The SLICC Inception Cohort recruited patients within 15 months of developing ≥4 1997 American College of Rheumatology (ACR) criteria for SLE, between 2000 and 2011. Details of PO and parenteral steroid use were captured at enrolment and each annual assessment, including type, dose and course dates. All CS data was converted to prednisolone equivalents and analysed using Stata 13.
**Results:** 1848 patients have been recruited to the Cohort. Those with follow up data (1686) are included in this analysis, providing data on 10,572 annual follow-up (FU) intervals. The mean (SD) total FU is 6.72 (3.60) years; 1072 (63.5%) patients contributed ≥5 years FU; 343 (20.3%) contributed ≥10 years FU.
The proportion of time spent on PO CS can be calculated for 10,098 (95.5%) FU intervals. For the majority of FU intervals (n=9103 (90.1%)), NONE (4494 (44.5%)) or ALL (4609 (45.6%)) of the time was spent on PO CS. In 995 (9.9%) FU intervals, only a proportion of the time was spent on PO CS. In those FU intervals where PO CS have been received (n=5604) the median (IQR) "average daily PO dose" was 6.5 (4.75–10) mg. The average daily CS dose decreased in later FU intervals: median (IQR) at FU 1=10 (5–15) mg and at FU 5=5.5 (4.8–10.0) mg. 558 (34.7%) patients have been on PO CS for ALL of their time in the study, 720 (44.8%) for some of it and 330 (20.5%) have never been on PO CS. 228 patients (13.5%) received parenteral CS prior to and/or at enrolment at a median (IQR) total dose of 1.5 (0.5–3.0) g. CS pulses were given during 429 (4.37%) FU intervals at a median (IQR) total dose of 679.5 (120–2500) mg. This compares to a median (IQR) cumulative total PO dose between FUs of 2565 (1575–4462) mg. PO CS use between FUs (using various definitions - see table 1) was higher in those FU intervals in which pulsed CS have also been given.

Table 1. Point estimates (medians) of various CS exposures, grouped according to the total dose of pulsed CS received between visits

| Total dose of of pulsed CS between visits* | Total cumulative PO CS dose in FU interval (mg) | Average daily PO CS dose in FU interval (mg) | Maximum daily PO CS dose in FU interval (mg) | Total time on PO CS (days) | Proportion of time between visits on PO CS |
|---|---|---|---|---|---|
| >1000mg (n=175) | 5184 | 14.0 | 30 | 364 | 1 |
| 250–1000mg (n=59) | 3960 | 10.0 | 20 | 352 | 1 |
| <250mg (n=143) | 1430 | 4.6 | 10 | 256 | 0.81 |
| 0mg (n=9841) | 600 | 1.5 | 10 | 163 | 0.39 |

*Total dose available for 377/429 intervals.

**Conclusions:** CS are widely prescribed in this international SLE cohort. 79.5% have been on CS at some point and 1 in 3 patients have taken CS throughout their entire disease duration. PO CS tend to be given at low daily doses for long periods of time but with a higher average daily dose earlier in the disease. Parenteral steroid use is associated with higher overall PO CS use, however PO CS contribute most to the total cumulative dose that patients receive. Current management of SLE still relies on CS use as a mainstay of therapy in a high proportion of patients.
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**Disclosure of Interest:** None declared
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## OP0044 SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) RESPONDER INDEX [SRI(4)] RESPONSE IS ASSOCIATED WITH GLOBAL BENEFIT IN PATIENTS WITH MODERATE TO SEVERE SLE

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**Background:** The SRI(4) is a composite endpoint used in SLE clinical trials. A *post-hoc* analysis of two Phase III studies of belimumab[1] showed that the achievement of an SRI(4) response at 52 weeks is associated with clinically meaningful benefits, irrespective of the treatment assignments. Confirmation of these findings in independent cohorts will enhance the wider acceptance of SRI(4) as a measure of clinically meaningful improvement.
**Objectives:** We assessed the global clinical benefit represented by the achievement of an SRI(4) response in patients with moderate to severe SLE.
**Methods:** Changes from baseline in clinical, laboratory, and patient reported outcome measures at Day 365 were compared between SRI(4) responders (n=396) and non-responders (n=340) in the combined dataset of two Phase II studies that evaluated sifalimumab and anifrolumab in moderate to severe SLE.
**Results** (detailed in Table): Baseline demographics were similar between the two studies. At Day 365, a greater percentage of responders than non-responders had a ≥7-point reduction in SLE Disease Activity Index 2000 (SLEDAI-2K) and achieved a reduction of oral corticosteroid dose to ≤7.5 mg/day. Responders also had a greater percentage change from baseline in clinical SLEDAI scores, greater improvements in the Physician's Global Assessment (PGA) score and the number of organ domains with improvement on SLEDAI-2K. The rates of British Isles Lupus Assessment Group (BILAG) "A" or "2B" flares were lower in SRI(4) responders compared with non-responders. Among patients with ≥8 swollen and ≥8 tender joints at baseline, a larger percentage of responders had a ≥50% improvement in swollen and tender joint counts. In patients with moderate to severe skin disease at baseline, defined as a Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score ≥10, a greater percentage of responders had ≥50% improvement in CLASI. In patients with abnormal baseline serological parameters, responders had greater improvements in anti-double stranded DNA concentrations; however, the differences in complement C3 and C4 concentrations were not significant. Responders also had greater improvements in patient-reported outcomes: percentage change from baseline in Patient Global Assessment, and absolute change in Short Form 36 Health Survey (SF-36) [Physical Component Summary (PCS) score; Mental Component Summary (MCS) score; Vitality domain], and Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue scores.

| | Responders (n=396) | Non-responders (n=340) | P-Value* |
|---|---|---|---|
| Day 365 | | | |
| SLEDAI-2K ≥7 point reduction, n (%)† | 223/360 (61.9) | 1/306 (0.3) | <0.001 |
| Reduction of oral corticosteroid dose to ≤7.5 mg/day, n (%)‡ | 76/235 (32.3) | 10/188 (5.3) | <0.001 |
| Percent change clinical SLEDAI, mean (SD) | -80.5 (21.5) | -14.4 (29.1) | <0.001 |
| Percent change in PGA, mean (SD) | -71.7 (26.6) | -13.6 (27.7) | <0.001 |
| Organ domains with improvement on SLEDAI-2K mean (SD) | 2.19 (0.73) | 0.29 (0.59) | <0.001 |
| BILAG "A" or "2B" flares, n (%)§ | 20 (5.1) | 73/333 (21.9) | <0.001 |
| ≥50% improvement in joint counts, n (%)¶ | 136/143 (95.1) | 26/143 (18.2) | <0.001 |
| ≥50% improvement in CLASI, n (%)# | 90/104 (86.5) | 19/100 (19.0) | <0.001 |
| Percent change in serology, mean (SD) [n]** | | | |
| anti-dsDNA | -13.5 (69.8) [200] | 6.0 (90.8) [112] | 0.051 |
| Complement C3 | 11.4 (25.4) [148] | 13.0 (29.1) [77] | 0.676 |
| Complement C4 | 31.7 (92.5) [88] | 36.6 (68.0) [50] | 0.728 |
| Change in SF-36, mean (SD) | | | |
| PCS | 6.3 (9.5) | 1.3 (5.8) | <0.001 |
| MCS | 4.3 (11.1) | -0.1 (6.9) | <0.001 |
| Vitality | 5.2 (9.3) | 0.1 (5.5) | <0.001 |
| FACIT–Fatigue, mean (SD) | 6.5 (11.3) | 0.7 (7.4) | <0.001 |

*P-value is from 2-sample t-test for continuous variables and chi-square test for categorical variables; †In patients with SLEDAI-2K ≥7 at baseline; ‡Reduction of OCS dose at Day 365 to ≤7.5 mg/day in patients who were receiving ≥10 mg/day at baseline; §BILAG "A" or "2B" flares at any time during the study up to Day 365; ¶≥50% decrease in swollen and tender joint count from baseline in patients with ≥8 swollen and ≥8 tender joints at baseline; #≥50% improvement in CLASI from baseline in patients with CLASI ≥10 at baseline; **Improvement of serological parameters in patients with abnormal baseline values
Anti-dsDNA, anti-double-stranded DNA; BILAG, British Isles Lupus Assessment Group; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; Clinical SLEDAI, at least a 4-point reduction in clinical components (no laboratory components) of Systemic Lupus Erythematosus Disease Activity Index; FACIT, Functional Assessment of Chronic Illness Therapy; MCS, Mental Component Summary; PCS, Physical Component Summary; PGA, Physician's Global Assessment; SD, standard deviation; SF-36, Short Form 36 Health Survey; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000

**Conclusions:** SRI(4) response in patients with moderate to severe SLE was associated with broad improvements in clinical, laboratory, and patient reported outcome measures. These results confirm previous findings, indicating that SRI(4) response is associated with a global clinically important benefit.
**References:**
[1] Furie R, et al. Lupus Sci Med 2014;1:e000031
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## LB0001 EFFICACY AND SAFETY OF SUBCUTANEOUS BELIMUMAB PLUS STANDARD CARE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) WITH LOW COMPLEMENT AND POSITIVE ANTI-DSDNA

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**Background:** In post hoc analyses of the BLISS trials, patients with SLE with positive anti-dsDNA and low complement (C3/C4) had a greater response to intravenous belimumab (BEL) compared with patients without these characteristics.[1]
**Objectives:** To assess the efficacy and safety of subcutaneous (SC) BEL plus

standard SLE care (SoC) in patients with SLE with low C3/C4 and positive anti-dsDNA.
**Methods:** BLISS-SC (BEL112341; NCT01484496) was a randomised, double-blind, multicentre, placebo-controlled trial. Patients with SELENA-SLEDAI (SS) ≥8 were randomised (2:1) to weekly BEL 200 mg SC or placebo (PBO), plus SoC. The primary endpoint was the SLE Responder Index 4 (SRI4; ≥4-point decrease in SS, <0.3 increase in Physician's Global Assessment, and no new BILAG A or ≤1 BILAG B organ domain scores, from baseline) at Week 52. Secondary endpoints included time to severe flare and reduction in steroid dose. Adverse events (AEs) were used to assess safety. Efficacy and safety data have been presented[2]; here, data are reported for a subset of patients who were anti-dsDNA positive and hypocomplementemic at baseline.
**Results:** Of 839 patients randomised, 356 had low C3/C4 and positive anti-dsDNA; baseline characteristics were similar between groups.

Baseline characteristics

| | PBO (n=108) | BEL 200 mg SC (n=248) |
|---|---|---|
| Mean (SD) age, years | 34.6 (10.38) | 34.6 (10.96) |
| Median (range) disease duration, years | 4.0 (0, 32) | 5.1 (0, 35) |
| Mean (SD) SS | 11.7 (3.14) | 11.5 (3.31) |
| Mean (SD) steroid dose (prednisone equivalent), mg/day | 11.4 (7.39) | 12.2 (8.34) |
| Antimalarials, % | 63.0 | 71.4 |
| Immunosuppressants, % | 54.6 | 47.2 |

At Week 52, SRI4 response was PBO 47.2% vs BEL 64.6% (odds ratio: 2.23 [95% CI 1.36, 3.64]; p=0.0014); SRI components were statistically significant. The BEL group was 62% less likely to experience a severe flare vs PBO (hazard ratio: 0.38 [95% CI 0.24, 0.61]; p<0.0001); median time to first severe flare among those having a severe flare was PBO 126.5 vs BEL 90.0 days. Numerically but not statistically (p=0.0844) more patients reduced steroid dose by ≥25% to ≤7.5 mg/day during Weeks 40–52 in the BEL group (20.7%) vs PBO (11.4%).
AE incidence was PBO 81.5%, BEL 78.2%; the most common (≥10% in either group) were headache (PBO 9.3%, BEL 10.5%) and nasopharyngitis (PBO 4.6%, BEL 10.1%).
Serious AE incidence was PBO 23.1%, BEL 13.3%; none occurred in ≥2.0% of patients. There were 5 deaths (PBO 1.9%, BEL 1.2%). The incidence of depression was PBO 2.8%, BEL 4.4%, with 1 case of suicide ideation (BEL 0.4%).
**Conclusions:** Patients with SLE with low C3/C4 and positive anti-dsDNA had significantly greater SRI4 responses and fewer severe flares with BEL 200 mg SC vs PBO (plus SoC). The treatment effect for SRI4 response was numerically larger compared with the overall population.[2] Safety in both groups was similar.
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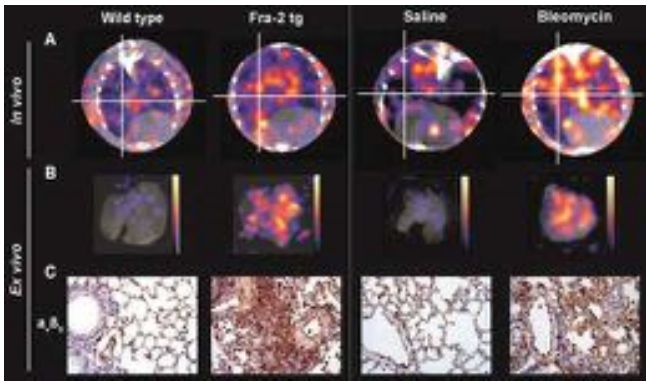
**FRIDAY, 10 JUNE 2016**

## Scleroderma, myositis and related conditions

### OP0045 EARLY DETECTION OF LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS USING MOLECULAR TARGETED IMAGING

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**Background:** Interstitial lung disease (ILD) is one of the leading causes of death in systemic sclerosis (SSc). Since routine diagnostics such as CT and pulmonary function tests only detect impaired organ function and/or damage, there is an unmet need for the non-invasive diagnosis of ILD at earliest, possibly still reversible disease stages.
**Objectives:** To assess nuclear imaging for the detection of SSc-ILD by using radiotracers specifically targeting integrin $\alpha_v\beta_3$ as a pathophysiologic key molecule of early inflammation-dependent fibrosis in the murine model of bleomycin-induced pulmonary fibrosis and in the multisystemic Fra-2 transgenic (tg) mouse model of SSc.
**Methods:** Expression of integrin $\alpha_v\beta_3$ was analysed in lung sections from patients with SSc-ILD, idiopathic pulmonary fibrosis (IPF), healthy controls (n=5) as well as from bleomycin-treated mice, Fra-2 tg mice and respective controls (n=4) using immunohistochemistry. *In vivo* imaging was performed using $^{111}$In-DOTA-RGD radioconjugates specifically targeting integrin $\alpha_v\beta_3$. SPECT (single photon emission computed tomography) was performed using a small-animal SPECT/CT scanner (NanoSPECT/CT, Mediso). Animals were scanned at early disease time points to visualise inflammation-dependent pulmonary fibrosis. The pulmonary accumulation of the radiotracer was confirmed by *ex vivo* SPECT/CT, biodistribution, and autoradiography studies. Nonparametric non-related data were expressed as median$_{(Q1,Q3)}$. For statistical analysis, the Mann-Whitney U test was applied. P-values <0.05 were considered statistically significant.
**Results:** In lung sections of patients with SSc-ILD and IPF, the expression of integrin $\alpha_v\beta_3$ was increased by 3.7-fold and 2.9-fold, respectively as compared to healthy controls (p<0.009, p<0.02). Lungs of bleomycin-treated and Fra-2 tg mice, but not of controls showed a significant increase in integrin $\alpha_v\beta_3$ expression (upregulation by 5.7-fold and 4.8-fold, respectively) as we have similarly observed in SSc-ILD and IPF patients (p<0.03 each, Fig. C). Integrin $\alpha_v\beta_3$ was primarily expressed on endothelial cells, inflammatory cells and myofibroblasts as indicated by sequential stainings with cell type-specific markers. Notably, at day 7 after intratracheal bleomycin installation, the peak of pulmonary inflammation, nuclear SPECT/CT with $^{111}$In-DOTA-RGD targeting integrin $\alpha_v\beta_3$, successfully visualised pulmonary inflammation and incipient fibrosis in the model of bleomycin-induced pulmonary fibrosis. Similarly, imaging of integrin $\alpha_v\beta_3$ in Fra-2 tg mice at 13 weeks of age, the starting point of pulmonary fibrosis, showed a higher pulmonary uptake of the radiotracer in Fra-2 tg mice than in controls (Fig. A). *Ex vivo* SPECT/CT of isolated lungs, biodistribution and autoradiography studies confirmed the *in vivo* results and validated the specific radiotracer uptake in lungs from bleomycin-challenged mice and Fra-2 tg mice as compared to controls (Fig. B).




**Conclusions:** Our data provide the first evidence that targeting pathophysiologic key molecules using nuclear imaging methods for the visualization of inflammation-dependent fibrosis is a promising non-invasive approach for the early detection of lung involvement in SSc.
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## OP0046 DECREASED CIRCULATING ILC2 LEVELS CORRELATE WITH SKIN FIBROSIS IN HUMAN SYSTEMIC SCLEROSIS AND ARE ASSOCIATED WITH A SKEWING OF THE ILC1/ILC2 BALANCE IN THE SKIN

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**Background:** Interleukin (IL)13 is considered as a key downstream mediator in the development of Systemic sclerosis (SSc) fibrosis[1]. The recently described type 2 innate lymphoid cells (ILC) produce higher amounts of IL13 than Th2 cells under certain stimulatory conditions[2]. Our recent work show that endothelial cells are an important source of thymic stromal lymphopoietin (TSLP) in SSc[3], which is an inducer of IL13 production by ILC2. Altogether, we assume that ILC2 could have a role in the promotion of SSc fibrosis.
**Objectives:** To analyse ILC populations in whole blood and skin of SSc patients and heatlhy donors (HD) and to correlate to clinical parameters.
**Methods:** 25 SSc and 15 HD were prospectively enrolled between September 2015 and January 2016 in the University Hospital of Bordeaux. Skin biopsies were performed in fibrotic skin for 2 SSc patients and in pieces of brachioplasty for HD. All patients signed informed consent. Analysis were done on fresh blood after Red Blood lysis and on cells from skin biopsies digested with liberase and DNase. ILC were measured by flow cytometry using Beckman Coulter and Miltenyi Biotech kits respectively. For peripheral blood and skin, results are expressed as median and means respectively. Mann-Whitney test is used for comparisons.
**Results:** In SSc patients, circulating ILC were significantly decreased both in frequency (0.0094% of total cells [0.0005–0.052] in HD vs. 0.0024% [0.0002–0.029] in SSc, p=0.006) and in absolute counts (0.146 [0.0089–1.641] in HD vs. 0.032 [0.0049–0.427] in SSc, p=0.0005). This global decrease was mainly due to the decrease of the ILC2 frequency (0.0077% of total cells [0.0009–0.031] in HD vs. 0.0024% [0.00–0.01] in SSc, p=0.0009) and absolute counts (0.123 [0.0153–0.574] in HD vs. 0.033% [0.00–0.167] in SSc, p<0.0001).
The number of ILC2 in peripheral blood was inversely correlated to skin fibrosis as assessed by the modified Rodnan skin score (r=-0.6, p=0.0041, using a Pearson test).
Analysis of ILC content in total cells showed that ILC2 are present in both normal and SSc skin. However, we showed a skewing towards ILC2 (83.6% of total ILC in SSc vs. 66.4% in HD) at the expense of ILC1 (7.5% in SSc vs. 18.85% in HD) in SSc skin, while ILC3 were not affected.
**Conclusions:** SSc patients are characterized by a decrease of the ILC2 subpopulation in peripheral blood inversely correlated to skin fibrosis and a skewing of the type 1/type 2 ILC balance in the skin towards ILC2. Altogether these results show for the first time flow cytometry analysis of ILC content in whole blood and skin of SSc patients, which pave the road for further extensive phenotypic analysis.
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**Disclosure of Interest:** None declared
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## OP0047 EXPRESSION OF HEAT SHOCK PROTEIN 90 IN MUSCLE TISSUE AND PLASMA IS INCREASED IN IDIOPATHIC INFLAMMATORY MYOPATHIES AND CORRELATES WITH DISEASE ACTIVITY, SKELETAL MUSCLE, HEART AND LUNG INVOLVEMENT

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**Background:** Heat shock proteins (Hsps) are chaperones playing important roles in skeletal muscle physiology, adaptation to exercise/stress, and activation of inflammatory cells.
**Objectives:** To assess Hsp90 expression in muscle biopsies and plasma of patients with idiopathic inflammatory myopathies (IIM) and to characterize its association with IIM-related features.
**Methods:** Total of 277 patients with IIM (198 females, 79 males; mean age 54.8; disease duration 4.1 years; dermatomyositis (DM, 104)/polymyositis (PM, 104)/cancer associated myositis (CAM, 42)/ necrotizing myopathy (IMNM, 27)) and 100 age-/sex-matched healthy individuals were included in plasma analysis and 50 muscle biopsy samples were stained for Hsp90 (PM-10, DM-10, IMNM-10, myodystrophy-10, myasthenia gravis-10). Patients with PM/DM fulfilled Bohan and Peter criteria and CAM was defined as cancer within 3 years of IIM diagnosis. Plasma Hsp90 was measured by ELISA (eBioscience, Vienna, Austria). Clinical disease circumstances were evaluated by Myositis Disease Activity Assessment (MYOACT), Myositis Intention to Treat Index (MITAX), Myositis Damage Index (MDI), physician and patient global activity using VAS and manual muscle testing (MMT8). CK, LD, ALT, *AST* and CRP were analyzed by routine techniques and IIM-specific autoantibodies by in-line blot and immunoprecipitation. Data are presented as median.
**Results:** In muscle biopsies Hsp90 expression was higher in IIM than in myodystrophy (myasthenia gravis used as another control was negative). Increased Hsp90 was detected in perifascicular degenerating and regenerating fibers, inflammatory cells (DM, PM), and necrotic and regenerating fibers (IMNM). Plasma Hsp90 levels were increased in IIM patients compared to healthy controls (20.2 vs. 9.2 ng/ml, p<0.0001), and in individual subgroups of IIM vs. healthy controls (PM: 19.4, DM: 22.4, CAM: 19.1, IMNM: 19.6 ng/ml, p<0.0001 for all). Hsp90 levels in all patients positively correlated with LD and AST (r=0.551, p<0.0001; r=0.372, p<0.0001, respectively), and there was a trend towards correlation with CK (r=0.111, p=0.068). Increased Hsp90 was associated with decreased MMT8 values (r=-0.136, p=0.029), in particular in proximal muscles. Hsp90 positively correlated with patient and doctor disease activity (r=0.222, p=0.0004; r=0.217, p=0.0005, respectively), pulmonary and muscle disease activity (r=0.201, p=0.001; r=0.146, p=0.018, respectively), MITAX and MYOACT (r=0.175, p=0.005; r=0.159, p=0.012, respectively), and with MDI extent/severity (r=0.215, p=0.003; r=0.120, p=0.041, respectively). Higher Hsp90 was found in patients with interstitial lung disease, cardiac involvement and dysphagia (25.4 vs. 18.9, p=0.004; 27.5 vs. 19.3, p=0.004; 25.0 vs. 18.2, p=0.018, respectively).
**Conclusions:** We demonstrate increased Hsp90 expression in IIM muscle biopsy samples, specifically in inflammatory cells, degenerating, regenerating and/or necrotic fibers. Increased Hsp90 plasma levels in IIM patients are associated with disease activity and damage, and with the involvement of proximal skeletal muscles, heart and lungs.
**Acknowledgement:** Supported by BT Cure, MHCR-23728.
**Disclosure of Interest:** None declared
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## OP0048 IL-31 IS AN INFLAMMATORY PRO-FIBROTIC FACTOR ELEVATED IN A SUBSET OF SCLERODERMA PATIENTS WITH SEVERE PRURITUS

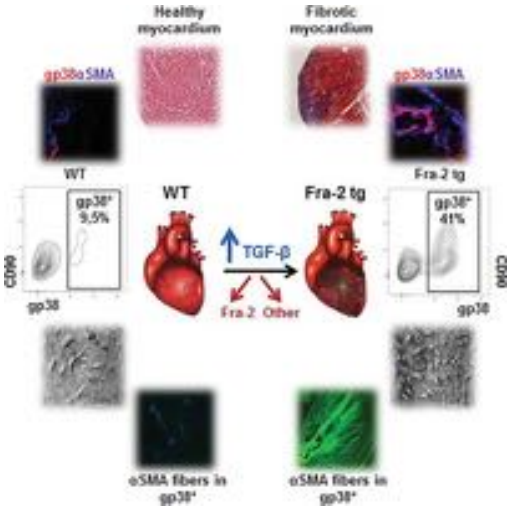
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**Background:** Systemic sclerosis (SSc) is an autoimmune rheumatic disease associated with fibroblast activation in the skin and visceral organs. In SSc, refractory pruritus is a common symptom in a subgroup of patients. IL-31 is a Th2 cell derived cytokine implicated in severe itch in other conditions including atopic dermatitis and T cell lymphoma. T-lymphocyte-derived factors provide a possible link between autoimmune inflammation and fibrosis reported in SSc. In this study we measured IL-31 levels in SSc tissue fluid and plasma, and sought correlation with itch severity and clinical parameters. Recombinant IL-31 was found to influence fibroblast and fibroblast precursor activity.
**Methods:** IL-31 was measured by ELISA of dermal tissue fluid samples obtained by a suction blister analysis method from the involved skin of SSc patients or matched site of healthy controls (SSc n=28, controls n=15), and matched plasma samples. IL-31 receptor mRNA expression was assayed by qPCR of SSc and control fibroblast lysates, as well as epithelial tissue biopsy samples. Normal skin fibroblasts as well as fat derived mesenchymal stem cells (MSCs) were treated with IL-31 (50 ng/ml) and migratory and fibrotic responses were assayed.
**Results:** IL-31 levels were increased in dermal interstitial fluid in SSc patients compared to controls (mean of 99.4 pg/ml vs 2.3 pg/ml in controls, P<0.0003) and in plasma samples (mean plasma IL-31 1370 vs 196 pg/ml, P<0.01). Dermal fluid IL-31 levels correlated strongly with itch severity in these patients R=0.72, P<0.0038). Raised blister fluid IL-31 was characteristic of a subgroup of SSc patients with severe pruritus, which included individuals from both limited and diffuse SSc clinical subsets. Both normal and disease fibroblast extracts contained IL-31 receptor mRNA (qPCR relative copy number 6.4 SSc vs 1.4 controls, p<0.01) which was also seen in epidermal tissue extracts (qPCR 18.4 SSc vs 8.2 in control, p NS). Treatment of normal dermal fibroblasts with IL-31 led to induction of type I collagen but not CTGF, and promoted fibroblast and MSC migration dependent on ERK and PI3kinase pathways.
**Conclusions:** This is the first analysis of IL-31 in systemic sclerosis and we have shown increased expression in the skin and plasma of a subgroup of SSc patients, correlating with severe itch. IL-31 protein induced fibroblasts and MSCs and may link T-cell autoimmune responses to fibroblast and precursor cell activation in SSc. Blocking IL-31 therapeutically may provide effective treatment in a subgroup of SSc patients identified clinically by severe pruritus.
**Disclosure of Interest:** None declared
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## OP0049 MYOCARDIAL FIBROGENESIS IN SYSTEMIC SCLEROSIS: INVOLVEMENT OF A NOVEL STROMAL SUB-POPULATION

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**Background:** Cardiac dysfunction is a significant cause of the high mortality in systemic sclerosis (SSc). Heart involvement in SSc patients resembles inflammatory dilated cardiomyopathy (iDCM) with inflammation and fibrosis. Myofibroblasts are the main players in cardiac fibrogenesis, but their origin remains unknown.
**Objectives:** Here, we aim to determine the role of specific myocardial stromal cell populations in myocardial remodeling in SSc.
**Methods:** The Fos-related antigen 2 (Fra2) tg mouse model of SSc/iDCM was studied. Immunohistochemistry (IHC) and immunofluorescence (IF) were performed on endomyocardial biopsies (EMBs) from SSc/iDCM patients (n=10) and on hearts from Fra2 tg mice (n=5). Flow cytometry analysis was used to identify subsets of myocardial stromal cells ($Ter119^-CD45^-CD31^-Sca1^+CD29^+$). Different stromal cell subsets were sorted, cultured and stimulated with TGFβ1. The differentiation potential was assessed by qPCR, IF, stress fiber staining, SIRCOL and contraction assay on sorted cells. The antisense oligonucleotide GapmeR was used to downregulate Fra2.
**Results:** Fra2 tg mice showed increased $CD45^+$ leukocyte infiltrates and massive collagen deposition in the heart tissue similarly to the myocardium of SSc/iDCM patients. Moreover, the myocardium of Fra2 tg mice revealed increased expression of pro-fibrotic markers such as αSMA, vimentin, collagen I and fibronectin compared to wild type mice.
Four myocardial stromal cell populations were identified: $gp38^+CD90.2^-$, $gp38^+CD90.2^+$, $gp38^-CD90.2^+$ and $gp38^-CD90.2^-$. The frequency of $gp38^+CD90.2^-$ (single positive) cells and $gp38^+CD90.2^+$ (double positive) cells was significantly higher in Fra2 myocardium compared to control mice (p=0.009; n=11).
Importantly, in the myocardium of Fra2 tg mice, the majority of $gp38^+$ cells co-expressed αSMA, vimentin, collagen and fibronectin indicating that myocardial $gp38^+$ stromal cells might proliferate and/or differentiate towards the myofibroblast phenotype.
Myocardial single and double positive stromal cells were cultured *in vitro*. After TGFβ1 stimulation, both cell populations up-regulated αSMA mRNA levels. Importantly, stromal cells from Fra2 tg mice showed the presence of αSMA fibers and stress fibers even without TGFβ1 stimulation as well as an increased contraction capability compared to control cells. These findings indicate that Fra2 overexpression might trigger the differentiation of these cells.
Consequently, Fra2 silencing resulted in a decreased differentiation capability of $gp38^+$ stromal cells: mRNA levels of the pro-fibrotic genes αSMA and collagen I were significantly downregulated (p=0.0075 and p=0.0073; n=5). Moreover, Fra2 downregulation impaired the secretion of collagens and the formation of αSMA fibers.




**Conclusions:** We suggest that cardiac $gp38^+$ stromal cell populations might serve as a cellular source of pathological myofibroblasts playing a pivotal role in TGFβ/Fra2-driven myocardial remodeling in SSc.
A better understanding of the mechanisms triggering myocardial dysfunction in SSc might be helpful in developing novel and effective therapies.
**Disclosure of Interest:** M. Stellato: None declared, M. Rudnik: None declared, F. Renoux: None declared, E. Pachera: None declared, K. Sotlar: None declared, K. Klingel: None declared, J. Henes: None declared, P. Blyszczuk: None declared, O. Distler Grant/research support from: Bayer, Sanofi, Ergonex, Boehringer Ingelheim, Actelion, Pfizer, Consultant for: from 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, EpiPharm, Ergonex, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Pharmacyclics, Pfizer, Serodapharm, Sinoxa, G. Kania: None declared
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## OP0050 SERUM LEVELS OF ADIPOKINES IN THE CATEGORIES OF BODY MASS INDEX (BMI) IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Adipose tissue is a source of factors stimulating the pro-oxidative-antioxidant system, such as adipokines, whose functions are closely associated with metabolic abnormalities and damage by oxidative stress. There are only few reports in literature about the correlation between body mass index (BMI), serum levels of adipokines and clinical manifestations of SSc.
**Objectives:** We evaluated serum levels of adipokines (leptin, resistin, visfatin, adiponectin) and cytokines (TNFα, IFNγ, IL-2, IL-10, IL-17) in SSc and controls (HD) and their pattern according the clinical and laboratory SSc features.
**Methods:** 89 SSc pts satisfying ACR EULAR criteria (age 52 ± 14.4 years and disease duration of 8.14 ± 6.6) and 26 HD were enrolled. Serum levels of Adiponectin, Leptin, Resistin, Visfatin, TNFα, IFNγ, IL-2, IL-10, IL-17A were measured using Bio-Rad kits and Multiplex Immunoassay tool. In all participants we collected clinical and laboratory features, such as visceral involvement, BMI, WHR (Waist to Hip Ratio), index of cardiovascular risk, acute phase reactants, cholesterol, triglycerides, smoking status, comorbidity and therapy. Data were analysed using IBM-SPSS Statistics 20 software. Mann-Whitney U-test or t-Student for unpaired data or Kruskal-Wallis test or ANOVA were used for comparison between groups. Spearman's or Pearson's test were used for correlations. A p-value $\leq$0.05 was considered statistically significant.
**Results:** The weight of SSc and HD differed ($p<0,05$) which was higher in HD. Serum levels of Leptin, Resistin, Visfatin and IL-10, IL-17 were increased in SSc compared to HD ($p<0.05$). In SSc, TNFα serum levels were not different from HD. Leptin levels positively correlated with body weight and BMI that in turn correlated with the values of ESR, CRP, WHR, triglycerides and cholesterol serum levels. Increased levels of IL-2, IL-10, IL-17, IFNγ, Leptin and Visfatin were found in overweight/obese SSc pateints ($p<0.05$) in respect to HD. TNFα was significantly increased in underweight patients (p=0.03) and there was a significant difference compared with normal weight (p=0.018). TNFα levels correlated with IL-2, IL-10, IL-17 and IFNγ levels and with esophageal involvement. There were no differences in cytokine levels between groups when correlated to skin subset, disease duration (Early/Late) and different class of cardiovascular risk. In HD, no statistically significant correlation between weight, TNFα and Leptin levels was detected.
**Conclusions:** Adipokines may play a role in inflammatory and immune pathways in SSc pathogenesis. The present data suggest a role for Leptin and TNFα as new potential SSc related circulating biomarker. Categories of modified BMI (underweight and obesity) seem to be associated to a different and a significant organ involvement in SSc. In underweight subjects, the increase of TNFα may be involved in the cachectic status, thus the role of TNFα needs be confirmed in further prospective longitudinal studies investigating also its correlation with disease severity and activity.
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[1] Pehlivan Y et al. Serum leptin, resistin and TNFa levels in patients with systemic sclerosis: the role of adipokines in scleroderma, Int J of Rheum Dis 15, 374–379, 2012
**Disclosure of Interest:** None declared
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## OP0051 DIPEPTIDYL-PEPTIDASE-4 (DPP4) CHARACTERIZES A SUBPOPULATION OF FIBROSIS-PROMOTING FIBROBLASTS AND IS A MOLECULAR TARGET FOR THE TREATMENT OF FIBROSIS

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**Background:** Dipeptidyl-peptidase-4 (DPP4/CD26) has been recently identified as a marker for a special fibroblast lineage responsible for the tissue remodeling during physiological wound healing. Fibrotic disease may be considered as a consequence of persistent, exaggerated and uncontrolled tissue repair processes. Systemic sclerosis (SSc) is associated with the highest mortality among the

connective tissue disorders and effective antifibrotic therapies are still lacking. DPP4 inhibitors are already used in treatment of diabetes.
**Objectives:** The aim of the study was to characterize the DPP4 positive cells, investigate the expression of DPP4 in SSc skin and to evaluate the antifibrotic effect of DPP4 inhibitors in preclinical models of systemic sclerosis.
**Methods:** Mouse fibroblasts were isolated and DPP4 positive cells characterized by fluorescence activating cell sorting. Expression of DPP4/CD26 in human and murine skin was analyzed by immunofluorescence. DPP4 inhibitors were tested in two different concentrations administered orally (Sitagliptin 3mg/kg/d and 10mg/kg/d, Vildagliptin 1,5mg/kg/d and 15mg/kg/d) in bleomycin induced skin fibrosis and in sclerodermatous chronic graft-versus-host disease mouse model (cGvHD). The antifibrotic effect on skin was assessed by hydroxyproline assay, alpha smooth muscle cells quantification and measuring the dermal thickness. Inflammatory infiltrate was assessed by CD45 immunofluorescence staining.
**Results:** We have demonstrated that DPP4/CD26 positive cells are a unique population of cells implicated in fibrosis. DPP4/CD26 positive cells were increased not only in experimental fibrosis, but also in skin biopsies from SSc patients as compared to healthy volunteers. Treatment with DPP4 inhibitor reduced dermal thickness in both mouse models ($p<0.05$). The differentiation of resting fibroblasts into myofibroblasts was also significantly decreased ($p<0.05$) in all treatment groups. Hydroxyproline content of the skin diminished by 40% in comparison with NaCl injected mice or syngeneic transplanted mice. Moreover, DDP4 inhibitors reduced the inflammatory infiltrate in a dose dependent manner in the bleomycin injected skin.
**Conclusions:** DPP4/CD26 identifies a subpopulation of fibrosis-promoting fibroblasts that plays a key role in the pathogenesis of fibrosis in SSc. Moreover, inhibitors of DPP4 show a significant antifibrotic effect in several mouse models of SSc in well tolerated doses. These results may have direct clinical implications as DPP4 inhibitors are already in clinical use for diabetes.
**Acknowledgement:** AS received an EULAR Scientific Training Bursary (2014) and was an Articulum Fellow (2015).
**Disclosure of Interest:** None declared
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## OP0052 AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IMPROVES FUNCTIONAL EVALUATION OF SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Systemic sclerosis (SSc) is associated with impairment of physical function, daily life activities and quality of life. Autologous hematopoietic stem cell transplantation (AHSCT) has been investigated as treatment for patients with severe SSc, promoting reduction of skin thickening and at least stabilization of pulmonary involvement.
**Objectives:** To evaluate the impact of AHSCT on skin involvement, functional capacity and quality of life (QoL) of SSc patients, and to compare these results with those from SSc patients under conventional immunosuppressive treatment.
**Methods:** This is a prospective longitudinal study of a cohort of SSc patients treated at a University Hospital in Brazil. Patients treated with AHSCT (transplant group) and patients under conventional immunosuppressive treatment (control group) were evaluated before, 6 and 12 months after treatment. The evaluations included respiratory muscle strength test (maximal inspiratory pressure – MIP and maximal expiratory pressure - MEP), hand function assessments (hand-grip strength, finger-to-palm distance - FTP, COCHIN questionnaire), six-minute walk test (6MWT), modified Rodnan's skin score (mRSS) and quality of life questionnaire (SF-36). Statistical significance was established at $p<0.05$.
**Results:** Nine SSc patients were included in the transplant group and 8 in the control group. When compared before, 6 and 12 months after AHSCT, patients presented improvement of MIP (p=0.0019), 6MWT distance (p=0.0459), right hand FTP (p=0.0086), right (p=0.0001) and left (p=0.0001) hand-grip strength, COCHIN (p=0.0005), mRSS (p=0.0007), and of the physical components score of SF-36 (p=0.0236). No significant differences were detected in the remaining evaluations. In the control group, no significant changes were observed 6 and 12 months after treatment at any of the evaluations. Patients from the transplant group presented better scores than those from the control group at the 6 months time point regarding MIP (p=0.0050), 6MWT distance (p=0.0418), right (p=0.0024) and left (p=0.0047) hand-grip strength, COCHIN (p=0.0088), mRSS (p=0.0272), and physical components score of SF-36 (p=0.0342). At the 12 months time point, transplanted patients presented better scores than controls concerning MIP (p=0.0242), right (p=0.0131) and left (p=0.0005) hand-grip strength, and physical components score of SF-36 (p=0.0350).
**Conclusions:** AHSCT promotes improvement of functional capacity, skin involvement and of physical components of quality of life in SSc patients. Scores are also significantly better than those from patients treated with conventional immunosuppressive treatment. These results can be interpreted as positive outcomes of AHSCT for SSc.
**References:**
[1] JAMA 2014;311:2490–8.
[2] Lancet 2013;381:1116–24.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4197

**THURSDAY, 9 JUNE 2016**

# Vasculitis

## OP0053 EULAR/ERA-EDTA RECOMMENDATIONS FOR THE MANAGEMENT OF ANCA-ASSOCIATED VASCULITIS

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**Background:** The European League Against Rheumatism (EULAR) Recommendation for primary and small vessel vasculitis were published in 2009.
**Objectives:** To update the 2009 recommendations with the focus being ANCA-Associated Vasculitis (AAV) using systematic literature review, as well as expert opinion where appropriate.
**Methods:** A combined taskforce from European League Against Rheumatism (EULAR), the European Renal Association (ERA-EDTA) and European Vasculitis Society (EUVAS) conducted a modified Delphi exercise to identify key areas of guideline for update. The identified themes were then used to generate keywords for literature searches. For the purpose of update a date period of 1st January 2007 to 1st February 2015 was chosen, to interrogate the main medical literature databases (MEDLINE, EMBASE, CENTRAL). From an initial 1,347 hits, 82 clinically relevant studies were identified. The evidence presented was discussed and summarized by the experts in the course of a consensus finding and voting process. Levels of evidence and grades of recommendations were derived and levels of agreement (strengths of recommendations) were determined.
**Results:** The 15 recommendations cover general aspects, such as attainment of remission and the need for shared decision-making between rheumatologists and patients. The more specific items relate to starting immunosuppressive therapy using a strategy in combination with glucocorticoids to induce remission, followed by a period of remission maintenance. For remission induction of life or organ-threatening AAV, cyclophosphamide and rituximab are considered to have similar efficacy. Azathioprine, rituximab and methotrexate are the preferred choices for remission maintenance. The recommendations address plasma exchange which is recommended, in the setting of rapidly progressive renal failure or severe diffuse pulmonary haemorrhage. To enable the recommendations to have maximum validity the voting process was also repeated amongst the members of EUVAS.
**Conclusions:** The recommendations have been updated and changes include; choice of drug therapy (both for induction, relapse and remission maintenance), monitoring for complications, the usefulness of repeated biopsy in those thought to having relapsing disease, monitoring for hypoimmunoglobulinaemia and recommendations on patient education. These recommendations are intended for use by healthcare professionals, doctors in specialist training, medical students, pharmaceutical industries and drug regulatory organisations.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1168

## OP0054 NEUROIMMUNOMODULATION OF NEUTROPHILS AS A NOVEL MECHANISM OF LEVAMISOLE-INDUCED VASCULITIS

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**Background:** Levamisole, an anti-helminth drug and known cholinergic agonist, has been implicated in cases of drug-induced autoimmunity in humans exposed to cocaine adulterated with levamisole for profit. Clinical manifestations of levamisole-

induced autoimmunity include cutaneous vasculitis and specific autoantibodies (e.g. anti neutrophil cytoplasmic antibodies, ANCA; antinuclear antibodies, ANA). Neutrophil extracellular trap (NET) formation is a novel cell death mechanism implicated in certain idiopathic autoimmune diseases that share features with levamisole-induced autoimmunity.
**Objectives:** The objective of this study was to determine the role of NET formation in the pathogenesis of levamisole-induced autoimmunity.
**Methods:** Human and mouse neutrophils were exposed to graded concentrations of levamisole. NET formation was visualized and quantified by fluorescence microscopy. To assess the pathways involved in levamisole-induced NETosis, the following inhibitors were tested: diphenylene iodonium (DPI), an inhibitor of reactive oxygen species, and Cl-amidine, an inhibitor of peptidylarginine deiminase (PAD) enzymes. Involvement of Akt and Raf-MEK-ERK kinase pathways was assessed by Western blot. The role of Toll-like receptors (TLRs) and muscarinic receptors (MR) in levamisole-induced NETosis was investigated. Pharmacologic inhibitors and MR knockout mice were used to study specific MR subtypes implicated in NETosis. MR subtype receptors on neutrophils from disease comparators and healthy controls were assessed by flow cytometry. Autoantibodies against specific NET-components were examined in cocaine users exposed to levamisole.
**Results:** Levamisole induced prominent NETs in human and murine neutrophils that contained the antigenic targets of ANCA. NETs were seen in vasculitic lesions from cocaine/levamisole users. NET formation induced by levamisole was dependent on phosphorylation of Akt and Raf-MEK-ERK kinase pathways. DPI and Cl-amidine significantly abrogated levamisole-induced NETosis, highlighting that levamisole stimulates NETs via generation of reactive oxygen species and activation of PAD enzymes. Both levamisole and acetylcholine induced NETs through MR engagement on the surface of neutrophils and not through stimulation of TLRs. Atropine, a non-selective MR antagonist, blocked levamisole mediated NETosis. Screening experiments with pharmacologic inhibitors and neutrophils from MR knockout mice demonstrated that levamisole-induced NETosis was mediated through engagement of the M3 muscarinic receptor. Increased M3 receptors were seen on neutrophils from patients with systemic lupus erythematosus compared to controls. In a cohort of 21 cocaine users, 100% had quantifiable levamisole in urine, and novel autoantibodies against NET components were detectable in sera. In longitudinal observations, ex-vivo spontaneous NET formation correlated with periods of active cocaine use.
**Conclusions:** Levamisole induces NETosis through engagement of M3 muscarinic receptors on the surface of neutrophils. These findings implicate a novel interaction between the cholinergic nervous system and innate immunity in the pathogenesis of levamisole-induced autoimmunity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2963

## OP0055 USING THE BIRMINGHAM VASCULITIS ACTIVITY SCORE AS A SCREENING TOOL IN PATIENTS WITH SUSPECTED VASCULITIS

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**Background:** The Birmingham Vasculitis Activity Score (BVAS) is validated to assess disease activity in systemic vasculitis, but has not been widely tested in conditions mimicking vasculitis.
**Objectives:** To explore the utility of BVAS in screening patients with suspected vasculitis.
**Methods:** We analysed data from the ACR/EULAR Diagnostic and Classification Criteria in Vasculitis Study (DCVAS), using the submitting physician's diagnosis (certainty >75%) as the gold-standard, with predetermined criteria to identify appropriate comparators for each vasculitis. BVAS score and frequency of individual items were evaluated in: giant cell arteritis (GCA); Takayasu arteritis (TAK); polyarteritis nodosa (PAN); and the anti-neutrophil cytoplasm antibody (ANCA) associated vasculitides (AAV) comprising granulomatosis with polyangiitis (GPA), eosinophilic GPA (EGPA) and microscopic polyangiitis (MPA); and their comparator conditions.
**Results:** 1122 patients with vasculitis and 487 comparators were analysed. The BVAS score (median (IQR)) was significantly higher ($p<0.0001$) in patients with each type of AAV vs comparators: GPA 19 (12–25) vs 11 (6–17); EGPA 18 (12–26) vs 11 (6–17); MPA 19 (14–24) vs 11 (5–17). Between 5–12 individual BVAS items were found significantly more frequently in each of these vasculitides than their comparators: bloody nasal discharge/nasal crusts, sinus involvement, pulmonary infiltrate, nodules/cavities in lung, proteinuria, haematuria for GPA; pulmonary infiltrate, wheeze, sensory peripheral neuropathy, mononeuritis multiplex, heart involvement (pericarditis, ischaemic pain, cardiomyopathy or congestive failure) for EGPA; fever, bloody nasal discharge/nasal crusts, pulmonary infiltrate, proteinuria, haematuria and any renal function abnormalities for MPA. These items were used to develop classification trees whose performance is shown in the table. We analysed whether including an ANCA result in the trees altered their performance (table). This led to an increase in sensitivity for MPA (from 71% to 98%), whereas only slight changes were recorded for GPA and MPA. For PAN, GCA and TAK there was no significant difference in BVAS score compared to comparators, and few or no BVAS items were discriminative.

Table 1. Classification tree performance

| | Sensitivity | | Specificity | |
|---|---|---|---|---|
| | Not including ANCA result | Including ANCA result* | Not including ANCA result | Including ANCA result |
| GPA | 82% | 88% | 81% | 81% |
| EGPA | 82% | 89% | 94% | 92% |
| MPA | 71% | 98% | 83% | 80% |

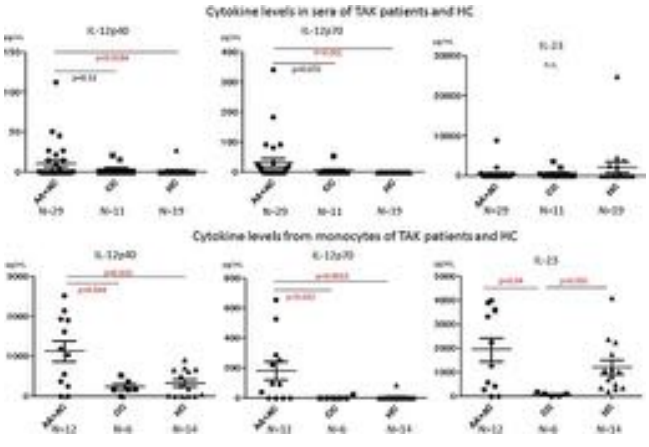
*For GPA: c-ANCA and/or PR3-ANCA were included; for EGPA and MPA: p-ANCA and/or MPO-ANCA.

**Conclusions:** BVAS consists of several items highly specific for GPA, EGPA and MPA, from which we have developed classification trees which can facilitate accurate and systematic screening of patients with suspected AAV based on clinical parameters alone. Whilst the ANCA result contributed to the classification of MPA, it had little additional value in distinguishing GPA or EGPA from their comparator conditions, limiting the value of ANCA testing for the purpose of screening for AAV. By contrast, BVAS is not effective in distinguishing PAN, GCA or TAK from comparator conditions.
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**Disclosure of Interest:** A. Floris Grant/research support from: Bursary by Italian Society of Rheumatology, N. Goodfellow: None declared, J. Sznajd: None declared, K. Wawrzycka-Adamczyk: None declared, H. Querin: None declared, A. Craven: None declared, J. Rosa: None declared, P. Merkel: None declared, R. Watts: None declared, R. Luqmani Grant/research support from: GSK, Nordic, Medimmune, Chemocentryx, Roche, UCB, Consultant for: GSK, Nordic, Medimmune, Chemocentryx
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## OP0056 ASSOCIATION OF IL-12P40 AND IL-12P70 WITH PATHOPHYSIOLOGY OF TAKAYASU ARTERITIS

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**Background:** We preliminarily found a SNP (rs6871626, A vs. C) in *IL-12B* region as a susceptibility gene to Takayasu arteritis (TAK) by genome-wide association study. *IL-12B* encodes IL-12p40 that is a component of both IL-12p70 and IL-23. The significance of IL-12p40 in pathophysiology of TAK has not been fully investigated yet. Moreover, there has been no consistent evidence about whether IL-12p70 or IL-23 is important in TAK.
**Objectives:** 1) To investigate the expression of IL-12p40 in patients with TAK, 2) reveal which is more important to pathophysiology of TAK, IL-12p70 or IL-23, and 3) examine the influence of SNP to the cytokine production.
**Methods:** We collected sera from 43 TAK patients and 19 healthy controls (HCs), and measured IL-12p40, IL-12p70 and IL-23 with ELISA. Next, we collected whole blood from 18 TAK patients and 12 HCs, and isolated monocytes with RosetteSep™. The monocytes were incubated with IL-6, IL-10 and GM-CSF, and then stimulated with INF-$\gamma$ and LPS. Then we measured the cytokines in culture supernatant with ELISA.
**Results:** IL-12p40 and IL-12p70 in sera of TAK patients were significantly higher than those of HCs ($p=0.031$ and $p<0.001$, respectively), whereas there were no differences in serum of IL-23 levels between TAK patients and HCs. IL-12p40 and IL-12p70 in sera of TAK patients whose allele at rs6871626 is AA or AC (defined as risk patients) were significantly higher than those of HCs ($p=0.018$



and p<0.001, respectively), whereas there were no differences in serum IL-23 levels among risk patients, TAK patients with CC allele (defined as non-risk patients) and HCs. Supernatant IL-12p40 and IL-12p70 levels from monocytes of risk patients were significantly higher than those of non-risk patients (p=0.044 and p=0.032, respectively) or those of HCs (p=0.032 and p=0.0015, respectively). Supernatant IL-23 from monocytes of risk patients were significantly higher than those of non-risk patients (p=0.04).
**Conclusions:** IL-12p40 and IL-12p70 but not IL-23 may play an important role in pathophysiology of TAK, and the risk allele of rs6871626 could contribute to production of these cytokines.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3475

## OP0057 URINARY AND SERUM KIM-1, MCP-1 AND TYPE IV COLLAGEN LEVELS IN THE ASSESSMENT OF ANCA-ASSOCIATED NEPHRITIS ACTIVITY

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**Background:** Kidney involvement is common in ANCA-associated vasculitis (AAV), but early detection of glomerulonephritis often presents a challenge.
**Objectives:** We evaluated diagnostic significance of urinary levels of kidney injury molecule-1 (uKIM-1), monocyte chemoattractant protein-1 (uMCP-1) and type IV collagen (uCollagenIV) and serum levels of MCP-1 (sMCP-1) and CollagenIV (sCollagenIV) and their relationship with nephritis activity and prognosis in AAV.
**Methods:** We enrolled 78 patients with AAV, diagnosed according to CHCC2012 definition (GPA=48, MPA=19, EGPA=11), 32 male, 46 female, aged 55 (45;61). To assess disease activity and kidney involvement we measured proteinuria, hematuria, serum creatinine (SCr), eGFR (CKD-EPI), BVAS and VDI. Urinary and serum concentrations of biomarkers were measured by ELISA.
**Results:** 28 patients had active renal AAV (35.9%, group 1), 26 had active nonrenal AAV (33.3%, group 2) and 24 were in long-term remission (30.8%, group 3). Median urinary levels of all biomarkers in active renal AAV were significantly higher than in groups 2 and 3 (Table), and did not depend on age and nosological form of AAV. Urinary excretion of all molecules was comparable in groups 2 and 3. There was a significant difference in sMCP-1 levels only between groups 1 and 3. sCollagenIV levels were similar in all groups.

| | Group 1, n=28 | Group 2, n=26 | Group 3, n=24 | |
|---|---|---|---|---|
| uKIM-1, pg/mL | 3724.4 (3023.6; 5428.7) | 1478.7 (1150.0; 2525.7) | 1890.0 (1218.1; 3280.3) | $p_{1-2}$=0.00001; $p_{1-3}$=0.0009; $p_{2-3}$=0.23 |
| uMCP-1, pg/mL | 407.4 (205.5; 795.2) | 120.9 (49.9; 197.2) | 124.3 (79.7; 335.3) | $p_{1-2}$=0.00002; $p_{1-3}$=0.002; $p_{2-3}$=0.49 |
| uCollagenIV, mcg/L | 3.88 (2.03; 7.06) | 1.6 (1.23; 2.67) | 1.68 (1.0; 2.59) | $p_{1-2}$=0.002; $p_{1-3}$=0.0006; $p_{2-3}$=0.76 |
| sMCP-1, pg/mL | 873,4 (609,7; 1095,8) | 708,6 (573,7; 836,85) | 589,9 (478,7; 750,8) | $p_{1-2}$=0.18; $p_{1-3}$=0.02; $p_{2-3}$=0.06 |
| sCollagenIV, mcg/L | 133,8 (107,64; 189,2) | 113,5 (93,3; 158,4) | 115,2 (97,0; 134,0) | $p_{1-2}$=0.22; $p_{1-3}$=0.10; $p_{2-3}$=0.87 |

Significant positive correlations were found between urinary excretion of all biomarkers and features of nephritis activity: hematuria, proteinuria, renal component of BVAS (all p<0.05). uCollagenIV level also had a significant positive correlation with SCr and a negative correlation with eGFR (all p<0.05).
sMCP-1 level showed no association with signs of nephritis activity, but had a positive correlation with CRP and total BVAS (p<0.05). sCollagenIV level had no association with disease activity but had a correlation with SCr and eGFR (all p<0.0001).
ROC-analysis showed that uMCP-1≥159 pg/mL identified renal involvement with sensitivity 89%, specificity 67% (AUC 0.80). uKIM-1≥2283.3 pg/mL had similar sensitivity (92%) and lower specificity (58%), AUC 0.76. uCollagenIV≥3.09 mcg/L showed the worst sensitivity (57%), but the highest specificity (86%), AUC 0.76.
**Conclusions:** Urinary excretion of all biomarkers was significantly increased in active renal vasculitis. We suggest that uKIM-1 and uMCP-1 levels reflect local renal inflammation, while elevated uCollagenIV is likely to represent both glomerular basement membrane damage and activation of renal fibrogenesis. Limited specificity or sensitivity of individual urinary biomarkes may justify their combined use to identify active renal AAV. In contrast serum MCP-1 and CollagenIV only show a weak correlation with overall inflammatory activity and kidney dysfunction respectively, but have no association with nephritis activity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5209

## OP0058 USING MASS SPECTROMETRY TO QUANTIFY RITUXIMAB AND PERFORM INDIVIDUALIZED IMMUNOGLOBULIN PHENOTYPING IN ANCA-ASSOCIATED VASCULITIS

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**Background:** Therapeutic monoclonal antibodies (mAbs) are used to treat patients with a wide range of disorders including autoimmune diseases. To perform pharmacokinetics analyses, they are commonly quantified using immunoassays (such as ELISAs) based on the specific affinity of the mAb to its target antigen. However the development of these tests is long and fastidious. A new method which could quantify any mAb without relying on their antigen specificity would be useful. Heavy and light chains from each therapeutic mAb have a specific molecular weight based on their unique amino acid sequence. New generation mass spectrometers have the mass accuracy and resolution to identify distinct mAbs using mass measurements and can quantify large peptides such as light chains in the serum of patients with high precision.
**Objectives:** To develop a new method based on mass spectrometry (MS) to quantify rituximab in the serum of patients treated for an autoimmune disease, and to compare its performance to a traditional ELISA test.
**Methods:** We analyzed 775 serum samples from the 99 patients included in the Rituximab for ANCA-associated vasculitis (RAVE) trial who received rituximab. Serum was first enriched for IgG then reduced to dissociate heavy and light chains. The molecular weight of each serum light chain was analyzed by microflow-liquid chromatography (LC) followed by ESI-Q-TOF MS. Rituximab was quantified using a unique software package developed by our group. Rituximab quantification by ELISA was performed as previously described.
**Results:** The peak corresponding to rituximab light chain molecular mass was easily recognized and quantified using our method (figure). The performance parameters of our assay were within acceptable limits (coefficients of variation: intra-day 5.0%, inter-day 14.1% at 50 μg/mL and 14.8% at 200 μg/mL; acceptable linearity from 0 to 250 μg/mL of rituximab; and lower limit of quantification of 14.3 μg/mL). The rituximab concentrations determined by MS were in good agreement with those found by ELISA ($R^2$=0.853/m=0.70). In addition, endogenous monoclonal and oligoclonal light chain immunoglobulins secreted into circulation during the course of treatment were documented using the LC-MS assay.

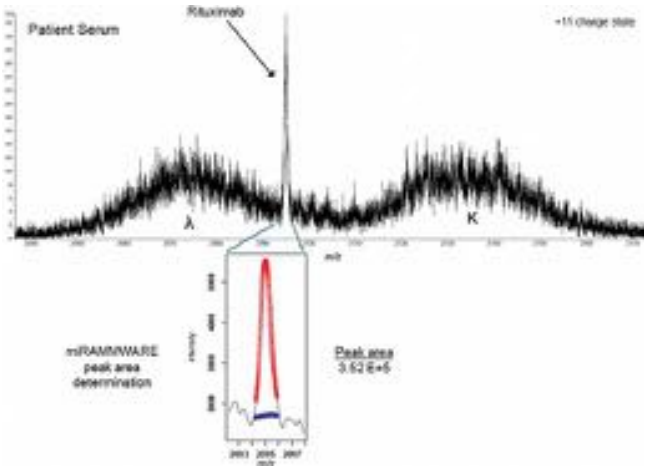



Figure 1

**Conclusions:** Our LC-MS assay was able to quantify a therapeutic mAb in a large cohort of patients in a clinical trial without the need for specific reagents. Our method could be applied to the quantification of any therapeutic mAb. This fact, coupled with the ability to phenotype a patient's polyclonal repertoire in the same analysis further shows the potential of this innovative approach to mAb analysis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5110

OP0059 **SERUM CXCL10 LEVELS ARE ASSOCIATED WITH CLINICAL MANIFESTATIONS AND DISEASE ACTIVITY IN BEHCET'S DISEASE**

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**Background:** Chemokines are multifunctional mediators that control leukocyte recruitment into the inflammatory sites and enhance immune responses. It remains to be investigated which chemokines are important in Behcet's disease (BD).
**Objectives:** The objective of this study was to investigate serum levels of (C-X-C motif) CXC chemokines in BD patients and its association with clinical manifestations and disease activity.
**Methods:** Blood samples were collected from 109 BD patients and 34 age-, sex matched healthy controls (HCs). Twenty two follow-up samples were collected in BD patients. Serum CXC chemokines were assayed for the neutrophil chemoattractants (CXCL1 and CXCL8) and lymphocyte chemoattractants (CXCL9, CXCL10, CXCL12, CXCL13 and CXCL16) by using a multiplex assay. Cell surface makers such as CD3, CD4 and CXCR3 in peripheral blood mononuclear cells were investigated by flow cytometry. The clinical features including disease activity, laboratory tests and current medication were evaluated at the time of blood collection. C-X-C chemokine receptor 3 (CXCR3) expression in skin and intestinal lesions from BD patients were assessed via immunohistochemistry.
**Results:** Serum levels of CXCL8, CXCL10 and CXCL12 were significantly higher in the BD patients than in HC (p=0.001, p=0.007 and p=0.003, respectively). Serum CXCL10 levels were significantly correlated with disease activity in both Behcet's Disease Current Activity Form (BDCAF) and Behcet's Syndrome Activity Score (BSAS) (rho =0.336, p<0.001 and rho =0.253, p=0.009, respectively) as well as with number of genital ulcer and erythema nodosum (EN) (rho =0.222, p=0.020 and rho =0.329, p<0.001, respectively). In follow-up BD patients, changes of serum CXCL10 levels were correlated with those of BDCAF (rho =0.425, p=0.048).
CXCR3 receptor expression was significantly increased on CD3 positive T cells versus CD3 negative cells in peripheral blood mononuclear cells of both BD patients and HCs (p=0.009 and p=0.031, respectively). Levels of serum CXCL10 were inversely correlated with percentage of CXCR3 expression on CD3 positive T cells in BD patients (rho = -0.523, p=0.022). In immunohistochemistry, the CXCR3 positive inflammatory cells were increased in skin lesions of BD patients than in those of HCs.
**Conclusions:** These results suggest that CXCL10/CXCR3 axis contribute to pathogenesis of BD particularly mucocutaneous lesions. Measurement of serum CXCL10 may help to assess disease activity in BD patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4219

LB0002 **DOES ADDING AZATHIOPRINE TO GLUCOCORTICOID INDUCTION INCREASE THE REMISSION RATE AND PREVENT RELAPSES IN PATIENTS WITH SYSTEMIC NECROTIZING VASCULITIDES WITHOUT POOR-PROGNOSIS FACTORS? A MULTICENTER, DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL**

X. Puéchal[1], C. Pagnoux[2], G. Baron[3], T. Quémeneur[4], A. Néel[5], C. Agard[5], F. Lifermann[6], E. Liozon[7], M. Ruivard[8], P. Godmer[9], N. Limal[10], A. Mékinian[11], T. Papo[12], A.-M. Ruppert[13], A. Bourgarit-Durand[14], B. Bienvenu[15], L. Geffray[16], B. Terrier[17], M. Groh[17], C. Le Jeunne[17], L. Mouthon[17], P. Ravaud[3], L. Guillevin for the French Vasculitis Study Group[17]. *[1]Hôpital Cochin, National Referral Center for Rare Systemic Autoimmune Diseases, Paris, Francse; [2]Mount Sinai Hospital, Toronto, Canada; [3]CHU Hôtel Dieu, Paris; [4]CH, Valenciennes; [5]CHU Hôtel Dieu, Nantes; [6]CH, Dax; [7]CHU, Limoges; [8]CHU, Clermont-Ferrand; [9]CH, Vannes; [10]Hôpital Henri Mondor, Créteil; [11]Hôpital Saint-Antoine; [12]Hôpital Bichat, Paris; [13]Hôpital Tenon, Paris; [14]CHU, Bondy; [15]CHU, Caen; [16]CH, Lisieux; [17]Hôpital Cochin, National Referral Center for Rare Systemic Autoimmune Diseases, Paris, France*

**Background:** Glucocorticoids (GC) achieve remission in most patients with systemic necrotizing vasculitides (SNVs) without poor-prognosis factors based on the 1996 Five-Factor Score. However, more than a third of them relapse, mainly during the first 2 years after treatment onset.
**Objectives:** This study aimed to determine whether combined GC and azathioprine (AZA) could achieve higher remission and lower relapse rates than GC alone in patients with newly diagnosed eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA) or polyarteritis nodosa (PAN), without increasing adverse events.
**Methods:** All patients included in this multicenter, randomized, double-blind trial received GC, initially 1 mg/kg/day, then gradually tapered over 12 months (asthmatic patients' doses were lowered as much as possible while controlling asthma symptoms) and were randomly assigned to receive concomitant 12 months of oral AZA (2 mg/kg/day) or placebo. Patients were followed for another 12 months, for 24 months of follow-up. The primary endpoint was rate of remission without subsequent relapses at month (M) 24. Analyses used a modified intent-to-treat strategy and were adjusted according to the vasculitis.
**Results:** 95 patients (51 EGPA, 25 MPA, 19 PAN) met the inclusion criteria and received at least 1 dose of AZA (n=46) or placebo (n=49). At endpoint, 52.2% AZA-arm patients achieved remission without subsequent relapse versus 51.0% placebo recipients (odds ratio [OR], 0.93; [95% CI, 0.40–2.17]). Secondary endpoints were also comparable between arms: remission rate (95.7% vs. 87.8%), number of patients with minor (30.2% vs. 28.5%) or major relapses (11.6% vs. 11.9%). Two (4.1%) AZA-arm patients died both at M11 (1 sudden death while in complete remission, 1 86-year-old died of congestive heart failure). Mean GC doses and area under the curve for GC use were also comparable between arms. At least 1 severe treatment-related adverse event occurred in 8 (17.4%) AZA-arm and 3 (6.1%) placebo-arm patients (OR, 3.23 [0.76–13.70]). For EGPA patients, neither the primary endpoint nor the numbers with exacerbated asthma/rhinosinusal disease differed between arms.
**Conclusions:** At study M24, AZA adjunction to GC induction compared to GC alone in non-severe SNVs did not improve remission rate or lower the risk of relapse, had no steroid-sparing effect, or did not reduce EGPA patients' rate of asthma/rhinosinusal disease exacerbations.
**Acknowledgement:** *CHUSPAN2 trial was funded by French Ministry of Health PHRC P060243 and sponsored by AP–HP; ClinicalTrials.gov number, NCT00647166.*
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6204

**THURSDAY, 9 JUNE 2016**

## Developing evidence-based non-pharmacological care

OP0060-HPR **CROSS-CULTURAL VALIDATION OF THE SYSTEMIC SCLEROSIS QUALITY OF LIFE QUESTIONNAIRE IN SIX EUROPEAN COUNTRIES: A TOOL VALIDATION STUDY**

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**Background:** The Systemic Sclerosis Quality of Life (SScQoL) questionnaire is a 29-item tool developed in UK to measure needs-based patient-reported quality of life in people with systemic sclerosis (SSc).
**Objectives:** To undertake a cross-cultural adaptation and validation of the SScQoL in six European countries.
**Methods:** This was a cross-sectional study involving six European countries: Germany, France, Italy, Spain, Sweden and UK. Adult patients with a definite diagnosis of SSc, who were willing and able to complete the SScQoL were eligible. The English SScQoL was adapted into the five European languages using a forward-backward translation process.[1] The translated SScQoL was completed by patients and the data was analysed using Rasch models. Where local response dependency was evident, items were grouped into subscales (function, emotion, sleep, social and pain) and re-analysed to test the scaling

Table 1

| | Item Fit Residual | | Person Fit Residual | | Chi Square Interaction | | Reliability | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Value (DF) | p-value | PSI | N |
| A. Analysis of the 29 individual items | | | | | | | | |
| UK | –0.232 | 1.043 | –0.233 | 0.680 | 48.932 (29) | 0.012 | 0.919 | 112 |
| Germany | –0.704 | 2.034 | –0.484 | 1.456 | 398 (116) | **<0.001** | 0.881 | 263 |
| France | –0.291 | 1.048 | –0.271 | 0.855 | 34.868 (29) | 0.209 | 0.893 | 111 |
| Sweden | –0.264 | 0.910 | –0.273 | 0.728 | 60.886 (29) | **<0.001** | 0.892 | 101 |
| Spain | –0.166 | 0.751 | –0.220 | 0.654 | 42.439 (29) | 0.051 | 0.906 | 95 |
| Italy | –0.205 | 1.051 | –0.285 | 0.756 | 88.662 (58) | **0.006** | 0.890 | 125 |
| Pooled | –0.416 | 1.676 | –0.229 | 0.882 | 410.802 (261) | **<0.001** | 0.896 | 807 |
| B. Analysis of the 5 subscales (testlets) | | | | | | | | |
| UK | 0.016 | 1.535 | –0.288 | 0.848 | 4.992 (5) | 0.417 | 0.896 | 109 |
| Germany | –0.698 | 2.795 | –0.285 | 0.873 | 61.952 (20) | **<0.001** | 0.852 | 263 |
| France | 0.020 | 1.380 | –0.280 | 0.895 | 2.368 (5) | 0.796 | 0.826 | 106 |
| Sweden | –0.136 | 0.793 | –0.253 | 0.819 | 25.665 (44) | 0.988 | 0.813 | 95 |
| Spain | –0.265 | 1.346 | –0.221 | 0.711 | 11.430 (5) | 0.043 | 0.846 | 92 |
| Italy | –0.137 | 1.888 | –0.315 | 0.831 | 4.281 (5) | 0.510 | 0.818 | 125 |
| Pooled* | –0.394 | 2.928 | –0.310 | 0.859 | 63.909 (45) | **0.033** | 0.840 | 536 |
| Pooled-Adj** | –0.420 | 2.724 | –0.310 | 0.862 | 65.579 (54) | 0.134 | 0.841 | 536 |

SD, Standard deviation; DF, Degrees of freedom; PSI, Person separation index reliability; Pooled* excludes Germany dataset; Pooled-Adj** adjusted to account for Italy differential response in the social subscale.

properties and cross-cultural equivalence, thus allowing calibration of the SScQoL into an interval scale.
**Results:** The adaptation of the SScQoL into European languages was seamless except in Germany, where patients reported problems in deciding yes/no responses for some items. Cross-cultural validation included 849 patients (mean age =57.9 years, SD =13.9), 87% of whom were women. All country-specific data except Germany had good fit to the Rasch model after correcting for local dependency. See table 1. After excluding Germany from the analysis, the scale was validated and calibrated with cross-cultural adjustment for Italy in the social subscale.
**Conclusions:** The SScQoL translated versions can be used as a valid common measure in France, Spain, Sweden, UK and Italy; the latter with adjustments in the social subscale. The German version requires further work.
**References:**
[1] Beaton DE, et al. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. 2000;25(24):3186–91.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1816

## OP0061-HPR THE EFFECT OF A CONTEXTUALLY RELEVANT NON-PHARMACOLOGICAL INTERVENTION ON THE FUNCTIONING OF SOUTH AFRICAN WOMEN WITH OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Osteoarthritis (OA) is more commonly found in women. Joint pain, stiffness, decreased levels of physical activity, obesity and chronic diseases are common problems experienced[1]. A non-pharmacological patient-centered management approach using exercise, education and self-management strategies, may help to ameliorate the impact of joint pain and chronic diseases of life style (CDL) on function, pain and health-related quality of life [2].
**Objectives:** To establish if an intervention programme incorporating physical activity and health education and using self-management principles would result in improved physical functioning, a decrease in pain and improved health related quality of life (HRQoL) in women.
**Methods:** Women with osteoarthritis and hypertension were randomized in two groups (experimental group and control group that received standard care in a form of a support group). The primary outcome was improved physical function using World Disability Schedule (WHODAS) and the Aggregated Locomotor Functioning Score (ALF). Secondary outcomes were decreased joint pain (BPI), improved HRQoL using EQ-5D, decreased Body Mass Index (BMI), decreased blood glucose levels and blood pressure. Measures were taken by a blinded observer at baseline, at six and twelve weeks. The intervention was offered on a weekly basis for six weeks and was led by a physiotherapist.
**Results:** Thirty-five participants were allocated to the experimental and 38 to the control group. There was no difference between the baseline outcome measurements, apart from blood glucose which was ranked higher in the control group (p=0.037). Post-intervention, the WHODAS score was significantly lower (better) (p=.032), the ALF was significantly lower (better, p=.013), joint pain was significantly less ($p<.001$); and the HRQoL significantly higher (Visual Analogue Scale p=.002) in the experimental group. Blood glucose remained lower in the experimental group (p=0.034) and within-group analysis indicated that whereas the control group had not lowered their glucose (p=.656), the experimental group had (p=.002). However, there was no difference in BMI (p=.340) or blood pressure category (p=.558).
**Conclusions:** The six week intervention significantly improved physical functioning, pain, HRQoL and blood glucose levels. However, it did not lower Blood pressure or BMI. It is recommended that this intervention be rolled out in primary health care clinics as it is relatively low cost and requires minimal exercise equipment. The results of this study support the inclusion of physiotherapists as members of the primary health care team in the management of osteoarthritis and chronic diseases of lifestyle.
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**Disclosure of Interest:** None declared
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## OP0062-HPR EFFICACY OF TAILORED EXERCISE THERAPY IN PATIENTS WITH KNEE OSTEOARTHRITIS AND COMORBIDITY: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Exercise therapy is a key intervention in the management of knee osteoarthritis (OA). It is an effective intervention to improve physical functioning and reduce joint pain in patients with knee OA. Comorbidity, which is highly prevalent in OA, interferes with the application of exercise therapy and contributes to non-adherence to exercise therapy.
**Objectives:** To evaluate the efficacy and safety of tailored exercise therapy on physical functioning in patients with knee osteoarthritis (OA) and comorbidity
**Methods:** A randomized clinical controlled trial was performed, comparing comorbidity-adapted exercise therapy with a control intervention. The study was conducted in an outpatient rehabilitation center. Patients with a clinical diagnosis of knee OA and at least one of the target comorbidities, i.e., coronary disease, heart failure, type 2 diabetes, COPD or obesity (body mass index$\geq$30kg/m) with severity scores $\geq$2 on the Cumulative Illness Rating Scale were included. The intervention group received a 20 weeks individualized, comorbidity-adapted exercise program, with 2 sessions of 30 -60 minutes a week. Participants in the control group received their current medical care for knee OA and were placed on a waiting-list for exercise therapy. Measurements were performed at baseline, at 10-weeks, 20-weeks (post-treatment) and 32 weeks (3-months post-treatment). Primary outcome measures: physical functioning (WOMAC subscale physical functioning and six minute walking test). Generalized Estimating Equation analysis was used to estimate group differences over time, adjusting for baseline value of outcome measure.
**Results:** In total, 126 participants were randomised, of which 63 participants in the experimental group and 63 in the control group. Statistically significant differences were found over time between the intervention and control group with respect to physical functioning WOMAC-pf and the six minute walk test in favour of the intervention group. The improvements in the experimental group were clinically relevant. The mean improvements in the intervention group on physical functioning were 33% on the WOMAC-pf scale and 15% on the six-MWT at 3 months follow up. No serious adverse events occurred during the intervention.
**Conclusions:** This is the first study showing that tailored exercise therapy is safe and effective in improving physical functioning, in patients with knee OA and comorbidities. These results should encourage clinicians to consider exercise therapy as a treatment option for patients with knee OA, even in the presence of comorbidity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3855

## OP0063-HPR HIGH PROPORTION OF NON-CONTRACTILE TISSUE IN THE VASTUS MEDIALIS MUSCLE IS ASSOCIATED WITH MUSCLE WEAKNESS IN PATIENTS WITH KNEE OSTEOARTHRITIS; RESULTS FROM THE AMS-OA COHORT

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**Background:** Muscle weakness is of clinical interest in knee osteoarthritis (OA). High proportion of non-contractile tissue including fatty tissue and connective tissue could contribute to muscle weakness in patients with knee OA.
**Objectives:** The study aims were to establish the association of non-contractile tissue in the vastus medialis muscle, assessed by magnetic resonance imaging, to muscle strength in patients with established knee OA.
**Methods:** A sample of 94 patients were included. Sagittal T1 weighted MRI, conducted at 3 Tesla, were performed using a phased array knee coil. Within a standardized region of interest located at the distal end of the vastus medialis, non-contractile tissue was distinguished from contractile tissue based on pixel grayscale values. The amount of non-contractile tissue was expressed as the percentage of non-contractile tissue pixels in proportion to the total amount of pixels. Muscle strength was assessed isokinetically (Nm). The GUG test was used as a measurement of physical function. Percentage of non-contractile tissue was dichotomized into low and high percentage non-contractile tissue groups. With Student's *t*-test, differences in demographics and clinical characteristics between the group of low percentage of non-contractile tissue versus a high percentage of

non-contractile tissue were calculated. In regression analysis the associations of the percentage of non-contractile tissue with muscle strength and GUG test were determined, controlled for BMI, gender, age and radiographic severity.
**Results:** Mean ± SD age and BMI were 61.68 ± 7.09 years and 29.13 ± 4.72kg/m$^2$, respectively. A K&L grade of 2 or higher was found in 68% of the participants. The mean ± SD of the percentage of non-contractile tissue was 16.03 ±15.31 with a median of 11%. The participants with a high percentage of non-contractile tissue (>11%) had on average less muscle strength, a longer GUG time and a higher BMI than participants with a low percentage of non-contractile tissue (≤11%) (*P*=0.031, *P*=0.021, *P*=0.026, respectively). In univariable regression analysis, associations of the percentage of non-contractile tissue to muscle strength and the GUG test were found (B= -19.04, 95% CI = -36.34 to -1.73, *P*=0.031; B=1.09, 95% CI = 0.17 to 2.01, *P*=0.021, respectively). Multivariate regression analysis, adjusting for BMI, gender, age and radiographic severity, showed that the percentage of non-contractile tissue was negatively associated with muscle strength (B= -13.94, 95% CI = -27.56 to -0.33, *P*=0.045), but no association was found with the GUG (B=0.674, 95% CI = -0.20 to 1.55, *P*=0.130).
**Conclusions:** In patients with established knee OA, non-contractile tissue in the vastus medialis muscle measured by clinical MRI is associated with muscle strength, but not with physical performance (GUG test) after adjustment for BMI, gender, age and radiographic severity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5506

## OP0064-HPR A MODEL INCLUDING FOOT-RELATED FACTORS IMPACTING ON QUALITY OF LIFE (QOL) IN SYSTEMIC SCLEROSIS

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**Background:** While foot problems in patients with systemic sclerosis (SSc) have been described previously and the association with disability noted, the impact of such problems on the quality of life (QoL) in people living with SSc has yet to be quantified.
**Objectives:** To identify the factors, including those arising from foot pathology, that impact on QoL in SSc.
**Methods:** Structural equation modelling (SEM) was used to explore the multi-factorial pathways impacting on QoL in a cross section cohort of people with SSc. Potential candidate factors were identified through: i) a literature review with expert consultation; and ii) a cross-sectional study capturing clinical features. QoL was measured using the disease-specific SScQoL questionnaire.
**Results:** One hundred and twenty one patients with SSc were recruited (106 female; median age 59, ranges 25 to 86 years) with a median disease duration of nine years (IQR:4,13) and a median modified Rodnan Skin Score of 2 (IQR:0, 5). The model that best explained the factors contributing to the SSc impact on QoL showed complex inter-relationships between 11 factors (Figure1) (c2=37.022, df=37, p=0.468, RMSEA=0.002, GFI=0.951, CFI=1.000). Combined, these factors explained 84% of the impact on QoL ($R^2$ =0.84) in patients with SSc. General disease factors, including physical function (standardised total effect 0.64), breathing problems (standardised total effect 0.493), and depression (standardised total effect 0.428) had the greatest impact. Foot problems had a substantial but indirect effect on quality of life (foot function and foot pain standardised total effect 0.343 and 0.327). A summary of the effects of the factors included in the model is provided in the Table 1.
**Conclusions:** The impact of SSc on QoL is substantial and complex. While loss of physical function is the most influential factor on QoL, followed by breathing difficulty and depression, foot problems significantly contribute to this impact.

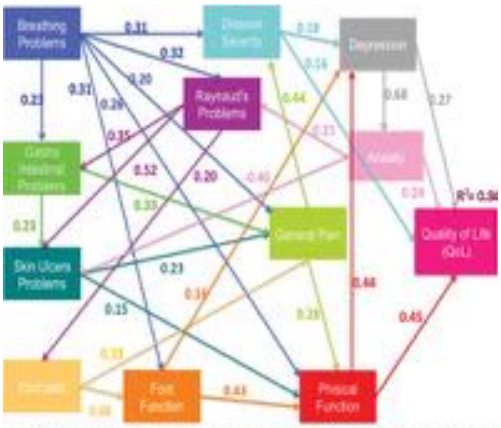



Figure 1: SEM for the factors contributing to QoL in Systemic Sclerosis (SSc) The arrows represent the direction in which the relationship is and the values on top of each line are the regression weights. The larger the regression weights the better predictor the variable is of the variable that the arrow is feeding into.

Table 1. Standardised direct, indirect and total effect of the variables as they relate to QoL, including foot problems

| Variable | Direct effect | Indirect effect | Total effect |
|---|---|---|---|
| Physical function | 0.454 | 0.186 | 0.640 |
| Breathing problems interference | 0.000 | 0.493 | 0.493 |
| Depression | 0.270 | 0.158 | 0.428 |
| Foot function | 0.000 | 0.343 | 0.343 |
| Foot pain | 0.000 | 0.327 | 0.327 |
| Raynaud's interference | 0.000 | 0.294 | 0.294 |
| General pain | 0.000 | 0.284 | 0.284 |
| Disease severity | 0.160 | 0.076 | 0.236 |
| Anxiety | 0.236 | –0.003 | 0.233 |
| DU interference | 0.000 | 0.162 | 0.162 |
| GI problems interference | 0.000 | 0.095 | 0.095 |

DU: digital ulcers; GI: gastro intestinal.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4402

## OP0065-HPR

WITHDRAWN

OP0066-HPR **PERFORMANCE-BASED MEMORY IS NOT IMPAIRED IN FIBROMYALGIA. A STUDY IN A LARGE SAMPLE ALSO TESTING GENDER DIFFERENCES. THE AL-ÁNDALUS PROJECT**

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**Background:** Many fibromyalgia (FM) patients experience a deteriorated cognitive function. This is one of the reasons why FM diagnosis has been moved from a pain-focused classification to a more encompassing diagnosis including cognitive difficulties. It is noteworthy that self-reported cognitive difficulties by FM patients are commonly inaccurate (1). Additionally, when cognitive function is measured by performance-based tests in FM patients, with some studies claiming the existence of cognitive deficits and other studies concluding a lack of such impairments. Finally, most of previous studies measuring performance-based memory was conducted in relatively small samples and did not examine gender differences.
**Objectives:** The aim of the present study was to compare performance-based memory of FM patients and non-FM controls and to assess potential gender differences.
**Methods:** A total of 507 FM patients (21 men) and 308 non-FM controls (57 men) participated in the present cross-sectional study. Four composite scores were obtained by means of the Rey Auditory Verbal Learning Test (RAVLT): learning rate, proactive and retroactive interference, and retention. Mixed-design analyses of covariance (ANCOVA) were performed on each of the RAVLT composite scores (within-subjects factor) with sample group (FM vs. non-FM controls) and gender as between-subjects factors, and education level as covariate.
**Results:** Performance-based memory observed in FM and non-FM participants was similar in every single composite score of the RAVLT (all $P>0.05$). There were not gender differences in proactive interference, retroactive interference and retention (all $P>0.05$), although women had a higher learning rate (i.e. greater number of words recalled) than men ($P<0.01$).
**Conclusions:** Our results do not support performance-based memory impairments in FM. Overall, gender differences were not observed in performance-based memory; except for learning rate, where women outperformed men regardless of sample group (i.e., FM or non-FM). Therefore, the gender differences observed seem to be an extension of the picture observed in general population rather than a disease-specific feature. Future research focusing on factors that are associated with the perception of memory deficits and the discrepancy between objective and subjective measures of memory performance is warranted.
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**Acknowledgement:** This study was funded by the Spanish Ministries of Economy and Competitiveness [I+D+I DEP2013–40908-R, I+D+I DEP2010–15639, BES-2014–067612, and BES-2011–047133] and Education [FPU12/00963; FPU14/12518, and FPU13/01088].
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5822

OP0067-HPR **EXCERSISE AS MEDICINE? DESCRIPTION OF OA TREATMENT IN DISCHARGE REPORTS**

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**Background:** The use of discharge reports (DR) as communication are mandatory in health care in most countries. Interprofesional collaboration is based on shared information and the DR is a minimum base for information sharing in most health care systems. To ensure treatment quality and patient safety, the information shared in DR must be precise and all terms used must be well understood by all professions in need of information regarding treatment modalities and treatment outcome.
Several studies have revealed that OA treatment is not in line with evidence based guidelines (1,2,3). This study assesses how physiotherapists are communicating their treatment of OA patients in the outpatient clinics to referring physician.
**Objectives:** To assesses how physiotherapists are communicating their treatment of OA patients in the outpatient clinics to referring physician.
**Methods:** Patient records in the hospital region of middle Norway were searched to identify patients with knee OA. A letter was sent to the identified patients (N=83) asking for information about which physiotherapist they had seen for treatment. A letter was then sent to the physiotherapists asking for the discharge report, which they are obliged to send to the referring physician. A survey of the content in the discharge reports was conducted by three independent well qualified health professionals.
**Results:** Response rate from patients was 93 percent (N=81). Of the 81, 13 (15 percent) had not been referred to physiotherapy treatment. Response rate from physiotherapists (N=68) was 39 (56 percent).
The information given in the DR's was incomplete and the language was imprecise regarding OA treatment. None of the DR met the criteria for what is supposed to be in a DR. In 11% of the DR's it was not possible to rule out what kind of treatment was provided to the patient. Descriptions used was "easy strength training", "hip and knee group", and "deep massage, hip and lumbal training"; these are all examples of complete information on knee OA treatment extracted from the DR's.
**Conclusions:** This study indicates that the physiotherapists do not list the information needed by other health care professions regarding OA treatment. There seem to be a need to stress the importance of describing exercise as if it was medication, in terms of what kind of medication (type of exercise), the dose (how intense), ratio (how often). If a patient is to be followed up of another health care provider (MD, PH or other) imprecise description,- or lack of description of treatment provided may be harmful for the patient. It may also make it difficult to compare different treatment regimes if the information in the DR's are incomplete or missing
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5873

**THURSDAY, 9 JUNE 2016**

## Cartilage, bone, synovium

OP0068 **WISP1 INDUCES PATHOLOGY IN EXPERIMENTAL OSTEOARTHRITIS AND PREDICTS DISEASE PROGRESSION IN EARLY OSTEOARTHRITIS PATIENTS**

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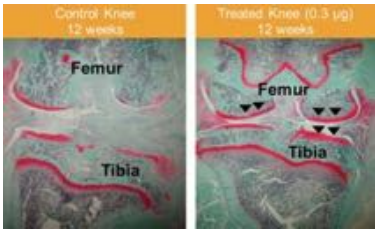
**Background:** Many osteoarthritis (OA) patients show synovial activation, which is suggested to be involved in joint destruction. Previously, we found strong upregulation of *Wnt2b* and *Wnt16* in the synovium of two experimental OA models. In addition, we found strongly increased *Wisp1* expression, a protein induced by canonical Wnt signaling.
**Objectives:** To determine whether there is a relation between *WISP1* expression and progression of OA in a cohort study of patients with early symptomatic OA. Furthermore, we will elucidate whether WISP1 plays a role during experimental OA by inducing OA models in wild type (WT) and *Wisp1*$^{-/-}$ mice.
**Methods:** Microarray analysis was performed on synovium from patients enrolled in the CHECK study, initiated to follow the progression of early symptomatic OA patients. Expression data were correlated with progression of OA (defined as a decrease in joint space width of $\geq$1mm and progression of osteophyte formation of $\geq$4x in size) between baseline and the five-year follow-up measurement. Human end-stage OA synovium was stimulated with WISP1. Joint pathology in WT or *Wisp1*$^{-/-}$ mice was assessed by histology after induction of collagenase-induced OA (CIOA), destabilization of the medial meniscus (DMM) and anterior cruciate ligament transection (ACLT) experimental models of OA. The aggrecan neoepitope NITEGE was visualized using immunohistochemistry. Gene expression in the synovial tissue was evaluated using qRT-PCR.
**Results:** Microarray analysis of synovial tissue from patients in the CHECK cohort showed significantly increased WISP1 expression at baseline in OA progressors versus non-progressors. To determine the mechanism of how WISP1 might be involved in OA pathology, we stimulated human OA synovium with WISP1. This increased the expression of *MMP2/3/9/13* and *ADAMTS4/5*. Next, we determined the *in vivo* role of WISP1. First, we found that spontaneous cartilage damage was not different between WT and *Wisp1*$^{-/-}$ mice at 3, 6 and 12 months of age. Next, we assessed joint pathology 42 days after induction of CIOA in WT and *Wisp1*$^{-/-}$ mice. Cartilage damage was significantly decreased in the tibio-femoral joints of the *Wisp1*$^{-/-}$ mice as compared with the WT controls. In line with the CIOA, we found significantly decreased cartilage degeneration in the *Wisp1*$^{-/-}$ mice in the DMM and ACLT at day 56 after induction. In addition we found decreased expression of *Mmp3*/*9* and the aggrecanases *Adamts4*/*5* in the synovium, 7 days after induction of CIOA in *Wisp1*$^{-/-}$ mice, in line with the increased expression of

these factors after stimulation of human OA synovium with WISP1. Furthermore, the expression of the protease inhibitor *Timp1* was decreased in the *Wisp1*$^{-/-}$ mice, whereas the expression of *Timp3*, an important inhibitor of ADAMTS-4/5, was unaffected. Finally, the protease activity in the cartilage, as assessed by the staining of the neoepitope NITEGE, was decreased in the *Wisp1*$^{-/-}$ mice.
**Conclusions:** Increased WISP1 expression may play an important role in OA pathology via increased synovial MMP/ADAMTS expression. Furthermore, because of the tight regulation and complexity of Wnt signaling and its role in many physiological processes, targeting WISP1 may more specifically target the OA-related pathological events, while minimizing interference with physiological processes.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2093

## OP0069 DISCOVERY OF A SMALL MOLECULE INHIBITOR OF THE WNT PATHWAY (SM04690) AS A POTENTIAL DISEASE MODIFYING TREATMENT FOR KNEE OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) is characterized by increased subchondral bone and thinning cartilage. The Wnt signaling pathway has the capacity to regulate both of these processes. Increased Wnt signaling induces stem cells in the joint to become osteoblasts while decreased Wnt signaling induces chondrogenesis[1]. Wnt signaling is increased in the joints of OA patients and polymorphisms in genes involved in Wnt signaling are associated with an increased susceptibility to development of OA[2].
**Objectives:** SM04690, a novel, small molecule inhibitor of the Wnt pathway, was evaluated in a series of preclinical studies to determine its capacity to induce chondrogenesis and improve joint health.
**Methods:** Inhibition of the Wnt pathway was determined with a cellular screen utilizing a luciferase reporter controlled by a Wnt-responsive promoter. Chondrogenesis was evaluated by histology using differentiation of mesenchymal stem cells (MSCs) to chondrocytes. Protease release from human chondrocytes was measured by ELISA. Pharmacokinetics of SM04690 were evaluated by intra-articular (IA) injection in rats and dogs followed by analysis of compound concentration in the joints and plasma. Safety of SM04690 was assessed by IA injection in rats and dogs followed by evaluation of clinical signs and histology. *In vivo* activity of SM04690 was evaluated in the rat instability model combining anterior cruciate ligament transection with medial meniscal tear. SM04690 was injected into the IA space of the damaged knee, followed by histological evaluation using OARSI scoring and measurement of biomarkers.
**Results:** *In vitro*, SM04690 reduced TCF7 expression leading to selective inhibition of Wnt pathway activation with an $EC_{50}$=3 nM. Consistent with Wnt's role in chondrogenesis, SM04690 induced MSCs to express chondrogenic genes and differentiate into chondrocytes. SM04690 inhibited production of proteases from human chondrocytes, while increasing expression of GAG suggesting it has the capacity to block cartilage degradation and stimulate matrix generation. *In vivo*, a single IA injection of SM04690 resulted in a joint concentration above the target $EC_{50}$ with no detectable systemic exposure. No systemic toxicity was observed after single or 9 monthly IA injections of doses >1400× the therapeutic dose in rats and dogs. In the rat instability model, a single IA injection of SM04690 2 weeks post-injury improved cartilage health in a dose-dependent manner relative to vehicle control. Representative histology showed increased cartilage thickness in SM04690-treated animals relative to vehicle control (Figure 1). At the optimal IA dose in rats (0.3 mg/knee) OARSI scores decreased significantly, p=0.006.




**Conclusions:** SM04690 has been shown in these experiments to inhibit the Wnt pathway, induce chondrogenesis, inhibit protease production and improve cartilage health in rodent models of OA after a single IA injection. SM04690 was maintained in the joint space with no detectable exposure in the plasma, indicative of a low potential for systemic toxicity. These data suggest that locally injected SM04690 has potential as a disease modifying therapy for OA.
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**Disclosure of Interest:** J. Hood Employee of: Samumed, C. Barroga Employee of: Samumed, Y. Hu Employee of: Samumed, V. Deshmukh Employee of: Samumed
**DOI:** 10.1136/annrheumdis-2016-eular.2386

## OP0070 PD-L2 – A NEW LINK BETWEEN INFLAMMATION AND BONE MODULATION IN RHEUMATOID ARTHRITIS

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**Background:** Inflammatory conditions affect bone turnover, as is seen in rheumatoid arthritis (RA). Inflammatory cytokines in RA stimulate osteoclasts and shift the balance between bone formation and resorption. Programmed death-1 (PD-1) and its ligands PD-L1 and PD-L2, are important for maintaining self-tolerance, and this pathway plays a prominent role in RA. Recently, repulsive guidance molecule b (RGMb) and bone morphogenetic protein (BMP) was identified as a novel receptor complex for PD-L2 (1). We previously showed the PD-1 pathway to be associated with radiographic progression in RA (2). The interaction of PD-L2 with the RGMb/BMP receptor complex could potentially provide a link between bone homeostasis and the PD-1 pathway.
**Objectives:** To investigate the possible association between bone homeostasis and the PD-1 pathway in RA.
**Methods:** We generated osteoclasts from RA synovial fluid mononuclear cells (SFMCs) (3), stimulated them with recombinant (rec) PD-1 and PD-L2, and subsequently evaluated these osteoclasts for TRAP activity, and expression of PD-1, PD-L2 and RGMb. We induced RA-like disease in PD-1-and PD-L2-KO mice by immunization with Freund's adjuvant and chick collagen, and evaluated clinical arthritis. After sacrifice, paws were paraffin embedded and stained for TRAP and osteocalcin. The femur was subjected to ex vivo DXA scanning. In addition, we stimulated normal mouse calvarial cells with the recombinant proteins in a BMP reporter assay to evaluate the potential of PD-1 and PD-L2 to affect BMP signaling.
**Results:** Recombinant PD-1 and PD-L2 increased TRAP activity in osteoclasts generated from RA SFMCs, at day 21 (p=0.046). Pre-osteoclasts in the culture expressed both PD-L2 and RGMb. The KO mice did not develop clinical signs of arthritis, ensuring intact mobility and constant bone load. DXA scan revealed that immunized PD-L2 KO mice had a higher bone mass density than other KO mice, WT and non-immunized PD-L2 KO (p=0.03). These mice did not differ histologically in TRAP and osteocalcin expression. Rec PD-L2 significantly decreased BMP signaling in the BMP reporter assay.
**Conclusions:** The clinical association between the PD-1 pathway and radiographic progression in early RA points to its importance in RA bone homeostasis. The increase in TRAP activity after incubation with recombinant PD-L2 supports this association. The increased bone mass density observed in immunized PD-L2 KO mice further supports a potential role for PD-L2 in bone homeostasis. The expression of PD-L2 in pre-osteoclasts also suggests a role for PD-L2 in bone homeostasis. These data provide a new insight into the close relation between the immune system and bone, as well as suggest a potential therapeutic target in diseases involving inflammatory bone changes.
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**Disclosure of Interest:** None declared
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## OP0071 ADIPOKINE EFFECTS ON DIFFERENTIATION OF OSTEOPOROSIS AND OSTEOARTHRITIS SPONGIOSA-DERIVED MESENCHYMAL STROMAL CELLS

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**Background:** Osteoporosis predominantly affects elderly people and is characterized by bone loss, increased fracture risk and reduced regeneration ability. Age-related bone loss and articular cartilage damage correlate with increased bone marrow fat infiltration. With respect to age and age-related osteoporosis, there is an inverse relationship between bone mass and bone marrow adiposity. Bone marrow adipose tissue is metabolically active: It releases proinflammatory (e.g. adipokines) and matrix-degrading proteins (e.g. matrix metalloproteinases, MMPs), which promote progressive bone loss observed in osteoporosis and osteoarthritis. Moreover, bone marrow adipocytes share the same precursor with osteoblasts, the mesenchymal stem cell (MSC). Adipocyte-derived factors might influence differentiation of bone marrow-derived MSCs into osteoblasts and adipocytes. However, information on interactions between adipose tissue-derived factors and MSC differentiation is limited.
**Objectives:** To analyze the presence of adipokines (visfatin, resistin and leptin) in the bone marrow cavity and their effects on differentiation of MSCs.

**Methods:** Spongiosa containing bone marrow from femoral heads of patients undergoing hip replacement after osteoporotic femoral neck fracture or osteoarthritis were collected. Primary spongiosa-derived mesenchymal stromal cells (hMSCs) as well as commercially obtained MSCs were cultured in adipogenic and osteogenic media 3 weeks with/without adipokines. mRNA expression of adipokines, bone marker genes, TIMPs and MMPs of stimulated hMSCs/MSCs and as well as of bone samples were evaluated by real time PCR.
**Results:** Expression of visfatin was significantly increased in osteoporotic bone (n=14) compared to non-osteoporotic bone. Higher expression of leptin was also detectable in osteoporotic bone (n=13). The stimulation with visfatin of hMSC during adipogenic differentiation significantly increased MMP13-expression (e.g. d21: 72-fold) but not leptin and resistin. In osteogenic differentiated cells, a reduction of MMP2 by stimulation of all adipokines could be observed (n=3). In contrast to adipogenic differentiation of hMSC, visfatin led to reduced expression of MMP13 during osteogenic differentiation (e.g. d21: 55-fold). In addition,visfatin decreased TIMP1 (e.g. d21: 2.86-fold), TIMP2 (e.g. d21: 3.17-fold), and RunX2 (e.g. d21: 5.85-fold) production, whereas leptin and resistin showed no effect on these molecules.
**Conclusions:** Visfatin and leptin levels were found to be increased in osteoporotic bone tissue. The altered MMP and TIMP production, mediated especially by visfatin, might therefore influence bone remodeling at the adipose tissue/bone interface. Moreover, high levels of leptin in the osteoporotic bone might enhance bone degradation. Although leptin had no local effect on MSCs differentiation *in vitro*, it may also modulate bone degradation by affecting other cell types such as inflammatory cells.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4181

## OP0072 INHIBITION OF NOTCH1 PROMOTES HEDGEHOG SIGNALING IN A HES1-DEPENDENT MANNER AND EXACERBATES EXPERIMENTAL OSTEOARTHRITIS

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**Background:** The Notch pathway is one of the so-called morphogen pathways, which are evolutionary conserved key-regulators of embryonic development. Notch signaling has recently been implicated in the pathogenesis of osteoarthritis (OA). However, cell-type and context dependent differences in outcome have been reported and the underlying molecular mechanisms are incompletely understood.
**Objectives:** OA is characterized by degeneration of articular cartilage, limited intraarticular inflammation with synovitis, changes in periarticular and subchondral bone and osteophyte formation by endochondral ossification. Several studies have identified Notch- and Hedgehog-signaling as essential pathways involved in cartilage development and bone remodeling.
**Methods:** Notch and hedgehog signaling were analyzed by real-time PCR and immunohistochemistry. Mice overexpressing a Notch-1 antisense construct (Notch-1 AS) were employed as a model of impaired Notch signaling. Experimental OA was induced by destabilization of the medial meniscus (DMM). The extent of cartilage destruction and osteophyte formation was analyzed by safranin-O staining with subsequent assessment of the OARSI and Mankin scores and $\mu$CT scanning. Collagen X staining was used as a marker of chondrocyte hypertrophy. The role of Hes-1 was investigated with knockdown and overexpression experiments.
**Results:** Notch signaling was activated in human and murine OA with increased expression of Jagged1, Notch-1, accumulation of the Notch intracellular domain (NICD1) and increased transcription of Hes-1. Notch1 AS mice showed exacerbated osteoarthritis with increases in OARSI scores, osteophyte formation, increased subchondral bone plate density, collagen X and osteocalcin expression and elevated levels of Epas1 and ADAM-TS5 mRNA. Inhibition of the Notch pathway induced activation of hedgehog signaling with induction of Gli-1 and Gli-2 and increased transcription of hedgehog target genes. The regulatory effects of Notch signaling on Gli-expression were mimicked by Hes-1.
**Conclusions:** Inhibition of Notch signaling activates hedgehog signaling, enhances chondrocyte hypertrophy and exacerbates experimental osteoarthritis including osteophyte formation. These data suggest that the activation of the Notch pathway may serve to limit aberrant hedgehog signaling in OA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3510

## OP0073 RNA-SEQ BASED IDENTIFICATION OF FACTORS INVOLVED IN KNEE JOINT REGENERATION AFTER INDUCED OSTEOARTHRITIS IN NOTOPHTHALMUS VIRIDESCENS

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**Background:** While tissue damage in mammals is mostly accompanied by fibrotic scar formation, many urodele amphibians including the red-spotted newt *Notophthalmus viridescens* are able to restore damaged organs or even lost appendages. To study endogenous knee joint regeneration in adult vertebrates, the newt has been established as a model organism in our working group. Like in murine models, osteoarthritis (OA) like symptoms can either be induced by surgical damage to articular cartilage or by intra-articular injection of enzymes, e.g. collagenase. In contrast to murine OA models, newts display symptoms including joint instability and luxation, but joint function is restored in these animals within 3 months.
**Objectives:** To evaluate the molecular pathways involved in knee joint regeneration.
**Methods:** To induce OA, animals were either treated by intra-articular injection of collagenase, mono-iodoacetate or by surgical manipulation of articular cartilage. To study gene expression changes on the transcriptional level during regeneration in the newt, RNA from knee joints was isolated and pooled. Subsequently, a quantitative transcriptome analysis using Illumina® next-generation sequencing (NGS) was performed. Relevant molecular pathways guiding regeneration were analyzed in all OA models tested. Candidate genes using public available databases have been selected, and pathway analyses of the gained data have been performed. Verification of selected candidate genes on the mRNA level has been done by Real Time PCR analyses. Adhesion of newt-derived cell lines and primary newt cells to Tenascin-C (TN-C) was analyzed *in vitro*. To compare molecular pathways guiding wound healing in amphibians and mice, the expression pattern of selected candidate genes (TN-C and cysteine-rich protein 61 (Cyr61/CCN1)) was also analyzed in murine OA models on the mRNA (Real Time PCR) and protein level (immunohistochemistry).
**Results:** During regeneration, several matricellular proteins including TN-C, CCN family members and their related pathways were found to be differentially regulated. In contrast to the murine OA models, Cyr61/CCN1 mRNA expression levels peaked at day 5 (5.9±0.72 in the collagenase model) and ceased afterwards, while mRNA expression levels in collagenase (day 10 0.6±0.07 to 2.5±0.61 at day 60) and surgically treated newts (day 10 3.39±0.64 to 1.6±0.2 at day 60) showed higher expression levels during later time points. On the protein level, CCN1 expression was detectable in chondrocytes and osteophytes in the collagenase induced murine OA model. In adhesion experiments using the newt-derived cell line B1H1 TN-C coating had anti-adhesive properties (TN-C vs. Control 42% reduction).
**Conclusions:** Extracellular matrix proteins are important during regenerative and repair processes, since they may alter cellular adhesion and guide migration. Identification of novel proteins and evaluation of their impact on cellular behaviour can help to understand the pathways involved. Future experiments on cells from OA patients might help in the development of new treatment options for human OA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5547

## OP0074 EBSELEN IS A POTENTIAL ANTI-OSTEOPOROSIS AGENT BY SUPPRESSING RECEPTOR ACTIVATOR OF NUCLEAR FACTOR KAPPA-B LIGAND-INDUCED OSTEOCLAST DIFFERENTIATION IN VITRO AND LIPOPOLYSACCHARIDE-INDUCED INFLAMMATORY BONE DESTRUCTION IN VIVO

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**Background:** Ebselen is a non-toxic seleno-organic drug with anti-inflammatory and antioxidant properties that is currently being examined in clinical trials to prevent and treat various diseases, including atherosclerosis, stroke, and cancer.
**Objectives:** We investigated the effects of ebselen on RANKL-induced differentiation of osteoclasts and their functions and the underlying molecular mechanisms. Furthermore, we determined the effects of ebselen on LPS-induced bone erosion *in vivo*.
**Methods:** To generate osteoclasts from BMMs, we cultured BMMs for 4 days in the condition of M-CSF and RANKL pretreated with ebselen. The cells were then stained with TRAP solution, rhodamine-conjugated phalloidin for F-actin ring labeling and DAPI solution to detect apoptotic body formation. The change of F-actin ring on mature osteoclasts induced by ebselen was quantified by calculating the ratio of actin ring positive (AR+) osteoclasts versus actin ring negative (AR-) osteoclasts. to detect the formation of apoptotic osteoclasts, we performed TUNEL (TdT-mediated dUTP-biotin nick end-labeling) assay. Primary calvaria osteoblasts and BMCs were co-cultured and were re-seeded in hydroxyapatite-coated plates or dentin slices with or without ebselen. ICR mice were divided into

4 experimental groups comprising 5 mice each: phosphate-buffered saline-treated (control) group, ebselen only-treated group, LPS only-treated group, and LPS- and ebselen-treated group. Ebselen (10 mg/kg) or PBS was administered orally every 8 days, and LPS was injected intraperitoneally on days 1 and 4. Micro-computed tomography (μ-CT) data containing 3D images and bone parameters and histological data were acquired

**Results:** Ebselen suppressed the formation of TRAP-positive multinucleated cells in an osteoblast/osteoclast co-culture by regulating the ratio of RANKL/osteoprotegerin secreted by osteoblasts. In addition, ebselen treatment in the early stage of osteoclast differentiation inhibited RANKL-dependent osteoclastogenesis by decreasing the phosphorylation of IκB, PI3K, and Akt in early signaling pathways and by subsequently inducing c-Fos and nuclear factor of activated T-cells c1. Further, ebselen induced apoptosis of osteoclasts in the late stage of osteoclast differentiation. In addition, ebselen treatment suppressed filamentous actin ring formation and bone resorption activity of mature osteoclasts. Reflecting these *in vitro* effects, administration of ebselen recovered bone loss and its μ-CT parameters in lipopolysaccharide-mediated mouse model. Histological analysis confirmed that ebselen prevented trabecular bone matrix degradation and osteoclast formation in the bone tissues. Finally, it was proved that the anti-osteoclastogenic action of ebselen is achieved through targeting N-methyl-D-aspartate receptor.

**Conclusions:** Finally, it was proved that the anti-osteoclastogenic action of ebselen is achieved through targeting N-methyl-D-aspartate (NMDA) receptor.

**Disclosure of Interest:** None declared

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### OP0075 SENSITIVE SPECT/CT IMAGING OF SYNOVIAL FAP EXPRESSION AFTER ANTI-IL-22 TREATMENT IN EXPERIMENTAL ARTHRITIS

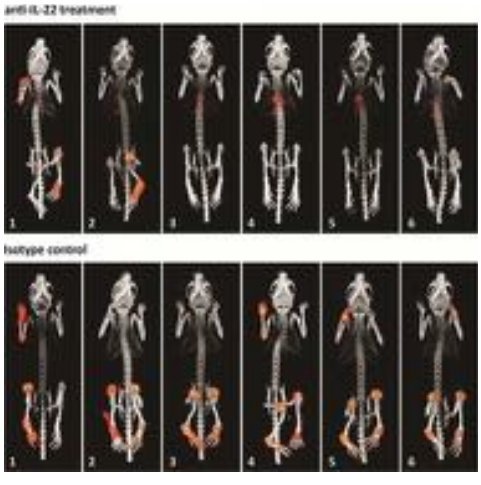
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**Background:** Rheumatoid arthritis (RA) synovial tissue has been demonstrated to express high levels of fibroblast activation protein (FAP) using anti-FAP-antibody 28H1. In addition, RA patients show elevated levels of IL-22 and IL-22-producing T helper cells that correlate to erosive disease, suggesting a role for this cytokine in the pathogenesis of RA.

**Objectives:** The purpose of this study was to determine the feasibility of $^{111}$In-28H1 SPECT/CT imaging of FAP-expressing synovium to monitor the therapeutic potential of neutralizing IL-22 during experimental arthritis.

**Methods:** Collagen-induced arthritis (CIA) was induced in male DBA/1J mice. Mice were treated 3 times per week with anti-IL-22 antibodies (8 mg/kg), while the control group received rat IgG1 isotype control antibodies. To monitor the therapeutic effect after 2 weeks of treatment, SPECT/CT images were acquired 24 h after injection of $^{111}$In-labeled DTPA-conjugated anti-FAP antibody, 28H1. After image acquisition, mice were euthanized and dissected. Imaging results were compared with the macroscopic arthritis scores and radiographic bone damage scores acquired by X-ray.

**Results:** Blocking IL-22 during CIA was a potent approach to prevent arthritis development, reaching a disease incidence of only 50%, versus 100% in the control group. SPECT/CT imaging using indium-labeled anti-FAP antibodies showed that joint uptake of the tracer was reduced highly significant (p=0.002) in anti-IL-22-treated mice (4.3 ± 3.4%ID/g) compared to the isotype control group (12.7 ± 3.7%ID/g) (See figure). This was confirmed by the corresponding macroscopic arthritis scores and radiographic bone damage scores that were significantly (p=0.047 and p=0.017 respectively) lower in the anti-IL-22-treated group. Besides its sensitivity, the in vivo FAP-based SPECT/CT had the great advantage to visualize sites of inflammation that were overlooked during clinical scoring, like in knee, hip, elbow and shoulder (See figure).




**Conclusions:** These findings demonstrate that IL-22 plays an important role in the development of experimental arthritis, and targeting this cytokine seems an attractive new strategy in RA treatment. Most importantly, SPECT/CT imaging of the inflamed synovium using the labeled anti-FAP antibody $^{111}$In-DTPA-28H1 can be used to specifically monitor response to therapy in an objective and quantitative way, and is potentially more sensitive in disease monitoring compared to the standard method of clinical arthritis scoring by macroscopic inspection.

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**THURSDAY, 9 JUNE 2016**

## SpA and PsA basic and translational research

### OP0076 AUTOANTIBODIES AGAINST CD74 – A NEW DIAGNOSTIC MARKER FOR SPONDYLOARTHRITIS (SPA)

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**Background:** Spondyloarthritis (SpA) is a common debilitating inflammatory disorder. Pathogenesis of axial SpA (axSpA) including ankylosing spondylitis (AS) is still largely unclear.

**Objectives:** Diagnosis is difficult, since abnormalities in conventional X-rays develop with a latency of several years and only HLA-B27 is used as laboratory marker. The presence of radiographic sacroiliitis is essential for SpA diagnosis. To prevent destructive effects early diagnosis and intervention in SpA patients may be important. To evaluate antibodies to the human leukocyte antigen class II-associated invariant chain peptide (anti-CD74) as a diagnostic marker of SpA.

**Methods:** Sera of 117 patients with axial SpA and 38 non-SpA patients were analyzed for IgA and IgG antibodies against CD74 by ELISA. HLA-B27 status was available in 112 patients. All donors provided informed consent for the study approved by the local ethics committee (project number 4928).

**Results:** Anti-CD74 antibodies were detected in 85.1% of SpA patients but only in 5% of non-SpA patients ($p \leq 0.0001$). Detection of both IgG and IgA anti-CD74 antibodies for diagnosing SpA revealed a sensitivity of 77% and a specificity of 90%. Remarkably, IgA autoantibodies against CD74 alone had a sensitivity of 67% and a specificity of 95%. IgA anti-CD74 antibodies were even more frequent in SpA patients with short disease duration and significantly correlate with more advanced radiological sacroiliitis and reduced spinal mobility.

**Conclusions:** Anti-CD74 IgA antibodies were strongly associated with SpA. Antibodies against CD74 could provide an important additional tool for diagnosis of SpA.

**Disclosure of Interest:** None declared

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### OP0077 IL-20 AND IL-24 LINK INNATE IMMUNE ACTIVATION AND NEW BONE FORMATION IN SPONDYLOARTHRITIS

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**Background:** The pathogenesis of spondyloarthritis (SpA) involves activation of the innate immune system, inflammation and new bone formation. The innate immune system is activated through pattern recognition receptors including Toll like receptor 4 (TLR4). Inflammation is a result of increased production of pro-inflammatory cytokines and chemokines including tumor necrosis factor alpha (TNFα) and monocyte chemoattractant protein 1 (MCP-1). New bone formation by osteoblasts is determined by a balance between the inhibitory effect of Dickkopf-1 (DKK1) and the stimulatory effect of bone morphogenetic proteins (BMPs) including BMP2. The two cytokines IL-20 and IL-24 have been shown to link innate immune activation and tissue homeostasis.(1) Previously, we have found increased plasma levels of IL-20 and IL-24 in SpA patients.

**Objectives:** We hypothesized that IL-20 and IL-24 are secreted as part of activation of the innate immune system and affect bone homeostasis. The aim was to describe associations of IL-20 and IL-24 and disease activity and magnetic resonance imaging (MRI) scores and to identify the sources and targets of the two cytokines in SpA.

**Methods:** Patients with axial SpA (n=83) were included in the study of associations between cytokine levels and disease activity and MRI scores. Patients with peripheral SpA (n=16) were included for studying sources and targets of IL-20 and IL-24 among synovial fluid mononuclear cells (SFMCs), peripheral blood mononuclear cells (PBMCs), and fibroblast-like synoviocytes (FLSs) using lipopolysaccharide (LPS) and TNFα as positive controls. Healthy human osteoblasts were used for studying the effect of the two cytokines on mineralization using BMP2 as a positive control. The secretion of IL-20, IL-24, MCP-1 and DKK1 were measured by enzyme linked immunosorbant assays and flow cytometry, and mineralization was measured by hydroxyapatite deposition. Plasma IL-20 and IL-24 levels were analyzed with the Mann-Whitney U test and the Spearman correlation. Supernatant cytokine concentration and flow cytometry median fluorescence intensity data were calculated as ratios, log-transformed and compared with the paired or unpaired t-test.
**Results:** The plasma IL-20 and IL-24 levels were increased in SpA patients compared with healthy controls (HCs) by 57% and 83%, respectively (both $p<0.0001$) and there was a trend towards associations with both future switch to biologic therapy (p=0.031 and p=0.11, respectively), and spine MRI chronicity score (p=0.10 and p=0.15, respectively). The production of IL-20 and IL-24 was increased by LPS, and this TLR4 induced secretion was greater in SpA PBMCs compared with HC PBMCs. IL-20 and IL-24 increased the production of MCP-1 by SpA SFMCs (but not by SpA FLSs), decreased the production of DKK1 by SpA FLSs (but not by SpA SFMCs) and increased mineralization by human osteoblasts. The IL-20 and IL-24 induced production of MCP-1 among the SFMCs was found in activated synovial monocytes only.
**Conclusions:** Taken together, our findings indicate that IL-20 and IL-24 are novel links between activation of the innate immune system and new bone formation.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1576

## OP0078 SYNOVIAL MYOFIBROBLASTS FROM SPONDYLOARTHRITIS PATIENTS PRODUCE IL-26 SPONTANEOUSLY AND THE PRODUCTION IS ENHANCED UPON IL-1, TNF-α AND LPS STIMULATION

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**Background:** New bone formation in spondyloarthritis involves myofibroblasts [1]. IL-26 is part of the IL-10 cytokine family and was recently reported to increase Th17 differentiation [2]. It was first discovered in herpesvirus saimiri–transformed T cells and thus suspected to be a T-cell cytokine [3]. However, more recent studies of RA patients show IL-26 expression in synoviolin-postive cells harvested from the synovia [2]. The knowledge about IL-26 is compromised by lack of IL-26 in mice and no studies of IL-26 in spondyloarthritis (SpA) and its regulation have been conducted.
**Objectives:** In the present study we aim to characterize IL-26 producing cells in spondyloarthritis (SpA).
**Methods:** IL-26 was measured by ELISA in plasma and synovial fluid (SF) of 14 SpA patients attending the clinic with a swollen joint and in plasma samples from 7 age and gender matched healthy controls. Synovial-fluid-mononuclear-cells (SFMC) and fibroblast-like-synoviocytes (FLS) were cultured and stimulated for 48 hours with IL-1β, TNFα, TGF-β, IL-17A and LPS. The supernatants were harvested and analyzed for IL-26 by ELISA. Tissue samples of inflamed synovial membrane were stained with a fluorochrome conjugated rabbit IL-26 antibody for immunofluorescence. Imaging of the sections was performed by confocal microscopy. For flow cytometry analysis, FLS were surface stained for CD90 and a live-dead marker, and subsequently permeabilized and stained intracellularly for α-Smooth-Muscle-Actin (αSMA) and IL-26. Samples were run on the flow cytometer within 24 hours of staining. Data are expressed as mean ± SD.
**Results:** IL-26 levels were significantly higher in synovial fluid compared with plasma; this applied to plasma from the healthy controls (HC) as well as SpA patients. (HC plasma: 5.8 ± 3.3 pg/ml, SpA plasma: 6.6 ± 1.8 pg/ml, SpA SF: 41.6 ± 6.8 pg/ml - P-values HC vs. SF: 0.0020, P-value SP vs. SF: <0.0001.) Staining of synovial membrane revealed IL-26 presence in synovial cells with fibroblast-like morphology. ELISA analysis of the supernatants from culturing and stimulation of FLS and SFMC showed a high level of IL-26 in both cell populations as well as drastic increase in IL-26 production after stimulation with IL-1, TNF-α and LPS. The vast majority of the IL-26 producing FLS were $\alpha SMA^+$ and $CD90^+$ myofibroblasts by flow cytometry.
**Conclusions:** IL-26 levels in synovial fluid are significantly higher than in plasma, suggesting a local production of IL-26 in the inflamed joint. We found IL-26 positive cells in the synovial membrane with fibroblast morphology and FLS from the inflamed joints of SpA patients produce high amounts of IL-26. By flow cytometry we established that these IL-26 producing fibroblasts seem to be myofibroblasts primarily.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4585

## OP0079 INCREASED FREQUENCIES OF IL-23R POSITIVE T CELLS AND IL-22 AND IL-17 PRODUCING MAIT CELLS IN THE PERIPHERAL BLOOD OF PATIENTS WITH ANKYLOSING SPONDYLITIS: PRELIMINARY RESULTS

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**Background:** Ankylosing spondylitis (AS) is the prototypic and most common form of spondyloarthritis (SpA). It was recently suggested that IL-23 could play a pivotal role in the pathophysiology of SpA. Indeed, there is a strong genetic association of SpA with polymorphisms of the *IL-23* receptor (IL-23R) gene. In experimental models, IL-23 is produced during the misfolding phenomenon of HLA-B27 heavy chain in the endoplasmic reticulum. Furthermore, in animal models, IL-23 overexpression induced a SpA-like disease via IL-23+ resident T cells infiltrating entheseal structures and producing IL-17 and IL-22. In addition, there is an increased number of circulating cells producing IL-17 in patients with AS. Recent data also suggested that IL-17A is a potential target in the treatment of patients with AS.
**Objectives:** Cells that expressed IL-23R as well as those producing IL-17 and/or IL-22 have been poorly characterized in AS and/or SpA. Thus, we aimed to better delineate the peripheral blood T cells that expressed IL-23R and the IL-17 and IL-22 producing cell subsets, notably conventional T cells as well as mucosal associated invariant T cells (MAIT) in patients with AS.
**Methods:** 36 patients with AS (modified NY criteria; 27 M; age: 44.7 ± 2.6, disease duration: 12.7 ± 1.6; all under NSAIDs or traditional DMARDs) and 31 healthy controls (HC) (8 M; age: 46 ± 2.3) were evaluated. For each subject, peripheral blood T cell subsets were assessed using multi-color flow cytometry. Intracellular cytokine IL-17A, IL-22 and IFN-γ were evaluated after phorbol myristate acetate and ionomycine activation and permeabilization and analysed by flow cytometry. MAIT cells were identified by using TCRVα7.2 specific monoclonal antibodies. IL-22 serum levels were determined by ELISA using commercially available kit.
**Results:** the number and percentage of CD3+ T cells, CD3+CD4+ and CD3+CD8+ T cells were comparable between patients and HC. Circulating IL-22 levels did not differ between patients and HC (22.6 ± 8.4 vs 15.1 ± 4.4 pg/ml, p=0.7). IFN-γ producing $CD4^+$ and $CD8^+$ T cells were decreased in AS compared to HC (4.6 ± 1.7 vs 11.4 ± 2.5% and 23.3 ± 1.9 vs 34.3 ± 2.3%, respectively, p=0.005 and p=0.002). $CD8^+$ T cells expressing IL-23R were significantly increased in AS: 72.8 ± 1.5 vs 65.2 ± 2% (p=0.009). The percentage of MAIT T cells did not differ between patients and HC but we found an increased percentage of MAIT cells that produced IL-17 and IL-22: MAIT IFN-$\gamma^-$ IL-$17^+$: 0.43 ± 0.1 vs 0.12 ± 0.008%, p=0.006; MAIT IFN-$\gamma^-$ IL-$22^+$: 0.83 ± 0.1 vs 0.3 ± 0.1%, p=0.004. No correlation was found between the percentage of $CD8^+$ IL-$23R^+$ T cells and measurements of disease activity as well as between IL-$17^+$ or IL-$22^+$ MAIT cells and disease activity.
**Conclusions:** These preliminary results suggest that the peripheral blood of patients with AS is enriched in $CD8^+$ IL-$23R^+$ T cells as well as IL-17 and IL-22 producing MAIT cells. Since MAIT cells are involved in antibacterial immunity and bacterial agents are potentially involved in SpA, our preliminary data suggest that this T cell subset could potentially play a role in AS via IL-17 and IL22 production. This remains to be clarified by future and complementary studies.
**Disclosure of Interest:** None declared
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## OP0080 HIGHER SERUM LEVEL OF LEPTIN MIGHT BE RESPONSIBLE FOR LESS STRUCTURAL DAMAGE IN THE SPINE IN FEMALE PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Fat tissue synthesizes and releases a series of biologically active substances (adipokines), which are involved in bone metabolism through effects on bone formation and resorption. There are gender-specific differences in the expression of adipokines and there are also gender specific-differences in the development of structural damage in the spine in patients with ankylosing spondylitis - AS. The reason for less structural damage in the spine in female AS patients is not well understood until now.
**Objectives:** The aim of this study was to investigate the gender-specific role of adipokines as predictors of radiographic spinal progression in patients with AS.
**Methods:** Altogether 120 patients (82 men and 38 women) from the ENRADAS

trial who completed the study per protocol were included into the analysis. Spinal radiographs (lumbar and cervical spine, lateral views) were scored independently by two trained readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) scoring system. Radiographic spinal progression was defined as 1) mSASSS worsening by ≥2 units after 2 years, and 2) development of at least one new syndesmophyte or progression of existing syndesmophytes (i.e., formation of a bridging syndesmophyte) after 2 years. Serum levels of adipokines (leptin, adiponectin, lipocalin-2, omentin, visfatin, resistin, and chemerin) were measured at baseline.

**Results:** A significant association with radiographic spinal progression was found for leptin only. Mean baseline leptin levels were significantly lower in patients with mSASSS worsening by ≥2 units after 2 years (n=29) as compared to those without progression (n=91): 10.3±8.8 vs. 15.9±13.7 ng/ml, respectively, p=0.002, and in patients with syndesmophyte formation (n=25) as compared to those without syndesmophyte formation (n=95): 10.1±9.6 vs. 15.7±13.4 ng/ml, respectively, p=0.002. This difference was especially evident in males, but not in females. However, in females the serum level of leptin at baseline was in general significantly higher than in males: 24.0±17.4 vs. 10.2±6.8 ng/ml, p<0.001 that was independent of body mass index.

In the ROC analysis leptin had an area under the curve (AUC) of 0.69 (95% CI 0.57–0.81) for no mSASSS worsening by ≥2 units and 0.70 (95% CI 0.57–0.82) for no syndesmophyte formation. Leptin level of 7.5 ng/ml was identified in the ROC analysis as an optimal threshold for the prediction of protection from radiographic spinal progression after two years – table.

In the logistic regression analysis, a protective value of higher leptin serum level regarding radiographic spinal progression could be confirmed: odds ratio (OR) =1.15 (95% CI 1.02–1.3) for no mSASSS worsening by ≥2 units, and OR =1.28 (95% CI 1.1–1.5) for no syndesmophyte formation (meaning a 15%/28% increase of the odds for no radiographic spinal progression after 2 years with each baseline leptin serum level increase by 1 ng/ml), both adjusted for baseline syndemophytes, elevated C-reactive protein (CRP), smoking, body mass index, sex, and NSAIDS intake score.

**Table.** Baseline serum leptin level >7.5 ng/ml (an optimal cut-off in the ROC analysis) as a predictor of protection from radiographic spinal progression after two years in patients with ankylosing spondylitis (n = 120).

| Outcome | Sensitivity, % | Specificity, % | OR, unadjusted | OR, adjusted* |
|---|---|---|---|---|
| No mSASSS worsening by ≥2 points | 78 | 55 | 4.4 (95% CI 1.8-10.6) | 9.2* (95% CI 2.5-34.0) |
| No syndesmophyte formation / progression | 77 | 56 | 4.2 (95% CI 1.7-10.6) | 11.7* (95% CI 2.8-47.8) |

*Adjusted for baseline syndemophytes, elevated CRP, smoking, body mass index, sex, and NSAIDs intake score

**Conclusions:** Higher serum levels of leptin seem to protect patients with AS from radiographic spinal progression. Female patients with AS have significantly higher leptin levels that might explain lesser extent of structural damage in the spine in female AS patients in general.

**Disclosure of Interest:** None declared

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## OP0081 TISSUE DEFICIENCY OF THE ATYPICAL CHEMOKINE RECEPTOR D6 IS ASSOCIATED WITH THE SELECTIVE INCREASE OF GUT-DERIVED PRO-INFLAMMATORY CXCR1HIGHLY6HIGHTL1A+IL-23+CCR7+ CELLS IN THE PERIPHERAL BLOOD, SYNOVIAL FLUIDS AND BONE MARROW OF AS PATIENTS

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**Background:** Gut derived innate lymphoid cells of type 3 (ILC)3 are increased in number in the circulation and inflamed tissues of AS patients. Factors influencing the maintainace of ILC3 in an activated status are not clear. The atypical chemokine receptor D6 is a decoy and scavenger receptor for most inflammatory CC chemokines and acts preventing exacerbated inflammatory reactions. Mice lacking D6 expression in the non-hematopoietic compartment display a significant increase of pro-inflammatory monocytes in the peripheral blood and in secondary lymphoid tissues. The role of D6 in human inflammatory disorders has not been inverstigated.

**Objectives:** To evaluate whether modulation of D6 expression occurs in the gut and in BM of AS patients and accompanied with a selective increase of pro-inflammatory CXCR1$^{high}$Ly6$^{high}$TL1A$^{+}$CCR7$^{+}$ cells in the circulation and inflamed tissues of AS and to study the effect of these cells in modulating ILC3 differentiation.

**Methods:** RT-PCR and immunohistochemistry were used to evaluate the expression of D6 in the gut and bone marrow of AS patients and controls. Different monocyte substes were analyzed by flow cytometry in the peripheral blood, gut, synovial fluids and bone marrow of AS patients and controls. Isolated peripheral CXCR1$^{high}$Ly6$^{high}$TL1A$^{+}$CCR7$^{+}$ cells were co-coltured with isolated peripheral ILC3 and changes in ILC3 frequency were evaluated by flow cytometry.

**Results:** D6 was significantly down-regulated in the ileum and in the bone marrow of AS patients compared to controls. D6 deficiency was accompanied by a complex monocyte/macrophage signature. Tissue resident CXCR1$^{high}$Ly6$^{low}$ macrophages were expanded in the ileum of AS patients compared to controls. A significant increase in the frequency of pro-inflammatory CXCR1$^{high}$Ly6$^{high}$ monocytes producing high levels of TL1A and IL-23 was observed in the ileum of AS patients. In the peripheral blood a statistically significant increase in the frequencies of both bone marrow derived CXCR1$^{low}$Ly6$^{High}$ and intestinal derived CXCR1$^{high}$Ly6$^{high}$CCR7$^{+}$TL1A$^{+}$IL-23$^{+}$ monocytes, the latest being also expanded in AS synovial fluids and bone marrow. Isolated pro-inflammatory CXCR1$^{high}$Ly6$^{high}$TL1A$^{+}$IL-23$^{+}$CCR7$^{+}$ monocytes from peripheral blood of AS induced the expansion and activation, evaluated through the production of IL-22 and IL-17, of ILC3.

**Conclusions:** In this study we provide the first demonstration that absence of D6 expression in the gut and in the inflamed tissues of AS patients selectively induced the intestinal accumulation and re-circulation of pro-inflammatory CXCR1$^{high}$Ly6$^{high}$TL1A$^{+}$IL-23$^{+}$CCR7$^{+}$ monocytes. Since the ability of these cells in promoting ILC3 expansion and activation, these cells may promote a sustained pro-inflammatory status in AS.

**Disclosure of Interest:** None declared

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## OP0082 INFECTIONS OF THE GUT, UROGENITAL AND RESPIRATORY TRACT AND APPENDICITIS DURING CHILDHOOD, AND THE RISK OF DEVELOPING ANKYLOSING SPONDYLITIS

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**Background:** Data supporting the role of specific environmental exposures in the development of AS are scarse. Microbial exposure, both in the form of infections and gut flora, has been implicated in the pathogenesis of several spondyloarthritis related conditions, such as reactive arthritis and inflammatory bowel disease (IBD). Gut dysbiosis has also been recognized in ankylosing spondylitis, but it is not known if this is a result of the disease or occurs before disease onset.

**Objectives:** To determine if infections during childhood, primarily gut, urogenital and respiratory tract infections (RTI) as well as appendicitis, predict a diagnosis of AS.

**Methods:** This is a register based study using several national registers. All individuals having ≥1 visit to specialized health care with an associated ICD-code for AS were identified in the national health care register, 1964–2009. For each index case 5 matched controls (sex, age, county) were retrieved from the population register. Cases and controls were linked to the National Patient Register (NPR) to identify hospitalization with an ICD-code indicating an infection (gastrointestinal, urogenital, respiratory tract or appendicitis) at an age of 0–16 years.

In order to ensure complete exposure information only cases and controls living in Sweden up until their 17th birthday were included. In order to increase the likelihood of a temporal relationship all cases and controls with any diagnosis of a rheumatic disease, psoriasis, IBD or iridocyclitis before the age of 17 and juvenile idiopathic arthritis ever were excluded.

Univariate conditional logistic regression analyses were used to determine odds ratios (OR) with confidence intervals (CI) for development of AS, with regard to the infectious exposures.

**Results:** Based on 2643 cases with AS and 11064 matched controls, childhood appendicitis reduced the odds for a later diagnosis of AS by 40% and hospitalization with a RTI increased the odds by 20%. Hospitalization for urogenital or gastrointestinal tract infections did not predict an AS diagnosis (Table 1). Similar (and statistically significant) results were obtained when excluding all cases/controls with a diagnosis of IBD up until 2 years after the first AS-diagnosis of the index case. The trend was stronger for men than women (data not shown).

| Table 1. Exposure | AS cases (N=2643) exposed | Controls (N=11064) exposed | OR | 95% CI |
|---|---|---|---|---|
| Appendicitis | 40 (1.5%) | 280 (2.5%) | 0.59 | 0.42 – 0.82 |
| Gastrointestinal tract infections | 84 (3.2%) | 336 (3.0%) | 1.03 | 0.80 – 1.32 |
| Respiratory tract infections | 225 (8.5%) | 808 (7.3%) | 1.18 | 1.01 – 1.39 |
| Urogenital tract infections | 11 (0.4%) | 47 (0.4%) | 0.96 | 0.49 – 1.85 |

**Conclusions:** Appendicitis during childhood decreased and RTI increased the risk of developing AS in this case-control study. Appendicitis/appendectomy has previously, repeatedly, been described to decrease the risk for ulcerative colitis, but has not been investigated for AS. Our findings suggest that early immune

phenotype, either affecting the risk for severe childhood infections, or being modulated by such infections, may represent an early pathophysiological phase of AS.
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## OP0083 MIR-125A DECREASED IN PSA SYNOVIUM AND PERIPHERAL BLOOD CD14+ MONOCYTES AND CORRELATES TO JOINT ANGIOGENESIS

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**Background:** Psoriatic Arthritis (PsA) is a chronic immune-mediated inflammatory disease, characterised by proliferation of synovial tissue and destruction of articular cartilage/bone with associated psoriasis. Dysregulated angiogenesis is one of the key early pathogenic processes in PsA. Monocyte subpopulations are increasingly recognized contributors to angiogenesis. Circulating monocytes can differentiate into tissue resident macrophages, monocyte derived dendritic cells and osteoclasts, which orchestrate both pro-inflammatory and pro-angiogenic signalling. These processes may be governed by microRNA (miRNA), a class of evolutionary conserved short non-coding RNAs which function as post-transcriptional repressors of gene expression. On such miRNA is miR-125a-5p, which in cancer, has been previously associated with altered angiogenesis, invasion and migration.
**Objectives:** To examine the expression and angiogenic associations of miR-125a-5p in PsA.
**Methods:** Synovial tissue biopsies were obtained from patients with PsA and osteoarthritis (OA). In parallel, CD14+ monocytes and CD3+ T cells were isolated from peripheral blood mononuclear cells. MiR-125a-5p levels were analysed by real-time PCR. To examine possible factors involved in regulating miR-125a-5p expression in endothelial cells,microvascular endothelial cells (HMVEC) were cultured with candidate pro-inflammatory stimuli including; TLR ligands (PAM, PolyIC, LPS), pro-inflammatory cytokines (TNFa, IL-1b, IL-17) and growth factors (VEGF, Ang2). Matrigel tube formation assays were performed with pre- and anti- 125a treated HMVEC to elucidate angiogenic function. Immunoistochemical analysis of synovial vasculature was performed using factor VIII (DAKO).Cliical markers assertained at the time of arthroscopy, includding synovitis and vascularity were correlated with synovial miRNA expression.
**Results:** Expression of miR-125a-5p was significantly decreased in PsA synovial biopsies (n=8) compared to OA (n=4) ($p<0.05$). CD14+ peripheral blood monocytes showed a significant decrease in miR-125a-5p compared to whole PBMC ($p<0.05$). No difference was observed for CD3+ T cells. Anti-125a-5p treated HMVEC displayed increased tube formations. Angiogenic growth factor, Ang2, induced miR-125a-5p in HMVEC ($p<0.05$). Lower synovial expression of miR-125a-5p displayed a higher degree of factor VIII staining compared to patients with higher miR-125a-5p expression. This was further demonstrated in representative arthroscopic images.
**Conclusions:** Our data demonstrates decreased expression of miR-125a in the joint and peripheral CD14+ monocytes in PsA patients. MiR-125a expression was associated with joint vascularity, a hallmark of PsA, suggesting its important role in mediating key pro-angiogenic and thereby pro-inflammatory mechanisms in the synovium. Correcting these microRNA deficiencies, either by conventional pharmacological agents or as novel targets, may provide a therapeutic benefit, especially in early disease stages.
**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

# SpA and PsA clinical

## OP0084 VALIDATION OF THE ASAS HEALTH INDEX: RESULTS OF A MULTICENTER INTERNATIONAL STUDY IN 23 COUNTRIES

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**Background:** The ASAS Health Index (ASAS HI) was developed to measure functioning and health in patients with spondyloarthritis (SpA) aiming to better define the impact of disease in these patients. The 17 questions of the questionnaire (range 0–17, with a lower score indicating a better health status) have now been translated into 18 languages worldwide. Face validity and feasibility (time of completion) have already been assessed in a field test.[1]
**Objectives:** To test construct validity, discrimination across relevant health states, reliability and responsiveness of the original English version and the 16 translations of the ASAS HI in 23 countries
**Methods:** A convenient sample of SpA patients fullfilling the ASAS classification criteria for either axial (axSpA) or peripheral SpA (pSpA) were included into the study from 33 centers of 23 countries worldwide. Data were collected by the local rheumatologist. Construct validity against other health outcomes was evaluated by Spearman correlation. Discrimination across patient reported health states was decribed. Test-retest reliability was assessed by intraclass correlation coefficient (ICC) in patients without treatment changes (stable disease state, interval 4–7 days). In those patients who required a therapeutic change because of high disease activity, responsiveness was tested (standardized response mean (SRM)) after 2–24 weeks depending on the type of medication.
**Results:** 1548 patients were included: 64.9% male, mean (SD) age 42.0 (13.4) years, mean (SD) BASDAI 4.1 (2.5)). There were 1299 patients with axSpA (375 nr-axSpA and 924 AS patients) and 256 patients with pSpA. The total score of the ASAS HI was 6.7 ± 4.3 (mean ± SD). Floor or ceiling effects were limited (0.8 and 6.9%, respectively). Convergent validity ranged as hypthesized with Spearman correlations from low (age: 0.10) to good (BASDAI: 0.70). ASAS HI scores showed a high internal consistency with a Cronbachs-$\alpha$ of 0.93. The ASAS HI discriminated well between patients with different stages of disease activity and function irrespective of the tool applied (ASDAS, BASDAI and BASFI) (table). The groups with greater disease activity and more impaired functioning had higher mean ASAS HI scores (indicating impaired functioning) than those with lower disease activity. Reliability (tested in 578 patients) was good (ICC: 0.87 (95%CI 0.84 to 0.89), $p<0.01$) and comparable across all disease subtypes. Sensitivity to change (tested in 246 patients) showed a moderate SRM of -0.44 for NSAIDs (n=75 patients), 0.69 for DMARDs (n=41) and -0.85 for TNFi (n=127). The smallest detectable change in this cohort was 3.0.

Table 1. Discriminative ability of the ASAS HI stratified by disease activity

| | ASDAS status groups | | | |
|---|---|---|---|---|
| | Inactive (n=245) | Moderate (n=283) | High (n=500) | Very high (n=289) |
| ASAS HI | 2.9±3.1 | 5.1±3.5 | 7.3±3.6 | 10.4±3.5 |
| BASFI | 0.9±1.4 | 2.1±1.9 | 3.7±2.5 | 5.9±2.5 |
| BASDAI | 1.2±0.9 | 2.7±1.3 | 4.7±1.7 | 7.0±1.6 |

All values given as mean ± SD.

**Conclusions:** The ASAS HI is a valid, reliable and responsive measure of disease severity in people affetcte by SpA. It should be used in clinical trials to evaluate the impact of SpA and its treatment on overall functioning and health.
**References:**
[1] Ann Rheum Dis 2014; 73 (suppl II): 463
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## OP0085 DOES THE PRESENCE OF MULTIPLE SPA-FEATURES IN PATIENTS WITH CHRONIC BACK PAIN ALWAYS LEAD TO DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS?

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**Background:** The number of clinical SpA-features plays an important role in the Assessment of SpondyloArthritis international Society (ASAS) modified Berlin algorithm for the diagnostic work-up of patients (pts) with a suspicion of axial SpA (axSpA).
**Objectives:** To investigate whether all pts with short duration chronic back pain (CBP) and multiple SpA-features are always diagnosed as axSpA by the rheumatologist and to describe the features of these patients.
**Methods:** The SPondyloArthritis Caught Early (SPACE)-cohort includes CBP pts ($\geq$3 months, $\leq$2 years, onset $<$45 years) from various European rheumatology centres. Baseline data were used for the analyses. Following a fixed protocol all pts underwent a full diagnostic work-up consisting of performance of MRI and radiographs of sacroiliac joints (MRI-SI and X-SI), acute phase reactants, HLA-B27 testing, and assessment of other SpA-features (inflammatory back pain (IBP), good response to NSAIDs, family history for SpA, peripheral arthritis, dactylitis, enthesitis, uveitis, inflammatory bowel disease (IBD), and psoriasis). Local radiologists or rheumatologists from the different centres interpreted MRI-SI and X-SI on presence of sacroiliitis (yes/no) using global assessment as part of routine clinical practice. Total number of SpA-features was calculated excluding sacroiliac imaging and HLA-B27 status. The treating rheumatologist provided clinical diagnosis of pts and the ASAS-criteria for axSpA were used for classification.
**Results:** A total of 522 pts were analysed in this study: before sacroiliac imaging and HLA-B27 testing 164/522 (31.4%) pts had no or 1 SpA-feature, 148/522 (28.4%) pts had 2 SpA-features, 85/522 (16.3%) pts had 3 SpA-features, and 125/522 (23.9%) pts had $\geq$4 SpA-features respectively. IBP, good response to NSAIDs, and positive family history for SpA were most common in all subgroups

(0 or 1 feature: 26.8%, 8.5%, and 16.5% of pts; 2 features: 72.3%, 34.5%, 39.9%; 3 features: 87.1%, 60.0%, 54.1%; ≥4 features: 94.4%, 83.2%, 68.0% respectively). Of the pts with 2 and 3 SpA-features with negative X-SI 20/132 (15.2%) and 9/78 (11.5%) did not have axSpA diagnosis despite being HLA-B27+ (Figure 1). All pts with ≥4 SpA-features and X-SI+ (n=28) were diagnosed with axSpA. In contrast to what would be expected by following the modified Berlin algorithm for pts with ≥4 SpA-features, 18/94 pts (19.1%) with negative imaging (of which 4 HLA-B27+), were not diagnosed with axSpA by their rheumatologist. Multivariate regression analysis of presence of SpA-features identified MRI-SI+ (OR 41.7;95%CI 17.3.1–100.5), X-SI+ (OR 31.5;95%CI 3.1–321.0), HLA-B27+ (OR 4.7;95%CI 2.5–8.6), uveitis (OR 4.3;95%CI 1.5–12.7), IBP (OR 2.5;95%CI 1.4–4.7), heel enthesitis (OR 5.5;95%CI 2.7–11.4), IBD (OR 3.2;95%CI 1.2–8.8), elevated CRP/ESR (OR 2.7;95%CI 1.4–5.3), and psoriasis (OR 2.5;95%CI 1.0–6.0) as significant independent predictors of axSpA diagnosis.

**Figure 1.** Diagnosis and classification of patients with 2, 3 and 4 or more SpA-features (after medical history taking, physical examination and measurement of acute phase reactants), followed by sacroiliac imaging and HLA-B27 testing.

| Number of SpA-features | X-SI status | HLA-B27/MRI status | Rheumatologist SpA diagnosis YES | Rheumatologist SpA diagnosis NO | ASAS axSpA classification YES | ASAS axSpA classification NO |
|---|---|---|---|---|---|---|
| 2 n=148 | X-SI+ n=16 | B27+/MRI+ | 14 | | 14 | |
| | | B27+/MRI- | 1 | | 1 | |
| | | B27-/MRI+ | 1 | | 1 | |
| | | B27-/MRI- | | | | |
| | X-SI- n=132 | B27+/MRI+ | 15 | | 15 | |
| | | B27+/MRI- | 15 | 20 | 35 | |
| | | B27-/MRI+ | 5 | 2 | 7 | |
| | | B27-/MRI- | 11* | 59 | | 71 |
| 3 n=85 [1] | X-SI+ n=5 | B27+/MRI+ | 3 | | 3 | |
| | | B27+/MRI- | 1 | | 1 | |
| | | B27-/MRI+ | 1 | | 1 | |
| | | B27-/MRI- | | | | |
| | X-SI- n=78 | B27+/MRI+ | 17* | | 18 | |
| | | B27+/MRI- | 11* | 9 | 21 | |
| | | B27-/MRI+ | 8 | | 8 | |
| | | B27-/MRI- | 8 | 21 | | 29 |
| ≥ 4 [1] n=125 | X-SI+ n=29 | B27+/MRI+ | 15 | | 15 | |
| | | B27+/MRI- | | | | |
| | | B27-/MRI+ | 8 | | 8 | |
| | | B27-/MRI- | 5 | | 5 | |
| | X-SI- n=94 | B27+/MRI+ | 16 | | 16 | |
| | | B27+/MRI- | 21 | 4 | 25 | |
| | | B27-/MRI+ | 8 | | 8 | |
| | | B27-/MRI- | 28* | 14 | | 43 |

[1] 2 patients missing X-SI, not included in subanalyses. [2] 2 patients missing X-SI, not included in subanalyses. * 1 patient diagnosis not available

**Conclusions:** In this cohort of pts with CBP having numerous SpA-features did not automatically lead to a clinical axSpA diagnosis but positive imaging was the main driving factor to diagnosis of axSpA.
**Disclosure of Interest:** None declared
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## OP0086 WHICH CELLS CORRESPOND TO THE TYPICAL SIGNALS FOR FATTY AND INFLAMMATORY LESIONS SEEN IN MAGNETIC RESONANCE IMAGING IN ANKYLOSING SPONDYLITIS? A PROSPECTIVE STUDY USING BIOPSY MATERIAL OBTAINED DURING SPINAL SURGERY -

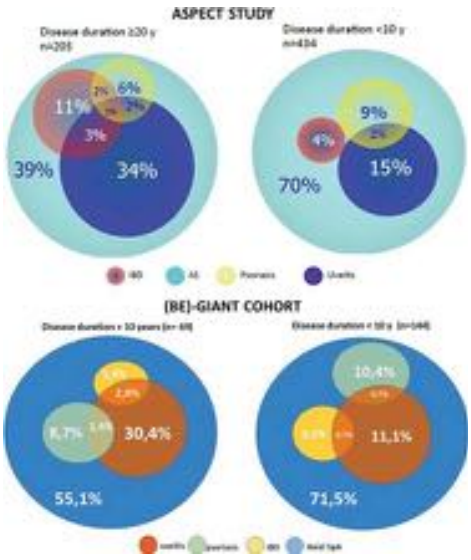
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**Background:** The occurrence of bone marrow edema (BME) and fat metaplasia detected by magnetic resonance imaging (MRI) were shown to be significantly associated with syndesmophyte formation in patients with ankylosing spondylitis (AS). The cell type responsible for the fat signal seen in MRI has not been defined to date.
**Objectives:** To histologically analyze the cells seen in fatty lesions (FL) as detected by MRI in spinal biopsies of AS patients and compare them with controls.
**Methods:** Spinal biopsies from vertebral edges of patients with AS and controls who underwent surgery for spinal deformity or spinal stenosis were prospectively collected. All patients had spinal STIR- and T1-weighted MRIs available exactly from the area of biopsy, and all biopsies were taken from areas that had a fat signal on MRI. The biopsies were analysed blinded to patients' diagnosis. Histomorphological analyses were performed to detect normal bone marrow, fat cells, inflammatory cells and fibroblasts. Histologic results were compared with MRI findings.
**Results:** Biopsies mostly obtained from the lower thoracic and the lumbar spine of 13 AS patients (mean age 56.3 years, mean disease duration 26 years) and 6 controls (mean age 53.4 years) were available. Similar proportions of AS patients, (12/16, 75%) and non-AS patients (4/6, 67%) had vital bone marrow. Fat cells were found in all 13 biopsies obtained from AS patients from the area of the fat signal vs. only 2 non-AS patients (33%), while inflammatory cells were found in 9 AS patients (56.3%), all of which also had BME on MRI, vs. 3 non-AS patients (50%). Fibroblasts were seen in 3 AS (18.9%) and 2 non-AS patients (33%).
**Conclusions:** The underlying cell types of FL and BME as detected by MRI in these long standing AS patients were fatty and inflammatory cells. The main difference between AS and non-AS patients was the proportion of biopsies containing fat cells. This suggests that fat cells are responsible for the MRI signal, at least in patients with longstanding ankylosing spondylitis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6005

## OP0087 THE ASSOCIATION OF EXTRA-ARTICULAR MANIFESTATIONS WITH DISEASE DURATION IN AXIAL SPA: RESULTS FROM THE (BE-) GIANT COHORT AND THE ASPECT STUDY

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**Background:** The prevalence of extra-articular manifestations (EAMs) in ankylosing spondylitis (AS) is well-known. However, as the diagnosis of axial spondyloarthritis (AxSpA) is now made much earlier in the disease the prevalence of the EAMs may be different. Moreover, the introduction of anti-TNF therapy may have altered the incidence of EAMs.
**Objectives:** to assess the association of EAMs with disease duration in AxSpA patients (n=215) in the post-anti-TNF era compared to a historic cohort of Belgian AS patients (n=847) from the pre-anti-TNF era.
**Methods:** The BelGian Inflammatory Arthritis and spoNdylitis cohorT (Be-Giant) and The Ghent Inflammatory Arthritis and spoNdylitis cohorT (GIANT) are post-anti-TNF observational cohorts that include consecutive patients since 2010, diagnosed with AxSpA by their treating rheumatologist. Patients who fulfill the ASAS classification criteria, are prospectively followed every 6 months. Follow-up consisted of patient-reported outcomes, a standardized clinical examination (peripheral joints, entheses, axial metrology), standard laboratory analysis and imaging. The ASPECT cohort is a Belgian pre-anti-TNF cross-sectional AS database containing information on 847 patients who fulfilled the New York modified criteria for AS between February 2004 and February 2005.
**Results:** In the (Be-)Giant cohort and ASPECT cohort respectively 47% and 67.9% of patients were male. Mean age was 34.5 (SD 9.6) in the (Be-)Giant cohort and 44.6 (SD 12.1) in the ASPECT cohort. Mean symptom duration was respectively 7.9 and 18.5 years. HLA-B27 was positive in respectively 76.5% and 83% of patients with HLAB27 determination. In a cross-sectional analysis of the baseline data of 215 AxSpA patients from the (Be-) GIANT cohorts, about 66.5% (143/215) of patients had not experienced any EAMs compared to only 58% (491/847) of AS patients in the ASPECT cohort. Additionally, 71.5% (112/144) of patients with a symptom duration of less than 10 years had not experienced any EAMs at baseline in the (Be-)GIANT cohort. However, in patients with more than 10 years of symptom duration, only about half of patients remained EAM- free (P=0.021). Similarly, in patients from the ASPECT cohort with a disease duration of less than 10 years, 70% of patients (304/434) had not experienced any EAM at baseline, whereas only 39% (79/203) of patients remained EAM- free after 20 years of disease. A subanalysis of 118 newly diagnosed non-radiographic AxSpA (nr -AxSpA) patients demonstrated a prevalence of 70.3% (83/118) of EAM-free patients at diagnosis.




**Conclusions:** The prevalence of extra-articular manifestations seems to increase with disease duration both in the pre-anti-TNF and the post-anti-TNF era, and may be linked to longer cumulative exposure to inflammation.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5827

## OP0088 INFLAMMATION ON MRI OF THE SPINE IS LONGITUDINALLY RELATED TO DISEASE ACTIVITY IN SMOKERS BUT NOT IN NON-SMOKERS IN AXIAL SPONDYLOARTHRITIS: 2-YEAR DATA FROM THE DESIR COHORT

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**Background:** In axSpA, the effect of disease activity on radiographic progression over time is more pronounced in males and smokers, but the reason for this is unclear. Recently, we have demonstrated a longitudinal relationship between MRI-inflammatory lesions and clinical disease activity measures (DA) in males, but not in females. However, whether or not there is also a disparity in this relationship based on the smoking status is unknown.
**Objectives:** To investigate the role of smoking status in the longitudinal relationship between inflammatory lesions on MRI of the spine and DA in patients with axSpA.
**Methods:** Two-year follow-up data from 164 patients fulfilling ASAS axSpA criteria in the DESIR cohort with ≥2 MRIs of the spine available during this period were analysed. Interactions were tested between smoking status and DA (ASDAS, BASDAI, patient's global disease activity, night pain, CRP and ESR) on the longitudinal relationship with MRI of the spine (Berlin score), analysed with a GEE model of i) absolute and ii) change scores. All models were adjusted for age, symptom duration and HLA-B27. Since there was a significant interaction with gender in previous analyses, analyses were repeated in males and females separately.
**Results:** Baseline characteristics of patients included were: 50% males, mean (SD) age: 33 (9) years, 39% smokers, 82% HLA-27+ and symptom duration: 18 (11) months. A significant interaction with smoking status was found for most of the DA, indicating that the relationship between MRI-inflammatory lesions and DA was different in smokers than in non-smokers. In the model of absolute scores (i), MRI-scores were statistically significantly related to most of the DA in smokers, while only CRP was significantly and weakly related in non-smokers (Table 1A). In the model of changes (ii), ASDAS and pain at night remained significantly related to MRI-inflammatory lesions, but no statistically significant relationship between MRI and DA was found in non-smokers (Table 1B). When stratifying for gender, the subgroups were small and the relationships were no longer statistically significant.

| | Smokers | | Non-smokers | |
|---|---|---|---|---|
| | Beta | 95% CI | Beta | 95% CI |
| **Table 1A** | | | | |
| ASDAS | **0.400** | **0.009 to 0.792** | 0.256 | –0.069 to 0.581 |
| BASDAI (0–10) | –0.002 | –0.162 to 0.157 | –0.064 | –0.131 to 0.002 |
| Night pain (0–10) | **0.191** | **0.050 to 0.332** | 0.0041 | –0.020 to 0.101 |
| Pt's gb disease (0–10) | 0.089 | –0.042 to 0.220 | 0.003 | –0.059 to 0.066 |
| ESR (mm/h) | 0.049 | –0.005 to 0.103 | 0.029 | –0.027 to 0.085 |
| CRP (mg/L) | **0.090** | **0.029 to 0.151** | **0.047** | **0.011 to 0.084** |
| **Table 1B** | | | | |
| ASDAS | **0.733** | **0.137 to 1.137** | 0.103 | –0.109 to 0.315 |
| BASDAI (0–10) | 0.214 | –0.047 to 0.529 | 0.018 | –0.058 to 0.094 |
| Night pain (0–10) | **0.298** | **0.101 to 0.495** | 0.042 | –0.005 to 0.089 |
| Pt's gb disease (0–10) | 0.187 | –0.030 to 0.403 | 0.055 | –0.002 to 0.111 |
| CRP (mg/L) | 0.020 | –0.001 to 0.041 | –0.003 | –0.032 to 0.025 |

**Conclusions:** In patients with axSpA, there is a longitudinal relationship between MRI inflammatory lesions of the spine and DA in smokers, but not in non-smokers. This disparity may explain the stronger effect of disease activity on radiographic progression observed in smokers.
Whether both gender and smoking have an effect on this relationship between MRI and DA remains to be elucidated.
**Acknowledgement:** Pfizer
**Disclosure of Interest:** None declared
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## OP0089 ARE INDIVIDUAL OR COUNTRY LEVEL SOCIO-ECONOMIC DETERMINANTS RELATED TO DISEASE ACTIVITY AND SELF-REPORTED PHYSICAL FUNCTION IN PATIENTS WITH SPONDYLOARTHRITIS? RESULTS FROM MULTI-NATIONAL CROSS-SECTIONAL STUDY ASAS-COMOSPA

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**Background:** In RA, previous studies observed inequalities in health across countries as well as across individual level socio-economic factors, and unequal uptake of biologic DMARDs (bDMARDs) played an important role in these inequalities. It is not known whether the same pattern is present for patients with spondyloarthritis (SpA).
**Objectives:** To assess: (1) independent associations of individual and country level socio-economic determinants with health outcomes in patients with SpA and (2) if confirmed, whether this relation is mediated by uptake of bDMARDs.
**Methods:** Data from the cross-sectional multinational COMOrbidities study in SpA (COMOSPA) were used. Contribution of individual socioeconomic factors (age, gender, education) and country of residence to ASDAS and BASFI was explored in regression models, adjusting for clinical confounders. Next, country of residence was replaced by gross domestic product adjusted for purchasing power parity (GDP PPP) (low, medium, and high, based on tertile distribution). Finally, the role of bDMARDs uptake in the relationship between education or GDP and ASDAS was explored by testing indirect effects.
**Results:** In total 3,984 patients with SpA from 22 countries were included: 65% males, mean age 44 (SD14), ASDAS 2.0 (±1.1) and BASFI 3.0 (±2.7). Five to 68% of patients were currently treated with bDMARDs. Females (vs. males) had higher ASDAS (β=0.21 [95%CI 0.13;0.28]) and BASFI (β=0.45 [95%CI 0.31;0.59]). The effect of age was negligible for both outcomes. Low vs high educated individuals had higher ASDAS and BASFI (β=0.29 [0.21;0.36] and β=0.46 [0.24;0.69], respectively) (Table). Independent of the individual confounders, large country differences were observed. Low GDP (vs. high GDP) was associated with higher ASDAS (β=0.27 [0.17;0.36]) and higher BASFI (β=0.20 [0.03;0.38] (Table). Current uptake of bDMARDs did not mediate relationship between education or GDP with ASDAS.

Table 1. Association between individual and country level (GDP) factors with ASDAS and BASFI

| | ASDAS-crp (β [95% CI]) | BASFI (β [95% CI]) |
|---|---|---|
| Age, years | –0.01 [–0.01; –0.00] | 0.02 [0.01; 0.02] |
| Gender (female vs male) | 0.21 [0.13; 0.28] | 0.45 [0.31; 0.59] |
| Education | | |
| Low education vs. University diploma | 0.29 [0.21; 0.36] | 0.46 [0.24; 0.69] |
| Secondary education vs. University diploma | 0.25 [0.14; 0.37] | 0.29 [0.15; 0.43] |
| Rheumatic diseases comorbidity index | | |
| (RDCI, 0–9) | 0.17 [0.14; 0.21] | 0.39 [0.32; 0.46] |
| Disease duration, years | Not included | 0.02 [0.01; 0.03] |
| Body Mass Index (BMI) | | |
| Underweight vs normal | 0.19 [–0.03; 0.41] | –0.13 [–0.53 ; 0.27] |
| Overweight vs normal | 0.08 [ –0.00; 0.16] | 0.21 [0.06; 0.36] |
| Obesity vs normal | 0.22 [0.11; 0.32] | 0.56 [0.38; 0.75] |
| Presence of axial SpA (yes vs no) | 0.18 [0.08; 0.28] | 0.58 [0.40; 0.76] |
| GDP | | |
| Middle vs High GDP | –0.09 [–0.18; 0.01] | –0.00 [–0.17; 0.16] |
| Low vs High GDP | 0.27 [0.17; 0.36] | 0.20 [0.03; 0.38] |

**Conclusions:** Health inequalities across individual and country level socio-economic factors exist also among SpA patients. Females, lower educated patients and patients from low income countries had higher disease activity and physical function.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1864

## OP0090 MRI LESIONS ORIGINATING FROM EITHER AXSPA OR DEGENERATION ARE RELATED TO SITE OF PAIN IN PATIENTS WITH CHRONIC BACK PAIN INCLUDED IN THE SPACE-COHORT

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**Background:** MRI-lesions in the spine (and SI-joints) are frequent in patients (pts) with axial spondyloarthritis (axSpA) and other pathologies like degenerative disease. It is relevant to know whether MRI-lesions (either axSpA or degenerative changes) are related with the site of back pain.
**Objectives:** To determine associations between MRI-lesions originating from either axSpA or degeneration and site of pain in pts with chronic back pain (CBP) of ≤2 years.
**Methods:** Pts with CBP (≥3 months, ≤2 years, onset <45 years) included in the SPACE cohort indicated site(s) of pain (thoracic, lumbar, buttock). Average MRI-scores from two readers for axSpA lesions and from two other readers for degenerative lesions were used. Readers were blinded for clinical data and scores of the other readers. AxSpA lesions considered inflammatory and fatty lesions, erosions and syndesmophytes/ankylosis on MRI-SI and MRI-spine. In addition, sclerosis was scored on MRI-SI. Each vertebral unit was scored for disc degeneration (Pfirrmann class >2), high intensity zone (HIZ), herniation, Schmorls' nodes and Modic changes (type I and type II). In addition, degenerative disc disease (DDD) was defined as degenerative complex with disc degeneration, an HIZ and herniation in an intervertebral disc.
Associations between MRI-SI lesions and buttock pain were investigated by logistic regression. Associations between axSpA or degenerative lesions and pain in the spine (thoracic and lumbar) were investigated by multilevel analysis with generalized estimating equations, taking the level of the spine into account. Interactions with gender, age, HLA-B27 and fulfilment of ASAS axSpA criteria were tested.

**Results:** In 348 pts (126 males, 127 fulfilling ASAS axSpA criteria, mean age 29.4 years) MRI-spine was available (in 342 pts also MRI-SI). Pain was present in thoracic (35.9%), lumbar (82.5%) spine and/or buttock (57.8%). The figure shows the significant associations between MRI-SI axSpA lesions and pain and between degenerative MRI-spine lesions and pain. AxSpA lesions on MRI-spine were not associated with pain at the same site (data not shown).

| AxSpA MRI-SI lesions (Logistic regression) | n | Stratification groups‡ | OR | 95% CI | P-value |
|---|---|---|---|---|---|
| Inflammatory lesions | 342 | No | 1.06 | 1.00 – 1.13 | 0.04* |
| Erosions | 178 | ≤29 years§ | 1.21 | 1.05 – 1.40 | 0.008* |
| | 164 | >29 years§ | 1.01 | 0.90 – 1.14 | 0.81 |
| **Degenerative lesions (Multilevel analysis)** | **n** | **Stratification groups‡** | **OR** | **95% CI** | **P-value** |
| Modic type 1 (BME) | 117 | <25 years§ | 0.92 | 0.09 – 9.05 | 0.94 |
| | 133 | 25-34 years§ | 1.31 | 0.39 – 4.39 | 0.66 |
| | 108 | ≥35 years§ | 5.19 | 1.90 – 14.19 | 0.001* |
| Degenerative disc disease | 117 | <25 years§ | 0.92 | 0.09 – 9.05 | 0.94 |
| | 123 | 25-34 years§ | 0.95 | 0.32 – 2.83 | 0.93 |
| | 108 | ≥35 years§ | 3.70 | 1.58 – 8.68 | 0.003* |
| High intensity zone | 132 | HLA-B27+ | 1.25 | 0.63 – 2.46 | 0.52 |
| | 216 | HLA-B27- | 2.88 | 1.58 – 5.23 | 0.001* |
| | 62 | ASAS+ & male | 0.65 | 0.18 – 2.38 | 0.51 |
| | 64 | ASAS- & male | 1.69 | 0.62 – 4.64 | 0.31 |
| | 65 | ASAS+ & female | 1.84 | 0.53 – 6.34 | 0.34 |
| | 157 | ASAS- & female | 5.09 | 1.99 – 13.04 | 0.001* |
| Herniation | 132 | HLA-B27+ | 1.45 | 0.83 – 2.26 | 0.10 |
| | 216 | HLA-B27- | 3.14 | 1.91 – 5.17 | 0.000* |
| | 127 | ASAS+ | 2.07 | 1.03 – 4.15 | 0.041* |
| | 221 | ASAS- | 4.66 | 2.24 – 8.97 | 0.000* |

‡Where a statistically and clinically relevant interaction was found, results are shown stratified for variable(s) indicated in this column. No stratification means no relevant interaction with age, sex, HLA-B27 status or fulfilment of ASAS axSpA criteria. *P-value <0.05. §Analyses were stratified according to age

**Conclusions:** Inflammatory axSpA lesions in the SI-joints were associated with buttock pain. Specific degenerative lesions -but not typical axSpA lesions- in the spine were associated with pain at the same location, especially in HLA-B27 negative pts without axSpA and pts ≥35 years.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2322

## OP0091 PSORIATIC ARTHRITIS COMORBIDITY INDEX: DEVELOPMENT AND VALIDATION OF A NEW SPECIFIC TOOL FOR CLASSIFYING PROGNOSTIC COMORBIDITY IN PSORIATIC ARTHRITIS PATIENTS

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**Background:** Specific comorbidity index can guide the management of psoriatic arthritis (PsA) patients and optimize their outcomes. So far, no disease-specific models are currently available for this purpose.
**Objectives:** 1. identify comorbidities with greatest impact on PsA patients' health status. 2. develop and validate a prospectively applicable comorbidity index for classifying PsA patients according to their comorbid conditions which might alter their risk of hospitalization and mortality.
**Methods:** This was a retrospective multicenter cohort analysis of PsA patients in a rheumatology clinical registry, assessing the effect of different comorbidities measured at patients' visits over 10-years period, on predicting future death and hospitalization. A weighted index that takes into account the number and seriousness of comorbid disease was developed in a cohort of 1707 PsA patients monitored over 10-years. Logistic and Cox Regression analyses were implemented to estimate the risk of mortality. Regression coefficients were used to develop the morbidity index score. ROC curve for the invented index was used to evaluate the discriminating ability of the index and identify different cutoff values that can delineate patients at different stages for risk of death. Disease activity parameters were considered.
**Results:** PsA patients who had higher incidence of comorbid condition and were at high risk of hospitalization were men, with older age at disease onset, high BMI at baseline ($p<0.05$). The most prevalent comorbidities strongly associated with the 10-year death risk or hospitalization in PsA patients were: Cardiovascular (7 comorbidities), osteoporosis, falls, depression/ anxiety, diabetes mellitus, renal and liver diseases, lung and GIT affection, as well as infection ($p<0.001$). Multivariate regression analysis identified Multidimensional Disease Relapse score (including 5 parameters: DAPSA, PASI, Functional disability score, ESR and CRP) as independent predictor for disease status associated with the 10-year death risk or hospitalization (Wald $\chi^2=9.2$, $p=0.002$, OR=24.6). Binary regression analysis revealed that: male gender, cardiovascular diseases, evident fall risk, diabetes, infection, anxiety, and the multidimensional relapse score were significant independent factors affecting the 10-years outcome of the disease. A comorbidity index weighted according to the regression coefficient of the variables extracted through the logistic regression analysis was developed. The score ranges from 0 to 38. A cut off point of 14.5 was associated with a sensitivity of 97.5% and a specificity of 87%. Validation using ROC curve revealed AUC of 98.5%.
**Conclusions:** The PsA-comorbidity index is a valid method for estimating risk of death in PsA patients. It enables the clinicians to include comorbidities assessment and management in their standard practice. It can be used to predict resource utilization, identify targets for reducing high costs, by prospectively identifying PsA patients at high risk. Rigorous application of systematic evaluation of comorbidities may permit earlier detection, which may ultimately result in an improved outcome of patients with PsA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4598

**THURSDAY, 9 JUNE 2016**

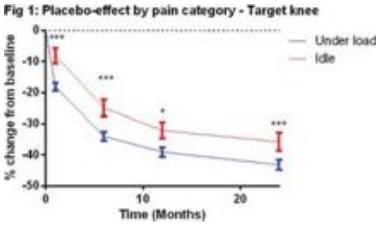
# New horizons in osteoarthiritis

## OP0092 IDENTIFICATION OF PAIN SUBTYPES ASSOCIATED WITH PLACEBO-RESPONSE: DATA FROM TWO PHASE 3 RANDOMIZED CLINICAL TRIALS IN SYMPTOMATIC KNEE OSTEOARTHRITIS

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**Background:** Pain is the principal clinical symptom of osteoarthritis (OA), and development of safe and effective analgesics for OA pain is needed. Trials of new analgesics for OA pain is impaired by substantial placebo-response (PR), and data describing characteristics and pain sub-types particularly associated with placebo-response is needed.
**Objectives:** The purpose of this post-hoc analysis was to investigate clinical characteristics and pain subtypes associated with PR as measured by the five pain questions of the Western Ontario and McMasters Arthritis (WOMAC) Index of the target (T)- and the non-target (NT) knees in the pooled data of two phase III randomized clinical trials of an oral treatment in OA.
**Methods:** Pooled data from the placebo-groups of two phase III randomized clinical trials (NCT00486434 and NCT00704847) in patients with knee OA followed for two years were analyzed. Main inclusion criteria for T knees were a Kellgren-Lawrence grade of 2 or 3, Joint-Space Width (JSW) of minimum of 2.0 mm at the medial tibio-femoral joint, and WOMAC pain ≥150 out of 500 mm. All analyses were performed on data from the T knees (N=771) and a sub-group of NT knees matching the pain inclusion criteria of the T knees (N=256). All subjects in the analysis belonged to the Per-Protocol population.
Pain of the T and NT knees was measured using the WOMAC pain sub-index, five questions: Q1; during walking on a flat surface, Q2; using stairs, Q3 at night while in bed, Q4; sitting or lying and Q5; while standing. Changes in percent from baseline pain were calculated at months 1, 6, 12 and 24, and differences between individual questions were assessed using a repeated measures ANOVA. Pain by category ("under load"; WOMAC questions 1, 2 and 5 and "idle"; WOMAC questions 3 and 4) were similarly analyzed for change over time, and compared in a repeated measures ANOVA. Selected patient baseline characteristics; pain by WOMAC question, Joint-space width (JSW), age, and BMI were assessed for association with PR defined as change in percent from baseline to year two using Spearman's correlation.
**Results:** Baseline pain was significantly higher in WOMAC Q2, compared to other pain questions ($p<0.001$). This was observed for both T- and NT knees. WOMAC Q2 was furthermore associated with the highest PR for both T, and NT knees (36.8% ±52.4 (SD) and 28.0% ±44.4, respectively) at year two. The observed PR was higher in the T knee, compared to the NT knee at all corresponding time-points.
The level of PR was significantly higher in questions related to pain while under load (Q1, Q2, Q5) compared to pain while idle (Q3, Q4), and this was statistically significant in the T knee ($p<0.005$) at month 1 and onwards (Fig. 1), but did not reach statistical significance for the NT knee.
Baseline BMI, age and JSW was not associated with PR. This indicates while no common clinical characteristics were associated with PR, other, perhaps psychological, factors may affect the susceptibility to PR.

**Fig 1: Placebo-effect by pain category - Target knee**




**Conclusions:** These results indicate that the level of PR is significantly different between pain subtypes, as pain under load is significantly more susceptible to lead to PR than pain while idle.
**Disclosure of Interest:** A. Bihlet Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, I. Byrjalsen Employee of: Nordic Bioscience, A.-C. Bay-

Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, C. Christiansen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, J. Andersen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, H. Gühring: None declared, C. Ladel: None declared, M. Michaelis: None declared, B. Riis Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, I. Valter: None declared
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## OP0093 DOES "PAIN ELSEWHERE" INFLUENCE THE ASSOCIATION BETWEEN KNEE STRUCTURAL PATHOLOGY AND KNEE PAIN?

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**Background:** The association between structural abnormalities and knee pain remains controversial. It may be that the association is weaker in those with generalized pain compared to localized pain.
**Objectives:** To determine the effect of pain at other sites on the association between knee structural pathology and knee pain in knee osteoarthritis (OA).
**Methods:** 1099 participants (average age 63 years; range 51 to 81 years) from the population-based Tasmanian Older Adult Cohort study were studied. Presence of pain (yes/no) at the neck, back, hands, shoulders, hips, knees and feet was assessed by questionnaire. T1-weighted or T2-weighted fat saturated MRI of the right knee was performed to measure cartilage defects, bone marrow lesions (BMLs) and effusion. Osteophytes and joint space narrowing (JSN) were assessed by X-ray. Data were analyzed using multi-nominal logistic regression with adjustment for potential confounders including age, sex, body mass index, physical activity, smoking history and pain medication.
**Results:** Knee pain only, knee plus any other site pain, and any other site pain were present in 3%, 44% and 41% of participants respectively. In multivariable analyses, knee pain only was strongly associated with the presence of cartilage defects (OR 16.96, 95% CI 4.03 to 71.32), BMLs (OR 3.27, 95% CI 1.01 to 10.53), effusion (OR 3.52, 95% CI 1.06 to 11.68) and osteophytes (OR 8.22, 95% CI 2.10 to 32.27). There were significant but weaker associations with knee pain plus any other site pain (OR=3.03 to 3.38, all $P<0.05$). Any other site pain was not found to be associated with any knee structural abnormalities. There was a dose-response relationship between number of knee structural abnormalities, and knee pain only and knee plus any other site pain (both P for trend$\leq$0.002).
**Conclusions:** Knee structural abnormalities are more strongly associated with localized knee pain than generalized pain, suggesting that pain elsewhere may influence the association of knee structural pathology and knee pain. The underlying mechanism may be due to central sensitization implicated in generalized pain which is no longer coupled to peripheral stimuli. Implication of this finding for clinicians and researchers is that pain at other sites needs to be considered while developing an approach to slow OA progression and alleviate symptom by targeting structural abnormalities.
**Disclosure of Interest:** None declared
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## OP0094 PHYSICIAN AND PATIENT ESTIMATES OF GLOBAL STATUS ARE MORE LIKELY TO BE DISCORDANT IN OSTEOARTHRITIS THAN IN RHEUMATOID ARTHRITIS

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**Background:** Concordance between global estimates of clinical status by physicians and patients may influence shared decisions concerning therapy toward better compliance and outcomes. However, discordance has been described in most rheumatology settings in which it has been studied carefully[1,2]. While osteoarthritis (OA) generally is regarded as a less severe medical problem than rheumatoid arthritis (RA), recent evidence suggests similar disease burdens in both OA and RA.
**Objectives:** To analyze discordance between physician global estimates (DOCGL) and patient global estimates (PATGL) in OA vs RA patients seen in a routine rheumatology academic setting.
**Methods:** In this setting, all patients complete a multidimensional health assessment questionnaire/routine assessment of patient index data (MDHAQ/RAPID3), which includes 0–10 scores for physical function, pain, and PATGL compiled into a 0–30 RAPID3, as well as fatigue VAS, a symptom checklist, and a RADAI self-report joint count, and demographic data. Patients with primary diagnoses of OA or RA were classified into 3 categories: PATGL$\geq$DOCGL by 2/10 units, PATGL=DOCGL, and DOCGL$\geq$PATGL by 2 units. The percentage of patients in each group was compared between RA and OA using chi-square. Variables were compared using ANOVA.
**Results:** The study included 216 patients with RA, 39 (18%) were discordant with PATGL>DOCGL and 243 patients with OA, 82 (34%) were similarly discordant. Concordance with PATGL=DOCGL was seen in 144 patients (67%) with RA and 136 patients (56%) with OA, while discordance with DOCGL>PATGL was seen in 33 patients (15%) of patients with RA and 25 (10%) with OA ($p<0.001$). Age did not differ in the groups, other than older patients with OA (72.6 yrs) curiously were among the fewer OA patients who were more likely to show DOCGL>PATGL than younger patients with OA (64.6–64.8 yrs). Patients with PATGL>DOCGL had lower formal education levels ($p<0.05$ in RA but not OA). Other MDHAQ measures were higher in OA patients than in RA patients with (Table). Highest MDHAQ scores were seen in patients with PATGL>DOCGL than in PATGL=DOCGL than in DOCGL>PATGL ($p<0.001$ other than symptoms and RADAI).

Table 1. Comparison of 3 groups of patients with RA and OA according to PATGL and DOCGL

| | PATGL>DOCGL | PATGL=DOCGL | DOCGL>PATGL | P values |
|---|---|---|---|---|
| Rheumatoid arthritis | 39 (18%) | 144 (67%) | 33 (15.1%) | |
| Age | 57.6 | 56.4 | 55 | 0.79 |
| Education | 12.7 | 14.3 | 15.3 | 0.03 |
| RAPID2 (0–20) | 10.8 | 6.8 | 3.8 | <0.001 |
| Pain (0–10) | 7.3 | 4.3 | 2.7 | <0.001 |
| Function (0–10) | 3.6 | 2.5 | 1.3 | <0.001 |
| Fatigue (0–10) | 5.8 | 3.8 | 1.9 | <0.001 |
| Symptom checklist (0–60) | 9.6 | 7.4 | 6.0 | 0.08 |
| Self-report RADAI joint count (48) | 18.3 | 9.4 | 4.5 | <0.001 |
| Osteoarthritis | 82 (34%) | 136 (56%) | 25 (10%) | |
| Age | 64.6 | 64.8 | 72.6 | 0.02 |
| Education | 13.0 | 14.3 | 13.6 | 0.06 |
| RAPID2 (0–20) | 11.2 | 8.3 | 7.0 | <0.001 |
| Pain | 7.8 | 5.7 | 4.9 | <0.001 |
| Function | 3.4 | 2.6 | 2.0 | <0.001 |
| Fatigue | 6.3 | 4.4 | 3.0 | <0.001 |
| Symptom checklist (0–60) | 12.3 | 9.7 | 6.9 | 0.005 |
| Self-report RADAI joint count (48) | 16.5 | 11.1 | 7.8 | 0.008 |

**Conclusions:** Patients with OA are more likely to have their clinical status underestimated by rheumatologists than patients with RA, although the burden of disease in OA in these patients was greater than in RA. These data suggest a need to revise generally held views that OA is less severe than RA.
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[1] Arthritis Care Res (Hoboken) 2014;66:934–42.
[2] Arthritis Care Res (Hoboken) 2012;64:206–14.
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## OP0095 RANDOMIZED, PLACEBO-CONTROLLED TRIAL TO EVALUATE CLINICAL EFFICACY AND STRUCTURE MODIFYING PROPERTIES OF SUBCUTANEOUS ETANERCEPT (ETN) IN PATIENTS WITH EROSIVE INFLAMMATORY HAND OSTEOARTHRITIS (OA)

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**Background:** Erosive OA involves interphalangeal joints (IPJs), resulting in a high disease burden, for which treatment options are limited. Although it is characterized by joint inflammation, earlier treatment with TNF blockers was equivocal.
**Objectives:** To investigate the 1-year efficacy of ETN in erosive OA.
**Methods:** In a European multicentre study (NTR 1192) patients were equally randomized to subcutaneous ETN (24 weeks 50 mg weekly, thereafter 25 mg weekly) or placebo. Patients with erosive ($\geq$1 IPJ with radiographic pre(erosive) anatomical phase ("J"/"E") according to Verbruggen-Veys system) inflammatory ($\geq$1 IPJ with soft swelling/erythema and with positive power Doppler at US) symptomatic (VAS pain >30/100 on NSAID use, flare after NSAID washout) OA were included. VAS pain, hand function (FIHOA), quality of life (SF-36), no. of tender joints and grip strength were assessed after 4, 8, 12, 24, 36 weeks and 1 year. Radiographic progression of IPJs was scored blindly in paired order (baseline, 24 weeks and 1 year) following the quantitative Ghent University Scoring System (GUSS, 0–300 per IPJ).
With linear mixed models VAS pain was compared between treatment groups at 24 weeks (primary outcome), and 1 year in intention-to-treat (ITT) analyses. With general estimated equations secondary outcomes were analysed. Adjustments were made for centre, baseline values and patient effects were appropriate. Completers fulfilling the extensive inclusion criteria were included in per-protocol (PP) analyses.
**Results:** Of 284 screened patients, 90 (mean age 60 years, 81% women, 96% fulfilled ACR hand OA criteria) were randomized; 22 discontinued the study prematurely. At baseline patient characteristics did not differ between the groups. VAS pain in all patients decreased -24.8 mm (95%CI -29.2;-20.5 ($P<0.001$)) at 24 weeks. In ITT differences in pain between the groups were in favour of ETN, but did not reach statistical significance. However, in PP the difference reached statistical significance (table). No differences were seen on secondary clinical outcomes. The PP analysis of GUSS showed a mean difference in favour of

ETN (table), indicating more remodelling in the ETN group. Additional analyses showed an interaction between soft swelling/erythema and ETN treatment on GUSS, resulting in a statistical significant ($P<0.05$) mean difference between ETN and placebo groups. More patients dropped out on placebo than on ETN (6 vs. 3) due to inefficacy, whereas more on ETN than on placebo (6 vs. 1) due to adverse effects.

Table. Joint pain and GUSS score at baseline by study drug, and mean differences between study groups for both intention-to-treat (ITT) and per-protocol (PP) analyses.

| | ETN | Placebo | Mean difference ETN-Placebo (95%CI) | | | |
|---|---|---|---|---|---|---|
| | Baseline | Baseline | 24 weeks | P | 1 year | P |
| ITT | N=45 | N=45 | N=90 | | N=90 | |
| Pain (mm) | 71.1 (15.7) | 68.4 (12.8) | -5.7 (-15.9; 4.5) | 0.27 | -8.5 (-18.6; 1.6) | 0.10 |
| PP | N=28 | N=33 | - | | N=61 | |
| Pain (mm) | 68.9 (13.3) | 65.9 (12.3) | - | | -11.8 (-23.0; -0.5) | 0.04 |
| PP | N=23 | N=31 | - | | N=54 | |
| GUSS score/ joint | 286 (37) | 288 (34) | - | | 3.1 (0.8; 5.4) | <0.05 |

Data represent mean (standard deviation) ; CI= confidence interval

**Conclusions:** In erosive OA ETN was not superior over placebo on VAS pain at 24 weeks. However in the symptomatic and inflammatory patients completing the study ETN was superior over placebo both on pain and structural damage assessed by GUSS; ETN was especially effective in joints with signs of inflammation.

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**Disclosure of Interest:** None declared

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## OP0096 MENISCAL EXTRUSION AND BONE MARROW LESIONS ARE INDEPENDENTLY ASSOCIATED WITH INCIDENT AND PROGRESSIVE KNEE OSTEOARTHRITIS

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**Background:** Whether meniscal extrusion and bone marrow lesions (BMLs) independently predict the risk of knee osteoarthritis (OA) remains to be clarified. Yet, while prospective cohort studies have shown that both meniscal extrusion and BMLs increase the risk of progressive knee OA, these studies have focused on the medial rather than the lateral knee joint, and examined people with established knee OA. It remains unclear whether these structural abnormalities predate incident knee OA, or whether meniscal extrusion or BMLs independently predict progressive disease.

**Objectives:** The aim of this 72 month longitudinal study was to examine whether compartmental baseline meniscal extrusion and BMLs were independently associated with incident and progressive knee OA, as measured by i) cartilage volume loss, ii) incident or progressive radiographic OA (ROA), and iii) total knee replacement (TKR).

**Methods:** Data was extracted from the Osteoarthritis Initiative (OAI) cohort. Participants were grouped according to the absence (Kellgren-Lawrence (KL) grade $\leq$1, n=2120) or presence (KL $\geq$2, n=2249) of ROA. Baseline meniscal extrusion, BMLs and cartilage volume were assessed on magnetic resonance imaging (MRI). Cartilage volume of the tibial plateau was assessed at baseline and 72 months, while ROA was assessed at baseline and 48 months. TKR was assessed at 72 months.

**Results:** In those with ROA, the presence of a baseline meniscal extrusion (independent of BMLs) was associated with accelerated cartilage loss (medial tibia: -2.1%/annum vs. -1.5%; lateral tibia: -2.6%/annum vs. -1.6%; both $p<0.001$), progressive ROA and TKR (OR range 1.4 to 1.8; 95% CI range 1.1 to 2.9, $p\leq0.04$). The presence of a baseline BML (independent of meniscal extrusion) was associated with accelerated cartilage loss (medial tibia: -2.1%/annum vs -1.6%; lateral tibia: -1.9%/annum vs -1.6%; $p\leq0.02$), progressive ROA and TKR (OR range 1.5 to 2.4; 95% CI range 1.1 to 3.4, $p\leq0.02$). In those with no ROA, a baseline medial meniscal extrusion was associated with accelerated cartilage loss (medial tibia: -2.1%/annum vs. -1.2%, $p<0.001$) and a baseline medial BML with incident ROA (OR 1.7, 95% CI 1.1 to 2.9, p=0.03).

**Conclusions:** Baseline meniscal extrusion and BMLs predict incident and progressive knee OA and represent important and independent structural targets for patient selection in disease-modifying OA drug (DMOAD) trials.

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## OP0097 IMMUNOSCINTIGRAPHIC DETECTION OF TNF BY RADIOLABELED CERTOLIZUMAB PEGOL IN PATIENTS WITH EROSIVE HAND OSTEOARTHRITIS IN RELATION TO DISEASE ACTIVITY AND STRUCTURAL PROGRESSION: A PROOF OF CONCEPT STUDY

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**Background:** A recent randomized clinical trial in erosive osteoarthritis (EOA) of finger joints with a TNF blocking agent, adalimumab, showed inhibition of radiographic progression in joints showing inflammatory signs (palpable swelling) at baseline (1). We anticipate the use of radio-labelled antibodies can help in identifying their *in vivo* abundance in joints (2) and might help to identify joints at particular risk for progression amenable for target therapies.

**Objectives:** To investigate the uptake of radiolabeled $^{99m}$Tc-certolizumab pegol in patients with EOA and study associations with other markers of active disease, including radiography, clinical examination and ultrasound (US).

**Methods:** Certolizumab Pegol was conjugated with S-HYNIC and radiolabeled with Tc99m. At baseline, static images of both hands of 5 patients with EOA (F/M: 4/1; median disease duration 8.4 years; median age 55.6 years) were acquired at 2 time points (immediately following administration (early phase) and after 4–6 hours post injection (late phase)). All 18 IP finger joints were scored according to the anatomical phase scoring system (3) on Xrays. All patients underwent clinical examination (presence of tenderness and palpable swelling of the joints) and Gray-scale and Power Doppler (PD) US one day prior to scintigraphy. Immunoscintigraphic findings were independently scored in a semi-quantitative way (uptake: 0 = absent, 1 = weak; 2 = strong). Descriptive statistics on joint level were calculated. Likelihood ratio (LR) for uptake in late phase was calculated in respect to tenderness, swelling, US and radiographic features (resp. with no tenderness, no swelling, no inflammatory US sign and normal phase as reference).

**Results:** In total, 90 IP joints were studied. Active tracer uptake was seen in 7 joints in early phase (7.8%) (all weak) and in at least 24 joints in late phase (26.7%) (19 weak, 5 strong). No uptake was seen in MCP joints.

Early and late uptake were present in 5 (15.2%) and 12 (36.4%) of 33 tender joints and in resp. 2 (3.5%) and 12 (21.1%) of 57 non-tender joints (LR =2.2, p = NS).

Interestingly, this relation was most pronounced with palpable joint swelling: early and late uptake were present in 5 (21.7%) and 14 (61.0%) of 23 swollen joints and in resp. 2 (3.0%) and 10 (14.9%) of 67 non-swollen joints (LR =8.9, $p<0.001$). Early and late uptake were present in resp. 6 (9.7%) and 18 (29.1%) of 62 sonographic active joints (= any presence of effusion or PD signal or synovial proliferation) and in resp. 1 (3.6%) and 6 (21.4%) non-inflammatory joints (LR =1.5, p = NS).

Immunoscintigraphic uptake was observed in all anatomical phases (i.e. N, S, J, E or R) but the strongest association was found with R phase (LR =1.86 with "N" as reference).

**Conclusions:** This is the first *in vivo* demonstration of TNF abundance in EOA. We found strong associations of certolizumab uptake with presence of swelling of the affected joints. The strongest association with TNF was found in the remodeling phases of the disease. These data further solidify the rationale for cytokine directed therapies in EOA.

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## OP0098 EFFECT OF ETANERCEPT ON SYNOVITIS AND BONE MARROW LESIONS IN EROSIVE HAND OSTEOARTHRITIS

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**Background:** Erosive osteoarthritis (OA), a subset of hand OA with high disease burden, is hypothesized to develop in distinct anatomical phases. These can radiographically be identified as loss of joint space (pre-erosive phase), followed by erosions and remodelling (E- and R-phase, according to the Verbruggen-Veys (VV) system). It is unknown which disease processes play a role in this development, although synovitis and bone marrow lesions (BMLs) on MRI

have shown to be associated with radiographic progression in OA finger joints. Therefore synovitis and BMLs could be a target for therapy.
**Objectives:** To investigate the presence of synovitis and BMLs in erosive compared to non-erosive joints, and to study the effect of TNF inhibition on these MRI abnormalities.
**Methods:** Analyses were performed in a subset of patients participating in a double-blind trial (NTR 1192), comparing etanercept (ETN, 25–50mg/week) to placebo. Patients with symptomatic erosive OA with clinical and ultrasonographic signs of inflammation in ≥1 interphalangeal joint (IPJ) were included. This analysis concerned 20 patients who underwent contrast-enhanced MRI of the 8 distal and proximal IPJs of one hand at baseline and 1 year. Images were scored for synovitis and BMLs (0–3 per joint, total score 0–24), blinded for patient characteristics, according to the OMERACT hand OA MRI score (HOAMRIS). Radiographs of the same hand were scored according to the VV system. Logistic regression with generalised estimating equations (GEE) were used to associate the presence of an MRI feature in a joint with being in an erosive (E/R) versus non-erosive anatomical phase (N=normal/S=stationary) (adjusted for age and sex, excluding IPJs from the ETN group at 1 year). A treatment effect of ETN on the change in MRI features over 1 year on joint level was also estimated with GEE.
**Results:** The total synovitis score was similar at baseline and 1 year in both the placebo (median (range): 10.5 (7–16) and 10.3 (6–14) respectively) and ETN group (7.0 (3–17) and 6.9 (3–14)). For BMLs, the total score was 5.4 (2–9) and 7.0 (0–9) in the placebo, versus 4.5 (3–9) and 3.7 (0–8) in the ETN group. The presence of BMLs was associated with being in E-phase (OR 12.5, 95% CI 2.1–74.7) and R-phase (OR 3.9, 1.2–12.0). Synovitis was not associated with these anatomical phases. Synovitis did not change in either group, whereas BMLs decreased more in the ETN compared to the placebo group (table). The same effect was observed in analyses on patient level (total score and number of IPJs with a feature, data not shown). Besides, an interaction was observed between ETN treatment and the presence of grade 2/3 synovitis at baseline in that IPJ (table).

| | Association with change in BML (beta (95% CI))† | p-value |
|---|---|---|
| Baseline synovitis grade 2/3 present | 0.01 (-0.23 to 0.25) | 0.95 |
| Treatment with etanercept | -0.22 (-0.35 to -0.09) | 0.001 |
| Baseline synovitis grade 2/3*treatment | -0.59 (-0.97 to -0.20) | 0.003 |

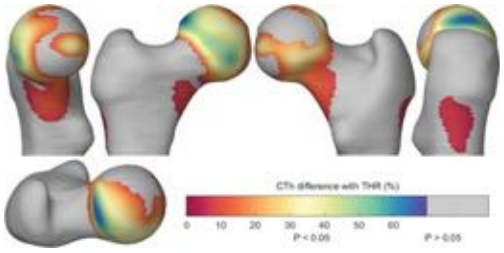
†Change between baseline and 1 year, negative score indicates a decrease over time (improvement), range 0-3. BML, bone marrow lesion; CI, confidence interval.

**Conclusions:** The presence of BMLs, but not synovitis, was associated with the presence of an erosive anatomical phase in a joint. Treatment with ETN appeared effective in inhibiting these lesions, suggesting a role for TNF in the pathophysiology of erosive OA, possibly through an effect on subchondral bone. The inhibitory effect of ETN on BMLs was more pronounced in IPJs with severe synovitis at baseline, suggesting that inflamed synovial tissue could be a source of TNF production in erosive OA.
**Disclosure of Interest:** None declared
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## OP0099 3D CORTICAL BONE MAPPING OF THE PROXIMAL FEMUR IN A LARGE PROSPECTIVE POPULATION-BASED STUDY SUPPORTS THE GANZ HYPOTHESIS OF HIP OSTEOARTHRITIS CAUSATION: THE AGES-REYKJAVIK STUDY

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**Background:** The mechanical aetiology hypothesis of hip osteoarthritis (OA) implicates focal mechanical wear of the joint surface from increased contact pressures, often associated with subtle abnormalities in 3D structure, such as those identified in femoro-acetabular impingement. Related to this, thickening of subchondral bone is emerging as an important disease feature in OA and may also be implicated in pathogenesis. Cortical bone mapping (CBM) is a proven technique that has been used to accurately measure structural properties of bone [1].
**Objectives:** CBM technique was applied to hip clinical computed tomography (CT) scans in a large prospective study of healthy older individuals to identify locations where cortical and subchondral bone in people who were destined for eventual total hip replacement (THR) to treat OA differed, on average, from healthy controls. We hypothesise that areas of thickening will coincide with lifelong habitual contact pressures, such as during walking.
**Methods:** We undertook a prospective nested case-control study within a cohort of 3133 subjects with an average 5-year follow-up from the Age, Gene/Environment Susceptibility-Reykjavik Study (AGES-REYKJAVIK). Using a previously published method [1], CBM was applied to clinical CT scans (slice thickness 1mm) to identify the regions where cortical thickness (CTh) in the proximal femur was significantly associated to eventual THR. After quality control 25 of the samples were rejected leaving 90 THR that were performed on 75 participants (49 female, 26 male, mean±sd age 74±4.7 yrs) at a mean±sd of 35.6±24.6 months after baseline CT scan, matched to 185 controls (117 female, 68 male, mean±sd age of 74±4.7 matched for calendar year of recruitment, sex and age). CTh measurements were spatially aligned onto an average femur surface and statistical parametric mapping used to analyse the results presented as percentage difference between cases and controls. The model allowed for size, the first five non-rigid shape modes, group (case*control), age, sex, weight and height.
**Results:** We found highly focal regions of up to 70% greater CTh in the proximal femur, especially at the femoral head, among men and women who had a subsequent THR when compared to controls. Cortical and subchondral bone plate thickening in OA coincides with simulated peak contact pressure areas of the human hip [2], but is absent in less loaded regions of the hip.




**Conclusions:** CBM and SPM show a pattern of femoral cortical bone and subchondral bone plate thickening in a large population destined for THR compared with controls in a novel 3D analysis that does not rely on subjective assessment of CT images. Such thickening patterns support the mechanical aetiology (Ganz) hypothesis of hip OA causation.
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**THURSDAY, 9 JUNE 2016**

# Clinical osteoporosis: new insights

## OP0100 SUPERIOR GAINS IN BONE MINERAL DENSITY AND ESTIMATED STRENGTH AT THE HIP FOR ROMOSOZUMAB COMPARED WITH TERIPARATIDE IN WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS TRANSITIONING FROM BISPHOSPHONATE THERAPY: RESULTS OF THE PHASE 3 OPEN-LABEL STRUCTURE STUDY

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**Background:** In a phase 2 study, treatment with romosozumab significantly increased bone mass in women with low bone mineral density (BMD).
**Objectives:** To report the results of STRUCTURE, a phase 3 study evaluating the effect of romosozumab or teriparatide (TPTD) in women with postmenopausal osteoporosis (PMO) transitioning from bisphosphonate (BP) therapy (NCT01796301).
**Methods:** This open-label study enrolled women with PMO who had taken an oral BP for ≥3 years prior to screening and alendronate (70 mg QW or equivalent) in the year prior to screening; had a BMD T-score ≤–2.5 at the total hip (TH), lumbar spine (LS), or femoral neck (FN); and had a history of nonvertebral fracture after age 50 or vertebral fracture. Women were randomized to receive SC romosozumab 210 mg QM or TPTD 20 μg QD for 12 months. The primary endpoint was percent change from baseline in BMD by DXA at the TH through month 12. Secondary endpoints included percent change from baseline at months

6 and 12 in BMD by DXA at the TH, LS, and FN; hip integral and cortical BMD by quantitative computed tomography (QCT); and estimated hip strength by finite element analysis.
**Results:** The 436 women enrolled in the study had a mean age of 72 years and mean TH, LS, and FN T-scores of –2.2, –2.9, and –2.5, respectively. Through 12 months, the mean (95% CI) percent change from baseline in TH BMD by DXA was 2.6% (2.2, 3.0) with romosozumab and –0.6% (–1.0, –0.2) with TPTD ($p<0.0001$ between groups). TH BMD changes at months 6 and 12 were significantly larger with romosozumab than with TPTD ($p<0.0001$): month 6, 2.3% (1.9, 2.7) vs –0.8% (–1.2, –0.4); month 12, 2.9% (2.5, 3.4) vs –0.5% (–0.9, 0), respectively. Romosozumab also resulted in significantly larger BMD gains at the LS at months 6 and 12 vs TPTD ($p<0.0001$): month 6, 7.2% (6.6, 7.8) vs 3.5% (2.9, 4.0); month 12, 9.8% (9.0, 10.5) vs 5.4% (4.7, 6.1), respectively. QCT assessments of the hip demonstrated significantly greater gains in integral and cortical BMD with romosozumab vs TPTD at months 6 and 12 ($p<0.0001$). Estimated hip strength gains were also significantly larger with romosozumab at both time points ($p<0.0001$) and declined from baseline in TPTD-treated subjects at month 6. The subject incidences of adverse events were generally balanced between treatment groups.
**Conclusions:** In subjects transitioning from BP therapy, romosozumab was well-tolerated and associated with greater BMD gains and improved estimated hip strength compared with TPTD.
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## OP0101 BISPHOSPHONATES DURING PREGNANCY: A PROSPECTIVE STUDY

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**Background:** Bisphosphonates (BPs) are sometimes prescribed to young women in childbearing age for bone disorders or corticosteroid induced osteoporosis. However their effects on pregnancy outcome have been poorly studied.
**Objectives:** The aim of our study was to determine pregnancy and newborn outcomes in women exposed to BPs during pregnancy.
**Methods:** Cases and controls were collected from the CRAT database (French Reference Centre of Teratogenic Agents),an ongoing prospective follow-up of drug-exposed pregnant women. Cases were all patients that received BPs within the 6 weeks before or during pregnancy between 1987 and 2014. Since pregnancy outcomes may be affected by the underlying maternal disease two sub-groups were defined: pregnant women with inflammatory diseases treated mainly for steroids-induced osteoporosis and pregnant women with bone diseases. Likewise, two control groups were selected from the CRAT database: pregnant women with inflammatory diseases and not exposed to BPs and healthy pregnant women non-exposed to teratogenic drugs. For each case, 4 controls were assigned. Pregnancy outcomes were compared between inflammatory cases and controls, and between bone disease cases and healthy controls.
**Results:** 39 women were identified as having be exposed to BPs during pregnancy. Median age was 33 [27;36] years and 20% of patients were primiparous. Among them, 23 had inflammatory diseases including systemic lupus erythematosus (n=5), rheumatoid arthritis (n=5), anti-phospholipid syndrome (n=1), vasculitis (n=6) or other connective/auto-immune disease (n=6) and 16 had bone diseases including osteoporosis (n=9), malignancy (n=3) and other bone disease (n=4). Characteristics are reported in table 1. Compared to their 92 matched controls, women with inflammatory diseases exposed to BPs were more likely to receive steroids (78% vs 47%, p=0.009), methotrexate (26% vs 5% p=0.008), and colchicine (17% vs 2%, p=0.014) but less likely to receive anti-malarial drugs (p=0.019). 26% of cases vs 13% of the controls had voluntary or therapeutic pregnancy termination (p=0.195, OR=2.33, IC95 [0.63; 7.94]). Among the remaining patients, the rate of live births did not differ (94% vs 80%, p=0.29, OR=3.96, IC95 [0.53; 177.94]). No difference was found on birth weightssizes or congenital malformations (9% vs 4%, p=0.345, OR 2.08 IC95 [0.18;15.7]).

**Table 1: Main characteristics of the patients and maternofetal outcomes**

| | Inflammatory cases | Inflammatory controls | | Bone cases | Healthy controls |
|---|---|---|---|---|---|
| | N= 23 | N=92 | | N= 16 | N=64 |
| Maternal characteristics | | | | | |
| Age (y) | 27 [25.5;34] | 30 [27;33] | | 34 [33;39] | 32 [29;35] |
| Previous pregnancy | 0 [0;1.5] | 1 [0;2] | | 1.5 [1;3] | |
| Previous delivery | 0.5 [0;1.25] | 1 [0;2] | | 1.5 [0;2] | |
| Disease | | | Disease | | |
| - Systemic lupus erythematosus (%) | 5 (22) | 40 (43) | - Osteoporosis | 9 (56) | 0 |
| - Rheumatoid arthritis (%) | 5 (22) | 24 (26) | - Malignance (%) | 3 (19) | 0 |
| - Anti-phospholipid syndrome (%) | 1 (4) | 12 (13) | - Other (%) | 4 (25) | 0 |
| - Systemic vasculitis (%) | 6 (26) | 3 (3) | | | |
| - Other inflammatory disease (%) | 6 (26) | 13 (14) | | | |
| Drug | | | Drug | | |
| - Risedronate (%) | 15 (65) | 0 | - Risedronate (%) | 1 (6) | 0 |
| - Alendronate (%) | 6 (26) | 0 | - Alendronate (%) | 9 (56) | 0 |
| - Etidronate (%) | 1 (4) | 0 | - Etidronate (%) | 2 (13) | 0 |
| - Ostevine (%) | 1 (4) | 0 | - Clodronate (%) | 1 (6) | 0 |
| | | | - Ibandronate (%) | 1 (6) | 0 |
| | | | - Pamidronate (%) | 3 (19) | 0 |
| Exposition | | | | | |
| - Within 6 weeks before pregnancy (%) | 1 (4) | 0 | | 4 (25) | 0 |
| - 1-3 month of pregnancy (%) | 21 (91) | 0 | | 9 (56) | 0 |
| - 3-4 month of pregnancy (%) | 4 (17) | 0 | | 3 (19) | 0 |
| - 4-9 month of pregnancy (%) | 4 (17) | 0 | | 0 | 0 |
| - All trimester (%) | 1 (4) | 0 | | 0 | 0 |
| Therapeutic or voluntary Abortion | 6 (26) | 12 (13) | | 3 (19) | 2 (3) |
| Live birth among the remaining patients (%) | 16/17 (94) | 64/80 (80) | | 9/13 (69) | 62/62 (100) |
| Congenital malformations | 1 (9) | 4 (6) | | 0 (0) | 1 (2) |

In women with a bone disease the rate of therapeutic or voluntary abortions tended to be higher than in controls (19% vs 3%, p=0.054). However, among the remaining women, those treated with BPs had a lower live birth rate than healthy controls (69% vs 100%, p=0.0005), partly due to 3 spontaneous abortions in the BPs group. No difference on birth weights, sizes, or congenital malformations (p=1.00) was observed. In both groups, no neonatal hypocalcemia occurred.
**Conclusions:** Despite its limited sample size, this study is to our knowledge the largest one on pregnancy outcomes among women exposed to bisphosphonates during pregnancy, especially during the first trimester. Results are reassuring and did not show any major teratogenic effect of BPs. However, we observed a higher rate of spontaneous abortions in patients with bone disease treated with BPs, potentially related to an underlying malignancy. Collecting characteristics of child's follow-up is ongoing and will provide additional data, particularly on post-natal growth.
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## OP0102 GENETIC EFFECTS ON TRABECULAR AND CORTICAL VOLUMETRIC BONE MINERAL DENSITIES AND BONE MICROSTRUCTURE MEASURED BY HRPQCT

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**Background:** While both genetic and environmental factors affect areal BMD (aBMD), as much as 80% of variation in BMD is attributable to genetic factors [1]. aBMD measured by dual x-ray absorptiometry (DXA) is used as a surrogate measure for bone strength and is the gold standard for diagnosis of osteoporosis. However, structural abnormalities independent of aBMD may contribute to bone fragility. Bone structural parameters quantified using high-resolution pQCT (HRpQCT) may help more accurately identify individuals at risk for fracture than aBMD alone [2]. The heritability of cortical and/or trabecular bone microstructure determined by HRpQCT are unknown.
**Objectives:** To estimate heritability of trabecular density (TD), cortical density (CD), trabecular thickness (TT) and cortical thickness (CT) at tibia and radius measured by HRpQCT and investigate the genetic correlations of these between the tibia and radius.
**Methods:** Participants were 174 mother-child pairs from 161 families (161 mothers, mean age 52 years; 174 children, mean age 26 years). Cortical and trabecular bone microstructure at tibia and radius were measured by HRpQCT. SOLAR software was used to conduct quantitative genetic analyses with adjustment for covariates.
**Results:** In multivariable analysis, maternal tibial TD, CD, TT and CT were independently associated with all corresponding bone microstructures in the children ($\beta$=0.14 to 0.37, all $P<0.05$) after adjustment for age, sex, weight, height, smoking history and physical activity. Additive genetic factors explained 67%, 36%, 33% and 46% of the variation in TD, CD, TT and CT, respectively (adjusted $P<0.05$). Similar results were observed at the radius, but the heritability estimates were lower than that at tibia (range, 12%>57%). Genetic correlations for TD and TT between tibia and radius ($r_g$=0.80 for TD; 0.86 for TT) were greater than that of CD and CT ($r_g$=0.47 for CD; 0.50 for CT).
**Conclusions:** Genetic factors appear to have an important role in the development of peak bone microarchitecture and are partly shared for the tibia and radius. The heritability estimates of radius were lower than that of tibia, suggesting tibia is affected by environmental factors to a greater extent than radius, possibly due to more loading at tibia.
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[2] Zheng HF, Tobias JH, Duncan E, Evans DM, Eriksson J, Paternoster L et al: WNT16 influences bone mineral density, cortical bone thickness, bone strength, and osteoporotic fracture risk. PLoS Genet 2012; 8:e1002745.
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## OP0103 FRACTURE LIAISON SERVICE IMPLEMENTED IN A METROPOLITAN TERTIARY CENTRE IN WESTERN AUSTRALIA IMPROVED TREATMENT AND RECURRENT FRACTURE RATES BY 12 MONTHS

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**Background:** Osteoporotic fractures impose a significant morbidity, mortality and economic burden (1). Research within our hospital confirmed low rates of identification and secondary prevention for patients discharged from Emergency Department (ED) with a fracture (2). The Fracture Liaison Service (FLS) aimed to identify, review and then manage these patients following their discharge from the ED.
**Objectives:** To evaluate the performance of a FLS in a Western Australian hospital.
**Methods:** Patients aged >50 yrs who presented to the Emergency Department after a fracture at Sir Charles Gairdner Hospital (SCGH) were invited to the FLS. A retrospective control group from SCGH determined the historical fracture risk without an active FLS intervention. Fremantle Hospital was used as a prospective control cohort.
Demographic data was collected at baseline then patients were followed up at 3 & 12 months. The follow-up survey collected information on: awareness of osteoporosis, investigations undertaken (e.g. BMD testing), had a diagnosis been made, medication usage, health care utilisation, falls & fracture information and quality of life (EQ-5D).
**Results:** The FLS reduced the recurrence of minimal trauma fractures over 12 months by between 9.2 to 10.2% compared to a retrospective cohort & a prospective control cohort. 167 or 69.3% of eligible patients agreed to attend the Fragile Bone Clinic. As the program becomes more main-stream the utilisation of the service is expected to increase.
The FLS demonstrated a 17.1% increase in patient *awareness of osteoporosis* compared to other sites and by 35.6% compared to the SCGH retrospective group over 12 months ($p<0.001$). The FLS had better prescription rates of calcium (57.4% vs 28.8%), vitamin D (59.8% vs 33.0%), optimised calcium & vitamin D (48.4% vs 19.8%) and anti-resorptive therapy (29.9% vs 16.2%) compared to the retrospective cohort at SCGH. At 12 months the FLS had the highest number (n=82) and rate (46.9%) of patients initiated on pharmacological treatment compared to other sites 17 (41.5%) and SCGH Retrospective 12 (16.0%). The FLS incrementally improved the prescription, adherence and compliance with of osteoporosis treatment.
**Conclusions:** By 12 months the Fracture Liaison Service demonstrated that it reduced the recurrent fracture rate and significantly improved rates of pharmacological treatment initiation & patient awareness of osteoporosis.
**References:**
[1] Briggs AM et al. (2015) Hospitalisations, admission costs and re-fracture risk related to osteoporosis in Western Australia are substantial: a 10-year review. ANZ J Public Health.
[2] Inderjeeth CA et al. (2010) A multimodal intervention to improve fragility fracture management in patients presenting to Emergency Departments. MJA
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## OP0104 BONE QUALITY, AS MEASURED BY TRABECULAR BONE SCORE, IN FEMALE POSTMENOPAUSAL PATIENTS WITH SYSTEMIC SCLEROSIS AND RHEUMATOID ARTHRITIS

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**Background:** Patients affected by Systemic Sclerosis (SSc) and Rheumatoid Arthritis (RA) might present an increased risk of low bone mass as a result of multisystemic disorder including treatment, low vitamin D levels and physical inactivity[1]. Trabecular Bone Score (TBS) is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone axial microarchitecture and allows to get informations about bone quality[2].
**Objectives:** The aim of this study was to assess bone quality in SSc patients using TBS in comparison with a "high-risk" population with RA.
**Methods:** 74 patients (mean age 65±9 years) affected by SSc, 98 RA patients (mean age 61±8 years) and 60 age-matched healthy controls (mean age 64±11 years) were studied. Bone Mineral Density (BMD, g/cm$^2$) of the lumbar spine (L1-L4) was analyzed using DXA scan (Lunar Prodigy). Lumbar spine TBS was derived for each spine DXA examination blinded to clinical parameters and outcomes using TBS iNsight Medimaps (Lunar Prodigy). TBS value >1.350 is considered normal whereas TBS value <1.200 indicates a degraded bone microarchitecture.
**Results:** Out of 74 enrolled patients with SSc, 56 (76%) presented bone loss; in particular 32 (43%) showed osteoporosis and 24 (32%) osteopenia. In RA patients bone loss was observed in 78 patients (80%); in particular 52 osteoporosis (53%) and 41 (42%) osteopenia. BMD was found significantly lower in SSc and RA patients compared with matched control group (respectively, Lumbar spine: 0.998±0.161 g/cm$^2$ and 0.862±0.194 g/cm$^2$ vs 1.240±0.932 g/cm$^2$; Femoral neck: 0.784±0.212 g/cm$^2$ and 0.668±0.141 g/cm$^2$ vs 0.845±0.164 g/cm$^2$; Ward 0.563±0.173 g/cm$^2$ and 0.486±0.221 g/cm$^2$ vs 0.657±0.106 g/cm$^2$; Trochanter: 0.666 ±0.104 g/cm$^2$ and 0.598±0.231 g/cm$^2$ vs 0.725±0.143 g/cm$^2$; Total hip: 0.827±0.182 g/cm$^2$ and 0.764±0.244 g/cm$^2$ vs 1.033±0.161 g/cm$^2$, all $p<0.001$). Lumbar spine TBS was found significantly lower in SSc and RA patients compared with matched control group (respectively, 1.032±0.163 and 0.904±0.148 vs 1.361±0.126, both $p<0.001$). There was no significant difference in mean lumbar spine TBS between patients with SSc and RA ($p=0.238$).
**Conclusions:** This detailed study shows a decreased BMD and TBS values in SSc and RA patients when compared to healthy controls. In addition TBS, evaluated at the lumbar spine, with lumbar and femoral BMD, could discriminate patients with alterated bone microstructure and could become a new clinical tool in the general diagnosis of osteoporosis in inflammatory rheumatic diseases, such as SSc and RA.
**References:**
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[2] Roux JP et al. Osteoporosis Int 2013; 24(9):2455–60.
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## OP0105 THE PREDICTORS FOR 12 MONTHS EFFICACY OF DENOSUMAB, AN ANTI-RANKL ANTIBODY, ON OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM MULTICENTER STUDY (TBCR-BONE)

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**Background:** Although medication of rheumatoid arthritis (RA) has been improved by early intensive treatment using MTX and biological agents (BIO) for decades, treatment of concomitant disease in RA patients, such as osteoporosis (OP), will be more important to improve activity of daily living of RA patients. Although denosumab (DMB), an anti-RANKL antibody, was approved for treatment of OP in Japan in 2013, clinical data in real world is lacking in patients with RA.
**Objectives:** To investigate the 12 months efficacy of DMB on OP in patients with RA (RA-OP) and predictors of efficacy from multicenter registry study in Japan (TBCR-BONE).
**Methods:** 64 female cases with RA-OP were included in this study. Bone mineral density (BMD) of lumbar spine (LS-BMD) and total hip (TH-BMD) and bone turnover markers (P1NP and TRACP-5b) were measured at baseline and every 6 months to 12 months.
**Results:** Mean age was 69 years old. Mean RA duration was 16 years. Mean DAS28-CRP was 2.7. 44% of cases had the past history of fracture. Mean FRAX was 26%. Daily teriparatide was used in 12 cases before DMB treatment. LS-BMD at 6m and 12m was significantly increased compared with baseline (4.3% and 5.9%) (Fig1). TH-BMD at 6m and 12m was significantly increased compared with

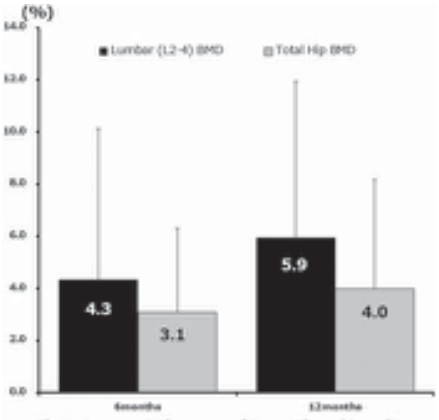


Fig 1. Average % increase of Bone Mineral Density

baseline (3.1% and 4.0%) (Fig1). Mean decrease in P1NP were 39.9% at 6m and 34.3% at 12m. Mean decrease in TRACP-5b were 31.5% at 6m and 27.2% at 12m. Next, all cases were divided into two group, good outcome group (GO group) and non-good outcome group (non-GO group), by mean %increase of LS-BMD and PF-BMD at 12 months. %increase of LS-BMD at 6m in LS-GO group (n=31) was significantly larger than that in LS-non-GO group (n=30) (7.6% vs. 0.9%). Baseline P1NP in LS-GO group was also larger than that in LS-non-GO group (62.5μg/l vs. 45.4μg/l). There were no significant differences in changes of BTMs between two groups. %increase of TH-BMD at 6m in TH-GO group (n=30) was significantly larger than that in TH-non-GO group (n=31) (5.0% vs. 1.2%). There were no significant differences in changes of BTMs between two groups.
**Conclusions:** DMB was effective in RA-OP. Early response of BMD and baseline P1NP level were suggested to be the predictors of the efficacy of DMB in RA-OP. Higher baseline P1NP and higher LS-BMD increase at 6m were the predictors of better LS-BMD increase at 12m. Higher TH-BMD increase at 6m was the predictors of better LS-BMD increase at 12m.
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## OP0106 CHANGE IN BONE MINERAL DENSITY WITH HIGH-DOSE PREDNISONE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Recently, we showed that treatment with COBRA-light therapy including prednisone with initially 30 mg/day, was as effective as the original COBRA scheme, with initially 60 mg/day [1,2], in the treatment of rheumatoid arthritis (RA). Since high-dose glucocorticoids are associated with bone loss and vertebral and nonvertebral fractures, we investigated the differences in bone mineral density (BMD) after one year of treatment in both arms.
**Objectives:** To compare 1-year changes in BMD (lumbar spine [L1-L4], total hip, and femoral neck) between the treatment groups.
**Methods:** An open-label, randomised controlled, non-inferiority trial of patients with active, newly diagnosed RA following a treat-to-target protocol.
**Results:** BMD data were determined in 144 out of 164 included RA patients, all randomized to either COBRA (n=71) or COBRA-light (n=73) therapy. Overall bone loss was very limited, and no significant difference in change in BMD between COBRA and COBRA-light was found at any site (*Table 1*). However, in secondary analyses, COBRA-light showed a significant decrease in BMD in the lumbar spine and total hip after 52 weeks, whereas the femoral neck and the COBRA group did not.

Table 1. Changes in bone mineral density between baseline and week 52 during COBRA and COBRA-light therapy

| | COBRA (n=71) | | | COBRA-light (n=73) | | |
|---|---|---|---|---|---|---|
| | baseline | week 52 | change | baseline | week 52 | change |
| Lumbar spine | 1.12 (0.17) | 1.12 (0.17) | 0.01% | 1.10 (0.15) | 1.09 (0.15) | −1.02%* |
| Total hip | 0.95 (0.14) | 0.95 (0.14) | 0.05% | 0.95 (0.12) | 0.94 (0.13) | −1.16%* |
| Femoral neck | 0.90 (0.16) | 0.89 (0.17) | −0.59% | 0.88 (0.12) | 0.87 (0.11) | −0.98%* |

*Significant change between baseline and week 52 ($p<0.05$). Values are reported as mean (SD), unless otherwise specified.

**Conclusions:** During the trial, overall bone loss was very limited and not significantly different between the treatments. These findings strengthen the hypothesis that positive effects associated with the large reduction in disease activity as a result of combination therapy and tight control treatment counteract the negative effects of (high-dose) prednisone on bone.
**References:**
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[2] Ter Wee MM, et al. Ann Rheum Dis 2015
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## OP0107 TERIPARATIDE AND DENOSUMAB COMBINATION THERAPY AND SKELETAL METABOLISM

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**Background:** Despite therapeutic options for osteoporosis have greatly expanded over the past few decades, the treatment of patients with established severe osteoporosis still remains challenging. Recently the combined teriparatide (TPD) and denosumab therapy was shown to increase bone mineral density (BMD) more than either agent alone.
**Objectives:** The aim of this study was to compare the changes in bone turnover markers and in inhibitors of the Wnt canonical pathway in patients treated with either denosumab alone or TPD alone or when TPD was added to patients previously treated with denosumab.
**Methods:** Open label prospective randomized study, involving 59 women over 65 years old affected by severe postmenopausal osteoporosis (with the evidence of at least two moderate-severe vertebral fractures), Bone turnover markers C-terminal telopeptide of type I collagen (CTX) and intact N-propeptide of type I collagen ad (P1NP) and inhibitors of the Wnt canonical pathway sclerostin (SOST) and Dickkopf-related protein 1 (DKK1) were evaluated.
**Results:** In the groups treated with TPD or with denosumab alone bone turnover markers rose and decreased, respectively. In TPD group a later significant increase in DKK1 was observed, while in denosumab group a progressive increase in SOST was associated with a progressive significant decrease in DKK1. In the group treated first with denosumab and in which TPD was added 3 months later, the rounded values of both CTX and P1NP increased 3 months after the beginning of TPD by approximately the same absolute and percentage value of the group of patients treated with TPD alone, showing that the strong effect of denosumab on bone turnover is easily reversed by TPD treatment. In this group, SOST increased as in the denosumab alone group, while DKK1 progressively increased as in the TPD alone group.
**Conclusions:** In conclusion, in this study we showed that TPD is able to express its biological activity even when bone turnover is fully suppressed by denosumab treatment. The combination therapy is associated with significant increases in both DKK1 and SOST, suggesting that the Wnt signalling pathway is not involved in the positive bone balance seen in the combination TPD-denosumab group.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

# Expanding therapeutic options in spondyloarthritis -

## OP0108 BIMEKIZUMAB, A MONOCLONAL ANTIBODY THAT INHIBITS BOTH IL-17A AND IL-17F, PRODUCES A PROFOUND RESPONSE IN BOTH SKIN AND JOINTS: RESULTS OF AN EARLY-PHASE, PROOF-OF-CONCEPT STUDY IN PSORIATIC ARTHRITIS

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**Background:** Bimekizumab (UCB4940) is a potent and selective monoclonal antibody inhibiting the activity of both IL-17A and IL-17F, which are key pro-inflammatory cytokines overexpressed in skin lesions of patients with psoriasis.[1] Blocking both IL-17A and IL-17F may provide a therapeutic advantage.
**Objectives:** To study the safety/tolerability and efficacy of multiple-dose bimekizumab in patients with PsA with inadequate responses to at least 1 DMARD and/or 1 biologic DMARD (NCT02141763).
**Methods:** 52 patients were randomized to receive either bimekizumab (N=38) or PBO (N=14). Four active dose-level groups were studied using a single loading dose (80–560 mg bimekizumab) administered at wk 0; further doses (40–320 mg bimekizumab) were administered at wks 3 and 6. ACR and PASI scores were examined; safety and PK variables were also investigated.
**Results:** At baseline, patients had a mean SJC (66) of 12.6 and TJC (68) of 29.6, and mean baseline CRP of 12.5 mg/mL. For patients with skin involvement of >3% (N=23) a mean baseline PASI of 15.9 (SD=14.6) was observed. Onset of response was rapid for both skin and joints: by wk 8, an ACR20 RR of 80% was observed for the top 3 doses (N=32) compared with 17% in the PBO group (N=12). Clinically relevant responses in disease activity measures were observed to wk 20. A summary of results in skin and joints is presented in the table.

| | Baseline | | Week 8 | |
|---|---|---|---|---|
| | PBO | Bimekizumab top 3 doses | PBO | Bimekizumab top 3 doses |
| Joints: | | | | |
| ACR20 RR [95% CI] | N/A | N/A | 17% [5%, 45%], N=12 | 80% [63%, 91%], N=30 |
| ACR50 RR [95% CI] | N/A | N/A | 8% [2%, 35%], N=12 | 40% [25%, 58%], N=30 |
| Mean DAS(CRP) [95% CI] | 5.1 [4.6, 5.6], N=11 | 5.0 [4.6, 5.4], N=30 | 3.9 [3.2, 4.6], N=11 | 3.1 [2.7, 3.6], N=29 |
| Skin: | | | | |
| PASI 90 RR [95% CI] | N/A | N/A | 0% [0%, 43%], N=5 | 87% [62%, 96%], N=15 |
| Mean PASI [SD] | 17.6 [18.0], N=5 | 11.1 [9.2], N=15 | 14.1 [17.9], N=5 | 0.2 [0.6], N=15 |

Bayesian analysis on wk 8 data indicated a >99% probability that ACR score improvement, and ACR20 RR, were greater than PBO and exceed the pre-defined clinically relevant threshold ($ACRn_{tr}$: 0.31 and ACR20: 25%). Additionally, there was a high posterior probability of >99% that the bimekizumab ACR20 RR

was greater than that reported for the current SOC biologic treatment, including anti-IL-17 therapies (59.7%) at wk 8.[2,3]
All doses of bimekizumab were well tolerated, with no unexpected safety findings. No patient discontinued due to treatment-emergent AEs. No treatment-related serious AEs were reported. Bimekizumab had a linear PK, with an expected half-life of ~24 days.
**Conclusions:** In patients with PsA, bimekizumab demonstrated rapid onset, sustained and deep efficacy on disease activity in skin and joints, and within this limited patient and exposure set, was safe and well tolerated. Bayesian analysis indicated that bimekizumab ACR20 RR is greater than that reported for current therapies including anti-IL-17A. Results support that inhibition of both IL-17A and IL-17F could provide additional clinical benefit in IL-17-mediated diseases.
**References:**
[1] Johansen et al. Br J Dermatol 2009;160:319–24;
[2] McInnes et al. Lancet 2015;386:1137–46;
[3] McInnes et al. Lancet 2013;382:780–9
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**Disclosure of Interest:** S. Glatt Shareholder of: UCB, Employee of: UCB, F. Strimenopoulou Employee of: UCB, P. Vajjah Shareholder of: UCB, Employee of: UCB, S. Shaw Shareholder of: UCB, Employee of: UCB, L. Ionescu Employee of: UCB, S. Popa: None declared, D. Baeten Grant/research support from: AbbVie, Pfizer, MSD, UCB, Novartis, Boehringer Ingelheim, Consultant for: AbbVie, Pfizer, MSD, UCB, Novartis, Boehringer Ingelheim, Roche, Eli Lilly, BMS
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## OP0109 EFFICACY AND SAFETY OF IXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: 52 WEEK RESULTS FROM A PHASE 3 STUDY (SPIRIT-P1)

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**Background:** Ixekizumab (IXE) is an IgG4 monoclonal antibody that binds with high affinity and specificity to the proinflammatory cytokine IL-17A. In this phase 3 study (SPIRIT-P1), IXE was superior to placebo (PBO) in achieving American College of Rheumatology 20 (ACR20) response at Week 24 in biologic disease-modifying antirheumatic drug-naive (bDMARD-naive) patients with active psoriatic arthritis (PsA)[1].
**Objectives:** To evaluate efficacy and safety of IXE over 52 weeks in patients with active PsA.
**Methods:** A total of 417 bDMARD-naive patients with active PsA were randomized 1:1:1:1 to IXE 80 mg once every 4 weeks (Q4W) or once every 2 weeks (Q2W) including a 160 mg starting dose, to 40 mg adalimumab (ADA), or to PBO (all subcutaneous dosing) during the Double-Blind Treatment Period (DBTP: Weeks 0 to 24). Of these, 381 patients completed the DBTP and entered the Extension Period (EP: Weeks 24 to 52) where they were assigned to 80 mg IXE Q4W or Q2W. Patients randomized to IXE at Week 0 continued the same dose regimen in the EP. Patients randomized to PBO or ADA at Week 0 were re-randomized (1:1) to 80 mg IXE Q4W or Q2W at Week 16 (inadequate responders) or 24. Those patients who initially received PBO started IXE at Week 16 or 24; patients who initially received ADA started IXE at Week 24 or 32 after an 8 week wash out period. Efficacy measures included ACR20/50/70 response, Health Assessment Questionnaire-Disability Index (HAQ-DI) Score, Disease Activity Score 28 diarthrodial joint count based on C-reactive protein (DAS 28-CRP), Psoriasis Area and Severity Index 75, 90, 100 (PASI 75/90/100), Leeds Enthesitis Index (LEI), and Leeds Dactylitis Index-Basic (LDI-B). Efficacy and safety were analyzed using the EP population defined as all patients who received at least 1 dose of study drug in the EP. Missing values were imputed by nonresponder imputation for categorical data and modified baseline observation carried forward for continuous data.

Table 1. Efficacy and Safety Outcome Measures at Week 52+ (Extension Period Population)

| | IXE Q4W (N=560) | IXE Q2W (N=560) | ADA (N=446) | ADA (N=446) | PBO (N=470) | PBO (N=470) | Total (N=1031) | Total (N=1030) |
|---|---|---|---|---|---|---|---|---|
| ACR20, n (%) | 67 (68.4) | 66 (68.8) | 38 (59.4) | 29 (76.3) | 26 (27.4) | 33 (71.7) | 127 (66.2) | 127 (66.3) |
| ACR50, n (%) | 51 (54.6) | 54 (53.1) | 29 (50.0) | 21 (43.8) | 19 (42.2) | 21 (45.7) | 101 (52.9) | 93 (48.5) |
| ACR70, n (%) | 38 (39.2) | 38 (39.6) | 17 (34.7) | 14 (29.2) | 9 (20.0) | 14 (30.4) | 64 (33.5) | 66 (34.7) |
| HAQ-DI, Mean (SD) CFB | -0.53 (0.56) | -0.55 (0.52) | -0.47 (0.48) | -0.42 (0.47) | -0.36 (0.53) | -0.42 (0.56) | -0.49 (0.53) | -0.49 (0.53) |
| DAS 28-CRP, Mean (SD) CFB | -2.16 (1.21) | -2.37 (1.35) | -2.15 (1.21) | -2.00 (0.95) | -1.85 (1.10) | -2.05 (1.06) | -2.09 (1.19) | -2.20 (1.19) |
| PASI 75, NR, n (%) | 52 (79.8) | 45 (81.8) | 23 (64.7) | 22 (68.7) | 19 (65.5) | 19 (65.5) | 93 (71.0) | 86 (72.5) |
| PASI 90, NR, n (%) | 44 (66.7) | 43 (78.2) | 17 (50.0) | 17 (53.1) | 16 (55.6) | 16 (52.1) | 77 (58.8) | 78 (65.7) |
| PASI 100, NR, n (%) | 37 (56.1) | 32 (57.3) | 12 (35.3) | 15 (46.9) | 15 (48.4) | 13 (44.8) | 64 (48.9) | 65 (54.6) |
| LEI, NR, Mean (SD) CFB | -1.9 (1.65) | -1.8 (1.58) | -2.0 (1.91) | -1.1 (2.26) | -1.1 (2.18) | -1.7 (2.06) | -1.8 (1.84) | -1.8 (1.87) |
| LDI-B, NR, n (%) | 36 (55.4) | 26 (50.0) | 14 (50.0) | 5 (26.1) | 8 (40.0) | 11 (42.3) | 59 (51.3) | 43 (42.6) |
| LDI-B, NR, Mean (SD) CFB | -3.7 (3.99) | -3.8 (3.87) | -5.4 (5.02) | -4.8 (5.61) | -3.1 (2.59) | -2.2 (1.94) | -3.8 (3.93) | -3.5 (3.93) |
| LDI-B (≥2), NR, n (%) | 32 (80.0) | 22 (81.5) | 7 (77.8) | 6 (72.7) | 9 (69.2) | 11 (57.9) | 48 (77.4) | 46 (73.0) |
| TEAE, n (%) | 54 (55.7) | 54 (56.3) | 26 (46.4) | 21 (43.8) | 28 (62.2) | 27 (58.7) | 102 (53.4) | 102 (53.7) |
| SAE, n (%) | 4 (4.1) | 9 | 5 (10.2) | 1 (2.1) | 1 (2.2) | 1 (2.2) | 10 (5.2) | 2 (1.1) |
| Discontinued due to AE, n (%) | 1 (1.0) | 0 | 0 | 0 | 1 (2.2) | 1 (2.2) | 2 (1.0) | 1 (0.5) |

Abbreviations: ACR20/50/70=American College of Rheumatology 20/50/70 index; ADA=adalimumab 40 mg; AE=adverse event; CFB=change from baseline; DAS 28-CRP=Disease Activity Score 28 diarthrodial joint count based on C-reactive protein; HAQ-DI=Health Assessment Questionnaire-Disability Index; IXE=ixekizumab; IXE Q2W=ixekizumab 80 mg once every 2 weeks; IXE Q4W=ixekizumab 80 mg once every 4 weeks; LDI-B=Leeds Dactylitis Index-Basic; LEI=Leeds Enthesitis Index; n=number of patients in the analysis population; n=number of responders; PASI 75/90/100=Psoriasis Area and Severity Index 75/90/100; PBO=placebo; SAE=serious adverse event; SD=standard deviation; TEAE=treatment-emergent adverse event;
+ For efficacy analyses, baseline was defined as the last non-missing assessment recorded on or prior to the date of first injection of study treatment at Week 0. For analyses of TEAEs, baseline was defined as AEs which started prior to the study drug injection at Week 24 with an exception of patients who were randomized to ADA during the entire Double-Blind Treatment Period and started IXE at Week 32 where baseline was defined as AEs which started prior to the study drug injection at Week 32.
‡ Only patients with psoriatic lesions ≥3% of BSA at baseline were included in the analysis.
¢ Only patients with enthesitis at baseline were included in the analysis.
Φ Only patients with enthesitis and LEI >0 at baseline were included in the analysis.
Ψ Only patients with dactylitis at baseline were included in the analysis.
ξ Only patients with dactylitis and LDI-B >0 at baseline were included in the analysis.

**Results:** A total of 304 patients completed the EP. Efficacy and safety results in the EP population are summarized in Table 1. Improvements from baseline in ACR20/50/70, HAQ-DI, DAS 28-CRP, PASI 75/90/100, LEI and LDI-B were observed at Week 52. The frequency of treatment-emergent adverse events (AEs) in the EP was similar to that observed in the DBTP; the majority were mild or moderate in severity. Serious AEs occurred in 12 patients and no deaths occurred in the EP population.
**Conclusions:** IXE demonstrated clinically significant improvement in signs and symptoms of PsA including arthritis, dactylitis and enthesitis as well as skin manifestations across treatment groups in the EP. The safety profile of IXE observed in the EP was similar to that observed in the DBTP and other phase 3 studies of IXE in patients with plaque psoriasis (UNCOVER studies).
**References:**
[1] Philip J. Mease et al. 2015 ACR/ARHP Annual Meeting, 6–11 November, San Francisco, CA 2015; [abstract 977].
**Disclosure of Interest:** P. Mease Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer; UCB Pharma, Consultant for: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Pfizer, UCB Pharma, M. Okada Grant/research support from: Lilly, Consultant for: Lilly, Speakers bureau: Santen Pharmaceutical, Mitsubishi Tanabe Pharma, Pfizer, Abbott Japan, M. Kishimoto Consultant for: Lilly, C. Shuler Shareholder of: Lilly, Employee of: Lilly, H. Carlier Shareholder of: Lilly, Employee of: Lilly, C.-Y. Lin Shareholder of: Lilly, Employee of: Lilly, J. Mou Shareholder of: Lilly, Employee of: Lilly, S. Moriarty Shareholder of: Lilly, Employee of: Lilly, C. Lee Shareholder of: Lilly, Employee of: Lilly, D. Gladman Grant/research support from: AbbVie, Amgen, Celgene, Janssen, Novartis, UCB Pharma, Consultant for: Abbvie, Amgen, BMS, Celgene, Lilly, Novartis, Pfizer, UCB
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## OP0111 ANTI-TNF THERAPY IN AXIAL SPONDYLOARTHRITIS: PREDICTION OF THERAPEUTIC RESPONSES USING IMMUNOLOGICAL SIGNATURES

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**Background:** The introduction of anti-TNF therapy has proven effective to reduce inflammation and clinical symptoms in several chronic inflammatory diseases. However, TNF-blockers are effective only in a subpopulation of patients and can be associated with serious side effects. Despite intense efforts, it is currently not possible to predict responsiveness of patients to anti-TNF treatment. To address this issue, we have asked whether the analysis of the immune functions of patients will allow us to define biomarkers that can predict therapeutic responses to TNF blockers.
**Objectives:** The goals of this project were to define (i) the impact of anti-TNF therapy on immune responses to microbial challenges and stimuli targeting specific immune pathways in axial spondyloarthritis (axSpA) patients and (ii) to identify immunological correlates associated with therapeutic responses to TNF blockers before the initiation of therapy.
**Methods:** We have recently developed a set of whole-blood, syringe-based assays to assess innate or adaptive immune responses to stimuli targeting different signaling pathways (e.g. cytokines and TLR/NLR agonists), or mimicking infections in patients (1). This "TruCulture" system is designed to capture immune cell activity in response to specific stimuli without introducing sample collection and manipulation variables. Using this assay system, we have investigated immune responses to 20 different stimuli in a pilot study involving 12 axSpA patients before and 3 months after initiation of anti-TNF therapy. We are currently validating our findings in a replication cohort.
**Results:** We noted a highly significant reduction of the secretion of IL-1ra, IL-1β, and MIP-1β in response to selected stimuli after treatment with TNF-blockers. In contrast, TNF blockers had only minor effects on cytokine/chemokine production in unstimulated cultures, indicating that the effects of anti-TNF therapy can be measured when immune cells are challenged, but not at steady state. We also tested whether there is a correlation between the responses of immune cells to specific stimuli and the clinical response to TNF-blockers. For this, we calculated the "Ankylosing Spondylitis Disease Activity Score" (ASDAS) before treatment and 3 months after initiation of anti-TNF therapy and determined the "Improvement Score" ($ASDAS_{before\ treatment} - ASDAS_{after\ treatment}$). We found that axSpA patients who secreted the highest levels of inflammatory cytokines and chemokines in response to specific immune stimuli before initiation of anti-TNF therapy had the best therapeutic responses (highest improvement score).
**Conclusions:** Our results show that TruCulture assays are an efficient and robust

tool to monitor immune functions in patients and that anti-TNF therapy induces specific changes in immune responses to selected stimuli. Our data also indicate that analyzing immune responses in patients before therapy is a promising strategy to develop biomarkers predicting therapeutic efficacy of TNF-blockers.

**References:**
[1] Duffy et al., Immunity. 2014 Mar 20;40(3):436–50

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## OP0112 EFFECT OF COMEDICATION WITH CONVENTIONAL SYNTHETIC DMARDS ON TNF INHIBITORS-RETENTION IN PATIENTS WITH SPONDYLOARTHRITIS: A PROSPECTIVE COHORT

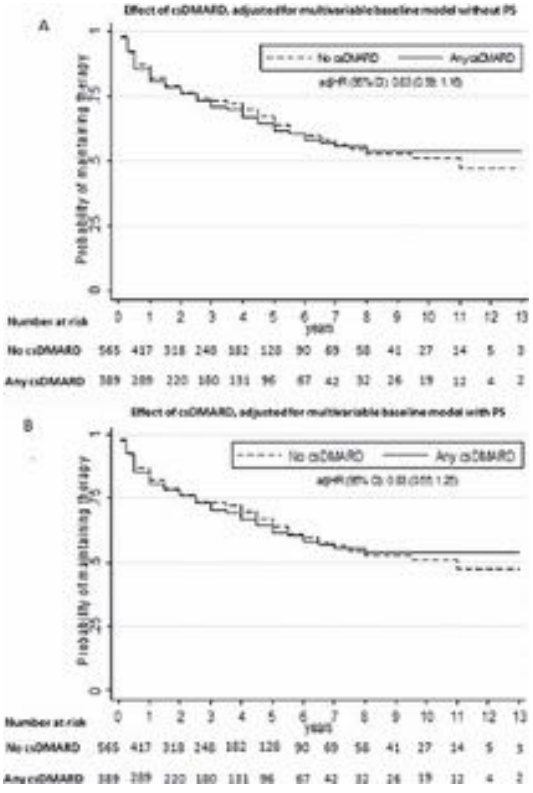
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**Background:** The effects of comedication with conventional synthetic disease modifying antirheumatic drugs (csDMARDs) on TNF inhibitors (TNFi)-retention in spondyloarthritis (SpA), are inconclusive. Results from previous observational studies may have easily led to spurious conclusions, since confounding, especially "confounding by indication", was not fully addressed.

**Objectives:** To evaluate if comedication with csDMARD influences TNFi-retention in patients with SpA, while performing a comprehensive set of adjustments to best handle confounding.

**Methods:** Patients with SpA (according to their treating rheumatologists) from the Rheumatic Diseases Portuguese Register (Reuma.pt), with first TNFi started between 2001 and 2014 were included in this prospective, multicenter, cohort study. Our main outcome was time to first TNFi discontinuation. Cox-regression was used to estimate the effect of csDMARD comedication on TNFi-retention in two types of models, one including baseline (time-fixed) variables and the other with time-varying variables, including socio-demographic features, measures of disease activity, physical function and co-treatment with other drugs (NSAIDs and oral steroids). To control for possible "confounding by indication", the effect of csDMARD comedication on TNFi-retention was also tested after propensity score (PS)-adjustment.

**Results:** In total, 954 patients (mean (SD) age 41.5 (12.0) years; 59.6% males; 13.7 (10.4) years of disease duration) were included and 289 (30.3%) discontinued their first TNFi after a median follow-up time of 2.5 years (range: 0.08–13 years). A large proportion of patients were treated with csDMARDs at baseline (389; 41%). Inefficacy was the most common reason for TNFi discontinuation (55.7%), followed by adverse events (31.1%). In the multivariable analysis comedication with csDMARDs had no effect on TNFi-retention, neither in the baseline model (HR: 0.83; 95% CI: 0.59; 1.16) (figure A) nor during follow-up adjusting for time-varying covariates (HR: 1.13; 95% CI: 0.71; 1.80). The effect of csDMARDs remained not statistically significant after PS-adjustment (figure B).




**Conclusions:** Comedication with csDMARDs does not prolong TNFi-retention in SpA patients in clinical practice suggesting no benefit in the concomitant use of these drugs.

**Disclosure of Interest:** None declared

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## OP0113 NO INCREASED INCIDENCE OF INFLAMMATORY BOWEL DISEASE AMONG SECUKINUMAB-TREATED PATIENTS WITH MODERATE TO SEVERE PSORIASIS, PSORIATIC ARTHRITIS, OR ANKYLOSING SPONDYLITIS: DATA FROM 14 PHASE 2 AND PHASE 3 CLINICAL STUDIES

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**Background:** Secukinumab (SEC), a fully human anti–interleukin-17A monoclonal antibody, has been evaluated and approved for the treatment of moderate to severe psoriasis (PsO), active psoriatic arthritis (PsA) and active ankylosing spondylitis (AS). Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is commonly associated with PsO, PsA and AS.[1,2] The risk of CD in PsO pts is ~4-fold higher than that in the general population; this risk is even higher among PsO pts with PsA, reported at a rate of 0.05 cases per 100 pt-years.[1] The rate of CD among placebo (Pbo) treated pts in AS trials has been reported as 0.7 cases per 100 pt-years.[3] Endoscopic subclinical inflammation occurs in up to 50% of AS patients.[2]

**Objectives:** To assess the incidence of CD and ulcerative colitis (UC) among SEC-treated pts in the PsO, PsA, and AS clinical trial programs.

**Methods:** This analysis included data from 10 Phase 2 and Phase 3 studies in moderate to severe PsO, 2 Phase 3 studies in active PsA, and 2 Phase 3 studies in active AS, pooled per indication. Most studies included short-term, Pbo treatment arms; 1 PsO study included an etanercept (ETN) active comparator arm. Pts with prior history of, but not active, IBD could be enrolled. Study durations varied; data from all pts receiving ≥1 SEC dose up to Week (Wk) 52 (PsO studies) or Wk 112 visit were included. Data are reported as crude frequency rates (%) in the short-term (Wk 12 in PsO studies and Wk 16 in the PsA/AS studies) and exposure adjusted incidence rates (EAIR; per 100 pt-years) over the entire treatment period.

**Results:** Overall, 3430, 974, and 571 pts received ≥1 SEC dose in the PsO, PsA, and AS studies, respectively. AEs of CD or UC were reported infrequently amongst SEC-treated pts in both the short- and long-term treatment periods (Table). Rates of CD and UC were similar across the PsO and PsA cohort, and rates with SEC were similar to those seen with ETN in PsO pts. Across all

Table: Incidence of CD and UC Across the PsO, PsA and AS Secukinumab Clinical Trial Programs

| | PsO Studies[#,1] | | | PsA Studies | | AS Studies | |
|---|---|---|---|---|---|---|---|
| **Short-term period, n (%)** | | | | | | | |
| | Any SEC (N=2877) | PBO (N=793) | ETN (N=323) | Any SEC (N=703) | PBO (N=300) | Any SEC (N=394) | PBO (N=196) |
| **Mean exposure, days** | 83.2 | 81.2 | 82.6 | 112.0 | 110.1 | 112.1 | 108.6 |
| **Crohn's disease** | 1 (0.03) | 0 | 0 | 0 | 1 (0.3) | 2 (0.5) | 0 |
| **Exacerbations[$]** | 1 | 0 | 0 | 0 | 0 | 2 | 0 |
| **Ulcerative colitis** | 1 (0.03) | 0 | 1 (0.3) | 0 | 0 | 1 (0.3) | 0 |
| **Exacerbations[$]** | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Entire treatment period, n (EAIR per 100 pt-years) [95% CI]** | | | | | | | |
| | PsO Studies[#,1] | | | PsA Studies | | AS Studies | |
| | Any SEC* (N=3430) | ETN (N=323) | | Any SEC* (N=974) | | Any SEC* (N=591) | |
| **Mean exposure, days** | 290.1 | 331.9 | | 542.4 | | 670.0 | |
| **Crohn's disease** | 3 (0.11) [0.02–0.32] | 0 [0–1.26] | | 1 (0.07) [0.00–0.39] | | 8[¶] (0.77) [0.33–1.51] | |
| **Exacerbations[$]** | 3 | 0 | | 0 | | 3 | |
| **Ulcerative colitis** | 4 (0.15) [0.04–0.38] | 1 (0.34) [0.01–1.90] | | 2 (0.14) [0.02–0.50] | | 3 (0.29) [0.06–0.84] | |
| **Exacerbations[$]** | 2 | 0 | | 1 | | 1 | |

[#]Final diagnosis was not confirmed in 2 cases; *Includes pts switched from placebo (PBO); [$]Exacerbations count to the overall incidence rate

indications, there was no dose dependency with respect to the incidence of CD or UC with SEC, and no pattern in time-to-onset (data not shown).
**Conclusions:** Events of CD and UC in the 14 clinical studies were reported infrequently in SEC-treated pts with PsO, PsA, or AS; rates were similar across the PsO and PsA cohorts. EAIR rates of CD and UC observed in SEC-treated patients are consistent with those reported in the literature in PsO, PsA, and AS pts.
**References:**
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**Acknowledgement:** The study was sponsored by Novartis Pharma AG.
**Disclosure of Interest:** S. Schreiber Grant/research support from: Abbvie, AstraZeneca/Medimmune, Boehringer, Celltrion, Ferring, Jansen, Novartis, MSD, Pfizer, Sanofi, Takeda, UCB, Consultant for: Abbvie, Celltrion, Ferring, MSD, Takeda, B. Sands: None declared, A. Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer, UCB, D. Baeten Grant/research support from: Boehringer Ingelheim, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Boehringer Ingelheim, BMS, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, UCB, J. Huang Shareholder of: Novartis, Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, C. Karyekar Shareholder of: Novartis, Employee of: Novartis, T. Fox Shareholder of: Novartis, Employee of: Novartis, C. Gaillez Shareholder of: Novartis, Employee of: Novartis
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## OP0114 SECUKINUMAB FOR THE TREATMENT OF ANKYLOSING SPONDYLITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS ADALIMUMAB USING A MATCHING-ADJUSTED INDIRECT COMPARISON

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**Background:** Secukinumab 150 mg (SEC) is approved for the treatment of active AS in adults with inadequate response to conventional therapy. The MEASURE 2 (M2) trial showed superiority for SEC over placebo for the primary outcome measure, ASAS20 response, at week 16 and for multiple secondary outcomes. Efficacy was sustained up to 2 years. The ATLAS trial compared adalimumab 40 mg (ADA) with placebo, but there is no head-to-head trial of SEC vs. ADA. Placebo patients could switch to active treatment as early as week 12 in ATLAS and at week 16 in M2. Matching-adjusted indirect comparison (MAIC) can assess comparative effectiveness by re-weighting patient level data (PLD) resulting in a reduced effective sample size (ESS), to match the baseline patient characteristics of another trial. Thus, MAIC is able to simulate head-to-head comparisons.
**Objectives:** To assess the relative efficacy of SEC vs. ADA using adjusted PLD from M2 and published ATLAS data.
**Methods:** PLD from the SEC arm in M2 (n=72) was re-weighted to match baseline characteristics of the ADA arm in ATLAS (n=208). Logistic regression was used to determine weights for age, sex, mean BASFI score, mean CRP level, and prior biologic use. Sensitivity analyses including adjustment for BASDAI score were performed. Correlation analyses of baseline characteristics with ASAS20/40 responses were not available before the regression analyses. Both trials reported non-responder imputation (NRI) results until week 24; beyond which ATLAS used LOCF with n=311, including placebo switchers. Weighted outcomes from M2 (ESS n=34) were compared with outcomes from ATLAS. Pairwise comparisons using relative risks (RR) were performed. Results are presented as probability of response (95% CI) and RR (95% CI).
**Results:** SEC treatment led to statistical significantly higher ASAS responses at week 24 vs. ADA for ASAS20 (72.3% [62–83]; RR 1.43 [1.12–1.84] $p$=0.004) and ASAS40 (61.4% [50–73]; RR 1.56 [1.14–2.14] $p$=0.006). The ASAS20 and 40 response rates for ADA were 50.5% (44–57) and 39.4% (33–46) respectively. At week 52, SEC led to higher ASAS responses vs. ADA. The ASAS20 and 40 response rates for SEC were 78.9% (69–89) and 57.6% (46–69) respectively, and for ADA were 65.4% (60–71) and 47.1% (42–53). The SEC vs. ADA comparison at ASAS20 approached significance (RR 1.21 [0.996–1.461] $p$=0.055). No significant differences were observed at week 12 and 16. Sensitivity analyses support these findings.
**Conclusions:** SEC demonstrated statistically significant higher symptomatic improvement in terms of ASAS20 and 40 responses vs. ADA at week 24 in this first MAIC in AS. A similar trend was noted up to week 52, even though SEC NRI data was compared with ADA LOCF data at week 52. Differences in study designs, such as the early-escape criteria and disease duration together with the small ESS (n=34) for SEC may result in potential limitations, warranting further MAIC analyses in AS.
**Disclosure of Interest:** W. Maksymowych Grant/research support from: Abbvie, Pfizer, Sanofi, Consultant for: Abbvie, Amgen, Boehringer, Eli-Lilly, Janssen, Merck, Pfizer, Sanofi, UCB, V. Strand Consultant for: Abbvie, Amgen Corporation, AstraZeneca, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, Glaxo-SmithKline, Janssen, Jazz Pharmaceuticals, Lilly, Novartis, Pfizer, Regeneron, Sandoz, Sanofi and UCB, D. Baeten Grant/research support from: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen and Boehringer Ingelheim, Consultant for: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS and Glenmark, P. Nash Grant/research support from: Novartis, Consultant for: Novartis, H. Thom Consultant for: Novartis Pharma AG and for a short time in 2015 for Eli Lilly, S. Cure: None declared, E. Palaka Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, H. Richards Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
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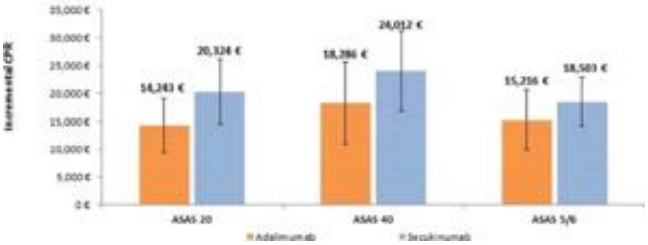
## OP0115 RELATIVE EFFICACY OF ADALIMUMAB VERSUS SECUKINUMAB IN ACTIVE ANKYLOSING SPONDYLITIS: A MATCHING-ADJUSTED INDIRECT COMPARISON

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**Background:** Two phase 3 clinical trials, MEASURE 1 and 2, demonstrated the efficacy of secukinumab for active ankylosing spondylitis (AS). However, there is limited data comparing the efficacy of secukinumab with established AS treatments.
**Objectives:** The objective of this study was to compare relative efficacy between adalimumab and secukinumab, estimate the number needed to treat (NNT), and evaluate the incremental cost per responder (CPR) for the treatment of active AS.
**Methods:** An indirect comparison was conducted using individual patient data from the adalimumab clinical trial (ATLAS)[1] and published data from the secukinumab trials (MEASURE 1 and 2).[2] Only dosages approved by the European Medicines Agency (adalimumab 40mg and secukinumab 150mg) were included in the analysis. To adjust for the cross-trial differences, individual patients in ATLAS were re-weighted to match the mean baseline characteristics in the MEASURE trials.[3,4] Specifically, age, weight, gender, duration of AS, baseline methotrexate use, baseline sulfasalazine use, presence of positive HLA-B27, BASDAI score and total back pain score were included in the baseline matching. The ASAS20, ASAS40 and ASAS 5/6 response rates relative to placebo at the end of the trial period (adalimumab: 12 weeks, secukinumab: 16 weeks) were compared. NNTs to achieve one additional ASAS20, ASAS40 and ASAS 5/6 responder and the corresponding incremental CPRs were also calculated. Drug costs in terms of 2015 Euros were obtained from the Lauer Taxe.[5]
**Results:** After matching, mean baseline characteristics were balanced across the ATLAS and MEASURE 1 and 2 populations. Compared to secukinumab (n=197), adalimumab (n=204) demonstrated similar efficacy in ASAS20/40 and ASAS 5/6. The mean differences (95% confidence interval) between adalimumab and secukinumab in relative ASAS20, ASAS40 and ASAS 5/6 response rates were 2.3% (-12.8%, 17.5%), -0.4% (-14.1%, 13.4%), and -3.1% (-17.3%, 11.2%),

respectively. The NNTs to achieve one additional responder were also comparable between adalimumab and secukinumab: 2.9 vs 3.1 in ASAS20, 3.7 vs 3.7 in ASAS40, and 3.1 vs 2.8 in ASAS 5/6. Incremental CPRs relative to placebo were lower for adalimumab compared to secukinumab across all efficacy measures (Figure 1).

**Figure 1.** Incremental CPR of ASAS 20, ASAS 40 and ASAS 5/6 relative to placebo of adalimumab (12 weeks) vs. secukinumab (16 weeks)




**Conclusions:** In the absence of head to head trials comparing adalimumab and secukinumab, the current indirect comparison reduced cross-trial differences and provides timely and reliable evidence for physicians and payers. After adjusting for cross-trial differences in baseline characteristics, adalimumab demonstrated similar efficacy as secukinumab in terms of ASAS20, ASAS40 and ASAS 5/6 responses and was associated with lower incremental CPR compared with secukinumab over the trial period among patients with active AS.

**References:**
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**Disclosure of Interest:** K. Betts Consultant for: AbbVie, M. Mittal Shareholder of: AbbVie, Employee of: AbbVie, J. Song Consultant for: AbbVie, M. Skup Shareholder of: AbbVie, Employee of: AbbVie, A. Joshi Shareholder of: AbbVie, Employee of: AbbVie
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**THURSDAY, 9 JUNE 2016**

## Designing solutions to support young people to address the challenges of living with a rheumatic or musculoskeletal disease

### OP0116-PARE DEVELOPMENT OF THE GUIDE FOR NATIONAL ONLINE YOUTH PLATFORMS INCLUDING IMPLEMENTATION IN THREE COUNTRIES

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**Background:** Several countries have interest in building an online platform for youth (18–35) with RMDs. However, they face the challenges of lack of experience, know-how and access to best practices on how to prepare and implement such a platform. For more than 10 years the Netherlands has a successful online youth platform, called Youth-R-Well.com. During its long-term existence the Dutch youth group has obtained in-depth experience regarding how to build and maintain such an online community.
**Objectives:** For many countries who want to build an online youth platform it is hard to initiate, build and maintain a successful platform. Youth-R-Well.com wants to support other countries through the development and dissemination of a practical guide. This guide instructs youth groups to build and maintain attractive and lively online platforms for young people with RMDs.
**Methods:** The guide for building online youth communities is based on our own experiences and the content of the current and previous online platforms of Youth-R-Well.com. The guide includes our best practices and addresses the challenges we faced on the way to establish the platform and to make it sustainable. The guide helps with tips and tricks and includes information about what an online platform is and what the basic principles are, especially for youth with RMDs. It covers topics about how to start, what kind of resources you need and how to involve people at your platform. The guide is already tested in practice by three different countries and can be used by other youth groups. In addition to the guide, Youth-R-Well.com conducted two knowledge transfer programs funded by EULAR PARE with Romania, Poland and Italy to implement the guide. These working days focused on sharing knowledge, experience and best practices related to the online platforms. We helped the participating countries in setting up their online youth platform and we received valuable feedback to improve our guide. By giving presentations and workshops, all the participating countries had a concrete plan at the end of the program to start an online youth platform.
**Results:** The main result of this project is a tested guide to establish and maintain online youth platforms. The guide can be used by patient organizations in any European country. Other outcomes are trained youth experts in several countries and a growing number of online platforms in the future. Each participating country (Romania, Poland and Italy) has made a promising start and will hopefully within a few years have developed a successful platform. The countries are satisfied with the guide as support in building an online platform for youth with RMDs.
**Conclusions:** The guide is a successful method to start an online youth platform. Within the upcoming years the guide can be used in more countries. In the future the guide can be used to get a national online youth platform in every European country.

**Disclosure of Interest:** None declared
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### OP0117-PARE ILOA ELÄMÄÄN – PEER SUPPORT AND NETWORKING EVENT FOR CHILDREN, YOUTH AND FAMILIES WITH MSD DISEASE

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**Background:** Rheumatism can be difficult and enduring disease for the individual and their family. The day-to-day life is challenging and hard for the entire family. Furthermore, finding joy and positive energy can seem impossible at times. Networking and peer support along with positive feeling such as joy are important factors for sustaining good mental health inside the family and to support them in their everyday challenges with MSD diseases in the family.
**Objectives:** The Finnish Rheumatism Association wanted to continue the successful Iloa Elämään (joy/happiness to life) campaign. The Iloa Elämään campaign's objective is to increase mental wellbeing mainly through events targeted for individuals with MSD. The event focus group was mainly on children from ages three to fifteen with MSD and to their families. The main instalment of Iloa Elämää campaign is a recreational day to create joy and experiences through fun activities focused towards the children. Simultaneously, bringing new energy into the families challenging lives with illness. The event was also a gateway for networking; meeting other individuals with the same challenges in their lives and to get in touch with organisations looking after their interests.
**Methods:** The Finnish Rheumatism Association planned to create the event in cooperation with Haaga-Helia University of applied sciences and their degree programme student group. The promoting of the events were done through contact and channels of Finnish Rheumatism Association and the resources of the student group. The Finnish Rheumatism Association funded part of the project by organizing money collections in ice-hockey matches and provided content for the event. The rest was from sponsors. Sponsors such as Hesburger, Haikko Kartano-Kokous-Spa, Haribo and Helsinki's Viihdepelit.
To measure the success of the event students planned and implemented mixed method customer satisfaction research. The event was organized with close cooperation with both organisations, The Finnish Rheumatism Association and Haaga-Helia University of applied sciences.
**Results:** The event was held at Finland Porvoo Campus 28th of November. The event lasted and had many activities throughout the whole day and had approximately 110 participants. The event peaked with a music performance with the favourite Finnish band among the teenagers, TCT.
Based customer satisfactory research 80 percent of the respondents had a family member with MSD disease, 70 percent weren't in the previous and event 93 percent though the event was successful and they enjoyed the event.
The Finnish Rheumatism Association noticed an increase in new members after the event. Moreover, it can be said some of the individuals in the event had found and joined the Finnish Rheumatism Association through the event. Many families made friends and found peer families. They have stayed in touch and supported each other still long after the event. For example a child with a rare arthritis met a peer with the same diagnosis for the first time in his life.




**Conclusions:** The event is an important service that needs to be provided to members of the Finnish Rheumatism Association and other individuals with MSD

disease. The participants enjoyed a day filled with fun activities, networking, information and support. The organizers and the participants offered support to the families living with MSD thus many were able to find new life-long friends. The event was able to reach new members and people.
**Disclosure of Interest:** M. Ekroth Employee of: CEO
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**THURSDAY, 9 JUNE 2016**

## New insights into imaging

### OP0118 DEVELOPMENT OF THE EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN THE CLINICAL MANAGEMENT OF OSTEOARTHRITIS

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**Background:** The increased availability of modern imaging in clinical practice has led to its more extensive use. In the field of osteoarthritis (OA), recommendations on the use of imaging in clinical trials have been developed, but there has been less focus on routine clinical management.
**Objectives:** To develop evidence-based recommendations for the use of imaging in the clinical management of OA.
**Methods:** A task force convened by the European League Against Rheumatism including rheumatologists, radiologists, generalists, methodologists and patients from 9 countries developed recommendations based on both evidence obtained through systematic literature review (SLR) and expert opinion. The task force initially identified the areas of application of imaging in OA and developed research questions to drive the SLR. Imaging modalities included were conventional radiography, ultrasound, magnetic resonance imaging, computed tomography, radioisotope scan. Anatomical areas of interest were knee, hip, hand and foot. Based on the priorities identified by the task force, the role of imaging in making a diagnosis of OA and identifying OA features (including soft tissue, bone and cartilage involvement), in detecting alternative diagnoses, the impact of imaging on disease management, in defining prognosis (natural history of the disease and response to treatment), in the follow up of the disease and to guide treatment were addressed. Research evidence was searched systematically for each question and separately for each anatomic area using PubMed and Embase.
**Results:** The systematic review retrieved 6858 references, after the assessment of 1317 full papers, 380 studies were included. The results of the systematic review were presented to the task force, and consensus recommendations derived. These cover areas such as (exact wording not included for brevity reasons): the lack of need for imaging in diagnosis of patients who present with usual OA symptoms; role of imaging in differential diagnosis; consideration of the challenges in using imaging for routine monitoring of OA where there is no change in clinical status; what should be the feasible first choice modality and what issues were relevant to how images were acquired; how anatomical site of OA may influence use and type of imaging; and the role of imaging and intra-articular injection. Significant gaps in the literature underpinned the recommendations for future research that were also developed.
**Conclusions:** Based on the results of a SLR and expert opinion, recommendations on the use of imaging in the clinical management of OA were developed.
**Disclosure of Interest:** None declared
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### OP0119 PREDICTORS OF RADIOGRAPHIC PROGRESSION IN EARLY RHEUMATOID ARTHRITIS PATIENTS TREATED BY AN AGGRESSIVE TIGHT CONTROL REGIME

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**Background:** With implementation of tight control strategies and defined treatment targets in rheumatoid arthritis (RA) care, a majority of early RA patients may reach remission and traditional predictors of joint damage might no longer be present.
**Objectives:** To identify baseline parameters predictive of 2-year radiographic progression in an early RA population treated by a semi-personalized treat-to-target strategy.
**Methods:** DMARD naïve RA patients with <2 years from first swollen joint were included in the ARCTIC study. Patients were followed for 24 months with DAS, radiographs and ultrasound (32 joints, each scored 0–3 for gray-scale (GS) and power-Doppler (PD)). Patients were treated according to an aggressive algorithm with treatment target of DAS <1.6 and SJC44=0, and in half the patients, absence of ultrasound PD signal. Patients with risk factors for progressive joint destruction (ACPA or RF positive with baseline erosions, or MRI bone marrow edema) could be escalated more aggressively to biologics. Radiographs were scored by two readers using the van der Heijde-Sharp method, with cut-off ≥1 unit change/year to be classified as progression. The SDC was 1.94 units. Potential baseline predictors were analyzed for collinearity, and remaining variables (gender, age, smoking, BMI, disease duration <3 months, ACPA, RF, tender joints, 44 SJC, ESR, total GS-score, total PD-score, patient global and radiographic joint damage) assessed by univariate logistic regression. Variables with p<0.25 from the univariate analysis were included in the multivariate model building, and a p-value of <0.05 was required to remain in the model.
**Results:** Mean [SD] age of the 222 patients was 51.1 [13.7] years, disease duration 7.2 [5.4] months, and mean DAS 3.5 [1.2]. 63% were female, 72% RF and 82% ACPA positive. 92 (41%) had radiographic progression at 24 months, and 68% were in DAS remission at 24 months. In 16% of patients treatment was escalated more rapidly from MTX monotherapy to biologics due to baseline risk factors. Smoking, tender joints, 44 SJC, ESR, PD-score, age and gender had a univariate p-value<0.25 but did not remain in the final model. In the multivariate model, RF positivity (OR 2.27, p-value 0.022), total van der Heijde Sharp score (OR 1.08, p-value 0.017) and ultrasound GS score (OR 1.03 per unit, p-value 0.019) were independent baseline predictors for radiographic progression at 24 months (table).

Table 1. Multivariate model for baseline predictors of radiographic progression at 24 months. Model corrected for age and gender

| Baseline variables | Radiographic progression at 24 months (n=92/222) | | | |
|---|---|---|---|---|
| | Univariate | | Multivariate | |
| | OR [CI] | P-value | OR [CI] | P-value |
| US GS-score (0–96) | 1.03 [1.01, 1.05] | 0.005 | 1.03 [1.00, 1.05] | 0.019 |
| RF positivity (IgM/IgA) | 1.78 [0.96, 3.29] | 0.07 | 2.27 [1.13, 4.57] | 0.022 |
| Total van der Heijde Sharp score | 1.11 [1.06, 1.17] | <0.001 | 1.08 [1.01, 1.14] | 0.017 |

**Conclusions:** RF positivity, radiographic joint damage and ultrasound gray-scale score were independent baseline predictors of joint damage in early RA patients treated according to an aggressive regimen aiming for remission. This indicates that extensive individualization of treatment based on risk factors might be needed to optimize disease outcomes, also in treat-to-target strategies.
**Disclosure of Interest:** None declared
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### OP0120 POST-PROCESSING TECHNIQUES FOR ENHANCED VISUALIZATION OF PULMONARY VASCULITIS AND PULMONARY THROMBOSIS BY MULTISLICE SPIRAL COMPUTED TOMOGRAPHY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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**Background:** Ground-glass opacification (GGO) is a common but non-specific radiological pattern on multislice spiral computed tomography (MSCT) scans which can refer to the interstitial or vascular involvement. Due to polymorphism of pulmonary pathology in patients with systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) GGO requires a multi-stage differential diagnosis the result of which will significantly affect the treatment regimen - a choice between antibiotic or cytostatic and high-dose hormonal therapy.
**Objectives:** The aim of this study was to optimize the ability of MSCT for differentiating between interstitial and vascular involvement and detecting pulmonary thrombosis using newly developed post-processing techniques.
**Methods:** 120 patients, aged 39.5 ± 13.7, with moderate-severe lupus activity were administrated a complex of laboratory, pulmonary function and imaging tests. It is the first time when post-processing techniques (PPTs) such as MPR (Multiplanar reformations), MIP (Maximum intensity projection), mIP (Minimum intensity projection) and especially color mapping were used for evaluation of vascular involvement on native MSCT scans of patients with SLE and APS. The criteria of pulmonary vasculitis on color maps were described as enhanced peripheral vascularization (vessel caliber enlargement and increase in vessel tortuosity) and perivascular edema. The criteria of pulmonary thrombosis - areas of micro-infarctions in the peripheral regions of lungs. CT angiography and pulmonary perfusion scintigraphy were chosen as methods of gold standard. Reconstructed scans were compared with native CT scans, CT angiograms and perfusion scans done by three diagnosticians.
**Results:** Statistics showed that the mean area under the receiver operating characteristic curve value increased significantly from 0.713 without the PPTs

to 0.925 with the PPTs ($P<0.05$) in differentiating between vasculitis and pneumonic infiltration and increased significantly from 0.527 without the PPTs to 0.724 with the PPTs ($P<0.05$) in detecting thrombosis. Compared with CT angiogram and perfusion scans no differences in the involved regions were detected. Variants that were associated with enhanced peripheral vascularization on color maps in a significant manner were: rate of diffusion capacity (p=0.006), hypocomplementemia (p=0.01), hypoxemia (p=0.003), pulmonary hypertension (p=0.01). The presence of lupus anticoagulant in patients with SLE was associated with the development of pulmonary thromboembolism (p=0.001) and pulmonary vasculitis complicated with thrombosis in situ (p=0.04).

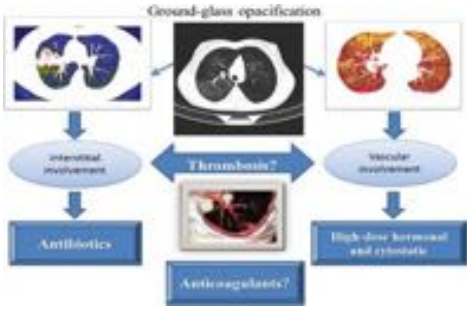



Image 1. Multi-stage differential diagnosis of GGO in patients with SLE and APS using PPTs.

**Conclusions:** PPTs are a useful addition to native MSCT scans in detecting early signs of pulmonary vasculitis, differentiating between vasculitis and pneumonic infiltration and evaluation of treatment-related changes. It equips radiologists to more easily detect areas with thrombosis especially thrombosis in situ due to pulmonary vasculitis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3989

## OP0121 SAFETY, TOLERABILITY AND FEASIBILITY OF MINIMALLY INVASIVE ULTRASOUND-GUIDED SYNOVIAL BIOPSY OF WRIST AND METACARPOPHALANGEAL JOINTS - AN ULTRASOUND FOLLOW-UP STUDY

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**Background:** Synovitis is the common feature of patients suffering from inflammatory arthropathies (IA). The development of ultrasound (US)-guided synovial biopsy will enable synovial tissue collection from small joints and will facilitate molecular studies, thus improving the understanding of mechanisms of IA as small joints are frequently involved in these diseases.
**Objectives:** To assess the safety, tolerability and feasibility to perform synovial biopsies from wrist and metacarpophalangeal (MCP) joints, using a minimally invasive US-guided technique in patients suffering from rheumatoid arthritis (RA), spondylarthropathies (SA) or undifferentiated arthritis (UA).
**Methods:** Two target joints (TJ) were biopsied: wrist and MCP. Patients with at least one clinically swollen joint at these levels, suffering from RA, SA, or UA underwent a US examination. The TJ chosen for the biopsy was the joint with the most important inflammatory changes on gray-scale (GS) US. GS synovitis and power-Doppler (PD) activity were assessed by OMERACT scores, on the day of the biopsy, as well as 2 weeks (w), 6w and 6 months (m) after the biopsy. In addition, tendon tears, hematoma, paratenonitis and tenosynovitis were searched by US. Patient-reported outcomes (PRO) included a standard questionnaire given to all patients on the day of the biopsy as well as 1w, 2w, and 6w after the biopsy. Tolerability and the patient-reported willingness to repeat the procedure was assessed using the 5-point Likert scale.
**Results:** Forty-one patients suffering from RA (27), SA (7) and UA (7) underwent US-guided biopsy of the wrists (20) and MCP (21) joints. A non-significant increase in pain was reported 24 h after the procedure. No difference in PRO of the biopsied joints was reported 2w and 6w after the biopsy, as compared to assessment before the biopsy. No infection or haemorrhage was observed after the biopsy. PRO did not differ significantly among patients suffering from RA, SA or UA. At the TJ, US scores tended to decrease 2w after the procedure. At 6w and 6m follow-up, no safety concerns were reported. Treatment response at the TJ was similar to the response of non-biopsied joints matched for the baseline US parameters.
**Conclusions:** With the exception of study of Kelly et al (Ann Rheum Dis. 2015;74:611–6117), data on safety, tolerability, feasibility and PRO using the minimally invasive US-guided biopsy technique are lacking. In this work, we confirm that US-guided biopsy of wrist and MCP joints is feasible, safe and well tolerated by RA patients. At 2w, 6w and 6m follow-up, no safety concerns were reported. Furthermore, no differences in PRO between RA, SA and UA were observed. This technique is therefore a promising approach to assess the presence and persistency of synovial inflammatory processes in patients with early and refractory IA, and to facilitate patients stratification according to transcriptomic profiles.

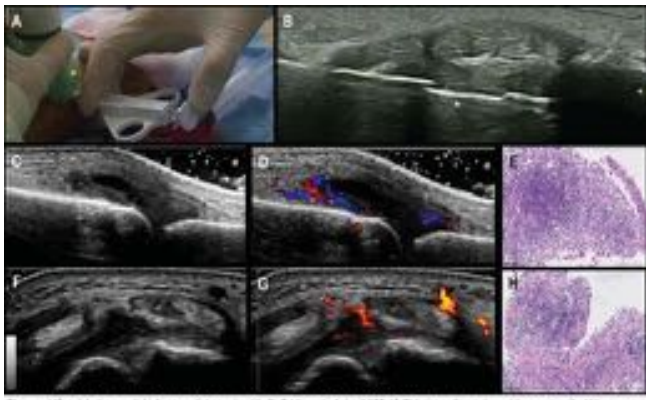


Figure. US-guided synovial biopsy of the wrist (A, B, F-H) and of the MCP (C-E) joints. Synovium biopsy needle (A) as seen with US (B) at the wrist level. A guillotine-type needle with an open throw (*) is used to cut the tissue. Prior to biopsy, MCP (C, D) synovitis is depicted by GS-US (C) and by color Doppler-US (D). Wrist synovitis (F, G) is depicted by GS-US and by PD-US (G). Histological images (E and H) of the corresponding GS-US (C and F) and Doppler US (D and G) images showing (*)oo, vessel proliferation and strong inflammatory infiltrates in the synovial sublining.

**Acknowledgement:** We acknowledge Pr C. Pitzalis and S. Kelly for giving us the opportunity to learn and further disseminate minimally invasive ultrasound-guided technique, and for fruitful discussions.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5386

## OP0122 INTER-READER AND INTRA-READER RELIABILITY OF THE NEW OMERACT ULTRASONOGRAPHIC CRITERIA FOR THE DIAGNOSIS OF CPPD

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**Background:** Ultrasonography (US) has been implemented recently as a possible diagnostic method for CPPD [1]. However, data on the reliability of US in CPPD diagnosis are lacking
**Objectives:** To assess the inter-reader and intra-reader reliability of US on detecting CPP deposition in fibrocartilage (FC), hyaline cartilage (HC), tendons (T) and synovial fluid (SF)
**Methods:** The OMERACT "US in CPPD" group defined firstly the US CPPD identification criteria according to methods described in an another abstract submitted in this congress. Subsequently, a two steps procedure for the assessment of the reliability has been followed. Firstly, the panel gave a dichotomous score on the presence absence of CPPD in 150 photos of FC, HC, T and SF equally distributed, on a web based platform. The assessment has

| Section | K inter-reader I round | K inter-reader II round | K intra-reader |
|---|---|---|---|
| | WEB based exercise | | |
| Fibrocartilage | 0.58 | 0.58 | 0.80 |
| Hyaline Cartilage | 0.73 | 0.73 | 0.85 |
| Tendons | 0.28 | 0.31 | 0.64 |
| Synovial Fluid | 0.50 | 0.47 | 0.76 |
| | Patient based workshop | | |
| ALL | 0.44 | 0.45 | 0.62 |
| - Knee | 0.47 | 0.52 | 0.65 |
| — Menisci | 0.65 | 0.64 | 0.73 |
| —— Medial Meniscus | 0.72 | 0.74 | 0.78 |
| —— Lateral Meniscus | 0.57 | 0.48 | 0.70 |
| — Synovial Fluid | 0.09 | 0.12 | 0.41 |
| — Tendon | 0.25 | 0.3 | 0.44 |
| —— Quadriceps Tendon | 0.13 | 0.19 | 0.28 |
| —— Proximal Patellar Tendon | 0.09 | 0.19 | 0.47 |
| —— Distal Patellar Tendon | 0.31 | 0.25 | 0.44 |
| — Hyaline Cartilage | 0.58 | 0.55 | 0.88 |
| - Wrist | 0.31 | 0.2 | 0.50 |
| — Triangular fibrocartilage | 0.27 | 0.15 | 0.47 |
| — Synovial Fluid | 0.15 | 0.1 | 0.36 |

Strength of agreement: < 0.20 Poor, 0.21 - 0.40 Fair, 0.41 - 0.60 Moderate, 0.61 - 0.80 Good, 0.81 - 1.00 Very good

been carried out twice in order to calculate both inter and intra-reader reliability. In the second step, the experts met for a real life-patient based assessment of CPPD in a workshop organised in Siena-Italy. In that occasion, FC/HC/T/SF of the right knee and FC and SF of the right wrist of 8 patients were assessed twice in a day by all experts giving again a dichotomous score for CPPD. 8 US scanners (ESAOTE mylab seven) equipped with the same probe and the same preset (made ad hoc before the meeting), have been used for the workshop.
**Results:** Reliability values of the web based exercise and of the workshop are presented in table 1. Tendons and synovial fluid analysis did not reach sufficient strength of agreement neither on the web based nor in the patient based exercise regarding the inter-reader kappa and independently of the site. However, in the static exercise, both tendons and SF reached a good intra-reader reliability meaning that scanning technique of these structures is very important for CPPD identification. On the other hand, menisci (but not triangular FC of the wrist) and HC reached good kappa values for inter-reader and intra-reader agreement both on static and web-based exercise
**Conclusions:** Knee cartilage and fibrocartilage structures resulted to be reliable enough for identification of CPPD. On the other hand, CPPD identification in tendons and synovial fluid is challenging and the actual OMERACT criteria for these sites do not ensure a safe classification of patients.
OMERACT US criteria for CPPD identification in knee menisci and HC allow a reliable classification of patients and should be used when CPPD is suspected.
**References:**
[1] Zhang W, Doherty M, Bardin T, et al. European League Against Rheumatism recommendations for calcium pyrophosphate deposition. Part I: terminology and diagnosis. Ann Rheum Dis 2011;70:563–70
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5183

## OP0123 MRI-DETECTED INFLAMMATION IS ASSOCIATED WITH FUNCTIONAL DISABILITY IN EARLY ARTHRITIS

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**Background:** MRI sensitively detects inflammation, but the clinical relevance of MRI-detected inflammation is undetermined in early arthritis. Therefore, this cross-sectional study investigated the association between MRI-detected inflammation of hands and feet and functional disability in early arthritis.
**Methods:** 514 early arthritis patients, consecutively included in the Leiden Early Arthritis Clinic, were studied. At baseline, unilateral 1.5T MRI of the wrist, metacarpophalangeal (MCP) and metatarsophalangeal-joints was made and functional disability was measured using the Health Assessment Questionnaire (HAQ). MRIs were scored for bone marrow oedema (BME), tenosynovitis and synovitis by two readers. The sum of these three features yielded the total MRI-inflammation score. Linear and non-linear regression analyses were performed with HAQ as dependent variable.
**Results:** The total MRI-inflammation score was associated with the HAQ-score ($\beta$=0.014, $p<0.001$), as were BME ($\beta$=0.015, $p<0.001$), tenosynovitis ($\beta$=0.046, $p<0.001$) and synovitis ($\beta$=0.039, $p<0.001$) separately. Analysing these three MRI-features in one multivariable model, revealed that only tenosynovitis was independently associated with HAQ-score ($\beta$=0.039, $p<0.001$). Also when correcting for age, gender, joint counts, acute phase reactants and auto-antibodies this association remained ($\beta$=0.034, $p<0.001$). MRI-detected inflammation at wrists or MCP-joints associated significantly with impairments in hand functioning (e.g. difficulties with opening milk cartons or jars). Exploring the relation between MRI-detected inflammation and HAQ-scores non-linear, suggested the presence of a ceiling effect, because after a certain inflammation-level, more inflammation was not associated with higher HAQ-scores.
**Conclusions:** MRI-detected inflammation, and tenosynovitis in particular, is associated with functional disability. This demonstrates the functional relevance of MRI-detected inflammation in early arthritis patients.
**References:**
[1] df
**Acknowledgement:** This work was supported by a Vidi-grant of the Netherlands Organisation for Scientific Research and the Dutch Arthritis Foundation
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2332

## OP0124 IMAGING REMISSION BY MUSCULOSKELETAL ULTRASOUND LEADS TO A BETTER FUNCTIONAL OUTCOME – RESULTS OF THE US IMPERA STUDY - US 7-SCORE IMPLEMENTATION STUDY IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Novel treatment options together with a treat-to-target strategy present new challenges to imaging procedures in terms of therapy monitoring.
**Objectives:** To evaluate the functional outcome measured by Health Assessment Questionnaire (HAQ) as the primary outcome in patients with early rheumatoid arthritis (RA) who were treated by standard clinical care (clinical cohort) in comparison to patients in whom treatment decisions were additionally based on musculoskeletal ultrasound (US) using the US7 score (US-cohort) in a nationwide investigator initiated study in Germany.
**Methods:** Functional (HAQ), clinical (DAS28, patient's Visual Analogue Scale [VAS] for disease activity) and laboratory parameters (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) were analyzed at seven different time points for a total of 18 months and compared between the two study cohorts. Treatment decision was made according to local standard of care (SOC) with a treatment goal of DAS28 <3.2. In the US-cohort, imaging remission criteria were defined as Gray-scale US (GSUS) <2 and Power Doppler-US (PDUS) =0 per joint level. In a subgroup analysis, US patients were analyzed separately with regard to imaging remission status and the parameters outlined above.
**Results:** Data of 313 patients (US-cohort [n=166], clinical cohort [n=147]) demonstrated a reduction of HAQ, DAS28, VAS and laboratory activity (ESR, CRP) to a low disease activity status 18 months after the beginning/change of antirheumatic therapy according to SOC (table 1). The results of functional and clinical outcome in both cohorts did not show significant differences. However, subgroup analysis of the US-cohort with imaging remission resulted in a significantly lower HAQ, DAS28 and VAS compared to patients not fulfilling these US remission criteria (table 1).

| | | HAQ | DAS28 | ESR (mm/h) | CRP (mg/l) | Patient's VAS (mm) |
|---|---|---|---|---|---|---|
| **Baseline** | | | | | | |
| Total population (n=313) | Clinical cohort (n=147) | 1.020 | 5.1 | 33.1 | 23.0 | 56.9 |
| | US-cohort in total (n=166) | 1.050 | 5.2 | 29.3 | 17.2 | 57.3 |
| | | p=0.600 | p=0.596 | p=0.194 | p=0.073 | p=0.998 |
| Subgroup analysis of US-cohort (n=166) | Non-remission group (n=87) | 1.120 | 5.3 | 32.2 | 20.6 | 57.1 |
| | Remission group (n=79) | 0.971 | 5.1 | 26.2 | 13.7 | 57.4 |
| | | p=0.200 | p=0.316 | p=0.182 | p=0.272 | p=0.945 |
| **Month 18** | | | | | | |
| Total population (n=313) | Clinical cohort (n=147) | 0.555 | 2.8 | 18.1 | 6.4 | 26.7 |
| | US-cohort in total (n=166) | 0.579 | 2.8 | 16.6 | 6.4 | 25.6 |
| | | p=0.758 | p=0.800 | p=0.174 | p=0.585 | p=0.397 |
| Subgroup analysis of US-cohort (n=166) | Non-remission group (n=87) | 0.741 | 3.4 | 18.4 | 7.8 | 33.9 |
| | Remission group (n=79) | 0.481 | 2.2 | 14.6 | 4.6 | 16.6 |
| | | p=0.002* | p=0.001* | p=0.406 | p=0.089 | p<0.001* |

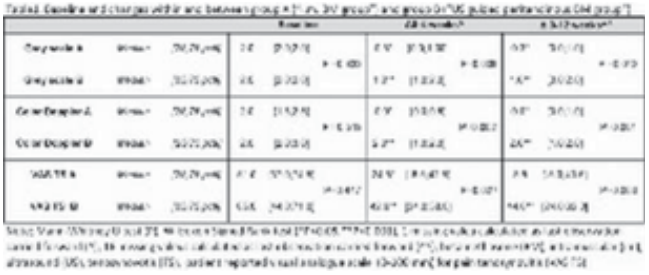
*p<0.05 for significant difference

**Conclusions:** Treatment strategies by a treat to target approach in early RA patients reduced disease activity and improved functional outcome of HAQ irrespective of imaging guidance. However, patients with imaging remission by US exhibited a significantly better functional outcome and lower disease activity status. Accordingly, an additional ultrasound examination aiming at imaging remission should be strongly considered in clinical practice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5892

OP0125 **A RANDOMISED, DOUBLE-BLIND, CONTROLLED STUDY OF INTRAMUSCULAR VERSUS ULTRASOUND GUIDED PERITENDINOUS BETAMETHASONE INJECTION FOR TENOSYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Intra-articular glucocorticoid (eg. betamethasone (BM)) injections are commonly used during flares in rheumatoid arthritis (RA)[1]. Currently, evidence on the best approach to treat tenosynovitis (TS) is lacking.
**Objectives:** To compare the effect of intramuscular (im) and ultrasound (US) guided peritendinous BM injection for TS in RA patients, after 4 and 12 weeks.
**Methods:** Fifty RA patients with TS were randomised into two double-blinded groups: Group A ("i.m. BM group") received im injection of 14 milligrams (2 ml) of BM and US-guided saline injection in up to two tendon sheaths (maximum 1 ml saline for each tendon sheath) and group B ("US guided peritendinous group") received 2 ml of saline im and US guided BM injection in up to two tendon sheaths (maximum 7 milligrams (1 ml) of BM for each tendon sheath). All patients were in stable anti-inflammatory treatment prior to and during the study. Patients were excluded, and considered non-responders, if treatment changes were made during the follow-up period. TS was assessed at baseline, 4 and 12 weeks using the semi-quantitative scoring system for Grey scale (GS) (0–3) and Colour Doppler (CD) (0–3) proposed by the OMERACT US group and a patient reported visual analogue scale (0–100 mm) for pain TS (VAS TS). If two tendon sheaths were treated, the mean score was used for statistical calculation. For US assessment a GE Logiq E9 US unit with a high frequency linear 6–15 ML probe and CD settings according to published recommendations were used. The predefined primary outcome was a US-TS GS score $\leq$1 and CD score =0, at week 4, with a non-responder imputation (NRI) used for missing data. The same outcome was used at week 12, with a NRI used for missing data.
**Results:** Forty-nine patients received treatment, 24 in group A and 25 in group B. The completion rate for group A/B was 23/25 at 4 weeks and 15/18 at 12 weeks. There was no significant baseline difference between the groups, except that two tendon sheaths were injected more often in group A (10) compared to B (3). The chance of achieving the primary outcome at week 4 was 0.25 (95% Confidence limits; 0.08; 0.42) in group A and 0.64 (0.45; 0.83) in group B and for 12 weeks 0.08 (0.00; 0.19) in group A and 0.40 (0.21; 0.59) in group B (Chi-Square; 4 weeks =0.008; 12 weeks =0.020). Likewise VAS TS showed significant better response in group B versus group A (Mann-Whitney U test; 4 weeks =0.027; 12 weeks =0.003). Baseline values and 4 and 12 weeks changes for GS, CD and VAS TS are presented in table 1.



**Conclusions:** In a randomized double-blind clinical trial, RA patients with tenosynovitis responded significantly better to US guided peritendineus glucocorticoid injection compared to i.m. glucocorticoid injection, both at 4 and 12 weeks, both when assessed by US and patient-reported outcomes.
**References:**
[1] Hetland ML, Ostergaard M, Ejbjerg B, et al. Short- and long-term efficacy of intra-articular injections with betamethasone as part of a treat-to-target strategy in early rheumatoid arthritis: impact of joint area, repeated injections, MRI findings, anti-CCP, IgM-RF and CRP. Annals of the Rheumatic Diseases 2012;71
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1707

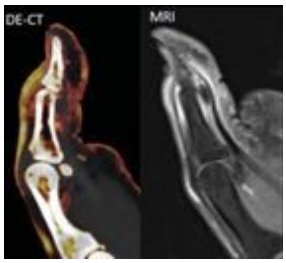
**THURSDAY, 9 JUNE 2016**

## Advancements in the imaging of PsA

OP0126 **DUAL ENERGY CT WITH IODINE MAP IS PROMISING NEW IMAGING MODALITY IN THE EVALUATION OF HAND PSORIATIC ARTHRITIS**

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**Background:** Magnetic resonance (MR) imaging allows to visualize inflammatory lesions of psoriatic arthritis (PsA). However, evaluation of the small joints of the hands remains a challenge. CT has a high spatial resolution, therefore it is suitable to evaluate small structures. In spite of this advantage, CT usage in inflammatory arthritis has been limited because of its poor contrast resolution. However, iodine map, the amount of iodine distribution in each voxel, can be created by the so-called three material decomposition from imaging data obtained with Dual-Energy CT (DE-CT)[1)]. Because DE-CT with iodine map has both high spatial resolution and high iodine contrast resolution, we hypothesized this technic can be useful in evaluation of inflammatory lesions of PsA
**Objectives:** To assess the feasibility of DE-CT with iodine map in the evaluation of hand PsA
**Methods:** Materials were 16 (11 male 5 female) consecutive psoriasis patients with finger joint symptoms. All patients fulfilled CASPER criteria. The Patients were scheduled for both contrast enhanced DE-CT and contrast enhanced MR imaging within 1 month. There was no therapeutic intervention between 2 examinations. Images were evaluated by 2 radiologists independently under blinded to clinical data and other images. For evaluation of both DE-CT and MR imaging, we modified the OMERACT Psoriatic Arthritis Magnetic Resonance Imaging Scoring System (PsAMRIS)[2)]. For inflammatory lesions (synovitis, flexor tenosynovitis, and extensor peritendinitis) graded as 0–3 and bone erosion graded as 0–10, inter-reader agreement was calculated with using weighted $\kappa$. For other inflammatory lesion (periarticular inflammation) and structural change (bone proliferation), which were scored as grade 0–1, inter-reader agreement was calculated with using $\kappa$. With using consensus score, sensitivity and specificity of DE-CT for inflammatory lesions were calculated with MR imaging as gold standard. As for structural changes, we used DE-CT as gold standard and calculated sensitivity and specificity of MR imaging.
**Results:** Inter-reader agreement of inflammatory lesions were good or very good (weighted $\kappa$=0.83 and $\kappa$=0.75 in DE-CT, weighted $\kappa$=0.81 and $\kappa$=0.87 in MR imaging). Although inter-reader agreement of MR imaging for bone proliferation was moderate ($\kappa$=0.44), it was good (weighted $\kappa$=0.77) for bone erosion. Inter-reader agreement of CT for structural changes were good ($\kappa$=0.66) for bone proliferation and very good (weighted $\kappa$=0.84) for bone erosion. Sensitivity and specificity of DE-CT for inflammatory lesions were 0.78 and 0.87. However, DE-CT detected 134 various inflammatory lesions which were not observed on MR imaging, out of 1120 evaluated inflammatory items. Of these 134 lesion, 69% (93/134) was located in the DIP joints. About structural changes, MR imaging had poor sensitivity (0.30) and high specificity (0.99).




**Conclusions:** DE-CT with iodine map has found to be a useful new imaging modality to evaluate PsA of hands, and may have higher detection capability of small joint inflammatory lesions compared with MR imaging.
**References:**
[1] Kuno H, et al. Radiology 2012: 265; 488–496.
[2] Ostergaard M, et al. J Rheum 2009: 36; 1816–1824.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3059

### OP0127 LOW FREQUENCY OF US DETERMINED EROSIONS IN EARLY PSORIATIC ARTHRITIS: RESULTS FROM THE LEEDS SPARRO COHORT

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**Background:** Ultrasound (US) is playing an increasingly important role in the early evaluation of psoriatic arthritis (PsA) being capable of detecting inflammatory changes at the enthesis, synovium and extra capsular tissues. Peri-articular radiographic erosions in PsA and rheumatoid arthritis are associated with a worse outcome. Further, US is shown to be a more sensitive imaging technique than conventional radiography (CR) to identify erosions in early RA. By contrast, there is a paucity of data in the literature on the prevalence of erosions and/or the capability of US to detect erosions in early PsA.
**Objectives:** To assess the prevalence of erosions in early PsA using CR and high resolution US.
**Methods:** We studied 860 joints of 43 patients (Table 1) with early PsA, all fulfilling CASPAR criteria from the Leeds Spondyloarthropathy Register for Research and Observation study (SpARRO) which is a prospective longitudinal observational cohort of patients with early spondyloarthritis. Radiographic and sonographic erosions of the wrists, MCPs (2, 3), PIPs (2, 3), and MTPs (1–5) bilaterally were independently evaluated. We looked at the frequency of erosions using both imaging methodologies. CR and US scoring systems used for defining erosions were the van der Heijde version of the Sharp and OMERACT respectively.
**Results:** Erosions were identified in a total of 8 patients, all negative for RF and CCP antibodies; 40% (3/8) of whom were ex-smokers. Four patients had six erosions at MTP4, MTP5, and PIP3 by CR whilst six patients had six erosions on US. The exact agreement between the 2 methods was 99%. Agreement on absence of erosions in both CR and US was 99% while agreement on their presence was 17%. The proportions of joints where the CR and US disagreed in either direction (US>XR, US

Table 1. Baseline clinical characteristics of the 43 patients

| | |
|---|---|
| Age, mean ± SD years | 42±13 |
| Female to male ratio | 1.5 |
| RF positive | 1/43 |
| CCP positive | 1/43 |
| Symptom disease duration in months, median (IQR) | 12 (6–25) |
| Disease pattern | |
| Asymmetrical | 29/43 |
| Symmetrical | 14/43 |
| Polyarthritis | 32/43 |
| Oligoarthrtis | 11/43 |
| SJC , median (IQR) | 2 (0–6) |
| TJC, median (IQR) | 7 (4–18) |
| Dactylitis at presentation | 19/43 |
| MASES at presentation, median (IQR) | 1 (0–3) |
| Nail psoriasis at presentation | 21/43 |
| PASI, median (IQR) | 2 (1–5) |
| Psoriasis at presentation | 39/43 |
| Medications at presentation | 22 (No treatment), 17 (NSAIDs only), 1 (Methotrexate), 1 (Prednisolone), 2 (Non-biologic DMARD+NSAID) |

**Conclusions:** In keeping with the emerging data in PsA, these results show a low frequency of erosions at clinical presentation on CR. Unlike studies in early RA, in this preliminary study of early PsA the burden of erosive disease detected using US was not measurably different.
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**THURSDAY, 9 JUNE 2016**

## When and how to treat Raynaud's phenomenon and related complications

### OP0128 EVALUATION OF PERIPHERAL BLOOD PERFUSION BY LASER SPECKLE CONTRAST ANALYSIS IN SYSTEMIC SCLEROSIS PATIENTS TREATED WITH AMINAPHTONE

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**Background:** Both primary (PRP) and secondary Raynaud's phenomenon (SRP) are characterized by impairment of the microvascular system, with clinical symptoms related to decreased peripheral blood perfusion (1,2). Different treatments are available to manage digital vasculopathy (3). Aminaphtone seems to downregulate endothelin-1 production in endothelial cells, and ameliorates RP symptoms (4,5). Laser speckle contrast analysis (LASCA) is a validated technique to assess blood perfusion (2).
**Objectives:** To evaluate short-time effects of aminaphtone treatment on blood perfusion by LASCA technique in patients affected by PRP or SRP.
**Methods:** Thirty-five patients with active RP were enrolled during routine clinical assessment in November 2015 (26 SRP, mean age 64±17 SD years, mean RP duration 10±7 years; 9 PRP, mean age 49±21 SD years, mean RP duration 5±3 years). Aminaphtone 75 mg twice daily was administered in addiction to current treatments (patients were on stable drug regimen from at least two months, and did not modify it during follow-up). Blood perfusion was assessed in all patients by LASCA at baseline (T0), after one (T1) and four weeks (T4) of treatment, at the level of fingertips, periungual areas, dorsum and palm of hands, tip of noise, zygoma, forehead, and perioral regions. Blood perfusion was calculated as perfusion units (PU) (2). Raynaud condition score (RCS), Raynaud's attach frequency and duration were also assessed at the same times.
**Results:** A progressive statistically significant increase of blood perfusion was observed from T0 to T4 in all skin areas (median PU at T0, T1, T4 respectively: fingertips 56, 93, 108; periungual areas 44, 81, 90; dorsum of hands 38, 64, 73; palm of hands 60, 85, 99; tip of noise 95, 114, 124; zygoma 134, 140, 150; forehead 113, 117, 130; perioral region 138, 144, 149; whole face 121, 132, 143. $p<0.0001$ for all areas). In particular, all patients treated with aminaphtone showed an increase of blood perfusion from T0 to T1, and 30 out of 35 patients had a further increase of blood perfusion from T1 to T4. A progressive statistically significant decrease of RCS (median at T0, T1, T4: 7, 6, 4) Raynaud frequency (median at T0, T1, T4: 2, 2, 1 attacks/day) and duration (median at T0, T1, T4: 20, 20, 10 minutes) was also observed from T0 to T4 ($p<0.0001$). The results were similar for both PRP and SRP. Two patients had to stop the drug due to headache.
**Conclusions:** This study demonstrates that the therapy with aminaphtone seems to increase in short-time and maintain skin blood perfusion, as well as seems to improve RP symptoms. Larger studies might further confirm the role of aminaphtone in the treatment of RP secondary to systemic sclerosis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3944

### OP0129 NAILFOLD CAPILLAROSCOPY IN RHEUMATOLOGY PRACTICE - A SINGLE CENTER EXPERIENCE

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**Background:** Nailfold capillaroscopy (NCP) is an easy, non-invasive and useful tool for the diagnosis and follow-up of Systemic Sclerosis (SSc) and other systemic rheumatic diseases.
**Objectives:** To present our single center experience with NCP, describing the main reasons for NCP request, and the major abnormalities detected in capillaroscopy.
**Methods:** Retrospective analysis of patients submitted to NCP assessment, from January 2013 to December 2015 in our center. We collected reasons for NCP request, demographic and clinical data, autoimmunity profile and NCP results.
**Results:** A total of 221 NPC, corresponding to 197 patients, 167 females (84.8%) and 30 males (15.2%) aged from 9 to 90 years were reviewed. One hundred and thirty eight (62.4%) patients had no definitive diagnosis, 53 patients (24%) had SSc, 7 (3.2%) had mixed connective tissue disease, 3 (1.4%) had dermatomyositis/polymyositis (DM/PM), and 3 (1.4%) antiphospholipid syndrome (APS).
Raynaud's phenomenon (RP) alone was the most frequent reason for requesting NCP (33% of the cases), and combined with ANA positivity accounted for another 30.8% of the requests. RP was present in 73.3% of the patients, acrocyanosis in 16.3%, livedo reticularis and puffy hands accounted for 8.6% each one.

Anti-nuclear antibodies (ANA) were positive in 59.7%, anti-centromere antibodies were present in 21.3%, anti-topoisomerase I and SSA/SSB in 5.1% of the cases. One hundred and fifty nine (71.9%) NCP were considered abnormal. The most frequent specific disease pattern was the early one (Cuttolo) in 15%. The most frequent findings were: capillary tortuosity in 112 (71.8%) cases, capillary dilatations in 95 (60.9%), and hemorrhages in 85 (54.5%). NCP was abnormal in 79.4% of patients with RP and ANA, 41.2% of them displaying specific findings of rheumatic diseases (Table 1).
In SSc patients the late and the early pattern (Cuttolo) were the most frequent, present in 15 and 13 NCP, respectively. Concerning specific NCP findings capillary dilatations (81%), hemorrhages (73.6%) and megacapillaries (71.7%) were the most frequent (Table 2).
Of the 138 cases without definitive diagnosis, 61. 6% had abnormal NCP, although mostly with non-specific patterns (50%). In 10 (7.2%) patients NCP helped to establish the diagnosis: VEDOSS (Very Early Diagnosis of Systemic Sclerosis) in 6, antiphospholipid syndrome in 3 and DM in one case.

| Reasons for requesting NCP / NCP results | Isolated RP N=73 | ANA positive N= 23 | RP + ANA N= 68 | Other reasons N= 57 |
|---|---|---|---|---|
| Normal (%) | 38.4 | 26.1 | 20.6 | 26.7 |
| Abnormal (%) | 61.6 | 73.9 | 79.4 | 73.3 |
| NCP with pathologic findings (%)* | 13.7 | 17.4 | 41.2 | 30 |

Table 1 – Relationship between the reasons why the clinicians asked a NCP (Nailfold capillaroscopy) and results of the exam. *Diseases specific NCP findings, detected in the abnormal capillaroscopy group.

| Diseases | SSc N=53 | MTCD N=7 | Sjogren S N=5 | RA N=4 | DM/PM N=3 |
|---|---|---|---|---|---|
| NCP findings | capillary dilatations (81%) | capillary dilatations (80%) | Capillary dilatations (80%) | Capillary tortuosity (75%) | Capillary dilatations (80%) |
| | Hemorrhages (73.6%) | Hemorrhages (80%) | neoagiogenesis (60%) | megacapillaries (50%) | Hemorrhages (80%) |

Table 2 – Most frequent NCP findings in Systemic sclerosis (SSc), Mixed connective tissue disease (DMTC), Primary Sjogren Syndrome (Sjogren S.), Rheumatoid arthritis (RA) and Dermatomyositis/Polymyositis (DM/PM) patients.

**Conclusions:** In our experience, NCP was helpful for the diagnosis of rheumatic systemic disease. Specific NCP findings were more frequent in patients with RP + ANA positivity, suggesting that this combination is associated with more disease incidence. Patients with isolated RF had less pathologic NCP findings than those with isolated. ANA positivity. The prospective follow up of those patients with abnormal NCP and no definitive diagnosis will help to establish the predictive value of observed alterations.

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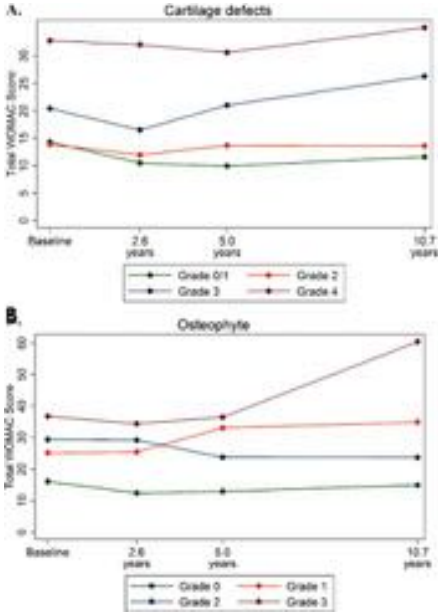
**THURSDAY, 9 JUNE 2016**

## Role of new imaging techniques as RMD outcomes -

### OP0130 RADIOGRAPHIC AND MAGNETIC RESONANCE IMAGING MARKERS PREDICT CARTILAGE VOLUME LOSS AND KNEE SYMPTOMS OVER 10.7 YEARS IN OLDER ADULTS

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**Background:** There are no long-term studies that describe the independent association of radiographic and magnetic resonance imaging (MRI) based markers and cartilage volume loss and knee symptoms in population-based older adults.
**Objectives:** To describe whether radiographic (joint space narrowing (JSN) and osteophytes) and MRI-based (cartilage defects, bone marrow lesions (BMLs), meniscal tears and meniscal extrusion) measures predict long-term cartilage volume loss and knee symptoms over 10.7 years.
**Methods:** 983 participants (mean age 62.8 years, 50% female) were randomly recruited from the local community of Tasmania and followed up at 2.6 years, 5.1 years and 10.7 years later. Osteophytes and JSN were assessed using OARSI atlas. A 1.5T MRI scan of the right knee was acquired at baseline (n=930), 2.6 years (n=399) and 10.7 years (n=484). Tibial and patellar cartilage volume was acquired using a manual segmentation method on the T1-weighted fat-saturated 3D GRE images. Cartilage defects were assessed on T1-weighted MRI using a modified Outerbridge scoring system (grade 0–4). BMLs were measured on T2-weigthed fat saturated FSE images using a modified Whole-Organ MRI scoring system (grade 0–3). Meniscal extrusion (grade 0–2) and meniscal tears (grade 0–3) were measured using the T1- and T2-weighted MRI. Analyses were performed using linear mixed-effects models for symptoms and linear regression for cartilage volume loss.
**Results:** After adjustment for age, sex, BMI and radiographic KOA status, cartilage defects and BMLs were associated with total WOMAC score ($\beta$=4.81, $p<0.01$ and $\beta$=2.20, $p<0.01$, respectively) and subscale (pain, stiffness and function, all $p<0.01$) scores in a dose-response pattern. Participants who had higher grades of cartilage defects, particularly grade 3 and 4, had higher WOMAC scores and remained higher over 10.7 years (Figure 1). The association of cartilage defects was independent of BMLs, meniscal pathology and effusion-synovitis, whereas the association of BMLs was dependent on cartilage defects and meniscal pathology but independent of effusion-synovitis. Tibiofemoral cartilage volume loss (not patellar) ($\beta$=1.91, $p<0.01$) and meniscal extrusion (not tears) ($\beta$=3.21, $p<0.01$) were independently associated with total WOMAC scores and pain over 10.7 years.
Baseline cartilage defects, BMLs and meniscal extrusion were significantly associated with annual loss of tibial cartilage volume over 10.7 years ($\beta$=0.27%, $p<0.01$, $\beta$=0.22%, $p<0.01$ and $\beta$=0.28%, $p<0.01$, respectively) independent of other structural abnormalities.
Radiographic osteophytes (but not JSN) were significantly associated with WOMAC score ($\beta$=8.49, $p<0.01$) over 10.7 years after adjustment for age, sex, BMI and other structural lesions. Conversely, radiographic JSN (but not osteophytes) was significantly associated with annual tibial cartilage volume loss ($\beta$=0.28%, $p<0.01$) over 10.7 years. These associations were independent of MRI structural lesions.




**Conclusions:** Baseline cartilage defects, cartilage volume loss, BMLs, meniscal extrusion, JSN and osteophytes are independent predictors of clinical and strcutural progression of knee osteoarthritis.
**Acknowledgement:** National Health and Medical Research Council of Australia funded this study
**Disclosure of Interest:** None declared
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### OP0131 TRABECULAR THINNING IN METACARPOPHALANGEAL JOINTS OF ANTICITRULLINATED PEPTIDE ANTIBODY POSITIVE PATIENTS WITH ARTHRALGIA

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**Background:** Rheumatoid arthritis (RA) is characterized by synovitis leading to

bone erosions and joint destruction, but little is known about bone structure in the joints of patients before they are diagnosed with RA.
High Resolution peripheral Quantitative Computed Tomography (HR-pQCT) is a new imaging technique allowing detailed automatic evaluation of bone structure.
**Objectives:** The aim was to quantify the cortical and trabecular bone structure in the metacarpophalangeal (MCP) joints of anticitrullinated peptide antibody (ACPA) positive patients with arthralgia and compare with healthy controls.
**Methods:** Using a cross-sectional study design patients were recruited from local rheumatologists and controls from a website for test subjects. All individuals underwent medical history interview, clinical examination, and biochemical screening including ACPA. Patient inclusion criteria were positive ACPA and arthralgia. Exclusion criteria were fulfillment of the 2010 ACR/EULAR criteria for RA and other rheumatologic or metabolic bone diseases. Exclusion criteria for controls were known rheumatologic or metabolic bone disease, current or prior arthralgia, arthritis, and positive ACPA.
The right hand MCP joints were imaged with HR-pQCT using an isotropic voxel size of 82 $\mu$m.
A region of 1.2 cm located proximal to the articular surface of the MCP head was evaluated in the 2nd and 3rd finger using a semiautomatic program. Volumetric bone mineral density (vBMD), bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tb.Sp), average cortical thickness (Ct.Th), and cortical area (Ct.Ar) were evaluated. Nine patients were rescanned after repositioning and the coefficient of variation (CV) was calculated. Values are mean (SD).
**Results:** Twenty-nine ACPA positive patients without clinical arthritis (age 51 (13)) and 29 healthy controls (age 50 (14)) were included. CV of the HR-pQCT parameters was 0.64–3.53%.
The overall bone density was similar in the groups since vBMD and BV/TV did not differ. In addition, the cortical bone was not affected in patients, as we found no difference in Ct.Th and Ct.Ar between the groups. In contrast, the trabeculae were significantly ($p < 0.05$) thinner in both 2nd (87.8 (11.1) $\mu$m vs 93.9 (9.8) $\mu$m) and 3rd (84.3 (13.5) $\mu$m vs 89.8 (9.8) $\mu$m) MCP head compared with controls, whereas Tb.N and Tb.Sp did not differ.
**Conclusions:** It has earlier been demonstrated that inflammation of the synovium and bone marrow is crucial for development of erosions in RA. In the present study we demonstrate that the trabecular thickness is affected very early, i.e. before the onset of clinical arthritis. Therefore, up-regulation of bone resorption in the bone marrow may be an early feature of RA. Bone loss before clinical RA warrants earlier diagnosis and treatment.
**Acknowledgement:** This work was supported by grants from the Danish Rheumatism Association and the Scandinavian Journal of Rheumatology.
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## "Fewer words - more action" - tailored care for men with rheumatic diseases?

### OP0132-HPR AXIAL SPONDYLOARTHRITIS KNOW-HOW: WHAT ARE THE BENEFITS OF A BRIEF EXERCISE AND SELF-MANAGEMENT EDUCATION GROUP PROGRAMME? A QUALITATIVE INVESTIGATION

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**Background:** Axial Spondyloarthritis (AS), a long-term sero-negative inflammatory arthritis is associated with inflammatory back pain, reduced spinal mobility, fatigue and work incapacity. Exercise and self-management education are key recommendations of the Assessment of Spondyloarthritis Society (ASAS) management guidelines. The Axial Spondyloarthritis Know-how (ASK) programme aims to increase knowledge, exercise participation and self-management and comprises a two hour group education, gym-based exercise and hydrotherapy session for up to six people, facilitated by a specialist physiotherapist and self-management education handbook.
**Objectives:** The qualitative focus group study aims to explore the acceptability and benefit of a brief exercise and self-management group programme for adults with Axial Spondyloarthritis.
**Methods:** A purposive sample of adults with AS (ASAS,2009) who attended the ASK group programme between April-June 2014 were enrolled into the study. Focus groups were facilitated by a rheumatology specialist physiotherapist not involved in the delivery of the ASK programme and followed a topic guide developed a priori. The focus groups were audio-recorded and transcribed verbatim. Manual coding was utilised to build categories (through naturalistic inquiry as a permutation of constructivist grounded theory) resulting in the identification of a thematic framework linking the theoretical concepts. The themes were checked for resonance with participants.
**Results:** Two focus groups including nine participants (5 male) with mean age 43 years (21–74) and mean disease duration 12.2 years (1–44) were conducted. Overall, patients reported the ASK programme was an acceptable and beneficial experience. Four over-arching themes were identified: 1) Exercise Behaviours: Participants described increased knowledge and confidence to exercise following attendance. Three participants commenced exercising with local National Ankylosing Spondylitis Society groups and four adapted the content of a home exercise programme. 2) Disease Positioning: Participants reported comparing their mobility and posture with others in the ASK group and positioned themselves along a "disease severity spectrum" in relation to other group members. 3) Temporal Effects of Self-Management Education: The time between diagnosis and attending the ASK group influenced the extent of learning acquired. Newly diagnosed interviewees reported that the ASK group provided information and promoted self-management whereas those with longer disease duration, who considered themselves to be knowledgeable, reported gaining less benefit. 4) The Group Effect: Participants reported that they learned from their peers, particularly self-management strategies for dealing with flares.
**Conclusions:** The ASK programme is an acceptable and beneficial experience for adults with AS. It promotes understanding of self-management, including exercise participation and flare-up management through learning from others. It may be easily implemented into clinical practice, however, may be more appropriate for those with early disease.
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**THURSDAY, 9 JUNE 2016**

## Recent advances in our understanding of macrophage biology

### OP0133 DNA DEMETHYLATION PATHWAY ANALYSIS IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS AND MACROPHAGES

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**Background:** Activated macrophages and synovial fibroblasts (SF) are found in the inflamed and hyperplastic synovial rheumatoid arthritis (RA) tissues. Our group has already reported a persistent global hypomethylation in RA tissues and RA synovial fibroblasts (RASF). Recent findings showed that the 5-methylcytosine (5-mC) modification of DNA can be converted to 5-hydroxymethylcytosine (5-hmC) through the activation of the family of Ten-Eleven-Translocation (TET1–3) enzymes which may explain the genomic hypomethylation in RA. It is known that TET enzymes require for their activation a-ketoglutarate (a-KG) which is produced from isocitrate during cell glycolysis by the enzyme Isocitrate dehydrogenase 1 (IDH-1).
**Objectives:** In the current study, we investigated the 5-hmC modification, TET1–3 and IDH-1 enzymes in RASF and monocyte derived macrophages stimulated with TNFa and LPS.
**Methods:** RASF cultures were prepared from joint replacement patients. The THP-1 cell line was differentiated into macrophages in the presence of 50nM phorbol myristate acetate (PMA). Macrophages were prepared by culturing CD14+ monocytes with macrophage colony stimulating factor (M-CSF) for 6 days. Macrophages and RASFs were transfected with siRNA for TET1 and stimulated with 100 ng/ml LPS for 2 hours or 10 ng/ml TNFa for 24 hours. Glucose uptake was measured using a colorimetric assay. The mRNA levels of TETs and IDH-1 were analyzed by quantitative Real-time PCR. The protein levels of TNFa and IL-6 were measured by ELISA. The global 5-hmC levels were determined by DNA dot blot assay. Hydroxymethylated DNA immunoprecipitation (hMeDIP) was applied to analyze the levels of 5-hmC in different promoter areas of the TNFa (TNFa 1–4) and the IL-6 locus.
**Results:** First, we screened different SF cultures and macrophages for the expression of 5-hmC using dot-blot assay and found that RASF cultures do not express 5-hmC in comparison to CD68+ macrophages. TNFa reduced the expression of TET1 and TET2 mRNA in RASF by 50% and 20% respectively. Interestingly, we observed a 40% reduction of IDH1 (n=3) and an increase of glucose uptake in RASF (n=2). Stimulation of the macrophages with LPS for 0.5h showed a significant increase of TET1 mRNA (TET1: 0.5h 1.93±0.7, fold change, n=4, p=0.03). Interestingly, LPS stimulation increased 5-hmC levels in the promoter of TNFa and IL-6 in monocyte derived macrophages (hMeDIP: TNFa 1.64±0.2, n=3, p=0.03; IL-6 1.74±0.2, n=3, p=0.03). Next, we knocked down TET1 with siRNA in THP1 differentiated macrophages and found that TNFa and IL-6 production was reduced by 46% and 44% as well as the 5-hmC levels were reduced by 25% respectively (n=4).
**Conclusions:** For the first time, we showed that TNFa reduces the glycolytic and epigenetic enzymes IDH1 and TET1 in RASF. In addition, we found that TET1 contributes to the activation of macrophages through the regulation of 5-hydroxymethylation in the promoter of pro-inflammatory cytokine genes. The IDH1 and TET1 enzymes could be promising molecular targets of RASF activation and macrophage chronic inflammation.
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### OP0134 THE RHEUMATOID ARTHRITIS SUSCEPTIBILITY GENE C5ORF30 ACTS AS AN IMMUNOMODULATOR IN MACROPHAGES

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**Background:** The variant rs26232 in the first intron of *C5orf30* has been associated with both risk of developing rheumatoid arthritis (RA) and severity of tissue damage. The gene encodes a protein of 206 amino acids that is highly expressed by RA synovial fibroblasts (RASF) and macrophages. Inhibition of C5orf30 in RASF results in increased cellular invasiveness and migration *in vitro*, furthermore, inhibition in the collagen-induced arthritis model markedly accentuated joint inflammation and damage, with elevated TNF and IL-1 expression (Muthana et al, 2015). There is no published data on the biological activities of C5orf30 in macrophages.
**Objectives:** To determine the role of C5orf30 in regulating monocyte-derived macrophage biology.
**Methods:** Experiments involving both the monocyte/macrophage cell line (THP1) and primary monocyte-derived macrophages (MDM) were employed. MDMs were isolated from healthy donor PBMCs and cultured on plastic for 8 days with m-CSF. Macrophage purity was confirmed via flow cytometry. Expression of C5orf30 mRNA was assessed by quantitative PCR and protein expression via Western blot. The effects of polarization to M1 and M2a phenotypes and stimulation with TNF and LPS on C5orf30 expression were compared. C5orf30 levels were manipulated using siRNA technology and functional effects on macrophage biology was assessed using cytokine response assays, matrigel transwell invasion assays, quantitative high throughput pathogen phagocytosis assays, gene expression and intracellular signaling.
**Results:** Treatment of macrophages with either TNF or LPS significantly reduced C5orf30 expression compared to untreated cells (TNF 0.51±0.26 $p$=0.001 and LPS 0.29±0.25 $p$=0.02). Furthermore, polarization to M2a phenotype trended to increased expression (1.34±0.59 $p$=0.13) whereas polarization to M1 macrophage phenotype resulted in significantly decreased expression of C5orf30 (0.68±0.13 $p$=0.01) compared to untreated cells, indicating an anti-inflammatory effect. Knockdown of C5orf30 significantly reduced the invasive capacity of macrophages (0.54±0.04 $p$=0.003); this was intensified upon incubation with either TNF (0.29±0.16 $p$=0.02) or LPS (0.34±0.11 $p$=0.01). Phagocytosis of labeled yeast particles was increased upon C5orf30 knockdown combined with co-incubation with TNF (1.14 $p$=0.02). C5orf30 knockdown also increased activation of the JNK pathway as measured by an increase in phosphoJNK but not total JNK. All knockdown experiments compared to non-targeting (scramble) siRNA control.
**Conclusions:** C5orf30 knockdown enhanced the proinflammatory (M1-like) macrophage phenotypes of pathogen phagocytosis and JNK pathway activation whilst diminishing the tissue-clearing (M2-like) phenotype of macrophage invasion. This data combined with the observation that proinflammatory cytokine stimulation reduced *C5orf30* expression indicates an important role for C5orf30 in the immunomodulatory regulation of macrophages and is consistent with our previous findings in RASF that C5orf30 is a negative regulator of tissue damage in rheumatoid arthritis.
**References:**
[1] Muthana M, Hawtree S, Wilshaw A, Linehan E, Roberts H, Khetan S, Adeleke G, Wright F, Akil M, Fearon U, Veale D, Ciani B and Wilson AG. C5orf30 is a negative regulator of tissue damage in rheumatoid arthritis. Proceedings of the National Academy of Sciences. 2015; 112(37):11618–23
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**THURSDAY, 9 JUNE 2016**

## Lubricants: potential as osteoarthritis treatment?

### OP0135 PREDICTIVE FACTORS OF FAILURE OF VISCOSUPPLEMENTATION IN PATIENTS WITH KNEE OSTEOARTHRITIS. RESULTS OF A POST-HOC ANALYSIS OF A DOUBLE BLIND, CONTROLLED NON INFERIORITY TRIAL

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**Background:** Viscosupplementation (VS) by intra-articular (IA) injections of hyaluronic acid (HA) is widely used worldwide to alleviate pain and improve function in patients with mild to moderate knee osteoarthritis (KOA). However, in most of the clinical trials, the rate of responders to treatment does not exceed 60 to 70%. One of the key points that remains to be clarified is the identification of predictive factors of success or failure to treatment.
**Objectives:** To identify clinical and radiographic predictive factors of treatment's response or failure in patients treated with VS for KOA.
**Methods:** We included in this post-hoc analysis, 166 patients, with fully available clinical and radiographic data, coming from the intent-to-treat population (n=205) of a controlled, multicentre, double-blind, randomized, clinical trial, which compared 2 HA viscosupplement in patients with symptomatic KOA. At baseline, demographic, anthropometric, clinical data (patient global assessment, WOMAC score, presence or lack of synovial effusion) radiologic data (Kellgren-Lawrence grade, OARSI score for joint space narrowing [JSN]) and all previous and present treatments for OA, previous IA steroids or HA injections were recorded. All patients received 3 weekly IA injections of HA. They were classified as Responders if they fulfilled the OMERACT-OARSI criteria, 6-month after injections. Mann-Whitney and chi-square tests were used to assess the association of quantitative or qualitative factors and OMERACT-OARSI response. Multivariate logistic regression analysis was used to identify predictors of response.
**Results:** Clinical and demographic characteristics at baseline as well as treatment effectiveness did not statistically differ between the 2 HA groups, so that the data could be pooled. The studied population consisted in 101 women and 65 men, mean age 65.2, mean disease duration 48.7, mean BMI 27.7. 47 patients were obese. Seventy three patients had grade 3 JSN. At baseline, mean WOMAC pain and function scores were 9.8 and 27.5, respectively. Before study inclusion, 95 had at least one VS or corticosteroid injection. At month 6, WOMAC pain and total scores decreased by 43.4% and 41.9% respectively. One-hundred-thirteen patients (68.1%) were classified as Responders. In univariate analysis, increased BMI and OARSI grade were significantly associated with lack of response (p=0.002 and p=0.005, respectively). Similar associations, although not statistically significant, were found with previous IA HA or steroids injection (p=0.11) and age >65 years (p=0.13). Multivariate analysis confirmed the association of obesity and radiological severity with lack of response. Finally, we found a strong cumulative impact of potential predictive factors (age >65, previous VS or steroid IA injection, obesity and severe JSN) on VS response. Thus, all patients without predictive factors were Responders, versus only 69.1% and 28.6% of those with 2 or 4 risk factors, respectively (p<0.0001).
**Conclusions:** VS should be chiefly considered in subjects with normal BMI and moderate tibio-femoral joint space narrowing. This study shows, for the first time, a strong cumulative impact of potential predictive factors of failure. This can be helpful for clinicians when they inform patients on the chance of success of VS.
**Acknowledgement:** To LABRHA for authorization tu use its database
**Disclosure of Interest:** None declared
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## Extraarticular complications of JIA

### OP0136 ABATACEPT TREATMENT DURING 1 YEAR PERIOD IN JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS WITHOUT PREVIOUS BIOLOGICS THERAPY

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**Background:** Biological DMARDs have an important role in the treatment of juvenile idiopathic arthritis (JIA) associated uveitis refractory to previous standard treatment.
**Objectives:** The aim of this prospective study was assessment of Abatacept (ABA) efficacy in JIA associated uveitis.
**Methods:** Among 17 patients with JIA and eye involvement included in the study, 9 children had oligo-articular JIA, 7 children – polyarticular, 1 patient had systemic disease. Study group included 13 girls and 4 boys. Mean age was 7,10 ± 2,16 years, age of disease onset was 3,70±3,05years; mean disease duration before ABA administration was 6,40±3,21. Disease onset with initial joint damage was observed in 10 children, with eye involvement- in 7 children.
Prior to ABA administration all children received immunosuppressive drugs: 12 children (70,58%) methotrexate (MTX) 10–15mg/m$^2$ of body surface per week, 2 children (11,8%) received Sandimunne Neoral as monotherapy and with methotrexate combination – 3 patients (17,6%), 2 children received oral corticosteroids (CS), 17 children (100%) received topical treatment of uveitis.
Number of active joints was 8,7±2,6, mean ESR was 20, 0±10,32mm/h, CRP 1,18±1,05mg/dl (ref. <0,8mg/dl). RF positive was detected in 2 children, negative - in 15 children, ANA positive in 14 children (82,35%) with 1:160- 1:180 rate.
VAS physician was 73, 4±15, 0, VAS patient/parent was 68, 7±16, 2. Mean functional disability in patients before ABA administration was 1, 03 ±0, 48.
All 17 patients had active uveitis at the moment of ABA administration. 9 (53%) patients had bilateral ocular involvement, 8 patients (47%) - unilateral.
**Results:** After 6 months of ABA therapy mean ESR decreased from 20, 0±12, 32 mm/h to 17.2±4,28mm/h, CRP – from 1, 18±1, 05 mg/dl to 1,05±0,75mg/dl. ACRpedi-30 was achieved in 10 from 17 (58,82) % patients, ACRpedi-50- in 4 patients (23,52%), ACRpedi -70- in 3 children (17,64%). Uveitis remission was achieved in 22% eyes; 46% showed a significant reduction in inflammatory activity, 32% had no significant dynamic.
After 12 months of ABA therapy number of active joints decreased from 8, 7±2, 6 to 5, 63± 1, 4. Mean ESR decreased from 20, 0±12, 32 mm/h to 10,0±4,6mm/h,

CRP –0±0,31mg/dl, VAS physician decreased from 73, 4±15,0 to 42,4±13,5, VAS patient/parent decreased from 68, 7±16, 2 to 50,0 ± 14,0. ACRpedi-50 was achieved in 13 patients (76,4%), ACRpedi-80 - in 2 children (11,76%). Regarding uveitis 21% eyes had uveitis remission; 36% – sub active process. Flares were observed in 43% eyes.
**Conclusions:** Abatacept treatment during 12 months period was effective in JIA associated uveitis with 82% ANA positivity without previous biologics therapy.
**Disclosure of Interest:** None declared
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### OP0137 DIABETES PREVALENCE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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**Background:** The majority of JIA categories are considered as autoimmune diseases. Autoimmune diseases seem to cluster in children and adolescents with JIA, which is attributed to shared susceptibility genes. Studies revealed an increase in the simultaneous JIA and juvenile type 1 diabetes mellitus (T1D) occurrence and an increased JIA prevalence in patients with T1D [1]. However, the frequency of T1D in JIA patients in comparison to the general population is unknown.
**Objectives:** To determine the frequency of T1D in JIA patients and to characterize patients having both JIA and T1D.
**Methods:** Diabetes comorbidity was recorded in the national paediatric rheumatologic database (NPRD) in 2012 and 2013. Data of the North Rhine-Westphalian diabetes register and the Diabetes data acquisition system for prospective surveillance (DPV) served as reference for the diabetes prevalence in the general population. NPRD data were indirectly standardized for age and sex for the comparison with the general population. The diabetes prevalence ratio (PR) was calculated using Poisson regression models.
**Results:** 9,359 JIA patients were included in the analyses. Patient mean age was 12 years (SD 4.5), mean disease duration 4.5 years (SD 3.8). 50 patients had T1D in addition to JIA, diabetes prevalence was 0.5%. Patients with versus without T1D did not differ significantly in the JIA category spectrum. Compared to the general population, the diabetes prevalence in JIA patients was significantly increased (PR: 1.96 [CI: 1.49;2.59], $p<0.001$). The PR for diabetes for girls was 1.92 (CI: 1.35;2.73, $p<0.001$) and for boys 2.04 (CI: 1.30;3.19, p=0.002). Diabetes onset in JIA patients was slightly earlier than in the age- and sex-matched population. More than half of the patients (58%) developed diabetes before JIA. Diabetes onset was on average 60 months before the JIA onset. Patients with JIA before T1D developed T1D on average 35 months after JIA onset. The majority of these patients had not received any DMARDs before diabetes onset.
**Conclusions:** Diabetes type 1 occurs more frequently in JIA patients than in the general population. The likelihood of T1D seems to be slightly higher before JIA manifestation and in patients who were not treated with DMARDs after JIA onset. The NPRD has been funded by the German Children Arthritis Foundation (Deutsche Kinder-Rheumastiftung).
**References:**
[1] Hermann G, Thon A, Mönkemoller K, Lilienthal E, Klinkert C, Holder M et al. Comorbidity of type 1 diabetes and juvenile idiopathic arthritis. J Pediatr 2015;166:930–5.
**Disclosure of Interest:** None declared
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## The elephant in the room: how to avoid biases in research?

### OP0138 SIMPLE POOLING OF DATA FROM DIFFERENT STUDIES IS INCREASINGLY USED BUT NOT IN LINE WITH METHODOLOGICAL RECOMMENDATIONS: A SYSTEMATIC REVIEW OF METHODS APPLIED IN THE FIELD OF RHEUMATOID ARTHRITIS

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**Background:** Combining data from different clinical trials (observational studies) is getting more frequent for the analysis of DMARD efficacy (effectiveness) and safety. The underlying objective is plausible: the generation of data with sufficient power for the investigation of rare adverse events or different treatment strategies. However, the approach of simply pooling data from different studies within an analysis has been shown to be prone to bias which applies for both, observational and clinical trial data [1,2].
**Objectives:** To describe the agreement of recommended and applied methods in the analyses of data originating from different studies.
**Methods:** A systematic literature review with PubMed and Web of Science was independently conducted by two researchers (RA, CJ) using a common strategy. We included full text publications if: ≥2 different data bases (clinical trial/observational data) with individual patient data were used, efficacy/effectiveness or safety were investigated and if the studies were conducted in patients with rheumatoid arthritis. We excluded studies using claims data, genetic/proteomic association studies and studies of prognostic markers. Outcomes of interest were the number of data bases, the analysis-type (pooled/separated/both) and the illustration and discussion of study heterogeneity.
**Results:** After screening 2002 search results, initial consent of the eligibility of each publication for this analyses was found in 58 publications (safety: n=34 (59%), effectiveness: n=20 (34%), both: n=4 (7%)). From these 28 publications (48%) were based on observational data, 24 (42%) on clinical trials and 6 (10%) based on a mixture of study types. The No. of databases in one publication ranged from 2–42 for clinical trial data, 2–10 in observational data and 4–13 if a mixture of databases was investigated. The analysis of pooled data (n=28, 48%) was more frequent in analyses with trials (n=18) than with data from observational studies (n=8). However, the latter studies were primarily conducted in recent years (Table). In only 1/8 publications (13%) from pooled observational data the baseline characteristics were shown separately for each database. Heterogeneity of study populations was discussed in only 2/8 (25%) publications based on pooled analysis, in 8/15 publications (53%) using a separate analysis of observational studies the heterogeneity of patients was discussed.

| | | No. of publications in 5-year intervals | | | | |
|---|---|---|---|---|---|---|
| Data origin: | Analysis: | ≤2000 | 2001-2005 | 2006-2010 | 2010-2015 | Total |
| Observational | Pooled | 0 | 1 | 2 | 5 | 8 |
| | Separate | 1 | 4 | 4 | 6 | 15 |
| | Pooled + Separate | 1 | 0 | 0 | 4 | 5 |
| Clinical trial data | Pooled | 3 | 5 | 6 | 4 | 18 |
| | Separate | 0 | 1 | 1 | 2 | 4 |
| | Pooled + Separate | 0 | 0 | 2 | 0 | 2 |

Table: Summary of full text publications but excluding Meta-Analysis of summary tables from published results. Pooled=no effects/estimates of individual studies shown; Separate=results of each study and combined results shown.

**Conclusions:** Collaborative analyses of several sources of observational data or multiple clinical trials may deliver superior results than individual studies but only if an appropriate analysis is applied. The approach of simply pooling the data neglects existing heterogeneity of patient cohorts, assessment of risk factors/events, missing data and dropouts. The use of individual patient data from multiple clinical trials could be superior to meta-analysis of published results but loses this advantage if the data are simply pooled. Regarding the considerable differences between observational studies, e.g. European register [3], the utility and the recent increase of pooled analyses from observational studies is disputable.
**References:**
[1] Hammad et al. Clinical Trials 8.5 (2011): 559–570.
[2] Van der Steen et al. Palliative medicine 2008;22:750–759.
[3] Kearsley-Fleet et al. Rheumatology 54.6 (2015): 1074–1079.
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## Digital applications for the benefit of the patient

### OP0139-PARE THE FIRST SERIOUS GAME EDUBIOT: A MODERN THERAPEUTIC EDUCATIONAL TOOL FOR ADULT PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASE, TREATED WITH BIOTHERAPY

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**Background:** Democratization of biotherapy for chronic inflammatory rheumatic disease has created new challenges in terms of therapeutic education for patient. Our goal has been to create the first modern serious game for adult patients with chronic inflammatory rheumatic disease treated with biotherapy.
**Objectives:** Our specification is based on the minimum self-care safety skills, a patient with a biotherapy must have acquired (issued by the SFR- Therapeutic Education section)[1].
**Methods:** An expert board was formed, with 5 rheumatologists, 1 pharmacist and 2 patients. Each game scenario was tested by patients.

It helps to promote the self-care safety skills in biotherapy by creating sequences increasingly complicated during the progress of the game. A "guardian" mode with password access, unlocks all the scenarios available in the game for use in a group of educational validated program. This free game will be available online on www.ludomedic.com. An update is planned after launching the application for the increment of new scenarios play.
A statistics module is also set up to quantify many indicators, such as number of players, the most frequent errors. These Statistics can guide the objectives of a therapeutic educational program patient at the individual level and the game will provide national statistics on the strengths and weaknesses of the level of knowledge of "patient players" in biotherapy.
**Results:** We opted for a video game called Serious Game. The principle is that the patient player must evolve an avatar having chronic inflammatory rheumatic disease treated by biotherapy. Different events disrupt the daily management of its biotherapy (fever, infections, pregnancy, surgery, travel etc.).
The player must take the right decisions and allowing it to gain or lose points on his influential level of quality of life, influenced in terms of its decisions and actions. 5 themes have been made (fever and infection management, parenting desire, surgical and dental care, information, prevention, and logistics and injection technique).
**Conclusions:** This is the first serious game dealing with the management of a biological therapy in adult patient treated by a biotherapy in France. A study of its impact on the level of knowledge of patients and the most common mistakes will be investigated after broadcast. It is the result of two years of a unique collaboration between two associations of patient and French rheumatologists to offer a unique and innovative patient education tool.
**References:**
[1] Gossec L & col. Safety of biologics: elaboration and validation of a questionnaire assessing patients' self-care safety skills: the BioSecure questionnaire. An initiative of the French Rheumatology Society Therapeutic Education section. Joint Bone Spine. 2013;80(5):471–623.
**Acknowledgement:** This serious game was created and produced in partnership with the ANDAR association and with the Institutional support of laboratories AbbVie
**Disclosure of Interest:** None declared
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## OP0140-PARE SELF-MANAGEMENT ONLINE: FROM CONCEPT TO DELIVERY, LIVING WELL WITH ARTHRITIS ONLINE

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**Background:** Over the past 10 years Arthritis Ireland has pioneered the development of services that enable people with arthritis to learn about self-management and put self-management tools into practice in their daily lives. Over the past 2 years we have embarked on a significant journey to bring these vital tools to even more people with arthritis through the development of an online education programme – *Living Well with Arthritis Online*.
**Objectives:** The objectives of the project were to 1)Compare and contrast the pros/cons of conventional class based self-management programmes with that of an online offering; 2) Develop a model of online delivery to attract large numbers of people with arthritis in an engaging format; 3) Develop comprehensive content to improve understanding of the various types of RMDs,the various self-management tools that could form part of a tool kit for daily living and the various medications that are now used to treat RMDs; 4) Develop appropriate mechanisms for reviewing and evaluating the impact of the programme; 5)Develop a comprehensive framework to promote and recruit participants to the programme.
**Methods:** Our journey with self-management began in earnest back in 2006 with the launch of the 6-week "*Living Well with Arthritis*" Stanford University self-management programme. Since that time we have delivered the programme to over 5,000 people across Ireland in community class settings.
Despite the myriad of benefits to the programme Arthritis Ireland recognises that not everyone approaches learning in the same way so it is important to provide alternative learning formats. We investigated the benefits and challenges of conventional self management courses with an online model. A number of reasons became apparent to us that impacted participation in class-cased programmes - time constraints; unsuitable course hours; location too far away; stigma of attending an "arthritis" course; not feeling comfortable talking about arthritis in a group; face to face course was less appealing to younger people.
In response to these challenges and to meet the growing challenge of how to reach greater numbers of people, Arthritis Ireland developed an online self-management programme – "*Living Well with Arthritis Online".* The programme was researched, developed and implemented by Arthritis Ireland during 2014 and 2015. It is designed to 1)improve a person's understanding of their arthritis 2) introduce them to key self-management tools that can be used on a daily basis and 3) improve understanding of the various medications now available to manage arthritis. The programme is highly interactive and learning take place through various video lessons with additional reading material available within each module.
**Results:** By the end of January 2016, over 800 people had registered for the programme within the first 3 months of operation. Results will be collated and findings reported at the 6-month stage.
**Conclusions:** What is clear so far is online education offers a unique learning opportunity to many people who would not otherwise attend a face to face class, at a reduced cost, with minimal ongoing financial outlay.
**Disclosure of Interest:** None declared
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# Optimization of MTX in RA treatment

## OP0141 WHICH STRATEGIES IN RHEUMATOID ARTHRITIS PATIENT WITH INADEQUATE RESPONSE TO METHOTREXATE MONOTHERAPY: THE STRATEGE STUDY

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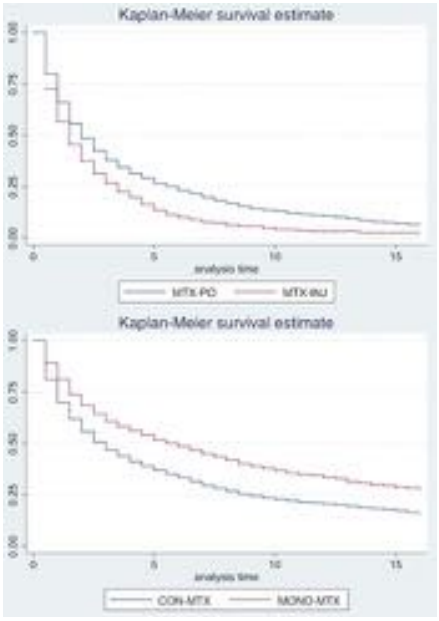
**Background:** Current EULAR and SFR (French Rheumatology Society) guidelines consider MTX as initial gold standard treatment for patients (pts) with RA. They also propose various strategies for MTX inadequate responders, among which the most frequent are optimization of MTX therapy (alone or in combination with other csDMARDs) or biological treatment.
**Objectives:** To explore the strategies applied in daily practice in RA pts with inadequate response to MTX.
**Methods:** STRATEGE is a prospective, observational, multicenter study, conducted in France. Main inclusion criteria were: confirmed RA diagnosis (ACR 1987 or ACR/EULAR 2010 criteria) and treatment by MTX monotherapy with clinical, structural, functional and/or therapeutic evolution leading to therapeutic management modification. Data presented here show the baseline pts characteristics and the therapeutic strategies chosen during the inclusion visit.
**Results:** Between Sept 2014 and July 2015, 176 rheumatologists, mainly with private (49.3%) or mixed private/public (42.1%) practice included 850 pts. Pts baseline characteristics were: mean age: 57.9 yrs (±13.7); RA duration: 5.4 yrs (±6.6); extra-articular manifestations: 10.4%; structural damage: 39.5%; mean DAS28: 3.98 (±1.35), with the following distribution: $<$2.6 for 12.4%, $>$3.2 for 75.8% and $>$5.1 for 17.1%; and mean HAQ: 1.1 (±0.84). All pts were receiving MTX monotherapy and for 83.8% it was the first-line treatment. 67.8% of pts were treated by oral MTX at a mean dose of 14.2 mg/wk (± 4.1), while parenteral mean dose was 16.4 mg/wk (± 3.8). 51.5% of pts treated with parenteral MTX were performing injections by themselves. 15.6% of pts had experience MTX dose tapering before the inclusion. Concomitant treatment included corticosteroids for 44.8% of pts and folic acid for 89.7%. After the inclusion visit, MTX prescription has been identically maintained (dose and route) for 26.2% of pts, interrupted for 2.9% and modified for 70.9% of them. Changes included dose increasing for 47.1%, dose tapering for 6.1% and a route modification for 20.3% (83% oral -> parent). Biologic treatment was initiated for 14.2%, in association with MTX for 95.8%. Other csDMARD treatment was initiated for 1.1% in monotherapy and for 3.8% in association with MTX. The mean dose of MTX after inclusion visit was 16.8 mg/wk (±4.2), with 10.6%, 35.3% and 34.9% pts receiving 10, 15 and 20 mg/wk respectively. The reasons for treatment modification were mainly high disease activity (70.2%), worsening of clinical and biologic parameters (30.8%), remission not achieved (13.1%), radiographic progression (14.1%), steroid dependence (11.4%), and MTX intolerance 4.8%.
**Conclusions:** Consistently with the recent European and National recommendations, first data of the large observational French study STRATEGE, revealed an important place held by initial MTX treatment optimization before initiation of a biotherapy.
**References:**
[1] Smolen JS, et al. EULAR recommendations for the management of RA with synthetic and biological DMARDs: 2013 update. Ann rheum Dis 2013; 0:1–18
[2] Gaujoux-Viala C, et al. Recommendations of the French Society for Rheumatology for managing RA. Joint Bone Spine 2014; 81(4):287–97
**Disclosure of Interest:** R.-M. Flipo Consultant for: Nordic Pharma, C. Gaujoux-Viala Consultant for: Nordic Pharma, C. Hudry Consultant for: Nordic Pharma, E. Zinovieva Employee of: Nordic Pharma, E. Leutenegger Employee of: Gecem, H. Herman-Demars Employee of: Nordic Pharma
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## OP0142 METHOTREXATE USE IN RA: WHAT 17 YEARS AND 22,621 PATIENTS CAN TEACH US

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**Background:** Methotrexate (MTX) remains the gold standard treatment for rheumatoid arthritis (RA), yet most recent research refers to it only as a referent or placebo without context of dose or form of administration.
**Objectives:** To examine the real-world use trends of MTX in the US since 1998.
**Methods:** Using a large observational cohort, the National Data Bank for Rheumatic Diseases (NDB), we characterized patients with RA who initiated MTX from 1998 through 2015. Baseline characteristics were assessed by MTX

administration route, injectable (INJ) and oral (PO), and by mono- vs. concomitant DMARD therapy. Discontinuation, described using Kaplan-Meier survival curves, was defined as either ending MTX or adding another DMARD. Sensitivity analyses were performed with alternative discontinuation definitions. GEE were also used to model change on MTX dose over time.
**Results:** In our study of 22,621 RA patients, MTX had widespread use with 73.5% ever being exposed, 59.4% using it during our study, and 11.4% initiating without any prior DMARD. The MTX-exposed baseline mean age was 59±13 years, 79% female, and 14±12 years RA duration. Of these, 21% used MTX-INJ and had worse disease severity and higher weekly doses compared to MTX-PO (PAS: INJ 4.1±2.2 vs. PO 3.6±2.2; Dose: INJ 16.2±4.2 vs. PO 13.8±5.5 mg). When initiating MTX, 42.8% took mono-therapy, and concomitant use was split 53/47% on synthetic/biologic DMARDs with trends of being younger, more employed, and more private insurance (34% vs 27% on mono-therapy). Overall median (IQR) survival time after initiating MTX was 2.5 (1–6) years per patient with 24,823 p-yr followup. Sensitivity analysis of discontinuation requiring ending MTX had 8 (2.5-.) years per patient, 38,290 p-yr followup. By route, the median (IQR) survival was 1.5 (0.5–3.5) years for INJ and 2 (1–5.5) years for PO with 16.2% of patients switching between routes. Also, survival was 6 (1.5–...) years for mono-therapy and 3 (1–9) years for concomitant therapy. MTX doses increased by 0.01 (95% CI 0.01 – 0.02) mg/yr/patient with 50% of patients increasing MTX dose a median (IQR) of 5 (2.5–10) mg and 3.3% of patients decreasing their dose.




**Conclusions:** Patients who tolerate MTX early tend to use it for several years even while adding concomitant DMARDs. We showed notable differences between patients by MTX route, with trends of increasing dose over time.
**Acknowledgement:** This study was funded by Pfizer Corp.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3777

**THURSDAY, 9 JUNE 2016**

## Joint replacement in OA: friend or foe?

### OP0143 THE EFFECT OF PHYSICAL ACTIVITY ON THE RISK OF TOTAL JOINT REPLACEMENT FOR SEVERE KNEE OR HIP OSTEOARTHRITIS: A POPULATION-BASED PROSPECTIVE COHORT STUDY

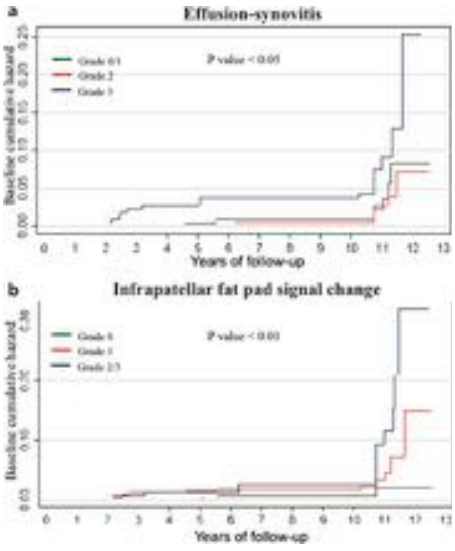
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**Background:** Studies examining physical activity and joint health are conflicting – with some showing a detrimental effect and others showing either no effect or a beneficial effect.
**Objectives:** To explore the association between physical activity and knee or hip osteoarthritis leading to knee or hip joint replacement surgery.
**Methods:** 536 community-dwelling adults aged 51–79 years were assessed at baseline, 2.7, 5 and 10 years. Physical activity was measured by pedometer (steps/day). The incidence of knee or hip replacement surgery was reported at each follow-up. Log-binomial regression was used to examine the association between steps/day with incident knee and hip replacement adjusted for age, sex, BMI, x-ray disease severity, and pain.
**Results:** Over 10 years, 36 participants reported having a knee replacement and 27 reported having a hip replacement. For every 1000 steps/day increase at baseline, there was a 0.84 times (95% CI 0.72 to 0.99) lower risk of hip replacement (P=0.036). There was no significant association between steps/day and knee replacement (RR 1.00 95% CI 0.9999 to 1.00, P=0.778). Baseline BMI significantly predicted knee replacement (RR per SD increase in BMI 1.42 (95% CI 1.03 to 1.97, P=0.032)) but not hip replacement (RR 1.00 95% CI 0.91 to 1.10, P=0.984).
**Conclusions:** Higher physical activity levels were protective against hip replacement while being overweight or obese increased the risk for knee replacement. This suggests different causal pathways for each site with regard to habitual activity and body composition.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3065

### OP0144 INFRA PATELLAR FAT PAD SIGNAL INTENSITY ALTERATIONS AND EFFUSION-SYNOVITIS PREDICT KNEE PAIN, CARTILAGE VOLUME LOSS AND TOTAL KNEE REPLACEMENT OVER 10.7 YEARS IN OLDER ADULTS

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**Background:** There are no long-term studies that describe the independent association of infrapatellar fat pad (IPFP) signal intensity alterations and effusion-synovitis with knee osteoarthritis (KOA) severity and progression.
**Objectives:** To describe the associations between baseline IPFP signal intensity alterations and effusion-synovitis and long-term knee pain, knee dysfunction, tibial cartilage volume loss and total knee replacement (TKR) over 10.7 years.
**Methods:** Participants (n=983, mean age 62.8 years, 50% female) were selected randomly from the local community of Tasmania and followed up at 2.6 years, 5.1 years and 10.7 years later. MRI was acquired at baseline and 10.7 year follow-up. Effusion-synovitis was measured on T2-weigthed MRI using a modified WORMS system (grade 0–3) at suprapatellar pouch, central portion, posterior femoral recess and subpopliteal recess. IPFP signal intensity alteration was assessed on T2-weighted MRI and was defined as discrete areas of increased signal within IPFP, and was graded as follows: grade 0 = none; grade 1 = $<$10% of the region; grade 2 = 10% to 20% of the region; grade 3 = $>$20% of the region. Cartilage volume at baseline and 10.7 years was measured using manual segmentation of T1-weighted MRI. Clinical symptoms and TKR data were recorded at each follow-up visit. Multivariable analyses were performed using linear mixed-effects models for clinical symptoms, linear regression for cartilage volume loss and cox proportional hazards for TKR.
**Results:** After adjustment for age, sex, BMI, radiographic KOA status, baseline IPFP signal intensity alteration was associated with total WOMAC score ($\beta$=2.19, 95% CI = 0.29, 4.09), WOMAC pain and WOMAC function scores (all $p<0.01$) over 10.7 years. However, these associations became borderline significance after further adjustment for cartilage defects, BMLs or effusion-synovitis. Baseline IPFP signal intensity alteration was independently associated with tibial cartilage volume loss ($\beta$=0.08 mm$^3$, 95% CI = 0.14, 0.02) and TKR (HR=1.89, 95% CI = 1.31, 2.74) over 10.7 years.
Baseline total effusion-synovitis and suprapatellar pouch effusion-synovitis were independently associated with total WOMAC score ($\beta$=2.08,95%CI=0.16,4.16) and pain and dysfunction scores (all $p<0.05$) over 10.7 years. However, there was no significant association between effusion-synovitis and cartilage volume loss. Total (HR=1.58,95%CI=1.01,2.49), sub popliteal recess (HR=1.53, 95%CI=1.11,2.



11) and suprapatellar pouch (HR=1.90,95%CI=1.25,2.89) effusion-synovitis was associated with TKR over 10.7 years. However, these associations were dependent of other structural pathologies except grade 3 suprapatellar effusion-synovitis.
**Conclusions:** Signal intensity alterations of IPFP at baseline were significantly associated tibial cartilage volume loss and TKR over 10.7 years independent of other structural pathologies. Effusion-synovitis (especially at suprapatellar pouch) was independently associated with knee pain and TKR. These results suggest that effusion-synovitis was associated with clinical progression and IPFP signal intensity alteration was associated with structural progression and TKR, and can be used as independent markers of progression of KOA.
**Acknowledgement:** National Health and Medical Research Council of Australia funded this study.
**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

## How to identify and follow patients with inflammatory back pain?

### OP0145 AN EVALUATION OF INFLAMMATORY BACK PAIN IN THE COMMUNITY – A NOVEL WAY OF USING SOCIAL MEDIA (FACEBOOK)

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**Background:** In the management of Spondyloarthropathy, early diagnosis is the key. Previous UK studies show an average delay in diagnosis of IBP of up to 8 years. This is partly due to a failure of individuals with IBP symptoms to present to their GP and partly to a failure of GPs to recognize the IBP patient subgroup. IBP classification criteria have recently been developed and used in clinical practice. We applied a novel recruitment method using Facebook to identify IBP sufferers in the community. This may help to raise awareness toreduce the delay in diagnosis of Spondyloarthropathy.
**Objectives:** Evaluate a novel way of recruiting potential patients with IBP, using social media.
Determine which of the two criteria sets for IBP, ie. ASAS or Calin, is fulfilled by more patients.
**Methods:** A novel recruitment method using Facebook was applied in a cross-sectional survey carried out in the UK over 5 months to identify adults ($\geq$18 years) with symptoms suggestive of IBP. Other methods, principally newspaper advertising, were used to generate a second group of participants for comparison. Online questionnaire-based surveys were completed to assess each group for IBP using the ASAS and Calin criteria. Data about previous diagnoses, GP, hospital consultations and back pain-related investigations, were also collected.
**Results:** Of the 585 participants, 455 (77.8%) were recruited through Facebook and 130 (22.2%) by a Non-Facebook method. Of the Non-Facebook group, 90 (15.4%) were recruited by a newspaper advert and 40 (6.8%) by another method. The mean age of the Facebook group was typical of IBP at 41.5 years, and the mean age of the Non-Facebook group was higher at 59.4 years. Most participants were female: 447 (76%).
Proportions of those previously diagnosed with Ankylosing Spondylitis, told that their back pain was associated with "inflammation", and were IBP positive on the questionnaire respectively, are shown in Table 1. In total 122 survey participants (21%) met the ASAS, and 292 (50%) met the Calin criteria for IBP at the time of the survey.
The majority of patients from each group reported consulting their GP, however few patients from either group had seen a rheumatologist (Table 1). The reason for non-referral to secondary care is unclear. Regarding further investigations, 45% (204) of the Facebook group reported having an MRI scan and 45% (205) an X-ray, whereas 50% (65) of the Non-Facebook group reported having an MRI scan and 59% (77) said they had been for an X-ray.
**Conclusions:**
– Facebook advertising recruited a younger group of respondents of whom more fulfilled the criteria for IBP, suggesting this may be a cost-effective way of identifying patients earlier.
– Most patients with chronic back pain had consulted their GP, but few who met the criteria for IBP had been referred to a rheumatologist indicating the need for additional GP education.
– In our study group the ASAS IBP criteria were fulfilled by fewer patients than the Calin criteria.
**Acknowledgement:** This study was sponsored by AbbVie and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.
The authors wish to thank Bobby Brown, who supported this work as a medical writer and Patients Direct, who designed and conducted the study.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3776

### OP0146 PATTERNS OF CLINICAL ASSESSMENT OF GENERAL PRACTITIONERS WHEN FACING A PATIENT SUSPECTED FOR SPONDYLOARTHRITIS; A STUDY WITH UNANNOUNCED STANDARDIZED PATIENTS IN DAILY PRACTICE

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**Background:** Timely recognition and referral of patients with spondyloarthritis (SpA) is challenging due to the insidious disease onset and frequent unawareness of the clinical picture by general practitioners (GPs). In a previous intervention study, we demonstrated that an educational programme targeted at recognition of SpA clearly improves referral of patients suspected for SpA.[1]
**Objectives:** To evaluate (1) the clinical assessment patterns of GPs and GP-residents when facing a patient suspected of having spondyloarthritis (SpA) and (2) the influence of an educational intervention on these clinical assessment patterns.
**Methods:** Alongside the intervention study, data were collected for this present qualitative study. GP (residents) were visited in 2 rounds by standardised patients (SPs) simulating either axial or peripheral SpA. In between, an educational intervention on SpA for half of the GP residents was organized. The other half and all GPs served as controls. Participants were visited by the SPs during their regular outpatient clinic and were unaware of the nature of the medical problem and study purpose. After the visit, SPs completed a case-specific checklist inquiring about disease-related items. These items were categorized into four subgroups: questions regarding (1) differentiation between a mechanical or inflammatory origin of the complaint, (2) presence of swollen joints, back pain or entheseal complaints (3) presence of extra-articular manifestations and (4) family history. Differences in patterns of clinical assessment were explored for the education versus the control group. Descriptive analyses were used to analyse demographic data.
**Results:** Sixty-eight (38 GP-residents (mean age 27.9 yrs, 32% male) and 30 GPs (mean age 52.5 yrs, 80% male) participated. Both rounds of SP-encounters were completed by 61 (90%) and 59 (87%) participants for the axial and peripheral SpA case, respectively.
Axial SpA case (Figure): participants who received education were in round 2, as compared to round 1, somewhat more likely to ask questions about the specific inflammatory character of the complaint. However, the most noticeable gain was seen in questions regarding the presence of extra-articular manifestations and family history of SpA. Despite that controls also tended to ask more questions regarding the inflammatory character of the complaint and family history of SpA in round 2, an evident increase in questions belonging to other subgroups (e.g. extra-articular manifestations) was not observed.
Peripheral SpA case (data not shown): in round 2, GP residents who received the educational intervention asked more questions regarding extra-articular complaints and family history of SpA. However, the observed gain was less evident as compared to the axial SpA case. In the control group, no difference was observed between both rounds.

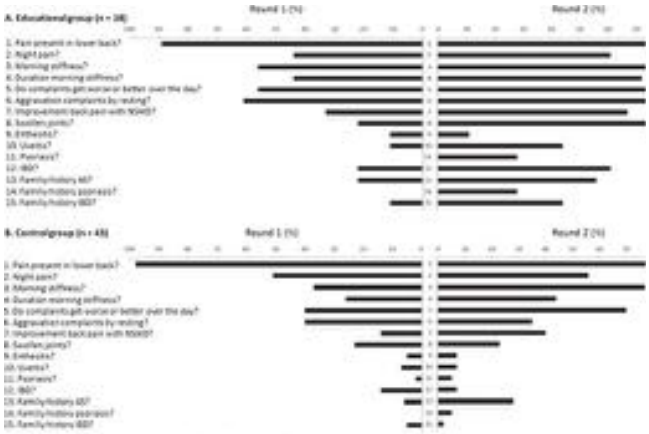


Figure. History taking pattern of GP (residents) facing a patient with axial SpA in round 1 and 2.

**Conclusions:** Targeted education can help GPs to improve their history taking and hence pattern recognition of patients suspected for SpA. Focusing on history taking alone already increases the chance of referral to the rheumatologist and targeted education should therefore be offered to all GPs to maximize a successful implementation of a referral strategy in primary care.
**References:**
[1] van Onna M, et al. RMD Open 2015;1:e000152.
**Disclosure of Interest:** M. Van Onna Consultant for: Janssen-Cilag and UCB, S. Gorter Speakers bureau: UCB, B. Maiburg: None declared, G. Waagenaar: None declared, A. van Tubergen Grant/research support from: Roche, Pfizer, Consultant for: Janssen-Cilag, UCB, Abbvie, MSD, Novartis, Speakers bureau: Abbvie, MSD, UCB, Pfizer
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**THURSDAY, 9 JUNE 2016**

## Physical activity assessment - what do we know, what do we do, how does it work?

### OP0147-HPR AEROBIC CAPACITY OVER 16 YEARS IN PATIENTS WITH RHEUMATOID ARTHRITIS; RELATIONS TO RISK FACTORS FOR CARDIOVASCULAR DISEASE

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**Background:** Patients with rheumatoid arthritis (RA) suffer from increased mortality due to cardiovascular disease (CVD) (1). Aerobic capacity ($VO_2$ max) is inversely and strongly related to cardiovascular disease in the general population (2). RA patients have shown very low levels of $VO_2$ max compared to normative values of healthy adults (3), which may be of importance for the increased CVD incidence in RA.
**Objectives:** To analyse the change of $VO_2$ max over time from disease onset and associated potential risk- and health factors in patients with RA.
**Methods:** 25 patients (20 f/ 5 m), diagnosed with RA 1995–2002 were tested at disease onset (<12 months from symptom onset) and after a mean of 16.2 years. Applied measurements were: sub-maximal ergometer test for $VO_2$ max, functional ability, joint- and muscle function, self-efficacy, ESR, CRP, number of tender and swollen joints and patient's global health. At follow-up, the risk of CVD was measured as blood levels of lipids, insulin and glucose, Body mass index (BMI), waist circumference and body composition measured by Dual-energy X-ray absorbtiometry (DXA). Pulse wave analysis (PWA), was used to register early endothelial dysfunction, arterial stiffness and systolic blood pressure in aorta besides peripheral blood pressure. Carotid Intima-Media Thickness (IMT) was measured by ultrasonography. Additionally, Fatigue Severity Scale was used at follow-up.
**Results:** All measures reflecting disease activity decreased significantly during the follow-up period. $VO_2$ max was (median (IQR)) 32.3 (14.2) ml $O_2$/kg x min at disease onset, and 33,2 (10.5) at follow-up ($p>0.05$). Aerobic capacity at inclusion was associated with follow-up values for age (r=-.469, p=.018), $VO_2$ max (r=.557, p=.004), BMI (r=-.401, p=.047), body weight (r=-.409, p=.043), waist circumference (r=-.498, p=.011) and periferal pulse pressure (r=-.415, p=.039). Variables at disease onset associated with $VO_2$ max at follow-up were $VO_2$ max (r=.557, p=.004) and self-efficacy for function, (r=.544, p=.029).
**Conclusions:** In patients with RA followed for 16 years from disease onset, $VO_2$ max was maintained. High aerobic capacity at disease onset was associated with favourable measures of $VO_2$ max and body weight at follow-up. The variables at disease onset that best correlated with a high $VO_2$ max at follow-up were high $VO_2$ max and self-efficacy for function. Our results may be important for preventive strategies in RA.
**References:**
[1] Wallberg-Jonsson, S., et al. J Rheumatol 1997;24(3):445–451.
[2] Kodama, S., et al. JAMA 2009;301(19):2024–2035.
[3] Metsios, G.S., et al. Rheumatology (Oxford) 2015;54(12):2215–2220.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5803

**THURSDAY, 9 JUNE 2016**

## How cell death shapes immunity and tolerance

### OP0148 FIRST IN CLASS THERAPEUTIC ACPA REDUCES INFLAMMATION BY INHIBITION OF NETOSIS

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**Background:** Neutrophils together with aberrant Neutrophil Extracellular Trap (NET) formation contribute to the induction and propagation of inflammation. A growing number of studies indicate that Peptidyl Arginine Deiminases (PADs) mediated conversion of arginine to citrulline residues in proteins are essential for NETosis, generation of auto-antigens, autoimmunity, and the breaking of tolerance in rheumatoid arthritis (RA). In RA patients, enhanced NETosis is observed in circulating and synovial neutrophils, and NET components are observed in blood and joints.
**Objectives:** Our objective is to develop a novel first in class NET-inhibiting therapeutic anti-citrullinated protein antibody (tACPA) treatment for RA and other auto-immune diseases in which aberrant NET formation adds to the severity of the disease.
**Methods:** Human neutrophils from blood donors have been used in order to visualize the NETosis inhibiting properties of tACPA. Furthermore, collagen antibody-induced (CAIA) as well as collagen-induced (CIA) arthritis mouse models have been used in order to test the therapeutic properties of tACPA.
**Results:** In human neutrophils, NETosis induction with calcium ionophore A-23187 or physiological stimuli like human synovial fluid is strongly inhibited by tACPA treatment (40–90% NET reduction compared to non-treated cells (n>40 different donors)). This observation has been confirmed by Myeloperoxidase and Neutrophil Elastase activity as well as immunohistochemistry read-outs. In both CAIA and CIA mouse models, NET-inhibiting tACPAs are able to prevent the onset and/or exacerbation of inflammation, and prevent or strongly reduce joint damage. Histological analysis of tACPA-treated inflamed mouse joints revealed a significant decrease in neutrophil influx. We identified the epitopes recognized by tACPA to be citrullinated domains of histones 2A and 4.
**Conclusions:** We have identified antibodies directed against a citrullinated epitope in murine and human histones 2A and 4. In RA mouse models, we demonstrate that tACPAs strongly prevents the occurrence of swelling and joint damage. We propose that the therapeutic effect of tACPA acts through the inhibition of NET and auto-antigen formation, clearance of formed NETs and toxic histones. In RA patients extinguishing auto-antigen production offers an orthogonal approach for treating this destructive autoimmune disease, potentially without impacting systemic immunity.
Citryll and ModiQuest are developing tACPAs as treatment for diseases where NETs and NETosis are driving or contributing to disease progression.
**Disclosure of Interest:** R. Chirivi Shareholder of: Citryll BV, Employee of: ModiQuest BV, J. van Rosmalen Employee of: ModiQuest BV, G. Schmets Employee of: ModiQuest BV, H. van Es Shareholder of: Citryll BV, Employee of: Citryll BV, J. Raats Shareholder of: Citryll BV and ModiQuest BV
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**THURSDAY, 9 JUNE 2016**

## "Smoke a joint to protect the joint". Cannabidoids & neuropeptides in pain and inflammation

### OP0149 DOPAMINE PATHWAY AND BONE METABOLISM IN RHEUMATOID ARTHRITIS

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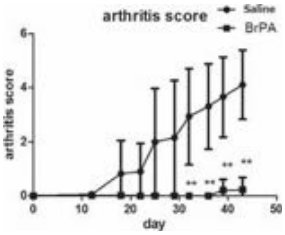
**Background:** A body of studies demonstrates the influence of the nervous system on the immune response. We recently described that dopamine, a neurotransmitter of the sympathetic nervous system, is locally produced by synovial fibroblasts of rheumatoid arthritis (RA) patients and influences *in vitro* cytokine release and inflammation (1). In addition, *in vivo* evidence confirmed the involvement of dopamine receptors (DR) in arthritis (2), and a subtype of DR was described to be expressed by *in vitro* differentiated human osteoclasts (3). These studies, together with the clinical evidence of an increased risk of osteoporosis in patients affected by Parkinson's disease, suggest an involvement of dopamine in joint destruction during RA. The aim of this study is therefore not only to investigate the role of the dopamine pathway on bone remodeling in RA patients, but also to unravel new pathways involved in joint destruction.
**Objectives:** The aim of this study is therefore not only to investigate the role of the dopamine pathway on bone remodeling in RA patients, but also to unravel new pathways involved in joint destruction.
**Methods:** Bone tissue was obtained from osteoarthritis (OA, n=6) and RA (n=4) patients during knee joint replacement surgery. Osteoblasts were isolated from the bone spongiosa. Immunohistochemistry of paraffin-embedded bone samples and immunocytochemistry of isolated osteoblasts were performed using antibodies against the five subtypes of DR (D1 to D5). Isolated osteoblasts were treated with specific DR agonists for 24 h or 7 d. IL-6 and IL-8 were quantified after 24 h stimulation by ELISA. Expression of tyrosine hydroxylase (TH), the rate limiting enzyme for dopamine production, was quantified in untreated isolated osteoblasts by real-time PCR. Mann Whitney test was used for statistical data analysis.
**Results:** Dopamine receptors D1, D3 and D4 could be detected by immuno-histochemistry in the bone remodeling zone of RA patients while OA samples did not express these receptors in the bone remodeling zone. Dopamine receptor subtypes D1, D2, D3 and D5 were present on isolated osteoblasts, with stronger expression in RA compared to OA. Stimulation of D1-like DR induced a significant dose-dependent increase of IL-6 release in RA compared to the untreated control (+79 ±43%, $P<0.005$). In contrast, no significant effects were detectable for OA osteoblasts. IL-8 release was not significantly altered in both RA and OA osteoblasts. TH was expressed in osteoblasts from 5 of 6 OA and from 2 of 4 RA patients, with expression levels even higher than in synovial fibroblasts (up to +50% in RA osteoblasts).
**Conclusions:** Dopamine receptors are upregulated in the bone remodeling zone of RA patients and their activation seems to have proinflammatory effects and to inhibit osteoblast activation. Expression of TH in osteoblasts suggests autocrine/paracrine effects of dopamine locally synthesized in the bone. These data underline the key involvement of the dopamine pathway in bone remodeling and joint erosion in RA.
**References:**
[1] Arthritis Rheumatol. 2014;66:2685–93
[2] Mod. Rheumatol. 2011;21:260–6

[3] Bone 2013;56:1–8
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2873

### OP0150 3-BROMOPYRUVATE AMELIORATES AUTOIMMUNE ARTHRITIS BY EXERTING A DUAL EFFECT ON BOTH TH17 AND TREG CELL DIFFERENTIATION AND DENDRITIC CELL ACTIVATION

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**Background:** Recent studies have shown that cellular metabolism plays an important role in regulating immune cell function. In the process of cell differentiation, both interleukin-17-producing T (Th17) cells and dendritic cells (DCs) show increase of glycolytic activity by upregulating glycolytic enzymes, such as hexokinase-II (HK-II). Blocking glycolysis by 2-deoxyglucose has recently been demonstrated to inhibit Th17 cell differentiation while promote regulatory T (Treg) cell generation, and then ameliorate experimental autoimmune encephalitis model.
**Objectives:** The aim of this study is to verify the effect of 3-bromopyruvate (BrPA), a specific inhibitor of HK-II, on the differentiation and function of immune cells and on experimental arthritis in SKG mice.
**Methods:** Arthritis was induced in SKG mice by Zymosan A injection. BrPA (5 mg/kg) was administered subcutaneously once daily. CD4+ T cells from splenocytes of unimmunized SKG mice were cultured with anti-CD3/anti-CD28, anti-IFN-γ, anti-IL-4, IL-6, TGF-β, and IL-2, with or without BrPA for 5 days, and then analyzed by flow cytometry. Bone marrow (BM) cells from unimmunized SKG mice were cultured with GM-CSF and IL-4 (for 3 days), and with LPS (for 1 day) with or without BrPA, and then analyzed by flow cytometry.
**Results:** Treatment with BrPA significantly ameliorated arthritis of SKG mice (Figure). Histological scores of arthritis in BrPA-treated mice were significantly reduced compared with those in control mice. Flow cytometric analysis revealed that significant increase of Treg cells, decrease of Th17 cells, and decrease of CD40+CD86+CD11b+CD11c+ activated DCs were observed in the splenocytes from BrPA-treated mice. BrPA did not affect IFN-γ-producing Th1 cells nor IL-4-producing Th2 cells. *In vitro*, BrPA facilitated the differentiation of Treg cells, while it inhibited the development of Th17 cells. In addition, treatment of BM cells with BrPA inhibited the differentiation of activated DCs and the production of TNF-α and IL-6 from DCs.




**Conclusions:** BrPA facilitates the differentiation of Treg cells, and inhibits the development of Th17 cells and the activation of DCs, and ameliorates arthritis in the SKG mice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5269

**THURSDAY, 9 JUNE 2016**

## Teaching clinical skills

### OP0151 A STUDY ON MEDICAL STUDENTS LEARNING ULTRASOUND IN RHEUMATOID ARTHRITIS (ASMSLURA)

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**Background:** Rheumatoid arthritis (RA) affects ~ 0.5% of the adult population worldwide. The current "standard" of teaching consists of didactic lectures and bedside teaching. It has been shown that musculoskeletal teaching is inadequate and needs improvement.[1–3] Ultrasound is safe and increasingly taught to postgraduates in specialties such as rheumatology and orthopaedics to improve their clinical skills. Literature suggests that ultrasound teaching may be beneficial for medical students.[4]
**Objectives:** This study aimed to assess whether the incorporation of ultrasound in teaching improved medical students' knowledge of rheumatoid arthritis and interest in musculoskeletal medicine.
**Methods:** This study was a single site, randomised, prospective, open, cross over trial comparing RA teaching in medical students, assisted with ultrasound, versus teaching via standard methods. The study included 3rd and 4th year students enrolled in the University of New South Wales 6 year undergraduate medical program. Students were randomised into 2 groups, and underwent both sets of teaching in different order. A written multiple-choice exam, was held before any teaching began, and after the first and second sets of teaching. An evaluation survey was administered at the conclusion of the two sets of teaching. Results from the MCQ exam was statistically analysed and the survey was qualitatively analysed.
**Results:** A total of 20 students completed the study (11 students from group 1 and 9 from group 2). The exam scores improved significantly ($p \leq 0.01$) for both groups after they undertook standard teaching. However, the exam scores did not improve for either group after ultrasound teaching. We also found that exam scores improved significantly ($p \leq 0.01$) for both groups at the conclusion of the entire teaching period. The order in which the students underwent teaching did not result in significantly different scores. The questionnaire revealed that most students thought ultrasound was of educational value and helped them improve their knowledge of anatomy. However they were equivocal about whether it helped their learning of RA. Both groups rated standard teaching highly.
**Conclusions:** This crossover trial demonstrates significant improvement in students' knowledge of RA after undergoing standard teaching as opposed to ultrasound teaching. Factors which may have contributed to this result and which deserve further exploration include using different assessment methods for ultrasound teaching, using different learning levels and using different teachers.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6194

**THURSDAY, 9 JUNE 2016**

## What is done for people with rare diseases? Can we do more?

### OP0152-PARE STARTING A DISEASE SPECIFIC YOUTH GROUP ON A NATIONAL LEVEL

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**Background:** A high proportion of individuals living with lupus (SLE) are young women, aged 25 to 35. At this age, they are getting ready to "begin" life with partners, children, education and careers. For most of them, this all stops at the time of diagnosis. They have to adjust to a lifelong struggle with pain, fatigue, headaches, cognitive problems and strong medications. As a result of this autoimmune disease, it is for instance, no longer risk-free to bear a child. This has to be done in close co-operation with various health professionals, and for some women, it is not an option at all.
**Objectives:** To help these young people to understand their disease and inspire them to live a full life, despite of coping with this incurable disease. A better understanding of the disease makes it easier to take control of treatment, and thereby having a more fulfilling life.
**Methods:** The goal was to start a youth group within our mother organisation. Although we already have a working and active SLE group in Denmark, that has existed for 22 years, we found out, that the young people were not joining in. The issues of a lupus patient changes considerably from when you are in your 20s, to your 50s (where most of our members were at that time). As a young person, you may not be comfortable with talking about your sex life with "older" ladies. We started with a theme day about sex and partnership, only for young people, and their spouses – and this was a great success.
**Results:** Out of this day, a Facebook group for young people (ages 18–35) was created, where the young people can discuss everything they want to. There are no taboos and people support each other with good advice or a shoulder to cry on. Besides the Facebook group, we now have a youth day with changing themes on our schedule every year. We have one person dedicated to the youth activities and this person also has a seat in our mother organisation, whereby youth issues are implemented in all our activities.
**Conclusions:** We now have a well functioning and active youth group, where young people with lupus can support each other and raise the issues important to them.
**References:**
[1] The web page of our mother association "SLE-diagnosenetværk DK": http://sle.dk and the Facebook group "Unge med Lupus/SLE": https://www.facebook.com/groups/1398750663726027/

**Acknowledgement:** The support of the Danish arthritis association "Gigtforeningen" has made it possible to fund our youth projects without having to go fundraising ourselves, which we are very grateful for.
**Disclosure of Interest:** None declared
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OP0153-PARE **REUMAMAMA'S EN –PAPA'S: INFO SESSIONS FOR (FUTURE) PARENTS WITH RMDS AND FOR PARENTS WITH CHILDREN WITH JUVENILE ARTHRITIS**

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**Background:** When diagnosed with a rheumatic condition (RMD), the first concern is managing and controlling the disease. More specific topics such as how you deal with a diagnosis as a parent of a child with an RMD or how to take care of children as a young parent with an RMD are less discussed with the rheumatologist. A lot of questions and concerns about heredity and pregnancy stay unanswered too.
**Objectives:** ReumaNet wants to offer tailor made information for young people with an RMD and a child wish and for parents of a child with an RMD.
**Methods:** ReumaNet, the Flemish organisation for people with RMDs, organised two info sessions in September-November 2015. The two target groups were 1) young (future) parents with an RMD and 2) parents with a child with an RMD. Both target groups first met informally for sharing their personal stories, concerns, experiences and expectations. During this first meeting, they noted down several questions and concerns regarding the topic. During the second session, different specialists such as a rheumatologist, a psychologist, a gynecologist, a pediatrician, ... tried to answer these specific questions and they gave more information on pregnancy and RMD's in the first group, and RMD's in children in the other group.
**Results:** Both sessions were well attended, although more people showed up during the second session. People obviously feel more safe when they mainly have to listen to information, instead of participating in a discussion.
(Future) parents with an RMD received information regarding heredity, pregnancy, delivery, (breast)feeding and practical tips and tricks regarding taking care of children. Parents with children with an RMD received not only practical information concerning juvenile arthritis (the diagnosis, the disease, future perspectives and impact in school), but also information regarding the psychological impact of receiving and dealing with the diagnosis as a parent.
**Conclusions:** There is a great need for information for either young parents with an RMD as well as for parents of a child with an RMD. Furthermore, these two groups will always be renewed throughout the years. This means the need for this kind of information will be ongoing. Along with organising ReuMaMaMa's, ReumaNet is also developing three brochures on these topics: "Pregnancy and heredity", "How to take care of infants", for parents with a RMD' and "Juvenile Arthritis". The live sessions will be repeated every two years.
**Disclosure of Interest:** None declared
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**THURSDAY, 9 JUNE 2016**

## The Health Professionals' approach to pain management in inflammatory arthritis and osteoarthritis

OP0154-HPR **SPINAL MOBILITY IS IMPAIRED IN PATIENTS WITH CHRONIC BACK PAIN OF SHORT DURATION, BUT DOES NOT DISCRIMINATE BETWEEN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND OTHER FORMS OF CBP**

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**Background:** Ankylosing spondylitis is associated with reduced spinal mobility. Little is known about the spinal mobility in early axial spondyloarthritis (axSpA) and how it compares to patients with other forms of chronic back pain (CBP).
**Objectives:** The aim was to compare spinal mobility in patients with CBP of short duration with reference mobility curves from the general population and to examine whether frequently used spinal mobility measures (SMM) can discriminate between axSpA and other forms of CBP.
**Methods:** The SPACE-cohort includes patients with CBP ($\geq$3 months, $\leq$2 years, onset $<$45 years) recruited from 5 centres in Europe. The CBP patients were classified as axSpA (fulfilling the ASAS criteria), possible axSpA (possSpA) (not fulfilling ASAS criteria but $\geq$1 axSpA feature) or not having SpA (noSpA).
Spinal mobility was assessed with lateral spinal flexion (LSF), chest expansion (CE), intermalleolar distance (IMD), modified Schober (MS), cervical rotation (CR) and occiput-to-wall distance (OWD).
SMM, except OWD, were defined as impaired if below the 5th percentile reference curve from general population, given their age and for CE and IMD also height, following the equations of mobility curves for each measures[1]. OWD $>$0 was considered impaired. The proportion of patients with impaired spinal mobility for each measure was compared across the patient groups using Chi square.
**Results:** In total 393 CBP-patients were included: 142 axSpA, 139 possSpA and 112 noSpA. Some characteristics of patients with axSpA were statistically significant different compared to possSpA and noSpA: a larger proportion (%) was male 48/28/27, reported less back pain (NRS 0–10) median 4.0/6.0/6.0 and patients with axSpA were taller (cm) than patients with possSpA mean 177/173/174.
In all CBP patients, the most frequently impaired mobility measure was LSF 40% followed by CE 22%, CR 18%, IMD 17%, MS 15% and OWD 11% (table 1). No statistically significant differences in proportion of patients with impaired spinal mobility were found between the CBP subgroups.

Table 1. Proportion of patients categorised with impaired[α] spinal mobility

| Measure | All chronic back pain (n=393) | axSpA (n=142) | possSpA (n=139) | noSpA (n=112) | p-value |
|---|---|---|---|---|---|
| Lateral spinal flexion (393) | 158 (40) | 50 (35) | 57 (41) | 51 (46) | 0.24 |
| Chest expansion[β] (374) | 80 (22) | 27 (20) | 31 (24) | 23 (21) | 0.79 |
| Cervical rotation (390) | 69 (18) | 21 (15) | 30 (22) | 18 (16) | 0.26 |
| Intermalleolar distance (371) | 63 (17) | 16 (12) | 28 (22) | 19 (18) | 0.13 |
| Modified Schober (394) | 57 (15) | 17 (12) | 20 (14) | 20 (18) | 0.42 |
| Occiput to wall[γ] (393) | 42 (11) | 18 (13) | 18 (13) | 6 (5) | 0.10 |

Values are number (percent). [α]Below the 5th percentile compared with age- (height) specific mobility curves [1], [β]the derivation of reference value included height, [γ]$>$0 categorised as impaired.

**Conclusions:** Among patients with CBP of short duration, between15–40% had a spinal mobility below the 5th percentile in the general population depending on the measurement used. The most affected SMM was LSF. Impaired spinal mobility was equally prevalent in patients with axSpA and other causes of CBP. Our findings suggest that the SMM recommended for axSpA may be of little differential diagnostic value.
**References:**
[1] Ramiro ARD 2015
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## News from kinase inhibitors

OP0155 **DEVELOPMENT OF A JAK3 SPECIFIC INHIBITOR CLINICAL CANDIDATE: FUNCTIONAL DIFFERENTIATION OF JAK3 SELECTIVE INHIBITION OVER PAN-JAK OR JAK1 SELECTIVE INHIBITION**

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**Background:** Janus kinase (JAK) inhibitors targeting multiple JAK isoforms, JAK1 and 2, or selective against JAK1 are currently utilized in clinical practice or being developed for the treatment of various inflammatory and oncological diseases. No truly JAK3-selective inhibitor has reached the clinic. JAK3 signal in pairs with JAK1 to transduce signal elicited from six known cytokines (IL-2, IL-4, IL-7, IL-9, IL-15 & IL-21) binding to the gamma-common (g-c) chain cytokine receptors. JAK1 in addition to be required for g-c chain cytokine receptors signaling can also signal in pair with JAK2 or TYK2 and is required for other cytokine receptors signaling such as type I and II interferons and IL-6 and IL-10 families of cytokines. Other cytokines such as IL-12 and IL-23 are signaling via JAK2 and TYK2. Additionally, hematopoietic cytokines such as EPO and TPO as well as cytokines such as IL-3 and IL-5 signal via homodimers of JAK2.
**Objectives:** Develop a JAK3 selective inhibitor that will inhibit signaling from the g-c chain cytokine receptors at therapeutic dosing without inhibiting signaling by other cytokines such as hematopoietic cytokines, type I and II interferons and IL-6, IL-12 and IL-10 families of cytokines.
**Methods:** A JAK3-specific covalent ATP competitive inhibitor was assessed functionally *in vitro* and *in vivo*. Functional differentiation of JAK3 selective inhibition as compare to pan-JAK inhibition (tofacitinib) or JAK1 selective inhibition was also assessed.
**Results:** The inhibitor showed JAK3 selective inhibition in biochemical and cellular assays. It inhibits Th1 and Th17 cell differentiation and function. Importantly, sparing JAK1 inhibition, through the selectivity of this inhibitor, preserved anti-inflammatory functions such as the differentiation of alternatively activated M2a macrophages. Unlike pan-JAK or JAK1-selective inhibitors, JAK3 selective inhibition also preserved IL-10-dependent suppression of the production of pro-inflammatory cytokines following LPS treatment in macrophages while maintaining the suppression of TNF and IL-1 responses in IL-27-primed macrophages. Further characterization of this compound in the rat adjuvant-induced arthritis (AIA) demonstrated efficacy at reducing disease pathology.
**Conclusions:** We have identified the first trully selective JAK3 inhibitor with potency and properties that make it suitable for further clinical development.
**Disclosure of Interest:** J.-B. Telliez Employee of: Pfizer, L. Wang Employee of:

Pfizer, J. Jussif Employee of: Pfizer, T. Lin Employee of: Pfizer, L. Li Employee of: Pfizer, E. Moy Employee of: Pfizer, W. Li Employee of: Pfizer, Y. Zhao Employee of: Pfizer, K. Crouse Employee of: Pfizer, P. Symanowicz Employee of: Pfizer, M. Hegen Employee of: Pfizer, M. E. Banker Employee of: Pfizer, F. Vincent Employee of: Pfizer, J. Clark Employee of: Pfizer, A. Thorarensen Employee of: Pfizer

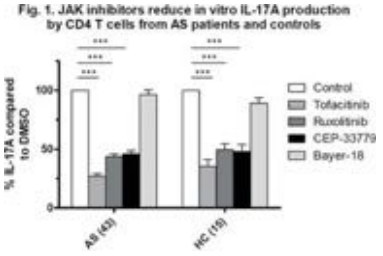
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### OP0156 DECIPHERING THE IN VITRO THERAPEUTIC POTENTIAL OF JAK INHIBITORS IN ANKYLOSING SPONDYLITIS

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**Background:** In Ankylosing Spondylitis (AS) therapeutic options include blocking of TNF and IL-17, but are expensive and limited compared to other rheumatic diseases. In addition there is no convincing evidence that either of these therapies is able to block new bone formation, the hallmark of AS. Small molecule inhibitors of Janus kinases (JAK) are potent inhibitors of other inflammatory diseases including Rheumatoid Arthritis (RA), and inhibit new bone formation in murine Spondyloarthritis[1,2].
**Objectives:** We evaluated the ability of 4 different JAK family inhibitors to reduce IL-17A production in vitro using blood and synovial fluid samples from patients with AS, Psoriatric Arthritis (PsA) and RA. We choose to study Tofacitinib, as it shows relative specificity to JAK3, Ruxolitinib (JAK1), CEP-33779 (JAK2) and Bayer-18 (TYK2), in order to decipher the most potent inhibitor for this disease.
**Methods:** CD4 T cells were isolated from PBMC of AS (n=43), PsA (n=13), RA patients (n=10) and Healthy controls (HC, n=15) and stimulated for 3 days under Th17-promoting conditions in the presence of JAK inhibitors. Cytokine secretion (IL-17A for all samples, IL-17F, IL-22, GM-CSF and IFN$\gamma$ for a representative subgroup) was assessed using ELISA, measured in pg/m, and expressed as relative to control. Cytotoxicity and proliferation were measured with Annexin V/7-AAD staining and CFSE dilution on Flow cytometry. TYK2 was silenced in primary human CD4 T cells with siRNA and effects were analysed using ELISA and Western Blot.
**Results:** All JAK inhibitors tested reduced secretion of IL-17A in CD4 T cells from AS, PsA, RA patients and HC (see Fig. 1 for data on AS and HC). In a small subset of 10 AS patients Tofacitinib showed statistically significant inhibition of IL-17F, IL-22, GM-CSF and IFN$\gamma$ secretion, and CEP-33779 of IL-22 and GM-CSF secretion. At the same time cytotoxicity and anti-proliferative capacity of the inhibitors was low. No correlation between inhibitory capacity of the different small molecules and clinical parameters was observed. Bayer-18 did not significantly reduce Th17 cytokine secretion, but siRNA-mediated knock down of TYK2 in primary human CD4 T cells inhibited IL-17A, IL-22 and IL-17F secretion, when knock-down efficacy exceeded 70%.

Fig. 1. JAK inhibitors reduce in vitro IL-17A production by CD4 T cells from AS patients and controls




**Conclusions:** All JAK inhibitors tested reduce IL-17A secretion from CD4 T cells in vitro. Despite the fact that our study does not address the specificity of the different JAK inhibitors, we find no clear evidence that targeting any one JAK family member is superior in reducing in vitro Th17 responses. Our siRNA knock-down data suggest that TYK2 is still a valuable target for developing new treatments in AS, even though blockade of its kinase activity was not efficacious in reducing IL-17A secretion. One explanation is that the IL-17A-inducing activity of TYK2 was not inhibited by Bayer-18 in our assays or that the scaffold function of TYK2 is more important in this pathway.
**References:**
[1] Fleischmann R. et al, Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. N Engl J Med. 2012;367(6).
[2] Lories R. et al, Tofacitinib inhibits inflammation and new bone formation in murine Spondyloarthritis but does not adversely inhibit human MSC function [abstract]. Arthritis Rheumatol. 2015;67 (suppl 10).
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**FRIDAY, 10 JUNE 2016**

## Crystal arthritis

### OP0157 PREVALENCE AND SIGNIFICANCE OF MEFV GENE MUTATIONS IN PATIENTS WITH GOUTY ARTHRITIS

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**Background:** Gouty arthritis is a chronic erosive autoinflammatory disease. Pyrin has anti-inflammatory effects in the regulation of inflammasome and is encoded by the MEFV gene. MEFV gene mutations trigger inflammatory cascade and cause familial Mediterranean fever The relationship between different rheumatic diseases and the MEFV gene mutations was demonstrated.
**Objectives:** The aim of this study was to determine the frequency of MEFV gene mutation in patients with gouty arthritis and identify a possible correlation with disease phenotype.
**Methods:** Ninety-three patients with gouty arthritis and 102 healthy controls, compatible with age, gender and ethnicity, were included in the study. MEFV gene was investigated by PCR method.
**Results:** Out of 93 patients with gouty arthritis, 36 (38.7%) showed MEFV gene mutation carriage, whereas 20.6% in healthy control group. Distribution of mutations identified in patients with gouty arthritis was as; R202Q in 18 (19.3%), E148Q in 5 (5.4%), K695R in 4 (4.3%), M680I in 2 (2.1%), V726A in 2 (2.1%), P369S in 2 (2.1%), R408Q in 2 (2.1%), M694V in 1 (1.1%), respectively. Three patients were identified with compound heterozygosity. Distribution of MEFV gene mutation carriage in healthy controls was; E148Q in 11 (10.7%), M694V in 2 (1.9%), M694I in 1 (0.9%), M680I in 2 (1.9%), V726A in 1 (0.9%), A744S in 1 (0.9%), K695R in 2 (1.9%), and P369S in 1 (0.9%) pateints, respectively. Higher MEFV gene mutation carrier frequency was observed in patients with gouty arthritis, compared with the control group (p=0.009). Heterozygous R202Q was the most common mutation detected in patients with gouty arthritis while heterozygous E148Q in healthy control group. Statistically significant difference was not detected between clinical findings of gouty arthritis and the MEFV gene mutations ($p>0.05$).
**Conclusions:** We determined higher prevalence of MEFV gene mutation in patients with gouty arthritis compared with the healthy control group. The most frequently detected mutation was heterozygous R202Q wheras E148Q in healthy controls. High carriage rates of MEFV gene mutation in gouty arthritis suggests that it may play an important role in the pathogenesis of the disease and predisposition to the disease. In this regard, prospective studies are needed with larger series of patients.
**Disclosure of Interest:** None declared
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### OP0158 MITOCHONDRIAL GENETIC VARIATION AND SUSCEPTIBILITY TO GOUT IN POLYNESIANS

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**Background:** Mitochondria appear to play a central role in the induction of an NLRP3 inflammatory response, an immune response critical for the development of gouty pathology. Mitochondria are in part self-encoding, possessing a 16.5 kB circular genome which encodes 36 genes. Therefore mitochondrial genetic variation may contribute to susceptibility to gout.
**Objectives:** The objective of this study was to test whether mitochondrial genetic variation and copy number among New Zealand Polynesians may be contributing to susceptibility to gout. The Māori and Pacific (Polynesian) populations of New Zealand exhibit a high prevalence of gout (6 and 8%, respectively).
**Methods:** 439 whole mitochondrial genomes belonging to Māori and Pacific men from New Zealand (327 cases, 112 controls) were sequenced to explore whether mitochondrial DNA (mtDNA) variation may contribute risk to gout. mtDNA copy number variation was also investigated by looking at relative read depth using Next Generation Sequencing data produced from whole genome sequencing and resequencing of urate loci. Quantitative PCR was undertaken for replication in an extended sample set of 540 Polynesian male and female cases and 530 controls.
**Results:** Within Polynesia, there is relatively little mitochondrial genetic diversity, with around 96% of those sequenced in this study belonging to the B4a1a and derived sub-lineages. A lineage-specific heteroplasmy in hypervariable region I was found to associate with a greater than three-fold higher risk of gout among the mitochondrial sequenced sample set (e.g. heteroplasmy at position 16179: OR 3.28, $P$=0.009; heteroplasmy at position 16181: 3.86, $P$=9x10$^{-5}$; heteroplasmy at position 16182: 3.43, $P$=0.005).
Quantitative PCR of mtDNA from the 1070 Polynesian gout cases and controls showed that individuals with gout possess less mtDNA, on average than healthy controls. With each unit increase in $\Delta$Ct (which reflects a decrease in mtDNA

content), there was a 33% increase in gout risk (OR 1.33, *P*=0.003). The effect was stronger when looking at those participants who possessed urate levels exceeding 0.40 mmol $L^{-1}$ (n=422, OR 1.69, *P*=0.0005).

**References:**

[1] It is unclear whether the reduced mtDNA copy number in gout is a result of the gouty pathology directly (i.e. the reduced mtDNA copy number is caused by the inflammatory processes underlying gout) or whether the reduced mtDNA copy number contributes to the risk of gout. The latter possibility is supported by the increase in risk using hyperuricemic controls suggesting that reduced mtDNA copy number plays a role in inflammation. Given emerging research is showing that mitochondria play a central role in the induction of the NLRP3 inflammasome, in particular with the co-localisation of the NLRP3 and ASC sub-units, a process essential for the generation of IL-1β, these observations may be significant. Exploring mitochondrial genetic variation may further elucidate the inflammatory processes underlying gout.

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## New pathways to treatment

### OP0159 IMPROVING B-CELL DEPLETION IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS: RESISTANCE TO RITUXIMAB AND THE POTENTIAL OF OBINUTUZUMAB

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**Background:** In patients with Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE), who have poor responses to standard doses of rituximab (RTX), enhanced B-cell depletion and improved clinical responses can be achieved with higher doses of RTX. Defects in complement, NK cell function and CD11b polymorphisms associated with SLE may impair the effector mechanisms evoked by RTX whilst high BAFF levels may confer B cells some resistance to apoptosis. Obinutuzumab (OBZ, a Type II anti-CD20 monoclonal antibody [mAb] with afucosylated Fc portion and enhanced affinity for Fcγ receptor III) is more efficient than Rituximab (RTX, a Type I mAb) at inducing malignant B cell cytotoxicity and has recently entered Phase II clinical trials in SLE.

**Objectives:** To compare the effects of RTX and OBZ against B cells from patients with RA and SLE in vitro and dissect any differences between the two mAbs in evoking effector mechanisms in RA and SLE.

**Methods:** We used flow cytometry to perform: in vitro whole blood B cell depletion assays to compare the efficiency of OBZ and RTX in depleting target B cells; surface fluorescence-quenching assays to determine the extent of mAb internalization; complement dependent cellular cytotoxicity (CDC) assays to assess the ability to recruit complement and lyse target cells; NK cell degranulation assays assessing surface expression of CD107a as a measure of antibody-dependent cellular cytotoxicity (ADCC); and neutrophil activation assays assessing the surface expression of CD62L and CD11B. Annexin V positivity represented cell death in direct cell death (DCD) assay. OBZ-gly (OBZ with Fc glycosylation similar to RTX) was used to assess the effects of afucosylation. All mAb were used at 1μg/mL except for the CDC and DCD assays (10μg/mL).

**Results:** OBZ was >2 fold more efficient than RTX at inducing cytotoxicity in B cells from patients with RA (n=31) and SLE (n=34) in whole blood assays. It was also internalized by isolated B cells from SLE patients (n=6) to a significantly lower extent than RTX with a median surface accessible mAb of 75% and 59%, respectively, after 6 hours of incubation. OBZ was at least twice as efficient at inducing NK cell activation, in RA (n=13) and SLE (n=19); and also activated neutrophils more efficiently than RTX in SLE (n=15) (Figure 3). In contrast, RTX was significantly more efficient than OBZ at evoking CDC of isolated B cells (SLE, n=6). OBZ was also more efficient at inducing direct cell death in CD19+ B-cells as a whole and in naïve (IgD+CD27-); and switched (IgD-CD27+) memory B-cells, a higher frequency of which is associated with poor clinical response after RTX.

**Conclusions:** Obinutuzumab is more efficient than rituximab at inducing B cell cytotoxicity in vitro in both RA and SLE samples. Enhanced direct cell death, reduced CD20 internalization and superior FcR-mediated effector mechanisms are observed, while complement mediated cytotoxicity is reduced. These data provide a mechanistic basis for considering Obinutuzumab as an alternative B cell depleting agent in RA and SLE, in particular.

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### OP0160 CHARACTERIZATION OF SYSTEMIC LUPUS ERYTHEMATOSUS SUBGROUPS WITH FEATURES OF ANTIPHOSPHOLIPID OR SJÖGRENS'S SYNDROME UTILIZING AFFINITY PROTEOMICS

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disease that covers a wide range of phenotypes, from subtle symptoms to life-threatening conditions. The heterogeneous presentation of SLE is a major obstacle in clinical trials and the lack of biomarkers also hampers accurate diagnosis and choice of treatment.

**Objectives:** In this study we explored biochemical pathways in two suggested subgroups of SLE utilizing affinity proteomics in order to characterize subgroups and identify biomarkers for personalized medicine.

**Methods:** We have utilized Karolinska SLE cohort consisting of 320 well-characterized SLE patients and 320 individually matched population based controls in a cross-sectional study. SLE subgroups were defined only based on patients' autoantibody profile: an Antiphospholipid Syndrome-like (APS-like, n=55) and a Sjögren's Syndrome-like (SS-like, n=58) subgroup. Based on literature and clinical knowledge we have made a targeted selection of 281 proteins targeted by in total 367 antibodies from the Human Protein Atlas. Antibodies were covalently coupled to color-coded magnetic beads. EDTA-plasma samples were labeled with biotin and screened in a 384 bead array format. The read-out was made by adding a streptavidin fluorophore and using suspension bead arrays.

**Results:** We identified differences in protein profiles comparing APS-like and SS-like SLE subgroups: The top most significantly different proteins were Integrin beta 1 (p=9.8e-8, Log2 fold change=1,5), renin (p=2.7e-5, Log2 fold change=0.5), glutamic-oxaloacetic transaminase 1 (p=2.9e-5, Log2 fold change=0,5) and Apolipoprotein M (p=3.4e-5, Log2 fold change=0,3) that all were increased in SS-like SLE, while Apolipoprotein H (β2-GPI, p=6.6e-5, Log2 fold change=-0,3) were increased in the APS-like subgroup.

**Conclusions:** The two suggested SLE subgroups were defined exclusively on autoantibody profile as the APS-like and the SS-like subgroups. Our results demonstrate that the two subgroups differ in their protein profiles and that these observations indicate underlying pathogenic differences between SS-like and APS-like SLE. A common etiology of the presence of β2-GPI in both APS and in APS-like SLE is suggested. Therefore, we believe that stratification of SLE patients should be further explored towards personalized medicine.

**Disclosure of Interest:** None declared

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### OP0161 CARDIAC MAGNETIC RESONANCE IMAGING OF LUPUS NEPHRITIS-INDUCED CARDIOVASCULAR DISEASE CORRELATES WITH MYOCARDITIS, FIBROSIS, AND ENHANCED PRO-INFLAMMATORY CYTOKINE EXPRESSION IN A MOUSE MODEL

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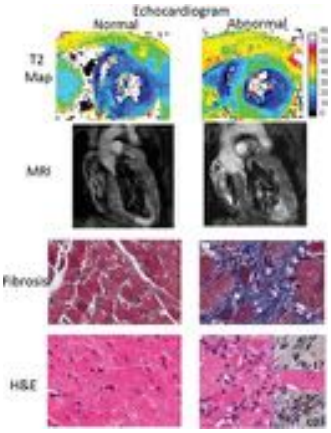
**Background:** Epidemiological data shows a bimodal pattern of mortality in lupus. The most deadly complications are associated with systemic lupus erythematosus (SLE) disease activities, including kidney disease and infections, in the first 10 years; subsequently, the primary cause of morbidity and mortality is cardiovascular disease (CVD). Previously, we used cardiac magnetic resonance imaging (CMR) with quantitative T2 mapping in human SLE and observed enhanced T2 signals in active patients during flares, which suggested sub-clinical levels of cardiac inflammation.

**Objectives:** Since patients may significantly benefit from non-invasive monitoring of CVD, we used CMR to examine the NZM2410 animal model of lupus nephritis (LN), which develops severe lupus-like glomerulonephritis at 22–40 weeks of age.

**Methods:** Myocardial edema was measured with T2 CMR mapping on the BioSpec 94/30 microMRI imaging system. Mice were monitored for cardiac abnormalities and physiological cardiac function using a high-frequency ultrasound echocardiogram (EC). Blood urea nitrogen (BUN) levels were measured to assess kidney function and ELISA was performed on cardiac tissue homogenates and serum. Heart tissue was collected for H&E, immunhistochemistry, and Masson's trichrome staining to measure tissue fibrosis.

**Results:** As NZM2410 mice aged, a significantly enhanced expression of IL-1β, IL-2, IL-6, IL-10, CXCL1, and TNF-α was detected in both the serum and cardiac tissue. CMR T2 mapping was performed at 20–25 weeks of age and EC was used to monitor for cardiac abnormalities. When ECs indicated increased left ventricular diameter and residual volumes as well as significantly decreased ejection fractions

relative to baseline, CMR with T2 mapping was performed again. Despite BUN levels and weight measurements showing no signs of end-stage renal disease, T2 signals were elevated and the myocardium thickened significantly to produce a prominent left ventricular hypertrophy upon MRI analysis. In addition, expression of IL-10, IL-2, IL-6, CXCL1, and TNF-α was significantly up-regulated in the serum of these mice. Histopathological examination revealed robust infiltrates in cardiac tissue with significant fibrosis. While immunohistochemical staining showed little to no detection of B-cells, neutrophils, or macrophages, IL-17 and CD3+ T-cells were observed in cardiac infiltrates.




**Conclusions:** Our results demonstrate that myocarditis is associated with pro-inflammatory cytokine expression and LN disease progression in NZM2410 mice prior to end-stage renal disease. Consequently, our data establish CMR as a novel non-invasive technique to explore the contribution of SLE-mediated inflammation on CVD and to develop therapeutic strategies to pharmacologically inhibit cardiac damage. Future work will identify biomarkers associated with cardiac damage and will further develop CMR with quantitative T2 mapping as a clinical tool to assess CVD in patients with SLE.

**References:**

[1] Ardoin, S, et al. CMR with Quantitative T2 Mapping in Patients with Active SLE [abstract]. Arthritis Rheumatol. October 2014; 66, S10. DOI: 10.1002/art.38914

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**Disclosure of Interest:** None declared

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## OP0162 TOLL-LIKE RECEPTOR 7-, BUT NOT TOLL-LIKE RECEPTOR 9-, MEDIATED INTERFERON-α PRODUCTION FROM PLASMACYTOID DENDRITIC CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Characteristic induction of interferon (IFN) signature is known to play a pivotal role in patients with SLE and plasmacytoid dendritic cells (pDC) are major source of Type I IFN. However, mechanisms of Type I IFN production from pDC in the pathogenesis of SLE remain unclear.

**Objectives:** To elucidate the function of pDC in SLE, we shed light upon Toll-like receptor (TLR) 7 and TLR9-mediated signaling during Type I IFN production from pDC in patients with SLE or healthy controls (HC).

**Methods:** Peripheral blood mononuclear cells (PBMCs) in 68 SLE patients without hydroxychloroquin treatment, 37 RA patients and 24 HC were analyzed in the presence of a TLR7 agonist loxoribine and a TLR9 agonist CpG 2216. The IFN-α production in Lin-HLA-DR+CD123+CD11c- pDCs was detected by flow cytometry.

**Results:** The spontaneous production of IFN-α in pDCs was marginal, but the TLR7 agonist markedly up-regulated IFN-α production from pDCs in SLE patients compared to that in HC. Such an up-regulation of IFN-α was not observed in pDCs in RA. On the other hands, TLR9-mediated IFN-α production from pDCs in SLE was down-regulated compared to that in HC. Furthermore, TLR7- and TLR9-mediated IFN-α production from pDCs in SLE patients were positively and negatively correlated with SLEDAI and dsDNA-ab titers, respectively. The expression of TLR7 and TLR9 on pDCs was comparable among SLE, RA and HC, indicating that the difference of TLR response was not depend on alterations of TLR expression levels. By in vitro experiments under pre-treatment with multiple cytokines, both Type I and Type II IFN up-regulated the TLR7-mediated IFN-α production from pDCs, but they down-regulated the TLR9-mediated IFN-α production, suggesting that up-regulation of TLR7 responses and down-regulation of TLR9 responses of pDCs in SLE patients were regulated by Type I and Type II IFNs.

**Conclusions:** This is the first report demonstrated the differential regulation of TLR7 and TLR9 by type I IFN in pDCs in SLE patients, namely, TLR7 and TLR9 response were regulated by Type I and Type II IFNs. Taken together, TLR7-mediated pDC response plays a pivotal role in the increase in IFN-signature in SLE patients and could be a potential therapeutic target for SLE.

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## OP0163 MESENCHYMAL STEM CELLS PREVENT PODOCYTE INJURY IN LUPUS PRONE MICE VIA EDUCATING MACROPHAGE INTO AN ANTI-INFLAMMATORY PHENOTYPE

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**Background:** Macrophage infiltration is a hallmark of severe lupus nephritis, contributing to podocyte injury. Mesenchymal stem cell (MSC) transplantation could alleviate lupus nephritis in both lupus mice and patients. However, the underlying mechanisms remain largely unknown.

**Objectives:** The study was designed to investigate the modulatory effect of MSCs on macrophage polarization and explore its role in preventing podocyte injury.

**Methods:** B6.MRL-Fas$^{lpr}$ (B6.*lpr*) mice were injected with umbilical cord MSCs (UCMSCs), while the control groups were administered with PBS or Fibroblasts. A 24-hour urine specimen was collected by putting mice in metabolic cages over a full 24-hour period every three weeks. 9 weeks later, all the mice were sacrificed. Histopathology scores of kidney were evaluated by hematoxylin-eosin (HE) staining. IgG and C3 deposits in glomeruli were assessed by immunofluorescence. Podocyte foot processes were observed under the transmission electron microscope. Mouse peritoneal macrophages were co-cultured with or without UCMSCs for 2 days, and further co-cultured with mouse podocytes for another 2 days. The expression of TNF-α, MCP-1, IL-1β and CD206 in macrophages and synaptopodin in podocytes were determined by real-time PCR. Flow cytometry was used to analyze podocyte apoptosis.

**Results:** UCMSCs treated B6.*lpr* mice showed lower levels of proteinuria, reduced glomerular deposition of IgG and C3, decreased renal histopathology scores and less foot process fusion. Besides, UCMSCs decreased macrophages infiltration while increased the expression of CD206 and synaptopodin in the kidney of B6.*lpr* mice. *In vitro* study demonstrated that macrophages co-cultured with UCMSCs expressed lower levels of inflammatory cytokines including TNF-α, MCP-1 and IL-1β, while higher levels of CD206. Moreover, UCMSCs treated macrophages induced less podocyte injury, with higher expression of synaptopodin and lower apoptotic rate.

**Conclusions:** UCMSCs prevented podocyte injury in lupus nephritis via educating macrophage into an anti-inflammatory phenotype, thus rescuing renal function.

**Disclosure of Interest:** None declared

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## OP0164 BLOCKADE OF IMMUNE COMPLEX-MEDIATED GLOMERULONEPHRITIS BY HIGHLY SELECTIVE INHIBITION OF BRUTON'S TYROSINE KINASE

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**Background:** Lupus nephritis (LN) causes significant morbidity and mortality in SLE patients. Autoantibody-containing immune complexes (ICs) can activate complement cascades and Fc receptors on resident and infiltrating cells within the kidney, thus promoting inflammation. Bruton's tyrosine kinase (BTK) is a tyrosine kinase important for B cell development, Fc receptor signaling, and macrophage polarization.

**Objectives:** To assess the role of BTK in the pathogenesis of nephritis in an inducible model of LN, and to evaluate the therapeutic potential of BTK inhibition.

**Methods:** A novel, highly selective, and potent (mouse whole blood CD69 $IC_{50}$=13±2 nM) BTK inhibitor, BI-BTK-1 (Boehringer Ingelheim), was tested in female 129 sv/J mice (10 weeks of age) injected with nephrotoxic serum (NTS), an experimental model which closely mimics LN. Mice pre-immunized with rabbit IgG (Day 0) were administered NTS containing rabbit anti-mouse glomerular antibodies (Day 5), inducing a severe IC-mediated crescentic glomerulonephritis. Mice that did not receive the NTS transfer were used as healthy controls. Mice were treated once daily with vehicle alone or BI-BTK-1 (0.3–10 mg/kg, n=16/group), before the transfer of NTS as a prophylactic assessment, or after the transfer of NTS as a therapeutic assessment.

**Results:** NTS-challenged mice treated with BI-BTK-1 exhibited a statistically significant, dose responsive protection from kidney disease. Compared to

vehicle treated mice, NTS-challenged mice treated with 10 mg/kg BI-BTK-1 had significantly less proteinuria (1220 mg/dl vs 10 mg/dl, respectively, $p<0.0005$), serum creatinine (0.74 mg/dl vs 0.48 mg/dl, respectively, $p<0.03$), and BUN (82 mg/dl vs 25 mg/dl, respectively, $p<0.03$) at the end of study (Day 11). Histology assessment confirmed marked renal protection in the BI-BTK-1 treatment groups. BI-BTK-1 treatment resulted in decreased recruitment of inflammatory monocytes from the splenic reservoir, and a decrease in infiltrating IBA-1+ cells as well as C3 deposition within the kidney. RNA-seq revealed that more than 500 genes were modulated by BTK treatment, with further analysis highlighting many of the modulated pathways being related to inflammation and glomerular injury in LN. Serum profiling and selective kidney gene expression analyses by Q-PCR revealed that BTK inhibition was associated with a significant decrease in the levels of key LN-relevant inflammatory cytokines and chemokines. Importantly, delayed treatment with 3 mg/kg of BI-BTK-1in mice with established proteinuria was able to reverse proteinuria and improve renal histopathology.

**Conclusions:** Our results further confirm the important role for BTK activation in the pathogenesis of immune complex-mediated nephritis, and highlight BTK as a valuable therapeutic target. Taken together with previously published studies and our preliminary results in spontaneous lupus models, these findings further strengthen the rationale for selective BTK inhibition as a promising approach to the treatment of LN.

**Disclosure of Interest:** S. Chalmers: None declared, J. Doerner: None declared, T. Bosanac Employee of: Boehringer Ingelheim, S. Khalil Employee of: Boehringer Ingelheim, D. Smith Employee of: Boehringer Ingelheim, C. Harcken Employee of: Boehringer Ingelheim, J. Dimock Employee of: Boehringer Ingelheim, E. Der: None declared, L. Herlitz: None declared, D. Webb Employee of: Boehringer Ingelheim, E. Seccareccia Employee of: Boehringer Ingelheim, D. Feng Employee of: Boehringer Ingelheim, J. Fine Employee of: Boehringer Ingelheim, M. Ramanujam Employee of: Boehringer Ingelheim, E. Klein Employee of: Boehringer Ingelheim, C. Putterman Grant/research support from: Boehringer Ingelheim
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## OP0165 BENEFICIAL EFFECTS OF AN ANTI-IFNAR1 MONOCLONAL ANTIBODY ON IMMUNE CELL DYSREGULATION AND COMPLEMENT SYSTEM ABNORMALITIES OF SYSTEMIC LUPUS ERYTHEMATOSUS: AN EXPLORATORY ANALYSIS OF PHASE IIB CLINICAL TRIAL OF ANIFROLUMAB

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**Background:** Anifrolumab is a fully human $IgG_1$ κ monoclonal antibody directed against subunit 1 of the type I interferon alpha receptor (IFNAR1). A Phase IIb randomized clinical trial of adult patients with systemic lupus erythematosus (SLE) has been conducted for anifrolumab.

**Objectives:** To assess downstream effects of anifrolumab on peripheral biomarkers and pathophysiologic pathways in patients with SLE.

**Methods:** In the MUSE study, 305 patients with moderate to severe SLE were randomized in a 1:1:1 ratio to receive a fixed intravenous dosage of placebo or anifrolumab (300 or 1,000 mg), in addition to standard of care medications, every 28 days for 1 year. Patients were stratified by IFN gene signature status (high vs. low) based on a 4-gene expression assay. Selected proteins were measured in sera of SLE patients procured at baseline, 85, 169, and 365 days post-administration along with 30 healthy controls (HCs) using a multiplex luminex immunoassay.

**Results:** Serum concentrations of 134 proteins were measured for 30 HCs and 304 SLE patients at baseline (missing sample for one patient), of which 229 had a high IFN signature (IFN-high) and 75 did not (IFN-low). Mann-Whitney U test identified 55 proteins with higher levels and 12 proteins with lower levels in IFN-high patients than IFN-low patients and/or HCs ($p<0.05$). Anifrolumab compared with placebo induced significant suppression of 15 proteins which were elevated at baseline, and up-regulation of 4 proteins with reduced baseline levels at more than one time point post-administration ($p<0.05$). Anifrolumab-driven suppression of T cell-targeting chemokines (CXCL10 & CXCL11), B cell-targeting chemokine (CXCL13), B-cell activator (TNFSF13B/BAFF), endothelial cell markers (VCAM1 & VWF & ANGPT2), and other lymphocyte-associated chemokines (CCL2 & CCL8 & CCL19) indicates reduction in T-cell, B-cell, and endothelial cell activation/movement after anifrolumab administration compared with placebo. Further, decreased concentration of FCN3, an initiator of the lectin pathway of complement, indicates inhibition of complement system activation, consistent with upregulation of complement C3 concentration by anifrolumab. In contrast, proteins upregulated by anifrolumab included; IL1R2 – a decoy receptor for IL-1 that is highly expressed in neutrophils, and TNFRSF10C – a decoy anti-apoptotic receptor for TRAIL that has been reported to be associated with SLE neutropenia. Cellular enumeration data demonstrated upregulation of both lymphocyte and neutrophil counts after administration of anifrolumab but not placebo. Suppression of lymphocyte-related chemokines and upregulation of neutrophil-associated proteins suggests different mechanisms for anifrolumab-induced upregulation of peripheral lymphocytes and neutrophils.

**Conclusions:** Our results demonstrate a distinct proteome profile of IFN-high patients compared with IFN-low patients and HCs. Anifrolumab administration elicits a widespread impact on peripheral biomarkers of patients with SLE. Beneficial effects on both immune cell dysregulation and complement system abnormalities may be key contributors to the mechanism of action of anifrolumab in SLE.

**Disclosure of Interest:** X. Guo Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, L. Wang Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, G. Illei Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, P. Brohawn Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, B. Higgs Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, W. White Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca
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## OP0166 IL-27 PARTICIPATES IN SJOGREN'S SYNDROME BY REGULATING LYMPHOCYTE SUBSETS

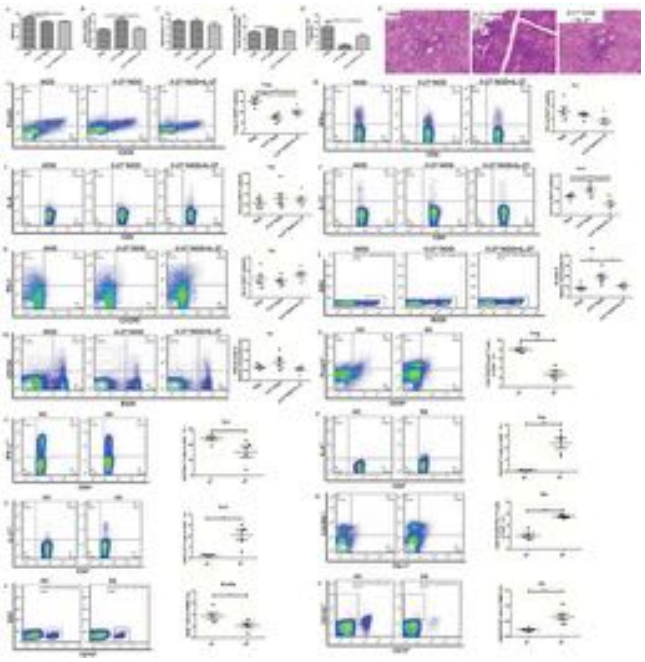
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**Background:** Primary Sjogren's syndrome (pSS) is a chronic, systemic autoimmune disorder characterized by inflammation of exocrine glands and functional impairment of the salivary and lacrimal glands [1]. The pathogenesis of pSS is complicated with many respects remaining elusive. Interleukin-27 (IL-27) is a new member of the IL-12 cytokine family. It is largely secreted by activated antigen-presenting cells, such as macrophages and dendritic cells (DCs). IL-27 participates in multiple autoimmune diseases by regulating T lymphocyte subsets. Recent studies showed that IL-27 was involved in anti-inflammatory functions in SS [2]. However, the underlying mechanism of IL-27 in SS is still unknown.

**Objectives:** In the present study, the changes of lymphocyte subsets were studied in Il-27 knock-out and wild-type pSS models and pSS patients for the purpose to explore the specific mechanism of IL-27 in pSS and provide the basis for clinical treatment.

**Methods:** The NOD mice, Il-27 knockout (*Il-27*$^{-/-}$) mice, Il-27 knockout mice with recombinant IL-27 treatment were studied. The saliva flow rates, weight, weight of submandibular glands and spleens were detected. Murine submandibular glands were fixed and paraffin sections were used for hematoxylin and eosin staining. The lymphocyte subsets of spleens from experimental mice and the peripheral blood from pSS patients were measured by flow-cytometric assay.

**Results:** Compared to WT NOD mice, the saliva flow rates decreased significantly, and the indexes of submandibular glands and spleens increased significantly in *Il-27*$^{-/-}$ mice (Fig 1A-E). The histological results showed that the number of lymphocytic infiltrates in submandibular glands of WT NOD was lower than *Il-27*$^{-/-}$ mice (Fig 1F). The splenic-Treg cells decreased significantly, but the levels of splenic Th17 and B cells increased significantly in *Il-27*$^{-/-}$ mice. After IL-27 treatment, the saliva flow rates, submandibular glands, Treg and Th17 cells were partially reversed in *Il-27*$^{-/-}$ mice (Fig 1G-M). Consistent with above observations, the changes of Terg and Th17 cells in pSS patients showed similar pattern. The Th2, Tfh and plasma cells increased significantly, whilst the B cells decreased significantly in pSS patients (Fig 1N-T). Compared with healthy control, the serum IL-27 decreased in pSS patients.



**Conclusions:** In general, these findings indicated that IL-27 deficiency dete-

riorated the disease symptoms of pSS and resulted in changes of Th17/Treg balance. In addition, pSS patients showed similar lymphocyte imbalance. Our data suggested that IL-27 might play an important role on the development and pathogenesis of pSS through regulating lymphocyte subsets, and targeting IL-27 and Th17/Treg balance may be a new direction of pSS treatment.

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**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Epidemiology of RMDs

### OP0167 PREVALENCE OF RHEUMATIC DISEASE IN LATIN AMERICAN INDIGENOUS POPULATION: A COMMUNITY BASED STUDY

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**Background:** GLADERPO group (Latin American Study Group on Rheumatic Diseases in Indigenous Peoples) is an organization aimed to conduct studies on indigenous populations with the purpose of closing the gap of information about rheumatic diseases and develop culturally-sensitive interventions.
**Objectives:** Estimate the prevalence of musculoskeletal disorders and rheumatic diseases in eight Latinoamerican indigenous communities using the COPCORD methodology.
**Methods:** A cross-sectional, house-by-house, community-based census study was performed. Bilingual staff members, who received standardized training, administered a cross-culturally validated version of the COPCORD questionnaire to adult indigenous population with the assistance of bilingual translators. Individuals with musculoskeletal pain, stiffness or swelling in the last 7 days and/or at any point during their lifetime were evaluated by participating physicians (general physicians and rheumatologist) to classify or diagnosed any rheumatic disease according to specific criteria.
**Results:** We surveyed 6,155 indigenous people having a mean age of 41.2 years (SD 17.6; range 18 to 105); 3,757 (61.0%) were women. Mean education was 5.0 years (SD 4.1); and 4,668 (75.8%) work for living.
MSK pain in the past and during the last 7 days occurred in 2,778 (45.1%; 95% CI 43.8–46.3) and 2,127 individuals (34.5%, 95% CI 33.3–35.7%), respectively. Of these, 1,195 (56.2%, 95% CI 54.1–58.3%) individuals associated pain to trauma. Pain was severe in 15.8% and according to localization, pain originated from the spine (26.7%), the knees (17.6%), shoulders (15.3%), and hands (10.6%) more frequently.
Point-prevalence of main rheumatic diseases was: low back pain (LBP) in 821 (13.3%; 95% CI: 12.4–14.2); osteoarthritis (OA) in 598 (9.7%; 95% CI: 8.9–10.4); rheumatic regional pain syndromes in 368 (5.9%; 95% CI: 5.3–6.6); rheumatoid arthritis (RA) in 85 (1.3%; 95% CI: 1.1–1.7); systemic lupus erythematosus in 7 (0.1; 95% CI: 0.004–0.2); nonspecific arthritis in 13 (0.2%; 95% CI: 0.1–0.3); spondyloarthritis in 12 (0.1; 95% CI: 0.1–0.3); and scleroderma in 3 (0.04%; 95% CI: 0.01–0.1).
There were marked variations in the prevalence of each rheumatic disease among the different communities, i.e.: RA prevalence was 2.4% in Qom (Argentina) and 0.4% in Mixtecos (Mexico).
**Conclusions:** The overall prevalence of MSK disorders in indigenous community of Latin-American was 35.4%. Low back pain and OA were the most prevalent rheumatic conditions, but wide variations according to population groups occurred.
**Acknowledgement:** National Council for Science and Technology (CONACYT)-Salud 2001–01–162154 (Mexico). Federico Wilhelm Agricola Foundation (Argentina). PDVSA East, SUELOPETROL and Bristol-Myers Laboratory (Venezuela).
**Disclosure of Interest:** None declared
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### OP0168 FIRST RESULTS FROM THE PROSPECTIVE GERMAN PREGNANCY REGISTER RHEKISS

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**Background:** There is limited evidence regarding the safety of pharmacologic treatments during pregnancy. With the increasing number of new medications available for the treatment of rheumatic and autoimmune diseases, there is a growing need for systematic collection of prospective real-world data on drug safety in pregnancy and lactation.
**Objectives:** To determine the safety of various drug treatments during pregnancy and the influence of the underlying rheumatic disease on outcome and child development.
**Methods:** The Rhekiss register is designed as a prospective nationwide, web-based longitudinal observational cohort study. Pregnant patients with confirmed diagnose of inflammatory rheumatic disease are eligible to be enrolled until the 20th week of pregnancy regardless of drug treatment. Rheumatologists as well as patients report three times during pregnancy (each trimester) and semi-annually after birth until the child's 2nd birthday. Patients can use the online documentation system remote or in the practice.
Information on all given drug treatments, details on the course of the maternal disease, the development of the pregnancy, maternal or fetal complications during pregnancy, pregnancy outcomes, and child development during the first two years of life are collected. At baseline, sociodemographic parameters, prior pregnancies, and comorbidities are reported.
The register is designed as uniform platform with specific modules for various inflammatory rheumatic diseases. Only pseudonymized data are used, data security issues conform with regulatory authorities have been implemented.
It can be easily extended and translated to other languages.
**Results:** The register started on 15th of September 2015. Until end of January 2016, 106 rheumatologists in outpatient clinic or private practices signed up for participation. Among these, 28 units recruited patients so far. 99 patients were enrolled until end of January. Of these, 26 had rheumatoid arthritis, 26 systemic lupus erythematosus, 17 other connective tissue diseases, 9 juvenile idiopathic arthritis, 8 spondyloarthritis, 7 psoriatic arthritis, 4 autoinflammatory syndromes and 2 systemic vasculitis.
Mean age of the patients was 31.1 (± 5.1) years, mean disease duration 6.5 (± 8.2) years. Mean disease activity, assessed by the rheumatologist on a numeric rating scale from 0–10, was 2.6 (± 2.1) over all diagnoses. On a disease severity scale ranging from 1 to 5 (highest grade), two thirds of the patients were reported as grade 2 or 3.
**Conclusions:** The German pregnancy register Rhekiss was initiated to fill the knowledge gap on the course and outcomes of pregnancies in patients with rheumatic diseases as well as on the current use and the safety of treatments during pregnancy and lactation. The fast uptake of patients shows that there is a substantial need for and a high interest in real-life data to guide treatment decisions. Rhekiss can be easily extended and translated to other languages.
At the time of the EULAR congress, data on the first seven months of the register will be available for presentation.
**Disclosure:** Rhekiss is a collaborative project of the DRFZ Berlin and the Rheumazentrum Rhein-Ruhr e.V. Düsseldorf, jointly funded by both institutions.
**Disclosure of Interest:** None declared
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### OP0169 ASSOCIATION BETWEEN USE OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS AND DIABETES IN PATIENTS WITH ANKYLOSING SPONDYLITIS, RHEUMATOID ARTHRITIS, OR PSORIASIS/PSORIATIC ARTHRITIS: NATIONWIDE, POPULATION-BASED COHORT STUDY OF 84,989 PATIENTS

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**Background:** Previous studies suggested anti-tumor necrosis factor (TNF) agents and hydroxychloroquine (HCQ) may inhibit the development of insulin resistance.
**Objectives:** Investigate the association between use of disease-modifying antirheumatic drugs (DMARDs) and diabetes mellitus (DM) in patients with ankylosing spondylitis (AS), rheumatoid arthritis (RA), or psoriasis (PSO)/psoriatic arthritis (PSA).
**Methods:** This retrospective cohort study used a nationwide, population-based administrative database to enroll 84,989 cases with AS, RA, or PSO/PSA who initiated treatment with anti-TNFs or nonbiologic DMARDs. Multivariable analysis was used to estimate effect of different therapies on risk of DM.
**Results:** There were 36,329 patients with AS, 33,112 patients with RA, and 15,638 patients with PS or PSA. All enrolled patients initiated treatment with an anti-TNF agent or a nonbiologic DMARD. We categorized patients into 4 mutually exclusive groups based on DMARD use: *(i)* anti-TNF agent with or without

another DMARD (n=6824); *(ii)* cyclosporine (CSA) without an anti-TNF agent or HCQ (n=1084); *(iii)* HCQ without an anti-TNF agent or CSA (n=27,033); and *(iv)* other nonbiologic DMARD without an anti-TNF agent, CSA, or HCQ (n=50,048), hereafter referred to as the reference group.The incidence rates of DM per 1000 person-years were 8.3 for users of anti-TNFs, 13.3 for users of cyclosporine (CSA), 8.4 for users of HCQ, and 8.1 for users of other nonbiologic DMARDs. Compared with users of nonbiologic DMARDs, the multivariate adjusted hazard ratios (aHRs) for DM were significantly lower for users of anti-TNFs with HCQ (aHR: 0.49, 95% CI: 0.36–0.66) and those who used HCQ (aHR: 0.70, 95% CI: 0.63–0.78), but not in those who used anti-TNFs without HCQ (aHR: 1.23, 95% CI: 0.94–1.60) or CSA (aHR: 1.14, 95% CI: 0.77–1.70).

Table 1. Univariate (crude HR) and multivariate (adjusted HR) analysis of factors associated with DM

| DMARD group | Crude HR (95% CI) | P-value | Adjusted HR (95% CI) | P-value |
|---|---|---|---|---|
| Other non-biologic DMARDs | Reference | | Reference | |
| Anti-TNF+HCQ | 0.73 (0.55, 0.97) | 0.028* | 0.49 (0.36, 0.66) | <0.001* |
| Anti-TNF alone | 1.52 (1.20, 1.92) | <0.001* | 1.23 (0.94, 1.60) | 0.125 |
| CSA | 1.64 (1.11, 2.41) | 0.013* | 1.14 (0.77, 1.70) | 0.510 |
| HCQ | 1.03 (0.95, 1.12) | 0.445 | 0.70 (0.63, 0.78) | <0.001* |

HR: hazard ratio; CI: confidence interval. *P<0.05 indicates a significant association with DM. Adjusted by age, sex, disease group, disease duration, pre-treatment Charlson comorbididy index and corticosteroid dose.

**Conclusions:** The aHR for DM was lowest for RA and PSO/PSA patients who initiated treatment with an anti-TNF agent with concomitant HCQ, followed by HCQ users.

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## OP0170 LOW INCOME IS ASSOCIATED WITH LOWER FUNCTIONAL CAPACITY AND HIGHER DISEASE BURDEN IN RA PATIENTS YOUNGER THAN 65

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**Background:** Low socioeconomic status is known to be a risk factor for unfavourable outcomes in rheumatoid arthritis (RA).

**Objectives:** The aim of this analysis was to assess the influence of low income on functional capacity and disease burden.

**Methods:** Patients with a diagnosis of RA (ICD-10 codes M05 or M06) in at least two quarters in 2013 from a large statutory health insurance in Germany (Barmer GEK) were randomly selected, stratified by age (18–49/50–64/65–80), sex and diagnosis (M05/M06). They were contacted by mail and asked to complete a questionnaire regarding self-reported diagnosis (for validation of claims diagnosis), sociodemographics, health behaviour, impact of RA on employment, the RA Impact of Disease questionnaire (RAID, 0: no impact, 10: highest impact) and the physical function questionnaire FFbH (0: total impairment-100: full function). General linear models were used to assess the association of income and other sociodemographic factors with the FFbH and the RAID.

**Results:** Of the 6,195 patients who were contacted, a total of 3,212 completed the questionnaire and 2,585 (80%) reported to have RA. Among those, 2,406 patients reported their household income. 31% of these had a low (<1,500 Euro), 54% a medium (1,500–3,200 Euro) and 15% a high (>3,200 Euro) household income.

Patients with a low income had a mean FFbH of 67 (standard deviation 23) and a mean RAID of 4.8 (2.3), patients with a medium income had a mean FFbH of 74 (22) and a RAID of 4.1 (2.3) and those with a high income had a mean FFbH of 83 (18) and a RAID of 3.5 (2.3). In patients <65 years (n=1353), FFbH and RAID differed between patients with low and medium/high income (table 1) while education and lifestyle (smoking, being stressed) were not associated, insufficient exercise was only associated with FFbH. This analysis was controlled for the following work-related parameters that were strongly associated with functional capacity and disease burden: being less efficient at work, being on sick leave >6 weeks, having applied for disability pension and fear of not being able to work until retirement.

Table 1. Results from two separate multivariable general linear models for patients <65 years. Parameters that are associated with functional capacity/disease burden are shown

| Parameter | Reference | Estimated effect on FFbH | Confidence interval (FFbH) | Estimated effect on RAID | Confidence interval (RAID) |
|---|---|---|---|---|---|
| Age | per 10 years | –2.8 | –3.9, –1.7 | 0.12 | 0.00, 0.23 |
| Body mass index | per unit | –0.41 | –0.61, –0.22 | 0.034 | 0.013, 0.056 |
| Male sex | female | 4.9 | 2.9, 6.8 | –0.46 | –0.67, –0.24 |
| Household income 1500–3200€ | <1500€ | 4.0 | 1.6, 6.3 | –0.51 | –0.78, –0.24 |
| Household income >3200€ | | 9.8 | 6.9, 12.6 | –1.03 | –1.34, –0.71 |
| Less efficient at work | | –7.9 | –9.9, –5.9 | 1.2 | 0.95, 1.4 |
| On sick leave >6 weeks | | –8.8 | –13.7, –3.8 | 1.1 | 0.54, 1.6 |
| Having applied for disability pension | | –22.5 | –25.7, –19.4 | 1.9 | 1.6, 2.3 |
| Fear of not being able to work until retirement | | –5.8 | –7.9, –3.8 | 1.0 | 0.77, 1.2 |
| Getting enough exercise | | 3.5 | 1.2, 5.8 | –0.08 | –0.34, 0.18 |

**Conclusions:** In patients with RA aged below 65, low income was strongly associated with higher disease burden und poorer function. The effect of income on function and overall disease burden remained after controlling for factors like considering or applying for disability pension, presenteism and absenteism.

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**Disclosure of Interest:** None declared

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## OP0171 PROGNOSIS OF STROKE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A POPULATION-BASED COHORT STUDY

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**Background:** Stroke is a severely disabling complication that occurs at a much earlier age in patients with systemic lupus erythematosus (SLE) compared to the general population.[1] Individuals with SLE have also a greater risk of stroke compared to the general population. However, it remains unclear if stroke patients with SLE have higher mortality after stroke.

**Objectives:** To assess the mortality after first-ever stroke in SLE patients compared to the general population.

**Methods:** In a prospective cohort of adult SLE patients (≥2 SLE visits, ≥1 with a specialist in the National Patient Register, NPR) and general population comparators identified from the Total Population Register, we identified those with first-ever stroke via the NPR (ischaemic, intracerebral haemorrhage, and unspecified), from 1998 to 2013. We linked them to the Swedish Stroke Register (Riksstroke) and followed them from occurrence of stroke until end of follow-up (death or the end of the study (Nov 2014)). We used age-adjusted Cox models to estimate the hazard ratio (HR) for all-cause mortality and stroke-specific mortality (defined using ICD codes from the Cause of Death Register) for SLE compared to non-SLE. For all-cause mortality, we estimated HRs for death within the first 30, 90, or 180 days after stroke. We additionally adjusted for comorbidities (hypertension, diabetes, congestive heart disease, atrial fibrillation and renal disease). In patients with Riksstroke records we further adjusted for smoking, aspirin and statin use at baseline (and thrombolysis for ischaemic stroke).

**Results:** We identified 467 individuals with SLE and 1775 non-SLE comparators with a first-ever stroke. SLE patients were younger than non-SLE at inclusion (mean age 66 yrs vs. 77 yrs). During follow-up, we identified 1293 deaths in both groups. After adjusting for age, stroke patients with SLE had a 50% higher rate of all-cause death for all stroke types compared to non-SLE, with the highest observed for intracerebral haemorrhage (HR=2.0; 95% CI=1.3–3.1). The HRs were similar after adjusting for comorbidities. Restricting to patients registered in Riksstroke, the HRs for mortality were similar, except for unspecified stroke. The hazard of death within the first 30 days was higher in the SLE group only for intracerebral haemorrhage (HR 1.99). Within 90 and 180 days, SLE patients are at higher risk of death compared to non-SLE for all stroke types. The stroke-specific mortality HR was 1.3 (95% CI=1.0–1.7) for all stroke types.

Table 1. All-cause mortality rate for stroke patients with SLE compared to non-SLE

| Stroke type | No. of deaths (%) SLE/non-SLE | HR (95% CI) | | |
|---|---|---|---|---|
| | | Age-adj. | Comorbidities-adj. | Riksstroke only |
| All | 243/1050 (52/59) | 1.7 (1.3–2.0) | 1.6 (1.3–1.8) | 1.6 (1.3–2.0) |
| Ischaemic | 178/822 (48/57) | 1.7 (1.4–2.0) | 1.5 (1.3–1.8) | 1.6 (1.2–2.1) |
| Intr. haemorrhage | 35/125 (66/63) | 2.0 (1.3–3.1) | 1.8 (1.1–2.9) | 2.0 (0.9–4.7) |
| Unspecified | 30/103 (75/74) | 1.9 (1.2–3.0) | 1.9 (1.1–3.1) | 5.7 (1.2–26.7) |

**Conclusions:** The rate of any cause and stroke-specific death after stroke is greater in patients with SLE than the general population, despite controlling for factors affecting mortality.

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OP0172 **A COST-EFFECTIVENESS ANALYSIS OF DIFFERENT INTENSIVE COMBINATION THERAPIES FOR EARLY RHEUMATOID ARTHRITIS: 1 YEAR RESULTS OF THE CARERA TRIAL**

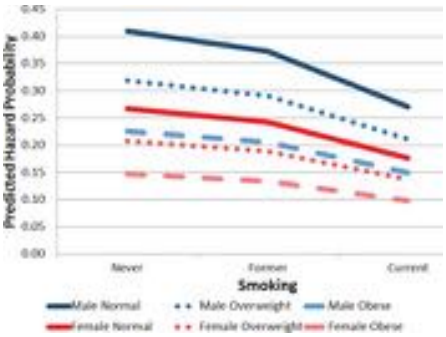
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**Background:** The (Care in Early RA) CareRA trial compared different treatment strategies in patients with early Rheumatoid Arthritis (ERA) with or without markers of poor prognosis. No significant differences were shown between the treatment arms in terms of remission rate and functionality at 16 and 52 weeks. The differential cost-effectiveness of these therapeutic strategies could aid in determining the optimal approach for ERA.
**Objectives:** To compare the cost-effectiveness of different therapeutic strategies used in the CareRA trial during the first treatment year in patients with early Rheumatoid Arthritis.
**Methods:** The CareRA trial is a 2-year investigator-initiated randomized pragmatic superiority trial comparing remission induction regimens in a treat-to-target approach. DMARD naïve ERA patients were stratified into a high- or low-risk group based on prognostic markers. High-risk patients were randomized to a COBRA Classic (Methotrexate (MTX) + Sulphasalazine + prednisone step-down from 60mg), COBRA Slim (MTX + prednisone step-down from 30mg) or COBRA Avant-Garde (MTX + Leflunomide + prednisone step-down from 30mg) scheme. Low-risk patients were randomized to MTX tight step-up (MTX-TSU) or COBRA-Slim. The direct costs for each patient in the trial were calculated by summing the cost of a rheumatology consultation, per protocol CareRA study medication and RA-related medication such as biologicals and extra glucocorticoids not stipulated in the protocol. The incremental cost-effectiveness ratio (ICER) was calculated using these costs and the treatment efficacy as observed in CareRA. Efficacy parameters investigated were the proportion of patients in remission (DAS28(CRP) $<2.6$) and the proportion with a clinically meaningful improvement of Health Assessment Questionnaire (HAQ change $>0.22$) at week 52.
**Results:** 349 out of 379 patients had sufficient cost information to be evaluated at week 52. Remission was achieved in 65,6% Classic, 61.7% Slim (high-risk) and 64.1% Avant-Garde patients; and in 56.8% MTX-TSU and 70.0% Slim (low-risk) patients. A clinically meaningful HAQ response was reached in 66.7% Classic, 70.2% Slim (high-risk) and 75.6% Avant-Garde patients; and in 58.3% MTX-TSU and 60.0% Slim (low-risk) patients. Mean ±SD total costs during year one were €1044.3 ± €871.0 €859.7 ±€431.3 and €1267.7 ±€632.7 for the Classic, Slim (high-risk) and Avant-Garde respectively; and €880.6 ±€917.4 and €867.5 ±€364.0 for MTX-TSU and Slim (low-risk) patients. In MTX-TSU patients, the high average cost ±SD of €268.6 ±€876.5 was remarkable. Cost-effectiveness analysis in the high-risk arm showed a higher ICER for Classic (€47.3/1% remission) and Avant-Garde (€170.0/1% remission) compared to Slim (high-risk); In the low-risk arm, the cost-effectiveness of MTX-TSU was shown to be comparable to Slim (low-risk), with an ICER of €-0.99/1% remission.
**Conclusions:** Cobra Slim, a combination of MTX with a moderately dosed glucocorticoid remission induction showed favorable cost-effectiveness in both ERA patients with or without poor prognosis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4139

OP0173 **HOW MUCH OF A BARRIER IS EXCESS WEIGHT AND SMOKING FOR ACHIEVING SUSTAINED REMISSION IN EARLY RA? RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT**

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**Background:** Relatively little is known about whether and to what extent modifiable lifestyle factors such as excess weight and smoking impact the likelihood of achieving sustained remission (SR).
**Objectives:** To explore the independent and combined effects of excess weight and smoking on achieving SR in early RA.
**Methods:** We examined the first 3 years of data of ERA patients enrolled in the Canadian Early Arthritis Cohort (CATCH), a multicenter prospective cohort study. Participants met 1987 or 2010 ACR/EULAR criteria for RA, had $<12$ months of symptom duration, were not in remission at entry, and had BMI and at least 2 consecutive DAS28 scores available. SR was defined as DAS28$<2.6$ at two consecutive visits. Independent effects of BMI class (normal weight: 18.5–24.9, overweight: 25–2.9, obese: 30+) and smoking on time to SR were estimated using Cox proportional hazards, adjusting for age, sex, ethnicity, education, comorbidities, smoking (current, former/never), symptom duration, disease activity, and treatment. Potential joint effects of smoking and weight class were tested using an interaction in the model. Higher order interactions with other covariates were also examined.
**Results:** The sample included 1,008 patients with a mean (SD) age of 53 (15), symptom duration of 5 (3) months, DAS28 of 5.3 (1.3); 728 (72%) were female and 813 (81%) were white. Among males, 131 (47%) were overweight, 93 (33%) obese, and 55 (20%) smoked. Among females, 220 (30%) were overweight, 241 (33%) obese, and 109 (15%) smoked. At entry, 741 (74%) patients were treated with MTX (mono or combination therapy), relatively few 28 (3%) with a biologic, and 522 (52%) with steroids. The proportion in SR rose steadily; at 3 years 408 (38%) had achieved SR with a median (IQR) time to SR of 11.3 (11.2) months. In fully adjusted Cox survival analyses, BMI class (p=0.003) and smoking (p=0.046) were significantly associated with SR, as was a 3-way interaction for BMI class, smoking, and gender (p=0.02). Figure 1 depicts the combined impact of smoking and BMI class on the probability of achieving SR in a prototypical male and female patient: 53-years old, white, with some postsecondary education, 5 months symptom duration, 2 comorbidities, DAS28 of 5, and initial treatment with MTX and steroids. A non-smoking male with a healthy BMI and these characteristics would have a 41% probability of achieving SR within 3 years vs. only 15% for an obese male smoker. A non-smoking female with a healthy BMI and these characteristics would have a 27% probability of achieving SR within 3 years vs. only 10% for an obese female smoker.




**Conclusions:** In this large "real-world" early RA cohort, two potentially modifiable lifestyle factors – smoking and excess weight – were prevalent and had significant independent and combined effects on the likelihood of achieving SR.
**Disclosure of Interest:** None declared
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OP0174 **THE DEVELOPMENT OF THE MODIFIED DAS28-CRP TO IMPROVE AGREEMENT WITH DAS28-ESR AND ENSURE APPROPRIATE DISEASE ACTIVITY STRATIFICATION IN RA**

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**Background:** Disease activity in rheumatoid arthritis (RA) has traditionally been measured using the 28-joint count disease activity score (DAS28) using ESR. Use of DAS28 with CRP in place of ESR is increasing. Evidence suggests these scores are not truly interchangeable and agreement varies dependant on disease activity. This study uses the BSRBR-RA to investigate agreement between these scores, proposing an optimised method to calculate the estimated DAS28-ESR using CRP (mDAS28-CRP) that offers higher interscore agreement than currently.
**Objectives:** To investigate and optimise agreement between the DAS28-ESR and DAS28-CRP scores using the BSRBR-RA.
**Methods:** Patients with concurrent measures of ESR and CRP were identified from the BSRBR-RA, enabling paired calculation of DAS28-ESR and DAS28-CRP using existing formulae. A non-linear regression model enabled prediction of ESR from CRP. Resulting values were used in the existing DAS28-ESR formula to calculate estimated disease activity (mDAS28-CRP). A Bayesian approach was used to acknowledge the uncertainty associated with the predictions and correctly propagate it through to mDAS28-CRP. Inference, including constructing credible intervals for predicted ESR and mDAS28-CRP, was performed using Markov-Chain-Monte-Carlo. Bland-Altman analysis and agreement matrices were used to compare agreement levels between mDAS28-CRP, DAS28-CRP and DAS28-ESR.
**Results:** 5457 patients (mean age 56 yrs, 76% female) with 31,084 data entries were identified where paired DAS28-ESR/DAS28-CRP scores could be calculated. Mean DAS28-ESR was 0.3 points greater than DAS28-CRP (4.4 (SD 1.7), 4.1 (SD 1.6) respectively) compared with mean mDAS28-CRP of 4.6

**Abstract OP0174** – Table 1. Comparison of agreement between DAS28-ESR, DAS28-CRP and mDAS28-CRP scores

| | | DAS28-ESR | | | | |
|---|---|---|---|---|---|---|
| | | Remission (<2.6) 15.6% (n=4857) | LDA (2.6 to ≤3.2) 11.1% (n=3440) | MDA (3.2 to ≤5.2) 38.0% (n=11810) | HDA >5.2 35.3% (n=10977) | Totals 100% (31084) |
| Remission (<2.6) | DAS28-CRP | **66.7% (4041)** | 25.4% (1541) | 7.9% (481) | 0 | 19.5% (6063) |
| | mDAS28-CRP | **84.6% (2720)** | 13.9% (446) | 1.6% (51) | 0 | 10.3% (3217) |
| LDA (2.6 to ≤3.2) | DAS28-CRP | 15.8% (646) | **32.0% (1303)** | 52.2% (2128) | 0 | 13.1% (4077) |
| | mDAS28-CRP | 42.1% (1487) | **39.2% (1384)** | 18.7% (662) | 0 | 11.4% (3533) |
| MDA (3.2 to ≤5.2) | DAS28-CRP | 1.4% (170) | 4.9% (591) | **73.7% (8881)** | 20.0% (2414) | 38.8% (12056) |
| | mDAS28-CRP | 5.0% (650) | 12.3% (1601) | **76.5% (9916)** | 6.4% (837) | 41.8% (13004) |
| HDA >5.2 | DAS28-CRP | 0 | 0.1% (5) | 3.6% (320) | **96.3% (8563)** | 28.6% (8888) |
| | mDAS28-CRP | 0 | 0.1% (9) | 10.4% (1181) | **89.5% (10140)** | 36.4% (11330) |

LDA, low disease activity; MDA, moderate disease activity; HDA, high disease activity.

(SD 1.6; Fig 1). mDAS28-CRP had superior agreement with DAS28-ESR across remission, low and moderate disease activity, with only a 6.8% reduction in agreement at high disease activity when compared with the DAS28-CRP (Table 1).

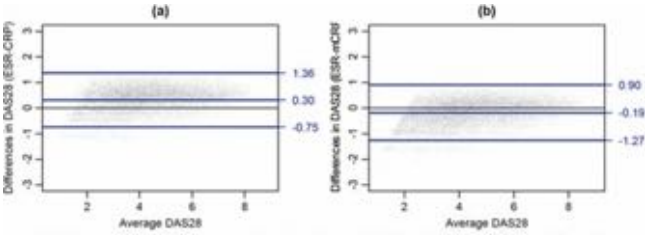



Figure 1. Reduction in interscore difference between DAS28-ESR and DAS28-CRP (a) and optimised mDAS28-CRP (b)

**Conclusions:** The mDAS28-CRP (online calculator pending) allows calculation of a disease activity score, using the same component parts of the DAS28-CRP, and has higher agreement levels with the original validated DAS28-ESR, than the current DAS28-CRP in this cohort. Disease activity scores are fundamental in clinical trials and practice, forming a central role in guiding availability of therapeutic agents. It is therefore essential that scores used are both valid and, if used interchangeably, have high agreement levels.

**Disclosure of Interest:** None declared

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**THURSDAY, 9 JUNE 2016**

## Prognosis and outcome in RA

### OP0175 RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS TAPERING TNF INHIBITORS IS PRIMARILY DRIVEN BY MEAN DISEASE ACTIVITY OVER TIME, NOT SO MUCH BY FLARING OR LOWER TNF INHIBITOR EXPOSITION

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**Background:** The Dose REduction Strategies of Subcutaneous tumor necrosis factor inhibitors (TNFi) study (DRESS), a randomized controlled strategy trial (RCT) investigating disease activity guided tapering of etanercept and adalimumab compared to usual care in rheumatoid arthritis (RA) patients, indicated that minimal radiographic progression is more frequent in patients that attempted TNFi tapering (1). Possible explanations include higher mean disease activity, higher incidence of flaring, and/or lower TNFi use in the tapering group.

**Objectives:** To investigate possible causes of a difference in minimal radiographic progression between patients that attempted tapering compared to patients that did not attempt to taper TNFi.

**Methods:** Eighteen months data were used. Mean change (Δ) in Sharp van der Heijde score (SvdH) and percentage of minimal radiographic progression, defined as >0.5 ΔSvdH, were calculated and used as outcome. Mean time weighted disease activity using DAS28-CRP (MTW-DAS28-CRP), occurrence and number of (major) flares per patient (flare: DAS28-CRP increase >1.2, or >0.6 and current DAS28-CRP ≥3.2; major flare: lasting >12 weeks), and TNFi use (normalized percentage of the defined daily dose) during the study were used in univariate and multivariate analyses. Thereafter, linear regression modeling was done with ΔSvdH as dependent variable and the above mentioned disease activity measures and TNFi use as independent variables, controlled for possible confounders (including age, sex, BMI, smoking, baseline SvdH, DAS28-CRP, CRP, RF and ACPA status, and concomitant synthetic DMARD). To check for effect modification by randomization group (tapering or usual care), all models were also done for both groups separately.

**Results:** All patients with 18 months data available (n=175) were included. Mean ΔSvdH was 0.75 and 0.15, and minimal radiographic progression was found in 39/121 (32%) and 9/59 (15%) patients in the tapering and usual care group respectively (both p<0.05, number needed to harm [NNH]=6). Mean DAS28-CRP and cumulative incidence of (major) flares were 2.3 (standard deviation [SD] 0.5) versus 2.1 (0.6) and 73% (12%) versus 27% (10%) in tapering and usual care (p<0.05). MTW-DAS28-CRP, but not incidence or number of (major) flares, was independently associated with radiographic progression. Effect modification was present for randomization group (p=0.01) (table 1). No significant confounding was present.

**Table 1:** linear regression model with effect modification

| Total group | Beta | P-value | 95% Confidence Interval (CI) |
|---|---|---|---|
| MTW-DAS28-CRP | 0.51 | 0.005 | 0.15 to 0.86 |
| constant | -0.4 | | |
| | | | |
| **Tapering group** | **Beta** | **P-value** | **95% CI** |
| MTW-DAS28-CRP | 0.64 | 0.013 | 0.14 to 1.14 |
| constant | -0.73 | | |
| | | | |
| **Usual care group** | **Beta** | **P-value** | **95% CI** |
| MTW-DAS28-CRP | 0.17 | 0.47 | -0.29 to 0.62 |
| constant | -0.20 | | |

**Conclusions:** The TNFi tapering strategy used in DRESS leads to higher risk for radiographic progression after 18 months than usual care. This is mainly caused by somewhat higher mean time weighted disease activity, but not so much by flaring after dose reduction attempts or lower TNFi use itself. Effect modification by randomization group was present. Dose tapering of TNFi still seems a safe long-term approach, but long term disease activity should be kept on the lowest possible level using treat to target, and radiologic progression should be checked regularly.

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[1] Van Herwaarden N et al. BMJ 2015;350:h1389

**Disclosure of Interest:** None declared

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### OP0176 FIVE YEAR OUTCOMES OF REMISSION STEERED TREATMENT INCLUDING DRUG TAPERING STRATEGIES IN EARLY ARTHRITIS PATIENTS

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**Background:** The window of opportunity hypothesis suggests that early initiation of treatment targeted at remission in early arthritis patients may avoid chronicity of inflammation and may result in early drug-free remission (DFR).

**Objectives:** To assess clinical outcomes of induction therapy followed by 5 years DAS-remission targeted therapy including rapid drug tapering strategies in early arthritis patients.

**Methods:** The IMPROVED study included 610 early rheumatoid arthritis (RA, 2010 criteria) or undifferentiated arthritis (UA) patients starting with methotrexate (MTX) and tapered high dose of prednisone. Patients in early DAS-remission (ER) (disease activity score (DAS)<1.6 after 4 months) stopped prednisone and if remission persisted at t=8 months also MTX. Patients not in ER (DAS≥1.6) were randomized to MTX+sulfasalazine+hydroxychloroquine+low dose prednisone (arm 1) or MTX+adalimumab (arm 2), 50 patients were not randomized and were treated "outside of protocol" (OP). Four monthly treatment adjustments aimed at DAS<1.6; if DAS<1.6 taper/stop medication and if DAS≥1.6 restart/intensify medication. Percentages of patients in (drug free) DAS-remission after 5 years were compared between RA and UA patients and the different treatment strategies. Logistic regression analysis was used to identify predictive factors of DAS-remission and DFR after 5 years.

**Results:** After 5 years mean±SD DAS decreased and functional ability improved in all treatment groups without differences between arm 1 and 2. 295/610 (48%) patients were in DAS-remission: 220/387 (57%) in the ER group, 31/83 (37%) in arm 1, 29/78 (37%) in arm 2 (p=0.768 arm 1 vs arm 2) and 15/50 (30%) in OP. 134/610 (22%) patients were in DFR: 105/387 (27%) in the ER group, 9/83 (11%) in arm 1, 12/78 (15%) in arm 2 (p=0.374 arm 1 vs arm 2) and 8/50 (16%) in OP. DAS-remission was achieved in similar percentages in RA and UA

patients and autoantibody positive (+) vs negative (–) patients. More UA than RA patients were in DFR at year 5 (33% vs 19%, p<0.001), and the same was true for anti-citrullinated protein antibodies (ACPA)– vs ACPA+ patients (31% vs 15%, p<0.001) and rheumatoid factor (RF)– vs RF+ positive patients (28% vs 17%, p<0.001). Between anti-carbamylated antibodies (anti-CarP)+ and – patients there was no difference in DFR rates.
Predictors of DAS-remission were age (OR 0.97 (95% CI 0.96–0.99)), symptom duration (0.99 (0.98–0.99)), baseline tender joint count (0.95 (0.90–1.00)) and achieving ER (1.95 (1.23–3.10)) (figure). Predictors of DFR were symptom duration (0.99 (0.97–1.00) and ER (2.67 (1.48–4.84)). ACPA+ was mostly associated with less DFR.

Figure: Multivariable logistic regression analysis with outcome DAS-remission and drug free remission at 5 years.

| Multivariable analysis Dependent DAS-remission at 5 years | OR | 95% CI | p-value |
|---|---|---|---|
| Baseline HAQ | 1.05 | 0.72-1.56 | 0.792 |
| Age | 0.97 | 0.96-0.99 | 0.004 |
| Female | 0.73 | 0.45-1.17 | 0.188 |
| Symptom duration (weeks) | 0.99 | 0.98-0.99 | 0.001 |
| Baseline Tender joint count | 0.95 | 0.90-1.00 | 0.053 |
| Baseline VAS global health | 0.99 | 0.98-1.00 | 0.100 |
| Early DAS-remission at 4 months | 1.95 | 1.23-3.10 | 0.004 |
| **Multivariable analysis Dependent DFR at 5 years** | | | |
| Baseline DAS | 0.86 | 0.65-1.15 | 0.312 |
| Female | 0.84 | 0.50-1.40 | 0.496 |
| Symptom duration (weeks) | 0.99 | 0.97-1.00 | 0.017 |
| Early DAS-remission at 4 months | 2.67 | 1.48-4.84 | 0.001 |
| RF- ACPA- anti-CarP- | Ref | | |
| RF+ ACPA- anti-CarP- | 1.11 | 0.48-2.54 | 0.811 |
| RF- ACPA+ anti-CarP- | 0.27 | 0.09-0.80 | 0.018 |
| RF- ACPA- anti-CarP+ | 3.94 | 0.43-35.93 | 0.224 |
| RF+ ACPA+ anti-CarP- | 0.23 | 0.11-0.50 | <0.001 |
| RF- ACPA+ anti-CarP+ | 0.25 | 0.05-1.25 | 0.091 |
| RF+ ACPA- anti-CarP+ | 0.50 | 0.08-3.01 | 0.447 |
| RF+ ACPA+ anti-CarP+ | 0.34 | 0.18-0.65 | 0.001 |

DAS: disease activity score, HAQ: health assessment questionnaire, VAS: visual analogue scale, DFR: drug-free remission, RF: rheumatoid factor, ACPA: anti-citrullinated protein antibodies, anti-CarP: anti-carbamylated protein antibodies, OR: odds ratio, CI: confidence interval, Ref: reference

**Conclusions:** After 5 years of DAS-remission steered treatment, 48% of early RA and UA patients were in DAS-remission and 22% in DFR. Remission results were better for patients who achieved ER and who had a shorter symptom duration. Remission results were similar for RA and UA patients, randomization arms and autoantibody status, but more UA than RA patients and more autoantibody? than + patients were in DFR.
**Disclosure of Interest:** G. Akdemir: None declared, L. Heimans: None declared, R. J. Goekoop: None declared, M. van Oosterhout: None declared, J. B. Harbers: None declared, C. Bijkerk: None declared, G. M. Steup-Beekman: None declared, L. Lard: None declared, P. B. J. de Sonnaville: None declared, B. A. M. Grillet: None declared, T. W. J. Huizinga: None declared, C. F. Allaart Grant/research support from: Year 1 of the IMPROVED study was sponsored by Abbott.
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## OP0177 ULTRASOUND IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS: RESULTS FROM THE RANDOMIZED CONTROLLED ARCTIC TRIAL

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**Background:** Application of ultrasound (US) in the management of patients with rheumatoid arthritis (RA) is rapidly growing.
**Objectives:** The randomized controlled ARCTIC trial (ClinicalTrials.gov NCT01205854) examined if the use of a treatment strategy based on structured US assessment[1] would lead to improved outcomes in RA, compared to a conventional strategy based on clinical and laboratory assessments alone.
**Methods:** Newly diagnosed DMARD naïve RA patients were randomized 1:1 to A) an ultrasound tight control (UTC) strategy targeting clinical and imaging remission (no ultrasound power-Doppler signal) or B) a conventional tight control (CTC) strategy targeting clinical remission. Patients in both arms were treated according to the same DMARD escalation strategy, starting with MTX, then triple therapy MTX/SSZ/HCQ, then biologic DMARD if target was not reached. The primary endpoint was the proportion of patients with a combination between 16 and 24 months of clinical remission, no swollen joints and non-progression of radiographic joint damage.
**Results:** A total of 238 patients were randomized, and patients with at least one follow-up visit were included in the full analysis set (UTC n=118, CTC n=112). Twenty-six patients (22.0%) in the UTC arm and 21 patients (18.8%) in the CTC arm reached the primary endpoint (mean difference 3.3%; 95%CI -7.1% to 13.7%). No significant differences were found between the groups for the components of the primary outcome, and secondary endpoints were similar (table).
**Conclusions:** The implementation and systematic use of ultrasound in the follow-up of early RA patients treated with an aggressive treat-to-target strategy is not justified based on the results of the ARCTIC trial.
**References:**
[1] Hammer HB et al Ann Rheum Dis 2011
**Disclosure of Interest:** E. Haavardsholm Grant/research support from: Pfizer, MSD, UCB, AbbVie, Roche, A.-B. Aga: None declared, I. Olsen: None declared, S. Lillegraven: None declared, H. Hammer Consultant for: AbbVie, Pfizer, BMS, Roche, UCB, T. Uhlig: None declared, H. Fremstad: None declared, T. Madland: None declared, Å. Lexberg: None declared, H. Haukeland Consultant for: UCB, AbbVie, E. Rødevand: None declared, C. Høili: None declared, H. Stray: None declared, A. Bendvold: None declared, I. Hansen: None declared, G. Bakland Consultant for: AbbVie, Pfizer, L. Nordberg: None declared, D. Heijde: None declared, T. Kvien: None declared
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## OP0178 IMPACT OF ANTI-CYCLIC CITRULLINATED PEPTIDE AND RHEUMATOID FACTOR STATUS ON RESPONSE TO ABATACEPT THERAPY: FINDINGS FROM A US OBSERVATIONAL COHORT

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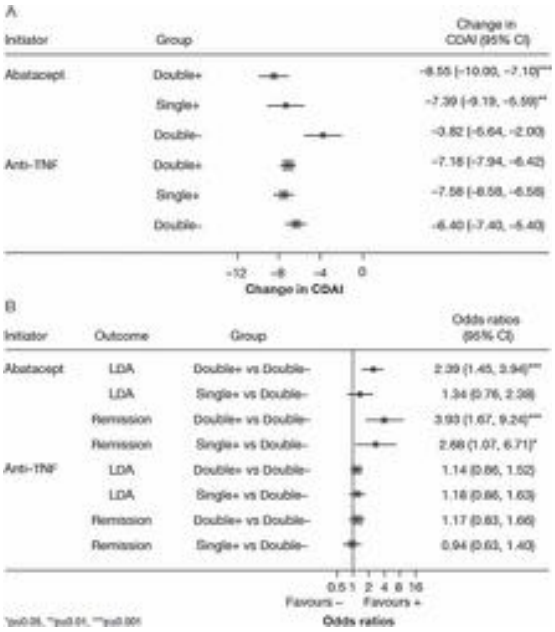
**Background:** It is unclear whether anti-cyclic citrullinated peptide (anti-CCP) and rheumatoid factor (RF) status are predictive of response to rheumatoid arthritis (RA) therapy.
**Objectives:** To assess whether baseline anti-CCP/RF status is associated with treatment response in patients with RA initiating abatacept (ABA) or a tumour necrosis factor-alpha inhibitor (TNFi).
**Methods:** Patients who initiated ABA or a TNFi within the Corrona RA registry between June 2002 and January 2015 were eligible if they had: anti-CCP and RF testing at or prior to initiation; a follow-up visit 6 months after initiation (±3 months); and Clinical Disease Activity Index (CDAI) measured at or within 4–6 months prior to initiation and after 6 months' treatment. Seropositivity was identified for anti-CCP (≥20 U/mL) and RF (≥40 U/mL). At 6 months, the primary

**Abstract OP0177** – Table 1

| Outcomes | Ultrasound tight control (n=118) | Conventional tight control (n=112) | Difference (95% CI) | p-value |
|---|---|---|---|---|
| Primary endpoint (between 16 and 24 months) | | | | |
| DAS<1.6, SJC44<1, ΔvdHSS<0.5, n (%) | 26 (22.0%) | 21 (18.8%) | 3.3 (–7.1 to 13.7) | 0.54 |
| Components of primary endpoint* and secondary outcomes | | | | |
| *No swollen joints 16–24 months, n (%) | 62 (52.5%) | 61 (54.5%) | –1.9 (–14.8 to 11.0) | 0.77 |
| *DAS remission (DAS<1.6) 16–24 months, n (%) | 64 (54.2%) | 58 (51.8%) | 2.5 (–10.4 to 15.4) | 0.71 |
| *No radiographic progression 16–24 months, n (%) | 49 (41.5%) | 39 (34.8%) | 6.7 (–5.8 to 19.2) | 0.29 |
| DAS remission (DAS<1.6) at 24 months, n (%) | 80 (67.8%) | 75 (67.0%) | 0.8 (–11.3 to 13.0) | 0.89 |
| SDAI remission (SDAI<3.3) at 24 months, n (%) | 71 (60.2%) | 56 (50.0%) | 10.2 (–2.6 to 23.0) | 0.12 |
| EULAR good/moderate response at 24 months, n (%) | 98 (83.1%) | 90 (80.4%) | 2.7 (–7.3 to 12.7) | 0.60 |
| Δ Modified Sharp score at 24 months, median (p25, p75) | 1.0 (0, 2.5) | 1.5 (0.5, 3.0) | –0.45 (–0.90 to 0) | 0.05 |
| Treatment at end of study | | | | |
| *MTX monotherapy, n (%)* | 63 (53.4%) | 80 (71.4%) | –18.0 (–30.3 to –5.8) | 0.004 |
| *MTX/SSZ/HCQ combination therapy, n (%)* | 21 (17.8%) | 13 (11.6%) | 6.2 (–2.9 to 15.3) | 0.18 |
| *Biologic treatment, n (%)* | 34 (28.8%) | 19 (17.0%) | 11.8 (1.1 to 22.6) | 0.03 |

outcome was ΔCDAI, with secondary outcomes being achievement of remission (CDAI ≤2.8 in those with low, moderate or high baseline disease activity) and low disease activity (LDA; CDAI ≤10 in those with moderate or high baseline disease activity). Unadjusted and adjusted linear and logistic regression analyses were performed by baseline anti-CCP/RF status: double positive (anti-CCP+/RF+), single positive (anti-CCP+/RF– or anti-CCP–/RF+) and double negative (anti-CCP–/RF–). Adjusted models controlled for baseline age, sex, BMI, CDAI score, co-morbidity index and number of prior biologic DMARDs.

**Results:** 566 patients starting ABA (244 double positive; 167 single positive; 155 double negative) and 1715 starting a TNFi (774 double positive; 470 single positive; 471 double negative) were identified. Most patients were female (ABA: 79–83%; TNFi: 74–80%) and middle-aged (mean age 57–58 years in ABA, 54–57 years in TNFi), with established disease (mean disease duration 9–11 years in ABA, 6–8 years in TNFi) and moderate disease activity (mean CDAI 18–23 in ABA, 18–19 in TNFi). For patients who initiated ABA, double positive status was associated with a significantly greater response compared with double negative status on all outcomes (ΔCDAI –8.9 vs –4.5, p=0.002; LDA 43% vs 26%, p=0.002; remission 15% vs 5%, p=0.001). Additionally, single positive status was associated with a greater likelihood of remission as compared with double negative status for ABA users (12% vs 5%, p=0.018). Conversely, there were no significant differences in responses between anti-CCP/RF groups in the TNFi users (double positive vs double negative: ΔCDAI –7.5 vs –6.8, p=0.46; LDA 39% vs 35%, p=0.20; remission 16% vs 14%, p=0.38). In adjusted models, there are significant differences in the outcomes based on anti-CCP/RF status among ABA users but not TNFi users (Figure).




**Conclusions:** These real-world data demonstrate that baseline anti-CCP+/RF+ is associated with better clinical response to ABA, with the strongest association observed for double seropositivity. In contrast, no relationship was evident between anti-CCP/RF status and response to a TNFi, suggesting that the predictive value of autoantibodies is dependent on drug mechanism of action.

**Disclosure of Interest:** L. R. Harrold Grant/research support from: Pfizer, H. J. Litman Employee of: Corrona, S. E. Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Kelly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, W. Hua Employee of: Corrona, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, L. Rosenblatt Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Rebello Employee of: Corrona, J. M. Kremer Shareholder of: Corrona, Grant/research support from: AbbVie, Bristol-Myers Squibb, Genentech, Lilly, Novartis, Pfizer, Employee of: Corrona, Speakers bureau: Genentech (non-branded talks only)

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## OP0179 COMPARING INITIAL TREATMENT STRATEGIES WITH METHOTREXATE ON FIRST USE OF BIOLOGIC THERAPY: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

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**Background:** Optimal treatment of early rheumatoid arthritis (ERA) involves a treat-to-target strategy aiming for remission. Initial use of combination DMARDs is associated with an increased likelihood of remission in ERA patients. Research suggests that combinations DMARDs can provide equivalent outcomes at lower costs than biologic DMARDs.

**Objectives:** To compare effects of initial treatment with methotrexate (MTX) monotherapy vs MTX combination therapy on time to first use of biologic DMARDs in a large multi-centre ERA cohort.

**Methods:** The Canadian Early Arthritis Cohort (CATCH) is a multi-centre prospective cohort study of patients with early RA diagnosed and treated by a rheumatologist. The present study included participants who met 1987 or 2010 ACR criteria for RA, with ≤12 months symptom duration, moderate or high disease activity based on the DAS28 at baseline and treated with MTX. Patients treated with a biologic at baseline were excluded. Patients were followed until they started a biologic or they were censored due to loss to follow up or the end of the 3-year study period. Cox proportional hazards survival analysis was used to estimate effects of oral MTX monotherapy, subcutaneous MTX monotherapy, and MTX combination therapy adjusting for age, gender, education level, symptom duration, comorbidities, seropositivity, baseline erosions, baseline DAS28, and corticosteroid use.

**Results:** 1214 patients were included with 212 first events of biologic use. At baseline, 865 (71.3%) were female with mean (sd) age of 54.4 (14.9) years, symptom duration of 5.5 (2.8) months, and DAS28 of 5.5 (1.2). Oral MTX monotherapy was used as initial treatment in 230 (19%), subcutaneous MTX monotherapy in 226 (19%), and MTX combination therapy in 730 (62%). In fully adjusted Cox regression models, patients treated with subcutaneous MTX monotherapy were half as likely to require biologics as patients treated with oral MTX monotherapy (HR =0.47, p=0.015). There was no difference between MTX combination therapy and oral MTX monotherapy (HR =0.95).

**Conclusions:** Treatment with subcutaneous MTX monotherapy was associated with a reduced use of biologics. This may be due to increased treatment efficacy compared to oral MTX. Combination DMARD therapy was not associated with longer time to biologic initiation, potentially due to funding models in Canada specifying that combination DMARD therapy must be used before biologics can be considered. This study suggests that early use of subcutaneous MTX can potentially delay the need for more expensive biologic therapies.

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## OP0180 OCCURRENCE OF REPAIR OF EROSIONS DURING EIGHT YEARS IN A LARGE INCEPTION COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS – A BARFOT-STUDY

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**Background:** Bone erosion is a central pathophysiological process in rheumatoid arthritis (RA) leading to joint destruction and functional limitations. Measurement of the degree of joint damage represents an important tool to assess disease progression and effectiveness of current treatments. Repair of existing bone erosions have been described but the extent and significance of this is so far unclear.

**Objectives:** The aim of this study was to examine the incidence of repair of erosions in patients with early RA during eight years and to look for possible factors linked to repair.

**Methods:** 473 patients from the BARFOT (Better Anti-Rheumatic FarmacOTherapy) inception RA cohort were included into the study71% were women, mean age 55 years, 63% were rheumatoid factor (RF)-positive and 59% current or previous smokers. All patients had radiographs of hands and feet at inclusion into the study (baseline), 1, 2, 5, and 8 years.

Erosion scores were measured by the Sharp-van der Heijde scoring (SHS) method. Sustained remission was defined as a DAS28 <2.6 at all follow-up visits. Repair was defined as complete healing or reduction in size of the erosion.

**Results:** After one year, presence of repair was found in 82 patients (17%), after two years in 140 (30%), after 5 years in 179 (38%) and after 8 years in 203 (51%). At 1, 2, 5 and 8 years these patients had 153, 260, 424 and 717 erosions with repair, respectively.

The number of repairs at the follow-up visits correlated weakly or moderately with the erosion scores, r=0.2–0.4, p=0.001.

The sum of the number of erosions showing repair recorded at each follow-up visit (*total repairs*) was 1.554 and the corresponding sum of erosion scores (*total erosion scores*) was 10.867. The *total repairs* correlated strongly with *total erosion scores*, r=0.7, p=0.001. The mean *total repairs* was associated with RF positivity, p=0.001 but not with gender, p=0.23.

The mean number of repairs was significantly higher in RF-positive patients at 2 and 8 years, 0.62 vs 0.37, (p=0.010) and 2.16 vs 1.18, (p=0.001). Presence of repair was significantly associated with RF-positivity at 2, 5, and 8 years and with gender at 8 years, 61% in men vs 47% in women (p=0.011).

The mean *total repairs* was significantly lower in patients in sustained remission compared with the rest of the patients, 2.3 vs 3.7, p=0.008.

There was no significant correlation between number of repairs and baseline DAS28 at any follow-up visit. Treatment with a combination of conventional DMARDs was associated with presence of repair after 1 (p=0.048) and 5 (p=0.001) years. After 8 years biologic DMARD therapy was more common in patients with some repair (p=0.011). Prednisolone treatment did not significantly influence repair.

**Conclusions:** In this cohort of patients with early RA, repair was more common than previously described. Repair of erosions occurred with increasing frequency during the 8 year study and was associated with rheumatoid factor positivity. Patients in sustained remission showed fewer repairs.

**Disclosure of Interest:** None declared

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## OP0181 PREDICTION OF FLARE AFTER STOPPING TNF-INHIBITOR BY BASELINE ULTRASONOGRAPHY AND PATIENT CHARACTERISTICS IN RHEUMATOID ARTHRITIS PATIENTS WITH LOW DISEASE ACTIVITY: 12-MONTH RESULTS

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**Background:** A significant number of rheumatoid arthritis (RA) patients can reach low disease activity (LDA) by using TNF-inhibitors (TNF-i), but this therapy can cause serious side-effects and is expensive. Therefore it could be expedient to stop in case of LDA, unless a relapse can be predicted. Ultrasonography of joints seems to be a predictor in this respect in smaller studies.

The Dutch POET (Potential Optimalisation of Expediency of TNF-i (TNF-inhibitor)) study, is a multicenter randomized prospective cohort study investigating if in patients with RA with LDA on TNF-i and conventional DMARD, the TNF-i can be stopped. Patients were randomized to continue or stop TNF-i. Part of this study is the POET-ultrasonography (US) study.

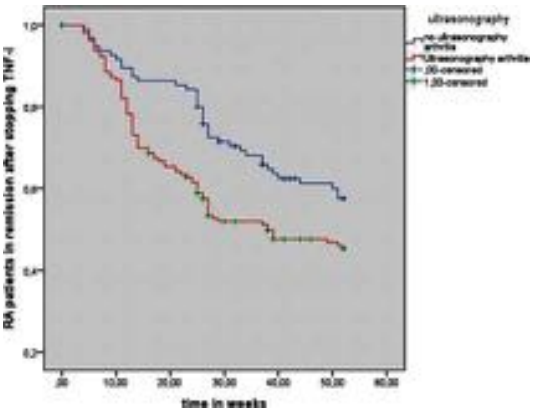
**Objectives:** To investigate whether US, at the time of stopping TNF-i in RA patients with LDA, is an additive predictor for flare besides clinical data.

**Methods:** Data were analysed of 251 patients who stopped TNF-i in the POET study. Participating patients had RA according to ACR 1987 criteria, >6 months a DAS28 <3.2 (LDA) and treatment with TNF-i >1 year next to a conventional DMARD, with no dose change 6 months prior to randomisation. Nineteen trained ultrasonographers performed at baseline of the study US (with different US machines) of 20 joints: MCP 1–5 dorsal and volar, wrist and MTP 2–5 dorsal aspect, all bilaterally. The joints were graded on grayscale (GS; 0–3) and power Doppler (PD; 0–3). US signs of arthritis were defined as GS>1 and/or PD>0. Trial visits were performed every 3 months during 12 months and intercurrently when flare was suspected. Flare was defined as DAS28 >3.2 and at least >0.6 increase compared to the baseline DAS28. Univariate and multivariate Cox-regression was performed guided by clinical factors described in the literature and US.

**Results:** The Kaplan Meier curve for patients with US signs of arthritis in one or more joints shows greater/higher risk of flare and shorter relapse-free period compared to the curve for patients without US signs of arthritis, p= (figure). At multivariate analysis (table), correcting for potentially clinical predictors, US detected arthritis stayed a statistically significant predictor of flare; HR 1.69; 95% CI 1.11 to 2.53. The predictive value of US seems not that strong that it can be used in individual patients.

| | Regression Coefficient | Hazard ratio (95% CI) |
|---|---|---|
| IgM RF (+) | –0.51 | 0.60 (0.35–1.05) |
| Anti-CCP (+) | 0.25 | 1.29 (0.76–2.17) |
| Erosiveness (+) | 0.23 | 1.26 (0.82–1.95) |
| Disease duration (years) | 0.24 | 1.27 (0.97–1.67) |
| Sex (male) | 0.06 | 1.06 (0.71–1.59) |
| BMI | 0.01 | 1.01 (0.97–1.06) |
| csDMARD (number) | –0.04 | 0.96 (0.72–1.27) |
| TNF-inhibitor (number) | –0.01 | 0.99 (0.89–1.11) |
| US (+)* | 0.52 | 1.69 (1.11–2.53) |

*P-value <0.05.




**Conclusions:** The presence of US arthritis is associated with an earlier flare and a higher flare rate compared to those with negative US taking into account demographic and clinical patient characteristics.

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## OP0182 PREVENTION OF RHEUMATOID ARTHRITIS BY B CELL DIRECTED THERAPY IN THE EARLIEST PHASE OF THE DISEASE: THE PRAIRI STUDY

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**Background:** Systemic autoimmunity may precede the development of clinical signs and symptoms of seropositive rheumatoid arthritis (RA), which offers a

window of opportunity to delay or prevent clinically manifest arthritis by targeted intervention. This could represent a paradigm shift from treatment to prevention[1].
**Objectives:** To explore if a single infusion of rituximab (anti-CD20 antibody) can prevent or delay the onset of clinically manifest arthritis in individuals at risk of developing autoantibody positive RA.
**Methods:** Eighty-two subjects with arthralgia who had never had clinically manifest arthritis and never used disease-modifying antirheumatic drugs were included in a multicentre, randomised, double-blind, placebo-controlled clinical trial. They were positive for both anti-citrullinated protein antibodies (ACPA) and rheumatoid factor and they had CRP levels ≥3 mg/l and/or subclinical synovitis on ultrasound or MRI of the hands. Subjects were randomized to receive a single iv infusion of either 1000 mg rituximab or placebo after 100 mg methylprednisolone premedication in each group. Subjects were prospectively followed to assess development of clinically manifest arthritis. We performed Kaplan-Meier survival analysis, Cox regression analysis and determined Treatment*Time Cox proportional hazards.
**Results:** Eighty-one individuals (52 females; mean age 53 (IQR 13.5) years) received treatment, which was generally well tolerated. One patient withdrew before treatment. The median follow up was 27.0 months (IQR 25.0), during which 30 subjects developed arthritis: 16/40 (40%) in the placebo group and 14/41 (34%) in the rituximab group, after a median period of 11.5 (interquartile range [IQR] 12.5) months in the placebo group versus 16.5 (IQR 19.0) months in the rituximab group. Whereas the risk for development of arthritis in the placebo group was 40%, we found a reduction of 53% of this risk in the rituximab group at 18 months follow up (HR (95%CI)=0.475 (0.190–1.191)). At the 25% quartile (75% free of arthritis) of the cumulative arthritis-free survival, there was a delay in the development of arthritis of 12.0 months (12 months in the placebo group versus 24 months in the rituximab group. As expected, this effect attenuated over time. Treatment*Time Cox proportional hazard analysis showed that the beneficial effect of rituximab was statistically significant (P<0.0001)
**Conclusions:** A single infusion of 1000 mg rituximab significantly delays the development of arthritis in subjects at risk of developing RA. This is the first study evaluating the effects of a biopharmaceutical in this population, and the results strongly support the rationale for future clinical trials aimed at prevention of RA by a targeted intervention.
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**FRIDAY, 10 JUNE 2016**

## SLE, Sjögren's and APS: clinical aspects (other than treatment)

### OP0183 HYPOCOMPLEMENTEMIA ASSOCIATES WITH THROMBOSIS IN SLE PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES

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**Background:** Low complement is common in systemic lupus erythematosus (SLE) and is considered in classification criteria and disease activity indices. Recent evidence supports the hypothesis that the activation of complement is also important in the antiphospholipid syndrome (APS), coating platelets and contributing to thrombus formation. The successful treatment of catastrophic APS with the terminal complement inhibitor, eculizumab, has been reported, supporting this hypothesis.
**Objectives:** This work was undertaken to evaluate the relationship between hypocomplementemia and thrombotic outcomes in SLE patients with antiphospholipid antibodies (APL).
**Methods:** As part of a longitudinal lupus cohort, the presence of antiphospholipid antibodies (lupus anticoagulant and anticardiolipin) and thrombotic events, both venous and arterial, were updated quarterly. Statistical analysis included only patients who were found on longitudinal follow up to have one or more APL, i.e. antibodies to cardiolipin, or the presence of the lupus anticoagulant (LAC). Patients were then categorized by thrombotic event, the presence of hypocomplementemia (low C3, low C4 and both low C3 and C4) and type of APL. Those with low complement were compared to those without and the odds ratio for each thrombotic outcome calculated.
**Results:** 2399 patients were included, 1140 (47.5%) had antibodies to cardiolipin and 624 (26.0%) a positive LAC. The relationship between the antiphospholipid antibodies, thrombotic outcomes and low C3, low C4 or both in combination is outlined in Table 1.
**Conclusions:** In patients with anticardiolipin antibodies, the presence of hypocomplementemia (both low C3 + C4) associates strongly with DVT and stroke. Hypocomplementemia in the setting of the LAC was also associated with stroke whilst low C4 alone associated with digital gangrene. These findings are supportive of the robust mechanistic data involving the complement system in APS. They also raise the question as to whether hypocomplementemia should be considered a further risk factor for thrombosis in SLE patients with positive antiphospholipid antibodies in whom to date many traditional risk factors have been implicated.
**Disclosure of Interest:** None declared
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### OP0184 CLINICAL SPECTRUM AND THERAPEUTIC MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED MACROPHAGE ACTIVATION SYNDROME. DATA FROM A FRENCH NATIONWIDE STUDY OF 81 EPISODES IN 67 ADULT PATIENTS

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**Background:** Macrophage activation syndrome (MAS) is a potentially life-threatening hyperinflammatory syndrome that can occur during systemic lupus erythematosus (SLE). In SLE, MAS can mimic a disease flare. This overlap in clinical presentations can hinder the recognition of incipient MAS and delay the selection of the most appropriate treatment. Data on MAS in adult SLE patients are very limited (1).
**Objectives:** Description of clinical, laboratory and pathological features, treatment strategies and prognosis of a large series of SLE-associated MAS
**Methods:** We conducted a nationwide retrospective study that included 81 episodes of MAS in 67 adult patients with SLE seen between 1990 and 2015. All patients fulfilled the 1997 ACR revised criteria for SLE and had at least one episode of MAS diagnosed according to Henter's criteria (2).
**Results:** No patient had familial history of MAS. Median age at first MAS episode was 32 (18–74) years. Median duration of follow up was 40 months. MAS was inaugural in 36 patients (44.4%). For the remaining patients median delay between the diagnosis of SLE and the first episode of MAS was 82 months. Eleven patients relapsed (2 had >2 relapses).
Patients had the following features: fever (100% episodes; mean ± SD: 39.5°C ± 0.57), splenomegaly (52%), increased serum levels of aspartate aminotransferase (AST) (96%; mean: 192UI/l ±167), LDH (96%; mean: 1155 UI/l ±863), CRP (96%; mean: 75.8 mg/l ±72), ferritin (94%; mean: 11497 ng/l ±20511), lymphopenia (mean: 0.49 G/l ±0.35). thrombocytopenia $<100\times10^9$/l was found in 90% of the cases, neutropenia $<1000\times10^9$/l in 65% and anemia <8 g/dl in 45%. Procalcitonin (PCT), measured in 32 episodes was found high in 85% of the cases. A concomitant infection was documented in 34/81 (42%) episodes (including 3 EBV infections).
Visceral complications included myocarditis (16 episodes), acute lung injury (15), seizures (8) pancreatitis (4). In 23 episodes, patients required hospitalization in an intensive care unit and 3 died (multiple organ failure).
80 episodes (98%) were treated with high dose steroids. In 38 cases additional treatments were required: immunoglobulins (n=21), cyclophosphamide (n=18), mycophenolate mofetil (n=8) Etoposide (n=7) and Rituximab (n=7). Etoposide

**Abstract OP0183** – Table 1. APL and thrombosis with hypocomplementemia

| Type of APL | Thrombosis | Low C3 OR (CI) | P value | Low C4 OR (CI) | P value | Both low C3+C4 OR (CI) | P value |
|---|---|---|---|---|---|---|---|
| Anticardiolipin antibody | Superficial | 0.8 (0.25, 2.51) | 0.6981 | 1.23 (0.34, 4.47) | 0.7543 | 1.15 (0.56, 2.37) | 0.7041 |
| | DVT | 1.43 (0.85, 2.42) | 0.1798 | 0.83 (0.37, 1.83) | 0.641 | 1.64 (1.13, 2.39) | 0.0095 |
| | Stroke | 1.01 (0.51, 1.98) | 0.9838 | 0.29 (0.07, 1.26) | 0.0993 | 1.64 (1.06, 2.56) | 0.0278 |
| | MI | 1.31 (0.51, 3.34) | 0.5768 | 0.37 (0.05, 2.84) | 0.3357 | 1.48 (0.76, 2.89) | 0.2501 |
| | Digital Gangrene | 2.03 (0.61, 6.77) | 0.247 | 2.49 (0.61, 10.2) | 0.2039 | 1.43 (0.54, 3.79) | 0.4766 |
| Lupus Anticoagulant | Superficial | 0.3 (0.07, 1.36) | 0.1199 | 0.67 (0.15, 3.04) | 0.6004 | 0.74 (0.36, 1.51) | 0.4024 |
| | DVT | 1 (0.57, 1.75) | 0.9886 | 0.96 (0.45, 2.06) | 0.9202 | 0.88 (0.59, 1.31) | 0.5376 |
| | Stroke | 1 (0.46, 2.21) | 0.9909 | 0.4 (0.09, 1.75) | 0.2221 | 1.89 (1.14, 3.15) | 0.014 |
| | MI | 0.79 (0.28, 2.25) | 0.6598 | 0.32 (0.04, 2.53) | 0.283 | 0.92 (0.46, 1.83) | 0.8164 |
| | Digital Gangrene | 4.21 (0.98, 18.04) | 0.0529 | 5.47 (1.06, 28.19) | 0.0421 | 2.25 (0.61, 8.28) | 0.222 |

and cyclophosphamide based regimens had a higher efficacy than immunoglobulins and conventional immunosuppressants.
**Conclusions:** This is the largest ever published case-series on SLE-associated MAS. It is a severe complication of SLE (28% ICU admissions) and is often inaugural. High fever and high levels of AST, LDH, CRP ferritin and PCT should be considered as red flags for early diagnosis. High dose steroids are often not sufficient to control disease.
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**Disclosure of Interest:** None declared
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## OP0185 CHARACTERISTICS OF PRIMARY SJÖGREN'S SYNDROME PATIENTS WITH IGG4-POSITIVE PLASMA CELLS IN LABIAL SALIVARY GLANDS

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**Background:** Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease affecting predominantly exocrine glands such as salivary and lacrimal glands. Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is a new clinical concept of multi-organ diseases, which is characterized pathologically by the infiltration of IgG4-bearing plasma cells into involved organs. However, some pSS patients showed infiltration of IgG4+ plasma cells in exocrine glands.
**Objectives:** We aim to investigate the characteristics of primary Sjögren's syndrome (pSS) patients with IgG4+ plasma cells in labial salivary glands (LSGs).
**Methods:** 336 patients with pSS were enrolled. The LSG tissues from pSS patients were stained with monoclonal antibodies to IgG4 and IgG. Patients were divided into three subgroups according to histopathologic infiltration degree of $IgG4^+$ plasma cells. The clinical and serological characteristics of patients were compared.
**Results:** 336 patients were divided into three groups according to infiltration degree of $IgG4^+$ plasma cells: slight-IgG4 group (n=194), moderate-IgG4 group (n=106) and high-IgG4 group (n=36). The results showed that the higher $IgG4^+$ plasma cells expression, the lower positive rates of serum anti-SSA, anti-SSB, anti-nuclear antibodies (ANA) and rheumatoid factor (RF). The comparison of extraglandular manifestations of three groups indicated that patients in high-IgG4 expression group showed a highest frequency of interstitial lung disease (30.6%) and tubulointerstitial nephritis (13.9%), whereas a lowest frequency of leucopaenia (13.9%), thrombocytopaenia (11.1%) and abnormal thyroidal function (0%).
**Conclusions:** The results showed that a considerable proportion of pSS patients could manifest abundant IgG4+ plasma cells infiltration in LSGs. These patients have unique laboratory and clinical characteristics. These findings may help further understand pSS, IgG4-RD, and the role of $IgG4^+$ plasma cells in autoimmune diseases.
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## OP0186 IMMUNE COMPLEX BOUND U1 AND Y1 RNA CORRELATES WITH INTERFERON-STIMULATED GENE EXPRESSION AND DISEASE ACTIVITY: AN OBSERVATIONAL STUDY OF SYSYTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Immune complexes (ICs) containing RNA are thought to play a central role in driving interferon (IFN) production and systemic inflammation in systemic lupus erythematosus (SLE) via activation of intracellular Toll-Like Receptors (TLRs). However, quantitation of IC-bound RNAs in SLE patient plasma has not previously been performed.
**Objectives:** To quantify IC-associated U1 and Y1 RNA and relate the findings to the interferon (IFN) signature and SLE clinical activity.
**Methods:** Medications and SLEDAI measurements were completed on 228 SLE patients. Autoantibodies were quantified by a Bioplex assay. Peripheral blood transcript profiles for 186 selected genes were quantified by a dynamic array QPCR analysis. ICs were isolated from plasma by protein A bead capture and associated RNA quantified by QPCR using primer/probes designed to detect small, noncoding U1 and Y1 RNA transcripts.
**Results:** The autoantibodies anti-SmRNP and anti-Ro60 displayed the strongest associations with IC-bound U1 and Y1 RNA levels, respectively. When patients were grouped into 4 categories based on the presence of ICs containing U1 and/or Y1 RNA, blood gene expression changes in the U1-/ Y1- group were significantly lower than observed in the three groups possessing U1 alone, Y1 alone, or both RNA molecules. Within the U1 RNA-positive groups, the top 10 up-regulated genes were increased 10–48 fold compared to healthy volunteers (associated p values exceeding $10^{-15}$) and corresponded to known IFN-inducible transcripts. IC-bound U1 and Y1 RNA levels showed significant correlations with each other and also with disease activity (SLEDAI) ($p<0.0003$).
**Conclusions:** The enhanced expression of IFN-inducible transcripts in blood from patients possessing IC-bound U1 and/or Y1 RNA lends further support to the hypothesis that these RNA molecules are involved in triggering TLR7 and stimulating interferon production in SLE patients.
Therapeutic strategies that seek to reduce the quantities of RNA associated with ICs may be an attractive approach to blocking downstream IFN production and immune system activation.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2747

## OP0187 ALL-CAUSE AND SPECIFIED CAUSES OF MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS: SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL TRIALS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease with a broad spectrum of clinical manifestations. Increased morbidity and mortality were observed despite early and aggressive treatment. A changing pattern of mortality has been observed recently.
**Objectives:** To summarize the incidence rate (IR) of all-cause and specified causes of mortality in SLE in clinical trials (CT).
**Methods:** A systematic review was performed by searching the Medline, Embase and Cochrane databases. The search strategy identified all synonyms of disease and was limited to CTs. Data from randomized CTs and open-label studies were combined to assess the IR of all-cause and specified causes of mortality using a random effects model.
**Results:** The search identified 2168 articles. After selection, 140 studies met the inclusion criteria (13,409 patients and 18,028.71 patients-year of exposure) and were included in the analysis. A total of 283 SLE patients died. IR of all-cause of mortality was 1.73 per 100 patients-year. IRs of specific causes are showed in the table. Stratified analysis showed higher IR for patients treated with higher dose of glucocorticoids ($\geq$1 mg/kg/day of prednisone) [IR was 3.13 (2.15–4.28) vs 1.22 (0.92–1.55)] and for studies with lower percentage of women (less than

**Abstract OP0187** – Table 1

| Mortality (100 patients-year) in studies | All-cause | Infection | Cardiovascular | Malignancies | Lupus nephritis | Lupus | Unknown | Suicide |
|---|---|---|---|---|---|---|---|---|
| All | 1.73 (1.37–2.11) | 0.62 (0.46–0.79) | 0.41 (0.31–0.51) | 0.17 (0.12–0.24) | 0.20 (0.14–0.27) | 0.15 (0.09–0.21) | 0.33 (0.24- 0.42) | 0.16 (0.11–0.23) |
| Rituximab | 1.14 (0.42–0.22) | 0.37 (0.03–1.06) | 0.37 (0.03–1.06) | 0.25 (0.007–0.84) | 0.25 (0.007–0.84) | 0.25 (0.007–0.84) | 0.50 (0.08–1.27) | 0.25 (0.007–0.84) |
| Cyclophosphamide | 3.79 (2.74–5.02) | 1.45 (0.89–2.13) | 0.97 (0.63–1.38) | 0.35 (0.16–0.61) | 0.40 (0.20–0.67) | 0.32 (0.14–0.56) | 0.51 (0.25–0.85) | 0.27 (0.11–0.51) |
| Mycophenolate | 2.35 (1.05–4.14) | 1.55 (0.66–2.82) | 0.45 (0.09–1.08) | 0.52 (0.12–1.19) | 0.45 (0.09–1.08) | 0.59 (0.16–1.30) | 0.67 (0.20–1.40) | 0.45 (0.09–1.08) |
| Azathioprine | 1.51 (0.54–2.98) | 0.66 (0.28–1.20) | 0.73 (0.33–1.30) | 0.28 (0.06–0.67) | 0.35 (0.09–0.77) | 0.17 (0.01–0.49) | 0.17 (0.01–0.49) | 0.33 (0.08–0.74) |
| Cyclosporine | 0.64 (0.27–1.19) | 0.17 (0.02–0.48) | 0.14 (0.01.-0.42) | 0.17 (0.02–0.48) | 0.14 (0.01–0.42) | 0.14 (0.01–0.42) | 0.51 (0.19–0.97) | 0.14 (0.01–0.42) |
| Leflunomide | 7.82 (0.79–21.11) | 2.64 (0.08–12.24) | 7.82 (0.79–21.11) | 2.64 (0.08–12.24) | 2.64 (0.08–12.24) | 2.64 (0.08–12.24) | 2.64 (0.08–12.24) | 2.64 (0.08–12.24) |
| Abatacept | 2.27 (0.89–4.30) | 0.79 (0.12–2.07) | 0.53 (0.03–1.56) | 0.23 (0.0001–0.89) | 0.23 (0.0001–0.89) | 0.23 (0.0001–0.89) | 0.63 (0.11–1.60) | 0.23 (0.0001–0.89) |
| Belimumab | 0.74 (0.39–1.22) | 0.18 (0.006–0.62) | 0.05 (0.0004–0.21) | 0.11 (0.0090–0.33) | 0.05 (0.0004–0.21) | 0.11 (0.0090–0.33) | 0.11 (0.0090–0.33) | 0.08 (0.003–0.29) |
| Tacrolimus | 3.34 (0.07–11.12) | 3.34 (0.07–11.12) | 1.65 (0.02–7.34) | 0.26 (0.16–0.39) | 1.65 (0.02–7.34) | 1.65 (0.02–7.34) | 1.65 (0.02–7.34) | 1.65 (0.02–7.76) |

91%) [IR was 2.10 (1.49–2.81) vs 1.32 (0.99–1.70)]. Differences in the IR in trials reflect a bias by indication.
**Conclusions:** Most frequent causes of death are still infections and cardiovascular disease. High doses of glucocorticoids were associated with higher rates of mortality.
**Disclosure of Interest:** None declared
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## OP0188 THE DOSE OF GLUCOCORTICOIDS TAKEN AT ONE YEAR, BUT NOT THE INITIAL DOSE PRESCRIBED, IS AN INDEPENDENT PREDICTOR OF DAMAGE ACCRUAL IN LUPUS NEPHRITIS

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**Background:** Several studies have demonstrated the pivotal role of glucocorticoids (GC) in damage accrual in lupus patients but very few studies were selectively performed in the subgroup of patients suffering from lupus nephritis (LN).
**Objectives:** To define the predictors of damage accrual in a LN population.
**Methods:** We reviewed the files of the 146 patients with biopsy-proven LN included in the Louvain Lupus Nephritis Cohort. The following data were retrieved: demographics, renal pathology, standard renal parameters at baseline and last followup, treatment, renal relapses and SLICC/ACR-DI over time.
**Results:** After a mean followup period of 124 months, 76/146 patients (52%) had some damage, *i. e.* a SLICC/ACR-DI $\neq 0$. The renal, musculoskeletal, cardiovascular and ocular items were the most represented. By univariate analyses, patients with a SLICC/ACR-DI $\neq 0$ were older, had a longer followup, took more GC at one year [methylprednisolone (MP): 8.8 mg/d *vs* 5.7], had suffered from more renal relapses and had develop more renal impairment, including end-stage renal disease. Similar data were obtained if a different SLICC/ACR-DI cutoff value was used ($>1$ *vs* $\leq 1$). In a multivariate analysis, using the logistic likelihood ratio test, only 3 variables independently predicted damage, namely the length of followup, the presence of renal relapses and the MP daily dose taken at one year. By contrast, gender, ethnicity, age of onset, standard renal parameters, renal pathology, starting oral MP daily dose, use of IV MP or IV CY did not predict damage. Time to first SLICC/ACR-DI point was statistically shorter, by Kaplan-Meier survival curves, in patients taking $\geq 4$ mg/d of MP after one year of treatment compared to $<4$ mg/d. Again the initial dose of MP was not influential. Every additional mg/d of MP taken at one year increased the risk of having a SLICC/ACR-DI $\neq 0$ by 26% (HR: 1.26; CI: 1.02–1.55).
**Conclusions:** We confirm that more than half of LN patients develop damage over time according to the SLICC/ACR-DI. Interestingly, the dose of GC taken at one year (and not the initial dose prescribed) is an independent predictor of damage accrual.
**Disclosure of Interest:** None declared
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## OP0189 RATE OF CERVICAL NEOPLASIA IN SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE COHORT-STUDY

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**Background:** Systemic lupus erythematosus (SLE) or its treatment might increase the risk of cervical neoplasia as evidenced by previous studies, although inconclusive. Cervical screening can detect subclinical cervical intraepithelial neoplasias and, in turn, offers effective protection against cervical cancer.
**Objectives:** To examine the risk of cervical neoplasia among women with SLE and across different treatment exposures incorporating findings from cervical screening.
**Methods:** By linking national Swedish registers we assembled a cohort of women with SLE and matched general population comparators. SLE patients were identified using the National Patient Register. Using the Prescribed drug register, two SLE subcohorts were defined by use of antimalarials and other immune-suppressive treatments (with or without antimalarials). Data on cervical screening came from the Swedish National Cervical Screening Registry, which gathers data on all Pap smears. A composite outcome of cervical dysplasia and invasive cervical cancer during follow-up (2006–2012) was defined using the Cervical Screening Registry and the Swedish Cancer Register. Secondary outcomes considered CIN 1, 2–3, and invasive malignancy separately. Cox models estimated hazard ratios (HR) adjusted for age, sex, education level, healthcare utilization, number of children, marital status, family history of cervical cancer, and prior cervical screening.
**Results:** Compared to the general population, there was a doubled rate of cervical dysplasia or invasive cancer among women with SLE (HR=2.12 95%CI 1.65–2.71). The rate was higher among those treated with systemic immune-suppressives than among those with only antimalarials (Table). Among women with SLE, immunosuppressive treatment was associated with an increased rate of cervical dysplasia or neoplasms compared to those on antimalarial therapy without additional immunosuppressive treatment (HR=1.83 95% CI 1.15–2.91). Results were generally similar for the secondary outcomes, however limited due to number of events and follow-up time, particularly in the antimalarial treated group.

Table 1

| Outcome definition | Cohort | Subjects | Number of events | Total follow-up, years | Adjusted[#] HR (95% CI) |
|---|---|---|---|---|---|
| Composite outcome of cervical dysplasia and cancer | Full SLE | 4550 | 121 | 23136 | 2.12 (1.65–2.71) |
| | Antimalarials* | 1783 | 26 | 6564 | 1.52 (1.00–2.33) |
| | Immune-suppressives* | 1981 | 73 | 9002 | 2.72 (2.01–3.67) |
| | General population | 28113 | 336 | 155543 | REF |

*Subsets of "Full SLE". Data on exposure from the Prescribed Drug Register 2006–. [#]Adjusted for level of education, healthcare utilization, number of children, marital status, family history of cervical cancer, prior cervical screening during the last 5 years before start of follow-up, and start year.

**Conclusions:** SLE is a risk factor for cervical neoplasia, even after adjusting for important risk determinants such as previous cervical screening. The clinical implication of our findings is that SLE patients treated with immune-suppressives are at increased risk of cervical neoplasia and should be adequately monitored, regardless of whether the risk increase is due to disease severity or treatment.
**Disclosure of Interest:** None declared
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## OP0190 INCREASED SERUM LEVELS OF IFN-Λ CORRELATE WITH TH17 AXIS CYTOKINES AND INDEPENDENTLY TO IFN-α IDENTIFY PATIENT GROUP WITH HIGHER ORGAN DAMAGE

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**Background:** Type I interferons (IFN), particularly IFN-αs, are considered to have a pivotal role in SLE. Recently, increased levels of type III IFNs (IFN-λs) have been described to be also associated with SLE.
**Objectives:** We measured circulating levels of IFN-λ, IL-17, IL-23, IP-10 and also IFN-α, in a cohort of SLE patients and investigated their association with clinical and laboratory manifestations of the disease. Population controls were investigated as comparators.
**Methods:** 261 SLE patients and 276 population controls, identified through the population registry and matched for age, sex, and region of living, were included. All participants were examined by clinician rheumatologist and assessed for current organ manifestations and disease related organ damage. Sera were collected at inclusion and stored at -70* C until analysis. Serum levels of IFN-α, IFN- λ, IL-17, IL-23 and IP-10 were measured in sera by commercial ELISA.
**Results:** IFN-λ was detected in 76 (29,1%) patients and IFN-α in 115 (44%). In 108 patients (41.4%) neither of the cytokines was detected. Both IFN-λ and IFN-α were detected more often and in higher levels in patients. IFN-λ levels did not correlate to the levels of IFN-α, and only in 38 (14.5%) patients had detectable levels of both. Levels of IL-17, IL-23 and IP-10 correlated with each other and with IFN-λ. In comparison, only a weak correlation between levels of IFN-α and IL-23 was observed. Detectable levels of IFN-λ were associated with lower incidence of fever, photosensitivity and also arthritis. Patients with detectable IFN-α had active mucocutaneous disease, serositis and lower levels of C3 and C4, and also presence of anti-Ro/SSA and anti-La/SSB. Incidence of nefritis and DVT was lower in this group. Co-detection of IFN-α and IFN-λ was significantly associated with lymphadenopathy, serositis, cortical dysfunction and presence of antiphospolipid antibodies. IFN-α was associated with overall lower disease damage. However, IFN-λ was associated with lower incidence of musculoskeletal, but higher frequency of cerebrovascular damage. The triple detection of IFN-λ, IL-17 and IL-23 was significantly associated with overall higher disease damage score, and particularly higher incidence of renal damage.
**Conclusions:** Our study demonstrates that in SLE patients the levels of IFN-α and IFN-λ do not correlate, but rather dissect patient's groups with different target organs. Triple positivity for IFN-λ, IL-17 and IL-23 is associated with the higher disease damage, in particular kidney damage.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5598

**FRIDAY, 10 JUNE 2016**

## Shared decision making

### OP0191-HPR USABILITY STUDY OF A NEW AUTO-INJECTOR IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease, for which the introduction of injectable treatments has had a major impact on quality of life. However, patients with RA may suffer from reduced manual dexterity, meaning that administering self-injections can be physically problematic.
**Objectives:** The primary objective of this French multicenter study was to evaluate the usability of a new auto-injector, based on the device design and instructions for use (IFU).
**Methods:** Three groups of subjects were enrolled in the trial: i/ professional nurses or caregivers; ii/ patients with established RA diagnosis with moderate to severe and iii/ from mild hand disability to normal hand function (assessed by Cochin scale above or fewer than 20, respectively). Injections (inj.) were performed with a water-filled device on a foam pad mimicking skin behavior. Each subject performed three inj. in different conditions (first phase (one inj.): just after reading the IFU without further instructions; second phase after explanations upon user's request (two inj.): first in an optimum environment then in a "worst case" environment (noise, dimmed light etc.)). The usability of the auto-injector was assessed by a questionnaire (success: $\geq$75% of positive responses) and by a score card reflecting injection performances, assessed by an independent observer (success: execution of $\geq$75% of handling steps).
**Results:** 42 subjects were enrolled in the study between November 2014 and March 2015. There were no major differences in subject profiles (group size, age, sex) between the 3 user groups. During the first phase, the great majority of subjects succeeded in the usability questionnaire (90.5%) and in the inj. performance (95.2%) with no major differences between the user groups. In the second phase, all subjects from all 3 user groups succeeded in the usability questionnaire and had a positive rate of device handling, regardless of the environment and of the user group. No safety concerns were raised during the study.
**Conclusions:** This study found a very high level of usability and subject acceptance of the auto-injector, regardless of the hand disability. The high performance rate in the first phase showed an intuitive device handling. The study also emphasized the importance of instructions provided to the patient for a 100% understanding and handling success.
**Disclosure of Interest:** C. Hudry Consultant for: Nordic Pharma, A. Lebrun Consultant for: Nordic Pharma, B. Moura Consultant for: Nordic Pharma, O. Backers Employee of: Disphar international, H. Herman-Demars Employee of: Nordic Pharma
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### OP0192-HPR TEACHING METHOTREXATE SELF-INJECTION TECHNIQUE TO THE PATIENTS IN A ROUTINE RHEUMATOLOGY OUT-PATIENT CLINIC: FACTORS FAVOURING OR COUNTERING ACCEPTABILITY

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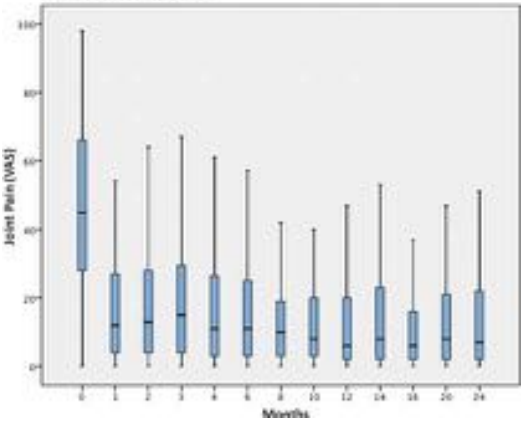
**Background:** In recent years, early aggressive targeted treatment for inflammatory joint diseases such as rheumatoid arthritis (RA) is recommended. Low dose Methotrexate (LD-MTX) is the "anchor drug" for RA and other inflammatory arthritidies. The administration of LD-MTX using subcutaneous route increases its therapeutic efficacy, ensures the maximum bioavailability and reduces gastrointestinal adverse effects. Therefore, it is preferred over the oral route. However, the acceptability of the injectable form of LD-MTX has several hurdles including fear of discomfort associated with the injection. This study tried to find out the factor(s) that directly influence the learning capabilities of patients with rheumatological diseases.
**Objectives:** To find out the factors influencing the learning ability of self-injection technique among patients with inflammatory rheumatic diseases.
**Methods:** This retrospective study included patients who were prescribed injectable LD-MTX for their treatment. Besides the demographic information (age, gender) and disease characteristics (diagnosis, duration, prior treatment), the patients were interviewed and counselled regarding the virtues of LD-MTX self-injection. Various other aspects including family and social support, educational background that could influence the learning ability of self-injection techniques were also discussed. Data were analysed statistically with appropriate tests.
**Results:** One hundred (n=100) consecutive patients who were advised weekly LD-MTX injections and taught the self-injection technique were enrolled in this study. On follow-up visit it was found that among them 57 patients ($n_1$) learned and started taking the subcutaneous injection of LD-MTX (either by self or by the attendant who had learnt techniques at the clinic) while the other 43 ($n_2$) did not. The various parameters were statistically analysed to find out which one of them were associated with acceptability for learning injection technique and which ones were impeded. Of the various variables studied, the family support was the only factor that proved to be highly significantly ("p" value 0.0001) associated with the acceptance to learn the self-injection technique. No other variable showed any influence on the learning of LD-MTX self-injection.
**Conclusions:** Among all the variable studied only family support showed a strong association ("p" =0.00001) with learning capabilities for the technique of subcutaneous injection of LD-MTX. Therefore, this preliminary study indicates that for the success of this route of self-administration of LD-MTX and making the patient independent, family support needs to be harnessed. This would improve drug efficacy and disease control
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**Disclosure of Interest:** R. Rawat: None declared, S. Baghel: None declared, R. Thakran: None declared, C. Messi: None declared, S. Kapoor Consultant for: Advisory board of IPCA, Janssen., S. Garg Consultant for: Advisory board of Roche and Intas, A. Malaviya Consultant for: Advisory board of IPCA, Janssen, Pfizer, Roche, BMS, Dr. Reddy's., Speakers bureau: dvisory board of IPCA, Janssen, Pfizer, Roche, BMS, Dr. Reddy's.
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### OP0193-HPR AIMING FOR REMISSION IN EARLY RA: IMPACT ON PAIN DURING THE FIRST 2 YEARS OF TREATMENT

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**Background:** Pain is the symptom people with rheumatoid arthritis (RA) have prioritized highest for improvement [1]. Treating to target and aiming for remission in early RA may reduce pain, but there is limited knowledge about the impact of modern treatment strategies on pain in RA patients classified using the 2010 ACR/EULAR criteria.
**Objectives:** The objective of this study was to explore and describe changes in the levels of pain in early RA during the first two years after starting DMARD treatment.
**Methods:** Patients with symptom duration of less than 2 years from first swollen joint who fulfilled the 2010 ACR/EULAR classification criteria for RA, and were DMARD naïve with indication for DMARD treatment were recruited from 11 rheumatology centres and followed for 2 years in the ARCTIC trial. The treatment target was remission, and DMARDs were prescribed using an algorithm developed according to international recommendations. Swollen joints and joints with ultrasound power Doppler synovitis were injected with intra-articular corticosteroids. Pain was recorded on a Visual Analogue Scale (VAS 0–100 mm) at every visit, and categorised according to Jensen et al. with cut points for no pain set at 0–4 mm, mild 5–44 mm, moderate 45–74 mm and severe pain 75–100 mm [2]. Short Form-36 (SF-36) bodily pain was recorded, and transformed to a scale from 0–100, with high scores indicating low bodily pain.
**Results:** A total of 205 early RA patients were included: 61.5% female, 82.4% ACPA positive, and mean (SD) age 52.2 (13.4) years. At initiation of DMARD treatment the mean (SD) 44-swollen joint count was 10.2 (7.2), Ritchie Articular Index 8.14 (6.5), ESR 24 (19) mm/hr and Patient Global Assessment 49 (24) mm. The mean (SD) DAS value was 3.4 (1.1); 20.1% were in low disease activity, 47.1% in moderate disease activity and 32.8% in high disease activity according to DAS. VAS pain at baseline was median (IQR) 45 (27–68) mm, and decreased

Figure: VAS pain 0–100 mm (box-and-whiskers plot including median and 25–75 percentiles)



to 12 (4–27) mm after 1 month, after 1 year to 6 (2–20) mm and after 2 years VAS pain was 7 (2–23) mm; see figure for details. Mean (SD) SF-36 bodily pain at baseline was 40 (21), and increased after 12 months to 73 (23) and 24 months to 74 (24). At baseline less than 3% of the patients reported no pain, after 3/6/12/24 months this proportion increased to 27/32/41/41%, respectively. In the interval 12 to 24 months more than 87% of patients reported exclusively either no or mild pain.

**Conclusions:** In this cohort of early DMARD-naïve RA patients treated according to modern treatment strategies aiming for remission, there was a substantial and significant reduction of pain after 1 month. Pain levels decreased further during the first year, and this reduction was sustained during the first 2 years of follow-up. Early intervention and treating to target in this population fulfils the patients' prioritised goal of minimising pain, leading to a decreased burden of pain in RA.

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## OP0194-HPR NURSING TRIAGE IN RHEUMATOLOGY: THREE MONTHS EXPERIENCE IN AN OUTPATIENT CLINIC OF THE UNIVERSITY OF FLORENCE (ITALY)

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**Background:** At present patients with rheumatic diseases are mainly assisted in outpatient settings. In our centre more than 150 patients with SSc (Systemic Sclerosis) and more than 100 patients with SPA (Spondyloathritis) are treated monthly. Rheumatic diseases are chronic conditions associated with disability, reduced quality of life and emotional and social consequences. Nurses' role is crucial in improving rheumatic patients' global health providing educational support, promoting self-management and helping accessing appropriate services when needed.

**Objectives:** To describe nursing triage in rheumatology – A nurse led service focused in monitoring disease activity, symptoms and complications and providing educational and clinical support. Nursing triage takes place before rheumatologists' assessment. Period of observation: 1/12/2013 – 28/2/2014

**Methods:** All SSc and VEDOSS patients were evaluated for Raynaud Condition Score (RCS), sHAQ, SScQoL, HAMIS, Cochin, Borg, IIEF5. DUs and other skin lesions were assessed. All SPA patients were evaluated for MASES, BASMI, BASDAI, BASFI, swollen and tender joints, tender points and sacroiliac joint pain. BP, BMI were available for all patients. A severity index based on the previous tests' scorings was obtained both for SSc and SPA patients. Severity index for SSc/VEDOSS was based on DUs presence, sHAQ, HAMIS, Cochin, Borg, RCS and ranges between 0 and 7 (0=lowest severity; 7=highest severity). Severity index for SPA was based on all the previous evaluations and ranges between 0 and 10 (0= lowest severity; 10= highest severity).

**Results:** 264 patients were treated in SSc/VEDOSS outpatient clinic (51 VEDOSS, 71 SSc, 7 primary RP, 98 secondary RP whose diagnosis had to be confirmed). DUs occurred in 29,41% of SSc patients, in 4,08% of patients with secondary RP, no DUs were found in VEDOSS patients. DUs were significatively associated with global and hand impairment and with reduced QoL ($p<0,05$). In SSc patients severity index, RP severity, overall and hand disability were more severe than VEDOSS patients ($p<0,05$). SPA patients had a mean severity index of 3,85; ds 2,67. The overall disability was low (BASFI mean value 2,32; ds 2,56), the disease activity was high (BASDAI mean value=4,09; ds 2,62).

**Conclusions:** SSc and VEDOSS patients with severity index=0 and SPA patients with severity index$\leq$1 may be followed mainly by nursing staff with interventions based on lifestyle modifications and non-pharmaceutical therapies. Adequate protocols must be approved by rheumatologists staff. In this context a nurse led helpline may be effective to select the most appropriate site and level of care for acute conditions in rheumatic diseases.

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## OP0195-HPR COMPARISON OF EDUCATIONAL MODELS FOR MAINTAINING OPTIMAL SAFETY IN THE SELF-MANAGEMENT OF BIOTHERAPY AMONGST RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS PATIENTS

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**Background:** Biotherapies prescribed in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA) are associated with risks that patients must be aware of. Patient education offers them to learn how to manage such treatments on a day-to-day basis. In our department, patients can benefit from 3 different educational models: individual informational consultation (Model 1), individual consultations including the 4 recommended steps (educational diagnosis, objectives, education and assessment) (Model 2) and individual consultations with group workshops (Model 3).

**Objectives:** To assess which educational model appears the most appropriate for maintaining optimal safety in the self-management of biotherapy.

**Methods:** This is an observational, monocentric, retrospective study on routine care. All patients on biotherapy with at least one educational consultation between 2009 and 2013 were subsequently divided up according to the undergone educational model (Models 1, 2, or 3). During normal management, patients filled out the BIOSECURE questionnaire, meant to assess their theoretical and practical knowledge (clinical cases), prior to consultation with an education nurse. The overall BIOSECURE score, its theoretical and practical subsections, the different dimensions of the questionnaire and the behaviors in risk situations were compared based on the 3 models.

**Results:** In total, 222 patients were included (67% women, age 53.9 years, disease duration: 10 years, RA n=137, SpA n=77 and uncategorized rheumatism n=8, anti-TNF 89.6%, rituximab 3.2%, abatacept 3.6%, and tocilizumab 3.6%. As regards the educational model, 106 patients (47.8%) benefited from Model 1, 88 (39.6%) from Model 2, and 28 (12.6%) from Model 3.

The overall BIOSECURE score was 76.6/100 without any significant difference depending upon the educational model (Model 1: 75.1, Model 2: 76.7, Model 3: 81.8; p=0.07). The BIOSECURE score was significantly higher amongst women (p=0.007), young people ($p<0.001$), working patients (p=0.005), higher education degree holders ($p<0.001$), patients whose diagnosis was most recent (p=0.008), as well as patients on etanercept (p=0.04) and those on intravenous biotherapies (p=0.004). Model 3 patients displayed a significantly higher practical score (clinical cases) than Model 1 ($p<0.001$) and 2 (p=0.003) patients. There was also a significant difference in BIOSECURE score in favor of Model 3 in certain skill areas, such as "Patient behavior in case of fever" (p=0.03) and "Behavior when faced with injuries, prevention of infectious complications and vaccination" (p=0.03). In terms of the implementation of acquired knowledge in risk situations, 64.5% of patients displayed appropriate behavior in the event of signs of infection, 68% in the case of surgical intervention, and 65% in the event of dental avulsion, without anydifference depending upon the model.

**Conclusions:** The educational model involving group workshops showed no significant variation from the overall BIOSECURE score amongst patients treated with a biotherapy for RA or SpA when compared to the models based solely on individual consultations. However, patients having participated in group workshops exhibited improvement in practical scores and certain skill areas.

**Disclosure of Interest:** None declared

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## OP0196-HPR DOSE REDUCTION OF BIOLOGIC DRUGS IN AXIAL SPONDYLOARTHRITIS IN CLINICAL PRACTICE

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**Background:** The practice of reducing the dose of anti-TNF agents during the treatment of patients with axial spondyloarthritis (axSpA) is often applied in clinical practice; it is not unusual for patients with axSpA to reduce the dose of anti-TNF agents despite the lack of supporting evidence from clinical trials or real-world investigations. Reasons for dose reduction include patient preference (fewer injections or infusions when the patient feels well) and cost reduction. The 2010 update of the ASAS recommendations for the use of anti-TNF agents in patients with axSpA does not consider dose reduction, nor do the 2015 draft BSR guidelines on the topic of biologics in axSpA. However, limited studies have indicated positive results.[1–3] Real-life data regarding dose reduction are therefore valuable and may inform further studies, potentially enabling a rational approach to dosing in clinical practice to be adopted in the future.

**Objectives:** To report the results of anti-TNF dose reduction in axSpA patients attending rheumatology practices in the UK.

**Methods:** In this retrospective study in SpA clinics at two UK hospitals, patients with axSpA who met NICE response criteria after 12 weeks of anti-TNF treatment,[4] and remained stable for at least 6 months, were considered for dose reduction. Dose reduction could have been suggested by either patient or practitioner. Dose reduction decisions were made on an individual basis and implemented by extending the interval between anti-TNF administration, reducing the dose of

each administration, or both. Dose reduction was calculated as a percentage of the standard recommended dose. Outcomes reported include BASDAI, BASFI and BASMI. Observed case data are reported.
**Results:** 47 patients had their dose reduced between June 2005 and December 2015 (25 adalimumab, 14 etanercept, 7 infliximab and 1 golimumab). Most patients (79%) were male and the mean age was 50.2 years (SD±10.5). At the time of anti-TNF initiation, mean BASDAI was 6.4 (SD±1.7), which improved to a mean of 1.8 (SD±1.4) at the time of dose reduction. BASFI and BASMI scores also improved from anti-TNF initiation to time of dose reduction (Table). The mean time interval between initiation of anti-TNF therapy and dose reduction was 3.8 years (SD±2.8).
At the time of analysis 39/47 (83%) remained on a reduced dose and were stable, with maintained efficacy up to 24 months post dose-reduction (Table). In these patients, the mean dose reduction was 36% (SD±16). 8 patients (17%) reverted to their original dose after a mean of 20.2 months (SD±18.7) of treatment with a mean dose reduction of 38% (SD±16).

**Table:** BASDAI, BASFI and BASMI scores at time of anti-TNF initiation, at time of dose reduction, and up to 24 months post-dose reduction in all patients (n=47) and in those in whom dose reduction was successful (n=39)

| | At anti-TNF initiation | | At dose reduction | | Post-dose reduction | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 6 months | | 12 months | | 24 months | |
| | n | Mean (SD) | n | Mean (SD) | n | Mean (SD) | n | Mean (SD) | n | Mean (SD) |
| **BASDAI** | | | | | | | | | | |
| All patients (n=47) | 46 | 6.4 (1.7) | 46 | 1.8 (1.4) | 40 | 2.1 (1.8) | 28 | 2.0 (1.4) | 25 | 2.3 (2.0) |
| Completers (n=39) | 38 | 6.5 (1.7) | 38 | 1.6 (1.3) | 33 | 1.6 (1.4) | 22 | 1.8 (1.4) | 19 | 1.9 (1.3) |
| **BASFI** | | | | | | | | | | |
| All patients (n=47) | 44 | 4.9 (1.9) | 46 | 2.3 (2.1) | 39 | 2.3 (2.1) | 27 | 2.2 (1.7) | 24 | 2.2 (1.6) |
| Completers (n=39) | 37 | 4.9 (1.9) | 38 | 2.0 (1.9) | 32 | 2.1 (2.0) | 21 | 2.1 (1.6) | 19 | 2.3 (1.6) |
| **BASMI** | | | | | | | | | | |
| All patients (n=47) | 40 | 4.4 (1.8) | 37 | 3.7 (1.8) | 29 | 3.6 (1.8) | 16 | 3.2 (1.6) | 21 | 3.4 (1.5) |
| Completers (n=39) | 33 | 4.3 (1.7) | 33 | 3.6 (1.7) | 25 | 3.5 (1.7) | 14 | 3.5 (1.6) | 18 | 3.4 (1.6) |

Completers: patients who were successful on dose reduction.

**Conclusions:** In this study, patients responding well to anti-TNF therapy successfully had their dose reduced while maintaining treatment response in real-life clinical practice in the UK. This approach to treatment may lead to cost savings in the care of these patients.
**References:**
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## OP0197-HPR PSYCHOSOCIAL PREDICTORS OF DMARD ADHERENCE IN THE FIRST THREE MONTHS OF TREATMENT FOR EARLY ARTHRITIS

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**Background:** To induce disease remission, early arthritis patients should adhere to their disease-modifying antirheumatic drugs (DMARD) in the first months after diagnosis.[1] It remains unknown why some patients do not adhere to their therapy.
**Objectives:** In this study we aimed to identify which patients are at risk for non-adherence in the first 3 months of treatment.
**Methods:** Adult DMARD-naïve early arthritis patients who started synthetic DMARDs were recruited for a cohort study. At baseline, patients filled out items on potential adherence predictors. These items were based on a literature review and focus group interviews.[2] Items included amongst others questions on coping with pain and the disease, anxiety and depression, and beliefs and expectations about medication. Adherence was in the first 3 months of treatment continuously measured with electronically monitored pill bottles. Items were reduced and clustered using principal component analysis. Per cluster of items, latent trait models were constructed to extract the most discriminating items. Per DMARD and per day non-adherence was defined as not opening the pill bottle when it should have been. We conducted a multilevel multivariable logistic regression model to find predictors for non-adherence.
**Results:** 301 patients agreed to participate of which 259 completed follow-up. Adherence was high and declined over time. Principal component analysis led to 7 dimensions, while the subsequent latent trait models analyses led to 15 dimensions. Of these dimensions, "information seeking" and "having positive expectations about the disease" were associated with adherence and the dimension "adjusting to the pain" was associated with non-adherence (see table 1).

Table 1. Results of the initial multivariable generalized linear mixed model and the results of the multivariable final model after backward selection and correction for over-optimism

| | Initial model | | | | Final model |
|---|---|---|---|---|---|
| Factor | OR | 95% CI | Regression coefficient | p | Regression coefficient |
| 1. Negative feelings | 1.92 | (0.66, 5.62) | 0.65 | 0.24 | |
| 2. Disability | 1.06 | (0.41, 2.72) | 0.05 | 0.91 | |
| 3. Depression | 1.11 | (0.40, 3.10) | 0.11 | 0.84 | |
| 4. Anxiety | 0.49 | (0.18, 1.29) | -0.72 | 0.14 | |
| 5. BMQ specific- necessity | 1.05 | (0.48, 2.38) | 0.05 | 0.91 | |
| 6. Modelling | 0.92 | (0.33, 2.57) | -0.09 | 0.87 | |
| 7. Adjusting / limiting activities | 1.20 | (0.43, 3.35) | 0.19 | 0.72 | 0.11 |
| 8. Information seeking | 0.70 | (0.40, 1.23) | -0.36 | 0.22 | -0.17 |
| 9. Not speaking about it | 1.97 | (0.91, 4.27) | 0.68 | 0.09 | |
| 10. Distancing | 0.90 | (0.35, 2.32) | -0.10 | 0.83 | |
| 11. BMQ - general harm/general overuse | 1.01 | (0.40, 2.55) | 0.01 | 0.98 | |
| 12. BMQ - specific concerns | 1.44 | (0.60, 3.46) | 0.37 | 0.41 | |
| 13. Internal locus of control | 1.36 | (0.53, 3.54) | 0.31 | 0.52 | |
| 14. Active coping | 1.31 | (0.57, 3.02) | 0.27 | 0.53 | |
| 15. Positive expectations | 0.35 | (0.14, 0.84) | -1.06 | 0.02 | -0.30 |

Abbreviations: OR: odds ratio, 95% CI: 95% confidence interval, BMQ: beliefs about medication questionnaire

**Conclusions:** Our findings suggest that patients who experience autonomy through information seeking behavior and having positive expectations about the course of the disease are more prone to be adherent than patients who feel less autonomous and become passive because of pain: these patients are at risk for non-adherence.
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## OP0198-HPR EXPLORING FACTORS WHICH INFLUENCE ANTI-TNF TREATMENT DECISIONS FOR RHEUMATOID ARTHRITIS IN ENGLAND – A QUALITATIVE ANALYSIS

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**Background:** Clinical guidance produced by the National Institute for Health and Care Excellence (NICE) recommends that patients in England with rheumatoid arthritis should be treated with the lowest cost anti-TNF[a]. In practice, however, it is possible that a number of factors may influence treatment choice.
**Objectives:** To explore the factors which influence consultant rheumatologists when prescribing anti-TNF therapies in England.
**Methods:** Individual semi-structured telephone interviews were conducted with a purposive sample of consultant rheumatologists (n=11) from hospitals across England between January and September 2015. The telephone interviews (mean duration =31 minutes) were recorded and transcribed verbatim. Interviewees were asked to discuss the influences on key treatment decisions, including: the decision to begin anti-TNF therapy; the choice of first-line anti-TNF; treatment decisions in remission. Interview transcripts were analysed by thematic framework analysis. Ethical approval was obtained from The University of Manchester's Research Ethics Committee (Project: 14147).
**Results:** Interviewees' responses clustered around six main themes. Cost was rarely a factor which influenced the participants' choice of first-line anti-TNF, unless their local service commissioners imposed the use of the least-expensive anti-TNF. In contrast, cautious optimism was expressed towards using biosimilar anti-TNF agents first-line on the grounds of potential cost savings. Patient involvement in decision making was viewed to be sacrificed in those units where using the cheapest anti-TNF was enforced. The interpretation of NICE guidance varied between interviewees with some claiming that the guidance was too restrictive whereas others saw benefits in the flexibility it provided. Interviewees tried to maintain clinical autonomy by careful manipulation of the DAS28 measure in patients with insufficient disease activity to receive anti-TNF therapy according to NICE guidance if they believed it to be clinically appropriate. Negotiated local exceptions to NICE guidance also facilitated clinical autonomy, while the use

(and success) of individual funding requests for treatments apparently varied between interviewees. Often advances in the clinical evidence were used to justify deviations from guidelines. However the influence of evidence had a lesser role in dose-optimisation decisions in remission, where the evidence to guide such decisions is limited.
**Conclusions:** The results suggest that a range of factors, other than just cost, may influence anti-TNF prescribing decisions including the emergence of evidence, the interpretation of clinical guidelines, patient involvement in decision making, a desire for clinical autonomy and the influence of clinical service commissioners. Such factors generate variability in the treatment received by patients with rheumatoid arthritis across England. Further research could explore whether the variation in deviations from NICE guidance leads to differences in patient outcomes or the cost-effectiveness of care.
**References:**
[1] a: NICE (2016). Technology Appraisal 375.
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## Novel insights into B and T cell immunity in rheumatic disease

### OP0199 IMMUNE RESPONSES TO PREVOTELLA COPRI IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Recently, Scher et al. showed that *Prevotella copri*, an intestinal microbe, was over-expanded in stool samples from patients with new-onset RA (NORA). However, it has been unclear whether over-expansion of *P. copri* is simply a marker for dysbiosis in the bowel, or whether the organism itself actually has a pathogenic role in RA.
**Objectives:** To determine whether *P. copri* may have a pathogenic role in RA, we investigated whether patients had T and/or B cell responses to the organism and looked for *P. copri* DNA in synovial fluid (SF).
**Methods:** To identify immunogenic proteins of *P. copri*, we identified microbial HLA-DR-presented peptides (T cell epitopes) in patients' synovial tissue, SF or peripheral blood (PB), using tandem mass spectrometry. The identified peptides were synthesized and tested for T cell reactivity with the matching patient's PBMC by IFN-g ELISpot assay. Immunoreactive peptides or source proteins were then tested for T and B cell responses using cells and sera from our cohort of DMARD-naive NORA patients, chronic RA (CRA) patients, and controls. All RA patients met the 2010 ACR/EULAR criteria for RA. Available serum and SF samples were analyzed for the presence of 16S rDNA of *P. copri* by nested PCR.
**Results:** From the HLA-DR-presented peptides isolated from the PB of one RA patient (HLA-DRB1*0401/0101), we identified an immunogenic T cell epitope derived from bacterial signal sequence of a 27-kDa protein of *P. copri* (*Pc*-p27), implying that this organism or components of it were present in this patient's circulating phagocytic cells. When testing was done in additional patients, 24 of 40 (60%) NORA patients had T cell reactivity with epitopes of *Pc*-p27 compared with none of 10 patients with Lyme arthritis (P=0.0007) and none of 15 healthy control subjects (P<0.0001). In addition, 10 of 78 NORA patients (13%) and 10 of 49 CRA patients (20%) had IgG antibodies to *Pc*-p27; 8 of 78 NORA patients (10%) and 6 of 49 CRA patients had IgA antibodies to this protein. Only 2 patients had both IgG and IgA antibody responses. Overall, 31 of 127 NORA or CRA patients (24%) had IgG or IgA antibody responses to *P. copri*, whereas low-level antibody responses to the organism were found in only 2 of 131 patients with Lyme arthritis, spondylarthropathy or lupus (P<0.0001) and in 2 of 50 healthy control subjects (P=0.001). Finally, synovial fluid yielded positive results for *P. copri* 16S rDNA in 3 of 5 RA patients with IgG antibody responses to *P. copri*, but in none of 13 patients with IgA *P. copri* antibodies or no response to the organism (P=0.01).
**Conclusions:** A subgroup of RA patients had *P. copri*-specific IgA or IgG antibody responses early or late in the disease, whereas patients with other types of arthritis rarely did, implying specificity of these responses in RA. IgA responses may occur because of interactions between host and immune cells in the gut mucosa, whereas IgG responses may be a sign of systemic spread of the organism to joints. These observations suggest that *P. copri* is more than a bystander in gut dysbiosis, and implies that the organism itself may have a pathogenic role in RA patients, creating a new paradigm to consider in RA pathogenesis.
**References:**
[1] Scher J. U. et al, Elife 2013
**Disclosure of Interest:** None declared
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### OP0200 CIRCULATING, AUTO-REACTIVE B CELLS SPECIFIC FOR CITRULLINATED ANTIGENS IN PATIENTS WITH RHEUMATOID ARTHRITIS DISPLAY AN ACTIVATED, PROLIFERATIVE PHENOTYPE

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**Background:** Rheumatoid arthritis (RA) is characterized by the formation of autoantibodies against citrullinated antigens (CA). Intriguingly, depletion of CD20+ B cells leads to significant clinical improvement in the majority of patients, despite the persistence of high titer autoantibodies. This indicates that the CD20+ B cell compartment, potentially more than the autoantibodies themselves, contributes to the pathogenesis and/or chronicity of RA. Auto-reactive B cells within this compartment could be the main drivers of this effect, but evidence for this hypothesis is lacking. We recently developed the technology to visualize and characterize CA-specific B cells in patients and demonstrated that a large proportion has a CD20+ memory phenotype[1].
**Objectives:** To study the phenotype of CA-specific B cells in comparison to tetanus-toxoid (TT)-specific B cells in peripheral blood of individual patients.
**Methods:** Differentially labeled CA and their arginine control variants were used as tetramers to identify CA-specific B cells in peripheral blood of patients with RA. TT-specific B cells were identified in the same samples using differentially labeled TT. Both antigen-specific cell populations were enumerated and phenotypically characterized by flow cytometry.
**Results:** CA-specific B cells and TT-specific B cells were detected in peripheral blood in comparable frequency (median 0.012% vs. 0.014%). Both CA- and TT-specific B cells displayed mainly markers of class-switched memory B cells. Intriguingly, CA-specific memory B cells showed remarkable overexpression of co-stimulatory molecules and markers of active proliferation.
**Conclusions:** This is the first phenotypic analysis of auto-reactive, CA-specific memory B cells in comparison to recall antigen-specific memory B cells in individual patients with RA. CA-specific memory B cells overexpress co-stimulatory molecules and proliferation markers, indicative of an active immune response against CA in these patients. These data support the hypothesis that CA-specific memory B cells contribute to RA pathogenesis and fuel efforts for their antigen-specific depletion.
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[1] Kerkman PF et al. Identification and characterisation of citrullinated antigen-specific B cells in peripheral blood of patients with rheumatoid arthritis. Ann Rheum Dis. 2015 Jun 1. doi: 10.1136/annrheumdis-2014-207182.
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### OP0201 SAFETY, TOLERABILITY, AND FUNCTIONAL ACTIVITY OF MGD010, A DART® MOLECULE TARGETING CD32B AND CD79B, FOLLOWING A SINGLE DOSE ADMINISTRATION IN HEALTHY VOLUNTEERS

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**Background:** MGD010, a bi-specific Dual-Affinity Re-Targeting, or DART®, molecule, inhibits activated B-cells by delivering a negative signal via simultaneous co-ligation of the inhibitory checkpoint molecule, CD32B (FcγRIIb), with the BCR component, CD79B. This novel-therapeutic approach leverages a physiologic B-cell inhibitory loop leading to signal suppression without B-cell depletion, while targeting all activated B cells rather than subsets, such as those dependent on BLyS for survival. MGD010 is being developed for the treatment of autoimmune disorders.
**Objectives:** A single ascending dose study among healthy volunteers was conducted to assess the safety, tolerability, pharmacokinetics, and functionality of MGD010.
**Methods:** This was a first-in-human, double-blind, placebo-controlled study in which 48 evaluable healthy volunteers were intravenously (IV) administered a single dose of MGD010. Eight (8) subjects were randomized [6:2 MGD010:Placebo] in each of the six (6) dose levels [0.01, 0.1, 0.3, 1.0, 3.0, and 10.0 mg/kg] and followed for safety evaluation. B-cell binding and functional assessment, as measured by ex-vivo calcium ($Ca^{2+}$) flux, was determined by flow cytometry in peripheral blood samples. Quantitation of immune cell populations, phenotyping of B-cell subsets, immunoglobulin levels and cytokines were also serially evaluated.
**Results:** MGD010 was well tolerated at all dose levels. All related adverse events (AEs) were ≤ Grade 2 and no serious AEs (SAEs) were reported. No subjects

had premature discontinuations or infusion reactions, systemic hypersensitivity reactions or injection site reactions. No clinically relevant changes in laboratory parameters, vital signs, or ECG parameters occurred. No substantial decrease in peripheral B-cell counts was observed at any dose level. MGD010 demonstrated linear pharmacokinetic and dose-dependent binding to circulating B lymphocytes. Consistent with its anticipated mechanism of action, administration of MGD010 was associated with a reduction in *ex vivo* BCR-induced $Ca^{2+}$ mobilization in B lymphocytes. Furthermore, a selective dose-dependent, prolonged downregulation of surface IgG BCR expression among circulating $CD27^{+}$ memory B cells was also observed, supporting a preferential effect on activated memory B cells.
**Conclusions:** These data demonstrate that MGD010 has an acceptable safety profile following a single-dose IV administration of up to the maximal tested dose level and showed pharmacodynamic activity consistent with its design. The results support continued development of MGD010 in patients with autoimmune disorders.
**Disclosure of Interest:** N. Pandya Shareholder of: MacroGenics, Employee of: MacroGenics, W. Chen Employee of: MacroGenics, J. Lohr Employee of: MacroGenics, X.-T. Yao Employee of: MacroGenics, R. Burns Employee of: MacroGenics, H. Li Employee of: MacroGenics, H. Li Employee of: MacroGenics, J. Muth Employee of: MacroGenics, R. Goldwater Employee of: Parexel, E. Bonvini Shareholder of: MacroGenics, Employee of: MacroGenics, S. Johnson Shareholder of: MacroGenics, Employee of: MacroGenics, P. Moore Shareholder of: MacroGenics, Employee of: MacroGenics, J. Wigginton Shareholder of: MacroGenics, Employee of: MacroGenics
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## OP0202 LONG-LIVED CD19-NEGATIVE HUMAN PLASMA CELLS ARE GENERATED AT THE PLASMABLAST TO PLASMA CELL TRANSITION

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**Background:** B-cells are key mediators in a wide variety of autoimmune disorders as evidenced by the clinical response to B-cell depletion. Lack of response in a proportion of patients could be due to long-lived plasma cells (PCs) that are resistant to B-cell depletion therapy. Thus long-lived PCs in addition to their central role in humoral immunity are also involved in autoimmunity. Absence of CD19 expression, a feature of neoplastic PCs, identifies a minor subpopulation of normal human bone marrow PCs potentially linked to long-lived cells [1]. Whether $CD19^{neg}$ PCs are "aged" cells that have gradually lost CD19 expression, or derive from a distinct differentiation decision is not established.
**Objectives:** We sought to ascertain whether human $CD19^{neg}$ PCs are derived at the plasmablast to PC transition or are established by gradual loss of CD19 expression with increasing PC age.
**Methods:** We performed a sensitive flow cytometric analysis of CD19 expression during the human acute immune responses to flu vaccination, and tracked the generation and maintenance of CD19-negative PCs using CD40:CD40L and TLR mediated in vitro human PC differentiation systems [2].
**Results:** Using intracellular staining for IRF4 alongside conventional surface markers such as CD27, CD38, CD95 and CD20, we robustly identify a $CD19^{neg}$ plasmablast population present in steady state peripheral blood. The $CD19^{neg}$ plasmablasts expanded during the acute plasmablast response to flu vaccination (p=0.063) but the degree of expansion was smaller compared to $CD19^{pos}$ plasmablasts. Influenza specific $CD19^{neg}$ plasmablasts were detectable 6 days after vaccination in the peripheral blood by ELISpot. $CD19^{neg}$ state was established at the plasmablast to PC transition in both CD40:CD40L and TLR mediated B-cell differentiation in vitro. $CD19^{neg}$ PCs increase as a percentage of surviving PCs with time in vitro at all the three subsequent time points compared to the previous time point (p=0.0009, 0.0015 and 0.0179). Flow-cytometrically sorted $CD19^{neg}$ PCs can be maintained independent of $CD19^{pos}$ PCs.
**Conclusions:** $CD19^{neg}$ PCs are independently established as an early event during human PC differentiation and predominantly do not derive by age-associated conversion from $CD19^{pos}$ PCs. Absence of CD19 expression does not provide evidence of PC age, but may identify PCs with greater potential for longevity in humans. Understanding the plasmablast to PC transition is vital in determining strategies for depletion of long-lived PCs and stages of immune response at which they can be employed for treatment of autoimmune disorders.
**References:**
[1] Mei HE, et al. Blood 2015, 125(11):1739–1748.
[2] Cocco M, et al. Journal of Immunology 2012, 189(12):5773–5785.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5760

## OP0203 IN RHEUMATOID ARTHRITIS SYNOVITIS IS NOT DOMINATED BY POLYMORPHIC LOCAL, BUT RATHER BY UNIFORM SYSTEMIC T CELL RESPONSES

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**Background:** Genetic and immunological evidence clearly points to a pathogenic role of T cell clones in rheumatoid arthritis (RA). Previous studies of T cell receptor (TCR) repertoires in the synovial tissue (ST) of individual inflamed joints showed highly expanded T cell clones; however, these clones had background frequencies in peripheral blood (PB)[1].
**Objectives:** To gain more insight into the potential role of these expanded T cell clones in RA, and to study whether single ST biopsies and synovial fluid (SF) samples are representative for the clonal T-cell disturbances observed, we analyzed the distribution of these highly expanded T cell clones in ST and SF samples from different joints in the same patient at the same time point.
**Methods:** In 7 RA-patients we simultaneously obtained ST biopsies from two inflamed joints via mini-arthroscopy together with paired PB and SF samples. ST biopsies were obtained from ankle or from the infrapatellar region of the knee. In 6 patients we took additional independent suprapatellar (SP) biopsies within the same knee joint. Samples were processed for RNA-based next generation sequencing. T cell clones were identified by their unique TCR β-chain sequence, the degree of expansion being expressed as a percentage of the total number of reads. To test for dissimilarity between different sites the Morisita index was used. This index originates from the field of biodiversity and gives a value between 0 and 1, values near 0 resemble no overlap between two locations while values close to 1 indicate similarity[2]. A One-tailed Mann-Whitney test was performed where applicable.
**Results:** We identified 1,114,386 clones in 7,890,571 TCR-sequences. Only a small proportion of the clones present in ST were retrieved in the same proportion in SF (Morisita Index 0.07, SD 0.20) and PB (0.006, SD 0.14). In contrast, considerable overlap was seen if we analyzed cellular infiltrate in ST biopsies from different regions of the same joint: 0.55 (SD 0.28). An identical overlap was seen if we analyzed ST from different joints in the same patient: 0.54 (SD 0.26). This overlap was significantly different from that between ST and PB ($p<0.005$) and ST and SF ($p<0.05$).

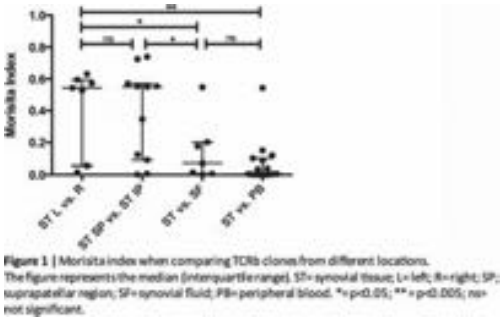


Figure 1 | Morisita index when comparing TCRb clones from different locations. The figure represents the median (interquartile range). ST= synovial tissue; L= left; R= right; SP; suprapatellar region; SF= synovial fluid; PB= peripheral blood. *= p<0.05; **= p<0.005; ns= not significant.

**Conclusions:** SF and PB T cells do not fully reflect the repertoire of dominant clones in the ST, suggesting that analysis of biopsies rather than SF or PB is preferred. ST biopsies taken from different locations within the same joint show substantial overlap suggesting that single biopsies, e.g. taken by ultrasound, show a representative snapshot of the ST T cell infiltrate. Interestingly, ST biopsies from different joints also show substantial overlap of the most dominant T cell clones in patients with active RA. This indicates that in individual patients a limited number of T cell clones dominate the adaptive immune response in the ST. Detailed cellular characterization of these clones seems warranted, and may help to devise more selective strategies for therapeutic targeting.
**References:**
[1] Klarenbeek P, et al. Ann. Rheum. Dis. 2012;71(6):1088–1093.
[2] Wolda H. Oecologia 1981;50:296–302.
**Disclosure of Interest:** A. Musters: None declared, P. Klarenbeek: None declared, M. Doorenspleet: None declared, R. Esveldt Employee of: BTCURE, a research project from the Innovative Medicines Initiative Joint Undertaking (grant No 115142–2)., B. van Schaik: None declared, A. Jongejan: None declared, S. Tas: None declared, A. van Kampen: None declared, F. Baas: None declared, N. de Vries Grant/research support from: BTCURE, a research project from the Innovative Medicines Initiative Joint Undertaking (grant No 115142–2).
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## OP0204 CLONAL EXPANSION OF CD4+ CYTOTOXIC T LYMPHOCYTES IN IGG4-RELATED DISEASE

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**Background:** IgG4-related disease (IgG4-RD) is a systemic condition of unknown etiology, characterized by highly fibrotic lesions with dense lymphoplasmacytic infiltrates rich in IgG4+ plasma cells and CD4+ T cells (1). Given the longstanding history of atopy that characterizes a proportion of patients with IgG4-RD, it has been suggested that TH2 cytokines contribute to the pathogenesis of this condition (2). However, we recently demonstrated that allergic manifestations are not increased in patients with IgG4-RD compared to the general population (3). Similarly, CD4+TH2 cells are expanded only in the peripheral blood of IgG4-RD patients with concomitant atopy, questioning the hypothesis of IgG4-RD as a TH2 driven condition (4).
**Objectives:** We aimed to characterize CD4+ T cell subsets in IgG4-RD subjects.
**Methods:** We used flow cytometry to identify CD4+ effector/memory T cells as well as Th1, Th2, and T regulatory cells in a cohort of 101 IgG4-RD patients. Gene expression analysis was used to further characterize expanded cells. Results were validated by flow cytometry. Next-generation sequencing of the T cell receptor β chain gene was performed on CD4+ T cells in a subset of patients to identify their clonality. Tissue infiltration by specific T cells was examined using quantitative multi-color imaging.
**Results:** CD4+ effector/memory T cells with a cytolytic phenotype (cytotoxic T lymphocytes (CTLs)) were expanded in IgG4-RD patients compared to healthy controls. Next-generation sequencing revealed prominent clonal expansions of these CD4+CTLs but not of CD4+GATA3+ memory TH2 cells in subjects with IgG4-RD. The dominant T cells infiltrating a range of inflamed IgG4-RD tissue sites were clonally expanded CD4+CTLs that expressed granzyme A and perforin. Clinical remission induced by rituximab-mediated B cell depletion was associated with a reduction in disease-associated CD4+ CTLs.
**Conclusions:** IgG4-RD is prominently linked to clonally-expanded CD4+ CTLs in peripheral blood as well as in inflammatory tissue lesions. A TH2 signature might be primarily linked to a concomitant atopic diathesis. CD4+ CTLs might be of pathogenic importance in other fibrotic conditions including IgG4-RD.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2447

## OP0205 CLINICAL AND PRECLINICAL ASSESSMENT OF THE ANTI-MCAM MONOCLONAL ANTIBODY PRX003, A POTENTIAL NOVEL TREATMENT FOR TH17-MEDIATED INFLAMMATORY DISEASES

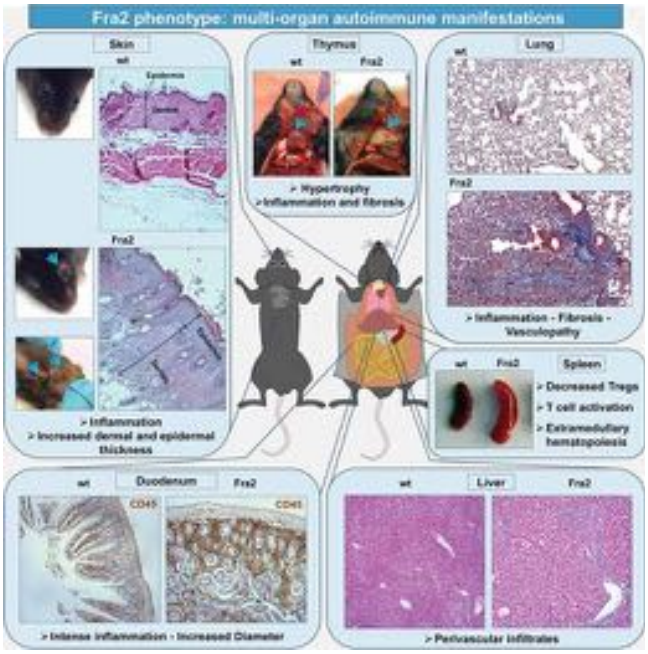
M. Koller[1], K. Flanagan[1], M. Skov[1], R. Goldblum[2], S.G. Griffith[3], R.M. Barbour[1], N. Ehsani-Chimeh[4], M.P. Marinkovich[4], W. Zago[1], T.A. Yednock[1], G.G. Kinney[1], D. Ness[1]. *[1]Prothena Biosciences Inc., South San Francisco; [2]Carlsbad Pharmaceutical Consulting, Inc.; [3]ClinPharma Services, Inc., San Diego; [4]Stanford University School of Medicine, Palo Alto, United States*

**Background:** Melanoma cell adhesion molecule (MCAM; CD146) is expressed on the surfaces of a small population of T cells that have the capacity to produce a multitude of cytokines; further, expression of MCAM is a defining characteristic of TH17 cells. As such, MCAM is hypothesized to be central to the pathogenesis of numerous autoimmune disorders, including psoriasis and psoriatic arthritis. Laminin α4 (LAMA4), the primary MCAM ligand, promotes T-cell transmigration into sites of inflammation. Thus, inhibition of MCAM/LAMA4 binding may limit cell infiltration and subsequent pathogenic inflammation. PRX003, a monoclonal antibody designed to bind an MCAM epitope critical for LAMA4 interactions, blocks adhesion of MCAM-expressing cells to LAMA4 rather than targeting an individual cytokine, thus preventing the infiltration of cells responsible for disease pathogenesis.
**Objectives:** Study objectives were twofold: (1) to demonstrate preclinical proof of concept for anti-MCAM antibodies in mice overexpressing RAC1, an aggressive transgenic model of psoriasis and (2) to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and immunogenicity of PRX003 in healthy human subjects.
**Methods:** The effects of anti-MCAM antibodies (murine homolog of PRX003) on the MCAM expression of circulating immune cells and on disease progression were assessed in RAC1 mice treated 3×/week with anti-MCAM antibodies (0.1 or 10 mg/kg) or isotype control from postnatal day 7 (when disease progression is evident) through postnatal day 34. In a first-in-human, randomized, double-blind, placebo-controlled, phase 1, single ascending dose-escalation study (NCT02458677), PRX003 was administered by intravenous infusion over approximately 60 minutes. Five escalating dose cohorts received 0.3, 1.0, 3.0, 10, or 30 mg/kg of PRX003 or placebo (6 subjects randomized to PRX003 and 2 to placebo per cohort) and were subsequently monitored in an inpatient unit for 24 hours and by periodic follow-up for 12 weeks. PD measurements in humans included MCAM expression on circulating T-lymphocytes and serum soluble MCAM.
**Results:** Anti-MCAM antibodies demonstrated target-mediated binding to circulating immune cells after administration to RAC1 transgenic mice. Furthermore, anti-MCAM antibody-treated mice experienced marked reductions in MCAM expression levels on circulating cells, resulting in diminished (by 40% to 60%) psoriatic disease progression, as evidenced by less erythema, scaling, and skin thickness than were observed in RAC1 transgenic mice treated with an isotype control antibody. PRX003 may thus have a beneficial impact on inflammatory diseases in humans. Data on the safety, tolerability, serum PRX003 PK, and immunogenicity of PRX003 in healthy human subjects, including PK/PD modeling of markers of target engagement, will be presented for the first time.
**Conclusions:** The results of these studies and of previously published reports support further examination of PRX003 in patients with inflammatory disease. A phase 1 multiple ascending dose trial of PRX003 in patients with plaque psoriasis (NCT02630901) is planned.
**Disclosure of Interest:** M. Koller Shareholder of: Prothena, Employee of: Prothena, K. Flanagan Shareholder of: Prothena, Employee of: Prothena, M. Skov Shareholder of: Prothena, Employee of: Prothena, R. Goldblum Consultant for: Prothena, Vascular BIogenics Limited, Sophiris, S. Griffith Consultant for: Prothena, R. Barbour Shareholder of: Prothena, Employee of: Prothena, N. Ehsani-Chimeh: None declared, M. Marinkovich: None declared, W. Zago Shareholder of: Prothena, Employee of: Prothena, T. Yednock Shareholder of: Prothena, Consultant for: Prothena, G. Kinney Shareholder of: Prothena, Consultant for: Janssen, Employee of: Prothena, D. Ness Employee of: Prothena
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## OP0206 FRA2 IS PLAYING A KEY ROLE IN THE CONTROL OF TREG DEVELOPMENT AND AUTOIMMUNITY

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**Background:** Decreased number or altered function of regulatory T cells (Tregs) has been reported in many inflammatory rheumatic diseases, and Tregs are considered promising therapeutic targets for autoimmune diseases. It is thus of high importance to delineate the pathways controlling Tregs biology and the onset of autoimmunity. Fra2 is a transcription factor belonging to the Fos family proteins which takes part in the AP-1 transcription complex. The role of Fra2 in Tregs is so far unknown.
**Objectives:** To characterize the potential role of Fra2 in controlling Tregs and autoimmunity in Fra2 transgenic mice.
**Methods:** Fra2 transgenic mice were generated, in which the Fra2 transcription factor is ubiquitously overexpressed under the control of an MHCI promotor. T lymphocyte populations were analyzed by flow cytometry, and pathological manifestations in multiple organs by histology. Bone marrow cells were transferred into lethally irradiated recipients to create Fra2-wt chimeric mice.
**Results:** At 3 weeks of age, Fra2 mice showed a striking decrease of the Treg population ($CD4^+CD25^+FoxP3^+$ in wt and Fra2 littermates spleens: 11.35 and 5.75% of $CD4^+$, respectively, p=0.0005, Mann-Whitney test, n=6). The strong decrease in Tregs was stable over time and also observed in $CD4^+$ single positive thymocytes, indicating that Fra2 mice have a defect in natural Treg development. Interestingly, from 7 weeks on, we could also detect the appearance of activated T cells ($CD4^+$ and $CD8^+$, with $CD62L^{high}CD44^{high}CD127^{low}$ profile) which represented up to 60% of total T cells by 16 weeks of age. While the phenotype of young mice was limited to decreased Tregs, macroscopic and histological observations in 16 week-old mice showed the presence of an extensive multi-organ autoimmune phenotype (see figure). Perivascular inflammatory infiltrates, containing T cells, B cells and numerous granulocytes were observed in the lung and liver. Extensive inflammation and fibrosis were observed in the thymus. Spleens were also enlarged with pronounced extramedullary haematopoiesis. Fra2 mice also developed dermatitis on eyelids and back-skin, with an increase in dermal and epidermal thickness. Finally, duodenum was enlarged due to acute inflammation and reactive hyperplasia.
To understand whether the effect of Fra2 is T cell intrinsic or extrinsic, we also performed bone marrow transfer experiments in which irradiated wt recipient mice received Fra2 transgenic bone marrow. Interestingly, chimera mice displayed a




decreased percentage of Tregs in blood, spleen, but also thymus, confirming an intrinsic role of Fra2 in natural Treg development.
**Conclusions:** These data suggest that Fra2 overexpression inhibits natural Treg development, resulting in 1: diminished Tregs, 2: activation of effector T cells and 3: development of inflammation in multiple organs. This is the first evidence for a role of Fra2 in controlling Treg development and autoimmunity. This murine model also provides a unique opportunity to delineate the function of the Fra2 pathway in T cells and Tregs and its impact on autoimmunity.
**Disclosure of Interest:** F. Renoux: None declared, M. Stellato: None declared, E. Pachera: None declared, D. Impellizzieri: None declared, C. Dees: None declared, J. Distler: None declared, G. Kania: None declared, O. Boyman: None declared, O. Distler Grant/research support from: Bayer, Sanofi, Ergonex, Boehringer Ingelheim, Actelion, Pfizer, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, EpiPharm, Ergonex, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Pharmacyclics, Pfizer, Serodapharm, Sinoxa
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**FRIDAY, 10 JUNE 2016**

## An inflammatory update!

### OP0207 TRANSMEMBRANE TNF-ALPHA REVERSE SIGNALING LEADING TO TGF-BETA PRODUCTION IS SELECTIVELY ACTIVATED BY ANTI-TNF-ALPHA TARGETING MOLECULES

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**Background:** Tumor necrosis factor (TNF)-a, a potent pro-inflammatory cytokine, is generated in a precursor form called transmembrane (m)TNF-a that is expressed on the surface TNF-a producing cells. TNF-a was shown to act both as a ligand by binding to TNF-a receptors, as well as a receptor that transmits outside-to-inside (reverse) signals back into the mTNF-a bearing cells. Anti-TNF-a targeting molecules which neutralize TNF-a with the same efficiency show disease specific effectiveness.
**Objectives:** The aim of the present study was to characterize mTNF-a signaling and to test whether known anti-TNF-a targeting molecules trigger mTNF-a signaling in human macrophages.
**Methods:** TNF-a expression and localization was studied in mouse bone marrow derived macrophages by RT-QPCR or FACS analysis and confocal microscopy. mTNF-a signaling was triggered by coated anti-TNF-a antibodies and tested by a Phospho-MAPK array. The cytokine induced was determined by RT-QPCR analysis and ELISA. The effect of mTNF-a signaling on lipopolysaccharide (LPS)-induced pro-inflammatory cytokine formation was tested with a cytokine array.
**Results:** Non-activated macrophages express basal levels of mTNF-a and respond to anti-TNF-a antibodies by triggering the mitogen-activated protein kinase kinase 4 signaling pathway leading transforming growth factor (TGF)-b production. Exposure to LPS further induced the expression of mTNF-a, and mTNF-a signaling suppressed the LPS-induced pro-inflammatory response via TGF-b. Since apoptotic cells downregulate their TNF receptors, they do not trigger mTNF-a for TGF-b production. Etanercept, a soluble TNF-a receptor, does not, while golimumab and infliximab, which are anti-TNF-a antibodies, do trigger TGF-b production in human macrophages.
**Conclusions:** Induction of TGF-b production by mTNF-a or by receptors triggered by apoptotic cells could be considered in the therapy of inflammatory diseases and may, in part, also account for differences in the actions of various TNF-a inhibitors.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1358

### OP0208 EMERGING ROLE OF IL-33/ST2 AXIS IN ENDOTHELIAL CELL INJURY OF LUPUS NEPHRITIS

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**Background:** "Alarmins" are prototypic endogenous pro-inflammatory factors as they are released from necotic cells and provoke local damage or systemic inflammation. Evidences are accumulating to support the inclusion of "Alarmins" as targets of autoreactivity as well as inducers in the pathogenesis of Systemic Lupus Erythematosus (SLE). Interleukin (IL)-33 is a novel member of the family of "Alarmins" because of its characteristics and functions in mediating host immune responses. On this background, we sought to determine the role of IL-33/ST2 axis in lupus pathogenesis. The role of IL-33/ST2 axis has not previously been described in lupus nephritis.
**Objectives:** We sought to determine the role of IL-33/ST2 axis in lupus pathogenesis. The role of IL-33/ST2 axis has not previously been described in lupus nephritis.
**Methods:** This project will study the followings: (1) To determine whether IL-33 was present in renal glomerular endothelial cells; (2) To assess the functional and intracellular signal transuction mechanisms regulating the link between IL-33/ST2-mediated innate immunity and inflammation in $CD4^+$ T cells-endothelial cells co-culture system of lupus patients.
**Results:** Immunofluorescence (IF) for IL-33 in the kidney were performed in both $MRL^{lpr}$ lupus mice and C57BL/6J mice. On double staining for IL-33 and lectin, IL-33 was clearly seen in glomeruli and also in peritubular areas. To determine whether the IL-33 staining in glomeruli and peritubular areas was in endothelium, double IF staining for IL-33 and von Willebrand factor (vWF) was performed. IL-33 co-localized with vWF in glomeruli and in peritubular areas. The increased levels of IL-33 mRNA transcripts were detected in kidney of $MRL^{lpr}$ lupus mice compared with C57BL/6J mice. Expression of cell-surface ST2 was increased on the $CD4^+$ T cells of lupus patients when compared with healthy controls. Serum sST2 level was significantly higher in SLE patients with *flare* than those without *flare* ($p<0.05$).
**Conclusions:** As a result of external stimuli or infection, renal glomerular endothelial cells undergo cellular death and release the "Alarmin", IL-33, to alert the lupus immune system. Released IL-33 interact with their target cells, $CD4^+$ T cells via their specific receptor ST2 to subsequently induce innate and adaptive responses, activate inflammatory pathways in the pathogenesis of lupus nephritis.
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[1] Yu SL, Wong CKTam LS. The alarmin functions of high-mobility group box-1 and IL-33 in the pathogenesis of systemic lupus erythematosus. Expert review of clinical immunology, 2013,9: 739–749.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1923

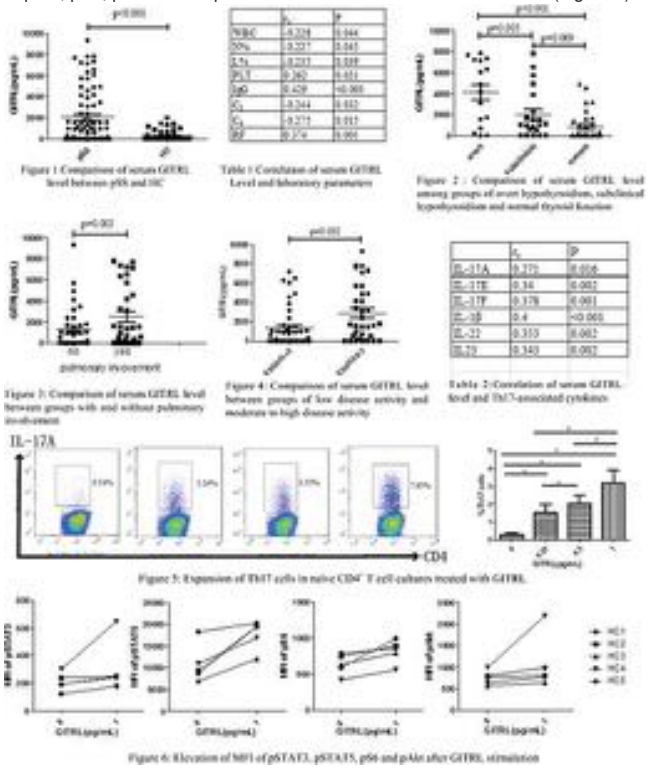
### OP0209 ELEVATED GITRL IS ASSOCIATED WITH MULTI-ORGAN INVOLVEMENT AND INCREASED DISEASE ACTIVITY OF PRIMARTY SJOGREN'S SYNDROME AND PROMOTES PATHOGENIC TH17 DIFFERENTIATION

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**Background:** Accumulating data has showed that Glucocorticoid-induced Tumor Necrosis Factor Receptor Family-related Protein (GITR), with its ligand (GITRL), plays an important role in promoting T-cell-mediated immunity and exacerbating autoimmunity in animal models, including transient inhibition of Tregs[1] and enhancement of Th17 cells[2]. But its pathogenesis role in primary Sjögren syndrome (pSS) remains unclear.
**Objectives:** Our study aimed to evaluate whether GITRL is related to disease severity and multi-organ involvement in pSS patients and explore the possible mechanisms.
**Methods:** 78 pSS patients and 44 healthy controls were recruited, and the serum level of GITRL was measured by ELISA, and the serum levels of interleukin (IL) -17A, IL-17E, IL-17F, IL-1β, IL-22 and IL-23 were tested by Luminex. $CD4^+$ T lymphocytes were isolated from PBMCs of 5 healthy donors by $CD4^+$ T Cell isolation kit and cultured in TexMACS™ GMP medium with anti-CD3

monoantibody (mAb), anti-CD28 mAb and rhIL-2. For Th17 cell differentiation and the pathway exploration of pAkt, pS6, pSTAT3 and pSTAT5, $CD4^+$T cells were treated either with recombinant human GITRL protein or without the protein for 5 days. Surface marker, intracellular cytokine and signal proteins were detected by flow cytometry. Clinical and laboratory data were also collected.

**Results:** *S*erum level of GITRL was significantly higher in pSS patients than in HC (Figure 1). There is a negative correlation between elevated levels of serum GITRL and WBC, Neutrophils%, PLT, $C_3$ and $C_4$, and positive correlation with Lymphocytes%, IgG and RF (Table 1). Interestingly, pSS patients with overt hypothyroidism showed higher level of serum GITRL comparing to those with subclinical hypothyroidism and normal thyroid function (Figure 2). Patients with pulmonary involvement had higher serum GITRL level (Figure 3), and patients of moderate to high disease activity (ESSDAI$\geq$5) also showed higher serum level of GITRL (Figure 4). Moreover, *S*erum GITRL level was positively correlated with IL-17A, IL-17E, IL-17F, IL-1β, IL-22 and IL-23 (Table 2). After GITRL treatment, we found an obvious expansion of $CD4^+IL\text{-}17A^+$T (Th17) cells and there might be a dose-dependent effect (Figure 5). We also found the mean fluorescence intensity (MFI) of pAkt, pS6, pSTAT3 and pSTAT5 increased after GITRL stimulation (Figure 6).



**Conclusions:** Our results identified the function of GITRL in exacerbating disease activity in pSS patients, and enhancing the differentiation of Th17 cells and the secretion of Th17-related cytokines, and the possible mechanisms might be through the pathways of pAkt, pS6, pSTAT3 and pSTAT5. This finding might provide the theoretical basis of anti-GITRL mAb[3] as a novel therapeutic tageting on Th17 cells in the treatment for pSS patients.

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## OP0210 APOLIPOPROTEIN E AGGRAVATES INFLAMMATION AND JOINT DESTRUCTION IN MURINE ANTIGEN-INDUCED ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by severe bone destruction which has been associated with altered lipid metabolism. Apolipoprotein E (Apo E) is a lipoprotein crucial in lipid metabolism, mainly produced by macrophages. Moreover ApoE has been recently described as an important anti-inflammatory mediator regulating innate immunity and bone turnover.

**Objectives:** In the present study we investigated the role of Apo E in inflammation and bone destruction during antigen-induced arthritis (AIA).

**Methods:** Experimental arthritis (AIA) was induced by injection of 60 μg mBSA into the right knee joint of $ApoE^{-/-}$ and wild type (WT) control mice previously immunized with mBSA/CFA.

Joint swelling was measured by uptake of $^{99m}$Technecium ($^{99m}$Tc) and expressed as a ratio of the uptake in right (injected) and the left (non injected) knee joint. Humoral immunity (mBSA antibody titer) was measured by ELISA. Joint inflammation and bone erosion were measured by histological analysis using an arbitrary scale from 0 to 3. $TRAP^+$ cells were determined using immunohistochemistry.

**Results:** $ApoE^{-/-}$ mice showed significantly less joint swelling at day 1, 3 and 7 after AIA induction compared to WT controls (21%, 17%, 18% lower, respectively). Serum mBSA antibody levels (total IgG, IgG1, IgG2a and IgG2b) are comparable between the two immunized mouse strains. At day 21, histology of the knee joints showed less infiltration of inflammatory cells (25% lower) and decreased bone erosion in the $ApoE^{-/-}$ mice compared to WT controls (25% lower from 1.5±0.2 to 1.1 ±0.1). In line with that, $ApoE^{-/-}$ mice showed a reduction of the number of osteoclasts present at the area of resorption within the arthritic knee joints (36% lower from 20±4 osteoclasts/section in WT mice to 12±5 in $ApoE^{-/-}$ mice), as measured by image analysis of TRAP staining.

**Conclusions:** ApoE aggravates bone destruction within the knee joints during AIA by increasing influx of inflammatory cells within the synovium and elevating the number of resorbing osteoclasts on the bone surface.

**Disclosure of Interest:** None declared

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## OP0211 REPROGRAMMING OF METABOLIC PATHWAYS INHIBITS TLR2-INDUCED INFLAMMATION IN RA

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**Background:** Recent studies have emphasized a tight link between the metabolic state and phenotype of immune/inflammatory cells. Metabolic turnover of the inflamed synovium may induce a cellular switch in energy production, characterised by a glycolytic flux, suppression of mitochondrial function and potentiation of inflammation. The role of Toll-like receptors (TLRs) in immune responses is well documented, however emerging evidence suggests they also play a role in metabolism.

**Objectives:** In this study, we examine mitochondrial function, cellular metabolism and synovial inflammation in response to TLR2 activation.

**Methods:** RA synovial explant cultures and RA synovial fibroblasts (RASFC) were cultured with TLR2-ligand Pam3CSK4 (1μg/ml). Mitochondria DNA (mtDNA) mutations were assessed using a Random Mutation Capture assay and reactive oxygen species (ROS), mitochondrial membrane potential (MMP) and ATP levels were quantified using fluorescent probes. Mitochondrial and glucose metabolism gene arrays were quantified by RT-PCR and the mitochondrial ultrastructure assessed by transmission electron microscopy (TEM). Surrogate markers of glycolysis PKM2, GLUT1, ATP5B and GAPDH were quantified in RA/OA synovium by immunohistochemistry. PKM2 was also assessed by western blotting and immunofluorescence. Finally, we examined the effect of glycolytic inhibitor 3-(3-pyridinyl)-1-(4-pyridinyl)-2-propen-1-one (3PO) (20μM) on TLR2–induced cytokine production, invasion/migration and signalling components NFκBp65, Notch-1IC and p-STAT3.

**Results:** Pam3CSK4 significantly induced mtDNA mutation frequency, ROS, and inhibited the MMP. In parallel, Pam3CSK4 differentially regulated key mitochondrial genes SOD2, BNIP3 and BBC3 (all $p<0.05$) and markedly altered the ultrastructure of mitochondria. Consistent with this, we demonstrated altered metabolic activity in RASFC, with induced PKM2 nuclear translocation, increased ATP levels and differential regulation of metabolic genes FBP1/2, PGAM2 and ACo2 (all $p<0.05$), resulting in metabolic shift in favour of glycolysis. This change in metabolic activity was mirrored *in-vivo* where expression of PKM2, GLUT1 and ATP5B were significantly higher in RA synovium compared to OA ($p<0.05$). Finally, reprogramming of metabolism using 3PO significantly inhibited TLR2-induced cytokine production, cell migration/invasion and transcriptional regulation of NFκBp65 and p-STAT3.

**Conclusions:** Reprogramming of metabolic activity in RA resulted in resolution of inflammation. These results show close interactions between innate immunity, metabolism and inflammation, further elucidation of these interactions may provide new insights to new therapeutic approaches in RA.

**Disclosure of Interest:** None declared

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## OP0212 PHOSPHOLIPID TRANSFER PROTEIN (PLTP): A LINK BETWEEN INFLAMMATION AND LIPIDS IN RHEUMATOID ARTHRITIS?

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**Background:** Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular events related to inflammation. In early RA, there is an imbalance between inflammation and lipids. The LXR (Liver X receptors) pathway regulates lipid metabolism and inflammation and it was recently shown to be the most upregulated pathway in RA synovial fluid macrophages compared to blood monocytes (1). Plasma phospholipid transfer protein (PLTP) is one of the LXR's upregulated targets genes. PLTP has been shown to be involved in lipids metabolism, atherosclerosis and, more recently, in the inflammatory response. PLTP was alternatively described as a proinflammatory factor when expressed in cells or as an anti-inflammatory agent through its ability to bind and neutralize LPS.
**Objectives:** We investigated PLTP expression in RA and its effects on synovial fibroblasts from RA (RAFLS).
**Methods:** PLTP expression was examined in FLS from RA patients by qPCR, WB analysis and immunochemistry. ABCA1 expression was analysed by flow cytometry. The effect of recombinant human PLTP on IL-8, IL-6, VEGF and MMP3 production, and on cell proliferation was assessed by ELISA and $^{3}$H-Thymidine incorporation, respectively. Inactivation of lipid transfer activity of PLTP was obtained by heating PLTP for 2 hours at 65°C. Lipid transfer activity of PLTP and pro-inflammatory cytokines were measured in synovial fluid (SF) from RA patients and controls (osteoarthritis (OA) patients).
**Results:** PLTP mRNA was increased in RAFLS (n=11) compared to OAFLS (n=5) but not statistically significant (p=0.08) whereas PLTP protein levels were significantly higher in RAFLS (p=0.04). RA synovial tissues showed higher PLTP staining than OA. ABCA1, a putative receptor of PLTP, was found on RAFLS both at the cell surface and at the intracellular level (n=5). Native PLTP and heat-inactivated recPLTP were able to significantly increase the production of inflammatory cytokines (IL-6 and IL-8), of the VEGF angiogenic mediator and of the MMP3 metalloproteinase in RAFLS. PLTP and heat-inactivated PLTP also significantly increased RAFLS proliferation (by 3.3±.1.2 and 5.5±2.1 fold, respectively). These effects were markedly impaired after treatment with anti-PLTP antibodies or glyburide (*i.e.* a chemical inhibitor of the ABCA-1 transporter). SF of RA patients were found to display elevated levels of PLTP activity compared to OA patients (p=0.0009). PLTP activity levels in RASF correlated with IL-6 and IL-1b (r=0.53, p=0.0086, and r=0.58, p=0.018, respectively), as well as with some lipid parameters.
**Conclusions:** It is shown for the first time that PLTP is highly expressed in the joint of RA patients. It is able to directly trigger inflammation and FLS proliferation, independently of its lipids transfer activity.
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**Disclosure of Interest:** None declared
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## OP0213 CD40-MEDIATED ACTIVATION OF NONCANONICAL NF-κB SIGNALLING IN DENDRITIC CELLS INDUCES EXTRATHYMIC AUTOIMMUNE REGULATOR (AIRE) EXPRESSION, WHICH IS IMPAIRED IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** The nuclear factor (NF)-κB family of transcription factors has a key role in the regulation of inflammation. We have previously demonstrated that activation of noncanonical NF-κB signalling in dendritic cells (DC) via CD40 stimulation is important for the induction of the immunoregulatory enzyme indoleamine 2,3-dioxygenase (IDO) [1]. This pathway is also involved in the expression of Autoimmune Regulator (AIRE) in the thymus, which is essential central tolerance. Peripheral extrathymic AIRE-expressing cells (mainly antigen presenting cells, including DC) can also induce tolerance. However, stimuli that induce extrathymic AIRE expression in DC are unknown. Therefore, we studied whether activation of noncanonical NF-κB signalling induces AIRE expression in monocyte-derived DC (moDC) and whether this induction is altered in moDC derived from patients with autoimmunity, using primary Sjögren's syndrome (pSS) as a prototypic systemic autoimmune disease.
**Objectives:** To study whether activation of non-canonical NF-κB signalling induces AIRE expression in moDC from healthy donors and pSS.
**Methods:** MoDC were generated by culturing monocytes for 6 days with GM-CSF and IL-4. Maturation was induced by addition of the non-canonical NF-κB stimulus anti-CD40 for 48 hours. Cleavage of p100 into p52, IDO and AIRE protein was analyzed by Western blot. Immunofluorescence staining for RelB was performed on cytospins of moDC. RelB protein was visualized by confocal microscopy. siRNA-mediated silencing of NF-κB-inducing kinase (NIK), the main activating kinase of the noncanonical pathway, was accomplished by neo electroporation.
**Results:** Anti-CD40 stimulation of moDC from healthy donors induced cleavage of p100 into p52 and nuclear translocation of RelB, which is indicative of noncanonical NF-κB signalling. This was accompanied by upregulation of IDO and AIRE expression, which was inhibited by siRNA-mediated silencing of NIK. Anti-CD40 stimulation of moDC derived from pSS patients also resulted in activation of noncanonical NF-κB signalling and upregulation of IDO. However, AIRE expression was to a much lesser extent upregulated in moDC derived from pSS patients compared to healthy donor DC.
**Conclusions:** Extrathymic AIRE expression can be induced in moDC via CD40-stimulation and is regulated by noncanonical NF-κB signalling. This is impaired in pSS patients. The functional consequences of this potentially defective immunoregulatory program are currently investigated.
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## OP0214 S100A8/A9 PRODUCED LOCALLY DURING EXPERIMENTAL OSTEOARTHRITIS INDUCES LOCAL AND SYSTEMIC CHANGES IN MONOCYTE POPULATIONS

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**Background:** The etiology of osteoarthritis (OA) is multi-factorial, and is mainly driven by an activated synovium wherein inflammation plays an important role. In response to pro-inflammatory cytokines, monocytes can be recruited from the bone marrow (BM) to the site of inflammation. In mice, two functionally distinct monocyte populations are described: pro-inflammatory Ly6C-high monocytes (C-C chemokine receptor type 2 (CCR2)$^{high}$) and patrolling Ly6C-low monocytes (CCR2$^{low}$). In the BM, monocyte chemoattractant protein-1 (MCP-1) is a key molecule that drives monocyte efflux via binding with CCR2.
**Objectives:** The objectives of our study are to investigate the systemic effects of locally induced OA on BM monocyte populations and their recruitment to the OA joint in collagenase induced OA (CiOA), and the role of the alarmins S100A8/A9 in that.
**Methods:** CiOA was induced by unilateral-articular collagenase-injection in C57BL/6 mice. At day 7, 21 and 42, mice were sacrificed together with age-matched naive mice (n=6/group), and synovial mRNA expression of several pro-inflammatory cytokines were measured. During CiOA and control conditions, the absolute amount of cells in the BM per femur was measured and the mRNA expression of BM MCP-1 and CCR2 was determined. Cells from BM, blood and synovial tissue were isolated and analyzed by FACS. Monocyte subsets were identified as (B220/CD90/CD49b/NK1.1/Ly6G)$^{low}$CD11b$^{high}$(F4/80/MHCII/CD11c)$^{low}$ and further distinguished by their Ly6C expression. In addition, we investigated synovitis in S100A9$^{-/-}$ mice during CiOA.
**Results:** Expression of the pro-inflammatory cytokines IL-1β, IL-6, TNF-α, S100A8 and S100A9 in the synovium were increased at day 7, but only expression of S100A8 and S100A9 remained high until day 21. Local induction of CiOA resulted in systemic effects within the BM as shown by the decrease in cell numbers at day 7 and 21 (15% and 14% respectively). Concurrently, the expression of MCP1 at day 7 in BM was increased (3.3-fold), suggesting an increased efflux of BM-cells. Relative number of BM-Ly6C-high monocytes was increased at day 7 (164%), being reflected by increased CCR2 expression (2.8-fold). This suggests a specific regulation of BM Ly6C-high monocytosis and recruitment during CiOA and emphasizes the systemic effects following CiOA. During the course of CiOA increased numbers of Ly6C-high monocytes were also observed in the synovium: 398% at day 7 and 510% at day 42, compared to naïve mice. These effects may be caused by the sustained S100A8/A9 levels; we therefore investigated synovitis in S100A9$^{-/-}$ mice during CiOA. The number of cell layers and cell influx in the synovium of S100A9$^{-/-}$ mice was decreased compared to C57BL/6 mice.
**Conclusions:** Local induction of OA induces systemic release of BM-derived cells and increased Ly6C-high monocyte populations systemically and locally in the synovium, a process that may be regulated by the sustained release of S100A8/A9 from the synovium.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Advances in paediatric rheumatology

### OP0215 SUBCUTANEOUS ABATACEPT IN PATIENTS WITH POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGIC OR NON-BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: PHARMACOKINETICS, EFFICACY AND SAFETY

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**Background:** IV abatacept (ABA) 10 mg/kg every 4 weeks is safe and effective in reducing signs and symptoms of polyarticular forms of juvenile idiopathic arthritis (pJIA) in children and adolescents.[1] SC ABA 125 mg weekly has therapeutically equivalent efficacy and comparable safety to IV ABA in adult RA, but similar data in pJIA are lacking.
**Objectives:** To assess the PK, efficacy and safety of SC ABA in children and adolescents with active pJIA.
**Methods:** This single-arm, open-label (OL), Phase III study (NCT01844518) enrolled patients (pts) aged 2–17 years (yrs) with pJIA and an inadequate response/intolerance to ≥1 DMARD. Pts received SC ABA weekly OL for 4 months (M), based on body weight tier (10–<25 [50 mg ABA], 25–50 [87.5 mg ABA] and >50 kg [125 mg ABA]). JIAACR criteria 30 (JIAACR30) responders at 4M could enter a 20M OL extension; JIAACR30 non-responders could continue SC ABA for 3M more and discontinued if JIAACR30 was not achieved by M7. The primary endpoint was steady-state blood trough concentration ($C_{minss}$) of ABA at 4M in the 6–17-yr-old pJIA pts (n=173); we report PK, efficacy and safety from the initial 4M OL phase for these pts.
**Results:** Baseline characteristics of the 173 pJIA pts were: mean age (SD) =12.3 (3.1) yrs; mean number of active joints (SD) =12.4 (8.3); 78.6% of patients used MTX (mean dose: 12 mg/m$^2$/week) and 26.6% failed prior biologic treatment. The target therapeutic $C_{minss}$ of 10 μg/mL was achieved (Figure); at 4M, mean (SD) $C_{minss}$ was 42.1 (14.7) μg/mL and was consistent across all three weight groups. Robust JIAACR responses were seen at 4M (Figure): JIAACR30, 80.9%; inactive disease, 29.5%. Biologic-naïve pts had a numerically higher JIAACR30 response than biologic-experienced pts at 4M. The number of pts with serious AEs and those who discontinued study drug due to AEs during the initial 4M were low (n=5 and n=3 [fatigue, exanthematous rash and ovarian germ cell teratoma] pts, respectively). AEs of interest reported included infections (31.8%) with 1 case of sepsis, injection-site reactions (5.2%) and malignancy (0.6%). No laboratory abnormalities or unexpected safety concerns were reported.

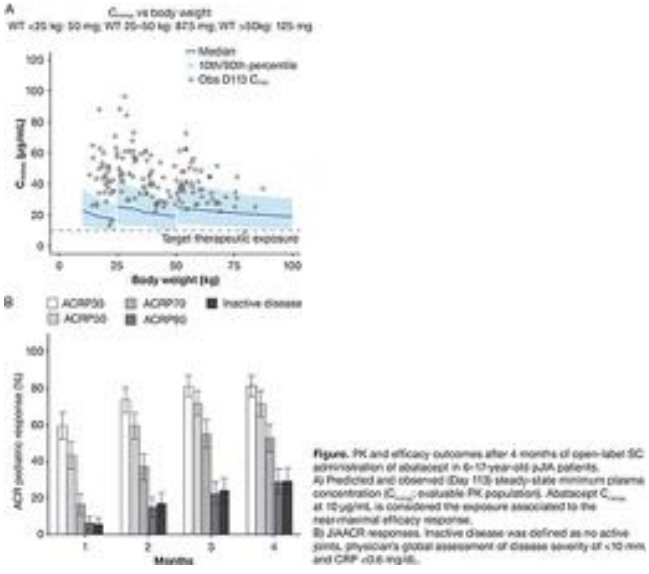



**Figure.** PK and efficacy outcomes after 4 months of open-label SC administration of abatacept in 6-17-year-old pJIA patients. A) Predicted and observed (Day 113) steady-state minimum plasma concentration ($C_{minss}$) evaluable PK populations. Abatacept $C_{minss}$ at 10 μg/mL is considered the exposure associated to the near-maximal efficacy response. B) JIAACR responses. Inactive disease was defined as no active joints, physician's global assessment of disease severity of <10 mm, and CRP <0.6 mg/dL.

**Conclusions:** The target therapeutic exposure for SC abatacept was achieved in pts aged 6–17 yrs with pJIA irrespective of weight group. The exposures for SC abatacept were within the range for IV abatacept in pJIA and comparable with SC abatacept in adult RA. Robust efficacy was observed with SC abatacept with no new safety concerns after 4M of treatment.

**References:**
[1] Ruperto N, et al. Lancet 2008;372:383–91.

**Disclosure of Interest:** N. Ruperto Grant/research support from: Gaslini Hospital, Bristol-Myers Squibb, Hoffman-La Roche, Janssen, Novartis, Pfizer, sanofi aventis, Schwarz Biosciences, Sobi, Consultant for: AbbVie, Amgen, Biogen Idec, Baxalta, Boehringer, Bristol-Myers Squibb, Celgene, EMD Serono, Hoffman-La Roche, Janssen, Novartis, Pfizer, Servier, Sinergie,Takeda, Speakers bureau: AbbVie, Amgen, Biogen Idec, Baxalta, Boehringer, Bristol-Myers Squibb, Celgene, EMD Serono, Hoffman-La Roche, Janssen, Novartis, Pfizer, Servier, Sinergie,Takeda, D. J. Lovell Grant/research support from: NIH, Consultant for: AstraZeneca, Bristol-Myers Squibb, AbbVie, Pfizer, Roche, Novartis, UBC, Forest Research Institute, Horizon, Johnson & Johnson, Biogen, Takeda, Genentech, GlaxoSmithKline, Boehringer Ingelheim, Celgene, Janssen, N. Tzaribachev Grant/research support from: UCB, Pfizer, Janssen, Roche, G. Vega-Cornejo: None declared, I. Louw: None declared, A. Berman: None declared, I. Calvo Grant/research support from: Novartis, Speakers bureau: AbbVie, Roche, Novartis, Sobi, R. Cuttica: None declared, G. Horneff Grant/research support from: Pfizer, AbbVie, Roche, F. Avila-Zapata: None declared, J. Anton Grant/research support from: Pfizer, Novartis, Speakers bureau: Pfizer, AbbVie, Novartis, Sobi, Roche, D. Viola: None declared, I. Foeldvari: None declared, V. Keltsev: None declared, D. Kingsbury: None declared, X. Li Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Nys Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, R. Wong Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, A. Martini Grant/research support from: The Gaslini Hospital, which is the public Hospital where I work as full time public employee, has received contributions from the following industries: Abbott, Bristol-Myers Squibb, "Francesco Angelini", GlaxoSmithKline, Hoffman-La Roche, Italfarmaco, Janssen, Novartis, Pfizer, sanofi aventis, Schwarz Biosciences, Sobi, Xoma, Wyeth, Consultant for: Abbott, AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Astellas, Boehringer, Italfarmaco, Janssen, MedImmune, Novartis, NovoNordisk, H. I. Brunner Consultant for: Pfizer, Bristol-Myers Squibb, UCB, Janssen, Amgen, Celgene, AstraZeneca, Novartis, Genentech, Speakers bureau: Novartis, Genentech
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### OP0216 SAFETY OF TOCILIZUMAB, INTERLEUKIN-1 INHIBITORS AND ETANERCEPT IN 262 SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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**Background:** Since the approval of first biologics for treatment of JIA, surveillance in Germany is monitored prospectively by the BIKER registry.
**Objectives:** To evaluate the safety of Tocilizumab (TOC), IL-1 inhibitors (Anakinra & Canakinumab) and Etanercept (ETA).
**Methods:** Safety assessments were based on adverse events reports.
**Results:** 205 sJIA pts received 269 treatment courses with biologics (TOC 71, Anakina 36, Canakinumab 19, ETA 143 and 57 pts. received MTX only. Median age was lower In the MTX cohort (4.8y) than with ETA (8.2); TOC (9.6); IL-1i (8.2) as was the disease duration. ETA was started in 80% of pts before 2008 while in the TOC cohort all pts and in the IL-1i cohort 74% started therapy after 2008. Pre-treatment consisted of systemic steroids in 75% starting MTX and in all patients starting biologics. Initial concomitant treatment with systemic steroids was significantly less frequent with TOC (44%, p<0,001) and IL-1i (44%, p<0.001) compared to 83% with ETA and 82 in MTX cohort. There were 30 adverse events (AE) in the MTX cohort, 71 in the ETA, 118 in the TOC and 81 in the IL-1i cohort. Rate of AE (per patient-year) was significantly higher in the TOC (RR 4.64; p<0.0001) and IL-1i-group (RR 3.04; p<0.01) (Table) and serious AE were also more frequent upon TOC (RR 5.5; p<0.01) and IL1i (6.39; p<0.01) but not upon ETA compared to the MTX cohort. There were 13 reports about Macrophage activation syndrome. Rates were not different. Of 125 infections, 13 were reported as serious. The infection rate was significantly higher in the TOC cohort (RR 4.3; p<0.001)and IL-1i cohort (RR 2.93; p<0.001) and significantly lower with ETA (RR 0.39; p<0.01) than in the MTX cohort. Hodgkin's lymphoma, Crohn's disease and demyelination occurred once in the ETA cohort, one case with a depression with suicidal thoughts occurred with IL-1i. Intolerance led to discontinuation of ETA in 3.5%, TOC in 8.3% and IL-1i in 2%. 2 pts died (septic shock & MAS) not related to biologics.
**Conclusions:** Higher rates of safety signals, especially infections were noted upon treatment with TOC and IL-1i. Beside infections, disease reactivation and

**Abstract OP0216** – Table 1

| | MTX (n=58); 131.6 PY | ETA (n=143); 355.8 PY | RR (95% CI) | TOC (n=72); 111.6 PY | RR (95% CI) | IL-1i (n=55); 116.8 PY | RR (95% CI) |
|---|---|---|---|---|---|---|---|
| AE (Rate/PY) | 30 (0.23) | 71 (0.20) | 0,88 (0,57–1,34) | 118 (1.06) | 4,64 (3.11–6.92)**** | 81 (0.69) | 3.04 (2.0–4.,62)**** |
| SAE (Rate/PY) | 3 (0.02) | 18 (0.05) | 2.22 (0.65–7.53) | 14 (0.13) | 5.5 (1.58–19.1)** | 17 (0.15) | 6.39 (1,87–21.8)** |
| JIA-Reactivation, N (Rate/PY) | 1 (0.01) | 4 (0.01) | 1.48 (0.17–13.2) | 7 (0.06) | 8.25 (1.01–67.1)* | 10 (0.86) | 11,3 (1.44–88.0)* |
| MAS; n (Rate/PY) | 2 (0.02) | 3 (0.01) | 0.12 (0.01–1.18) | 5 (0.05) | 2.95 (0.57–15.2) | 3 (0.03) | 1.69 (0.28–10.1) |
| Hypersensitivity; n (Rate/PY) | 1 (0.01) | 5 (0.01) | 1.85 (0.22–15.8) | 4 (0.04) | 4.72 (0.52–42.3) | 2 (0.02) | 2.25 (0.20–24.9) |
| Infections, N (Rate/PY) | 15 (0.12) | 16 (0.05) | 0.39 (0.20–0.80)** | 55 (0.49) | 4.3 (2.44–7.65)**** | 39 (0.33) | 2.93 (1.62–5.31)*** |

Compared to MTX-cohort; *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001.

MAS, further adverse events were rare and overall tolerability was acceptable. However, steroids were markedly spared upon IL6- and Il-1 inhibitors.

**Disclosure of Interest:** G. Horneff Grant/research support from: Abbvie, Roche, Chugai, Pfizer, A. Schultz: None declared, A. Hospach: None declared, G. Ganser: None declared, I. Foeldvari: None declared, A. Thon: None declared, R. Trauzeddel: None declared, F. Weller: None declared, K. Minden: None declared, J. Haas: None declared

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## OP0217 ADJUDICATION OF INFECTIONS IN THE PHARMACOVIGILANCE IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS (PHARMACHILD) TREATED WITH BIOLOGIC AGENTS AND/OR METHOTREXATE

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**Background:** The Pharmachild study is aimed at observing children with JIA undergoing treatment primarily with biologics±methotrexate (MTX). It is conducted by the participating centres of over 60 countries belonging to PRINTO and PReS.
**Objectives:** Primary endpoint of the study is safety in JIA patients undergoing immunosuppressive therapy. A preliminary analysis of infections has been performed by an independent Safety Ajudication Committee of 6 experts (3 pediatric rheumatologists and 3 pediatric infectious disease specialists).
**Methods:** The centres were asked to report all infections encountered by the patients followed for JIA. Data were checked by PRINTO and the medical monitor based on MedDRA dictionary. Upon completion of these steps, all eligible cases for adjudication, represented by serious/severe/very severe infections, were submitted to the expert Committee. The experts were asked to answer 6 questions. The events with consensus of at least 4/6 experts on more than 3/6 questions were considered. An additional analysis was performed on opportunistic infections, with referral to the recommendations by Withrop *et al.*[1], and on the correlation between infections and 3 treatment phases: MTX only, first biologic±MTX and at least 2 sequential biologics±MTX after failure of the first biologic.
**Results:** 7817 patients were enrolled in Pharmachild at the time of preliminary analysis, with 27% of total safety events reported as infections. 360 events were submitted to the Safety Adjudication Committee. 94 infections (26.1%) achieved maximum consensus among the experts (6/6 questions), 237 (65.8%) consensus on 4/6 or 5/6 questions, the remaining events were discarded. 330 infections were finally retained for the analysis, mostly represented by serious infections of moderate/severe intensity. With regard to the other questions, 74.2% infections were adjudicated as common, appropriately treated, with no clear correlation to the immunosuppressive therapy. The experts achieved consensus on 18 infections adjudicated as opportunistic. Referring to the list of opportunistic infections provided by Winthrop *et al.*[1], we identified 89/330 (27%) opportunistic infections, mostly represented by EBV and herpes zoster infections. 98.8% of events were not recoded. A doubled risk of infections was found in the group of patients who were started on their first biologic±MTX or who had been treated with at least 2 sequential biologics±MTX (1.3 and 1.9 infectious events per 100 py, respectively), compared to the MTX only group (0.8 infectious events per 100 py). The same was found for serious and opportunistic infections.
**Conclusions:** Our preliminary analysis showed a significant number of infections in JIA patients on immunosuppressive therapy, with one third classified as opportunistic infection. The introduction of biologics in therapy increased the risk of opportunistic and serious infection.

**References:**
[1] Winthrop et al. Ann Rheum Dis. 2015;74:2107–16.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2320

## OP0218 EVALUATION OF THE ACR AND SLICC CLASSIFICATION CRITERIA IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL ANALYSIS

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**Background:** Juvenile-onset systemic lupus erythematosus (JSLE) is a severe multi-system inflammatory disease with very varied presentation and disease course. Diverse clinical manifestations means classification of JSLE can prove challenging. The Systemic Lupus International Collaborating Clinics (SLICC) group proposed revised classification criteria for systemic lupus erythematosus (SLICC-2012 criteria)[1].
**Objectives:** This study aimed to compare the SLICC-2012 criteria with the widely used American College of Rheumatology classification criteria (ACR-1997 criteria)[2,3] in a national cohort of JSLE patients and evaluate how classification criteria that individual patients meet evolved over time.
**Methods:** Data from patients in the UK JSLE Cohort Study with a senior clinician diagnosis of probable, evolving or definite JSLE was reviewed. Patients were classified using both criteria within one year of diagnosis and at latest follow-up (following a minimum twelve month follow-up period). Sensitivity of each classification criteria was compared using McNemar's test.
**Results:** 226 patients were included. The SLICC-2012 was more sensitive than ACR-1997 at diagnosis (92.9% vs 84.1% p<0.0001) and after follow-up (100% vs 92.0% p<0.0001). Figure 1 provides an overview of our results. Of those patients meeting the SLICC-2012 criteria and not the ACR-1997 criteria 59% of patients at diagnosis and 61% of patients at follow-up, scored more than one additional point on the SLICC-2012. In particular, the inclusion of hypocomplementaemia on SLICC-2012 facilitated classification of more patients using these criteria.

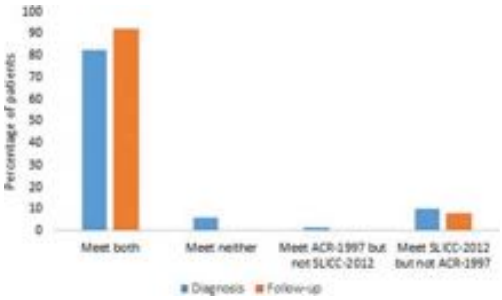



Figure 1. Summary of classification criteria met by patients at diagnosis and at follow-up

**Conclusions:** The SLICC-2012 was better able to classify patients with JSLE than the ACR-1997 and did so at an earlier stage in their disease course. SLICC-2012 should be considered for classification of JSLE patients for the purpose of observational studies and clinical trial eligibility. It may also be useful in daily practice to corroborate clinician diagnosis of JSLE.

**References:**
[1] Petri M, Orbai A, Alarcon G, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012;64:2677–86.
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**Disclosure of Interest:** None declared
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## OP0219 UPDATE ON MALIGNANCIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS IN THE GERMAN BIKER REGISTRY

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**Background:** While TNFα-inhibitors improved outcome of JIA markedly, concerns have been raised about an increased risk for malignancies especially lymphoma, probably already due to the disease itself.
**Methods:** The BIKER data base was used to identify cases of suspected and confirmed malignancies
**Results:** Until 2015, 3695 pts treated with MTX and /or TNFα inhibitors were prospectively followed with 13198 observation years (OY). 12 cases of suspected malignancies, including 7 lymphoid neoplasms, have been reported. 11 pts had received MTX, 2 CSA, single patients received Sulfasalazine, Azathioprine or Leflunomide. 9 pts received Etanercept (ETA), 2 Adalimumab, and 1 case consecutively ETA, Infliximab and Abatacept. A case of myelodysplasia, with spontaneous recovery and a cervical dysplasia were labelled as suspected. Confirmed cases included 2 Hodgkin's lymphoma, 1 non-Hodgkin's lymphoma, 2 ALL and 2 lymphoproliferative disorders, who recovered after discontinuation of immunosuppressive therapy. Singular confirmed cases were thyroid carcinoma, yolk sac carcinoma, cervical dysplasia and anaplastic ependymoma. The total rate of malignancies observed in the registry (0.91/1000Y) exceeds the rate expected according to data of the German cancer registry (0.16/1000Y, $p<0.001$). The calculated risk-ratio in the MTX cohort (n=3: 1 lymphoma, 2 acute lymphatic leukaemias) was significantly increased for both all malignancies (RR 4.5; 95% CI1.5–14.0) and for haemato-lymphatic malignancies (RR 10.1; 95% CI 3.2–31.2). The risk ratio in the ETA cohort also was significantly increased (RR for all malignancies 8.1; 95% CI 4.2–15.5; RR for leukaemia/lymphoma 10.4 (3.9–27.7). No difference was found between the incidence rate of malignancies within the ETA cohort compared to the MTX cohort (p=0.39). Rates did not markedly differ if suspected malignancies (cervical dysplasia, myelodysplasia) were excluded. 6 of the 7 haemato-lymphatic malignancies occurred in ps <15 y of age. There was a higher rate within MTX (0.93/1000Y; 95%CI 0.30–2.89) than with ETA (0.56/1000Y; 95%CI 0.18–1.74). 4 of 5 solid tumours occurred after the age of 15, all in the ETA cohort. One patient never exposed to biologics but to MTX died of ALL, all other recovered.

Table 1. Risk ratios (RR) and 95% CI compared to the German Childhood Cancer Registry report 2015 (1657/2056 cancers in children <15/<18 years of age in $10.5/12.9\times10^6$ children)

| | Malignancies | N (Incidence/1000 PY) | RR (95% CI)* | P (Wald test) |
|---|---|---|---|---|
| MTX <15 y (3224 PY) | All | 3 (0.93) | 5.90 (1.90–18.3) | 0.002 |
| | Lymphoma & leukemia | 3 (0.93) | 13.74 (4.42–42.71) | <0.0001 |
| ETA <15 (5333 PY) | All | 3 (0.56) | 3.56 (1.15–11.1) | 0.028 |
| | Lymphoma & leukemia | 3 (0.56) | 8.31 (2.67–25.82) | 0.0003 |
| MTX <18 y (4182 PY) | All | 3 (0.72) | 4.50 (1.45–13.97) | 0.009 |
| | Lymphoma & leukemia | 3 (0.72) | 10.05 (3.23–31.21) | <0.0001 |
| ETA <18 Y (6998 PY) | All | 9 (1.29) | 8.07 (4.19–15.53) | <0.0001 |
| | Lymphoma & leukemia | 4 (0.57) | 8.01 (3.00–21.38) | <0.0001 |

**Conclusions:** Malignancies were more frequent than expected. Whether the increased risk is through the rheumatic disease or through treatment remains unclear. Treatment with ETA seems not to further increase the malignancy risk. Long-term observation of JIA patients treated with TNFα inhibitors into adulthood remains an important challenge.
**Disclosure of Interest:** None declared
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## OP0220 PERSONAL EXPOSURE TO AIR POLLUTION INFLUENCED DISEASE ACTIVITY AND EXHALED BREATH BIOMARKERS: A PROSPECTIVE STUDY IN A CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS POPULATION

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**Background:** Recently, we showed that exposure to outdoors pollutants was associated with an increase of hospitalizations in paediatric rheumatic diseases (1) and higher risk of disease activity in our childhood-onset systemic lupus erythematous (cSLE) patients (2).Exhaled breath biomarkers measurements, such as exhaled breath condensate (EBC) and fractional concentration of exhaled nitric oxide (FeNO) may indicate airways inflammation related to air pollutant exposure. To our knowledge, this was the first study that showed the effects of daily exposure to $PM_{2.5}$, assessed by personal real time monitoring, on airway inflammation and increased risk of disease activity in cSLE patients.
**Objectives:** To investigate the association between daily individual real-time exposure to air pollutants and disease activity in cSLE patients.
**Methods:** A longitudinal panel study was carried-out in 108 consecutive visits of cSLE patients. During four consecutive weeks, daily personal measures of nitrogen dioxide ($NO_2$), fine particulate matter ($PM_{2.5}$), ambient temperature and humidity were obtained.This cycle was repeated every 2.5 months along one year and pH of exhaled breath condensate (EBC pH), fractional exhaled NO (FeNO) and disease activity parameters were collected weekly. Specific generalized estimation equation models were used to assess the impact of these pollutants on the risk of moderate/severe disease activity (SLEDAI-2K≥8), EBC pH and FeNO considering the fixed effects for repetitive measurements. The models were adjusted for inflammatory indicator, body mass index, infection, medication and weather variables.
**Results:** For an interquartile range increase of 18.12μg/m$^3$ in $PM_{2.5}$ daily concentration we observed an increased short-term effect in FeNO at the first three days (lag 0 to lag 2) after exposure. The 3-day moving average effect on FeNO was an increase of 0.75 ppb (95%IC: 0.38–1.29). Decreases in EBC pH were evidenced at days 7 and 10 after exposure [0.09 (95%IC: 0.15–0.02); 0.09 (95%IC: 0.17–0.01) respectively]. Regarding the risk of SLEDAI-2K ≥8, an increase of 18.12 μg/m$^3$ in $PM_{2.5}$ was associated with increases in the risk of SLEDAI-2K ≥8 at four [RR 1.45 (95%CI: 1.24–1.66)] and 11 days [RR 1.34 (95%CI: 1.05–1.62)] after exposure.

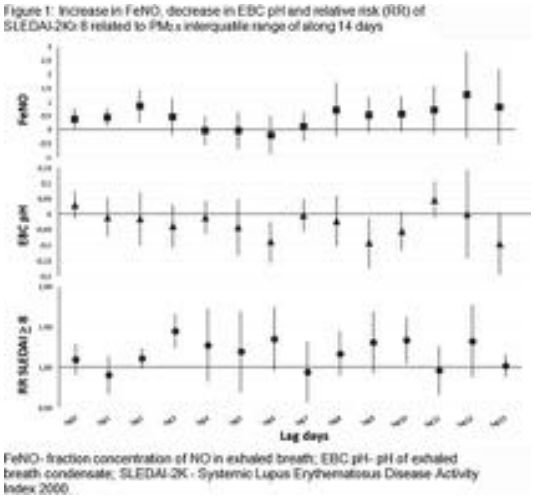


Figure 1. Increase in FeNO, decrease in EBC pH and relative risk (RR) of SLEDAI-2K≥ 8 related to $PM_{2.5}$ interquartile range of along 14 days
FeNO- fraction concentration of NO in exhaled breath; EBC pH- pH of exhaled breath condensate; SLEDAI-2K - Systemic Lupus Erythematosus Disease Activity Index 2000

**Conclusions:** Real-time exposure to air pollution may have a role in triggering disease activity and airways inflammation in cSLE patients.
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**Disclosure of Interest:** None declared
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## OP0221 EFFICACY AND SAFETY OF TUMOUR NECROSIS FACTOR-ALPHA ANTAGONISTS IN A LARGE COHORT OF JUVENILE DERMATOMYOSITIS PATIENTS

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**Background:** Some patients with juvenile dermatomyositis (JDM) have a disease course which is refractory to multiple drug treatments. There is evidence that prolonged disease activity is associated with increased mortality and morbidity. High levels of anti-TNFα have been reported in JDM patients with a long disease course, suggesting it may play a significant role in refractory disease. There are no published clinical trials of this therapy but some are in progress.
**Objectives:** To evaluate the efficacy and safety of anti-TNFα treatment in UK JDM Cohort and Biomarker Study patients.
**Methods:** Data were analysed from children who were recruited to the UK JDM Cohort and Biomarker Study, met Bohan-Peter criteria and were on anti-TNF treatment at the time of analysis, and had had at least 3 months of therapy. Childhood Myositis Assessment Scale (CMAS), Manual Muscle Testing (MMT8),

muscle enzymes and physicians global assessment (PGA) were recorded. Skin disease was assessed using modified skin Disease activity score (DAS).
**Results:** 66 patients with JDM actively treated with anti-TNF agents were analyzed. 41 patients were female (62%). The current mean (±SD) age of these patients was 16.8±5.6 years old, the mean age at diagnosis was 7.31±4.04 years old and the mean disease duration was of 9.6±4.6. Mean disease duration at the beginning of anti-TNF treatment was 3.49±2.80 years and mean duration of anti-TNF therapy was of 2.76±2.09 years. Muscle involvement significantly improved, with median [IQR] CMAS and MMT8 values at initiation of anti-TNF therapy of 45.50 [39.75–52.25] and 74 [59.5–79.5] respectively, and at current evaluation (or date of anti-TNF treatment completion) of 53 [50–53] and 79 [74.5–80] ($p<0.0001$ and p=0.0097; Mann Whitney test), respectively. For skin involvement the initial modified DAS was 4 [2–5] and final 1 [0–3] ($p<0.0001$; Mann Whitney test). Assessing global disease activity the initial PGA was 2.9 [1.3–4.3] and final 0.5 [0–1.45] ($p<0.0001$; Mann Whitney test). Sixteen patients (24%) switched their anti-TNF treatment. 62.5% of the switches were due to therapy failure, 25% due to adverse events and 12.5% for patient preference in subcutaneous administration. Of 21 adverse reactions registered, 7 were considered severe (anaphylactic reactions on infliximab infusion). One patient died due to small bowel perforation (not felt to be related to the use of TNF antagonists). The remaining adverse reactions were not severe and 77% (n=10) of them were due to infections causes. In 4 of the mild to moderate adverse reactions the drug had to be discontinued and switched to another TNF antagonist, while in the remaining patients temporarily withholding the drug proved sufficient. No tuberculosis case was registered.
**Conclusions:** This study is one of the largest to explore the efficacy and safety of TNF antagonist treatment in a large independent cohort of JDM patients. Both muscle and skin involvement appeared to improve after anti-TNF treatment.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5062

## OP0222 PREGNANCY OUTCOME IN PATIENTS AFFECTED BY JUVENILE IDIOPATHIC ARTHRITIS (JIA) EXPOSED TO BIOLOGICAL AGENTS: A MONOCENTRIC EXPERIENCE IN A TERTIARY CENTRE OF MILAN

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**Background:** During the last sixteen years, biologics have been used in our centre in an open prospective study for the treatment of refractory JIA not only in paediatric age but also in young adults.
**Objectives:** To underline the capability to become pregnant, not negatively influenced by biologics and to describe the pregnancy outcome of our young patients who got pregnant during the biologics treatment, since this event seems to be facilitated from a low disease activity under biologics.
**Methods:** Seventeen women affected by refractory JIA became pregnant during biologic therapy. Two males affected by JIA, both treated with Adalimumab have been achieved as indirect pregnancies. All patients had a long lasting refractory polyarticular disease not responsive to DMARDs. Patients were treated with biological agents like Etanercept (9 patients), Adalimumab (4 patients), Golimumab (3 patient), Infliximab (1 patient) and Rituximab (2 patients) as monotherapy and most of the cases after multiple switches.
**Results:** 3 patients decided for an elective termination; 16 patients had a normal pregnancy resulted in live born infants, full term, with no structural abnormalities and still in good health. The median time of exposure to biologics was 48 months (min 10- max 72 months). No abnormalities were achieved neither in the live born infants nor in the fetuses of the pregnancies which ended with an elective termination. The paternal exposure did not influence conception and was not associated with negative outcome of pregnancy.
**Conclusions:** The availability of therapies like antiTNFa and other biologics has raised important questions about pregnancy outcome in female and male patients affected by JIA exposed to biologics. Other data regarding limited populations affected by Crohn's disease or Rheumatoid Arthritis treated with antiTNFa have been published. It doesn't seem to be an increased risk to pregnancy loss. Even if there is no increase in miscarriage or malformation or birth defect, as reported in letterature, TNFa inhibitors are raccomended to be discontinued after pregnancy detection. In our experience no complications or unexpected side effects on the course of pregnancy were observed.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3266

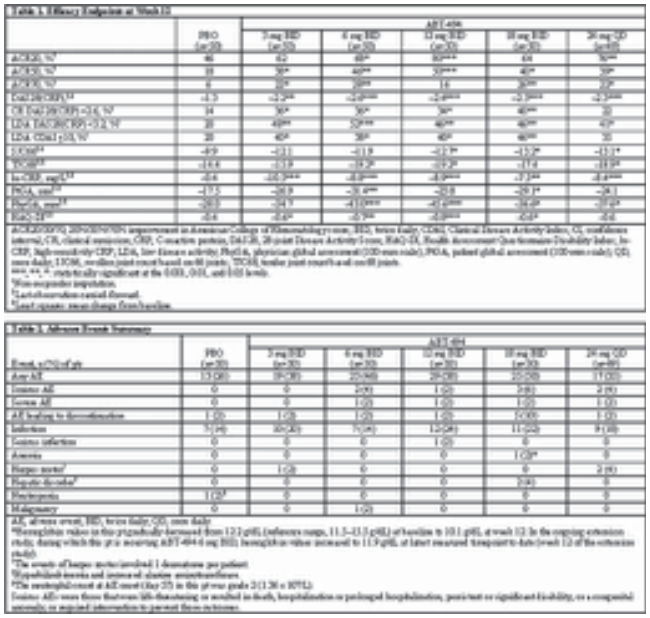
**FRIDAY, 10 JUNE 2016**

# Developments in the treatment of RA

## OP0223 SAFETY AND EFFICACY OF ABT-494, A NOVEL SELECTIVE JAK1 INHIBITOR, IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WITH AN INADEQUATE RESPONSE TO METHOTREXATE

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**Background:** ABT-494 is a novel selective JAK1 inhibitor.
**Objectives:** The safety and efficacy of ABT-494 was characterized vs placebo (PBO) in patients (pts) with moderate to severe RA and an inadequate response to stable background methotrexate therapy (MTX-IR).
**Methods:** In a phase 2b, 12-week, randomized, double-blind PBO-controlled study, MTX-IR pts with active RA on stable background MTX were randomized 1:1:1:1:1:1 to ABT-494 3, 6, 12, and 18 mg twice daily (BID), 24 mg once daily (QD), or matching PBO. The primary efficacy endpoint was ACR20 response at week 12.
**Results:** Baseline demographics and characteristics of the 299 randomized, treated pts were similar across groups. ACR20 response rates were significantly higher with ABT-494 at 6 mg BID (68%), 12 mg BID (80%), and 24 mg QD (76%) vs PBO (46%; non-responder imputation; Table 1). ACR50 and ACR70 response rates and change from baseline in DAS28(CRP) were also statistically significantly better for all ABT-494 doses (except ACR70 in 12 mg BID) vs PBO. Clinical remission by DAS28(CRP) was achieved by significantly more pts on ABT-494 (except 24 mg QD) vs PBO. Onset of action was rapid for ACR20, ACR50, and ACR70 responses, with significant ($P \leq 0.027$) differences in ACR20 observed at week 2 for all dose groups vs PBO. DAS28(CRP) $\leq$3.2 and CDAI $\leq$10 were achieved by significantly more pts on ABT-494 (except 24 mg QD for CDAI) vs PBO.
AE incidence was numerically higher with ABT-494, with a trend of dose dependence (Table 2). The incidence of infections was similar across groups. One serious infection (community acquired pneumonia) occurred with ABT-494 12 mg BID. One pt receiving ABT-494 3 mg BID and 2 pts receiving 24 mg QD had non-serious zoster infections (single dermatomes). A pt in the 6-mg BID dose group, aged 79 y and smoking 40 y, was diagnosed with lung cancer 8 days after study completion and died 3 months later. No deaths occurred during the study. ABT-494 treatment resulted in dose-dependent increases in LDL and HDL cholesterol. Liver function test elevations were sporadic, with no clear dose dependence. Mean hemoglobin values remained stable or increased at lower doses, most notably in pts with elevated CRP at baseline. Dose-dependent decreases in hemoglobin were seen at higher doses, without clinical impact.



**Conclusions:** This phase 2b study evaluated a broad dose range to understand the boundaries of JAK1 selectivity and demonstrated the efficacy of ABT-494 vs PBO in MTX-IR pts with active RA on stable background MTX. ABT-494 had an acceptable safety and tolerability profile.
**Acknowledgement:** The design, study conduct, analysis, and financial support of the clinical trial (NCT02066389) were provided by AbbVie. AbbVie participated

in the interpretation of data, review, and approval of the content. All authors had access to all relevant data. Mariana Ovnic, PhD, Katherine Groschwitz, PhD, and Michael J. Theisen, PhD of Complete Publication Solutions, LLC, provided medical writing support. This presentation contains information on the investigational product ABT-494.

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## OP0224 FILGOTINIB (GLPG0634), AN ORAL JAK1 SELECTIVE INHIBITOR IS EFFECTIVE IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: RESULTS FROM A 24-WEEK PHASE 2B DOSE RANGING STUDY

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**Background:** Filgotinib (GLPG0634) is a novel oral selective JAK1 inhibitor that was evaluated in a 24-week phase 2B study in combination with methotrexate (MTX) in active rheumatoid arthritis (RA) with inadequate response to MTX. The primary endpoint of proportion of patients achieving ACR20 response after 12 weeks of treatment was met.

**Objectives:** To present the results of the 24-week analysis.

**Methods:** Patients with active RA on stable dose of MTX were randomized 1:1:1:1:1:1:1 in a double blinded manner to receive either placebo (PBO) or one of three doses of filgotinib (50mg, 100mg or 200mg) as once (qd) or twice daily (bid) regimen for 24 weeks (DARWIN 1 study). At Week 12, patients on placebo and 50mg dose whose tender and swollen joint counts did not improve by 20% (non-responders (NR)) were reassigned to 100mg daily.

**Results:** 594 randomized and treated patients, mean duration of RA of 7–10 years and mean DAS28(CRP) at baseline 6.0–6.2. At Week 12, statistically significant and dose dependent higher ACR20, ACR50, ACR70, DAS28(CRP) and CDAI responses versus PBO were observed in patients on filgotinib. These responses were maintained or continued to improve through 24 weeks (Table 1). Increase in filgotinib dose from Week 12 lead to improved efficacy in PBO and 50mg NR groups (at Week 24 ACR20 57% and 42% respectively). Serious Adverse Events and Treatment-Emergent Adverse Events (TEAE) were distributed over the groups including PBO: TEAE 51% PBO and 52% filgotinib groups. No opportunistic infections or cancers occurred; one death was reported. Infections occurred in 19% PBO and 25% filgotinib groups. Laboratory parameters remained stable between 12 and 24 weeks. Increase in haemoglobin was noted in patients on filgotinib.

Table 1. Summary of the efficacy responses after 12 and 24 weeks treatment

| | | Once-daily dosing | | | Twice-daily dosing | | |
|---|---|---|---|---|---|---|---|
| | Placebo n=86 | 50mg n=82 | 100mg n=85 | 200mg n=86 | 25mg n=86 | 50mg n=85 | 100mg n=84 |
| Week 12 | | | | | | | |
| ACR20, NRI[1], % | 44 | 56 | 64* | 69** | 57 | 60 | 79*** |
| ACR50, NRI, % | 15 | 33* | 38** | 43*** | 28* | 34* | 55*** |
| ACR70, NRI, % | 8 | 16 | 21 | 24* | 14 | 19 | 31** |
| DAS28(CRP), mean change from BL[2], LOCF[3] | −1.2 | −1.8** | −2.2*** | −2.5*** | −1.9** | −2.1*** | −2.8*** |
| CDAI[4], mean change from BL, LOCF | −17 | −20 | −24** | −26*** | −21* | −23** | −29*** |
| Week 24 | | | | | | | |
| ACR20, NRI, % | 42 | 55 | 61* | 73*** | 56 | 60* | 80*** |
| ACR50, NRI, % | 16 | 35** | 47*** | 50*** | 35** | 35** | 55*** |
| ACR70, NRI, % | 9 | 22* | 33** | 29** | 21* | 24* | 39*** |
| DAS28(CRP), mean change from BL, LOCF | −1.2 | −2.0*** | −2.7*** | −2.8*** | −2.2*** | −2.4*** | −3.2*** |
| CDAI, mean change from BL, LOCF | −16 | −21** | −29*** | −29*** | −24*** | −27*** | −32*** |

*p<0.05 vs. placebo; **p<0.01 vs. placebo; ***p<0.001 vs. placebo; ACR scores based on ITT analysis. [1]Non-responder imputation. [2] Baseline. [3]Last observation carried forward. [4]Clinical Disease Activity Index.

**Conclusions:** Significant improvement in signs and symptoms of active RA was observed after 12 weeks and sustained or increased up to Week 24 with filgotinib in combination with MTX. The safety profile was overall acceptable.

**Disclosure of Interest:** R. Westhovens Grant/research support from: Roche, BMS, Janssen, Galapagos NV: investigator DARWIN 1, R. Alten Grant/research support from: Galapagos NV: investigator DARWIN 1, D. Pavlova Grant/research support from: Galapagos NV: investigator DARWIN 1, F. E. Enriquez Sosa Grant/research support from: Galapagos NV: investigator DARWIN 1, M. Mazur Grant/research support from: Galapagos NV: investigator DARWIN 1, M. Greenwald Grant/research support from: Galapagos NV: investigator DARWIN 1, A. Van der Aa Employee of: Galapagos NV, F. Vanhoutte Shareholder of: Galapagos NV, Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, P. Harrison Employee of: Galapagos NV

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## OP0225 THREE MONTHS' CLINICAL OUTCOMES FROM A NATIONWIDE NON-MEDICAL SWITCH FROM ORIGINATOR TO BIOSIMILAR INFLIXIMAB IN PATIENTS WITH INFLAMMATORY ARTHRITIS. RESULTS FROM THE DANBIO REGISTRY

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**Background:** According to national guidelines issued in 2015, a non-medical switch from originator infliximab (IFX) (Remicade) to biosimilar Remsima was conducted in all Danish patients with inflammatory rheumatic diseases treated in routine care.

**Objectives:** To investigate 3 months' clinical outcomes in Remicade-treated patients (pts) with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthrits (SpA) who switched to Remsima and were monitored prospectively in the DANBIO registry.

**Methods:** Disease activity at 3 mths before switch (pre-switch), at the switch and after 3 mths (70–120 days) (post-switch) and changes over time (∆pre-switch and ∆post-switch) were calculated. Disease flare was defined as ∆DAS28≥1.2 (RA/PsA) or ∆ASDAS≥1.3 (SpA). Reasons for withdrawal (adverse events (AE), lack of effect (LOE) or other) were registered.

**Results:** 647 of 693 switching pts (300 RA, 96 PsA, 219 SpA, 32 other) had available data (52% women, age (median (IQR) 56 (45–66) yrs)). Prior Remicade treatment duration was 6.7 (4.1–9.4) yrs and in 77% it was the first biological treatment. Remsima dose was in RA+PSA 3.3 (3.0–4.8) mg/kg every 7 (6–8) wks and in SpA 4.8 (3.6–5.1) mg/kg every 6 (6–9) wks. Concomitant MTX was given in 69% (RA+PsA)/25% (SpA). Median follow-up time was 139 (98–160) days.

Disease activity remained largely unchanged 3 months prior to vs. after the switch (Table). The proportion of patients with disease flare pre-/post switch was 10%/10% (RA+PsA) (p=1.0) and 10%/0% (SpA) (p=1.0) (related samples McNemar test).

Overall, 45 ptts (7%) stopped Remsima treatment during follow-up (AE 16 (allergic 3, infection 2, rash 2, unspecific 9), LOE 20, remission 3, cancer 2, other 4). Prior Remicade treatment duration in these patients was 5.9 (3.5–9.1) yrs.

Table 1

| | Disease activity, median (IQR) | | | Delta-values, median (IQR) | | P* |
|---|---|---|---|---|---|---|
| | 3 months pre-switch | Switch | 3 months post-switch | Pre-switch | Post-switch | |
| RA/PSA | | | | | | |
| DAS28 | 2.3 (1.8–3.0) | 2.3 (1.8–3.2) | 2.3 (1.9–3.2) | 0.0 (−0.3–0.5) | 0.1 (−0.2–0.5) | 0.07 |
| HAQ | 0.6 (0.1–1.1) | 0.6 (0.1–1.1) | 0.5 (0.3–1.1) | 0.0 (0.0–0.1) | 0.0 (−0.1–0.1) | 0.5 |
| CRP, mg/l | 4 (2–7) | 4 (2–8) | 6 (3–9) | 0 (−2–1) | 0 (−1–3) | 0.03 |
| VAS pt's global, mm | 26 (11–52) | 27 (11–56) | 26 (11–55) | 0 (−7–8) | 0 (−7–9) | 0.04 |
| SpA | | | | | | |
| BASDAI, mm | 26 (12–47) | 23 (7–41) | 23 (7–41) | 0 (−4–5) | 0 (−3–3) | 0.5 |
| CRP, mg/l | 4 (1–8) | 2 (1–5) | 5 (1–9) | 0 (−2–2) | 0 (−2–2) | 0.5 |
| VAS pt's global, mm | 28 (15–57) | 31 (15–56) | 24 (10–52) | 1 (−4–8) | −2 (−9–2) | 0.3 |
| ASDAS | 2.0 (1.3–2.7) | 1.9 (0.7–3.2) | 1.8 (1.2–2.7) | 0.0 (−0.3–0.5) | 0.0 (−0.4–0.2) | 0.8 |

*Delta values for disease activity pre-switch vs. post-switch, Wilcoxon matched-pair signed rank test.

**Conclusions:** In 647 patients with inflammatory rheumatic diseases treated with Remicade for >4 years, disease activity was largely unaffected in the majority of patients 3 months after non-medical switch to biosimilar Remsima and comparable to the fluctuations observed in the 3 months prior to the switch. However, several patients (~6%) stopped treatment due to LOE or AE. This warrants further investigation before such a non-medical switch can be recommended.

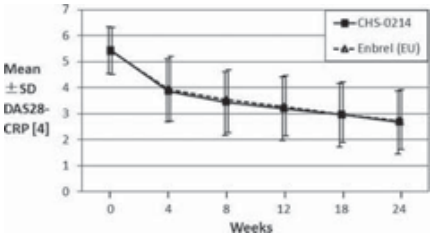
**Disclosure of Interest:** None declared

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## OP0226 RANDOMIZED, DOUBLE-BLIND STUDY COMPARING CHS-0214 WITH ETANERCEPT IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS (RA) DESPITE METHOTREXATE (MTX) THERAPY

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**Background:** CHS-0214 is a proposed biosimilar of etanercept, a fusion protein inhibiting tumor necrosis factor that is approved for several inflammatory autoimmune diseases.
**Objectives:** This Phase III multi-center study compared the efficacy, safety, and immunogenicity of CHS-0214 with etanercept for 24 weeks (Part 1) in patients with moderate/severe RA who had an inadequate response to MTX; then all patients received open-label CHS-0214 for 24 weeks with a final evaluation at Week 52 (Part 2).
**Methods:** Patients were randomized to 50 mg of CHS-0214 or etanercept subcutaneously QWx24 weeks (Part 1). The primary endpoint was the ACR20 response rate at Week 24. To establish the equivalence of CHS-0214 to etanercept, the 95% confidence interval (CI) of the treatment difference between groups had to be within [–15%, 15%]. Secondary efficacy endpoints (ACR50, ACR 70, and change in DAS28-CRP), safety, and immunogenicity were also evaluated.
**Results:** In 13 countries, 644 patients on MTX were randomized and received treatment. Baseline characteristics were comparable between treatment groups. Part 1 results are reported here. At 24 weeks, 512 patients were evaluable for efficacy. The ACR20 response rate was 91.0% (233/256) in the CHS-0214 group and 90.6% (232/256) in the etanercept group. The 95% CI of the treatment difference was [- 4.55, 5.37], which was within the pre-defined equivalence range. The response rates at 24 weeks were 67.6% vs. 63.7% for ACR50 and 38.3% vs. 37.9% for ACR70 in the CHS-0214 and etanercept groups, respectively. Mean (±SD) DAS28-CRP scores were 5.45 (± 1.00) and 5.42 (±1.00) at baseline and decreased to 2.67 (± 1.18) and 2.73 (±1.14) at 24 weeks in the CHS-0214 and etanercept groups, respectively (See Figure).
Among the 644 patients, adverse events (AEs) occurred in 60.8% and 65.0% of patients in the CHS-0214 and etanercept groups, respectively, including all infections combined in 34.3% and 32.2%, respectively. Investigator-designated treatment-related AEs occurred in 16.4% and 21.9% of patients, respectively, and most commonly included: injection site reactions (2.2% and 13.4%) and all infections combined (7.7% and 5.3%). Treatment-related serious AEs occurred in 3 (0.9%) patients treated with CHS-0214 (cholecystitis, increased blood creatinine phosphokinase, and bronchospasm) and 1 (0.3%) patient treated with etanercept (sepsis). Binding anti-drug antibodies occurred in 1.3% and 4.7% of patients in the CHS-0214 and etanercept groups.

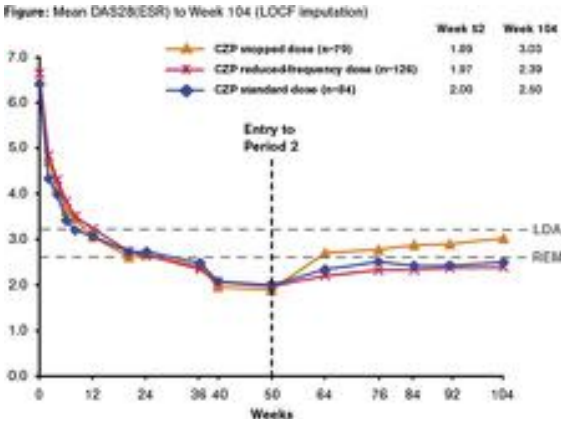



**Conclusions:** These results demonstrated equivalence of CHS-0214 to etanercept with respect to efficacy as measured by the primary endpoint (ACR20 at Week 24) and other measures (ACR50, ACR70, and DAS28-CRP). CHS-0214 was well tolerated with no clinically meaningful differences to etanercept with regard to safety and immunogenicity.
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## OP0227 A RANDOMIZED DOUBLE-BLIND TREATMENT STRATEGY STUDY EVALUATING CONTINUATION OR REDUCED-FREQUENCY DOSING OF CERTOLIZUMAB PEGOL VERSUS WITHDRAWAL TO MAINTAIN LOW DISEASE ACTIVITY IN EARLY RA PATIENTS (C-EARLY PERIOD 2)

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**Background:** MTX plus anti-TNF therapy is an effective treatment for early RA. It is becoming increasingly important to understand whether the dose of anti-TNF can be reduced or stopped in patients (pts) receiving long-term therapy.
**Objectives:** To demonstrate that for patients (pts) who achieved sustained low disease activity (sLDA) after 1 year (yr) with CZP 200mg Q2W+optimized MTX, continuation of certolizumab pegol (CZP) as a standard (200mg Q2W) or reduced-frequency dose (200mg Q4W) is superior to stopping CZP for maintaining pts in LDA from Week (Wk) 52 through Wk104.
**Methods:** CZP+MTX-treated pts achieving sLDA (DAS28[ESR]$\leq$3.2 at Wks40 and 52) in C-EARLY Period 1 (NCT01519791)[1] entered Period 2 (NCT01521923); pts were randomized 2:3:2 to CZP standard dose (200mg Q2W+MTX), CZP reduced-frequency dose (200mg Q4W+MTX) or CZP stopped (PBO+MTX). Pts were evaluated every 8–12 wks. The Period 2 primary endpoint was the proportion of pts who maintained LDA (DAS28[ESR]$\leq$3.2) from Wk52 through Wk104 without flare, using non-responder imputation for missing values. CZP standard dose was compared with CZP stopped; if $p<0.05$ was achieved then, as per the hierarchical testing scheme, CZP reduced-frequency dose was compared with CZP stopped. The assumptions were that 455 pts would achieve sLDA in C-EARLY Period 1 and enter Period 2, with a response of 95%, 90% and 75% at Wk104 for standard, reduced-frequency and stopped dose respectively. Given $\alpha$=0.05, there would be 99% and 92% power to detect a difference between CZP standard and reduced-frequency dose vs stopped dose.
**Results:** In Period 2, 289 pts (who had achieved sLDA in Period 1) were included in the full analysis set: CZP Q2W+MTX (n=84), CZP Q4W+MTX (n=126) or PBO+MTX (n=79). From Wk52 through Wk104, a greater proportion of pts continuing CZP (either Q2W or Q4W)+optimized MTX maintained LDA vs PBO+MTX (48.8% and 53.2% vs 39.2%; p=0.112 and $p<0.05$ [nominal p value; first hierarchical test not significant]). Pts stopping CZP tended to worsen over time, as demonstrated by the increase of the mean DAS28(ESR) values from 1.89 at Wk52 to 3.03 to Wk104 (Figure). No new safety signals were observed.




**Conclusions:** Early RA pts with prognostic factors for severe disease progression achieving sLDA after 1yr of standard dose CZP+optimized MTX can taper to CZP reduced-frequency dose and maintain comparable disease activity control to CZP standard dose. Pts who stopped CZP had a tendency to have more relapses; despite this, 39.2% of these pts maintained LDA through Wk104. Further work will aim to identify the characteristics of pts who can successfully stop CZP.
**References:**
[1] Weinblatt M. Arthritis Rheumatol 2015;67(S10)
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## OP0228 BARICITINIB DOSE STEP-DOWN FOLLOWING DISEASE CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Ph3 studies demonstrated clinical efficacy of 2 different once-daily (QD) doses of baricitinib (bari) (2mg and 4mg) in patients (pts) with active rheumatoid arthritis (RA) and an inadequate response (IR) to conventional synthetic DMARDs[1] or biologic DMARDs[2]. In general, larger, more rapid and more consistent treatment effects were observed for the 4mg dose across measures.

**Objectives:** To investigate the effects of bari dose step-down in patients who had achieved sustained low disease activity (LDA) or remission with bari 4mg QD.

**Methods:** Pts who completed a bari Ph3 Study (RA-BEGIN, RA-BEAM, RA-BUILD, or RA-BEACON) could enter a long-term extension study, RA-BEYOND. In RA-BEYOND, pts who had received bari 4mg for at least 15 months and who had achieved sustained LDA or remission (defined by CDAI score at 2 consecutive visits at least 3 months apart) were re-randomized in a double blind manner to continue receiving bari 4mg or to step down to a 2mg QD dose. Disease activity was assessed at a 12 week (wk) landmark following re-randomization.

**Results:** Among pts who achieved satisfactory and sustained disease control with bari 4mg QD, randomized, double blind dose reduction to 2mg QD was associated with modest, statistically significant increases in disease activity across measures at a subsequent 12 wk landmark assessment (Table). However, a large majority of pts (in both the continued 4mg and reduced to 2mg groups) retained the state of LDA or remission that led to their re-randomization.

| | RA-BEAM, RA-BUILD, RA-BEACON combined | |
|---|---|---|
| Efficacy measure† Wk12 | Continued bari 4 mg (N=147) | Stepped down to bari 2 mg (N=146) |
| CDAI LDA ≤10§, n (%) | 136 (92.5) | 123 (84.2)* |
| CDAI remission ≤2.8§, n (%) | 57 (38.8) | 54 (37.0) |
| ΔCDAI | 0.60 (3.44) | 2.04 (6.29)* |
| ΔTJC 68 | 0.3 (3.0) | 1.2 (3.8)* |
| ΔSJC 66 | 0.1 (1.7) | 0.8 (2.7)* |
| ΔHAQ-DI | 0.04 (0.26) | 0.06 (0.28) |
| ΔPain | 0.7 (14.7) | 2.5 (16.4) |
| ΔPtGA | 1.2 (14.3) | 2.5 (14.5) |
| ΔPhGA | –0.0 (9.6) | 2.7 (13.6)* |
| ΔCRP | 0.68 (7.16) | 1.68 (7.82) |
| ΔDAS28-CRP | 0.14 (0.70) | 0.36 (0.77)* |
| ΔDAS28-ESR | 0.10 (0.73) | 0.35 (0.89)* |
| ΔSDAI | 0.69 (3.55) | 2.19 (6.33)* |

†Values other than CDAI LDA or remission are mean change from baseline (SD) with missing data imputed using modified last observation carried forward; §Missing data imputed using non-responder imputation; RA-BEAM = MTX-IR pts; RA-BUILD = csDMARD-IR pts; RA-BEACON = bDMARD-IR pts; Δ = change from baseline; CDAI = Clinical Disease Activity Index; CRP = C-reactive protein; DAS28 = Disease Activity Score modified to include the 28 diarthrodial joint count; ESR = erythrocyte sedimentation rate; HAQ-DI = Health Assessment Questionnaire-Disability Index; PhGA = Physician's Global Assessment of Disease Activity; PtGA = Patient's Global Assessment of Disease Activity; SD = standard deviation; SDAI=Simplified Disease Activity Index; SJC = swollen joint count based on 66 joints; TJC = tender joint count based on 68 joints; *p≤0.05 vs. bari 4 mg.

**Conclusions:** Consistent with completed studies, these data indicate that 4mg QD was the most efficacious dose of bari for pts with RA in clinical studies. Most pts who had achieved sustained disease control with bari 4mg sustained LDA or remission 12 wks after randomized, blinded dose taper to 2mg QD.

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## OP0229 BOTH HIGH TITER OF RF/ACPA AT BASELINE IS CLOSELY LINKED WITH HIGH LEVEL OF BASELINE PLASMA TNF LEVEL WHICH RESULTED IN LOW DRUG LEVEL AND LOW CLINICAL RESPONSE IN INFLIXIMAB TREATMENT IN RA PATIENTS: POST-HOC ANALYSIS OF A DOUBLE-BLIND CLINICAL STUDY (RISING STUDY)

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**Background:** Baseline RF or ACPA positivity is reported to be linked with clinical response of some non-TNF bDMARDs in RA. However, its impact on the efficacy of TNF inhibitors was controversy.

**Objectives:** To evaluate the influence of baseline RF and ACPA "titers" on the patients characteristics and efficacy of infliximab (IFX) in RA patients using data of the RISING study, a randomized double-blind clinical study in MTX-refractory RA (ref-1, NCT00691028).

**Methods:** In the RISING study, after patients received 3 mg/kg IFX infusion at Weeks 0, 2, and 6, they were randomly assigned to infusion of 3, 6, or 10 mg/kg IFX, every 8 weeks from Week 14 to Week 46 in a double-blind manner (n=307, all patients received 3 mg/kg treatment until Week 14). Serum IFX levels and clinical responses based on DAS28-CRP were evaluated at Weeks 14 and 54.

**Results:** Both baseline RF and ACPA titers showed significant positive correlation with baseline plasma TNF level. We hypothesized that "both RF-High and ACPA-High" was correlated with higher TNF level. Then, we stratified the patients into 3 classes using baseline RF/ACPA titers; "Low/Low" (RF: <55 U/ml, ACPA: <42 U/ml), "High/High" (RF: ≥160 U/ml, ACPA: ≥100 U/ml), and "Middle" (did not meet above criteria for either class), and compared baseline patient characteristics, serum IFX level, and DAS28-CRP among these 3 classes.

Among above 3 classes, significant difference was observed in plasma baseline TNF level, which was previously reported to be closely correlated with low serum IFX level, and low clinical response (ref-2); low TNF level in Low/Low class, high TNF level in High/High class, and intermediate value in Middle class (median: 0.73, 1.15, and 0.91 pg/ml, respectively, p<0.0001). In addition, high serum

Table. Comparison of patient characteristics, serum IFX levels and clinical responses among 3 classes stratified using baseline RF/ACPA

| | Low/Low (n=53) | Middle (n=183) | High/High (n=71) | p * |
|---|---|---|---|---|
| Baseline | | | | |
| RF, U/ml | 11 (5, 30) | 87 (50, 139) | 384 (248, 604) | <0.0001 |
| ACPA, U/ml | 7 (2, 22) | ≥100 (38, ≥100) | ≥100 (≥100, ≥100) | <0.0001 |
| DAS28-CRP | 5.54 (4.92, 6.42) | 5.39 (4.69, 6.01) | 5.74 (5.12, 6.37) | 0.1406 |
| TNF, pg/ml | 0.73 (<0.55, 1.09) | 0.91 (<0.55, 1.23) | 1.15 (0.72, 1.82) | <0.0001 |
| IL-6, pg/ml | 26.5 (12.3, 56.5) | 28.5 (12.4, 70.2) | 33.6 (15.1, 61.8) | 0.3595 |
| Week 14 (at 3 mg/kg) | | | | |
| Serum IFX, μg/ml | 1.5 (0.8, 2.1) | 0.7 (<0.1, 2.0) | 0.4 (<0.1, 1.1) | 0.0004 |
| DAS28-CRP | 3.17 (2.49, 3.69) | 3.53 (2.63, 4.36) | 3.82 (2.62, 4.97) | 0.0256 |
| Week 54 | | | | |
| 3 mg/kg group | (n=23) | (n=47) | (n=29) | |
| Serum IFX, μg/ml | 1.0 (0.8, 2.2) | 0.2 (<0.1, 1.9) | 0.1 (<0.1, 0.5) | 0.0075 |
| DAS28-CRP † | 2.39 (1.81, 3.19) | 3.68 (2.18, 4.38) | 3.17 (2.44, 4.20) | 0.0342 |
| 6 mg/kg group | (n=20) | (n=62) | (n=22) | |
| Serum IFX, μg/ml | 3.6 (2.3, 5.9) | 1.9 (<0.1, 3.9) | 3.0 (0.3, 4.3) | 0.2445 |
| DAS28-CRP † | 2.31 (1.66, 3.43) | 2.66 (1.57, 4.08) | 2.96 (1.73, 3.99) | 0.6372 |
| 10 mg/kg group | (n=10) | (n=74) | (n=20) | |
| Serum IFX, μg/ml | 8.1 (7.1, 13.5) | 5.2 (0.9, 8.9) | 3.8 (1.5, 8.3) | 0.1313 |
| DAS28-CRP † | 2.78 (1.91, 3.36) | 2.51 (1.78, 3.64) | 2.31 (1.48, 3.97) | 0.5540 |

Data are median (IQR).
* Spearman rank correlation coefficient, † evaluated using LOCF method.

IFX level and low DAS28-CRP in Low/Low class, low serum IFX level and high DAS28-CRP in High/High class, and intermediate values in Middle class were observed at Week 14. In Low/Low, Middle, High/High classes, median IFX levels at Week 14 were 1.5, 0.7, and 0.4 μg/ml, respectively (p=0.0004), and median DAS28-CRP at Week 14 were 3.17, 3.53, and 3.82, respectively (p=0.0256). Similar tendency was observed at Week 54 in patients who continued 3 mg/kg treatment, but not in those who received dose-escalation from 3 to 6 or 10 mg/kg after Week 14.

**Conclusions:** High titers of both RF/ACPA at baseline is correlated with high baseline plasma TNF level which might be resulted in low IFX level and low clinical response in patients with continuing 3 mg/kg treatment, but not in patients receiving 6 or 10 mg/kg treatment. Baseline RF/ACPA might be the index of dose-escalation of IFX in RA.

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### OP0230 MULTI DRUG RESISTANCE (MDR) PROTEIN ACTIVITY OF ACTIVATED T LYMPHOCYTES IS A PREDICTOR OF BIOLOGICAL TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS

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**Background:** Multi-Drug Resistance (MDR) protein function is an independent prognostic marker in certain haematological malignancies. Immune activation is also linked to the expression of MDR proteins in autoimmune disorders. Furthermore, MDR protein function may predict patient response to traditional DMARD, as well as biological treatment helping the physician to tailor the therapy. Switching the patient to biologicals is often challenging due to unpredictable drug susceptibility and high cost, especially in patients with mildly elevated DAS28 scores. However, MDR protein activity values can objectively reflect the actual disease activity of RA patients.

**Objectives:** In this observational cohort trial, we wished to assess lymphocyte MDR protein activity in RA patients on biological therapy in comparison to healthy controls in order to predict response to treatment.

**Methods:** We measured the activity of three clinically relevant MDR proteins (MRP1/ABCC1, MDR/ABCB1, BCRP/ABCG2) expressed in MDR activity factor (MAF) values in CD3+, CD4+ and CD19+ cells of 23 responder and 8 primary non-responder RA patients before (at 0 week) as well as at 2, 6 and 12 weeks after patients were switched to biological therapy according to the EULAR guideline. For this purpose, a novel flow cytometry based, CE-IVD certified diagnostic kit was applied. DAS28 scores, CRP, IL-6, aCCP and RF values were also recorded on each occasion. 35 age-matched, healthy controls were included.

**Results:** There was an inverse correlation between MAF of BCRP/ABCG2 in CD3 and CD4 cells and DAS28 at 0 week in RA patients. Multiple correlations between MAF values and inflammatory parameters were also observed. While DAS28 and IL-6 values decreased as the treatment progressed, MAF of MRP1/ABCC1 on CD3 cells was increased at 12 weeks. A positive correlation was noted between MAF of BCRP/ABCG2 on CD3 cells at 0 week and IL-6 at 12 weeks (p=0.0274, r =0.4095) in RA patients. MAF of CD3 BCRP/ABCG2 and CD3 MRP1/ABCC1 were higher in non-responders compared to responders at 0 week.

**Conclusions:** Our results suggest that low BCRP/ABCG2 and MRP1/ABCC1 MAF activities on CD3 cells may predict the need to start biological therapy in RA patients whose symptoms do not improve on classical DMARD treatment. Further decrease of CD3 BCRP/ABCG2 and increase in CD3 MRP1/ABCC1 MAF upon follow-up may indicate a good therapeutic response to biological therapy.

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**FRIDAY, 10 JUNE 2016**

## Emerging concepts in genomics & genetics

### OP0231 DIFFERENTIAL TRANSCRIPTION FACTOR BINDING COULD EXPLAIN THE GENETIC ASSOCIATION OF ANKYLOSING SPONDYLITIS WITH POLYMORPHISMS IN THE IL23R-IL12RB2 INTERGENIC REGION

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**Background:** Genome-wide association studies have revealed the polygenic nature of ankylosing spondylitis (AS). More than 60 genetic influences have been identified but most of these are non-coding sequences (1–3). Protection against AS is afforded by a loss of function mutation in the cytoplasmic tail of the IL23 receptor (IL23R), but there is also a second independent association in this region (2).

**Objectives:** This study explores the functional basis for the second independent association between AS and single nucleotide polymorphisms (SNPs) in the *IL23R-IL12RB2* intergenic region.

**Methods:** We performed conditional analysis on genetic association data at *IL23R* and used epigenetic data on chromatin remodelling and transcription factor (TF) binding to identify the primary AS-associated SNP. Functional effects were tested in luciferase reporter assays in HEK293T cells and allele-specific TF binding was investigated by electrophoretic mobility gel shift assays. The involvement of candidate TFs in DNA binding was investigated by antibodies in these experiments. We measured mRNA expression levels of nearby genes in CD4+ T-cells and compared these between cases homozygous for the risk "A" allele and the protective "G" allele. The proportions of IL-17A+ and IFN-γ+ CD4+ T-cells were measured by FACS and also correlated to patient genotype.

**Results:** Conditional analysis identified *rs11209032* as the primary causal SNP within a putative enhancer between *IL23R* and *IL12RB2*. Reduced luciferase activity was seen for the risk "A" allele ($p<0.001$), and reduced H3K4me1 methylation observed in CD4+ T-cells from "A/A" homozygotes (p=0.02). Nuclear extract binding to the risk "A" allele was decreased ~3.5-fold compared to the protective allele ($p<0.001$). Reduced nuclear factor binding was observed when antibody to TWIST1 was included. The proportion of IFN-γ+ CD4+ T-cells was increased in "A/A" homozygotes (p=0.004), but neither *IL23R* nor *IL12RB2* mRNA was affected.

**Conclusions:** The *rs11209032* SNP downstream of *IL23R* forms part of an enhancer, allelic variation of which may influence Th1-cell numbers. Homozygotes for the risk "A" allele have more Interferon gamma-secreting (Th1) cells compared to those with the protective "G" allele. Further work is necessary to explain how TWIST1 contributes to these important observations.

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### OP0232 C1QTNF4 MUTATION IDENTIFIED BY EXOME SEQUENCING IS ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND DYSREGULATION OF TNF-INDUCED APOPTOSIS

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**Background:** Whole exome sequencing of DNA samples from 30 UK SLE trios identified a *de novo* nonsynonymous mutation in *C1QTNF4* gene associated with juvenile onset, severe SLE. *C1QTNF4* encodes the secretory protein C1q/TNF-

related protein 4, a member of the C1q family, characterized by two highly conserved C1q domains with structural similarity to adiponectin. C1QTNF4 has been implicated in NF-κB signalling and regulation of energy metabolism.
**Objectives:** To characterize the structural and functional consequences of the *C1QTNF4* C594G mutation (p.His198Gln) on TNF signalling and NF-κB activation.
**Methods:** Whole exome sequencing of 90 individuals from 30 UK SLE trios was analysed to identify a list of *de novo* mutations associated with SLE. Resulting mutations were then filtered by likelihood of being deleterious and confirmed by Sanger sequencing of affected families. *In silico* modelling of wild type C1QTNF4 and C1QTNF4 p.His198Gln protein conformation was performed using Phyre2 and Pymol. The C1QTNF4 p.His198Gln mutation was reproduced *in vitro* by site-directed mutagenesis of pCMV6-C1QTNF4 vector, confirmed by Sanger sequencing. Secreted supernatants of C1QTNF4 and mutant C1QTNF4 p.His198Gln expressed in HEK293 cells were analysed for effects on secretion and oligomerization by chromatography and western blot. The effect of C1QTNF4 p.His198Gln on TNF-induced NF-κB activation was assessed in HEK293-NF-κB reporter cell line. The effect of the mutation on TNF-induced apoptosis was studied in L929 cells by luminescent cell titre assay.
**Results:** The G594C mutation in *C1QTNF4* results in a histidine to glutamine substitution at position 198 within the second globular C1q domain, resulting in significant change to the conformation of the second domain according to computational 3D modelling. The p.His198Gln mutation had no effect on protein secretion or oligomerization comparing C1QTNF4 and mutant C1QTNF4 p.His198Gln. Functional experiments revealed an inhibitory effect of secreted C1QTNF4 p.His198Gln on TNF signalling. Although wild type C1QTNF4 had no effect on TNF-stimulated activation of NF-kB and TNF-induced cell death, secreted C1QTNF4 p.His198Gln demonstrated significant inhibition of TNF-stimulated activation of NF-κB ($p<0.01$) and inhibition of TNF-induced apoptosis in L929 cells ($p<0.0001$).
**Conclusions:** Using exome sequencing, we have identified a novel *de novo* mutation G594C (p.His198Gln) in *C1QTNF4* associated with development of SLE, which results in a gain-of-function change in conformation of the second C1q domain of C1QTNF4. Secreted C1QTNF4 p.His198Gln inhibited both TNF mediated activation of NF-kB and TNF-induced apoptosis. Thus the association of *C1QTNF4* G594C with SLE is consistent with the known role of dysregulated apoptosis in SLE pathogenesis, and the association of TNF blockade with development of SLE-type autoimmunity.
**Disclosure of Interest:** None declared
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## OP0233 GENOME-WIDE PATHWAY ANALYSIS REVEALS THAT VEGF GENETIC PATHWAY IS ASSOCIATED WITH ORAL ULCERS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a genetically complex rheumatic disease with heterogeneous clinical manifestations. Recent studies have suggested the existence of a genetic basis for the diverse SLE clinical phenotypes. Also, there is increasing evidence indicating that a substantial part of the genetic variation associated with complex diseases is explained by small-effect genes from common genetic pathways.
**Objectives:** The objective of the present study was to identify new genetic variation associated with SLE phenotypes using a genome-wide association study at the pathway level.
**Methods:** A total of 598,258 SNPs were genotyped in a discovery cohort of n=482 SLE patients of southern European ancestry using the Illumina platform Quad610. After quality control analysis, including ancestry estimation using principal-component analysis, genome-wide pathway analysis was performed. A total of 14 clinically relevant SLE phenotypes were tested for association with n>700 reference genetic pathways. Significantly associated pathways (corrected P-value <0.05) were subsequently tested for validation in an independent cohort of n=425 SLE patients from the same ancestry. Both discovery and validation cohort patients were Caucasian European and from Spanish origin, and were recruited by rheumatology departments from n=15 Spanish university hospitals. The validated genetic pathways were functionally characterized using *in silico* analysis on cell types of relevance in SLE pathogenesis.
**Results:** In the discovery stage, two genetic pathways were significantly associated with the presence of oral ulcers and antinuclear antibodies in SLE ($P_{FDR}<0.05$). In the replication stage, we validated the association between oral ulcers and vascular endothelial growth factor (*VEGF*) genetic pathway ($P$=1.3e-2). Analyzing the transcriptional effect of the topical immunotherapies used for the treatment of oral ulcers in SLE, we found a significant differential expression of *VEGF* pathway genes ($P<0.05$).
**Conclusions:** In this work we have performed the first genome-wide association study for clinically relevant SLE phenotype using a pathway-based approach. With this new approach, we have identified and validated the association of VEGF genetic pathway with oral ulcers in SLE. These findings represent an important step towards the characterization of the genetic basis of phenotype heterogeneity in SLE.
**Disclosure of Interest:** None declared
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## OP0234 RHEUMATOID ARTHRITIS SUBSETS DEFINED BY SUB-SPECIFICITIES OF ANTI-CITRULLINATED ANTIBODIES (ACPAS) HAVE UNIQUE HLA ASSOCIATIONS

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**Background:** Antibodies (Ab) towards citrullinated (cit) peptides (ACPA) are specific serological markers for a subset of rheumatoid arthritis (RA) patients with distinct genetic and environmental associations [1,2]. On the autoantigen-derived peptide level, the ACPA responses in RA patients are heterogeneous. Better understanding of the relationships between immunity to defined peptides, and structural variants of HLA molecules may provide novel insights concerning HLA-driven pathology in RA.
**Objectives:** To investigate whether RA specific Ab towards cit peptides can detect subsets of patients with distinct associations to different HLA structures.
**Methods:** We used a multiplex peptide array [3] to detect reactivities in sera of patients (n=6400) and selected controls (n=12000) across cohorts from Sweden (EIRA), United Kingdom (WTCCC), and the United States (NARAC). Genetic data from the immunochip platform was used to investigate variation in the HLA region. First, we tested the association between AA-alleles of HLA molecules and Ab defined strata of RA patients. In order to quantify the similarity between different peptide reactivities we used permutation, scaled Jaccard distance metrics and hierarchical clustering. Next, we assessed genetic associations with antibody titers in RA cases, and estimated interactive effects on susceptibility to Ab-positive RA.
**Results:** Comparing 20 different ACPAs reactive with different cit peptides, we observed that reactivities to specific peptides are highly correlated across patients (>87% pairs co-occurs more than expected). The majority of Abs are highly co-expressed in patients who have high frequencies of HLA-alleles known to be associated to ACPA-positive RA. AA at positions 11/13 of HLA-DRB1 display the strongest susceptibility to 18 fine-specific ACPAs (omnibus $p \leq 9.3 \times 10^{-64}$), the exceptions being reactivities towards cit Fibrinogen (Fib) β 62–81 with citrullination at position 72 or 74. The reactivities towards two Fib peptides are not highly co-occurring with other Ab; The expression of Ab against cit Fib α peptide 36–50 is independent of HLA variants and for Ab towards cit Fib β 62–81 (72) there is even a negative association to HLA-variants previously shown to associate with ACPA-positive RA. Finally, we observed several allelic combinations showing interactive effects on fine specific ACPAs, and not or weakly with CCP2.
**Conclusions:** RA patients often co-express many different RA specific Ab, and the expressions of most of these are associated to HLA variants linked with ACPA-positive RA. However we also identified ACPAs with distinct expression profiles and HLA associations.
**References:**
[1] Klareskog L et al. PMID: 18173373
[2] Raychaudhuri S et al. PMID: 22286218
[3] Hansson M et al. PMID: 23025688
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3896

## OP0235 IDENTIFICATION OF NOVEL CD4+ LYMPHOCYTE EXPRESSION QUANTITATIVE TRAIT LOCI IN UNTREATED EARLY ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is a CD4+ lymphocyte-mediated disease of immune dysregulation. Genome-wide association scans (GWAS) have shown common variants at approximately 100 genetic loci to be associated with RA. However, the associated single nucleotide polymorphisms (SNPs) often lie in intergenic regions and the gene upon which they act has not been defined. Examining how RA-associated SNPs influence gene expression in relevant biological contexts will begin to address this.
**Objectives:** To map *cis* eQTLs at established RA risk loci in CD4+ lymphocytes of a well-characterised early arthritis cohort, and so gain insight into mechanisms of genetic risk.
**Methods:** Patients attending the Newcastle Early Arthritis Clinic, naïve to immunomodulatory therapy, donated high integrity RNA and DNA extracted from 98% pure CD4+ lymphocytes within 4 hours of blood draw. Detailed baseline and longitudinal clinical data were recorded for all participants, who were followed up for $\geq$1 year. Genotyping and global gene expression measurement was carried out using the Illumina Human CoreExome array, and either HT12v4 or WG6v3 BeadChip arrays, respectively, and expression data was batch-corrected and normalised using standard algorithms. Data were analysed using the R package. Variants in linkage disequilibrium (LD) with $>$100 confirmed RA- SNPs[1] ($r^2>0.8$), and probes within 4MB of these LD blocks, were included in the analysis, seeking evidence of cis-eQTLs.
**Results:** Data from 249 white Caucasian early arthritis patients were available for analysis; diagnoses (confirmed at follow-up) were RA (n=88), spondyloarthropathy/other inflammatory arthritis (n=86), osteoarthritis/other non-inflammatory arthralgia (n=70) and undifferentiated arthritis. Analysis of 1,247 SNPs and 8,023 probes identified strong evidence for cis-eQTLs at a number of RA risk loci in this population overall (experiment-wide $p<0.05$). Previously observed genes subject to eQTLs in primary human CD4+ lymphocytes replicated by our study include *BLK*, *FADS1* and *FADS2*. Genes whose expression specifically in these cells has, to our knowledge, been associated with RA risk variants for the first time include *RPS26*, *RNF167* and *IKZF3*.
**Conclusions:** We present the first detailed eQTL analysis in the pathophysiologically relevant setting of early arthritis CD4+ lymphocytes, free of confounding immunomodulatory treatment. Interactions of clinical parameters (including disease phenotype) with eQTL effects remains the subject of ongoing analyses, to be presented. Our findings have the potential to modify the biological candidate gene landscape of RA.
**References:**
[1] Okada Y et al. 2014 Nature. 506(7488):376–81
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3385

## OP0236 WHOLE TRANSCRIPTOME INVESTIGATION OF RESPONSE TO ANTI-TNF TREATMENT IN RHEUMATOID ARTHRITIS

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**Background:** Despite the revolutionary impact of anti-TNF treatments on rheumatoid arthritis (RA) patients, good disease control is only achieved in 30% of patients. In current clinical practice, RA drugs are administered on a trial and error basis and there are no clinical biomarkers of response to guide treatment decisions. Whilst non-responding patients can be switched to alternative therapies at 3 months, many remain on ineffective therapy for longer periods. Identification of early predictors of response could support timely switching in patients whose disease activity is not controlled by a particular drug.
**Objectives:** To investigate gene expression levels in whole-blood collected from patients with RA, between the start of treatment (baseline) and following 3-months of treatment, to identify a biological biomarker of response to the anti-TNF drug adalimumab.
**Methods:** EULAR good responders (GR) and non-responders (NR) to adalimumab were selected from the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS) cohort. Total RNA was isolated from Tempus™-stabilised baseline and 3-month blood samples using the MagMAX™ RNA Isolation Kit and quality assessed using the Agilent Bioanalyzer 2100. Samples with an RNA integrity number $>$4 were amplified and converted into biotinylated sense-strand DNA using the Affymetrix WT PLUS Kit and hybridised to Affymetrix GeneChip® Human Transcriptome Arrays. Quality control and differential transcription analysis was performed using the Affymetrix Expression and Transcriptome Analysis Console™.
**Results:** Whole genome expression profiling was performed on 44 patient samples (31 GR and 12 NR to adalimumab treatment). Gene level paired-analysis of variance revealed the significant downregulation of 1776 transcripts and upregulation of 943 transcripts following 3 months of adalimumab treatment in GR (FDR p-value $<$0.05, fold change $>$1.2 or $<$ -1.2) (Figure). There were no significant differences in gene expression between baseline and 3 months in NR. Pathway analysis using the Database for Annotation, Visualization and Integrated Discovery (DAVID) revealed that both differentially expressed and differentially spliced genetic variants in GR were heavily enriched for relevant processes including antigen processing and presentation, ribosome biogenesis and T- and B-cell receptor signalling. Many of the most significantly upregulated genes encoded immunoglobulin and MHC II components, which may indicate immune cell migration from the synovium into the blood in a positive response to adalimumab therapy in GR.

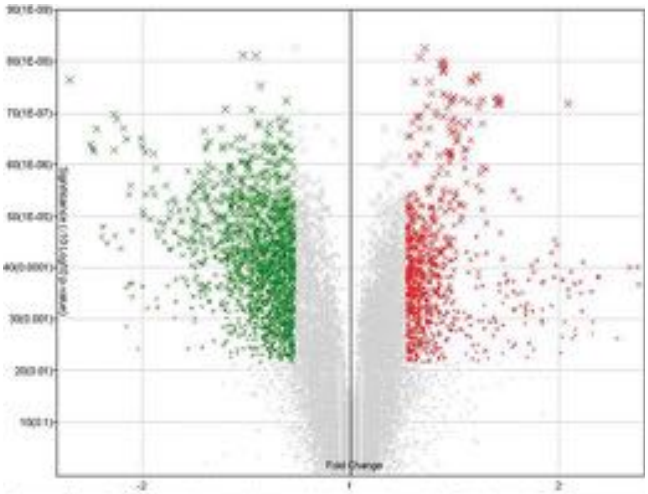



**Figure:** Differentially expressed transcripts between baseline and 3 months of adalimumab treatment in good responders. Green represents downregulated genes (FDR p<0.05, fold-change <-1.2); red represents upregulated genes (FDR p<0.05, fold-change>1.2).

**Conclusions:** A blood-based biomarker for good-response to anti-TNF treatment at 3 months could allow prompt identification of non-response, reducing the impact of long-term radiological damage and facilitating more responsible pharmacological spending. To support the promising immune signature of good-response at 3 months identified herein, subsequent work will include replication in additional patients and integration with corresponding genotype and serum microRNA data.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2883

## OP0237 POLYMORPHISMS OF GENE IMPLICATED IN TYPE 1 INTERFERON PATHWAY ARE ASSOCIATED WITH THE CLINICAL RESPONSE OF RITUXIMAB AT 24 WEEKS IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) treatment may target B-cells using rituximab (RTX), a chimeric monoclonal antibody directed against the B-cell marker CD20. Transcriptome of PBMCs from RA patients before RTX has suggested that responders differs from non-responders on the expression of genes regulated by type 1 interferon (IFN) (1) suggesting a possible contribution of type 1 IFN pathway genes such as interferon regulatory factor 5 (*IRF5*),

tyrosine kinase 2 (*TYK2*), signal transducer and activator of transcription 4 (*STAT4*), osteopontin (*SPP1*) and interferon regulatory factor 7 (*IRF7*).
**Objectives:** To study 8 *IRF5*, *TYK2*, *STAT4*, *SPP1* and *IRF7* variants as candidate predictors of the clinical response to RTX in RA at 6 months defined by a good or moderate EULAR response.
**Methods:** Patients from the SMART study who signed consent for genetic studies were included (2). The association between the EULAR response at 24 weeks and the polymorphism of the 8 chosen SNPs was analyzed by logistic regression. Response rates were compared across *risk* genotypes using the $\chi^2$ test or the Fisher exact test, when appropriate. Significant variables after univariate regression ($P<0.15$) were entered into a stepwise multivariate model adjusted to the sex, the age and the DAS28-CRP score.
**Results:** Among the 115 included patients, 92 were women, mean age was 56 years, 93 patients were anti-CCP positive. At M6, 30 patients were considered as good responders (26.1%), 62 as moderate responders (53.9%) and 22 as non-responders (19.1%). Univariate analysis showed that *IRF5* rs2004640 was significantly associated with a good/moderate EULAR response at week 24 ($P$=0.038) whereas *IRF7* rs1131665 and *SPP1* rs9138 were near statistical significance ($P$=0.092 and $P$=0.089, respectively). Since it was previously reported an association between *TNFSF13B* (the gene coding the BAFF cytokine) rs9514828 and RTX response in RA in the same cohort (2), this variant was also included in the multivariate analysis. The multivariate analysis with logistic regression analysis including *IRF5*, *SPP1*, *IRF7* and *TNFSF13B* revealed that a genotypic combination of *IRF5* rs2004640, *SPP1* rs9138 and *TNFSF13B* rs9514828 was strongly associated with good/moderate response to RTX at M6: $P=9.34\text{x}10^{-6}$, OR =11.37 [4.03–35.28] with a PPV of 91% and a NPV of 53% (Fig. 1).

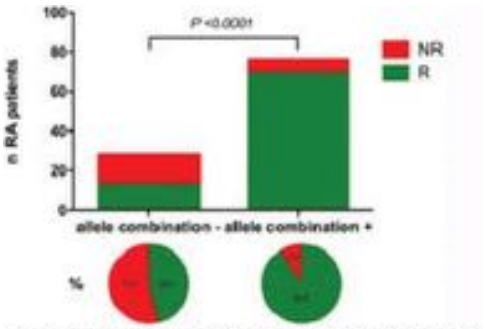



Fig.1 Number and corresponding percentages of EULAR responders and non-responders according to the genotypic combination.
R: responders, NR: non responders

**Conclusions:** We found an association between a combination of type 1-interferon genes and response to RTX treatment in RA. To further validate the magnitude of the association detected an independent replication in a larger cohort is required. If validated, our model could be helpful before the decision of initiating RTX in RA.
**References:**
[1] Vosslamber S, et al. Ann Rheum Dis 2011.
[2] Ruyssen-Witrand A, et al. Rheumatology 2013.
**Acknowledgement:** Unrestricted grant from Roche-Chugai and SFR
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1309

## OP0238 FCGR2B AND MULTIPLE HLA LOCI ARE ASSOCIATED WITH SUSCEPTIBILITY TO IGG4-RELATED DISEASE

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**Background:** IgG4-related disease (IgG4RD) is an emerging concept of an autoimmune disease entity including autoimmune pancreatitis, IgG4-related sialadenitis and IgG-related kidney disease (Ref 1–3). Comprehensive genetic landscape of IgG4RD is unknown.
**Objectives:** To perform a genome-wide association study of IgG4RD to detect susceptibility loci and uncover the pathophysiology underlying IgG4RD.
**Methods:** We conducted a two-staged genome-wide association study composed of a total of 850 cases and 2,082 controls by genotyping 2,310,564 single nucleotide polymorphisms (SNPs). Allele frequencies were compared between cases and controls by logistic regression analysis and followed by meta-analysis with use of inverse-variance method. Comprehensive analysis in the *HLA* region using imputation of amino acid residues of classical *HLA* alleles in combination with direct sequencing was also performed. The associations between clinical manifestations and correlates especially genetic components were analyzed.
**Results:** We identified *FCGR2B* and the *HLA* region as susceptibility loci to IgG4RD ($p\leq1.2\text{x}10^{-11}$). We also found evidence that the *HLA* region contained at least two independent associations in *HLA-DRB1* and *HLA-A* regions. The amino acid position 11 in the HLA-DRB1 peptide-binding groove, the strongest susceptibility position to other autoimmune diseases, was strongly associated with IgG4RD ($p=1.3\text{x}10^{-22}$). We also found a significant synergistic effect in combination of the two SNPs in *FCGR2B* and *HLA-DRB1* loci ($p\leq0.024$). The susceptibility SNP in *FCGR2B* was in linkage disequilibrium with a functional missense variant of *FCGR2B* and showed an association with the decreased gene expression ($p\leq1.0\text{x}10^{-10}$). None of rare or coding variants found by direct sequencing in the *FCGR2B* region and copy number variations could explain the association. The SNP in *FCGR2B* and age at diagnosis were independently associated with recurrence of IgG4RD ($p\leq0.013$). When we assessed common genetic architectures between IgG4RD and other autoimmune diseases, SLE-susceptibility loci showed a trend of opposite directions in IgG4RD susceptibility in contrast to RA, which showed a trend of common directions with IgG4RD ($p$=0.027).
**Conclusions:** A total of three susceptibility markers to IgG4RD were identified. *FCGR2B* may play critical roles in developing and the progression of IgG4RD. HLA-DRB1 amino acid position 11 is important for IgG4RD. Common molecular pathways are suggested to underlie IgG4RD and other autoimmune diseases.
**References:**
[1] Umehara H, Okazaki K, Masaki Y, et al. A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details. Modern rheumatology/the Japan Rheumatism Association 2012;22:1–14.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3046

**FRIDAY, 10 JUNE 2016**

# Novel clues solved in RA development

## OP0239 DISSECTING THE MOLECULAR BASIS OF IMMUNE CELL ACCUMULATION IN THE INFLAMED JOINT USING A MURINE MODEL OF RHEUMATOID ARTHRITIS

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**Background:** The molecular control of the “ebb and flow” of inflammatory cells into and out of the joint during the initiation, maintenance and resolution of inflammation in Rheumatoid Arthritis (RA) remains unclear.
**Objectives:** To characterise the ingress and egress of immune cells into inflamed joints, and identify the key molecular pathways regulating their migration in real time *in vivo*.
**Methods:** We developed a “breach of self tolerance” murine model of articular inflammation [1]. Using this model in conjunction with mice expressing the photoswitchable fluorescent protein kaede [2], we characterized the migration of cells from the inflamed joint (after photoswitching) to the draining lymph nodes. Flow cytometry of excised lymph nodes allowed the identification and phenotypic characterization of photoswitched cells that could only have originated from the inflamed joint. Using the same approach we identified and sorted cells that migrated to the draining lymph nodes and those that remained in the joint. RNA-seq analysis of these populations identified genes differentially regulating cellular retention in, and egress from, the inflamed joint to the draining lymph node.
**Results:** The key populations identified exiting the inflamed joint and entering the draining lymph node were $CD4^+$ and $CD8^+$ T cells, $FoxP3^+$ Treg, B cells and $CD11c^+$ DCs. The populations present in the inflamed joint comprised mainly $CD4^+$ T cells, $CD11c^+$ DCs and $Ly6G^+$ neutrophils. Analysis of RNA-seq data revealed pathways and genes previously highlighted as characteristic of RA in patient studies. More specifically focusing on cell migration, adhesion and movement pathways has indicated genes associated with the egress of immune cells from the inflamed joint.
**Conclusions:** We have identified key gene expression profiles that may be important for the migration of cells from the inflamed joint, which may provide targets for therapeutic manipulation.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2701

## OP0240 SYNOVIAL LYMPHOCYTIC AGGREGATES ASSOCIATE WITH HIGHLY ACTIVE RA AND PREDICT EROSIVE DISEASE PROGRESSION AT 12 MONTHS: RESULTS FROM THE PATHOBIOLOGY OF EARLY ARTHRITIS COHORT

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**Background:** The synovial cellular infiltrate in RA has for some time been recognised to organise into lymphocytic aggregates with a number observations suggesting they are immunologically competent and can support chronic inflammation. However, their clinical significance has been controversial with conflicting publications reporting diverse associations with disease outcome.
**Objectives:** The aim of this study was to examine in a cohort of therapy naïve, early RA patients whether baseline synovial pathotype: i)associated with specific clinical phenotypes, ii)predicted response to DMARD therapy, and iii)predicted joint damage progression
**Methods:** 135 DMARD-naïve early RA patients were recruited as part of the Pathobiology of Early Arthritis Cohort at Barts Health NHS Trust. Following pre-treatment synovial biopsy clinical data was collected at baseline and 12 months. Following immunohistochemical staining the degree of synovial infiltration by CD20+B cells, CD3+T cells, CD68+macrophages and CD138+plasma cells was determined. Patients were then categorised into synovial pathotypes: lymphoid, myeloid or fibroid according to the degree of immune cell infiltration. Samples also underwent nanostring analysis of 238 genes. Significant differences in clinical parameters at baseline and progression in radiographic damage at 12 months between synovial pathotypes was determined.
**Results:** At baseline a lymphoid pathotype significantly associated with ACPA+ve (0.017) and highly active disease (DAS28, CRP, ESR and swollen joint count, $p<0.01$). Furthermore a significantly higher number of patients with a baseline lymphoid pathotype (vs myeloid/fibroid) developed radiographic progression (9/26 vs 5/53, p=0.026). A cohort of 79 genes were identifed from the nanostring analysis that were differentially upregulated in patients with joint damage progression. Logistic regression analysis was used to develop a clinical model for predicting radiographic progression (final model ESR, RF and ACPA) with an AUC of 0.86. Integration of synovial gene expression profiles into the clinical model improved the AUC to 0.96.
**Conclusions:** The demonstration in this early RA cohort of a significant association between a lymphoid pathotype and a severe clinical phenotype/sero positivity for ACPA supports a direct role for synovial lymphoid structures in disease pathogenesis. Furthermore patients with a lymphoid pathotype were significantly more likely to develop radiographic damage. Integration of synovial gene expression profiles into a clinical model of radiographic progression enhanced performance. This data strongly supports a role for integration of synovial biomarkers into clinical prediction models of radiographic progression in early RA with critical implications for future patient stratification.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3229

## OP0241 REPETITIVE PROLONGED PHYSICAL WORKLOAD IS ASSOCIATED WITH INCREASED RISK OF DEVELOPING RHEUMATOID ARTHRITIS: RESULTS FROM THE SWEDISH EIRA-STUDY

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**Background:** Physical workloads and physical activities/exercises differ in quantity, intensity and duration of mechanical stress exerted on the joint and synovia. There are various types of repetitive prolonged physical workload (RPPW) that have been hypothesized to provide stress to the joints and possibly influence the development of arthritis. To our knowledge, there is no study that investigates the association of various types of RPPW and risk of rheumatoid arthritis (RA).
**Objectives:** To investigate the association between exposure to 7 different types of RPPW and risk of rheumatoid arthritis; to study the potential interactions between different RPPWs and the genes in the human leukocyte antigen (HLA) region.
**Methods:** Data from the Swedish Epidemiological Investigation of Rheumatoid Arthritis (EIRA), a population-based case-control study involving incident cases of RA (3680 cases and 5935 controls), were analyzed. Information on different types of self-reported RPPW exposures (see figure 1), anti-citrullinated protein antibody (ACPA) status and *HLA-DRB1* genotypes of cases and controls were retrieved. RPPW exposed subjects were compared with that of unexposed subjects. Odds ratios (ORs) with 95% confidence intervals (CI) of RA (overall), ACPA-positive RA and ACPA-negative RA associated with various RPPW exposures were estimated using an unconditional logistic regression model. Age, sex, residential area, smoking status, alcohol consumption, body mass index and education were considered as potential confounders and added as covariates in the statistical model. RPPW-HLA interactions were evaluated using the principle of departure from additivity of effects, by calculating the attributable proportion (AP) due to interaction.
**Results:** As shown on figure 1, the estimated ORs of developing RA associated with various RPPW exposures ranged from 1.3 (95% CI, 1.1–1-4) to 1.8 (95%CI, 1.6–2.0). No major difference in the ORs between ACPA-positive and ACPA-negative RA was found. Significant interactions between RPPW exposures and *HLA-DRB1* shared epitope genes were observed among ACPA-positive RA (AP values ranging from 0.3 (95% CI, 0.1–0.5) to 0.4 (95%CI, 0.2–0.6)).

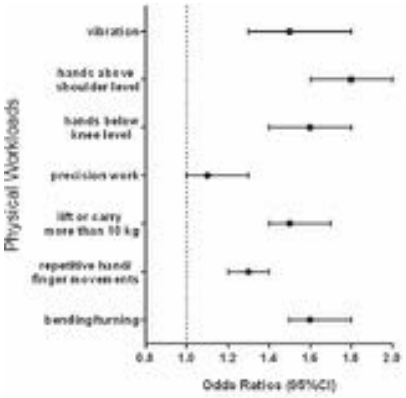



**Figure 1** Odds ratios of developing rheumatoid arthritis among subjects exposed to repetitive prolonged physical workload 5 years before diagnosis compared with unexposed subjects

**Conclusions:** Repetitive prolonged physical workload (RPPW) is associated with the risk of both ACPA-positive and ACPA-negative RA. The interactions between some RPPWs and *HLA-DRB1* shared epitope may be involved in the etiology of ACPA-positive RA.
**Acknowledgement:** The authors thank the investigators and participants from the EIRA study. The authors also thank Marie-Louise Serra and Lena Nise for data collection and Lena Israelsson for performing ELISA analysis.
**Disclosure of Interest:** None declared
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## OP0242 SELECTIVE DELETION OF FAP EXPRESSING CELLS ATTENUATES SYNOVIAL INFLAMMATION AND PROTECTS AGAINST INFLAMMATORY BONE CHANGES

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**Background:** Despite their role as key effector cells driving synovial inflammation and joint damage, fibroblast like synoviocytes (FLS) have yet to be targeted therapeutically. Fibroblast activation protein (FAP) is a cell surface serine protease, known to be expressed at a low level in resting FLS but up-regulated during inflammation (1). Genetic deletion of FAP has been shown to protect against cartilage damage despite no protective effect on inflammation or bone erosion (2). The pathogenic role of FLS expressing FAP is currently unknown.
**Objectives:** To determine the role of FAP expressing FLS in a murine model of autoantibody mediated inflammatory arthritis.
**Methods:** We utilized a transgenic mouse in which FAP expressing cells were conditionally ablated (FAP-DTR) by administration of diphtheria toxin (3) in either in a prophylactic or therapeutic regime. Inflammatory polyarthritis was induced by the passive transfer of K/BxN serum into naïve mice. Mice were scored for clinical signs of arthritis and flow cytometry of digested synovial tissue was performed to determine the expression of fibroblast subsets. In addition, MicroCT

was performed on hind-limbs of mice 15 days following induction of arthritis to evaluate inflammatory bone changes.
**Results:** We found that FAP expression in the human synovium predicts disease persistence in patients with early synovitis.FAP was dynamically expressed by FLS during inflammatory arthritis and defined a population of activated fibroblasts that co-express the lining layer marker Podoplanin (gp38). Therapeutic deletion of FAP+ cells during either the induction or peak phases of inflammatory arthritis significantly attenuated synovial inflammation leading to a reduction in the clinical severity of arthritis reduced inflammatory cell infiltration and protection against inflammatory bone changes as measured by micro CT. In contrast, prophylactic deletion of FAP expressing cells led to a delayed onset of inflammatory arthritis, but did not impact on subsequent clinical severity.
**Conclusions:** These data support a pathogenic role for FAP expressing FLS in inflammatory arthritis and provide a rationale for the selective targeting of FAP+ fibroblasts as a novel therapeutic approach.
**References:**
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[2] Wäldele et al. Arthritis Res Ther. 2015:20;17:12.
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**Acknowledgement:** This woirk was supported by an individual Wellcome Trust Postdoctoral Clinical Research Fellowship awarded to APC.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5983

## OP0243 SINGLE NUCLEOTIDE POLYMORPHISMS (SNP) IN THE IL-4 RECEPTOR, IL-4, AND CD40 LOCI AND OUTCOME PREDICTION IN PATIENTS WITH EARLY IMMUNE-MEDIATED INFLAMMATORY POLYARTHRITIS

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**Background:** Clinicians need reliable biomarkers of disease progression contributing additional information sufficient to personalize treatments in patients with early immune-mediated inflammatory polyarthritis (EPA) and rheumatoid arthritis. Some single nucleotide polymorphisms (SNP) in immune-related genes impact the expression of encoded proteins.
**Objectives:** To determine whether SNP in the Interleukin (IL)-4 Receptor (IL-4R), IL-4, and CD40 genes are associated with EPA disease outcomes.
**Methods:** We studied patients from the Early Undifferentiated PolyArthritis (EUPA) cohort. These patients were evaluated early (median 3.8 months), treated to remission and followed up at pre-specified intervals. Radiographs were scored according to Sharp/van der Heijde (SvH); significant damage was $\geq$5. SNPs were genotyped using an allele-specific primer extension (ASPE) assay and Luminex 100 analyzer. HLA-DR alleles were determined using the LABType rSSO assay (One Lambda). SNP and HLA-DR alleles were correlated to total (SvH $\geq$5) or erosive (Erosion $\geq$5) joint damage, functional incapacity (Modified Health Assessment Questionnaire (M-HAQ) $\geq$1.0) and remission according to Simplified disease activity index (SDAI $\leq$3.3) using generalized estimating equation (GEE) with repeated measures over 5 years. Results were presented with relative risk (RR) and 95% confidence intervals (CI). General linear model (GLM) with repeated measures was used for continuous outcomes.
**Results:** The allelic distribution for the SNPs is presented in Table. IL-4 SNPs rs2243250 and rs2070874 were strongly correlated (r2=0.99); only rs2243250 is presented.
The (G) allele at rs1801275 (IL-4R) was significantly associated with decreased radiographic damage (GLM: Estimate (standard error): 0.035 (0.017), p=0.043).
A (T) allele at rs2243250 (IL-4) was positively associated with erosive damage (GEE: RR 1.26 (1.02–1.55), p=0.034) and functional incapacity (M-HAQ $\geq$1.0; GEE: RR 1.25 (1.00–1.55), p=0.048).
A (T) allele at rs4810485 (CD40) was associated with a higher likelihood of reaching SDAI remission (GEE: RR 1.36 (1.13–1.64), p=0.001).
As previously published[1], the presence of at least one copy of the DERAA protective alleles was significantly associated with decreased erosive damage (GEE: RR 0.75 (0.58–0.96), p=0.02), a trend to decreased functional incapacity (GLM: M-HAQ $\geq$1.0; RR: 0.79 (0.61–1.02), p=0.07) and increased chance of SDAI remission (GEE: RR 1.19 (1.01–1.4), p=0.04).
Combined presence of at least one copy of the DERAA alleles and two copies of rs2243250 (C) allele of IL-4 further reduced erosive damage (GEE: RR 0.67 (0.51–0.90), p=0.007), functional incapacity (GLM: RR 0.75 (0.56–1.00), p=0.051) and slightly increased the chance for SDAI remission (GEE: RR 1.21 (1.02–1.44), p=0.03).

| Allelic distribution of EUPA patients | | |
|---|---|---|
| | Total | n (%) |
| rs1801275 (IL-4R) [A;G] | | |
| A/A | 663 | 391 (59.0) |
| A/G | | 240 (36.2) |
| G/G | | 32 (4.8) |
| rs2243250 (IL-4) [C;T] | | |
| C/C | 662 | 474 (71.6) |
| C/T | | 172 (26.0) |
| T/T | | 16 (2.4) |
| rs1883832 (CD40) [C;T] | | |
| C/C | 559 | 320 (57.2) |
| C/T | | 135 (24.2) |
| T/T | | 104 (18.6) |
| rs4810485 (CD40) [G;T] | | |
| G/G | 559 | 322 (57.6) |
| G/T | | 132 (23.6) |
| T/T | | 105 (18.8) |
| Shared epitope | | |
| -/- | 560 | 308 (55.0) |
| -/+ | | 200 (35.7) |
| +/+ | | 52 (9.3) |
| Protective epitope DERAA | | |
| -/- | 615 | 450 (73.2) |
| -/+ | | 151 (24.6) |
| +/+ | | 14 (2.3) |
| DERAA -/+ or +/+ AND rs2243250 (IL-4) C/C | 610 | 128 (21.0) |

**Conclusions:** Genotyping the SNP rs1801275 (IL-4R), rs2243250 (IL-4), rs1883832/rs4810485 (CD40) and determining the HLA-DR allele of EUPA patients provided a set of stable genetic predictors of disease progression, both clinically and on radiographs. Their association together and with other stable predictors may contribute to develop reliable biomarker signatures suggesting significant associations with poor disease outcomes.
**References:**
[1] Carrier N et al. Arthritis Rheum 2009;60:698–707
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3695

## OP0244 SUSTAINED SUPPRESSION OF RHEUMATOID ARTHRITIS DISEASE MARKERS BY MAVRILIMUMAB BUT NOT GOLIMUMAB IN ANTI-TUMOR NECROSIS FACTOR-INADEQUATE RESPONDERS: AN EXPLORATORY ANALYSIS IN THE PHASE IIB EARTH EXPLORER 2 CLINICAL TRIAL

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**Background:** Treatment of rheumatoid arthritis (RA) patients by anti-tumour necrosis factors (anti-TNFs), such as golimumab, has substantially improved patient outcomes. However, unmet therapeutic needs exist for the significant proportion of patients who do not respond to current biologics treatment. Mavrilimumab is a fully human monoclonal antibody which inhibits the granulocyte-macrophage colony-stimulating factor receptor $\alpha$ (GM–CSFR-$\alpha$). Recently, a Phase IIb study has been completed to evaluate the efficacy and safety of mavrilimumab and golimumab in both disease-modifying antirheumatic drug (DMARD)-inadequate responder (IR) and anti-tumor necrosis factor-inadequate responders (anti-TNF-IR) patients (EARTH EXPLORER 2, NCT01715896).
**Objectives:** To assess peripheral biomarkers and pathophysiological pathways modulated by mavrilimumab in comparison with golimumab in both DMARD-IR and anti-TNF-IR RA patients.
**Methods:** In total, 75 DMARD-IR and 63 anti-TNF-IR patients were randomized in a 1:1 ratio to receive subcutaneous 100 mg mavrilimumab (n=70) every other week (Q2W) or 50 mg golimumab (n=68) Q2W alternating with placebo, in combination with methotrexate (7.5–25.0 mg/week) for 24 weeks. Serum levels of 18 RA-associated proteins as well as 3 protease-derived protein fragments were measured in 71 DMARD-IR and 61 anti-TNF-IR RA patients at baseline and 4 time points post-administration. Transcriptome sequencing was used to measure gene expression changes in whole blood of RA patients at baseline and day 169 post-administration.
**Results:** Serum levels of CCL22 and CCL17 were suppressed by mavrilimumab but not golimumab, while CXCL13 and ICAM1 levels were suppressed by golimumab but not mavrilimumab. Those four proteins may be specific pharmacodynamic markers for the two biologics respectively. More interestingly, both mavrilimumab and golimumab demonstrated early and sustained suppression of multiple inflammatory markers in DMARD-IR patients, including CRP, SAA, MMP1, MMP3, IL6, VEGF, IL2R, and CD163. However, golimumab-induced early changes rapidly returned towards baseline levels in anti-TNF-IR patients, while serum protein suppression by mavrilimumab was maintained through day 169 in anti-TNF-IR patients. Similarly, mavrilimumab administration was associated with durable suppression of extracellular matrix markers, C1M, C3M, and P4NP7S, while golimumab only induced a transient change of the three markers in anti-TNF-IR patients. Furthermore, RNA sequencing results demonstrated significant regulation of 1547 transcripts at day 169 after mavrilimumab administration while golimumab had no impact on whole blood gene expression in anti-TNF-IR patients. In contrast, significant changes of 1042 and 2058 transcripts were observed in DMARD-IR patients at day 169 after mavrilimumab and golimumab administration respectively.
**Conclusions:** Our study demonstrated sustained suppression of RA disease markers by mavrilimumab but not golimumab in anti-TNF-IR patients, suggesting the potential of greater long-term disease control by mavrilimumab than golimumab in this population of RA patients.

**Disclosure of Interest:** X. Guo Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, S. Wang Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, A. Bay-Jensen Employee of: Nordic Bioscience, M. Karsdal Employee of: Nordic Bioscience, A. Godwood Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, D. Close Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, P. Ryan Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, L. Roskos Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca, W. White Shareholder of: MedImmune/AstraZeneca, Employee of: MedImmune/AstraZeneca
**DOI:** 10.1136/annrheumdis-2016-eular.4475

## OP0245 HS1,2A ENHANCER POLYMORPHISM IN RHEUMATOID ARTHRITIS DETERMINES HIGH DISEASE ACTIVITY, HIGH NF-KB ACTIVITY IN B CELLS AND LEADS TO A DIFFERENTIAL RESPONSE TO THERAPY

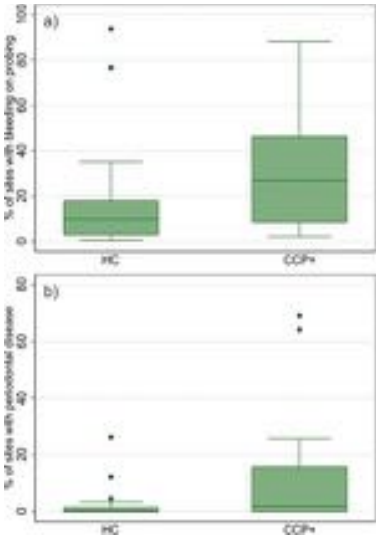
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**Background:** Several autoimmune chronic inflammatory diseases have been associated with a polymorphism of the HS1,2A enhancer located in the 3' regulatory region of the locus for the immunoglobulin heavy chain (IgH 3'RR-1) (1,2). Its main biologic role resides in the immunoglobulin isotype switching and somatic hypermutation, but the interest in the regulatory region relies also on the demonstration that the allele*2 has a binding site for NF-kB, not present in allele*1.
**Objectives:** To study the HS1,2A enhancer polymorphism as a possible biomarker of disease, disease activity and of response to therapy in the earliest phases of Rheumatoid Arthritis (ERA). To evaluate whether the polymorphism is related to a different NF-kB pathway activation on B cells of ERA patients carrying 2/2 or 1/1 genotypes.
**Methods:** Three-hundred and twenty nine ERA patients, treated according to a tight control strategy were enrolled in the study. At each visit, clinical improvement and remission were evaluated according to ACR/EULAR criteria (3). ERA patients were genotyped for HS1,2A enhancer polymorphism, as previously described (4). At diagnosis, circulating B cells were isolated from PB of 8 naïve RA patients (4 with the 2/2 genotype and 4 with the 1/1 genotype) and analysed for specific genes expression through Real-Time PCR (PCR Array). The Ingenuity Pathway Analysis (IPA) software was used to examine biological networks associated with the polymorphism and to identify functionally related genes that correspond to specific canonical pathways.
**Results:** Twenty-eight percent of ERA patients had the HS1,2A enhancer 2/2 genotype and 10.9% the 1/1 genotype, comparable with the already published data on RA (1). ERA patients carrying the 2/2 genotype had more active disease at baseline compared to 1/1 genotype (in terms of ESR, CRP, circulating IL6 and DAS), reaching less likely a good-EULAR response and remission at 3 months FU (good-EULAR response: 35.9% vs 56.4%, OR (95%CIs): 0.43 (0.24–0.78); EULAR-remission: 14.1% vs 34.6%, OR (95%CIs): 0.31 (0.14–0.67), respectively). Moreover, at 6 months FU, a higher percentage of subjects carrying the 2/2 genotype needed TNF-blockers addition compared to patients without the 2/2 genotype (26.1% vs 12.2%, p=0.01). Finally, we performed the IPA analysis of PB derived B cells from ERA patients carrying the 2/2 and 1/1 genotypes, finding that the focus genes were mapped to 3 networks related mainly to cell death and survival, immunological disease and cell-to-cell signaling and interaction. Moreover, the 2/2 genotype was linked to the top canonical pathway "NF-kB signaling" with TNF-alpha, CD40 and CD40 ligand as top upstream regulators.
**Conclusions:** We demonstrate that carrying allele*2 of HS1,2A enhancer influences the disease activity and the response to therapy in RA already at the earlier phases of the disease and that this genetic background is strongly related to NF-kB activation. Based on these findings we suggest that the enhancer HS1,2A polymorphism is a genetic biomarker that should be included in an individual matrix able to define a possible personalized therapy in RA.
**References:**
[1] Tolusso B et al. Ann Rheum Dis 2009;
[2] Frezza D et al. Ann Rheum Dis 2012;
[3] Felson DT et al. Arthritis Rheum 2011;
[4] Giambra V et al Gene 2005
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4596

## OP0246 INCREASED PREVALENCE OF PERIODONTAL DISEASE IN ANTI-CCP POSITIVE INDIVIDUALS AT RISK OF PROGRESSION TO INFLAMMATORY ARTHRITIS: A TARGET FOR PREVENTION?

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**Background:** The prevalence of periodontal disease is increased in rheumatoid arthritis (RA) patients (1) but has not been reported in seropositive at risk individuals. Comprehensive periodontal examination requires expert evaluation of six sites per tooth for bleeding on probing (BOP), clinical attachment loss (CAL) and pocket depth (PD). Periodontal disease is associated with *Porphyromonas gingivalis*, which, through its unique ability to citrullinate arginine residues (2) may trigger RA-related mucosal autoimmunity. Salivary IgA anti-CCP antibodies have been reported in RA patients (3) but their presence in at risk individuals has not been described.
**Objectives:** To investigate the prevalence of periodontal disease and to describe evidence of RA-related mucosal autoimmunity in anti-CCP positive subjects at risk of progression to inflammatory arthritis.
**Methods:** Anti-CCP positive individuals with no evidence of synovitis (CCP+), healthy controls (HC) and anti-CCP positive RA patients were recruited. All patients underwent periodontal examination by a dentist; six sites per tooth were assessed for BOP (present/absent), CAL (mm) and PD (mm). Dentists later agreed a consensus clinical diagnosis for each case, blinded to patient group. Unstimulated saliva and serum samples were collected. CAL$\geq$2mm and PD$\geq$4mm at the same site signified periodontal disease (PDD). The % of evaluable sites with BOP (%BOP) and % with PDD (%PDD) were calculated per patient. Anti-CCP antibodies (anti-CCP2; immunocap assay, Phadia) were measured in paired saliva & serum samples. IgA anti-CCP titres exceeding the 95th centile in HCs were considered positive. Mann-Whitney U tests were used to compare groups. Spearman rho is reported for associations.
**Results:** We recruited 31 CCP+, 20 HC and 12 RA patients. Groups were balanced for sex, smoking and number of missing teeth. Dentists classified 77% of CCP+ and 45% of HC as having clinical periodontal disease. %BOP was higher in CCP+ than HC (CCP+=26.9 [8.6, 46.3], HC=9.8 [3.1, 17.9]; p=0.033) (fig 1a). %PDD was higher in CCP+ compared to HC (CCP+=1.9 [0.0, 15.7], HC=0.3 [0.0, 1.4]; p=0.050) (fig 1b). PDD was recorded at $\geq$1 site in 65% of CCP+ and 50% of HC. Similar results were obtained for percentage of sites with both PDD and BOP present. 4 patients (CCP+ n=3, RA n=1) had positive saliva IgA anti-CCP results ($>$6$\mu$g/L). 21% of CCP+ (n=6) and 17% of RA (n=2) had positive serum IgA anti-CCP results ($>$15$\mu$g/L); these were not associated with periodontal disease measures. RA patients were slightly older (mean age CCP+=52, HC=50, RA=62) and on disease-modifying treatments; the latter may account for similar %BOP and lower %PDD in this group compared to HC. Age was not associated with %BOP (rho=0.05, p=0.714) or %PDD (rho=0.03, p=0.833).




**Conclusions:** We provide preliminary evidence of both an increased prevalence of periodontal disease and the presence of salivary IgA anti-CCP antibodies in anti-CCP positive individuals at risk of arthritis development. These findings support the concept that periodontal inflammation precedes joint inflammation as a potential trigger or early target of RA-related autoimmunity.
**References:**
[1] A Abou-Raya et al. Scan J Rheum,2005.
[2] W McGraw et al. Infect Immun, 1999.
[3] A Svard et al. Immunobiology, 2013.
**Disclosure of Interest:** K. Mankia: None declared, L. Hunt: None declared, E. Hensor: None declared, J. Nam: None declared, V. Clerehugh: None declared, A. Speirs: None declared, A. Tugnait: None declared, T. Do: None declared, D. Devine: None declared, P. Emery Consultant for: Pfizer, Abbvie, Roche, MSD, BMS, Novartis, Samsung, Lilly, Sandoz, UCB
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**FRIDAY, 10 JUNE 2016**

## PARE abstract session

### OP0247-PARE SURVEY: WHAT DO PATIENTS THINK ABOUT THEIR CARE, CARETAKERS AND THE ROLE OF PATIENT ORGANISATIONS?

N. Caeyers on behalf of ReumaNet vzw. *ReumaNet vzw, Mol, Belgium*

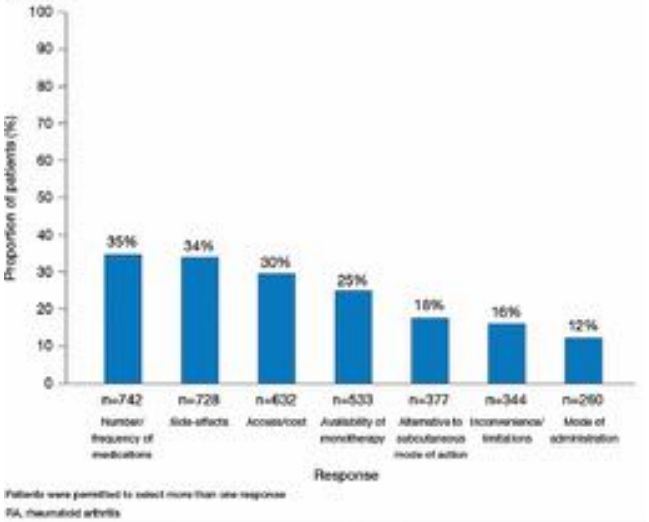
**Background:** When diagnosed with a rheumatic condition (RMD), we turn to rheumatologists and other specialists for the best treatment possible. We rely on medication and exercise to minimize the impact of our conditions. While living with a chronic disease, people develop a certain expertise themselves. An expertise that differs from what rheumatologists know, but nevertheless is extremely valuable.
**Objectives:** ReumaNet wanted to know what patients think about their care and how they believe things can be improved. By communicating the results to health care providers, policy makers and industry, ReumaNet wants to start a unique collaboration between professionals and patient experts to improve care for people with RMD's.
**Methods:** ReumaNet, the Flemish patient organisation for people with RMDs, developed a survey together with its partners (= rheumatologists, health professionals, industry). The survey was launched in February 2015 and ran until June 2015. It contained 40 online questions for people with an RMD and covered the following items: information, treatment, research, relation with Health Professionals (rheumatologist, physiotherapist, general practitioner and pharmacist), communication between these care takers and the role of patient organisations (POs).
**Results:** 711 people completed the questionnaire. Most people completed the questionnaire online, 50 surveys were filled in on paper by people not familiar with a pc. The majority had RA (48%), but also AS, PsA, JIA, CTD, fibromyalgia, OA and osteoporosis or a combinations of different RMD's were represented. The results were analysed in different ways: conditions, age, gender, time of diagnosis. A part of the survey was also analysed based on medication.
Only 48% considered themselves well informed about their condition and only 34% were well informed about their treatment and medication. Specially people with a diagnosis of less than 6 months are in great need of more info. A fear of side effects are the main reason not to take medication as prescribed (51%).
Fatigue and heredity are the most important issues that should be on the research agenda, according to patients. Rheumatologists score 7/10 on the question: "How satisfied are you with your rheumatologist". Not listening to the patient and not taking him or her seriously are the biggest concerns. Communication between rheumatologist and GP only scores a low 6/10. Most patients do not even know if there is some form of communication and if there is, this obviously is not satisfying for all parties involved.
Other HP's score around 80%, which means people with RMD's are happy with their interactions.
Spreading information among patients is the biggest task for POs (82%). Young people have the greatest need to meet with peers, but 21% of the same group does not even know a PO exists.
**Conclusions:** The results were presented during the World Arthritis Day Symposium of ReumaNet, where the different target groups were present. A debate started the first discussions on these important topics. Health care providers, industry and policy makers were asked how they would tackle the issues in the next five years. ReumaNet is currently meeting with all stakeholders to work together towards better care for all people with RMD's. Opening a 'Reuma Expertise Huis', a place where all expertise on RMD's can come together, was a first step.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2087

### OP0248-PARE UNDERSTANDING THE IMPORTANCE OF A PATIENT'S ROLE IN THE MANAGEMENT OF RA: RESULTS FROM A PATIENT-BASED SURVEY DEVELOPED BY THE RA NARRATIVE GLOBAL ADVISORY PANEL

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**Background:** Rheumatoid arthritis (RA) is a chronic, debilitating disease for which there is no cure.
**Objectives:** To identify and better understand the perspective of patients (pts) regarding pt/healthcare provider (HCP) interactions, RA treatment and RA management, based on results from a pt-based survey developed by the RA NarRAtive global advisory panel.
**Methods:** The RA NarRAtive initiative comprises an advisory panel of 39 RA experts (including rheumatologists and pt advocacy group leaders [many with RA themselves]) from 17 countries. A pt-based survey designed by the working group was fielded online across 13 countries between Sept 2014 and Jan 2015. Results are presented for all respondents who consented to the survey.
**Results:** Total of 3649 pts responded to the survey: mean age 52.8 yrs (SD ±15), 59% female. Median time since diagnosis of RA (pt-reported) was 7 yrs. Only 34% of pts (n=1251) described their current overall health as excellent/good. Respondents represented a wide spectrum of self-reported disease activity from mild (39%) to moderate to severe (30%) to severe (8%). Overall, 93% and 50% of pts were under the care of an HCP or rheumatologist/RA specialist, respectively. In total, 59% (2139) of pts were receiving prescribed RA medication, including pain relievers (70%), disease-modifying antirheumatic drugs (DMARDs) (38%), steroids/corticosteroids (32%), and biologic DMARDs (16%). Of these, 38% were not taking their medication as prescribed. Overall, 78% of pts currently taking RA medication were satisfied with their treatment regimen, however 70% desired fewer medications, 57% were worried their medications would fail and 56% wanted more medication choices. The number or dosing frequency of medications was the most frequently cited aspect that pts would most like to change with respect to their current prescribed medications (Figure). Almost half of pts under HCP care (48%) acknowledged that dialogue with the HCP would optimise management of their RA. However, 62% of respondents felt uncomfortable raising treatment/disease concerns to their HCP. Of those currently seeing an HCP to manage their RA, 34% strongly/somewhat agreed that if they ask too many questions, their HCP will consider them a difficult pt and this may affect the quality of care they receive. The current treatment goal for physicians is to achieve clinical remission or low disease activity.[1] However, successful treatment was most commonly defined by pts as a reduction of pain and/or joint swelling/inflammation (81%) and improvements in quality of life (77%).

Figure: Aspects of current, prescribed treatment for RA that patients (n=2139) would most like to change




**Conclusions:** This pt-based survey highlights the importance of treatment conversations between pts and HCPs. Although many pts are satisfied with their RA treatment, non-adherence persists and many would like to discuss and/or change their currently prescribed treatment. Further understanding the responses from this survey will be important to facilitate communication between pts and HCPs, with the aim of improving treatment outcomes.
**References:**
[1] Smolen JS et al. Ann Rheum Dis 2015; 75: 3–15.
**Acknowledgement:** These surveys were funded by Pfizer Inc. Editorial support was provided by S Johnson, PhD, of Complete Medical Communications, and funded by Pfizer Inc.
**Disclosure of Interest:** C. Koehn Shareholder of: Arthritis Consumer Experts, Grant/research support from: Canadian Institutes of Health Research, Arthritis Research Canada, St. Paul's Hospital, Employee of: Arthritis Consumer Experts, A. Dikranian Consultant for: Pfizer Inc, AbbVie, Speakers bureau: Pfizer Inc, AbbVie, A. Maniccia Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, E. Bananis Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
**DOI:** 10.1136/annrheumdis-2016-eular.3217

### OP0249-PARE 25 YEARS OF CAMP FREEDOM - A 6 DAY CAMP FOR CHILDREN 7-17 YEARS OLD WITH ARTHRITIS

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**Background:** Camp Freedom was developed by the Arthritis Foundation of Western Australia in conjunction with Princess Margret Hospital for Children in 1990 for children with arthritis, with a camp manual having been produced as a guide into the preparation and development of each camp.
**Objectives:** The aim of Camp Freedom is to empower young people with all forms of Arthritis to make informed choices with regards to lifestyle, education and disease management. The camp is designed to offer friendship, fun and exciting activities as well as educational workshops. This also provides respite for the family.
**Methods:** Preparation for camp begins with the selection of the campsite, forming

an enthusiastic team is our next step, our team consists of a Camp Coordinator and our volunteers are a Pediatric Rheumatology Nurse Specialist, a Pediatric Rheumatologist and 7–10 Peer leaders over the age of 21, most having been previous campers.
A programme is created to keep the children occupied most of the time during the 6 day camp, with confidence building a prime outcome to most of our activities, with abseiling, flying fox, sports and fun actvities planned.
Our education sessions are undertaken in two sections, for our junior and senior campers, the subjects and methods are very different, with our health professionals providing age appropriate information and subject matter. Junior camper topics are generally related to understanding the mechanics of their joints,how Arthritis affects them and how to handle bullying. Whereas with the senior campers more detailed interactive subjects such as Transition, peer pressure and social issues are discussed, generally in two sessions, the first with peer leaders and the second with our Health professionals in attendance to answer the questions from the previous session.
**Results:** At the end of each camp we ask the participants to fill in a feedback form to make sure we are providing them with activities and information they need and to give us information to change and improve our programme. We think the biggest accolade is that the parents allow their children to attend camp year after year, if they didn't think they benefited from camp they wouldn't allow them to attend.
Seeing the change that has happened to many of the campers, arriving as shy, negative, closed children who hate their difference to their other friends, at the end of camp to be kids who are vibrant outgoing young people who have made lifelong friends all because they just "get each other". They don't have to explain why they take medications, or why they have a limp today but not yesterday, or why they have to sit down for a while after exercise, they are all in the same boat, although at different levels. Camp gives the kids the chance to discuss their condition with someone just like them, to know they aren't alone and can share their experiences, without having to explain themselves.
**Conclusions:** Many of our outcomes are not measurable on a piece of paper but having been involved with Camp Freedom for 18 years seeing the campers grow up and now returning as adult peer leaders is a very rewarding outcome. Camp Freedom is very successful and growing due to the caring and nurturing nature of the week. The kids are allowed to be kids; they don't have well meaning but overprotective parents around to stop them from "having a go".
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4998

## OP0250-PARE SHARED DECISION MAKING IN RHEUMATOID ARTHRITIS - PATIENTS/DOCTORS WORKSHOP

E. Kritza on behalf of the Arthritis Foundation of Crete. *The Arthritis Foundation of Crete, Heraklion, Crete, Greece*

**Background:** As in most countries in Greece, medical consultations for RA are too short especially in public hospitals. Therefore there isn't enough time for doctors to educate patients about their disease, to discuss treatment options, to review the side effects and finally to adjust treatment strategies according to their patient's life and priorities.
**Objectives:** After campaigning for change for so many years, we wanted answers to our main questions: a. Do doctors and patients view the importance of Shared Decision Making in the same way b. Is shared decision making possible within the current social, economic and cultural climate?
**Methods:** Two full day mixed workshops were organized to discuss the realities of SDM in Greece today, to share ideas and explore solutions. One in Heraklion on 6/6/2015 involving 30 experienced patients and 6 Healthcare Professionals (4 rheumatologists, 1 GP, 1 nurse, 1 Anesthesiologist specializing in chronic pain).
The second workshop took place in Chania on 29/11/2015 involving 25 patients and 4 Healthcare Professionals (1 rheumatologist, 1 GP, 1 orthopedic, 1 nurse).
After a short introduction the participants were divided into two groups: a doctors' group facilitated by a patient and a patients' group facilitated by a doctor. Both groups were asked to rate the degree of implementation of SDM in clinical practice, its usefulness for patients and to justify their ratings.
*The patient Sub Group* rated the usefulness of SDM 10 out of 10 but, the rate of its implementation was only 5 out of 10.They believe that SDM is more likely to occur after the 1st year of diagnosis and depends on: levels of mutual respect and doctor/patient trust, available time, patient preparation before the visit, level of education and information both patients and doctors have, and the weaknesses within the healthcare system.
*The HCP Sub Group* rated the usefulness of SDM 8–9 out of 10 but, the rate of its implementation was only 5 out of 10.The HCPs felt that the implementation of SDM depends on: the patients' age, educational level, willingness to participate and the doctors' attitude
Then the participants were split into three mixed groups and asked to explore the same topics such as: FEASIBILITY, BARRIERS, and SOLUTIONS and propose PRACTICAL STEPS
**Results:** The implementation of SDM is very difficult under current conditions in the healthcare system. As main barriers were identified: lack of time, breakdown in the doctor/patient relationship, weakness in hospital systems & structures and lack of personal responsibility for decision making among some patients.To overcome these barriers a lot of interesting ideas were put forward such as: allow more time during the first consultation, prepare patients before their consultation for better use of time, recruit trained nursing staff who will be in more active contact with patients and the management of their disease, exploit new technologies for patient data transfer to doctors and vice versa, educate patients and doctors to appreciate the benefits of SDM.
**Conclusions:** SDM allows the patient, to be an equal partner in their health care, working with their doctor, nurse or other health professional to make an informed decision about their treatment. However to be implemented in clinical practice doctors and patients need to be educated.
**Disclosure of Interest:** E. Kritza Grant/research support from: Bristol-Myers Squibb Greece
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## OP0251-PARE PATIENT AND PUBLIC INVOLVEMENT IN DESIGN, ANALYSIS AND REPORTING OF A PUBLIC PRIORITY SETTING EXERCISE FOR RESEARCH IN OSTEOPOROSIS

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*[1]Research Institute for Primary Care & Health Sciences, Keele University, Keele; [2]Oxford University Hospitals NHS Trust, Oxford University, Oxford; [3]Haywood Rheumatology Centre, Haywood Hospital, Burslem, United Kingdom*

**Background:** Patient and public involvement (PPI) in identifying topics for research ensures relevant, impactful research questions and is expected by research funders. We have undertaken a two-stage national priority setting exercise to identify public views on research priorities in osteoporosis. Four focus groups were undertaken with members of the National Osteoporosis Society (NOS) and a research cohort of people who had experienced fracture. A national e-survey was sent to members of the NOS. PPI was embedded throughout to inform study design, analysis and reporting.
**Objectives:** To describe the role and impact of a Research User Group in co-designing priority setting methods for osteoporosis research.
**Methods:** Three face-to-face advisory group meetings were held with members of the Research Institute's Research User Group (RUG). All members have bone and muscle pain. Meeting 1 occurred before the focus groups. A draft topic guide was discussed. Meeting 2 occurred after all focus groups were completed and before the e-survey went live. Before this meeting researchers undertook some analysis of focus group data to identify specific research questions or uncertainties about treatments and produced a draft e-survey. Each section and question was discussed with the RUG alongside relevant data from the focus groups to clarify concepts and wording. Meeting 3 focussed on e-survey results and co-design of recommendations on research priorities.
**Results:** Five RUG members participated. In meeting 1 RUG members advised on general topics to include in the focus group discussion and the order of questions to be asked. The group had innovative ideas about how best to ask participants to prioritise topics discussed and suggested using "post-it" notes which the researchers subsequently implemented. In meeting 2 researchers presented how emerging themes from the focus groups could be turned into questions for the e-survey. Some themes were felt to be "straightforward", and for these RUG members advised on question wording. Some themes were less well crystallised (e.g. support, confidence), and for these, the RUG members interpreted meaning from quotes. Discussions led to clarity about what the question should be about and wording amended. The RUG identified overlap between questions and the need to simplify the introduction to the e-survey. Researchers redrafted and re-circulated the survey. RUG members fed back further comments by email, particularly regarding the order of presented questions and suggesting reordering in line with patient experiences. This meant moving the questions about diagnosis to an earlier part of the questionnaire. The final meeting was held after the e-survey closed. Summary results from the e-survey were presented and RUG members discussed how results should be presented in a final report.
**Conclusions:** Patient and public involvement was integral to the design and analysis of this UK osteoporosis research priority setting exercise at three key points. This iterative process enabled active involvement throughout and impacted on focus group and e-survey design and the development of research strategy recommendations.
**Acknowledgement:** We would like to thank the PPI team at Keele who helped to set up the RUG groups and the focus group participants and people who responded to the e-survey.
**Disclosure of Interest:** None declared
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## OP0252-PARE INCREASING THE INTEREST IN RESEARCH IN RHEUMATOLOGY

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**Background:** The Swedish Rheumatism Association has a research fund which distributes money to research in rheumatology but also research on pain, osteoarthritis and other conditions related to musculoskeletal disease. Our long term commitment is to reduce the burden of rheumatic disease, increase the

quality of life for people with rheumatic disease and ultimately prevent the onset of rheumatic disease and its consequences. The fund distributes about 20 million Swedish krona yearly. In 2015 the Swedish Rheumatism Association published a report on the research that is financed by their fund.
**Objectives:** The report had several objectives 1) to increase the awareness of the Swedish Rheumatism Association's function as a funder of research 2) to interest decision makers in different parts of society in the field 3) to be used for fundraising.
**Methods:** The Swedish Rheumatism Association worked together with a content agency (OTW, Stockholm, Sweden) in the production of the report. The report was based around six major areas of research, rheumatoid arthritis, juvenile arthritis, juvenile idiopathic arthritis, systemic autoimmune rheumatic disease, pain, osteoarthritis and life style. Each theme contained a number of articles on different projects that the Swedish Rheumatism Association has helped to fund. The different articles were written by, or in collaboration with, the principal investigator.
**Results:** The report contains 18 articles on research. It addition, it contains four cases where four patients tell their story. The report was printed and first released to the public during a research seminar arranged by the Swedish Rheumatism Association. The report is also distributed as a PDF via the Swedish Rheumatism Association's webpage and a few of the individual articles have been reworked to suit the web better.
**Conclusions:** The Swedish Rheumatism Association have published a report on the research they finance in order to use it both for lobbying purposes and for fundraising. For the coming year a series of activities will be arranged around the report. For example it will be used at a research seminar that is arranged for young medical students in order to interest them in research as a career path. It will also be used in different meetings with various decision makers as well as for fundraising purpose.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4039

## OP0253-PARE "SAMEN REUMA"- A CLOSED GROUP ON FACEBOOK FOR PEOPLE WITH RHEUMATIC DISEASES

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**Background:** With a website with 250.000 visitors monthly, a fanpage on Facebook with over 17.000 fans and a Twitteraccount with about 2.400 followers the Dutch Arthritis Foundation is in touch with a very large group of people with rheumatic diseases. We noticed there is a demand for an online place to meet for people with RMDs in the Netherlands. A place to share their feelings and to ask each other questions. Nowadays there are a lot of social communities on the internet. Although we do have a Fanpage on Facebook, where we share our extensive knowledge about all kinds of rheumatic diseases, the page is accessable for everybody and less suited for more personal conversations. For this reason we started a closed Facebook group for people with RMDs where they can get in touch with peers in a more private setting (within the possibilities of Facebook) to exchange tips, give support and to find answers to more private matters.
**Objectives:** Many people with rheumatic diseases would like to be able to get in touch with peers. On the other hand the Dutch Arthritis Foundation would like to stay in touch with patients and get more insight into what is going on in the community. For that reason we've created a private community on Facebook where patients can meet each other and can exchange knowledge amongst themselves and with us.
**Methods:** In the beginning of 2015 we developed a plan to start an online community on Facebook. As not only the support of the patient community is important, but also the support from the organisation we tried to involve both as much as we could. Our goal was to reach 200 members within half a year and to have activity in the community 3 to 4 times a week.) After we set up the group on Facebook (without any members yet) we made a list of rules and in June started to ask patients to help us find members. About ten people were interested in helping and invited their friends to the group. When somebody had a question they made sure that the question got answered. In this way we started the group low profile. In July we asked two key members of the group if they would like to be a moderator, which they agreed to do. For moderation purposes we created a secret (untraceable) group on Facebook. In August we announced the group on all of our media channels (Facebook public fanpage, Twitter, website, newsletter etc) after which the group grew rapidly.
**Results:** Our goal at six months was to have at least 200 members, by the end of 2015 we counted more than 1.700 members!
The group is very active and the amount of subjects is enormous. At least every two hours somebody posts a question or reacts on someone else's question, if not more often. The converstation contains subjects like medical problems, health insurance and solutions for daily activities. The members introduce themselves, ask questions, support each other en share their experiences and knowledge.
**Conclusions:** As the group got off at a tremendous pace, we can conclude that it satisfies the (online) needs of people with rheumatic diseases. People are positive about the group and are likely to stay and help each other. It is still a quest for the Dutch Arthritis Foundation to decide what topics we can contribute to. While we do believe in the power of peer to peer conversations, we also think people with RMDs can benefit from our knowledge. The big question for us at this moment however is when and how often to contribute ourselves.
**Disclosure of Interest:** None declared
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## OP0254-PARE RHEUMATOID ARTHRITIS PATIENT CHARACTERISTICS AND WILLINGNESS TO PARTICIPATE IN RESEARCH AMONG MEMBERS OF THE CREAKYJOINTS ARTHRITIS PATIENT COMMUNITY: RESULTS FROM A PATIENT SURVEY

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**Background:** CreakyJoints (CJ) is an international online arthritis patient community offering support, blogs, education, advocacy and the opportunity to participate in research.
**Objectives:** To identify willingness to participate in research among rheumatoid arthritis (RA) patients in an online community.
**Methods:** CJ patient community completed an online form preparatory to launch of a PCORI-funded research network (ArthritisPower.org). The online survey captured self-reported demographic, diagnosis, treatment, and willingness to participate in research.
**Results:** As of January 2016, a total of 8923 patients had registered. Among respondents, 2147 identified themselves as patients who had RA; a subgroup of 970 completed the survey on willingness to participate in research. *Demographics (N=2147):* Respondents were mostly female (93%) and white, non-Hispanic (85%) with mean age of 51.7 years (SD 11.6). *Conditions & Treatments (N=2147):* The most frequent concomitant conditions reported by RA respondents were osteoarthritis (32%), fibromyalgia (31%), and osteoporosis (13%). A majority reported taking a classical DMARD (e.g. MTX) (59%) or a biologic (50%) including anti-TNF biologics (33%); only 23% indicated they were taking neither. *Willingness to Participate in Research (N=970):* Most patients (68%) had never taken part in research. Among U.S. respondents, a majority (75%) would refuse to participate in research that requires sharing Social Security Number (SSN) and 50% for the last 4 digits of SSN compared with only 20% for email and 34% for medical records. Top 3 reasons patients would not be interested in being part of medical research were: project not recommended by doctor (30%), individual results may not be kept private/confidential (28%), and project will take a lot of time (25%). Table 1 shows percentage of patients interested in research based on the source of the invitation.

Table 1. Interest in research participation by source of invitation

| | Not Interested | Somewhat Interested | Very Interested |
|---|---|---|---|
| Your own doctor | 7% | 27% | 66% |
| Medical school or hospital | 13% | 40% | 47% |
| Non-profit | 21% | 46% | 33% |
| Government (e.g., U.S. NIH) | 27% | 42% | 31% |
| Drug company | 36% | 45% | 18% |
| Private company (e.g., food or retail) | 50% | 38% | 12% |
| Insurance company | 54% | 34% | 12% |

**Conclusions:** Results from this patient community survey indicate substantial willingness to participate in rheumatology research yet identify a number of potential barriers. Considering patients as unique stakeholders is vital to maximize the relevance and patient-centeredness of future research endeavors.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

# Cormobidities

## OP0255 RHEUMATOID ARTHRITIS COMORBIDITY INDEX: DEVELOPMENT AND VALIDATION OF A NEW SPECIFIC TOOL FOR CLASSIFYING PROGNOSTIC COMORBIDITY IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis patients are clinically complex, and the interplay of their prognostically important conditions leads to morbidity as well as

mortality. Separate patterns of comorbidity are identified in patients with different rheumatic diseases. These patterns include the type of comorbid variables reported and their associations with age and disease duration. The available comorbidity tools face some tough challenges particularly most of them are non-specific and were developed before the era of biologic therapy, early inflammatory arthritis as well as Treat to Target concepts.
**Objectives:** 1. identify comorbidities with greatest impact on Rheumatoid Arthritis (RA) patients' health status. 2. develop and validate a prospectively applicable comorbidity index for classifying RA patients according to their comorbid conditions which might alter their risk of hospitalization and mortality.
**Methods:** This was a retrospective multicenter cohort analysis of RA patients in a rheumatology clinical registry assessing the effect of different comorbidities measured at patients' visits over 10-years period, on predicting future death and hospitalization. A weighted index that takes into account the number and seriousness of comorbid disease was developed in a cohort of 2029 patients with early RA monitored over 10-years. Logistic and Cox Regression analyses were implemented to estimate the risk of mortality. Regression coefficients were used to develop the morbidity index score. ROC curve for the invented index was used to evaluate the discriminating ability of the index and identify different cutoff values that can delineate patients at different stages for risk of death. Disease activity parameters were considered.
**Results:** Comorbidities (18 conditions) were strongly associated with the 10-year death risk, and composed the RA-comorbidity index. These include Cardiovascular (7 comorbidities), infection, osteoporotic fractures, falls risk, Depression/anxiety, functional status (HAQ >2), diabetes mellitus, steroid therapy >5mg, DAS-28 >3.2), renal/liver/lung disease and tumors. A comorbidity index weighted according to the regression coefficient of the variables extracted through the logistic regression analysis was developed. The score ranges from 0 to 40. A cut off point of 20 was associated with a sensitivity of 90.2% and a specificity of 89.3%. Validation using ROC curve revealed AUC of 97%.

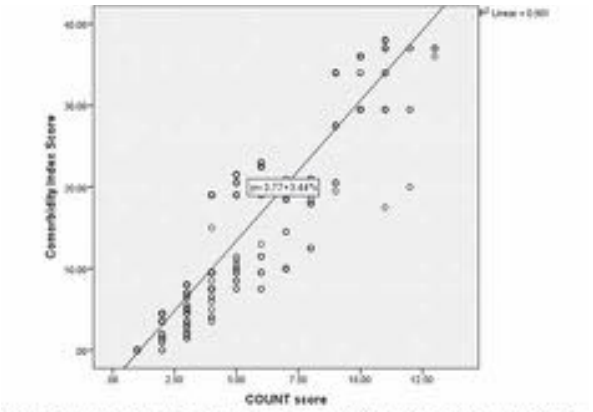


Figure Scatterplot displaying correlation between COUNT score and Comorbidity Index

**Conclusions:** The RA-comorbidity index is a valid method for estimating risk of death in RA patients. It enables the clinicians to include comorbidities assessment and management in their standard practice. It can be used to predict resource utilization, identify targets for reducing high costs, by prospectively identifying RA patients at high risk.
**Acknowledgement:** Omar El Miedany: data entery and analysis
**Disclosure of Interest:** None declared
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## OP0256 PRESENCE OF RISK FACTORS FOR CARDIOVASCULAR DISEASE PREDATES THE ONSET OF SYMPTOMS OF RHEUMATOID ARTHRITIS

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**Background:** Patients with rheumatoid arthritis (RA) are at increased risk of developing cardiovascular (CV) comorbidity compared with the general population. Contradictory results concerning CV disease prior to onset of RA have been reported. Of the known CV risk factors, a more atherogenic lipid profile and smoking have been presented prior to RA onset.
**Objectives:** In this study, lifestyle factors, lipid levels, presence of hypertension, and diabetes were evaluated in individuals prior to onset of symptoms of RA and matched population controls from northern Sweden.
**Methods:** A nested case-control study was based on information from The Västerbotten Intervention Programme (VIP) and the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA). Data were collected by questionnaire (socioeconomic and lifestyle factors), assessments by a nurse (body mass index;BMI, waist and blood pressure), and blood sampling (lipids and glucose loading). The registers of patients with RA (ARA criteria) attending the Department of Rheumatology, Umeå was co-analysed with the registers from VIP and MONICA. This study included 547 pre-symptomatic individuals (mean age 51.5years; 372f/175m, median (IQR) predating time 5.0 (7.0) years), and 1654 controls (mean age 51.6years; 1123f/531m). CV risk factors were defined as: hypertension (systolic≥140 mmHg, diastolic≥90 mmHg), ApoB/ApoA1 ratio (females ≥0.7, males ≥0.8), BMI≥25, diabetes, and ever smoker.
**Results:** Lower levels of ApoA1 (OR=2.0 (95%CI1.25, 3.25) and increased ApoB/ApoA1 ratio (OR=2.25 95%CI1.25, 4.06) were associated with RA development, particularly in females besides smoking, BMI and waist range. Plasma glucose at baseline was related to disease development, particularly in males (OR=1.18 95%CI1.01, 1.37). Blood pressure did not differ between the groups. Conditional logistic regression models identified elevated ApoB/ApoA1 ratio (OR=1.25 95%CI1.01, 1.56), being ever smoker (OR=2.00 95%CI1.63, 2.47), BMI≥25 (OR=1.33 95%CI1.09, 1.63) and diabetes (OR=1.98 95%CI1.06, 3.68) but not hypertension (OR=0.89 95%CI 0.72–1.11) to be associated with RA development. The pre-symptomatic individuals had significantly higher frequency of these risk factors, 32.3% of these individuals had ≥3 of these factors compared with 23.2% of the matched controls (OR=2.52 95%CI1.67, 3.83).
**Conclusions:** Several of the CV risk factors are present in individuals already years before onset of symptoms of RA. One third of the pre-symptomatic individuals had at least 3 of these factors present. These results urge early CV prevention in patients with RA.
**Acknowledgement:** The Medical Biobank of northern Sweden is acknowledged.
**Disclosure of Interest:** None declared
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## OP0257 RHEUMATOID ARTHRITIS-SPECIFIC CARDIOVASCULAR RISK CALCULATORS ARE NOT SUPERIOR TO RISK CALCULATORS ESTABLISHED FOR THE GENERAL POPULATION: A VALIDATION ANALYSIS IN A COHORT OF RA PATIENTS FROM 7 COUNTRIES

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**Background:** Cardiovascular disease (CVD) risk calculators developed for the general population do not accurately predict CVD events in patients with rheumatoid arthritis (RA).
**Objectives:** To externally validate risk calculators recommended for use in patients with RA including the European League Against Rheumatism (EULAR) 1.5 multiplier, the Expanded Cardiovascular Risk Prediction Score for Rheumatoid Arthritis (ERS-RA) and QRISK2.
**Methods:** Seven RA cohorts from United Kingdom, Norway, Netherlands, United States, South Africa, Canada and Mexico were combined. Data on baseline CVD risk factors, RA characteristics and CVD outcomes (including myocardial infarction, ischemic stroke and cardiovascular death) were collected using standardized definitions. Performance of QRISK2, EULAR multiplier and ERS-RA was compared to other risk calculators (ACC/AHA, Framingham Adult Treatment Panel III [FRS-ATP] and Reynolds Risk Score) using c-statistics and net reclassification index (NRI).
**Results:** Among 1796 RA patients without prior CVD (mean age: 54.0 [SD: 14.0] years, 74% female), 100 developed CVD events during a mean follow-up of 6.9 years (12430 person-years). Estimated CVD risk by ERS-RA (mean: 8.8%, SD: 9.8%) was comparable to FRS-ATP (mean: 9.1%, SD:8.3%) and Reynolds (mean: 9.2%, SD: 12.2%), but lower than ACC/AHA (mean: 9.8%, SD: 12.1%) and QRISK2 (mean: 15.5%, SD: 13.9%) estimates. Discrimination was not improved for ERS-RA (c-statistic=0.69), QRISK2 or EULAR multiplier applied to FRS-ATP and ACC/AHA (c-statistic=0.72 for all) compared to ACC/AHA and FRS-ATP (c-statistic=0.72 for both). The NRI for ERS-RA were low (-0.8% vs. ACC/AHA and 2.3% vs. FRS-ATP). The NRI for QRISK2 compared ACC/AHA was low (-2.4%). The NRI for QRISK2 compared to FRS-ATP was higher, but not significant (NRI: 25.0%, 95% CI: -9.4–34.7%). The EULAR multiplier only reclassified 6 patients above the 7.5% treatment threshold for the ACC/AHA calculator and 3 patients above the 20% treatment threshold for the FRS-ATP calculator, so the NRI was negligible.
**Conclusions:** The QRISK2, EULAR multiplier and ERS-RA algorithms did not predict CVD risk more accurately in patients with RA than CVD risk calculators developed for the general population.
**Acknowledgement:** The ATACC-RA consortium: S Gabriel, C Crowson, E Matteson, G Kitas, K Douglas, A Sandoo, AG Semb, S Rollefstad, E Ikdahl, T Kvien, P Van Riel, E Arts, J Fransen, S Rantapää-Dahlqvist, S Wållberg-Jonsson, L Innala, G Karpouzas, P Sfikakis, E Zampeli, P Dessein, L Tsang, MA Gonzalez-Gay, A Corrales, H El-Gabalawy, C Hitchon, V Pascual Ramos, I Contreras Yáñez, M van de Laar, H Vonkeman, I Meek, E Husni, R Overman, I Colunga, D Galarza
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## OP0258 OPTIMIZING THERAPY IN INFLAMMATORY ARTHRITIS: PREDICTION OF RELAPSE AFTER TAPERING OR STOPPING DMARDS/ BIOLOGIC AGENTS BY ULTRASONOGRAPHIC ASSESSMENT IN RHEUMATOID ARTHRITIS PATIENTS WHO ACHIEVED CLINICAL REMISSION

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**Background:** In contrast to initiation of biologic therapy, guidelines regarding stopping of this treatment are missing. As a result, the decision of discontinuation is still a challenging aspect in the use of biologic therapy. Currently this is typically based on an estimated, case-by-case, benefit-risk ratio.
**Objectives:** To assess whether joint ultrasonography can predict disease relapse in RA patients in sustained remission, either continuing, tapering or stopping Disease modifying drugs (DMARDs) or biologic therapy in a prospective randomized study.
**Methods:** 157 RA patients in clinical remission, (Disease Activity Score in 28 joints [DAS-28] $<$2.6 for more than 6-months) receiving treatment with DMARDs and biologic therapy, were randomized into four arms: Arm 1: continue full dose DMARDs and taper biologic therapy by 50% (31 patients); Arm 2: taper both DMARDs and biologic therapy dose by 50% (32 patients); Arm 3: taper DMARDs by 50% and stop biologic therapy (31 patients); Arm 4: stop both DMARDs and biologic therapy (31 patients). Patients' joints were assessed ultrasonographically (Gray scale and Power Doppler) at 40 joints (DAS28 joints + ankles + metatarsophalangeal joints) and were prospectively followed up bi-monthly for 12-months. Control group (32 RA patients) continued their DMARDs and biologic therapy at the same doses. Physicians who evaluated the patients during the study period were blinded to the baseline ultrasound findings. The primary endpoint was sustained remission during 12 months. Patients were considered as having a relapse when the DAS-28 score was $>$3.2 and anti-rheumatic treatment was escalated.
**Results:** The incidence of relapses was related to study arms: Arm 1: relapse 41.9%, arm 2: 59.3%; arm 3: 67.7%; Arm 4: 77.4%. Kapler-Meier Analysis revealed that time to relapse also varied in the 4 study subgroups: Arm 1: 6.8 ± 2.46; Arm 2: 5.3 ± 2.6; Arm 3: 4.7 ± 2.2; Arm 4: 3.9 ± 2.1 months. Relapse rates were significantly higher in patients whose total ultrasound scores at discontinuation were high than in those whose total ultrasound scores were low ($P<0.001$ for both total gray-scale and power Doppler scores). Positive and negative predictive values were 84.7% and 71.2% for the total Gray-scale score and 89.8% and 73.5% for the total power Doppler score, respectively. Multivariate logistic regression identified anti-citrullinated protein antibodies (ACPA) positivity (p=0.027) and treatment reduction (in comparison to continuation) as predictors for relapse (arm 1: p 0.004, arm 2: p=0.002; arm 3: p=0.003, arm 4: p=0.001).
**Conclusions:** Less than 40% of the patients remained in remission after tapering or stopping DMARDs and biological therapy. In RA patients in clinical remission, residual synovial inflammation determined by joint ultrasonographic assessment predicted relapse within a short term after discontinuation of the treatment. Relapses occurred mainly in the first 6 months after treatment reduction or stoppage and were associated with the presence of ACPA. This data endorse the establishment of ultrasound-based strategies before optimizing biologic/ DMARs therapy in RA is considered.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4909

## OP0259 IMPACT OF SUSTAINED REMISSION ON RISK FOR INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS ENROLLED IN A US REGISTRY

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**Background:** High disease activity has been shown to be associated with increased risk of infection in patients with rheumatoid arthritis (RA).[1] The potential benefit of lower disease activity on the risk of serious infection has not been examined.
**Objectives:** This study was conducted to assess the impact of sustained remission on infection risk.
**Methods:** We identified patients in the Corrona registry with at least two Clinical Disease Activity Index (CDAI) measures, at least 1 follow-visit, and met the criteria based on CDAI for sustained remission or sustained low disease activity (two incident consecutive visits in remission [CDAI $\leq$2.8] or LDA [CDAI between 2.8 and 10] and following the second visit (index visit) had an average disease activity in remission or LDA over follow-up using the area under the curve method based on the trapezoidal rule. Patients were followed until the earliest of: first serious infection (infection requiring either hospitalization or treatment with IV antibiotics) or last follow-up visit. Covariates identified at the index date included demographic and clinical characteristics. The incidence rates (IR) per 100 patient-years of serious infections in patients in sustained remission vs sustained LDA were calculated and crude incidence rate ratios (IRRs) calculated.
**Results:** There were a total of 3355 RA patients in the sustained remission group and 3912 in the sustained LDA group. The majority of patients were female (75%) with mean age of 60 years, with an average disease duration of RA of 9.9 years for the sustained remission patients and 12.1 years for the sustained LDA patients ($P<0.001$). During follow-up, the sustained remission and sustained LDA groups reported 115 and 260 serious infections, respectively. Incidence rates between the two disease activity groups differed significantly, with the sustained LDA group having a nearly twofold (crude IRR=1.8 [1.45, 2.24]) higher rate of infections (IR=2.01 [1.78, 2.27]) than the sustained remission group (IR=1.12 [0.93, 1.34]).

Table 1. Incidence rate and incidence rate ratio between sustained LDA vs sustained remission cohorts

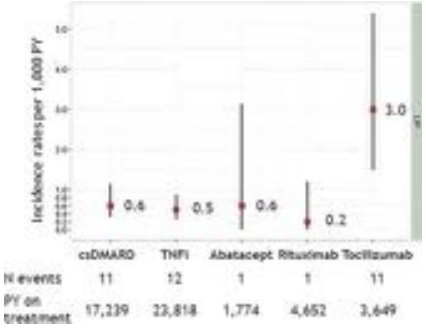
| | Sustained remission | Sustained LDA | p |
|---|---|---|---|
| Serious infections, N | 115 | 260 | |
| Person-yrs follow-up | 10282 | 12909 | |
| Incidence Rate [95% CI] (per 100 person-year) | 1.12 [0.93, 1.34] | 2.01 [1.78, 2.27] | $<$0.001 |
| Crude Incidence rate ratio (IRR) | Ref. | 1.80 [1.45, 2.24] | $<$0.001 |

**Conclusions:** Patients in sustained remission have a lower risk of serious infections compared to those in sustained LDA. These findings may help motivate those who only attain LDA to strive to reach remission if possible.
**References:**
[1] Au K, Reed GW, Curtis JR, Kremer JM, Greenberg JD, Strand V, Furst DE. High disease activity is associated with an increased risk of infection in patients with rheumatoid arthritis. Ann Rheum Dis 2011 May;70(5):785–791.
**Acknowledgement:** This study is sponsored by Corrona, LLC. The Corrona RA registry has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, BMS, Crescendo, Genentech, Horizon Pharma USA, Janssen, Eli Lilly, Novartis, Pfizer, and UCB.
**Disclosure of Interest:** J. Curtis Grant/research support from: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, Abb Vie, Consultant for: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, Abb Vie, M. Liu Employee of: Corrona, LLC, S. Rebello Employee of: Corrona, LLC, M. Trivedi Shareholder of: Amgen, Inc., Employee of: Amgen, Inc., T. Lesperance Shareholder of: Amgen, Inc., Employee of: Amgen, Inc., Y. Li: None declared, N. Accortt Shareholder of: Amgen, Inc., Employee of: Amgen, Inc.
**DOI:** 10.1136/annrheumdis-2016-eular.1803

## OP0260 LOWER INTESTINAL PERFORATIONS ARE MORE FREQUENT AND PRESENT UNTYPICALLY IN PATIENTS TREATED WITH TOCILIZUMAB COMPARED TO OTHER BIOLOGIC OR CONVENTIONAL SYNTHETIC DMARDS

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**Background:** During randomized controlled trials with tocilizumab, an IL-6 inhibitor, perforations of the lower intestinal tract (LIP) occurred only in the exposed patient population, not in the control group. The relevance of this finding for daily practice is unclear because we know little about the background risk for LIP in rheumatoid arthritis (RA) patients on different treatments.
**Objectives:** To examine the incidence of LIP and their appearance in RA patients treated with different biologics (bDMARDs) or conventional synthetic DMARDs (csDMARDs).
**Methods:** We used data from the prospective longitudinal German biologics register RABBIT with 14,300 RA patients included since May 2001 starting a csDMARD or bDMARD. All serious gastrointestinal adverse events reported until 30th April 2015 which were possibly associated with perforations (including haemorrhages) were filtered (n=137). All events were validated (twice, with additional external validation) based on medical records or specific queries. Reviewers were blinded for treatment exposure. Only events with a definite, non-traumatic and non-iatrogenic perforation of the lower intestinal tract were selected for the analysis. Treatment exposure was defined as treatment given in the last three months before occurrence of the event.



**Results:** In total, 36 LIPs (colon/sigma: 31, appendix: 4, terminal ileum: 1) were observed in 48,102 patient years (PY). In total, 27 of the 36 patients with LIP had concomitant GCs, with a daily dose of ≥7,5mg in 12 patients. In the multivariate analysis higher age, GC use and treatment with TCZ were significantly associated with a higher risk of LIP (hazard ratio (HR) 1.3 per 5mg increase in GC dose [95%CI=1.2, 1.4], and HR 1.5 [1.3, 1.8] per 5 years increase in age). Compared to csDMARDs, treatment with TCZ was associated with a 5 times higher risk for LIP (HR 5.2 [2.4,11.6]) whereas no association was found for TNF inhibitors, abatacept or rituximab.
None of the patients with LIP had a history of diverticulitis known to the treating rheumatologist. In patients treated with TCZ the presentation of LIP events was untypical: acute and localized pain was only reported by some patients, diffuse abdominal pain was more frequent. CRP was completely suppressed or only slightly elevated. In total, 11 (31%) of the patients died after LIP: 2 of 11 csDMARD, 3 of 12 TNFi and 6 of 11 TCZ treated patients.
**Conclusions:** This first comparative analysis of all bDMARDs available for the treatment of RA showed a significant risk of LIPs in patients treated with TCZ. It confirms a signal detected in clinical trials and specified the localization to lower GI tract only. TCZ patients with LIP present untypically. In order to ensure timely intervention, patients should be advised that symptoms of LIP might be mild and that CRP is not a valid diagnostic marker in their case.
**Disclosure:** RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celltrion, Hospira, MSD Sharp & Dohme, Pfizer, Roche, and UCB.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2901

## OP0261 7-YEAR TOLERABILITY PROFILE OF GLUCOCORTICOIDS USE IN EARLY RHEUMATOID ARTHRITIS: DATA FROM THE ESPOIR COHORT

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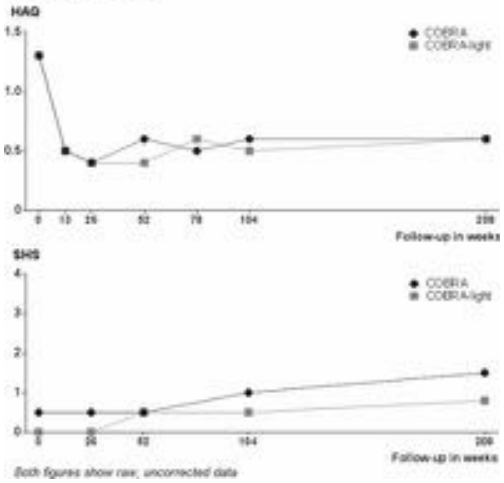
**Objectives:** To explore the 7-year tolerability profile of glucocorticoids (GC) use in patients with early rheumatoid arthritis (RA).
**Methods:** Six-hundred and two RA patients from the early arthritis ESPOIR cohort (less than 6 months disease duration) were included. They were stratified in two groups, based on whether they received or not GC treatment during their follow-up. The group "with GC" comprised RA patients who took a systemic GC therapy at least once during their entire follow-up, while the control group "without GC" included RA patients who had never taken GC. The main outcome was a composite of death, cardiovascular diseases (including myocardial ischemia, cerebrovascular accident and heart failure), severe infections and fractures. We used Cox proportional-hazard model, adjusting for confounding factors and propensity score (Inverse Probability of Treatment Weighting).
**Results:** Among the 602 RA patients (476 women, mean age of 48 ± 12 years), the group "with GC" included 386 patients (64.1%) and the group "without GC" comprised 216 patients. RA patients in the group "with GC" received low dose prednisone treatment during their follow-up (mean dosage 3.1 mg/day ±2.9), most of them starting GC during the first six months (n=263, 68.1%). Compared to patients "without GC", RA patients "with GC" significantly received more DMARDs and biological agents, more NSAIDs, and were more frequently diabetics and smokers. Additionally, RA patients "with GC" suffered from a more active disease, with significantly higher DAS-28 CRP and HAQ scores, and higher CRP and ACPA levels. Among a total of 65 events (7 deaths, 14 cardiovascular diseases, 19 severe infections and 25 fractures), 21 (9.72%) occurred in the "without GC group", and 44 (11.4%) in the "with GC group". No significant difference was found between groups in univariate analysis (p=0.520). However, a trend toward more infections was evidenced in RA patients "with GC" (p=0.09). Propensity score included baseline HAQ, and DAS-28 CRP scores, baseline ACPA level, history of diabetes and baseline modified Sharp score. Cox model adjusted on propensity score, age, gender, and history of hypertension, showed no significant difference between groups (p=0.628).
**Conclusions:** This 7-year data analysis of the ESPOIR cohort did not show any significant difference with regards to major safety events in RA patients exposed to GC treatment compared to RA patients who had never received GC. These data support the good safety profile of short term low-dose GC therapy in early RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4321

## OP0262 SIMILAR CLINICAL AND RADIOLOGICAL OUTCOME IN THE COBRA AND COBRA-LIGHT TREATMENT GROUP 4 YEARS AFTER INITIATION OF THE COBRA-LIGHT TRIAL

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**Background:** COBRA and COBRA-light combination therapy are equally effective treatments for early rheumatoid arthritis (RA) after 26 and 52 weeks [1,2], but the long-term effect of start with COBRA-light therapy is unknown.
**Objectives:** To investigate the efficacy of initial COBRA and COBRA-light combination therapy after a 4 year follow-up period. A detailed analysis of long-term safety will be presented separately.
**Methods:** In the COBRA-light trial, 164 patients with recent-onset RA were randomized to either COBRA (prednisolone 60 mg/day, tapered to 7.5 mg/day in 6 weeks; MTX 7.5 mg/week and sulfasalazine 2 g/day; n=81) or COBRA-light therapy (prednisolone 30 mg/day, tapered to 7.5 mg/day in 8 weeks and MTX escalated to 25 mg/week in 8 weeks; n=83). In the period of 26 to 52 weeks; treatment intensification of MTX and addition of etanercept was protocollized (treat-to-target). After 52 weeks, treatment was continued without protocol. Four years after trial initiation, all patients who had initiated therapy (n=162) were invited to participate in the COBRA-light extension study. Main outcomes were: Disease Activity Score in 44 joints (DAS), Health Assessment Questionnaire (HAQ), Sharp – Van der Heijde radiographic Score (SHS) and ACR/EULAR Boolean remission. Longitudinal mixed modeling (DAS), TOBIT (HAQ), and GEE analyses (SHS: log negative binomial; Boolean remission: logit binomial) were performed in STATA.
**Results:** A total of 149 out of 162 original trial patients participated in the extension study (77 COBRA and 72 COBRA-light patients); 2 COBRA vs. 3 COBRA-light patients had died, 1 vs. 5 patients were not able or willing to participate, and 1 vs. 1 patient were in drug-free remission and out of care. After the 52 weeks trial period, 43% COBRA vs. 42% COBRA-light patients used prednisolone for ≥90 days, 34% vs. 44% patients switched to other DMARDs, and 39% vs. 28% patients used biologicals during the follow-up period. After mean 4 years follow-up, 49% COBRA vs. 47% COBRA-light patients had DAS<1.6, 50% vs. 48% had HAQ≤0.5, and 29% vs. 36% had SHS=0. Boolean remission occurred significantly more in the COBRA-light group (12% COBRA vs. 26% COBRA-light; p=0.04). Longitudinal data analyses showed equal effects of both COBRA and COBRA-light therapy on DAS, HAQ, SHS and Boolean remission over time. HAQ and SHS, both indicators of long-term efficacy, showed equal progression in both treatment groups during the 4 year follow-up period (Fig. 1).

Figure 1. HAQ and SHS during the 4 year follow-up period of the COBRA-light extension trial (n=149)




**Conclusions:** Early RA patients initially treated with COBRA or COBRA-light therapy showed similar outcome over a 4 year follow-up period.
**References:**
[1] Den Uyl, ARD 2014,73:1071–8;
[2] Ter Wee, ARD 2015,74:1233–40
**Disclosure of Interest:** N. Konijn: None declared, L. van Tuyl: None declared, M. Boers Consultant for: MundiPharma, Pfizer, D. den Uijl: None declared, M. ter Wee: None declared, P. Kerstens: None declared, A. Voskuyl: None declared, D. van Schaardenburg: None declared, M. Nurmohamed: None declared, W. Lems Grant/research support from: This study was supported by an unrestricted grant from Pfizer
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**FRIDAY, 10 JUNE 2016**

## Biomarkers: powerful or powderpuff?

### OP0263 SYNOVIAL B-CELL GENE SIGNATURE PREDICTS RESPONSE TO RITUXIMAB THERAPY

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**Background:** Predicting response to biologic therapies in RA remains a clinical challenge. The anti-CD20 monoclonal antibody Rituximab effectively depletes peripheral blood B-cells, however response rates are approximately 60%. We hypothesized that expression of CD20 in diseased tissue may be an important predictor of response, since up to 40% of patients have few/no B-cells present in the synovium.
**Objectives:** To ascertain whether a synovial B-cell gene signature can enhance prediction of responsiveness to Rituximab therapy and identify genes involved in response/non-response to treatment.
**Methods:** Synovial tissue was obtained using ultrasound-guided synovial biopsies from 20 patients with active RA who were treated with Rituximab therapy after failure of conventional DMARD and anti-TNF therapy. High-throughput quantitative real-time PCR for 190 genes was performed in collaboration with MedImmune (MedImmune, LLC) using the Fluidigm platform. Samples were classified as B-cell "rich" or "poor" according to levels of MS4A1 expression. Using an empirical Bayes statistical model, a further 17 significant ($p<0.05$) genes were identified to create a baseline B-cell gene expression signature. Hierarchical clustering and receiver operating characteristic curve analysis was used to assess ability to predict EULAR criteria response at 16 weeks. Gene expression was compared pre- and post-treatment in responders versus non-responders and correlated with delta DAS-28. Logistic regression with backward and forward selections using AIC was applied to identify further predictive models.
**Results:** Seventeen genes were identified that clustered with MS4A1 expression to create the B-cell signature. Fifteen of these are directly involved in B-cell and plasma-cell signaling or differentiation pathways and immunoglobulin synthesis. Two genes identified within this signature play a pivotal role in antigen presentation and TH17 differentiation. The baseline B-cell signature had an area under ROC curve (AUC) of 0.87 (95%CI 0.76–1.0) to predict response to Rituximab therapy at 16 weeks. Three additional genes were identified segregating responders from non-responders; that when combined with the baseline B-cell signature the AUC improved to 0.95. Additionally, ten genes were identified that significantly correlated with delta DAS-28. High expression of genes involved in the formation of ectopic lymphoid structures and the TH17 lineage correlated with non-response to Rituximab therapy (all $p<0.05$).
**Conclusions:** This study shows that a B-cell rich gene signature has high sensitivity to predict response to Rituximab therapy. High expression of TH17 related genes correlates with non-response to B-cell depletion, indicating that in a subset of patients, these pathways may play a more pivotal role in disease pathogenesis. The observed high expression of ELS associated genes in non-response may relate to variable synovial B-cell depletion; disruption of these follicles may be the key to response, particularly with repeat cycles. These findings warrant confirmation in a larger cohort of patients; however they strongly support the notion that a stratified approach to treatment relies upon the identification of biomarkers, both in the synovium and peripheral blood that reflect heterogenous molecular disease pathways in RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5428

### OP0264 RELATIVE FREQUENCIES OF CIRCULATING T FOLLICULAR HELPER AND T FOLLICULAR REGULATORY CELLS IN AUTOIMMUNE PATIENTS AND HEALTHY CONTROL DONORS AND THE EFFECT OF DISEASE MODULATING THERAPY

A.J. Macdonald[1], K. Cerosaletti[2], J. Chen[2], T.-S. Nguyen[2], S. Posso[2], G. Marchesini[2], M. Abashian[1], A.P. Martin[1], D. De Rosa[1], T. Samanta[1], J. Poorbaugh[1], R.J. Benschop[1], J. Buckner[2]. *[1]ELI. LILLY & Co, Indianapolis; [2]Benaroya Research Institute, Seattle, WA, United States*

**Background:** T follicular helper cells are critical in the formation of autoantibody-producing ectopic germinal centers in seropositive autoimmune diseases and have attracted interest as potential biomarkers of autoimmune disease activity. A further subset with regulatory properties (Tfr) has also been described but, as yet, not well characterized in autoimmune diseases.
**Objectives:** The purpose of this study was to (1) determine the frequencies of Tfh in a range of autoimmune diseases by flow cytometry and a new commercially available Tfh epigenetic marker assay, (2) ascertain if Tfr frequencies vary among AI diseases, (3) determine effect of treatment on Tfh/Tfr frequencies in the autoimmune groups.
**Methods:** Patients were recruited from the Rheumatology or Neurology clinics at the Virginia Mason Clinic in Seattle WA. Healthy controls were recruited from the Seattle community. AI samples were selected regardless of length of disease or therapy; healthy control samples were matched with AI samples for age, gender and race. Cryopreserved peripheral blood mononuclear cells (PBMC) from 50 each of systemic lupus erythematosus (SLE), systemic sclerosis (SSc), multiple sclerosis (MS), rheumatoid arthritis (RA) and healthy volunteers (HV) were analyzed by multicolor flow cytometry for Tfh and Tfr frequencies. Tfh frequencies were also analyzed by a PCR-based assay from Epiontis GmbH, Germany. Initial experiments established that results obtained from fresh versus frozen PBMC were not significantly different. Relative frequencies of Tfh and Tfr were compared among disease/control groups, and in relation to disease activity and concurrent therapies – none, DMARDs, depleting (biologics, Cytoxan, MMF)
**Results:** Elevated frequencies of Tfh were seen in SSc, MS and RA compared with healthy controls, but not in SLE. TFh counts by flow cytometry and Epiontis epigenetic assay were significantly correlated within groups and globally. Tfr percentages were increased in RA, SSc and SLE compared with healthy controls, and the ratio of Tfh/Tfr was reduced in SLE compared with the other study groups. Tfh frequencies were positively correlated with inflammation (ESR) in SLE. Depleting therapy reduced Tfh and/or Tfr frequencies in patients with SLE and SSc.
**Conclusions:** A novel epigenetic marker assay to count Tfh proved to be robust and correlated well with flow cytometry counts. This supports the use of the PCR-based epigenetic marker assay as a replacement for multi-color flow cytometry. This would facilitate standardization of Tfh counts in clinical trials and studies where multiple sites are involved. A range of Tfh and Tfr frequencies were observed in the peripheral blood of patients with autoimmunity, but levels were significantly elevated in SSc, MS and RA patients. In SLE patients, Tfh levels correlated with ESR values and may be indicative of ongoing inflammation. Tfh and/or Tfr levels in SLE and SSc may be modulated though the use of biologics or cytotoxic therapies and further longitudinal studies are indicated.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3344

**FRIDAY, 10 JUNE 2016**

## The role of nuclear medicine in rheumatology

### OP0265 FEVER OF UNKNOWN ORIGIN (FUO) AND INFLAMMATION OF UNKNOWN ORIGIN (IUO): IS 18F-FDG-PET/CT A USEFUL FIRST LINE DIAGNOSTIC STRATEGY?

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**Background:** Fever of unknown origin (FUO) and inflammation of unknown origin (IUO) are rare but diagnostically challenging clinical problems. Because of the abundance of differential diagnoses, a generally accepted diagnostic guideline has not yet been established. Besides a thorough medical history, physical examination, and laboratory testing, imaging techniques are important tools in the diagnostic workup of FUO and IUO. In the last few years, $^{18}$F-FDG-PET/CT has been found to be a suitable diagnostic tool for FUO/IUO, as it is able to detect inflammatory and malignant processes with a high spatial resolution.
**Objectives:** The present study is carried out at to quantify the utility of $^{18}$F-FDG-PET/CT for the diagnosis of FUO and IUO. The study, moreover, evaluates special clinical markers, that increase the possibility of diagnosing FUO or IUO with a $^{18}$F-FDG-PET/CT.
**Methods:** All patients presenting with FUO or IUO at the University Clinic of Erlangen between 2007 and 2015 were clinically documented and subjected to $^{18}$F-FDG-PET/CT scanning. $^{18}$F-FDG-PET/CT scans were considered positive when a focal uptake of the tracer was detected additionally to the standard areas of physiological tracer uptake. $^{18}$F-FDG-PET/CT results were compared to the final diagnosis and classified as helpful or non-helpful in establishing the final diagnosis. Multivariate logistic regression was used to identify clinical parameters that correlated with a helpful $^{18}$F-FDG-PET/CT in patients with and without FUO as well as in patients with and without IUO.
**Results:** Of the 240 patients enrolled 72 presented with FUO, 142 with IUO and 26 did not fulfill FUO or IUO criteria. 235 patients were included in the multivariate logistic regression model. Final diagnosis was established in 190 patients (79.2%). In 136 (56.7% of all patients and 71.6% of the patients with a diagnosis), the $^{18}$F-FDG-PET/CT was helpful in finding the diagnosis. The chance was higher in patients without fever (p=0.003), those aged >50 years (p=0.002; p=0.005, respectively) and those with a CRP level >30 mg/dl (p=0.003; p=0.008, respectively).

| Category | N (%) FUO patients in category | N (%) IUO patients in category | N (%) non-FUO/IUO patients in category |
|---|---|---|---|
| Infection | 11 (15.3%) | 17 (12.2%) | 0 (0%) |
| Malignancy | 5 (6.9%) | 11 (7.9%) | 2 (8.0%) |
| Chronic inflammatory diseases | 35 (48.6%) | 86 (61.9%) | 10 (40.0%) |
| Miscellaneous | 1 (1.4%) | 2 (1.4%) | 6 (24.0%) |
| No diagnosis | 20 (27.8%) | 23 (16.5%) | 7 (28.0%) |
| Total | 72 (100%) | 142 (100%) | 26 (100%) |

**Conclusions:** Our study shows that if the standard diagnostic tests (laboratory, chest x-ray and abdominal ultrasound) did not identify the cause of FUO/IUO, $^{18}$F-FDG-PET/CT scanning should be applied in the early stage of the diagnostic

process. An early use of an $^{18}$F-FDG-PET/CT is especially helpful to establish a final diagnosis in patients with an elevated C-reactive protein and age over 50 years.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2255

### OP0266 BASELINE 89ZR-RITUXIMAB PET MAY PREDICT THERAPEUTIC RESPONSE 24 WEEKS AFTER INITIATION OF RITUXIMAB TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS

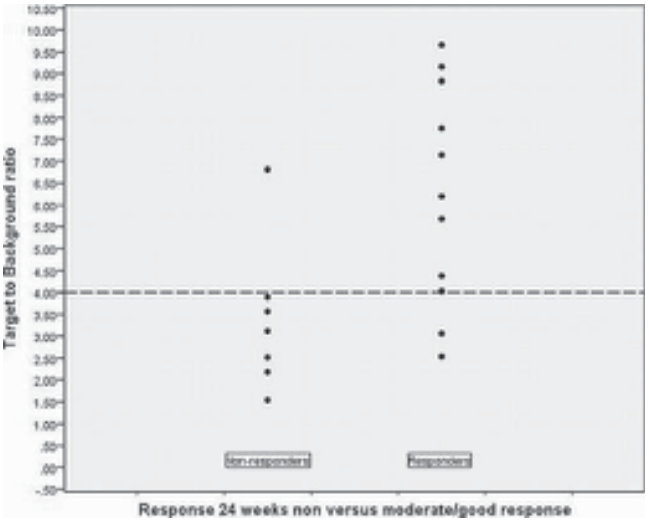
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**Background:** Rituximab (RTX) is an effective treatment of rheumatoid arthritis (RA) after failure or intolerance to TNF blockers. Nevertheless, still 30–50% of RA patients does not respond. Therefore, identifying patients with favourable response to RTX is important in order to further optimize treatment for the individual patient. *In vivo* imaging of biodistribution of radiolabelled RTX in RA by Positron Emission Tomography (PET) might provide a tool to fulfil this unmet clinical need.

**Objectives:** To investigate the association of *in vivo* biodistribution of Zirconium-89 (89Zr-)RTX in RA patients starting with RTX treatment and clinical response at 24 weeks post injection (p.i.).

**Methods:** We included 20 anti-B cell therapy naïve RA patients (female18/20; age 53±11; DAS28 5.4±1.2) who started RTX treatment according to standard clinical protocol (without methylprednisolone). The first RTX infusion (1000 mg) was directly followed by infusion of 10 mg-18 MBq 89Zr-RTX. Whole body and PET-CT images of wrists/hands (n=22 joints/patient) were performed three days p.i. After 24 weeks of therapy, response was defined according to the EULAR response criteria (DAS28 at endpoint $\leq$5.1 and/or deltaDAS28$>$0.6) (1). 89Zr-RTX uptake was assessed visually (blinded for clinical data) and quantitatively by drawing volumes of interest (VOI) on PET positive tissues/joints. Standardized uptake values (SUVs) were calculated and background ROIs were drawn on metacarpal bone to calculate target-to-background (T/B) ratios.

**Results:** At 24 weeks 13/20 patients were moderate to good responders to RTX. Whole body PET images showed 89Zr-RTX distribution in liver, spleen, kidneys, blood pool, lymph nodes (LN) (9/20pts) and in shoulders/elbows (9/20pts), without statistically significant SUV differences between responders and non-responders. Detailed hand images showed PET positive joints in 18/20 patients (ranging 1–20 joints/patient). Clinical responders had significantly higher 89Zr-RTX uptake in visually positive joints than non-responders (SUV: 3.2±1.4 vs 2.1±1.1 [p=0.04]; T/B ratios 6.2±2.5 vs. 3.4±1.7 [p=0.015], respectively). Using a T/B cut-off value of 4.0, positive predictive value and negative predictive value for response were respectively 90% and 75%, at a sensitivity of 82% and specificity of 86% (Fig 1). In contrast, no association was found between any clinical disease or serological (including a-CCP/RF) parameters and clinical response at 24 weeks.




**Conclusions:** 89Zr-RTX PET-CT clearly visualizes arthritic joints in RA patients. Significant differences in baseline quantitative 89Zr-RTX uptake in PET positive hand joints were found between responders and non-responders to RTX treatment at 24 weeks. Our data point at a promising clinical value of 89Zr-RTX PET to predict at baseline the therapeutic response to RTX and therefore has potential for stratification of RTX treatment in RA. Further validation is required in larger cohorts.

**References:**

[1] Van Gestel et al; Arthritis Rheum 1998

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**FRIDAY, 10 JUNE 2016**

## PROMs/PROs in rheumatological research - time for a critical appraisal?

### OP0267-HPR A SURVEY OF PATIENT REPORTED EXPERIENCE, PATIENT REPORTED OUTCOME AND WORK IN PATIENTS WITH INFLAMMATORY ARTHRITIS SEEN IN NURSE LED RHEUMATOLOGY CLINICS IN THE UK

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**Background:** Measuring patient experience (PREMs) and Patient reported outcomes (PROs) in the health care setting have become a priority in health care in the past 5 years. Collection of these measures enables quality, safety and value of care delivered to be demonstrated. In response to a need to collect patient outcomes both the National Rheumatoid Arthritis Society and the British Society for Rheumatology in the UK have devised PREMs and PROs questionnaires to support the commissioning, provision and performance of rheumatology services. Additionally the British Society for Rheumatology is piloting these questionnaires across the UK as part of the Health Quality Improvement Programme (HQIP).

**Objectives:** The WMRNSN piloting PREMS, PROs and Work questionnairs in clinic practice. To demonstrate quality of care provided and identifying gaps quality of patient care.

**Methods:** The format of the questionnaire following approval by a local rheumatology patient group and research and development approval obtained from 7 hospital Trusts across the West Midlands. The questionnaire was then used to survey 309 inflammatory arthritis patients seen in rheumatology nurse led clinics during May – July 2015. Patients completed and submitted the questionnaire anonymously following a clinic visit and the author extracted and analysed the data.

**Results:** The WMRNSN have shown 309 patients with inflammatory arthritis seen in rheumatology nurse led clinics had a positive experience of care in the past year. Negative experiences were patients reporting not being aware of the following:

1. Referral to other members of the multidisciplinary team was available
2. Information available was available about UK based national support groups
3. There was opportunity to attend a self- management course
4. Family members could attend consultations to help them make treatment decisions
5. They could discuss personal and intimate issues.

Patient reported if appointments were suddenly cancelled or if they needed to be seen sooner they wait 4 weeks or more to be seen. A third of patients reported poor disease control preventing them from managing day to day which was concordant with the PROs visual analgoue scores which were on average 4.9 or great for pain, sleep, fatigue, physical disability, emotional wellbeing, physical well being and pain. The work questionnaire reported unhelpful data in that; the age ranges do not reflect working ages within the UK nor identify the nature of work e.g. Studying, working from home, raising children, homemakers or retired. Additionally it does not capture hours worked or the difficulties experienced by patients regarding work. A fact sheet has been developed by the WMRNSN to provide patient information on these issues.

**Conclusions:** We suggest collection of PROMS and work data is more useful to patients when used individually during their appointment. The Trusts who took part have their results and as evidence for nurses' revalidation. Finally PREMS, PROs and Work data we recommend routinely collecting this data to demonstrate quality, improve patient experience and health outcome. Resources and IT needs to be available to facilitate this.

**References:**

[1] BSR http://www.rheumatology.org.uk/resources/audits/national_ra_audit/information_pack.aspx

**Acknowledgement:** Thanks to the 7 particpatint Trusts and the West Midlands Rheumatology Nurse Specialist Network

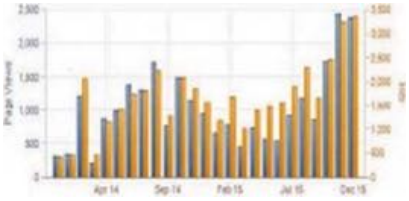
**Disclosure of Interest:** None declared

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OP0268 **THE EULAR OUTCOME MEASURE LIBRARY, AN EVOLUTIONAL DATABASE OF VALIDATED PATIENT-REPORTED OUTCOMES: USE AND DISSEMINATION IN THE FIRST TWO YEARS**

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**Background:** Patient reported outcomes (PROs) are being more frequently used in rheumatology to evaluate treatment response and to guide clinical decisions. In order to standardize and enhance the use of these measures a structured database including the main cross-culturally validated PROs in rheumatic and musculoskeletal diseases was developed: the EULAR Outcomes Measure Library (OML)[1]. This is an in-progress library led by rheumatologists freely available online since November 2013 (http://oml.eular.org/) and connected to the main EULAR website.
**Objectives:** To evaluate the use and dissemination of the EULAR OML during the first two years of functioning.
**Methods:** The EULAR OML includes to date 138 measures covering any domain of health identified through systematic reviews. The PROs are generic (across diseases) or specific, being the most represented diagnosis rheumatoid arthritis (RA) (33 instruments), osteoarthritis (OA) (27), spondylarthritis (23), fibromyalgia (21), systemic lupus (20), low back pain (15), osteoporosis (12), and juvenile idiopathic arthritis (6). The PROs search can be performed by disease, domain, or language. All PROs are validated at least in English but versions in other languages are also included being the most frequent cross-validated versions in French (54 instruments), Spanish (53), Dutch (49), and German (46). A glossary with validation aspects is available for educational support. The OML is regularly updated using search strategy alerts in PubMed and based on a network of volunteers, who may propose the inclusion of new instruments. A summary of the statistics of the website is presented.
**Results:** Over the first two years, the OML has been increasingly used with an accumulated 41,641 page views and 25,926 visits (Figure). The mean of visits per month is 571 with a mean of 333 new visitors per month. Tuesdays and Wednesdays are the peak days for visits. The PROs being downloaded most frequently are: the evaluation of ankylosing spondylitis quality of life (EASI-QOL) (11.6%), the multidimensional health assessment questionnaire (MDHAQ) (8.8%), the RA quality of life scale (RAQoL) (7.4%), and the Western Ontario McMaster OA index (WOMAC) (3.4%). The devices more frequently used are iPad (42%), android (31%), and iPhone (26%). The European countries with most users are France and Germany (15% each), The United Kingdom (13.7%), Ukraine (9.4%), and Spain (6.7%). Other non-European countries are also users of the Library, in particular the United States of America (19.8%), and China (12.5%).



**Conclusions:** The use of the EULAR OML freely available website is increasing over time. This website includes a detailed description of each instrument, recommendations for use, information about validation, and versions in different languages. There are many instruments that still need to be included. We expect that unified access to this information will contribute to a better use of PROs. We invite everyone to contact us if willing to contribute to keep the EULAR OML updated and useful.
**References:**
[1] Castrejon I, Carmona L, Agrinier N, et al. Clin Exp Rheumatol 2015;33:910–6
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2377

**FRIDAY, 10 JUNE 2016**

## Collaboration for success. User-centred design for improvement of health services

OP0269-HPR **PATIENT PARTICIPATION IN MULTIDISCIPLINARY TEAM CARE: VIEWS OF PATIENTS AND HEALTH CARE PROFESSIONALS**

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**Background:** A hallmark feature of multidisciplinary team care is patient-centeredness; every aspect of patient's health status is systematically evaluated and the treatment goals and plans for interventions are jointly set, evaluated, attuned.[1] But the perceptions and values of patients and health care professionals (HCPs) about the role and degree of active involvement of patients in team care has received little attention.
**Objectives:** To explore patients' and HCPs views on the meaning and role of patient participation in team care, and to explore the experiences of patient membership in team conference.
**Methods:** This study was conducted before and after the introduction of patients in team conference. To explore the views about patient participation semi-structured face-to-face interviews were held with 10 patients with rheumatic diseases eligible for or participating in multidisciplinary treatment and 12 HCPs. After the introduction of patients' membership in the team conference, telephone interviews with 8 patients and a focus group (n=5) with HCPs were held. The interviews and the focus group were audiotaped and described verbatim. Thematic content analysis of the interviews were performed by two researchers independently and discussed until consensus was reached. Similarly, data of the telephone interviews and focus group were analysed and identified topics were discussed by a rheumatology nurse and a researcher.
**Results:** Participants described patient participation in terms of an active participatory behaviour of the patient (e.g. willingness to change, motivation, asking questions, expressing their own opinions, treatment adherence), an open respectful dialogue between patients and HCPs based on trust and equality, and (shared) responsibility of treatment. Participants indicated that patients' involvement in team care varied, from passive receiver to meaningful exchange between patients and HCPs. Opportunities for improvement were identified: improving information about the treatment, facilitating patient involvement in goal-setting, planning and evaluation of treatment, and stimulating patient's responsibility of care. After the introduction of patients in team conference, the evaluation of patient membership revealed that although some patients felt tense the atmosphere felt safe and they experienced a honest, transparent and respectful interaction between themselves and HCPs. Patients felt they were taken seriously and that their needs were taken into account, the treatment goals were set in mutual agreement and the resulting therapeutic interventions were clear and satisfactorily. HCPs valued patient's membership in team conference, although they needed to get used to it. HCPs experienced an open, honest and truthful team dialogue and a truly shared treatment plan leading to more patient commitment to treatment. The limited time, prior to team conference, to formulate a draft treatment plan to be discussed during the team conference, was seen as a disadvantage, especially in complex cases.
**Conclusions:** Patients and HCPs highly valued patient's membership in the multidisciplinary team conference. Treatment plans were developed in partnership between patients and HCPs, and team interaction was based on mutual trust and respect. This study underscores the value of stimulating partnership in team care.
**References:**
[1] Vliet Vlieland et al. (2006). Does everybody need a team? J Rheumatol 33(9): 1897–9.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2171

**FRIDAY, 10 JUNE 2016**

## ER stress & rheumatic disease

OP0270 **TARGETING IL-23 CAN ATTENUATE PROGRESSION OF SPINAL ANKYLOSIS IN ANKYLOSING SPONDYLITIS**

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**Background:** IL-23 has been implicated in the development of ankylosing spondylitis (AS). The role of IL- 23 in AS pathogenesis has emerged as a therapeutic target. This study aimed to clarify that anti IL-23 blockade can prevent progression of bony ankylosing in AS patients.
**Objectives:** We investigated endoplasmic reticulum (ER) stress and IL-23 cytokine could play a role in human bone-derived osteoblast cells and blocking it leads to regulation of bone-related genes and/or preventing bone ankylosis in AS.
**Methods:** Primary human osteoblast cells were isolated from diced bones of facet joints which were taken from surgical operation of 8 AS patients and 8 healthy controls (HC). The tissues of facet joints in AS were stained and compared with those of HC. Osteoblast differentiation- and ER stress-related genes were determined by quantitative RT-PCR, immunoblotting, immunofluorescence, and immunohistochemistry. Osteoblast activity of all bones-derived osteoblast cells was confirmed by Alkaline Phosphatase activity (ALP) and Alizarin Red (ARS) staining. The ER stress by BIX, selective BIP inducer X, in the regulation of IL-23 expression and secretion was evaluated by quantitative RT-PCR and ELISA.
**Results:** We found that elevated RUNX2, BIP, and IL-23 protein expressions were observed at osteoblast cells in human AS compared to HC. In addition, mRNA levels of bone differentiation (ALP, BMP2, COL1A, RUNX2, C/EBPβ, OPG, and OCN) and ER stress (BIP and CHOP)-related genes were highly expressed in human AS. In particular, IL-23 and RUNX2 expressions were

significantly increased in AS. BIX-mediated ER stress stimulated induction of osteoblast activity and IL-23 secretion via modulating RUNX2 and C/EBPβ genes. Intriguingly, RUNX2 Knockdown by shRNA impeded ER stress-induced effects. Moreover, osteoblast activity and RUNX2 expression in AS were significantly reduced by IL-23 blockers, but not TNFα blockers.
**Conclusions:** This is the first report to show that ER stress, osteoblastic activity, and IL-23 expression in AS were increased compared to HC, suggesting that sustained ER stress induces osteoblast activity and IL-23 expression. Notably, these effects in AS were reduced by IL-23 blockade. Taken together, our results supported that blocking IL-23 may represent a promising therapeutic target to assist and prevent bony progression in AS.
**Disclosure of Interest:** None declared
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### OP0271 PERK PATHWAY CHARACTERIZATION IN LABIAL SALIVARY GLANDS OF SJÖGREN SYNDROME'S PATIENTS: COULD IT BE AN ADAPTIVE RESPONSE?

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**Background:** Labial-salivary-glands (LSG) of Sjögren's syndrome (SS) patients show an altered exocytic route that can induce endoplasmic reticulum (ER)-stress and activate the unfolded-protein-response (UPR)[1,2]. UPR helps to recover and preserve cellular homeostasis, reducing the load of unfolded proteins in the ER, through various mechanisms of cell survival. UPR is mediated by the activation of IRE1α, PERK and ATF6 sensors.Chronic activation of ER-stress sensors exhibits a time course-kinetics with attenuation of IRE1α pathway and sustained signaling of PERK and ATF6 pathways[3]. We have observed in SS-patients a decrease of IRE1α pathway activity[4] and an increase of ATF6 pathway activity[5].
**Objectives:** Considering that PERK pathway reduces levels of unfolded proteins by increasing expression of pro-survival or pro-apoptotic components, here our purpose was to evaluate the expression of PERK pathway components and its relation with an adaptive response of LSG from SS-patients.
**Methods:** RNA and proteins were extracted from LSG of 11 SS-patients and 12 controls. Expression of PERK pathway components was determined by q-PCR and Western-blot. Localization was addressed by immunofluorescence.
**Results:** Compared to controls, LSG of SS-patients showed a significant increase of pPERK/PERK ratio but no changes of peIF2α/eIF2α ratio. Also, an increase of ATF4 and CHOP protein levels were observed, which correlated with clinical parameters including scintigraphy and serology. On the contrary, significantly decreased expression of ERO1α, PDIA1 and PDIA4 (proteins involved in protein folding), and NRF2 (transcription factor) protein levels, an additional PERK substrate involved in the response to oxidative stress, were detected. Interestingly, SS-patients showed a significant increase of expression of Xc- system subunits, which is involved in glutathione synthesis. PERK, ERO1α, PDIA1, PDIA4, eIF2α and peIF2α were located in the basal cytoplasm of acinar cells, while eIF2α and peIF2α were also observed in the nucleus. NRF2 localized in cytoplasm and lateral plasma-membrane, next to E-cadherin.
**Conclusions:** PERK pathway is activated in LSG of SS-patients and controls; indicating that both are developing UPR. Considering that ATF4 mediates an integrated response to cellular stress[6], its increased expression in SS-patients and its correlation with clinical data and $Xc^-$ expression, suggest that ATF4 could be part of an adaptive response against cellular stress. In addition, expression of ERO1α, PDIA1 and PDIA4 suggests alterations of the protein folding process. Finally, NRF2 protein levels and its location suggest an altered oxidative stress response.
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**Acknowledgement:** Supported by Fondecyt-Chile [#1120062] (MJG, SA, CM, SG), PhD fellowship Conicyt-Chile (MJB and JC).
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**FRIDAY, 10 JUNE 2016**

## Joint EULAR - EFIS session: Do stromal cells house and cure immune cells?

### OP0272 IDENTIFICATION OF NEW INHIBITORS OF ANGIOGENESIS IN A NOVEL 3D MODEL OF RHEUMATOID ARTHRITIS SYNOVIAL ANGIOGENESIS

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**Background:** Angiogenesis contributes to rheumatoid arthritis (RA) pathogenesis, however, many models focus solely on endothelial cells (EC). We developed a 3D-spheroid model including both EC and RA fibroblast-like-synoviocytes (FLS) to study angiogenesis associated with RA and to test the efficacy of several inhibitors targeting this process. Previous work demonstrated a role for the non-canonical NF-κB pathway and its main regulator, NF-kB inducing kinase (NIK), in pathological angiogenesis and thus we aim to use the 3D model to further characterize its contribution to neovascularization.
**Objectives:** Generate a representative 3D *in vitro* model of RA synovial angiogenesis and screen the effects of targeting the non-canonical NF-κB pathway using siRNA or small molecule pharmacological inhibitors.
**Methods:** Human primary EC were co-cultured with RA FLS after pre-incubation with cell tracker dyes and incubated overnight to form spheroids. Subsequently, spheroids were plated in collagen gel and stimulated with 10% RA SF, growth factors (GF) or well-known activators of non-canonical NF-kB signaling (lymphotoxin beta (LT) or LIGHT). To establish NIK dependency, EC were pre-transfected with NIK-targeting siRNA before incorporation into spheroids. Furthermore, several pharmacological inhibitors were screened for their ability to block sprout formation. Spheroids were imaged by confocal microscopy and quantified using Leica QWin Plus software.
**Results:** We established a robust 3D model of angiogenesis containing both EC and RA FLS. LT, LIGHT, RA SF and GF stimulations led to significant increases in sprout formation as compared to basal conditions ($p<0.05$). The LT and LIGHT induced sprout formation proved to be NIK dependent as spheroids containing EC transfected with NIK targeting siRNA had significant reductions in vessel formation as compared to the non-targeting controls ($p<0.05$). Sprouting promoted by GF and RA SF was significantly blocked by the angiogenesis inhibitor Anginex ($p<0.05$). Finally, targeting of the non-canonical pathway using a small molecule pharmacological NIK inhibitor significantly reduced sprout formation caused by LT and LIGHT, and importantly also RA SF-induced sprout formation ($p<0.05$).
**Conclusions:** We developed a novel 3D model that incorporates essential elements of synovial inflammation, namely EC, RA FLS and RA SF, which proves to be an effective tool for studying synovial angiogenesis. Using this system, we have further demonstrated a role for the non-canonical NF-kB pathway, and its central regulator NIK, in neovascularization associated with RA. Moreover, we have shown that the 3D model is useful for testing small molecule inhibitors of angiogenesis and found that targeting non-canonical NF-kB signaling is an effective method to block pathological angiogenesis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3481

### OP0273 EFFECTS OF TUMOR NECROSIS FACTOR ALPHA ON CYTOKINE SECRETION OF SYNOVIAL FLUID-DERIVED MESENCHYMAL STEM CELL-LIKE CELLS

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**Background:** Rheumatoid arthritis is characterized by painful joint swelling, cartilage and bone destruction, chronic inflammation of the synovium (synovitis) with the accumulation of synovial fluid into the joint cavity. Within the synovial fluid the number of MSC-like cells (SYF-MSC) is increasing during the active phase of the disease. MSC are able to mediate immunosuppression via cell-cell contact and secreted factors respectively.
**Objectives:** Our goal was to screen the secreted proteins by SYF-MSCs under pro-inflammatory conditions.
**Methods:** Synovial fluid was harvested from patients with active RA (according to the Guidelines of the Helsinki Declaration). The isolated fluid/cells were cultured *in vitro,* their expression of well-known MSC markers as well as their differentiation potential was tested. SYF-MSCs were treated with human recombinant TNF alpha (TNFa) for 24 hour than the secreted cytokines were determined by high throughput protein array.
**Results:** SYF-MSCs secreted aggrecan, angiogenin, chitinase 3 like-1, Dkk-1, DPPIV, EMMPRIN, FGF-19, GM-CSF, IGFBP-3, IL-6, IL-17A, MCP-1, PDGF-AA, Pentraxin-3, Resistin, SDF-1α and Thrombospondin-1 under normal condition. Treatment by TNFa decreased the level of the secreted chitinase 3 like-1 (544003±56200.85; Pixel density, Mean±SD) and Dkk-1 (388062.5±10488.51) compared to untreated controls (721671.5±10434.77 and 705830±16013.14).

Beside this phenomenon the pro-inflammatory provocation increased the secretion of IL-6 (from 79140±6940.96 to 615191±73256.26), MCP-1 (283985.5±25964.25 to 846348±81354.05), furthermore induced the release of IL-(8743315±71580.42) IL-24 (32189±29555.65) and RANTES (641698±26383.57). Unlike untreated cells no resistin, empirin and SDF-1 could be detected after TNFa exposure.
**Conclusions:** The *in vitro* data suggest that TNFa is able to turn SYF-MSCs to a pro-inflammatory phenotype, which may play a role in the inflammatory processes of RA prolonging the active phase of the disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1359

**FRIDAY, 10 JUNE 2016**

## Role of imaging in childhood-onset rheumatic diseases

### OP0274 QUANTIFICATION OF DYNAMIC MRI EXAMINATIONS IN JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** In chronic inflammatory conditions, the need for a more objective measurement of disease activity has been identified. Imaging biomarkers based on the automated quantification of dynamic contrast enhanced magnetic resonance images (DCE-MRI) have been studied in adult patients with rheumatoid arthritis (RA)[1]. In children with juvenile idiopathic arthritis (JIA) similar knowledge is very limited.
**Objectives:** To compare treatment changes of clinical scores in patients with JIA and automated DCE-MRI quantitative parameters analysed with a dedicated software - Dynamika[tm].
**Methods:** In 8 Caucasian patients (7 girls, median age 13,6 years) with polyarticular JIA, who underwent standardized DMARD treatment, DCE-MRI of the metacarpophaleangeal (MCP) 2–5 joints in the most affected hand were performed at 3 time points: baseline (BL), month 3 and 6 of treatment using 0.2 Tesla Esaote C-Scan. Clinical scores included active joints (AJ), swollen joints (SJ), tender joints (TJ) and joints with limited range of motion (LJ) divided into 3 levels: joint level (the MCP), region level (the hand) and global level (all joints). DCE-MRI were analyzed using a region of interest covering synovium of MCP 2–5. Output parameters included DEMRIQ-ME (Maximum Enhancement) and -IRE (Initial Rate of Enhancement). DEMRIQ is a perfusion/inflammation imaging biomarker and combines the volume of synovial inflammation (GD-map based statistics) and the degree of perfusion (ME-map or IRE-map based statistics), either as volume (classified pixels) or intensity (ME/IRE) or a combination of both (DEMRIQ score).
Differences in DEMRIQ scores between visits, were analyzed using the t-test ($p<0.05$ = statistically significant, $p<0.25$ = clinically meaningful). Correlations were also assessed using the Pearson's Correlation Coefficient.
**Results:** At 3 months all patients showed statistically significant and/or clinically meaningful changes mainly in DEMRIQ-ME, 6 patients in parallel with clinical improvement. Two patients worsened in DEMRIQ-ME despite clinical improvement. At 6 months, six patients continued clinical improvement. In all but one, DEMRIQ-ME persisted or worsened (compared to previous examinations) and patients had a clinical flare within 2 to 6 months after last DCE-MRI. One patient had persistent clinical activity with corresponding DEMRIQ-ME score. Another patient showed clinical worsening and improvement in DEMRIQ-ME, where clinical improvement followed later during disease course. Thus a persistent/rising DEMRIQ-ME compared to previous examinations predicted clinical flare in a timeframe between 2 and 6 months after last DCE-MRI, despite of global clinical improvement.
**Conclusions:** Dynamika based scores (mainly DEMRIQ-ME) show to be useful for depicting disease activity in JIA. In particular, the DEMRIQ-ME correlated with clinical activity over time especially after 3 months. Moreover, persistence or worsening of Dynamika based scores could predict clinical flares (in this study within 2–6 months) despite of global clinical improvement. Dynamika based DCE-MRI calculations could be of high importance for disease management and a supportive tool in treatment decisions in pediatric rheumatology.
**References:**
[1] Eur J Radiol. 2010 Jun;74(3):e67–72.
**Disclosure of Interest:** N. Tzaribachev Grant/research support from: UCB, Janssen, Pfizer, Roche, R. Hagoug Employee of: Image Analysis Ltd, P. Louka Employee of: Image Analysis Ltd, C. Trentin Employee of: Image Analysis Ltd, O. Kubassova Employee of: Image Analysis Ltd, M. Hinton Employee of: Image Analysis Ltd, M. Boesen: None declared
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### OP0275 PREVALENCE OF ULTRASOUND-DETECTED FINDINGS IN FOOT IN JUVENILE IDIOPATHIC ARTHRITIS VERSUS HEALTHY CHILDREN: ASSOCIATION TO PAEDIATRIC FOOT POSTURE

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**Background:** Foot problems have been reported in several JIA categories, even though children rarely complain symptoms. Besides synovitis, peri-articular manifestations have been associated with reduced joint ranges-of-motion and deformities. Musculoskeletal ultrasound (US) is more sensitive than clinical examination for detecting signs of inflammation. It becomes an accessible tool with an ongoing role on the foot care in JIA. Consequently, the clinical relevance of what is considered as a normal or pathological US finding needs to be more precisely clarified.
**Objectives:** 1. To determine and to compare prevalence of US-detected findings in JIA patients and healthy children. 2. To examine associations of foot US-findings to foot abnormalities using objective podiatry assessment.
**Methods:** Eighty-four children (168 feet), 29 children with a definitive diagnosis of JIA (ILAR criteria) and history of foot/ankle complains were recruited from the outpatient paediatric rheumatology clinic at our Hospital as well as 55 healthy children. The participants underwent clinical, podiatrist and US assessment. The sonographer, who was blinded to the clinical and podiatrist details, performed gray- scale and power Doppler (PD) bilateral evaluation at each site of study (8 joints, 8 tendons and 2 entheseal insertions per foot). Joint recess distension, tenosynovitis, abnormal echogenicity or thickening of entheseal insertion, and PD signal were assessment (dichotomous score: absence or presence). The podiatry assessment included the following measures: 1) footprint evaluation on podoscope, 2) the calcaneus relaxed position test (RCSP), 3) the foot postural index (FPI-6), 4) the standing heel-rise test (SHRT) the Jack test or Hubscher maneuver.
**Results:** The JIA group included 17 girls and 12 boys (mean age, 9.3 ± 4.6 years old), oligoarthritis was the commonest category and disease duration was 53.4 ± 49 months. No statistical differences were found for demographic characteristics between the two groups.
Forty-six children had at least one US abnormality (20, JIA and 26, control). Distension of the dorsal recess in the first metatarsophalangeal (MTP1) was the most frequently detected finding (32 JIA feet and 46 controls; 52% and 41.8% of feet in each group respectively) without statistical differences ($p>0.05$). The presence of distension of the anterior tibiotalar joint (TA) and anterior subtalar joint was always associated with the presence of disease. The presence of tenosynovitis and enthesitis was associated as well.
The podiatry assessment showed several findings: joint hypermobility of MTF1was frequently detected in the study population, mostly in JIA ($p=0,001$), and the association between abnormal FPI/ footprint and US findings (distension of the anterior subtalar and MTP2 joints) ($p<0.05$).
**Conclusions:** This study describes the prevalence and location of US findings in the paediatric foot. Distension of the MTP1 joint was quite common in childhood and it was associated to joint hypermobility. FPI seems to be associated with the presence of anomalies of TA, subtalar and MTP2 joints in children with JIA. Further studies are needed to confirm these results.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Physician-patient relationship in the era of interactive media

### OP0276 POSTGRADUATE RHEUMATOLOGY EDUCATION FOR HEALTH PROFESSIONALS IN RHEUMATOLOGY: AVAILABILITY, NEEDS AND BARRIERS

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**Objectives:** To explore the availability of postgraduate education for rheumatology health professionals (HPs) in Europe, to define HPs' educational needs, including Eular's role and its activities across Europe, and to identify potential barriers.
**Methods:** An interview guide to obtain information from national representatives of rheumatology HPs' organisations and an online survey for individual HPs were prepared by a team of HPs from multiple disciplines, two rheumatologists and a patient representative (Educational subcommittee of the Eular Standing Committee of Health Professionals in Rheumatology). The interviews were conducted by telephone or in person by members of the team. The English online survey was translated into Czech, Danish, French, German, Portuguese, Spanish, Swedish and Turkish. The interviews and survey comprised questions on: availability of postgraduate education, familiarity with Eular and its educational offerings, needs regarding the contents and mode of delivery of education and

potential barriers to participate in education (0–10 scales). Access information for (translated versions of) the online survey was circulated to national representatives of rheumatology HPs' organisations for dissemination among their contacts, to individual HPs who had once visited the Eular annual congress, and was announced on the EULAR Website and in the Eular HPs' newsletter.
**Results:** Interviews with representatives from 17 countries were conducted. Overall, the number of countries where postgraduate rheumatology education was reported to be available was 13/17 for nurses, 8/17 for physical therapists and 7/17 for occupational therapists, and 3 or less countries for other disciplines. There were 1041 responses to the online survey (216 English and 824 translated version), from 19 European countries. The mean (SD) age of the respondents was 41 (11) years, 897 (86%) were female. 545 (56%) were familiar with Eular, 201 (21%) had once or more attended the Eular annual conference, and 137 (14%) were familiar with Eular online courses. Educational need scores were highest for "Inflammatory arthritis" (6.5 SD 2.8) and "Connective Tissue Diseases" (6.5 SD 2.7) regarding content and for "Courses in English organised in own country" (5.7 SD 3.5) and "Eular online course" (5.7 SD 3.4) concerning mode of delivery. The most important perceived barriers to participate in educational offerings included "Lack of resources" (7.2 SD 2.8), "Lack of time" (5.8 SD 2.9) and "Lack of mastery of the English Language" (5.8 SD 3.4; Participants in translated survey only).
**Conclusions:** With the exception of education for nurses, there is a lack of postgraduate rheumatology education for HPs in the majority of countries. There are opportunities to raise familiarity with Eular and its educational offerings, with considerable interest in online courses and courses provided in HPs' own country with lack of English language skills being an important aspect to take into account.
**Acknowledgement:** This project was financially supported by Eular.
**Disclosure of Interest:** None declared
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### OP0277-PARE PATIENT RESEARCH PARTNERS INVOLVED IN A PROJECT TO ENHANCE DISEASE-ASSOCIATED COMMUNICATIONS SKILLS OF RHEUMATOID PATIENTS

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**Background:** Patients with chronic diseases often have to conduct conversations that are associated with their disease, either to pursue their own interests or to justify their personal restrictions. The ability to communicate with confidence may be considered a precondition for social participation. Because social participation is one of the key concerns of the Deutsche Rheuma-Liga (DRL), the DRL has funded a research project for enhancing the communication skills of people suffering from rheumatic diseases. The project involved key participation by DRL's- patient research partners (PRPs), who related their own communication limitations as well as providing input to the design of a novel programme of communication skill training. The experience gained and the various contributions of the PRPs will be presented.
**Objectives:** The aim of the project was the inclusion of PRPs in a scientific study that identifies, and subsequently seeks to enhance, those areas of life in which patients with rheumatic diseases experience the most problems during conversations.
**Methods:** PRPs were trained during a two-day interactive training course based on EULAR recommendations. Obstacles during disease-associated conversations were identified via an online questionnaire. The results of this analysis fed into a new programme of communication skills training.
**Results:** The PRPs felt they were being treated on equal terms and that they were being taken seriously by the researchers. Their proposals were implemented by the researchers, if possible, and they took part in all substantial meetings of the research project. The PRPs were actively involved in: i) the preparation of the information leaflet describing the online questionnaire; ii) the preparation of the online questionnaire itself; iii) designing the course of the interviews; iv) disseminating information about the study. Thereafter, the PRPs participated in: v) designing the various modules of the communication skill training; vi) the training handbook's preparation; vii) the information leaflets promoting and describing the skill training. Moreover, the PRPs will operate the first test runs of the skill training. Altogether, the participation in the research project was acclaimed as interesting and enriching by the PRPs.
**Conclusions:** The implementation of the patient's perspective through inclusion of the PRPs was successful and gave important impetus. The usefulness and effectivity of the new training programme will be evaluated in a future randomised, controlled trial.
**Acknowledgement:** The authors wish to thank the following patient research partners for participating in the study: R. Choijnacki, U. Garske and I. Kimmerle. We also thank the following investigators: J. Lamprecht, W. Mau, M. Schlöffel and A. Schöpf.
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## It's in your hands

### OP0278-PARE PATIENT EMPOWERMENT: NATIONAL ACTION WEEK WITH INFORMATIVE LECTURES IN LAYMAN'S TERMS FOR THOSE WHO ARE AFFECTED BY RHEUMATISM

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**Background:** Rheumatic diseases can cause significant restrictions for sufferers in virtually all aspects of everyday life. Those who are affected often feel like they are on their own with their symptoms. Information about their illness, treatment options and the responsibilities of corresponding specialists is often not issued in layman's terms. Studies have shown that patients who have received adequate information handle their illness better and are able to positively influence the progression of their illness [1].
**Objectives:** Patient Empowerment should be achieved by providing the patient with information about a) their illness, b) treatment options and c) specialists and contacts. Those who are affected should feel empowered as responsible patients to be able to participate in decision-making processes regarding the types of treatment available and to have a discussion with a doctor on an equal footing. Those who are affected should also be able to carry out movement exercises independently and integrate joint protection strategies into their everyday lives. What is more, a platform should be created for those who are affected, so that they can directly contact specialists, health professionals and others who are affected.
**Methods:** Rheumaliga Schweiz organises a National Action Week on a specific topic in September every year in several cities throughout Switzerland. Specialists (rheumatologists, surgeons, physiotherapists, occupational therapists, psychologists and others) offer information on specific symptoms and the treatment options available in layman's terms. The events are free of charge. The national office provides its member organisations with a concept for the event that has been compiled by a specialist group. The lectures are compiled by experts in their field and are adapted accordingly so that they are suitable for the general public. In this way, it is guaranteed that both up-to-date and technically flawless contents are presented at all events. Speakers are even on hand to offer personal advice to visitors during the breaks. Other specialists present their offerings at information stands. Emphasis is placed on regional roots both in terms of the speakers and the information stands.
**Results:** The National Action Week has become a fixed series of events for people who are affected by rheumatism in recent years. In the meantime, we have been able to organise approximately 15 events each year with the support of our member organisations. On average, each individual event is attended by 150 participants. This means that on the whole, over 2,200 people across Switzerland can benefit from an information event every year. In a survey carried out, 94% of participants stated that they had benefited considerably from the event.
Focussing the event in a period of a single week makes it possible to use resources sparingly on the one hand, whilst also facilitating media work.
**Conclusions:** Rheumaliga Schweiz will continue to hold an annual action week for people affected by rheumatism in the future. There is a good balance between the expenses incurred for this by Rheumaliga Schweiz and the benefits gained by those who are affected.
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**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## The EULAR School of Rheumatology - a new era of education

### OP0279 DEVELOPING AND RUNNING A RHEUMATOLOGY EMERGENCY SIMULATION COURSE

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**Background:** The UK Joint Royal College Of Physicians 2010 rheumatology curriculum states that "trainees should be able to diagnose, choose appropriate investigations, formulate an appropriate management plan, communicate effectively and involve appropriate specialities where necessary" [1].
However rheumatology emergencies are rare, and trainees may not get adequate exposure to be able to develop these competencies. A survey performed in the Yorkshire region (UK) showed that up to 62.5% of trainees were not confident in dealing with some emergency presentations.
Currently there are no simulation courses covering this aspect of training for rheumatology trainees.
**Objectives:** Our objective was to develop and run a pilot simulation course

for rheumatology trainees that will provide education in the identification and management of rheumatology emergencies, and aid development of non-technical skills.

**Methods:** Scenarios were developed and mapped against the curriculum requirements. They were run in a simulated ward environment using a high fidelity simulator. Faculty included one actor acting as ward staff, 2 senior simulation fellows, 1 technician, and 3 senior rheumatology Consultants.

5 scenarios were used in the pilot one day course run on the 1st May 2015. These were; Scleroderma renal crisis, methotrexate pneumonitis, acute lupus myocarditis, catastrophic antiphospholipid syndrome and ANCA positive vasculitis presenting with pulmonary haemorrhage. The running of the scenarios lasted 20 minutes, with debriefing taking between 30–40 minutes.

Delegates were provided with a reading pack at the end of the course, consisting of literature. Post course questionnaires assessing confidence scores, session rating, as well as general feedback were used to assess the course.

**Results:** Post course feedback was provided using a 5 point Liket scoring sheet, with a rating of 5 – extremely confident in managing independently, and 1 – unable to manage:

Delegates rated between 3–5 in their overall ability to identify and manage rheumatological emergencies (50% giving a rating of 5, and 40% rating a 4, 10% rating a 3), and between 3–5 in their ability to manage the five emergency scenarios. With the majority rating a 4, one delegate rated a 3 in two scenarios, while one delegate rated a 5 in four of the scenarios.

All delegates felt that the session had added to their knowledge and rated the course as either very good or excellent.

**Conclusions:** The pilot course was felt to overall improve trainee confidence in identifying and managing these rheumatology emergencies. It also highlighted non-technical skills and was felt to be a satisfactory teaching method by all the participants and trainers.

This course has obtained training programme director support for the Yorkshire and Humber region (UK) as well as funding and will run on a yearly basis in the region.

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[2] A framework for technology enhanced learning. A DOH report 2011

**Disclosure of Interest:** None declared

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**FRIDAY, 10 JUNE 2016**

## Advances in large vessel vasculitis

### OP0280 IMPROVED SURVIVAL IN GIANT CELL ARTERITIS: A POPULATION-BASED STUDY

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**Background:** Giant cell arteritis (GCA) is associated with significant morbidity and mortality, but previous studies on mortality in GCA have yielded conflicting results. Furthermore, mortality trends are largely unknown, particularly in the general population.

**Objectives:** To address this knowledge gap, we evaluated mortality trends in individuals with GCA in a general population-context from January 1, 1997 – December 31, 2012.

**Methods:** Using an administrative health database from the province of British Columbia, Canada (population approximately 4.5 million), we identified all incident cases of GCA and up to 10 non-GCA sex-, age- and entry-time-matched controls. The case definition for GCA included at least one prescription of oral glucocorticoids between one month before and six months after the index date. Study cohorts were divided into two sub-groups based on the year of diagnosis (i.e., 1997–2004 and 2005–2012). Mortality rates were calculated, as well as hazard ratios (HR) using a Cox proportional hazard model. HRs were adjusted for potential confounders (e.g., Charlson's comorbidity index, number of outpatient visits and hospitalizations, cardiovascular drugs, glucocorticoids, cox-2 inhibitors, NSAIDs within 12 months prior to index date).

**Results:** The early cohort (i.e., 1997–2004) of GCA patients had considerably higher mortality rates than the late cohort (i.e., 2005–2012) (i.e., 373.7 vs 87.5 cases per 1000 person-years), while the non-GCA cohort experienced a much smaller improvement in mortality rates between the two time periods (i.e., 70.9 vs 52.0 cases per 1000 person-years). The resulting HRs for mortality for the early and late cohorts were 4.58 (95% CI, 3.70–5.67) and 1.46 (95% CI, 1.16–1.84), respectively. Testing for difference between incident cohorts via an interaction term were all significant.

**Conclusions:** This population-based study shows that survival of GCA patients has improved in recent years, suggesting that new treatment strategies and improved management of GCA and its associated complications has led to significant improvements in GCA-associated mortality.

**Acknowledgement:** This study was funded by the Canadian Arthritis Network, The Arthritis Society of Canada/the British Columbia Lupus Society (Grant 10-SRP-IJD-01) and The Canadian Institutes of Health Research (THC-135235).

Table 1. Incidence rates and hazard ratios (HR) for associations between giant cell arteritis and death according to sub-cohort

| | 1997–2004 | | 2005–2012 | |
|---|---|---|---|---|
| | GCA Cohort | Non-GCA Cohort | GCA Cohort | Non-GCA Cohort |
| **Overall** | 349 | 714 | 652 | 1304 |
| Number of deaths | 235 | 172 | 135 | 196 |
| Mean follow-up Time (person-years) | 1.80 | 3.40 | 2.36 | 2.89 |
| Death rate (deaths per 1000 person-years) | 373.74 | 70.92 | 87.50 | 52.04 |
| Fully adjusted HR (95% CI)* | 4.58 (3.70–5.67) | 1.0 (ref) | 1.46 (1.16–1.84) | 1.0 (ref) |
| **Men** | 101 | 206 | 168 | 336 |
| Number of deaths | 70 | 57 | 41 | 60 |
| Mean follow-up time (person-years) | 1.47 | 3.03 | 2.19 | 2.77 |
| Death rate (deaths per 1000 person-years) | 472.07 | 91.44 | 111.41 | 64.45 |
| Fully adjusted HR (95% CI)* | 2.78 (1.77–4.38) | 1.0 (ref) | 1.06 (0.62–1.80) | 1.0 (ref) |
| **Women** | 248 | 508 | 484 | 968 |
| Number of deaths | 165 | 115 | 94 | 136 |
| Mean follow-up time (person-years) | 1.94 | 3.55 | 2.43 | 2.93 |
| Death rate (deaths per 1000 person-years) | 343.40 | 63.82 | 80.01 | 47.97 |
| Fully adjusted HR (95% CI)* | 5.41 (3.96–7.40) | 1.0 (ref) | 1.69 (1.22–2.35) | 1.0 (ref) |

**Disclosure of Interest:** None declared

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### OP0281 SURVIVAL OF BIOPSY-PROVEN GIANT CELL ARTERITIS IN ITALY DURING A 26-YEAR PERIOD: CORRELATION WITH HISTOLOGICAL PATTERN

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**Background:** No study have evaluated if there is a correlation between histological pattern of temporal artery biopsy and survival in patients with biopsy-proven giant cell arteritis (GCA).

**Objectives:** To investigate the relationship between histological pattern of temporal artery biopsy and survival in patients with biopsy-proven GCA in a defined area of Northern Italy.

**Methods:** All patients with incident temporal artery biopsy-positive GCA diagnosed between 1986 and 2012 living in the Reggio Emilia area were identified using pathology register and by reviewing all histopathological specimens. Patients were followed from the time of diagnosis until either their death or until December 31st, 2013. On the basis of the localization of the inflammation, positive TABs were classified into 4 categories: transmural inflammation (TMI), (229 cases, 81.8% of the positive biopsies); inflammation limited to adventitia (ILA), (14 cases, 5% of the positive biopsies); vasa vasorum vasculitis (VVV), (13 cases, 4.6% of the positive biopsies); and small vessel vasculitis (SVV), (24 cases, 8.6% of the positive biopsies). A semiquantitative 4 grade scale was used to describe the severity of mural inflammation (no mural inflammation, 81 cases, 28.9%, mild mural inflammation, 43 cases, 15.4%, moderate mural inflammation, 75 cases, 26.8%, severe mural inflammation, 81 cases, 28.9%). For each case, we identified one control from the same geographic area matched for age and gender. Mortality rates and specific causes of death were reported and compared between cases and controls and between cases with different histological pattern. TAB histological pattern and severity of mural inflammation entered in a Cox proportional regression analysis along with demographical, clinical and laboratory data at disease onset.

**Results:** There were 280 incident cases of biopsy-proven GCA (205 women, mean age at disease onset 74.3 + 7.5 y, mean duration of follow-up 95 + 58 months) during the 26-year study period with complete clinical, laboratory and survival data. During the follow- up period 159 (56.8%) patients died (mean survival time from disease onset 101 + 60 months). Patients with histological pattern ILA and VVV had reduced hazard ratio mortality as compared to TMI type (0.38 and 0.12 respectively). Survival of patients with different histological TAB pattern of GCA was not different from controls. The most frequent causes of death were cardiovascular diseases, cancer, and respiratory diseases. No significant differences in causes of death were observed comparing the 4 pattern of histological TAB involvement.

**Conclusions:** The histologic spectrum of inflammatory lesions in TAB positive GCA have correlation with survival.

**Disclosure of Interest:** None declared

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**FRIDAY, 10 JUNE 2016**

## When and how to diagnose and treat vitamin D deficiency?

### OP0282 EXPRESSION OF VITAMIN D RECEPTOR ASSOCIATED GENES IN THE AORTA OF CORONARY ARTERY DISEASE PATIENTS WITH AND WITHOUT RHEUMATOID ARTHRITIS

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**Background:** Vitamin D has an important role in the immune system, and has been linked to inflammation, rheumatoid arthritis (RA) and coronary artery disease (CAD)[1, 2]. However, the exact mechanisms how vitamin D is involved in these processes are still unclear.
**Objectives:** To compare expression of vitamin D receptor (VDR) associated genes in the aortic adventitia of CAD patients with and without RA.
**Methods:** RNA was isolated, and Affymetrix microarray was used to determine the gene expression profile in specimens from the ascending aorta in 8 patients with CAD and 8 patients with CAD and RA from the Feiring Heart Biopsy Study. Partek Genomics Suite software was used to identify differentially expressed genes by one-way ANOVA ($p<0.05$; FC>1.1), and differences in expression of VDR associated genes were determined by Ingenuity Pathway Analysis.
**Results:** Among the 15586 transcripts that were identified, pathway analysis determined two genes within the VDR signaling pathway, Growth arrest and DNA-damage-inducible protein 45 alpha (GADD45A) ($p=0.006$; FC=1.474) and Nuclear Receptor Corepressor 1 (NCOR1) ($p=0.005$; FC=1,210), that where both up-regulated in RA patients.
**Conclusions:** We found that GADD45A and NCOR1 were upregulated in the aorta of RA patients. GADD45A induces cell cycle arrest, DNA repair and apoptosis in response to various environmental stresses [3], while NCOR1 has an important role as a gene-specific integrator of positive and negative signals that control inflammation [4]. Based on this finding, we hypothesize that the accelerated atherosclerosis in RA might be related to the up-regulation of GADD45A and NCOR1 through the VDR signaling pathway.
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**Disclosure of Interest:** None declared
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### OP0283 A RANDOMIZED DOUBLE-BLIND COMPARATIVE CLINICAL TRIALS TO EVALUATE EFFICACY OF VITAMIN D IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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**Objectives:** To assess the efficacy and safety of ergocalciferol in combination with standard care in patients with systemic lupus erythematosus (SLE)
**Methods:** A randomized, double-blinded, placebo-comparative study was conducted in SLE with mild-moderate disease activity. The patients were randomized to receive either high doses of vitamin D (100,000 IU of ergocalciferol weekly for 4 weeks followed by 40,000 IU of ergocalciferol weekly for 20 weeks) or placebo. All patients received 800 unit of cholecalciferol daily for 24 weeks. Concurrent medications could be adjusted as clinically required. Efficacy measures were SLE disease activity index (SLEDAI) score, SLE Flare Index (SFI), inflammatory markers, and dosage of immunosuppressive drugs. The study was approved by the ethic committee and institutional review board
**Results:** Of the 104 patients enrolled, 88 patients completed the study. Baseline characteristics were similar. At 24 weeks, the mean ± standard difference (SD) of serum 25(OH)D in patients who received high doses of vitamin D was significantly higher than placebo group (41.2 ± 14.4 vs. 27.2 ± 10.1, $p<0.001$). There was no difference between patients who received high doses of vitamin D and placebo in respect of SLEDAI, SFI, inflammatory markers, and dosage of immunosuppressive drugs. However, at 12 and 24 weeks, the number of patient who can reduce prednisolone dosages in patients who received high doses of vitamin D were significantly greater than that of the placebo (39.6% vs.17.6%, p=0.008) and (43.4% vs. 23.5%, p=0.013). Adverse reactions in both groups were similar. Serum calcium levels did not change within and between groups of treatment.
**Conclusions:** This study could not demonstrate the efficacy of high dose ergocalciferol in controlling SLE disease activity. However, high dose ergocalciferol could be an adjunctive therapy that safe and has a corticosteroid-sparing effect on patients with SLE
**Disclosure of Interest:** None declared

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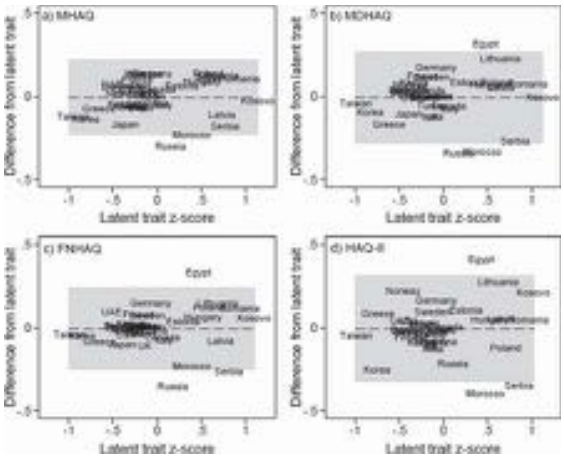
**FRIDAY, 10 JUNE 2016**

## Data harmonization across (rheumatoid arthritis) clinical cohorts and registers

### OP0284 COMPARABILITY OF THE HEALTH ASSESSMENT QUESTIONNAIRE BETWEEN COUNTRIES: PSYCHOMETRIC EXAMINATION OF CROSS-NATIONAL MEASUREMENT EQUIVALENCE

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**Background:** The HAQ disability index is the most widely used measure of function in rheumatological conditions. Translated versions of thr original HAQ and several revisions are increasingly used to make comparisons between countries in epidemiological studies. Such comparisons assume cross-national measurement equivalence. That is, total scores are not biased due to responses to individual items being influenced by subtle differences in interpretation across languages or cultures. Despite its wide use, this measurement property has not been tested across a wide range of countries.
**Objectives:** To examine the cross-national measurement equivalence of four versions of the HAQ: modified HAQ (MHAQ), multidimensional HAQ (MDHAQ), functional HAQ (FNHAQ) and HAQ-II.
**Methods:** Data are from the QUEST-RA cross-sectional survey of 10,150 patients with RA from 34 countries (74% female, mean age 55 years). Respondents completed an item pool of 33 items, excluding devices, relating to the original HAQ and four revisions. Item response theory (IRT) models were estimated. Likelihood ratio tests compared models for each HAQ version fixing IRT parameters to be the same across all countries (equivalent) or estimating separate parameters for each country (non-equivalent). Further analysis with Bayesian multiple-group IRT models identified items with non-equivalent IRT parameters for each country using an alignment method.
**Results:** All versions of the HAQ exhibited good psychometric properties with a single latent disability variable explaining around two-thirds of the variance in item responses. Compared to other versions, the HAQ-II exhibited greater precision (i.e. reliability) in differentiating between people with low levels of disability. For each version of the HAQ the non-equivalent model provided a significantly better fit compared to the equivalent model (all $p<0.001$), indicating comparisons of scores across countries are biased. Further analysis indicated this non-equivalence across countries was generally due to differences in the level of disability required to respond positively to an item, rather than variation



in an items ability to discriminate level of disability. Examining the aligned means for each country using the limits of agreement method (Figure) indicated that the overall impact of non-equivalence was likely to be minimal for most countries and that scores for the MHAQ were least affected. Scores for Russia, Serbia and Morocco were overestimated, and Egypt underestimated.
**Conclusions:** All versions of the HAQ have good psychometric properties. Due to differences in item interpretation across translations, caution should be taken when drawing inferences about disability levels across countries. For most countries such inferences are likely to be valid due to the relatively low level of bias introduced by individual items. Although measurement properties at the individual level are more favourable for the HAQ-II, it is more prone to bias in cross-national comparisons where the MHAQ may be favoured.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3985

### OP0285 THE EULAR TASK FORCE FOR STANDARDISING MINIMUM DATA COLLECTION IN RHEUMATOID ARTHRITIS OBSERVATIONAL RESEARCH: RESULTS OF A HIERARCHICAL LITERATURE REVIEW

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**Background:** There is considerable variation in the type of information used in rheumatoid arthritis (RA) observational studies. This, in turn, makes collaborative RA observational research challenging. As part of a larger initiative (EULAR Task Force) a step-wise approach was designed in order to achieve a consensus on a standardized minimum core dataset (MCD) with items (i.e. "what to collect") and instruments (i.e. "how to collect").
**Objectives:** To undertake a literature review designed to construct a comprehensive list of items and instruments currently collected across observational RA studies in Europe. This will ultimately inform the development of a MCD for collaborative RA research.
**Methods:** A hierarchical literature review of published articles that were I) observational cohorts or registers II) including RA patients and III) were initiated in Europe, was performed. Results were compared and cross-checked with EULAR recommendations for data reporting in RA clinical trials and trial extension studies for management of RA, The EULAR outcome measures library (OML) and the results of an initial survey undertaken by our group[1]. The latter was a web-survey involving a smaller sample of RA registers and clinical cohorts. The current literature review expanded to involve all existing RA registers and cohorts in published literature. From the literature, information of what is collected (item) and how (instrument) was extracted and the frequency of data collection was calculated.
**Results:** Published articles from 67 different European RA registers and cohorts were included. The number of patients recruited in each register ranged from 130 to more than 50,000. A total of 40 different items were identified comprising >100 different instruments Most studies included a measure of disease duration, disease activity, current DMARD use or physical function although the choice of instrument within each item varied widely in many cases (table 1). For example, 8 different composite scores of disease activity are being captured. Relative agreement on specific items did not always, however, entail agreement in terms of instruments.

Table 1. Commonly captured items in the literature, their frequency and the number of different instruments (i.e. how) used to collect the information

| Item | Frequency of collection | Number of instruments |
|---|---|---|
| Age | 67/67 (100%) | 1 |
| Gender | 67/67 (100%) | 1 |
| Current DMARD | 63/67 (94%) | 7 |
| Disease Duration | 62/67 (93%) | 1 |
| Composite Score of Disease Activity | 61/67 (91%) | 8 |
| Serology | 60/67 (90%) | 4 |
| Tender Joint Count | 58/67 (87%) | 5 |
| Swollen Joint Count | 58/67 (87%) | 5 |
| Acute phase reactants | 58/67 (87%) | 2 |
| Physical Function | 55/67 (81%) | 5 |
| Steroids | 53/76 (79%) | 5 |
| Patient Global | 52/67 (78%) | 6 |
| Pain | 48/67 (72%) | 4 |

**Conclusions:** Information captured in registers is heterogeneous. The frequency of collection of items and instruments informed voting in the first face-to-face meeting, alongside the expert panel survey.
**References:**
[1] Radner H. el al. Consistency and utility of data items across European rheumatoid arthritis clinical cohorts and registers. Arthritis Care Res 2015

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4631

**FRIDAY, 10 JUNE 2016**

## Telemedicine and e-health in community care

### OP0286-HPR THE EFFICACY OF MOTIVATIONAL COUNSELLING AND SMS-REMINDERS ON DAILY SITTING TIME IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RANDOMISED CONTROLLED TRIAL

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**Background:** Patients with rheumatoid arthritis (RA) are more sedentary than the general population, which can have serious health consequences. Reducing sedentary behaviour (SB) and increasing light intensity physical activity is advocated as a potentially more achievable health promotion focus in patients with chronic diseases and mobility problems. Intervention studies have shown that behavioural approaches are effective in reducing SB in healthy populations. Whether this applies to patients with RA is yet to be determined.
**Objectives:** To test the efficacy of a 16-week individually tailored, behavioural intervention in reducing daily sitting time, pain and fatigue and improving health-related quality of life, self-efficacy, physical function and cardio-metabolic disease risk in patients with RA.
**Methods:** Parallel-group, observer-blinded randomised controlled trial (N=150). RA patients >18 years of age, self-reported daily sitting time >5 hours and Health Assessment Questionnaire (HAQ) score <2.5 were consecutively recruited from a rheumatology outpatient clinic. The intervention group (n=75) received three individual motivational counselling sessions with a health professional and text messages aiming at improving motivation for light intensity physical activity through reduction of SB. The control group (n=75) was encouraged to maintain usual lifestyle. Primary outcome was change from baseline in daily sitting time measured objectively by ActivPAL, analysed using ANCOVA with a factor for group and adjustment for the outcome level at baseline. Primary analyses were based on the intention-to-treat population. Secondary outcomes included patient-reported outcomes and cardio-metabolic biomarkers (blood pressure, cholesterol levels, blood glucose, body weight and waist circumference).
**Results:** After 16 weeks, three participants were lost to follow-up. There was a mean decrease in daily sitting time of 1.61 hours (h)/day with the intervention and an increase of 0.59 h/day in the control group; between-group difference was -2.20 h/day (95%CI: -2.72 to -1.69; p<.0001) in favour of the intervention group. Most of the secondary outcomes were also in favour of the intervention; VAS-pain: -22.36 (-29.27 to -15.44); VAS-fatigue: -26.80 (-34.32 to -19.30), physical function (HAQ): -0.42, (-0.54 to -0.30) and total cholesterol: -0.37 (-0.50 to -0.24) mmol/l.
**Conclusions:** An individually tailored, behavioural intervention effectively reduced daily sitting time by on average more than two hours in patients with RA and additionally improved patient-reported clinical outcomes and cholesterol levels. The results may be important for clinical practise and physical activity recommendations for patients with RA and can most likely be generalised to other populations with chronic disease and mobility limitations.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4668

**FRIDAY, 10 JUNE 2016**

## Inflammasome as therapeutic target in inflammatory diseases

### OP0287 CALCIUM PYROPHOSPHATE DIHYDRATE CRYSTALS INDUCE IL-1β PRODUCTION BY MONOCYTES THROUGH A POTASSIUM EFFLUX-DEPENDENT PATHWAY

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**Background:** Osteoarthritis (OA) is the most common adult rheumatic disease characterized by cartilage degradation, synovial inflammation and subchondral bone remodeling. Risk factors associated with OA are age, genetics, mechanical overload and presence of calcium-containing microcrystals. Calcium pyrophosphate crystals including monoclinic and triclinic dihydrate phases (m- and t-CPPD) are found in 40% of end-stage OA patients. Frequently asymptomatic, it can

give rise to synovitis contributing to OA lesion worsening. CPP crystal-induced inflammation is orchestrated mainly by interleukin (IL)-1β. Secretion of IL-1β required a cytokine maturation process which depends on the NLRP3 inflammasome activation. This intracellular multiprotein complex can be stimulated by ATP-dependent potassium ($K^+$) efflux, reactive oxygen species (ROS) generation, lysosomal or mitochondrial alterations.
**Objectives:** The objectives were to identify intracellular pathways induced by CPPD crystals and leading to NLRP3 activation and IL-1β production.
**Methods:** The effects of CPPD crystals were assessed in human THP-1 cell line and bone marrow-derived macrophages (BMDM) from wild type (wt), NLRP3 (*nlrp3*$^{-/-}$) or P2X7 receptor (*p2x7*$^{-/-}$) knock out mice. Cells were primed before stimulation with synthetic m- and t-CPPD crystals in presence or absence of $K^+$-enriched media (KCl 50mM – to block $K^+$ efflux), N-acetyl-L-cystein (NAC 50mM – an intracellular ROS scavenger) or oxidized ATP (oxATP 200μM – an antagonist of ATP). NLRP3 expression was determined by western blotting, IL-1β and extracellular ATP (ATPe) concentrations were measured in cell culture supernatants whereas ROS production and mitochondrial membrane potential were evaluated using fluorescent probes (DFDA and JC-1, respectively).
**Results:** First, IL-1β production induced by CPPD crystals was lacking in *nlrp3*$^{-/-}$ BMDM but important in wt BMDM. Second, we showed that m-CPPD crystals induced a higher NLRP3 expression and IL-1β production than t-CPPD suggesting a differential modulation of NLRP3 activation. We observed that CPPD-induced IL-1β secretion was completely abrogated when $K^+$ efflux or intracellular ROS were inhibited. Moreover, we demonstrated a stronger decrease in mitochondrial membrane potential following m-CPPD than t-CPPD crystal stimulation, combined with a *de novo* ROS generation. These two latter effects were inhibited when $K^+$ efflux was blocked. Finally, we found that m- and t-CPPD crystals differentially brought on an ATP release and that IL-1β production was partially inhibited by oxATP. However, although ATPe can trigger $K^+$ efflux through P2X7 receptor opening, crystal-mediated IL-1β production was similar between wt and *p2x7r*$^{-/-}$ BMDM.
**Conclusions:** IL-1β production triggered by m- and t-CPPD crystals occurred through a modulation of ROS production and mitochondrial disruption. Interestingly, $K^+$ efflux, associated with ATP release, could be the initial signal of CPPD-induced IL-1β maturation, independently of P2X7 receptor involvement. These results highlight a new molecular pathway of crystal-dependent OA inflammation.
**Disclosure of Interest:** None declared
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**FRIDAY, 10 JUNE 2016**

## Potential targets in inflammatory fibrotic conditions in SSc

### OP0289 MICRORNAS AS POTENTIAL REGULATORS OF MONOCYTE DIFFERENTIATION AND FUNCTION IN HEART FIBROSIS IN SYSTEMIC SCLEROSIS

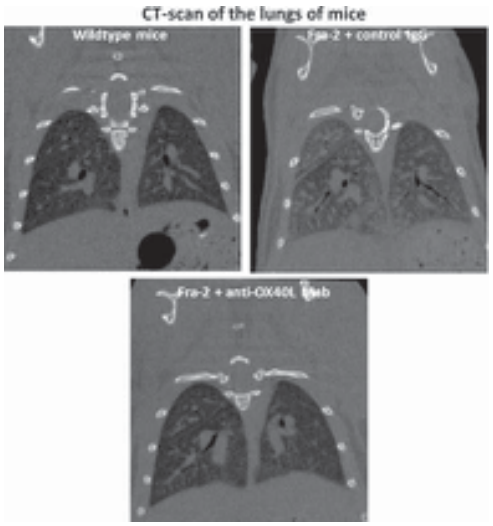
M. Rudnik[1], M. Stellato[1], P. Blyszczuk[2], E. Pachera[1], R. Dobrota[1], B. Maurer[1], K. Klingel[3], J. Henes[4], K. Sotlar[5], O. Distler[1], G. Kania[1]. *[1]Division of Rheumatology, University Hospital Zurich; [2]Center of Molecular Cardiology, University of Zurich, Zurich, Switzerland; [3]Department of Molecular Pathology; [4]Division of Rheumatology, University Hospital Teubingen, Teubingen; [5]Insitute of Pathology, Ludwig Maximilians University, Munich, Germany*

**Background:** Heart involvement in patients with systemic sclerosis (SSc) resembles the inflammatory dilated cardiomyopathy (iDCM) phenotype with predominance of inflammation, fibrosis, vasculopathy and heart dysfunction. Animal studies of iDCM indicated bone marrow originated cells as a major source of pathological myofibroblasts. MicroRNAs are key regulators of immune cell function and are involved in many cardiac pathological processes. However, their roles in monocyte differentiation and fibrogenesis are unclear.
**Objectives:** To determine the role of circulating monocytes and microRNAs in the onset and progression of myocardial fibrosis in SSc, we examined monocyte differentiation and their microRNAs expression profile in SSc.
**Methods:** Endomyocardial biopsies from SSc/iDCM patients and healthy controls were screened by immunohistochemistry. $CD14^+$ monocytes isolated from peripheral blood of SSc patients and healthy donors were differentiated towards the myofibroblast phenotype by stimulation with TGF-β1, IL-4, IL-10 and IL-13. In addition, $CD14^+$ monocytes were co-cultured with dermal fibroblasts originated from SSc patients and healthy subjects. After 7 days, myofibroblast gene expression and cytokines secretion profile were evaluated. MicroRNA candidates were selected using DIANA-TarBase v7.0 and TargetScan Release 7.0 and further analysed by qPCR.
**Results:** Myocardium of SSc/iDCM patients (n=10) revealed extensive fibrosis and accumulation of inflammatory cells including $CD14^+$ monocytes. Moreover, fibrotic myocardium from SSc patients exhibited the presence of $CD14^+$/$Fra\text{-}2^+$ monocyte-derived fibroblast-like cells. Bioinformatical analysis indicated several potential microRNAs being involved in monocyte differentiation, and qPCR confirmed predicted candidates. We observed decreased basal levels of let-7i (Mann-Whitney U test, p=0.005), miR-10b (p=0.005), miR-21 (p=0.005), miR-29a (p=0.005), miR-155 (p=0.002), miR-199a (p=0.008) and miR-544a (p=0.002), and increased levels of miR-29b (p=0.03) in circulating $CD14^+$ monocytes isolated from SSc patients (n=10) compared to healthy controls (n=4). Stimulated monocytes acquired a myofibroblast-like phenotype with increased expression of collagen I, fibronectin, α smooth muscle actin and Fra-2 in comparison to untreated cells. Similarly, $CD14^+$ monocytes exposed to dermal fibroblasts acquired myofibroblast features. $CD14^+$ monocytes from SSc patients were characterised by higher production of IP-10, MIP-3α, LIF and NT-3. The process of monocyte to myofibroblast differentiation employed Fra-2/TGF-β signalling. Inhibition of the canonical SMAD-dependent pathway with TGFβR1 inhibitors resulted in the abrogation of monocyte-to-myofibroblast differentiation.
**Conclusions:** Here we demonstrated the capability of peripheral blood monocytes to differentiate towards the myofibroblast phenotype, indicating these cells as one of the potential sources of pathological tissue myofibroblasts in SSc. Different miRNA expression profiles in SSc monocytes indicate a primary activation state. Further studies of miRNAs regulation pathways might lead to novel treatment strategies, particularly for heart involvement.
**Disclosure of Interest:** M. Rudnik: None declared, M. Stellato: None declared, P. Blyszczuk: None declared, E. Pachera: None declared, R. Dobrota: None declared, B. Maurer: None declared, K. Klingel: None declared, J. Henes: None declared, K. Sotlar: None declared, O. Distler Grant/research support from: Bayer, Sanofi, Ergonex, Boehringer Ingelheim, Actelion, Pfizer, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, EpiPharm, Ergonex, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Pharmacyclics, Pfizer, Serodapharm, Sinoxa, G. Kania: None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2682

### OP0290 OX40L BLOCKADE PROTECTS AGAINST SKIN AND LUNG INFLAMMATION-DRIVEN FIBROSIS

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**Background:** Systemic sclerosis (SSc) is a severe fibrotic disease with no effective treatment. The OX40-OX40L axis is emerging as a new potential target in autoimmune diseases offering the advantage of a targeted approach on co-stimulatory signals with limited impact on the whole immune response and very preliminary data suggested its involvement in SSc.
**Objectives:** To investigate the contribution of OX40L in SSc
**Methods:** We assessed the expression of OX40L in fibrotic skin and in the serum of SSc-patients. The efficacy of a targeted therapy against OX40L *in vivo* was evaluated using complementary experimental mouse models.
**Results:** Expression of OX40L protein was higher in fibrotic skin of SSc-patients as compared to healthy controls (p=0.003), particularly in diffuse cutaneous forms. Soluble OX40 levels were significantly higher in SSc-patients (n=177) than in healthy controls (n=100). Longitudinal analyses of our cohort showed that high level of serum OX40L at baseline was highly predictive of worsening of dermal and lung fibrosis during the follow-up (HR: 8.28 [2.11–32.50] and 4.60 [1.52–12.18], $P<0.001$). This was confirmed in a replication Norwegian cohort (n=241) dedicated to lung fibrosis analysis. In this cohort, in multivariate analyses, OX40L was a strong predictor of lung fibrosis including known risk factors for lung fibrosis.



Invalidation of OX40L prevented dermal fibrosis in the bleomycin mouse model with a decrease in dermal thickness, hydroxyprolin content and myofibroblasts count. OX40L invalidation was associated with a decrease in T cell, B cell and macrophage infiltrates and in cytokine release (IL-6, TNF-α) in lesional skin of mice. A transcriptomic approach identified two main pathways regulated by OX40L blockade: NF kappa B and AP 1 signaling. Then pharmacologic approaches, using a monoclonal anti-OX40L antibody, demonstrated that the blockade of OX40L not only prevented dermal fibrosis, but also induced regression of established fibrosis. Thereafter, the use of this monoclonal antibody demonstrated in the fra-2 transgenic mouse model marked protection from fibrosing alveolitis (measured by CT-scan (Figure) and histology) and vessel remodeling leading to pulmonary arterial hypertension.

**Conclusions:** Altogether, our results show that OX40L is as an attractive target in inflammation-driven fibrosis. OX40L appears as a very promising biomarker in SSc and an appealing potential therapy to reduce both skin and lung fibrosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4589

**SATURDAY, 11 JUNE 2016**

## SLE: What will it be and how will it be treated 5 years from now

### OP0291 ANIFROLUMAB, AN ANTI-INTERFERON-ALPHA RECEPTOR MONOCLONAL ANTIBODY, IN MODERATE TO SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

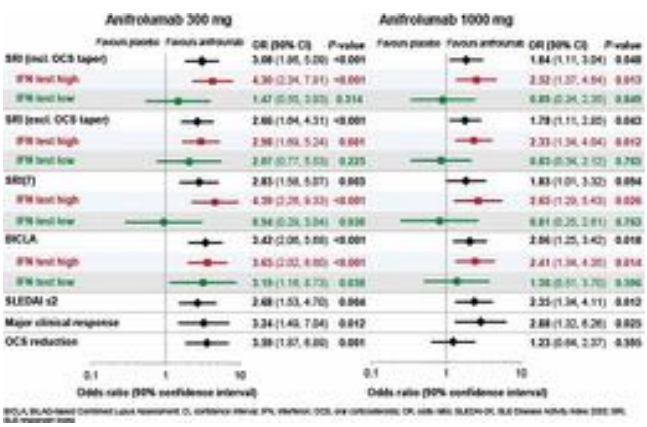
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**Background:** Increased activity of the type I interferon (IFN) pathway is central to the pathogenesis of SLE. Blocking the type I receptor may reduce SLE activity more effectively than inhibiting IFN-α alone.

**Objectives:** Efficacy and safety of anifrolumab were assessed in a Phase IIb, randomized, double-blind, placebo-controlled study of adults with moderate to severe SLE (the MUSE study).

**Methods:** 305 patients were treated for 48 weeks with intravenous anifrolumab (300 mg or 1000 mg) or placebo, in addition to standard-of-care medications. Randomization was stratified by SLE Disease Activity Index 2000 (SLEDAI-2K) score (<10 or ≥10), oral corticosteroid (OCS) dose (<10 or ≥10 mg/day), and IFN gene signature status (high vs. low) based on a 4-gene expression assay. The primary endpoint was the percentage of patients achieving an SLE Responder Index [SRI(4)] response at Day 169 with sustained reduction of OCS (<10 mg/day and ≤Day 1 dose from Day 85 to 169).

**Results:** The primary endpoint was met by more anifrolumab-treated patients [placebo vs. 300 mg vs. 1000 mg: 17.6%, 34.3% ($p$=0.014), 28.8% ($p$=0.063)] with greater effect sizes observed in the 75% of patients who had a high baseline IFN signature [13.2%, 36.0% ($p$=0.004), 28.2% ($p$=0.029)]. At Day 365 more anifrolumab-treated patients achieved SRI(4) responses [40.2%, 62.6%, ($p$<0.001), 53.8%, ($p$=0.043)], BILAG-based Composite Lupus Assessment (BICLA) [25.7%, 53.5% ($p$<0.001), 41.2% ($p$=0.018)], modified SRI(6) [28.4%, 49.5% ($p$=0.002), 44.7% ($p$=0.015)], and SLEDAI-2K ≤2 [17.6%, 35.4% ($p$=0.004), 32.7% ($p$=0.012)]. Major clinical response (BILAG "C" or better in all domains at Day 169 maintained to Day 365) was achieved by 6.9%, 19.2% ($p$=0.012), and 17.3% ($p$=0.025) of patients. BILAG "A" flares were reported in more placebo- vs. anifrolumab-treated patients (16.7%, 9.1%, 10.6%). In patients with baseline Cutaneous Lupus Erythematosus Disease Area and Severity Index activity score ≥10, more anifrolumab-treated patients attained a ≥50% reduction by Day 365 [30.8%, 63.0% ($p$=0.013), 58.3% ($p$=0.077)]. In patients with ≥8 swollen and ≥8 tender joints at baseline more anifrolumab-treated patients achieved ≥50% decrease in joint count [48.6%, 69.6% ($p$=0.038), 64.6% ($p$=0.156)]. Although steroid tapering was not mandated, OCS reduction to ≤7.5 mg/d at Day 365 was achieved by 26.6%, 56.4%, and 31.7% of patients. The observed benefits were driven by results in the IFN-high subpopulation (figure). Median suppression of 21 IFN-regulated genes was ~90% for both doses of anifrolumab. Patients in the placebo group had the lowest incidence of *Herpes zoster* (2.0%, 5.1%, 9.5%) and cases reported as influenza (2.0%, 6.1%, 7.6%); there were no differences in the incidence of serious adverse events (18.8%, 16.2%, 17.1%). The incidence of infusion-related reactions was similar (5.9%, 2.0%, 3.8%).




**Conclusions:** Anifrolumab significantly reduced disease activity across all clinical endpoints. Enhanced effects in IFN-high patients support the pathobiology of this treatment strategy.

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**Disclosure of Interest:** R. Furie Consultant for: MedImmune, J. Merrill Grant/research support from: MedImmune; Genentech/Roche, Consultant for: Medimmune, Genentech/Roche, Neovacs, V. Werth Consultant for: MedImmune, M. Khamashta: None declared, K. Kalunian Grant/research support from: MedImmune, Consultant for: AstraZeneca, P. Brohawn Shareholder of: AstraZeneca, Employee of: MedImmune, G. Illei Shareholder of: AstraZeneca, Employee of: MedImmune, J. Drappa Shareholder of: AstraZeneca, Employee of: MedImmune, L. Wang Employee of: MedImmune, S. Yoo Shareholder of: AstraZeneca; Regenx Bio, Consultant for: Regenx Bio

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**SATURDAY, 11 JUNE 2016**

## Clinical outcomes for PMR/GCA

### OP0292 INTERSPINOUS BURSITIS EVALUATION BY ULTRASOUND IS VERY USEFUL FOR DIAGNOSIS OF POLYMYALGIA RHEUMATICA EXTENSION STUDY

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**Background:** Polymyalgia rheumatica (PMR) is a common inflammatory disease of the elderly, and 2012 provisional classification criteria were suggested, however it is provisional and not meant for diagnosis purpose[1)]. Ultrasound (US), MRI and other modalities were often detected interspinous bursitis in patients with PMR[2)]. To develop 2012 provisional classification criteria, adding interspinous bursitis evaluation by US. We reported the usefulness of interspinous bursitis evaluation by US at 2015 American college of rheumatology annual meeting.

**Objectives:** In this time, we compared 2012 provisonal classification criteria to adding interspinous bursitis evaluation by US, and checked the association between US evaluation of conventional (shoulder and hip) bursitis and interspinous bursitis.

**Methods:** This is a prospective cohort study. Candidate criteria were evaluated 161 patients with new onset untreated PMR, and 174 patients non-PMR comparison subjects with conditions mimicking PMR. We compared the diagnosis ability of 2012 provisional classification criteria with 2012 provisional classification criteria, adding interspinous bursitis evaluation by US. US evaluation was checked cervical and lumbar spine added conventional shoulder and hip. In PMR patients, we evaluated the prevalance of interspinous bursitis without hip or shoulder bursitis, the association between interspinous bursitis and shoulder or hip bursitis.

**Results:** 2012 provisional classification criteria scoring system had 66% sensitivity and 82% specificity. Adding interspinous bursitis by US had significantly increased sensitivity to 89%,and not significantly decreased specificity to 77%.(ROC anaylysis: p<0.05)

PMR patients without hip or shoulder bursitis were 56 patients. Surprisingly, PMR patients without hip or shoulder bursitis had interspinous bursitis with high prevalence. (85%, 48 patients) No correlation was found between interspinous bursitis and shoulder or hip bursitis (r=0.09, $P$=0.36).

**Conclusions:** Interspinous bursitis by US is important evalution in patients with PMR. Interspinous bursitis by US should be added classification criteria for PMR. If patients were suspected of PMR, interspinous bursitis by US might be performed despite hip and shoulder bursitis.

**References:**

[1] Dasgupta B, et al. 2012 Provisional classification criteria for polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis. 2012 Apr;71(4):484–92. doi: 10.1136/annrheumdis-2011-200329.

[2] Camellino D, et al. Interspinous bursitis is common in polymyalgia rheumatica, but is not associated with spinal pain. Arthritis Res Ther. 2014 Dec 1;16(6):492. [Epub ahead of print]

**Disclosure of Interest:** None declared

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OP0293 **PATIENT PRIORITIES FOR PMR RESEARCH: A PRIMARY CARE SURVEY**

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**Background:** Polymyalgia rheumatica (PMR) is a common inflammatory disorder of older (>50 years) adults, frequently managed in primary care. PMR remains under-researched despite the significant impact this condition has on patient's quality of life. Existing research is typically focused in secondary care settings and as such may not be generalizable to the wider PMR patient population. The importance of involving patients in research is increasing recognised as best practice, yet to date patient priorities for PMR research have not been examined.
**Objectives:** To identify patient priorities for PMR research.
**Methods:** All adults aged ≥50years registered with 150 English general practices who had a first Read code for PMR in their medical records in the preceding 3 years were mailed a self-completion questionnaire (n=704). Survey items included questions on patient demographics and PMR symptoms. Questions regarding patient priorities for PMR research were developed in collaboration with patient members of the leading UK patient group (PMRGCAuk). Patients were asked to indicate what their priorities for research were from a predefined list of 8 items and an additional free-text option.
**Results:** 550 patients responded (78%). The mean (SD) age was 74.2 (8.4) years and 365 (66%) were female. Non-responders did not differ significantly from responders in terms of age (mean age 75 (9.2) vs 74.2 (SD 8.4), p=0.21) or gender (73% vs 66% females, p=0.14).Priorities areas for research were focused on how to manage pain, stiffness and fatigue (440, 80%), improving the diagnosis of PMR (391, 71%), steroid management (341, 62%) and improving self-management (330, 55%). The development of giant cell arteritis (74, 13%), a key concern for clinicians, was the item rated as least important by participants for future research.
**Conclusions:** Meaningful involvement of patients in the research process is essential if we are to generate evidence that improves outcomes for those suffering with this painful and disabling condition. This survey of PMR patients in primary care suggests that symptom management and managing medication are key areas for patients for future research. Researchers and funding organisations should be aware of these priorities if we to generate research findings that are relevant to the widest range of stakeholders.
**Acknowledgement:** This abstract presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.
**Disclosure of Interest:** None declared
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**SATURDAY, 11 JUNE 2016**

## Getting active against rheumatoid arthritis fatigue —

OP0294-HPR **SLEEP QUALITY, SLEEP DISTURBANCES AND PHYSICAL ACTIVITY: A NATIONAL SURVEY OF IRISH PEOPLE WHO HAVE INFLAMMATORY ARTHRITIS**

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**Background:** Restorative sleep has an important role in maintaining health with disrupted or lower levels of sleep being related to serious outcomes such as increased risk of morbidities and reduced levels of physical activity. Sleep disturbances and poor sleep quality are prevalent complaints in people with Inflammatory Arthritis. Poor sleep quality and disturbances may exacerbate pain in this population, which may further lead to reduced levels of physical activity. Due to a dearth of information in this area, establishing same among Irish People with Inflammatory Arthritis is important.
**Objectives:** To investigate sleep quality, sleep disturbances and physical activity among Irish people who have Inflammatory Arthritis
**Methods:** Members from Arthritis Ireland were invited to participate in a cross-sectional survey hosted on SurveyMonkey(R)TM. Ethics approval was received through the University of Limerick. Descriptive statistics, Chi-square tests/Fisher's exact tests were used to analyse the data using SPSS v22.
**Results:** Ninety (90) people with Inflammatory Arthritis responded and report an average of 5.7 (SD 1.46) hours sleep per night. Results found 77% of respondents were female, with a mean number of years with inflammatory arthritis to be 10.09 (SD 9.92). Over half had a third level qualification (54%), while a third (33%) were in full-time employment. A majority (61%) report their sleep quality as fairly bad/very bad, with 31% having taken medications at least once a week to help their sleep, over the previous month. Ninety three percent (93%) reported arthritis pain in the previous week, while 23% were limited a lot and 62% limited a little with moderate activities. A large majority report "pain" (95%), "waking up in the middle of the night or early morning" (97%) and "cannot get to sleep within 30 minutes" (91%), as sleep disturbances. There was a statistically significant association between longer years with symptoms (p=0.004), taking medication at least once a week (p=0.009) and limited in their activities (p=0.004), when rating their sleep quality as bad. When using the SQUASH questionnaire, patients' physical activity levels were a low 1,210 minutes per week, compared to other physical activity surveys from their healthy counterparts, even-though 72% believe it is important to measure physical activity.
**Conclusions:** Irish people with Inflammatory Arthritis fall far below the "sleep needs spectrum" with those having symptoms longer, taking medications regularly and having limitations with their activities, reporting poorer sleep quality. More research is needed with regards to investigating poor sleep quality and disturbances in order to promote health and well-being in people with Inflammatory Arthritis. In addition the effects of physical activity interventions on poor sleep needs to be examined to show if it is a positive non-pharmacological treatment approach for the management of poor sleep in patients with Inflammatory arthritis.
**Disclosure of Interest:** None declared
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OP0295-HPR **INCREASING PHYSICAL ACTIVITY IN ANKYLOSING SPONDYLITIS (INPACT-AS): A RANDOMISED CONTROLLED TRIAL**

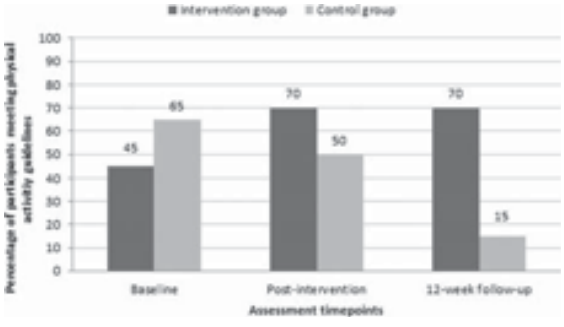
T. O'Dwyer[1], A. Monaghan[1], J. Moran[1], F. Wilson[1], F. O'Shea[2]. *[1]Physiotherapy, Trinity College Dublin; [2]Rheumatology, St. James's Hospital, Dublin, Ireland*

**Background:** The numerous benefits of physical activity (PA) are well established, and guidelines recommend adults obtain ≥150 minutes of moderate-intensity PA per week in bouts lasting ≥10 minutes ($PA_{BOUTS}$)[1]. PA, including exercise, is a key component of the management of ankylosing spondylitis (AS), however participation in PA in this cohort is low[2,3].
**Objectives:** The INPACT-AS trial explored the effects of a PA behaviour change intervention on habitual PA of adults with AS; secondary aims explored effects on spinal mobility and AS-related features.
**Methods:** This single-blind, parallel-group randomised controlled trial recruited adults diagnosed with AS. Exclusion criteria were the presence of comorbidities limiting PA, or recent changes in medication usage. Forty participants (26 males) were randomised to an intervention group (IG) or a control group (CG). Over a 12-week period, the IG had individual consultations with a physiotherapist, aiming to optimise habitual PA. The CG continued with 'usual care'. Blinded outcome assessments were conducted at baseline, post-intervention, and 12-week follow-up. Habitual PA was measured during waking hours with ActiGraph GT3x accelerometers. Questionnaires administered included the Bath AS Disease Activity Index, Bath AS Functional Index, and the AS Quality of Life questionnaire (ASQoL). The Bath AS Metrology Index (BASMI) measured spinal mobility. An intention-to-treat analysis was performed.
**Results:** Mean (SD) age was 38.9 (7.6) years in the IG and 44.8 (9.7) years in the CG. Mean symptom duration was 17.7 (9.5) years in the IG and 24.4 (13.6) years in the CG. Other baseline socio-demographic, AS, medication, and PA-related features were similar across groups ($p>0.05$). No adverse effects were reported during the study. Median number of IG consultations was 5 (IQR 1). Post-intervention, there were significant between-group differences in health-related PA, of large effect size (Tab. 1). After follow-up, significantly more participants in the IG met PA guidelines than in the CG [$\chi^2(1)=12.379$, $p<0.0005$] (Fig. 1). BASMI score changes significantly favoured the IG [ANOVA: $F(2, 76)=5.691$, $p=0.005$]. ASQoL scores significantly improved in the IG [Friedman's test, $\chi^2(2)=8.400$, $p=0.015$].

Table 1. Health-enhancing physical activity

| Variable | Group | Baseline | 12-weeks | 24-weeks | *p*-value[a] | Effect size[b] |
|---|---|---|---|---|---|---|
| Moderate/vigorous intensity PA, min/week | IG | 238 (310) | 309 (278) | 296 (269) | **<0.0005** | **0.205** |
| | CG | 302 (283) | 298 (244) | 197 (128) | | |
| $PA_{BOUTS}$, min/week | IG | 124 (226) | 192 (188) | 198 (171) | **<0.0005** | **0.281** |
| | CG | 173 (188) | 142 (144) | 69 (74) | | |

Median (interquartile range). [a]Mixed-design repeated measures ANOVA. Significant *p*-value <0.05. [b]Partial $\eta^2$: small >0.01, medium >0.06, large >0.14.




**Conclusions:** This was the first behaviour change intervention targeting PA in an AS cohort. Health-enhancing PA, spinal mobility and quality of life were significantly improved after the intervention, and improvements were maintained at three-month follow-up.

**References:**
[1] WHO. Global recommendations on physical activity for health. Geneva, Switzerland: WHO, 2010
[2] Millner JR, et al. (2015) Exercise for ankylosing spondylitis: an evidence-based consensus statement. Semin Arthritis and Rheum. [epub]
[3] O'Dwyer T, et al. (2015) Decreased physical activity and cardiorespiratory fitness in adults with ankylosing spondylitis. Rheumatol Int. 35:1863–72
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3581

**SATURDAY, 11 JUNE 2016**

## Endothelial to mesenchymal transition and angiogenesis as driving mechanisms in systemic sclerosis.

### OP0296 COMPARISON OF BOSENTAN AND MACITENTAN EFFECTS ON ENDOTHELIAL-TO-MESENCHYMAL TRANSITION PROCESS INDUCED BY ET-1 IN CULTURED HUMAN MICROVASCULAR ENDOTHELIAL CELLS

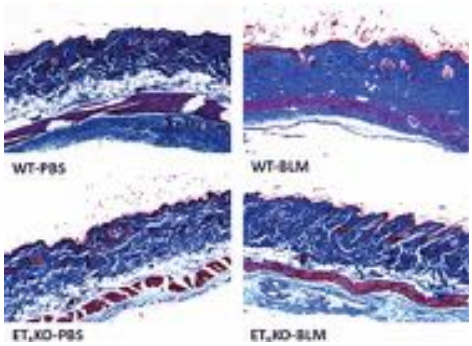
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**Background:** In systemic sclerosis (SSc), the damage of microvascular endothelial cells (ECs) and their phenotype alteration are considered early events responsible for myofibroblast activation and the development of fibrosis (1). Endothelin (ET)-1 and transforming growth factor (TGF)β1 induce ECs to acquire features of extracellular matrix-producing myofibroblasts through the induction of the endothelial-to-mesenchymal transition process (EndoMT) (2).
**Objectives:** To compare the ability of ET-1 receptor antagonists ($ET_{A/B}$RAs), bosentan and macitentan, to support the *in vitro* endothelial damage repair and to contrast the EndoMT induced by ET-1 in cultured human microvascular ECs (HMVECs).
**Methods:** HMVECs, at 3rd culture passage, were grown in endothelial cell medium (EGM2-MV). A part of these cultured HMVECs was untreated or treated with either ET-1 (100nM) or TGFβ1 (10ng/mL) for 6 days. Another part of cultured cells was treated for 1hr with bosentan (10μM) or macitentan (1μM) and then stimulated with ET-1 for 6 days (2,3). At the end of treatments, cultured HMVECs were scraped with a 200μL tip to create a linear injury, whose area was determined at baseline and after 24hrs of culture in EGM2-MV by ImageJ analysis software, to evaluate the *in vitro* endothelial damage repair. The gene expression of specific markers of the EndoMT, such as α-smooth muscle actin (α-SMA), fibroblast specific protein-1 (S100A4), fibronectin (FN), platelet endothelial cell adhesion molecule (CD31), and vascular endothelial (VE)-cadherin was evaluated by quantitative real time polymerase chain reaction (qRT-PCR). Statistical analysis was performed by Man-Whitney non-parametric *U*-test.
**Results:** ET-1 treated HMVECs showed a significantly lower ability to promote the *in vitro* endothelial damage repair compared to untreated cells ($p<0.05$). A similar effect was observed in TGFβ1-treated cells ($p<0.01$). On the contrary, cultured HMVECs treated with $ET_{A/B}$RAs significantly improved the *in vitro* endothelial damage repair compared to ET-1-treated cells ($p<0.05$ for bosentan and macitentan). ET-1 significantly up-regulated the gene expression of α-SMA, S100A4, and FN ($p<0.0001$ for all proteins) and down-regulated that of CD31 and VE-cadherin compared to untreated cells ($p<0.05$, $p<0.01$) as observed by qRT-PCR.
Bosentan contrasted the up-regulation of α-SMA as well as significantly contrasted the up-regulation of S100A4 and FN induced by ET-1 ($p<0.01$, $p<0.05$ vs. ET-1 treated cells). Macitentan significantly reduced the ET-1-induced increase in α-SMA, S100A4, and FN ($p<0.01$; $p<0.01$; $p<0.05$), as well as it antagonized the down-regulation of CD31 and VE-cadherin compared to ET-1 treated cells ($p<0.05$ for both proteins), as observed by qRT-PCR.
**Conclusions:** Both macitentan (at very low concentration) and bosentan seem to allow *in vitro* endothelial damage repair and to efficiently contrast the EndoMT induced by ET-1 in cultured HMVECs. Therefore, $ET_{A/B}$ receptor antagonism might contrast the damage of ECs and their phenotype transition that seems to contribute the early phases of the fibrotic process in SSc.
**References:**
[1] Denton CP. Clin Exp Rheumatol.2015;33 (Suppl 92):S3–7.
[2] Cipriani P et al. J Rheumatol.2015;42:1808–16.
[3] Cutolo M et al. J Rheumatol.2015;42:456–63.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3883

### OP0297 KNOCKOUT OF ENDOTHELIN TYPE B RECEPTOR SIGNALING ATTENUATES BLEOMYCIN-INDUCED SKIN SCLEROSIS IN MICE

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**Background:** Endothelin-1 (ET-1) is important in the pathogenesis of systemic sclerosis (SSc). It has been reported that plasma concentration of ET-1 are higher in SSc patients, and that endothelin receptor expression are also increased in lungs and skins in the patients. ET-1 binds two receptors, endothelin type A ($ET_A$) and endothelin type B ($ET_B$). Dual $ET_A$/$ET_B$ receptor antagonists and a selective $ET_A$ receptor antagonist are used clinically to treat SSc, and the effect of these antagonists on fibroblast activation has been described. However, the role of $ET_B$ receptor signaling in fibrogenesis is less clear.
**Objectives:** This study was conducted to evaluate the profibrotic function of $ET_B$ receptor signaling in a murine model of bleomycin (BLM)-induced scleroderma.
**Methods:** We used $ET_B$ receptor–knockout ($ET_B$KO) mice, which are genetically rescued from lethal intestinal aganglionosis by an $ET_B$ receptor transgene driven by the human dopamine β-hydroxylase (Dβ H)-gene promoter, and wild-type mice with DβH-ETB (WT). BLM or phosphate-buffered saline (PBS) was administered subcutaneously by osmotic minipump, and skin fibrosis was assessed by dermal thickness, subcutaneous fat atrophy, and alpha-smooth muscle actin (αSMA)-expressing myofibroblast count in the dermis. Dermal fibroblasts isolated from $ET_B$KO and WT mice were cultured *in vitro*, stimulated with BLM or ET-1, and the expression of profibrotic genes was compared by quantitative PCR.
**Results:** Dermal thickness, subcutaneous fat atrophy, and myofibroblast counts in the dermis were significantly reduced in $ET_B$KO mice compared to WT mice, after BLM treatment. Compared with wild-type, dermal fibroblasts isolated from $ET_B$KO mice showed lower gene expressions of *αSMA* and *collagen 1α1* in response to BLM or ET-1 stimulation *in vitro.*




**Conclusions:** ET-1–$ET_B$ receptor signaling is involved in skin sclerosis and in collagen synthesis by dermal fibroblasts.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2613

**SATURDAY, 11 JUNE 2016**

## Cell-cell interaction in joint inflammation

### OP0298 ANTI-CITRULLINATED PROTEIN ANTIBODIES PROMOTE SYNOVIAL FIBROBLASTS MIGRATION AND ADHESION THROUGH A PEPTIDYLARGININE DEIMINASES (PAD) DEPENDENT PATHWAY

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**Background:** Synovial fibroblasts (SFs) contribute to rheumatoid arthritis (RA) pathogenesis by growing into the synovial space and by producing pro-angiogenic and tissue remodelling factors, chemokines and inflammatory cytokines that recruit and stimulate various immune cells. We have recently demonstrated that anti-citrullinated proteins antibodies (ACPAs) promote osteoclast development. In the present work we investigated whether ACPAs can also modulate SFs.
**Methods:** SFs were isolated from synovial tissue of RA patients by enzymatic digestion. Polyclonal ACPA and others non-ACPA IgGs were separated from plasma of RA patients by affinity purification on cyclic citrullinated peptide (CCP)-2 column. Monoclonal ACPAs were generated from synovial B-cells. Antibodies were tested in scratch-assays for SF migration and the results were evaluated

by NIH ImageJ software. SF adhesion was analyzed by xCELLigence System Real-Time Cell Analyzer (ACEA bioscience). ACPA-induced signalling pathways were examined using inhibitors of phosphoinositide 3-kinase (PI3K), phosphatase and tensin homolog (PTEN), G-protein coupled receptors, focal adhesion kinase (FAK) and peptidylarginine deiminases (PAD) in the migration assays. Protein phosphorylations were monitored by western blot.
**Results:** Polyclonal ACPAs but not others IgGs induced both SFs migration (a fold increase of 2.6±0.5, mean±SD, $p<0,05$) and SFs adhesion (a fold increase of 1.3±0.1 at 6 hours, $p<0.05$). Similar effects were observed with two (D10 and B02) out of three tested monoclonal ACPAs, with a fold increase of the migration index of 2.4±0.4 for D10 antibody and 2.2±0.4 for B02 antibody ($p<0.05$ for both). IL-8, a chemokine that is upregulated in developing ostecolasts by ACPAs, synergistically increased the ACPA-induced SF migration. Inactivation of the PAD enzymes completely abolished the ACPA-induced SFs migration. GPCR and PI3K blocking completely abolished ACPAs effects, indicating an important role for GPCR and PI3K but not for FAK in the ACPA effects.
**Conclusions:** ACPAs promote SFs migration and adhesion acting synergistically with IL-8 through a PAD-dependent pathway. Our findings suggest that SFs may have a potential role in the ACPA-dependent disease propagation from the bone marrow to synovial tissue.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2748

## OP0299 SUSCEPTIBILITY TO ANKYLOSING SPONDYLITIS IS INFLUENCED INDEPENDENTLY BY TWO CLOSELY ADJACENT RUNX3 SNPS, THAT SHOW STRONG FUNCTIONAL EFFECT IN DIFFERENT CELL TYPES

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**Background:** More than 60 genes are associated with ankylosing spondylitis (AS), many of which (*RUNX3, EOMES, TBX21, ZMIZ1, IL23R, IL6R, ERAP-1, IL7 and IL7R)* are involved in diverse immunological processes.[1] To understand the functional basis for these genetic associations is one of the greatest scientific challenges in complex polygenic diseases. For example, the association between AS and the single nucleotide polymorphism (SNP) *rs4648889* located in a 2kb regulatory *locus* upstream the promoter of *RUNX3* can be explained by allele-specific effects on transcription factor (TF) recruitment (including IRF4) that alter gene expression, specifically in CD8+ T-cells.[2]
**Objectives:** 22 SNPs in the *RUNX3* locus were initially found to be associated with AS. Here we focus on an independently associated SNP adjacent to *rs4648889* which affects gene regulation in CD14+ monocytes.
**Methods:** We used the Encyclopedia of DNA Elements (ENCODE) data to dissect the epigenetic and transcriptional landscape of the RUNX3 locus; we performed *in silico* analysis and *in vitro* functional studies to characterize the effects of this particular genetic variant, providing critical functional evidence for its role in AS.
**Results:** (1) Conditional analysis on 4230 AS cases and 9700 matched controls established the primacy of *rs4648889* association ($1.3\times10^{-14}$) with AS in this region. However, there was also an independent second signal ($1.7\times10^{-7}$) with *rs4265380*, adjacent to *rs4648889*, highlighting the importance of this *locus* and a likely functional role for *rs4265380*. (2) ENCODE data on CD14+ monocytes, revealed a robust peak for DNA accessibility (DNase1 Hypersensitivity) and TFs ChIP-seq overlapping *rs4265380*. There was also a strong overlying peak for histone modification H3K4Me1, normally associated with active regulatory region. (3) The effect of the *rs4265380* dimorphism on TF binding was evaluated by electrophoretic mobility shift assays (EMSA) using nuclear extract from U937 and THP-1 (monocyte-derived cell lines) focusing on specific TFs involved in monocyte regulation, inflammation and chromatin modifiers (C-Fos, p300 i.e.). (4) Analysis of the expression of inflammasome-related genes revealed some striking differences (i.e CARD6 and IL-6, upregulated of 5 and 177 fold, respectively) influenced by the *rs4265380* genotype.
**Conclusions:** We have identified functional differences in the transcriptional regulation of *RUNX3* associated with AS-associated SNPs at this locus. Two individual adjacent SNPs exert their independent effects in two separate cell types (CD8+ T-cells and monocytes). These observations are critically important not only in identifying cell types that play a pathogenic role in AS but also in defining potential therapeutic drug targets.
**References:**
[1] IGAS et al. Nat Genet. 2013 Jul;45(7):730–8
[2] Vecellio M. et al, Ann Rheum Dis. 2015 Oct 9 pii: annrheumdis-2015–207490
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2252

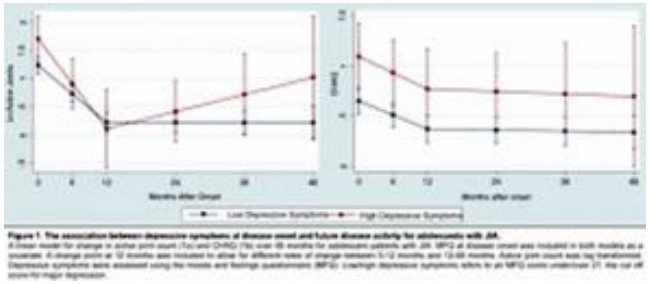
**SATURDAY, 11 JUNE 2016**

# Transition of care

## OP0300 DO DEPRESSIVE SYMPTOMS AT DISEASE ONSET ASSOCIATE WITH FUTURE DISEASE ACTIVITY FOR ADOLESCENT PATIENTS WITH JIA? RESULTS FROM THE CHILDHOOD ARTHRITIS PROSPECTIVE STUDY (CAPS)

L. Hanns[1], L. Cordingley[2], J. Galloway[3], S. Norton[3], L.A. Carvalho[1], D. Christie[1], D. Sen[1], R. Carrasco[2], A. Rashid[2], H. Foster[4], E. Baildam[5], A. Cheing[6], J. Davidson[7], L. Wedderburn[8], K. Hyrich[2], W. Thomson[2], Y. Ioannou[1] on behalf of Childhood Arthritis Prospective Study (CAPS).
*[1]University College London, London; [2]University of Manchester, Manchester; [3]Kings College London, London; [4]University of Newcastle, Newcastle; [5]Alder Hey Children's Foundation NHS Trust Liverpool, Liverpool; [6]Royal Manchester Children's Hospital, Manchester; [7]Royal Hospital for Children Glasgow, Glasgow; [8]University of Manchester, London, United Kingdom*

**Background:** Adolescents with rheumatic disease have a four times higher incidence of depression than healthy peers. Studies in adults have shown an association between depression and worse disease in rheumatoid arthritis, yet this association has never been explored in detail for patients with JIA or in a purely adolescent population.
**Objectives:** This study investigates the association between depressive symptoms and 1) disease activity at onset and 2) future disease activity.
**Methods:** Data are from JIA patients in the Childhood Arthritis Prospective Study, a nationwide inception cohort of childhood onset arthritis. Patients are recruited within 6 months of disease onset and the first study visit is identified as "baseline". Patients were included in this analysis if they were aged 11–16 at baseline. Depressive symptoms were assessed using the Mood and Feelings Questionnaire (MFQ). Associations at baseline were analysed using Spearman's correlation. Separate piecewise linear mixed-effect models for change in active joint count and disability (Childhood Health Assessment Questionnaire (CHAQ)) over 48 months was estimated. A change point at 12 months allowed for different rates of change between 0–12 months and 12–48 months. MFQ score at baseline was included as a covariate
**Results:** 102 patients were included. At baseline, mean age was 12.7 years (SD1.4) and 15.7% were taking DMARDS. 56.7% were female, 52.0% had persistent oligoarticular arthritis, 30.4% had polyarticular arthritis and 17.6% had enthesitis related arthritis. 14.7% scored over the MFQ cut-off for probable depression (>27) at baseline. At baseline, depressive symptoms significantly associated with disability ($r=0.51$, $p<0.000$) and active joint count ($r=0.32$, $p=0.001$). Longitudinal analysis showed that depressive symptoms, active joint count and disability rapidly decreased during the first 12 months after baseline and then stabilised. After 12 months, baseline depressive symptoms no longer associated with active joint count whereas disability for those with high baseline depressive symptoms continued to be higher than those with low depressive symptoms (Figure 1).



**Conclusions:** At disease onset, 14.7% adolescents with JIA have significant depressive symptoms. Those with more depressive symptoms have higher numbers of inflamed joints and more disability. In the 12 months after disease onset, a reduction in disease activity is mirrored by improvements in mental health. After the first year, baseline depression no longer associates with subsequent disease activity but remains associated with higher disability. This highlights the importance of psychological health assessment for adolescent patients with JIA and underlines the need for psychological support fully integrated into their routine care.
**Disclosure of Interest:** None declared
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### OP0301 ADOLESCENT AND YOUNG ADULT CARE IN ADULT RHEUMATOLOGY: HOW WELL DO WE KNOW OUR HEEADDSS?

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**Background:** Most rheumatology departments will have a significantly larger cohort of older adolescents and young adults (AYAs) that enter adult services de-novo than will have transitioned from paediatric services. The current move towards a hub and spoke model of care makes it increasingly important that both secondary and tertiary care services are aware of AYA specific needs.
**Objectives:** Our aim was to evaluate AYA care within two different adult Rheumatology clinics, in particular focusing on use of the HEEADDSS psychosocial interview.
**Methods:** A review of clinical correspondence for 120 patients aged 16–25yrs attending adult rheumatology clinics at a secondary and tertiary care hospital in Greater Manchester, UK.
Data collected focussed on evaluating the documentation of components of the HEEADDSS screen.
**Results:** At both sites the "did not attend" rate was equal at 13%. The tertiary hospital had significantly more AYAs with Juvenile Idiopathic Arthritis (JIA) (22 patients) than the secondary care hospital (4 patients).
There were differences in recording of the HEEADDSS criteria. The three most frequently documented at the tertiary hospital were drugs, education, home (41%, 36%, 19% respectively), least documented was sleep (5%). The three most often documented at the secondary care hospital were, education, exercise, activities (24%, 15%, 13% respectively), least documented was sex (1%).
**Conclusions:** There were significantly more AYAs with JIA in the tertiary hospital. Documentation of HEEADDSS criteria varied between the two hospitals, documentation of any component was achieved in less than 50% of AYAs.
A hub and spoke model of healthcare requires all adult rheumatologists to have an understanding the unique needs of AYAs.
**Disclosure of Interest:** None declared
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**SATURDAY, 11 JUNE 2016**

## New approaches to understanding and managing chronic musculoskeletal pain

### OP0302-PARE SUPPORTING PEOPLE WORKING WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES (RMDS)

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**Background:** Work is proven to be good for your health and it is important to people with rheumatic and musculoskeletal diseases (RMDs), both financially and for their quality of life and wellbeing. There is also an enormous social cost. In Ireland, RMDs account for 7 million days in absenteeism - half of the total. That amounts to €750 million each year. €295 million is paid out in illness benefit. Arthritis Ireland is working to improve the supports available to people with RMDs so that they can continue in their jobs or get back to work.
**Objectives:** The objectives of the project were to 1) develop succinct informative guides to working with RMDs for both employees and employers 2) develop an online educational programme to provide information, guidance and support to employees, employers and healthcare professionals on working with RMDs.
**Methods:** In 2011, Arthritis established Fit for Work Ireland – a coalition of stakeholders including employer and employee representatives and health professionals with the key goal of improving employees' ability to work with RMDs and reducing the impact of RMDs on workplace absenteeism.
Arthritis Ireland has developed a number of educational tools to support people with RMDs in the workplace as part of our Fit for Work Programme. 2014 saw the development of two comprehensive guides for employees and employers to help address these challenges. 1) "*Working with arthritis, back pain & related conditions: A guide for employees*" provides up to date and accurate information and advice to make sure an individual can find the help they need to stay in their job. If a person is worried or concerned following a recent diagnosis of an MSD, they can find more information about what kind of support they are entitled to. This guide also discusses the options of re-training or moving to different types of jobs within an organisation. 2) "*Arthritis, back pain & related conditions: A guide for employers*" provides a practical source of information and guidance for employers to help them to understand what MSDs are; understand how MSDs may affect employees and support employees working with MSDs.
In 2015 Arthritis Ireland developed an online education programme "*Fit for Work Online*" which focuses on the tripartite relationship between the employee, employer and healthcare professional.
**Results:** The two published guides for employees and employers have been distributed widely to rheumatology clinics, physiotherapy clinics and GP surgeries. The guides are also available for order or for download on the Arthritis Ireland website. The information has been positively received but employees, employers and healthcare professionals alike.
"*Fit for Work Online*" will launch formally in February 2016.
**Conclusions:** Despite the staggering incidence and the fact that RMDs are the leading cause of work absence in Ireland, these conditions often remain overlooked by policy makers and employers. This project has aimed to improve employee's ability to work with RMDs through the provision of clear and quality information and support.
**Disclosure of Interest:** None declared
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### OP0303-PARE RAISING PUBLIC AWARENESS ON OSTEOARTHRITIS THROUGH AN EDUCATIONAL CAMPAIN

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**Background:** The Swedish Rheumatism Association has in collaboration with Netdoktor.se, Sweden's leading public portal for health issues, developed an online test with the aim of improving public awareness of osteoarthritis. There are many myths surrounding osteoarthritis that we need to address, for example that osteoarthritis is just something one needs to accept rather than it being treatable.
**Objectives:** There is a lack of knowledge in the Swedish society about osteoarthritis. With this online test we want to improve the understanding of the condition. Without basic knowledge it is hard for a patient to demand one's right in the health care system.
**Methods:** The Swedish Rheumatism Association has in collaboration with Netdoktor.se put together a team of experts to review all information in the test. The experts have different backgrounds from both the medicine, IT and PR.
**Results:** This far the test has been very successful, a total of 9 720 individuals have completed the whole test and 35 388 have visited the website for more information.
The test shows that among women with symptoms of osteoarthritis, who had sought medical advice, only 40% have received any explanation on what may cause their joint pain. And out of these women, 23% use naturopathic drugs for their condition. The numbers are almost the same for men; only 41% have received an explanation on what may cause their joint pain and 20% uses naturopathic drugs.
Out of the category which already has been diagnosed with osteoarthritis, 62% have not been invited to join an evidence based supportive osteoarthritis self-management program lead by a physiotherapists. The program helps the patient to gain knowledge to improve their health condition, a program which the Swedish Rheumatism Association recommends.
**Conclusions:** The Swedish Rheumatism Association is able to use the different statistic that the test generates to raise awareness about osteoarthritis. Approximately 800 000 Swedes suffer from osteoarthritis in one or more joints. It is in other words a huge public health issue and more needs to be done for a better care of this patient group. Our aim is that the health care system will increasingly recommend their patients to the supportive osteoarthritis self-management program.
**Disclosure of Interest:** None declared
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**SATURDAY, 11 JUNE 2016**

## Picking knowledge from other medical disciplines for SSc

### OP0304 ESTROGENS INHIBIT THE PROFIBROTIC EFFECTS OF TGF-BETA AND PROTECT FROM THE DEVELOPMENT OF EXPERIMENTAL DERMAL FIBROSIS

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**Background:** Systemic sclerosis (SSc) primarily affects postmenopausal women. This sex bias could partly be explained by the action of estrogens on the immune system and/or fibrogenesis. Since little is known about their direct role in fibrogenesis.
**Objectives:** Our aim was to evaluate the effects of estrogens i) on the pathological activation of dermal fibroblasts induced by transforming growth factor-b (TGF-β) and ii) in the development of experimental dermal fibrosis.
**Methods:** Effects on estrogen inhibition by gene inactivation (knockout mice for the estrogen receptor-α, ERKOα) or targeted molecular strategy (tamoxifen, a selective estrogen receptor modulator that display anti-estrogenic properties) were evaluated in the mouse model of bleomycin-induced dermal fibrosis and in the tight skin (Tsk-1) mouse model.
SSc dermal fibroblasts were stimulated with TGF-β and incubated with different concentrations of 17-β-estradiol and/or tamoxifen. Collagen release from fibroblasts was evaluated by mRNA levels of col1a1 and col1a2 and by measuring the concentrations of collagen in cell culture supernatants with the SirCol collagen assay. Differentiation of fibroblasts into myofibroblasts was assessed by the ex-

pression of alpha smooth muscle actin (α-SMA). Activation of the TGF-β pathway was evaluated by the expression of phospho-smad-2/3.
**Results:** Estrogen inhibition increased the activation of canonical TGF-β signaling and exacerbated skin fibrosis both in the bleomycin model and in Tsk-1 mice. Upon bleomycin injections, ERKO-α mice treated with tamoxifen had a significant increase of dermal thickness (17%, p=0.03 and 20%, p=0.04), hydroxyproline content mice (16%, p=0.02 and 36%, p=0.003, respectively) and number of myofibroblasts (22%, p=0.01 and 20%, p=0.04 respectively) compared to control mice. In Tsk-1 mice, treatment with tamoxifen led to significantly enhanced skin fibrosis, with a 31±8% increase of hypodermal thickening (p=0.03) and a 17% increase of hydroxyproline content (p=0.01) compared to control mice.
In SSc dermal fibroblasts, treatment with 17-β-estradiol significantly decreased the stimulatory effects of TGF-β on collagen synthesis and myofibroblast differentiation, decreased activation of canonical TGF-β signaling, and markedly reduced the expression of TGF-β target genes. Tamoxifen reversed the inhibitory effects of estrogens by restoring Smad2/3 phosphorylation and TGF-β-induced collagen synthesis.
**Conclusions:** Our results demonstrate a beneficial effect of estrogen in experimental dermal fibrosis. Estrogens reduce TGF-β dependent activation of SSc dermal fibroblasts and estrogen inhibition leads to a more severe experimental dermal fibrosis. These findings may partly contribute to the occurrence of SSc in postmenopausal women and the greater severity of the disease in men and open avenue to potential hormonal therapies.
**Disclosure of Interest:** None declared
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## OP0305 PSYCHOLOGICAL PROFILE OF SCLERODERMA PATIENTS DESCRIBED BY MULTIDIMENSIONAL MINNESOTA MULTIPHASIC PERSONALITY INVENTORY (MMPI II) AND BECK DEPRESSION INVENTORY TESTS (BDI II)

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**Background:** Scleroderma is a systemic multiorgan autoimmune disease with high mortality and morbidity rates. In serious disease with organ manifestation, quality of life and perception of health is deeply influenced in these patients. The face changes and fibrosis of skin, digital ulceration contribute to the psychological trauma of these patients. Only little is known about the objective evaluation of systemic scleroderma psychological impact.
**Objectives:** The aim of study is detection of psychological profile and manifestation of depression in scleroderma patients.
**Methods:** From March 2015 to January 2016 we examined 42 patients with scleroderma Patients were evaluated by MMPI-II (The Minnesota Multiphasic Personality Inventory test, standardized psychometric test of adult personality and psychopathology) and BDI-II tests (Beck Depression Inventory test of depression). The data obtained from the multidimensional pachological testing were correlated with the clinical and laboratory pheonotype of the disease (smoking status, BMI, arterial hypertension, diabetes, lipid profile, family history of cardiovascular event, lung manifestation, pulmonary hypertension, digital ulceration, damage of gastrointestinal tract, myositis, renal crisis, autoantibody profile, and presence of cardiovascular events) Statistical tests (descriptive statistic, Student t-test, Spearman test, ANOVA) were performed and p-value $\leq$0.05 was considered as significant.
**Results:** In this study42 patient were included (6 men, 36 women. mean of age – 57,8±9.4y., duration of disease 8,6±8.2y. duration of Raynauds phenomenon 13,4±11,2y.), 12 patient have diffuse form and 30 patient limited form of scleroderma. Subjective perceived depression detected by BDI II test was present in 16 patients (32.1%, mild 7, moderate 7 and 2 severe). BDI-II correlated with anticentromer antibodies (p=0.05), total cholesterol (p=0.008), LDL (p=0.05) and, gastrointestinal manifestation (p=0.002). Scale L, F and K in MMPI-II test in typical sequence for depressive score was detected in 38 patients (90%). The main scales of MMPI-II test were detected in followed percentage values: – Hypochondria (54.7%), Depression (33.3%), Converse hysteria (28.6%), Psychopathic (14.3%), Masculinity/Felinity (7.1%), Paranoia (9.5%), Psychastenia (26.2%), Schizophrenia (21.4%), Hypomania (11.9%) and Social introverse (33.3%).
**Conclusions:** The limitation of these data is fact, that these tests showed some of trends of symptoms typical for psychological and personal manifestation; they could not be regarded as a diagnostic test. Patients with scleroderma have high prevalention of subjective perceived depression. In this study we detected high prevalence of depression, social introversion and trend toward somatisation. It will be very useful to be aware of this subjective perception of scleroderma patient and cooperated with psychologist or psychiatrist to improve quality of life and sometimes also morbidity of these seriously ill patients.
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**SATURDAY, 11 JUNE 2016**

# Paget's and other rare bone diseases

## OP0306 TEN YEARS OF DENOSUMAB TREATMENT IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS: RESULTS FROM THE FREEDOM EXTENSION TRIAL

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**Background:** Osteoporosis is an important chronic disease, requiring prolonged treatment. Long-term efficacy and safety data are therefore of great importance. Denosumab (DMAb) is used in over 80 countries or administrative districts worldwide for the treatment of postmenopausal women with osteoporosis. The effects of DMAb treatment for up to 10 years have been evaluated in the 3-year FREEDOM study and its 7-year extension.
**Objectives:** Report results through the final year of the FREEDOM extension, representing up to 10 years of continued DMAb treatment.
**Methods:** During the extension, all subjects were to receive 60 mg DMAb every 6 months and calcium and vitamin D daily. In this analysis, the long-term group received 10 years of DMAb treatment (3 years in FREEDOM and 7 years in the extension), and the cross-over group received 7 years of DMAb treatment (3 years of placebo in FREEDOM and 7 years of DMAb in the extension).
**Results:** Of the 4,550 subjects who entered the extension, 2,784 (61%) continued to participate at the beginning of year 10. Of these, 2,212 (80%) have completed their final 10-year visit, 120 (4%) discontinued, and 452 (16%) were ongoing at the time of this submission. In the long-term group, further significant increases in BMD occurred with mean cumulative 10-year gains of 21.6% (lumbar spine) and 9.1% (total hip) from FREEDOM baseline. The cross-over group had mean cumulative 7-year gains of 16.3% (lumbar spine) and 7.3% (total hip) from the extension baseline (Figure 1; all $P<0.0001$ compared with FREEDOM baseline, extension baseline, and previous measurement). Similar and sustained reductions in bone turnover markers were observed in both groups, with the characteristic attenuation of effect at the end of the dosing period. Yearly rates of new vertebral and nonvertebral fractures remained low. Overall incidence rates of adverse events (AEs) and serious AEs were consistent with data reported previously in the extension study.

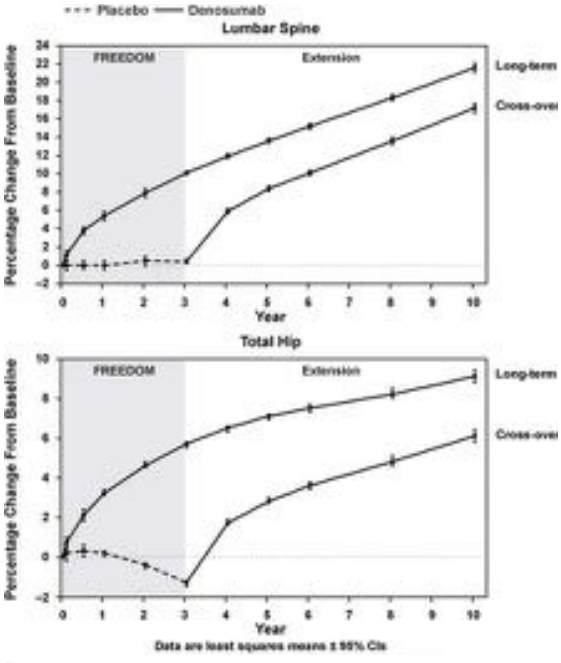



Figure 1

**Conclusions:** DMAb treatment for up to 10 years was associated with persistent reduction of bone turnover, continued increases in BMD without therapeutic

plateau, and low fracture incidence. The benefit/risk profile for DMAb in an aging population of postmenopausal women remains favorable.

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**SATURDAY, 11 JUNE 2016**

## Analytical issues of complex databases

### OP0307 NO LONG-TERM EFFECT ON DISEASE ACTIVITY AND PAIN OF PHYSICAL ACTIVITY FOUND IN PROSPECTIVE OBSERVATIONAL STUDY OF EARLY RHEUMATOID ARTHRITIS

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**Background:** Physical activity was once perceived as potentially harmful for patients with rheumatoid arthritis (RA), but intervention trials in the past decade have shown that physical activity on the contrary is well tolerated in established RA. [1] Further, small, short-term intervention studies have in addition shown potential positive effects of physical activity/exercise on the symptoms of RA [2].

**Objectives:** Prospectively investigate the long-term effect of physical activity on the prognosis of rheumatoid arthritis (RA) in terms of disease activity, measured as DAS28, and pain, measured on the VAS-scale.

**Methods:** We used incident RA cases from the population-based EIRA-study with clinical follow-up in the Swedish Rheumatology Quality Register (2006–2010). We investigated the effect of self-reported physical activity 1 year after diagnosis (>150 min. of moderate/intense or >75 min intense activity/week), on the probability of remission (DAS28<2.6) and remaining pain (CRP<10mg/l and VAS-pain>20mm) after 3 years, using modified Poisson regression, adjusted for sex, age at diagnosis, BMI, education, smoking, physical activity before diagnosis and baseline level of DAS28/pain, respectively. Further, we estimated the longitudinal effect from assessment of physical activity, using mixed models, and also the effect of the combination of physical activity 5 years before/1 year after diagnosis in four groups (low-low, low-high, high-low and high-high).

**Results:** 555 RA-patients were included in this study, the mean age at diagnosis was 54 years and 74% was female. One year after diagnosis, when physical activity was assessed, the mean DAS28 was 2.92 and the mean VAS-pain was 30. We could not detect any effect of physical activity after diagnosis; the adjusted risk ratio for remission was 1.07 (95%CI:0.74–1.53) and for remaining pain 1.12 (95%CI:0.75–1.67). Similarly, no effect was found using longitudinal analysis (p-value for difference in DAS28, comparing active and non-active patients: 0.32, corresponding p-value for difference in VAS-pain: 0.71) or when we investigated the combination pattern of physical activity 5 years before RA-diagnosis and 1 year after.

**Conclusions:** In this prospective cohort study we did not find evidence of an effect of self-reported physical activity on the prognosis of RA, either measured as pain or disease activity. Such lack of improvement could e.g. occur if the effect of physical activity would be short-lasting. There is no reason to doubt the beneficial effect of physical activity on the general health of RA-patients, similar to the effect for the general population.

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**Disclosure of Interest:** None declared

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**SATURDAY, 11 JUNE 2016**

## Intimate life and sexual relations in RA

### OP0308-HPR PRECIPITATING, PREDISPOSING AND MAINTENANCE FACTORS ASSOCIATED WITH SEXUAL DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Sexuality is an important dimension of personality and human body, therefore any involvement in this area should be considered as important. Sexual disturbances in rheumatoid arthritis (RA) patients are poorly described in literature.

**Objectives:** The aim of this study using CIE-10 was to describe different type of factors that may influence the prevalence and worsening of sexual disturbances in patients with RA and relationship with disease activity.

**Methods:** A descriptive cross-sectional study was performed in a specialized clinic dedicated to Ra patients care. Patients seen by the area of psychology, information was collected through semi-structured interviews and non-probability sampling. Descriptive epidemiology was done, using averages and percentages for categorical and qualitative variables; we used chi2 test to study a possible relationship between the level of disease activity with precipitating, predisposing and maintenance factors.

**Results:** Total sample of patients was 1298, 1048 (80%) were women and 250 (19%) were men. Patients had a DAS28 2.6 in average ± 1.1; mean age was 55.1 ± 8.8 years; 451 (40%) women reported no sexual activity, while 627 (60%) reported sexual activity. 77 (31%) of men reported no sexual activity, while 173 (69%) reported sexual activity. 377 (36%) of women and 85 (34%) men referred to have any sexual disturbances (lack of sexual desire, non-satisfactory sexual life, dyspareunia, orgasmic dysfunction, premature ejaculation). The relationship between having a sexual disturbance and the disease activity was not statistically significant. *precipitating factors:* In women 110 (33%) manifested infidelity, 107 (32%) insecurity in sexual role, biological or physical causes 56 (17%) while in men 42 (16%) manifested insecurity in sexual role, 38 (15%) inadequate information, 15 (6%) infidelity, and 7 (3%) biological or physical causes. *predisposing factors:* Of those who had any predisposing factor, in woman 155 (14%) were related to image changes (14%), infidelity 135 (13%), anxiety 23 (2%) and loss of attraction 15 (1.4%), while in men 53 (21%) were related to image changes, 24 (10%) loss of attraction, 18 (7%) infidelity, and 5 (2%) anxiety. *maintenance factors:* In women, 120 (11%) reported maintenance factors related with biological causes followed by 100 (9%) infidelity, 93 (9%) general alteration of couple relationship, 37 (3%) partner's sexual dysfunction and 20 (1.9%) depression and anxiety; while in men, 47 (19%) general alteration of couple relationship followed by 39 (15%) reported maintenance factors related with biological causes, 14 (5%) depression and anxiety, 10 (4%) infidelity and 2 (0.8%) partner's sexual dysfunction. The relationship between precipitating, predisposing or maintenance factors and disease activity was not statistically significant.

**Conclusions:** According to these findings sexual disorders are present in a half of patients with RA both men and women. There are many factors that may influence the prevalence and worsening of sexual disturbances; however the sexual disturbances do not affect disease activity.

**Disclosure of Interest:** None declared

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**SATURDAY, 11 JUNE 2016**

## Bone and heart: common molecular mechanisms in osteoporosis and atherosclerosis

### OP0309 ASSOCIATION OF BONE MINERAL DENSITY AND CAROTID ATHEROSCLEROSIS IN PATIENTS WITH DIABETES TYPE 2

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**Background:** Many epidemiological studies have shown that low bone mineral density (BMD) and atherosclerosis appear to be related. However, their precise correlation is not completely understood [1,2].

**Objectives:** The aim of this study was to examine the relationship between bone mass and carotid measurements in patients with diabetes type 2 (DT2).

**Methods:** 105 patients both sexes with type 2 diabetes aged 54.69±11.07 years were studied. Control group included 84 healthy subjects the same age. Osteoporosis was defined as a femoral neck BMD T score below -2.5. Carotid intima media thickness (cIMT) and carotid plaque occurrence were determined by B-mode ultrasound and BMD by dual-energy X-ray absorptiometry. The plaques were measured in both common and internal carotid arteries.
**Results:** BMD and cIMT were inversely associated both in patients and controls. The correlation was stronger in females than in males, and in females, the correlation was stronger after menopause. Patients with DT2, with carotid plaque had higher cIMT at low BMD than at normal BMD, p=0.020. Multiple linear regression analysis reveals that age ($p<0.001$), smoking (p=0.016), and osteoporosis (p=0.001) were significantly associated with increased cIMT. In women, cIMT was significantly related to age (p=0.01) and osteoporosis (p=0.03). In men, though there was no significant relationship, a trend toward old age and having osteoporosis was observed in increased cIMT (p=0.054, p=0.075).
**Conclusions:** The association between carotid atherosclerosis and bone metabolism has become an increasing focus of interest in recent years [3], and accumulating evidence has shown that atherosclerosis and osteoporosis frequently co-exist. We found inverse association between BMD and carotid measurements in both diabetic patients and controls. Diabetes type 2 patients, especially postmenopausal women, with decreased BMD may have a higher risk of developing coronary atherosclerosis.
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**Disclosure of Interest:** None declared
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### OP0310 ASSOCIATION OF NEUTROPHIL EXTRACELLULAR TRAPS WITH ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS

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**Background:** Neutrophil extracellular traps (NETs) have recently been implicated in vascular damage and atherothrombosis. Extruded DNA fibers containing multiple proinflammatory and thrombotic molecules induce the activation and recruitment of monocytes and dendritic cells to the vessel wall. Enhanced NETosis occurs in rheumatoid arthritis (RA), which has been shown related to the pathogenesis of this disorder. However, the relevance of this abnormality in the development of atherosclerosis has not been elucidated yet.
**Objectives:** To evaluate the association of netosis-derived products with the development of atherosclerosis in RA.
**Methods:** One hundred RA patients and 30 healthy donors were included. Carotid intima media thickness (CIMT) was used as atherosclerosis marker. Inflammatory and prothrombotic molecules, nitric oxide (NO), total antioxidant capacity (TAC) and protein nitration (NTyr) were analyzed in plasma. Neutrophils were isolated from RA patients and controls. Spontaneous and induced NETs formation from RA and control neutrophils was assessed in vitro through fluorescence microscopy. Oxidative stress status (JC1 and DCFH) and myeloperoxidase (MPO), neutrophil elastase (NE) protein expression were measured in neutrophils through flow cytometry. Cell-free DNA plasma levels were analyzed using Sytox staining. mRNA expression of peptidyl arginine deiminase 4 (PAD4) was analyzed in neutrophils by RT-PCR. Receiver operator characteristic (ROC) curves were calculated.
**Results:** Induced NETosis was increased in RA patients alongside MPO and NE protein expression in neutrophils. Cell-free DNA plasma levels were found significantly increased in RA patients. ROC curve analysis showed an area under the curve (AUC): 84, with a high sensitivity (69%) and specificity (86%). Those DNA levels strongly correlated with clinical parameters such as evolution time, DAS28, CRP and ESR and autoimmunity state (RF and anti-CCPs levels). In addition, high levels of cell-free DNA were associated with elevated levels of IL-6, MCP-1, spSelectin and tPA in plasma. Moreover, high levels of cell-free DNA correlated with increased NTyr and TAC and decreased NO. At cellular level, cell-free DNA plasma levels correlated with increased oxidative status in RA neutrophils (JC1 and DCFH) and mRNA expression of PADI4. Those patients having pathologic CIMT showed increased cell-free DNA plasma levels (ROC curve analysis: AUC 77, sensitivity 60%, specifity 72%).
**Conclusions:** 1) Elements associated with the extrusion of NETs are significantly enhanced in RA compared with healthy controls. 2) NETosis-derived products, such as cell-free DNA strongly correlated with clinical parameters, inflammatory and oxidative status in RA patients. Thus, NETosis-derived products demonstrated diagnostic potential for atherosclerosis, which might be a complementary tool to discriminate between normal and pathologic CIMT in RA patients.
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**SATURDAY, 11 JUNE 2016**

## Adiposity as a driver of arthritis through inflammatory mechanisms

### OP0311 SYNOVIAL LIPODYSTROPHY INDUCED BY HYPERCHOLESTEROLEMIA AGGRAVATES SYNOVITIS IN AN EXPERIMENTAL MODEL OF OSTEOARTHRITIS IN RABBITS

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**Background:** Metabolic syndrome (MetS) is a risk factor for osteoarthritis (OA). While obesity contribution is well characterized, less known is the effect of each component of this syndrome on its own. Particularly interesting is the role of hypercholesterolemia, given the high incidence of cardiovascular events and atherosclerosis in OA patients.
**Objectives:** To study the effect of hypercholesterolemia without any other component of MetS in the synovial inflammation in knee OA.
**Methods:** 16 New Zeland rabbits were fed with a high fat diet (HFD, 0.5% cholesterol+4% peanut oil). Six weeks later, OA was induced by anterior cruciate ligament transection and partial medial meniscectomy, in 10 of these animals (OA+HFD group), and in 10 regular chow fed rabbits (OA group). 10 healthy rabbits fed with regular chow were simultaneously followed (Control group). Twelve weeks after OA induction, animals were euthanized and SM isolated for histological and molecular biology studies.
**Results:** HFD, OA and OA+HFD animals gain significantly less weight than control rabbits at the end of the study. We did not find significant differences in systolic blood pressure, serum glucose or oral glucose tolerance between the groups. HFD fed rabbits showed higher total serum cholesterol, triglycerides and C-Reactive Protein levels than rabbits fed a normal diet. Synovitis score was increased in HFD and OA rabbits, and particularly in OA+HFD group, with the more severe score. Synovitis in OA+HFD was characterized by a massive infiltration of foam RAM11+ cells, with higher presence of multinucleated foam cells and stromal fibrosis than in OA. A huge decrease in the adipose tissue area (%ATA)t ogether with a marked decrease in the adipocyte size was observed in the SM of OA+HFD in comparison to OA and control animals. Furthermore, perilipin1a synthesis was significantly decreased in OA+HFD in comparison to OA and control rabbits. In comparison to controls, synovial leptin and adiponectin gene expressions were markedly decreased in HFD and OA rabbits, and especially in OA+HFD animals ($p<0.01$ vs OA), and positively correlated with %ATA in these animals. By contrast, serum leptin was increased in HFD and OA+HFD in comparison to control rabbits. We did not find significant differences in the SM gene expression of the proinflammatory cytokines IL-1$\beta$, COX-2 or MCP-1, between OA and OA+HFD animals. However, TNF SM expression was significantly increased in OA+HFD vs. OA, and significantly correlated with the presence of RAM11+ cells in the SM of these rabbits.
**Conclusions:** Our data show that hypercholesterolemia is an aggravating factor for OA synovitis, inducing an increased infiltration of macrophages and the disappearance of adipose tissue in the SM. Hypercholesterolemia induced a profound decrease in the adipocyte content in the OA SM, together with a remarkable increase in synovial TNF expression. HFD induced a decrease in the synovial expression of leptin and adiponectin in OA rabbits. However, high levels of serum leptin, probably due to systemic synthesis such as that derived from the liver were found in HFD fed animals. Our data indicate that synovial adipocytes and dyslipemia could play pivotal roles in OA joint deterioration in patients with MetS, and support the concept that the link between obesity and OA transcends mechanical loading
**Disclosure of Interest:** None declared
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### OP0312 DIABETES-ACCELERATED EXPERIMENTAL OSTEOARTHRITIS IS PREVENTED BY AUTOPHAGY ACTIVATION

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**Background:** Type 2 Diabetes (T2D) is a risk factor for Osteoarthritis (OA) (1). Autophagy, an essential mechanism in articular cartilage, is defective in T2D and OA (2). However, how T2D may influence OA progression is still unknown.
**Objectives:** We aimed to determine how diabetes affects cartilage integrity and whether pharmacological activation of autophagy has disease-modifying efficacy in diabetic mice with OA.
**Methods:** Experimental OA was performed in the right knee of 9 weeks-old C57Bl/6 male mice (Lean group, N=8) and of 9 weeks-old B6.BKS (D)-*Leprdb* male mice (db/db group, N=16) by transection of medial meniscotibial and medial collateral ligaments. Left knee was employed as control knee. Rapamycin (2 mg/kg weight/day) or Vehicle (dimethyl sulphoxide) were administered intraperitoneally 3 times a week for 10 weeks. Body weight and fasting blood glucose levels were monitorized weekly. Insulin levels in plasma were determined by ELISA at the end of the study. Histopathology in articular cartilage and synovium was evaluated by using semiquantitative scoring and synovitis grading systems, respectively. Immunohistochemistry was employed to evaluate the effect of diabetes and Rapamycin on cartilage integrity and OA biomarkers.
**Results:** Diabetic mice have increased body weight, fasting blood glucose levels and insulin levels compared to lean mice. Importantly, Rapamycin treated mice have significantly reduced body weight and blood glucose and insulin compared to control db/db mice. Moreover, rapamycin treatment significantly reduced the phosphorylation of rpS6, a direct target of mTOR and increased phosphorylation of AMPK. The results indicated that cartilage damage was significantly increased in db/db mice compared to lean group after surgical induction of OA, while no differences are observed in the control knee. mTOR inhibition protects against surgical-induced OA in db/db mice joints. Cartilage damage and OA severity was significantly reduced in the treated group. This reduction was accompanied with a significant reduction in synovium inflammation and in the expression of OA biomarkers, such as MMP-13 and ADAMTS-5 and decreased IL-12 levels. Furthermore, LC3 lipidation, a marker of autophagosome formation, was increased and cartilage cellularity was maintained after treatment, suggesting that autophagy activation protects chondrocytes against death.
**Conclusions:** Our findings indicate that diabetic mice exhibit accelerated-joint damage after experimental OA, and that autophagy activation might be an effective therapy for diabetes-accelerated OA.
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**SATURDAY, 11 JUNE 2016**

## There is more than drugs

### OP0313-PARE THE SWEDISH RHEUMATISM ASSOCIATION'S BLOG ABOUT TRAINING – A NEW WAY OF LEARNING

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**Background:** Regardless of whether we live with a rheumatic disease or not recommendations on physical activity and training apply to all of us. For a person with rheumatic disease easily accessible knowledge and how-to-do ideas on physical activity and training is central. It contributes not only to a reduction of current symptoms but it also contributes to a higher level of sustained health over time, both physically, psychologically and socially. In synergy with the development of IT and different social media, blogging has become a tool of communication also in the public sector. A blog often approaches its reader in a readily accessible way, with updated information and often with a personal tone. By using a blog large groups of people can be reached in a cost effective way.
**Objectives:** To use a blog as a tool to support and encourage individuals with rheumatic disease in both their understanding of and their performance of physical activity and training.
**Methods:** Plan, do, study, act (PDSA) which is a method for systematic improvement of processes was applied.
*Plan:* The Swedish Rheumatism Association's training blog (SRA-tb) was initially set up as a project in 2011. The reader was invited to follow a person with rheumatic disease as she prepared for, performed and evaluated two challenges. The challenges were a cross-country ski race (30k) and a run (5k). The emphasis was placed on the perceived health in relation to disease activity rather than the results in the races. Foremost, symptoms and effects of training in relation to the disease became the focus. A physiotherapist with special competence in rheumatology was appointed editor of the blog.
*Do:* During 2011, 135 posts were made on the SRA-tb. Several of the published posts contained practical information such as examples of exercises, suggestions for self-help but also articles on the latest research on physical activity and training for people with rheumatic disease were also published.
**Results:** *Study:* In 2011 the project resulted in a total of 17351 viewings. The statistics showed that the postings that contained practical advice or was of a more instructing character (i.e. training programs) rendered most viewings. Moreover, the search terms that were used by the readers were monitored. The tool for the blog also allowed for the readers to comment or ask questions, which opened up for dialog and interaction.
**Conclusions:** *Act:* Since the start of the SRA-tb over 850 posts have been made and the blog has become a part of the Swedish Rheumatism Association's communication strategy. During 2015 the blog had 41497 viewings and 198 posts were published. The increase in viewings in relation to the number of posts can be explained by a systematic review and analysis of which topics and search terms that renders most interest. Also, the blog is now often linked to other social media published by the Swedish Rheumatism Association, mainly Facebook.
The Swedish Rheumatism Association is currently facing the challenge to use social media in a more efficient way. As a part of meeting that challenge the Swedish Rheumatism Association is building a digital health platform with the ambition that this will become a knowledge base for life style questions related to rheumatic disease and rheumatology. The blog about training will become a part of this knowledgebase. Our goal is that the digital health platform will help empower our members to influence the course of their disease and to live a healthier life.
**Disclosure of Interest:** None declared
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### OP0314-PARE GROUP EXERCISE THERAPY IN ANKYLOSING SPONDYLITIS (AS): THE PATIENTS' PERSPECTIVE

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**Background:** Group exercises have been recommended for patients with AS with, some exercise classes having been instituted more than 20 years ago. Current practice may therefore not be consistent with the current needs and preferences of AS patients and new scientific insights into required components and dosage (exercises improving joint mobility, strength, cardiopulmonary fitness and neuromotor abilities) dosage (intensity x duration/repetitions, dependent on age and health status), frequency (at least 2–3 times a week).
**Objectives:** To determine to what extent patients with AS are satisfied with a long-existing group exercise programme and what their preferences are regarding the current and required features of group exercise classes.
**Methods:** A survey was administered to patients participating in a group exercise programme used in a randomised trial (1). The programme, once a week during 2.5 hours, consisted of mobility exercises, sports activities (e.g. volleyball, badminton) and hydrotherapy, addressing strength, mobility and fitness without specification of dosage, regular monitoring or home exercises. The survey investigated experiences with the dosage of the programme components (too high/too low), its subjective effects, patients' preferences regarding potentially novel elements (heart rate controlled training, regular standardized assessments of mobility, physical function and activity limitations) and increased exercise frequency (in favour/not in favour/don't know).
**Results:** 43 of 48 patients (90%) returned the survey, 31 (72%) were male, their median age was 58 years (range 33–80). Overall, there were patients finding the dosage of various programme components either high/too high or low/too low and/or deserving less or more attention. The top 3 of most frequently perceived positive effect of the programme were the prevention of deterioration (74%), moving less stiff (61%) and an improved cardiopulmonary fitness (30%). Regarding potential adaptations, the majority of patients favoured implementing

Satisfaction of 43 AS patients regarding a group exercise programme

| Patients' opinions regarding programme components | Exercise therapy | Sports | Hydrotherapy |
|---|---|---|---|
| Duration too short/too long | 4 (9)/3 (7) | 7 (16)/4 (9) | 4 (9)/1 (2) |
| Intensity too high/not high enough | 3 (7)/6 (14) | 3 (7)/9 (21) | 3 (7)/8 (19) |
| **Patients' opinions regarding exercise modalities** | **Muscle strength** | **Joint mobility** | **CP-fitness** |
| Too little attention | 10 (23) | 4 (9) | 12 (28) |
| Enough attention | 32 (74) | 37 (86) | 29 (67) |
| Too much attention | 0 | 0 | 1 (2) |

heart rate-guided cardio-vascular training (63%) and standardized and periodic assessments (74%), whereas a minority favoured increasing the frequency of exercise classes (23%).

**Conclusions:** The variety regarding patients' perception with a group exercise programme of its intensity and preferred components underlines the need for individual adaptions, according to results of regular assessments. As only a minority of patients favours group exercises more than once a week, the delivery of home-based exercises meeting minimum requirements to enhance health status in patients with AS is a future challenge.

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# Poster Presentations

## Adaptive immunity (T cells and B cells) in rheumatic diseases

### THU0001 TERTIARY LYMPHOID ORGANS IN TAKAYASU ARTERITIS: ARE LOCALLY MATURED B CELLS INVOLVED IN THE PATHOGENESIS?

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**Background:** Takayasu arteritis (TA) is a large vessel vasculitis involving the aorta and its major branches. T cell mediated autoimmunity is thought to play a major role in its pathogenesis while the role of B cells is still unclear.
**Objectives:** To study the presence of tertiary lymphoid organs (TLOs) in the aortic wall of TA patients and analyzing if their presence could be associated with the activity of the disease.
**Methods:** Hematoxylin and eosin–stained sections from aorta specimens from patients with TA were screened for tertiary lymphoid organs (TLOs). The presence of B cell aggregates (CD20), follicular dendritic cells (FDCs, CD21), and high endothelial venules (HEVs, PNAd) was investigated by immunohistochemistry. Immune cells from the adventitial layer of one patient were characterized by flow cytometry. Demographic, medical history, laboratory, imaging, treatment and follow up data were extracted from medical records.
**Results:** Aorta specimens from Bentall procedures were available from 7 patients (five female, aged 22 to 57 years) with TA in whom surgery was performed between 2009 and 2014. Surgical treatment was performed at TA diagnosis (n=4) or at a median of 108 [84–156] months after TA diagnosis. Disease was active at surgery in four patients according to NIH score. B cell aggregates-TLOs containing HEVs were observed in the adventitia of all but one patient. Ectopic follicles containing FDCs were found in 5 patients and appeared associated with aortic FDG uptake assessed by PET. In addition, flow cytometry analysis confirmed the accumulation of memory/germinal center–like B cells in the adventitial layer and showed the presence of antigen-experienced T follicular helper cells (Tfh).
**Conclusions:** Apparently functional ectopic lymphoid neogenesis takes place in the aortic wall of a subset of patients with TA. Our data suggest that the B cells play a key role in the pathogenesis of TA.
**Disclosure of Interest:** None declared
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### THU0002 PREVALENCE OF MONOCLONAL B-CELL DISORDERS IN PATIENTS WITH AUTOIMMUNITY IN THE UK

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**Background:** Persistent inflammation as seen in patients with autoimmune disorders can potentially lead to the development of monoclonal B-cell disorders. The incidence of non-Hodgkin's lymphoma is more than 2-fold higher in RA patients compared to the general population [1]. Monoclonal B-cell lymphocytosis (MBL) refers to the asymptomatic presence of monoclonal B-cells in the peripheral blood with a risk of progression to lymphoproliferative disease. MBL includes CLL-type (CD5 positive) MBL (5.1%), which is more common in the UK and less common non-CLL type (CD5 negative) MBL (1.8%) [2].
**Objectives:** To assess whether the prevalence of monoclonal B-cell disorders is higher in autoimmune disorders compared to the native general population.
**Methods:** Peripheral blood B-cells from patients with autoimmune disorders were analysed using a panel of CD19 PerCP-Cy5.5, CD20 APC-H7, Kappa BV421, Lambda FITC, CD45 BV510, CD305 PE and CD5 PE-Cy7. The presence of MBL was defined according to standard criteria [3], briefly the detection of a monoclonal B-cell population in the peripheral blood with an overall kappa:lambda ratio $>$3:1 or $<$0.3:1, or greater than 25% of B cells lacking or expressing low level surface immunoglobulin, or the presence of a disease-specific immunophenotype in the absence of any other feature diagnostic of a B-lymphoproliferative disorder.
**Results:** Peripheral blood from a total of 128 patients with autoimmune disorders were analysed by flow cytometry for the presence of monoclonal B-cells. This included 101 RA patients, 11 patients with SLE, 7 patients with GPA and 8 patients with other autoimmune disorders. The patient group was predominantly females with female to male ratio of 2.7:1 (93:35). The median age of the patients was 57 years (18–85). 45 patients were between 40 – 60 years old and 55 patients were between 60 – 80 years old. 23 patients were less than 40 years old and 5 patients were more than 80.
The presence of a monoclonal B-cell population was detected in 10.1% (13/128) of the patients. One of these patients was already known to have CLL. The prevalence of CLL type MBL was 2.4% (3/127) and non-CLL type MBL was 7.1% (9/127). Of these 12 patients, 7 patients had RA, 2 patients had GPA, 2 patients had SLE and one patient had an overlap of RA and Sjogren's syndrome. Five patients were between 60–80 years old, three in their 30s, three in their 80s, and one in their 50s.
**Conclusions:** Non-CLL type MBL may be more common in patients with autoimmune disorders compared to the general population in the UK. The apparent relative increase in CD5neg MBL could be associated with the effective control of the inflammatory disease process or the direct effect of therapies used for the treatment of autoimmune diseases on B-cells. More extensive studies are required to understand the implications of current treatment strategies on the selective pressure for expansion of monoclonal B-cell populations.
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### THU0003 MOUSE B CELL CYTOKINE PRODUCTION REQUIRES OXIDATIVE PHOSPHORYLATION MEDIATED BY GLYCOLYSIS AND FATTY ACID OXIDATION

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**Background:** B cells contribute to disease pathophysiology through several mechanisms, including cytokine secretion. A wide variety of stimuli can activate B cells to produce cytokines including B cell receptor (BCR) and Toll-like receptor (TLR) engagement. Recently, numerous observations have established the role of metabolic pathways in the diverse array of immune cell functions. It is unknown though how these metabolic pathways influence B cell cytokine production.
**Objectives:** Delineate the array of cytokines generated by B cells and their metabolic requirement following activation.
**Methods:** B cells were isolated from the spleens of C57Bl/6J mice and activated overnight individually by the following agents: anti-$\mu$ antibody (B cell receptor), anti-CD40 agonist antibody, poly(I:C) (TLR3), LPS (TLR4), ssPolyU (TLR7/8), and CpG (TLR9). Supernatants were collected and analyzed for the quantification of cytokines using the Milliplex Multiplex cytokine kit (EMD Millipore). Real-time analysis of extracellular acidification rates (ECAR) and oxygen consumption rates (OCR) of activated B cells were performed using the XF-96 Extracellular Flux Analyzer (Seahorse Bioscience). Three or more consecutive measurements were obtained under basal conditions and after the sequential addition of 1 $\mu$M oligomycin, to inhibit mitochondrial ATP synthase; 1.5 $\mu$M FCCP (fluoro-carbonyl cyanide phenylhydrazone), a protonophore that uncouples ATP synthesis from oxygen consumption by the electron-transport chain; and 100 nM rotenone plus 1 $\mu$M antimycin A, which inhibit the electron transport chain. To assess 3-carbon sources for oxidative phosphorylation, inhibitors to fatty acid oxidation (etomoxir, which irreversibly inhibits carnitine palmitoyltransferase-1), pyruvate transfer to mitochondria (UK-5099), and glutamine usage (BPTES, which inhibits mitochondrial glutaminases) were used.
**Results:** Both LPS and CpG activation of B cells independently generated the highest levels of cytokine secretion. In addition, these stimuli generated high OCR and ECAR values, reflecting the need for oxidative phosphorylation and lactate production respectively. Both LPS and CpG required free fatty acids and glucose as a carbon sources, as addition of etomoxir and UK-5099 abrogated both cytokine secretion and oxidative phosphorylation.
**Conclusions:** We catalogued the breadth of cytokines secreted by B cells via various stimulatory agents. High-dose LPS and CpG required free fatty acids and glucose for the elaboration of LPS or CpG-induced cytokine production. These data suggest that B cell cytokine secretion can be manipulated by altering the local metabolic environment, and may represent an interesting therapeutic approach for modulating B cells in autoimmune diseases.
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## THU0004 ACTIVATED PLASMACYTOID DENDRITIC CELLS (PDCS) ALTER THE COMPOSITION OF THE BLOOD B CELL SUBSETS

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**Background:** Many autoimmune rheumatic diseases, such as systemic lupus erythematosus (SLE), display multiple aberrations in their B cell functions together with a continuous type I interferon (IFN) production by plasmacytoid dendritic cells (pDCs). Type I IFN has a broad range of immunomodulatory effects but less is known about the impact of direct B cell and pDC interactions.
**Objectives:** We asked whether the peripheral blood B cell phenotype is affected by interactions with pDCs and SLE-related immune complexes (IC).
**Methods:** B cells and pDCs were isolated from peripheral blood of healthy individuals and stimulated with immune complexes consisting of IgG from SLE patients and U1snRNP particles (RNA-IC). The cells were cultivated alone or in cocultures for 6 days. Expression of activation markers, cell surface molecules and proliferation were analyzed by flow cytometry and the production of IL-6, IL-10 and IFN-$\alpha$ were analyzed by immunoassays.
**Results:** Both B cells and pDCs displayed an increased expression of activation markers in the cocultures compared to cultures of B cells or pDCs alone. No increased proliferation of the B cells was detected in the RNA-IC-stimulated cocultures. The production of IL-6 was enhanced in the stimulated cocultures compared to the single cultures of B cells or pDCs, in a similar manner as we earlier have described for IFN-$\alpha$ production by pDCs. Cocultivation of B cells with pDCs resulted in a 7-fold increased frequency of $CD24^{hi}CD38^{hi}$ B cells, independently of RNA-IC. This B cell subset is considered to have a regulatory character, however, the IL-10 production was low in the stimulated cultures. Interestingly, we found a highly increased frequency of double negative $CD27^{-}IgD^{-}$ B cells, from 7% among fresh B cells to 37% in the RNA-IC-stimulated cocultures. This was accompanied by a decreased frequency of memory and naïve B cells. In addition, $CD95^{+}$ expression was induced in a small fraction (1.4%) of the double negative B cells in the RNA-IC-stimulated cultures. We could also confirm a higher frequency of the double negative $CD27^{-}IgD^{-}$ B cells in SLE patients compared to healthy individuals.
**Conclusions:** The pDCs and SLE-related ICs are able to alter the composition and activation of the peripheral blood B cell subsets. Notably, a prominent enrichment of double negative $CD27^{-}IgD^{-}$ B cells, resembling those found in SLE, required presence of both pDCs and SLE related ICs. The functional role of the double negative B cells in SLE is so far unknown, but their presence are reported to correlate with anti-dsDNA autoantibodies and nephritis. Thus, activated pDCs may contribute to the regulation and expansion of potentially pathogenic B cell subpopulations, especially in patients with circulating interferogenic ICs and an ongoing type I IFN production.
**Disclosure of Interest:** None declared
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## THU0005 DRUG RE-PURPOSING WITH A COMMERCIALLY AVAILABLE CHEMICAL LIBRARY IDENTIFIES NOVEL B-CELL INHIBITORY COMPOUNDS

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**Background:** Self-reactive antibodies produced by B-cell derived plasma cells play a crucial role in the pathogenesis of autoimmune disorders. By targeting the source of these pathogenic antibodies, B-cell modulation is one treatment option. However, newly emerging therapeutics directed at specific molecules are not universally available and the current therapies of autoimmune diseases still rely on the systemic use of corticosteroids. Hence, a development of new treatment strategies is required.
**Objectives:** We investigated a hypothesis that some drugs, which are already used for other treatment purposes, might possess unknown B-cell modulatory effects. By using a drug library consisting of 1,200 commercially available, off-patent compounds, an *in vitro* screening evaluating the drug effect on human B cell proliferation was performed. Afterwards, the selected drugs were tested *in vivo* to confirm their effect on adaptive immunity and potential use as therapeutic agents in autoimmune diseases.
**Methods:** Human B cells were obtained from healthy donors. Under the stimulation with IL-21 and anti-CD40 antibody, isolated B-cells were cultured for five days in the presence or in the absence of 1$\mu$M drugs from the library, and the drug effect on cell proliferation was assessed by 5-Bromo-2'-Deoxyuridine (BrdU) ELISA. Dose-dependency and cytotoxicity test with candidate drugs inhibiting B cell proliferation were performed as validation. IgM and IgG production in the culture supernatant was measured by ELISA. For *in vivo* validation, further selected drugs were tested in an experimental animal model of epidermolysis bullosa acquisita (EBA), an autoimmune skin blistering disease characterized by antibody production against type VII collagen which triggers the blister formation [1]. One day prior to the disease induction by immunizing B6.S mice with vWFA2, a subdomain of the pathogenic antigen in EBA [1], drug or vehicle treatment was initiated and continued for eight weeks. Disease severity was recoded weekly, and the antigen-specific B cell as well as plasma cell numbers in the draining lymph nodes were evaluated by flow cytometric analysis.
**Results:** Out of 1,200 drugs, BrdU ELISA screening identified 48 compounds inhibiting human B cell proliferation and the validation narrowed the number of candidates to six. Immunoglobulin production was negatively affected in the presence of these compounds with a dose-dependent manner. Experimental EBA mice treated with the selected drugs showed >50% less disease development compared to the vehicle-treated group. Furthermore, mice treated with one of the candidate drugs had significantly fewer numbers of B cells as well as antigen-specific B cells in the draining lymph nodes ($p<0.05$).
**Conclusions:** The present results suggest unknown properties of "old" drugs in B cell biology as well as the subsequent adaptive immunity and their potential "new" roles in the treatment of autoimmune diseases. In addition, such a drug screening method would save time and be more cost efficient than the conventional approach used to develop new therapeutic agents.
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## THU0006 NOVEL CHANGES IN B AND T-CELL PHENOTYPES WITH BELIMUMAB IN AN AUTOANTIBODY MEDIATED DISEASE

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**Background:** Belimumab is a B-lymphocyte stimulator (BLyS)-specific inhibitor indicated for the treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus. Belimumab has also been shown to reduce anti-phospholipase A2 receptor (PLA2R) autoantibodies and proteinuria in a mechanistic study in primary membranous nephropathy (PMN)[1]. Here we report an interim analysis of B and T cell phenotypes in PMN subjects treated with belimumab to further elucidate the mechanism of action in autoantibody mediated disease.
**Objectives:** To characterize changes in B and T lymphocyte phenotypes in PMN patients treated with belimumab, as a comparison with known pharmacodynamic (PD) effects in SLE[2], and to assess correlation with anti-PLA2R autoantibody.
**Methods:** 14 anti-PLA2R autoantibody positive PMN patients received 10mg/kg iv belimumab every 4 wks (or 2 wks) for up to 100 wks. 11 of these completed at least 28 wks treatment. Whole blood was collected at baseline, Wks 8, 16 and 28 for analysis of B and T-cell phenotypes by flow cytometry. Serum levels of anti-PLA2R antibodies were measured by ELISA (Euroimmun). Statistical analysis to identify PD-induced changes in lymphocyte subsets was carried out by paired t-test (2 tailed) against baseline.
Correlations between anti-PLA2R antibody and B and T-cell subsets, either at a specific time point or in the linearised trend over time, were calculated using Pearson's correlation coefficient (r).
**Results:** There was a significant reduction (-63%, p=0.002) in absolute numbers of naive B cells (CD19+ CD27-) at Wk 8 which was sustained through to Wk 28. There was a significant increase in absolute numbers of memory B cells (CD19+ CD27+) at Wk 8 (70%, p=0.023) which increased further through to Wk 28. Plasmablasts (or SLE subset, CD19lo CD38hi CD27hi) showed a trend at Wk 8 to decrease (-64%, p=0.20) but with high variance and low cell numbers.
In addition, the expression (mean fluorescence intensity) of BAFF-R (B-cell activating factor receptor) on B-memory cells increased through Wk 28, while expression of TACI (transmembrane activator and calcium modulator and cyclophylin ligand interactor) decreased. Activated cells as identified by surface CD95 expression, decreased as a proportion of B-memory cells through Wk 28. No clear trend was seen in T-regulatory or T-activated cells.
There was a significant negative correlation between decrease in absolute numbers of naive B-cells and immunological efficacy defined as level of anti-PLA2R antibody remaining at Wk 28 (r=-0.87, p=0.0005). Correlations were also seen between antibody and changes in proportion of B-memory CD95+ cells.
**Conclusions:** This mechanistic trial of belimumab in PMN has enabled a novel analysis of PD endpoints, confirming but also extending the PD effects previously reported in studies of SLE. Changes in B-cell subsets were associated with improvements in levels of autoantibody in PMN which in turn correlates with proteinuria. Further analysis of longer term anti-PLA2R antibody kinetics as related to early changes in B and T cell phenotypes may also be informative.
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**Disclosure of Interest:** C. Barrett Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, R. Henderson Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, N. Galwey Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, S. Flint Grant/research support from: GlaxoSmithKline, A. Gibson Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, C. Savage Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline
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## THU0007 ENHANCED IGG4 PRODUCTION BY FOLLICULAR HELPER TYPE 2 T CELLS IN IGG4-RELATED DISEASE

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**Background:** IgG4-related disease (IgG4-RD) is characterized by elevated serum IgG4 and increased circulating plasmablasts[1]. The high degree of somatic hypermutation and emergence of distinct plasmablast clones at disease relapse suggests the de novo recruitment of naïve B cells into T-cell–dependent responses[1]. Follicular helper T (Tfh) cells play a major role in T-cell–dependent B cell responses, and their counterparts and subsets (Tfh1, Tfh2 or Tfh17 cells) have only been recognized in peripheral blood[2]. We previously reported that Tfh2 cells were increased in IgG4-RD[3], although the functional role of Tfh2 cells remains to be elucidated.
**Objectives:** To elucidate the function of Tfh2 cells and involvement in the pathogenesis of active, untreated IgG4-RD.
**Methods:** Active, untreated IgG4-RD (n=17) were compared to healthy controls (HC) (n=12), patients with primary Sjögren syndrome (pSS) (n=20) and multicentric Castleman's disease (MCD) (n=5). Tfh2 cells (CD3+CD4+CD45RA-CXCR5+CXCR3-CCR6-cells), activated Tfh2 cells ($CCR7^{lo}PD\text{-}1^{hi}$ subset in Tfh2 cells) and plasmablasts (CD19+CD20-CD27+CD38+cells) were detected by flow cytometry. The function of Tfh2 cells was evaluated by co-culture with autologous naïve B cells in vitro. Disease activity was evaluated by IgG4-RD Responder Index (IgG4-RD RI) score.
**Results:** The percentage of Tfh2 cells was significantly increased in IgG4-RD compared to pSS, MCD or HC, and correlated with serum IgG4 levels ($\rho$=0.7377, $P$ =0.0011) or the percentage of plasmablasts ($\rho$=0.6127, $P$=0.0104). In vitro, Tfh2 cells induced a greater percentage of differentiation of naïve B cells into plasmablasts in IgG4-RD and HC compared to Tfh1 and Tfh17 cells. Of note, while IgG production in culture supernatants of Tfh2 cells were comparable between IgG4-RD and HC, IgG4 production was significantly higher in IgG4-RD compared to HC. Accordingly, IgG4/IgG ratio in culture supernatants was also significantly higher only with Tfh2 cells from IgG4-RD. In addition, the percentage of activated Tfh2 cells was significantly increased in IgG4-RD (8.0 ± 1.6%) compared to pSS (1.4±0.2%, $P<0.0001$), MCD (1.6±0.5%, $P<0.0001$) or HC (1.2±0.2%, $P<0.0001$), and correlated strongly with IgG4-RD RI score ($\rho$=0.7984, $P$=0.0002). In particular, the percentage of activated Tfh2 cells associated with the number of affected organs ($\rho$=0.8152, $P$=0.0001), and decreased with glucocorticoid treatment in parallel with disease improvement. Of note, the percentage of activated Tfh2 cells was re-elevated at disease relapse.
**Conclusions:** Tfh2 cells, but not Tfh1 or Tfh17 cells, induce the differentiation of naïve B cells into plasmablasts and IgG4 production in patients with active, untreated IgG4-RD. This increase in activated Tfh2 cells is linked to disease activity, suggesting that Tfh2 cells play a pivotal role in the pathogenesis of IgG4-RD.
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**Acknowledgement:** We thank the patients and healthy individuals who participated in this study. We thank Mr. Noriyasu Seki, Mr. Humitsugu Yamane, Mrs. Yoshiko Yogiashi and Ms. Yuki Otomo for their technical assistance.
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## THU0008 LEUCINE-RICH ALPHA 2 GLYCOPROTEIN PROMOTES THE DIFFERENTIATION OF TH17 AND DETERIORATES COLLAGEN INDUCED ARTHRITIS THROUGH ENHANCEMENT OF TGF BETA SIGNALING

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**Background:** We have identified leucine-rich alpha 2 glycoprotein (LRG) as a disease marker of rheumatoid arthritis (RA) [1)]. Although LRG is produced in site of inflammation such as synovial tissues, its function is still unclear. Recently, LRG is reported to bind with TGF-β and enhance of Smad2 phosphorylation [2)]. TGF-β is essential for differentiation of Th17. Th17 plays important roles in the pathogenesis of RA, for example, by regulating osteoclast differentiation. In collagen induced arthritis (CIA), a mouse model of RA, phosphorylation of Smad2 in CD4 T cells is important for the Th17 differentiation and the induction of arthritis [3)]. Thus, LRG may be involved in the pathogenesis of RA through the regulation of T lymphocyte differentiation.
**Objectives:** In this study, we aimed to elucidate the function of LRG on T lymphocyte differentiation and to examine the involvement of LRG in the pathogenesis of RA.
**Methods:** Naïve T lymphocyte were isolated from WT or LRG KO mice to examine the effects of LRG on the differentiation into Th17 and Treg in the absence or presence of recombinant LRG. Male C57BL/6 mice and LRG KO mice were subjected to collagen-induced arthritis (CIA).
**Results:** In the presence of TGF-β alone, the differentiation of Treg was promoted by LRG. However, in the presence both TGF-β and IL6, LRG enhanced the differentiation into Th17 by increasing both Smad2 and STAT3 phosphorylation. The phosphorylation of p38 was also increased by LRG. In addition, the expression of IL6 receptor in naïve T cells was significantly lower in LRG KO mice than in WT mice. In CIA model, arthritis score was significantly lower in LRG KO mice than in control group. The numbers of Th17 in regional lymph nodes and serum levels of IL17 were significantly lower in LRG KO mice than in WT mice.
**Conclusions:** LRG promoted TGF-β-induced Smad2 phosphorylation under Th17 differentiation condition. Since Smad2 signal increases the expression of IL6 receptor in naïve T cells [4)], LRG might increase the expression of IL6 receptor through Smad2 signal, leading to enhanced the phosphorylation of STAT3 which is an essential transcription factor in the differentiation of Th17 [4)5)]. LRG also enhanced phosphorylation of p38 MAPK which is involved in the proliferation of helper T cells. In addition, recent study reported that p38 MAPK plays an important role in the production of IL17 [6)7)]
Taken together, our study suggested that LRG promotes both the proliferation and Th17 differentiation of naive T cells under inflammatory state, leading to deterioration of arthritis.
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## THU0009 ADIPONECTIN-ADIPOR1-STAT3 DEPENDENT PATHWAY IS A CRITICAL REGULATOR OF TH17 CELL DIFFERENTIATION IN COLLAGEN-INDUCED ARTHRITIS

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**Background:** We previously showed that adiponectin (AD) acts to promote Th17 cell differentiation, suggesting that AD plays an important role in mediating joint inflammation and damage in collagen-induced arthritis (CIA).
**Objectives:** The aim of this study was to investigate whether STAT3 expression is regulated by AD, and if so, whether knockdown AdipoR1 could inhibit STAT3 and Th17 expression and prevent disease progression in CIA.
**Methods:** Expression of Th17, AD and STAT3 in joint tissue of CIA was detected by real-time PCR and flow cytometry. STAT3 promoter activity was analyzed using a Dual-Luciferase Reporter Assay. The effect of AD on STAT3 expression in *vitro* and *vivo* was assessed using histological analysis, real-time PCR and flow cytometry.
**Results:** Expression of STAT3 was up-regulated and positively correlated with highly expressed AD in joint tissue of CIA. Moreover, AD treatment markedly enhanced STAT3 expression both in *vitro* and *vivo*. Moreover, we found that the anti-Th17 differentiation effect of STAT3 inhibitor can be stimulated by addition of exogenous AD partly. Mechanistically, we showed AD activated STAT3 transcription by binding to the promoter region of the STAT3 gene. Further, using the CIA model, we showed that treatment with the AdipoR1 RNA interference led to reduction of STAT3 levels, decrease of Th17 response, and attenuation of inflammation and disease progression in *vivo*.
**Conclusions:** Our results not only reveal a new role of AD in promoting Th17 development via upregulation of STAT3 expression. Our study also suggests that the pro-Th17 cell differentiation effect of AD is mediated through AdipoR1.
**Disclosure of Interest:** None declared
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## THU0010 LACK OF CRP RESPONSE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS - WHAT ARE THE IMMUNOLOGICAL CAUSES, AND HOW CAN WE HARNESS THIS DATA TO IMPROVE DISEASE OUTCOMES

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**Background:** Using musculoskeletal ultrasound (US) to assess joint erosions and disease activity in patients with rheumatoid arthritis (RA) an atypical subgroup was identified with active disease demonstrated by significant Power Doppler, but normal C-reactive protein (CRP) levels. We questioned whether this presentation was associated with delayed diagnosis or relative under treatment, risking worse disease outcome and/or disability. We hypothesized that understanding the underlying immune pathology in this atypical subset of patients could directly influence therapeutic targeting in patients whose needs are not currently met.

**Objectives:** Define the immunological and clinical phenotype of RA patients with active disease and either normal or high CRP levels. Investigate whether lack of CRP response is associated with altered inflammatory cytokine signaling and exploit the immunological and clinical phenotype of this patient subgroup to propose a more appropriate treatment algorithm.
**Methods:** 44 RA patients with active synovitis were recruited, defined by ≥1 joint with Power Doppler detected by US, 29 had normal (n)CRP (≤5mg/L) and 15 had high (h)CRP (>5mg/L) levels. Peripheral blood mononuclear cells (PBMCs) and serum as well as detailed clinical and disease activity scores were collected. Blood from 18 age and sex matched healthy donors was obtained. Multicolour flow cytometry was used to perform in depth PBMC immunophenotyping and serum cytokines were assessed using a Cytometric Bead Array.
**Results:** The erosion accrual rate was elevated in patients with nCRP compared to hCRP suggesting more disease-associated joint damage, while no significant differences were detected between patient groups in terms of autoantibody levels, ESR and disease activity scores. Inflammatory cytokine levels were elevated in both the nCRP and hCRP patients including IL1β ($p$=0.0364; 0.0233) and IL6 ($p$=0.0009; 0.0007) which are known to trigger CRP production. This suggested that nCRP patients could have defects in downstream IL6 signaling, or alternatively, the disease mechanism may not be IL6-dependent in the nCRP group. Since IL6 is known to support T-cell and T-follicular helper-cell (Tfh) activation and differentiation we compared the T-cell phenotype in the two patient groups. As expected, $CD4^+$ T-cells from hCRP patients with RA were activated compared to healthy donors ($p$=0.0054) and had increased central memory (p=0.0380, T-CM) and Th17 populations. Similarly, only Tfh-cells in hCRP patients were activated compared to nCRP ($p$=0.0026). In contrast, nCRP patients had a less inflammatory phenotype characterized by the highest level of regulatory T-cells (T-reg) compared to healthy donors ($p$=0.0036) and hCRP ($p$=0.0303) and raised serum IL10 suggesting increased immune modulation in these patients. This was supported by a significant correlation between Treg and TCM populations in the nCRP ($p$=0.05) but not the hCRP patients.
**Conclusions:** Overall, this supports altered immunological mechanisms in nCRP compared to hCRP patients which could have therapeutic implications.
**Disclosure of Interest:** None declared
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## THU0011 CD32+ B LYMPHOCYTES AND IL21R+ T LYMPHOCYTES ARE ASSOCIATED WITH DISEASE ACTIVITY AND INCREASED LEVELS OF PROINFLAMMATORY CYTOKINES IN PATIENTS WITH RHEUMATOID AND PSORIATIC ARTHRITIS

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**Background:** Autoimmunity is presumed to be a major driving force in the pathogenesis of chronic rheumatic diseases, including rheumatoid arthritis (RA) and psoriatic arthritis (PSA). Although these forms of arthritis differ in their clinical features, both are marked by persistent inflammation and osteoresorption underpinned by aberrant lymphocyte populations and disturbed cytokine network.
**Objectives:** Various subpopulations of both T and B lymphocytes have been implied in RA and PSA, but their relevance to disease onset and progression remains largely unclear. The aim of our study was to define the association of T, B and NK cell subpopulations with cytokine levels and clinical parameters in RA and PSA patients.
**Methods:** Mononuclear cells were isolated from peripheral blood of healthy controls (n=35), RA (n=36) and PSA (n=13) patients, after obtaining Ethical approval and informed consent. Flow cytometry was applied to discriminate between T lymphocyte subpopulations: Th1/2 (CD3+CD4+CCR6-), Th17 (CD3+CD4+CCR4+CCR6+), Tfh (CD3+CD4+CXCR5+), Tc (CD3+CD8+) and memory Tc (CD3+CD8+CCR4+); B lymphocyte subpopulations: naïve (CD19+IgD+CD27-), unswitched memory (CD19+IgD+CD27+), class-switched memory (CD19+IgD-CD27-) and plasmablasts (CD19+IgD+CD27hiCD38+); and NK cells (CD3-CD19-CD56+). Markers of lymphocyte maturation (CD32), activation (CD86, IL21R, CD25) and migration (CD11b) were also analyzed. Frequencies of lymphocyte subpopulations were correlated with clinical parameters, including DAS28 (for RA and PSA) and BASDAI (for PSA with spondylitis). Finally, serum levels of various cytokines (TNF, IL4, IL6, IL10, IL17, CCL2, CCL3, CCL4, CCL5) were measured by flow cytometry bead based assay.
**Results:** Several subpopulations were found to be significantly expanded: CD32+ naïve (Ctrl 1.8%, RA 5.8%, PSA 6.0%) and memory B lymphocytes, both class-switched (Ctrl 1.8%, RA 5.3%, PSA 3.8%) and unswitched (Ctrl 4.0%, RA 16.8%, PSA 13.7%); memory Tc lymphocytes (Ctrl 4.8%, RA 6.8%, PSA 9.1%); and CD11b+ B lymphocytes (Ctrl 15.1%, RA 20.9%, PSA 20.2%). Significant correlations between lymphocyte subpopulations and clinical parameters included: positive association of IL21R+ T lymphocytes with DAS28 in RA (ρ=0.45) and negative with BASDAI in PSA (ρ=-0.86); negative association of class-switched memory B lymphocytes with DAS28 in RA (ρ=-0.52), but positive with BASDAI in PSA (ρ=0.71). Correlation of lymphocyte subpopulations with cytokine levels showed: significant positive association of CD32+ naïve B lymphocytes with TNF and CCL5 (ρ=0.55 and 0.54); CD32+ class-switched and unswitched memory B cells with TNF (ρ=0.47 and 0.55) and CCL4 (ρ=0.47 and 0.54); CD11b+ B lymphocytes with CCL4 (ρ=0.47); and IL21R+ T lymphocytes with TNF, CCL3 and CCL4 (ρ=0.42, 0.47 and 0.49).
**Conclusions:** Our results indicate novel T and B lymphocyte subpopulations induced in both RA and PSA. CD32+ B lymphocytes, as well as IL21R+ T lymphocytes, may be of particular interest as possible therapeutic targets, since their frequency is associated with disease activity and increased levels of proinflammatory and proresorptive cytokines.
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## THU0012 REGULATORY T- CELLS IN PERIPHERAL BLOOD OF DMARD-NAIVE PATIENTS WITH VERY EARLY RHEUMATOID ARTHRITIS: ASSOCIATION WITH DISEASE ACTIVITY AND SYSTEMIC DISEASE MANIFESTATIONS

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**Background:** Regulatory T (Treg) cells play a critical role in the regulation of peripheral immune tolerance.The ability of Tregs to suppress T-cell responses,and thereby to regulate immune reactions,points to their key role in the pathophysiology of autoimmune diseases
**Objectives:** To investigate the percentage and absolute number of Treg cells in peripheral blood of healthy donors and DMARD-naive very early rheumatoid arthritis (VERA) patients (pts) by immunocytometry and to analyze the association between Treg cells subsets and RA activity
**Methods:** Peripheral blood of 20 healthy donors and 39 VERA DMARD-naive pts (34F/5M, Me;IQR age 50; 32–58 years, disease duration 5.0; 4.0–6.0 months, DAS28 5.1; 4.3–5.8, RF positive-66.7%, anti-CCP positive-87.2%) were assessed for Treg-cell subpopulations. Human blood mononuclear cells were isolated from whole venous blood by Ficoll–Hypaque centrifugation and subjected to multicolor flow cytometry analysis. Tregs were stained for different surface markers, and proportions of marker-positive subsets (FoxP3+CD25+; CD152+surface; CD152+intracellular; FoxP3+CD127-; CD25+CD127-; FoxP3+ICOS+; FoxP3+CD154+; FoxP3+CD274+) between healthy controls and pts were compared
**Results:** We found the lower percentage of FoxP3+CD25+T-cells in pts with VERA,compared to healthy donors: 5.5% (4.1–6.5) vs 6.9% (5.8–7.9); the percentage and the absolute number of FoxP3+ICOS+T-cells: 6.9% (2.1–11.5) vs 10.8% (9.3–13.7); 0.0035 (0.0013–0.0067) vs 0.0068 (0.0039–0.009);the percentage and the absolute number of FoxP3+CD154+T-cells: 0.47% (0.19–0.83) vs 1.5% (1.12–2.08); 0.0002 (0.0001–0.0005) vs 0.0009 (0.0005–0.0014); the percentage and the absolute number of FoxP3+CD274+-cells: 0.6% (0.3–1.5) vs 1.9% (1.2–2.2); 0.0003 (0.0002–0.0007) vs 0.001 (0.0006–0.0016), $p<0.05$ for all cases. We found a negative correlation between the percentage of FoxP3+CD25+ T-cells and CRP in pts with VERA (r=-0,4), ESR (r=-0,43); the percentage of CD152+ intracellular T-cells and DAS28 (r=-0,4), ESR (r=-0,52), CRP (r=-0,55); the percentage of FoxP3+CD127- T-cells and ESR (r=-0,41), CRP (r= -0,48); the percentage of CD25+CD127-T-cells and DAS28 (r=-0,53), SDAI (r=-0,5), CDAI (r=-0,44), ESR (r=-0,56), CRP (r=-0,53), $p<0.05$ for all cases. Low percentage of CD25+CD127–cells compared to pts with low/moderate disease activity was observed in the group of pts with high disease activity (DAS28>5.1 SDAI>26 CDAI>22, n=27) (5.1% (4.9–5.6) vs 6.9% (6.4–7.9), $p<0.05$). A lower percentage of FoxP3+CD127- T cells: 4.2% (2.8–5.4) vs 6.4% (4.9–7.3) and the percentage of CD25+CD127- cells: 5.1% (3.5–5.1) vs 6.6 (5.6–7.9) was found in pts with systemic disease manifestations (n=7), $p<0.05$ for all cases
**Conclusions:** VERA pts have demonstrated the lower frequency of FoxP3+CD25+regulatory T cells and the percentage and the absolute number of FoxP3+ICOS+, FoxP3+CD154+, FoxP3+CD274+ cells in comparison to healthy donors. These markers characterize activated Treg cells, capabale of effective immunosuppression, thus lower levels of these markers on Treg surface and reduced numbers of marker-positive cells, suggest that Treg function is reduced in VERA pts. Diminished T-reg cell counts are associated with higher disease activity and systemic disease manifestations
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3983

## THU0013 NORMAL CD19-NEGATIVE PLASMA CELLS ARE BIOLOGICALLY DISTINCT FROM OTHER NORMAL PLASMA CELLS AND LIKELY TO BE INVOLVED IN LACK OF RESPONSE TO B-CELL DEPLETION FOR AUTOIMMUNE DISORDERS

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**Background:** Plasma cells (PCs) are heterogeneous in terms of function and lifespan. Long-lived PCs are not depleted by B-cell depletion therapy for autoimmune disorders and therefore likely to be responsible for lack of clinical response in a significant proportion of patients. Until recently [1], the phenotype of long-lived PCs was not known. Understanding the biological features of long-lived PCs could greatly facilitate identification of therapeutic targets. Long-lived PCs contribute to humoral memory, and may represent the cell of origin for myeloma while neoplastic PCs are generally distinguished by lack of CD19 expression. However, polyclonal $CD19^{Neg}$ PCs constitute approximately 15–35% of total PCs in people aged over 50 years. Here we further characterize normal $CD19^{Neg}$ PC populations in the context of normal and therapeutically perturbed bone marrow.
**Objectives:** To establish the phenotypic and functional differences between normal $CD19^{Pos}$ and $CD19^{Neg}$ human PCs
**Methods:** Extensive phenotyping of surface and intracellular proteins of normal and myeloma PCs were performed by flow cytometry. The regeneration of normal PCs was monitored following bone marrow ablation for myeloma [2] and B-cell depletion with alemtuzumab [3] in a series of clinical trials. The immunoglobulin heavy chain variable (IGHV) region of normal $CD19^{Pos}$ and $CD19^{Neg}$ human PCs were sequenced as described previously [4] to identify phylogenetic relationships.
**Results:** $CD19^{Neg}$ PCs are phenotypically distinct from normal $CD19^{Pos}$ plasma cells with weaker CD95 ($p<0.0001$) and stronger ($p<0.0001$) BCL2 expression. Normal $CD19^{Neg}$ PCs share some characteristics with neoplastic PCs including variable expression of CD28, CD56, and CD45, but neoplastic PCs are reliably distinguished from normal $CD19^{Neg}$ PCs by differential expression of CD27, CD81 and CD117 as well as CD56 in some cases. After effective myeloablation for myeloma $CD19^{Pos}$ PCs recovered in 74 out of 80 samples, while $CD19^{Neg}$ PCs remained at less than 1% of total PCs in 30 out of 80 samples. Therapeutic B-cell depletion with alemtuzumab for chronic lymphocytic leukaemia results in loss of $CD19^{Pos}$ PCs ($p<0.0001$) whereas $CD19^{Neg}$ PCs persist. There was little overlap between the IGHV repertoire with only 2.1 to 3.7% of unique IGHV@ rearrangements shared between the $CD19^{Pos}$ and $CD19^{Neg}$ fractions, suggestive of a largely discrete immunoglobulin repertoire in the two fractions at steady state.
**Conclusions:** $CD19^{Pos}$ and $CD19^{Neg}$ PCs are biologically distinct with different immunoglobulin repertoires and production kinetics consistent with $CD19^{Neg}$ PCs having greater potential lifespan. Identifying the developmental pathway of normal $CD19^{Neg}$ PC is likely to allow selectively targeting PC compartments for autoimmune disorders.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5652

## THU0014 CCR6 EXPRESSION REGULATES ARTHRITIS IN A T CELL DEPENDENT MANNER

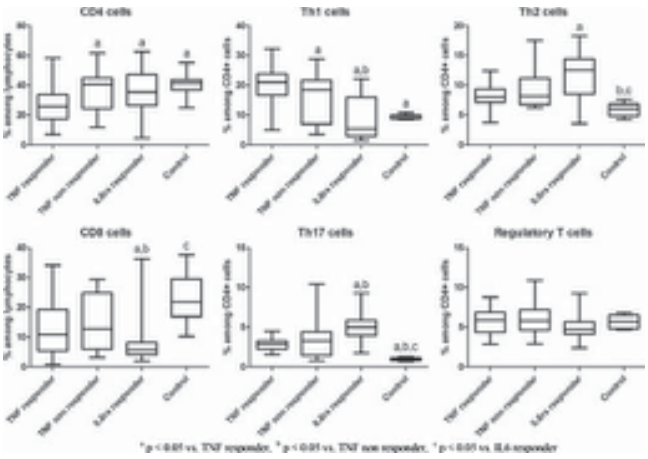
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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease, characterized by synovial infiltration of various inflammatory cells. Chemokines are involved in controlling the recruitment of different cell types into the synovial membrane. Increased production of MIP-3-a and accumulation of CCR6 expressing mononuclear cells can be found in joints of RA patients. CCR6 expression has also been reported on $CD4^+$ T cells, in particular regulatory as well as Th17 cells. Recent data suggest that $CD25^-Foxp3^+$ T cells upregulate CCR6 and promote arthritis.
**Objectives:** In this study, we investigated the role of CCR6 in the pathogenesis of arthritis using different arthritis models.
**Methods:** Clinical as well as histological signs of arthritis were investigated in the collagen-induced arthritis (CIA), K/BxN serum transfer arthritis and in the human tumor necrosis factor (hTNFtg) arthritis model, comparing *wt* and *CCR6–/–* mice. We analyzed the phenotype of lymph node cells by flow cytometry and cytokine concentrations in serum. Anti-collagen antibodies and cytokines were measured by enzyme-linked immunosorbent assay.
**Results:** Since CCR6 is an important component of the innate immune system we compared the development of arthritis in *CCR6–/–* mice in 2 different arthritis models known to be T cell independent, the K/BxN serum transfer arthritis and hTNFtg arthritis. In both models, we did not detect any significant differences in clinical signs of inflammation or histological severity of arthritis between wt and CCR6–/– mice. In additon, we could not detect differences in bone density between *wt* and *CCR6–/–* mice. To investigate the role of CCR6 as part of the adaptive immune system in the development of arthritis we induced CIA in *wt* and *CCR6–/–* mice. *CCR6–/–* mice were almost completely protected from CIA. Analyses of T cell subsets by flow cytometry revealed a significant reduction of $CD25^-Foxp3^+$ T cells.
**Conclusions:** These data suggest that CCR6 is not crucially involved in innate immunity driven arthritis, but is necessary for the development of autoimmune arthritis. Importantly, CCR6 is necessary for the generation of pathogenic $CD25^-Foxp3^+$ T cells in CIA, suggesting an important function of CCR6 on T cells in the development of autoimmune arthritis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2983

## THU0015 THE IMPACT OF BIOLOGIC THERAPIES ON CD4+ AND CD8+ CELL SUBSETS IN RHEUMATOID ARTHRITIS: A LONG TERM FOLLOW-UP STUDY

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**Background:** Rheumatoid arthritis (RA) is characterized by abnormal prevalence of Th1, Th2, Th17, and regulatory (Treg) subsets. Some data suggest that these subsets are influenced by anti-RA agents. Biologic therapies target different elements in autoimmune process. These agents are regarded as therapeutically equivalent clinical alternatives in RA. However, there are still some slight differences in their action, individual responses, and side effect profile. Follow-up studies monitoring T cell phenotype in response to biologic therapies are limited. We investigated the alteration of CD4+ and CD8+ T cell subset distribution during long term follow-up of anti-TNF and IL-6 receptor antagonist (IL6ra) therapies.
**Methods:** We enrolled RA patients including 28 anti-TNF responders, 38 IL6ra responders and 19 secondary anti-TNF non responders. Blood was taken at least half year after the initiation of biologic therapies. Ten volunteers served as controls. The T cell phenotype was assessed with flow cytometry.
**Results:** In anti-TNF responders, CD4+ prevalence was lower than in anti-TNF non responders, IL6ra responders and controls (Figure). CD4/CD45RA prevalence was lower in all RA groups than in controls. CD4/CD69 prevalence was higher in IL6ra responders than in anti-TNF responders and anti-TNF non responders. CD4/HLADR prevalence was higher in anti-TNF and IL6ra responders than in controls. CD4/CD25 prevalence was lower in all RA groups than in controls and CD4/CD25 prevalence was higher in IL6ra responders than in anti-TNF responders. In IL6ra responders, Th1 prevalence decreased, while Th2 prevalence increased compared to anti-TNF treated groups and controls; and anti-TNF responders and controls, respectively. Th17 prevalence was higher in all RA groups than in controls and Th17 prevalence was also higher in IL6ra responders compared to anti-TNF treated groups. Treg prevalence normalized in all RA groups (Figure) (1). CD8+ prevalence was lower in IL6ra responders than in anti-TNF treated groups and controls (Figure). CD8/CD45RA and CD8/CD45RO prevalence were lower in all RA groups than in controls. CD8/CD69 prevalence was higher in IL6ra responders than in anti-TNF treated groups and controls. CD8/HLADR prevalence was higher in anti-TNF responders than in controls.




**Conclusions:** Biological therapies exhibit marked effects on all the cell populations investigated; some significant differences in this action exist between anti-TNF and IL6ra therapies. This study on peripheral blood samples has provided

comprehensive information regarding the long term impact of biologic therapies on CD4+and CD8+ cell distributions.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2525

## Cartilage, synovium and osteoimmunology

### THU0016 HEPARANASE IS ACTIVE IN HUMAN OSTEOARTHRITIC CARTILAGE AND DRIVES CATABOLIC RESPONSES IN PRIMARY HUMAN CHONDROCYTES

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**Background:** Osteoarthritis (OA) affects hundreds of millions of people worldwide, resulting in significant morbidity. Articular cartilage homeostasis is governed by resident chondrocytes that can either contribute to cartilage anabolism by producing tissue constituents or drive catabolic events by secreting aggrecanases and collagenases. The chondrocytes' pericellular matrix (PCM) acts as a mechanosensor by sequestering growth factors that are bound to heparan sulfate (HS) proteoglycans, such as perlecan.
Heparanase is the sole mammalian enzyme with HS degrading activities. Heparanase enzymatic activity releases HS-bound growth factors, cytokines, chemokines and other ligands stored within the extracellular matrix. Through both enzymatic and non-enzymatic activities, heparanase influences the expression of a number of important genes and has been implicated in numerous processes involved in cancer progression, inflammation and remodeling of the ECM. Little is known about whether heparanase plays a role in cartilage homeostasis.
**Objectives:** To ascertain whether heparanase may have a role in modulating the anabolic or catabolic responses of human articular chondrocytes.
**Methods:** Heparanase enzymatic activity was measured in collagenase digests of osteoarthritic articular cartilage using solid-phase-bound radiolabeled heparan sulfate as substrate. Primary human chondrocytes obtained from OA patients undergoing joint replacement surgery, were incubated with or without recombinant human pro-heparanase. In some experiments, the heparanase inhibitor, PG545, was also added. Heparanase was also added together with fibroblast growth factor 2 (FGF-2) or interleukin 1 (IL-1). The association of pro-heparanase with the chondrocytes and its conversion to active heparanase was evaluated by Western blot. Induction of the catabolic genes *MMP13*, *ADAMTS4* and *ADAMTS5* and the anabolic genes *ACAN* (encoding the aggrecan core protein) and *COL2A1* (encoding the alpha chain of type II collagen), was analyzed by real time reverse-transcriptase PCR. MMP13 enzymatic activity in the culture medium was measured with a specific fluorescent assay. ERK phosphorylation was evaluated by Western blot.
**Results:** The collagenase-digested cartilage (but not the collagenase blend alone), liberated small fragments compatible with HS-degradation products, indicated active heparanase is present in osteoarthritis cartilage. Cultured chondrocytes rapidly associated with the inactive 62-kDa pro-heparanase, which was then cleaved to the active 50-kDa enzyme. Addition of heparanase to cultured human chondrocytes activated the catabolic genes *MMP13* and *ADAMTS4* by 4 hours and reduced the expression of anabolic genes *ACAN* and *COL2A1* by 20 hours. Heparanase also induced human chondrocytes to secrete active MMP13 to the culture medium by 20 hours and induced intracellular ERK phosphorylation by 30 minutes. A synergistic effect was observed between heparanase and FGF-2, but not between heparanase and IL-1. PG545, a heparan sulfate mimetic, reversed the effects of heparanase.
**Conclusions:** Heparanase is active in osteoarthritic cartilage and induces catabolic responses in cultured primary human chondrocytes. This response seems to be due, at least in part, to the release of heparan sulfate-bound growth factors such as FGF-2.

**Disclosure of Interest:** None declared

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### THU0017 DEFEROXAMINE SUPPRESSES COLLAGEN CLEAVAGE IN CULTURED HUMAN OSTEOARTHRITIC ARTICULAR CARTILAGE VIA A PROCESS INVOLVING DOWNREGULATION OF PROTEASE ACTIVITY, PROINFLAMMATORY CYTOKINES AND TYPE X COLLAGEN EXPRESSION AND UPREGULATION OF AMPK AND CITRIC ACID CYCLE GENES

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**Background:** Osteoarthritis (OA) involves degenerative changes in articular cartilage, remodelling of subchondral bone and limited synovial inflammation. Osteoarthritic changes in articular cartilage are associated with progressive proteolytic degradation of the extracellular matrix (ECM), which is composed mainly of type II collagen and aggrecan. Their destruction leads to eventual cartilage loss that is accompanied by phenotypic hypertrophy-related changes in chondrocytes.
**Objectives:** Here we studied the effects of the iron chelator deferoxamine (DFO) on collagen cleavage, inflammation and chondrocyte hypertrophy in relation to energy metabolism-related gene expression in OA articular cartilage. We hypothesised that DFO treatment of human OA articular cartilage explants might decrease collagen cleavage activity, generation of pro-inflammatory cytokines and recover an often-altered chondrocyte phenotype by changing the cellular energy balance in favour of improving of mitochondrial function and restoring an anabolic matrix phenotype. We tested this hypothesis in cultured OA cartilage while also examining and comparing whole-body AMPK expression by peripheral blood mononuclear cells (PBMCs) in OA versus normal patients.
**Methods:** Full-depth explants of human OA knee articular cartilage from arthroplasty were cultured with exogenous DFO (1–50$\mu$M). Type II collagen cleavage and phospho-adenosine monophosphate activated protein kinase (pAMPK) concentrations were measured using ELISAs. Gene expression studies in the knee articular cartilage employed real-time PCR and included AMPK analyses in PBMCs.
**Results:** In OA explants collagen cleavage was frequently downregulated by 10–50 $\mu$M DFO. PCR analysis of five OA patient cartilages revealed that 10 $\mu$M DFO suppressed expression of MMP-1, IL-1b and TNFa, and a marker of chondrocyte hypertrophy, COL10A1. No changes were observed in the expression of glycolysis-related genes. In contrast, expressions of genes associated with the mitochondrial citric acid cycle (TCA) and AMPK were upregulated. Gene expressions of HIF1$\alpha$ and COL2A1 were also upregulated in individual patients but not significantly in the whole group. AMPK gene expression was reduced in OA cartilage and increased in PBMCs from the same patients compared to healthy controls.
**Conclusions:** Our studies demonstrate that DFO is capable of suppressing excessive collagenase-mediated type II collagen cleavage in OA cartilage and reversing phenotypic changes. The concomitant upregulation of pro-anabolic TCA-related gene expressions points to a potential for availability of energy generating substrates required for matrix repair by end-stage OA chondrocytes. This might normally be prevented by high whole-body energy requirements indicated by elevated AMPK expression in PBMCs of OA patients.

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### THU0018 REGULATION OF XYLOSYLTRANSFERASE-1 EXPRESSION BY FIBRONECTIN FRAGMENT IN HUMAN ARTICULAR CHONDROCYTES

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**Background:** Xylosyltransferase-1 (XT-1), encoded by *xylt1* gene, is an essential anabolic enzyme to catalyze the initial and rate-determining step in glycosaminoglycan chain synthesis. The effect of fibronectin fragments (FN-fs), generated by proteolytic cleavage of FN and known as damage-associated molecular pattern (DAMP) molecules, on cartilage metabolism was poorly characterized.
**Objectives:** In this study we examined 29-kDa amino-terminal fibronectin fragment (29-kDa FN-f)-mediated XT-1 expression mechanism and its signaling pathway, determining the role of 29-kDa FN-f in cartilage matrix synthesis.
**Methods:** Human articular chondrocytes were enzymatically isolated from articular cartilage and cultured in monolayer. In 29-kDa FN-f-stimulated chondrocytes, the relative levels of mRNA and protein for XT-1 were analyzed by real-time quantitative reverse transcription-polymerase chain reaction and Western blot analysis, respectively. In order to investigate the effects of 29-kDa FN-f on XT-1, human chondrocytes were transfected with small interfering RNAs (siRNAs) targeting TLR-2.
**Results:** The level of aggrecan and XT-1 in human osteoarthritis cartilage was significantly decreased compared to normal cartilage. XT-1 expression in cultured primary articluar chondrocytes showed a periodic oscillation in both mRNA and protein level. 29-kDa FN-f significantly suppressed the mRNA and protein levels of XT-1 at 14 h and 24 h, respectively. Knockdown of toll like receptor-2 (TLR-2) using small interference RNA revealed that the decrease of XT-1 expression by 29-kDa FN-f is mediated by TLR-2 signaling pathway. Inhibition of mitogen activated protein kinase (MAPK) and nuclear factor-$\kappa$B (NF- $\kappa$B) signaling pathway restored 29-kDa FN-f-inhibited XT-1 expression. In addition, reduction of XT-1 expression by 29-kDa FN-f- was associated with activation of activator protein 1 (AP-1) signaling pathway. Finally, 29-kDa FN-f enhanced the expression of Sp3

and inhibited the expression of Sp1. Knockdown and overexpression experiments confirmed that XT-1 expression was modulated by Sp3 and Sp1, which are ubiquitous transcriptional proteins and compete for the same DNA binding site.
**Conclusions:** These results demonstrated that 29-kDa FN-f plays a detrimental role in the regulation of cartilage extracellular matrix formation including XT-1 expression.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3483

## THU0019 AGE-RELATED HISTOLOGICAL CHANGES IN CALCIFIED CARTILAGE AND SUBCHONDRAL BONE PLATE IN COMPLETE HUMAN FEMORAL HEADS

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**Background:** Age is the most important risk factor for osteoarthritis (OA). However, the pathogenesis of OA is not fully understood, but the subchondral bone plate may be thickened in osteoarthritis. How aging of the joint corresponds to OA changes is poorly elucidated, but preliminary OA alterations may occur in healthy old individuals and progress into symptomatic OA.
**Objectives:** The objective was to investigate the age-related changes in different tissue compartments of the femoral head hypothesizing that a positive correlation with age would be found for 1) volume of the femoral head; 2) volume and thickness of the subchondral bone plate and calcified cartilage.
**Methods:** Sixty-one femoral heads from 29 females (median, range) (49, 20–74 years) and 32 males (47, 23–78 years), who had accidently died, were obtained by autopsy from the Institute of Forensic Medicine. Individuals were excluded in case of known bone or joint diseases, or macroscopic cartilage erosions.
Design-based stereological methods using systematic uniform random sampling were applied to estimate absolute volume. The femoral heads were randomly rotated around a vertical axis and sawn in 5–8 slabs with a thickness of 7 mm. The slabs were halved and alternating right or left half were embedded in methylmethacrylate from where 7-μm thick sections were cut. The sections were stained with Masson-Goldner trichrome or May-Grünwald toluidine blue. The total absolute volume of the femoral head, calcified cartilage, and the subchondral bone plate were estimated using the Cavalieri estimator. Orthogonal thicknesses of the calcified cartilage and the subchondral bone were measured in uniform randomly selected sampling points and related to the overlying articular cartilage alterations using the OARSI score of histological osteoarthritis. Linear regression was used to test the effect of age on the parameters and t-tests were applied for comparing men and women.
**Results:** The volume and thickness of the subchondral bone did not correlate with age (Table 1). Calcified cartilage volume and thickness correlated positively with age only in women. The volume of the femoral head correlated positively with age only in men. Women and men did not differ in OARSI-stage or grade.

| | Mean Values ± SD | | | Changes per 10 years | | |
|---|---|---|---|---|---|---|
| | All | Women | Men | All | Women | Men |
| Femoral Head volume ($cm^3$) | 34.3 ± 10.4 | 25.8 ± 3.7 | 41.9 ± 8.3§ | 1.3 | 0.1 | 1.9* |
| Calcified cartilage volume ($mm^3$) | 276 ± 121 | 282 ± 149 | 271 ± 89 | 34** | 51*** | 19 |
| Subchondral bone plate volume ($mm^3$) | 681 ± 252 | 585 ± 258 | 767 ± 211§ | -13 | -27 | -6 |
| Calcified cartilage thickness (μm) | 88 ± 34 | 100 ± 40 | 76 ± 21§ | 8* | 15*** | 2 |
| Subchondral bone plate thickness (μm) | 222 ± 61 | 216 ± 69 | 229 ± 52 | -7 | -9 | -6 |
| Mean OARSI-grade | 0.34 ± 0.29 | 0.35 ± 0.34 | 0.33 ± 0.23 | 0.08*** | 0.08 | 0.09*** |
| OARSI-stage (%) | 18.1 ± 13.4 | 19.4 ± 15.6 | 16.9 ± 11.1 | 4.5*** | 4.3* | 4.7*** |
| -OARSI-grade 0 | 81.9 ± 13.4 | 80.6 ± 15.6 | 83.1 ± 11.1 | -4.5*** | -4.3* | -4.7*** |
| -OARSI-grade 1 | 9.0 ± 7.2 | 9.9 ± 7.9 | 8.1 ± 6.3 | | | |
| -OARSI-grade 2 | 4.6 ± 5.4 | 5.6 ± 6.5 | 3.7 ± 4.0 | | | |
| -OARSI-grade =3 | 4.6 ± 5.5 | 3.9 ± 5.6 | 5.1 ± 5.3 | | | |

Data is represented as mean±SD and changes per 10 years.
Linear regression was used to check for statistical correlation with age and is denoted as * p<0.05, ** p<0.01 and ***p<0.001.
Students T-test or Mann-Whitney Rank Sum test was applied for comparing men and women and a statistical difference is denoted as § p<0.05.

**Conclusions:** In complete human femoral heads obtained from a cross-sectional population without macroscopic OA changes, we found no correlation with age for the volume or thickness of the subchondral bone plate. Surprisingly, the two genders differed in the effect of age on volume of the femoral head and volume and thickness of the calcified cartilage even though they had corresponding damage of the articular cartilage.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1765

## THU0020 IMMATURE DENDRITIC CELL ARE POTENT OSTEOCLASTS PRECURSORS IN RA AND ARE TARGETED BY RA-SPECIFIC ANTIBODIES

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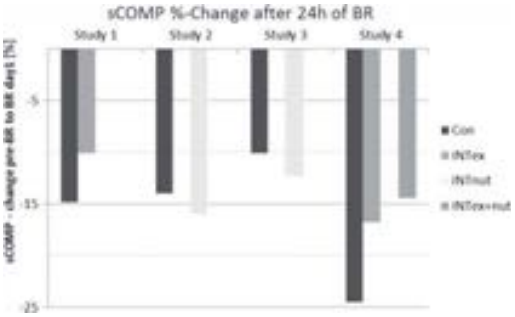
**Background:** We have recently shown that the immature dendritic cells (iDC) developing in dense cultures in presence of high lactic acid levels can efficiently differentiate into osteoclasts (OC).
**Objectives:** We aimed to investigate influence of Anti-citrullinated protein antibodies (ACPA) on iDC differentiation to OC in rheumatoid arthritis (RA).
**Methods:** CD14+ monocytes from PB of ACPA+ RA patients and healthy individuals were first used to generate iDC and MΦ and these cells were then differentiated to OC with RANKL and M-CSF. Mass spectrometry analysis was performed on different stages of differentiation of iDC and MΦ derived OC. ACPA positive and negative polyclonal IgGs were isolated from synovial fluid (SF, n=26) and peripheral blood (PB, n=38) samples of RA patients and the effects of these antibodies was tested in OC cultures. Cytokines were measured by CBA in cultures supernatants. Immunoflourescence was done on OCs with monoclonal ACPAs derived from single SF derived B cells. The effect of IL-8 and PAD inhibition was tested on OC differentiation.
**Results:** Principal component analysis confirmed distinct proteomics profiles in sparse or dense DC cultures and in MΦ but both DC and MΦ precursors differentiated into OC with similar protein composition. Citrullinated-actin was identified during iDC-OC maturation and citrullinated-vimentin in matured OC. With immunofluorescent staining we demonstrated the presence of citrullinated proteins on the surface of both iDC precursors and iDC-derived mature OCs. PAD2 and PAD4 showed faint staining in CD14 monocytes with increased staining intensity in both iDC precursors and more mature OCs with PAD activity present both in dendritic cells and osteoclasts. Polyclonal ACPAs enhanced osteoclastogenesis and bone resorption from iDC (fold increase 1.6±0.2 for OC number and 2.0±0.3 for bone resorption area). Similar effect was observed when the iDC were derived from ACPA+ RA patients (fold increase of 2.3±0.9 for OC number and 2.6±0.1 for bone resorption area). Monoclonal ACPA's with certain specificities were able to induce osteoclastogenesis. The importance of citrullination and PAD enzymes for ACPA mediated iDC transdifferentiation to OC was confirmed by a dose-dependent inhibition of OC differentiation using the PAD inhibitor Cl-Amidine. Increased osteoclastogenesis was associated with significantly higher levels of IL-8 levels in ACPA treated culture supernatants (fold increase of 2.4±0.5). Neutralization of IL-8 blocked ACPA induced osteoclastogenesis.
**Conclusions:** Our results shows iDC can efficiently transdifferentiate in to OC in RA and this process is enhanced by ACPA. We provide evidence on the importance of the IL-8 and PAD enzyme in ACPA mediated osteoclastogenesis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4735

## THU0021 IMPACT OF IMMOBILIZATION ON SERUM LEVELS OF CARTILAGE OLIGOMERIC MATRIX PROTEIN AND IMPLICATIONS FOR CLINICAL PRACTICE IN MUSCULOSKELETAL DISORDERS

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**Background:** Healthy articular cartilage is important for proper joint function. The impact of unloading due to disease or injury on healthy and diseased articular cartilage is not well understood and bed rest (BR) studies offer a unique and well-standardized model to study the effects of immobilization. Cartilage oligomeric matrix protein (COMP) is a structural protein found in cartilage and is a marker of cartilage turnover [1]. Increased serum concentrations (sCOMP) have been associated with cartilage degradation in osteoarthritis [2] and rheumatoid arthritis [3] but also physiological loading [4, 5]. sCOMP decreases with with immobilization [6].
**Objectives:** To investigate the impact of duration of immobilization (CON) and effectiveness of exercise (INT ex) and nutrition interventions (INTnut) on sCOMP concentration in healthy male subjects during medium-term BR-studies.
**Methods:** Four BR-studies were conducted, each in cross-over design: study 1 (INTex; N=8) had a 14-days of BR, Study 2 (INTnut; N=7), Study 3 (INTnut; N=9) and Study 4 (INTex+nut; N=8) had 21 days of BR. Blood samples were taken after overnight fast. sCOMP concentration was analyzed using commercial enzyme immunoassays (COMP® ELISA, AnaMar Medical AB, Lund, Sweden). Statistical

analysis (IBM SPSS Statistics, 19.01) was performed using repeated measures ANOVA ($p<0.05$).
**Results:** BR lead to a reduction in sCOMP after 24h for all interventions and the control condition (Fig.1). sCOMP recovered to baseline after the end of BR for all conditions (study 1: INTex: +26%, CON: +28.6%; study 2: INTnut: +25%, CON: +25%; study 3: INTnut: +28.9%, CON: + 28.6%; study 4: INTex: +35.0%, INTex+nut: +33.2%, CON: +32.8%). INTnut and INTex did not affect the results. COMP data of 24 individuals from studies 1–3 were re-analyzed for the adaptation of sCOMP during BR. Baseline values of sCOMP decreased by -16% after 24h of BR and further by -5% until BRday 14.




**Conclusions:** sCOMP concentration is sensitive to immobilization. After the distinct initial decrease in sCOMP during the first 24hrs of BR, sCOMP is significantly lowered at BR day 14 compared to the first 24h of BR. These results suggest that beside a reduced diffusion of molecules from the joint, cartilage turnover is decreased during prolonged immobilization. This presumably also negatively affects tissue properties. Thus the combined effects of disease and immobilization on cartilage health in arthritis patients need to be considered and require further investigation. High standardization of blood sampling with regards to mechanical loading is essential for data quality when evaluating sCOMP concentration.
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**Disclosure of Interest:** None declared
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## THU0022 HYPERGLYCEMIA-RELATED ADVANCED GLYCATION END-PRODUCTS IS ASSOCIATED WITH THE ALTERED PHOSPHYTIDYLCHOLINE METABOLISM IN OSTEOARTHRITIS PATIENTS

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**Background:** Accumulating evidence suggests an independent association between osteoarthritis (OA) and type 2 diabetes mellitus (DM). Our recent work [Zhang, *et al.* Metabolomics, 2015] found phosphatidylcholine acyl-alkyl C34:3 (PC ae C34:3) and phosphatidylcholine acyl-alkyl C36:3 (PC ae C36:3) were associated with both OA and DM. Both synovial and plasma concentrations of these two metabolites were reduced in knee OA and DM patients, and OA patients with DM had lowest concentration of these two metabolites, suggesting the altered unsaturated phosphatidylcholine metabolism may be responsible for the association between OA and DM.
**Objectives:** We hypothesized hyperglycemia-related production of advanced glycation end-products (AGEs) was involved in the altered phosphatidylcholine metabolism in OA patients and tested this hypothesis in the current study.
**Methods:** Synovial fluid and plasma samples were collected from OA patients with and without DM. Hyperglycemia-related AGEs including methylglyoxal (MG) and methylglyoxal-derived hydroimidazolone (MG-H1) levels were measured in both synovial fluid and plasma samples using UPLC/MS method. The correlation between MG, MG-H1, and PC ae C34:3 and PC ae C36:3 were examined.
**Results:** 84 knee OA patients, including 46 with DM and 38 without DM, were included in the study. We did not find a significant difference in plasma MG-H1 concentration between OA with and without DM. However, we found that log transformed synovial concentrations of MG-H1 in the groups of OA with diabetes were 2.56±0.27 ng/ml which was significantly higher than that in the group of OA without diabetes (2.39 ±0.25 ng/ml, P=0.012). Similarly, synovial concentration of MG was 2.05±0.11 ng/ml in the group of OA with diabetes which was significantly higher than 1.99±0.11 ng/ml in the group of OA without diabetes (P=0.046). The significance remained after adjusting the age, BMI and sex. The correlation between MG-H1 and PC ae C34:3, MG-H1 and PC ae C36:3, MG and PC aeC34:3, and MG and PC ae C36:3 were -0.15, -0.32, -0.23 and -0.06, respectively.
**Conclusions:** We demonstrated that both MG-H1 and MG concentrations in synovial fluid were elevated in OA patients with DM and associated with the levels of PC ae C34:3 and PC ae C36:3, suggesting that hyperglycemia-related AGEs may be responsible for the altered phosphotidylcholine metabolism in OA.
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**Disclosure of Interest:** None declared
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## THU0023 EXPRESSION OF OSCAR IN THE SYNOVIUM OF EARLY RA PATIENTS

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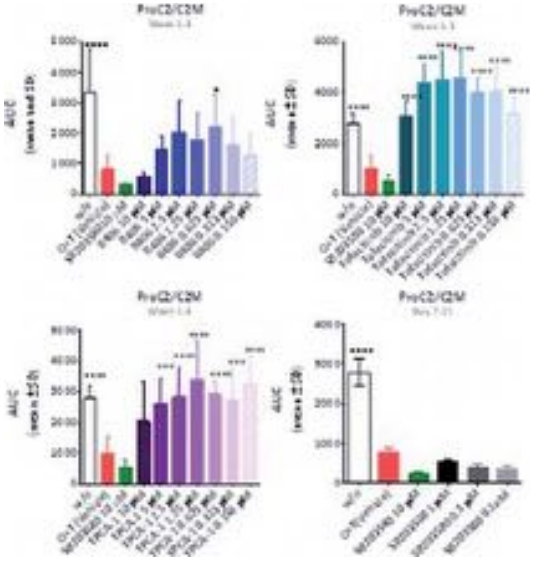
**Background:** Osteoclast-associated receptor [OSCAR] is expressed by monocyte, endothelial and dendritic cells. OSCAR is a co-stimulation receptor involved in transducing immunoreceptor tyrosine-based activation (ITAM) signals for differentiation from monocytes into active osteoclasts (OCs). Endothelial OSCAR expression may induce monocyte adhesion increasing monocyte extravasation available for osteoclastogenesis in affected joints. Higher expression of OSCAR by endothelial and pre-OCs, as detected by immunohistochemistry, is present in active RA compared with OA and healthy synovial samples (Crotti ART 2012). Inflammation in RA may increase OSCAR expression as supported by increased monocyte (Herman ART 2012) and endothelial cell (Crotti ART 2012) OSCAR expression in response to TNF-alpha in vitro. OSCAR expression in early RA (less than 6 months post diagnosis) and cartilage pannus junction (CPJ) and non-CPJ samples from established RA has not been reported.
**Objectives:** To examine OSCAR expression in the synovium of early RA patients at diagnosis and 6 months following treatment. OSCAR was also assessed in the CPJ and non-CPJ tissues of patients with established RA.
**Methods:** Samples included synovial biopsies from 15 patients newly diagnosed for RA at 0 and 6 months. CPJ and non-CPJ samples from established RA joints were also assessed (n=14). Serial sections for both cohorts were stained for OSCAR, TRAP (to identify pre-OCs/OCs) and von Willebrand factor (to identify vessels). Positive cells were counted (TRAP) or scored semiquantitatively (OSCAR) in 6x 2mm$^2$ fields. A paired T test was used to detect significance.
**Results:** OSCAR was associated with the synovial lining cells and distributed sparsely in association with monocytes in the subsynovial tissue or lymphoid aggregates in both early and established RA. A subset of samples from both cohorts showed a very mild staining associated with the vasculature and lumen. In early RA there was no significant difference in OSCAR expression within lining, sublining and vessels (p=0.217, 0.622, 0.906 respectively) between 0 and 6 months. The expression of OSCAR in the sublining reduced in 10/15 patients by 6 months. Very few TRAP positive cells were detected at either time point. The CPJ and non-CPJ established RA cohort had higher expression of OSCAR than the early cohort. The number of TRAP positive cells was significantly higher in the CPJ versus non-CPJ (p=0.015, mean=88.5 vs 44).
**Conclusions:** OSCAR positive cells were observed in all synovial tissues, particularly in the lining, in both early RA and established RA. This has not been previously reported. Expression of OSCAR by sublining cells including OC precursors, possibly dendritic cells, macrophages and endothelial cells is consistent with previous reports. Low numbers of TRAP positive cells may relate to early disease and/or site of biopsy as distant from the actual CPJ due to limitations of arthroscopic technique. In established RA, higher numbers of TRAP and OSCAR positive cells were present in both CPJ and non-CPJ tissues. The reduced sublining OSCAR expression in the majority of patients following treatment suggests modulation of OSCAR by DMARDS and may implicate OSCAR as an inflammation and bone erosion predictive biomarker.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2109

## THU0024 ANTI-INFLAMMATORY INHIBITORS TARGETING JAK AND IKK HAVE AN ANABOLIC EFFECT ON TYPE II COLLAGEN TURNOVER EX VIVO

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**Background:** Rheumatoid arthritis (RA) and a subpopulation of osteoarthritis, inflammatory OA (iOA) are degenerative joint diseases with an inflammatory

component. However, the degree of inflammation is much higher in RA than iOA. There are many signaling pathways involved with the inflammation-driven extracellular matrix (ECM) degradation in RA and iOA cartilage that have been suggested as anti-inflammatory targets. However, the results on joint structure in clinical trials have been varying. A better understanding of the intracellular signaling pathways and the downstream effect on ECM turnover could be beneficial for the selection of novel anti-inflammatory treatments for RA and iOA.
**Objectives:** The aim of this study was to investigate the direct effect of the anti-inflammatory inhibitors R406 (the active metabolite of Fostamatinib), Tofacitinib, TPCA-1 and SB203580 on the cartilage ECM turnover.
**Methods:** Full depth bovine cartilage *ex vivo* cultures were cultured for 3 weeks with OSM [10 ng/mL] and TNFα [2 ng/mL] (O+T) or together with R406, Tofacitinib or TPCA-1 at 10 μM and a two-fold dilution to 0.16 μM. SB203580 was tested at 3 μM, 1 μM and 0.3 μM. As negative control, untreated explants were included. The ECM turnover of the cartilage was assessed with the biomarkers; C2M, ProC2, AGNx1 and/or ARGS. Additionally, histology of the explants was examined with Safranin O and fast green staining.
**Results:** Aggrecanase mediated degradation of aggrecan was assessed with ARGS or AGNx1. The Syk inhibitor R406, the Jak inhibitor Tofacitinib, and the IKK inhibitor TPCA-1 inhibited the release of ARGS or AGNx1, while the p38 inhibitor, SB203580, had no effect. The turnover of type II collagen was measured by the formation of type II collagen (ProC2) and MMP-mediated degradation of type II collagen (C2M). The ratio between ProC2 and C2M was calculated for week 1–3. Tofacitinib and TPCA-1 increased the area under the curve (AUC) of ProC2/C2M significantly compared to O+T ($p<0.001$). SB203580 and R406 had no effect at 10 μM, 5 μM, 0.31 μM and 0.16 μM, but tended to increase ProC2/C2M at 2.5–0.625 μM compared to O+T (Figure 1). Safranin O and fast green staining of the explants showed that O+T, SB203580 and 0.16 μM of R406, Tofacitinib, and TPCA-1 lead to loss of proteoglycans from the cartilage explants compared to the untreated explants. R406 at 10 μM retained the proteoglycans in the deep and middle zone of the cartilage, while the proteoglycans of the superficial layer was lost. 10 μM of Tofacitinib and TPCA-1 retained the proteoglycans in all layers of the cartilage explants.



**Conclusions:** The four inhibitors tested had a positive effect on the degradation of aggrecan and type II collagen. However, only Tofacitinib and TPCA-1 had an increased anabolic effect on type II collagen turnover. The anabolic effect from Tofacitinib and TPCA-1 on top of the anti-catabolic effect indicates that the chondrocytes can repair the cartilage during treatment opposite to the p38 inhibitor that inhibits the catabolic and the anabolic response.
**Disclosure of Interest:** C. Kjelgaard-Petersen: None declared, A.-C. Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/s, M. Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, P. Hägglund: None declared, C. Thudium Employee of: Nordic Bioscience A/S
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## THU0025 OVER-EXPRESSED PGC-1β IN CD14+ MONOCYTES OF RHEUMATOID ARTHRITIS PATIENTS AND ITS DOWN-REGULATION CAN SUPPRESS OSTEOCLASTOGENESIS AND BONE RESORPTION THROUGH INHIBITION OF CATHEPSIN K AND TRAP

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**Background:** Peroxisome proliferator-activated receptor-gamma coactivator-1 (PGC-1) is a transcriptional coactivator that plays important roles in regulating energy metabolism and cytokine signaling pathways. Our previous study showed that down-regulating PGC-1β could inhibit rheumatoid arthritis fibroblast-like synoviocytes induced osteoclastogenesis by RAW264.7 (used as precursor of osteoclasts).
**Objectives:** To investigate the expression of PGC-1β in CD14+ monocytes from RA patients and its effect and underlying mechanism on osteoclastogenesis and bone resorption.
**Methods:** (1) Peripheral blood mononuclear cells (PBMCs) were collected from 3 patients with active RA and 3 healthy controls and CD14+ monocytes were selected by flow cytometry. PGC-1β expression was detected by immunofluorescence staining or flow cytometry. (2) PGC-1β in RAW264.7 was depleted by lentivirus short hairpin RNAs and then cultured with recombinant murine RANKL (50ng/ml) and M-CSF (25ng/ml). Tartrate-resistant acid phosphatase (TRAP) staining and western blot (WB) for detecting the expression of DC-STAMP, cathepsin K and TRAP were performed at day 7. Toluidine blue staining for examining resorption pits by reflected light microscopy and image analysis system was performed at day 14. (3) After PGC-1β knockdown in RAW264.7, cytoplasmic protein was extracted for WB determining the expression of JNK, p-JNK, p38, p-p38, p-ERK1/2, NFATc-1, NF-κB and IκB, while nuclear protein was extracted for WB determining the expression of PGC-1β, p- NF-κB, ERK1/2, c-jun and c-fos.
**Results:** (1) Immunofluorescence staining showed that the percentage of PGC-1β positive PBMCs in RA was significantly higher than that in healthy controls (94±3% vs. 57±7%, *P*=0.021, Figure 1A). Flow cytometric analyses showed that PGC-1β expression in CD14+ monocytes from RA patients was higher than that of healthy controls (Figure 1B) and the mean fluorescence intensity was significantly higher than that of healthy controls (274±23 vs. 167±15, *P*=0.034).(2) At day 7, the number of TRAP-positive multinucleated osteoclasts in sh-PGC-1β group was significantly lower than that in sh-GFP group (33.4 ± 3.4 vs. 192.5 ± 5.1 cells/per well, *P*=0.021, Figure 1C). At day 14, the pit area of bone resorption lacunae on the slices of sh-PGC-1β group was significantly reduced than that of sh-GFP group (13 ± 2 vs. 197 ± 15 $\mu m^2$/per slice, *P*=0.012, Figure 1C). (3) WB assay showed that the protein expression of cathepsin K and TRAP,but not DC-STAMP, were obviously suppressed in sh-PGC-1β group (Figure 1D). Further analysis of signaling pathways showed the expression of NFATc1 and phosphorylate NF-κB p65 were also significantly decreased (Figure 1E).

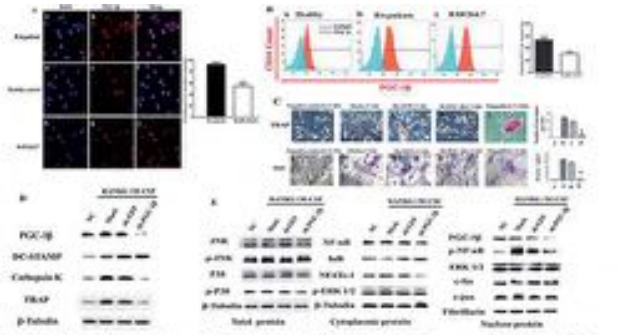


**Figure 1. A.** Elevated expression of PGC-1β in RA-PBMC. **B.** Elevated expression of PGC-1β in CD14+ monocytes. **C.** PGC-1β knockdown decreases the number of osteoclasts and resorption lacunae area induced by RANKL and M-CSF. **D.** PGC-1β knockdown inhibits the expression of cathepsin K, TRAP. **E.** PGC-1β knockdown dampens the activation of NF-κB.

**Conclusions:** Our results showed that over-expressed PGC-1β in CD14+ monocytes of RA patients and down-regulation of PGC-1β can suppress RANKL induced osteoclastogenesis and bone resorption through inhibition of cathepsin K and TRAP by NF-κB and NFATc1 pathway.
**Acknowledgement:** This work was supported by National Natural Science Foundation of China (81471597), Specialized Research Fund for the Doctoral Program of Higher Education (20130171110075) and Guangdong Natural Science Foundation (2014A030313074).
**Disclosure of Interest:** None declared
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## THU0026 MICRORNA-365 REGULATES EXPRESSION OF CATABOLIC FACTORS VIA MODULATING IL-1β-INDUCED EPAS-1 EXPRESSION IN SW1353 CELLS AND HUMAN PRIMARY CHONDROCYTES

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**Objectives:** Endothelial PAS domain protein-1 (EPAS-1/HIF-2α), encoded by *EPAS1* gene, is a catabolic transcription factor to regulate osteoarthritis (OA) cartilage destruction. In this study we examined whether microRNA-365 (miR-365) can regulate interleukin (IL)-1β-induced expression of catabolic factors in SW1353 cells and human articular chondrocytes via regulation of EPAS-1.

**Methods:** Total RNA was isolated from normal and OA cartilage tissues, human chondrocytes, and SW1353 cells. The level of miR-365 was quantified by TaqMan assay. The effects of miR-365 on expression of EPAS-1 and EPAS-1-modulated genes were measured by quantitative real-time polymerase chain reaction (qRT PCR), Western blot analysis, and enzyme-linked immunosorbent assay (ELISA). To examine the direct interaction of miR-365 with 3' untranslated region (UTR) of EPAS-1 mRNA, luciferase reporter assay was performed.
**Results:** The level of miR-365 in human OA cartilage was significantly decreased compared to normal cartilage. The overexpression of miR-365 significantly suppressed IL-1β-induced expression of EPAS-1 in both SW1353 cells and human articular chondrocytes. QRT PCR analysis using pharmacological inhibitors revealed that mitogen activated protein kinase and nuclear factor-κB signaling pathway was involved in IL-1β-induced miR-365 decrease and subsequent increase of EPAS-1 expression. Luciferase reporter assay using DNA construct containing binding site of miR-365 within 3'UTR of human EPAS-1 mRNA demonstrated that the overexpression of miR-365 significantly suppressed IL-1β-induced up-regulation of EPAS-1. Furthermore, miR-365 overexpression significantly suppressed IL-1β-induced expression of catabolic factors, including cyclooxygenase-2, inducible nitric oxide synthase, and matrix metalloproteinase-1, -3 and -13, in SW1353 cells and human chondrocytes.
**Conclusions:** MiR-365 regulates IL-1β-stimulated catabolic effects in SW1353 cells and human chondrocytes via modulating the expression of EPAS-1.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3345

## THU0027 INDUCTION OF REGULATORY T CELLS AND ITS REGULATION WITH INSULIN-LIKE GROWTH FACTOR/INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-4 BY HUMAN MESENCHYMAL STEM CELLS

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**Background:** Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by synovitis and subsequent joint destruction. Biological agents and Janus kinase inhibitors have proven to be more effective than conventional treatments. However, no effective treatment for repairing damaged joints has yet been established. Human mesenchymal stem cells (hMSCs) are multipotent and are expected as potential therapeutic tools for promoting tissue repair at various sites, including joints in RA. Human MSCs also have the capacity to modulate immune responses, but the underlying mechanism remains elucidated.
**Objectives:** In the present study, we investigated the regulatory mechanism of induce regulatory T cells (Treg cells) induction through the growth factors released by hMSCs.
**Methods:** Human naïve $CD4^+$T cells were stimulated with anti-CD3/28 antibodies and co-cultured with hMSC culture supernatant for 48 hours. The proliferation and cytokine production of $CD4^+$T cells and surface molecule expressions on $CD4^+$T cells were evaluated.
**Results:** The proliferation of anti-CD3/28 antibody-stimulated $CD4^+$T cells was suppressed by the addition of hMSCs culture supernatant, but production of IL-10 and IL-4 from $CD4^+$T cells were induced the supernatant. The hMSCs supernatant induced $CD4^+FoxP3^+$Treg cells. The induced $CD4^+FoxP3^+$Treg cells expressed CD25, CTLA-4, GITR, and IGF (insulin-like growth factor)-1R and IGF-2R and revealed anti-proliferative activity against $CD4^+$T cells. In addition, the induction of Treg cells by the hMSCs supernatant was enhanced by addition of rhIGF-1/2 and suppressed by inhibition of IGF-1R. The MSCs supernatant include not only IGF-1 and IGF-2 but also a significant amount of IGFBP-4, an inhibitor of IGF action. After neutralization of IGFBP-4 in the hMSCs culture supernatant by anti-IGFBP-4 antibodies, the number of the Treg cells increased significantly as compared to the neutralization of IGFBP-3.
**Conclusions:** Human MSCs induced $CD4^+IGF1R^+IGF2R^+FoxP3^+$Treg cells responsive to IGF signaling thorough the secretion of soluble factors. On the other hand, hMSCs are also involved in a negative regulatory mechanism, which suppresses Treg cells proliferation by releasing IGFBP-4, indicating differential regulation of Treg cells by the MSCs: positive regulation by IGF and negative regulation by IGFBP-4. The present results also suggest that the inhibition of IGFBP-4 may be necessary for the efficient application of MSC therapy in the context of joint repair in RA
**Disclosure of Interest:** I. Miyagawa: None declared, S. Nakayamada: None declared, K. Nakano: None declared, K. Yamagata: None declared, K. Sakata Employee of: Mitsubishi Tanabe pharma corporation, K. Yamaoka: None declared, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-Kirin, Abbvie, Bristol-Myers, Consultant for: Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, Santen
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## THU0028 MICRORNA-381 AMELIORATES ARTHRITIS BY CONTROLLING FUNCTIONS OF FIBROBLAST-LIKE SYNOVIOCYTES, WHICH ARE AFFECTED BY A TO I RNA EDITING

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**Background:** MicroRNAs (miRNAs) play as regulators of rheumatoid arthritis (RA) and other diseases. MicroRNA is edited by the adenosine deaminase double-stranded RNA (ADAR) as well as mRNA and other noncoding RNA after transcription. A to I RNA editing is occurred limited variety of miRNAs. MicroRNA-381 (MiR-381) is one of limited miRNAs and was down regulated in synovium derived from patients with RA. However, the function of miR-381 and A to I RNA editing against RA is not clear.
**Objectives:** To clarify a role of miR-381 and A to I RNA editing in synovium derived from RA or OA.
**Methods:** 1) RNA was purified from the synovium derive from patients with RA (n=6) or OA (n=6) and analyzed with next generation sequencing (NGS). MiRNA editing was annotated containing 2 nucleotide mismatch. 2) The expression of wild type (WT) and edited miR-381 of synovium derived from RA (n=10) was compared to OA (n=10) with real time PCR. 3) Fibroblast-like synoviocytes (FLS) purified from RA synovium (n=3) were treated TNFα and IL-1β to clear miR-381 expression mechanism. 4) FLS were transfected with WT or edited miRNA expression vectors. These migration, proliferation and MMP production were analyzed. The target genes was predicted and determined by luciferase assay. 5) Male DBA/1 mice were intraperitoneally injected anti-collagen antibodies (collagen antibody-induced arthritis, CAIA) on day0 and LPS on day3. MiR-381 mimic was injected intra articular space on day0 and 3 after antibody injection. Arthritis was evaluated by arthritis score and histological score.
**Results:** 1) Two types of A to I RNA editing were detected in miR-381 seed sequence using NGS (edit1/edit2). 2) These expression of both WT, edit1 and edit2 miR-381 in RA synovium were lower than OA ($p<0.05$). 3) The expression of series of miR-381s were decreased by TNFα and IL-1β stimulation. 4) Overexpression of WT and edit1 miR-381 reduced the migration of FLS ($p<0.01$). Overexpression of edit1 and 2 miR-381 repressed proliferation of FLS ($p<0.01$), which may be caused by reducing CUL3 mRNA expression. CUL3 was regulator of cell cycle and was a direct target gene of edited miR-381s by luciferase assay. All types of miR-381 reduced MMP13 expression ($p<0.05$). 5) Treatment with miR-381 mimic increased expression of miR-381 in synovium but not in other tissues and significantly reduced arthritis score (scramble vs. miR-381 mimic: 11.5±0.76 vs. 8.4±2.06) and cartilage destruction.
**Conclusions:** These findings suggested that miR-381 was added functions by A to I RNA editing and controls FLS and arthritis.
**Disclosure of Interest:** Y. Tanaka Grant/research support from: Resesarch Fellow of Japan Society for the Promotion of Science, S. Takada Grant/research support from: CREST, Japan Science and Technology Agency, H. Iizasa: None declared, A. Hatzigeorgiou: None declared, S.-I. Miyazawa: None declared, T. Furumatsu: None declared, K. Nishida: None declared, H. Asahara Grant/research support from: CREST, Japan Science and Technology Agency
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# Rheumatoid arthritis - prognosis, predictors and outcome

## THU0029 PREDICTING DAS28-CRP <2.6 AND LOW DISEASE ACTIVITY STATUS AT 6 MONTHS BASED ON EARLY CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** For patients (pts) with rheumatoid arthritis (RA), early attainment of remission or low disease activity (LDA) predicts better long-term outcomes. Predicting non-response to therapy early in the disease course may avoid additional exposure to ineffective treatments and reduce a patient's potential risk of adverse events.
**Objectives:** To develop an instrument for predicting clinical outcomes for individual RA pts at 6 months based on observed 3-month responses.
**Methods:** A 3-step method was used to predict DAS28-CRP (28-joint disease activity score based on C-reactive protein) <2.6 and LDA (<3.2) at 6 months, using data from the OPTIMA trial in early RA pts: First, baseline (BL) and post-BL candidate predictors including demographics, laboratory assessments and genetic assays, were screened using the Least Absolute Shrinkage and Selection Operator (LASSO) method (1). To obtain an individual prediction score

of achieving Week (wk) 26 DAS28-CRP <2.6 or LDA, logistic regression was performed using predictors chosen based on LASSO results and clinical feasibility. Lastly, cutoff values were established by applying the Recursive Partitioning and Regression Tree (2) (RPART) method on the individual predictive score. Prediction rules were recommended based on satisfactory positive and negative predictive values (PPV/NPV), and validated using data from the DE013, DE019, MUSICA and CONCERTO trials in patients with early or established RA. Responders and non-responders (NR) are defined based on attainment of DAS28-CRP <2.6 or LDA at 6 months.

**Results:** Wk 12 DAS28-CRP, physician global assessment of arthritis, and health-assessment questionnaire-disability index (HAQ-DI) were selected from the final list of predictors to calculate the individual prediction score (Table footnote). Individual prediction scores were calculated for 866 pts in OPTIMA, who had both Wk 26 DAS28-CRP <2.6 status and Wk 12 predictors. The prediction rule was applied to 541/866 (62%) pts based on their Month 3 prediction score. Out of 427 predicted NR at Wk 26, 401 predictions were correct (NPV of 94.61%) (Table). Out of 114 predicted responders at Wk 26, 97 predictions were correct (PPV of 85.19%). For the 38% of pts in the hard-to-classify category, the treatment outcome at Wk 26 was unclear due to lack of proper early response indicators; however, a higher prediction score corresponded to a higher rate of DAS28-CRP <2.6. Similarly, for DAS28-CRP LDA, the NPV was 90.80% and the PPV was 90.15%. Prediction accuracy in the validation datasets was consistent with that in OPTIMA; for MTX NR, accuracy was consistently >90% in all the trials.

**Table 1**

| Summary of Prediction Rule for DAS28-CRP <2.6 in OPTIMA | | | | |
|---|---|---|---|---|
| **Score Cutoff** | **N [%]** | **Prediction** | **PPV** | **NPV** |
| <0.1726 | 427 (5.39) | Non-Responder | | 94.61 |
| ≥0.1726, <0.4421 | 202 (28.22) | Hard-to-classify | | |
| ≥0.4421, <0.7072 | 123 (60.16) | Hard-to-classify | | |
| ≥0.7072 | 114 (85.19) | Responder | 85.19 | |
| **Summary of Prediction Rule for DAS28-CRP LDA in OPTIMA** | | | | |
| <0.2467 | 348 (9.20) | Non-Responder | | 90.80 |
| ≥0.2467, <0.4497 | 146 (29.45) | Hard-to-classify | | |
| ≥0.449, <0.7234 | 169 (60.95) | Hard-to-classify | | |
| ≥0.7234 | 203 (90.15) | Responder | 90.15 | |

Equation for logit of prediction score of DAS28 <2.6: Logit = 3.719 - 1.126*DAS28_wk12 - 0.623*HAQ_wk12 - 0.16*PhGA_wk12. Equation for logit of prediction score of LDA: Logit =4.626 - 1.121*DAS28_wk12 - 0.636*HAQ – 0.143*PhGA_wk12; Logit is the natural logarithm of the odds of DAS28 <2.6 (or LDA) status respectively, at Wk 26. Individual prediction score is $\frac{\exp(\text{Logit})}{1+\exp(\text{Logit})}$. N=number of pts in subgroup defined by score cutoff, % = percentage of pts achieving DAS28 <2.6/LDA at Wk 26. LDA, low disease activity; PPV=positive predictive value; NPV=negative predictive value; HAQ, health assessment questionnaire; PhGA, physician's global assessment of arthritis activity

**Conclusions:** Using this instrument derived from clinical study data, DAS28-CRP <2.6 or LDA at 6 months could be individually predicted for about 60% of RA pts based on clinical outcomes at 3 months. This instrument-based predictive capability may provide quantified guidance for switching non-responders to more effective therapy as early as 3 months.

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**Disclosure of Interest:** J. Smolen Grant/research support from: AbbVie, Consultant for: AbbVie, X. Wang Shareholder of: AbbVie, Employee of: AbbVie, I. Sainsbury Shareholder of: AbbVie, Employee of: AbbVie, A. Kavanaugh Grant/research support from: AbbVie, Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Consultant for: AbbVie, Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB

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## THU0030 ULTRASOUND INFLAMMATION IN ARTHRALGIA PATIENTS PREDICTS THE DEVELOPMENT OF ARTHRITIS

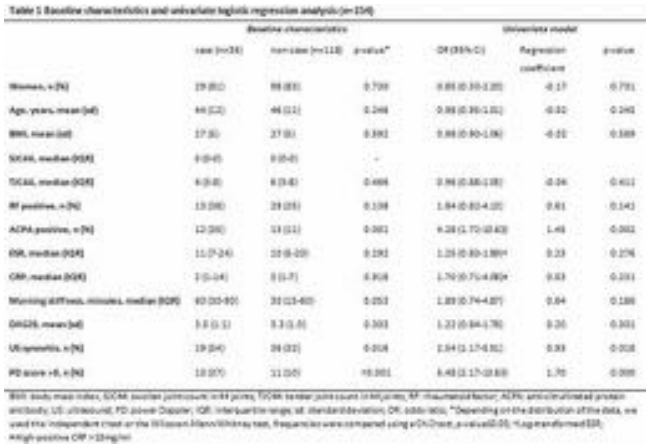
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**Background:** To decrease burden of disease of rheumatoid arthritis (RA) we need to identify patients at risk for RA as early as possible, preferably as no clinical apparent synovitis could be detected yet. Previous studies suggest that this should be in the arthralgia phase or even before that. Up to now it has been fairly difficult to identify those arthralgia patients who develop inflammatory arthritis (IA), but recent studies in ultrasound (US) suggest that earlier detection is possible [1].

**Objectives:** We aim to identify which arthralgia patients will develop clinical apparent IA within a year using US to detect subclinical synovitis at first consultation.

**Methods:** In a multi-centre prospective cohort study we followed arthralgia patients with ≥2 painful joints of hands, feet or shoulders without clinical apparent synovitis. Patients had a symptom duration of <1 year which could not be explained by other conditions (e.g. fibromyalgia). We collected data at baseline, 6 months and 12 months follow-up, which included physical examination, laboratory variables (ESR, CRP, auto-antibodies), diagnosis and medication used (including DMARDs at 6 and 12 months). At baseline we examined patients by US, which included 26 joints (MCP2–5, PIP2–5, wrists, MTP2–5) graded on greyscale (GS; 0–3) and power Doppler (PD; 0–3) according to a semi-quantitatively scoring system of Naredo et al. US synovitis was defined as GS grade 2 or 3 and/or PD grade 1, 2 or 3. After one year follow-up we determined the incidence of IA (clinical soft tissue swelling or start of DMARD treatment). We performed a complete-case analysis. For univariate logistic regression we tested demographic characteristics, clinical characteristics, and ultrasound findings and their association for development of IA. For multivariate logistic regression we selected the strongest variables ($p<0.2$).

**Results:** In total, 196 patients were included of whom 154 completed the 12 months follow-up. At baseline 72 (38%) arthralgia patients had US synovitis and in 29 (15%) patients a positive PD signal was detected. At 12 months follow-up 36 (23%) patients had developed IA of whom 22 patients initiated DMARD treatment. Table 1 shows baseline characteristics of cases and non-cases and the results of the univariate analysis. Strongest variables were ACPA, RF, morning stiffness >30 minutes and PD signal. In the multivariate logistic regression positive ACPA (OR 4.56: 95% CI 1.26–16.46) and the presence of PD signal (OR 5.79: 95% CI 1.75–19.19) at baseline were associated with the development of IA during one year follow-up.



**Conclusions:** In this early arthralgia cohort 38% of patients showed US synovitis at baseline. At 12 months 23% of the patients developed IA. In a multivariate analysis positive PD signal and positive ACPA were significantly associated with the development of IA after one year.

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## THU0031 BASELINE CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WHO ACHIEVE DEEP REMISSION IN RHEUMATOID ARTHRITIS

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**Background:** It is unclear which patients with rheumatoid arthritis (RA) may benefit from treatment discontinuation or dose reduction without diminished therapeutic effect. Previously, deep remission (DAS28-ESR ≤1.98) has been demonstrated as a good indicator of sustained remission upon anti-TNF treatment withdrawal.[1]

**Objectives:** Investigate baseline characteristics and treatment outcomes of patients with RA who achieve deep remission with etanercept (ETN).

**Methods:** Randomised patients with moderate/severe RA who participated in 3 ETN clinical trials[2–4] were included in this post-hoc analysis. Patients who achieved deep remission (DAS28-ESR≤1.98), remission (1.98<DAS28-ESR<2.6), or low disease activity (LDA; 2.6≤DAS28-ESR<3.2) during the full-dose ETN open-label (OL) period of each study were randomised into ETN tapering or withdrawal arms. Treatment outcomes (maintenance of response or non-failure) were assessed per the studies' primary endpoints (Table). Last observation carried forward (LOCF) analyses were conducted.

**Abstract THU0031** – Table 1. Sustained clinical response (LOCF) according to response category during OL period

| Study | Study primary endpoint | Randomised treatment | Patients sustaining clinical response per study primary endpoint, n/N (%) | | |
|---|---|---|---|---|---|
| | | | LDA | Remission | Deep Remission |
| PRESERVE[2] | DAS28-ESR LDA with discontinuations due to lack of efficacy treated as failures at 88 weeks | ETN 50 mg + MTX | 27/35 (77.1) | 56/65 (86.2) | 82/98 (83.7) |
| | | ETN 25 mg + MTX | 32/39 (82.1) | 52/74 (70.3) | 73/86 (84.9) |
| | | MTX | 9/39 (23.1) | 32/73 (43.8) | 43/85 (50.6)* |
| PRIZE[3] | DAS28-ESR remission at weeks 76 and 91 in patients not requiring corticosteroid boost from week 52 to 64 | ETN 25 mg + MTX | – | 13/29 (44.8) | 27/34 (79.4)* |
| | | MTX | – | 10/29 (34.5) | 16/37 (43.2) |
| | | PBO | – | 4/28 (14.3) | 11/36 (30.6) |
| EM T2T[4] | DAS28-ESR LDA at week 52 | ETN 50 mg + MTX ± DMARDs | 36/101 (35.6) | 14/37 (37.8) | 21/25 (84.0)** |
| | | MTX ± DMARDs | 8/107 (7.5) | 12/43 (27.9) | 9/18 (50.0)** |

Statistically significant trend; *P<0.01, **P≤0.0001. DMARD, disease-modifying anti-rheumatic drug; MTX, methotrexate; PBO, placebo.

**Results:** 1117 patients were included across clinical trials (n=594 PRESERVE, n=192 PRIZE, n=331 EM T2T). In PRESERVE, patients who achieved deep remission at week 36 were significantly younger at baseline (P<0.001), had lower baseline ESR (P<0.01), and lower baseline mean DAS28 (P<0.01) than those who achieved DAS28 remission or LDA. In PRIZE, demographics and disease characteristics were not significantly different across response categories at week 52. In EM T2T, the week 24 deep remission category had significantly younger patients (P<0.05), more males (P<0.05), and patients had lower mean baseline DAS28-ESR, DAS28-CRP, CDAI, SDAI, CRP, ESR, HAQ, PGA, SGA, and General Health scores (all P<0.01). Generally, patients who achieved deep remission during the OL-period were more likely to sustain their clinical response following ETN dose-tapering than those who achieved remission or LDA, across clinical trials (Table).
ClinTrials.gov:NCT00565409 (PRESERVE), NCT00913458 (PRIZE), NCT01981473 (EM T2T).
**Conclusions:** Sustained clinical response is more likely in patients who achieved deep remission prior to ETN withdrawal.
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## THU0032 DIAGNOSTIC ACCURACY OF HAND AND FOOT MRI FOR EARLY RHEUMATOID ARTHRITIS

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**Background:** Early diagnosis and treatment of rheumatoid arthritis (RA) is advocated. However, in part of the RA-patients a classifiable diagnosis cannot be made at first presentation; these patients present with unclassified arthritis (UA). The use of MRI for early diagnosis of RA is recommended, yet the evidence is limited.
**Objectives:** To assess the performance of hand and foot MRI for early diagnosis of RA.
**Methods:** Unilateral contrast-enhanced 1.5T MRI of the hand and foot was performed in 589 early arthritis patients included in the Leiden Early Arthritis Clinic, of whom 229 presented with RA, 159 with other arthritides and 201 with UA. MRI-findings observed in symptom-free controls served as reference to define an abnormal MRI. In preliminary investigations, patients that presented with RA were compared with symptom-free controls and with patients that presented with other arthritides. Thereafter, the accuracy of MRI was determined in UA-patients that were followed for 1-year on fulfilling the 1987-RA-criteria (primary outcome); the secondary outcome was start of disease-modifying drugs.
**Results:** The results of the preliminary investigations were promising and showed that MRI-detected tenosynovitis was more discriminative than other types of MRI-inflammation. Of all UA-patients, 29 (14%) developed RA and 75 (37%) started disease-modifying treatment. MRI-detected tenosynovitis was associated with RA-development independent of other types of MRI-inflammation (odds ratio (OR) 7.5 95%CI 2.4–23) and also independent of age and commonly used measures of inflammation (number of swollen joints and C-reactive protein) (OR 4.2 95%CI 1.4–12.9). Within UA-patients, the negative predictive value (NPV) of abnormal tenosynovitis was 95% and the positive predictive value (PPV) 25%. The performance was best in the subgroup UA-patients presenting with oligo-arthritis (18% developed RA): PPV was 36%, NPV 98%, sensitivity 93%, and specificity 63%. Decision curve analysis revealed a higher net benefit for a model including MRI-detected tenosynovitis.
**Conclusions:** MRI-detected inflammation, MRI-detected tenosynovitis in particular, contributes to identification of the UA-patient that will develop RA.
**Disclosure of Interest:** None declared
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## THU0033 EFFECTS OF EARLY REMISSION ON WORK ABILITY AND ABSENTEEISM IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Treatment of RA is increasingly aimed at remission. A small scale study on patients who were clinically regarded to be in remission felt that they were able to continue their normal everyday activities at home, at leisure and at work (1). However, whether achieving early disease remission by tight control treatment can predict improvement in work ability remained uncertain.
**Objectives:** To ascertain whether achieving early remission will influence work ability and absenteeism in early RA patients treated by a protocol-driven, tight-control strategy after 1 year.
**Methods:** Early RA patients with symptom onset of less than 2 years were recruited for this prospective cohort study. All patients were treated according to a tight control protocol aiming at remission. Early remission was defined as achieving Disease Activity Score (DAS) or Simplified Disease Activity Index (SDAI) remission after treatment for 3 months. Work ability was assessed by the self-perceived working ability index (WAI) compared to life time best (score from 0–10, with 10 as best). WAI was evaluated at both baseline and 1 year after treatment. The days of sick leave were also retrieved. Logistic or linear regression models were used to assess baseline clinical and demographic predictors, with the need to take sick leave and month 12 WAI during the 1-year period following RA diagnosis as outcome.
**Results:** 103 early RA patients (79 female and 24 male, mean age: 55.7±13.1 years) completed 1 year follow-up. At baseline, the mean baseline WAI was 4.97±2.9. 12/103 patients (12%) were unable to work as a result of the disease. After treatment for 3 months, 38 (36.9%) achieved DAS remission and 18 (17.5%) achieved SDAI remission. After treatment for 1 year, the WAI increased significantly to 6.45±2.6 ($p$<0.001) and 6/12 (50%) were able to go back to the work force again. Using univariate analysis, the baseline physician global assessment score (PhyGA), patient global assessment score (PatGA), tender joint count, swollen joint count, DAS-ESR, DAS-CRP, SDAI and HAQ were negatively associated with month 12 WAI. Early DAS remission ($r$=0.233, $p$=0.018) and SDAI remission ($r$=0.336, $p$=0.001) were positively associated with month 12 WAI. Using multivariate linear regression, early SDAI remission (β=2.256, 95% CI: 0.945–3.566, $p$=0.001) was an independent predictor for higher month 12 WAI after adjustment for the baseline characteristics. The working population (n=65, 15 achieved early SDAI remission and 29 achieved early DAS remission) was further analyzed. Significantly less patient required sick leave ≥1 day(s) if early SDAI remission was achieved [3 (20.0%) vs 12 (80%), $p$=0.010] but not DAS remission [12 (41.4%) vs 17 (58.6%), p=0.256]. Using univariate logistic regression, baseline PhyGA, DAS-CRP, WAI, HAQ, SF36 Physical component score were associated with ≥1 day(s) of sick leave, while patients not achieving early SDAI remission (OR=5.524, 95%CI:1.384–22.049, $p$=0.016) was more likely to require any sick leave. Using multivariate logistic regression, not achieving early SDAI remission was the independent predictor for taking sick leave (5.317, 1.314–21.516, $p$=0.019).
**Conclusions:** Early RA patients who achieved early SDAI remission had better self-perceived working ability and were less likely to require sick leave after adjustment of baseline characteristics.
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**Disclosure of Interest:** None declared
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## THU0034 USE OF RITUXIMAB COMPARED TO ANTI-TNF AGENTS AS SECOND AND THIRD-LINE THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS. A 6-YEAR FOLLOW-UP REPORT FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

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**Background:** The order of use of biologic agents after failing a TNF inhibitor remains a question for debate. Phase III trial data in TNF-IR patients show comparable efficacy results across biologic agents, and limited head-to-head studies have been published. Prospective registries offer a unique opportunity to observe the effectiveness of these agents in a real-world clinical setting where all single diagnostic patient treated in the center are included. We report here a six-year follow-up.
**Objectives:** Our aim is to assess if patients with rheumatoid arthritis (RA) treated with rituximab (RIT) after failing a first or a second anti-TNF agent (TNF-IR) have different six-year retention rates than patients similarly prescribed anti-TNF agents (pooled adalimumab, etanercept or infliximab) and compare the treatment strategies of using RIT as second or third biologic treatment.
**Methods:** Data from TNF-IR RA patients prescribed adalimumab (ADA), etanercept (ETA), infliximab (INF) or rituximab (RIT) as second or third biologic agents on or after January 1st, 2007 was extracted and subjects taking either ADA, ETA or INF were pooled to form the anti-TNF cohort. Baseline demographics included age, disease duration, HAQ-DI, fatigue and pain visual analog scale evaluations (VAS), TJC, SJC, DAS-28(ESR) and CDAI. Six-year drug retention rates were estimated and compared using Kaplan-Meier survival estimates. Statistical analysis was performed using SAS version 9.4. RHUMADATA® is a software used in daily clinical practice at the IRM and CORQ. All patients with RA are included.
**Results:** The data from 231 RA patients was extracted, 155 and 76 having respectively failed a first and a second anti-TNF agent. No clinically significant differences in baseline variables were observed between treatment groups in second and third intention. The 6-year retention rates of second-line RIT and anti-TNF users were 80.1% and 19.1% respectively (overall survival log-rank $p<0.0001$). After two failures, subsequent use of RIT and anti-TNF agents respectively demonstrated 6-year retention rates of 53.6% and 37.2% (overall survival log-rank p=0.0473). Second versus third-line use was numerically (80.1% vs. 53.6%) and statistically better (overall survival log-rank p=0.0029). Of the censored patients treated with a second TNFi, 41%, were in remission, 27% had low disease activity (LDA), and 23% had moderate disease activity (MDA) according to DAS28(CRP) criteria. In patients treated in second intention with RIT, 23% were in remission, and 27% and 42% were respectively in LDA and MDA. Among censored patients treated with a third TNFi, 33%, 11% and 44% were in remission, had LDA and MDA respectively compared to 39%, 6% and 39% in RIT exposed patients.
**Conclusions:** As second and third-line agent used in TNF-IR patients, RIT demonstrates a better 6-year retention rate than anti-TNF agents. Second-line use showed a statistically better retention rate than third-line use. This suggests that using RIT as a second agent after failing a first anti-TNF agent is a better strategy than waiting to use it after two successive anti-TNF failures.
**Disclosure of Interest:** None declared
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## THU0035 SIX YEARS TOCILIZUMAB USE IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH ONE PREVIOUS ANTI-TNF AGENT EXPOSURE: COMPARISON WITH ADALIMUMAB AND ETANERCEPT FROM THE PROVINCIAL ELECTRONIC DATABASE AND REGISTRY RHUMADATA®

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**Background:** Tocilizumab, an intravenous agent, is approved for rheumatoid arthritis (RA) treatment in Canada since April 30th, 2010. It was the sixth approved agent after adalimumab, etanercept, abatacept, infliximab and rituximab. It has been demonstrated effective in the treatment of RA either in mono or combo therapy after non-biologic or biologic DMARDS.
**Objectives:** The goal of this analysis is to describe the six-year effectiveness of tocilizumab used in patients with RA failing a first anti-TNF agent and to compare it with adalimumab and etanercept used in the same clinical situation.
**Methods:** All patients with RA having failed a first anti-TNF agent and subsequently exposed to tocilizumab after the 1st of January 2008 were extracted from the Rhumadata® database. Three cohorts were created according to the time tocilizumab or the subsequent anti-TNF agents were introduced: One cohort of patients starting tocilizumab and two other cohorts starting either adalimumab or etanercept. Demographics and baseline characteristics including age, gender, disease duration, rheumatoid factor and anti-CCP antibodies, CRP and ESR, the number of previously failed treatments, DAS-28(ESR) and CDAI, HAQ-DI were included for each cohort. Kaplan-Meier model and were used to compare retention rates and Cox proportional hazard models were used to generate adjusted hazard ratios.
**Results:** The data from 128 patients prescribed either tocilizumab (44=34%), adalimumab (38=30%) or etanercept (46=36%) as a second biologic agent was extracted from the Rhumadata® registry and clinical database. Most subjects were female (77.3%), and the average age of cohort subjects was 54.4 (SD=13.2). 69.3% and 62.2% of patients were respectively $RF^+$ or anti-$CCP^+$. Mean CRP and ESR were respectively 14.8 (SD=21.5) mg/L and 28.6 (SD=24.2) mm/hr. No clinically significant differences at baseline were observed between groups. The six-year retention rates of tocilizumab, adalimumab, and etanercept as second-line biologic agents were respectively 54.6% (95% CI=35.9–70.0), 22.8% (9.7–39.1), 21.9% (8.9 -38.6) respectively. Kaplan-Meier survival analysis revealed significant differences in drug retention rates (log rank p=0.0007). Multivariate analysis adjusting for patient characteristics yielded hazard ratios of 2.66 (1.10–6.44), 5.33 (2.30–12.38) when respectively comparing adalimumab and etanercept to tocilizumab. Of the censored patients taking tocilizumab, 35% and 12% were in remission and had low disease activity (LDA) respectively, according to the DAS-28(CRP) criteria. In patients treated with anti-TNF agents, 50% and 17% were in remission and LDA.
**Conclusions:** In RA patient having failed their first anti-TNF agent, tocilizumab, an Il-6 inhibitor, is a more valuable alternative than cycling to a second anti-TNF agent. Similarly to previously presented analysis, in a patient having failed a first anti-TNF agent, it seems that using an agent with a different mode of action such as abatacept, rituximab or tocilizumab as opposed to a second anti-TNF agent delivers better long-term retention.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1605

## THU0036 IDENTIFYING CLINICAL FACTORS ASSOCIATED WITH LOWER DISEASE ACTIVITY DURING PREGNANCY IN PATIENTS WITH RHEUMATOID ARTHRITIS TO SELECT THOSE PATIENTS IN WHOM MEDICATION CAN BE SAFELY TAPERED

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**Background:** Pregnancy is the only natural condition in which Rheumatoid Arthritis (RA) remits spontaneously in approximately half of the pregnancies [1]. Many physicians try to taper or stop medication when a women conceives in order to prevent drug related side effects for mother and child. However, 50% of the patients still has active disease in the third trimester of pregnancy[1]. Factors that can identify patients in whom medication can be safely tapered during pregnancy are therefore needed.
**Objectives:** To determine clinical factors associated with lower disease activity in the third trimester during pregnancy in women with Rheumatoid Arthritis (RA) and thereby to identify patients in whom medication can be safely tapered during pregnancy.
**Methods:** This study is embedded in the Pregnancy induced Amelioration of Rheumatoid Arthritis (PARA)-study, a nationwide prospective cohort study. There was data available on 190 pregnancies from first trimester unto delivery. Disease activity was measured using the Disease Activity Score in 28 joints (DAS28). A multivariate linear regression analysis was performed on the DAS28 in the third trimester. Independent covariates in these models: the DAS28 in the first trimester, prednisone and sulfasalazine use in the first trimester, parity, methotrexate use in past, autoantibody status (either rheumatoid factor or ACPA positive), presence of erosions and duration of RA.
**Results:** In the multivariate linear regression model, see table 1., a higher DAS28 in the first trimester, the use of prednisone and the presence of autoantibodies were statistically significantly associated with a higher DAS28 in the third trimester (p-values $<0.001$, 0.032 and 0.014 respectively).

Table 1. Factors associated with RA disease activity in the third trimester, a multivariate linear regression model for DAS28 in the third trimester.

| N=190 | Linear regression DAS28 in the third trimester | | | |
|---|---|---|---|---|
| | Multivariate | | Multivariate* | |
| | Coeff. | P-value | Coeff. | P-value |
| DAS28 1st trimester | 0.542 | <0.001 | 0.544 | <0.001 |
| Sulfasalazine use 1st trimester | -0.184 | 0.192 | -0.186 | 0.177 |
| Prednisone use 1st trimester | 0.301 | 0.030 | 0.287 | 0.032 |
| Parity | -0.165 | 0.195 | -0.164 | 0.195 |
| MTX use ever | -0.041 | 0.760 | - | - |
| Autoantibody status | 0.410 | 0.009 | 0.367 | 0.014 |
| Presence of erosions | -0.065 | 0.658 | - | - |
| Duration RA | 0.012 | 0.291 | - | - |

DAS28 = Disease Activity Score in 28 joints, RA= rheumatoid arthritis, MTX= methotrexate.
*Multivariate model after backward selection (limit for exclusion P≥0.20)

**Conclusions:** The DAS28 in the first trimester, the autoantibody status and the use of prednisone were associated with RA disease activity in the third trimester. Female RA patients who have a lower DAS28 in the first trimester are

likely to have lower disease activity in the third trimester, especially if they are autoantibody negative and if they do not use prednisone. In these patients, it may be considered to safely taper their medication.

**References:**
[1] de Man YA, Dolhain RJ, van de Geijn FE, Willemsen SP, Hazes JM. Disease activity of rheumatoid arthritis during pregnancy: results from a nationwide prospective study. Arthritis Rheum 2008;59:1241–8.

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**Conflicts of interest:** None.
**Disclosure of Interest:** None declared
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## THU0037 PERSONALITY TRAITS IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN UNRECOGNIZED PREDICTOR OF MORTALITY

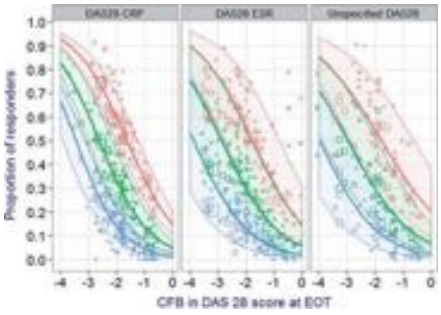
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**Background:** Psychosocial factors, such as pessimistic explanatory style, are shown to affect the course of treatments in many illnesses (Cardiovascular diseases, lung cancer, Parkinson's disease). Little is known about how pessimistic explanatory style affects rheumatoid arthritis (RA).
**Objectives:** The aim of this study was to determine if pessimistic explanatory style altered the risk for and mortality rates of RA patients.
**Methods:** The study used a subset of patients who completed the Minnesota Multiphasic Personality Inventory (MMPI) from among a population-based cohort with incident RA in 1955–2007 and an age- and sex-matched non-RA comparison cohort. Only patients who were ≥18 and fulfilled the American College of Rheumatology (ACR) 1987 criteria for RA were included. Pessimistic explanatory style was measured using the Optimism-Pessimism scale (PSM≥60). Logistic regression and Cox models were used to examine the associations between pessimistic explanatory style and development of RA or mortality rates.
**Results:** There were 148 RA and 135 non-RA subjects who completed the MMPI. Pessimistic explanatory style was associated with development of rheumatoid factor positive (RF+) RA (odds ratio [OR]:1.74; 95% confidence interval [CI]: 0.99–3.04; p=0.053 adjusted for age, sex, smoking and obesity). Among patients with RA, mortality risk adjusted for age, sex, year, smoking, and Charlson Comorbidity Index was increased with a pessimistic explanatory style (hazard ratio [HR]:2.88; 95%CI: 1.02–8.14), similar to mortality risk in RF+ RA patients (HR:2.28; 95%CI:1.10–4.73). A significant interaction between RF+ and pessimistic explanatory style indicated that having both did not confer an additive effect (p=0.037). The 10 year survival percentages were highest for those with RF-RA who were not pessimistic (93%) and were similar for patients with RF+RA who were not pessimistic (73%), those with RF-RA who were pessimistic (77%), and those who were both RF+RA and pessimistic (84%). This association did not change after adjusting for the MMPI depression scale or a history of depression prior to diagnosis of RA.
**Conclusions:** Having a pessimistic explanatory style was associated with an increased risk of developing RA and increased mortality rate in patients with RA. In these patients, the effects of RF+ and pessimistic style were not additive. The patient's psychological state strongly affects treatment decisions and outcomes and can inform about the usefulness of mindful interventions (e.g. cognitive behavioral therapy). Understanding the explanatory style is an important step in the holistic management of disease and a vital component of integrated care.
**Disclosure of Interest:** None declared
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## THU0038 QUANTITATIVE ASSESSMENT OF THE RELATIONSHIP BETWEEN THE DAS28 CONTINUOUS SCORES AND THE PROPORTION OF RESPONDERS BASED ON THE ACR CRITERIA IN RHEUMATOID ARTHRITIS: A META-ANALYSIS

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**Background:** ACR scores are widely accepted binary endpoints in Rheumatoid Arthritis (RA) clinical trials to characterize response to treatment. The Disease Activity Score calculated from twenty-eight tender and swollen joints (DAS28) is often assessed as a secondary endpoint in RA trials and is believed to be a more sensitive measure of dose-response due to the continuous nature of the scale.
**Objectives:** To characterize the quantitative relationship between the change from baseline (CFB) in DAS28 score and the proportion of responders based on ACR20/50/70 criteria using summary level data available in the literature from RA trials reporting both measures of response.
**Methods:** Summary level data from RA trials reporting DAS28-CRP, DAS28-ESR or unspecified DAS28 and ACR20/50/70 variables at the primary time point (with a minimum of 20 subjects per arm) were included in the analyses. The dataset included 82 unique trials with information from more than 12,000 patients (trial durations from 4 to 104 weeks). Three separate mixed-effects logistic regression analyses of the relationships between CFB in each DAS28 score and ACR20/50/70 responses with random inter-trial variability (in the intercept) were conducted and the sample size for each trial was used for weighting
**Results:** The observed and model-estimated relationships between DAS28 and ACR20/50/70 are presented in Figure 1. For a CFB in DAS28 CRP of -1 point, the point estimate [90% prediction interval (PI)] for ACR20, ACR50 and ACR70 responders is 33% [25% to 43%], 13% [8% to 22%] and 4% [2% to 7%], respectively. For a treatment that increases the CFB in DAS28 CRP from -1.0 to -2.0 points, the increase in ACR20, ACR50 and ACR70 responders is estimated to be 26% [24% to 26%], 19% [13% to 24%] and 9% [6% to 14%], respectively. For a treatment that increases the CFB in DAS28 CRP from -2.0 to -3.0 points, the increase in ACR20, ACR50 and ACR70 responders is estimated to be 22% [18% to 25%], 27% [24% to 28%] and 22% [16% to 28%], respectively. The relationship between the ACR scores and DAS28 was estimated to be slightly shallower and more variable for DAS28 ESR than DAS28 CRP.
Figure 1: The relationship between DAS28 continuous scores (DAS28 CRP, DAS28 ESR and unspecified DAS28) and the proportion of responders based on the ACR criteria. The solid lines and the shaded areas depict the median and 90% prediction interval for the proportion of responders at the end of treatment (EOT) for ACR20 (red), ACR50 (green) and ACR70 (blue) responders. The symbols represent the observed relationships for the analyzed trials with the symbol size weighted by the arm sample size.




**Conclusions:** A quantitative relationship between the continuous DAS28 score and proportion of subjects achieving ACR response has been established. The relationship between the DAS28 scores and ACR responders is estimated to be non-linear, most prominently for the deeper ACR responses. DAS28 CRP was better correlated with the ACR scores than DAS28 ESR based on the lower heterogeneity estimated in the relationship
**Disclosure of Interest:** M. Minocha Shareholder of: AbbVie, Employee of: AbbVie, J. Mandema Consultant for: AbbVie, A. Othman Shareholder of: AbbVie, Employee of: AbbVie
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## THU0039 MORE THAN ONE IN THREE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AT THE ULTRASOUND EXAMINATION OF THEIR HANDS ARE MISCLASSIFIED AS BEING IN REMISSION BY THEIR CLINICIANS: RESULTS FROM A LARGE COHORT STUDY

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**Background:** Assessment of active synovitis in rheumatoid arthritis (RA) is complex but essential for diagnosis and ongoing management. Clinical assessment is supported by serum laboratory analysis of inflammatory markers, high sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR). Musculoskeletal power Doppler ultrasonography (PDUS) has recently demonstrated greater sensitivity over clinical assessment and serum inflammatory markers in detecting active synovitis.
**Objectives:** To investigate the association between findings on PDUS, clinical assessment, serum hsCRP and ESR in the assessment of active synovitis in RA.
**Methods:** This cross-sectional study evaluated 218 consecutive RA patients (82% female) referred to ultrasound (US) clinic. Two assessors performed US examination using a 22 hand joint protocol, assessing wrists, metacarpophalangeal and proximal interphalangeal joints bilaterally (OMERACT scoring system). HsCRP and ESR were measured within 1 month of US scan. Patients with ≥3 swollen (SJ) and ≥3 tender joints (TJ) in hands were considered to have significant clinical synovitis (active or chronic).
**Results:** Of 218 patients with RA, 100 (46%) had positive PDUS signal in at least one joint. Raised hsCRP was found in 25% and raised ESR in 45%. Seventy-two of 202 patients (36%) had ≥3 TJ and ≥3SJ (clinically active synovitis). Whilst tender joint count was not correlated with positive PDUS (OR 1.01, p=0.334), swollen joint count (SJC) demonstrated strong association, with >30% increase in odds for positive PDUS for increase in SJC by one (OR 1.3, p<0.001). Of 96 patients with positive PDUS, 46 (48%) had ≥3TJ and ≥3SJ. Of 105 patients with negative PDUS, 26 (25%) had ≥3TJ and ≥3SJ (p=0.001).
Of 196 patients with ESR and PDUS data available, 44 (47%) of PDUS positive

and 45 (44%) of PDUS negative patients had raised ESR, showing no significant association (p=0.667). There was no difference in proportion of patients with raised CRP (25%) in PDUS positive vs. negative groups (p=0.748).
ESR and SJC were only very weakly correlated (Spearman's rho =0.16, p=0.03). Of 138 patients with either clinical or serological evidence of disease activity, 73 (53%) had positive PDUS. Among asymptomatic patients with normal hsCRP and ESR, 21 (38%) were PDUS positive (p=0.058).
**Conclusions:** Both hsCRP and ESR correlated poorly with clinical examination and PDUS detection of active synovitis. This should raise awareness among clinicians that hsCRP, ESR and clinical examination are misleading in appreciating the risk of ongoing inflammation in some patients with RA, as 38% of active RA patients in our study fell into this category. Further research into establishing the appropriate hsCRP cut-off value to distinguish between a subclinical inflammatory state and disease remission might yield better understanding of the role of hsCRP in monitoring disease activity in RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1086

## THU0040 IMPACT OF BASELINE CONVENTIONAL DISEASE ACTIVITY VARIABLES, IMAGING ASSESSMENT OF RA ACTIVITY (JOINT US AND MRI SYNOVITIS SCORES), MMP-3 AND CALPROTECTIN LEVELS ON ACHIEVEMENT OF ACR70 RESPONSE IN RA PATIENTS AFTER ETANERCEPT TREATMENT

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**Background:** Monitoring of RA activity is important in daily practice and clinical trials, in particular for subjects receiving biologics. As a result, new imaging tools and more objective biomarkers of synovial inflammation and joint destruction have been developed.
**Objectives:** To evaluate role of imaging methods (joint MRI, US), biomarkers (calprotectin-CP and MMP-3) and RA activity parameters in achievement of ACR70 response after Etanercept (ETN) therapy
**Methods:** 25 pts (mean age 49,4±13,7 yrs) with active RA despite stable doses of cDMARDs (DAS28 6,12±0,97) had received ETN 50 mg weekly sc for 24 weeks. RA duration was 6,38±5,9 yrs, 92% were women, 64%>RF+. Clinical and laboratory evaluation was done at weeks 0 and 25. US exam was performed before start of ETN treatment and after 6 month of ETN therapy by the same independent sonographer. 7-joint score (grade 0–3) included wrist, intercarpal, 2–3 MCP, 2–3 PIP joints of the clinically dominant hand and knee was used. MRI was done at baseline and after end of ETN treatment. Assessment of 2–5 MCP joints of the clinically dominant hand (0-no synovitis, 1–10-severity of synovitis) was done by the same independent radiologist.CP and MMP-3 serum levels (ELISA) were measured at the same time points. Changes of all parameters since baseline were assessed. Predictive factors of achievement ACR70 responce were explored.
**Results:** All clinical, laboratory, MRI and US parameters of RA activity had significantly improved during ETN therapy (p<0,05).We detected statistically significant difference only in baseline MRI synovitis score between responders and non-responders according ACR70 (p=0,0074). (table 1)

Table 1. The difference in baseline variables between ACR70 responders and non-responders

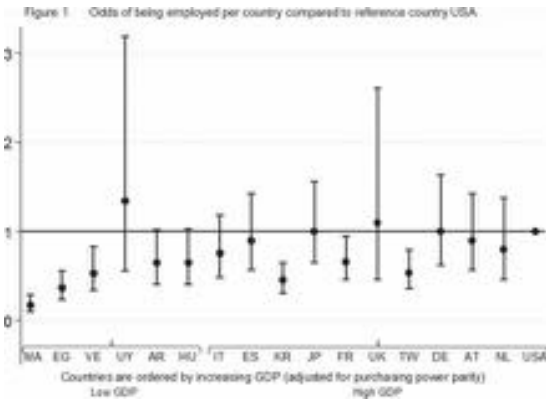
| Baseline parameters | Responders | Non-responders | p |
|---|---|---|---|
| SJC/66, Me [$Q_{25}$–$Q_{75}$] | 13 [10–16] | 10 [8–13] | 0.156 |
| ESR, mm/h, M±SD | 45±29 | 41±23 | 0.977 |
| CRP, mg/ml, Me [$Q_{25}$–$Q_{75}$] | 9.8 [8.2–51.9] | 16.4 [7–34.5] | 0.886 |
| DAS28 | 6.23 [5.84–6.62] | 5.96 [5.43–6.72] | 0.587 |
| CDAI, Me [$Q_{25}$–$Q_{75}$] | 35.6 [32.1–39.1] | 31 [26.7–39.7] | 0.139 |
| SDAI, Me [$Q_{25}$–$Q_{75}$] | 38 [33–42.8] | 32.9 [30.3–41.3] | 0.287 |
| CP, μg/ml, Me [$Q_{25}$–$Q_{75}$] | 4.54 [2.13–8.83] | 3.53 [1.88–12.01] | 0.977 |
| MMP-3, ng/ml, Me [$Q_{25}$–$Q_{75}$] | 1.14 [0.36–2.44] | 0.85 [0.44–1.23] | 0.51 |
| BM, Me [$Q_{25}$–$Q_{75}$] | 5.5 [2–10] | 8 [3–11] | 0.627 |
| PD, Me [$Q_{25}$–$Q_{75}$] | 1 [0.5–3] | 1 [1–2] | 0.797 |
| MRI, Me [$Q_{25}$–$Q_{75}$] | 1.5 [0–2] | 3 [3–4] | **0.0074** |

We did not find any significant difference between groups in MeΔ at weeks 0–12 of ESR, CRP, CP and MMP-3, whereas MeΔ of SJC distinguished in ACR70 responders and non-responders (p=0,0494).
**Conclusions:** 1. US and MRI synovitis sum scores decreased significantly in parallel with CP and MMP-3 serum levels and RA activity variables during ETN therapy. 2. Low baseline MRI synovitis sum score is more useful in comparison with baseline US, CP, MMP-3 and conventional RA activity factors as predictive tool of good responce in RA during anti-TNF therapy. 3. Decrease of ESR, CRP, CP and MMP-3 at week 12 had not impact on ACR70 response at week 25.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2235

## THU0041 LARGE COUNTRY DIFFERENCES IN WORK OUTCOMES IN PATIENTS WITH RA – AN ANALYSIS IN THE MULTINATIONAL STUDY COMORA

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**Background:** Better insight into country- or system related differences in work outcomes is important when trying to take country specific measures aiming to improve short- and long-term work outcomes of patients with rheumatoid arthritis (RA).
**Objectives:** We aimed to explore whether country of residence and specific country characteristics are associated with work outcomes in patients with RA.
**Methods:** Data from the cross-sectional multinational study COMORA (17 countries) were used. Work outcomes were measured by the Work Productivity and Activity Impairment Questionnaire (WPAI) assessing employment (yes/no), absenteeism (% of time) and presenteeism (% of normal productivity). The contribution of country of residence, gross domestic product (GDP), human development index (HDI), unemployment rate, social protection expenditures (SPE) and world region to the work outcomes was investigated in logistic or ordinal logistic regression models after adjusting for clinical and sociodemographic factors.
**Results:** The study sample consisted of 3,920 patients of whom the mean age was 56 (SD 13), 3,191 (82%) were female and 1,197 (31%) were employed. Large country differences were found for all work outcomes. The country with the best work outcome was used as reference. Morocco showed the lowest adjusted employment compared to the USA (OR 0.17; [95%CI 0.10; 0.30]) followed by Egypt (OR 0.37 [95% CI 0.24; 0.56]), Korea (OR 0.45 [95% CI 0.31; 0.65]), Venezuela (OR 0.53 [95% CI 0.34; 0.84]), Taiwan (OR 0.54 [95% CI 0.36; 0.80] and France (OR 0.66 [95% CI 0.46; 0.95]) (figure 1). Compared to Japan, absenteeism was highest in Morocco (OR 12.63 [4.45; 35.89]) followed by Hungary (OR 6.49 [95%CI 2.45; 17.23]) and Argentina (OR 3.25 [95%CI 1.25; 8.45]). Compared to Venezuela, presenteeism was highest in Taiwan (OR 13.81 [5.95; 32.04]) followed by Korea (OR 10.59 [95%CI 4.77; 25.13]) and Italy (OR 8.96 [95%CI 3.53; 22.76]). All country indices except SPE were significantly associated with the outcomes. Low GDP countries had lower odds of employment (OR 0.66; [0.54; 0.80]), higher odds of absenteeism (OR 2.68 [1.91; 3.76]), but a lower odds of presenteeism (OR 0.45 [0.32; 0.62]) compared to high GDP countries.




**Conclusions:** Substantial differences in work outcomes among RA patients were observed between countries. Lower economic and human welfare were associated with worse employment, higher absenteeism but paradoxically also with lower presenteeism.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1334

## THU0042 EVALUATION OF SYNOVITIS AT THE LARGE JOINT USING ULTRASONOGRAPHY AND HISTOLOGICAL FINDINGS FOR RA PATIENTS

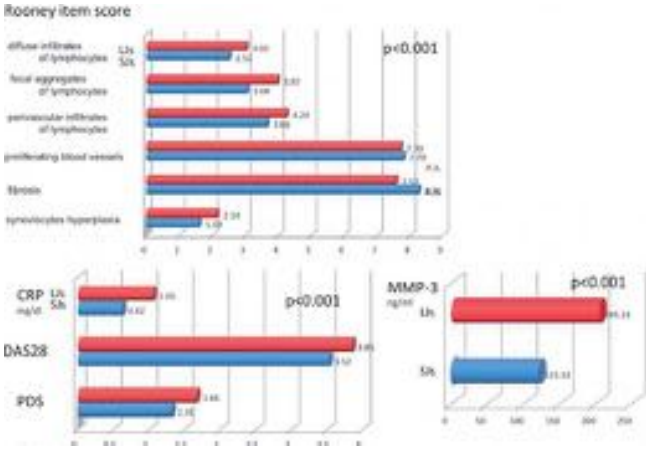
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**Background:** After starting to use biological DMARDs (bDMARD), the number of small joint (SJ) arthroplasty increased as compared with large joint (LJ) at our rheumatic center. Additionally, ultrasonography (US) for the examination of the affected joints widely utilized and it became a tool by which the rheumatologist should learn to diagnose RA and to evaluate disease activity.
**Objectives:** To clarify relationship among systemic disease activity, local disease

activity using US and synovial histopathological evaluation, we examined serum CRP, MMP-3 and DAS28, and US at the surgical site before surgery. After surgery, histopathological examination of the gathered synovium at the surgical site was performed.

**Methods:** Between March, 2011 and September, 2015, 668 joints underwent surgical treatment and synovial biopsies were performed. There were 152 LJs including 8 shoulders, 60 elbows and 84 knees, and 516 SJs including185 fingers, 118 toes, 192 wrists and 21 ankles. Male: female ratio was 1:7. The bDMARD (IFX20, ETN62, ADA17, TCZ44, ABT16, CZP4, GLM13) was used in 176 cases. Maximum power Doppler (PD) signal grade of US was determined ranging from 0 to 3. They were compared with serum CRP, MMP-3, DAS28 and local disease activity using histopathological evaluation using Rooney score (RS).

**Results:** Systemic disease activity correlated with local PD signal intensity both in LJs and SJs. Also, total RS and its item score excepting "proliferating blood vessels" correlated well with PD signal intensity. Systemic disease activity, local synovial proliferation and lymphocyte infiltration were more severe in LJs than in SJs. Though sensitivity of synovitis at LJs lower than at SJs, there was not a significant difference in PD signal intensity and RS between at LJs and at SJs. RS reflected systemic disease activity more in LJs than in SJs.




**Conclusions:** US is an excellent tool to reflect local synovitis as well as systemic disease activity both in LJs and SJs.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.1565

## THU0043 MINIMAL IMPORTANT DIFFERENCE IN HAQ: A VALIDATION FROM HEALTH ECONOMIC PERSPECTIVES IN PATIENT WITH RHEUMATOID ARTHRITIS USING REAL-WORLD DATA FROM ADELPHI DATABASE

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**Background:** A change of 0.25 in HAQ score has been considered as clinically meaningful.

**Objectives:** This study is to evaluate the clinical meaningfulness of the HAQ change from health economic perspectives in patients with rheumatoid arthritis using real-world data.

**Methods:** This is a retrospective cross-sectional study using data in ADELPHI Disease-Specific Program collected in 2014 (EU5 and US). Patients with clinically diagnosed RA (N=1032) were enrolled and completed self-reported outcomes measures including physical function by Health Assessment Questionnaire-disability index (HAQ-DI), employment status, work productivity by Work Productivity and Activity Impairment Questionnaire-General Health (WPAI-GH) and general health status by EQ visual analogue scale (EQ VAS). Clinical characteristics include disease activity defined by DAS28. Correlations between HAQ-DI score and other outcomes were analyzed using univariate or multiple regression analysis.

**Results:** The majority of patients were female (72.1%) with average age of 55 years old and disease duration of about 9 years. The mean (SD) HAQ-DI score was 0.76 (0.69) with 42.2% having a HAQ-DI score $\geq$1, indicating moderate to severe physical disability. 58% of patients were currently unemployed. Patients with a HAQ-DI score of $>$1.0, 77% were unemployed with a EQ VAS of 54.2, while patients with normal HAQ score of $\leq$0.5, 40% were unemployed with a EQ VAS of 75.6. HAQ-DI score was significantly correlated with the unemployed in multivariate logistic regression model ($p<0.001$), and correlated with time lost from work ($p<0.001$) and general health status by EQ VAS ($p<0.001$) by multivariate linear regression model. After adjustment for demographic characteristics including age, gender, and disease duration, an 0.25 increase in HAQ-DI score was associated with a 30% increase in likelihood for unemployed status (OR=1.30, 95% CI=1.22, 1.39).

**Conclusions:** Physical function measured by HAQ-DI is a valid measure to predict employment status and general health status in patients with RA.

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## THU0044 EFFICACY OF TREAT-TO-TARGET BIOLOGIC THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARED TO DELAYED INITIATION OF BIOLOGICS: A REAL WORLD STUDY

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**Background:** Rheumatoid arthritis (RA) is a chronic, devastating disease with involvement of small and large joints. Treat-to-target strategy aims to improve the outcome of patients with RA and rapidly reduce disease activity by using properly and aggressively all the therapeutic options[1].

**Objectives:** To estimate the efficacy of the first bDMARD, overall and by specific bDMARD, in RA patients, when administered according to international recommendations[2], compared to delayed initiation of bDMARDs (usual care) in an outpatient clinic.

**Methods:** Disease activity was regularly measured by DAS-28 until the end of treatment with the first bDMARD. Good response to treatment was considered when remission or low disease activity was achieved. Cox proportional-hazards analyses and Kaplan-Meier (KM) plots were performed to assess the likelihood (hazard ratio, HR) of achieving a good response.

**Results:** There were 113 patients in T2T and 250 patients in usual care group (study-sample characteristics, Table 1). Efficacy of treatment was measured at 3, 12, 24, 36 months and at the end of treatment (Table 2), with significant advantage of the T2T group ($p<0.001$). The IR for T2T group was 37.16 (95% CI 30.29–45.58) and for usual care group 17.26 (95% CI 14.54–20.50). The IRR between the 2 groups was 2.15.

The KM plots (Figure 1) depicted that the likelihood for a good response was significantly higher among patients of the T2T group ($p<0.001$), with comparable efficacy of the 3 classical bDMARDs: infliximab (p=0.008), adalimumab (p=0.018) and etanercept ($p<0.001$) (Figure 2). The HR of the likelihood of achieving good response was 1.71 (95% CI 1.18–2.47, p=0.004) in favor of the T2T group. Etanercept and the newer bDMARDs seemed to be more effective than infliximab or adalimumab whereas total steroid dose $>$500mg and swollen joint count (6–10) were found to be negative predictive factors for a good response.

**Conclusions:** Treat-to-target treatment with bDMARDs offers a rapid and better long-term outcome to patients with RA, compared to delayed initiation of biologic treatment[3,4,5].

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## THU0045 14-3-3ETA POSITIVITY IS ASSOCIATED WITH RADIOGRAPHIC PROGRESSION DESPITE PATIENTS ACHIEVING CLINICAL REMISSION

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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease characterized by synovial inflammation which may lead to irreversible joint damage, reduced mobility and decreased quality of life. Although clinical remission can often be achieved with DMARD therapy, remission is often not observed on imaging and the presence of bone edema on MRI is the current best predictor of radiographic progression. Another marker associated with radiographic outcomes is 14–3-3$\eta$, which is a joint-derived protein whose serological expression is independent of CRP[1], modifiable over time[2], and linked with the upregulation of factors that drive the joint damage process[3].

**Objectives:** Examine whether patients who achieve clinical remission at year 1 (Yr1) but remain 14–3-3$\eta$ positive have worse radiographic outcomes by year 3 (Yr3).

**Methods:** Baseline (BL) and Yr1 plasma 14–3-3η protein titres were measured in a cohort of 360 early RA patients from the Reade Institute; all patients were treatment naïve at BL. 14–3-3η positivity was based on the cut-off ≥0.19 ng/ml. Mean (SD) patient age was 55 (12) years and 74% were female. Radiographic progression at Yr3, across the whole cohort and in those patients that achieved Yr1 DAS28 ESR remission (<2.6), was assessed as well as ΔSHS of ≥1, 3 and 5 points from Yr1 to Yr3. Mann-Whitney and Fisher Exact testing was performed to determine the significance (p≤0.05) of group differences and the association with marker positivity, respectively.

**Results:** At BL and Yr1, 245 (68%) and 210 (58%) of patients were 14–3-3η positive. Patients who were positive at baseline or Yr1 had significantly worse radiographic progression by Yr3 than 14–3-3η negative patients; BL 14–3-3η positivity (+ve vs.-ve): [2.0 (0.0–7.5) vs. 0.0 (0.0–4.0), p=0.019] and Yr1 14–3-3η positivity (+ve vs. -ve): [2.0 (0.0–8.0) vs. 0.0 (0.0–4.0), p=0.0012]. A total of 109 (30%) patients achieved Yr1 DAS28 remission. Patients who achieved remission yet were 14–3-3η positive at Yr1 experienced significantly worse radiographic progression by Yr3 than negative patients [1.0 (0.0 -5.0) vs. 0.0 (0.0–2.0), p=0.016]. A similar and significant trend for radiographic progression was observed in patients who did not achieve clinical remission and were 14–3-3η positive at Yr1 versus those who were 14–3-3η negative [2.0 (0.0–11.0) vs. 1.0 (0.0–5.0), p=0.029]. The table below demonstrates that positivity for 14–3-3η at both BL and Yr1, across the whole cohort as well as in those achieving clinical remission, is associated with radiographic progression. Yr1 positivity was more strongly associated with ΔSHS ≥5 than BL.

| Yr1 to Yr3 | ΔSHS≥1 | | ΔSHS≥3 | | ΔSHS≥5 | |
|---|---|---|---|---|---|---|
| | OR (95%CI) | p-value | OR (95%CI) | p-value | OR (95%CI) | p-value |
| Whole Cohort, n=360 | | | | | | |
| BL Pos, n=245 | 1.6 (1.0-2.5) | 0.024 | 1.6 (1.0-2.5) | 0.034 | 1.5 (0.9-2.5) | 0.076 |
| Yr1 Pos, n=210 | 1.8 (1.2-2.8) | 0.004 | 1.8 (1.2-2.8) | 0.005 | 1.9 (1.2-3.1) | 0.005 |
| Non-Remitters, n=251 | | | | | | |
| BL Pos, n=174 | 1.6 (0.9-2.8) | 0.062 | 1.6 (0.9-2.7) | 0.074 | 1.4 (0.8-2.5) | 0.150 |
| Yr1 Pos, n=151 | 1.6 (1.0-2.7) | 0.050 | 1.6 (1.0-2.7) | 0.050 | 1.4 (0.8-2.5) | 0.117 |
| Remitters, n=109 | | | | | | |
| BL Pos, n=71 | 1.6 (0.7-3.5) | 0.179 | 1.6 (0.6-3.8) | 0.234 | 1.6 (0.5-4.9) | 0.280 |
| Yr1 Pos, n=59 | 2.3 (1.0-4.9) | 0.029 | 2.4 (1.0-5.7) | 0.038 | 5.8 (1.6-21.4) | 0.003 |

**Conclusions:** Patients who achieve DAS28 remission at Yr1 but remain 14–3-3η positive are at risk of future radiographic progression. As expected with a modifiable biomarker such as 14–3-3η, serial assessment is more informative than baseline assessment.

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## THU0046 A 3-YEAR STUDY OF WORK IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON THE IORRA COHORT

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**Background:** Indirect costs of rheumatoid arthritis (RA) due to losses such as reduced productivity are an important social issue in addition to rapidly increasing direct costs; however, work disability in patients with RA have not been thoroughly assessed in Japan. With the recent changes in socioeconomic structure, the number of female paid workers has been increasing; thus, the impact of RA on the work impairment of Japanese patients has been rapidly increasing. In addition, work status is strongly influenced by cultural differences among races. Furthermore, with the recent improvement of RA treatment strategy, it has not been evaluated whether work disability in patients with RA improved or not in a real world settings. Hence, we evaluated longitudinally work impairment in patients with RA in daily practice using a large cohort database.

**Objectives:** To study how the magnitude of work impairment in Japanese patients with rheumatoid arthritis (RA) has changed over the past 3 years in routine clinical practice.

**Methods:** Patients with RA who participated in both of the IORRA studies conducted in April 2012 and April 2013 and those who worked for pay on both surveys and were aged 55 years or younger at baseline were identified. Changes over the 3 years in the absenteeism (AB), presenteeism (PR) and overall work impairment (OWI) scores as determined by the Work Productivity and Activity Impairment (WPAI) were evaluated in those patients. In addition, patients with work impairment, defined as AB >0% or PR ≥30%, at baseline were classified according to whether or not they still had work impairment at 3 years to identify differences in their characteristics.

**Results:** Among 4,214 patients with RA who participated in both of the IORRA studies, 1,310 patients were selected in this study cohort (mean age, 51.5 years; females, 80.1%; Japanese version of the HAQ [J-HAQ], 0.37). The AB, PR, OWI scores in the 1310 patients were 1.8%, 16.4% and 17.3%, respectively, at baseline, which remained unchanged at 3 years (2.1%, 16.4% and 17.6%, respectively). At baseline, 206 patients (15.7%) had work impairment, of whom 117 patients (56.8%) (mean age, 43.8 years; females, 85.5%; DAS28, 3.1 [2.8 at 3 years]; J-HAQ, 0.80 [0.75 at 3 years]; 73.5% [76.9% at 3 years] of patients received methotrexate; 36.8% [38.5% at 3 years] received biologics) continued to have it at 3 years, and 89 patients (43.2%) (mean age, 44.2 years; females, 84.3%; DAS28, 3.2 [2.1 at 3 years]; J-HAQ, 0.54 [0.25 at 3 years]; 77.5% [82.0% at 3 years] of patients received methotrexate; 24.7% [39.3% at 3 years] received biologics) were free from work impairment.

**Conclusions:** In the overall population of Japanese patients with RA, work impairment has not been improved over the past 3 years; however, as many as 43.2% of patients with work impairment at baseline have experienced improved work productivity. In these patients, more intensive RA therapy has resulted in a greater reduction in disease activity or functional impairment.

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## THU0047 ARTHROSCOPIC MACRO-ASSESSMENT OF SYNOVIA IN RHEUMATOID ARTHRITIS PATIENTS HIGH ANTI-CCP

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**Background:** Antibodies to cyclic citrullinated peptide (anti-CCP) are valuable immunological marker for early diagnostic of rheumatoid arthritis (RA). They are highly sensitive and highly specific in RA. In addition, anti-CCP used as prognostic marker of severe RA. Arthroscopy is a minimally invasive technique, safe and efficient for visualization and biopsy of synovia (S) in rheumatology. Changes and structure of S are different for stages of RA. Detailed study of S changes features depending on the RA clinical course is an actual problem in rheumatology, as it allows early diagnostic of the disease, clinical course prognosis and individual therapy prescription.

**Objectives:** to define a peculiarities of S macro-assessment on arthroscopy in RA patients depending on the blood level of anti-CCP

**Methods:** knee arthroscopy was performed in 33 patients with RA (diagnosis is verified according to the criteria ACR/EULAR, 2010). Patients were divided into two groups depending on the blood level of anti-CCP. The first group ("–" anti-CCP), with negative or low positive level, included 13 patients (40%) (anti-CCP level was ≤40 IU/ml). The second group ("+" anti-CCP) positive and highly positive - 20 patients (60%) (anti-CCP level was >40 IU/ml). The patients of the two groups were not statistically different for clinical and demographic indicators.

All arthroscopy was performed in the same sterile operating room via arthroscope (Karl Storz GmbH, Tuttlingen, Germany) of 2.4 mm with an angle of 30°. Arthroscopy was performed in accordance with Helsinki Declaration. All chambers of the joint were inspected. The joint lavage for visualization was perfomed throughout the procedure, but minimized (usually it is about 500 to 1000 ml). All the arthroscopy procedure was recorded on video for the further evaluation of the macroscopic picture of the knee joint changes. Parameters of the changes were estimated: the type of S hyperplasia, S vascularization, atrophic changes in S, presence of pannus and fibrin, shape of S villi

**Results:** Indices of inflammatory and of villous S hyperplasia were equally often (62% and 76%, 69% and 75%, respectively) in the patients of the two examined groups. S hyperemia and expressed vascular pattern predominated in "+" anti-CCP group of the patients - 76% of cases, compared with the group "–" anti-CCP - 36% ($\chi^2$=4.17, p=0.04). Growth of S with clavate villi tended to increase in the patients of "+" anti-CCP group. Presence of pannus significantly prevalent in patients with "+" anti-CCP group (75%) when compared with "–" anti-CCP groups - 31% ($\chi^2$=4.63, p=0.03). The presence of fibrin tended to increase in incidence in patients of "+" anti-CCP, but it was not statistically significant. The percentage of patients with atrophic changes of S was practically the same in the compared groups.

**Conclusions:** RA patients with anti-CCP blood level of >40 IU/ml have S hyperemia with increased vascular pattern twice more often, and the presence of pannus on S arthroscopy was 2.5 times more often in them. The data shows the intensity of inflammation and angiogenesis in S of high anti-CCP blood level patients. This contributes to an aggressive course of RA in these patients with the rapid development of cartillage-bone destruction

**Disclosure of Interest:** None declared

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## THU0048 TESTING OF 14-3-3ETA IN EARLY UNDIFFERENTIATED POLYARTHRITIS CAN ASSIST WITH PRIORITIZING REFERRALS OF HIGH JOINT DAMAGE RISK PATIENTS TO RHEUMATOLOGISTS

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**Background:** Achievement of radiographic remission in RA is dependent on early patient identification and effective triaging to enable prompt referral to enable tight control treatment strategies. Assessment within 12 weeks of symptom onset i.e. the "window of opportunity" is reportedly associated with less joint destruction and a higher likelihood of achieving remission. Based on RF or anti-CCP2 testing at the primary care level, approximately one half of early RA patients may test negative and not be referred. Further, since referral times can often be lengthy, rheumatologists in consult with GPs require more sensitive, disease specific tools to prioritize the referral of patients who are at greatest risk for radiographic progression. 14–3-3η is a soluble diagnostic RA marker that is involved in the pathophysiology of the disease and informs joint damage progression.
**Objectives:** The aim of this study was to examine the combined benefit of 14–3-3η and anti-CCP2 testing in early undifferentiated polyarthritis to inform radiographic progression rate.
**Methods:** Serum 14–3–3η levels were measured at baseline in 331 patients with recent onset polyarthritis (Sherbrooke EUPA), for which a follow up of at least 60 months was completed. Mean (SD) age was 60 years, 62% were female, and median (IQR) duration of symptoms was 4 (1.7–5.7) months. Radiographic progression was defined as a change in Sharp/van der Heijde score, $\Delta SHS \geq 1$ at 18, 30, 42, and 60 months. Differences in mean ΔSHS based on 14 -3-3η positivity was assessed using the Mann-Whitney U-test at the diagnostic cut-off of ≥0.19 ng/ml. ANOVA analysis was performed to assess the significance of 14–3-3η and anti-CCP2 co-expression with radiographic progression over 60 months.
**Results:** At baseline, 46% and 40% of patients were positive for 14–3-3η and anti-CCP2, respectively. Together, 14–3-3η or anti-CCP2 captured 55% of patients. Of these, 58% were positive for both markers whereas 42% were positive for one or the other. Over the course of 60 months, mean (SD) radiographic progression from baseline was significantly higher in 14–3-3η seropositive patients when compared with seronegative patients, 10.0 (15.6) vs. 6.3 (13.40) p=0.022. Radiographic progression based on biomarker co-expression analysis shows that patients who were positive for both anti-CCP2 and 14–3-3η had the most significant changes in radiographic outcomes over 60 months.

| Timepoint | Group | n | Mean ΔSHS ± SD | p-value |
|---|---|---|---|---|
| Baseline to 60 months | Both negative | 144 | 6.22±13.91 | 0.024 |
| | Only 14–3–3η positive | 47 | 6.43±12.09 | |
| | Only anti-CCP2 positive | 25 | 6.40±10.01 | |
| | Both positive | 100 | 11.66±16.76 | |

**Conclusions:** Early undifferentiated polyarthritis patients who are positive for 14–3-3η and anti-CCP2 have more radiographic progression over 60 months. 14–3-3η positive status can assist with prioritization of high joint damage risk patient referrals to rheumatologists.
**References:**
[1] de Rooy DPC et al. Rheum. 2011. 50:93.
**Disclosure of Interest:** G. Boire Grant/research support from: The 14–3-3eta measurements were performed free of charge by Augurex, Augurex remaining totally blinded to clinical data. All the analyzes were performed in Sherbrooke without sharing of clinical data of individual patients with Augurex personnel., N. Carrier: None declared, A. de Brum Fernandes: None declared, P. Liang: None declared, A. Masetto: None declared, Y. Gui Employee of: Augurex Life Sciences Corp., J. Savill Employee of: Augurex Life Sciences Corp., S. Michienzi Employee of: Augurex Life Sciences Corp., H. Menard: None declared, W. Maksymowych Consultant for: Augurex Life Sciences Corp., (Co-inventor of 14–3-3η), A. Marotta Employee of: Augurex Life Sciences Corp., (Co-inventor of 14–3-3η)
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## THU0049 IS PATIENT GLOBAL ASSESSMENT IN BOOLEAN-BASED REMISSION IN RHEUMATOID ARTHRITIS REALLY REQUIRED INSTEAD OF PHYSICIAN GLOBAL ASSESSMENT? A COMPARATIVE STUDY WITH ULTRASOUND

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**Background:** Patient global assessment (PtGA) is included in all the current remission definitions for RA despite the fact that PtGA is not exclusively related to disease activity.
**Objectives:** In this study in order to objectively identify whether patient's assessment is better than physician's (Ph) or not, we compared disease activities assessed with ultrasound (US) of Boolean remission patients with PtGA and with PhGA.
**Methods:** RA patients in clinical remission (DAS28 ESR<2.6) for at least 3 months were included. Boolean based remission definition and modified version by substitution of PtGA with PhGA were determined. A standard gray scale (GS) and power Doppler (PD) US examination of 28 joints (included in DAS28) for the presence of synovitis was performed by an experienced sonographer (NI) blinded to clinical data. US synovitis GS and PD signals were semiquantitatively graded from 0 to 3 and were recorded as sum scores of PD and GS, respectively.
**Results:** A total of 88 out of 389 RA patients (22.6%) in DAS28 remission were enrolled (F/M=55/33, mean age 53.4±12.0, disease duration 10.5±6.3 years, bDMARDs 44.3%, RF/Anti-CCP positivity 72%). Of 88 patients, 33 (37.5%) fulfilled the Boolean remission criteria. When PtGA was substituted with PhGA, Boolean remission rate increased to 61.4% (n=54) ($P$<0.001). Regarding US disease activity no PD, no GS and no PD+GS signals were observed in 13 (39.4%) vs 16 (29.6%), 10 (30.3%) vs 11 (20.4%) and 9 (27.3%) vs 10 (18.5%) patients in Boolean remission with PtGA and PhGA, respectively (Table 1). When PD and GS signals > grade 1 were taken into account, % of patients without PD, GS or both signals were also similar Table 1). US disease activity parameters of Boolean PtGA and Boolean PhGA remission and their counterpart nonremission patients were compared as well, Boolean remission either with PtGA or PhGA had significantly lower PD scores compared to Boolean nonremission groups with PtGA or PhGA (1 [0–4] vs 3 [1–7], $P$=0.016 and 1.5 [0–4] vs 4 [0.75–7], $P$=0.027, respectively).

**Table 1. US disease activity parameters of remission patients according to Boolean based criteria with PtGA and PhGA***

| | Boolean REM with PtGA (n=33) | Boolean REM with PhGA (n=54) | *P* value |
|---|---|---|---|
| PD synovitis sum score (0-84) | 1 (0-4) | 1.5 (0-4) | 0.43 |
| PD synovitis sum score (without counting grade 1 signals) | 0 (0-3) | 0 (0-4) | 0.58 |
| GS synovitis sum score (0-84) | 3 (0-8.5) | 3 (1-8) | 0.58 |
| GS synovitis sum score (without counting grade 1 signals) | 2 (0-4) | 2 (0-6) | 0.58 |
| US joint count with PD signal (0-28) | 1 (0-2.5) | 1 (0-3) | 0.44 |
| US joint count with PD signal (without counting grade 1 signals) | 0 (0-1.5) | 0 (0-2) | 0.58 |
| US joint count with GS signal (0-28) | 1 (0-4) | 2 (1-4) | 0.43 |
| US joint count with GS signal (without counting grade 1 signals) | 1 (0-2) | 1 (0-3) | 0.58 |
| PD≥1 | 21 (63.6) | 31 (57.4) | 0.61 |
| GS≥1 | 16 (48.5) | 24 (44.4) | 0.71 |
| PD≥1 and GS≥1 | 14 (42.5) | 22 (40.7) | 0.68 |
| US JC with GS≥1 | 14 (42.5) | 24 (44.4) | 0.71 |
| ESR, mm/h | 18 (11-26) | 17 (10-28) | 0.43 |
| CRP, mg/L | 3.2 (2.1-3.9) | 3.2 (2.7-3.8) | 0.83 |
| Tender joint count, median (min-max) | 0 (0-1) | 0 (0-1) | 0.58 |
| PD sum score in the tender joints, median (min-max) | 0 (0-0) | 0 (0-0) | 0.50 |

*The values were presented as median (IQR). †The values were presented as n (%).

**Conclusions:** RA patients in Boolean remission with PhGA do not have higher disease activity that is verified by US, compared to patients in Boolean remission with PtGA. Furthermore Boolean remission with PhGA differentiates patients with US evinced inflammation, especially PD scores, as good as PtGA. These data suggest that PtGA might be substituted with PhGA in Boolean criteria with higher remission achievement rates. Prospective follow up and recruitment of more patients will clarify the consistency of these results over time and impact of this substitution on functionality.
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## THU0050 ORTHOPEDIC SURGICAL INTERVENTION AIMING AT HIGHER LEVEL OF QUALITY OF LIFE AND MENTAL WELLNESS FOR THE PATIENTS WITH RHEUMATOID ARTHRITIS. A PROSPECTIVE COHORT STUDY OF 276 SURGICALLY-TREATED PATIENTS

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**Background:** By the biologic treatment of rheumatoid arthritis (RA), uncontrollable synovitis in the past has been well comtrolled. However, some patients with established RA are still difficult to reach comprehensive disease control, thus surgical reconstruction for the damaged joint is required. Recently, patients desired to achieve functional remission aiming at the higher level of quality of life (QOL) and the mental wellness.
**Objectives:** The objective of this study was to clarify the effect of orthopedic surgical intervention for the disabled patients with RA using the assessment of patient-reported outcome (PRO) and disease activity.

**Methods:** Surgical reconstruction of the damaged joint was scheduled on 276 sites in 276 patients (male: 34, female: 242) with RA between October 2012 and September 2014. The average age was 64 (19–89) years old and the average duration of the disease was 16 (1–60) years. The surgical site was shoulder in 6 patients, elbow in 26, wrist in 74, hand in 63 (combined with wrist in 18), hip in 13, knee in 50, ankle in 12, and forefoot in 50. The procedure included alloarthroplasty (shoulder: 5, elbow: 22, hand: 36, hip: 13, knee: 47), arthroplasty without prosthesis (wrist: 30, hand: 10, forefoot: 67), arthrodesis (wrist: 37, hand: 33, ankle: 11, forefoot: 5), and synovectomy (shoulder: 1, elbow: 4, wrist: 15, hand: 6, knee: 3, ankle: 1). MTX was used in 176 patients (64%) with the average dose of 7.7mg/w, and PSL was used in 175 patients (63%) with the average dose of 4.0mg/d. Biologics was used in 69 patients (25%) including ETN: 20, TCZ: 17, IFX: 11, GLM:9, ADA: 8 patients. PRO was assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), and patient's general health using visual analogue scale of 100mm (Pt-GH). Disease activity was assessed by 28-joint Disease Activity Score using C reactive protein (DAS28-CRP). They were measured just before surgery (baseline), at 6 and 12 months after surgery.
**Results:** As a whole, physical function (HAQ-DI), QOL (HAQ-DI, EQ-5D, Pt-GH) and mental wellness (BDI-II, Pt-GH), disease activity (DAS28-CRP) significantly improved at 6 and 12 months after surgery compared to those at baseline ($p<0.01$) (Table1, Figure1). The rate of clinical remission in DAS28-CRP (<2.3) at baseline, 6 and 12 months after surgery was 23%, 55% and 53%, respectively. The rate of functional remission in HAQ-DI (<0.5) was 25%, 31% and 30%, respectively. The rate of minimal depression in BDI-II (≤13) was 58%, 64% and 65%, respectively.

Table 1. Change in patient-reported outcome and disease activity (n=276)

| | HAQ-DI | EQ-5D | BDI-II | Pt-GH | DAS28-CRP |
|---|---|---|---|---|---|
| Baseline | 1.1 ± 0.7 | 0.69 ± 0.11 | 13.0 ± 8.8 | 39 ± 25 | 3.1 ± 1.0 |
| 6mos.after surgery | 1.0 ± 0.8* | 0.74 ± 0.14* | 11.7 ± 8.2* | 26 ± 21* | 2.4 ± 1.5* |
| 12mos.after surgery | 1.0 ± 0.8* | 0.75 ± 0.14* | 11.6 ± 8.5* | 27 ± 21* | 2.4 ± 0.8* |

mean ± SD, *:p<0.001 compared to baseline

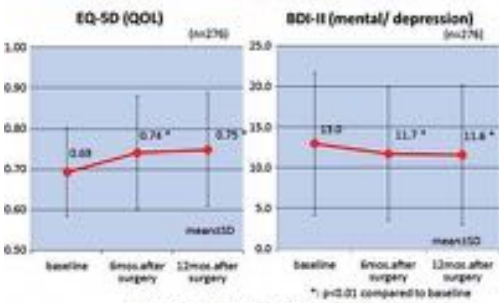



Figure 1: Change in EQ-5D and BDI-II

**Conclusions:** Favorable effects of orthopedic surgical intervention on QOL and mental wellness as well as physical function were confirmed in the disabled patients with RA. To improve QOL and mental wellness, surgical treatment for the damaged joint should be considered in combination with tight medical control. It also had an ameliorating effect on disease activity.
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## THU0051 THE LEVELS OF SERUM PENTRAXIN 3, IL 6, FETUIN A AND INSULIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The pathogenesis of RA is not well understood, but genetic, environmental and immunologic factors are known to be involved in the development of the disease. The long pentraxin, pentraxin-3 (PTX-3), is an inflammatory marker and a member of pentraxin superfamily which contains CRP and serum amyloid P. There are some published studies showing the relationship between RA and PTX-3. (1–3). We investigated that PTX3, IL 6, fetuin- A, insulin and HOMA-IR might also have a role in the pathogenesis of RA.
**Objectives:** The aim of this study was to evaluate the relationship between disease severity and biochemical parameters such as pentraxin-3, fetuin-A, IL-6,insulin and HOMA-IR levels in patients with rheumatoid arthritis.
**Methods:** This study included 60 patients with RA and 20 healthy controls. Serum pentraxin-3, fetuin-A, IL-6 and insulin concentrations were determined. Also, HOMA-IR values were calculated. Disease activity was assessed with Disease Activity Score (DAS28). Quality of life was evaluated by the use of the Health Assessment Questionnaire disability index.
**Results:** The serum values for ESR, CRP, pentraxin-3 and fetuin-A in patients with RA were elevated than control subjects (p values=0.001, 0.001, 0.000, 0.000, 0.01, 0.02, respectively) A positive correlation was evident between the DAS 28 score and IL6 levels (r =0.263, p=0.045). We found no correlation between the DAS28 score and HOMA-IR, the levels of pentraxin 3, fetuin A, insulin ($p<0.05$). Fetuin A levels was positively correlated with cumulative steroid dose (r=0.382, p=0.035). A statistically significant correlation was evident between presence of cardiovascular disease and HOMA-IR values in RA patients (r=0.437, p=0.032). In addition, DAS-28 score values were not in correlation with insulin, fetuin-A, HOMA-IR, IL-6 and pentraxin-3 levels ($p>0.05$).
**Conclusions:** Elevated levels of pentraxin-3, fetuin-A, CRP, ESR might play a role in the pathogenesis of RA. Levels of IL-6, fetuin-A, insulin HOMA-IR, pentraxin -3, CRP, ESR concentrations were not associated with clinical severity of the RA.
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## THU0052 ASSOCIATION BETWEEN ANTIPHOSPHOLIPID ANTIBODIES AND ARTERIAL THROMBOTIC EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Antiphospholipid antibodies (aPL) were reported to be found by variable range from 5 to 75% in patients with rheumatoid arthritis (RA) but their clinical significance remains undetermined.
**Objectives:** The aim of this study is to investigate the association of the presence of aPL with thrombotic events in patients with RA.
**Methods:** aPL profile, including lupus anticoagulant (LAC), anti-cardiolipin antibodies (aCL), and anti-$\beta_2$ glycoprotein I antibodies (a$\beta_2$GPI), was evaluated in 360 patients with RA according to the standard guideline. Clinical and radiographic data were collected retrospectively.
**Results:** aPL were identified in 36 patients (10.0%). LAC was the most common type (n=23, 6.4%) and aCL and a$\beta_2$GPI were detected in 5 and 12 patients (1.4 and 3.4%), respectively. Compared to aPL-negative group, aPL-positive group included more male patients (16 (44.4%) vs. 51 (15.7%), $P<0.001$) and had higher rate of ever-smoker (14 (38.9%) vs. 51 (15.7%), $P=0.005$) while there was no difference between two groups in the age, disease duration, and body mass index as well as in the rate of diabetes, hypertension, and dyslipidemia. There was also no significant difference in the positive rate of rheumatoid factor and anti-cyclic citrullinated peptide antibody, values of inflammatory indices and radiographic scores of hand x-ray between two groups. Of note, arterial thrombotic events more commonly developed in aPL-positive group than aPL-negative (5 (13.9%) vs. 7 (2.2%), $P=0.004$) while venous thrombosis did not differ between two groups (0 (0.0%) vs. 3 (0.9%), $P=1.000$). In multivariate regression analysis, the presence of aPL, old age, hypertension, and high value of baseline C-reactive protein were independently associated with arterial thrombotic events ($P<0.05$).
**Conclusions:** A proportion of RA patients was aPL-positive, and the presence of aPL was independently associated with arterial thrombosis. This result suggests that aPL might be contributable to increased risk for arterial thrombosis in patients with RA.
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**Disclosure of Interest:** None declared

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## THU0053 NO EXCESS MORTALITY IN A POPULATION-BASED DANISH RHEUMATOID ARTHRITIS COHORT FROM THE LATE PRE-BIOLOGIC ERA

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**Background:** Patients with rheumatoid arthritis (RA) from hospital-based series have an increased mortality, in particular from cardiovascular diseases. Estimates of standardized mortality ratios (SMR) from population-based inception cohorts have been inconsistent and mortality in RA patients may be modified by treatment and preventive strategies. Furthermore, human senescence in the general population has been delayed since 1950.(1) We therefore wanted to investigate the all-cause SMR in a Danish population-based inception RA cohort from the late pre-biologic era seen at a regional hospital with documented focus on intention-to-treat (2, 3) and cardiovascular screening (4).
**Objectives:** To investigate SMR in an unselected inception cohort of Danish RA patients from 1995 to 2002.
**Methods:** The case base was the population of the County of South Jutland according to the Danish Civil Registration System (CVR). Incident RA cases were identified at the referral center for rheumatic diseases in the County where the observed completeness of registrations from the case base was 97%.(5) The registry was scrutinized for all RA patients fulfilling the 1987 American College of Rheumatology criteria for RA from 1995 to 2002. Linkage of cases to CVR and the Danish Register of Causes of Death was based on unique personal identification numbers. Cases were followed from inclusion until emigration, death or end of follow-up (31.12.2013). Statistics Denmark provided mortality rates for the total Danish population from 1995 to 2013.
**Results:** A total of 509 cases were identified (Females 68%; mean age 61 years; rheumatoid factor positive 77%; erosive 23%). During 6079 person-years (py) of follow-up 200 (39%) patients had died (Females 32%; males 55%). The main causes of death are seen in table 1. There were no statistically significant differences in the causes of death according to sex (Chi-squared test=12.2, degrees of freedom: 7, p=0.092). The median follow-up time was 13 years and the average mortality rate 33/1000 py (Females 26/1000 py; males 50/1000 py). The overall SMR was 1.04 (95%>confidence interval (CI): 0.91–1.19), in females 0.96 (95%>CI: 0.79–1.43) and in males 1.16 (95%>CI: 0.95–1.43).

Table 1. Main causes of death in 200 Danish patients with RA (numbers (%)

| Diseases (ICD-10 codes) | n (%) |
|---|---|
| Cardiovascular (I00-I99) | 68 (34) |
| Neoplasms (C00-D48) | 52 (26) |
| Pulmonary (J00-J99) | 23 (12) |
| Skin, bone connective tissue (L00-M99) | 10 (5) |
| Gastrointestinal (E00-E90) | 8 (4) |
| Metabolic (E00-E90) | 8 (4) |
| Infectious (A00-B99) | 5 (3) |
| Other (other codes) | 26 (13) |

**Conclusions:** In this population-based study there were no significant excess mortality compared to the general population. The predominant causes of death were cardiovascular-, neoplastic- and pulmonary disease.
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## THU0054 GLYCATED ALBUMIN INCREASES WITH DISEASE ACTIVITY IN RHEUMATOID FACTOR POSITIVE RHEUMATOID ARTHRITIS PATIENTS WITH NORMAL FASTING GLUCOSE AND HBA1C

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**Background:** Rheumatoid arthritis (RA) is a prototypical autoimmune disease, characterized by the symmetric inflammation in multiple joints, leading to progressive destruction of joints. Glycated albumin (GA) is a newly suggested parameter for the glycemic status. GA was reported to be correlated with inflammatory burdens such as (C-reactive protein) CRP and inflammatory cytokines levels [1,2].
**Methods:** We consecutively screened 250 RA patients in this study, and finally analyzed data of 205 RA patients. We collected 12 hourfasting blood samples and performed laboratory tests. In this study, we used disease activity score (DAS) 28 using both erythrocyte sedimentation rate (ESR) (DAS28-ESR) and CRP (DAS28-CRP), and we defined DAS28 >3.2 as active RA.
**Results:** Patients with active RA showed significantly higher GA level than those with inactive RA (13.8 ± 1.8 vs. 12.8 ± 1.4%, P<0.001 (DAS28-ESR) and 14.4 ± 1.7 vs. 13.0 ± 1.5%, P<0.001 (DAS28-CRP)). Patients with active RA had significantly higher alkaline phosphatase (ALP) level than those with inactive RA (P=0.003 (DAS28-ESR) and P=0.033 (DAS28-CRP)). On multivariate logistic regression analysis, GA ≥12.95%, CRP ≥1.65 mg/L and ALP ≥60.5 IU/L were independent predictors of active RA based on DAS28-ESR (OR 4.881, P<0.001, OR 12.972, P<0.001, and OR 3.573, P=0.001). Also GA ≥13.95% could independently predict active RA based on DAS28-CRP better than ESR ≥43.5 mm/hr (OR 6.399, P<0.001 vs. OR 4.509, P<0.001), but ALP ≥60.5 IU/L could not.
**Conclusions:** GA level increased with disease activity in rheumatoid factor positive RA patients with normal laboratory results, who had no medical history. GA level showed the potential to predict active RA, comparable with ESR and CRP.
**References:**
[1] Pu LJ, Lu L, Xu XW, Zhang RY, Zhang Q, Zhang JS, et al.Value of serum glycated albumin and high-sensitivity C-reactive protein levels in the prediction of presence of coronary artery disease in patients with type 2 diabetes. Cardiovasc Diabetol 2006;5:27.
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**Disclosure of Interest:** None declared
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## THU0055 BONE RESORPTION WAS CORRELATED WITH RADIOLOGIC PROGRESSION IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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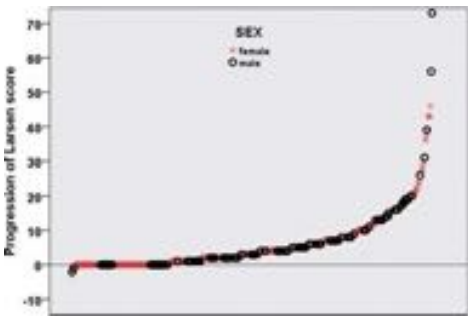
**Background:** Rheumatoid arthritis (RA) itself is associated with osteoporosis that may be localized or generalized. Joint inflammation in RA induces local periarticular osteoporosis. And the bone loss in the hands and generalized osteoporosis was reported to be correlated.
**Objectives:** To determine the levels of bone turnover markers in patients with rheumatoid arthritis (RA) and the correlation with disease activity index, bone mineral density (BMD) and radiographic progression.
**Methods:** Sixty-eight postmenopausal women with RA were recruited in our study. Serologic measurement including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF) and anti-cyclic citrullinated peptid (anti-CCP) were analyzed. Calcium, vitamin D, bone alkaline phosphatase (BAP) β-crosslaps were also detected. Bone mineral density (BMD, g/cm$^2$) was measured at the lumbar spine and the left femoral neck by dual-energy X-ray absorptiometry (DXA). DAS28 and Sharp score were separately calculated for disease activity and radiographic progression evaluation. Spearman correlation analysis was conducted between clinical biomarkers and disease indexes.
**Results:** The overall rate of patient with abnormal BMD was 94.12%, with osteopenia 29.41% (20/68) and osteoporosis 64.71% (44/68), respectively. ESR, CRP and DAS28 was significantly correlated with each other showing consistent disease activity (p<0.05). Serum β-crosslaps level (452.87±202.40 ug/l) was not correlated with any of disease acidity markers (p all >0.05) and positively correlated with Sharp score (150.76±59.71) in postmenopausal women with RA (r=0.776, p=1×10–6).
**Conclusions:** Osteopenia and osteoporosis was predominant in RA which might be related to disease activity and/or structural damage. β-crosslaps implies radiographic progression instead of disease activity.
**References:**
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**Disclosure of Interest:** None declared
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## THU0056 WOMEN, MEN, AND RHEUMATOID ARTHRITIS: RADIOGRAPHIC PROGRESSION OVER TEN YEARS IN THE CURRENT MILLENNIUM

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**Background:** Radiographs of hands and feet represent an objective outcome measure of rheumatoid arthritis (RA). Joint damage is a result of cumulative disease activity over years. Unlike other clinical measures, radiographic damage is caused mainly by disease inflammatory activity. Therefore, radiographs are a proper measure to analyze whether RA behaves differently in women and men over time.
**Objectives:** To compare radiographic progression in women and men over 10 years after diagnosis of early RA.
**Methods:** All 1046 patients who were diagnosed with RA in 1997 – 2005 at a single rheumatology center were scheduled for a 10 year follow-up with radiographs of hands and feet at years 0, 2, 5, and 10. Larsen score (0 - 100) was employed including MCPs, wrists and 2–5 MTP joints. Radiographic progression over 10 years was calculated and compared between women and men.
**Results:** Among 1046 patients (66% women, mean age 58, 60% seropositive, 13% with erosions at baseline), 5-year radiographs were available in 85% and 10-year radiographs in 71% of patients. A 5-year radiographic progression was similar between women and men: among 539 seropositive patients the median (IQR) Larsen score was 2 (0, 6) in 359 women and 2 (0, 7) in 180 men. In 346 seronegative patients the figures were 0 (0, 2) and 0 (0, 2) in 245 women and 101 men, respectively. Overall, 50% of seropositive women and 52% of seropositive men showed erosions and in seronegative patients the respective proportions were 17% and 23%. Also the 10-year radiographic progression was similar between women and men (Figure 1). Among 480 seropositive patients, the median (IQR) Larsen score was 4 (0, 10) in 333 women and 4 (1, 9) in 147 men. In 263 seronegative patients the figures were 0 (0, 2) and 0 (0, 3) in 187 women and 76 men, respectively. Overall, 59% of seropositive women and 63% of men showed erosions and in seronegative patients the proportions were 21% and 28%, respectively. Among seropositive women vs men similar proportion had been treated with various anti rheumatic medications including 90% vs 87% MTX, 22% vs 29% subcutaneous MTX, 75% vs 84% SSZ, 76% vs 71% HCQ, 17% vs 16% LEF, 14% vs 12% im gold, 78% vs 77% Pred, and 22% vs 20% biologic agents. Mortality (a total of 15% of women and 30% of men died over 10 years) was the main reason for missing data.




**Conclusions:** Radiographic progression is similar in women and men who are treated for RA in the current millennium.
**Disclosure of Interest:** None declared
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## THU0057 VALIDATION OF THE BASELINE ADAMTS5 MRNA LEVELS AS A PREDICTION BIOMARKER FOR THE EFFICACY OF INFLIXIMAB; A MULTICENTER CLINICAL TRIAL

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**Background:** A disintegrin and metalloproteinase with thrombospondin motifs 5 (ADAMTS5) has been reported to play a key role in aggrecan degradation in cartilage. Lower level of the baseline blood ADAMTS5 mRNA level has been also reported to predict the better response to infliximab (IFX) in RA patients using a single-center study.
**Objectives:** In this study, we performed a prospective, multicenter, and observational study to derive and validate the baseline blood ADAMTS5 mRNA that would be predictive of the efficacy of IFX in RA patients.
**Methods:** Forty-one RA patients (Age, 54.1±12.3 y/o; Disease duration, 4.5±7.1 years; DAS28_ESR, 5.07±1.07; SDAI 23.5±1.03; Bio naïve, 91.7%) were enrolled and treated with IFX. Peripheral blood samples were collected at baseline and ADAMTS5 mRNA was quantified using real-time PCR as the ratio of b-actin mRNA (Index as BiologicMate®).
**Results:** Five patients dropped out of this study while 44.1%, 14.7%, 29.4%, 41.1%, 23.5%, and 23.5% of the remaining patients achieved good responder, none responder, DAS_ESR remission, DAS_CRP remission, SDAI remission, and Boolean remission at 14 weeks' treatment with IFX, respectively. Baseline ADAMTS5 mRNA levels in the SDAI remission group was significantly ($p=0.049$) lower than that in the non-SDAI remission group at 14 weeks' treatment with IFX. Area under curve (AUC) of the ROC curve for predicting the SDAI remission (SDAI $\leq$3.3) using the baseline ADAMTS5 mRNA at 14 weeks was 0.67, and the cut-off value of ADAMTS5 mRNA was calculated as 2.1 Index. There observed no difference in the general patient backgrounds (average age, disease duration, dose of MTX, dose of steroid, baseline SDAI, etc) between Low-ADAMTS5 ($<$2.1 Index) group and High-ADAMTS5d group. However, DAS28, CDAI, and SDAI at 14 weeks after treatment were significantly ($p=0.031$) lower in Low-ADAMTS5 group than those in High-ADAMTS5 group. The accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the baseline Low-ADAMTS5 ($<$2.1 Index) for predicting the SDAI remission (SDAI $\leq$3.3) at 14 weeks after treatment with IFX were 76.5%, 66.7%, and 85.7%, respectively. Interestingly, we observed positive correlation between baseline ADAMTS5 mRNA and SDAI score at 14 weeks after treatment with IFX.
**Conclusions:** The baseline blood ADAMTS5 mRNA level was validated as a biomarker for the prediction of the response to IFX in RA patients using the multicenter clinical trial.
**Disclosure of Interest:** K. Tsuzaka Shareholder of: Kaytee Bio, Co.&Ltd., M. Nagata: None declared, K. Amano: None declared, T. Mimura: None declared, S. Kagami: None declared, Y. Miwa: None declared, K. Ikeda: None declared, T. Mitsuka: None declared, H. Kanai: None declared, I. Sekigawa: None declared
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## THU0058 PREDICTION OF SUCCESSFUL DOSE REDUCTION OR DISCONTINUATION OF BIOLOGICS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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**Background:** Tapering of biologics has been shown feasible, effective and safe in rheumatoid arthritis (RA) patients with stable low disease activity. Tapering of biologics is done using a trial-and-error disease activity guided strategy, because it is not known in advance which patient can successfully taper. Prediction of successful dose reduction or discontinuation of a biologic could prevent flares and would save time and drug exposition. In the last years, several studies have investigated biomarkers for predicting successful tapering. However, these results have not yet been systematically summarised.
**Objectives:** To systematically review studies that address prediction of successful dose reduction or discontinuation of biologics in RA patients.
**Methods:** A literature search was performed in PubMed, EMBASE and Cochrane Library (November 2015). Clinical (un)controlled trials were included if they investigated the predictive value of clinical patient characteristics, biochemical tests or imaging measures assessed prior to protocolised dose reduction or discontinuation of a biologic (abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab) in RA patients with a low disease activity state. Two review authors independently selected studies, extracted data and assessed risk of bias. Qualitative best-evidence synthesis was separately performed for the prediction of successful dose reduction and successful discontinuation. A biomarker was classified as potential predictor if the univariate association was either strong (odds ratio (OR) or hazard ratio (HR) $>$2.0 or $<$0.5) and/or significant ($p<0.05$). If no univariate OR or HR was provided, other univariate association measures, multivariate results or textual conclusions were used. Potential predictors that were studied multiple times and were consistently ($\geq$75% of findings in same direction) associated with successful dose reduction or discontinuation of a biologic were regarded as predictors.
**Results:** Out of 3029 non-duplicate articles, 16 articles on 15 cohorts were included. A total of 17/55 and 33/65 biomarkers were studied in more than one cohort for the prediction of successful dose reduction and successful discontinuation of a biologic. Three predictors were identified: higher adalimumab trough level for successful dose reduction; and lower Sharp/van der Heijde erosion score and shorter symptom duration at the start of a biologic for successful discontinuation. Noteworthy, all three biomarkers were only studied twice, meaning that more frequently investigated biomarkers yielded no consistent predictors. In addition, 13/38 and 8/32 biomarkers studied in only one cohort were classified as potential predictor for successful dose reduction and discontinuation, respectively.
**Conclusions:** The predictive value of a wide variety of biomarkers for successful dose reduction or discontinuation of a biologic has been investigated, but we have found only three biomarkers that were predictive in just two studies. The strength of the evidence is limited by the low quality of included studies and the likelihood

of publication bias and multiple testing. Therefore, validation of the found potential predictors in well-designed predictive studies is needed.
**Disclosure of Interest:** None declared
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## THU0059 TRENDS IN THE ACHIEVEMENT OF LOW DISEASE ACTIVITY AMONG A US NATIONAL SAMPLE OF RHEUMATOID ARTHRITIS PATIENTS INITIATING BIOLOGICS

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**Background:** There is a growing emphasis on treating patients to a target level of low disease activity (LDA) or remission in order to improve outcomes associated with rheumatoid arthritis (RA).
**Objectives:** Our objective was to examine trends in the achievement of LDA over the past decade among RA patients receiving their first, second and third or more biologic agent.
**Methods:** Using the Corrona registry, we identified initiators of biologic therapy (stratified by prior experience: 1st, 2nd, ≥3rd) in distinct periods of calendar time over the last decade (2002–2004, 2005–2007, 2008–2010, 2011–2013) with moderate or high disease activity at the time of the initiation based on the Clinical Disease Activity Index (CDAI >10), and a follow-up CDAI measured at 1 year (±3 months). The primary outcome was achievement of LDA (CDAI ≤10) at 12 months. Trends over time between the groups were examined using Chi square tests. Multivariable logistic regression models were performed adjusting for baseline covariate.
**Results:** We identified 6,534 biologic initiators (1st: 2,769, 2nd: 2181, ≥3rd: 1584) who met inclusion criteria. Between 2011 and 2013, LDA occurred in 51%, 42% and 35% of those initiating their 1st, 2nd and ≥3rd biologic respectively. There was a significant trend over time in achievement of LDA in those initiating their first biologic. In adjusted models, treatment in the earlier time periods for those who initiated their 1st or ≥3rd biologic was associated with a reduced likelihood of achieving LDA (Table).

| Achievement of LDA | Year category | | | | P value for trend |
|---|---|---|---|---|---|
| | 2002–2004 | 2005–2007 | 2008–2010 | 2011–2013 | |
| 1st Biologic | N=282 | N=615 | N=684 | N=1188 | |
| Unadjusted (%) | 43 | 53 | 58 | 51 | 0.0003 |
| Adjusted* OR (95% CI) | 0.68 (0.51–0.90) | 0.93 (0.75–1.15) | 1.21 (0.99–1.49) | 1 | |
| 2nd Biologic | N=127 | N=419 | N=657 | N=978 | |
| Unadjusted (%) | 40 | 38 | 42 | 42 | 0.55 |
| Adjusted* OR (95% CI) | 0.85 (0.50–1.43) | 0.84 (0.65–1.09) | 1.00 (0.81–1.25) | 1 | |
| ≥3rd Biologic | N=55 | N=170 | N=460 | N=899 | |
| Unadjusted (%) | 20 | 32 | 37 | 35 | 0.09 |
| Adjusted* OR (95% CI) | 0.44 (0.22–0.89) | 0.95 (0.66–1.37) | 1.13 (0.88–1.44) | 1 | |

*Adjusted for age, gender, body mass index, disease duration, baseline CDAI, patient pain, functional status and insurance.

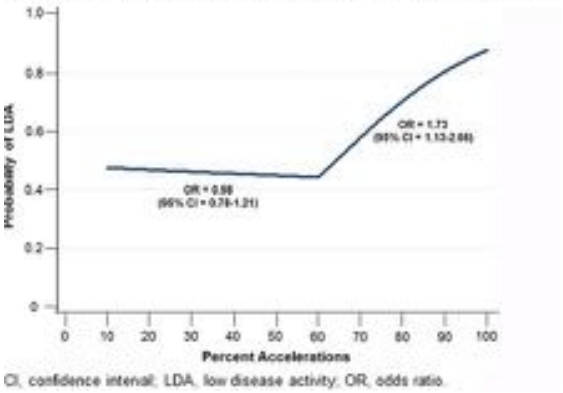
**Conclusions:** In the latest time period, achievement of LDA was influenced by biologic experience (50% in 1st biologic vs. 35% ≥3rd biologic initiation). Patients who initiated their 1st or ≥3rd biologic in earlier time periods had a reduced likelihood of achieving LDA (Table). Additional investigation is needed to understand the factors contributing to the trend in improved disease as well as the barriers in order to inform efforts to further increase the proportion of patients who achieve LDA.
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## THU0060 THE RELATIONSHIP BETWEEN ADHERENCE TO A TREAT-TO-TARGET APPROACH FOR CLINICAL CARE OF US PATIENTS WITH RHEUMATOID ARTHRITIS AND ACHIEVEMENT OF LOW DISEASE ACTIVITY

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**Background:** Little is known about the relationship between adherence to the treat-to-target (T2T) paradigm and clinical outcomes in US patients with rheumatoid arthritis (RA).
**Objectives:** To evaluate the relationship between adherence to T2T care and achievement of low disease activity (LDA) using a post hoc analysis of a cluster-randomized behavioral intervention trial evaluating a T2T implementation approach vs usual care (UC) in patients with RA.
**Methods:** Twenty-eight rheumatology practices from the Corrona network recruited patients with RA between July 29, 2011, and July 30, 2013. Eligible patients with moderate or high disease activity (Clinical Disease Activity Index [CDAI >10]) were followed for 12 months. Regardless of randomization in the trial (T2T vs UC), sites were categorized based on rate of acceleration (e.g., initiation or dose increase of cDMARD or biologic at visits with CDAI >10 and no treatment acceleration in the prior 3 months). Sites that accelerated therapy at ≥60% of eligible visits (top tertile) were considered high acceleration (HA) sites; sites with <60% acceleration rates were deemed low acceleration (LA) sites. The primary endpoint was achievement of LDA (CDAI ≤10) at 12 months. Baseline characteristics of the groups were compared using standardized differences. An intent-to-treat analysis was performed with logistic regression models adjusting for clustering by site and covariates associated with |standardized differences| >0.10.
As a sensitivity analysis, logistic regression models were fitted using acceleration rates as a linear association. The first model was as a continuous covariate (1 unit representing a 10% change in acceleration). The second model allowed for a threshold effect and used a linear spline with a knot at 60% acceleration.
**Results:** Overall, there were 10 HA sites (195 patients) and 18 LA sites (337 patients). The groups were similar in terms of sex, race, ethnicity and baseline disease activity. However, HA site patients were younger (mean age, 56 vs 58 years) and had shorter disease duration (mean, 6 vs 9 years). Over the study period, 17% of HA site patients (34/195) and 18% of LA site patients (62/337) dropped out ($P$=0.832). The rates of achievement of LDA at the last visit were 60.5% in the HA group vs 52.5% in the LA group (odds ratio [OR] 1.78; 95% CI 0.96–3.27) in multivariable models adjusting for demographics and disease characteristics. In the sensitivity analyses, use of acceleration rate as a continuous covariate was associated with an OR of 1.15 (95% CI 0.99–1.24). In the model with the spline (Figure), acceleration rates <60% were associated with an OR of 0.98 (95% CI 0.78–1.21), while rates ≥60% had an OR of 1.73 (95% CI 1.13–2.66).

**Figure.** Association of treatment acceleration rate with the probability of achieving LDA




CI, confidence interval; LDA, low disease activity; OR, odds ratio

**Conclusions:** Increased site adherence to a T2T approach was associated with a greater likelihood of achieving LDA. Evidence suggests there may be a threshold effect, indicating a lack of benefit with inconsistent adherence to the T2T approach.
**Acknowledgement:** The Corrona T2T study is sponsored by Corrona, LLC, with support from a development and subscription agreement/contract with Genentech and additional support from AbbVie and Crescendo.
**Disclosure of Interest:** L. Harrold Grant/research support from: Corrona, LLC, Employee of: Corrona, LLC, G. Reed Employee of: Corrona, LLC, A. John Employee of: Genentech, Inc, C. Barr Employee of: Corrona, LLC, K. Saunders Employee of: Corrona, LLC, K. Soe Employee of: Corrona, LLC, R. Magner: None declared, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: AstraZeneca, Celgene, Genentech, Janssen, Novartis, Pfizer, Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Grant/research support

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## THU0061 PATIENTS' PERCEPTIONS OF RISK, RISK COMMUNICATION AND PREDICTIVE TESTING FOR RHEUMATOID ARTHRITIS

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**Background:** Early treatment of rheumatoid arthritis (RA) is associated with improved clinical outcomes. There is a growing research interest in the identification of biomarkers to predict the development of RA in order to facilitate early treatment and preventive interventions. First degree relatives of individuals with a diagnosis of RA are at an increased risk of developing RA and are therefore likely candidates for predictive/preventive approaches. However access to this group is currently dependent on the cooperation of existing RA patients.
**Objectives:** To understand patients' perceptions of risk and predictive testing for RA, and their likelihood of communicating with their relatives about the risk of developing RA in the future.
**Methods:** Twenty-one RA patients (15 females and 6 males; aged 35 – 80 years) took part in semi-structured interviews. The interviews explored perceptions of risk of RA, family communication about risk, predictive testing, and risk reduction strategies. Interviews were audio-recorded, transcribed verbatim and analysed using thematic analysis.
**Results:** Many patients were aware of genetic risk factors for RA and identified one or more relatives who they felt were at risk of developing RA in the future. Some patients described feelings of responsibility or guilt for their relatives' increased risk of developing RA. Environmental risk factors such as infection and psychosocial stress were also suggested, though few patients mentioned that smoking is associated with an elevated risk of RA. Patients described a lack of public awareness about RA and the causes of RA. They also referred to a lack of understanding, by their relatives as well as by the general public, of the negative impact that this condition has on their quality of life.
Many patients held positive views of predictive testing for RA and were of the opinion that prediction would typically be associated with timely and positive preventive intervention. Those with negative views attributed these to their uncertainty about the accuracy of predictive tests, the availability of approaches (including therapeutic ones) to reduce RA risk and the potential for risk knowledge to cause unnecessary worry.
Patients generally expressed willingness to communicate with their relatives about their risk of RA. However many patients identified relatives that they were not in contact with, or communicated with infrequently. Some mentioned that they would not pass on information to particular relatives who they did not get on with. Patients referred to choosing which relatives to communicate with, and described likely variation amongst relatives in their receptivity to risk information, and their likelihood of acting on such information. Reasons suggested for this included relatives being too busy, being in denial of their susceptibility, preferring to deal with things when they happen, being likely to worry, and feeling that RA is not serious enough to warrant action.
**Conclusions:** Accurate information about risk factors for RA, and the potential impact of RA on quality of life, is needed to support family communication about RA risk. Strategies for the management of RA that target relatives of existing patients need to take into account that communication of risk information via patients is likely to be restricted and/or selective.
**Disclosure of Interest:** None declared
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## THU0062 PROGNOSIS OF EARLY RHEUMATOID ARTHRITIS PATIENTS WITH EROSIVE DISEASE AT BASELINE

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**Background:** In 2013, a new EULAR definition of erosive disease for use in the 2010 ACR/EULAR rheumatoid arthritis (RA) classification criteria was published [1]. We were interested in the characteristics of early RA patients with erosive disease according to this new definition, including their propensity to reach ACR/EULAR Boolean remission [2].
**Objectives:** To characterize the clinical course of early RA patients with erosive disease participating in a clinical trial, at baseline and after a 4-year follow-up period.
**Methods:** The presence of erosive disease was assessed at the baseline visit of early RA patients who were treated in the context of the COBRA-light trial [3,4]. After 52 weeks, treatment was continued without protocol. Erosive disease was defined as: "an erosion (defined as a cortical break) seen in at least three separate joints at any of the following sites: the proximal interphalangeal, the metacarpophalangeal, the wrist (counted as one joint) and the metatarsophalangeal joints on radiographs of both hands and feet" [1]. Radiographs were scored by two independent trained assessors according to the Sharp/van der Heijde (SHS) method. ACR/EULAR Boolean remission was assessed at 3, 6, 9 months; and 1, 1.5, 2 and 4 years after trial initiation.
**Results:** Only 8 (5%) of the 162 trial patients had erosive disease at baseline; these were somewhat older than patients without erosive disease at baseline (p=0.10). No differences in rheumatoid factor and ACPA status were found between erosive and non-erosive patients at baseline. After the 52 weeks trial period, 43% COBRA vs. 42% COBRA-light patients used prednisolone for ≥90 days, 34% vs. 44% patients switched to other DMARDs, and 39% vs. 28% used biologicals during the follow-up period. After a mean follow-up period of 4 years (data of 149 patients available), patients with erosive disease reported significantly higher disease activity (p=0.04) and pain (p=0.03) than patients without erosive disease, and a trend for more functional limitations (p=0.05) (Table 1). Likewise, the physician reported significantly higher disease activity (p=0.03); and both the SHS at 4 year (p<0.01) as well as SHS progression since baseline were higher for patients with erosive disease than patients without erosive disease (p=0.09). None of the erosive patients reached Boolean remission at any visit during the 4-year follow up-period, whereas 45% of the non-erosive patients did (p=0.01).

Table 1. Characteristics of RA patients with and without erosive disease

| | Baseline visit (n=162) | | 4 year visit (n=149) | |
|---|---|---|---|---|
| | Erosive (n=8) | Not erosive (n=154) | Erosive (n=8) | Not erosive (n=141) |
| Female, n (%) | 3 (38) | 107 (70) | 3 (38) | 97 (69) |
| Age in years | 59 (11) | 52 (13)* | 64 (11) | 56 (12)* |
| DAS | 4.5 [3.5;4.8] | 4.0 [3.4;4.4] | 2.1 [1.2;2.5] | 1.5 [1.0;2.3] |
| Tender joint count in 53 joints | 19 [16;22] | 14 [9;19] | 4 [0;10] | 2 [0;7] |
| Swollen joint count in 44 joints | 14 [9;19] | 12 [9;16] | 0 [0;2] | 1 [0;3] |
| HAQ | 1.5 [1.3;2.3] | 1.3 [0.9;1.6] | 1.1 [0.5;2.0] | 0.5 [0;1.1]* |
| Change in HAQ (Δ baseline - 4 year) | - | - | -0.5 [-1.2;0.2] | -0.6 [-1.1;-0.2] |
| SHS | 17 [14;21] | 0 [0;14]* | 19 [15;35] | 1.0 [0;3.5]* |
| SHS progression (Δ baseline - 4 year) | - | - | 2.0 [0.5;18.5] | 0.5 [0;2.3]* |
| CRP in mg/l | 22 [5;63] | 13 [4;37] | 4 [2;6] | 3 [2;5] |
| Patient assessment of disease activity | 64 [43;80] | 66 [50;79] | 33 [17;67] | 14 [4;37]* |
| Patient assessment of pain | 72 [23;87] | 62 [41;77] | 42 [26;59] | 18 [5;43]* |
| Patient global assessment | 63 [23;94] | 66 [45;76] | 38 [32;55] | 22 [7;51]* |
| Physician assessment of disease activity | 52 [45;63] | 48 [40;60] | 41 [21;51] | 18 [7;39]* |

* Significant difference between patients with erosive vs. non-erosive disease (p<0.05)
† Trend for significant difference between patients with erosive vs. non-erosive disease (p<0.10)

**Conclusions:** In this exploratory study of early RA, erosive disease at baseline appeared to be rare. However, such disease is associated with a poor prognosis: more active disease, no remission, and worse 4-year outcomes despite a treat-to-target regime aimed at clinical remission.
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[4] er Wee, ARD 2015,74:1233–40.
**Disclosure of Interest:** N. Konijn: None declared, L. van Tuyl: None declared, M. Boers: None declared, D. den Uijl: None declared, M. ter Wee: None declared, P. Kerstens: None declared, A. Voskuyl: None declared, D. van Schaardenburg: None declared, M. Nurmohamed: None declared, W. Lems Grant/research support from: This study was supported by an unrestricted grant from Pfizer
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## THU0063 OUTCOMES OF TREAT-TO-TARGET STRATEGY IN ESTABLISHED RHEUMATOID ARTHRITIS: A LONG-TERM PROSPECTIVE COHORT STUDY

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**Background:** Treating rheumatoid arthritis (RA) to a target has become a landmark strategy to be pursued in every patient. Compared to usual care, treat to target (T2T) has decreased radiographic progression and improved quality of life and physical function[1]. Nonetheless, few studies have addressed the true long-term impact of a T2T strategy in a real-world setting with established RA patients[2,3].
**Objectives:** To examine the long-term effectiveness of a treat-to-target strategy in patients with established rheumatoid arthritis in daily practice.
**Methods:** Rheumatoid arthritis patients previously treated under usual care condition were started on a T2T strategy between March 2005 and February 2007 and followed through December 2014. Participants were seen every 3 months until remission/low disease activity was reached and every 6 months afterwards. After DMARD change, participants were assessed monthly for three consecutive months. Treatment escalation followed a step-up strategy, according

to national recommendations. Disease activity was measured by DAS28 and CDAI, and physical function by HAQ. Data were extracted by standardized chart and research forms review. Change in disease activity and physical function was compared using Wilcoxon's test and Generalized estimate equations.

**Results:** Significant improvements were seen in both composite scores during follow-up period. There was a significant reduction in DAS28 (4.6±0.1 vs. 3.1±0.1; $p<0.001$) and in CDAI (21.2±1.0 vs. 7.9±0.7; $p<0.001$). Physical function also improved, as demonstrated by reduction in HAQ-DI (1.3±0.05 vs 1.0±0.1; $p<0.001$). The reduction in DAS28, CDAI and HAQ-DI was nonlinear. The percentage of participants in remission increased significantly from 11% to 35% by DAS28 and from 6% to 19% by CDAI ($p<0.001$). Likewise, there was an improvement in LDA from 10% to 28% by DAS28 and from 22% to 52% by CDAI ($p\leq0.001$). At the end of follow up, 62% of the cohort achieved the target by DAS28 and 71% by CDAI. As well as 30% of participants reached HAQ$\leq$0.5 and DAS$\leq$3.2.

**Conclusions:** Treat-to-target strategy aiming for remission or low activity disease is effective in patients with established RA. The access to biologic DMARDs might have contributed to achieve disease activity control in a substantial proportion of the patients.

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**Disclosure of Interest:** None declared

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## THU0064 SHORT AND SUSTAINED PERIODS OF ACR/EULAR REMISSION PREDICT GOOD FUNCTIONAL OUTCOME, BUT NOT STABLE RADIOGRAPHIC OUTCOME IN EARLY RHEUMATOID ARTHRITIS

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**Background:** The ACR/EULAR remission criteria were validated against their potential to predict future prognosis of rheumatoid arthritis (RA) [1]. Sustained remission was not studied, but is likely to be an even stronger predictor of RA prognosis. Furthermore, the patients in the validation study mainly had established RA, whereas results might be different for early RA patients.

**Objectives:** To investigate whether remission at single and consecutive visits predicts good outcome in early RA.

**Methods:** The presence of remission according to ACR/EULAR and other criteria (Boolean clinical, CDAI, DAS, DAS28, RAPID3) was assessed in early RA patients during the first year of the COBRA-light trial [2,3]. Likelihood ratios were used to assess whether meeting the remission criteria at single visits (13, 26, 39 or 52 weeks) and consecutive visits (13+26, 26+39 or 39+52 weeks) predicted good outcome in the second year (52–104 weeks). Good outcome was defined for function (HAQ consistently $\leq$0.5 and no deterioration), radiographic damage progression (no deterioration in Sharp-Van der Heijde scores) and both ("overall good outcome").

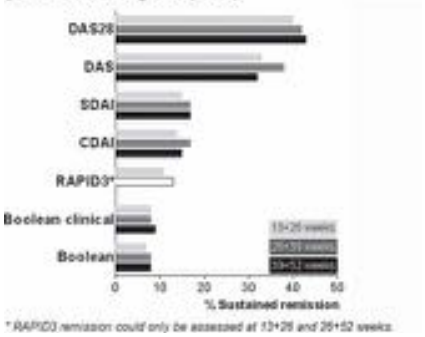
**Results:** Of the original 164 trial patients, 144 had evaluable data. In the second year, good functional outcome was observed in 35%, good radiographic outcome in 79%, and both in 28% of the patients. Highest sustained remission rates at 13+26, 26+39, and 39+52 weeks were observed for DAS28, followed by DAS, SDAI, CDAI, RAPID3, Boolean clinical and Boolean criteria (Figure 1). Almost all criteria predicted good functional and good overall outcome, at both single and consecutive visits; only single DAS remission did not significantly predict good overall outcome (p=0.07). Sustained remission periods resulted in higher likelihood ratios than remission at single visits (Table 1). None of the criteria predicted good radiographic outcome.

Table 1. Predictive value of remission at single and consecutive visits (n=144)

| | LR+ of remission at single visits | | | LR+ of remission at consecutive visits | | |
|---|---|---|---|---|---|---|
| | Good functional outcome | Good radiographic outcome | Good overall outcome | Good functional outcome | Good radiographic outcome | Good overall outcome |
| Boolean | 3.6* | 1.3 | 2.8* | 29.2* | 0.6 | 4.8* |
| Boolean clinical | 3.3* | 1.2 | 2.6* | 31.0* | 0.7 | 5.2* |
| CDAI | 2.3* | 1.2 | 2.0* | 6.8* | 0.8 | 3.1* |
| SDAI | 2.3* | 1.3 | 2.1* | 7.0* | 0.7 | 3.3* |
| DAS | 1.4* | 1.0 | 1.2* | 2.4* | 1.0 | 2.1* |
| DAS28 | 1.4* | 1.1 | 1.3* | 1.8* | 1.3 | 1.8* |
| RAPID3† | 3.5* | 0.9 | 2.7* | 12.8* | 1.0 | 5.2* |

*Indicates significant predictor ($p<0.05$); †RAPID3 remission could only be assessed at 13, 26 and 52 weeks, not at week 39; LR+ = Positive likelihood ratio.

Figure 1. Sustained remission in early RA patients during the first year of the COBRA-light trial (n=144)




* RAPID3 remission could only be assessed at 13+26 and 26+52 weeks.

**Conclusions:** Early RA patients who reach remission according to ACR/EULAR and other criteria during short or sustained periods are likely to retain good physical function in the subsequent months. Sustained remission periods are a stronger predictor than remission at single visits. However, in the setting of low overall damage progression, (sustained) remission was not predictive of good radiographic outcome.

**References:**

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[2] Den Uyl, ARD 2014;

[3] Ter Wee, ARD 2015.

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## THU0065 POTENTIAL PREDICTORS FOR ACHIEVING AND/OR MAINTAINING LOW DISEASE ACTIVITY OR REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Treatment with tumor necrosis factor inhibitors (TNFi) such as etanercept (ETN) is effective in patients with rheumatoid arthritis (RA). However, not all patients respond to treatment. Physicians would be able to better provide the best treatment to their patients if there were criteria that identified potential good responders to TNFi therapy.

**Objectives:** To evaluate criteria at baseline for their predictive value for (1) initial response to ETN treatment at week 24, and (2) for maintaining low disease activity (LDA) or remission at week 52 using data from the T2T trial (NCT01981473).

**Methods:** Patients with moderate-to-severe RA were treated with 50 mg ETN (ETN50) on a background of methotrexate ± disease-modifying anti-rheumatic drugs (DMARDs) for 24 weeks (open-label, Period 1 (P1)). Patients achieving LDA (Disease Activity Score-28 joints (DAS28)–erythrocyte sedimentation rate (ESR)<3.2) at week 24 were randomized to continue ETN50 or switched to placebo (PBO) for another 28 weeks (Period 2 (P2)). Baseline variables were analyzed for the probability of patients achieving DAS28-ESR or Clinical Disease Activity Index (CDAI) LDA (<3.2) at the end of P1 and to determine whether patients in remission maintained it at the end of P2. All data were evaluated using logistic regression analysis.

**Results:** Evaluable data were available for 473 of the 491 patients enrolled in P1. After 24 weeks of ETN treatment (end of P1), only being female (p=0.031) and using DMARDs (p=0.029) were predictive of patients being able to achieve DAS28-ESR LDA (<3.2). Younger patients and patients with lower DAS28-ESR, ESR, and Health Assessment Questionnaire–Disability Index (HAQ-DI) showed a statistically significant greater probability to achieve remission (DAS28-ESR<2.6) at the end of P1. Patients with lower DAS28-ESR, DAS28-C-reactive protein (CRP), CDAI, Simplified Disease Activity Index (SDAI), HAQ-DI, and shorter time to LDA in P1 at week 24 prior to entering P2 showed a statistically significant greater probability to maintain DAS28-ESR LDA or remission at week 52 for both patients who continued on ETN or were switched to PBO during P2. Younger patients (p=0.006) and patients with shorter disease duration (p=0.008) showed

a statistically greater probability to achieve CDAI remission at week 24. Lower DAS28-ESR, DAS28-CRP, CDAI, SDAI, HAQ-DI, and shorter time to LDA in P1 at week 24 prior to entering P2 showed a statistically significant greater probability to maintain CDAI LDA or remission at week 52 for both patients who continued on ETN or were switched to PBO during P2. The proportion of patients who maintained LDA or remission was consistently greater in the ETN arm compared with the PBO arm. None of the other baseline variables were predictive of patients being able to achieve LDA or remission.

**Conclusions:** In this post-hoc analysis, younger patients and patients with lower disease activity at baseline or shorter time to achieve LDA were more likely to achieve and maintain LDA or remission.

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## THU0066 DO PREDICTORS OF IV ABATACEPT RETENTION DEPEND ON THE LINE OF RHEUMATOID ARTHRITIS TREATMENT: 12-MONTH INTERIM ANALYSIS OF THE OBSERVATIONAL, PROSPECTIVE ACTION STUDY

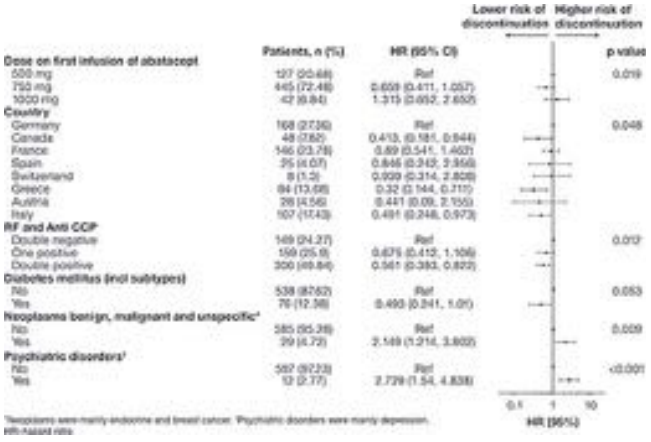
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**Background:** ACTION (NCT02109666) is an ongoing study to provide prospective, real-world data on IV abatacept (ABA) retention in RA. Prognostic factors for IV ABA retention were previously identified in a 12-month interim analysis of patients (pts) enrolled May 2008–Jan 2011 who failed ≥1 prior biologic DMARD.[1]

**Objectives:** To compare rates and identify predictors of IV ABA retention by treatment line (biologic naïve vs biologic failure) in a 12-month interim analysis.

**Methods:** ACTION is a 2-year, observational study of pts with moderate-to-severe RA who initiated IV ABA in Europe and Canada. Enrolment periods: May 2008–Dec 2010 (biologic naïve/failed prior biologics); Sept 2010–Dec 2013 (biologic naïve); Oct 2011–Dec 2013 (failed prior biologics). Data cut-off was May 2015. Crude retention rates were estimated by Kaplan–Meier analysis and compared using a log-rank test. Known risk factors and factors with significance in univariate models ($p \leq 0.20$) and no collinearity were entered into a multivariate Cox proportional hazards regression model. Factors with $p \leq 0.10$ after backward selection were retained. Efficacy assessments at 12 months included EULAR response and DAS28 (CRP) score.

**Results:** 2364 pts were enrolled and 2350 were evaluable: 674 (28.7%) were biologic naïve and 1676 (71.3%) had failed ≥1 prior biologic: 728/1676 (43.4%) failed 1 biologic, 948/1676 (56.6%) ≥2 biologics; 1605/1676 (95.8%) had failed anti-TNFs. Biologic-naïve pts had similar baseline characteristics vs biologic-failure pts, except for shorter disease duration, fewer erosions in combination with RF or anti-citrullinated protein antibody (ACPA) positivity, prior conventional DMARDs failed and ABA monotherapy, and more co-morbidities (COPD, cardiac disorders and neoplasms). Crude retention rates over 12 months were statistically higher in biologic-naïve (78.1%; 95% CI 74.7, 81.2) vs biologic-failure pts (69.9%; 95% CI 67.6, 72.1; $p<0.001$). Predictors of higher retention for biologic-naïve pts are shown (Figure). Neoplasms and psychiatric disorders were associated with lower retention and need investigation. In both treatment lines, RF/ACPA double positivity was associated with higher retention vs double negativity after stratifying for erosion status, but was significant only in pts with erosive disease at baseline. A numerically greater proportion of biologic-naïve vs biologic-failure pts had a good/moderate EULAR response (83.8 vs 73.3%) and DAS28 (CRP) <2.6 (44.5 vs 35.0%); unadjusted.




**Conclusions:** These data confirm the high levels of IV abatacept retention in the real world, particularly when used in earlier lines of treatment. Poor prognostic factors in RA, including RF/ACPA double positivity combined with erosions at baseline, positively impact retention, independently of treatment line.

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**Disclosure of Interest:** R. Alten Grant/research support from: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, H. Nüßlein Consultant for: Bristol-Myers Squibb, AbbVie, Celgene, Chugai, UCB, Pfizer, MSD, Novartis, Roche, Speakers bureau: Bristol-Myers Squibb, AbbVie, Celgene, Chugai, UCB, Pfizer, MSD, Novartis, Roche, M. Galeazzi: None declared, H. M. Lorenz Consultant for: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, Sobi, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, Speakers bureau: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, Sobi, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, X. Mariette Grant/research support from: Biogen, GSK, Pfizer, Speakers bureau: Bristol-Myers Squibb, GSK, Pfizer, sanofi, UCB, A. Cantagrel Grant/research support from: UCB, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Chugai, Lilly, MSD, Novartis, Pfizer, Roche, M. Chartier Consultant for: Bristol-Myers Squibb, Y. Elbez Employee of: Bristol-Myers Squibb, C. Rauch Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Le Bars Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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## THU0067 IS TREAT-TO-TARGET REALLY WORKING? A LONGITUDINAL ANALYSIS IN BIODAM

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**Background:** A Treat-to-Target approach (T2T), treating patients with RA towards a target, either remission or low disease activity (T2T-REM or T2T-LDA) is nowadays recommended. However it has never been assessed whether such a strategy in daily clinical practice really leads to more patients meeting that target.

**Methods:** BIODAM is a 2-year prospective cohort including patients in daily practice with RA from 10 countries, who were started or changed on DMARD and/or anti-TNF treatment and were followed-up every 3 months. Participating physicians were required to practice T2T per protocol. Per visit was decided whether a patient was treated according to T2T or not. T2T-REM was considered met: i) if a patient had already a disease activity score below the target (DAS28-CRP<2.6); or ii) if treatment was intensified (by increasing dosage or adding drugs) upon a DAS28≥2.6. T2T-LDA was computed using the benchmark for low disease activity (LDA) (DAS28<3.2) (T2T-LDA). The main outcome was the presence or absence of ACR/EULAR-boolean remission 3 months after T2T-REM or T2T-LDA. Another outcome analysed was sustained remission (present >6 months). The relationship between T2T and ACR/EULAR Boolean remission 3 months later (or sustained remission) was investigated using generalized estimating equations with auto-regression.

**Results:** In total 3084 visits of 539 patients (mean (SD) age: 56 (13) years, 76% female, disease duration 6 (8) years). In 68% of the visits, T2T-REM was applied (in 79% of the visits T2T-LDA was applied). ACR/EULAR-boolean remission was reached in 15% of the visits. Appropriate application of T2T-REM led to a 50% higher likelihood of ACR/EULAR-boolean remission 3 months later than not applying T2T-REM. Both T2T-REM and T2T-LDA strategies led to lower disease activity (with an exception of DAS28 remission or DAS28-LDA). Only 9% of the treatment intensifications followed upon a DAS28 between 2.6 and 3.2, and 79% of the intensifications were applied upon a DAS>3.2. Following T2T strategies led to higher achievement of sustained remission (table).

Table - Effect of treat-to-target approach on disease activity outcomes 3 months later

| | REMISSION ACHIEVEMENT | | | | | SUSTAINED REMISSION |
|---|---|---|---|---|---|---|
| | ACR/EULAR boolean remission (OR (95% CI)) | DAS28 remission (OR (95% CI)) | CDAI remission (OR (95% CI)) | SDAI remission (OR (95% CI)) | DAS28-LDA (OR (95% CI)) | ACR/EULAR boolean sustained remission (OR (95% CI)) |
| TT2-REM | **1.50 (1.20; 1.87)** | 0.97 (0.83; 1.13) | **1.48 (1.18; 1.84)** | **1.63 (1.32; 2.02)** | 1.08 (0.93; 1.27) | **1.64 (1.27; 2.10)** |
| TT2-LDA | **2.01 (1.50; 2.71)** | **1.35 (1.12; 1.62)** | **2.31 (1.70; 3.14)** | **2.63 (1.95; 3.53)** | **1.28 (1.07; 1.54)** | **1.66 (1.23; 2.24)** |

**Conclusions:** A treat-to-target approach, even with a modest benchmark (DAS28 = 3.2), works and leads to a higher achievement of (sustained) ACR/EULAR-remission. Our study illustrates the importance of acting upon the data that is routinely collected in a clinical encounter. Rheumatologists should be encouraged to follow a treat-to-target approach in order to improve the outcome of their patients.

**Disclosure of Interest:** None declared

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## THU0068 ABSOLUTE MONOCYTE COUNTS ARE ASSOCIATED WITH ADVERSE EULAR RESPONSE AFTER 6 MONTHS OF TREATMENT WITH A BIOLOGIC AGENT FOR RHEUMATOID ARTHRITIS

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**Background:** Absolute monocyte counts after 3 months of treatment have been found to be predictive of clinical response to adalimumab at 6 months in rheumatoid arthritis (RA) patients[1]. It has also been shown that resistance to spontaneous apoptosis of monocytes *in vitro* predicts inadequate response to etanercept[2]. We hypothesise that absolute monocyte counts obtained from routine pre-treatment blood testing has predictive utility for treatment response to biologic agents.

**Objectives:** To assess whether monocytes and other white blood cell subtypes are associated with treatment response at 6 months in RA patients.

**Methods:** Full blood count (FBC) data was collected from patients attending 2 centres participating in the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS), Manchester Royal Infirmary and Royal Lancaster Infirmary, from 2009–2015. BRAGGSS is a UK-based multi-centre inception cohort of secondary-care RA patients. Spearman correlation was carried out to explore relationships between pre-biologic differential white cell count (WCC) and absolute DAS28 (and its components) at treatment start (baseline) and 6 months. Logistic regression was used to explore associations between differential WCC and EULAR response at 6 months. Stata v13.1 was used for all statistical analyses.

**Results:** 130 patients had WCC data available for analysis. They all satisfied American College of Rheumatology 1987 classification criteria for RA. 104 patients (80%) were female, with a mean age of 56.21 (SD 13.07). Mean baseline DAS28 score was 5.96 (SD 0.92) and mean monocyte count at baseline was $0.62*10^9$/L (SD 0.22). Patients were on a variety of biologics: etanercept (n=56), adalimumab (n=24), rituximab (n=13), abatacept (n=10), golimumab (n=5), tocilizumab (n=12) and certolizumab (n=10).

Pre-treatment monocyte count was not associated with DAS28 at baseline, but correlated with DAS28 at 6 months (rho=0.19, p=0.028). When a cut-off of $0.62*10^9$/L was used, high monocyte count was associated with DAS28>3.2 at 6 months (OR1.72 [95% CI 1.12–2.64], p=0.013), and with poor EULAR response (OR 2.82 [95% CI 1.12–7.13], p=0.028).

Neutrophil count was associated with DAS28 at both baseline (rho=0.22, p=0.013) and 6 months (rho=0.21, p=0.019). Neutrophil count was significantly associated with reduced odds of achieving a good EULAR response at 6 months (OR 0.82 [95% CI 0.69, 0.96], p=0.017). These neutrophil counts likely reflect ongoing inflammation, contributing to poor response to biologic therapy[3].

**Conclusions:** Monocyte counts were associated with increased DAS28 at 6 months, but not baseline, and with poor EULAR response at 6 months. This could provide a useful and widely available predictive biomarker, as FBC is routinely carried out in all patients commencing disease-modifying therapy in the UK. In future, monocyte count at baseline may be used to predict treatment response to biologics in RA patients at 6 months. Further studies with increased sample size are required to confirm these findings.

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**Disclosure of Interest:** None declared

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## THU0069 INFLUENCE OF THE DIFFERENCE BETWEEN PATIENT AND PHYSICIAN GLOBAL ASSESSMENT ON DISEASE ACTIVITY STATUS IN HIGH AND LOWER INCOME COUNTRIES: DATA FROM THE METEOR DATABASE

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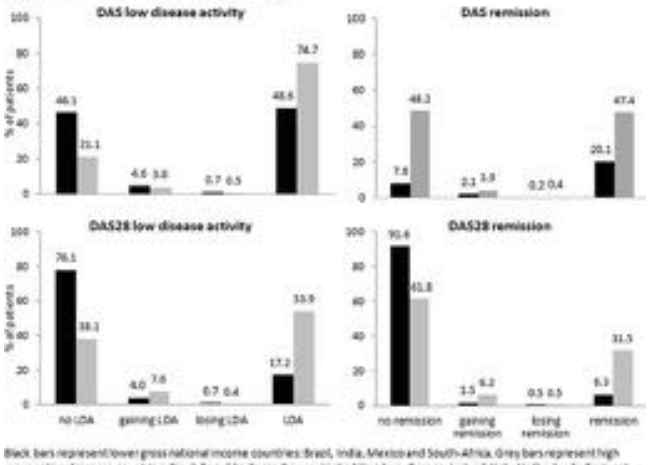
**Background:** Patients with rheumatoid arthritis (RA) score their global disease activity (ptGD) on average higher than physicians (phGD). This difference can vary between countries with high and lower gross national income (GNI)[1]. Also, patients with RA in lower GNI countries have less access to biologic and synthetic DMARDs[2]. With targeted treatment aiming at low disease activity (LDA) or remission, this could influence treatment.

**Objectives:** To compare differences between ptGD and phGD in high and lower GNI countries and to assess how these potential differences influence disease activity measures.

**Methods:** RA patients included in the METEOR (Measurement of Efficacy of Treatment in the Era of Outcome in Rheumatology) database were selected from countries ≥30 patients with >1 visit, available phGD and DAS or DAS28. Countries were divided in high and lower GNI (World Bank definition, high income GNI per capita ≥$12746). ptGD and phGD were measured on a 100mm visual analogue scale (100 worst score); A difference ≥20 mm between ptGD and phGD (GDdif=ptGD–phGD) was considered clinically relevant. Next, ptGD was replaced by phGD in the DAS and DAS28, to assess potential changes in the number of patients in LDA or remission.

**Results:** From high GNI countries, 6928 patients were included, from lower GNI countries 5136 patients. DAS was available in 10420 patients (6179 from high GNI countries), DAS28 in 11173 patients (6839 from high GNI countries). Patients from lower GNI countries had higher disease activity [mean (SD) DAS28 4.6 (1.8) vs 3.4 (1.8); DAS 2.5 (0.9) vs 1.8 (0.9)], longer disease duration at diagnosis [55 (69) vs 27 (59) weeks] and less often reached LDA [DAS28 49% vs 75%; DAS 20% vs 48%] or remission [DAS28 7% vs 32%; DAS 20% vs 48%] than patients from high GNI countries. Compared to high GNI countries, in lower GNI countries, more patients had a GDdif ≥20 mm with ptGD>phGD (44% vs 30%) and fewer patients had a GDdif <20 mm (47% vs 67%). Also, more patients had a GDdif ≥20 mm with ptGD<phGD (9% vs 3% in lower vs high GNI countries). Replacing ptGD by phGD resulted in a mean (SD) change in DAS and DAS28 of 0.09 (0.1) and 0.4 (0.6) in high GNI countries and 0.9 (0.1) and 0.4 (0.7) in lower GNI countries. For both DAS and DAS28, the percentage of patients changing disease activity status is low in all countries [mean change in DAS LDA 4.8%, remission 3.3%; DAS28 LDA 6.4%, remission 4.4%], with most patients gaining LDA or remission (Fig. 1).

Figure 1. Percentage of patients changing DAS and DAS28 disease activity status after replacement of the patient global assessment by the physician global assessment.




Black bars represent lower gross national income countries: Brazil, India, Mexico and South-Africa. Grey bars represent high gross national income countries: Czech Republic, Spain, France, United Kingdom, Greece, Ireland, Italy, Netherlands, Portugal, Qatar and United States. Outer bars describe patients not changing disease activity status. The inner two bars describe patients changing disease activity status. LDA = low disease activity.

**Conclusions:** Compared to high GNI countries, patients from lower GNI countries had higher disease activity and less often reached LDA or remission. Clinically relevant differences between ptGD and phGD existed in more than 1/2 of the patients in lower GNI countries and 1/3 of the patients in high GNI countries, thereby influencing disease activity stronger in lower GNI countries as compared to high GNI countries. These results indicate a different access to good RA care in lower and high GNI countries.

**References:**

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[2] Putrik et al ARD 2015; doi:10.1136/annrheumdis-2015-207738

**Disclosure of Interest:** None declared
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## THU0070 RANKL, OPG AND OSCAR BUT NOT DKK-1 PREDICT RADIOGRAPHIC PROGRESSION IN AN INCEPTION COHORT OF SEROPOSITIVE RHEUMATOID ARTHRITIS (RA) TREATED-TO-TARGET WITH COMBINATION CONVENTIONAL DMARD THERAPY

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**Background:** Traditional markers associated with erosive disease in RA do not reliably predict radiographic progression. There are limited data regarding the role of bone biomarkers in erosive disease in early RA treated with conventional DMARDs and no longitudinal data on osteoclast-associated receptor (OSCAR) with therapy.
**Objectives:** To determine whether bone biomarkers associated with osteoclast activation (RANKL, OSCAR and Dkk-1) or inhibition (OPG) are associated with erosion progression over 3 years, independent of disease activity in an inception cohort of RA receiving treat-to-target combination DMARD therapy without oral corticosteroids.
**Methods:** Dual RF and anti-CCP positive patients with early RA (<1 year; fulfilling ACR 1987 and/or 2010 classification criteria; n=50) received triple therapy (methotrexate, sulfasalazine and hydroxychloroquine) escalated to achieve DAS28 remission. RANKL, OPG and Dkk-1 were analysed by Luminex kits, OSCAR by ELISA at baseline, 6 and 12 months. For radiographic outcomes annual hand and feet radiographs were scored by the van der Heijde modified Sharp (SvH) method. Changes in bone biomarkers and associations with predictor variables were assessed using a linear multi-response random effects model. Relationships between bone biomarkers in the first year and DAS28 remission and radiographic erosion score outcomes over 3 years were analysed using logistic and negative binomial mixed regression respectively.
**Results:** Mean (SD) baseline DAS28ESR was 5.55 (1.14), 76% were females, 70% were current/past smokers and mean duration of symptoms prior to diagnosis was 18 (12) weeks. Median (IQR) total SvH score was 2 (7); 24% had erosive disease. With treatment, there was a reduction in DAS28 at 1 year to 3.14 (1.31), significant reduction in RANKL, slight increase in OPG and no significant change in Dkk-1 and OSCAR. DAS28 remission, assessed over 3 years, was less likely to occur both in the presence of detectable RANKL (p=0.01) and/or in the presence of higher average Dkk-1 levels (p=0.007). Baseline erosion scores were higher in the presence of RANKL (p=0.046) and lower OSCAR (p=0.021). There was a trend towards higher erosion scores in the presence of lower OPG levels (p=0.16). Unexpectedly, those with higher mean OPG over the first 12 months had a higher annual increase in erosion scores over 3 years (p=0.018), which may reflect the dynamic processes of bone inflammation.
**Conclusions:** Conventional DMARD treatment results in reduction of RANKL, but not OPG, OSCAR or Dkk-1 levels. Higher RANKL levels, lower OSCAR levels and higher mean OPG were associated with erosions. Failure of bone biomarkers to respond to treatment may warrant escalation of therapy to prevent erosion progression. Bone biomarkers may also provide an explanation for the apparent dissociation between disease activity and bone damage in RA.
**Disclosure of Interest:** M. D. Wechalekar: None declared, S. Lester: None declared, S. Nagpal Employee of: Johnson & Johnson, S. Cole Employee of: Johnson & Johnson, A. Das Employee of: Johnson & Johnson, P. Hissaria: None declared, T. Crotti: None declared, L. Spargo: None declared, J. Walker: None declared, M. Smith: None declared, S. Proudman: None declared
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## THU0071 TIME TO REMISSION IN EARLY RHEUMATOID ARTHRITIS IS SHORTER IN EARLY ARTHRITIS CLINIC COMPARED TO MIXED OUTPATIENT CLINIC

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**Background:** Early diagnosis of rheumatoid arthritis (RA) is of paramount importance as early effective treatment reduces long-term morbidity and mortality (1,2). Evidence suggests that simple clinical criteria, facilitates earlier referral of patients with suspected RA from general practitioners (GP's) to the rheumatologist (3).
**Objectives:** Our hypothesis: Supplementary education of GP's to identify RA and refer to an Early Arthritis Clinic (EAC) shortens time to remission compared to referral to a mixed outpatient clinic.
**Methods:** In July 2011, an EAC was established in Holbæk Hospital. GP's in the hospitals catchment area were informed of the clinic, educated in the referral criteria and encouraged to refer patients suffering unspecific arthritis symptoms at early disease stages. A standardised referral form was contrived to simplify the referral process. Patients referred and diagnosed with RA were followed until remission. Patients in the trial were enrolled from July 2011 to April 2015. Controls were patients referred prior to the establishment of the EAC. The main outcome parameter was time from referral to low DAS28 <3.2 or remission at DAS28 <2.6. All patients were registered in the mandatory nationwide database DANBIO (4). Patients were evaluated and monitored by rheumatologists or rheumatology specialist nurses in the DANBIO at regular intervals and DAS28 was calculated at each visit. A Kaplan-Meier plot was calculated and compared using the log-rank test. The two groups were compared using the X2-test.
**Results:** As shown in the table, the two groups, EAC vs. controls, were similar in gender distribution. A relatively large proportion in each group already appeared to be in remission at the entry point, up to 16%, probably reflecting the proportion with only slight or minor disease activity. There was a significant proportion in the EAC that achieved both DAS28<3.2 and DAS28<2.6 compared to the control group. Likewise, a conspicuous difference was observed among the patients never achieving remission. The two Kaplan-Meier plots show the timely difference was highly significant indicating that time of remission was achieved very early.

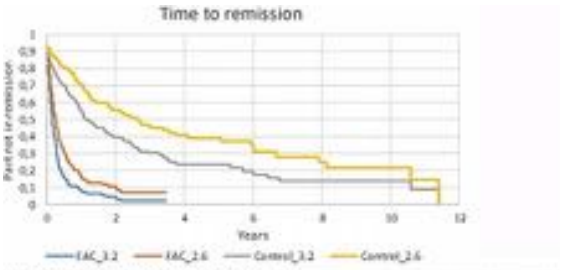



Fig. 1: Kaplan-Meier plot of EAC vs. Controls showing the remission probability DAS28<3.2 and DAS28<2.6 respectively.

| Log Rank test vs | | p |
|---|---|---|
| EAC_3.2 | EAC_2.6 | 0.41 |
| Control_3.2 | Control_2.6 | 0.003 |
| EAC_3.2 | Control_3.2 | <0.0001 |
| EAC_2.6 | Control_2.6 | <0.0001 |

| | EAC | Control | p (X2-test) |
|---|---|---|---|
| n, total | 190 | 160 | |
| Males | 59 | 48 | n.s. |
| Females | 131 | 112 | n.s. |
| DAS28<3,2 | | | |
| Already in remission, n | 29 | 16 | n.s. |
| Achieved remission, n | 153 | 92 | p<0.01 |
| Never achieved remission, n | 8 | 52 | p<0.0001 |
| Median time to remission, days | 62 | 238 | |
| DAS28<2,6 | | | |
| Already in remission | 22 | 11 | n.s. |
| Achieved remission | 116 | 73 | p=0.05 |
| Never achieved remission | 24 | 76 | p<0.0001 |
| Median time to remission, days | 70 | 341 | |

**Conclusions:** Establishing an early arthritis clinic and supplementary RA education of GP's shortens time to early disease activity or remission in patients with RA.
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**Disclosure of Interest:** None declared
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## THU0072 A NOVEL DOSE REDUCTION THERAPY USING BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS TO TARGET MATRIX METALLOPROTEINASE 3 NORMALIZATION TOGETHER WITH A SIMPLIFIED DISEASE ACTIVITY INDEX ≤3.3 YIELDS EFFECTS NON-INFERIOR TO STANDARD CARE IN RHEUMATOID ARTHRITIS WITH REGARDS MAINTAINING REMISSION

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**Background:** While there have been previous studies into reduction of biological disease-modifying anti-rheumatic drugs (bDMARDs) in rheumatoid arthritis (RA)

patients in clinical remission or with low disease activity, there have been no strategy studies which demonstrated non-inferiority to standard care with regard to maintaining clinical remission while reducing bDMARDs.
**Objectives:** To evaluate whether a therapy strategy using reduced doses of bDMARDs [bDMARDs: etanercept (ETN); tocilizumab (TCZ); abatacept (ABT)] achieving both a simplified disease activity index (SDAI) score of less than 3.3 and normalization of matrix metalloproteinase (MMP) 3 levels is non-inferior in maintaining disease control in patients with RA compared with standard care (rT-4 study).
**Methods:** 223 RA patients demonstrating both SDAI remission and MMP-3 normalization using bDMARDs for ≥3months were randomly allocated to one of four strategy groups: Standard care (SC group; n=56); SDAI-driven therapy (S group; n=54); MMP-3-driven therapy (M group; n=57); or both SDAI and MMP-3-driven therapy group (Twin; T group; n=56). Method of dose reduction (every 3 months): ETN - period between injections increased by one week; TCZ - dose reduced by 80mg or period between injections increased by one week; ABT - dose reduction by 250 mg or period between injections increased by one week; up to a minimum dose of: ETN - 25 mg every 5 weeks; TCZ - 80 mg every 5 weeks or 162 mg every 5 weeks; ABT - 250 mg every 5 weeks or 125 mg every 5 weeks. The dose was reversed to the previous level in the event that the target scores were exceeded, and the lower dose was eventually reattempted after the target was re-achieved. The primary outcome was the difference in the proportion of patients who maintained remission at 12 months among the four groups, compared against a non-inferiority margin of 10%. Secondary outcomes included functional and radiographic progression.
**Results:** Patient characteristic demographics are summarized in Table 1. One hundred ninety-three patients completed the observation period of 12 months and three patients dropped out. Consequently, one hundred ninety-six patients were analyzed (non responder imputation). There was no difference for the rate of reduction dose of bDMARDs at 12 months in S group, M group, and T group: 37.8, 42.3 and 42.9%, respectively (p=0.4176). The M and T groups were non-inferior to the SC group (proportion of patients who maintained remission during the 12 months: 32.7% and 40.0% v 38.2%; a variation of -1.8% and 5.5%, respectively; with 95% CIs of 3.8% to 5.3% and -1.9% to 5.3%, respectively). At month 12, functional status and radiographic progression did not differ between the SC and T groups.

Table 1 Baseline patient characteristics

| | Standard Care (n=56) | SDAI-driven therapy (n=54) | MMP-3-driven therapy (n=57) | Twin-driven therapy (n=56) | p Values |
|---|---|---|---|---|---|
| Age (years)* | 60.8 (15.9) | 65.4 (12.5) | 64.5 (11.6) | 62.8 (13.1) | 0.5108 |
| Female sex, n (%) | 35 (62.5) | 43 (79.6) | 40 (70.2) | 44 (78.6) | 0.1453 |
| Disease duration, years† | 4.9 (2.1-10.5) | 5.5 (1.4-10.1) | 4.2 (1.3-12.1) | 3.3 (1.3-8.3) | 0.4571 |
| IgM RF positivity, % (N) | 83.9 (47) | 88.9 (48) | 80.7 (46) | 78.6 (44) | 0.5033 |
| ACPA positivity, % (N) | 69.6 (39) | 77.8 (42) | 61.4 (35) | 78.6 (44) | 0.1071 |
| SDAI † | 2.2 (0.9-2.9) | 2.6 (1.1-3.3) | 2.6 (0.7-3.2) | 2.4 (1.0-3.3) | 0.3011 |
| MMP-3* (Female) | 42.6 (13.8) | 46.5 (10.9) | 43.0 (15.8) | 42.9 (11.3) | 0.4609 |
| (Male) | 93.0 (20.8) | 104.8 (20.8) | 85.7 (30.7) | 90.2 (16.4) | 0.2919 |
| HAQ-DI† | 0 (0-0.05) | 0 (0-0.05) | 0 (0-0.1) | 0 (0-0.15) | 0.6194 |
| Total mTSS* | 48.4 (63.7) | 42.7 (47.1) | 51.7 (76.1) | 39.0 (44.3) | 0.8896 |
| Methotrexate Use, % (N) | 80.4 (45) | 74.1 (40) | 77.2 (44) | 66.1 (37) | 0.3445 |
| Methotrexate Dose (mg/week) * | 8.0 (0.4) | 9.0 (0.4) | 8.2 (0.4) | 8.4 (0.5) | 0.1094 |
| Other DMARDs‡ Use, % (N) | 37.5 (21) | 46.4 (24) | 49.1 (28) | 44.6 (25) | 0.6637 |
| Etanercept Use, % (N) | 50.0 (28) | 55.6 (30) | 61.4 (35) | 58.9 (33) | 0.6427 |
| Tocilizumab Use, % (N) | 16.1 (9) | 42.6 (23) | 33.3 (19) | 30.4 (17) | 0.0239 |
| Abatacept Use, % (N) | 0 (0) | 0.2 (1) | 3.5 (2) | 3.6 (5) | 0.0666 |

*Mean (standard deviation)
†Median (interquartile range)
‡sulfasalazine, bucillamine, iguratimod, mizoribine
SDAI, simplified disease activity index ; MMP, matrix metalloproteinase (MMP); Twin, both a SDAI less than 3.3 and normalization of MMP-3 levels; Ig M, immunoglobulin; RF, rheumatoid factor;ACPA, anti-citrullinated peptides antibody;HAQ DI, Health Assessment Questionnaire-disability index ;mTSS, modified total Sharp score;DMARDs, disease-modifying anti-rheumatic drugs.

**Conclusions:** Results of the rT-4 study reveal that a twin target strategy can achieve effects non-inferior to standard care with regard to maintaining clinical remission.
**Disclosure of Interest:** None declared
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## Rheumatoid arthritis - comorbidity and clinical aspects

### THU0073 DAS28-CRP AND DAS28-ESR CUTOFFS FOR HIGH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS ARE NOT INTERCHANGEABLE

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**Background:** Rheumatoid arthritis (RA) clinical trials have shown that mean DAS28 calculated using C-reactive protein (CRP) is lower than DAS28 calculated using erythrocyte sedimentation rate (ESR). We demonstrated that DAS28-CRP cutoffs equivalent to DAS28-ESR for remission and low disease activity (LDA) were 2.4 and 2.9, respectively, rather than 2.6 and 3.2.[1] Use of DAS28-ESR cutoffs to assess high disease activity (HDA) using DAS28-CRP likely underestimates the number of patients with HDA, although these values are often used interchangeably in clinical trials, and by payers and health organizations, probably excluding patients who should be eligible for advanced therapies.
**Objectives:** To analyze baseline (BL) data from 2 etanercept (ETN) clinical trials to determine the DAS28-CRP cutoff corresponding to the validated DAS28-ESR cutoff for HDA in RA.
**Methods:** Data were pooled from COMET and PRIZE, clinical studies in early moderate to severe RA. Descriptive statistics for DAS28-CRP and DAS28-ESR were determined for each treatment: weekly ETN 50 mg + methotrexate (MTX) or MTX only. DAS28-CRP and DAS28-ESR were compared according to the DAS28-ESR cutoff point for HDA (>5.1) using sensitivity, specificity, kappa coefficients, and proportion of discordance. Based on the DAS28-ESR cutoff, the corresponding DAS28-CRP cutoff was determined for each study and treatment group using cumulative distribution plots, receiver operator curves, and maximum concordance. These DAS28-CRP cutoffs were averaged for each study and treatment, then averaged overall. This produced the DAS28-CRP HDA cutoff corresponding best to the DAS28-ESR HDA cutoff.
**Results:** At BL, fewer patients met the value of >5.1 by DAS28-CRP than by DAS28-ESR (table). DAS28-CRP >5.1 and DAS28-ESR >5.1 had modest agreement (kappa coefficients of 0.45 and 0.53), with high sensitivity but low specificity. In the ETN+MTX group (N=571), mean (95% CI) DAS28-CRP and DAS28-ESR were 5.7 (5.6, 5.8) and 6.2 (6.2, 6.3), respectively, with a difference of 0.6 (0.5, 0.6). In the MTX group (N=262), mean (95% CI) DAS28-CRP and DAS28-ESR were 6.0 (5.9, 6.1) and 6.5 (6.4, 6.6), respectively, with a difference of 0.5 (0.5, 0.6). We determined that DAS28-CRP of 4.6 was similar to DAS28-ESR of 5.1.

Table 1. Statistical measures comparing DAS28-CRP >5.1 and DAS28-ESR >5.1 at baseline, pooled data

| | DAS28-CRP >5.1 | DAS28-ESR >5.1 | Proportion of discordance between parameters | Sensitivity | Specificity | Kappa coefficient | *P*-value |
|---|---|---|---|---|---|---|---|
| ETN+MTX | 394/571 (69.0) | 486/571 (85.1) | 98/571 (17.2) | 99.2% | 46.3% | 0.532 | <0.0001 |
| MTX | 204/262 (77.9) | 243/263 (92.4) | 38/262 (14.5) | 100.0% | 34.5% | 0.450 | <0.0001 |

Sensitivity and specificity based on standard DAS28-CRP >5.1. *P*-value from kappa test of agreement between DAS28-CRP >5.1 and DAS28-ESR >5.1. Values are n/N (%) unless otherwise noted.

**Conclusions:** More patients met the HDA cutoff according to DAS28-ESR than DAS28-CRP, and mean values for DAS28-CRP were lower, suggesting that use of the DAS28-ESR cutoff for DAS28-CRP for HDA underestimates disease activity. Use of the new HDA cutoff of >4.6 for DAS28-CRP, and the new DAS28-CRP cutoffs of ≤2.9 for LDA and <2.4 for remission will enable more accurate measurement of disease activity when DAS28-CRP is used.[1]
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**Disclosure of Interest:** R. Fleischmann Consultant for: Pfizer, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Celgene, Daiichi, Eli-Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Employee of: Director of Imaging Rheumatology bv, P. Gardiner: None declared, A. Szumski Employee of: inVentiv Health, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer, E. Bananis Shareholder of: Pfizer, Employee of: Pfizer
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### THU0074 IMPACT OF THE DISCORDANCE BETWEEN C-REACTIVE PROTEIN AND ERYTHROCYTE SEDIMENTATION RATE ON CLINICAL RESPONSE TO COMBINATION ETANERCEPT-METHOTREXATE THERAPY IN RHEUMATOID ARTHRITIS

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**Background:** Clinical response remains difficult to predict in patients with rheumatoid arthritis (RA). Acute phase reactants (APRs) C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are regularly measured in standard care, and abnormal CRP and ESR are frequently used as inclusion criteria for RA clinical trials. Alone or in combination with demographic, clinical, and imaging parameters, these APRs are often considered important in treatment decisions in RA. However, results of these tests for inflammation are discordant in a substantial proportion of patients,[1–3] and the clinical implications of discordant CRP:ESR findings have not been well studied.
**Objectives:** To explore the relationship between clinical response and baseline CRP:ESR discordance in RA.
**Methods:** Randomized patients with moderate-severe RA who participated in 3 etanercept (ETN) clinical trials[4–6] and had both APR measurements were included in these post hoc analyses. To allow comparison, baseline CRP and ESR were standardized to the same scale by subtracting the respective means and dividing by the respective standard deviations for each patient. Standardized CRP was subtracted from standardized ESR and differences categorized by quartile (cutoffs: Q1, –0.5; median, 0; Q3, 0.5). DAS28 (ESR) low disease activity (LDA) and remission after 16 or 52 weeks of treatment with ETN + methotrexate (MTX) were analyzed by quartile of CRP:ESR discordance.

**Results:** Across clinical trials, 693 patients received ETN+MTX and had CRP and ESR measured. After 16 or 52 weeks of ETN+MTX treatment, significantly higher proportions of patients achieved DAS28 LDA and remission in the group with higher CRP than ESR at baseline (lower ESR/higher CRP); lower proportions of responders were seen in the group with similar CRP and ESR (ESR≈CRP), and the lowest proportion in the group with lower CRP than ESR (higher ESR/lower CRP) (Table).

Table. Proportions of patients achieving DAS28 LDA and remission after 16 or 52 weeks of ETN+MTX treatment by quartile of standardized CRP:ESR* discordance at baseline in RA clinical studies.

| Study (Weeks) | Clinical Outcome | Patients, % (n/N) Discordance Quartile: ESR−CRP≤−0.5 (↓ ESR / ↑ CRP) | −0.5<ESR−CRP≤0 (ESR=CRP) | 0<ESR−CRP≤0.5 (ESR=CRP) | ESR−CRP>0.5 (↑ ESR / ↓ CRP) | P Value† |
|---|---|---|---|---|---|---|
| Klareskog et al, 2004[4] (52) | LDA | 63 (42/67) | 53 (31/58) | 48 (23/50) | 46 (26/56) | 0.048 |
| | Remission | 57 (38/67) | 31 (18/58) | 32 (16/50) | 29 (16/56) | 0.002 |
| Emery et al, 2008[5] (52) | LDA | 71 (46/65) | 70 (46/66) | 66 (48/73) | 49 (30/61) | 0.013 |
| | Remission | 55 (36/65) | 58 (38/66) | 53 (39/73) | 31 (19/61) | 0.008 |
| Kim et al, 2012[6] (16) | LDA | 48 (23/48) | 49 (26/53) | 42 (16/38) | 21 (12/58) | 0.002 |
| | Remission | 21 (10/48) | 19 (10/53) | 24 (9/38) | 5 (2/58) | 0.020 |

*Standardized CRP and ESR for each patient: (CRP−mean CRP)/SD CRP; ESR−mean ESR)/SD ESR. means and SDs used in standardized formula were obtained separately for each study.
†Cochran-Mantel-Haenszel test, non-zero correlation.

**Conclusions:** In clinical trials, elevated CRP relative to ESR at baseline was a significantly better predictor of the ability of active treatment to show clinical response after 4 months or 1 year of combination etanercept-methotrexate therapy than similar CRP and ESR or lower CRP vs higher ESR. These findings underscore the importance of incorporating this readily available biomarker (CRP) into clinical trial settings; whether this is true in clinical practice cannot be determined from this data set but should be investigated prospectively.

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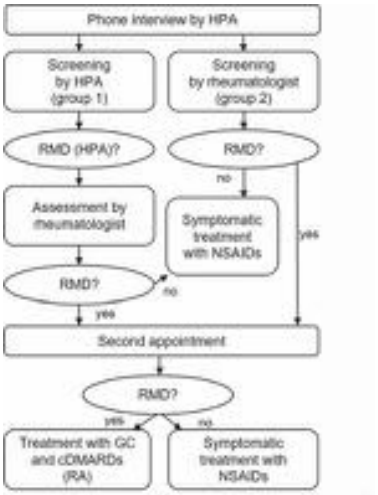
**Disclosure of Interest:** R. Fleischmann Consultant for: Pfizer, A. Szumski Employee of: inVentiv Health, H. Jones Shareholder of: Pfizer, Employee of: Pfizer

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## THU0075 EFFICIENT SCREENING SYSTEM FOR EARLY ARTHRITIS – A PROJECT OF THE T2T INITIATIVE IN GERMANY

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**Background:** Early stages of rheumatic diseases (0–12 weeks) including rheumatoid arthritis (RA) are still difficult to diagnose. For this reason, incorrect referrals to a rheumatologist result in a high use of resources in outpatient clinics.
**Objectives:** Implementation of a structured screening system for selecting and treating patients (pts) with RA or other rheumatic and musculoskeletal diseases (RMD).
**Methods:** 98 pts visited a screening appointment for early arthritis (EA) between February 2015 and September 2015 in special EA departments. Inclusion criterion was arthritis ≥ one joint for less than one year recorded by phone. Qualified health professional assistants (HPA) conducted the phone call. Upon screening, all pts filled in a tablet based questionnaire to be developed for future online use about their symptoms. Subsequently, 53 pts (group 1) were seen first by an HPA who analysed the questionnaire and performed the joint count. Based on these findings, the HPA made a suspected diagnosis. Afterwards, also a rheumatologist saw these pts and made a suspected diagnosis. In comparison, the rheumatologist directly examined 45 pts without an HPA (group 2). In both groups, typical clinical findings led to a new appointment, or in acute cases, treatment was started immediately. If an RMD was suspected or laboratory parameters were abnormal, pts received a second appointment as well. The documentation of the real-life data was carried out by the Medpath© system based on medical and flexible adaptable paths.
**Results:** Mean duration between phone call and screening was 19.6±12.8 days. Pts had an age of 18–80 years (mean 51.1±15.5 years), and 73 pts (74.5%) were female. Although all pts had reported symptoms of less than one year over the phone, only 70 pts (71.4%) fulfilled this criterion when asked in the questionnaire. In group 1, according to the HPA 22 of 53 (41.5%) pts had an RMD upon screening. The suspected diagnoses of HPA and rheumatologist corresponded in 43 of 53 (81.1%) pts in the screening. In group 2, the rheumatologist suspected 14 of 45 (31.1%) pts having an RMD in the first visit.
59 (60.2%) pts had no RMD. 23 (23.5%) pts had RA that was seropositive in 14 (14.3%) pts. All RA pts were recommended a therapy with conventional disease modifying antirheumatic drugs (cDMARDs) and glucocorticoids (GC), which 21 (21.4%) pts started 17.2±27.6 days after screening. 3 (3%) pts initially had a preclinical seropositive RA, which changed into definite RA in need for treatment with cDMARDs after 191 days in one patient. 3 (3%) pts received inpatient treatment and systemic lupus erythematosus was diagnosed in one case.




cDMARDs, conventional disease modifying antirheumatic drugs; GC, glucocorticoids; HPA, Health professional assistent; NSAIDs, Nonsteroidal anti-inflammatory drugs; RA, rheumatoid arthritis; RMD, rheumatic and musculoskeletal disease.

**Conclusions:** The structured screening system efficiently selects pts with RMDs and leads to treating RMD at an early stage in times of limited resources.
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**Disclosure of Interest:** None declared

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## THU0076 ASSOCIATION BETWEEN BODY MASS INDEX AND QUALITY OF LIFE AT ONE AND THREE YEARS POST DIAGNOSIS OF RHEUMATOID ARTHRITIS: RESULTS FROM AN INCEPTION COHORT

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**Background:** Due to large increases in the prevalence of obesity, there is a growing need to understand the relationship between obesity and rheumatoid arthritis (RA) outcomes. RA patients with high body mass index (BMI) have a greater of risk of disease persistence and higher disease activity scores compared to RA patients with lower BMI (1,2). This leads to higher levels of pain and disability, and can reduce quality of life (QoL) for RA patients in higher BMI groups. So far, most of the research looking at obesity in RA has focused on the QoL in terms of physical outcomes, but there has been relatively little investigation on the psychological impact on QoL amongst these patients.
**Objectives:** To assess whether BMI at baseline predicts physical and mental health-related quality of life (HRQoL) for patients over three years in newly-diagnosed RA patients
**Methods:** Data were from the Early Rheumatoid Arthritis Network (ERAN), a longitudinal observational study involving 21 rheumatology centres in the UK. Between 2002 and 2011 1,236 participants (397 male) were recruited. Sociodemographic and standard clinical variables were recorded at baseline, 6 months, 12 months and and then annually until loss to follow-up or the end of study follow up in 2013. QoL was measured using the Short Form 36 Health Survey Questionnaire (SF-36), a wide-ranging measure of health related QoL. Responses are grouped to form two higher-order constructs: Physical Component (PCS) and Mental Component (MCS). Linear regression models was estimated to determine if BMI as baseline was a predictor of the PCS and MCS scores at one year and 3 years, controlling for potential confounders
**Results:** he analysis was restricted to 873 (71%) with data for both BMI and SF-36. Patients with complete data were younger (56.3 vs 58.7 years, p=.01) but did not differ in terms of gender (33% vs 30% male, p=.31), health assessment questionnaire disability (1.09 vs 1.07, p=0.68) or disease activity score (4.5 vs 4.5, p=0.88). Mean BMI at baseline was 27.6 kg/m$^2$, increasing to 28.3 kg/m$^2$ at 3 years – equivalent to a gain of 2.1 kg for an average height male (175cm), or 1.8 kg for an average height female (160cm). At baseline 66.6% of the sample

fell into a WHO BMI category of overweight or obese. BMI at baseline associated with physical but nor mental QoL ($b_{PCS}$=-0.2, p=0.003; $b_{MCS}$=-0.04, p=0.58). After controlling for age, gender, baseline disease activity and baseline PCS and MCS score, BMI at baseline was a significant predictor of both physical and mental QoL at 3 years ($b_{PCS}$=-0.5, p=0.001; $b_{MCS}$=-0.3, p=0.004). Change in BMI between baseline and one year was not related to PCS or MCS at three years ($b_{PCS}$=0.5, p=0.11; $b_{MCS}$=0.2, p=0.58).

**Conclusions:** Obesity is prevalent at the onset of disease in rheumatoid arthritis and, on average, patients gain weight over time. BMI at baseline is a predictor of poor long terms physical and mental QoL. Tailoring self-management interventions to account for obesity may help to improve long term outcomes.

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**Disclosure of Interest:** None declared

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## THU0077 INSUFFICIENT CARDIOVASCULAR TREATMENT IS A MAJOR RISK FACTOR FOR STROKE IN RA PATIENTS: A MATCHED CASE CONTROL STUDY FROM THE GERMAN BIOLOGICS REGISTER RABBIT

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**Background:** Patients with rheumatoid arthritis (RA) are at increased risk for stroke. The particular impact of RA and its treatment in addition to known risk factors is not clear.

**Objectives:** To examine the impact of RA on the risk of stroke taking risk factors of cardiovascular disease (CVD) and age into account.

**Methods:** We performed a nested case-control study within the prospectively observed cohort of the German biologics register RABBIT. Since May 2001, RA patients are enrolled at start of a conventional synthetic (cs)DMARD or biologic (b)DMARD after ≥1 csDMARD failure. Rheumatologists report clinical characteristics, RA treatment, comorbidities and the respective therapy in a standardized manner. We considered all non-haemorrhagic strokes reported until April 2015 as cases. Two control patients, also observed in RABBIT, were matched to each case by an extensive algorithm [1] using sex, age, enrolment period, smoking status, body mass index and comorbidities at baseline (hypertension, heart failure, coronary disease or prior cerebrovascular event, diabetes). 16 cases could not be matched to a control. A multivariable Cox proportional hazard model with a random component (shared frailty model) was applied to address the matched design. Missing data were considered by multiple imputations.

**Results:** The matching algorithm generated utmost agreement of cases and controls in baseline characteristics (Table 1). Compared to the remaining cohort, cases and controls were older and had more CVD. Similarity between cases and controls was also found regarding the treatment of comorbid osteoporosis and diabetes whereas the treatment of CVD was significantly different. This significant difference was confirmed in multivariable analysis. Compared to patients without prevalent CV comorbidities, patients with treated CVD had a moderately elevated risk for stroke (hazard ratio (HR): 1.44 [95% CI: 0.72, 2.89]), whereas patients with untreated CVD had a highly increased risk (HR: 4.27 [2.04, 8.94]. Hospitalization for a serious adverse event within six months before stroke (correspondent index date in controls) and time-varying log-transformed C-reactive protein were further predictors for stroke (HR: 2.42 [1.46, 4.02] and 1.25 [1.06, 1.47]). Treatment with TNF inhibitors or other bDMARDs was not associated with the development of stroke (HR: 0.86 [0.56, 1.31] and 1.04 [0.61, 1.75], Reference: csDMARDs).

Table 1: Baseline characteristics of patients in the cohort, cases and their matched controls

| Parameter | Cohort | Cases | Controls | Matching |
|---|---|---|---|---|
| N | 11557 | 148 | 296 | 1:2 |
| Age, years (SD) | 55.9 (12.5) | 63.4 (10.9) | 63.4 (10.6) | X |
| Female gender | 8817 (76.3%) | 111 (75%) | 222 (75%) | X |
| Hypertension | 4285 (37.1%) | 80 (54.1%) | 160 (54.1%) | X |
| Diabetes | 1142 (9.9%) | 21 (14.2%) | 42 (14.2%) | X |
| Prior cerebrovascular disease | 148 (1.3%) | 2 (1.4%) | 4 (1.4%) | X |
| BMI ≥ 30mg/kg² | 2742 (23.7%) | 34 (23.0%) | 55 (18.6%) | X |
| Smoking, ever | 5324 (46.1%) | 78 (52.7%) | 156 (52.7%) | X |
| DAS28, mean (SD) | 5.2 (1.3) | 5.5 (1.3) | 5.6 (1.3) | |
| CRP, mean (SD) | 18.6 (26.6) | 24.8 (32) | 21.4 (29.9) | |
| Hyperlipoproteinemia | 931 (8.1%) | 22 (14.9%) | 31 (10.5%) | |
| Osteoporosis | 2078 (18%) | 46 (31.1%) | 82 (27.7%) | |
| Osteoporosis w/o treatment | 327/2078 (15.7%) | 6/46 (13.0%) | 10/82 (12.2%) | |
| Diabetes w/o treatment | 232/1142 (20.3%) | 3/21 (14.3%) | 7/42 (16.7%) | |
| CVD w/o treatment | 1037/4780 (21.7%) | 31/90 (34.4%) | 25/169 (14.8%) | |
| TNFi at baseline | 5857 (51%) | 77 (53.5%) | 153 (52%) | |
| Other bDMARDs at baseline | 1851 (16.1%) | 27 (18.8%) | 39 (13.3%) | |

Abbreviations: CVD, cardiovascular disease; w/o, without.

**Conclusions:** Within a strictly matched design providing the same baseline risk for stroke in cases and controls, we found that higher inflammation levels during follow-up and hospitalization were associated with a higher risk for the development of stroke. However, underlying CVD which is not medically treated was found to be the strongest risk factor for a future stroke in the RABBIT cohort. These results strengthen the need for a better CVD management in RA patients.

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## THU0078 MODERATE ALCOHOL CONSUMPTION IS NOT ASSOCIATED WITH SERUM LIVER ABNORMALITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS TAKING METHOTREXATE: DATA FROM THE CLINICAL PRACTICE RESEARCH DATABASE (CPRD)

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**Background:** Methotrexate (MTX) is the most commonly prescribed disease modifying anti-rheumatic drug in the treatment of rheumatoid arthritis (RA). Patients taking MTX are advised to restrict their alcohol consumption because of a theoretical hepatotoxic interaction between alcohol and MTX. However data are limited to support this advice.

**Objectives:** To quantify the association between alcohol consumption and abnormal serum liver function tests (LFTs) in patients with RA taking MTX, using routinely collected clinical data.

**Methods:** Patients with RA in the Clinical Practice Research Database (CPRD) starting MTX between 1987 and 2011 were studied. Patients were included if they had alcohol consumption details recorded in CPRD and ≥6 LFTs per year, indicating adequate monitoring. Patients were grouped by reported weekly alcohol consumption. Crude rates of abnormal LFTs (defined as alanine transaminase or aspartate aminotransferase level ≥3 times the upper limit of normal) per 1000 person-years follow up were calculated. Cox proportional hazards models described the association between alcohol consumed and development of abnormal LFTs whilst taking MTX univariately, then adjusting for age and gender. Patients were censored at time of first abnormal LFT, death or the end of follow up (31/12/2011).

**Results:** 8801 patients were included in the study, 6285 (71%) female, mean age (SD) was 58 (14) years. There were 241 abnormal LFTs in 38000 person-years follow up. There was no difference in rates of abnormal LFTs between drinkers and non-drinkers, adjusted hazard ratio (HR) (95% confidence interval (CI)) 1.12 (0.82–1.51). Crude rates of abnormal LFTs appeared to increase with increasing levels alcohol consumption (table 1); similarly when treated as a continuous variable, each increased unit of alcohol consumed was associated with a higher risk of abnormal LFTs, adjusted HR (95%CI) 1.01 (1.00–1.02). In the adjusted Cox model, moderate alcohol consumption (≤14 units per week) was not associated with a statistically significant risk of developing abnormal LFTs (table 1). There was a non-significant trend to higher HR with higher levels of alcohol consumption, however power was limited in the patients consuming >14 units per week.

| Units of alcohol per week | Number of events[§†] | Crude rate (95% CI) Per 1000 person years | Hazard ratio (95% CI) Univariate | Hazard ratio (95% CI) Age & gender adjusted |
|---|---|---|---|---|
| 0 | 24 | 5.58 (3.74–8.33) | ref | ref |
| 1–7 | 83 | 5.57 (4.49–6.91) | 1.01 (064–1.58) | 1.02 (0.65–1.60) |
| 8–14 | 23 | 5.99 (3.98–9.01) | 1.07 (0.60–1.89) | 1.15 (0.65–2.06) |
| 15–21 | 11 | 7.58 (4.20–13.68) | 1.36 (0.67–2.78) | 1.59 (0.76–3.30) |
| 21–28 | 3 | 8.61 (2.78–26.70) | 1.51 (0.46–5.03) | 1.91 (0.56–6.47) |
| >28 | 6 | 9.05 (4.07–20.15) | 1.60 (0.66–3.92) | 1.92 (0.76–4.89) |

[§]Event=abnormal LFT. [†]Not all patients who were defined as drinkers/non-drinkers had alcohol consumption defined in units.

**Conclusions:** In patients with RA taking MTX, increasing alcohol consumption is associated with an increased risk of developing abnormal LFTs. The clinical importance of this increased risk may be small when drinking ≤14 units per week.

**Disclosure of Interest:** None declared

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## THU0079 HDL, IGG ANTI-HDL ANTIBODIES AND PON1 AXIS IN RHEUMATOID ARTHRITIS PATIENTS: A NEW TARGET FOR CV DISEASE

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**Background:** High Density Lipoproteins (HDL) seem to develop cardioprotective functions beyond the reverse cholesterol transport, thus pointing to their antioxidant activity as a crucial player. Paraoxonase 1 (PON1) is a HDL-associated antioxidant enzyme which has an important role in avoiding lipid oxidization. Although genetic polymorphisms are known to modulate PON1 activity, its involvement in cardiovascular disease (CVD) in Rheumatoid Arthritis (RA) is controversial, suggesting that other factors may modulate its function.
**Objectives:** since anti-HDL antibodies have been related to an impaired lipid profile and CVD in RA, we aimed to evaluate the associations between PON1 activity, anti-HDL antibodies and CVD in RA according to PON1 rs662 genetic variants.
**Methods:** serum PON1 activity, using paraoxon as substrate, and IgG anti-HDL antibodies were quantified in 212 RA patients and 110 healthy controls (HC). The PON1 rs662 genotype (Q>R) was determined with TaqMan probes. An additional group of 13 biologic-naïve RA patients was prospectively followed for three months.
**Results:** PON1 activity was decreased in RA compared to HC (p=0.005). PON1 rs662 variants influenced serum PON1 activity in both groups, QQ homozygotes exhibiting the lowest activity. Distribution of genotypes did not differ between groups (p=0.215) and Hardy-Weinberg equilibrium was observed in both populations. Interestingly, PON1 activity was not associated with disease activity, ESR or CRP. A multivariate ANOVA analysis confirmed an independent role of both rs662 ($p<0.0001$) and anti-HDL antibodies (p=0.026) on PON1 activity, but differences were noted when patients were stratified by genotypes. Anti-HDL antibodies were associated with an impaired PON1 activity (p=0.010), decreasing HDL levels (r=-0.680, $p<0.001$) and higher prevalence of CV events in univariate and multivariate models in patients carrying the QQ genotype, but not in their QR or RR counterparts. Finally, change in anti-HDL antibodies upon TNFα-blockade independently predicted improved PON1 activity (B [95% CI], p: -0.369 [-0.669, -0.069], p=0.024) after adjusting by clinical response, change in ESR and change in HDL levels.
**Conclusions:** PON1 activity is impaired in RA in association with rs662 status and anti-HDL antibodies. The presence of anti-HDL antibodies in patients with the low activity genotype was correlated with a decreased PON1 function and associated with a higher prevalence of CV events in these patients. Therefore, anti-HDL antibodies are crucial mediators to understand the link between rs662 polymorphism and CVD.
**Disclosure of Interest:** None declared
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## THU0080 LIPID TESTING AND MANAGEMENT AMONG RHEUMATOID ARTHRITIS PATIENTS COMPARED TO PATIENTS WITH DIABETES AND THE GENERAL POPULATION

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**Background:** Patients with rheumatoid arthritis (RA) have high coronary heart disease (CHD) burden. Limited data suggest that these patients may be screened less frequently than other patients with similar CHD risk.
**Objectives:** To evaluate the rate of lipid testing and management among RA patients and compare it both to the general population and diabetes (DM) patients.
**Methods:** We used a mix of private and public health plans claims data from 2006 to 2010 with medical and pharmacy coverage. Eligible participants were required to 1) have at least 12 months of continuous medical and pharmacy coverage (baseline period), and 2) have 2+ physician diagnosis and relevant medications to categorize them as having 1) RA and DM; 2) RA only; 3) DM only; 4) Neither RA nor DM. Patients with prevalent myocardial infarction (MI)/stroke/CHD during baseline were excluded. We calculated the proportion of patients with low density lipoprotein (LDL) lab test. In a subgroup analysis, we determined the proportion of patients with lab results available with LDL ≥130 mg/dL that initiated treatment with statins. We use chi-square tests to compare differences between the 4 cohorts in the proportion tested for LDL and initiating statins.
**Results:** There were 428,109 eligible patients distributed between the 4 cohorts (Table). Overall, 60% were women. The overall age distribution was: 12% ≤40; 29%, 41–65; and 59% >65 years old. RA patients were less frequently tested for LDL compared to DM patients, with or without RA (p-value <0.001 for all comparisons). Conditional on having LDL ≥130 mg/dL, RA patients were less likely to be started on a statin compared to DM patients (p-value <0.001), and were marginally more likely to be initiated on statins compared to the general population (p-value =0.045). There was no difference in the statin prescription trend after an LDL ≥130 mg/dL between DM and RA patients compared to only RA patients (p-value =0.083)

Table 1. Frequency of lipid testing among patients with rheumatoid arthritis, diabetes, both or neither condition

| Outcome | RA Only N=20,148 | Diab Only N=100,971 | RA & Diab N=3,358 | Neither N=303,632 |
|---|---|---|---|---|
| Screening: LDL checked during 2-year period, % | 46 | 63 | 62 | 45 |
| Treatment: statin initiation (among subgroup of patients with lab results available and LDL ≥130 mg/dL not already on therapy), % | 13 | 26 | 28 | 9 |

**Conclusions:** RA patients are less frequently screened and managed for hyperlipidemia compared DM patients. Despite higher CHD risks in RA patients, hyperlipidemia screening and treatment rates in RA patients were no better than the general population. Further studies to investigate the reasons and potential interventions to ameliorate this care gap among RA patients are needed.
**Disclosure of Interest:** None declared
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## THU0081 ROLE OF THE SOLUBLE FORM OF DIPEPTYDIL PEPTIDASE-4(DPP4) IN THE INSULIN RESISTANCE OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Dipeptidyl peptidase 4 (DPP-4) is an enzyme which plays a fundamental role on glucose homeostasis through degradation of the incretine hormones glucagon like peptide 1 and gastric inhibitory polypeptide.
**Objectives:** To analyze if DPP-4 levels differ between Rheumatoid arthritis (RA) patients and healthy controls, as well as to investigate if they correlate with the insulin resistance (IR) that RA patients express.
**Methods:** 406 subjects, 178 patients with RA and 228 controls adjusted by age and sex, were selected. We determined in both groups glucose, insulin and C peptide levels, *Homeostatic Model Assessment* (HOMA2) index for insulin and C peptide, and blood levels of the soluble form of DPP-4. We studied with multivariant analysis adjusted for the intake of steroids and other classic factors associated with IR, the differences between patients and controls as well as the correlation of DPP-4 with the activity of the disease and with IR in both groups.
**Results:** Patients had higher levels of insulin (16±26 vs 10±7 microU/mL, p=0,001) and C peptide (1,15±1,02 vs 0,50±0,26 nmol/L, $p<0,001$) compared to controls. Equivalently, insulin resistance index HOMA-IR (1,81±1,82 vs 1,35±0,93, p=0,002) and HOMA2-IR-peptide C (2,59±2,45 vs 1,10±0,55 nmol/L, $p<0,001$) were higher in patients with RA. DPP-4 levels were lower in patients with RA than controls (beta coef. -162 [-259–65] ng/ml, p=0.001), after adjustment for age, sex, body mass index and classic factors for IR. Patients with high or moderate activity (633±270 vs 844±757 ng/ml, p=0.06) and low activity (761±340 vs 844±756 ng/ml, p=0.40) had a lower expression of DPP-4 levels compared to those patients in remission, although this difference did not reach statistical significance.
**Conclusions:** Patients with RA express lower levels of DPP-4. This decrease could be explained by the activity of the disease and could play a role in the development of insulin resistance that RA patients express.
**Disclosure of Interest:** None declared
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## THU0082 MEDICATION IMPACT ON THE RISK OF INCIDENT DIABETES MELLITUS IN PATIENTS WITH RHEUMATOID ARTHRITIS: HYDROXYCHLOROQUINE AND ABATACEPT PROTECT WHILE GLUCOCORTICOIDS AND STATINS WORSEN

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**Background:** Chronic inflammation and some anti-inflammatory medications in rheumatoid arthritis (RA) are not only responsible for accelerated atherosclerosis but also have effects on the development of traditional risk factors, among which type 2 diabetes mellitus (DM) is the most important. Although hydroxychloroquine

(HCQ) and TNF inhibitors have been reported to decrease incident DM risk in RA, there are still a number of unanswered questions regarding the impact of newer biologics, statins, and the timing, dosing, and sustainability of this effect.
**Objectives:** To investigate the impact of specific DMARDs and statins on the risk of incident DM in patients with RA.
**Methods:** Study patients were participants without baseline DM and at least 1 year in the National Data Bank for Rheumatic Diseases (NDB) from 2000 through 2015. DM was determined by patient self-report or use of DM-specific medication. Multivariable Cox proportional hazard models were adjusted for age, sex, ethnicity, socioeconomic and smoking status, comorbidities, body mass index (BMI), and RA severity while examining the time-dependent association of HCQ, other DMARDs, glucocorticoids (GC), and statins.
**Results:** During the 71,668 person-year followup of 13,669 RA patients, 1,139 developed DM. Adjusted HR (95% CI) for DM were 0.67 (0.57–0.80) for HCQ, 0.52 (0.31–0.89) for abatacept, 1.31 (1.15–1.49) for GC, and 1.56 (1.36–1.78) for statins *(Table)*. There was no evidence of risk change through MTX, other synthetic and biological DMARDs. Although the risk reduction was significantly associated with higher HCQ doses and longer (>4 years) treatment durations, HCQ dose of <400mg/day, HR 0.71 (0.52–0.96), and ≥2-year duration, HR 0.72 (0.56–0.91), were also protective. DM-free survival of the patients who discontinued HCQ were quite similar to the patients who started HCQ and kept receiving the drug. Concomitant use of GC did not adversely affect the protective effect of HCQ, HR 0.69 (0.51–0.93). However, there was significant increased risk with statins and GC, HR 2.03 (1.65–2.50). In concomitant use of HCQ and statins, the protective effect of HCQ and increased risk with statins disappeared, HR 0.92 (0.68, 1.25).

Table 1. Association of different treatments with incidence of DM in RA patients

| Time-dependent treatment | Unadjusted HR (95% CI) | *P*-value | Adjusted HR* (95% CI) | *P*-value |
|---|---|---|---|---|
| HCQ | 0.66 (0.55–0.78) | <0.001 | 0.67 (0.57–0.80) | <0.001 |
| Glucocorticoid | 1.43 (1.26–1.61) | <0.001 | 1.31 (1.15–1.49) | <0.001 |
| Statin | 1.73 (1.52–1.97) | <0.001 | 1.56 (1.36–1.78) | <0.001 |
| Concomitant synthetic or biologic DMARDs | | | | |
| MTX alone (referent) | 1.0 | | 1.0 | |
| Any abatacept | 0.82 (0.52–1.29) | 0.39 | 0.52 (0.31–0.89) | 0.02 |
| Any other combination with MTX | 0.98 (0.82–1.18) | 0.88 | 0.87 (0.72–1.05) | 0.15 |
| Other or no DMARDs | 1.36 (1.17–1.58) | <0.001 | 1.11 (1.36–1.78) | 0.19 |

*Adjusted for age, age$^2$, sex, disease duration, employment, income, ethnicity, smoking, hypertension, comorbidity index, BMI, HAQ, NSAID usage, and year of entry.

**Conclusions:** The risk of incident DM in RA was reduced with HCQ and abatacept and increased with GC and statins. HCQ not only confers a sustainable, dose and treatment duration-dependent protective effect but also abolishes the increased risk of DM as a consequence of GC or statins.
**Disclosure of Interest:** None declared
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## THU0083 SIMPLIFIED PATIENT-DERIVED DISEASE ACTIVITY SCORE (SPDAS2): A SIMPLIFIED VERSION WITHOUT EARLY MORNING STIFFNESS

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**Background:** Treat-to-target is the standard of care in rheumatoid arthritis (RA). Integral to this is the regular assessment of disease activity. Several tools have been developed and validated to allow patients with RA to self-assess disease activity. One of these tools is the Patient-derived Disease Activity Score (PDAS). Two versions pf PDAS are available: PDAS1 and PDAS2. PDAS-2 is a composite score that includes patient global assessment of disease activity (PGA), modified health assessment questionnaire (MHAQ), patient self-assessed 28 swollen joint count (ptSJC28) and early morning stiffness score (EMS). PDAS2 correlated with DAS28ESR and Clinical Disease Activity Index (CDAI).
**Objectives:** In order to reduce patient burden, we developed a simplified PDAS2 (sPDAS2) by removing the need to assess EMS.
**Methods:** Data from 311 patients with established RA were analysed. The original model for calculating PDAS2 was: PDAS2 = 2.667 + [(0.021 x PGA) + (0.483 x MHAQ) + (0.033 x patient 28 SJC) + (0.002 x EMS)]. Linear regression was used to develop a sPAS2 using DAS28ESR as a dependent variable and including PGA, MHAQ and ptSJC28. R-squares were used to examine the statistical model fit of sPDAS2 compared with PDAS2. sPDAS2 was further validated using data from a different cohort of 204 patients with established RA. Correlation of sPDAS-2 with DAS28 and CDAI was examined to assess criterion and construct validity.
**Results:** Based on data from 311 patients with RA. The following model for sPDAS2 was developed: sPDAS2 =2.447 + 0.028 x PGA + 0.422 x HAQ + 0.053 x patients 28SJC.
The R-square for PDAS2 (including EMS) was 0.601. R-square for sPDAS (without the EMS) was 0.594. A difference of 0.007 indicating minimal loss of statistical fit.
Using data from a different cohort of RA patients. sPDAS2 correlated well with DAS28ESR (r=0.72, p<0.001) and CDAI (r=0.74, p<0.001) demonstrating criterion and construct validity.
**Conclusions:** A sPDAS2 has been developed and validated for patients with RA to self-assess disease activity. The components of sPDAS2 included PGA, mHAQ and ptSJC28 and do not require assessment of early morning stiffness.
**Acknowledgement:** The original developed of PDAS was supported by a grant from Arthritis Research UK. The CREATE Centre is funded by Arthritis Research UK and Health and Care Research Wales.
**Disclosure of Interest:** None declared
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## THU0084 TREATMENT RESPONSE IN PATIENTS WITH SIMULTANEOUS THYROID DISEASE AND RHEUMATOID ARTHRITIS IS SIGNIFICANTLY WORSE THAN PATIENTS WITH ISOLATED RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory polyarthritis with a prevalence of 0.5–1% of general population.[1] Various comorbidities can complicate the course of the disease and have direct effects on the long-term prognosis and management of RA.[2] Previous studies showed that there is an increased prevalence of thyroid disease (TD) among RA patients, probably due to autoimmunity; however the association of RA disease characteristic and TD has not been evaluated before.[3]
**Objectives:** To determine the association between TD and RA and reveal the prevalence of TD among RA patients.
**Methods:** All patients diagnosed with RA since 1st of January 2010 were included in this cross sectional study. Patients' demographic data (age, sex, year of diagnosis), serology test results including rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (anti-ccp) and antinuclear antibody (ANA) as well as disease activity score in 28 joints (DAS28) at the time of diagnosis and after 4 months (±1–2 months) of treatment were extracted in December 2015. Patients' previous medical history as well as medications and laboratory tests were evaluated to find out if the patients have been diagnosed with thyroid disease as well. Patients with subclinical thyroid diseases were also considered to perform statistical analysis. Chi-square test and t-test were used to compare different variables in patients with/without TD.
**Results:** Of 439 included patients 60.14% were female. The mean of age and disease duration were 64.64±15.03 and 2.59±1.66 years respectively. Prevalence of TD was 69/439 (15.7%). The mean of ∆DAS28 in patients with simultaneous TD and RA was 1.0±1.4 and in patients with isolated RA 1.5±1.4 (P<0.05). The results of our study showed that presence of TD among RA patients is associated with female gender (P<0.001), ANA positivity (P<0.05) and anti-ccp ≥100 AU/ml (P=0.05). Furthermore, coexistence of TD and RA resulted in poor response to treatment (P<0.05). We did not find any association between TD and disease duration as well as RF positivity.
**Conclusions:** Considering the higher prevalence of TD among RA patients in comparison with general population, we recommend the routine measurement of thyroid stimulating hormone to detect TD at an earlier stage, leading to earlier treatment initiation and improve prognosis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2230

## THU0085 LEVEL OF CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS WITH SUBCLINICAL HYPOTHYROID DYSFUNCTION

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**Background:** Patients with rheumatoid arthritis (RA) with subclinical hypothyroid dysfunction (SHTD) have early mortality due to cardiovascular complications. There for it is necessary to study this problem. Investigation of the SHTD effect on RA in these patients will help to define the prognosis and optimize the efficiency of integrated diagnostic and therapeutic tactics.
**Objectives:** To determine the cardiovascular risk (CVR) level in RA patients with SHTD
**Methods:** 98 patients with RA were examined. All the patients were divided into 2 groups. Group I – 59 (60,2%) patients with RA and SHTD, the second – 39 (39.8%) patients with RA without SHTD. Thyroid gland condition was determined according to international standards of SHTD diagnosis. All subjects were female. Patients in group I and II have not differed by age and RA duration. All patients

underwent clinical and functional investigation for RA diagnosis. Blood levels of total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol cholesterol (LDL-C), very low density lipoproteins (VLDL) and atherogenic index (AI) were assessed. All patients underwent ultrasound detection of vascular endothelial dysfunction. CVR is calculated by Score scale. The results were multiplied by 1,5 factor according to the latest European guidelines for CVR in RA patients. The CVR level was also evaluated by Procam scale.

**Results:** CVR factors were significantly higher in the group I, than in group II (respectively 91.7%, 69.6%). Family history of cardiovascular disease was observed in 48.1% of patients I and 35.1% II group, higher BMI – respectively at 88.8% and 27.02% ($p<0.001$), dyslipidemia – at 79.6% and 43.2% ($p<0.001$), increased blood pressure – at 62.9% and 37.8% (p=0,003), menopause – at 57.4% and 24.3% ($p<0.001$). The total risk of cardiovascular death by Score scale in group I patients was 5.7%, in II – 3.2%, and by Procam scale in I – 18.5%, in II – 13.7%, it is significantly different ($p<0.001$).

Parameters of lipid profile in group I compared with group II showed a significant increase of all investigated indices $p<0.001$, except for level of HDL cholesterol. In the study of endothelial function in both groups of patients the decrease of endothelium-dependent vasodilation (EDVD) and endothelium-independent vasodilation (EIVD) from standard indicators (EDVD brachial artery is (BA) greater or equal to 10%, and EIVD BA is more than 15%) was found. The average thickness of the complex intima-media (CIM) in patients of group I was 1.11±0.058 mm, and the II – 0.71±0.072 mm (p=0.009), which got statistical significance. Correlations between CIM and total cholesterol levels (r=0.297, p=0.021), LDL cholesterol (r=0.36, p=0.005), AI (r=0.335, p=0.008) in group I patients; and correlations between CIM and the level of LDL cholesterol (r=0.301, p=0.18) and AI (r=0.268, p=0.024) in patients of group II were defined.

**Conclusions:** The results show more significant changes of lipid profile and endothelial function indices in RA patients with concomitant SHTD, increasing CVR in these patients. This raises the need for physicians to pay more attention to thorough survey of RA patients for early diagnosis and correction of comorbid conditions, aggravating RA course

**Disclosure of Interest:** None declared

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## THU0086 AN AUDIT ON RHEUMATOID ARTHRITIS PATIENTS WITH LUNG DISEASE ON METHOTREXATE AT A DISTRICT GENERAL HOSPITAL

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**Background:** Interstitial lung disease (ILD) is associated with Rheumatoid arthritis (RA) in 3.7% - 7.7% of patients.[1] Methotrexate induced pneumonitis is a rare and unpredictable toxicity leading to withdrawal of treatment in 1:108 patient years.[2] British Society of Rheumatology (BSR) guidelines for pre- methotrexate treatment screening include chest x-ray and in certain cases pulmonary function tests and high resolution CT scan (HRCT). It is also recommended that methotrexate is best avoided in established cases of interstitial lung disease.[3]

**Objectives:** The aim of our audit was to check compliance with BSR guidelines.

**Methods:** We have conducted a retrospective audit on 40 RA patients treated with methotrexate with preferential selection of patients with lung disease. We looked at their records to obtain details of screening chest investigations and also any subsequent chest investigations carried out and the reasons prompting the investigations and the actions taken.

**Results:** Our cohort included patients with the median age of 63 years (Range 25 -87). There was an equal gender distribution. 80% of the patients were seropositive. Patients had pre-existing lung disease in 20% of which 50% had COPD, 25% Fibrosis, 25% benign pathology. A screening chest X-ray was performed in 97.5% of the patients with 31% being reported as abnormal. Fifty eight percent of the patients with abnormal chest x ray were symptomatic with shortness of breath (SOB) (86%) followed by cough. All these patients had subsequent HRCT revealing ILD in 57%, combination of emphysema and fibrosis in 29% and pneumonitis in 14%. All these patients were subsequently referred to a respiratory physician and methotrexate was withdrawn.

Fifty five percent of the patients with normal chest x-ray at screening subsequently developed chest symptoms (SOB (53%) and cough (34%)). Sixty seven percent of these patients had abnormal chest x rays. HRCT was requested in 80% of these patients revealing ILD in 47%. One symptomatic patient was found to have lung cancer. All of the ILD patients were subsequently referred to a respiratory physician and methotrexate was withdrawn.

The duration of methotrexate to onset of symptoms and withdrawal varied from 14 months to 12 years.

**Conclusions:** Appropriate pre-treatment screening for lung disease was performed in all patients commencing methotrexate. All patients with established ILD had methotrexate withdrawn. There is evidence for continuing methotrexate in RA patients who develop ILD with careful monitoring. However currently there are no guidelines concerning continuation or withdrawal of methotrexate in patients who develop ILD during the course of treatment.

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## THU0087 SUBCLINICAL CAROTID ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS: ROLE OF SERUM CATHEPSIN S AND CYSTATIN C

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**Background:** Although Cystatin C relation with atherosclerosis has been studied before in RA patients, cathepsin S association with subclinical atherosclerosis has not been previously considered in RA patients. This could help to better stratify or predict the development of cardiovascular diseases in RA.

**Objectives:** To assess if serum cathepsin S and cystatin C, two novel markers of cardiovascular disease risk (CVDR), are associated with subclinical carotid atherosclerosis in RA patients.

**Methods:** Serum cystatin C and cathepsin S levels, carotid intima-media thickness (cIMT) and carotid plaques were assessed in a cross-sectional study involving 178 RA patients. All of them were 18 years or older and fulfilled the 2010 ACR/EULAR classification criteria.

**Results:** Patients with a mean ± SD age of 55 ± 11 years were included. Regarding cardiovascular risk factors, 35% of the patients had hypertension, 32% dyslipidemia and 15% diabetes. Disease duration was 7 (IQR 4–15) years. Patients had moderate-active disease as shown by DAS28 (3.74 ± 1.91). One third (35%) of them were taking prednisone, 86% were under disease-modifying antirheumatic drugs and 22% were taking anti-TNF-alpha or other biologic therapies. The mean cIMT was 0.670 ± 0.143 mm, and 66 patients (37%) had carotid plaques in the carotid ultrasound assessment. Both cystatin C and cathepsin S were significantly associated with hypertension, diabetes and dyslipidemia. However, neither positive rheumatoid factor nor prednisone use were associated with cystatin C or cathepsin S. A trend for lower levels of cystatin C was observed in patients undergoing anti-TNF-alpha therapy (*log* beta coef. -0.20 (-0.44–0.04), p=0.09). An association between disease activity scores with higher levels of cystatin C but not with cathepsin S was found. Cystatin C levels were also associated with cIMT in the subgroup of patients included in the higher quartile of cIMT (OR 1.31, 95%CI [1.00–1.72], p=0.04) after adjusting for traditional cardiovascular risk factors, age and sex. An association between serum cystatin C levels and carotid plaques was also found in the univariate analysis (OR 1.37, 95%CI [1.06–1.76], p=0.02). However, this significant association was lost after adjusting for traditional cardiovascular risk factors and age. Cathepsin S was not associated with cIMT or carotid plaques.

**Conclusions:** High cystatin C serum levels identify a subgroup of RA patients with high risk of subclinical atherosclerotic disease.

**Disclosure of Interest:** None declared

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## THU0088 IRON DEFICIENCY AND LOW ERYTHROPOIETIN CONCENTRATIONS ARE FREQUENT ANEMIA CAUSING FACTORS IN RHEUMATOID ARTHRITIS

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**Background:** Anemia was recently re-evaluated as a predicting parameter for radiographic joint damage progression in addition to standard disease activity measures in rheumatoid arthritis (RA) [1].

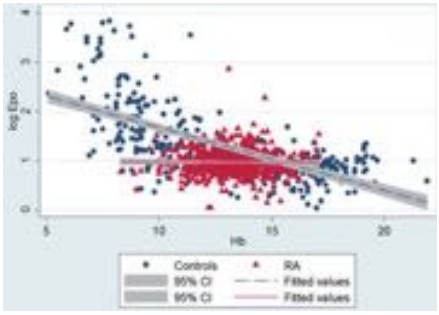
**Objectives:** To characterize the origin of anemia in RA.

**Methods:** All patients in the Swiss SCQM-RA cohort with available hemoglobin concentrations and a biobank sample were included. Anemia was defined according to WHO definitions (hemoglobin <12g/dl in women and <13 g/dl in men). Mean corpuscular volume (MCV) and hemoglobin (MCH) were locally acquired. Serum samples were collected and stored according to stringent pre-analytical quality requirements. Serum iron, transferrin, ferritin, soluble transferrin receptor (sTfR) and erythropoietin (EPO) concentrations were measured using standard procedures in an accredited central laboratory. Non-RA patients with normal CRP served as control for logEPO/Hb quotient interpretation. Iron deficiency anemia (IDA) was defined according to [2] in case of 1. t-sat ≤20% & ferritin ≤30 μg/l or 2. sTfR index, the quotient of sTfR divided by log-transformed ferritin concentrations ≥1mg/μg. Anemia of chronic disorders (ACD)

was diagnosed by signs of inflammation plus 1. T-sat ≤20% & ferritin ≥100 μg/ml or 2. sTfR index <1mg/μg & ferritin ≥30 μg/l. Serum hepcidin-25 was quantified using commercially available ELISA kits from Peninsula Laboratory, LLC, San Carlos, CA.

**Results:** 106 (14%) of the 779 patients included were anemic at the time of sample collection. Anemic patients were significantly older, had more comorbidities, higher DAS-28 and used more often corticosteroids, but did not differ in NSAID, conventional (75%) or biological (70%) DMARD use. They had lower MCV, lower MCH and lower transferrin levels ($p<0.04$) than non-anemic patients, but other serum parameters were not significantly different. sTfR was more sensitive than transferrin concentrations to detect possible iron deficiency (14% versus 1%).

IDA was detected in 98 (92%) of the 106 anemic patients. ACD was diagnosed in 61 (58%) of the anemic cases, when active disease was defined by CRP >10 mg/l or ESR >30 mm/h, or in 82 (77%) of subjects after including DAS-28 >3.2 as additional marker of inflammation. Only 3 respectively 6 cases could be attributed to ACD alone, while 58 (55%) respectively 76 (72%) of anemia cases had ACD and IDA in combination, dependent of the definition of inflammation. In a multivariate linear regression analysis ($r^2=0.38$, n=1075, $p<0.0001$), logEPO concentrations depended on hemoglobin concentrations (-0.1, 95%CI -0.11 to -0.09, $p<0.0001$), which increased significantly less in RA (-0.29, 95%CI -0.34 to -0.24, $p<0.001$) with decreasing hemoglobin concentrations than in controls.




**Conclusions:** Iron deficiency was the most common cause of anemia in this large RA cohort with representative prevalence of anemia for an intensively treated RA population. We further found inadequately low EPO levels in relation to observed hemoglobin concentrations among RA patients, which may further contribute to anemia in these patients. Their relation to radiographic damage progression needs to be determined.

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**Disclosure of Interest:** B. Möller Grant/research support from: VIFOR Pharma, Villars-sur-Glâne, Switzerland, A. Leichtle: None declared, P. Meyer: None declared, M. Fiedler: None declared, A. Finckh: None declared, D. Kyburz: None declared, C. Gabay: None declared, P. Villiger: None declared

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## THU0089 RHEUMATOID ARTHRITIS AND PERIODONTAL DISEASE IN ALGERIAN PEOPLE

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**Introduction:** Rheumatoid arthritis (RA) and periodontitis (PD) are two chronic inflammatory affections that share many similarities. Many studies report the increased frequency of periodontitis during rheumatoid arthritis. The porphyromonas gingivalis, periodontopathogenic bacterium plays a main role through peptidylarginine-deiminase an enzyme capable of citrullinating endogenous proteins and generates an autoimmune reaction.

**Objectives:** The aim of this study was to determine the prevalence of periodontitis during rheumatoid arthritis and its relationship with RA severity, treatment and patient characteristics.

**Methods:** This is a multicentre,cross-sectional, prospective study. Were included adults RA. We identified sociodemographic factors, the periodontal disease status and anaerobic germs, clinical activity of RA with the Disease activity score (DAS 28-VS), the Health Assessment Questionnaire (HAQ), extraarticular manifestations, Sharp Score and periodontal anaerobic bacteria. Were determined correlations between PD and patient characteristics, treatment and RA severity.

**Results:** a total of 204 RA were included. The mean age of the patients was 50.338±12.428 years. Sex-ratio: 0.13. The mean duration disease was 10.259±8.232 years. 43% of patients had extaarticular manifestations: 43%. The DAS vs-28 =4.615±1.440. HAQ =1.140±0.821.0. The ACPA rate was 229.855±241.902. Sharp mean: 112.995±93.965. 65.7% patients were treated by methotrexate. 32.8% by biological. 77, 4% patients were under corticoids. The periodontitis frequency was 37.3% (51.1% related to the porphyromonas gingivalis (PG). The tooth loss frequency was 31, 4%.the comparison of the subjects with periodontitis and patients without it showed no significant differences. the comparison of the patients with severe periodontitis and those without showed: age p=0.0004, menopause p=0.002, DAS p 0.47, Sharp p=0.06, HAQ p=0.95.

**Conclusions:** These results suggest a high prevalence of periodontitis during RA, PG is often responsible. The tooth loss frequency is also high. There is no correlation between periodontitis and RA severity and no relationship between PD and RA treatment. On the other hand periodontitis severity is related to the age and the menopause.

**Disclosure of Interest:** None declared

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## THU0090 ASSOCIATION OF THE RHEUMATOID ARTHRITIS PROGNOSTIC FACTORS ANTI-CITRULLINATED PEPTIDE ANTIBODIES, RHEUMATOID FACTOR AND EROSIONS WITH DISEASE ACTIVITY AND WORK PRODUCTIVITY

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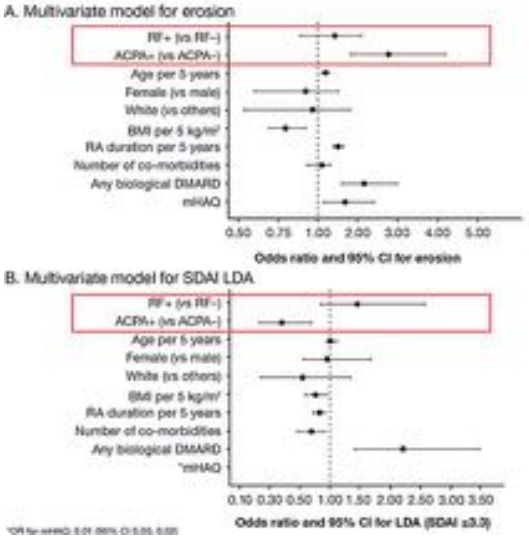
**Background:** Autoantibody production, including RF and anti-citrullinated protein antibody (ACPA), may play a role in RA disease pathogenesis.[1] ACPA positivity(+) in patients (pts) with RA is a strong predictor of joint erosions and radiographic progression.[1,2] However, data evaluating the association of seropositive, erosive disease with disease activity and resource use (RU) are limited.

**Objectives:** To evaluate the association of ACPA+/RF+ with erosions and disease activity; to compare activity, RU and work productivity (WP) in ACPA+ pts with erosions vs all other RA pts.

**Methods:** Pts enrolled in the BRASS Registry were analysed. BRASS comprises mostly pts with established RA who were evaluated annually on clinical measures and semi-annually on clinical pt-reported outcomes and resource utilization parameters. Baseline (BL) visit was the time of enrolment into BRASS. ACPA levels at BL and annual follow-up were measured using a validated ELISA (Inova Diagnostics, San Diego, CA) until its discontinuation in 2011, and the Euro-Diagnostica assay (IBL-America, Minneapolis, MN) thereafter. RF levels at BL and follow-up were measured during the annual rheumatologist visit. RU and WP were measured at 6 months (M) via pt questionnaires. Subgroups at BL were described using Wilcoxon rank-sum test (continuous variables) and Pearson's chi-square test (categorical variables); multivariate logistic regression models (binary outcome variables) and ordinary least-square regression analysis (continuous outcome variables) were used. Covariates included in the multivariate models were age, sex, race, BMI, RA duration, number of co-morbidities and treatment.

**Results:** Among 1309 pts with ACPA data, 82% were female, mean (SD) age was 56.5 (14.1) yrs and DAS28(CRP) was 3.7 (1.6). Pts had mean (SD) TJC of 14.3 (14.0), ACPA levels of 128.3 (151.9) units/mL and RF levels of 127.7 (301.6) units/mL. After controlling for covariates, odds ratio (OR) for erosive disease was 2.72 (95% CI: 1.77, 4.18) for ACPA+ and 1.36 (0.88, 2.08) for RF+ (Fig. 1a). The OR for attaining SDAI LDA (<3.3) was 0.37 (0.21, 0.66) for ACPA+ and 1.45 (0.82, 2.56) for RF+ (Fig. 1b). ACPA titres were associated with erosive disease: 61 vs 32% of pts had erosive disease in the high vs low ACPA quartiles. ACPA+ pts with erosions (n=498) had higher mean SDAI (28.0 vs 18.1) and joint counts (19.2 vs 11.1), and greater proportions (60 vs 38%) were treated with biologic (b)DMARDs compared with all other RA pts. In multivariate analyses, the OR for SDAI remission in ACPA+ pts with erosions was 0.19 (0.10, 0.37); a significantly ($p<0.05$) greater proportion of these pts had durable equipment use (30.6 vs 22.1%) and all-cause hospitalizations (20.1 vs 13.1%) compared with all other RA

**Figure 1.** Association of ACPA+ and RF+ with erosion and disease activity.



pts at 12M. This group also had lower employment (38.7 vs 53.5%) and higher long-term disability (25.4 vs 17.3%) and retirement (32.5 vs 22.1%).
**Conclusions:** ACPA+ has a stronger association with erosions and disease activity. The presence of ACPA+ and erosions (vs absence) is associated with higher disease activity, lower odds of remission and lower WP, even when treated with standard-of-care bDMARDs.
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**Disclosure of Interest:** E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, C. Iannaccone: None declared, M. Frits: None declared, N. Shadick Grant/research support from: Bristol-Myers Squibb, Crescendo Biosciences, Amgen, UCB, Questcor, M. Weinblatt Grant/research support from: Bristol-Myers Squibb, Crescendo Bioscience, UCB, Amgen, Consultant for: Bristol-Myers Squibb, Crescendo Bioscience, UCB, AbbVie, Roche, Janssen, Pfizer, Lilly, Amgen
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## THU0091 TREATMENT PATTERN AND DISEASE ACTIVITY SCORES IN RHEUMATOID ARTHRITIS PATIENTS; DATA TAKEN FROM QATAR RHEUMATOID ARTHRITIS REGISTRY

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**Background:** To date, there is no rheumatoid arthritis registry in Middle East. Rheumatoid arthritis registry in Qatar was established in 2013 with the aim of collecting data on RA patients seen in routine care at Hamad General Hospital, Qatar. It is observational study collecting data about demographic features of RA, RF and Anti CCP status, type of medication and their adverse reactions. CDAI, SDAI, DAS28, RAPID3 and HAQ questionnaire are also recorded.
**Objectives:** To describe demographic, disease activity score and treatment pattern in rheumatoid arthritis patients in Qatar.
**Methods:** All consecutive rheumatoid arthritis patients who were attending routine rheumatology outpatient clinic at Hamad General Hospital from period of June 2013 to September 2015 were included in this study.
**Results:** Data of 496 patients were analyzed: 75.8% female, 54.2% Arabs, 45.8% non Arabs, 74.9% were positive for rheumatoid factor, 79.8% were positive for anti CCP and 31.3% have erosion at the time of data collection. One hundred thirty one patients (26.4%) were receiving biologic drugs: (9.3% etanercept, 6% rituximab, 5.6% tocilizumab, 4.4% adalimumab, 0.4% abatacept, 0.4% certolizumab, and 0.2% infliximab). Among patients who are receiving biologic therapy, 42 patients (32%) are on biologic monotherapy. (9.9% on rituximab monotherapy, 9.9% on tocilizumab, 6.9% on etanercept and 5.3% on adalimumab monotherapy). Similarly, 49.23% of those patients receiving biologic, are also using concurrent methotrexate.
Methotrexate (MTX) was the most commonly prescribed synthetic DMARD (65.3%); 27% MTX monotherapy, 9.9% combined MTX and hydroxychloroquine, 6% combined MTX and sulfasalazine, 4.8% combined MTX and leflunomide and 3.6% triple therapy. Hydroxychloroquine was used by 29.4% of patients (4.6% patients were only on hydroxycholoquine monotherapy). Sulfasalazine was used by 21.2% patients (3.2% were only on sulfasalazine monotherapy). Leflunomide was used by 13.7% of patients (3.4% were only on leflunomide monotherapy). Good number of patients (39.7%) was receiving corticosteroid in our cohort. Mean dose of methotrexate, sulfasalazine and prednisolone was 15.88 ± 4.98 mg per week, 1.64 ± 0.57 gram daily and 5.45 ± 1.81 mg per day respectively.
Different disease activity scores in our cohort were as follows: DAS28 (4) 3.2 ± 1.2, CDAI 8.5 ± 7.9 and SDAI 9.7 ± 9.1. Mean HAQ score was 0.9 ± 0.7. Disease activity categorized by these indices differs considerably; 18% and 17.5% patients were in remission according to CDAI and SDAI scores respectively while 30.3% patients were in DAS 28 remission. Similarly, 23.1% patients were in low disease activity according to DAS28 (4) score while 51.6% patients were in low disease activity according to CDAI and SDAI scores.
**Conclusions:** This observational study describes a cohort of RA patients seen at Hamad General Hospital, Doha Qatar. Treatment pattern is somewhat similar to what is reported worldwide. One fourth of patients are receiving biological DMARD. Approximately two third of patients are categorized as having low disease activity or in remission. Disease activity categorized by various scores differs considerably.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1203

## THU0092 EFFECT OF DISEASE MODIFYING ANTI RHEUMATIC DRUG METHOTREXATE ON THE LIPID PROFILE OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Cardiovascular morbidity and mortality appear to be increased in rheumatoid arthritis (RA), which might be due to increased prevalence of risk factors for cardiovascular disease, such as an accelerated progression of atherosclerosis. Patients with active RA frequently show an atherogenic lipid profile, which has been linked with the inflammatory reaction.
**Objectives:** The AIM of this study is to determine the effect of treatment with methotrexate on the lipid profile of patients with rheumatoid arthritis.
**Methods:** We studied 25 patients with newly diagnosed rheumatoid arthritis who had not been treated with corticosteroids or disease-modifying antirheumatic drugs. We measured serum lipid profile of patients, who achieve remission according to DAS28 scores, at baseline and 3, 6 and 12 months post methotrexate to study the effect of the drug on the lipid levels.
**Results:** Twenty five patients were included in this prospective study 22 females (88%) and 3 males (12%). The mean age of patients was (46.40 ± 13.00). In these patients, mean high density lipoprotein (HDL) increased by 18.8 ± 11.3% ($p<0.001$), 21.9 ± 12.5% ($p<0.001$) and 26.8 ± 12.3% ($p<0.001$) and total cholesterol (TC) increased by 16.39 ± 22.12% ($p<0.001$), 14.38 ± 18.18% ($p<0.001$) and 12.94 ± 16.81% ($p<0.001$) at 3, 6, and moths respectively. Increase in Light density lipoprotein (LDL) was statistically significant at 3 months {9.89 ± 18.84% ($p<0.042$)} where as significant decrease in the level of triglycerides was noted at 6 months 2.69 ± 3.94% ($p<0.003$) and at 12 months2.62 ± 4.52% ($p<0.010$). Despite the increase in HDL, LDL and TC the atherogenic ratios (TC/HDL and LDL/HDL ratios) showed improvement at 3, 6 and 12 months post MTX treatment. There was negative association between changes in DAS28(ESR) after 3 months therapy and changes in HDL, LDL and TC levels.
**Conclusions:** Lipid profile and atherogenic ratios (TC/HDL and LDL/HDL ratios) improves substantially following effective treatment with methotrexate of rheumatoid arthritis. This improvement may reduce the risk of cardiovascular disease. With a decline in disease activity, a rising trend was observed for all lipids. However, changes in disease activity (DAS28) were only significantly related to changes in HDL cholesterol and LDL cholesterol levels.
**Acknowledgement:** I dedicate this thesis to my beloved parents; my father Jeet Singh Sidhu and my mother Amarjit kaur.
**Disclosure of Interest:** G. sidhu Shareholder of: no, Grant/research support from: no, Consultant for: no, Employee of: no, Paid instructor for: no, Speakers bureau: no
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## THU0093 EFFICIENCY OF NON-BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS) IN RHEUMATOID ARTHRITIS (RA) PATIENTS WITH COMORBIDITY

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**Background:** The impact of comorbidity on the course and results of RA treatment isn't investigated enough.
**Methods:** 402 RA patients (pts) (50.0% with early RA, including 12.4% pts with very early RA) were studied. Mean age at inclusion was 49.6±0.58 yrs, disease duration – 52.3±3.15 month. 84.1% of the pts were women; 63.2% were positive for rheumatoid factor and 75.2% - for antibodies against cyclic citrullinated peptides. 175 pts had extra-articular manifestations (EAM): mostly rheumatoid nodules (22.1%), lymphadenopathy (13.3%) and weight loss or fever (10.1%), less frequently - Sjögren's syndrome, vasculitis, eye disease, serositis. Pts were treated with methotrexate (mean dose – 11.6±0.29 mg/w, n=157), leflunomide (19.2±0.28 mg/d, n=95), sulfasalazine (2 g/d, n=76) or combined basic therapy (n=74). Effectiveness outcomes were evaluated after 2 yrs of treatment by ΔDAS28 and modified Sharp-van der Heijde score (ΔSHS).
**Results:** Comorbidity was observed in 58.7% RA pts, 25.0% of them had several comorbid conditions. The following most common comorbidities were recorded in pts with RA: arterial hypertension (AH) (22.5% of comorbidities), thyroid disease (11.9%), osteoarthritis (9.17%), chronic pyelonephritis (5.96%), diabetes mellitus (5.50%), peptic ulcer disease (5.05%), liver pathology (5.05%).
After 2 years clinical response to the treatment was significantly less in pts with comorbidity versus pts without comorbidity (ΔDAS28 2.12±0.13 vs 2.63±0.17, $p<0.05$), while a degree of radiological progression was only slightly higher (ΔSHS 11.7±1.20 vs 10.0±1.39, $p>0.05$).
The impact of the most common comorbidities in RA (AH and thyroid disease) on clinical and radiological response to treatment was assessed. Our results suggests that DMARDs efficiency doesn't depend on AH presence (ΔDAS28/ΔSHS – 2.0±0.19/9.05±1.55 vs 2.38±0.17/10.0±1.39 in pts with and without comorbidity respectively). However, in pts with thyroid disorders clinical response to treatment was significantly lower (ΔDAS28 – 1.57 ± 0.29) versus pts without comorbid diseases (2.38 ± 0.17, $p<0.05$), radiological progression in the compared groups did not differ significantly (ΔSHS – 11.5±2.77 vs 10.0±1.39).
To study the possible mutual aggravating influence of comorbidity and EAM of RA the effectiveness of DMARDs in the relevant subgroups was analyzed: in pts with comorbidity and EAM (n=94) or without EAM (n=142), pts without comorbidity, but with EAM (n=68) or without EAM (n=98). The clinical response in pts without comorbidity and EAM of RA was better (ΔDAS28 2.52±0.20) then in pts with comorbidity and with or without EAM (2.01±0.21 and 1.87±0.17 respectively, $p<0.05$). The lowest rate of radiographic progression (ΔSHS 8.85±1.13) in pts without comorbidity and EAM was observed (comparing 12.1±1.12 in pts with comorbidity and EAM, $p<0.05$).
**Conclusions:** 1. Comorbidity in more than half of Ukrainian pts with RA is observed, mostly arterial hypertension and thyroid disease.

2. The presence of comorbidity in pts with RA is associated with a worse clinical efficacy of DMARDs and the trend to greater radiological progression of RA.
3. Pts without comorbidity and EAM of RA have the best clinical response to non-biological DMARDs treatment (significantly better then pts with comorbidity, without EAM) and the lowest degree of radiological progression (vs pts with comorbidity and EAM).

**Disclosure of Interest:** None declared
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## THU0094 SYSTEMIC EFFECT OF WRIST SURGERY ON QUALITY OF LIFE AND MENTAL WELLNESS FOR THE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** By a remarkable advance in the medical treatment of rheumatoid arthritis (RA), uncontrollable synovitis in the past has been well comtrolled. However, some patients still have a problem in their wrist due to structural damage and smoldering synovitis. Surgical reconstruction for the wrist is required, if the conservative treatment failed. Recently, patients desired to achieve functional remission aiming at the higher level of quality of life (QOL) and the mental wellness.
**Objectives:** The objective of this study was to clarify the systemic effect of wrist surgery on the disabled patients with RA using the assessment of patient-reported outcome (PRO) and disease activity.
**Methods:** Surgical reconstruction was scheduled on 74 wrists in 74 patients (male:10, female:64) with RA between October 2012 and September 2014. The average age was 62 (19–88) years old and the average duration of the disease was 14 (1–60) years. Correction of the thumb and the finger deformities were combined in 18 wrist surgeries. The procedure included Darrach procedure (ulnar head resection) in 55 wrists, radiolunate arthrodesis in 31, Sauvé-Kapandji operation in 11, extensor tendon reconstruction in 11 etc. Steinbrocker stage I, II, III, IV was 2, 22, 29, 21 patients, and Steinbrocker class I,II, III, IV was 7, 47, 20, 0 patient(s), respectively. MTX was used in 48 patients (65%) with the average dose of 8.7mg/w, and PSL was used in 45 patients (61%) with the average dose of 4.1mg/d. Biologics was used in 12 patients (16%) including ETN:2, TCZ:3, IFX:3, ADA:3 patients. PRO was assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), and patient's general health using visual analogue scale of 100mm (Pt-GH). Upper extremity function was assessed by Disabilities of the Arm, Shoulder and Hand (DASH). Disease activity was assessed by 28-joint Disease Activity Score using C reactive protein (DAS28-CRP). They were measured just before surgery (baseline), at 6 and 12 months after surgery.
**Results:** As a whole, physical function (HAQ-DI, DASH), QOL (HAQ-DI, EQ-5D, Pt-GH) and mental wellness (BDI-II, Pt-GH), disease activity (DAS28-CRP) significantly improved at 6 and 12 months after surgery compared to those at baseline ($p<0.01$) (Table1,Figure1). The rate of clinical remission in DAS28-CRP ($<2.3$) at baseline, 6 and 12 months after surgery was 14%, 60% and 57%, respectively. The rate of functional remission in HAQ-DI ($<0.5$) was 28%, 35% and 41%, respectively. The rate of minimal depression in BDI-II ($\leq 13$) was 54%, 70% and 68%, respectively.

Table 1. Change in patient-reported outcome and disease activity (n=74)

| | HAQ-DI | DASH | EQ-5D | BDI-II | Pt-GH | DAS28-CRP |
|---|---|---|---|---|---|---|
| Baseline | 1.0 (0.9) | 40 (21) | 0.72 (0.12) | 13.5 (9.4) | 58 (21) | 3.2 (0.9) |
| 6mos.after surgery | 0.8* (0.7) | 34* (18) | 0.77* (0.14) | 11.6* (8.5) | 23* (22) | 2.2* (0.8) |
| 12mos.after surgery | 0.7* (0.6) | 30* (19) | 0.77* (0.14) | 11.3* (8.8) | 24* (20) | 2.3* (0.8) |

mean(SD), *p<0.001 compared to baseline

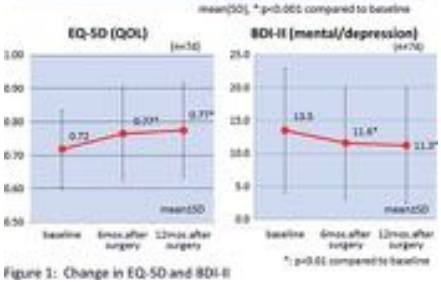



Figure 1: Change in EQ-5D and BDI-II

**Conclusions:** Favorable effects of wrist surgery on QOL and mental wellness as well as physical function were confirmed in the disabled patients with RA. To improve QOL and mental wellness, surgical treatment for the damaged wrist should be considered in combination with tight medical control. It also had an ameliorating effect on disease activity.

**References:**
[1] Ishikawa H, Murasawa A, Nakazono K, et al. The patient-based outcome of upper-extremity surgeries using the DASH questionnaire and the effect of disease activity of the patients with rheumatoid arthritis. Clin Rheumatol 2008;27:967–973.

**Disclosure of Interest:** None declared
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## THU0095 CLINICAL CHARACTERISTICS OF ELDERLY ONSET RHEUMATOID ARTHRITIS (EORA) COMPARED TO YOUNG ONSET RHEUMATOID ARTHRITIS (YORA) IN YOUNG AND OLD

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**Background:** As aging society and treatment of rheumatoid arthritis (RA) progress, problem of elderly onset RA (EORA) raised up in developed countries recent decade. Number of patient who suffers RA in elderly days has increasing. Grasping characteristics of EORA compared to young onset RA (YORA) is beneficial information for daily clinical practice for RA.
**Objectives:** RA patient's clinical courses were investigated from our small cohort study, and clinical characteristics of EORA were evaluated.
**Methods:** 549 RA patients visited as RA as diagnosed with 2010 ACR/EULAR classification criteria since August 2010, when treat to target strategy (T2T) have been accepted in our clinic, and have continued to be treated consecutively. Our clinic is the only medical institute in where rheumatologists that is certified Japan College of Rheumatology work in the area that consists of hundred thousand of population.
In these, patients who had been thrown of methotrexate before first visit, and dead patients before November 2015 were eliminated, then 436 patients have been investigated in this study. Patients were classified according to age at onset. We defined EORA as their onset age is sixty-five or more. The other patients (YORA) were also classified according to age at last visit. Patient who is younger than 65-year-old was classified as yYORA, and another group was defined as oYORA. Average values of disease activity score with 28 joints with C-reactive protein (DAS28-CRP), CRP, patient's pain score with visual analogue scale (PS-VAS), and health assessment questionnaire (HAQ-DI), for first visit (@BL), six months later (@6M), and average value throughout follow up (@AV), concomitant methotrexate (MTX) and glucocorticoid (GCS) thrown ratio, and average dosage of these drugs for first 24 weeks were calculated and compared with Mann-Whitney's U-test, unpaired T-test and chi-square test among groups and two of the three groups.
**Results:** 176 EORA, 123 oYORA, and 137 yYORA were picked up. Average DAS28-CRP were 3.83, 3.59, 3.71 @BL, 1.82, 1.85, 1.73 @6M, 1.99, 2.03, 2.22 @AV, while CRP were 1.61, 0.88, 0.83 @BL, 0.58, 0.46, 0.54 @6M, 0.73, 0.62, 0.57 @AV, and PS-VAS were 37.87, 30.73 33.74 @BL, 20.78, 17.32, 22.57 @6M, 25.79, 24.74, 26.19 @AV, and HAQ-DI were 0.53, 0.50, 0.26 @BL, 0.27, 0.20, 0.15 @6M, 0.46, 0.40, 0.26 @AV, for EORA, oYORA, and yYORA, respectively.
MTX and GCS thrown ratio were 47.7%, 38.9%, 45.3%, and 27.8%, 15.9%, 10.8% for EORA, oYORA, yYORA, respectively. Thrown dosage of MTX were 7.99, 8.25, 8.87mg, while GCS were 3.24, 3.07, 3.44mg, for EORA, oYORA, yYORA, respectively.
In Table 1, their statistical significances have been described.

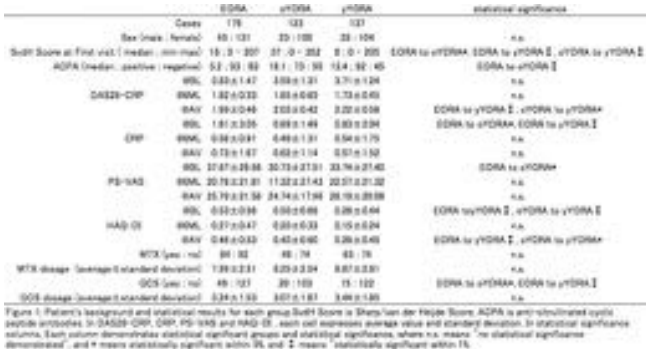


Figure 1. Patient's background and statistical results for each group Sharp/van der Heijde Score, ACPA is anti-citrullinated cyclic peptide antibodies, in DAS28-CRP, CRP, PS-VAS and HAQ-DI , each cell expresses average value and standard deviation. In statistical significance columns, Each column demonstrates statistical significant groups and statistical significance, where n.s. means "no statistical significance demonstrated", and * means statistically significant within 5% and ‡ means " statistically significant within 1%.

**Conclusions:** EORA patient has tendency to demonstrate higher CRP and PS-VAS at baseline than YORA, As well as CRP, DAS28-CRP is likely to demonstrate relatively higher, however, also demonstrates sensitive response for treatment including for GCS, then reduces PS-VAS as well as DAS28-CRP. However, elderly RA patient tends to remain in higher level of HAQ-DI than yYORA.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1346

## THU0096 SERUM INFLAMMATION IDENTIFIES INCREASED RISK OF FRAILTY IN RHEUMATOID ARTHRITIS

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**Background:** Frailty is defined as "excess vulnerability to stressors, with reduced ability to maintain or regain homeostasis after a destabilizing event"[1]. Frailty is closely related to body composition and physical functioning, and is associated with increased risk of poor health outcomes including death. Serum inflammation is associated with differences in body composition and physical functioning in the general population and individuals with chronic disease. The ability of serum markers of inflammation to identify increased frailty among individuals with rheumatoid arthritis (RA) is unknown.
**Objectives:** We tested whether serum erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP) are associated with increased risk of frailty among men and women with RA.
**Methods:** Participants were individuals in a longitudinal RA cohort. ESR and high sensitivity CRP were assessed from blood samples using standard clinical assays. Individuals with 3 or more of the following physical deficits were classified as frail[1]: 1) body mass index $\leq$18.5, 2) low grip strength (adjusted for sex and BMI, measured by handheld dynamometer), 3) severe fatigue (measured by the Fatigue Severity Inventory), 4) slow 4-meter walking speed (adjusted for sex and height), 5) low physical activity (measured by the International Physical Activity Questionnaire). Individuals with 1 or 2 deficits were classified as pre-frail, and those with no deficits as robust.[1] Multinomial logistic regression analyses controlling for age, sex, smoking status, RA disease duration, prednisone use, tumor necrosis factor inhibitor use, appendicular lean mass, and pain modeled the effects of ESR and CRP on severity of frailty.
**Results:** Of the 141 participants, 60% were female; mean age was 58 (±11) years, duration of RA was 19 (±11) years, ESR was 19 (±19) mm/h, and hsCRP was 5 (± 8) mg/L. Sixteen participants (11%) were frail, 86 (61%) pre-frail, 22 (16%) robust, and 17 (12%) were missing grip strength data. In adjusted models, higher ESR was associated with significantly increased risk of frailty (Table 1). Similar trends were observed between CRP and risk of frailty, but did not reach statistical significance in adjusted models.

Table 1. Multinomial logistic regression relative risk ratios (95% CIs) for the effect of serum sedimentation rate and C-reactive protein on risk of frailty category among individuals with RA

| | ESR | | CRP | |
|---|---|---|---|---|
| | Unadjusted | Adjusted[#] | Unadjusted | Adjusted[#] |
| Frail | 1.69 (0.94, 3.07) | 2.56* (1.16, 5.65) | 1.49 (0.88, 2.52) | 1.96$^{+}$ (0.96, 4.03) |
| Pre-Frail | 1.43 (0.95, 2.15) | 1.92* (1.05, 3.48) | 1.26 (0.85, 1.86) | 1.66$^{+}$ (0.94, 2.94) |
| Robust | Ref. | Ref. | Ref. | Ref. |

[#]Adjusted for age, sex, smoking status, disease duration, prednisone use, TNF inhibitor use, appendicular lean mass, and pain due to rheumatoid arthritis. *$p<0.05$, $^{+}p<0.1$.

**Conclusions:** Frailty and pre-frailty were common in our cohort of individuals with RA, with a greater prevalence than that of geriatric populations. ESR levels were associated with approximately twice the risk of being frail or pre-frail compared to being robust. CRP demonstrated similar effects on risk of frailty, though trends did not reach statistical significance. These findings underscore the burden of frailty among individuals with RA, and they may suggest a clinical role for serum ESR and CRP to identify individuals with RA at greatest risk of frailty.
**References:**
[1] Fried J Am Geriatr Soc 2001;56:M146
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1526

## THU0097 DESCRIPTIVE ANALYSIS OF LARGE SINGLE CENTER EXPERIENCE OF PATIENTS WITH INTERSTITIAL LUNG DISEASE AND RHEUMATOID ARTHRITIS

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**Background:** ILD may present as a rare but serious extraarticular manifestation in patients with RA and can have dramatic effect on morbidity and mortality.
**Objectives:** To evaluate the course of pulmonary disease in a large prevalence cohort of patients with RA who have ILD.
**Methods:** Prevalent cases of RA with ILD from 01/01/1998 to 01/01/2014 were identified in a single center's electronic medical record using advanced software to identify cases using ICD-9 diagnosis codes. All cases were manually reviewed and screened for inclusion. RA characteristics and pulmonary findings including high-resolution computed tomography (HRCT) and pulmonary function testing (PFT) were evaluated. Descriptive statistics were used to summarize the data.
**Results:** Two-hundred and one patients with ILD and RA were identified. Patients were predominately Caucasian (97%); 54% were males; mean age was 66.6 years (±10.9) at ILD diagnosis. Mean follow-up from ILD diagnosis was 4.1 years (±4.0) and median time from RA to ILD diagnosis was 4.9 (range -15.7 to 45.6) years. Seventy-three (37%) were never smokers. Eighty-seven (43%) had usual interstitial pneumonia (UIP) and/or idiopathic pulmonary fibrosis (IPF) and sixty-seven (33%) had non-specific interstitial pneumonia (NSIP) by HRCT. Anti-citrullinated protein antibody (ACPA) was present in 110 (77%) of 142 tested patients, and rheumatoid factor (RF) was present in 161 (84%). Erosive disease was present in 52 (28%) of patients and 103 (51%) had other extraarticular manifestations of RA prior to or at time of ILD diagnosis. The baseline predicted PFTs at time of ILD diagnosis included a forced vital capacity (FVC) of 72% (± 21), a forced expiratory volume in 1 second (FEV1) of 71% (±21), and a diffusing capacity for carbon monoxide (DLCO) of 55% (±19). Ninety-four (49%) patients required supplemental oxygen with a mean requirement at last followup of 2.9 liters (±1.6). At last follow-up 79 had died, with pulmonary disease accounting for 23 (29%) of deaths.

Table 1. Interstitial lung disease (ILD) with rheumatoid arthritis (RA) cohort summary

| Characteristic | Value* |
|---|---|
| Age at ILD diagnosis (years) | 66.6 (±10.9) |
| Age at RA diagnosis (years) | 57.9 (±13.4) |
| Sex, male | 108 (54%) |
| Smoking status | |
| never | 73 (37%) |
| former | 120 (60%) |
| current | 7 (4%) |
| Years from ILD to last follow-up | 4.1 (±4.0) |
| RA disease duration at ILD diagnosis | |
| median | 4.9 |
| range | –15.7 to 45.6 |
| RF positive | 161 (84%) |
| ACPA positive, % of patients tested | 110 (77%) |
| Erosive disease | 52 (28%) |
| Extra-articular RA other than pulmonary disease | 98 (49%) |
| Type of lung disease | |
| UIP/IPF | 87 (43%) |
| NSIP | 67 (33%) |
| Other | 47 (23%) |
| Pulmonary function tests (baseline) | |
| FEV1 percent predicted | 70.5 (±21.0) |
| FVC percent predicted | 71.5 (±20.5) |
| DLCO percent predicted | 55.4 (±19.4) |
| Required supplemental oxygen | 94 (49%) |
| Oxygen requirement at last visit (liters) | 2.9 (±1.6) |

**Conclusions:** In this largest single-center reported cohort of patients with RA-ILD, most patients were seropositive, male, and had a prior history of tobacco use. UIP was more common than NSIP. Almost half of patients required supplement oxygen, and nearly one third died from pulmonary disease which was the most common known cause of death.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2199

## THU0098 NO RELATIONSHIP BETWEEN LOW SERUM 25-HYDROXYVITAMIN D LEVEL AND DECREASED BONE MASS OR BONE QUALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS – TOMORROW STUDY

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**Background:** Vitamin D deficiency in patients with rheumatoid arthritis (RA) is commonly observed. Previous studies have investigated the relationship between vitamin D deficiency and RA and increased risk of cardiovascular events and the role of immunomodulation. While RA is recognized as a risk factor for osteoporosis, there are few reports examining the relationship between vitamin D level and bone mass or metabolism markers in RA patients compared with healthy controls.
**Objectives:** To examine the relationship between serum 25-hydroxyvitamin D (25(OH)D) level, bone mineral density, and bone metabolic markers of RA patients compared with age-and sex-matched healthy volunteers (Vo group) using a cross-sectional method.
**Methods:** In 2010, we began a prospective cohort study called the TOMORROW Study (UMIN000003876) which compares data from RA patients with age- and sex-matched controls (Vo) recruited through mass media. Laboratory data were collected for all participants, including 25(OH)D level, insulin resistance, bone metabolic markers (urinary pentosidine, homocysteine, collagen type 1 cross-linked N-telopeptide (NTX), and osteocalcin), and anthropometric parameters. Bone mineral density of the lower extremities and body composition were determined using whole-body dual-energy X-ray absorptiometry (DXA). The parameters were compared with healthy controls, and multiple regression analysis was carried out in the RA population only. In RA patients, disease activity score 28 was measured by clinical assessment.
**Results:** There were 413 participants (208 RA patients, 205 Vo group; 349 females; mean age of 58 years) enrolled in the study. In RA patients (mean disease duration of 13 years), bone density was significantly lower ($p<0.01$; Student's

*t*-test), and urinary NTX ($p<0.01$), pentosidine ($p<0.01$), and homocysteine ($p<0.05$) were higher compared with the Vo group. The serum 25(OH)D level was lower in RA patients compared with the Vo group ($p<0.01$) (Table). Multiple linear regression analysis in the RA population revealed no significant relationship between DXA and vitamin D level (p=0.18) or pentosidine (p=0.61).

Table 1. Differences between RA patients and healthy controls (Vo) (Student's *t*-test)

| Variables | Vo (n=205) | RA (n=208) | P-value |
|---|---|---|---|
| HbA1c | 5.1 | 5.2 | 0.37 |
| HOMA-R | 1.06 | 1.25← | 0.03 |
| Serum 25(OH)D (ng/dL) | 21.6 | 18.5↓ | <0.001 |
| DXA (g/cm$^2$) | 1.03 | 0.97↓ | <0.001 |
| Urinary NTX (nM/mM Cr) | 44.3 | 59.0← | <0.001 |
| Osteocalcin (ng/mL) | 7.3 | 7.2 | 0.81 |
| Urinary pentosidine (pmol/mg Cr) | 54.1 | 72.6← | <0.001 |
| Homocysteine (nmol/mL) | 9.1 | 10.9← | <0.001 |

**Conclusions:** No relationship was found between low vitamin D level and decreased bone mass or bone quality in RA patients.
**Disclosure of Interest:** K. Inui: None declared, T. Koike Speakers bureau: Takeda Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Chugai Pharmaceutical, Eisai, Abbott Japan, Teijin Pharma, Banyu Pharmaceutical and Ono Pharmaceutical, Y. Sugioka: None declared, T. Okano: None declared, K. Mamoto: None declared, M. Tada: None declared, H. Nakamura: None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1831

## THU0099 CARDIOVASCULAR MR (CMR) EVIDENCE FOR REDUCED LV MASS IN RHEUMATOID ARTHRITIS (RA), SUGGESTING PATHOLOGY OTHER THAN ATHEROSCLEROSIS FOR HEART FAILURE

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**Background:** An increased risk of heart failure in RA exists[1]. Aetiology is unclear with some evidence that cardiomyopathy may occur early in RA, from pathology distinct to atherosclerosis[3]. Large well characterised CMR-RA studies to investigate pathogenesis are few[2].
**Objectives:** To evaluate sub-clinical CVD in an asymptomatic-CVD established RA cohort compared to healthy controls (HC), using reference standard CMR-measured outcomes & novel CMR-measures of carotid artery.
**Methods:** 76 ACR1987 RA patients (pts) with dis.>5yrs, no CVD/diabetes, assessed for CV traditional risk factor (TRFs)/RA profile, pulse wave velocity (PWV), non-contrast 3T CMR (heart & carotids) reported by CMR-cardiologists, compared to 26 HC. Carotid measures inc. mean (MWT) & maximum (MxWT) wall thickness, wall (WVol) & luminal (LVol) volume & WVol-index (WVol-I, WVol/(WVol+LVol)). UVA variables (var.)=TRFs, BMI, waist/hip ratio (WHR), HOMA-IR, NTproBNP, dis. duration (ddur), 3vDAS28, ACPA, HAQ-DI, joint surgery hx, biologic use & PWV. MVA var.=age/sex/known associated (ass.) var./UVA r>0.3.
**Results:** Mean (SD) age (yrs) of RA pts; 60 (9.2), 74% female; HC 52 (11.4), 54% female. Median (IQR) ddur 16.5 (10.7, 25.7)yrs, 81% ACPA+ve, DAS28CRP 2.59 (1.30, 3.33), 67% on biologic. There were no significant differences in lipids/glucose/HOMA-IR between RA/HC. Trend for higher NT-proBNP in RA seen. In MVA (inc. age/sex), increasing ddur ass. with NTproBNP (0.5% rise in NTproBNP per 1% increase in ddur, p0.034). RA pts (after adj. for age/sex/TRFs) had reduced LVmass/BSA, LVEF, native T1 values & increased strain (Mid-S') vs HC; no difference seen for LVEDV, LVESV, SV, LVmass/EDV, torsion or arterial stiffness (PWV/distensibility). No significant differences in carotid measures between RA/HC seen. In RA pts, 10yr JBS2 CV risk score correlated with WVol (r0.377 p=0.004) & LVol (r0.441 p=0.001). TRFs ass. with cardiac & carotid measures in RA.

Table 1. CMR results

| CMR measure | Mean difference (95% CI) RA vs HC, p value adj. for age/sex/TRFs | RA group ass. var.: UVA (p) & MVA B (95% CI, p) |
|---|---|---|
| LVEF, % | **–2.9 (–5.1, –0.6), 0.016** | UVA: –<br>MVA: Male sex –3.26 (–5.76, –0.75) p0.012 $R^2$=0.13 |
| LVmass/BSA, g/m$^2$ | **–4.6 (–8.9, –0.2), 0.041** | UVA: Male sex p<0.001, sys BP p0.003, WHR p0.005, PWV p0.027,<br>MVA: Male sex 13.99 (9.17, 18.78) p<0.001, sysBP 0.14 (0.02, 0.25) p0.020, ever smoked 3.60 (0.03, 7.16) p0.048 $R^2$=0.62 |
| Mid S' | **0.2 (0.1, 0.3), <0.001** | – |
| Native T1, ms | **–34.8 (–64.1, –5.5), 0.021** | UVA: Ever smoked p0.035, –ve TC/HDL p0.039.<br>MVA: Ever smoking 27.10 (1.26, 52.95) p0.04 $R^2$=0.143 |
| MWT, mm | –0.01 (–0.08, 0.06), 0.790 | UVA: –; MVA:– |
| MxWT, mm | –0.05 (–0.24, 0.15), 0.646 | UVA: Ever smoked p0.049, –ve BMI p0.026.<br>MVA: – |
| WVol, ul | –5.5 (–29.0, 18.0), 0.644 | UVA: Age p0.007, ever smoked p0.010, PWV p0.047.<br>MVA: Age 1.13 (–0.25, 2.64) p0.007 $R^2$=0.25 |
| WVol-I | 0.00 (–0.03, 0.03), 0.952 | UVA: –ve HOMA-IR p0.035, –ve Hx joint surgery p0.043.<br>MVA: – |

–ve = negative correlation.

MVA (inc. age/sex), increasing ddur ass. with NTproBNP (0.5% rise in NTproBNP per 1% increase in ddur, p0.034). RA pts (after adj. for age/sex/TRFs) had reduced LVmass/BSA, LVEF, native T1 values & increased strain (Mid-S') vs HC; no difference seen for LVEDV, LVESV, SV, LVmass/EDV, torsion or arterial stiffness (PWV/distensibility). No significant differences in carotid measures between RA/HC seen. In RA pts, 10yr JBS2 CV risk score correlated with WVol (r0.377 p=0.004) & LVol (r0.441 p=0.001). TRFs ass. with cardiac & carotid measures in RA.
**Conclusions:** CMR evidence for reduced LV mass in RA, suggesting pathology other than atherosclerosis as the cause of heart failure; perhaps microvascular dysfunction. TRFs, not RA features, are important determinants of CMR measures of subclinical CVD in RA.
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## THU0100 SERUM LEPTIN AS A BIOMARKER OF FAT MASS EXCESS IN RHEUMATOID ARTHRITIS BRAZILIAN PATIENTS

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**Background:** although obesity is a risk factor for developing coronary artery disease[1] and cardiovascular diseases account for approximately half of the deaths among rheumatoid arthritis (RA) patients[2], anthropometric measures are not accurate for fat mass quantification in this population.[3]
**Objectives:** to identify a serum biomarker of fat excess in patients with RA.
**Methods:** cross-sectional study in adults with established RA. Disease activity was assessed by DAS28 and CDAI. Anthropometric measures included waist circumference (WC), weight and height for body mass index (BMI) calculation. Body composition by DXA (Hologic Discovery W, software 3.3.01) was used to fat mass excess quantification.[4] Circulating levels of IL-6, TNF alpha, IL- 1β and leptin were measured in a single sample of peripheral blood using the technique of Bead-Based Multiplex Immunoassays- Luminex; while adiponectin was measured by Enzyme-Linked Immunosorbent Assay-ELISA.
**Results:** 99 patients were included, 89.9% women, with mean age of 54.5 (±11) years and mean disease duration of 16.5 (±9.3) years. The frequency of obesity was 31.3% by BMI, 85.9% by WC and 57.6% by DXA. Mean serum leptin concentration was 24.5 (± 22.5) ng/ml. Leptin correlated with obesity by the three methods: BMI, WC and DXA. This correlation was stronger with DXA. The correlation between leptin and DXA was not influenced by DAS28, C-reactive protein, erythrocyte sedimentation rate, nor by inflammatory cytokines levels (IL -6, TNF-alpha, IL- 1β). Analysis by ROC curve determined the cut-off point of 6.52 ng/ml of leptin as obesity marker, with a sensitivity of 96.43% and a specificity of 23.81%.
**Conclusions:** serum concentration of leptin presents as a fat mass excess biomarker, being useful since more accurate diagnostic methods for measuring fat mass are not available in clinical practice.
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## THU0101 THE PREDICTORS OF FRAGILITY FRACTURE IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN OBSERVATIONAL STUDY

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**Background:** Rheumatoid arthritis (RA)is a well known risk factor for osteoporosis (OO) and is an independent risk factor in the FRAX ™ tool, additionally the femoral neck Bone mineral density (BMD) is included in the tool as a risk factor for fracture, but not the lumbar spine.
**Objectives:** To determine the predictors of fragility fractures in an observational cohort of patients with RA referred for BMD estimation, and whether using lumbar spine BMD would predit risk.
**Methods:** Patients referred for BMD estimation in a scanner in the North west of England between 2004 and 2014 with a history of RA were identified from a dual X-ray absorptiometry (DEXA) database. Demographics and other risk factors

were also recorded. Fragility fractures were also recorded. Initially those who had sustained a fracture were compared to those who had not sustained a fracture using chi squared test for categorical variables and Student's T test for continous variables. Subsequently univariate and multivariate logistic regression models were fitted. Variables included age at scan, gender, weight, height and body mass index (BMI),family history of fracture, alcohol, smoking, current steroid exposure, causes of secondary OP as per the FRAX™ definition, in addition to BMD in the lumbar spine (L1-L4) and the non-dominant femoral neck.

**Results:** 1527 patients were scanned in the referral period. Mean age at scan was 64.3 year (SD 11.6), 1207 (79.0%) were female, 406 (26.6%) had sustained a fracture. Patients who had sustained a fracture were more likely to be female 347/860 (28.8%) vs 59/320 (18.4%) ($p<0.001$) and older 65.6 years (SD11.6) vs 63.9 years (SD11.5) (p=0.01). They also had lower BMD in the lumbar spine and the femoral neck. Results of the univariate analysis unadjusted and adjusted for age and gender are shown in table 1 with significant predictors marked with an asterisk (*).

| Predictor | Unadjusted Odds ratio (95% CI) | Adjusted OR (95% CI) |
|---|---|---|
| Age at scan in decades | 1.14 (1.03,1.26*) | – |
| Female gender | 1.78 (1.31,2.43*) | – |
| Lumbar spine BMD | 0.14 (0.08,0.25*) | 0.17 (0.09,0.32)* |
| Femoral neck BMD | 0.10 (0.05,0.22*) | 0.14 (0.06,0.33)* |
| Height | 0.97 (0.96,0.98*) | 0.98 (0.97,1.00)* |
| Weight | 0.98 (0.98,1.00*) | 0.99 (0.98,1.00) |
| Smoking | 0.96 (0.76.1.21) | 1.03 (0.82,1.31) |
| Excess alcohol | 1.40 (0.81,2.42) | 1.81 (1.03,3.19)* |
| Secondary osteoporosis | 1.68 (1.21,2.33*) | 1.52 (1.09,2.12)* |
| Family history of fracture | 1.30 (0.92,1.84) | 1.31 (0.92,1.86) |
| Current Steroid exposure | 0.86 (0.68,1.08) | 0.92 (0.73,1.15) |
| Body mass index kg/m$^2$ | 0.99 (0.97,1.01) | 0.99 (0.97.1.01) |

In the multivariate model, the variables that predicted fractures in this cohort the BMD in the lumbar spine (OR 0.33 95%CI 0.14,0.80), BMD in the femoral neck (OR 0.29 95%CI 0.09,0.94)and alcohol excess (OR 2.01 95%CI 1.12,3.61)family history (OR 1.49 95%CI 1.01,2.19)and secondary osteoporosis (OR 1.50 95%CI 1.03,2.18). Using the lumbar spine only gave an area under the curve (AUC) of the model of 0.640 whilst using the lumbar spine only gave an AUC of 0.633, using both gave an AUC of 0.646.

**Conclusions:** In univariate analysis, many risk factors are associated with fracture in this cohort with RA. Using the lumbar spine BMD improved the prediction of fractures, this is not included in the FRAX™ tool and would underestimate the fracture risk in this cohort. Further models including the L1l4 BMD should be developed to more accurately predict fractures in patients with RA.

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## THU0102 PLATELET ASSOCIATED IGG IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Thrombocytopenia was sometimes shown in clinical medical treatment in patients with rheumatoid arthritis (RA). The causes of thrombocytopenia in patients with RA are various. Drug induced thrombocytopenia and idiopathic thrombocytopenia are ones of these causes. The diagnosis of thrombocytopenia is important because the method of treatment depends on it.

**Objectives:** Increased levels of platelet associated IgG (PAIgG) found in patients with idiopathic thrombocytopenia. We investigated in the relationship between platelet and PAIgG to evaluate the clinical significance in patients with RA.

**Methods:** Total 266 patients (60 males: 206 females) with RA were enrolled in this study. The serum level of PAIgG were examined. We evaluated age at onset of RA, age of PAIgG test, disease duration of RA, platelet number, platelet bindable IgG (PBIgG), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (ACPA), matrix metalloproteinase-3 (MMP-3), Disease activity score including a 28-joint count (DAS28)-CRP, DAS28-ESR, simplified disease activity index (SDAI), clinical disease activity index (CDAI), and methotrexate (MTX) dose between PAIgG(+) and (–) groups.

**Results:** PAIgG were positive in 60.9% (162/266). There were no significant differences in age at onset of RA, age of PAIgG test, disease duration of RA, PBIgG, CRP, ESR, ACPA, MMP-3, DAS28-CRP, DAS28-ESR, SDAI, CDAI, and MTX dose between PAIgG(+) and (–) groups. There were significant differences only in RF and platelet number between PAIgG(+) and (–) groups. RF were higher in PAIgG(+) than those in (–) significantly (126.4 IU/mL vs. 84.4 IU/mL, p=0.03). RF(+) rate were also higher in PAIgG(+) than those in (–) significantly (75.3%: 122/162 vs. 61.5% 64/104, p=0.02). Platelet number were lower in PAIgG(+) than those in (–) significantly (207,000/μL vs. 218,000/μL, p=0.03). However, the PAIgG(+) patients whose platelet number were under normal limit were only 11.1% (18/162). There was no significant difference compared with PAIgG(–) patients whose platelet number were under normal limit (8.7%: 9/104).

**Conclusions:** PAIgG shows high value in immune thrombocytopenia, systemic lupus erythematosus, etc. However, we found high PAIgG(+) rate in RA which usually shows thrombocytosis. Although platelet number in PAIgG(+) were lower significantly, the mean value was within normal limit. The rates under normal limit between 2 groups were not different significantly. Although PAIgG had small effect on platelet number in RA, RF were higher in PAIgG(+) significantly. Further investigation is needed to evaluate the clinical significance of PAIgG in patients with RA.

**Disclosure of Interest:** None declared

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## THU0103 IS INTERLEUKIN 17 IMPLICATED IN OSTEOPOROSIS PATHOGENESIS IN RHEUMATOID ARTHRITIS? RELATION BETWEEN IL-17 SERUM LEVEL AND FRAX INDEX IN PREMENOPAUSAL RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is one of the most common form of inflammatory arthritis. It is characterized by being chronic, progressive with systemic inflammation. Patients with RA are at an increased risk of osteoporosis (OP) and consequentaly osteoporotic fractures (OFs). Interleukin-17 (IL-17) is a cytokine expressed in inflammatory and autoimmune diseases. It plays an important role in the pathogenesis of RA and OP. Fracture Risk Assessment Tool (FRAX)is a computer-based algorithm used to measure the 10-year probability of a major osteoporotic fractures and the 10-year probability of hip fracture. Current studies focus on better assessment of risk factors of OFs in RA patients aiming to prevent them and their subsequent complications.

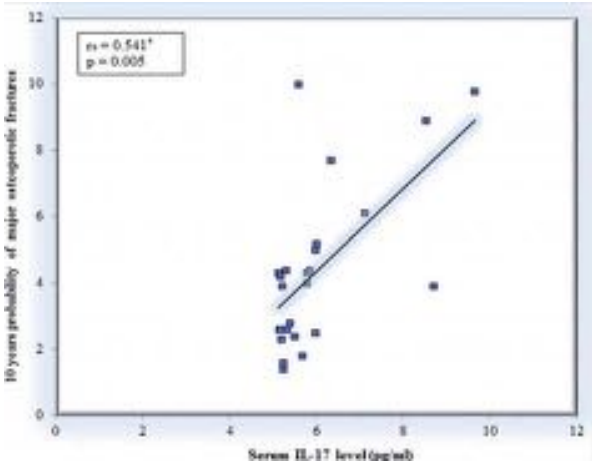
**Objectives:** To study the correlation between serum IL-17 level and FRAX index scores in pre-menopausal RA patients.

**Methods:** This study included 25 premenopausal RA patients and 20 healthy controls. Serum IL-17 level was measured by using ELISA technique, bone mineral density (BMD) measured using DEXA scan and FRAX index was calculated by using online FRAX calculator (Femoral neck BMD was used to enhance fracture risk prediction).

**Results:** Serum IL-17 level among RA patients was significantly higher than healthy controls, (5.99 ± 1.22pg/ml), (3.73 ± 2.15pg/ml) respectively with a $p<0.001$. Serum IL-17 levels showed a positive significant correlation with the FRAX index scores in RA patients.

| | Serum IL-17 | |
|---|---|---|
| | $r_s$ | *p* |
| Major osteoporotic fracture | 0.541 | 0.005* |
| Hip fracture | 0.492 | 0.013* |

$r_s$: Spearman coefficient. *Statistically significant at $p \leq 0.05$.




**Conclusions:** IL-17 is highly suspected to be implicated in the pathogenesis of OP in RA patients which may spotlight that the emergence of IL 17 blockade as a future therapy in RA is to be highlighted.

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## THU0104 LIMITED SAFETY SIGNALS, BUT NO ADVANTAGE OF COBRA-LIGHT OVER COBRA COMBINATION THERAPY 4 YEARS AFTER INITIATION OF THE COBRA-LIGHT TRIAL IN EARLY RHEUMATOID ARTHRITIS

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**Background:** COBRA and COBRA-light combination therapy are equally effective and safe treatments for early rheumatoid arthritis (RA) after 26 and 52 weeks [1,2], but long-term safety of COBRA-light therapy is unknown.
**Objectives:** To investigate survival and comorbidities of initial COBRA and COBRA-light combination therapy after a 4 year follow-up period. A detailed analysis of long-term efficacy will be presented separately.
**Methods:** In the COBRA-light trial, 164 patients with recent-onset RA were randomized to either COBRA (prednisolone 60 mg/day, tapered to 7.5 mg/day in 6 weeks; MTX 7.5 mg/wk and sulfasalazine 2 g/day; n=81) or COBRA-light therapy (prednisolone 30 mg/day, tapered to 7.5 mg/day in 8 weeks and MTX escalated to 25 mg/wk in 8 weeks; n=83). Between 26 and 52 weeks; treatment intensification of MTX and addition of etanercept was protocollized (treat-to-target). After 52 weeks, treatment was continued without protocol. Four year after trial initiation, all patients who had initiated therapy (n=162) were invited to participate in the COBRA-light extension study. All patients were interviewed and clinical records were protocollized examined for new comorbidities developed during the follow-up period.
**Results:** A total of 149 out of 162 original trial patients participated in the extension study (77 COBRA and 72 COBRA-light). During the follow-up period, 5 five patients had died: 2 COBRA (both cancer) and 3 COBRA-light (1x dementia; 2x unknown); 6 were not able or willing to participate, and 2 were in drug-free remission and out of care. After the 52 weeks trial period, 43% COBRA vs. 42% COBRA-light patients used prednisolone for ≥90 days, 34% vs. 44% switched to other DMARDs, and 39% vs. 28% used biologicals during the follow-up period. After mean 4 years follow-up, 118 patients (79% in each treatment group) had developed new comorbidities. Cardiovascular events, hypertension, hypercholesterolemia and diabetes mellitus were equally prevalent in both treatment groups (Table 1), notably angina pectoris and heart failure were not seen. Bone quality tended lower in the COBRA-light group, as evidenced by prevalence of osteoporosis on DXA (1% COBRA vs. 6% COBRA-light, p=0.20); clinical fractures (8% vs. 18%, p=0.06), and especially vertebral and rib fractures (0% vs. 6%, p=0.05). Seven patients developed cancer during follow-up: 2 COBRA (both lung cancer, both deceased during follow-up), and 5 COBRA-light (3x lung cancer, 1x basal cell carcinoma and 1x meningioma).

**Table 1.** New comorbidities developed during the 4 year follow up period of the COBRA light extension trial (n=149)

| | COBRA (n=77) | COBRA-light (n=72) |
|---|---|---|
| Any cardiovascular event | 5 (7) | 7 (10) |
| – Myocardial infarction | 1 (1) | 1 (1) |
| – Stroke [1] | 2 (3) | 5 (7) |
| – Arrhythmia | 3 (4) | 1 (1) |
| – Peripheral vascular disease | 1 (1) | 1 (1) |
| Hypertension | 7 (9) | 5 (7) |
| Hypercholesterolemia | 5 (7) | 7 (10) |
| Diabetes mellitus | 1 (1) | 3 (4) |
| Any clinical fracture | 6 (8) | 13 (18)* |
| – Hip and pelvis | 1 (1) | 2 (3) |
| – Vertebra and rib | 0 (0) | 4 (6)* |
| – Leg and ankle | 2 (3) | 1 (1) |
| – Arm and wrist | 1 (1) | 3 (4) |
| – Hand and feet | 3 (4) | 5 (7) |
| Osteoporosis at 4 year DXA (T score < -2.5 at spine and/or hip) [2] | 1 (1) | 4 (6) |
| Vertebral fracture at 4 year spine X-ray [3] | 7 (10) | 8 (13) |
| Bone necrosis | 0 (0) | 1 (1) |
| Any infection with antibiotic or antiviral drugs | 39 (51) | 38 (53) |
| Any gastrointestinal event | 3 (4) | 4 (6) |
| Glaucoma | 0 (0) | 1 (1) |
| Cataract | 5 (7) | 3 (4) |
| Cancer [1,4] | 0 (0) | 5 (7) |

*Results are reported as frequencies (%); [1]No CVA, 5x TIA, 1x eye infarct and 1x venous occlusion left eye; [2]Based on DXA's of 135 patients; [3]Based on spine X-rays of 134 patients; [4]No significant difference between treatment groups when taking into account the 2 deceased COBRA cancer patients; *In each treatment group, 1 patient had a basal cell carcinoma relapse during the follow-up period; *Trend for significant difference between treatment groups (p=0.10)*

**Conclusions:** Over a 4 year follow-up period, early RA patients initially treated with COBRA and COBRA-light therapy showed limited and similar safety signals in terms of survival and major comorbidities, except for the higher incidence of clinical fractures in the COBRA-light group, which could not be explained by a significant higher prevalence of osteoporosis. Overall, attenuating the original COBRA regimen did not further improve its favorable safety profile.

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[1] Den Uyl, ARD 2014;
[2] Ter Wee, ARD 2015

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## THU0105 FRAX 10-YEAR FRACTURE RISK IN RHEUMATOID ARTHRITIS - ASSESSMENTS WITH AND WITHOUT BONE MINERAL DENSITY MAY LEAD TO VERY DIFFERENT RESULTS IN THE INDIVIDUAL PATIENT

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**Background:** Osteoporosis is a well-known complication in patients with rheumatoid arthritis (RA). The FRAX tool is an online computer-based algorithm developed by WHO to evaluate the 10-year risk of an osteoporotic hip fracture and major fracture (hip, clinical spine, proximal humerus or forearm fracture) (ref). Clinical risk factors include age, height and weight and dichotomized risk factors comprising prior fragility fracture, parental history of hip fracture, current tobacco smoking, ever use of long-term oral glucocorticoids, RA, other causes of secondary osteoporosis and alcohol consumption. Bone mineral density (BMD, g/cm$^2$) of the femoral neck can be optionally included as a risk factor but FRAX does not provide recommendations on which side to measure BMD. The usability of fracture risk assessment without BMD has been evaluated on group level, but the agreement between fracture risks assessed with and without BMD in individual patients has not met much attention.
**Objectives:** To investigate the intra-individual agreement between 10-year fracture risk calculated with and without BMD in patients with RA.
**Methods:** Data from 50 RA patients registered in the Danish rheumatology registry (DANBIO) were used for analysis. BMD of the left and right femoral neck was measured using a Lunar iDXA-scanner (GE, Lunar) by experienced laboratory technicians. The intra-individual agreement between fracture risk assessed with and without BMDs was examined using the Bland-Altman method. 95% lower and upper limits of agreement (LLoA and ULoA) were estimated as the mean difference (bias) in percent point (pp) between paired measurements ± 1.96SD (2.5% - 97.5% range for side comparison due to screwed distribution). Student's t-test was used for comparison on the group level.
**Results:** Mean age was 63.6 ± 11.7 (range 40–50) years, mean disease activity score (DAS28-CRP) 3.3 ± 3.5 and the mean femoral neck T-score -1.4 ± 1.2. 64% of the patients were on oral steroids, 50% on DMARDs and 46% on biological treatment (±DMARD). The mean 10-year risk of a major fracture and a hip fracture calculated with BMD was 22.9 ± 15.8% and 8.5 ± 10.8%, respectively. There was an overall trend of a greater bias, the higher the FRAX fracture risk but the bias was lower and LoA more narrow in osteopenic and osteoporotic patients compared to patients with normal BMD. The LLoA and ULoA [bias] for major fracture risk calculated with and without BMD (side with lowest value) were -14.5 pp and 20.4 pp [2.93 pp, $p<0.05$]. For hip fracture risk, LLoA and ULoA were -14 pp and 23.2 pp [4.6 pp, ($p<0.001$)]. When calculating fracture risk based on the side with lowest versus highest BMD, the LLoA and ULoA for hip fracture were 0 pp and 6.8 pp [0.8 pp, $p<0.001$] and for major fracture 0 pp and 7.3 pp [1.0 pp, $p<0.001$].
**Conclusions:** The FRAX 10-year fracture risk estimated with and without BMD may disagree to a substantial degree in individual RA patients and should therefore not be considered inter-changeable in the daily clinic. Choice of measurement side may also impact the fracture risk assessment, especially in the individual patient.

**References:**
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## THU0106 IDENTIFICATION OF MARKERS ASSOCIATED WITH THE OCCURRENCE OF INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is a systemic autoimmune disease, the most severe manifestation being interstitial lung disease (ILD). Therapeutic options are undefined and ILD is one of the leading causes of mortality for RA patients. A better characterization of RA-ILD–associated factors may improve the risk stratification of RA patients.
**Objectives:** To identify variables associated with ILD occurrence in RA.
**Methods:** RA-ILD patients (RA-ILD+) in a French multicentric cohort were compared to monocentric RA cases without ILD (RA-ILD-). All patients fulfilled 2010 ACR/EULAR criteria for RA and had a HRCT chest scan for suspected ILD or during a pre-biologic assessment. ILD was defined by HRCT results. Because ILD occurrence increases with RA duration, RA-ILD+ and RA-ILD- patients were matched by disease duration (1:1). Demographic data, clinical features of RA and treatment modalities before the ILD diagnosis were collected. Results significant on univariate analysis ($P<0.15$) were selected for multivariate analysis to identify variables independently associated with RA-ILD. Duration of methotrexate (MTX) and anti-TNF agent use was adjusted to mean MTX or anti-TNF duration before ILD diagnosis.
**Results:** Among 253 consecutive RA patients, 81 were male (32.02%), 112 (48.07%) were smokers, mean age at RA onset was 48.11 ± 16.33 years, and mean RA duration 11.69 ± 10.10 years; 199 patients (85.78%) were ACPA-positive and 171 (71.85%) had erosive status; 134 (60.63%) received MTX and 63 (28.25%) a TNF inhibitor. Among the 253 patients, 138 (54.55%) had ILD. Among the RA-ILD+ patients, 72 (74.23%) had UIP and 25 (25.77%) NSIP. On univariate analysis, ILD was associated with older age at RA onset (52.69 ± 15.00 *vs* 42.86 ± 16.26 years, P=0.0001), male sex (40.68% *vs* 21.74%, P=0.001), ACPA rate ≥60 N (20.63% *vs* 6.41%, P=0.012), less use of anti-TNF agents and MTX (14.55% *vs* 41.59%, P=0.001, and 50.94% *vs* 69.57, P=0.005, respectively) and lower MTX dosage (15.26 ± 4.44 *vs* 16.83 ± 4.31 mg/week, P=0.046). There was no difference for erosive status. On multivariate analysis, ILD was independently associated with older age at RA onset ($P<0.0001$), male sex ($P=0.0006$), less use of MTX ($P=0.015$) with lower dosage ($P=0.005$) and less use of anti-TNF agents ($P=0.004$).
**Conclusions:** As previously reported, ILD was independently associated with male sex as well as older age at RA onset and, of interest, less use of MTX and anti-TNF biologics before ILD diagnosis, even though patients did not differ in erosive status. Larger prospective studies are required to further elucidate the role of DMARDs and anti-TNF biologics in ILD occurrence and progression in RA patients.
**Disclosure of Interest:** None declared
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## THU0107 PREVALENCE OF POSITIVE QUANTIFERON-GOLD TEST IN ADULT PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND ITS SIGNIFICANCE IN DEVELOPING COUNTRIES

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**Background:** The detection of latent TB infection (LTBI) and institution of appropriate prophylactic therapy is an essential requirement before prescribing biologic disease modifying anti-rheumatic drugs (DMARDs) to patients with rheumatoid arthritis. With several biologics going off-patent and a mushrooming of biosimilars, biologics which were hitherto unaffordable and unavailable in the developing world are soon likely to be widely available. In view of the high prevalence of active tuberculosis (TB) and LTBI in these regions, the increased prescribing of biologics will raise some pertinent questions in the context of LTBI testing, test result interpretation and management.
**Objectives:** The objective of this study was to identify the prevalence of latent TB infection in a geographically diverse population of patients with Rheumatoid Arthritis eligible for treatment with biologic DMARDs.
**Methods:** A retrospective analysis of QuantiFERON-TB Gold (QFT-G) test results of samples received at Quintiles Central Laboratories from Jan 2010 to Dec 2013 was conducted. All samples were from adult subjects who were consented and screened for clinical trials. All subjects had active Rheumatoid arthritis of at least 6-month duration as per ACR 1987 criteria and had inadequate response to conventional DMARDs including MTX therapy.
**Results:** The QFT-G test results of 4471 samples were analyzed. Samples were received from 40 countries with 66% from Europe, 18% from USA and Canada, 18% from APAC region and 5% from Latin America.
The total incidence of positive QFT-G in this sample size was 12.3% with range of positivity extending from 2.4% in Canada to 37.8% in China. Romania, Korea, Bosnia and Mexico also had significant QFTG positivity of 31.5%, 30.2%, 28.7% and 20.3% respectively. The total incidence of indeterminate results to QFT-G test was 5.2%.
The Asian countries predictably showed a higher prevalence of LTBI, with 25.2% of test results being positive. Eastern Europe and Latin America followed with 13.1% and 11.5%, while Western Europe had 8.2% and USA & Canada had only 4.5% positive QFT-G test results
**Conclusions:** With increasing availability of biologics in regions with high tuberculosis disease burden there appears to be a requirement to develop country-specific guidelines for prophylaxis of latent TB tailored to the needs of the populace. In terms of duration of prophylaxis, will the recommended 6-month INH prophylactic regimen be adequate to effectively prevent re-activation of TB in the developing countries? As patients with Rheumatoid Arthritis continue to take biologic DMARDs for longer durations of time, will a life-long preventive strategy be necessary? There is also concern for presence of INH resistance in these regions, effectively bringing into play more toxic prophylactic regimens for prevention of tuberculosis. National guidelines for patient pathways and selection of biologic may be the required solution to enable patients of rheumatoid arthritis to avail of better therapies while avoiding potential risks.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1050

## THU0108 CLOSING THE AUDIT CYCLE: HAVE CARDIOVASCULAR RISK ASSESSMENT AND MANAGEMENT IN RHEUMATOID ARTHRITIS PATIENTS IMPROVED?

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**Background:** Patients who suffer from rheumatoid arthritis have an increased risk of morbidity and mortality from cardiovascular disease. This is due to the high prevalence of traditional risk factors and the effect of systemic inflammation.
**Objectives:** The aim of the audit was to determine whether the cardiovascular risk assessment and management in rheumatoid arthritis patients at Mater Dei Hospital is in concordance with the recommendations by the European League Against Rheumatism (EULAR).
**Methods:** An audit was carried out retrospectively on 91 patients who suffer from rheumatoid arthritis by using the medical notes to collect data on demographics, co-morbidities, drug history and cardiovascular risk assessment and management over a two year period (August 2010 to July 2012). The results of the first audit were then disseminated through the rheumatology department and a form for cardiovascular risk assessment and management in rheumatoid arthritis patients was implemented. The audit was repeated on 107 patients and data was collected retrospectively over the two year period starting from January 2013 to December 2014.
**Results:** Documentation of cardiovascular risk factors over the two year period audited improved as follows from the first to the second audit: weight in 27.5% to 52.3%, height in 0% to 27.1%, BMI in 0% to 10.3%, smoking status in 72.5% to 93.5%, blood pressure in 72.5% to 92.5%, blood glucose in 72.5% to 97.1% and lipid profile in 54.9% to 96.3%. Documentation of smoking cessation advice improved from 15.8% to 41.1% and advice on other lifestyle changes improved from 14.3% to 18.7%. Moreover calculation of DAS28 over a one year period improved from 20.9% to 51.4%.
In the first audit, 13.8% of patients who had complete data and in whom the ten year cardiovascular risk could be calculated (29 patients), would benefit from the use of a statin according to the guidelines (and were not currently receiving one). In the re-audit, this decreased to 8.6% of such patients (93 patients).
In the second audit it was noted that the form that had been introduced for cardiovascular risk assessment was used in 15% (16 patients). The documentation of lifestyle advice was significantly higher ($p<0.001$) in the group of patients in whom the form was used. The same applies for documentation of weight ($p<0.001$), height ($p<0.001$), BMI ($p<0.001$) and calculation of DAS28 over a one year period ($p<0.001$).
The prevalence of diagnosed hypertension in our cohort of rheumatoid arthritis patients was 49.0%; diabetes was 19.7%; hyperlipidaemia was 21.8%; and ischaemic heart disease was 8.8%.
**Conclusions:** Cardiovascular risk factors are highly prevalent in rheumatoid arthritis patients. This audit showed that cardiovascular risk assessment and management improved through raising awareness of its importance in the rheumatology department as well as the implementation of the cardiovascular risk assessment form.
**References:**
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risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis, Feb 2010; 69: 325–33.
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## THU0109 VACCINATION RATES IN ADULTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES AND THE PATIENTS' PERSPECTIVE ON THEIR INFECTION RISK

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**Background:** Patients suffering from autoimmune rheumatic diseases are at increased risk of developing infections, especially if they are on immunomodulatory treatment.
**Objectives:** The aim of the study was to determine whether vaccination in adult patients with autoimmune inflammatory rheumatic diseases (AIIRD) attending the Rheumatology Clinic at Mater Dei Hospital, is in concordance with the European League Against Rheumatism (EULAR) guidelines.
**Methods:** 60 patients with AIIRD attending the Rheumatology Clinic were recruited for the audit. Demographic data and vaccination status were completed using the medical notes. Further information on their vaccination history and their perceived importance of vaccination was obtained by interviewing the patients. Approval to carry out this study was obtained from the University Research Ethics Committee.
**Results:** The study included patients with a variety of AIIRD including rheumatoid arthrtitis, systemic lupus erythematosus, ankylosing spondylitis and psoriatic arthritis. 58% were females and the mean age was 62.4 years (range 24 to 81 years). Out of the 60 patients audited, 43 were on a synthetic disease modifying anti-rheumatic drug (sDMARD) alone, 6 were on a biologic drug alone, and 3 were on a combination of both a biologic drug and sDMARD. 13 patients were on glucocorticoids; of which 12 were also receiving a sDMARD. Information on vaccination history was found in the medical notes in only 2 cases.
The influenza vaccine was taken in 44 patients (73.3%) of which it was taken yearly in 30 patients. Out of those who had taken the influenza vaccine, most of them claimed they had been advised to do so either by their general practitioner (43.2%) or through public health campaigns (27.3%). 32 patients (53.3%) claimed that they had the intention to take it the following year. The proportion of patients who took the influenza vaccine yearly was significantly higher in those above 65 years ($p<0.001$) and in those who had co-morbidities (including lung disease, diabetes and ischaemic heart disease) ($p=0.024$). 5 patients (8.3%) claimed they had taken the pneumococcal vaccine. All of these claimed they had been advised to do so by a hospital doctor. 38.3% claimed that they knew that they were at increased risk of infections because of their condition or treatment. Only 6.7% stated that they had been advised to take vaccination because of this.
**Conclusions:** Even though this study may have under-estimated vaccination rates and advice given to patients because of recall bias, it has clearly shown that improved patient education on their infection risk and need for vaccination is required. This can be encouraged by having structured documentation of patients' vaccination status in the medical notes and by raising awareness of its importance within the Rheumatology Department.
**References:**
[1] Van Assen S, Agmon-Levin N, Elkayam O et al. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 2001; 70:414–422.
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## THU0110 EFFECTIVENESS OF BIOLOGIC AND NONBIOLOGIC ANTIRHEUMATIC DRUGS ON ANEMIA IN ADULT PATIENTS (PTS) WITH RHEUMATOID ARTHRITIS (RA): NEW EVIDENCE FROM REAL-WORLD DATA

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**Background:** Anemia, a common complication of RA, has a negative impact on RA symptoms and QOL and is associated with a more severe form of RA. Roles of biologic DMARDs (BDMARDs), including the IL-6 pathway–inhibiting biologic tocilizumab (TCZ), in the pathophysiology of anemia have not been well explored at the population level.
**Objectives:** Evaluate the impact of treatment (Tx) with nonbiologic (NB) and BDMARDs on hemoglobin (Hb) and hematocrit (Hct) in a real-world setting.
**Methods:** Using the GE EMR database, a longitudinal cohort study was conducted on 153,672 adult RA pts in the US who had ≥6-mo follow-up. 4 mutually exclusive DMARDTx groups (TxGs) were identified: TCZ, tofacitinib (TOFA), other BDMARDs (OBDMARD), and other NBDMARDs (ONBDMARD). To evaluate changes in Hb and Hct at 6 and 12 mo from index date (ID) in different TxGs, unadjusted and adjusted mean (95% CI) changes were obtained, adjusting for age, sex, smoking status, RA duration, concomitant medications, CRP, and other covariates. Separate analyses were conducted for pts with Hb <12/13.5 g/dL for women/men (anemic).
**Results:** Demographics of the cohort were: 55 y mean age, 76% female, 59% white, 57% current or ex-smokers, 44% obese (mean BMI 30 kg/m$^2$). 2% of pts had ischemic heart disease, 2% renal disease, and 7% diabetes. Mean Hb and Hct levels at ID across TxGs were 13.3 g/dL and 40%. Average CRP (1.6 mg/dL) and ESR (23 mm/h) were clinically similar across TxGs at ID. Adjusting for covariates, increases in Hb and Hct levels at 6 and 12 mo were significantly higher in the TCZ group vs the other TxGs (Table). Among anemic pts at ID, increases in Hb and Hct at 6 mo were significantly higher in the TCZ group vs the other TxGs. Significantly greater reductions in ESR and CRP levels over all follow-up periods were observed in the TCZ group vs the other TxGs.
**Conclusions:** This study suggests significant increases in Hb and Hct levels after TCZ therapy vs other nonbiologic and biologic therapies in RA pts with anemia, in line with the potential role of IL-6 in RA pts with anemia. Further study is needed to better evaluate the role of IL-6–based OBDMARDs as a Tx option for RA pts with anemia.
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## THU0111 BIOLOGICS DISCONTINUATION AND BMI PREDICT RA FLARE RISK AFTER HIP AND KNEE ARTHROPLASTY

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**Background:** Immunosuppressive medications are often stopped prior to arthroplasty to mitigate infection risk, but this may increase the risk of disease flares post surgery in patients with rheumatoid arthritis (RA).
**Objectives:** To describe rates, characteristics, and risk factors for flare after total hip (THA) and total knee (TKA) arthroplasty surgery.
**Methods:** Pre- and post-operative characteristics were examined in 58 RA patients undergoing TKA/THA. Perioperative medication use was standard of care: biologics were stopped before surgery, while steroids and methotrexate (MTX) continued. Clinicians evaluated RA clinical characteristics, on average, 0–2 weeks before and 6 weeks post-surgery. Post-surgery, patients completed weekly questions about RA symptoms, impact, and flare status using the OMERACT Flare Questionnaire. Baseline characteristics were compared using t-tests and chi-square, and multivariate logistic regression was used to identify baseline characteristics associated with post-surgical RA flares.
**Results:** Of 68 patients, 10 (15%) were flaring prior to surgery and were excluded. 88% met 2010/1987 RA criteria; those who did not meet criteria were included by rheumatologist diagnosis. Patients had a mean [SD] age of 61 [12], BMI of 30.6 [7.2], and RA duration of 16 [12] yrs. 59 (87%) were female, 53 (78%) were white, 33 (49%) were having THA, and 35 (52%) were on biologics. 35 (60%) had flared by 6 weeks post surgery. At baseline, flarers had significantly ($p<.05$) higher BMI, higher disease activity indicators (DAS28, RAPID3), inflammatory markers (ESR, CRP), and pain, and more were undergoing THA and used biologics (Table 1). After controlling for age, surgical joint, and baseline DAS28, the odds of flaring by 6 weeks post-surgery were significantly higher in patients who had

**Abstract THU0110** – Table 1. Adjusted mean (95% CI) change in study parameters at 6 and 12 mo after initiation of Tx

| TxG | Follow-up, mo | All, n | Anemia at ID, n [%] | Δ Hb, g/dL | | Δ Hct, % | |
|---|---|---|---|---|---|---|---|
| | | | | All | Anemia at ID | All | Anemia at ID |
| TCZ | 6 | 2,008 | 384 [19] | 0.22 (0.18, 0.27) | 0.59 (0.47, 0.71) | 0.38 (0.24, 0.52) | 1.18 (0.81, 1.54) |
| | 12 | 1,470 | 267 [18] | 0.23 (0.17, 0.29) | 0.73 (0.57, 0.90) | 0.49 (0.32, 0.67) | 1.45 (1.00, 1.90) |
| TOFA | 6 | 900 | 171 [19] | –0.10 (–0.16, –0.03) | 0.23 (0.05, 0.41) | –0.34 (–0.54, –0.14) | 0.57 (0.03, 1.10) |
| | 12 | 412 | 74 [18] | 0.03 (–0.09, 0.15) | 0.28 (–0.12, 0.69) | –0.03 (–0.37, 0.31) | 1.07 (–0.10, 2.25) |
| OBDMARD | 6 | 41,881[a] | 7,982 [19] | 0.08 (0.07, 0.09) | 0.37 (0.35, 0.39) | 0.18 (0.16, 0.21) | 0.76 (0.70, 0.82) |
| | 12 | 35,632[b] | 6,764 [19] | 0.08 (0.07, 0.09) | 0.46 (0.44, 0.49) | 0.20 (0.18, 0.23) | 1.02 (0.95, 1.10) |
| ONBDMARD | 6 | 59,307 | 11,922 [20] | –0.05 (–0.05, –0.04) | 0.25 (0.24, 0.27) | –0.11 (–0.13, –0.09) | 0.53 (0.48, 0.59) |
| | 12 | 47,898 | 9,627 [20] | –0.05 (–0.06, –0.04) | 0.34 (0.32, 0.36) | –0.08 (–0.11, –0.06) | 0.74 (0.67, 0.80) |

[a]95% TNF-α inhibitors. [b]96% TNF-α inhibitors.

discontinued biologics (OR 14.9, 95% CI 2.0, 112.0) or were obese (OR 6.0, 95% CI 1.1, 33.0).

Table 1. Characteristics of RA patients who did and did not flare in the first 6 weeks post hip or knee arthroplasty (N=58)

| | Flare (n=35) | No Flare (n=23) | Significance |
|---|---|---|---|
| Age (yrs) | 58.2 (13.5) | 63.9 (10.4) | 0.073 |
| Female Sex | 32 (91%) | 18 (78%) | 0.155 |
| **BMI** | **32.6 (7.2)** | **28.6 (6.5)** | **0.040** |
| Minority Race | 10 (29%) | 2 (9%) | 0.099 |
| **Hip arthroplasty** | **22 (63%)** | **6 (26%)** | **0.006** |
| HOOS | 39.8 (21.9) | 52.2 (22) | 0.230 |
| KOOS | 44.0 (27.5) | 44.9 (14.2) | 0.914 |
| RA Duration (yrs) | 16.4 (12.0) | 16.1 (13.2) | 0.920 |
| **DAS28** | **4.1 (1.2)** | **2.9 (1.3)** | **0.001** |
| **RAPID3** | **16.0 (4.1)** | **13.2 (5.4)** | **0.032** |
| **ESR (mm/hr)** | **23.9 (20.2)** | **11.0 (11.2)** | **0.003** |
| **CRP (mg/dl)** | **2.3 (3.6)** | **0.9 (0.8)** | **0.043** |
| MD Global | 4.1 (1.6) | 3.3 (1.9) | 0.092 |
| Patient Global | 5.1 (1.9) | 4.0 (2.5) | 0.064 |
| **Pain (10mm VAS)** | **7.0 (2.0)** | **5.7 (2.7)** | **0.053** |
| MD HAQ | 3.9 (1.6) | 3.5 (1.5) | 0.282 |
| **Biologics** | **24 (69%)** | **7 (30%)** | **0.004** |
| MTX | 20 (57%) | 14 (61%) | 0.778 |

Data shown as mean (SD) or n (%).

**Conclusions:** Flares are frequent in RA patients undergoing arthroplasty, particularly THA. Discontinuing biologics and obesity significantly increased the risk of flaring post-arthroplasty.
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## THU0112 PREVALENCE AND RISK FACTORS FOR NEW VERTEBRAL FRACTURES IN PATIENTS WITH RA: FIVE-YEAR FOLLOW-UP OF THE TOMORROW STUDY

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**Background:** Rheumatoid arthritis (RA) is one cause of secondary osteoporosis [1]. Multifactorial osteoporosis can be due to the disease itself, a decrease in physical activity, treatment with glucocorticoids, and being postmenopausal. Accelerated generalized bone loss often leads to increased risk of vertebral fractures [2]. We started a prospective cohort study (TOtal Management Of Risk factors in Rheumatoid arthritis patients to lOWer morbidity and mortality: TOMORROW study, UMIN000003876) to compare risk factors for osteoporosis between patients with RA and controls.
**Objectives:** We previously reported that the prevalence of vertebral fractures is significantly higher in patients with RA than controls. We compared the prevalence of new vertebral fractures and associated risk factors between patients with RA and controls based on the 5-year follow-up findings of the TOMORROW study.
**Methods:** This study included 208 patients with RA (among whom 112 were medicated with biological agents and 96 received conventional therapy) and 205 age- and sex-matched healthy volunteers (n=413). Vertebral fractures evaluated using thoracolumbar spine X-rays, whole body bone mineral density (BMD) assessed using a QDR-4500 (Hologic, Marlborough, MA, USA) and bone metabolic markers were compared in 2010, 2011, and 2015. The prevalence of new vertebral fractures and associated risk factors were evaluated.
**Results:** Thoracolumbar spine radiographs and clinical data were analyzed from 182 patients with RA and 190 controls. More new vertebral fractures were found in the patients than in the controls (26 [14.3%] vs. 14 [7.4%]; *P*=0.03) and they were likely to be more severe in the patients. The SQ grade was $\geq$2 in 53.8% and 42.9%, respectively, and more than one new vertebral fracture was found in 26.9% and 21.4%, respectively of the patients and controls. Logistic regression analysis of patients with RA selected previous vertebral fracture (adjusted OR, 7.88; 95% CI, 2.00–31.0), persistent low BMD (adjusted OR, 5.11; 95% CI, 1.13–23.1), glucocorticoid use (adjusted OR, 3.71; 95% CI, 1.14–12.0), and age (adjusted OR, 1.07; 95% CI, 1.01–1.14) as risk factors for new vertebral fractures.

Table 1. Logistic regression anlysis

| | New vertebral fractures (n=25) | No new fractures (n=157) | OR (95% CI) | *P* value |
|---|---|---|---|---|
| Age | 71.8 (8.0) | 62.0 (12.6) | 1.07 (1.01–1.14) | 0.034 |
| Female | 23 (92.0) | 130 (82.8) | 0.22 (0.03–1.44) | 0.114 |
| Weight | 51.7 (9.3) | 55.1 (10.5) | 0.99 (0.93–1.04) | 0.615 |
| Bisphosphonate medication | 12 (48.0) | 54 (34.4) | 0.33 (0.10–1.04) | 0.058 |
| Previous vertebral fracture | 22 (88.0) | 60 (38.2) | 7.88 (2.00–31.0) | 0.003 |
| Glucocorticoid use | 8 (32.0) | 27 (17.2) | 3.71 (1.14–12.0) | 0.029 |
| Persistent low BMD | 5 (20.0) | 6 (3.8) | 5.11 (1.13–23.1) | 0.034 |

**Conclusions:** New vertebral fractures were significantly more frequent in patients with RA during follow-up for five years. Pre-existing vertebral fracture and persistent low BMD were risk factors for new vertebral fractures.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1870

## THU0113 GENETIC VARIATIONS IN THE ALANINE-GLYOXYLATE AMINOTRANSFERASE-2 (AGXT-2) GENE ARE NOT RELATED TO LEVELS OF DIMETHYLARGININES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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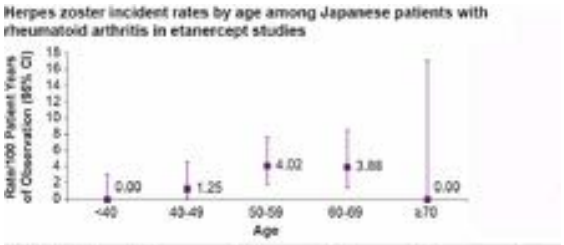
**Background:** Rheumatoid arthritis (RA) is associated with high rates of cardiovascular (CV) events and increased CV morbidity and mortality mainly due to coronary and cerebrovascular atherosclerotic disease. Asymmetric (ADMA) and symmetric (SDMA) dimethylarginines are endogenous inhibitors of nitric oxide synthase and have been repeatedly linked with adverse CV outcomes in the general population and various disease settings. ADMA and SDMA levels differ in RA individuals compared to non-RA subjects but whether such abnormalities are driven by genetic variations remains under investigation.
**Objectives:** The aim of the current study was to investigate the effect of alanine-glyoxylate aminotransferase-2 (AGXT-2) gene polymorphisms on circulating levels of ADMA and SDMA in RA patients.
**Methods:** Serum ADMA and SDMA levels were measured in 201 individuals with RA [155 females median age 67 (59–73)]. Two tag SNPs in AGXT-2 gene – rs37369 and rs28305 – were genotyped. Distributions of SDMA and ADMA were skewed, hence comparisons across the gene polymorphisms were performed using Mann-Whitney tests, and summarised using medians and interquartile ranges. Multivariate analysis examined each of the genes after adjustment for parameters of systemic inflammation, insulin resistance and renal function namely [erythrocyte sedimentation rate (ESR), quantitative insulin sensitivity check index (QUICKI) and estimated glomerular filtration rate (EGFR)] which we have previously shown affect ADMA and SDMA levels in RA.
**Results:** Univariable analysis found no evidence to suggest that either SDMA or ADMA differed significantly between the categories of rs37369AGXT2 (p=0.911, 0.507) or rs28305AGXT2 (p=0.233, 0.501). A multivariable analysis was then performed, which accounted for potential confounding factors. This showed ESR ($p<0.001$) and EGFR (p=0.007) to be significantly associated with ADMA, whilst QUICKI (p=0.029) and EGFR ($p<0.001$) were significantly associated with SDMA.
**Conclusions:** Our study in a well-characterized RA population did not show any associations between serum concentrations of dimethylarginines and gene variants of AGXT2, as reported to occur in the general population and patients with diabetic mellitus.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2082

## THU0114 INCIDENCE OF HERPES ZOSTER AND MALIGNANCY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ETANERCEPT

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**Background:** Both herpes zoster (HZ) and malignancies have been reported

in patients treated with TNF blockers such as etanercept (ETN). In Japanese patients with RA, information regarding the incidence of HZ and malignancy following long-term treatment with TNF blockers is limited.
**Objectives:** The objective of this study was to analyse the incidence rates (IR) of HZ and malignancy in Japanese patients with RA treated with ETN in order to expand the safety data set available for this patient population.
**Methods:** Data were pooled from 4 clinical trials of ETN in Japanese patients with RA. Two studies were double-blind trials of 10 and 25 mg ETN vs placebo (study 202) or methotrexate (study 315-JA), and were of 12 and 52 weeks duration, respectively. The other 2 studies were open-label, long-term trials of ETN (studies 310-JA and 313-JA) and were of 183 and 134 weeks duration, respectively. Crude IR for HZ and malignancy per 100 patient-years, with 95% confidence intervals (95% CI), were calculated and the rates were stratified by age and time of symptom development.
**Results:** A total of 521 patients with RA were included in this analysis. Mean age was 51.9 years and 81.6% of patients were female. Mean and standard deviation (SD) duration of RA was 5.2 ± 6.5 years, and the mean (SD) disease activity score 28-erythrocyte sedimentation rate was 6.15 ± 1.20. Following ETN treatment, 18 incidences of HZ in 17 patients were reported. The IR/100 years [95% CI] for the entire population was 2.5 [1.45, 4.00]. IR of HZ was highest in the 50–59 age bracket, followed by the 60–69 age bracket (Figure). IR [95% CI] was highest during the first 6 months of treatment with ETN (3.81/100 patient years [1.74, 7.23]) and subsequently declined with a stable cumulative IR seen up to 48 months of treatment (2.50/100 patient years [1.45, 4.00] across the entire treatment period). In addition, 4 incidences of malignancy in 4 patients were reported following treatment with ETN. There was 1 incidence of hypopharyngeal cancer which occurred in the first 6 months of treatment, 2 incidences of breast cancer, each occurring between Months 6–12 of treatment, and 1 incidence of liposarcoma, which occurred between Months 30–36 of treatment with ETN. IR/100 patient years [95% CI] for malignancy was 0.57 [0.15, 1.46].




**Conclusions:** In Japanese patients with RA treated with ETN, increased IR of HZ in patients aged over 50 was observed. This trend is consistent with previous observations in the Japanese general population. IR of HZ was similar to that seen in a study of Japanese patients with RA treated with the IL-6 blocker tocilizumab (2.29/100 patient years),[1] and might be higher compared with a large cohort study of Japanese patients with RA (2005–2010) where only 3% of patients used a biological treatment for RA (0.91/100 patient years).[2] Malignancies occurred in a small number of patients with limited exposure, and there was no increase in the cumulative IR of malignancy during the treatment period.
Tsutomu Takeuchi and Naonobu Sugiyama are equally credited first authors.
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**Disclosure of Interest:** T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahikasei Pharma Corp., and Taisho Toyama Pharmaceutical Co., Ltd.,SymBio, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., and Asahi Kasei Medical K.K.,abbivie GK, Daiichi Sankyo Co.,Ltd., Bristol–Myers K.K., Nipponkayaku Co.Ltd., Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co,. Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Astellas Pharma, and Diaichi Sankyo Co.,Ltd., Celtrion, Nipponkayaku Co.Ltd, N. Sugiyama Shareholder of: Pfizer, Employee of: Pfizer, N. Miyasaka Grant/research support from: AbbVie, Astellas, Chugai, Eisai, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Corporation and Takeda., Y. Morishima Shareholder of: Pfizer, Employee of: Pfizer, H. Yuasa Shareholder of: Pfizer, Employee of: Pfizer, N. Sugiyama Shareholder of: Pfizer, Employee of: Pfizer
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## THU0115 DEPENDENCE OF ARTERIAL PRESSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS ON THE GENOTYPE OF BCL1 POLYMORPHISM IN GLUCOCORTICOID RECEPTOR GENE

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**Objectives:** The objective is to study the incidence of arterial hypertension in patients with rheumatoid arthritis in regard to the genotype of BCL1 polymorphism in the glucocorticoid receptor gene.
**Methods:** 161 subjects with rheumatoid arthritis aged 40 years and older were investigated by means of instrumental, clinical and laboratory examinations. Rheumatoid arthritis was diagnosed according to ACR/EULAR Classification Criteria (2010). Arterial hypertension was diagnosed, when systolic arterial pressure was at or above 140 mmHg and diastolic arterial pressure – at or above 90 mmHg. Bcl1 polymorphism in exon 2 was defined by means of polymerase chain reaction with subsequent analysis of restriction fragment length polymorphism by I. Fleury et al. (venous blood was taken for the study). Statistical analysis was performed using SPSS–17 program.
**Results:** The patients with rheumatoid arthritis revealed the following: 10 patients had hypotension (6.2%); 60 subjects had normal arterial pressure (43.5%); 91 patients had arterial hypertension (56.5%). Of those having hypotension, 4 patients had C/C genotype (8.9%), 4 individuals presented with C/G genotype (5.1%) and 2 – with G/G genotype. Among the patients with normal pressure, 22 subjects were homozygous for the C allele (48.9%), 32 were heterozygous (40.5%) and 6 were homozygous for the G allele (16.2%). In the hypertensive group 19 individuals were homozygous for the C allele (42.2%), 43 were heterozygous (C/G allele) (54.4%) and 29 were homozygous for the pathologic G allele (78.4%). A significant difference was determined by Pearson's chi-squared test (p=0.02) as for the genotype distribution in patients with rheumatoid arthritis and different levels of arterial pressure. Analysis of frequency of arterial pressure levels in these patients demonstrated an association between arterial hypertension and G/G genotype.
**Conclusions:** An association was found between the Bcl1 polymorphism in glucocorticoid receptor gene and arterial pressure level in patients with rheumatoid arthritis. A strong association between arterial hypertension and G/G genotype was proved.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1126

## THU0116 SINGAPORE PATIENTS WITH RHEUMATOID ARTHRITIS HAVE A HIGHER INCIDENCE OF SOLID-ORGAN MALIGNANCIES THAN THE GENERAL POPULATION: FINDINGS FROM THE TTSH RA REGISTRY

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**Objectives:** Patients with rheumatoid arthritis (RA) have been shown to have an increased risk of developing malignancies. This study was undertaken to determine the incidence and patterns of malignancy in RA patients and identify risk factors of malignancy among patients with RA.
**Methods:** Patients from the TTSH RA Registry were followed up longitudinally and those who developed malignancies from 2001 to 2013 after the onset of

**Abstract THU0116** – Table 1. Demographics, disease characteristics and treatment history of patients without malignancy and those who develop malignancy

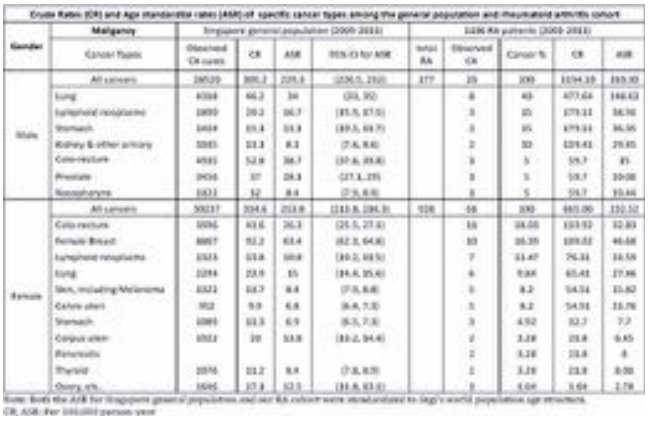
| | | Total No. of patients n=1106 (%) | No. of patients without maligancy n=1025 (%) | No. of patients with maligancy after 1st study entry n=81 (%) | Univariate test p-value (t-test or chi2) |
|---|---|---|---|---|---|
| Demographics | | | | | |
| Age at RA onset (yrs) | mean (SD) | 45.03 (13.40) | 44.58 (13.20) | 50.77 (14.59) | 0.0001 |
| Age at RA diagnosis (yrs) | mean (SD) | 47.31 (13.69) | 46.74 (13.55) | 54.43 (13.52) | <0.0001 |
| Duration of RA onset to RA diagnosis (mths) | mean (SD) | 27.34 (66.63) | 26.02 (64.86) | 43.96 (84.61) | 0.0196 |
| Gender | Male | 177 (16.02) | 157 (15.33) | 20 (24.69) | 0.0390 |
| Diease characteristics | | | | | |
| ESR at 1st study visit | mean (SD) | 37.58 (27.06) | 36.98 (26.60) | 45.15 (31.54) | 0.0102 |
| CRP at 1st study visit | mean (SD) | 20.23 (23.21) | 19.11 (22.24) | 33.56 (30.59) | 0.0248 |
| No. of tender joints at 1st study visit | mean (SD) | 1.84 (3.80) | 1.78 (3.69) | 2.54 (4.94) | 0.0817 |
| No. of swollen joints at 1st study visit | mean (SD) | 2.34 (3.59) | 2.26 (3.45) | 3.37 (4.90) | 0.0072 |
| DAS28 at 1st study visit | mean (SD) | 3.35 (1.41) | 3.33 (1.39) | 3.61 (1.57) | 0.0894 |

RA were identified. Age-standardised rates (ASRs) of various cancers were analyzed and compared with the Singapore Cancer Registry data. Risk factors for developing malignancy, including demographics and disease characteristics at baseline, were analyzed using Chi-squared test and student's t test.

**Results:** Of the 1,134 patients in the registry, 28 patients were excluded as they developed malignancy prior to study enrollment. 1,106 patients were included in the final analysis. Of the 1,106 patients, 81 patients developed malignancies at a mean interval of 15.1 (SD 9.7) years after the onset of RA. The mean age of the 81 patients was 65.9 (SD 10.8) years, of which 61 (75.31%) were females and 69 (85.19%) were Chinese. There were 70 (86.4%) with solid-organ tumours and 11 (13.6%) haematological malignancies.

The ASR of cancer in RA patients was 310.3 for males and 232.5 for females per 100,000 person-years, compared with 229.3 (95%CI 226.5–232) for males and 218.3 (95%CI 213.8–216.3) for females in the general population. By cancer type, there is an increased risk of lung cancer, lymphoid neoplasms and stomach cancer in RA compared with the general population.

The risks factors for developing malignancy ($p<0.05$) include male gender, non-Indian ethnicity, onset of RA at an older age, untreated RA and higher disease activity.



**Conclusions:** The incidence of solid-organ malignancies was higher than hematological malignancies, unlike that in the literature. The overall risk of malignancy is higher in RA patients. Chronic inflammation from RA is associated with increased risk of malignancy.

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**Disclosure of Interest:** None declared

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## THU0117 DIAGNOSTIC VALUES OF ANTI-SA AND ANTI-RA33 ANTIBODIES IN RHEUMATOID ARTHRITIS: A META-ANALYSIS

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**Background:** Anti-Sa antibody was identified in 1994 and belongs to a class of antibodies that target citrullinated antigens. Anti-Sa antibody is highly specific for diagnosing rheumatoid arthritis (RA, but it is associated with low prevalence and sensitivity. Anti-RA33 antibody was identified in 1989 and targets RA33 complex or heterogeneous nuclear ribonucleic protein. In contrast to anti-Sa antibody, anti-RA33 antibody does not target citrullinated antigens. Both anti-Sa and anti-RA33 antibodies are considered as specific serological markers for RA. However, studies assessing the diagnostic value of these antibodies in RA have provided inconsistent results.

**Objectives:** The aim of this study is to evaluate the diagnostic performance of anti-Sa and anti-RA33 antibodies in RA.

**Methods:** PubMed, Embase, and Cochrane library databases were searched for relevant studies and 2 meta-analyses were performed to determine the diagnostic accuracy of anti-Sa and anti-RA33 antibodies in patients with RA.

**Results:** The meta-analysis included 17 studies. Of these, 9 studies, which included 1,095 patients and 1,667 controls, were on anti-Sa antibody and 8 studies, which included 905 patients and 835 controls, were on anti-RA33 antibody. Pooled sensitivity and specificity of anti-Sa antibody were 39.5% (95% confidence interval [CI], 36.5–42.4) and 96.8% (95% CI, 95.9–97.4), respectively, and those of anti-RA33 antibody were 31.8% (95% CI, 28.7–35.0) and 90.1% (95% CI, 87.8–92.1), respectively. PLR, NLR, and DOR of anti-Sa antibody were 14.11 (95% CI, 7.076–28.13), 0.607 (95% CI, 0.558–0.703, and 22.76 (95% CI, 11.10–46.69), respectively, and those of anti-RA33 antibody were 3.429 (95% CI, 2.039–5.765), 0.761 (95% CI, 0.681–0.851), and 4.597 (95% CI, 2.602–8.121), respectively. AUC and $Q^*$ index for anti-Sa antibody were 0.558 and 0.543, respectively, while those for anti-RA33 antibody were 0.501 and 0.500, respectively.

**Conclusions:** Our meta-analysis indicated that both anti-Sa and anti-RA33 antibodies were highly specific and the PLR of anti-Sa antibody was very useful for diagnosing RA, although they were not sensitive for diagnosing RA.

**Disclosure of Interest:** None declared

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## THU0118 TREND OF ATYPICAL FEMORAL FRACTURES IN RHEUMATIC PATIENTS IN THE HIGHLY SUPER AGING AREA OF NORTH JAPAN

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**Background:** A number of recent case reports and series have identified atypical fractures of the femoral shaft. Atypical femoral fractures (AFFs) with lack of trauma or less-energy have been reported to relate using of the bisphosphonates (BPs) and glucocorticoids (GCs) for a long time, affecting collagen diseases[1,2].

**Objectives:** We have analyzed the AFFs in rheumatic patients in the highly super aging area of North Japan, in which the rate more than 65 year-old people in the population was 28%.

**Methods:** We investigated retrospectively all cases of AFF summarized by the American Society for Bone and Mineral Research (ASBMR) Task Force 2013[1] including affected rheumatic disease patients in all hospitals of our prefectural area from 2009 to 2014. Two independent orthpaedic surgeons have diagnosed blindly AFF and estimated proximal femoral geometry by using radiographic analyses. Observation end of this study was settled on Feb 2016.

**Results:** We have 86 cases 99 AFFs in our prefectural area from 2009 to 2014 (1.43 cases/100,000 person/year). The rheumatic patients with AFFs were eleven femurs in eight women in that periods and increased year by year (Fig. 1). Three cases have bilateral AFFs (six femurs, 55%). The mean age of them was 54.9 year-old (33–80). As comorbid conditions, five patients have systematic lupus erythematosus, two dermatomyositis and rheumatoid arthritis, one polyarteritis nodosa and systemic sclerosis. Fracture types were seven subtrochanteric and four diaphyseal femoral fractures. Mean femoral neck angle was 133 degrees (120–141) and femoral shaft angle was 6.1 degree (3–10). Six patients with AFF had prodromal pain (55%). All patients received BPs and all but one prednisolone (PSL). Mean duration of receiving those drugs was 52 months (24–120) and 109 months (36–120), respectively. Mean dosage of PSL was 14 mg/day (0–30). In addition, bilateral AFF group has more PSL dose and duration of PSL, more varus deformity of their femur compared to unilateral AFF group ($p<0.05$). After affecting the fractures, BPs were quitted in seven femurs except four. The surgery using intramedullary nail fixation were performed in all cases excluding one femur using a locking plate. Teriparatide and therapy of low-intensity pulsed ultrasound was induced for five cases after healing their operated wounds. Mean duration of post-operative observation was 28 months (12–70). At the latest follow-up, ten femurs were observed the sign of union at fracture site on X-ray or computed tomography of their femurs, but not one femur. Mean duration of union of the fracture site was 12.6 months (6–24) in ten femurs.

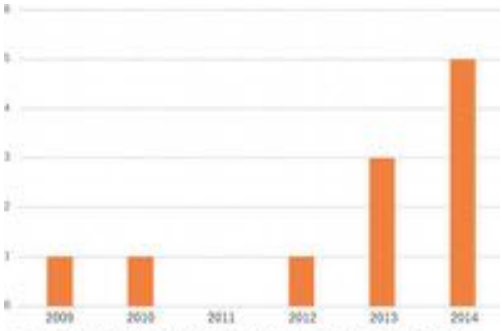



Fig. 1 The trend of atypical femoral fractures in rheumatic patients in the highly super aging area of North Japan

**Conclusions:** Eleven AFFs were observed in 2009–14 in rheumatic patients and the numbers were increased year by year in the highly super aging area of North Japan. The careful management and treatment for the AFFs in rheumatic patients are required even after the surgery, because our all cases have been observed the delayed union or non-union of fracture site at their latest follow-up[3]. In addition, AFF patients who show varus deformity of their femurs and receive much dose of PSL have highly risk of contralateral AFF.

**References:**

[1] Shane E, et al. JMBR, 2014,
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[3] Thompson RN, et al. JBJS, 2012.

**Acknowledgement:** We really appreciate all members of Yamagata Prefectural Committee of Atypical Femoral Fractures Study group.

**Disclosure of Interest:** None declared

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### THU0119 RHEUMATOID ARTHRITIS AND PERIODONTAL DISEASE: ASSOCIATION BETWEEN SALIVARY CITRULLINE, ACPA LEVELS AND CLINICAL PRESENTATION

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**Background:** Periodontitis and other dental conditions have been associated with the pathogenesis of rheumatoid arthritis (RA). In addition, these dental pathologies are also important comorbidities for RA.
**Objectives:** We wished to evaluate the periodontal involvement of rheumatoid arthritis (RA) patients, and we correlated with various laboratory biomarkers including lipids, autoantibodies, serum vitamin D levels, markers of bone metabolism in relation with the periodontal condition and cariological indices; and also correlated them with salivary citrulline and anti citrullinated protein autoantibody levels with the above mentioned clinical and blood test findings.
**Methods:** Twenty-three RA patients were recruited for the study. Saliva samples were taken following whole scale periodontal and cariological examination. Protein concentration, peptidyl-citrulline and anti-cyclic citrullinated protein (anti-CCP) levels were measured from saliva samples. Blood test results were provided by rheumatologists. Citrullinated enolase protein-1 (CEP-1) level from serum was also measured.
**Results:** Periodontal diagnoses (scores) seem to have a positive dependency on LDL (R=0.722, p=0.008), PTH1 (R=0.586, p=0.022), $D_3$ vitamin level (R=0.586, 0.022), the sum of D3/D2 (R=0.634, p=0.011) respectively, in these patients. Anti-CEP-1 positive patients had significantly higher periodontal scores (2.71±0.11 vs 2.50±0.09, $p<0.05$) compared to anti-CEP-1 negative subjects. Interestingly, anti-CEP-1 positive patients had significantly higher triglyceride levels compared to seronegative ones (1.81±0.17 vs 1.42±0.05 mmol/l; $p<0.05$). Salivary citrulline and salivary anti-CCP, (p=0.007, R: 0.583) level has a correlation with the maximum of clinical probing depth.
**Conclusions:** Our results may add further pieces to the mosaic of RA-periodontitis connection. The possible role of antimicrobial immunity, as well as the possible role of lipids and bone metabolism have also been delineated. Future therapies should aim the disruption of this framework.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1360

## Rheumatoid arthritis - anti-TNF therapy

### THU0120 LONG TERM SAFETY AND EFFICACY OF BIOSIMILAR INFLIXIMAB AMONG PATIENTS WITH INFLAMMATORY ARTHRITIS SWITCHED FROM REFERENCE PRODUCT

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**Background:** Biologic medications are effective treatments for inflammatory arthritis, however they are expensive, costing around €15,000 per patient per year, or 5% of the annual healthcare budget in Ireland. Measures to reduce this cost without sacrificing efficacy or safety are important. Studies switching patients to cheaper approved biosimilar products are few.
**Objectives:** To evaluate the efficacy and safety of biosimilar Infliximab in adult patients with inflammatory arthritis switched from reference product in our centre.
**Methods:** In April 2014 all patients attending our rheumatology service for Infliximab infusions were switched from reference product to a biosimilar infliximab following verbal consent and hospital approval. Our local I.R.B. approved a retrospective review of these patients following requests from other centres for information on our experience.
**Results:** 34 patients with inflammatory arthritis were switched from reference product Infliximab in 2014: 50% female, mean (SD) age 55 years (12.9), mean disease duration 14.8 years (9.7), mean duration on infliximab 70 months (59.6) and two thirds were taking oral DMARDs. There was no difference in efficacy or safety in the first 6 months of therapy. By the end of 2015, the mean follow-up on biosimilar infliximab was 15.8 months (6.3). Our results show no significant difference in HAQ score, patient global assessment of disease activity, number of disease flares or medication dose between the originator and the biosimilar Infliximab. However reported pain and CRP values were significantly higher during the longer follow-up period (*p* value 0.028, 0.001 respectively). There was no significant difference in the number of adverse events or infusion reactions during similar follow-up periods, or the number of patients who discontinued therapy (3 Vs 5). 1 frail patient with multiple co-morbidities died during follow-up. Substantial savings were obtained by using the biosimilar product.
**Conclusions:** Our patients experienced similar efficacy and safety for managing their arthritis with biosimilar infliximab as reference product Infliximab, but at a much lower cost.
**Acknowledgement:** National University of Ireland, Galway for statistical software support.
**Disclosure of Interest:** A. Abdalla: None declared, N. Byrne: None declared, R. Conway: None declared, T. Walsh: None declared, G. Mannion: None declared, M. Hanly: None declared, M. O'Sullivan: None declared, A. Curran: None declared, J. Carey Consultant for: Consulting fees and speaker fees by MSD Ireland and Hospira and received travel support and grants from MSD Ireland and Centrecor,USA
**DOI:** 10.1136/annrheumdis-2016-eular.2924

Table 1. Main study outcomes

| | Reference infliximab Duration = 6 months | Biosimilar infliximab Duration = 15.8 months | *P*-value |
|---|---|---|---|
| Death | 0 | 1 | – |
| Infusion related adverse events | 1 | 1 | – |
| Serious adverse events | 2 | 3 | – |
| PGA, mean (SD) | 28.3 (23.2) | 35.2 (25.6) | 0.111 |
| HAQ, median (range) | 0.38 (0–2.63) | 0.69 (0–2.63) | 0.111 |
| Pain level, mean (SD) | 28.8 (23.1) | 38.1 (26.3) | 0.028 |
| CRP, median (range) | 1.95 (0.6–25.9) | 4 (0.6–21.3) | 0.001 |
| Dose in Mg, mean (SD) | 298.2 (110.5) | 302.3 (125.4) | 0.494 |
| Flares No. | 10 | 14 | 0.177 |

### THU0121 LOW DISEASE ACTIVITY AND ACR70-RESPONSE IS ASSOCIATED WITH THE INHIBITION OF PERIARTICULAR BONE LOSS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH CERTOLIZUMAB PEGOL PLUS METHOTREXATE

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**Background:** Anti-TNF treatment with certolizumab pegol is an effective therapy in patients with rheumatoid arthritis (RA).
**Objectives:** The aim of this study, based on a post-hoc analysis of the data set used in the RAPID 1 trial (1), focuses on the associations between metacarpal bone mineral density as estimated by Digital X-ray Radiogrammetry and disease activity as well as ACR70-Response in RA patients treated with certolizumab pegol plus methotrexate (CZP+MTX).
**Methods:** The post-hoc analysis of the RAPID 1 trial evaluates a total of 345 patients: 34 patients who received placebo plus methotrexate (PBO+MTX), 155 patients who received CZP 200 mg (every two weeks) plus MTX and 156 patients who received CZP 400 mg (every two weeks) plus MTX. All patients underwent x-rays of the hand at baseline and week 52 as well as computerized calculations of bone mineral density (BMD) by DXR (2). ACR70-response was evaluated.
**Results:** The highest CRP reduction was observed for patients treated with CZP 400 mg + MTX (-63.6%, $p<0.05$) and CZP 200 mg + MTX (-55.9%, $p<0.05$) compared to the PBO+MTX (-24.7%, $p<0.05$). An equal constellation was revealed regarding the DAS28-CRP (CZP 400 mg + MTX: -50.5%, $p<0.05$; CZP 200 mg + MTX: -49.3%, $p<0.05$ and PBO + MTX: -31.3%, $p<0.05$). In accordance with these results, DXR-BMD showed a minor significant bone loss for the treatment groups undergoing therapy with CZP 400 mg + MTX and CZP 200 mg + MTX with -1.1% ($p<0.05$) versus -1.3% ($p<0.05$), and an advanced periarticular metacarpal bone loss of -5.5% ($p<0.05$) in the PBO+MTX. The patients treated in the small PBO+MTX group revealed no significant ACR70-Response. Both CZP+MTX groups revealed a significant ACR70-Response. In the case of ACR70-Response no significant change of the DXR-BMD was observed.
**Conclusions:** The study highlights that patients treated with CZP+MTX showed a high reduction of CRP and DAS28-CRP in association to a less accentuated periarticular bone loss as estimated by DXR in comparison to patients treated with PBO+MTX. Additionally, patients with ACR70-Response revealed no periarticular demineralisation. The reduced periarticular demineralization functions as a surrogate marker for the bone protective effects of certolizumab pegol.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2787

## THU0122 ETANERCEPT TREATMENT DOES NOT ADVERSELY AFFECT TRADITIONAL CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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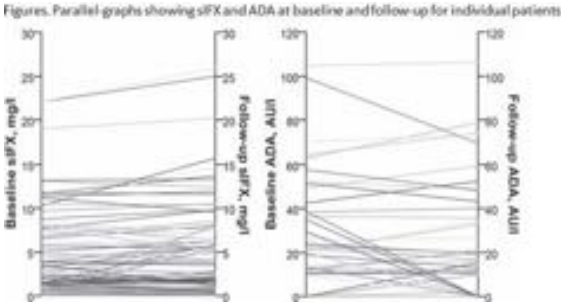
**Background:** Patients with rheumatoid arthritis (RA) are at increased risk of cardiovascular (CV) disease.
**Objectives:** To evaluate changes in metabolic and lipid CV risk factors in patients with RA treated with etanercept (ETN)
**Methods:** This was an exploratory analysis in a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of ETN in patients with moderate RA despite disease-modifying antirheumatic drug therapy. Adults with active, moderate RA (3.2 < DAS28-CRP ≤ 5.1) for ≥6 months and receiving a stable dose of methotrexate for ≥8 weeks were randomized 1:1 to receive ETN 50 mg or placebo (PBO) weekly for 12 weeks; after week 12, all patients received ETN 50 mg weekly for 12 weeks. Laboratory tests evaluated baseline, week-12, and week-24 levels of metabolic and lipid analytes, and shifts in grade (low, normal, or high).
**Results:** In total, 210 patients enrolled: 104 PBO and 106 ETN; 77% female, 86% white, and mean (SD) age 56 (12) years. There were 14% with a medical history of type 2 diabetes and 30% a medical history of hyperlipidemia or hypercholesterolemia; 22% were receiving statins, 10% oral antidiabetic medications, 3% insulin, and 52% prednisone. Baseline, week-12, and week-24 values for each analyte are listed below. Over 24 weeks, there were no significant changes in metabolic or lipid analytes. Patients with diabetes and hyperlipidemia resembled the overall study population, except for decreases in fasting glucose and insulin through week 12 and slight decreases in hemoglobin A1C through week 24 in diabetics receiving ETN (n=17). For the majority of patients, all analytes were in the normal range at baseline and remained normal at week 24.There were no gross abnormalities in liver function tests. Safety results are consistent with the current safety profile.
**Conclusions:** Treatment with ETN did not adversely affect the levels of traditional metabolic and lipid CV risk factors in patients with RA. Results in patients with diabetes are hypothesis generating and might be clinically relevant if demonstrated in a larger study.
**Disclosure of Interest:** A. Deodhar Grant/research support from: AbbVie, Amgen Inc., Boehringer Ingelheim, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen Inc., Boehringer Ingelheim, Janssen, Novartis, Pfizer, and UCB, B. Bitman Shareholder of: Amgen Inc., Employee of: Amgen Inc., Y. Yang Shareholder of: Amgen Inc., Employee of: Amgen Inc., D. Collier Shareholder of: Amgen Inc., Employee of: Amgen Inc.
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## THU0123 NON-MEDICAL SWITCH FROM ORIGINATOR TO BIOSIMILAR INFLIXIMAB AMONG PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASE – IMPACT ON S-INFLIXIMAB AND ANTIDRUG-ANTIBODIES. RESULTS FROM THE NATIONAL DANISH RHEUMATOLOGIC BIOBANK AND THE DANBIO REGISTRY

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**Background:** According to national guidelines issued in 2015, a non-medical switch from originator infliximab (IFX) to biosimilar IFX was conducted in all Danish patients with inflammatory rheumatic diseases treated in routine care.
**Objectives:** To investigate effects of the switch on serum (s) IFX and anti-drug antibodies (ADA) in patients with rheumatoid arthritis (RA), axial spondyloarthrits (SpA) and psoriatic arthritis (PsA).
**Methods:** We included originator infliximab treated patients, who switched to and were treated with biosimiilar infliximab for >2 months with 2 available trough level serum samples (baseline immediately before switching/follow-up 2–4 months after switching time of 2nd–4th infusion). Patients stopping treatment earlier were not included. Trough sIFX <3mg/l was considered low and ≤1mg/l very low. If sIFX <5mg/l, ADA was measured. ADA ≤30AU/l was considered low and ADA >30AU/l median-high. sIFX and ADA were analyzed using automated in-house assays at OUS-Radiumhospitalet. Characteristics and outcomes were registered in the DANBIO registry. Remission was defined by disease activity indices (DAS28 <2.6 (RA, PsA) and ASDAS <1.3 (SpA)). Comparisons were by Mann Whitney U test (unpaired) and Wilcoxon signed rank test (paired). Outcomes are shown as medians (interquartile ranges).
**Results:** 96 pts (192 samples) from 4 departments (49 RA, 27 SpA, 10 PsA, 10 other) were included (age 52 (43–62) years, 47% women). Previous IFX treatment duration was 7.5 (5.1–10.3) years. Follow-up was after 81 (71–90) days. 58 patients (60%) received concomitant methotrexate (15 (10–20) mg/wk). Baseline IFX dose was 3.1 (3.0–4.8) mg/kg every 7 (6–9) weeks. At baseline, 60% of pts had low sIFX and 29% very low and at follow-up it was 57% and 29%, respectively. At baseline, 14 pts (15%) had medium-high ADA, at follow up 16%. Median sIFX was lower at baseline vs. follow-up (1.8 (0.8–5.8) vs 2.4 (0.8–6.2) mg/l, p=0.006) whereas ADA were similar (p=0.7). Six of 58 pts with low baseline sIFX had high sIFX at follow-up, and 3 of 38 pts with high baseline sIFX had low sIFX at follow-up. Similar numbers for low vs. medium–high ADA at baseline and follow-up were 2/81 and 3/15. For the rest, sIFX and ADA remained stable between baseline and follow-up in 87/96 (91%) and 91/96 (95%), respectively (Figure). MTX use was not associated with sIFX or ADA (both p>0.05). Patients with low sIFX received lower IFX doses than pts with sIFX ≥3mg/l (255 (200–320) mg vs. 300 (250–400) mg, p=0.02) and with longer intervals (8 (6–10) weeks vs. 6 (6–6)weeks, p<0.01). Remission rates at baseline (56%/11%/75%) or follow-up (52%/21%/100%) for RA/SpA/PsA were not associated with sIFX (all p>0.05).

Figures. Parallel graphs showing sIFX and ADA at baseline and follow-up for individual patients




**Conclusions:** In this highly selected group of patients treated with originator infliximab for >5 years, non-medical switch to biosimilar IFX had no negative impact on sIFX or ADA 2–4 months following switch. At baseline, 60% of patients had low sIFX but few patients had ADA, perhaps indicating low immunogenicity in these patients.
**Disclosure of Interest:** None declared
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## THU0124 VARIABILITY OF INTENDED COPIES FOR ETANERCEPT IN FIVE COUNTRIES

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**Background:** The term "intended copy" (IC) is used to describe biotherapeutic medicinal products that have not been approved via a regulatory pathway aligned with WHO's Similar Biotherapeutic Product (SBP) guidelines to ensure quality,

**Abstract THU0122** – Table 1

| Analyte, mean (SD) | Baseline | | Week 12 | | Week 24 | |
|---|---|---|---|---|---|---|
| | PBO-ETN (N=104) | ETN-ETN (N=106) | PBO-ETN (N=104) | ETN-ETN (N=106) | PBO-ETN (N=104) | ETN-ETN (N=106) |
| Fasting glucose, mg/dl | 99.0 (30.7) | 98.6 (30.3) | 95.9 (22.3) | 97.3 (26.6) | 101.0 (22.8) | 100.1 (24.0) |
| Fasting insulin, mIU/L | 14.3 (17.6) | 16.0 (34.9) | 15.3 (22.4) | 13.2 (13.5) | 15.0 (18.4) | 12.0 (12.1) |
| Hemoglobin A1C, % | 5.7 (0.9) | 5.7 (0.7) | 5.7 (0.9) | 5.6 (0.6) | 5.6 (0.9) | 5.6 (0.6) |
| Total cholesterol, mg/dl | 195.2 (44.2) | 186.6 (37.1) | 190.9 (40.7) | 184.8 (37.4) | 197.0 (41.7) | 191.1 (39.6) |
| HDL, mg/dl | 62.0 (18.1) | 62.1 (21.7) | 60.5 (17.1) | 61.6 (18.3) | 62.1 (18.5) | 62.2 (22.9) |
| LDL, mg/dl | 105.6 (36.3) | 97.8 (30.0) | 103.2 (35.4) | 96.9 (33.2) | 105.5 (35.4) | 101.7 (31.0) |
| Triglycerides, mg/dl | 135.2 (91.6) | 133.1 (80.1) | 139.2 (85.5) | 131.8 (69.4) | 149.6 (104.0) | 136.6 (76.2) |
| Apolipoprotein A1, mg/dL | 159.6 (27.8) | 160.5 (35.4) | 159.2 (28.1) | 162.0 (32.8) | 163.7 (32.1) | 161.6 (38.0) |
| Apolipoprotein B, mg/dL | 91.6 (25.5) | 86.2 (22.2) | 89.5 (24.7) | 84.9 (23.8) | 91.8 (24.2) | 88.7 (25.0) |
| Adiponectin, mg/L | 11.6 (6.8) | 11.5 (8.7) | 11.7 (7.4) | 11.6 (8.8) | 12.3 (7.2) | 11.6 (9.1) |
| Leptin, μg/L | 29.3 (20.9) | 33.5 (28.5) | 30.1 (22.7) | 35.6 (30.9) | 30.8 (22.7) | 34.5 (28.9) |
| Plasma NT-ProBNP, ng/L | 242.0 (554.1) | 170.1 (334.6) | 232.2 (630.8) | 168.2 (297.8) | 244.2 (687.5) | 164.2 (315.7) |

safety and efficacy. In some countries, the WHO SBP guidelines are not being consistently adopted or implemented and ICs of etanercept (ETN), originally developed by Pfizer (Wyeth), are being marketed as biosimilar versions, although rigorous regulatory criteria for analytical testing and clinical demonstration of biosimilarity may not have been fully assessed.

**Objectives:** Pfizer conducted an analytical assessment of multiple lots of 4 ICs, and a single lot of 1 IC of ETN that have received marketing approval in various global markets. The results for critical quality attributes are compared with the licensed specifications of ETN.

**Methods:** ICs of ETN manufactured by Shanghai CP Guojian (China), Lafrancol (Colombia), Cipla (India), Probiomed (Mexico) and AryoGen (Iran) were assessed. Analyses included a subset of the release tests for ETN, together with evaluation by additional characterization methods to provide appropriate comparative detail on biochemical composition. Results for each product were evaluated against licensed specifications and historical ranges for ETN and ETN reference standard for the additional characterization test results.

**Results:** None of the ICs met all of the individual product quality criteria that Pfizer apply for analytical comparability, although each product met some of the requirements. Principal differences were observed during assessments of *identity* (as measured by tryptic peptide map high-performance liquid chromatography [HPLC]), *purity* (as measured by hydrophobic interaction chromatography [HIC]), degree of *aggregation* (size exclusion [SE] HPLC), distribution of *charged species* (isoelectric focusing [IEF]/anion exchange [AEX] chromatography) and *carbohydrate profile* (N-linked oligosaccharide map). These are shown in the table.

| Key structural differences* | IC Manufacturer | | | | |
|---|---|---|---|---|---|
| | Shanghai CP Guojian | Lafrancol | Cipla | Probiomed | AryoGen |
| Identity (tryptic peptide map HPLC): Atypical | | | | | Y |
| Aggregation (SE HPLC): above specification limit | Y | Y | Y | | |
| Charged species (IEF/AEX chromatography): Differences in distribution vs ETN | Y | Y | Y | | Y |
| Purity (HIC): Atypical profile | Y | Y | Y | | |
| Carbohydrate profile (N-linked oligosaccharide map): Atypical (additional species not in ETN profile) | | | | Y | Y |

*Relative to ETN release specifications and additional characterization historical data. Y, yes.

**Conclusions:** While a degree of structural similarity with ETN was observed for each of the ICs analyzed, a number of significant structural and biochemical differences were noted. None of the products analyzed meet the combination of release specification and additional characterization criteria Pfizer typically apply to support a comparability assessment with ETN.

**Disclosure of Interest:** M. Scheinberg Consultant for: Pfizer Boehringer Mannenheim, Genzyme, Orygen, GSK, G. Castaneda Hernandez Consultant for: Abbvie, Bayer, Boehringer-Ingelheim, Eli-Lilly, Laboratorios Liomont, Laboratorios Sophia, Medix, Merck-Serono, Merck, Sharp and Dohme, Novartis, Pfizer, Roche and Sanofi, Speakers bureau: Amgen, Abbvie, Astra-Zeneca, Bayer, Eli-Lilly, Janssen-Cilag, Laboratorios Liomont, Laboratorios Sophia, Medix, Merck-Serono, Merck, Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi and UC, M. Li: None declared, U. R. Rao Consultant for: Pfizer, Sanofi, E. Singh Shareholder of: Pfizer, Employee of: Pfizer, E. Mahgoub Shareholder of: Pfizer, Employee of: Pfizer, J. Coindreau Shareholder of: Pfizer, Employee of: Pfizer, J. O'Brien Shareholder of: Pfizer, Employee of: Pfizer, S. M. Vicik Shareholder of: Pfizer, Employee of: Pfizer, B. Fitzpatrick Shareholder of: Pfizer, Employee of: Pfizer, B. Hassett Shareholder of: Pfizer, Employee of: Pfizer

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## THU0125 DRUG RETENTION AND REASONS FOR DRUG DISCONTINUATION OF ANTI-TNF THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS. A NETWORK META-ANALYSIS

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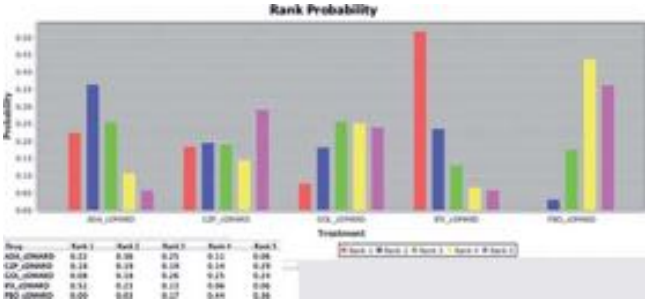
**Background:** Drug retention is considered an indicator of the overall effectiveness, safety and tolerability of a treatment. It is a useful guide to decide the best anti-TNF therapy in patients with R.A.

**Objectives:** To determine which of the TNF inhibitors has the highest retention rate in patients with R.A and to analyze the different reasons for drug discontinuation.

**Methods:** A search of MEDLINE, CENTRAL and EMBASE identified 201 randomized controlled trials (RCTs). We included those comparing a TNF inhibitor (standard dose) with a placebo group, plus concomitant use of conventional DMARDs. We excluded those allowing rescue therapy or not reporting the outcomes of interest. These outcomes were: drug discontinuation and reasons, adverse events, serious adverse events, infections, serious infections and acute infusion events or injection site reactions. A mixed-treatment comparisons analysis was constructed to indirectly compare each study group to one another. Calculation of the probability that each treatment is best was implemented using the Bayesian Markov chain Monte Carlo method.

**Results:** 18 RCTs, including 6948 patients, were extracted. The mean length of study was 6.6 months. On average, patients were 52 years old with active R.A of 5.5 years duration, with 24 TJC, 15 SJC and CRP of 2.3 mg/dl at baseline.

All TNF inhibitors were associated with relatively high rates of drug survival and no statistically significant differences were noted. By rank probability, Infliximab had the highest probability (52%) of retaining patients, and Golimumab (26%) and Certolizumab (29%) had the highest probabilities of being least likely to retain patients (see graphic). Regarding discontinuation due to lack/loss of efficacy, Certolizumab was the most likely and Infliximab the least likely drug to be discontinued. With respect to discontinuation due to adverse events, Infliximab had a 77% probability of being the most likely drug to be discontinued and Certolizumab (30%) was the least likely drug to be discontinued. Additionally, regarding adverse event-related outcomes, several observations were notable. Both Adalimumab and Golimumab were statistically significantly less likely than Infliximab to cause infections and, by rank probability, Infliximab had a 96% chance of being the drug most likely to cause infections. Regarding infusion/injection reactions, both Certolizumab and Infliximab were associated with very high probabilities (51% and 47%, respectively) relative to the other agents of being most likely to cause infusion reactions.




**Conclusions:** Infliximab had the highest retention rate and was the least likely drug to be discontinued due to lack or loss of efficacy, but had the highest discontinuation rate due to adverse events. More data is needed with longer study periods to further reinforce these findings.

**References:**

[1] Neovius M, Arkema E V, Olsson H, et al. Drug survival on TNF inhibitors in patients with rheumatoid arthritis comparison of adalimumab, etanercept and infliximab. Ann Rheum Dis 2013; 0: 1–7

**Acknowledgement:** To Helene Walcoff, Medical Librarian, for helping with the literature search.

**Disclosure of Interest:** None declared

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## THU0126 DOSE TITRATION OF BIOLOGICS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Increasingly, clinicians treating rheumatoid arthritis (RA) or ankylosing spondylitis (AS) are trying to dose-titrate biologics, due to cost, patient preference, and safety. Recent clinical guidelines recommend down titration for RA. However, evidence of safety and efficacy is limited.

**Objectives:** Conduct a systematic literature review to assess breadth and quality of published data and evaluate whether sufficient evidence exists to support dose titration of biologics in RA or AS.

**Methods:** Medline, Embase, and the Cochrane library were electronically searched on February 2, 2015, and conference abstracts from 2010 to November 2015 were hand searched. Eligible studies included: randomized controlled trials (RCTs), non-RCTs, observational, and pharmacoeconomics. Biologics included: abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab. Outcomes were (1) efficacy and sustained remission, (2) flares and retreatment, (3) economic impact.

**Results:** The search yielded 21,585 records; after screening, 73 studies in 90 publications/abstracts were retained, including 15 full-text RCTs, 15 full-text non-RCTs and 43 conference abstracts. Efficacy and economic data were limited. Heterogeneity in disease duration, dosing strategies, and definition of treatment success/failure complicated the interpretation and comparison of regimens. Dose titration rationale varied greatly, and few studies used established definitions of flare (table). Level of evidence was low, with most studies presented as conference abstracts.

**Abstract THU0126** – Table 1. Decisions driving downward dose-titration in RA and definitions of flare, according to study/publication type and biologic

| | # RCTs | # Observational studies | # Congress abstracts |
|---|---|---|---|
| Decisions driving dose-titration | | | |
| Sustained DAS28 remission or LDA | 2 ETN | 1 ADA, 2 ETN, 3 INF | 2 ETN, 4 TCZ |
| Clinical remission or LDA (no additional information) | | | 1 ADA, 2 ETN |
| EULAR response (moderate or good) | 1 RTX | | 2 RTX |
| Good sustained response or clinical judgment | | | 1 ADA, 1 ETN, 1 RTX, 1 TCZ |
| Not specified | | | 1 RTX |
| Flare definition | | | |
| No sustained DAS28 LDA, SDAI remission (≤3.3), ACR/EULAR Boolean remission, or normal HAQ (≤0.5) | 2 ETN | | |
| DAS28 clinical classification | | 1 ADA, 2 ETN, 1 INF | 1 ADA, 2 ETN |
| EULAR: Increase in DAS28 ≥1.2; once DAS28 >3.2 is reached, then increase in DAS28 ≥0.6 | | 2 INF | 1 RTX |
| Loss of efficacy or increase in corticosteroid/DMARD dose, physician judgment, or side effect | 1 RTX | | 2 RTX, 2 TCZ |
| Not specified | 1 RTX | | 1 ADA, 3 ETN, 5 RTX, 4 TCZ |

ACR, American College of Rheumatology; ADA, adalimumab; DAS28, disease activity score-28 joints; DMARD, disease modifying anti-rheumatic drug; ETN, etanercept, EULAR, European League Against Rheumatism; HAQ, health assessment questionnaire; INF, infliximab; LDA, low disease activity; RTX, rituximab; SDAI, simplified disease activity index; TCZ, tocilizumab.

**Conclusions:** Studies evaluating dose titration of biologics are heterogeneous in design and lack standardized definitions. Little evidence of safety and efficacy exists to support dose titration of biologics in RA or AS; RCTs with defined indicators of treatment success and failure are needed.

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## THU0127 INTRAVENOUS GOLIMUMAB THERAPY IMPROVES HEMOGLOBIN, RESULTING IN REDUCED ANEMIA, IMPROVED PHYSICAL FUNCTION AND FATIGUE IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: RESULTS FROM GO-FURTHER PHASE III CLINICAL TRIAL

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**Background:** Clinical studies demonstrated that patients with rheumatoid arthritis (RA) experience lower hemoglobin level and higher prevalence of anemia than general population.

**Objectives:** This study was to examine the treatment effect of intravenously administered golimumab on improving hemoglobin (Hgb) level, and relieving anemia and anemia-related outcomes among patients with RA using data from the phase III clinical trial GO-FURTHER.

**Methods:** In the GO-FURTHER trial, adult patients with active RA were randomized to placebo + MTX (PBO group) or GLM (2mg/kg) plus MTX at week 0, 2, and every 8 weeks thereafter (GLM group). Patients in placebo group with <10% improvement in tender and swollen joint count from baseline at week 16 entered early escape (EE) and received a 2 mg/kg golimumab infusion at Weeks 16 and 20. In this post hoc analysis, Hgb was assessed at baseline, week 4, 12, 20, 28, 44. Anemia was defined based on World Health Organization (WHO) criteria as Hgb <12 g/dl in women and <13 g/dl in men. Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT fatigue) Scale, SF-36 vitality scale, and Health Assessment Questionnaire (HAQ) were collected. Pearson's correlation and linear regression model were used to test correlation. Comparisons between groups at Week 12 before EE were performed using t-test for numeric variables or Mantel-Haenszel Chi-square test for dichotomous variable.

**Results:** At baseline, mean (SD) of Hgb was 12.1 (1.39) g/dl in female and 13.8 (1.29) g/dl in male, and 40.8% female patients and 23.4% male patients had anemia. Significantly greater improvement in hemoglobin in the GLM-treated patients than patients in the placebo group was observed as early as Week 4. At Week 12, mean improvement in Hgb was 0.34g/dl in male and 0.69g/dl in female in the GLM group, compared to an improvement of 0.01g/dl in male ($p<0.001$) and 0.07g/dl in female ($p<0.001$) in the PBO group; and greater proportion of patients in the GLM group achieved an increase of ≥1g/dl in Hgb than PBO group. Among patients who had anemia at baseline, prevalence of anemia at Week 12 was 66.4% in female, and 26.3% in male in the GLM-treated patients, compared to 75% in female and 33.3% in male in placebo-treated patients. After adjusting for baseline anemia and gender difference, GLM-treated patients were more likely to have an improvement of ≥1g/dl in Hgb with a Relative Risk (RR) of 1.87 ($p<0.001$), and less likely to have anemia (RR =0.73, $p<0.001$) at Week 12. Improvement in Hgb at Week 12 was correlated with improvement in HAQ-DI (r=0.16, $p<0.001$), FACIT-fatigue (r=0.10, $p<0.001$) and SF-36 vitality score (r=0.12, $p<0.01$). Treatment effect of intravenous golimumab on Hgb was maintained through Week 112.

**Conclusions:** Intravenously administered golimumab therapy improves Hgb, resulting in reduced anemia, improved physical function and fatigue in patients with moderate to severe active RA despite MTX.

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## THU0128 MAINTENANCE OF IMPROVEMENTS IN WORKPLACE AND HOUSEHOLD PRODUCTIVITY AND PHYSICAL FUNCTION AT 2 YEARS IN EARLY RA PATIENTS WITH SEVERE PROGRESSIVE DISEASE WHO ACHIEVED SUSTAINED LOW DISEASE ACTIVITY FOLLOWING 1 YEAR OF INITIAL THERAPY, WITH TWO DOSING FREQUENCIES OF CERTOLIZUMAB PEGOL

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**Background:** RA leads to high burden on patient (pt) work, functioning and quality of life. Certolizumab pegol (CZP)+MTX improves physical function,[1] and workplace and household productivity,[2,3] in established and early active RA. Here we report impact of maintaining, reducing frequency or stopping CZP from Week (Wk) 52 to 104 in pts who achieved sustained low disease activity (sLDA) following 1 year (yr) of CZP+optimized MTX.

**Objectives:** To assess effect of 2 dosing frequencies of CZP+MTX vs stopping CZP on physical function and workplace/household productivity in Period 2 of C-EARLY, a phase 3 study in early RA pts with severe progressive disease.

**Methods:** CZP+MTX-treated pts achieving sLDA (DAS28[ESR]≤3.2 at Wks40 and 52) in C-EARLY Period 1 (NCT01519791)[4] entered Period 2 (NCT01521923), a randomized, double-blind study. Pts were randomized 2:3:2 to CZP standard dose (200mg Q2W+MTX), CZP reduced-frequency dose (200mg Q4W+MTX) or CZP stopped (PBO+MTX). Physical function (HAQ-DI) and %pts achieving normative physical function (HAQ-DI≤0.5) from Wk52 to 104 are reported (ANCOVA model with factors treatment, region, time since diagnosis at BL [≤4 vs >4 months], and BL/Wk52 values as covariate and logistic regression models [treatment, region and time since diagnosis at BL as factors] respectively; CZP stopped as comparator; LOCF). Workplace/household productivity (Work Productivity Survey, WPS)[5] at Wk52 and 104 are reported (LOCF); non-parametric bootstrap-t method (CZP stopped as comparator).

**Results:** In Period 2, 289 pts were included in the full analysis set: CZP Q2W+MTX (n=84), CZP Q4W+MTX (n=126) or PBO+MTX (n=79). Improvements in physical function were maintained from Wk52 to 104 in CZP Q2W+MTX (HAQ-DI mean [SD] 0.32 [0.42] to 0.37 [0.48], respectively) and CZP Q4W+MTX (0.33 [0.49] to 0.41 [0.57]), whereas deterioration was seen in PBO+MTX (0.33 [0.47] to 0.57 [0.65]). %pts with normative function was generally maintained between Wk52 to 104 in CZP Q2W+MTX (80.7% to 71.4%) and CZP Q4W+MTX (80.2% to 70.6%), but decreased in PBO+MTX pts (75.9% to 57.0%). At Wk104, employed CZP Q2W+MTX and CZP Q4W+MTX pts maintained on average the improvements in workplace productivity, whereas worsening was seen in pts stopping CZP (Table). Similar trends were observed in household productivity and need for regular assistance (Table).

**Conclusions:** Pts continuing CZP treatment (both dose frequencies) after 1yr further maintained improvements at 2yrs in physical function and workplace/household productivity, compared with pts who stopped CZP.

**Table:** C-EARLY Period 2: Improvements in workplace and household productivity, and need for assistance with daily activities at Wk52 and Wk104

| | | CZP stopped (FBO+MTX) n=79 | CZP reduced-frequency (QHW+MTX) n=126 | CZP standard dose (Q2W+MTX) n=84 |
|---|---|---|---|---|
| **Employment status, % [a]** | | | | |
| Employed | Wk52 | 51 (64.6) | 84 (66.7) | 49 (59.0) |
| | Wk104 | 52 (65.8) | 79 (62.7) | 51 (60.7) |
| **Productivity in the workplace (employed patients only), mean (SD), median [a]** | | | | |
| Absenteeism [b] | Wk52 | 0.2 (0.7), 0.0 | 0.1 (0.5), 0.0 | 0.1 (0.4), 0.0 |
| | Wk104 | 0.5 (1.5), 0.0 | 0.2 (0.9), 0.0 | 0.3 (0.9), 0.0 |
| Presenteeism [c] | Wk52 | 0.2 (0.9), 0.0 | 0.4 (1.2), 0.0 | 1.0 (4.5), 0.0 |
| | Wk104 | 1.5 (4.9), 0.0 | 0.6 (2.0), 0.0 | 0.8 (2.3), 0.0 |
| Level of RA interference with work productivity [d] | Wk52 | 0.7 (1.3), 0.0 | 0.7 (0.9), 0.0 | 1.2 (2.1), 0.0 |
| | Wk104 | 2.3 (2.8), 1.0 | 0.9* (1.6), 0.0 | 1.2* (2.2), 0.0 |
| **Household productivity, mean (SD), median [a]** | | | | |
| Household work days missed per month [e] | Wk52 | 0.1 (0.5), 0.0 | 0.3* (1.1), 0.0 | 0.4* (1.3), 0.0 |
| | Wk104 | 1.4 (3.4), 0.0 | 0.7 (2.3), 0.0 | 0.8 (2.6), 0.0 |
| Household work days with productivity reduced by ≥50% per month [f] | Wk52 | 0.4 (2.0), 0.0 | 0.6 (1.6), 0.0 | 0.5 (1.2), 0.0 |
| | Wk104 | 1.8 (4.5), 0.0 | 0.9 (3.0), 0.0 | 1.0 (3.4), 0.0 |
| Level of RA interference with household productivity [d] | Wk52 | 0.6 (1.2), 0.0 | 0.8 (1.3), 0.0 | 1.0 (1.8), 0.0 |
| | Wk104 | 2.0 (2.6), 1.0 | 1.0** (1.5), 0.0 | 1.1* (2.0), 0.0 |
| **Need of regular assistance with usual activities, % [g]** | | | | |
| From a relative/friend | Wk52 | 1.3 | 0.0 | 2.4 [h] |
| | Wk104 | 7.6 | 4.8 | 2.4 [h] |

Full analysis set, LOCF imputation. *p<0.05, **p<0.001 vs CZP stopped, non-parametric bootstrapt method.
[a] Assessed through Work Productivity Survey; [b] Absenteeism=Days missed per month due to arthritis;
[c] Presenteeism=Days with productivity reduced by ≥50% per month due to arthritis, does not include days counted in absenteeism; [d] 0–10 scale, 0=no interference and 10=complete interference; [e] Days missed of household work per month due to arthritis; [f] Days with household productivity reduced by ≥50% per month due to arthritis, does not include days counted in days missed; [g] Assessed through Case Report Form modules; [h] n=83.

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## THU0129 CLINICAL OUTCOMES OF IMMUNOGENICITY IN RHEUMATOID ARTHRITIS PATIENTS UNDER ANTI-TNF BIOLOGICS: RESULTS FROM AN OBSERVATIONAL STUDY

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**Background:** Anti-drug antibodies (ADA) develop in up to one third of patients treated with biologic agents, immunogenicity being one of the main reasons for loss of efficacy and tolerance of the biodrug.
**Objectives:** To investigate the clinical relevance of anti-drug antibodies, drug levels and their relationship with disease outcomes in rheumatoid arthritis (RA) patients receiving TNF-inhibitors (TNF-i).
**Methods:** We performed a prospective observational study in a cohort of forty-eight consecutive RA treated with adalimumab (ADL; 24), infliximab (IFX; 15) or etanercept (ETN; 9). Disease activity, clinical outcomes and adverse events were evaluated at baseline and during study visit, while serum TNF-i and ADA levels collected as a single-point data in both bio-naïve and bio-experimented patients.
Lab assays (IgG-ADA, TNF-i) were measured following the manufacturer's instructions using ELISA Progenika kits, with detection limit set at 10AU/mL for anti-ADL, 142AU/mL for anti-ETN and 5AU/mL for anti-IFX, 0.024μg/mL ADA, 0.035μg/mL ETN, 0.035μg/mL IFX.
Statistical analysis was conducted in SPSS-19 ($p<0.05$).
**Results:** ADA were detected in 8/48 (16.7%) patients (5/24 ADL, 20.8%; 3/9 IFX, 33.3%; while no anti-ETN) and associated with lower functional serum drug (2.17 vs 5.53μg/mL ADL; 2.10 vs 3.82μg/mL IFX; $p<0.01$), higher disease activity (DAS28: 3.5 vs 3.3 in ADL-group $p<0.05$; 3.6 vs 3.0 in IFX-group), less remission ($p<0.01$) compared to ADA negative. Moreover, high ADA levels predict therapy discontinuation ($p<0.01$).
Treatment failure was demonstrated in 12/48 (25%) cases, strongly associated with ADA status ($p<0.01$) and drug levels ($p<0.01$), with a specific profile for secondary non-responders meaning ADA positivity at higher titers (62.51 vs 101.54AU/mL anti-ADL; 5.41 vs 39.80AU/mL anti-IFX; $p<0.01$), lower free serum TNF-i (6.14 vs 1.64μg/mL ADL; 3.01 vs 4.08μg/mL IFX; $p<0.01$), lower biologic exposure (32.2 vs 38.58 months for ADL, 40.17 vs 73.33 months for IFX; $p<0.01$), lower DAS28 at baseline (6.14 vs 6.7 for ADL, $p<0.05$; 6.88 vs 7.04 for IFX; $p<0.05$).
No difference in immunogenicity for ETN-treated cases ($p>0.05$), although lower levels of drug in non-responders (1.92 vs 2.89μg/mL, $p<0.05$). In addition, adverse events happened more often in ADA positive then ADA negative status ($p<0.01$)
**Conclusions:** Immunogenicity to ADL and IFX but not to ETN have large impact on clinical practice (disease activity, treatment failure) and may represent key findings towards optimizing biological therapeutics in RA during long-term follow-up.

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## THU0130 COMORBIDITIES AND EFFICACY OF ANTI-TNF THERAPIES: HISTORY OF DEPRESSION AS A POSSIBLE INDICATOR OF LOWER RESPONSE

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**Background:** Little is known about the influence of specific comorbidities on response to biologic therapy.
**Objectives:** To examine the impact of comorbidities on anti-TNF therapy efficacy in rheumatoid arthritis (RA) patients (pts) within the US CORRONA RA registry.
**Methods:** A retrospective cohort of adult RA pts with moderate-to-severe RA (CDAI>10) who initiated anti-TNF biologics after June 1, 2009 and had a 6 month follow up (in a window of 3–9 months) were included. Comorbidity assessments included a modified Charlson comorbidity index (CCI) [HIV status was not assessed]) and diagnoses of diabetes, cardiovascular disease (CV) and history of depression. Propensity score (PS) method was employed to match pts with and without select comorbidities. Variables used for PS matching were selected if standardized differences were ≥0.1 between groups. PS were stratified by line of therapy. The primary outcome was achievement of low disease activity (LDA) at 6 months (CDAI ≤10). Secondary outcomes included DAS28(ESR) LDA (DAS<3.2), modified ACR 20/50/70. Post hoc analysis was performed on the CDAI components to estimate pt and MD reported outcomes.
**Results:** A total of 4064 anti-TNF initiations were included. For CCI, diabetes and CV, there were no significant differences in response in the matched populations. For patients with a history of reported depression (hxdep), LDA rates were significantly lower (29% for hxdep vs 39% for no hxdep, $p<0.001$ OR=0.65 [0.56, 0.75]). In the matched population (n=1810) LDA rates remained significantly different: 31% vs 36% (hxdep vs no hxdep), p=0.027, OR=0.80 [0.66, 0.98]. Matched patients differed in mean (SD) patient fatigue (VAS 0–100): hxdep: 61.4 (26.2) and no hxdep: 54.7 (27.9) $p<0.001$. In pts matched on factors including patient fatigue (n=1252) there was no significant difference in response rates: 31.8% vs 31.8% OR=1.0 [0.79, 1.27]. Similar results were found in the secondary outcomes. Estimates of the CDAI components [Table 1] showed the Pt Global and Tender Jts were the largest contributors to CDAI change.

| Outcome Difference in mean Δ | Unadjusted N=4064 | Matched patients N=1810 | Matched including Pt fatigue N=1452 |
|---|---|---|---|
| ΔMD Global* | 0.48 [0.32, 0.64] | 0.20 [–0.02, 0.42] | 0.025 [–0.22, 0.27] |
| ΔPt Global* | 0.37 [0.18, 0.56] | 0.56 [0.30, 0.82] | 0.057 [–0.23, 0.34] |
| ΔTender Jts | 1.12 [0.61, 1.63] | 0.64 [–0.08, 1.35] | 0.13 [–0.66, 0.92] |
| ΔSwollen Jts | 0.90 [0.51, 1.28] | 0.09 [–0.44, 0.61] | 0.06 [–0.52, 0.64] |

*VAS 0–10.

**Conclusions:** Of the comorbidities examined, a history of reported depression in RA patients is an indicator of lower response rates to TNFi. CDAI was primarily influenced by patient responses. Patient fatigue may be a manifestation of depression and explained response rate differences. Further analyses are needed to explore this relationship.
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## THU0131 MIRNA PROFILING USING HTG-EDGESEQ PLATFORM PREDICTS RESPONSE TO ANTI-TNF ALPHA THERAPY IN RHEUMATOID ARTHRITIS

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**Background:** Millions of patients suffering Rheumatoid Arthritis (RA) are treated with TNF-α inhibiting agents, however, response rate is low (30 to 40%) and no tool exists to predict the treatment response.
**Objectives:** Using the HTG-Edgeseq platform, an innovative combination of nuclease protection assay and next generation sequencing, we identified sets of miRNAs that discriminate responders from non-responders to anti TNF-α therapy.
**Methods:** Sixty-seven patients diagnosed with RA, eligible for treatment with 1st line anti-TNFα and for whom DMARD therapy had failed were enrolled in the study. Twelve to 14 weeks after anti-TNFα therapy, patients were categorized as responders or non-responders based on DAS28 index. Patients' miRNA profile was established from 15μl of plasma using HTG-Edgeseq Whole Transcriptome Assay (WTA) miRNA panel (2256 miRNA). Results were normalized based on the median of the sample and Random forest was used as the classification model. For 8 patients, miRNA were also analyzed with the qPCR Exiqon miRNA panel V4 to determine HTG-Edgeseq accuracy. Method reproductibility was assessed by analyzing 4 times an independent sample on different sites, with different instruments/days/operators.
**Results:** Results obtained from both HTG-Edgeseq and qPCR methods showed an overall correlation of 0.63 for the 341 miRNA common between those 2 kits, and correlations factors between the 4 independent experiments ranged from 0.993 to 0.999. Statistical analysis of patients' miRNA profile identified 2 panels of 6 and 52 miRNAs with significant predictive power to discriminate responders from non-responders (sensitivity was 0.898 and 0.918, and AUC 0.773 and 0.824 respectively).
**Conclusions:** In conclusion, miRNA profiling in RA patients using HTG-EdgeSeq allowed us to build 2 predictive models for response to anti-TNF-α drugs. Moreover, we showed that HTG-Edgeseq platform offers accurate and sensitive miRNA expression measurement. Its low sample input requirement and compatibility with all biological material makes it an invaluable tool for biomarkers discovery.
**Disclosure of Interest:** None declared
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## THU0132 COMPARATIVE EFFECTIVENESS OF TNFI AND TOFACITINIB MONOTHERAPY IN CLINICAL PRACTICE: RESULTS FROM CORRONA REGISTRY

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**Background:** TNF inhibitors (TNFi) can be used as monotherapy (mono) or in combination (combo) with conventional DMARDS (cDMARDS). Clinical trial data and European registry data have shown evidence of better effectiveness of TNFi combo therapy than mono. Effectiveness of mono vs combo in US clinical practice, in particular among biologic naïve and experienced patients, has not been assessed.
**Objectives:** This study was carried out to quantify the prevalence and effectiveness of TNFi monotherapy use in US clinical practice. A secondary objective was to contrast this with tofacitinib (tofa) monotherapy use and effectiveness.
**Methods:** RA patients initiating a TNFi (adalimumab, etanercept, infliximab, golimumab, certolizumab pegol) or tofa with a six month follow-up in Corrona US were identified. A subcohort of TNFi initiations after 11/6/2012 (market approval of tofa) were used for comparisons with tofa initiators. We defined combo therapy as TNFi or tofa used with MTX alone and mono as no use of any cDMARD. The primary outcome was achieving low disease activity (LDA) or remission based on CDAI ($\leq$10) at 6 months. Patients switching to another biologic prior to 6 months were defined as non-responders. Secondary outcomes included modified ACR20/50/70 and mean change in CDAI. Combo and mono initiators were matched within line of therapy using a propensity score. Covariates for the model were selected if the standardized mean difference between the groups $>$0.1.
**Results:** There were 7076 TNFi initiations in Corrona, with 2091 (30%) mono initiations. Mono by line of therapy was 21%, 35% and 41% for 2nd, 3rd and 4th line therapy, respectively. There were 325 tofa initiations with 201 (61%) mono and mono rates of 50%, 65% and 63% for 2nd, 3rd and 4th line therapy, respectively. In the matched populations, across outcome measures (Table 1), TNFi combo was more effective than TNFi mono in 2nd line therapy (55.6% LDA vs 47.1% LDA) and similar in 3rd and 4th line therapy. Tofa combo therapy was similar to mono in the matched populations (35.4% LDA vs 32.3% LDA). Tofa mono was similar to TNFi combo therapy in the matched populations (33.3% LDA vs 33.3% LDA).
**Conclusions:** TNFi monotherapy is common in U.S. clinical practice. TNFi monotherapy is less effective than combination therapy especially in biologic naïve patients. There is no evidence that tofa monotherapy is less effective than tofa combination therapy or TNFi combination therapy.
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## THU0133 STATISTICAL ASSESSMENT ACROSS MULTIPLE EARLY TIME POINTS VALIDATES BIOSIMILARITY OF BOW015 TO REFERENCE INFLIXIMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS ON STABLE METHOTREXATE DOSES

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**Background:** No formal guidelines exist to inform the selection of appropriate equivalence margins or the timing of efficacy assessment for comparative effectiveness trials of biosimilars in rheumatoid arthritis (RA). Studies to date have specified a single time-point for assessment of the primary outcome and an equivalence margin based on experience in placebo-controlled trials of the reference product. Neither of these adequately describes the dynamic early responses to TNF inhibition nor provides an optimally sensitive measure to assess bioequivalence. However, by applying multiple statistical analyses across frequent early time points, a "totality-of-the-evidence" might be generated that could sufficiently demonstrate clinical similarity.
**Methods:** To compare the statistical evaluation of bioequivalence using aggregate information from early time-points to that using data from the primary endpoint at week 16, 189 subjects with active RA on stable doses of oral methotrexate were randomized 2:1 to receive double-blinded treatment with BOW015 or reference infliximab (rIFX) and assessed for efficacy at weeks 0, 2, 6, 14, and 16. The pre-specified primary endpoint was the proportion of subjects achieving an ACR20 response at week 16, as previously reported. In this novel post-hoc analysis,

**Abstract THU0132** – Table 1. Matched patients

| | TNFi Combo vs TNFi Mono | | | Tofa Combo vs Tofa Mono | TNFi Combo vs Tofa Mono |
|---|---|---|---|---|---|
| | 2nd line* (n=1130) | 3rd line (n=1044) | 4th line (n=680) | 3rd & 4th line (n=130) | 3rd and 4th line (n=186) |
| LDA OR [95% CI] | 1.4 [1.1–1.8] | 1.1 [0.9–1.5] | 0.7 [0.5–1.0] | 1.2 [0.5–2.5] | 1.0 [0.4–1.8] |
| mACR20 OR [95% CI] | 1.6 [1.2–2.1] | 1.2 [0.9–1.5] | 1.2 [0.8–1.8] | 0.6 [0.3–1.6] | 0.9 [0.5–1.8] |
| ΔCDAI mean△ [95% CI] | –2.0 [–3.4–0.6] | –0.9 [–2.5–0.6] | –2.1 [–4.1–0.1] | 0.2 [–4.8–5.2] | –1.6 [–4.8–1.7] |

*2nd line was defined as prior use of at least one cDMARD and no prior use of any biologic.

a generalized estimating equation, logistic regression, and an exponential time response model were applied to aggregate data from the early time-points in this trial. Aggregated and integrated analysis were compared to the assessment of bioequivalence using data only from the primary endpoint.

**Results:** At the week 16 primary endpoint, comparable proportions of BOW015- and rIFX treated-patients achieved an ACR20 response, yielding a 95% confidence interval (CI) for the treatment difference of -12.6% to 19.3% by the protocol-specified 2-sided Fisher's Exact test methodology. Analyses to assess the average proportion of ACR20 responders over multiple time-points during the first 16 weeks provide a more stringent assessment of equivalence, with 95% CIs for the treatment difference that fall within a narrower range than that achieved using the Exact test at week 16 (Table 1). Non-linear modeling further confirmed this comparable time-response profile across 16 weeks in agreement with averaged findings.

Table 1

| Method of Analysis | Reference Infliximab %ACR20 responders | BOW015 %ACR20 responders | Difference | Exact 95% CI |
|---|---|---|---|---|
| Exact test, week 16 | 86.44% | 89.83% | –3.39% | (–19.27, 12.60) |
| GEE, week 0–16 | 67.49% | 67.47% | 0.02% | (–15.95, 15.95) |
| Logistic regression, week 0–16 | 66.65% | 67.97% | –1.70% | (–17.61, 14.28) |
| Logistic regression, week 2, 6 | 49.1% | 46.37% | 2.73% | (–13.44, 18.44) |
| Logistic regression, week 2, 6, 14 | 57.58% | 56.88% | 0.70% | (–15.11, 16.78) |

CI, Confidence interval.

**Conclusions:** Assessment of therapeutic equivalence by aggregating multiple time-points during the steep phase of the time response curve, using appropriate statistical methods to validate attainment of bioequivalence margins, can provide a more comprehensive assessment of biosimilarity than a measure taken at a single timepoint.

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## THU0134 GOOD RESPONSE ON ADALIMUMAB TREATMENT FOR PATIENTS WITH RHEUMATOID ARTHRITIS PERSISTS FOR UP TO 9 YEARS

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**Background:** With the advent of biological therapy a range of new drugs have become available for patients with rheumatoid arthritis (RA). Adalimumab was one of the first biologicals to become widely available, and as many patients use biologicals indefinitely, data on very long-term efficacy and safety in daily clinical practice is important as results obtained in short-term clinical registration trials might differ from those observed in long-term daily clinical practice, especially after many years of continuous use.

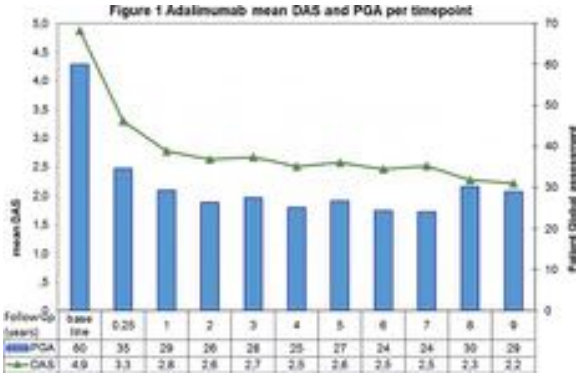
**Objectives:** To ascertain the efficacy and safety of very long- term adalimumab treatment for RA.

**Methods:** From December 2004 to October 2013, 587 consecutive patients have been included in the adalimumab for RA (AdRA) cohort at the Jan van Breemen research center at Reade in Amsterdam, the Netherlands.

**Results:** The mean age was 54 years (SD:13), and 469 (80%) were female. At baseline, the median disease duration was 7 (3–15) years, and 399 (70%) were Rheumatoid factor positive. At baseline, 373 (64%) used methotrexate, 183 (31%) used prednisolone, and 144 (25%) a DMARD other than MTX and 176 (39%) had used at least one other biological prior to start. On average patients had used 3.2 (SD:2.1) DMARDs. A total of 237 (40%) patients are currently on drug, and 350 (60%) patients have dropped out. The median follow-up duration was 4.0 (IQR:1.0–7.2) years for patients currently still on adalimumab treatment, and 0.7 (0.3–2.2) years for drop-outs. The maximum follow-up duration was 9.2 years, the total was 1507 patients years. The main reason for discontinuing adalimumab treatment were failure (121, 35%), followed by adverse events (69, 20%). Eight (2%) patients discontinued because of remission and 3 (1%) patients died while on drug (one of sepsis, one of lung cancer, and one at age 84 of unknown causes). In total 1892 adverse events were reported by patients, who deemed 137 to be severe, 51 times patients required hospitalization, and 317 times antibiotics were given.

The mean DAS-28 drops significantly from 4.9 (SD: 1.3) at baseline to 3.3 (1.4) at 16 weeks. This improvement was sustained, and steadily improved further over the whole 9 years with a DAS-28 of 2.8 (1.3), 2.6 (1.2), 2.6 (1.2) and 2.2 (0.6) at 1, 2, 5 and 9 years, respectively (see Figure 1). The patient reported outcome of patient global assessment (PGA) was also good, the mean PGA drops from 60 (23) to 35 (25) at 16 weeks of treatment, and remains stable after that with a mean PGA of 29 (23), 26 (22), 27 (22) and 29 (28) at 1, 2, 5 and 9 years, respectively (see Figure 1).

Figure 1 Adalimumab mean DAS and PGA per timepoint




**Conclusions:** The initial good response on adalimumab persists for the 9 years of follow-up, with the decrease in DAS28 continuing for the entire 9 years. Over time, a satisfactory response in DAS28 and PGA is sustained during further follow-up for 9 years.

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## THU0135 THE IMPACT OF EARLY TREATMENT WITH ADALIMUMAB ON RHEUMATOID FACTOR AND ANTI-CITRULLINATED PEPTIDE ANTIBODY LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE OPTIMA TRIAL

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**Background:** In patients (pts) with rheumatoid arthritis (RA), rheumatoid factor (RF) and anti-citrillunated peptide antibody (ACPA) are associated with higher disease activity and damage progression.

**Objectives:** To explore whether early initiation of combination therapy with the TNF-inhibitor, adalimumab (ADA) + methotrexate (MTX) is associated with conversion in RF or ACPA status.

**Methods:** Data were from the OPTIMA trial[1], where pts with early RA were initially treated for 26 weeks (wks, period 1) with ADA+MTX, or placebo (PBO) +MTX. In total, 708/900 (78.7%) were RF+, 728/884 (82.4%) were ACPA+ at wk 26. If pts on ADA+MTX attained 28-joint disease activity score based on C - reactive protein (DAS28-CRP) $<$3.2 at wks 22 and 26 (responders), they were randomized to withdraw ADA, continue PBO+MTX, or continue ADA+MTX until wk 78 (period 2). Pts on PBO+MTX, who were responders at wks 22 and 26, received PBO+MTX until wk 78. Pts who did not reach DAS28-CRP $<$3.2 either on ADA+MTX or MTX alone (non-responders, NR), received Open Label (OL) ADA+MTX until wk 78. Levels of RF and ACPA were measured at baseline (BL), wks 26, 52 and 78. Results obtained in OPTIMA were validated with data from PREMIER (early RA; RF levels at BL, wks 26 and 52)[2] and DE019 trials (established RA; RF at screening, wks 24 and 52).[3]

**Results:** In OPTIMA, pts on ADA in period 1 tended to have lower RF levels than pts in the PBO+MTX arm at wks 26 and 78, irrespective of the treatment after wk 26. In pts who switched to or continued ADA in period 2 [ADA+MTX/ADA+MTX, ADA+MTX/OL ADA+MTX and PBO+MTX/ADA+MTX arms], RF levels decreased from wk 26 to 78 (table); pts in the PBO+MTX/ADA+MTX arm had the largest decrease from wk 26, in line with a decrease of clinical disease activity. In pts who switched to or continued on PBO+MTX in period 2 (ADA+MTX/PBO+MTX and the PBO+MTX/PBO+MTX arms), the RF levels increased from wk 26 to 78, despite overall maintenance of a low disease activity. A similar pattern was observed for ACPA levels. In PREMIER, combination ADA+MTX therapy was also more effective in reducing RF levels vs ADA or MTX monotherapy (table). More pts on ADA+MTX (19.4%) vs ADA (10.2%) or MTX (8.8%) monotherapy, who were RF+ at BL became RF- after 26 wks. In DE019, ADA+MTX therapy was effective in reducing RF levels compared to PBO (on background MTX), and more pts in the ADA arms vs PBO, who were RF+ at screening became RF- after 24 wks (ADA 20 mg: 7.5%; ADA 40 mg: 7.1%; PBO: 2.3%).

Table 1. Change (Δ) in RF and ACPA levels with treatment, in OPTIMA, PREMIER and DE019, Least Square Means (SE) adjusting for BL RF and BL DAS28

| Treatment arm | ΔRF | ΔACPA |
|---|---|---|
| OPTIMA PERIOD 1: Δ BL to wk 26 | | |
| ADA+MTX | -125.5 [5.47]* | -20.6 [2.54] |
| PBO+MTX | -101.1 [5.48] | -17.4 [2.53] |
| OPTIMA PERIOD 2: Δ wk 26 to wk 78 | | |
| ADA+MTX / PBO+MTX | 20.9 [16.67]† | 5.1 [5.1]§,* |
| ADA+MTX / ADA+MTX | -16.6 [15.43] | -8.9 [4.79] |
| ADA+MTX / OL ADA+MTX | -10.6 [10.56] | -9.0 [3.21] |
| PBO+MTX / PBO+MTX | 22.8 [16.21]† | 4.1 [4.88]§,* |
| PBO+MTX / OL ADA+MTX | -24.7 [8.9] | -15.5 [2.73] |
| PREMIER | | |
| | ΔRF BL to wk 26 | ΔRF BL to wk 52 |
| MTX | -159.9 [18.95] | -205.9 [29.38] |
| ADA 40mg | -77.9 [18.56] | -59.0 [29.95] |
| ADA 40mg +MTX | -245.0 [17.97]# | -267.3 [27.60]# |
| DE019† | | |
| | ΔRF BL to wk 24 | ΔRF BL to wk 52 |
| PBO+MTX | 37.9 [30.32] | 24.0 [29.84] |
| ADA 20mg +MTX | -96.5 [27.90]‡ | -129.3 [26.76]‡ |
| ADA 40mg +MTX | -94.5 [28.04]‡ | -128.2 [27.18]‡ |

*P<.05 vs PBO+MTX; §P<.05 vs PBO+MTX/OLADA+MTX; †P<.05 vs ADA+MTX/OLADA+MTX; ‡P<.001 vs PBO+MTX/OLADA+MTX; #P≤.05 vs ADA or MTX monotherapy; *P<.001 vs ADA; §P≤.001 vs PBO. †In DE019, screening visit was considered as BL.

**Conclusions:** Early combination treatment with ADA+MTX resulted in lower levels of RF and ACPA. The withdrawal of ADA led to increases in levels of RF and ACPA. These data suggest that effective therapy reduces autoantibody levels. Further studies are needed to elucidate the consequences of these changes.

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## THU0136 USE OF A GLOBAL RISK SCORE TO IDENTIFY PATIENTS WITH RHEUMATOID ARTHRITIS AT RISK OF SERIOUS INFECTIOUS EVENTS DURING CERTOLIZUMAB PEGOL TREATMENT

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**Background:** Anti-TNF drugs are an effective therapy for patients (pts) with rheumatoid arthritis (RA) but are associated with an increased incidence of serious infectious events (SIEs). We have previously identified baseline (BL) age and comorbidity as risk factors for SIEs in certolizumab pegol (CZP)-treated RA pts.[1]

**Objectives:** To identify RA pts at high/low risk of developing SIEs during long-term CZP treatment, using a BL age-adjusted comorbidity index (AACI).

**Methods:** CZP safety data from anti-TNF naïve patients were pooled from the RAPID1 and RAPID2 randomized controlled trials (NCT00152386/NCT00160602) and their open-label extensions (NCT00175877/NCT00160641). Post-hoc analyses of SIEs with onset after the first CZP dose and ≤84 days after the last CZP dose or withdrawal are presented. Pts' AACI was based on the Charlson index: it included medically-treated comorbidities (diabetes mellitus, chronic obstructive pulmonary disease/asthma, cardiac disorder, hypertension, lipidemia, transient ischemic attack or cerebrovascular disorder; each with score=1) and the resulting score was increased by 1 for each decade over the age of 40 years (yrs) at BL.[2] Incidence rates (IRs) of SIEs were calculated per 100 pt-yrs (PY), with 95% confidence intervals (CIs); time at risk = time from first CZP dose to the first SIE, or the total CZP time at risk for pts without SIEs. A multivariate Cox proportional hazards model (selection criteria: p≤0.25) was used to estimate the relative risk (hazard ratio [HR]) of BL pt covariates to the first SIE. BL covariates analyzed were AACI (≤1; 2; 3; ≥4), BMI (<20; 20–30; >30 kg/m$^2$), DAS28(CRP), disease duration (<2; ≥2 yrs), HAQ-DI, joint erosion score, MTX dose (≤15; >15 mg/week) and systemic steroid use (Yes; No). High/low risk pt groups were defined based on co-occurrence of the highest/lowest risk categories in the Cox model, respectively.

**Results:** 201/1506 anti-TNF naïve CZP pts reported ≥1 SIE over ~6 yrs of CZP treatment (IR 3.66/100 PY, 95% CI 3.17–4.21; total exposure 5778.6 PY). Overall, the observed IR of SIEs increased with AACI (Figure 1A). According to the Cox model, AACI ≥3 was a risk factor for SIEs; AACI=2, BL systemic steroid use, disease duration <2 yrs and DAS28(CRP) also contributed to SIE risk (Figure 1B). 195 pts (12.9%) were identified as "low risk" at BL (AACI≤1, no systemic steroid use) and 141 pts (9.4%) as "high risk" (AACI≥4, systemic steroids used). Over time, high risk pts reported more SIEs than low risk pts; across all pt groups, the observed IR was highest in the first yr of CZP treatment (Figure 1C). Results should be interpreted with caution, as it was not possible to compare the absolute risk of SIEs between CZP and placebo pts with similar AACI, due to limited placebo exposure.

**Figure 1:** Impact of baseline age-adjusted comorbidity score (AACI) on the risk of SIEs in CZP-treated patients with RA

A) Overall incidence of SIEs in CZP patients categorized by baseline AACI (n=1506)

| | Baseline AACI | | | |
|---|---|---|---|---|
| | ≤1 (n=530) | 2 (n=408) | 3 (n=312) | ≥4 (n=256) |
| Events (n [a]), % | 57 (52, 9.8) | 69 (58, 14.2) | 58 (50, 16.0) | 52 (41, 16.0) |
| IR/100 PY (95% CI) | 2.53 (1.89, 3.32) | 3.61 (2.74, 4.66) | 4.71 (3.49, 6.20) | 5.37 (3.85, 7.28) |

B) Multivariate analysis of baseline predictors of SIEs [b]

| | HR | (95% CI) | p value |
|---|---|---|---|
| Disease duration (years), ≥2 vs <2 | 0.75 | (0.53, 1.06) | 0.103 |
| Systemic steroid use, Yes vs No | 1.27 | (0.95, 1.69) | 0.109 |
| AACI, 2 vs ≤1 | 1.42 | (0.97, 2.07) | 0.070 |
| AACI, 3 vs ≤1 | 1.81 | (1.23, 2.68) | 0.003 |
| AACI, ≥4 vs ≤1 | 2.07 | (1.37, 3.12) | <0.001 |
| DAS28(CRP) imputed | 1.12 | (0.95, 1.32) | 0.182 |




C) Observed incidence of SIEs in high risk and low risk patient groups over time

| | IR/100 PY (95% CI) [c] | | |
|---|---|---|---|
| | Low risk patients (n=195) | High risk patients (n=141) | Remaining patients (n=1170) |
| Overall | 1.98 (1.11, 3.26) | 5.00 (3.05, 7.72) | 3.83 (3.27, 4.46) |
| Time since first CZP dose | | | |
| 6 months | 3.21 (0.66, 9.39) | 10.74 (4.32, 22.12) | 5.59 (3.80, 7.93) |
| 1 year | 4.47 (1.93, 8.80) | 11.85 (6.48, 19.89) | 5.38 (4.08, 6.97) |
| 2 years | 2.99 (1.43, 5.50) | 6.85 (3.75, 11.50) | 5.10 (4.15, 6.20) |
| 3 years | 2.76 (1.47, 4.72) | 5.81 (3.32, 9.43) | 4.55 (3.79, 5.42) |
| 4 years | 2.53 (1.41, 4.16) | 5.05 (2.94, 8.09) | 4.27 (3.61, 5.02) |
| 5 years | 2.13 (1.19, 3.51) | 4.95 (2.98, 7.72) | 4.03 (3.44, 4.69) |

[a] Number of patients with SIEs; [b] A covariate was defined as a risk factor for SIEs if p≤0.05 (highlighted in red), or as a contributing factor if p≤0.25; missing BL values were imputed by linear regression using non-missing components; [c] IR of SIEs observed up to the indicated time since the first CZP dose.

**Conclusions:** In RA pts treated with CZP, higher age-adjusted comorbidity index was associated with a greater relative risk of SIEs. The stratification of RA pts at BL using a global risk score may help clinicians to better assess the risks and benefits of long-term CZP treatment.

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**Disclosure of Interest:** J. R. Curtis Grant/research support from: Roche/Genentech, UCB Pharma, Janssen, CORRONA, Amgen, Pfizer, BMS, Crescendo, AbbVie, Consultant for: Roche/Genentech, UCB Pharma, Janssen, CORRONA, Amgen, Pfizer, BMS, Crescendo, AbbVie, K. Winthrop Grant/research support from: BMS, Consultant for: UCB Pharma, Pfizer, BMS, Eli Lilly, AbbVie, Roche, M. de Longueville Employee of: UCB Pharma, C. O'Brien Employee of: UCB Pharma, M. N. Ndlovu Employee of: UCB Pharma, B. Haraoui Grant/research support from: Abbott, Amgen, BMS, Janssen, Pfizer, Roche, UCB Pharma, Consultant for: Abbott, Amgen, BMS, Janssen, Pfizer, Roche, UCB Pharma, Speakers bureau: Abbott, Amgen, BMS, Janssen, Pfizer, Roche, UCB Pharma

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## THU0137 NON-ADHERENCE TO SUBCUTANEOUS BIOLOGICAL THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS. ARCO STUDY

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**Background:** Lack of adherence to medication in rheumatoid arthritis (RA) can

worsen disease activity, but data on adherence to biological drugs is scarce.
**Objectives:** To evaluate RA patients adherence to the subcutaneous (SC) biological treatment prescribed by the physician during the first year of treatment.
**Methods:** Retrospective study in RA patients ≥18 years-old from 42 Spanish hospitals, which had been prescribed a SC biological drug 12 to 18 months prior to the study visit. Data were collected from patients' clinical records and hospital pharmacy drug-dispensing logs. Adherence was evaluated through the Medication Possession Ratio (MPR) (actual number of days covered by the taken medication/theoretical number of days covered by the prescribed medication). The number of days theoretically covered was calculated considering the interval of administration of the prescribed biological drug, if induction dose was prescribed, and if there were suspension periods or changes in the dose. The actual number of days covered was calculated with the number of vials that the patient had taken from the hospital pharmacy during the study period. Non-adherence was diagnosed if MPR was ≤80%.
**Results:** 364 patients were included (age 54.9 years [12.5]; 77.5% women, median RA duration 7.8 years). The initial interval of administration of the biological drug was weekly (44.2%), biweekly (39.1%) and monthly (17.3%); the median duration of the period studied was 14.8 months. For the primary analysis, 363 patients were valid, of which 52 patients were non-adherent (MPR ≤80%) to the prescribed schedule (14.3%; 95% CI: 11.1–18.3). There were no differences in adherence by age ranges, gender or other socio-demographic factors, such as level of education, smoking habit or alcohol intake, employment status, comorbidities or polypharmacy (all, p= NS). Non-adherence was less frequent in patients with a monthly administration schedule (6.4%) than in patients with a weekly (17.4%, p=0.034) or biweekly administration (14.4%, p=0.102), and slightly more frequent in those receiving induction (21.6% vs 12.5% without induction, p=0.068). No differences were observed between patients who used syringes or pen devices, or in patients who had periods of treatment interruption.
**Conclusions:** In RA patients, 14.3% were non-adherent to the prescribed SC biological medication during the first year of treatment, with no differences related to socio-demographic variables. Adherence was higher in those patients with monthly subcutaneous administration.
**Acknowledgement:** The ARCO study was funded by Merck Sharp & Dohme of Spain.
**Disclosure of Interest:** None declared
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## THU0138 SECONDARY EFFICACY RESULTS UP TO WEEK 24 FROM A PHASE III STUDY COMPARING SB5 (AN ADALIMUMAB BIOSIMIAR) WITH ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS DESPITE METHOTREXATE THERAPY

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**Background:** SB5 is a biologic agent developed as a biosimilar of the adalimumab reference product (ADL). Pharmacokinetic equivalence was demonstrated in a phase I study in healthy subjects[1]. Primary efficacy and safety results from a phase III study in rheumatoid arthritis (RA) patients showed equivalent efficacy and comparable safety and were reported previously[2].
**Objectives:** To compare secondary efficacy endpoints up to Week 24 in the phase III study of SB5 vs. ADL in patients with moderate-to-severe RA despite methotrexate (MTX) treatment.
**Methods:** Patients with moderate to severe RA despite MTX treatment were randomly assigned to receive 40 mg of either SB5 or ADL administered subcutaneously every other week for 24 weeks. At Week 24, patients on ADL were randomised again to receive 40 mg of either SB5 or ADL subcutaneously every other week for an additional 28 weeks. Patients on SB5 continued to receive SB5. The primary endpoint was the ACR20 response rate at Week 24. Secondary efficacy endpoints up to Week 24, including ACR20, ACR50, ACR70, disease activity score based on 28 joints (DAS28), simplified disease activity index (SDAI), clinical disease activity index (CDAI), and health assessment questionnaire-disability index (HAQ-DI), were compared for patients receiving SB5 and ADL.
**Results:** 544 patients were randomised and 542 patients were included in the full analysis set (SB5 [N=269] or ADL [N=273]) for assessment of secondary efficacy endpoints. ACR response rates (ACR20/50/70) were comparable between the two treatment groups at every visit up to Week 24. DAS28, SDAI, and CDAI were also comparable up to Week 24. The mean change in DAS28 from baseline to Week 24 was –2.74 for SB5 and –2.68 for ADL; the 95% confidence interval of the difference in the least square means between each treatment group was –0.26 to 0.17, which was within the pre-defined equivalence margin of –0.6 to 0.6. Comparable proportions of patients on SB5 and ADL achieved low disease activity and remission at Week 24, as assessed by DAS28, SDAI, and CDAI. Patient reported outcomes, assessed by HAQ-DI, were also comparable between SB5 and ADL up to Week 24. Other efficacy endpoints (ACR-N, EULAR response) were comparable up to Week 24.

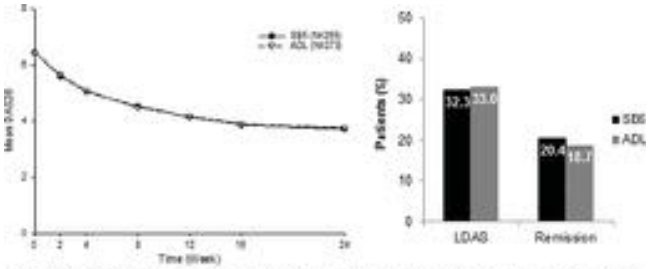



Figure 1. Mean DAS28 up to Week 24 and Proportion of Patients with Low Disease activity and Remission Based on DAS28 at Week 24

DAS28: disease activity score measured by 28 joints based on erythrocyte sedimentation rate.
Remission is defined as DAS28 < 2.6 and low disease activity is defined as DAS28 < 3.2 at Week 24.

**Conclusions:** Efficacy of SB5 and of ADL was comparable up to Week 24 for all secondary efficacy endpoints, as well as for the primary efficacy endpoint.
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[1] Shin D et al. Ann Rheum Dis. 2015; 74 (Suppl2: 459–460), FRI0110
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**Disclosure of Interest:** J. Kay Grant/research support from: AbbVie, Eli Lilly and Company, Pfizer, Genentech, Roche Laboratories, Consultant for: Alexion Pharmaceuticals, Amgen, AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb Company, Crescendo Bioscience, Eli Lilly and Company, Epirus Biopharmaceuticals, Genentech, Hospira, Janssen Biotech, Merck Sharp & Dohme Corp., Novartis Pharmaceuticals Corporation, Pfizer, Samsung Bioepis, Sandoz, Roche Laboratories, UCB, M. Weinblatt Consultant for: AbbVie, Samsung Bioepis, Amgen, E. Keystone Grant/research support from: Pfizer, Roche, Janssen, Amgen, Consultant for: Pfizer, Roche, Janssen, Amgen, BMS, Merck, Celltrion, Samsung Bioepis, M. C. Genovese Consultant for: Samsung Bioepis, A. Baranauskaite Grant/research support from: AbbVie, Samsung Bioepis, S. Y. Cheong Employee of: Samsung Bioepis, J. Ghil Employee of: Samsung Bioepis
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## THU0139 COMPARISON OF THE EFFICACY AND TOLERANCE OF THE "TRIPLE ORAL THERAPY" VERSUS "ANTI-TNF PLUS METHOTREXATE" IN RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: A SYSTEMATIC LITERATURE REVIEW

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**Background:** For patients with rheumatoid arthritis (RA) who have an inadequate response to methotrexate (MTX), there is some uncertainty about the relative effectiveness of combination of conventional DMARDs compared with combination of TNF inhibitors and MTX, as second line therapy.
**Objectives:** To compare efficacy and tolerance of triple oral DMARD therapy versus anti-TNF associated with MTX in patients with RA after MTX failure.
**Methods:** A systematic search of literature up to Mars 2014 was performed, in Medline, Embase, the Cochrane library and abstracts from the ACR and EULAR congresses from 2006 to 2013. Studies were included if they were randomised and controlled trial in patients receiving a triple oral combination therapy (MTX + sulfasalasine + hydroxychloroquine) compared with biologic agents plus methotrexate. Treatment effects on disease activity (DAS 28), American College of Rheumatology and the European League Against Rheumatism response criteria and structural damage using Sharp score were studied.
**Results:** Our search identified 263 articles, among them only 5 responded to the selection criteria. At six months and two years, there is a significantly larger number of participants achieving an ACR 70 response in the anti-TNF group. At one year, a significantly higher percentage of patients in the anti-TNF group reached a good EULAR response. Patients treated with TT have a significantly greater increase in modified Sharp than patients treated with MTX-infliximab at two years.
Analysis based on ACR-EULAR response criteria, the DAS 28 score and Sharp score were in favor of anti-TNF combined with MTX. There was no difference between treatments on functional disability (HAQ) and rates of adverse events.
**Conclusions:** In patients with RA in whom MTX has failed, addition of tumour necrosis factor antagonist to MTX is a valid option with better clinical outcomes and better radiographical results. Addition treatment with DMARDs is an appropriate treatment option in the absence of poor prognostic factors and/or in case of TNF inhibitors contraindications in a health-economic restreint context.
**Disclosure of Interest:** None declared
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## THU0140 EFFICACY AND SAFETY ANALYSIS BY OVERALL ANTI-DRUG ANTIBODY RESULTS UP TO WEEK 30 IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SB2 (AN INFLIXIMAB BIOSIMILAR) OR INFLIXIMAB REFERENCE PRODUCT IN PHASE III STUDY

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**Background:** SB2 is developed as a biosimilar of the infliximab reference product (INF). The clinical results of this Phase III study have been reported[1,2].
**Objectives:** To compare efficacy results (ACR responses, ACR-N, DAS28, and proportion of patients with remission/low disease activity based on DAS28, SDAI or CDAI) and safety results including infusion related reaction by anti-drug antibody (ADA) status up to Week 30 in patients with rheumatoid arthritis (RA) treated with SB2 or INF.
**Methods:** This study is a randomised, double-blind phase III study. A total of 583 patients with RA were treated with 3 mg/kg of SB2 or INF with background methotrexate (MTX). Efficacy, safety and immunogenicity were measured.
**Results:** Patients who developed ADA up to Week 30 were 55.1% in SB2 and 49.7% in INF. In both ADA positive and ADA negative subgroups, the ACR responses and other efficacy endpoints were comparable between SB2 and INF up to Week 30. There was a trend towards decreased efficacy in ADA positive subgroups compared with ADA negative subgroups for all efficacy parameters evaluated in both treatment arms. Safety profiles were also comparable between SB2 and INF in both ADA positive and negative subgroups. Within each treatment group, safety profiles were comparable between ADA positive and negative subgroups. Two patients (1.6%) treated with SB2 and 4 patients (2.7%) treated with INF in the ADA negative subgroups, and 8 patients (5.1%) treated with SB2 and 9 patients (6.2%) treated with INF in the ADA positive subgroups reported an infusion related reaction.

**Table 1. Efficacy Results at Week 30 by 30-week Overall ADA Results**

| | (-) ADA, SB2 (N=129) | (-) ADA, INF (N=147) | (+) ADA, SB2 (N=158) | (+) ADA, INF (N=145) |
|---|---|---|---|---|
| ACR20 | 80/110 (72.7%) | 94/132 (71.2%) | 81/143 (56.6%) | 79/133 (59.4%) |
| ACR50 | 49/110 (44.5%) | 57/132 (43.2%) | 40/143 (28.0%) | 42/133 (31.6%) |
| ACR70 | 29/110 (26.4%) | 27/132 (20.5%) | 16/143 (11.2%) | 23/133 (17.3%) |
| Change in DAS28 from Week 0 | −2.7 (1.44) | −2.4 (1.39) | −2.0 (1.31) | −2.3 (1.57) |
| Change in SDAI from Week 0 | −26.0 (13.12) | −24.0 (12.84) | −22.0 (14.57) | −23.0 (15.94) |
| Change in CDAI from Week 0 | −25.0 (13.08) | −23.0 (12.79) | −22.0 (13.96) | −23.0 (15.45) |
| LDA (DAS28) | 39/110 (35.5%) | 37/132 (28.0%) | 26/143 (18.2%) | 31/133 (23.3%) |
| Remission (DAS28) | 27/110 (24.5%) | 25/132 (18.9%) | 10/143 (7.0%) | 17/133 (12.8%) |

Data are presented in n/n' (%) or mean (SD)
Remission is defined as DAS28 < 2.6 and low disease activity is defined as DAS28 ≤ 3.2

**Conclusions:** Regardless of the overall 30-week ADA status, efficacy results were comparable between SB2 and INF. Efficacy tends to be lower in ADA positive subgroups compared with ADA negative subgroups of patients treated with either SB2 or INF. Safety profiles including infusion related reactions were also comparable between SB2 and INF regardless of ADA status, but a higher proportion of patients reported infusion related reactions in ADA positive subgroups compared to ADA negative subgroups in both treatment groups.
**References:**
[1] Choe JY et al. Ann Rheum Dis. 2015–207764 [Epub ahead of print]
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**Disclosure of Interest:** J.-Y. Choe Grant/research support from: Samsung Bioepis, Consultant for: Samsung Bioepis, J. S. Smolen Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, Celgene, Glazo, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung Bioepis, Sanofi, UCB, E. Keystone Grant/research support from: Pfizer, Roche, Janssen, Amgen, Consultant for: Pfizer, Roche, Janssen, Amgen, BMS, Merck, Celltrion, Samsung Bioepis, M. C. Genovese Consultant for: Samsung Bioepis, J. Choi Employee of: Samsung Bioepis, Y. H. Rho Employee of: Samsung Bioepis
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## THU0141 A NON-INTERVENTIONAL CLINICAL STUDY EVALUATING THE USE OF GOLIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), PSORIATIC ARTHRITIS (PSA), AND ANKYLOSING SPONDYLITIS (AS) IN A REAL-LIFE SETTING IN GERMANY

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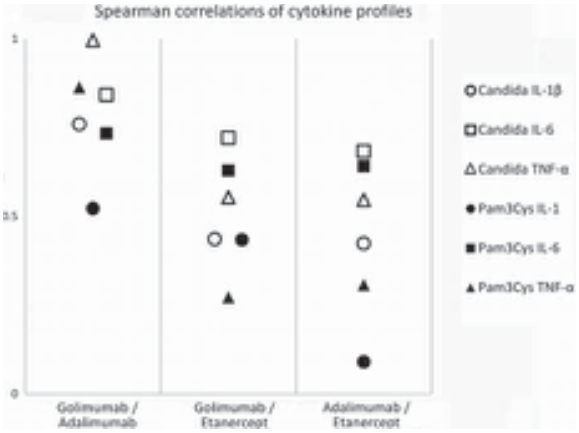
**Background:** Golimumab (GOL) has shown its efficacy and safety in various randomized clinical trials with patients eligible for clinical studies. Data from daily clinical practice in Germany are still lacking.
**Objectives:** To gather data in daily clinical practice from German patients with RA, PsA, AS starting a treatment with GOL sc once monthly. The aim was to monitor safety, effectiveness, socio- and health economic parameters, as well as patient reported quality of life in a real-life setting.
**Methods:** Patients were enrolled in the non-interventional study GO-NICE at 168 German sites to explore days of sick leave, ability to work, data of quality of life and clinical effectiveness by DAS28, PsARC and BASDAI as well as safety.
**Results:** 1,613 patients were documented. A total of 1,458 (90.4%) patients were eligible for final analysis, and had a baseline assessment as weel as at least one additional visit. 664 (41.2%) completed the 24-month observational period.
*RA-patients* (n=474): Mean age was 54.9 years, 72.8% were female, 45.7% were employed and 64.7% were biologic-naïve at baseline (BL). DAS28 was initially 5.0 and dropped to 2.9 within 24 months ($p<0.0001$). After 3 months of therapy, 33.7% of patients were in remission (DAS28 <2.6), and after 24 months 44.6%.
*PsA-patients* (n=501): Mean age was 50.5 years, 54.1% were female, 55.7% were employed, 56.5% were biologic-naïve at BL. 197 patients had a nail involvement (39.3%), 106 dactylitis (21.2%) and 70 enthesitis (14.0%) at BL. 54.1% showed a good response (mod. PsARC) after 3 months with a further increase to 67.9% after 24 months.
*AS-patients* (n=483): Mean age was 43.6 years, 66.5% were male, 69.6% were employed, 61.0% were biologic-naïve at BL. The most common extra-articular manifestations were iritis (15.1%), enthesitis (12.4%), IBD (5.8%) and dactylitis (3.5%). The mean BASDAI score (1–10) decreased from 5.1 (month 0) to 2.4 (month 24) ($p=0.0001$).
*Days of absenteeism* from work due to the underlying disease in the last 6 months were evaluated at BL and after 2 years of treatment. These dropped from 16.2 to 4.1 (RA), from 10.6 to 2.0 (PsA) and from 14.7 to 3.9 days (AS). The disease impact on *quality of work* within the last 6 months, determined by 0 (no impact) to 10 (very severe impact) decreased within 24 months of treatment from 4.8 to 2.4 (RA-), from 4.8 to 2.2 (PsA-) and from 4.8 to 2.0 (AS-patients).
An improvement of *quality of life* (EQ-5D-3L) and *functional ability* (FFbH) was seen in all three patient groups after 6 months and was maintained over 24 months.
After 24 months the treating rheumatologists rated more than 80% of the treatment courses as "successful", 10–15% as "partially successful", and less than 4% as "unsuccessful".
The *safety profile* of GOL was consistent with that observed in other studies of GOL. 4 deaths occurred: 1 patient unlikely related, and 3 patients not drug-related to treatment of GOL.
**Conclusions:** GOL sc once monthly was an effective treatment in patients with RA, PsA and AS in a real-life setting in Germany. It showed remarkable improvements in clinical effectiveness, health economic and patient-reported quality of life parameters. No new safety signals were detected.
**Disclosure of Interest:** K. Krüger Grant/research support from: AbbVie, BMS, Celgene,Janssen Biologics, Pfizer, Roche, Sanofi-Aventis, G. Burmester Grant/research support from: AbbVie, Bristol-Myers Squibb, MSD Sharp & Dohme, Pfizer, Roche, UCB, S. Wassenberg Grant/research support from: AbbVie, Chugai, Janssen Biologics, MSD, Novartis, Pfizer, Roche, M. Bohl-Bühler Grant/research support from: AbbVie, Hexal, MSD, Roche, UCB, M. Thomas Employee of: MSD Sharp Dohme GmbH
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## THU0142 HIGH SIMILARITY BETWEEN EX-VIVO INHIBITED CYTOKINE PROFILING BY GOLIMUMAB AND ADALIMUMAB AS A PUTATIVE EXPLANATION FOR INFERIOR TREATMENT RESPONSE TO GOLIMUMAB AFTER ADALIMUMAB FAILURE IN RHEUMATOID ARTHRITIS

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**Background:** Better prediction of treatment response to biologics in rheumatoid arthritis (RA) would contribute to optimal individualised treatment. Clinical data suggest that the response of RA patients to treatment with golimumab is much lower among those who switched from adalimumab compared with those who had previously received etanercept or infliximab.[1] In order to elucidate the mechanism behind this difference in response to sequential biologic treatment, we have performed ex-vivo inhibited cytokine profiling.
**Objectives:** To compare the ex-vivo effect of six different biologics on multi-cytokine profiles of RA patients.
**Methods:** In a prospective longitudinal prediction cohort study (BIO-TOP [Biologic Individual Optimised Treatment Outcome Prediction]), blood samples were obtained from patients at baseline (before start biologic). Within 24 hours peripheral blood mononuclear cells (PBMCs) were isolated, washed and pre-incubated for one hour with the therapeutic concentration of six different biologics (adalimumab and golimumab (anti-TNF-$\alpha$), etanercept (TNFR-Fc) abatacept (CTLA4-Ig), rituximab (anti-CD20) and tocilizumab (anti-IL-6R)). Subsequently, the cells were stimulated with Candida albicans or Pam3Cys. Supernatants were harvested after 24 hours and stored at -20C. The cytokine concentrations of IL-1$\beta$, IL-6 and TNF-$\alpha$ were determined by ELISA. The correlation of absolute changes of cytokine levels after inhibition by each biologic were calculated and analysed by means of Spearman rank correlations ($r_s$).
**Results:** Ex-vivo cytokine profiling was performed in 71 patients. The absolute change of cytokine level after inhibition by golimumab was significantly ($p<0.001$)

correlated with the absolute change of cytokine level after inhibition by adalimumab for both IL-1β, IL-6 and TNF-α (Figure). In other words, the cytokine profile after inhibition by golimumab or adalimumab was moderately to highly correlated with each other, while the correlation with the cytokine profile after inhibition by etanercept was much lower for both. Correlations between the cytokine profiles after inhibition by any of the three TNF inhibitors and cytokine profiles after inhibition by any non-TNFi were all weak (data not shown; all $r_s < 0.6$).




**Conclusions:** The high similarity between ex-vivo inhibited cytokine profiling by golimumab and adalimumab provides a putative explanation for the previously found inferior treatment response to golimumab after adalimumab failure in RA. This interesting finding is relevant for clinical practice, because it seems that RA patients who are non-responsive to adalimumab should not switch to golimumab and vice-versa. Furthermore, the similarity in both cytokine profile and clinical outcome for golimumab and adalimumab suggests that ex-vivo inhibited cytokine profiling could be a predictor of individual treatment response to biologics. This is currently being investigated in the BIO-TOP study.

**References:**

[1] Smolen JS et al. Insights into the efficacy of golimumab plus methotrexate in patients with active rheumatoid arthritis who discontinued prior anti-tumour necrosis factor therapy: post-hoc analyses from the GO-AFTER study. Ann Rheum Dis 2014;73:1811–1818

**Disclosure of Interest:** None declared

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## THU0143 SINGLE-ARM STUDY OF ETANERCEPT (ETN) IN ADULT PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS (RA) WHO FAILED ADALIMUMAB (ADA) TREATMENT

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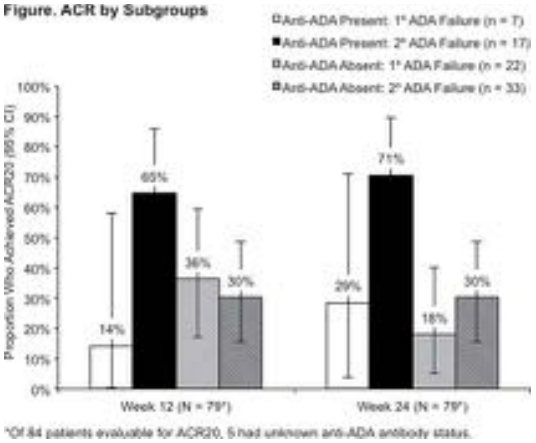
**Background:** EULAR guidelines for RA[1] recommend adding a biologic disease-modifying antirheumatic drug (bDMARD) to a conventional synthetic DMARD (csDMARD) like methotrexate (MTX) if poor prognostic factors are present or response to csDMARD treatment alone is insufficient. If a first bDMARD fails, another bDMARD should be used, such as switching from one tumor necrosis factor inhibitor (TNFi) to another TNFi. It is not known whether antibodies to one TNFi influence the effectiveness of a different TNFi.

**Objectives:** This phase 4, single-arm study evaluated the efficacy and safety of ETN in adult RA patients who had failed ADA.

**Methods:** Adults (age ≥18 years) with moderate to severe RA (disease activity score using 28-joint count and C-reactive protein [DAS 28-CRP] ≥3.2) who failed to respond to ADA+MTX (1º ADA failure) or lost a satisfactory response to ADA+MTX (2º ADA failure) were enrolled. After ≥2 weeks without ADA, ETN 50 mg once weekly for 24 weeks was added to ongoing MTX treatment. Visits occurred at weeks 0, 4, 8, 12, 18, and 24. Assessments included American College of Rheumatology 20% (ACR20), 50% (ACR50), and 70% (ACR70) improvement criteria, and DAS28-CRP. The primary efficacy endpoint was ACR20 at week 12.

**Results:** Of 85 patients who received ETN, 80% were women; mean age was 56.6 years. Overall, 28% had anti-ADA antibodies (42% were neutralizing and 58% non-neutralizing), including 21% (7/33) with 1º ADA failure and 33% (17/52) with 2º ADA failure. Median duration of prior ADA therapy was 46 weeks (range, 12–466 weeks). Of 84 evaluable patients, 30 (36%) achieved ACR20 at week 12 (95% confidence interval [CI]: 26%, 47%) and 29 (35%) achieved ACR20 at week 24. The rates for ACR50 and ACR70 with ETN were 11% and 2%, respectively, at week 12, and 16% and 4%, respectively, at week 24. ACR20 rates by visit are shown by subgroup in the figure. Of the subgroups, patients with 2º ADA failure and anti-ADA antibodies were most likely to have an ACR20 response with ETN at week 12 (65%; odds ratio vs no anti-ADA antibodies 5.2; 95% CI: 2.0, 13.5; $P < 0.001$). DAS28-CRP improved by a mean of 0.8–2.0 in each subgroup at week 12 of ETN, with the greatest improvement in patients with anti-ADA antibodies and 2º ADA failure. Most patients (82%) in this subgroup had DAS28-CRP improvement ≥1.2 at week 12 of treatment with ETN. ACR20 responses at week 12 occurred in patients with anti-ADA binding antibodies that were either neutralizing (4/10; 40%) or non-neutralizing (8/14; 57%). Safety results (≥1 adverse event in 73% of patients and no fatal adverse events) were consistent with the known safety profile of ETN.

**Figure. ACR by Subgroups**




*Of 84 patients evaluable for ACR20, 5 had unknown anti-ADA antibody status.

**Conclusions:** In patients who fail ADA, ETN could be considered as a therapeutic option. The presence of anti-ADA antibodies in patients with 2º ADA failure may guide treatment decisions.

**References:**

[1] Smolen JS, et al. Ann Rheum Dis. 2014;73:492–509.

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## THU0144 PHARMACOKINETICS AND SAFETY OF GP2015, A PROPOSED ETANERCEPT BIOSIMILAR, ADMINISTERED SUBCUTANEOUSLY BY AN AUTOINJECTOR OR PREFILLED SYRINGE IN HEALTHY MALE SUBJECTS

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**Background:** Rheumatoid arthritis (RA) being a joint-destructive disease, patients with advanced stages of the disease face difficulties in operating conventional or pre-filled syringes (PFS) for subcutaneous (sc) administration. Therefore, GP2015, a proposed etanercept biosimilar, is planned to be presented in a ready to use, fixed dose, disposable autoinjector (AI), identical to secukinumab autoinjector, allowing one-hand injection without requiring fine finger manipulations.

**Objectives:** To compare the pharmacokinetics (PK) and safety of GP2015 administered via AI or PFS in healthy male subjects.

**Methods:** In this open-label, randomised, 2-way cross over study, male healthy subjects (N=51), ≥18–≤55 years of age, were randomised to receive a single 50 mg sc dose of GP2015 via AI or PFS followed by a wash-out period of at least 35 days and a second 50 mg sc injection of GP2015 via PFS or AI vice versa. Subsequent follow up was 28 days. Randomisation was stratified by body weight (50–79.9 kg, 80–99.9 kg, 100–140 kg), allocating 17 subjects per each weight category.

**Results:** Out of 51 subjects enrolled into the study, 48 were evaluable for PK analysis. Subjects exhibited a mean body weight of 91.5 kg (range: 54.4–133.7 kg) and a mean body mass index (BMI) of 27.7 kg/m$^2$ (range: 19.3–39.0 kg/m$^2$). The 90% confidence intervals (CIs) for the ratios of geometric means of maximum observed serum concentration ($C_{max}$), area under the serum concentration-time curve measured from the time of dosing to the last measurable concentration ($AUC_{0\text{-last}}$), and AUC measured from the time of dosing and extrapolated to infinity ($AUC_{0\text{-inf}}$) were contained within the limits of 80–125% confirming bioequivalence between GP2015 applied via AI or PFS (Table). Within each body weight category, the serum concentration profiles of GP2015 were similar for both treatment administrations. The 90% CI for the ratios of geometric means of all PK parameters were within 80–125% in low and medium weight groups. In

the high weight group, due to a single subject with low exposure after dosing by PFS, the upper limit of the 90% CI was above 125%, while without this outlier the upper limit of CI was below 125%. The most common adverse events (AEs) regardless of relationship to the study drug were headache [GP2015-AI, n=8 (16%); GP2015-PFS, n=5 (10%)] and neutropenia [GP2015-AI, n=5 (10%); GP2015-PFS, n=5 (10%)]. All treatment related AEs were of mild severity and resolved during the study. None of the neutropenias (range: 1.1–1.7 x $10^9$/L; reference range: 1.8–7.9 x $10^9$/L) were considered clinically significant. No serious AEs or deaths occurred during the study. Three subjects had a mild injection site reaction [GP2015-AI, n=1 (2%); GP2015-PFS, n=2 (2%)]. No anti-drug antibodies were detected in any of the subjects.

**Table. Geometric LS means and 90% Confidence intervals for PK parameters**

| PK parameters | LS means | | Ratio GP2015-AI/GP2015-PFS | |
|---|---|---|---|---|
| | GP2015-AI | GP2015-PFS | Estimate | 90% Confidence Interval |
| $C_{max}$ (µg/mL) | 3.7 | 3.6 | 1.01 | (0.94, 1.08) |
| $AUC_{0\text{-}tlast}$ (h*µg/mL) | 684.1 | 678.4 | 1.01 | (0.95, 1.07) |
| $AUC_{0\text{-}inf}$ (h*µg/mL) | 745.2 | 737.4 | 1.01 | (0.96, 1.07) |

Using an analysis of variance (ANCOVA) model with treatment, period and sequence as fixed effects, body weight as covariate, and subject within sequence as random effect.
AI, autoinjector; $AUC_{0\text{-}tlast}$ area under the serum concentration-time curve measured from the time of dosing to the last measurable concentration; $AUC_{0\text{-}inf}$ area under the serum concentration-time curve measured from the time of dosing and extrapolated to infinity; $C_{max}$ maximum observed serum concentration; LS, least squares; PFS, pre-filled syringe; PK, pharmacokinetic

**Conclusions:** This study demonstrated PK bioequivalence of GP2015 administered by AI or PFS. Both administrations were bioequivalent, including when analysis was stratified by body weight. A single dose of 50 mg GP2015 administered by AI or PFS was well tolerated, with a safety profile consistent with previous reports for etanercept. These results suggest that the AI is an effective application form of GP2015 with a similar safety profile compared to the PFS.
**Disclosure of Interest:** M. Afonso Employee of: Hexal AG, affiliate of Novartis, D. Kollins Employee of: Hexal AG, affiliate of Novartis, L. Macke Employee of: Hexal AG, affiliate of Novartis, H. Woehling Shareholder of: Hexal AG, affiliate of Novartis, Employee of: Hexal AG, affiliate of Novartis, G. Wuerth Employee of: Hexal AG, affiliate of Novartis
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## THU0145 PHARMACOKINETICS AND SAFETY OF GP2015, A PROPOSED ETANERCEPT BIOSIMILAR, AND ETANERCEPT ORIGINATOR PRODUCT IN HEALTHY MALE SUBJECTS: A RANDOMISED TWO-WAY CROSSOVER STUDY

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**Background:** GP2015 is a proposed etanercept (tumor necrosis factor inhibitor) biosimilar.
**Objectives:** To compare the pharmacokinetics (PK) and safety of GP2015 and etanercept originator product (EU-authorised) in healthy subjects.
**Methods:** Healthy subjects (N=54) were randomised to receive a single 50 mg subcutaneous (sc) injection of GP2015 or etanercept originator product, followed by a wash-out period of at least 35 days, and a single 50 mg sc injection of originator product or GP2015, respectively. Subsequent follow up was 28 days. The primary PK parameters were normalised by the protein content of the administered dose before fitting in the analysis of variance model (dose normalised PK analysis). Bioequivalence between GP2015/etanercept originator product for primary PK parameters [maximum observed serum concentration ($C_{max}$), area under the serum concentration-time curve measured from the time of dosing to the last measurable concentration ($AUC_{0\text{-}tlast}$) and AUC measured from the time of dosing and extrapolated to infinity ($AUC_{0\text{-}inf}$)] was demonstrated if the 90% confidence intervals (CIs) for the ratio of geometric means were completely contained within the predefined bioequivalence limits of 0.80–1.25.
**Results:** The 90% CIs for the ratios of geometric means of dose normalised primary PK parameters ($C_{max}$, $AUC_{0\text{-}tlast}$ and $AUC_{0\text{-}inf}$) were within the interval of 0.80–1.25 (Table). For the respective nominal dose (not dose normalised) primary PK parameters, the 90% CIs of the ratios of geometric means were also within the interval of 0.80–1.25 (Table). The most common AEs regardless of relationship to study drug were neutropenia [GP2015, n=7 (13%); originator product, n=8 (14.8%)], headache [GP2015, n=5 (9.3%); originator product, n=5 (9.3%)] and nasopharyngitis [GP2015, n=4 (7.4%); originator product, n=4 (7.4%)]. All treatment-related AEs were of mild or moderate intensity. No serious AEs and deaths occurred during the study. Three subjects had low titer and non-neutralising anti-drug antibodies (ADAs) at the 28-day follow-up visit (treatment sequence GP2015/etanercept originator product).

**Table. Mean ratio and 90% confidence intervals for PK parameters**

| PK parameters (dose normalised) | GP2015/the etanercept originator product | |
|---|---|---|
| | Mean ratio (%) | 90% confidence interval |
| $C_{max}$ (ng/mL) | 1.03 | (0.98 – 1.09) |
| $AUC_{0\text{-}tlast}$ (h*ng/mL) | 0.92 | (0.88 – 0.95) |
| $AUC_{0\text{-}inf}$ (h*ng/mL) | 0.90 | (0.87 – 0.94) |
| **PK parameters (nominal dose)** | | |
| $C_{max}$ (ng/mL) | 1.11 | (1.05 – 1.17) |
| $AUC_{0\text{-}tlast}$ (h*ng/mL) | 0.98 | (0.94 – 1.02) |
| $AUC_{0\text{-}inf}$ (h*ng/mL) | 0.96 | (0.93 – 1.00) |

Using an analysis of variance (ANOVA) model with treatment, period and sequence as fixed effects, and subject within sequence as random effect.
$AUC_{0\text{-}tlast}$ area under the serum concentration-time curve measured from the time of dosing to the last measurable concentration; $AUC_{0\text{-}inf}$ area under the serum concentration-time curve measured from the time of dosing and extrapolated to infinity; $C_{max}$ maximum observed serum concentration; PK, pharmacokinetic

**Conclusions:** This study demonstrated PK bioequivalence between GP2015, a proposed etanercept biosimilar and the etanercept originator product with no relevant differences in safety. The safety and immunogenicity profiles observed in this study are consistent with previous reports on etanercept originator product.
**Disclosure of Interest:** M. Afonso Employee of: Hexal AG, affiliate of Novartis, S. Sanguino Heinrich Employee of: Hexal AG, affiliate of Novartis, J. Poetzl Employee of: Hexal AG, affiliate of Novartis, H. Woehling Shareholder of: Hexal AG, affiliate of Novartis, Employee of: Hexal AG, affiliate of Novartis
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## THU0146 IMPACT OF ANTI-DRUG ANTIBODIES ON EFFICACY AND SAFETY UP TO WEEK 24 FROM A PHASE III STUDY COMPARING SB5 (AN ADALIMUMAB BIOSIMILAR) WITH ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS DESPITE METHOTREXATE THERAPY

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**Background:** SB5 is a biologic agent developed as a biosimilar of the adalimumab reference product (ADL). The primary efficacy and safety results from a phase III study in rheumatoid arthritis (RA) patients have been reported previously[1]. Immunogenicity to monoclonal antibodies may affect patients' safety and efficacy.
**Objectives:** To compare efficacy and safety results by anti-drug antibody (ADA) status in patients with RA treated with SB5 or ADL (with background Methotrexate, MTX) up to Week 24.
**Methods:** Patients with moderate to severe RA despite MTX treatment were randomly assigned to receive 40 mg of either SB5 or ADL administered subcutaneously every other week. Efficacy, safety, and immunogenicity were measured.
**Results:** The ADA incidence up to Week 24 was 32.8% in SB5 and 31.5% in ADL. In both ADA positive and ADA negative subgroups, ACR responses and other efficacy endpoints were comparable between SB5 and ADL up to Week 24. Within SB5, there was a trend towards decreased efficacy (ACR20, ACR50, ACR-N, change in DAS28 from baseline, and in patients with remission based on DAS28, SDAI or CDAI) in the ADA positive subgroup compared to the ADA negative subgroup. Within ADL, there was a trend towards decreased efficacy for patients in remission based on DAS28, SDAI or CDAI in the ADA positive subgroup compared with the ADA negative subgroup, but other efficacy endpoints were comparable. The safety profiles of SB5 and ADL were generally comparable in both ADA positive and ADA negative subgroups. Within each treatment group, the safety profiles were comparable between ADA positive and ADA negative subgroups. Among ADA negative subgroup, 2.2% in SB5 and 3.8% in ADL experienced ISR and among ADA positive subgroup, 4.5% in SB5 and 1.2% in ADL experienced ISRs.

**Table 1. Efficacy Results at Week 24 by 24-week Overall ADA Results**

| | (–) ADA, SB5 (N=178) | (–) ADA, ADL (N=183) | (+) ADA, SB5 (N=88) | (+) ADA, ADL (N=86) |
|---|---|---|---|---|
| ACR20 | 134/171 (78.4%) | 125/174 (71.8%) | 49/85 (57.6%) | 59/84 (70.2%) |
| ACR50 | 73/171 (42.7%) | 68/174 (39.1%) | 25/85 (29.4%) | 32/84 (38.1%) |
| ACR70 | 31/171 (18.1%) | 36/174 (20.7%) | 16/85 (18.8%) | 14/84 (16.7%) |
| Change in DAS28 from Week 0 | −2.9 (1.24) | −2.7 (1.30) | −2.5 (1.39) | −2.7 (1.24) |
| Change in SDAI from Week 0 | −26.9 (12.85) | −24.7 (12.36) | −24.1 (14.08) | −25.6 (11.35) |
| Change in CDAI from Week 0 | −26.4 (12.47) | −24.1 (12.13) | −23.4 (13.55) | −24.8 (11.85) |
| LDA (DAS28) | 59/170 (34.7%) | 63/173 (36.4%) | 28/85 (32.9%) | 27/84 (32.1%) |
| Remission (DAS28) | 41/170 (24.1%) | 39/173 (22.5%) | 14/85 (16.5%) | 12/84 (14.3%) |

Data are presented in n/n' (%) or mean (SD)
Remission is defined as DAS28 < 2.6 and low disease activity is defined as DAS28 ≤ 3.2

**Conclusions:** The efficacy was comparable between SB5 and ADL regardless of 24-week overall ADA status. Patients with positive ADA status were more likely to have reduced efficacy in SB5, but there was a weaker correlation between the presence of ADA and clinical efficacy in ADL. The safety was generally comparable between SB5 and ADL regardless of the 24-week overall ADA status. Safety was generally comparable between ADA negative and ADA positive subgroups in both treatment groups
**References:**
[1] Weinblatt ME et al. Arthritis Rheumatol. 2015; 67 (suppl 10), 8L
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## THU0147 DRUG SURVIVAL OF GOLIMUMAB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS IS INDEPENDENT OF METHOTREXATE AND PREDNISOLONE CONCOMITANCE: RESULTS FROM THE MULTICENTER BIOLOGICS REGISTRY

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**Background:** When using biological agents, particularly tumor necrosis factor (TNF) inhibitors, in patients with rheumatoid arthritis (RA), the use of methotrexate (MTX) or prednisolone (PSL) can cause considerable problems for patients because they cause adverse events. Therefore, safety would be increased if MTX and PSL could be tapered or stopped. The objective of this report was to determine the drug retention rate of golimumab (GLM) in Japanese patients with RA and identify potential predictors associated with treatment discontinuation.
**Methods:** A prospective analysis was performed on 152 patients with RA who were treated with GLM in our multicenter biologics registry. We assessed the age, body weight, disease duration, use of pre-biological agents, Disease Activity Score 28-Erythrocyte Sedimentation Rate, and use and dose of MTX and PSL as baseline characteristics of the patients, and we compared cumulative survival among these factors.
**Results:** The overall 52 weeks drug survival rate of GLM was 71.6%. The patients with a body weight of <50 kg had a better drug survival rate than those with a body weight of >50kg (see Table). The use and dose of MTX and use of PSL did not show statistical differences in drug survival rate (see Table).

Table 1. Characteristics of patients with RA receiving GLM at baseline

| Characteristic (unit) | Group range (number) | *P* value† |
|---|---|---|
| Body weight (kg) | <50 (41) | |
| | 50–60 (54) | 0.040* |
| | >60 (26) | 0.010* |
| Number of biologics used before GLM | 0 (80) | 0.363 |
| | 1 (48) | |
| | >1 (24) | 0.015* |
| DAS28-ESR | <3.2 (14) | |
| | 3.2–5.1 (48) | 0.722 |
| | >5.1 (67) | 0.589 |
| MTX use | negative (45) | |
| | positive (103) | 0.829 |
| MTX dose (mg/w) | <8 (30) | 0.177 |
| | 8 (32) | 0.185 |
| | >8 (41) | |
| PSL use | negative (74) | |
| | positive (75) | 0.520 |

†*P* value was calculated using log-rank test in each variable against its controls. **P* value of <0.05 was considered to indicate statistical significance.

**Conclusions:** In daily practice, patients with RA taper or stop their MTX or PSL use while undergoing treatment with biological agents if their RA disease activities are low. On the other hand, MTX with biological agents, particularly TNF inhibitors, would produce better efficacy than higher dose. Our result indicates that Japanese patients with RA receiving GLM may be able to taper or stop MTX and PSL use, which could increase safety and raise the drug retention rate in these patients. These data would be of value in selecting biological agents for MTX-intolerant RA patients.
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## THU0148 ECONOMIC CONSIDERATIONS AND PATIENTS' PREFERENCES AFFECT TREATMENT SELECTION FOR RHEUMATOID ARTHRITIS PATIENTS: A DISCRETE CHOICE EXPERIMENT AMONG EUROPEAN RHEUMATOLOGISTS

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**Background:** Economic considerations and patient preferences are increasingly important when choosing treatments. It is not known to what extent rheumatologists across Europe account for these factors when changing drug therapies in patients with active rheumatoid arthritis (RA).
**Objectives:** To compare the value that rheumatologists across Europe attach to patients' preferences and economic aspects when choosing treatments for rheumatoid arthritis (RA) patients.
**Methods:** In a discrete choice experiment European rheumatologists chose between two hypothetical drug treatments for a patient with moderate disease activity. Treatments differed in five attributes: efficacy (improvement and achieved state on disease activity), safety (probability of serious adverse events), patient's preference (level of agreement), medication costs and cost-effectiveness (incremental cost-effectiveness ratio (ICER)). A Bayesian efficient design defined the fourteen choice sets and a random parameter logit model was used to estimate relative treatment preferences for rheumatologists across countries.
β Coefficients presented in table 1 indicate whether the attribute has a negative or positive effect on the rheumatologists' preference
Cluster analyses and latent class models were applied to understand preference patterns across countries and among individual rheumatologists.
**Results:** Responses of 559 rheumatologists from 12 European countries were included in the analysis (49% females, mean age 48 years). In all countries, efficacy dominated the treatment decision followed by economic considerations and patient's preferences. Across countries, patient's agreement with the treatment was associated with an increased treatment preference of rheumatologists and a stronger, negative impact on rheumatologists treatment preference was seen when patents dislike treatments. The economic aspect also played an important role. Higher economic burden was consistently associated with decreased treatment preference. Interestingly, medication costs contributed significantly in all countries, whereas cost-effectiveness was only significant in 9 of 12 countries (table).Latent class models revealed four respondent profiles: one of which traded off all attributes, and the remaining three classes that disregarded ICER. Among individual rheumatologists, 57% disregard ICER in treatment choices, and these were more likely to be located in Italy, Romania, Portugal or France (cluster 2, table)



**Conclusions:** Overall, European rheumatologists are willing to trade between treatment efficacy, patients' treatment preferences and economic considerations. However, the degree of trade-off differs between countries and among individuals.
**Disclosure of Interest:** None declared
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## THU0149 THE 54-WEEK RESULTS OF INTERFERON-γ RELEASE ASSAY IN A PHASE III STUDY COMPARING SB2, AN INFLIXIMAB BIOSIMILAR, TO INFLIXIMAB REFERENCE PRODUCT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Patients who are being treated with anti-TNF therapy are at increased risk of developing active tuberculosis (TB) by reactivation of latent TB infection (LTBI) or de novo infection. SB2 is developed as a biosimilar of the infliximab reference product (INF). The primary results (30-week) and 54-week results of Phase III study have been reported[1,2].
**Objectives:** To evaluate the prevalence of positive interferon-γ release assay (IGRA) at Screening, the incidence of positive seroconversion in IGRA, and the incidence of active TB in the patients receiving SB2 or INF for 54 weeks.
**Methods:** This study is a randomised, double-blind phase III study. IGRA (QuantiFERON® Gold in-tube test) was performed at Screening, Week 22 and Week 54. Patients who have been diagnosed as active TB were excluded from the study. Patients with a positive IGRA test without any evidence of active TB could be enrolled after receiving TB prophylaxis treatment. Patients who newly seroconverted during the study also were recommended to receive TB prophylaxis.

**Results:** Of 804 patients with IGRA results at Screening, 143 patients (17.8% of 804) had positive results. Among them, 46 patients (19 patients in SB2 and 27 patients in INF) were randomised after the 30-days of TB prophylaxis treatment and the others were excluded from the study. At Week 22 and 54 or early termination visit, respectively, 19 (6.6%) and 7 (2.4%) patients in SB2 and 20 (6.8%) and 7 (2.4%) patients in INF had newly positive IGRA results. Among the patients with positive IGRA results at Week 22, 73.7% (14/19) in SB2 and 50.0% (10/20) in INF were treated with anti-TB treatment. During the study period, there was 1 active TB case in each treatment group (tuberculous pleurisy in SB2 [Korea] and pulmonary tuberculosis in INF [Lithuania]) and there was no case of active TB reported in patients with positive IGRA results at Screening or Week 22.

Table 1. Positive interferon-γ release assay[a] rate during the study

| IGRA test time | SB2 (N=290) | | INF (N=293) | |
|---|---|---|---|---|
| | Positive IGRA n (%) | Seroconversion[b] n (%) | Positive IGRA n (%) | Seroconversion[b] n (%) |
| Screening[c] | 19 (6.6%) | | 27 (9.2%) | |
| Week 22 | 28 (9.7%) | 19 (6.6%) | 36 (12.3%) | 20 (6.8%) |
| Week 54 or early termination | 26 (9.0%) | 7 (2.4%) | 24 (8.2%) | 7 (2.4%) |

[a]Patients, whose first and second interferon-γ release assay results were indeterminate, were considered to have the positive IGRA (at Screening 1 patient in each SB2 and INF; at Week 22, 4 patients in SB2 and 5 patients in INF for both positive IGRA and seronconversion; at Week 54, no patient in each SB2 and INF). [b]Seroconversion defined as negative to positive test change at each test time. [c]Randomised patients only.

**Conclusions:** The incidence of positive seroconversion in IGRA was comparable between the two treatment groups. Among patients with positive IGRA results at Screening or Week 22, there were no cases of active TB and only 2 cases of active TB were reported in this study. IGRA is therefore an useful method to prevent active TB in anti-TNF treated RA patients.

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## THU0150 LONG-TERM SAFETY AND EFFICACY OF SB4 (ETANERCEPT BIOSIMILAR) IN PATIENTS WITH RHEUMATOID ARTHRITIS: COMPARISON BETWEEN CONTINUING SB4 AND SWITCHING FROM ETANERCEPT REFERENCE PRODUCT TO SB4

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**Background:** SB4 is approved by the European Medicines Agency as a biosimilar of the etanercept reference product (ETN). The phase I clinical study results and 52-week results of phase III clinical study have been reported previously.[1–3]

**Objectives:** To evaluate the long term safety, immunogenicity, and efficacy of continuing SB4 vs. switching (as will occur in clinical practice) from ETN to SB4 in patients with moderate to severe RA.

**Methods:** The phase III randomised, double-blind study period consisted of 52 weeks of treatment with either weekly dose of subcutaneous 50 mg SB4 or ETN with background methotrexate (MTX) in patients with moderate to severe RA. After 52 weeks of treatment, patients in Czech Republic and Poland were enrolled into the open-label, extension period and received SB4 for additional 48 weeks. Efficacy, safety, and immunogenicity were assessed up to Week 100.

**Results:** At Week 52, 245 patients from the randomised, double-blind study period enrolled into the extension study: 126 patients continued to receive SB4 (SB4/SB4) and 119 patients switched from ETN to SB4 (ETN/SB4). Among them, 119 (94.4%) patients of SB4/SB4 and 113 (95.0%) patients of ETN/SB4 completed 100 weeks of treatment. SB4 was well tolerated and the safety profile was comparable between SB4/SB4 and ETN/SB4 during the open-label, extension period (Table 1). Adverse events were those newly occurring after Week 52 in 47.6% of SB4/SB4 and 48.7% of ETN/SB4. There were no cases of injection site reactions reported after Week 52. The overall incidence of anti-drug antibodies after Week 52 was 0.8% in SB4/SB4 and 0.9% in ETN/SB4. Efficacy was sustained and comparable between SB4/SB4 and ETN/SB4 up to Week 100 (Table 2).

**Conclusions:** SB4 was well tolerated and effective over 2 years in patients with RA. Efficacy, safety, and immunogenicity were comparable between the SB4/SB4 and ETN/SB4, demonstrating that switching produced no treatment emergent issues such as loss of efficacy, increase in adverse events, or increase in immunogenicity.

Table 1. Safety and Immunogenicity Outcome During the Open-label, Extension Period (From Week 52 to Week 100)

| Number of patients with | SB4/SB4 (N=126) | | ETN/SB4 (N=119) | |
|---|---|---|---|---|
| | n | (%) | n | (%) |
| At least 1 TEAE | 60 | (47.6) | 58 | (48.7) |
| At least 1 SAE | 6 | (4.8) | 2 | (1.7) |
| Serious infections | 1 | (0.8) | 1 | (0.8) |
| Active tuberculosis | 0 | (0.0) | 0 | (0.0) |
| Injection site reactions[a] | 0 | (0.0) | 0 | (0.0) |
| Malignancy[b] | 1 | (0.8) | 0 | (0.0) |
| Death[b] | 1 | (0.8) | 0 | (0.0) |
| ADA positive[c] | 1 | (0.8) | 1 | (0.9)[d] |

ADA: anti-drug antibody; SAE: serious adverse event; TEAE: treatment-emergent adverse event
[a] Defined as high level group terms of administration site reactions
[b] Hepatic cancer was reported in SB4/SB4
[c] Defined as at least one ADA positive up to Week 100 after Week 52
[d] Percentage is based on the number of patients with ADA results (117 patients)

Table 2. ACR Response Rates During the Open-label, Extension Period (From Week 52 to Week 100)

| ACR response | Timepoint | SB4/SB4 (N=126) | | ETN/SB4 (N=119) | |
|---|---|---|---|---|---|
| | | n/n' | (%) | n/n' | (%) |
| ACR20 | Week 52 | 99/125 | (79.2) | 98/119 | (82.4) |
| | Week 76 | 102/125 | (81.6) | 90/117 | (76.9) |
| | Week 100 | 95/122 | (77.9) | 91/115 | (79.1) |
| ACR50 | Week 52 | 65/125 | (52.0) | 64/119 | (53.8) |
| | Week 76 | 74/125 | (59.2) | 62/117 | (53.0) |
| | Week 100 | 73/122 | (59.8) | 70/115 | (60.9) |
| ACR70 | Week 52 | 48/125 | (38.4) | 39/119 | (32.8) |
| | Week 76 | 49/125 | (39.2) | 44/117 | (37.6) |
| | Week 100 | 52/122 | (42.6) | 48/115 | (41.7) |

ACR: American college of rheumatology

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## THU0151 MULTICENTER, OPEN-LABEL STUDY TO EVALUATE THE PREDICTABILITY OF DISEASE CONTROL AT WEEK 52 BASED ON EARLY RESPONSE TO CERTOLIZUMAB PEGOL (IN COMBINATION WITH METHOTREXATE) IN ITALIAN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: THE CZP-SPEED STUDY

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**Background:** Early identification of patients (pts) unlikely to achieve good long-term disease control with anti-TNF therapy in rheumatoid arthritis (RA) is important for physicians following treat-to-target recommendations. Predictability of response has previously been demonstrated in RA pts treated with certolizumab pegol (CZP), with previous work focusing on the predictability of long-term (1-year) response based on response at Week (Wk) 12.[1] In addition to clinical and patient-reported outcomes, musculoskeletal ultrasonography (US) is an increasingly important tool for assessing pt disease activity.

**Objectives:** To assess the impact of CZP treatment on clinical, patient-reported and US outcomes, and to assess the ability of early treatment response to predict long-term outcomes in Italian pts with RA.

**Methods:** CZP-SPEED (NCT01443364) was a 52-wk, open-label, prospective, interventional, multicenter study. Pts were biologic-naïve, had active RA ($\geq$6 swollen and $\geq$6 tender joints), and had failed treatment with $\geq$1 DMARD. All pts received CZP (400mg at Wks 0, 2 and 4, followed by 200mg every 2 wks). Positive predictive value was defined as the percentage of pts with clinical response (reduction from baseline in DAS28(ESR)$\geq$1.2) at an early time point who also had clinical response at Wk52. Early time points were Wks 1, 2, 4, 6, 8 and 12. Clinical and patient-reported outcomes were DAS28(ESR), ACR20/50/70, HAQ-DI, Pain (VAS) and PtGADA. US was assessed using the composite power Doppler/US (PDUS) score, defined as the sum of synovial fluid

and proliferation, Doppler signal/blood flow, cartilage damage and bone erosion scores. US operation parameters were harmonized across all study sites. Data are reported descriptively with NRI imputation for dichotomous data and LOCF for continuous data.

**Results:** 132 pts were enrolled and received CZP (safety set; SS), of whom 131 (99%) provided ≥1 baseline and ≥1 post-baseline DAS28(ESR) assessment (full analysis set; FAS), and 91 (69%) completed to Wk52. Pts had a mean age of 54.8, 82% were female, and disease duration was relatively short (median 1.8 years). Between 64–70% of pts who responded at Wk 2, 4, 6, 8, or 12 maintained response at Wk52 (Figure). Rapid improvements in clinical and US outcomes were observed at Wk8 and were maintained to Wk52 (Table). There were 301 adverse events (AEs) in 94 pts (71.2%) and 25 serious AEs in 16 pts (12.1%). No deaths or cases of tuberculosis were observed. No new safety signals were observed for CZP.

**Figure:** Positive predictive value (PPV) for clinical response at Week 52 based on clinical response at Weeks 1, 2, 4, 6, 8, and 12 (FAS, N=131)




Clinical response at Weeks 1–12 and Week 52 was defined as reduction in DAS28(ESR)≥1.2 from baseline.

**Table:** Clinical and ultrasound outcomes over 52 weeks of CZP treatment (FAS, N=131)

| | Baseline | Change from baseline to Week 8 | Change from baseline to Week 52 |
|---|---|---|---|
| DAS28(ESR), mean (SD) | 5.9 (1.1) | -2.2 (1.1) | -2.3 (1.5) |
| ACR20, n (%) | - | 86 (65.6) | 81 (61.8) |
| ACR50, n (%) | - | 57 (43.5) | 62 (47.3) |
| ACR70, n (%) | - | 27 (20.6) | 39 (29.8) |
| HAQ-DI, mean (SD) | 1.3 (0.7) | -0.5 (0.6) | -0.6 (0.7) |
| Pain, mean (SD) | 56.5 (23.4) | -25.2 (25.6) | -26.2 (29.9) |
| PtGADA, mean (SD) | 57.3 (23.2) | -25.8 (26.6) | -26.5 (30.9) |
| PDUS, mean (SD) [a] | 20.5 (11.7) | -4.5 (5.5) | -4.8 (7.5) |

[a] Measured in the PDUS subgroup (n=66). PDUS: power Doppler/ultrasonography; PtGADA: patient's global assessment of disease activity.

**Conclusions:** In Italian RA pts treated with CZP, clinical response up to Wk12 was predictive of long-term response at Wk52. In addition to the rapid and sustained clinical improvements observed in this cohort, this is the first report of the maintenance of US improvements over 52 wks in CZP-treated pts. Coupled with the clinical predictability data, US evaluation may allow rheumatologists to make decisions earlier in the treatment journey.

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## THU0152 OPTIMIZATION STRATEGIES OF BIOLOGICAL THERAPY IN RHEUMATOID ARTHRITIS. CREATE REGISTRY RESULTS AFTER TWO YEARS OF FOLLOW-UP

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**Background:** Treat to Target (T2T)is an international initiative to define Rheumatoid Arthritis (RA) treatment targets and recommendations to measure disease severity and encourage earlier diagnosis and optimize treatment. The primary target for treatment of RA should be a state of clinical remission.After reaching remission there are different therapeutic approaches to consider. In recent years, optimization of Biological Therapy (BT)is a strategy employed in patients with RA in remission, consists in a dose reduction or an extended dose interval, searching a minimum effective dose for each patient, which limits the occurrence of adverse effects and promotes economic saving

**Methods:** RA patients (ACR criteria 1987)of CREATE registry that November 1, 2013 had clinical remission (DAS28 value <2.6)of at least 6 months constituted the cohort of patients who were optimized. According to the consensus of the Spanish Society of Rheumatology and Hospital Pharmacy, dose optimization involved the reduction of between 20 and 50% of it.Decisions about treatment and dose reduction was performed by a multidisciplinary team of clinical rheumatologists and pharmacists in a tertiary hospital,which involved the application of protocols and patients revision at least every 2 months

**Results:** We performed a prospective observational cohort study in 70 RA optimized patients. (81.4% were women with a mean age at onset optimization of 56.9 ± 13.7 years. 68.8% were RF positive and 66.7% ACPA positive). Optimization occurred in 41.4% of patients in the first year and 58.8% in the second year (p=0.001).64 patients completed 24 month of follow-up, suffering 36 of these patients (56.3%) clinical relapse (mean DAS28 2.81 (0.88) at 1 year, reason why it was decided to return to the usual dose again reaching clinical remission in all patients after 2 years (DAS 28 2.59 (0.58).43.8% patients maintained optimization after 2 years of follow-up without suffering relapse (mean DAS28 2.19 (0.84)). Statistically significant differences were found when comparing the mean baseline DAS 28 between both groups, being lower in the subgroup of patients who maintains remission compared to the relapsing group (1.97 (0.85) vs 2.44 (0.66) (p=0.012)

**Conclusions:** -The use of an extended dose interval maintained remission status in patients with established RA who are in sustained clinical remission it is possible in 41.2% patients after 2 years of follow-up in clinical practice (CREATE registry)-This strategy is possible in patients with controlled disease persistently and in view of our results, we might consider that those patients who have a lower level of activity at onset optimization, are less likely to relapse and therefore maintain this strategy-After 2 years of follow up all patients maintained clinical remission (DAS28 <2.6),even the patients who relapsed at 12 months and returned to their usual dose

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## THU0153 HEMOGLOBIN IS A BETTER PREDICTOR FOR RADIOGRAPHIC PROGRESSION THAN DAS28 IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS-ANALYSIS FROM INTRAVENOUSLY ADMINISTERED GOLIMUMAB GO-FURTHER STUDY

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**Background:** Clinical studies demonstrated that baseline disease activity including C-reactive protein (CRP) level was a predictor variable for radiographic joint damage in patients with rheumatoid arthritis (RA).

**Objectives:** To identify variables associated with radiographic joint damage in patients with RA treated with intravenously administered golimumab (GLM) + Methotrexate (MTX) or MTX + placebo (PBO).

**Methods:** GO-FURTHER was a multicenter, randomized, placebo-controlled study. Adult patients with active RA despite MTX therapy (≥6 tender and swollen joints, CRP ≥1.0 mg/dL, and RF and/or anti-CCP positive) were randomized to placebo (PBO) + MTX or GLM (2mg/kg) plus MTX at week 0, 2, and every 8 week thereafter (GLM group). Patients in PBO group with <10% improvement in tender and swollen joint count from baseline at week 16 entered early escape (EE) and received a 2 mg/kg GLM infusion at weeks 16 and 20 and every 8 weeks subsequent. Radiographic progression was measured using Total *Sharp score* (TSS). The correlations of TSS with hemoglobin, disease activity score (DAS28-CRP)and physical function evaluated with Health Assessment Questionnaire (HAQ) were assessed using Spearman's correlation or multivariable liner regression model. Anemia was defined based on World Health Organization (WHO) criteria as Hgb <12 g/dl in women and <13 g/dl in men.

**Results:** Moderate to severe RA was demonstrated by a mean DAS28 score of 5.9 with TSS of 48.5 in all patients group at baseline. In linear regression models, baseline DAS28, HAQ score, and Hgb level was correlated with baseline TSS with Spearman's correlation coefficient (r) of 0.148 (p<0.01), 0.0.193 (p<0.001) and -0.129 (p<.001), respectively. Similar correlation relationships of TSS score with DAS28, HAQ and Hgb were observed at Week 24. In multiple linear regression models, after adjusting for effect of other factors, Hgb level demonstrated significant correlation with TSS at the baseline or Week 24. The change in Hgb at Week 20 also was correlated with change in TSS at Week 24 after adjusting for change in DAS28 and HAQ. GLM IV + MTX-treated patients demonstrated less radiographic damage than MTX+PBO-treated patients regardless of their anemia status at baseline or week 20.

**Conclusions:** Hemoglobin level is an independent variable predicting radiographic progression in MTX refractory RA patients.
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## THU0154 EFFECTS OF ETANERCEPT BIOMIMICS ON LIPID PROFILES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Objectives:** To compare the modifications in lipid profiles among patients with RA receiving anti-TNF-α agents – one Etanercept biomimics plus disease modifying anti-rheumatic drugs (DMARDs) versus DMARDs, explore the relationship between dyslipidemia, inflammation in RA patients.
**Methods:** 100 newly diagnosed RA patients were randomly divided into biological agent treatment group and non-biological agent treatment group, each group included 50 patients. At baseline and at 12 and 24 weeks, levels of lipids, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), as well as the atherogenic index of plasma (AIP) was calculated, antibodies against cyclic citrullinated peptide (ACCP), carotid intima-media thickness (CIMT)were studied at baseline and 24 weeks. Statistical analyses are performed with SPSS software version 19.0.
**Results:** Baseline values for lipid levels were similar in both groups. Pearson correlation test was carried out and found that CIMT and ESR, CRP, AIP were positively correlated, and HDL, Apo-AI were negatively correlated at baseline. At 12 weeks and 24 weeks in the biological agent treatment group, the levels of HDL, Apo-AI were increased and levels of Lpa, AIP were decreased when compared to the baseline, and at 24 weeks, CIMT was decreased compared to the baseline. At 24 weeks in the non-biological agents treatment group, the level of HDL was increased, levels of LDL, Lpa, CIMT, AIP were all decreased compared to the baseline. At 12 weeks in the biological agent treatment group, the levels of AIP, Lpa were lower than non-biological agent group, levels of TC, HDL, Apo-AI were higher than non-biological agent group, and at 24 weeks in the biological agent treatment group, the levels of Apo-B, Lpa were lower than non-biological agent group, level of LDL, Apo-AI were higher than non-biological agent group (all $P<0.05$).
**Conclusions:** (1) Inflammatory status may affect the lipid profiles and the endothelial function and is associated with the atherosclerosis. (2) The Etanercept biomimics and DMARDs both can improve lipid profiles, and the protective effect of the Etanercept biomimics on cardiovascular complications is superior to traditional DMARDs, but the medication's effect lasts shorter lengths of time, therefore further studies and large samples are needed in the future.
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## THU0155 ANALYSIS OF BIO-FREE CONDITION OF ADALIMUMAB (ADA) AND EARLY INTRODUCTION OF ADA IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** HOPEFUL-1 trial and HIT HARD trial showed the effect of combination therapy of methotrexate (MTX) plus adalimumab (ADA) for MTX naïve patients with active early rheumatoid arthritis (RA). Although the biologic disease modified anti rheumatic drugs (bDMARDs) are the most effective treatment of RA, the costs are much higher than that of conventional synthetic DMARDs (csDMARDs). Considering the total medical cost, strategies such as tapering and withdrawal of bDMARDs without disease flare can be an important option. However, the condition for discontinuation of bDMARDs in a real clinical setting has not been fully investigated.
**Objectives:** To analyze the bio-free condition of ADA and the effect of early introduction of ADA in RA patients in a real world.
**Methods:** We used ADA in 132 RA patients. Study 1: Twenty three patients discontinued ADA. We analyzed 14 patients who were followed up for more than 24 weeks after discontinuation. Study 2: Twenty four patients started ADA within 3 months from the introduction of MTX. Two patients stopped ADA due to inefficacy. We analyzed 14 patients who were followed up for more than 52 weeks.
**Results:** Study 1. Patients were 54.6 ± 10.5 years old, disease duration 3.2 ± 2.7 years, Bio-naïve: 13 patients, switch: 1 patient, Prednisolone was increased in 1 patient. csDMARDs were added in 8 patients (4 patients before and 4 patients after discontinuation of ADA). DAS28-CRP did not change until 24 weeks and no patient re-started bDMARDs. Study 2. Patients were 45.0 ± 14.9 years old, disease duration 1.5 ± 2.7 years, 6 patients used MTX alone as csDMARD and 5 patients among them started other csDMARDs additionally. DAS28-CRP decreased from 4.9 ± 1.1 to 1.8 ± 0.6 ($p<0.0001$), 9 patients achieved clinical remission (64.3%), and 3 patients (21.4%) achieved bio-free condition without relapse.
**Conclusions:** In Study 1, ADA made bio-free condition in 17.5% of RA patients without relapse until 24 weeks, which indicates the possibility of sustainable bio-free in the real clinical setting. In Study 2, patients with early RA who started ADA within 3 months from the introduction of MTX achieved clinical remission (64.3%) and bio-free condition (21.4%). This result shows early introduction of ADA for bio-free condition might be a good choice in terms of reducing a total medical cost in the long term. In these studies, additional use of csDMARDs after bDMARDs discontinuation is thought to be important for maintaining bio-free condition without disease flare.
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## THU0156 ACHIEVEMENT OF LOW DISEASE ACTIVITY IN PATIENTS INITIATING INFLIXIMAB WITH AND WITHOUT DOSE ESCALATION

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**Background:** Dose escalation is a common strategy for patients (pts) having an inadequate response to a medication.
**Objectives:** To examine low disease activity (LDA) among pts receiving infliximab (IFX) who did and did not escalate therapy above 3mg/kg in CORRONA, a US national registry of rheumatoid arthritis (RA) pts.
**Methods:** We identified all RA pts who initiated IFX on or after 6/2009 at a dose ≤3mg/kg and with moderate or high disease activity (CDAI>10). Eligible pts required at least 6 mos of follow-up after initiation or after dose escalation. Dose escalation was defined as an increase of >1mg/kg or reduction in infusion intervals by ≥1 wk. We divided pts into 3 groups: pts achieving LDA (CDAI ≤10) without dose escalation; pts not achieving LDA and not dose escalating; pts dose escalating. The last group was further divided into pts achieving LDA after dose escalation and pts not achieving LDA after dose escalation. We compared the populations at time of initiation by demographics, BMI in categories of normal (BMI<25), overweight (25≥BMI<30), obese (BMI ≥30), disease characteristics and activity, comorbidities (including diabetes), and medications (prior and current conventional disease modifying anti-rheumatic agents or biologics). For dose escalators, we determined the last dose at time of LDA or in those not achieving LDA, the last dose. The dose is normalized to mg/kg/8wk for comparative purposes.
**Results:** There were 286 pts who met inclusion criteria. 124 (43.4%) reached LDA without escalation; 50 (17.5%) either switched without escalation or had not reached LDA by at least 9 mos; 112 (39.2%) escalated. Of the escalators, 64 (57.1%) reached LDA and 48 (42.9%) switched or did not reach LDA by at least 9 mos. Pts who reached LDA without escalation were more likely to be biologic naïve (67.7%) than those who escalated but did not reach LDA (45.8%, p=0.008). Pts reaching LDA without escalation had lower disease activity measures at initiation (tender joints, physician global assessment, pt global assessment, pt pain) than pts not reaching LDA with or without escalation ($p<0.05$ for all measures). However, swollen joint counts were not significantly different. Pts escalating had higher rates of obesity (57%) and diabetes (13.4%) than pts reaching LDA without escalating (obesity: 41% [p=0.02] and diabetes: 5.7% [p=0.046]). Pts not reaching LDA after escalation had the highest rate of obesity (62.5%). Pts reached LDA at a median dose of 6.0mg/kg/8wks, Interquartile Range (IQR): [5, 8]; pts not reaching LDA had a final median dose of 6.7mg/kg/8wks, IQR: [5, 8.5]. There was no significant difference in last dose by BMI group.
**Conclusions:** Pts more likely to reach LDA without dose escalation are biologic naïve and have lower disease activity measures at initiation. Both high BMI (obese) and diabetes are associated with requiring dose escalation to achieve LDA. In this analysis, ≤25% of patients received dose escalation beyond 8mg/kg/8wks, which may have clinical relevance.
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## THU0157 CLINICAL OUTCOMES AT WEEK 104 AND ANALYSIS OF ASSOCIATED BASELINE FACTORS AFTER AN INITIAL 1 YEAR OF CERTOLIZUMAB PEGOL AND MTX TREATMENT IN MTX-NAÏVE PATIENTS WITH EARLY RA: RESULTS FROM THE SECOND YEAR OF THE C-OPERA STUDY

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**Background:** The efficacy and safety of certolizumab pegol (CZP) treatment in combination with optimized-dose MTX in Japanese MTX-naïve early rheumatoid arthritis (RA) patients (pts) with poor prognostic factors have previously been reported (1-year [yr] results from the C-OPERA study).[1]
**Objectives:** 1. Investigate whether the clinical impact of initial 1-yr treatment with CZP+MTX was maintained to Week (Wk) 104 with MTX therapy alone; 2. Identify factors associated with the final outcomes of the 2-yr therapy by post-hoc logistic regression analysis.
**Methods:** MTX-naïve early RA pts were eligible to enter C-OPERA (NCT01451203). Pts were randomized to CZP+MTX (n=159) or placebo (PBO)+MTX (n=157); oral MTX was escalated to 16mg by Wk8, or maximum tolerated dose (optimized-dose). After pts completed the 52-wk double-blind (DB) period, CZP or PBO was discontinued and MTX monotherapy continued up to Wk104. Full analysis set population was analyzed using LOCF for SDAI remission, and linear extrapolation for mTSS in patients who withdrew before Wk104. Post-hoc univariate logistic regression analysis was used to investigate factors associated with radiographic non-progression (change from baseline [BL] in mTSS$\leq$0.5 at Wk104) or SDAI remission at Wk104, and factors with p$<$0.1 were included in a multivariate analysis.
**Results:** After stopping CZP at Wk52, the radiographic non-progression rate was higher at Wk104 in the Yr 1 CZP+MTX treatment group vs Yr 1 PBO+MTX treatment group (84.2% vs 67.5%, p$<$0.001). Although SDAI remission rates of the Yr 1 CZP+MTX treatment group decreased after CZP discontinuation, higher rates were maintained up to Wk104 vs PBO+MTX (41.5% vs 29.3%, p=0.026). Initial treatment with CZP, lower BL HAQ-DI and mTSS were considered to be associated with radiographic non-progression, whereas SDAI remission at Wk104 associated with male gender, lower BL DAS28(ESR) and initial treatment with CZP (Table). Incidence of overall adverse events was similar between groups, with no new safety signals.

**Table:** Logistic regression analyses to identify factors associated with Week 104 outcomes

| | Radiographic non-progression [a] | | | | SDAI remission [b] | | | |
|---|---|---|---|---|---|---|---|---|
| | Univariate | | Multivariate | | Univariate | | Multivariate | |
| | Odds ratio (95% CI) | p value | Odds ratio (95% CI) | p value | Odds ratio (95% CI) | p value | Odds ratio (95% CI) | p value |
| Age | 1.01 (0.98, 1.03) | 0.488 | - | - | 0.99 (0.97, 1.01) | 0.322 | - | - |
| Gender (female) | 0.50 (0.23, 1.06) | 0.070 | 0.46 (0.20, 1.05) | 0.064 | 0.51 (0.29, 0.91) | 0.022 | 0.51 (0.28, 0.92) | 0.026 |
| BMI | 1.00 (0.93, 1.07) | 0.974 | - | - | 0.94 (0.88, 1.01) | 0.082 | 0.93 (0.87, 1.00) | 0.051 |
| DAS28(ESR) | 0.71 (0.56, 0.90) | 0.004 | 1.08 (0.79, 1.48) | 0.630 | 0.63 (0.51, 0.79) | <0.001 | 0.70 (0.53, 0.92) | 0.012 |
| HAQ-DI | 0.45 (0.30, 0.67) | <0.001 | 0.46 (0.27, 0.76) | 0.004 | 0.56 (0.38, 0.80) | 0.002 | 0.78 (0.48, 1.26) | 0.309 |
| mTSS (Log +1) | 0.65 (0.51, 0.83) | <0.001 | 0.68 (0.52, 0.89) | 0.005 | 0.77 (0.61, 0.98) | 0.032 | 0.80 (0.62, 1.02) | 0.077 |
| RF (Log) | 0.75 (0.59, 0.97) | 0.028 | 0.79 (0.60, 1.04) | 0.094 | 1.00 (0.81, 1.24) | 0.994 | - | - |
| anti-CCP antibody (Log) | 0.84 (0.62, 1.14) | 0.268 | - | - | 0.93 (0.72, 1.21) | 0.591 | - | - |
| MMP-3 (Log) | 0.67 (0.50, 0.90) | 0.007 | 0.88 (0.63, 1.24) | 0.477 | 0.86 (0.66, 1.11) | 0.249 | - | - |
| DB treatment (CZP+MTX) | 2.56 (1.49, 4.40) | <0.001 | 2.75 (1.53, 4.93) | <0.001 | 1.71 (1.07, 2.73) | 0.024 | 1.65 (1.01, 2.69) | 0.047 |

[a] mTSS change from baseline ≤0.5; [b] SDAI ≤3.3.

**Conclusions:** Primary analyses showed the clinical benefit of initial 1-yr CZP+MTX therapy in MTX-naïve early RA pts with poor prognostic factors was maintained to 2yrs with MTX alone. Different BL factors were identified as associated with clinical remission and radiographic non-progression. Effectiveness of initial 1-yr CZP treatment on both clinical and radiographic 2-yr outcomes was confirmed by multivariate logistic regression adjusting for BL factors.
**References:**
[1] Atsumi T. Ann Rheum Dis 2016;75:75–83
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## THU0158 WHICH PATIENT CHARACTERISTICS INFLUENCE THE CHOICE OF BIOLOGICAL THERAPY AFTER FIRST TNF INHIBITOR THERAPY IN RA? A NATIONWIDE STUDY OF CHANNELING IN SWEDEN 2010-2012

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**Background:** The past decade has seen the introduction of many biological DMARDs (bDMARDs) for treating RA, but there is only limited evidence from comparative studies to guide the choice of therapy for specific patients. Whilst a TNF inhibitor (TNFi) is typically used as the first bDMARD, many patients will switch from this initial therapy. The choice of the next bDMARD is, however, largely a matter of patient and physician preference. Perceived or established differences between available bDMARDs may lead to non-random allocation of treatment, a quantification of which is essential for a correct assessment of comparative effectiveness and safety in observational studies.
**Objectives:** To describe baseline patient characteristics at initiation of different bDMARDs after a switch from a TNFi as first bDMARD
**Methods:** Patients with RA who initiated a second bDMARD in 2010–2012 within one year of discontinuing initial TNFi treatment were identified using the

Swedish Rheumatology register (SRQ). Data on disease history, defined as ever diagnosed with relevant co-morbidities, were retrieved by linking to the nationwide and virtually complete Swedish Patient Register.

**Results:** The most common bDMARDs after initial TNFi therapy were rituximab and etancercept; the least common was infliximab. Across drugs, there were only modest differences in demographics and RA characteristics, and moderate differences in disease history. Those initiating a second TNFi were slightly younger, less often RF+, and had slightly lower DAS28 than those initiating a non-TNFi bDMARD. Initiators of rituximab had longest disease duration, highest proportion RF+ and with history of malignancy or COPD, while etanercept-initiators had the lowest proportion with history of malignancy. Those initiating a second TNFi had more often switched due to adverse events, though lack of effect was the most common reason for all drugs.

| | RIT | TOC | ABA | ETA | ADA | CZP | GOL | INF |
|---|---|---|---|---|---|---|---|---|
| N | 176 | 109 | 67 | 168 | 137 | 69 | 54 | 33 |
| Age, yrs | 62 (54–68) | 58 (47–65) | 62 (53–70) | 58 (48–65) | 59 (43–65) | 56 (45–62) | 56 (46–67) | 59 (46–67) |
| Female | 75 | 80 | 84 | 74 | 82 | 81 | 87.0 | 75.8 |
| Education | | | | | | | | |
| <9 yrs | 32 | 28 | 33 | 21 | 23 | 19 | 17 (31.5) | 11 (34.4) |
| 9–12 yrs | 47 | 43 | 44 | 48 | 47 | 47 | 25 (46.3) | 17 (53.1) |
| 12+ yrs | 21 | 28 | 23 | 31 | 30 | 34 | 12 (22.2) | 4 (12.5) |
| RF+ | 94 | 80 | 86 | 75 | 78 | 73 | 81.6 | 87.9 |
| Dis. dur., yrs | 12 (5–20) | 8 (3–14) | 10 (5–21) | 9 (4–19) | 9 (4–20) | 11 (5–19) | 11 (5–172) | 8 (4–18) |
| HAQ | 1.3 (0.8–1.9) | 1.1 (0.9–1.6) | 1.4 (0.9–1.9) | 1.1 (0.8–1.6) | 1.1 (0.6–1.6) | 1.3 (0.8–1.5) | 1.1 (0.8–1.6) | 1.5 (1.1–2.0) |
| DAS28 | 5.2 (4.1–6.0) | 5.1 (4.4–6.1) | 5.1 (4.5–5.5) | 4.8 (3.6–5.4) | 4.7 (3.6–5.5) | 5.0 (3.8–5.7) | 4.5 (3.6–5.5) | 4.9 (4.0–6.2) |
| Disease history | | | | | | | | |
| Malignancy | 10.8 | 6.4 | 4.5 | 1.2 | 4.4 | 4.3 | 1.9 | 3.0 |
| Joint replacement | 12.5 | 19.3 | 17.9 | 13.1 | 16.8 | 10.1 | 13.0 | 24.2 |
| COPD or ILD | 9.1 | 1.8 | 4.5 | 5.4 | 2.2 | 2.9 | 3.7 | 6.1 |
| Ischemic heart disease | 3.4 | 3.7 | 4.5 | 3.0 | 3.6 | 4.3 | 5.6 | 0.0 |
| Reason for switching | | | | | | | | |
| Adv. Ev. | 24.1 | 23.4 | 32.8 | 42.4 | 34.6 | 36.8 | 37.7 | 26.7 |
| Lack of Eff. | 53.4 | 68.2 | 48.4 | 46.1 | 46.6 | 48.5 | 39.6 | 43.3 |
| Other | 22.4 | 8.4 | 18.8 | 11.5 | 18.8 | 14.7 | 22.6 | 30.0 |

Numbers are median (IQR) or %.

**Conclusions:** We observed some evidence for channeling regarding disease history, both by class and by drug within class. These differences were small compared to previously reported channeling to non-TNFi as first bDMARD, but should still be taken into account in observational studies of comparative effectiveness and safety of different biological therapies.

**Disclosure of Interest:** None declared

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## THU0159 A LARGE-SCALE PROSPECTIVE SINGLE COHORT OBSERVATIONAL STUDY OF WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ADALIMUMAB: THE FINAL ANALYSIS OF 48-WEEK DATA FROM THE ANOUVEAU STUDY

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**Background:** Rheumatoid arthritis (RA) significantly impairs work productivity and daily activities, for which therapeutic approaches have still to be investigated.

**Objectives:** To examine the effectiveness of adalimumab (ADA) with respect to RA-related work productivity and activity impairment, as well as associations between changes in work outcomes and changes in disease activity, in Japanese patients with different employment statuses. The first 24-week interim results from the 48-week, multicenter, prospective, single-cohort observational study of self-reported work productivity and activity impairment (ANOUVAEU study) were presented at EULAR in 2013, and here we report the final 48-week results from the study.

**Methods:** Data were obtained from 1973 Japanese RA patients enrolled in the ANOUVAEU study. Work-related outcomes were measured using the Work Productivity and Activity Impairment questionnaire for RA (WPAI/RA), including employment status [paid-worker (employed for ≥35 hr/week), home-worker (employed for <35 hr/week) or non-employed], absenteeism (work time missed), presenteeism (impairment while working), overall work impairment (OWI) and activity impairment (AI) due to RA. The Health Assessment Questionnaire Disability Index (HAQ-DI), EQ-5D, disease activity score based on 28 joint count (DAS28), Clinical Disease Activity Index, and Simplified Disease Activity Index were used to assess clinical response. Factors associated with improvement of WPAI/RA domain scores were analyzed by multivariate analysis, and correlations between changes in WPAI/RA domain scores and clinical responses were estimated.

**Results:** Overall, absenteeism, presenteeism, OWI and AI scores were significantly improved by treatment with ADA, and the observed improvements at week 24 were sustained until week 48 (Table). HAQ-DI and EQ-5D were also consistently improved from week 12 until week 48 ($p<0.0001$). In parallel with these improvements, the clinical remission rate as determined by DAS28-CRP significantly increased from 9.0% at baseline to 32.5% at week 12 and 41.1% at week 48 ($p<0.0001$). Additional results including factors associated with improvement of WPAI/RA domain scores and correlations between changes in WPAI/RA domain scores and clinical responses will be discussed.

Table 1. Effects of treatment with ADA on WPAI/RA

| | Week 0 | Week 24 | Week 48 |
|---|---|---|---|
| Absenteeism, % | 8.17±20.64 (825) | 3.01±12.65 (617) p<0.0001 | 1.25±8.13 (426) p<0.0001 |
| Presenteeism, % | 40.09±28.83 (888) | 19.51±21.94 (655) p<0.0001 | 12.71±16.44 (454) p<0.0001 |
| OWI, % | 41.85±30.00 (812) | 20.65±23.75 (611) p<0.0001 | 13.37±17.15 (420) p<0.0001 |
| AI, % | 48.43±28.09 (1538) | 24.67±23.87 (1128) p<0.0001 | 19.08±20.68 (774) p<0.0001 |

Values are mean ± SD (n). P-values were calculated by paired t-test.

**Conclusions:** ADA demonstrated significant sustained improvements in RA-related work productivity and activity impairment in Japanese RA patients. Treatment with ADA for RA patients may reduce their potential risks of becoming unemployed and financially impaired.

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## THU0160 EXCELLENT OUTCOMES SUSTAINED EVEN IN LONG-TERM WHEN TARGETED TREATMENT WITH A COMBINATION OF TRADITIONAL DMARDS IS USED IN EARLY RHEUMATOID ARTHRITIS. THE 10-YEAR FOLLOW-UP RESULTS OF A RANDOMIZED CLINICAL TRIAL, THE NEO-RACO TRIAL

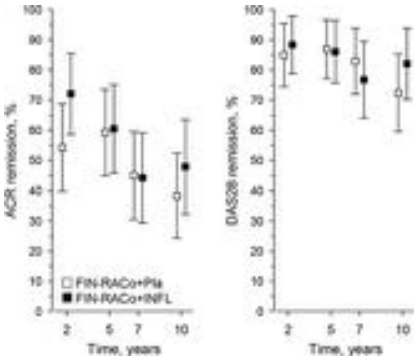
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**Background:** The short term outcomes of remission-targeted treatments of rheumatoid arthritis (RA) are well established, but the long-term success of such strategies is less clear, as is the role of initial add on biologics.

**Objectives:** To assess the evolution of clinical and radiograpich outcomes over 10 years in patients with early RA treated with initial remission-targeted combination-DMARD therapy and additional infliximab or placebo infusions for the first six months

**Methods:** Ninety-nine patients with early, DMARD-naïve RA were treated with a triple combination of DMARDs, starting with methotrexate (max 25mg/week), sulfasalazine (max 2g/day), hydroxychloroquine (35mg/kg/week), and with prednisolone (7.5mg/day), and randomized to double-blindly receive either infliximab (3mg/kg; FIN-RACo+INFL) or placebo (FIN-RACo+PLA) infusions during the first 6 months. After 2 years the treatment strategies became unrestricted, but the treatment goal was strict ACR remission. At 10 years the clinical and radiographic outcomes were assessed using the intention-to-treat principal.

**Results:** Ninety patients (91%) were followed after 2 years, 43 in the FIN-RACo+INFL and 47 in the FIN-RACo+PLA group. At 10 years, the respective proportions of patients in strict ACR and in DAS28 remissions in the FIN-RACo+INFL and FIN-RACo+PLA groups were 48% and 38% [p=0.37 (NNT=10)], and 82% and 72% [p=0.30 (NNT=11)] (Figure 1). The radiographic progression remained slow in most of the patients up till 10 years, the mean (SD) total Sharp van der Hejde score (TSS) was 9.8 (14.8) in the FIN-RACo+INFL and 7.3 (8.1) in the FIN-RACo+PLA group (p=0.34). Only 15% of the patients had TSS>20, and 22% had TSS 0. By ten years, 26% of the FIN-RACo+INFL group patients and 30% of the FIN-RACo+PLA group patients were using biologics (p=0.74). After 5 years, 56% of the patients were at least sporadically using prednisolone, the mean (SD) daily dose was 1.8 (1.6) mg in the FIN-RACo+INFL group and PLA 1.6 (1.4) mg in the FIN-RACo+PLA group.




**Conclusions:** In early RA, excellent results can be maintained up till 10 years in most patients treated with initial combination DMARDs and targeted treatment strategy. Adding initial infliximab for 6 months does not improve these outcomes.
**Acknowledgement:** The NEO-RACo Trial Group.
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## THU0161 PREDICTION OF FLARING IN RHEUMATOID ARTHRITIS PATIENTS UPON BIOLOGICS DOSE TAPERING: A CHART REVIEW STUDY IN TAIWAN

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**Background:** The OuTcomes Associated with taPering biologics among patiEnts with Rheumatoid arthritis (TAPER) is a retrospective chart review study to assess real-world implication of Taiwan policy on tapering/withdrawing biologics in stable rheumatoid arthritis (RA) patients.[1]
**Objectives:** To assess RA flare rates before and after anti-TNF dose tapering and to identify predictors of flaring upon tapering.
**Methods:** Medical chart data were collected from RA patients tapering adalimumab (ADA) or etanercept (ETN) (methods described elsewhere).[1] RA flares were assessed for 6-month pre-tapering, and for short-term (6 months) and longer-term (12 to 18 months) post-tapering. Three alternative flare definitions were used: 1) TAPER: defined *a priori* the Institutional Review Board submission as a) increase in DAS28≥1.2, b) increase in number of swollen/tender joints, or c) use of injectable steroids during outpatient/ER visits; 2) OMERACT: a) increase in DAS28>1.2, or b) increase in DAS28>0.6 if prior DAS28≥3.2; and 3) Taiwan National Health Insurance Administration: a) increase in DAS28≥1.2 and b) erythrocyte sedimentation rate (ESR) >25mm/h and c) increase in ESR>25%. Logistic regression models were developed to identify factors significantly associated with post-tapering flare.
**Results:** Data came from medical charts of 261 patients (ADA=40.6%; ETN=59.4%). More than half patients had a 12- to 18-month follow-up (58.6%: ADA=40.5%; ETN=59.5%). All three flare criteria showed that a greater proportion of patients had flare post-tapering (see table). During the short-term post-tapering, the risk factors of flaring included a longer disease duration (odds ratio=1.05, p=0.049) and having prior concomitant therapy on Cox-2 inhibitors (OR=2.61, p=0.003); being in remission (DAS28<2.6) prior to tapering was associated with a reduced risk (OR=0.41, p=0.037). Over a longer-term, a longer disease duration (OR=1.13, p=0.028) and having a flare within 6-month post-tapering were associated with an increased risk of flaring (OR=9.99, p<0.001).

| | Pre-Tapering | Post-Tapering short-term | Post-Tapering longer-term |
|---|---|---|---|
| **TAPER Criteria** | | | |
| Flare rate (per patient per year) (SD) | 0.47 (0.98) | 1.18 (1.43) | 1.60 (1.30) |
| Patients with at least one flare, n (%) | 54 (20.7) | 115 (44.1) | 113 (73.9) |
| **OMERACT Criteria** | | | |
| Flare rate (per patient per year) (SD) | 0.05 (0.30) | 0.52 (1.08) | 0.62 (0.96) |
| Patients with at least one flare, n (%) | 6 (2.3) | 53 (20.3) | 65 (42.5) |
| **Taiwan National Health Insurance Administration Criteria** | | | |
| Flare rate (per patient per year) (SD) | 0.01 (0.12) | 0.12 (0.47) | 0.16 (0.40) |
| Patients met dose returning criteria, n (%) | 1 (0.4) | 14 (5.4) | 28 (18.3) |

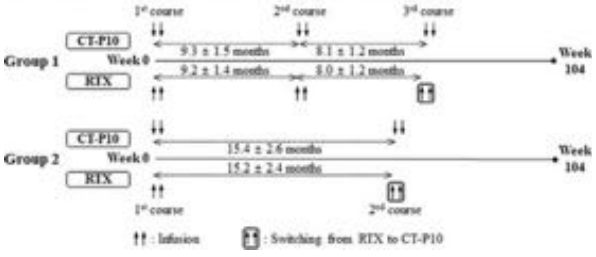
**Conclusions:** Careful considerations are needed when tapering a biologic in stable RA patients in order to avoid potentially increased risk of disease flaring. This could include assessing disease duration and remission status prior to tapering, and whether there is a flare within 6-month of tapering when considering for in long-term.
**References:**
[1] J Rheum Dis 2015;18(Suppl1):22
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## THU0162 COMPARABLE TIME TO RETREATMENT WITH CT-P10 AND INNOVATOR RITUXIMAB UP TO 2 YEARS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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**Background:** A randomised controlled trial (RCT) and its open label extension trial (OLE) demonstrated comparable pharmacokinetics (PK), efficacy and safety between CT-P10 and innovator rituximab (RTX) (including switched from RTX to CT-P10) up to 2 years in rheumatoid arthritis (RA) patients (NCT01534884 and NCT01873443).[1,2]
**Objectives:** To compare time to retreatment and confirm clinical similarity in efficacy and safety by the number of treatment courses in the RCT between CT-P10 and RTX in RA patients up to 2 years.
**Methods:** One hundred fifty three patients were randomised in 2:1 ratio and received up to 2 treatment courses of either CT-P10 or RTX in RCT, and they had a chance to receive up to 2 additional courses of CT-P10 in OLE. Retreatments were given based on disease activity. Post-hoc analyses using combined data obtained from the RCT and OLE studies were performed in 2 different groups according to the number of treatment courses in RCT as following; Group 1: patients who received 2 courses in RCT; Group 2: patients who received 1 course in RCT.
**Results:** A total of 82 patients (59 received CT-P10 and 23 received RTX) were in Group 1 and 20 (13 received CT-P10 and 7 received RTX) were in Group 2. Time to retreatment was similar between CT-P10 and RTX (including switched to CT-P10) in each group (Figure 1).

**Figure 1. Overall Schema of Retreatment Interval up to 2 Years**




DAS28 improvement at Week 24 of each course was similar between CT-P10 and RTX (including switched to CT-P10) in both groups (Table 1).

Table 1. DAS28 Improvement at week 24 in each course

| Mean ± SD (n) | Group 1 (2 courses in RCT) | | Group 2 (1 course in RCT) | |
|---|---|---|---|---|
| | CT-P10 | RTX | CT-P10 | RTX |
| DAS28-CRP | | | | |
| Baseline | 6.2±0.8 (59) | 6.0±0.7 (23) | 5.4±1.0 (13) | 5.4±0.6 (7) |
| Changes after 1st course | –2.0±1.1 (59)* | –1.9±1.1 (23)* | –1.9±1.1 (13)* | –1.6±1.2 (7)* |
| Changes after 2nd course | –2.3±1.2 (57)* | –2.0±1.3 (19)* | –1.8±1.3 (10) | –1.7±0.9 (6)§ |
| Changes after 3rd course | –2.4±1.1 (23) | –2.5±1.3 (10)§ | N/A | N/A |
| DAS28-ESR | | | | |
| Baseline | 7.0±0.8 (59) | 6.8±0.8 (23) | 6.5±1.0 (13) | 6.2±0.6 (7) |
| Changes after 1st course | –2.1±1.2 (59)* | –2.1±1.2 (23)* | –2.3±1.1 (13)* | –1.5±1.3 (7)* |
| Changes after 2nd course | –2.5±1.2 (57)* | –2.0±1.2 (19)* | –2.5±1.2 (11) | –2.1±0.8 (6)§ |
| Changes after 3rd course | –2.7±1.2 (23) | –2.7±1.6 (10)§ | N/A | N/A |

RTX, innovator rituximab; DAS28, disease activity score in 28 joints; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SD, standard deviation. *Course(s) treated during RCT up to 72 weeks. §DAS28 improvement after switching to CT-P10 from RTX.

Infusion related reactions by treatment course up to 2 years was similar between

the CT-P10 and RTX groups and tended to decrease over time in line with RTX historical data.[3] Incidence rate of adverse event, serious adverse event and infection was comparable between CT-P10 and RTX groups.

**Conclusions:** The results of the post-hoc analyses demonstrated comparable duration of disease control between CT-P10 and RTX (including switched to CT-P10) with clinical similarity in efficacy for 2 years. The safety profile of CT-P10 was similar to that of RTX and in line with RTX historical data.

**References:**
[1] Yoo DH, et al. Arthritis Rheum 2013; 65 (Suppl10): S736
[2] Yoo DH, et al. Arthritis Rheum 2015; 67 (Suppl10): 2449–245
[3] van Vollenhoven RF, et al. EULAR 2013 (Madrid, Spain): Poster SAT0131

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## THU0163 EARLY RESPONSE AS A PREDICTOR OF LONG-TERM CLINICAL RESPONSE IN DMARD-NAÏVE PATIENTS WITH SEVERE, ACTIVE AND PROGRESSIVE RA TREATED WITH CERTOLIZUMAB PEGOL PLUS OPTIMIZED MTX VERSUS OPTIMIZED MTX ALONE

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**Background:** C-EARLY (NCT01519791) assessed the efficacy and safety of certolizumab pegol (CZP)+optimized MTX vs placebo (PBO)+optimized MTX in inducing and maintaining a sustained clinical response, and inhibiting radiographic damage, in DMARD-naïve patients (pts) with active, severe, progressive RA.[1] Here, we examine the association between an inadequate response to PBO+MTX or CZP+MTX treatments at Week (Wk) 12 (lack of improvement from baseline [BL] in DAS28[ESR], DAS28[CRP] or CDAI) and corresponding response at Wk 52.

**Objectives:** To examine the association between Wk12 response and Wk52 clinical response (remission [REM]/low disease activity [LDA]) in recently diagnosed DMARD-naïve pts with active, severe, progressive RA, treated with CZP+optimized MTX vs PBO+optimized MTX.

**Methods:** This multicenter, double-blind, randomized controlled trial enrolled pts who were DMARD-naïve with active, severe, progressive RA (<1yr since diagnosis, fulfilling 2010 ACR/EULAR criteria). 879 pts were randomized 3:1 to CZP (200mg Q2W+MTX; n=660) or PBO Q2W+MTX (n=219). MTX was initiated at 10mg/wk and increased to 25mg/wk by Wk8; maximum tolerated dose per pt (mean optimized dose, CZP: 21mg/wk, PBO: 22mg/wk) was maintained to Wk52. Negative predictive values (NPV) were defined as probability of failing to achieve Wk52 REM (DAS28[ESR]/[CRP]<2.6 or CDAI≤2.8) or LDA (DAS28[ESR]/[CRP]≤3.2 or CDAI≤10) after failing to achieve a corresponding defined response at Wk12; change from BL in DAS28(ESR)/(CRP)≥0.6 or ≥1.2/CDAI≥6 and ≥12. DAS28(CRP) LDA/REM definitions are not validated. Observed data were utilized for Wk12 responses; missing Wk52 values were imputed using non-responder imputation.

**Table:** Probability of failing to achieve Week 52 clinical response after failing to respond at Week 12

| | PBO+MTX patients (n=213) | | | | | |
|---|---|---|---|---|---|---|
| | DAS28(CRP) | | DAS28(ESR) | | CDAI | |
| Week 12 reduction from baseline (observed case) | <0.6 (n=23) | <1.2 (n=49) | <0.6 (n=18) | <1.2 (n=42) | <6 (n=13) | <12 (n=28) |
| Week 52 LDA (NRI) | 87% (n=20) | 76% (n=37) | 94% (n=17) | 81% (n=34) | 69% (n=9) | 68% (n=19) |
| Week 52 remission (NRI) | 87% (n=20) | 84% (n=41) | 94% (n=17) | 83% (n=35) | 77% (n=10) | 79% (n=22) |
| | CZP+MTX patients (n=655) | | | | | |
| | DAS28(CRP) | | DAS28(ESR) | | CDAI | |
| Week 12 reduction from baseline (observed case) | <0.6 (n=45) | <1.2 (n=87) | <0.6 (n=36) | <1.2 (n=86) | <6 (n=23) | <12 (n=48) |
| Week 52 LDA (NRI) | 80% (n=36) | 72% (n=63) | 89% (n=32) | 86% (n=74) | 91% (n=21) | 73% (n=35) |
| Week 52 remission (NRI) | 82% (n=37) | 79% (n=69) | 92% (n=33) | 93% (n=80) | 91% (n=21) | 90% (n=43) |

Week 52 LDA: DAS28(ESR)/(CRP)<3.2, CDAI ≤10; Week 52 remission: DAS28(ESR)/(CRP)<2.6, CDAI ≤2.8.

**Results:** The NPV of Wk12 responses were high (Table): PBO+MTX pts who did not achieve DAS28(ESR) improvements from BL ≥0.6 had 94% probability of not being in REM or LDA at Wk52. CZP+MTX pts who did not achieve DAS28(ESR) improvements from BL ≥1.2 had 93% probability of not being in REM at Wk52. NPV of changes in DAS28(CRP) and CDAI at Wk12 were less informative for predicting remission at 1yr (Table).

**Conclusions:** In early RA pts treated with optimized-dose MTX, failure to achieve a ≥0.6 DAS28(ESR) reduction from BL at Wk12 was associated with a low probability (6%) of DAS28(ESR) REM/LDA at Wk52, supporting treatment step-up at 3 months. For pts with active, severe RA with poor prognostic factors where CZP has been initiated as first-line treatment, failure to achieve a rapid decrease of 1.2 points was associated with a reduced likelihood of achieving REM (7%). These findings in DMARD-naïve pts are consistent with the negative predictability outcomes for CZP in established RA.[2]

**References:**
[1] Weinblatt M. Arthritis Rheumatol 2015;67(S10);
[2] van der Heijde D. J Rheumatol 2012;39:1326–33

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## THU0164 EFFICACY OF INFLIXIMAB FOR SUPPRESSING RADIOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE; TWO YEARS OF FOLLOW-UP – A MULTICENTER REGISTRY STUDY

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**Background:** Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab (IFX), anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13 and 14. However there is still few studies of efficacy of against RA cervical lesions of IFX comparison with methotrexate (MTX).

**Objectives:** To evaluate the efficacy of IFX for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 2 years.

**Methods:** We used MTX or MTX+IFX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 40 and 88 patients received continuous MTX and IFX treatment for at least 2 years. MTX was used in all patients receiving IFX. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1,2.

**Results:** In the patients receiving MTX (n=40) and IFX (n=88), the number of female were each 33 (83%) and 75 (85%) cases (p=0.794). The mean age was 62.5 ± 10.7 and 53.9 ± 12.9 years old (p<0.001); disease duration was 9.3 ± 10.0 and 10.7 ± 9.2 years (p=0.127) and the mean dose of MTX was 7.3 ± 2.4 and 7.8 ± 2.1 mg/w (p=0.414). Clinical findings related to RA were as follows; CRP 1.3± 2.0 and 3.1± 2.8 mg/dl (p<0.001); ESR 28.1 ± 21.1 and 49.9 ± 29.1mm/h (p<0.001); MMP3 170 ± 303 and 337 ± 309ng/ml (p<0.001); DAS28 4.07 ± 1.42

and 5.47 ± 1.25 (p<0.001); ADI 2.6 ± 1.6 and 3.6 ± 1.9mm (p=0.001); SAC 20.2 ± 2.7 and 18.1 ± 2.7mm (p<0.001) and Ranawat value 16.0 ± 1.5 and 14.5 ± 2.2mm (p<0.001). The respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.25 ± 0.44 and 0.22 ± 0.44 mm (p=0.591); SAC: –0.18 ± 0.39 and –0.16 ± 0.40 mm (p=0.716); and Ranawat value: –0.13 ± 0.34 and –0.15 ± 0.36 mm (p=0.733). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.53 ± 0.72 and 0.35 ± 0.59 mm (p=0.193); SAC: –0.48 ± 0.64 and –0.27 ± 0.60 mm (p=0.038); and Ranawat value: –0.35 ± 0.58 and –0.26 ± 0.47 mm (p=0.486) (Fig. 1). The numbers of patients who did not showed progression in ADI, SAC and Ranawat value were each 24 (60%) and 62 (70%) cases (p=0.310); 24 (60%) and 67 (76%) cases (p=0.058) and 28 (70%) and 66 (75%) cases (p=0.666) after 2 years. Also the number who was able to suppress progression in all three parameters were each 24 cases (60%) receiving MTX and 58 cases (66%) receiving IFX (p=0.555) after 2 years (Fig. 2).

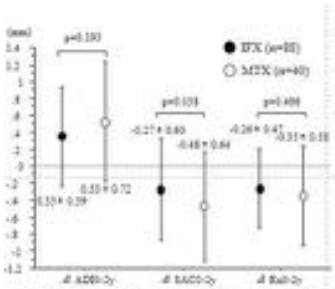



Figure 1 : Respective changes in ADI, SAC and Rana value from Year 0 to Year 2 between MTX and IFX patients

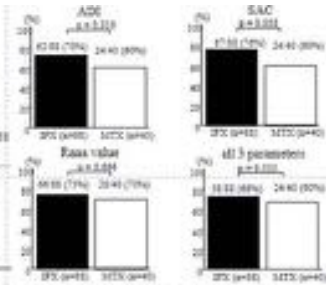



Figure 2 : The rate of patients who did not showed progression in ADI, SAC, Rana value and all three parameters after 2 years

**Conclusions:** This study suggested that IFX treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.
**Disclosure of Interest:** Y. Kanayama: None declared, T. Kojima Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, AbbVie,Bristol-Myers Squibb, and Pfizer, Janssenn Pharmaceutical Companies, Astellas Pharma and Chugai Pharma., Y. Hirano Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, and Bristol-Myers Squibb., N. Takahashi Speakers bureau: Abbvie Japan Co. Ltd, Eisai Co. Ltd, UCB Japan Co. Ltd, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Company Ltd, Pfizer Co. Ltd, Chugai Pharmaceutical Co. Ltd,Janssen Pharmaceutical K.K., and Bristol-Myers Squibb Co. Ltd., Y. Yabe: None declared, N. Ishiguro Grant/research support from: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, TaishoToyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai Pharmaceutical, Mitsubishi Tanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan, Speakers bureau: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai Pharmaceutical, Mitsubishi Tanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan.
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## Rheumatoid arthritis - non-biologic treatment and small molecules

### THU0165 LONG-TERM RADIOGRAPHIC AND PATIENT-REPORTED OUTCOMES BASED ON CLINICAL DISEASE ACTIVITY INDEX RESPONSES WITH TOFACITINIB AT 6 MONTHS

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of RA.
**Objectives:** This analysis assessed if patients achieving Clinical Disease Activity Index (CDAI) remission (REM) or low disease activity (LDA) at Month 6 had less radiographic progression and improved patient-reported outcomes (PROs) at Month 24 and compared results between tofacitinib and MTX.
**Methods:** ORAL Start (NCT01039688) and ORAL Scan (NCT00847613) were Phase 3 randomised controlled trials (RCTs) in MTX therapeutically naïve and MTX inadequate response (IR) patients with RA, respectively. In ORAL Start and Scan, patients received tofacitinib 5 or 10 mg twice daily (BID) monotherapy vs MTX monotherapy or tofacitinib 5 or 10 mg BID + MTX vs placebo + MTX, respectively. This was an observed analysis of patients with radiographs at Months 6, 12 and 24, excluding placebo-treated patients in ORAL Scan. Patients were classified according to CDAI responses at Month 6: REM (CDAI ≤2.8); LDA (CDAI >2.8 to ≤10); or incomplete-responders (CDAI >10). Outcomes included the proportion of patients with no radiographic progression (change in modified Total Sharp Score [mTSS] ≤0) and/or HAQ-DI ≤0.5 (defined as normative) at Month 24, and mean changes from baseline in mTSS and HAQ-DI.
**Results:** In ORAL Start, 250, 269 and 98 patients received tofacitinib 5 mg BID, tofacitinib 10 mg BID and MTX, respectively. In ORAL Scan, 193 and 201 patients received tofacitinib 5 and 10 mg BID, respectively. Baseline demographics were generally similar between subpopulations within each RCT; however, incomplete responders generally had higher baseline disease activity. In both ORAL Start and Scan, patients in REM or LDA with tofacitinib at Month 6 were more likely to be radiographic non-progressors and achieve normative HAQ-DI scores at Month 24 (Table). Tofacitinib-treated patients in REM at Month 6 generally had better HAQ-DI scores at Month 24 than LDA patients. In ORAL Start at Month 6, a higher proportion of tofacitinib- than MTX-treated patients were in REM or LDA (Table). CDAI incomplete responders receiving tofacitinib had improved HAQ-DI scores and less radiographic progression compared with MTX-treated counterparts. Overall, more tofacitinib-treated patients who achieved REM or LDA were non-progressors or achieved HAQ-DI scores ≤0.5 compared to those treated with MTX.



**Conclusions:** More MTX-naïve or MTX-IR tofacitinib-treated patients achieving CDAI REM or LDA at Month 6 were radiographic non-progressors or achieved normative HAQ DI scores at Month 24, compared with CDAI incomplete responders. In ORAL Start, more tofacitinib-treated than MTX-treated MTX-naïve patients achieved CDAI REM or LDA at Month 6 with better PROs and radiographic outcomes at Month 24.
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### THU0166 SAFETY PROFILE OF BARICITINIB IN PATIENTS WITH ACTIVE RA: AN INTEGRATED ANALYSIS

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**Background:** Baricitinib (bari; an oral JAK 1/JAK 2 inhibitor) is in development for patients (pts) with active RA.
**Objectives:** To assess the safety of bari in pts with active RA across 8 completed studies (4 Ph3, 3 Ph2, 1 Ph1b) and 1 ongoing long-term extension (LTE) study.
**Methods:** Primary safety analysis was based on 6 studies with bari 4 mg QD and placebo (PBO) arms and dose response assessments on 4 studies with bari 2 and 4 mg QD and PBO arms. In addition, the all-bari RA set included all patients exposed to any bari dose. 2 studies contained active comparators.
**Results:** 3464 pts were exposed to bari (4214 pt-yrs (PY); 2166 pts (62.5%) >1 yr; 467 (13.5%) >2 yrs). In controlled periods of the program, no increases in deaths, AEs leading to study drug discontinuation, malignancies, MACE, or serious infections were seen for bari vs PBO/active treatment. Herpes zoster was reported more frequently for bari vs PBO. In randomized, controlled periods

of the program, TB was reported in 2 pts: 1 bari 4 mg, 1 adalimumab; in uncontrolled periods, 6 TB events were reported (bari 4 mg: 2 with incomplete TB screening, 3 without organism confirmed). All TB occurred in endemic areas. Two GI perforations were reported (0.05/100 PY). No confirmed opportunistic infections were reported. Bari treatment has been associated with changes in selected hematology/clinical chemistry analytes; few patients (<1%) discontinued due to abnormal lab results. There was no observed increased risk over time for the above outcome measures with longer exposure.

Table 1. Safety outcomes - Data are reported as "n" and "(IR)"

| | Death | AE leading to perm DC | Malignancy ex. NMSC | MACE | Serious infection | Herpes Zoster |
|---|---|---|---|---|---|---|
| 6-study Data Set, Wks 0–24 | | | | | | |
| PBO (N=1070) | 2 (0.5) | 35 (8.9) | 2 (0.5) | 2 (0.5) | 17 (4.2) | 4 (1.0) |
| Bari 4 mg (N=997) | 3 (0.7) | 47 (11.5) | 2 (0.5) | 2 (0.5) | 16 (3.8) | 18 (4.3)* |
| 4-study Data Set, Wks 0–24 | | | | | | |
| PBO (N=551) | 2 (1.0) | 21 (11.1) | 0 | 2 (1.2) | 10 (5.1) | 2 (1.0) |
| Bari 2 mg (N=479) | 0 | 20 (10.8) | 1 (0.5) | 0 | 8 (4.2) | 6 (3.1) |
| Bari 4 mg (N=479) | 1 (0.5) | 26 (13.9) | 0 | 2 (1.1) | 11 (5.7) | 10 (5.2) |
| RA-BEGIN (DMARD naïve), Wks 0–52 | | | | | | |
| MTX (N=210) | 3 (1.7) | 11 (6.4) | 1 (0.6) | 2 (1.1) | 8 (4.6) | 2 (1.1) |
| Bari 4 mg (N=159) | 0 | 11 (7.7) | 1 (0.7) | 1 (0.7) | 6 (4.1) | 4 (2.7) |
| Bari 4 mg + MTX (N=215) | 0 | 23 (12.2) | 3 (1.6) | 0 | 5 (2.6) | 5 (2.6) |
| RA-BEAM (MTX-IR), Wks 0–24 | | | | | | |
| PBO (N=488) | 0 | 17 (8.6) | 2 (1.0) | 0 | 7 (3.5) | 2 (1.0) |
| Bari 4 mg (N=487) | 2 (0.9) | 25 (11.6) | 2 (0.9) | 1 (0.5) | 5 (2.3) | 7 (3.2) |
| Adalimumab (N=330) | 0 | 7 (4.9) | 0 | 0 | 2 (1.4) | 4 (2.8) |
| RA-BEAM (MTX-IR), Wks 0–52 | | | | | | |
| Bari 4 mg (N=487) | 2 (0.5) | 36 (8.4) | 3 (0.7) | 2 (0.5) | 10 (2.3) | 11 (2.5) |
| Adalimumab (N=330) | 1 (0.4) | 15 (5.5) | 0 (0.0) | 1 (0.4) | 5 (1.8) | 5 (1.8) |
| All Bari RA | | | | | | |
| Phases 1–3 (N=3464) | 13 (0.3) | 255 (6.1) | 29 (0.7) | 16 (0.5) | 137 (3.2) | 143 (3.4) |

ex. = excluding, IR = incidence rate/100 PY, MACE = major adverse cardiovascular event, NMSC = non-melanoma skin cancer, perm DC = permanent discontinuation of study drug. With the exception of AE leading to perm DC, analyses include follow-up observation. *Significantly different vs comparator (95% CI: 2.6, 6.8).

**Conclusions:** In the context of reported efficacy,[1,2] bari had an acceptable safety profile in pts with moderate-to-severe active RA.

**References:**

[1] Dougados M. Ann Rheum Dis. 2015;74(S2):79.
[2] Taylor PC. Arthritis Rheumatol. 2015;67(suppl 10).

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## THU0167 THE EFFECT OF FILGOTINIB (GLPG0634), AN ORAL JAK1 SELECTIVE INHIBITOR ON PATIENT-REPORTED OUTCOMES: RESULTS FROM TWO 24-WEEK PHASE 2B DOSE RANGING STUDIES

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**Background:** Filgotinib (GLPG0634) is a novel oral, potent and selective JAK1 inhibitor that showed rapid and sustained improvements of signs and symptoms of active rheumatoid arthritis (RA) in patients with inadequate response to methotrexate (MTX) in two 24-week Phase 2B studies, with an acceptable safety profile.

**Objectives:** To investigate the effect of filgotinib add-on to MTX or monotherapy on patient-reported outcomes (PROs).

**Methods:** In DARWIN 1 (add-on to MTX) and DARWIN 2 (monotherapy), patients with active RA were randomized in a double blinded manner to placebo (PBO) or one of the three daily doses of filgotinib (50mg, 100mg or 200mg) for 24 weeks. In DARWIN 1, once (qd) and twice daily (bid) regimens were assessed. At week 12, patients on PBO (in DARWIN 1) and 50mg daily dose (in DARWIN 1 and DARWIN 2) whose tender and swollen joint counts did not improve by at least 20% were reassigned to 100mg daily dose. In DARWIN 2, all patients on PBO were reassigned to 100mg daily dose. Assessed PROS were patient evaluation of disease activity & pain, physical function, fatigue and HRQoL-SF36.

**Results:** In total 594 and 283 patients were randomized and treated in DARWIN 1 and DARWIN 2, respectively. Mean HAQ-DI baseline value was 1.74 and 1.81, respectively, indicating severe impairment. Filgotinib demonstrated rapid and significant improvement in PROs (patient assessment of disease activity and pain, physical function, fatigue and HRQoL-SF36) in both studies, with the 200mg daily dose showing statistically significant effects as early as week 1–2 on HAQ-DI and the patient VAS global disease and pain and from week 4 on the FACIT and SF-36-PCS. After week 12, these responses were maintained or continued to improve through 24 weeks. At week 24 with identical daily doses, the filgotinib effect was comparable between qd and bid regimens (in DARWIN 1) and between add-on and monotherapy (between study comparison)"

Table 1. PRO responses for the 200mg daily dose

| | | Mean change from baseline (LOCF) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Patient's VAS disease activity | Patient's VAS pain | HAQ-DI | FACIT | SF-36 PCS | SF-36 MCS |
| DARWIN 1 | | | | | | | |
| PBO (N=86) | Wk12 | –16.7 | –16.9 | –0.38 | 5.6 | 3.2 | 4.3 |
| | Wk24 | –17.9 | –17 | –0.37 | 6.0 | 2.8 | 4.7 |
| 200mg qd (N=86) | Wk12 | –34.2*** | –31.4** | –0.75*** | 11.4*** | 8.9*** | 8.1 |
| | Wk24 | –34.9** | –34.6*** | –0.82*** | 11.6** | 9.7*** | 7.2 |
| 100mg bid (N=84) | Wk12 | –35.6*** | –37.9*** | –0.84*** | 11.3*** | 10.5*** | 6.2 |
| | Wk24 | –39.1*** | –37.9*** | –0.90*** | 12.8*** | 11.6*** | 7.1 |
| DARWIN 2 | | | | | | | |
| PBO (N=72) | Wk12 | –11.5 | –13.3 | –0.23 | 3.9 | 3.0 | 2.7 |
| | Wk24 | – | – | – | – | – | – |
| 200mg qd (N=69) | Wk12 | –28.2*** | –31.3*** | –0.74*** | 11.2*** | 8.6*** | 6.8** |
| | Wk24 | –35.1 | –37.7 | –0.85 | 13.7 | 9.7 | 8.5 |

*p<0.05; **p<0.01; ***p<0.001 vs. PBO. Subjects who switched at wk 12 were handled as if they discontinued at wk 12. In DARWIN 2 statistical comparison vs. PBO is not possible after wk 12.

**Conclusions:** In the DARWIN 1 and DARWIN 2 studies, filgotinib led to a rapid decrease in disease burden as demonstrated by the significant improvement in all assessed PROs. After 24 weeks of treatment, filgotinib in combination with MTX as qd or bid or as monotherapy demonstrated comparable benefit in improving PROs in RA patients with high disease activity.

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## THU0168 BARICITINIB INHIBITS RADIOGRAPHIC PROGRESSION OF STRUCTURAL JOINT DAMAGE AT 1 YEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AND AN INADEQUATE RESPONSE TO CSDMARDS

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**Background:** Baricitinib (bari), a JAK1 and JAK2 inhibitor, was efficacious in a 24-week (wk) Ph 3 study in patients (pts) with active RA and an inadequate response (IR) to conventional synthetic DMARDs (csDMARDs) (RA-BUILD)[1].

**Objectives:** To evaluate radiographic progression of structural joint damage in RA-BUILD pts with IR or intolerance to ≥1 csDMARD over 48 wks of bari treatment in the long-term extension study, RA-BEYOND.

**Methods:** In the 24-wk RA-BUILD study, pts were randomized to placebo (PBO; N=228), bari 2mg (N=229) or bari 4mg (N=227) once daily (QD), with rescue possible from Wk16. Pts completing RA-BUILD and entering RA-BEYOND continued to receive the bari dose received at the end of RA-BUILD. Pts receiving PBO at the end of RA-BUILD were switched to bari 4mg in RA-BEYOND. Pt and investigator blinding was maintained in RA-BEYOND. Joint damage was measured using the van der Heijde modified total Sharp score (mTSS). To account for missing scores and scores obtained after rescue or discontinuation of study drug, data were analyzed using 1) linear extrapolation (LE), and 2) last observation carried forward (LOCF). The observed/LOCF method used all

available observed data, including after rescue or switch, with pts analyzed according to original treatment assignment.

**Results:** Using LE, progression of mTSS, bone erosion, and joint space narrowing (JSN) at 24 and 48 wks was statistically significantly lower for both bari 2 or 4mg compared to PBO (Table). Only bari 4mg demonstrated statistically significant inhibition of progressive radiographic joint damage compared to PBO using observed/LOCF at Wk 48 or based on categorical measures.

| | Wk 24 | | | Wk 48 | | |
|---|---|---|---|---|---|---|
| | PBO† | 2 mg QD | 4 mg QD | PBO/ 4 mg QD† | 2 mg QD | 4 mg QD |
| Linear extrapolation | | | | | | |
| Change in (D) mTSS | 0.72 | 0.27* | 0.25* | 1.36 | 0.43** | 0.45** |
| D Erosion | 0.43 | 0.20* | 0.17* | 0.82 | 0.31** | 0.32** |
| D JSN | 0.29 | 0.08* | 0.08* | 0.55 | 0.12* | 0.13* |
| D mTSS ≤0, n (%) | 150 (78) | 169 (81) | 167 (84) | 150 (78) | 175 (80) | 169 (83) |
| D mTSS ≤0.5, n (%) | 157 (82) | 179 (86) | 175 (88) | 150 (78) | 183 (84) | 174 (85) |
| D mTSS ≤SDC, n (%) | 165 (86) | 188 (90) | 186 (94)* | 162 (84) | 195 (89) | 186 (91)* |
| Observed/LOCF | | | | | | |
| D mTSS | 0.57 | 0.26* | 0.25* | 0.69 | 0.41 | 0.32* |
| D Erosion | 0.36 | 0.18* | 0.17* | 0.43 | 0.24 | 0.23* |
| D JSN | 0.21 | 0.08* | 0.08* | 0.26 | 0.17 | 0.10 |
| D mTSS ≤0, n (%) | 152 (78) | 169 (81) | 169 (85) | 151 (74) | 172 (79) | 169 (82) |
| D mTSS ≤0.5, n (%) | 163 (83) | 183 (87) | 178 (89) | 166 (81) | 188 (86) | 179 (87) |
| D mTSS ≤SDC, n (%) | 171 (87) | 192 (91) | 188 (94)* | 182 (89) | 205 (94) | 193 (94) |

Data are least squares mean change from baseline, unless otherwise stated; †Pts were switched to treatment with bari at rescue or at Wk 24. SDC: smallest detectable change. Wk 24 SDC=1.1; Wk 48 SDC=1.7; Comparisons analyzed using ANCOVA; *p≤0.05, **p≤0.01 vs. PBO.

**Conclusions:** Once daily oral bari inhibited radiographic progression of structural joint damage in pts with an IR or intolerance to csDMARDs over 48 wks of treatment. The most robust benefit across measures of radiographic progression was seen for the 4mg dose.

**References:**

[1] Dougados M et al. Ann Rheum Dis 2015;74(S2):79. Abstract LB0001.

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## THU0169 PERSISTENCE OF TOFACITINIB IN THE TREATMENT OF RHEUMATOID ARTHRITIS IN OPEN-LABEL, LONG-TERM EXTENSION STUDIES UP TO 7 YEARS

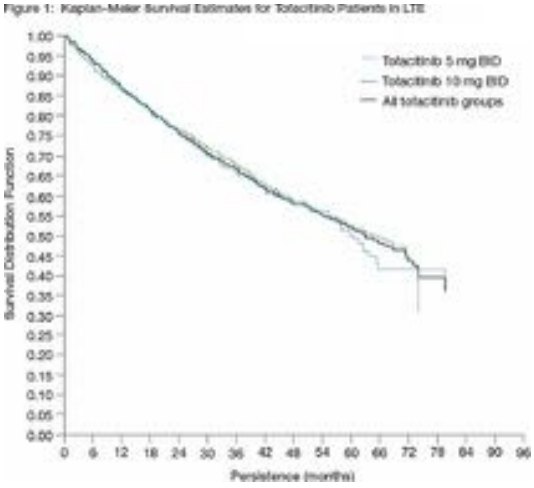
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**Background:** Tofacitinib is an oral JAK inhibitor for treatment of rheumatoid arthritis (RA). Open-label, long-term extension (LTE) studies have enrolled tofacitinib-treated patients (pts) to evaluate safety and efficacy over time. Time on treatment is considered a composite measure of efficacy and safety; discontinuation (D/C) is often due to lack of efficacy (LOE) and/or adverse events (AEs) for disease-modifying antirheumatic drugs (DMARDs).[1]

**Objectives:** To estimate drug survival of tofacitinib up to 84 months (mo) in LTE studies and describe reasons for D/C.

**Methods:** Data were pooled from two LTE studies (NCT00413699 [up to April 2014; study ongoing, database unlocked] and NCT00661661 [completed]). Of 6553 pts from Phase (P) 1, 2 and 3 studies, 4858 pts (74.1%) received treatment in LTE studies. Tofacitinib 5 or 10 mg BID were initiated as monotherapy or with background DMARDs; pooled data and data for each dose ± background DMARDs were analysed. Pts were assigned tofacitinib 5 or 10 mg BID based on average daily dose in LTE. Kaplan-Meier (K-M) analyses estimated drug survival in tofacitinib-treated pts who withdrew for any reason, due to LOE or due to AE in the LTE, including pts who had previously responded to and tolerated treatment in P1P2P3 studies. Ongoing pts were censored as of April 2014, while pts completing the trial(s) were censored at their completion date. Safety data were included over 84 mo and efficacy data up to 72 mo due to limited pt numbers after 72 mo for efficacy. Retention data were divided into dose and mono vs combination therapy.

**Results:** 4858 pts were treated for a mean (maximum) duration of 2.5 (6.9) years (yrs) (results previously reported).[2] Overall, median survival for all tofacitinib treated pts was 5.2 yrs [95% CI 5.0, 5.6] (Figure 1). Median survival for pts receiving tofacitinib with background DMARDs or as monotherapy was 5.3 [4.9, 5.7] and 5.4 [4.8, not evaluable] yrs, respectively. K-M estimates appear similar between 5 and 10 mg BID, median survival was 5.4 [4.9, 5.9] and 5.0 [4.7, 5.5] yrs, respectively (Figure 1). The D/C rate due to LOE was considerably lower than due to AEs (AEs: 17.8%, 22.9%, 15.6%; LOE: 2.7%, 3.3%, 2.5% for all tofacitinib, 5 or 10 mg BID, respectively). The most commonly reported reasons for D/C due to AEs by class were infections/infestations (7.2%, 7.8%, 7.0%), investigations (3.1%, 4.6%, 2.5%) and neoplasms (benign, malignant, unspecified) (2.7%, 3.9%, 2.1%) for all tofacitinib, 5 or 10 mg BID, respectively.




**Conclusions:** Drug survival in LTE studies provides early information on the long-term safety, efficacy and tolerability of a therapy. In this analysis, median survival of tofacitinib was approximately 5 yrs, with D/C more commonly associated with AEs than LOE. Similar survival medians were observed for the 5 and 10 mg BID dose groups and monotherapy vs background DMARD therapy. These data support the use of tofacitinib for long-term management of RA.

**References:**

[1] Neovius M et al. Ann Rheum Dis 2015; 74: 354–360.
[2] Wollenhaupt J et al. Arthritis Rheumatol 2014; 66: S375.

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## THU0170 ADHERENCE TO PARENTERAL METHOTREXATE IN RHEUMATOID ARTHRITIS IS NOT A MAJOR ISSUE AND DOES NOT INFLUENCE THE OCCURRENCE OF MAJOR CARDIOVASCULAR EVENTS

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**Background:** Cardiovascular (CCV) burden in rheumatoid arthritis (RA) is well defined. Several studies showed benefits from methotrexate (MTX) in reducing overall CCV morbidity and mortality [1]. Thus, MTX adherence could be crucial not only to achieve its disease modifying properties on articular signs and symptoms, but also to maximize long-term disease-related outcomes, including major CVV events.

**Objectives:** To explore the impact of MTX adherence on the occurrence of hospitalized major CCV events in real life RA patients while persisting in MTX medication.

**Methods:** Data including demographics, drug delivery, out-patient services and hospital admissions were extracted from health care administrative databases of the Lombardy Region (Italy) for the period between 1/1/2004 and 31/12/2013. Patients with RA were identified by a validated algorithm [2]. RA patients with a new course of treatment with parenteral MTX (new users) and at least 12

months of persistence were included. Hospitalizations/deaths for CCV events (acute myocardial infarction, stroke, heart failure) were evaluated through the Hospital Discharge Forms based on relevant ICD-9CM codes. The association between adherence to MTX - calculated as Proportion Days Covered (PDC) ≥80% - and risk of hospitalization for CCV event was assessed by survival models for competing risks. The results are presented as hazard ratios (HR) and 95% CI, crude and adjusted for sex, age, disease duration, Charlson comorbidity index, concomitant use of corticosteroids, NSAIDs, biologic disease modifying anti-rheumatic drugs/bDMARDs and combination of conventional synthetic DMARDs/csDMARDs.

**Results:** A total of 5337 RA patients [F 3629, 68%; mean age (SD) 62.78 (12.7) years] were included in the analysis. Patients were mainly early onset RA [4015 (75%) <1 year disease duration], generally taking MTX as monotherapy [29 (1%) and 1218 (23%) patients on concomitant bDMARDs and non-MTX csDMARDs, respectively] in association with corticosteroids [3055 (57%)] and NSAIDs [2037 (38%)]. Mean (SD) Charlson comorbidity index was 1.34 (0.83). Most patients [4284 (80%)] resulted adherent to MTX. During 17.104 patient-years of observation, 440 hospital admissions due to major CVV events were registered (344 in adherent versus 96 in non adherent patients). Adherent vs non adherent patients did not significantly differ in the occurrence of CVV events (HR 0.82 CI95% [0.66–1.04]) causing hospital admission, even after adjusting for confounders (Table).

Table 1

| Variable | Adjusted Hazard ratio (95% CI) |
|---|---|
| Adherence to MTX | 0.85 (0.67–1.07) |
| Age (year) | 1.08 (1.06–1.09) |
| Sex (F) | 0.56 (0.46–0.68) |
| Disease duration (>1 year) | 1.11 (0.89–1.38) |
| Charlson index | 1.25 (1.14–1.36) |
| Concomitant Corticosteroids | 0.98 (0.81–1.20) |
| Concomitant csDMARDs | 1.06 (0.84–1.34) |
| Concomitant bDMARDs | 0.84 (0.12–6.02) |

**Conclusions:** In a cohort of real life RA patients from Italy, adherence to parenteral MTX is very high and does not significantly affect the occurrence of major CVV events, even after taking into account potential confounders. These results suggests persistent use of MTX, beside the adherence to it, still carries benefits in preventing from CCV events and that the parenteral administration route of MTX fosters adherence to treatment in RA.

**References:**

[1] Marks JL, et al. Ther Adv Musculoskel Dis 2012.
[2] Carrara G, Scirè CA, Zambon A, et al. BMJ Open 2015.

**Disclosure of Interest:** None declared

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## THU0171 EFFECT OF FAST ESCALATION OF THE DOSE OF SUBCUTANEOUS METHOTREXATE ON THE NEED FOR BIOLOGICAL DMARDS IN PATIENTS WITH VERY EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS

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**Background:** The ongoing REMARCA study (Russian acronym: Russian InvEstigation of MethotrexAte and biologics in eaRly aCtive inflammatory Arthritis) included patients with early and established active RA, who did not use subcutaneous methotrexate (SC MTX) and/or biologics. The main goal of the study is an adaptation of "Treat to target" (T2T) recommendations for clinical practice.

**Objectives:** The purpose of this part of REMARCA trial is to compare two regimens of escalation of the dose of SC MTX in pts with very early (duration of symptoms ≤6 months) and established RA.

**Methods:** 191 patients (pts) with active severe RA (34 males, 157 females, 51,8% with very early RA, 80,1% RF(+), 81,2% anti-CCP(+), DAS28 5,52±1,12, SDAI 30,8±14,7, CDAI 27,3±12,5) were followed up for at least 12 months, among them 115 pts (18 males, 97 females, 60% with very early RA) were followed for 24 months. All patients received SC MTX as a fist-line therapy. We used two regimens of SC MTX dose escalation: 1) fast escalation – starting dose 15 mg/week increasing with increments of 5 mg every 1–2 week to achieve 20–30 mg/week in 4–6 weeks; 2) "slow" escalation (usual recommendations) - starting dose 10 mg/week increasing with increments of 2,5–5 mg every 2–4 week to achieve maximal dose in 8–12 weeks. Fast and "Slow" regimens were prescribed in random manner (with exception of pts who had signs of probable safety problems, such as liver, kidney disease etc., when "slow" regimen used). Use of oral steroids was limited to continuation of previously administered low doses (in 14,7% pts) and intra-articular injections (2 doses per 3 months). Therapy revision and initiation of biological DMARDs in combination with SC MTX (adalimumab, certolizumab, or abatacept), was made every 3 months (or more often if indicated) in order to reach T2T targets.

**Results:** After 12 months, 73 (38,2%) pts achieved SDAI low disease activity (LDA) and 65 (34%) achieved SDAI remission. In the group followed up to 24 months, 45 (39%) and 49 (42,6%) achieved stable SDAI LDA or remission respectively. At 12 month 36,1% pts responded well to monotherapy with SC MTX, and 63,9% required a switch to a combination therapy with biologics. In the group followed up to 24 months the proportion of pts left on MTX monotherapy and switched to biologics was 32,2% and 67,8% resp. Fast escalation regimen used in 87 (45,5%) pts was associated with less need for biologic therapy (see table). When fast escalation used in pts with very early RA (n=47, 24,5%), monotherapy with SC MTX was sufficient in 68,1–66,7% of pts.

**Conclusions:** Early administration of SC MTX with fast escalation of the dose leads to the achievement of T2T goals without need for combination with biological DMARDs in 2/3 of patients with severe active RA.

**Acknowledgement:** Trial State registration number: 01201454666 (http://www.rosrid.ru/search)

**Disclosure of Interest:** None declared

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## THU0172 RISK FOR SERIOUS ADVERSE EVENTS ASSOCIATED WITH ORAL CORTICOSTEROID THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A UK POPULATION-BASED STUDY

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**Background:** Rheumatoid arthritis (RA) is a chronic, erosive form of inflammatory arthritis characterized by a distinctive pattern of bone and joint destruction. Along with disease-modifying antirheumatic drugs and newer biologic therapy, treatment can include oral corticosteroids (oCS), predominantly prednisolone or prednisone. CS are associated with a variety of adverse effects.[1]

**Objectives:** Using data from the UK's Clinical Practice Research Datalink, we estimated the incidence rates (IRs) and incidence rate ratios (IRRs) of known oCS-related serious adverse events (SAEs) of interest in an RA cohort and in a non-RA general population (GP) comparison group matched on age, sex, and time. We also explored the role of oCS use on the risk for SAEs of interest by comparing RA patients of varying exposure levels of oCS.

**Methods:** Patients with a first-time diagnosis of RA who were ≥18 years of age were identified and matched to patients in a non-RA GP comparison group of equal size. Group IRs and IRRs were estimated for diabetes, osteoporosis, fractures, glaucoma, hypertension, thrombotic stroke or myocardial infarction (MI), gastrointestinal (GI) perforation or bleeding, and death for the RA group and the GP group. We then performed a series of nested case-control analyses examining the effect of oCS use on the risk for SAEs of interest. We used conditional logistic regression to calculate the unadjusted and multivariate adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for the association between oCS use and the risk for each separate outcome of interest. We stratified the analyses according to increasing cumulative and average daily oCS use.

**Results:** The cohort consisted of 34,047 RA patients and 34,047 matched non-RA GP patients. Mean follow-up time was ~8 years. The incidence for most SAEs was greater in the RA group than in the GP group. IRRs (95% CIs) for SAEs of interest were diabetes (1.21; 1.13–1.31), osteoporosis (2.11; 1.96–2.27), fractures (1.16; 1.08–1.24), glaucoma (1.08; 0.94–1.22), hypertension (1.13; 1.09–1.18), thrombotic stroke or MI (1.22; 1.11–1.34), GI perforation or bleeding (1.3; 1.15–1.47), and death (1.17; 1.11–1.22). In multivariate analyses, increasing risks for diabetes, osteoporosis, fractures, thrombotic stroke or MI, and death were observed with increasing cumulative oCS use ($p$ <0.05 for trend). RA patients receiving an average daily dose >7.5 mg/day had an increased adjusted OR (95% CI) for diabetes (1.49; 1.21–1.84), osteoporosis (1.41; 1.20–1.66), fractures (1.22; 1.03–1.45), thrombotic stroke or MI (1.61; 1.27–2.04), and death (1.49; 1.27–1.74).

**Conclusions:** Patients with RA experienced an increased incidence of diabetes, osteoporosis, fractures, hypertension, thrombotic stroke or MI, GI perforation or bleeding, and death compared with age- and sex-matched controls. Increasing cumulative oCS doses and average daily oCS doses were associated with increased odds of diabetes, osteoporosis, fractures, thrombotic stroke or MI, and death.

**References:**

[1] Venables PJW. Rheumatoid arthritis treatment (beyond the basics). UpToDate,

**Abstract THU0171** – Table 1

| | 12-month follow-up, n=191 | | 24-month follow-up, n=115 | |
|---|---|---|---|---|
| | SC MTX monotherapy (n=69) | SC MTX + biologics (n=122) | SC MTX monotherapy (n=37) | SC MTX + biologics (n=78) |
| Fast vs "Slow" escalation of SC MT | 49.4% vs 25%* | 50.6% vs 75%* | 46.3% vs 19.7%* | 53.7% vs 80.3%* |
| Fast escalation of SC MT + very early RA vs All other pts | 68.1% vs 25.7%* | 31.9% vs 74.3%* | 66.7% vs 19%* | 33.3% vs 81%* |

*p<0,01 between groups.

Inc. 2016. http://www.uptodate.com/contents/rheumatoid-arthritis-treatment-beyond-the-basics. Accessed January 21, 2016.

**Disclosure of Interest:** J. Wilson: None declared, K. Sarsour Shareholder of: Roche, Employee of: Roche, S. Gale Shareholder of: Roche, Employee of: Roche, A. Pethö-Schramm Employee of: F. Hoffmann-La Roche, S. Jick: None declared, C. Meier Shareholder of: Hoffmann-La Roche, Grant/research support from: Hoffmann-La Roche

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## THU0173 FILGOTINIB (GLPG0634), AN ORAL JAK1 SELECTIVE INHIBITOR IS EFFECTIVE AS MONOTHERAPY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: RESULTS FROM A 24-WEEK PHASE 2B DOSE RANGING STUDY

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**Background:** Filgotinib (GLPG0634) is a novel oral, selective JAK1 inhibitor that was evaluated in a 24-week phase 2B study as monotherapy in active rheumatoid arthritis (RA) with inadequate response to methotrexate. The primary endpoint of proportion of patients achieving ACR20 response after 12 weeks of treatment was met.

**Objectives:** To present the results of the 24-week analysis.

**Methods:** Patients with active RA were randomized 1:1:1:1 in a double blinded manner to receive either placebo (PBO) or one of three doses of filgotinib (50mg, 100mg or 200mg) as a once daily regimen for 24 weeks (DARWIN 2 study). At Week 12 all patients on PBO and on 50mg daily whose tender and swollen joint counts did not improve by at least 20% (non-responders (NR)) were reassigned to 100mg daily.

**Results:** Of 283 randomized and treated patients, mean duration of RA of 9 years and DAS28(CRP) at baseline between 6.0–6.2. At Week 12, a statistically significant higher ACR20, ACR50, ACR70, DAS28(CRP) and CDAI response versus PBO was observed in filgotinib groups. These responses were similar or continued to improve through 24 weeks (Table 1). Increase in filgotinib dose from Week 12 improved efficacy in PBO and 50mg NR groups (at Week 24 ACR20 55% and 60% respectively). Serious Adverse Events and Treatment-Emergent Adverse Events (TEAE) were distributed over the dose groups including PBO: TEAE 39% PBO and 41% filgotinib groups. Infections occurred in 10% PBO and 19% filgotinib groups. No opportunistic infections, cancers or deaths occurred. In filgotinib groups, for the first 4 weeks, a dose dependent decrease in mean neutrophil and a small reduction in platelet counts was seen; mild increase in mean creatinine was apparent. These changes subsequently plateaued and remained stable up to Week 24. A dose dependent increase in haemoglobin was seen during the first 12 weeks and levels remained stable up to Week 24. Over 24 weeks no meaningful difference in transaminase changes was apparent.

Table 1. Summary of the efficacy responses after 12 and 24 weeks treatment

| | Placebo (n=72) | 50mg (n=72) | 100mg (n=70) | 200mg (n=69) |
|---|---|---|---|---|
| 12 weeks | | | | |
| ACR20, NRI[1], % | 29 | 67*** | 66*** | 73** |
| ACR50, NRI, % | 11 | 35** | 37*** | 44*** |
| ACR70, NRI, % | 3 | 8 | 19** | 13* |
| DAS28(CRP), LOCF[3], mean change from BL[2] | –1.0 | –1.8*** | –2.0*** | –2.3*** |
| CDAI[4] mean change from BL, LOCF | –12 | –21*** | –24*** | –25*** |
| 24 weeks | | | | |
| ACR20, NRI, % | n/a | 57 | 79 | 67 |
| ACR50, NRI, % | n/a | 33 | 39 | 45 |
| ACR70, NRI, % | n/a | 19 | 26 | 25 |
| DAS28(CRP), LOCF, mean change from BL | n/a | –2.0 | –2.6 | –2.6 |
| CDAI mean change from BL, LOCF | n/a | –22 | –30 | –28 |

*p<0.05 vs. placebo; **p<0.01 vs. placebo; ***p<0.001 vs. placebo. ACR scores based on ITT analysis. [1]Non-responder imputation. [2]Baseline. [3]Last observation carried forward. [4]Clinical Disease Activity Index.

**Conclusions:** Significant improvement in signs and symptoms of active RA was observed after 12 weeks treatment with filgotinib monotherapy. Efficacy responses were sustained or increased at Week 24. The safety profile was acceptable.

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## THU0174 A SAFETY ANALYSIS OF TOFACITINIB 5 MG TWICE DAILY ADMINISTERED AS MONOTHERAPY OR IN COMBINATION WITH BACKGROUND CONVENTIONAL SYNTHETIC DMARDS IN A PHASE 3 RHEUMATOID ARTHRITIS POPULATION

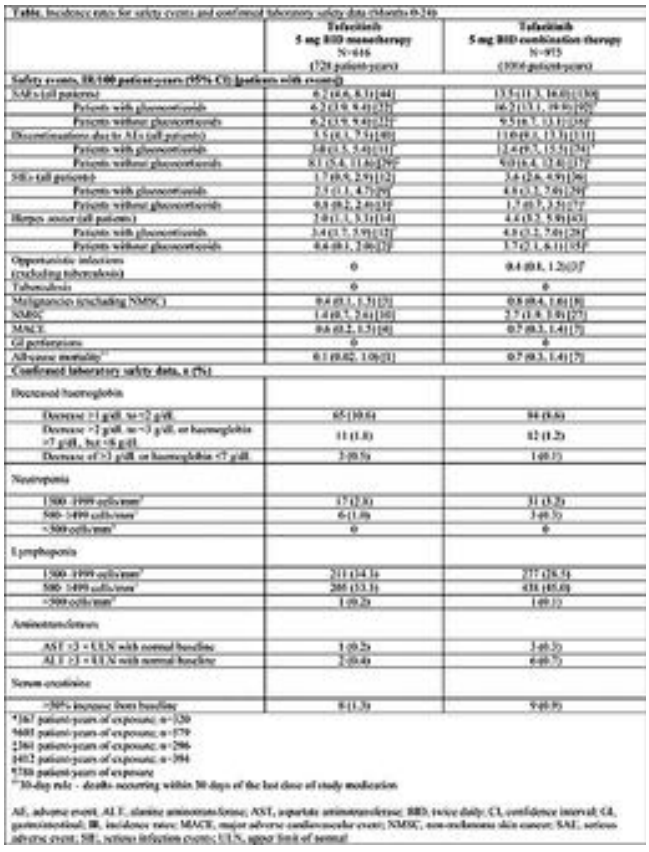
A. Kivitz[1], B. Haraoui[2], J. Kaine[3], V. Castellano[4], E. Bananis[4], C.A. Connell[5], H. Fan[5], L. Takiya[6]. *[1]Altoona Center for Clinical Research, Duncansville, United States; [2]Institut de Rhumatologie de Montréal, Montréal, Canada; [3]Sarasota Arthritis Research Center, Sarasota; [4]Pfizer Inc, Collegeville; [5]Pfizer Inc, Groton; [6]Pfizer Inc, New York, United States*

**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of RA. In Phase 3 studies, tofacitinib demonstrated safety and efficacy at 5 and 10 mg BID when used as monotherapy or with conventional synthetic (cs) DMARDs (csDMARDs).

**Objectives:** To examine the safety profile of tofacitinib 5 mg BID as monotherapy and combination therapy in the Phase 3 clinical development RA program.

**Methods:** Safety data for tofacitinib were obtained from six double-blind Phase 3 studies of 6–24 months' duration and stratified by whether tofacitinib was administered as monotherapy (NCT00814307, ORAL Solo; NCT01039688, ORAL Start) or with csDMARDs (NCT00960440, ORAL Step; NCT00847613, ORAL Scan; NCT00856544, ORAL Sync; and NCT00853385, ORAL Standard). Patients in ORAL Start were methotrexate (MTX)-naïve while patients in all other studies had an inadequate response to cs or biologic DMARDs. Endpoints included: serious adverse events (SAEs), discontinuations due to adverse events (AEs), serious infection events (SIEs), opportunistic infections, herpes zoster (HZ), malignancies, major adverse cardiovascular events, gastrointestinal perforations, all-cause mortality and laboratory safety data.

**Results:** Tofacitinib 5 mg BID was administered as monotherapy in 616 patients (243 from ORAL Solo and 373 from ORAL Start, mean age 51.1 years [yrs], mean RA duration 4.9 yrs, 49.8% received glucocorticoids [GC]) and combination therapy in 973 patients (mean age 53.4 yrs, mean RA duration 8.9 yrs, 57.8% received GC). Incidence rates (IRs) for SAEs, discontinuations due to AEs, SIEs and HZ were generally lower in patients receiving tofacitinib monotherapy vs combination therapy. A similar trend was observed when patients were stratified by GC use; however confidence intervals were wide and overlapping for some outcomes (Table). IRs for SIEs and HZ were greater for patients who received GC compared with those who did not, irrespective of whether tofacitinib was given as monotherapy or in combination. Similar proportions of patients in the monotherapy and combination therapy groups had confirmed laboratory decreases in haemoglobin, neutrophil and lymphocyte counts, and increases in liver enzymes and serum creatinine (Table).



**Conclusions:** In this analysis, IRs for SAEs, discontinuations due to AEs, SIEs and HZ were lower in the tofacitinib 5 mg BID monotherapy group vs the combination therapy group; however, IRs should be interpreted with caution as the data are from controlled studies of limited duration and MTX-naïve patients with shorter disease duration were included in the monotherapy group only.
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## THU0175 COMPARISON OF TWO COMMONLY USED INTRA-ARTICULAR STEROID PREPARATIONS IN ACUTELY SWOLLEN KNEE JOINT IN PATIENTS WITH CHRONIC ARTHRITIS – A RANDOMIZED CONTROLLED TRIAL

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**Background:** Rheumatoid arthritis (RA) and Spondyloarthropathies (SpA) are the commonest chronic inflammatory arthritides and intra-articular corticosteroid therapy is commonly used to control flares in one or few joints. However, it is surprising that despite more fifty years of experience with intra-articular corticosteroids use and evidence to attest their usefulness, evidence in the form of controlled trials to evaluate individual agents and their comparison remains sparse.
**Objectives:** To compare the efficacy of intra-articular injection of methylprednisolone acetate with triamcinolone acetonide in treatment of acutely swollen knee joint in patients with chronic arthritis (RA and SpA) over a follow up period of 24 weeks using time to relapse and patient reported outcomes between the two groups.
**Methods:** Patients with RA/SpA and swollen knee joint were recruited in this double-blind, randomized controlled trial. They were randomized in 1:1 ratio to receive either intra-articular methylprednisolone acetate (80 mg) or triamcinolone acetonide (80 mg) and followed up over a period of 24 weeks with follow-up visits at 4,12 and 24 weeks. Patients continued to take their DMARDs and other medications, with the dose of oral corticosteroids kept $\leq$7.5 mg/day prednisolone or equivalent. At each visit, relapse in the target joint was assessed using clinical measures, which included joint tenderness and swelling. Numerical rating scales for joint swelling and pain in the target joint, disease activity (using DAS28 (3)/BASDAI) and functional status assessment using the Health assessment questionnaire (HAQ) were secondary outcomes.
Trial #CTRI 006187.
**Results:** This study included 100 patients of RA and SpA (RA:SpA=89:11,M:F=24:76) with mean age being 41.9 (± 25.2) years and mean disease duration 5.38 years. Among these, 50 patients each received intra-articular methylprednisolone 80 mg or triamcinolone acetonide 80 mg. After 24 weeks follow-up, there was no significant difference in the relapse rate or time to relapse between the two groups, each group having 9 relapses (relapse rate in the two groups was 18.4% vs.18.8%) with an average time to relapse of 6.44 (±8.24) weeks and 7.44 (±9.74) weeks in methylprednisolone and triamcinolone groups (p=0.991). Reduction in NRS-pain was 5.50 and 5.38 and in NRS-swelling was 5.52 and 5.45 respectively in methylprednisolone and triamcinolone groups at 24 weeks. The reduction in DAS28 at 24 weeks was 1.78 in both the groups. There was no significant difference in functional status between the two groups, the average reduction in HAQ scores being 0.85 and 0.86 in methylprednisolone and triamcinolone groups respectively
**Conclusions:** Our study suggests that there is no significant difference between intra-articular methylprednislone and triamcinolone in terms of efficacy.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5171

## THU0176 EFFICIENCY OF COMPLEX THERAPY OF RHEUMATOID ARTHRITIS USING RAMIPRIL

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**Background:** Angiotensin II (AnII) is not only involved in the pathogenesis of endothelial dysfunction (ED) due vasoconstrictor effect, but also has a powerful pro-inflammatory and remodeling properties, stimulating the production of proinflammatory cytokines (TNFα, IL-1, IL-6 et al.), adhesion molecules (ICAM-1), and growth factors (vascular endothelial growth factor - VEGF), which play an important role in the pathogenesis of rheumatoid arthritis (RA). The use of ACE inhibitors in vivo and in vitro on cell cultures demonstrated anti-cytokine and anti-inflammatory effect.
**Objectives:** to study the effectiveness of combined therapy of RA with ramipril use
**Methods:** The study included 84 patients with RA. Mean age was 40.12 ± 10.2 years. Mean RA disease duration was 4.22 ± 3.43 years. The concentration of ICAM-1, VEGF and TNFα in blood was determined by enzyme immunoassay. Endothelial regulation of vascular tone was studied in all the patients (by Celermayer-Sorensen method, 1992), which revealed the presence of ED in examined patients: reduction of endothelium-dependent vasodilation (EDVD) till less than 10%, endothelium-independent vasodilation (EIVD) – till less than 15%, the coefficient of the sensitivity of the endothelium to the (transverse strain) shere stress (K) <0.59. The average value of the examined EDVD RA patients was 9.2 ± 2.3%, ENVD – 13.9 ± 2.9%, K – 0.37 ± 0.21.
All the patients studied were randomly divided into two groups: I - 43 patients received standard RA therapy according to protocols of rheumatic diseases treatment, II - 41 patients received 12 months complex treatment, which included standard therapy with an ACE inhibitor addition - ramipril 2.5 -5 mg per day. The initial dose was 2.5 mg/day for a week, then the dose was increased to 5 mg/day under the blood pressure control. Patients of the I and II groups were not statistically different in all investigated indices prior to treatment.
**Results:** The dynamics of indicators of ED in the groups (Table. 1) revealed that all parameters in the both groups significantly improved ($p<0.001$) after treatment, but the increase was significantly more in group II ($p<0.05$). The positive dynamics of immune inflammation RA activity markers (CRP, TNFα, DAS28) after the treatment was in both groups, but the gain power was statistically more significant in group II ($p<0.05$). It should be noted, that DAS28 in group II decreases by more than 1.2 (according to the EULAR criteria for the RA treatment effectiveness), while in group I - only by 0.65.
Thus, inclusion of ramipril in the complex therapy of RA led to an improvement in endothelial regulation of vascular tone, helped to reduce blood levels of ICAM-1 by 16%, VEGF by 36%, CRP by 13%, TNFα by 12% as opposed to standard therapy.

Table 1. Dynamics of ED indices post treatment in the studied groups, Me (LQ; UQ)

| Indices | I group (n = 43) | | | II group (n = 41) | | | U | p |
|---|---|---|---|---|---|---|---|---|
| | Prior treatment | Post treatment | Gain (%) | Prior treatment | Post treatment | Gain (%) | | |
| EDVD, % | 9.3 (8.7; 9.7) | 9.4 (9.1; 10.7) | 1 | 9.2 (8.6; 10.3) | 11.3* (9.7; 11.8) | 23 | 3.6 | <0.001 |
| EIVD, % | 14.1 (13.6; 15.5) | 14.3 (13.3; 16.6) | 1 | 14.2 (13.6; 15.6) | 17.4* (16.1; 17.9) | 21 | 2.29 | 0.02 |
| K | 0.38 (0.29; 0.47) | 0.4 (0.34; 0.68) | 5 | 0.36 (0.28; 0.59) | 0.68* (0.5; 0.74) | 89 | 2.53 | 0.01 |
| ICAM-1, pg/ml | 8.2 (7.8; 10.1) | 8.3 (7.1; 9.3) | 1 | 8.03 (7.5; 10.1) | 6.7* (5.6; 7.34) | -17 | 4.48 | <0.001 |
| VEGF, pg/ml | 457 (324; 579) | 472 (290; 567) | 3 | 498 (341; 636) | 305* (191; 389) | -39 | 4.03 | 0.002 |

Source: Authors
* - differences are reliable after the treatment within one group by Wilcoxon test, $p < 0.05$

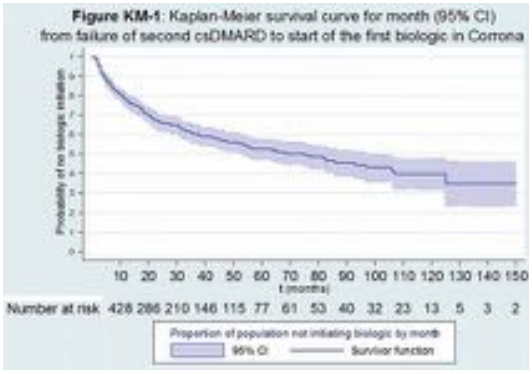
**Conclusions:** The use of ramipril in the treatment of RA for one year contributed to the effective reduction of markers of autoimmune inflammation, improved endothelial dysfunction, and significantly reduced the activity index of the disease compared with standard therapy.
**Disclosure of Interest:** None declared
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## THU0177 DELAY IN INITIATION OF BIOLOGICS AMONG BIO-ELIGIBLE PATIENTS WITH RHEUMATOID ARTHRITIS IN US: EVIDENCE FROM THE CORRONA REGISTRY

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**Background:** Biologic agents can help achieve low disease activity or remission in patients with rheumatoid arthritis (RA) who do not respond adequately to therapy with one or two conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) (1).

**Objectives:** To understand the prevalence of RA patients with inadequate response to therapy with 2 csDMARDs and describe time to initiation of a biologic agent for this patient population.
**Methods:** Patients enrolled in the Corrona RA registry as of January 2015 were included in this analysis. "Inadequate response" to 2 csDMARDs was defined as being on moderate or high disease activity (CDAI >10) six months after the initiation of 2 csDMARDs. The index visit was defined as the first visit after 6m of being on moderate or high CDAI after the initiation of 2 csDMARDs. The population of biologic naïve patients at index visit, with at least 6 months of additional follow up were observed longitudinally to calculate the time to initiation of a biologic agent. Kaplan-Meier method was used to estimate the time to biologic initiation.
**Results:** 2723 RA patients treated with 2 csDMARDs for at least 6 months were identified. At the time of the index visit: 1774 (65.1%) patients had responded to 2 csDMARDs, 192 (7.1%) had started a biologic, and 135 (4.9%) patients with inadequate response to 2 csDMARDs and did not have at least 6 months of additional follow up post-index visit. The final number of inadequate responders to 2 csDMARDs included in this analysis was 622 (22.9%) patients (79.1% female, 60.9±12.7 mean age, 9.0±9.9 mean duration of RA, 19.5±8.9 mean CDAI at index visit). The median follow up time for this population was 32.5 months. Among the 622 patients, 227 initiated a biologic during the follow up time. The median time to initiation of a biologic was 75 months (95% CI: 53–97 months). Among the 227 patients who initiated the biologic, the mean (SD) time to initiation was 17.7 (±21.7) months (figure 1). While for some patients disease activity fluctuated between low/remission and moderate/high until the initiation of a biologic agent, for 57.3% of patients remained persistently in moderate or high disease activity over the follow-up.



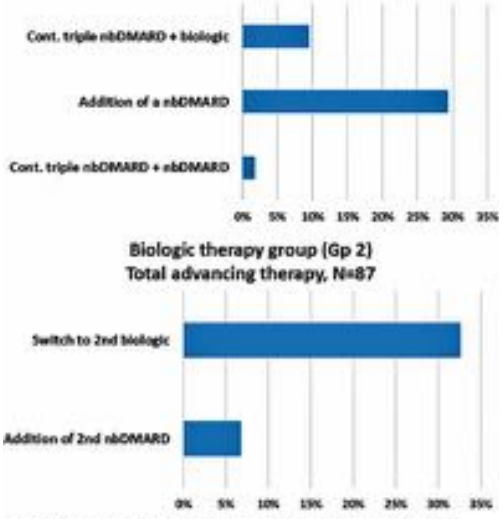

**Conclusions:** A significant percentage of RA patients treated with 2 csDMARDs did not respond adequately to such therapy in the population studied. Prolonged time until the initiation of a biologic agent was noted for this patient population.
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**Acknowledgement:** This study is sponsored by Corrona, LLC. The Corrona, LLC. RA registry has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, Astra Zeneca, BMS, Crescendo, Genentech, Horizon Pharma USA, Janssen, Eli Lilly, Novartis, Pfizer, and UCB. The design, study conduct, and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.
**Disclosure of Interest:** D. Pappas Employee of: Corrona, LLC, Paid instructor for: Novartis, C. Karki Employee of: Corrona, LLC, M. Liu Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie, Amgen, BMS, Genentech, GSK, Lilly, Medimmune, Pfizer, Sanofi, Employee of: Corrona, LLC, Speakers bureau: Genentech (for non-branded talk only), J. Greenberg Shareholder of: Corrona, LLC, Consultant for: AstraZeneca, Celgene, Genentech, Janssen, Novartis and Pfizer, Employee of: Corrona, LLC, V. Garg Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc.
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## THU0178 NEED TO ADVANCE THERAPY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TRIPLE NBDMARD VS BIOLOGIC COMBINATION THERAPY: RESULTS FROM THE CORRONA REGISTRY

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**Background:** Some studies have suggested that efficacy of triple non-biologic disease modifying anti-rheumatic drug (nbDMARD) therapy for Rheumatoid Arthritis (RA) is similar to biologic combination therapy (1).
**Objectives:** To examine the difference in need to advance therapy after treatment with triple nbDMARD (Group 1) or TNF inhibitors in combination with methotrexate (MTX)) (Group 2).
**Methods:** RA patients enrolled in Corrona between 10/2001 – 8/2015 initiating either triple nbDMARD therapy or a biologic agent in combination with MTX and with at least 1 follow-up visit were included. Group 1 included patients who started either concurrently or sequentially MTX, hydroxychloroquine and sulfasalazine. TNF inhibitors could be started concurrently with or added to MTX in Group 2. Advancement of therapy was compared for the two groups after propensity score (PS) matching and defined as discontinuing one or more of triple nbDMARD and adding a biologic/adding another nbDMARD for Group 1 and adding a second nbDMARD/switching to a different biologic for Group 2. Index visit was defined as initiation of triple therapy for Group 1 and date of biologic initiation for Group 2. Kaplan-Meier estimates were used to determine time to advancement of therapy.
**Results:** There were 236 and 2,938 in Gp 1 and 2 respectively. After PS matching, N=221 were included in each group. Groups were well balanced with a mean age of 58.5 yrs vs 58.6 yrs, mean disease duration of 10.5 yrs vs 10.6 yrs and mean clinical disease activity index (CDAI) of 15.9 vs 16.1 for groups 1 and 2 resp. About 76% (95% CI: 69.5%, 81.3%) of the Gp 1 patients continued on initial therapy compared to 82% (95% CI: 76.4%, 86.8%) in Gp 2 at 12 months of follow-up. Median time to therapy advancement was 49 months (95% CI: 35, 59) for group 1 and 69 months (95% CI: 46, 100) for group 2. About 40% of patients in triple nbDMARD group had to advance therapy during 12 months of follow-up, vs 39% in group 2. Types of first advancement of therapy is shown in table 1.

**Figure 1: Categories of advancement of therapy in triple nbDMARD and biologic therapy group during follow-up**




nbDMARD: non-biologic disease modifying anti-rheumatic drug

**Conclusions:** Therapy with a biologic agent resulted in a numerically but not statistically significant prolonged time to advancement therapy compared to triple nbDMARD therapy. Future examination of the need to advance therapy with a larger sample size may provide further insights for treatment practices.
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**Acknowledgement:** This study is sponsored by Corrona, LLC. The Corrona, LLC. RA registry has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, BMS, Crescendo, Genentech, Horizon Pharma USA, Janssen, Eli Lilly, Novartis, Pfizer, and UCB. The design, study conduct, and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.
**Disclosure of Interest:** D. Pappas Employee of: Corrona, LLC, Paid instructor for: Novartis, C. Karki Employee of: Corrona, LLC, H. Litman Employee of: Corrona, LLC, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: AstraZeneca, Celgene, Genentech, Janssen, Novartis and Pfizer, Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie, Amgen, BMS, Genentech, GSK, Lilly, Medimmune, Pfizer, Sanofi, Employee of: Corrona, LLC, Speakers bureau: Genentech (for non-branded talk only), V. Garg Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc.
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## THU0179 DISCONTINUATION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN RHEUMATOID ARTHRITIS PATIENTS WITH LOW DISEASE ACTIVITY

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**Background:** Although nonsteroidal anti-inflammatory drug (NSAIDs) is effective in relieving joint pain in rheumatoid arthritis (RA) patients, long-term use of NSAIDs can cause adverse effects on gastrointestinal or cardiovascular organs. When patients discontinue daily use of NSAIDs, there is often a dichotomous clinical response in patient-reported outcomes (PRO).
**Objectives:** We aimed to examine the clinical outcome especially joint pain, and its associated factors in RA patients with low disease activity (LDA) after discontinuing NSAIDs.
**Methods:** This study was a 16-week, multi-center prospective open-label trial conducted at eight rheumatology clinics in Korea. RA patients who achieved LDA (DAS28 <3.2) who were on NSAIDs for more than 2 consecutive months, discontinued the NSAID. Acetaminophen (AAP) was used as the rescue medication. During the study period, changes of DAS28 and PRO including pain visual analogue scale (VAS) and Routine Assessment of Patient Index Data 3 (RAPID-3) score were assessed. NSAIDs were restarted when patient's 1) pain was uncontrolled with AAP and 2) PRO were aggravated. The endpoint was to analyze the group of patients who continued to withdraw NSAIDs within the study period. Patients were further classified to have "sustained effectiveness" who met the following: 1) 16-week pain VAS ≤30 mm or increase less than 20% from baseline and 2) 16-week RAPID-3 score ≤6 or increase less than 20% from baseline.
**Results:** A total of 121 RA patients with LDA were enrolled in the study. Four patients were lost to follow-up. At the end of the study, 18 (15.3%) patients had restarted NSAIDs owing to uncontrolled pain. In general, there was a difference in pain VAS between baseline (median 15 mm (IQR 5–20)) and 16 weeks (median 17 mm (IQR 5–40)) ($p$=0.022). Changes of DAS28 and RAPID-3 were insignificant in patients taking on-demand AAP (n=99) (0 versus 16 weeks; DAS28, $p$=0.111; RAPID-3; $p$=0.339). Moreover, 60% of the total patients (73/117) ended up to show sustained effectiveness without restarting NSAIDs. By using a multivariate logistic regression model, we found out that joint swelling was the detrimental factor compromising sustained effectiveness (OR 0.312, 95% C.I. 0.125–0.777, $p$=0.012).
**Conclusions:** Discontinuation of NSAIDs can be attempted in RA patients with LDA, especially in those without swollen joints at the time point of its cessation.
**Disclosure of Interest:** None declared
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## THU0180 LACK OF EARLY CHANGE IN DISEASE ACTIVITY SCORE PREDICTS THE LIKELIHOOD OF ACHIEVING LOW DISEASE ACTIVITY AT MONTH 6: TOFACITINIB MONOTHERAPY VERSUS METHOTREXATE IN METHOTREXATE-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Treatment guidelines recommend targeting remission or low disease activity (LDA), herein defined as Disease Activity Scores ≤3.2 based on 28 joint counts (DAS28≤3.2) and adjusting therapy after 3–6 months[1] (Mos). Predicting the likelihood of clinical response may help inform early treatment decisions.
**Objectives:** To understand the relationship between timing and magnitude of early changes in DAS28, erythrocyte sedimentation rate (DAS28-4[ESR]) and the likelihood of achieving LDA at Mo 6 in RA patients (pts) naïve to methotrexate (MTX).
**Methods:** In a Phase 3 study (ORAL Start; NCT01039688), MTX-naïve RA pts were randomised 2:2:1 to the following monotherapies: tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID or MTX. Conditional probability of pts achieving LDA at Mo 6 were calculated, given failure to achieve DAS28-4(ESR) improvement from baseline (range ≥0.3 to 1.8) at Mo 1 or 3. One-year data with non-responder imputation for missing values was used.
**Results:** 948 pts received treatment; tofacitinib 5 mg BID (n=370), tofacitinib 10 mg BID (n=394) or MTX (n=184); results previously reported.[2] In this post-hoc analysis, of those patients who failed to achieve DAS28-4(ESR) improvement from baseline ≥1.2 at Mo 3, 6.8% for tofacitinib 5 mg BID, 11.3% for tofacitinib 10 mg BID and 6.2% for MTX achieved LDA at Mo 6 (Table). A minority of pts (74/353 [20.9%]) receiving tofacitinib 5 mg BID failed to achieve DAS28-4(ESR) improvement ≥1.2 from baseline at Mo 3, while a greater proportion failed for MTX (65/171 [38.0%]). Failure to achieve DAS28-4(ESR) improvement from baseline at Mo 3 (range ≥0.30–1.8) for tofacitinib 5 mg BID and MTX was associated with a low probability (≤10%) of achieving LDA at Mo 6. For tofacitinib 5 mg BID, failure to achieve lower thresholds of DAS28-4(ESR) improvement (range ≥0.3 to 0.9) at Mo 1 was associated with lower probability of LDA at Mo 6 than higher DAS28-4(ESR) thresholds (≥1.2–1.8) (Table).

| Given failure to achieve DAS28-4(ESR) improvement at Month 1 or 3 | | Percentage of patients achieving LDA at Month 6 | | |
|---|---|---|---|---|
| DAS28-4(ESR) improvement≥ | Month | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | MTX* |
| 0.3 | 1 | 3.9 | 14.3 | 12.7 |
| | 3 | 0.0 | 15.4 | 5.0 |
| 0.6 | 1 | 9.8 | 18.2 | 12.8 |
| | 3 | 0.0 | 8.7 | 5.0 |
| 0.9 | 1 | 12.1 | 15.4 | 10.9 |
| | 3 | 6.0 | 11.4 | 7.8 |
| 1.2 | 1 | 14.7 | 19.5 | 10.0 |
| | 3 | 6.8 | 11.3 | 6.2 |
| 1.5 | 1 | 18.5 | 21.1 | 10.6 |
| | 3 | 8.7 | 11.1 | 6.5 |
| 1.8 | 1 | 22.6 | 23.5 | 12.8 |
| | 3 | 10.0 | 10.7 | 7.5 |

BID, twice daily; DAS28-4(ESR), disease activity score, erythrocyte sedimentation rate; LDA, low disease activity.
*MTX dose – starting dose of 10 mg per week (mg/wk), with increments of 5 mg/wk every 4 weeks to 20 mg/wk by Week 8. Mean dose of MTX was 18.6 mg/wk

**Conclusions:** Failure to achieve DAS28-4(ESR) improvement ≥1.2 from baseline at Mo 3 was associated with a low probability of achieving LDA at Mo 6 (≤6.8%) for tofacitinib 5 mg BID and MTX. For the minority of MTX-naïve RA pts treated with tofacitinib 5 mg BID or MTX who failed to achieve a minimal clinical response (DAS28-4[ESR] improvement ≥1.2) by Mo 3, another treatment option can be considered at Mo 3, as there is a low probability of reaching LDA at Mo 6.
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**Disclosure of Interest:** E. Keystone Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, R. F. van Vollenhoven Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, B. Wilkinson Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Fallon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L.-J. Hwang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Chapman Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. DeMasi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, E. B. Lee Consultant for: Pfizer Inc
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## THU0181 EFFICACY AND SAFETY OF CONCOMITANT METHOTREXATE AND LEFLUNOMIDE USE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS. CROSS -SECTIONAL STUDY

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**Background:** Treatment of RA is based on the use of DMARDs, both synthetic and biological,and the mayor goal is to achieve clinical remission. Several Scientific Societies (EULAR, ACR, SER) recommend that all patients with RA should be treated with DMARDs as soon as the clinical diagnosis is established. Methotrexate (MTH) is the first line treatment. In case of unsatisfactory response (development of toxicity or failure), it is recommended to use Leflunomide (LEF), Sulfasalazine or an anti-TNF agent as a second line treatment, in monotherapy or associated with MTH
**Objectives:** To describe the current situation, baseline characteristics and reasons for discontinuing or changing treatment of RA patients seen during 1 year in our department,that were or had been treated with concomitant MTH-LEF therapy
**Methods:** Observational cross-sectional study. Clinical records of RA patients, attended in our Rheumatology Department during 2014 who were or had been treated with MTH-LEF, were reviewed. Demographic (age and sex), clinical (years of disease progression, RF/ACPA, ESR/CRP, NTJ/NSJ, DAS28) and treatment

variables (duration in months, other treatments, reasons for discontinuing or changing)were analyzed
**Results:** 483 patients were analyzed, 104 were finally included. Mean age was 55.18 years (±11,82), 88.6% were women. 39.4% were currently receiving MTH-LEF therapy, with a mean disease course in years of 6.15 (±5.03) and a mean duration of treatment in months of 22,84 (±17.45).53.7% took corticosteroids and 12.2% NSAIDs on a daily basis. RF/ACPA was positive in 85.4%/51.2%; mean NTJ/NSJ was 0.41 (±1.16)/0.32 (±069); the mean value of ESR/CRP was 32.13 (±17.99)/6.92 (±10.61). According to DAS28 score, 14.6% of patient were in remission, 70.7% at low disease activity, 12.2% at moderate disease activity and 2.4% at high disease activity. *Patients no longer with MTH-LEF therapy* had similar baseline characteristics except for ACPA positive in a higher % (77.97% vs. 51.2%,p=0.05). No differences in drug dosing were found, being the higher doses the most used ones (MTH>15 mg/week, LEF 20 mg/day). The main reason for combined therapy discontinuation was inefficacy (54%), followed by adverse effects in 35% (gastrointestinal intolerance 36.36%, nonspecific skin disorders 18.18% and hematological disorders, cough, headache and others) and low clinical activity (11%). No significant differences between patients according to the reason for discontinuation of treatment were observed. Higher drug dose use was not found in patients who experienced adverse effects (as it would have been expected). A longer disease course was found in patients presenting inefficiency as so a higher positive % of RF/ACPA
**Conclusions:** The 39.4% of patients responded to the MTH-LEF therapy, avoiding the use of biological agents. It appears to be a valid alternative for our patients, since 85.3% of them had low clinical activity. However, it had to be discontinued in up to 60.6% of patients, noting in this group a higher % of ACPA+ patients. The main causes for treatment discontinuation were ineffacy and gastrointestinal intolerance. No significant differences were seen regarding the therapy discontinuation cause, although it seems to be more common in RF/ACPA positive patients and we observed a longer disease course if inneficacy happened. No differences in drug dosing were found.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5420

## THU0182 EX VIVO FUNCTIONAL COMPARISON OF BARICITINIB AND TOFACITINIB FOR CYTOKINE SIGNALING IN HUMAN LEUKOCYTE SUBPOPULATIONS

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**Background:** Baricitinib (bari) and tofacitinib (tofa) are selective JANUS kinase inhibitors (JAKi). In biochemical assays, bari exhibits greatest potency against JAK1 and JAK2, whereas that for tofa is against JAK1 and JAK3.
**Objectives:** To determine whether differences in JAKi specificity translate to differences in cellular signal transduction in leukocyte subpopulations stimulated by cytokines, indicated by inhibition of signal transducers of activator transcription (STATs) phosphorylation.
**Methods:** Peripheral blood mononuclear cells (PBMC) were obtained from healthy donors (n=6). Leukocyte preparations were incubated with JAKi using a 7 point dose range, 2.44–10,000 nM, for 1 hour before cytokine stimulation. The half maximum inhibitory concentration ($IC_{50}$) values were determined by plotting the mean fluorescence intensity of cytokine-stimulated and nonstimulated samples in phenotypically gated leukocyte subpopulations.[1]
**Results:** $IC_{50}$ values for bari and tofa were similar for interleukin-6 (IL-6) across leukocyte subsets. Differences were observed for other cytokines. The $IC_{50}$ across leukocyte subpopulations stimulated with the same cytokine varied 2–3 fold per compound (Table). The most significant differences between JAKi $IC_{50}$ values were for cytokines that use JAK1/3. Tofa was a more potent inhibitor of IL-2, IL-4, IL-15, and IL-21 induced STAT phosphorylation than bari. Both compounds inhibited IL-10 stimulation of pSTAT3 and IFN-α stimulation of pSTAT1, pSTAT3, and pSTAT5 similarly. Inhibition of IFN-α pSTAT3 and pSTAT5 were similar for both JAKi, although less potent in inhibiting STAT1 phosphorylation. Bari and tofa inhibited GM-CSF (JAK2) and G-CSF and IFNg signaling, with bari exhibiting a greater effect in monocytes than tofa.
**Conclusions:** The differences in $IC_{50}$ for key cytokine stimuli suggest fundamental functional differences across classes of JAKi. The potency of JAKi varied between different leukocyte subpopulations and is STAT substrate dependent. At the clinical level, therefore, these agents should not be considered biologically equivalent. A practical consequence is that determination of JAKi potency on $IC_{50}$ based solely on a nongated whole blood assay would not detect differential responses of leukocyte subpopulations by JAKi.

$IC_{50}$ Values for baricitinib and tofacitinib in cytokine-stimulated human PBMC preparations

| Cytokine/ pSTAT | B cells | | CD4+ T cells | | CD8+ T cells | | NK cells | | Monocytes | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Bari (nM) | Tofa (nM) | Bari (nM) | Tofa (nM) | Bari (nM) | Tofa (nM) | Bari (nM) | Tofa (nM) | Bari (nM) | Tofa (nM) |
| IL-2/5 | NDS | | 23 | 9*** | 24 | 9** | 43 | 15*** | NDS | |
| IL-4/6 | 135 | 61** | 50 | 18*** | 27 | 10*** | 17 | 6*** | 50 | 39* |
| IL-6/3 | NDS | | 44 | 41 | NDS | | NDS | | 51 | 42 |
| IL-10/3 | 82 | 76 | 59 | 48 | 63 | 57 | 71 | 61 | 165 | 121* |
| IL-15/5 | NDS | | 37 | 14*** | 64 | 24*** | 73 | 24*** | NDS | |
| IL-21/3 | 86 | 28*** | 63 | 22*** | 65 | 22*** | 61 | 21*** | NDS | |
| IFN γ/1 | 17 | 20 | NDS | | NDS | | NDS | | 46 | 54*** |
| IFN α/1 | 246 | 195 | 77 | 59* | 117 | 91 | 137 | 110** | 139 | 99* |
| IFN α/3 | 27 | 19* | 25 | 19* | 26 | 20 | 25 | 18 | 17 | 12* |
| IFN α/5 | 25 | 18 | 21 | 15* | 26 | 18* | NDS | | 13 | 9** |
| G-CSF/3 | NDS | | NDS | | NDS | | NDS | | 69 | 103** |
| GM-CSF/5 | NDS | | NDS | | NDS | | NDS | | 116 | 163** |

*p<0.01; **p<0.001; ***p<0.0001. CSF = colony stimulating factor; G = granulocyte; $IC_{50}$ = half maximum inhibitory concentration; IFN = interferon; IL = interleukin; M = macrophage; NDS = no detectable signal; NK = natural killer; PBMC = peripheral blood mononuclear cells; pSTAT = phosphorylated signal transducers of activatortranscription.

**References:**
[1] Krutzik, et al. Nat Methods. 2006 May;3(5): 361–368.
**Disclosure of Interest:** I. McInnes Grant/research support from: Pfizer, UCB, Janssen, Astra Zeneca, Consultant for: Eli Lilly and Company, Pfizer, Galapagos, AbbVie, UCB, Janssen, Novartis, R. Higgs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, G. Rocha Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, X. Zhang Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, J. Lee Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, T. Wehrman: None declared, W. Macias Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Zuckerman Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Taylor Grant/research support from: UCB, GlaxoSmithKline, Celgene, Consultant for: UCB, Eli Lilly and Company, Pfizer, Galapagos, Merck, GlaxoSmihKline, AbbVie, Takeda, Bristol-Myers Squibb
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## THU0183 TREATMENT WITH TOFACITINIB INHIBITS HUMAN NAÏVE B LYMPHOCYTE DEVELOPMENT AND FUNCTION IN VITRO

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**Background:** B cells are pivotal to the pathogenesis of many autoimmune diseases including rheumatoid arthritis (RA). Tofacitinib, a JAK inhibitor, is effective and safe in the treatment of RA. Tofacitinib interferes with signal transduction via cytokine receptors using the common γ-chain.
**Objectives:** Despite of extensive data on T lymphocytes, the impact of tofacitinib on B lymphocytes is poorly understood. In this study we assess the effect of tofacitinib on the differentiation of naive B-lymphocytes and their function.
**Methods:** Sorted human B cells from cord blood or buffy coat were stimulated in the presence of increasing doses of tofacitinib. B cell phenotypes were determined by flow cytometry. Immunoglobulin concentrations were measured by ELISA. The expression of B cell fate determining genes PRDM1, IRF4, XBP1, and AICDA was analyzed by quantitative RT-PCR.
**Results:** Tofacitinib treatment strongly impaired plasmablast development, immunoglobulin secretion and induction of PRDM1, IRF-4, and XBP-1 from naive B cells. Interestingly, class switch and AICDA induction from activated naive B cells was only slightly reduced. B cells purified from buffy coats, including naive and memory B cells, stimulated in the presence of tofacitinib, showed only a moderate reduction in plasmablast formation, immunoglobulin secretion and proliferation.
**Conclusions:** We demonstrated that tofacitinib has a direct impact on human naive B-lymphocytes, independently from its effect on T lymphocytes, by impairing their development into plasmablasts and immunoglobulin secretion. Tofacitinib predominantly affects naive B lymphocytes, while its effect on total peripheral B cells containing naive and memory B cells is less pronounced. Our data are of clinical importance as they suggest that vaccinations should be performed prior to tofacitinib treatment. Furthermore, impairement of B cell function by tofacitimib may directly contribute to its therapeutic effects. This fact has implications for the potential use of tofacitinib in B cell-mediated diseases.
**Disclosure of Interest:** None declared
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## THU0184 REPAIR OF BONE EROSION IN RHEUMATOID ARTHRITIS BY DENOSUMAB: AN HR-PQCT STUDY

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**Background:** Blockade of receptor activator of nuclear factor kappa B ligand (RANKL), using denosumab retards bone damage in RA. Whether RANKL blockade allows repair of existing bone erosions is so far unclear.

**Objectives:** To compare the reparative effect of denosumab and alendronate on erosions in female RA patients with low bone mass using HR-pQCT.
**Methods:** This is a post-hoc analysis of a randomized-controlled trial. 40 patients with bone erosions were randomized in a 1:1 ratio to receive either subcutaneous denosumab (60mg) once or oral alendronate (70mg) weekly for 6 months. The size of individual bone erosions and the presence and degree of marginal osteosclerosis around the second metacarpophalangeal joint of the non-dominant hand were measured both semi-quantitatively and quantitatively at baseline, 3- and 6-months.
**Results:** At baseline, the mean (±SD) width, depth and volume of the bone erosion were similar for both groups (Table). At 6 months, erosion size significantly decreased in the denosumab group, and significantly increased in the alendronate group. The between group differences in all size criteria were statistically significant at 6 months (all $p<0.01$). The degree of marginal osteosclerosis was similar between both groups at baseline. At 6-month, more than half of the patients (57.1%) in the alendronate group showed no osteosclerosis (grade 0). In contrast, most patients (80.9%) in the denosumab group showed osteosclerosis (grade 1 or 2). Mean (±SD) pixel attenuation of the erosion margin was similar between both groups at baseline. Mean pixel attenuation was significantly increased at 6 months in the denosumab group though unchanged in the alendronate group. Between group differences for change in mean pixel attenuation between baseline and 6 months were also significant ($p<0.05$).

| Parameter | Alendronate | | Denosumab | |
|---|---|---|---|---|
| | Baseline (n=21) | 6 months (n=21) | Baseline (n=21) | 6 months (n=21) |
| Shape and size of erosion | | | | |
| Width (mm) | 2.91±1.64 | 3.22±1.59* | 3.16±1.21 | 2.69±1.28** |
| Depth (mm ) | 1.86±0.94 | 2.48±1.08** | 1.46±0.68 | 1.15±0.66** |
| Volume ($mm^3$) | 4.72±5.62 | 5.39±6.07* | 4.97±7.60 | 4.06±6.76** |
| Change in width (mm) | | 0.19±0.26 | | –0.23±0.24## |
| Change in depth (mm) | | 0.32±0.35 | | –0.16±0.086## |
| Change in volume ($mm^3$) | | 1.38±1.40 | | –0.91±1.054## |
| Marginal osteosclerosis | | | | |
| Grade 0 | 10 (47.6%) | 12 (57.1%) | 13 (61.9%) | 4 (19.1%) |
| Grade 1 | 9 (42.9%) | 8 (38.1%) | 8 (38.1%) | 12 (57.1%) |
| Grade 2 | 2 (9.5%) | 1 (4.8%) | 0 | 5 (23.8%) |
| Pixel attenuation (HU) | 2252±1635 | 2091±1423 | 1647±710.5 | 2066±946.5** |
| Change in pixel attenuation (HU) | | –161.6±577.6 | | 418.9±611.1# |

All data expressed as mean ± SD or n (%). Pixel attenuation refers to the mean pixel attenuation of the area surrounding the bone erosion. *$p<0.05$, **$p<0.01$, within group comparison between baseline and 6 months. #$p<0.05$, ##$p<0.01$, comparison between alendronate and deonsumab groups.

**Conclusions:** Bone erosions in RA patients treated with denosumab show evidence of limited repair in contrast to bone erosions in patients treated with alendronate, indicating a favourable impact of RANKL inhibitor on the local bone remodeling.
**Disclosure of Interest:** None declared
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## THU0185 TOFACITINIB, AN ORAL JAK INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS: SAFETY AND CLINICAL AND RADIOGRAPHIC EFFICACY IN OPEN-LABEL, LONG-TERM EXTENSION STUDIES OVER 7 YEARS

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA).
**Objectives:** To report tofacitinib safety, tolerability and clinical response over 84 months (mo), and radiographic data over 12 mo, in long-term extension (LTE) studies.
**Methods:** Data were from two open-label studies (NCT00413699 [ongoing; database unlocked at March 2015 data-cut] and NCT00661661]) of patients (pts) with RA who completed randomised Phase (P)1/2/3 tofacitinib studies. Pts received tofacitinib 5 or 10 mg BID as monotherapy or with background DMARDs; data were pooled. Primary endpoints: AEs and lab safety. Confirmed data are reported for decreased Hgb, neutrophil and lymphocyte counts, and increases >50% from BL in creatinine. Secondary endpoints: DAS28-4(ESR), HAQ-DI and mTSS. Safety data were included up to 96 mo and efficacy up to Mo 84 ($n\leq30$ post-Mo 84).
**Results:** 4867 pts were treated (mean [max] duration: 1107 [2895] days). BL data were from P1/P2/P3 index studies for 90.9% of pts. Total tofacitinib exposure was 14926 pt-years (py); 79.2% of pts maintained initial dose. In total, 2132 pts (43.8%) discontinued (AEs: 1051 [21.6%]; insufficient clinical response: 153 [3.1%]). Most common AE classes: infections and infestations (67.6%) and musculoskeletal/connective tissue disorders (37.3%). Most common AEs: nasopharyngitis (18.1%), upper respiratory tract infection (16.2%) and bronchitis (11.7%). SAEs occurred in 26.8% of pts (incidence rate [IR] 9.7/100 py [95% CI 9.2, 10.2]), and serious infection events (SIEs) in 8.4% of pts (IR 2.8/100 py [95% CI 2.5, 3.0]). Malignancies excluding NMSC were reported in 3.0% of pts (IR 1.0/100 py [95% CI 0.8, 1.1]). IRs for SIEs and malignancies through Mo 96 did not increase vs reported data through Mo 84.[1] Decreased Hgb (>30% decrease from BL/Hgb <8 g/dL) occurred in <1.0% of pts. Increased aminotransferases (>3×ULN) occurred in 5.4% (ALT) and 3.1% (AST) of pts. Moderate to severe neutropenia (absolute neutrophil count [ANC] 0.5–$1.5\times10^3/mm^3$) was noted in 1.5% of pts; there were no confirmed cases of ANC <$0.5\times10^3/mm^3$. Confirmed absolute lymphocyte counts <$0.5\times10^3/mm^3$ occurred in 1.3% of pts. Increases >50% from BL in creatinine were seen in 2.4% of pts. Mean DAS28-4(ESR) was 6.29 at BL, 3.74 at Mo 1 and 3.20 at Mo 84. Mean HAQ-DI score was 1.42 at BL, 0.81 at Mo 1 and 0.78 at Mo 84. Radiographic data were available for 1099 pts. Mean mTSS was 24.0 at BL (last P1/P2/P3 index value), 25.1 at Mo 6 and 24.3 at Mo 12. Mean change from BL in mTSS was 0.3 at Mo 6 and 0.2 at Mo 12.
**Conclusions:** Consistent safety and sustained efficacy over 84 mo was seen in pts with RA receiving tofacitinib 5 or 10 mg BID in LTE studies. Changes in mTSS were minimal at Mo 12 in LTE studies.
**References:**
[1] Wollenhaupt J et al. Arthritis Rheumatol 2014; 66: S375.
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## THU0186 DOES EARLY STEROID USE INCREASE THE LIKELIHOOD OF ACHIEVING REMISSION AT 6 MONTHS IN EARLY RA? RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

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**Background:** In RA, synthetic glucocorticoids (steroids) are often used as "bridge therapy" to rapidly control symptoms while allowing slower-acting DMARDs time to reduce disease activity. Whether early use of steroids in conjunction with conventional DMARDs has an added benefit for achieving early remission is unknown.
**Objectives:** To describe the frequency of early steroid use in a national observational cohort of ERA patients seen by rheumatologists in routine clinical practice and to estimate the extent to which early use of steroids is associated with achieving early remission at 6 months.
**Methods:** We analyzed baseline and 6-month follow up data from the prospective multi-center Canadian early ArThritis CoHort (CATCH). The study sample included participants meeting 1987 or 2010 ACR/EULAR criteria for RA, symptom duration ≤12 months, with DAS28 moderate-high disease activity at enrolment and medication information and follow-up DAS28 scores at 6 months. Mixed-effects logistic regression was used to estimate independent effects of early steroid use on remission status at 6 months after adjusting for sociodemographics (age, sex, education, comorbidities, smoking), and RA characteristics (symptom duration; presence of erosions, DAS28 and HAQ at baseline) including treatment at enrolment. A random effect for study center was specified to appropriately account for dependencies in the data.
**Results:** The analytic sample included 1170 CATCH participants and was mostly female (n=855; 73%) with a mean [SD] age of 54 [15] and symptom duration of 6 [3] months. At entry, 640 (55%) used steroids (oral only 264 [23%]; parental only 295 [25%]; both: 81 [7%]). Patients receiving steroids were older, male, had shorter symptom duration, a higher DAS28, and more swollen and tender joints ($p<0.003$). Steroids were most commonly used with MTX (frequency [%]: 513 [80%]; MTX mono: 194 [30%]; MTX combo; 319 [50%]; biologics: 10 [2%]; other treatment strategies: 117 [18%]). At 6 months, 393 (34%) were in DAS28 remission. After adjusting for treatment and other covariates, neither oral not parenteral steroids were independently associated with remission status at 6 months, though there was a trend ($p=.07$) for patients receiving both oral and parenteral steroids to have a lower odds of being in remission (see table).

Impact of early steroid use on remission status at 6 months

| | Odds Ratio | 95% Confidence Interval |
|---|---|---|
| Oral only | 0.79 | 0.53–1.17 |
| Parenteral only | 0.85 | 0.59–1.23 |
| Oral and parental | 0.56 | 0.31–1.04 |

**Conclusions:** Findings from this large national ERA cohort showed that steroids were commonly used as early adjunctive therapy in routine practice and that patients receiving steroids were more likely to be older, male, have higher disease activity and more affected joints. Early steroid use (oral or parenteral) was not independent associated with early remission at 6 months, although use of both may be a negative prognostic indicator.
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## THU0187 SAFETY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR: INTEGRATED DATA ANALYSIS FROM THE GLOBAL CHRONIC PLAQUE PSORIASIS CLINICAL TRIALS

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis that is being investigated for psoriasis.
**Objectives:** To report pooled trial safety data in patients with psoriasis to expand knowledge around the safety profile of tofacitinib in inflammatory diseases.
**Methods:** The 1-year randomised controlled trials (RCT) group included patients with psoriasis who received ≥1 dose of tofacitinib 5 or 10 mg BID in three 1-year Phase 3 RCTs. The integrated safety group included patients with psoriasis who received ≥1 dose of tofacitinib in four Phase 3 studies (5 or 10 mg BID) or a long-term extension (LTE) study. In the LTE study, patients entered following one Phase 2 study or the Phase 3 studies and received 10 mg BID (for 3 months), then 5 or 10 mg BID (ongoing, database not locked, data cut-off April 4, 2014). Incidence rates (IR; patients with events/100 patient-years) were calculated for the 1-year RCT and integrated safety groups. For the integrated safety group, data were pooled across doses.
**Results:** In the 1-year RCT group, 2436 patients received tofacitinib (5 mg BID, n=1217; 10 mg BID, n=1219), with a median of 253 days of tofacitinib exposure (range: 1–431, first and third quartiles: 168, 364). In the integrated safety group, 3623 patients received tofacitinib, with a median of 527 days of tofacitinib exposure (range: 1–1344, first and third quartiles: 261, 766). Serious infection IRs were 1.37 and 2.42 respectively for 5 and 10 mg BID in the 1-year RCT group, and 1.68 in the integrated safety group. Herpes zoster IRs were 1.00 and 2.32 for 5 and 10 mg BID in the 1-year RCT group, and 2.55 in the integrated safety group. Malignancy (excluding non-melanoma skin cancer [NMSC]) IRs were 1.12 and 0.81 for 5 and 10 mg BID in the 1-year RCT group, and 1.00 in the integrated safety group. NMSC IRs were 0.63 and 1.27 for 5 and 10 mg BID in the 1-year RCT group, and 0.74 in the integrated safety group. Major adverse cardiovascular event IRs were 0.50 and 0.23 for 5 and 10 mg BID in the 1-year RCT group, and 0.37 in the integrated safety group. In the 1-year RCT group, 95% confidence intervals for 10 vs 5 mg BID hazard ratios included 1 for each of these events.
**Conclusions:** Serious infection, herpes zoster and NMSC IRs were numerically, but not statistically, higher with 10 vs 5 mg BID. IRs were similar in the RCT group and the integrated safety group, indicating that IRs are stable over time. Tofacitinib was well tolerated in patients with plaque psoriasis – including up to 44 months of exposure for some patients in the ongoing LTE study at data cut-off.
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## THU0188 EFFICACY AND SAFETY OF ADD-ON TREATMENT OF TACROLIMUS VERSUS LEFLUNOMIDE IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO METHOTREXATE: A 24-WEEK DOUBLE-BLINDED RANDOMIZED NON-INFERIORITY STUDY

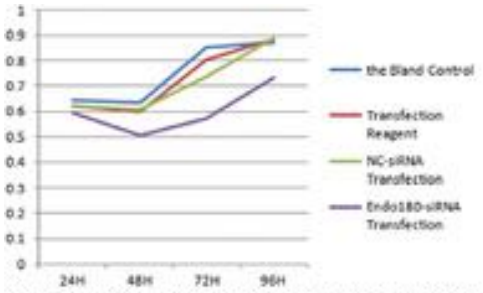
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**Background:** Tacrolimus (TAC) is used as a disease modifying antirheumatic drug (DMARD) in rheumatoid arthritis (RA). Combination of TAC with methotrexate (MTX) has been shown to be effective and safe in RA, yet comparative clinical studies are insufficient to date.
**Objectives:** To investigate the efficacy and safety of TAC versus leflunomide (LEF) when combined with MTX in RA patients
**Methods:** The PLATINUM-X study is a 24-week multi-center, double-blinded randomized non-inferior (phase 4) study targeting RA patients with moderate to active disease activity (DAS28(ESR) >3.2) that had a inadequate clinical response to MTX. Patients were randomized into the TAC or LEF (add-on) group. The initial daily dose of TAC and LEF were 1.5 mg and 10 mg, respectively for 4 weeks, then increased to 3 mg, 20 mg until the end of the study. Clinical (DAS28, Korean (K-) HAQ) and laboratory data were obtained at 4, 8, 16, and 24 weeks. The primary endpoint was to compare DAS28 in both groups at 24 weeks. Non-Inferiorly was established if the upper limit of the 95% confidence interval (CI) for DAS28 difference was less than 0.7. Secondary endpoint variables included DAS28, K-HAQ as well as swollen/tender joint counts at each visit. Safety profiles were assessed at each patient's visit. The per protocol set was used for statistical analysis.
**Results:** Eighty seven patients were screened in 9 centers, and 75 patents were randomized into 2 groups. Baseline demographics of patients were comparable with baseline DAS28 being 4.54 ± 0.61 and 4.91 ± 1.01 in the TAC and LEF group, respectively. TAC was non-inferior to LEF in terms of reduction of DAS28 at 24 weeks (mean difference -0.0565, CI -0.6513, 0.5384). Improvement of DAS28, K-HAQ throughout each visit was not statistically different between the 2 groups. Yet, reduction in tender joint count was significant in the TAC group compared with LEF (-5.97 ± 4.89 versus -3.08 ± 5.55 at 24 weeks, $p$=0.0145). There was more numbers of adverse events (AE) or adverse drug reactions in the LEF group (89 in LEF and 64 in TAC); 6 patients presented transaminitis in the LEF group compared with 2 in TAC.
**Conclusions:** The efficacy of TAC plus MTX is non-inferior to LEF combined the MTX, with reasonable safety profile in RA patients with moderate to active disease activity (cris.nih.go.kr KCT0000781).
**References:**
[1] Tacrolimus in RA patients receiving concomitant MTX. Kremer et al. Arthritis Rheum 2003
[2] Efficacy and safety of tacrolimus in patients with RA. Youcum et al. Arthritis Rheum 2003
**Disclosure of Interest:** None declared
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## THU0189 INCREASED EXPRESSION OF THE COLLAGEN INTERNALIZATION RECEPTOR ENDO180 IN FIBROBLAST-LIKE SYNOVIOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Hyperproliferative and invasiveness are the characteristics of fibroblast-like synoviocytes in rheumatoid arthritis (RA-FLSs), which contribute mainly to RA disease progression and ultimately to joint destruction. Endo180 is a recycling endocytic receptor that has functions to regulate cell migration and bind to internalize collagens. However, the expression of Endo180 in RA-FLSs and its underlying mechanisms remain unclear.
**Objectives:** The aim of this study was to examine the expression of Endo180 in RA-FLSs and the role it played in RA pathological process.
**Methods:** Tissues were collected from RA patients with joint replacement surgery or arthroscopy and RA-FLSs were obtained by tissue culture;Westren blotting was used to measure the expression of Endo180 in RA-FLSs. Chemically synthesized small interference RNA (siRNA) specifically targeting Endo180 gene was transfected into RA-FLSs by cationic liposome; The interference efficiency of Endo180-siRNA on the production of Endo180 RNA and protein was determined by RT-qPCR and Western blotting respectly; The proliferative inhibition rate was examined by CCK8 assay and the migration of RA-FLSs were examined by Transwell assay.
**Results:** Expression of Endo180 was obviously higher in fibroblast-like synoviocytes in RA than OA and the traumatic patients. And its expression level has positive correlation with disease activity described as DAS28. The proliferative inhibition rate was obviously higher in the Endo180-siRNA group than the control groups ($P<0.05$) after transfection for 48h (16.31%±1.17%), 72h (23.53%±2.62%), 96h (18.01%±1.96%). Transwell migration assay demonstrated the RA-FLSs through the transwell membrane in Endo180-siRNA group (21.27±6.35) were lesser than the NC-siRNA group (80.20±11.12) ($P<0.05$) and the blank control group (82.17±10.36) ($P<0.05$).




Knocking-down Endo180 in RA-FLSs decreases cell proliferation. RA-FLSs were transfected with Endo180-siRNA or a negative control for 24h, 48h, 72h, and 96h respectively and the cell proliferation was assessed by the CCK8 assay.

**Conclusions:** Endo180 may play a role in the regulation of proliferation and migration of RA-FLSs, which may provide beneficial therapeutic effects in RA.
**References:**
[1] Melander MC, Jürgensen HJ, Madsen DH,et al. The collagen receptor uPARAP/Endo180 in tissue degradation and cancer (Review).Int J Oncol. 2015 Oct;47(4):1177–88. doi: 10.3892/ijo.2015.3120. Epub 2015 Aug 12.
[2] Madsen DH, Jurgensen HJ, Ingvarsen S, et al. Endocytic collagen degradation:a novel mechanism involved in protection against liver fibrosis. J Pathol. 2012 May;227(1):94–105. doi: 10.1002/path.3981. Epub 2012 Feb 17.
**Disclosure of Interest:** None declared
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## THU0190 A SIX-WEEK PROGRESSIVE RESISTANCE TRAINING CLASS IMPROVES FUNCTION AND FATIGUE IN RA PATIENTS

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**Background:** Rheumatoid arthritis (RA) is associated with adverse changes in body composition and physical function that persist despite pharmaceutical treatment. Randomised control trial evidence has shown that Progressive Resistance Training (PRT) is safe and efficacious in restoring lean mass and function in patients with RA. We set up our own PRT programme for RA patients to explore whether similar results could be achieved in an NHS setting.
**Methods:** RA patients were invited to attend a PRT programme of six, weekly class held under the supervision of a Senior Physiotherapist. Newly diagnosed and established RA were included. The exercises used within the circuit are: wall slides, chest press, leg extension, rowing, balance board work, triceps extensions, bicep curls, clam, bridging, standing calf raises and step ups. Classes included up to 10 patients at a time. Data collected at induction and after six weeks included demographics, BMI, percentage body fat, grip strength, 60 second Sit to Stand test, HAQ and FACIT (fatigue) scores. After the six-week PRT programme patients were encouraged to continue at home or referred to their local gym.
**Results:** Of 34 RA Patients invited, 27 started and 21 completed the 6 week PRT course. Mean age 54 (range 17–78) years; 71% F; 50% RF positive. 11 (32%) patients were diagnosed within 3 months of starting the class. There was no difference in results between recently diagnosed and established RA patients. After six weeks there was a significant improvement in: HAQ mean (range) 1 (0–2.9) vs 0.8 (0–2.5) p=0.03; Body Fat Composition mean (range) 38.0% (21.5%>51%) vs 36.9% (26.3%>48.2%) p=0.02; Sit to Stand mean (range) 20.0 (8–36) vs 23 (9–42) p=0.02. There was a trend towards improvement mean (range) in: handgrip strength 22.0 (2–54) vs 25.8 (5–54) p=0.21 and FACITF score 29.5 (18–49) vs 35.6 (19–49) p=0.05.

| | BMI | Sit to stand (60 secs) | Grip strength right (kg) | Grip strength left (kg) | FACITF | Body fat % | HAQ |
|---|---|---|---|---|---|---|---|
| Baseline mean | 30.9 | 20.0 | 22.5 | 22.0 | 29.5 | 38.0 | 1 |
| 6 week mean | 30.3 | 23.0 | 27.3 | 25.8 | 35.6 | 36.9 | 0.8 |
| p | 0.49 | 0.02 | 0.08 | 0.21 | 0.05 | 0.02 | 0.03 |

**Conclusions:** We present an effective model for PRT workable in the NHS, which encourages patient to take control of their own exercise regimes. The class setting fosters motivation, confidence and a belief in exercise as part of effective treatment. This brief intervention was associated with significant improvement in various aspects of physical function, Grip strength, HAQ and Fatigue scores.
**Disclosure of Interest:** None declared
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## THU0191 JAK-STAT PATHWAY STIMULATION, A NEW CAUSE OF INFLAMMATORY ARTHRITIS

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**Background:** Downregulation of the JAK-STAT signalling pathway with agents such as tofacitinib (a JAK inhibitor) is emerging as effective in the management of rheumatoid arthritis. It is conceivable therefore that upregulation of this pathway could result in inflammatory arthritis. The thrombopoietin receptor agonists eltrombopag and romiplostim, used to treat immune thrombocytopaenia (ITP), stimulate the JAK-STAT pathway. A frequent side effect of these drugs is arthralgia, in up to 26% of patients.
**Objectives:** To highlight thrombopoetin receptor agonists as a potential cause of inflammatory arthritis.
**Methods:** We present a 62-year-old male who developed florid inflammatory arthritis following initiation of eltrombopag for ITP.
**Results:** Mr H was first diagnosed with ITP in 1997, with splenectomy in 1998. Rituximab treatment in 2014 was ineffective for his persistent thrombocyopaenia. Eltrombopag was commenced and titrated to 50mg daily. Three months later he developed new left knee pain with an effusion. Following a dose increase to 50/75mg (alternate days), the arthritis progressed to involve the shoulders, wrists and hands bilaterally. He noted joint stiffness, worse in the mornings, particularly in the small joints of the hands with associated swelling and difficulty making a fist. On examination, he displayed bilateral swollen wrists, metacarpophalangeal and proximal interphalangeal joints with reduced range of movement. Blood tests showed CRP <5mg/L, ESR 16mm, uric acid 326μmol/L, with rheumatoid factor, anti-CCP antibodies and ANA all being negative. Plain radiographs identified moderate degenerative changes in the hands, however MRI of the left knee showed a significant joint effusion. Ultrasonography showed moderately severe synovitis of the right wrist and mild synovitis of the left wrist, with increased power Doppler signal. Three months after eltrombopag dose reduction to 50mg daily, the arthritis in the hands improved such that he could form a fist. Eltrombopag was reduced and weaned, leading to further improvement in his symptoms.
**Conclusions:** To our knowledge this is the first case of a patient developing inflammatory arthritis following treatment with JAK stimulation. Interestingly, our patient was seronegative for both rheumatoid factor and anti-CCP, but had synovitis on ultrasound. The temporal and dose-related correlation between eltrombopag initiation and inflammatory arthritis, in the absence of other causes, suggests an association. Mechanistically this is likely to be via the binding of eltrombopag to dendritic cell thrombopoietin receptors with subsequent JAK2-STAT5 activation. Conversely inhibition of JAK signalling by methotrexate or the JAK inhibitors tofacitinib and baracitinib is used in the treatment of inflammatory arthritis. While most rheumatologists are aware of the therapeutic benefits of JAK inhibitors, the effects of potential stimulators of the pathway are less well known. It is possible that increasing use of these drugs may result in a rise in inflammatory arthritis.
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## THU0192 EVALUATING PHARMACOKINETIC PREDICTORS OF TOFACITINIB CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS

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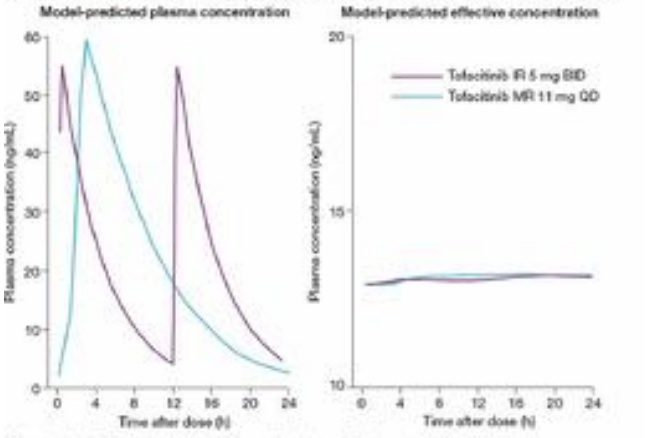
**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). A extended-release (XR) formulation to provide a once-daily (QD) dosing alternative to the available 5 mg twice daily (BID) immediate-release (IR) formulation has been developed.[1]

**Objectives:** To determine the most relevant pharmacokinetic (PK) parameter driving the clinical response of tofacitinib to inform clinical development of the MR formulation.

**Methods:** Clinical efficacy data (Disease Activity Score [DAS] and ACR 20/50/70 responses) from 5 Phase 2 RA dose-ranging studies of IR 1–30 mg BID and IR 20 mg QD across ~1500 patients were analysed. Dose- and exposure-response (E-R) models were developed to characterise the time course of changes in DAS, including quantifying the delay between concentration and response, and to compare the predictive abilities of various PK parameters (total drug exposure as measured by area under the concentration-time profile [AUC], and peak [$C_{max}$] and minimum [$C_{min}$] plasma concentrations). Non-clinical efficacy data from a dose-fractionation study of multiple IR QD and BID doses using the murine collagen-induced arthritis (mCIA) model were also analysed to delineate the predictive ability of PK parameters. The relationship between tofacitinib exposure metrics and incidence of safety outcomes was explored using linear logistic models.

**Results:** The E-R model yielded an equilibration half-life of 3.2 weeks for changes in DAS, substantially longer than the PK half-life of tofacitinib (~3 hours). Application of this model to plasma PK profiles of MR and IR yielded superimposable predicted effective concentrations for both regimens (Fig 1). In a dose-ranging Phase 2 study, analyses of the IR 20 mg QD dose (similar AUC to the IR 10 mg BID dose, but 86% lower $C_{min}$ and ~2-fold higher $C_{max}$) demonstrated similar efficacy to the IR 10 mg BID dose. DAS mean (standard error) change from baseline was -1.72 (0.14) for IR 20 mg QD vs -1.82 (0.15) for IR 10 mg BID; ACR 20/50/70 rates were 56/36/24% for IR 20 mg QD vs 58/28/12% for IR 10 mg BID at Week 12. Statistical comparison of PK parameters favoured AUC as a better predictor ($p<0.05$) of DAS changes than $C_{max}$ or $C_{min}$, with little added value of $C_{max}$ or $C_{min}$. In the mCIA model, BID and IR QD E-R curves were well aligned for AUC as the predictor, as demonstrated by concordance of concentrations producing 50% of maximum response. Comparing the predictive ability of AUC, $C_{max}$ and $C_{min}$ for safety events of interest (eg serious infections) also supported AUC as the most relevant PK parameter (data not shown).

**Figure 1. Predicted Steady-State Tofacitinib Concentration-Time Profiles in Plasma and in the Virtual Effect Compartment Following IR 5 mg BID Doses and MR Doses in RA Patients**




BID, twice daily; IR, immediate release; MR, modified release; RA, rheumatoid arthritis

**Conclusions:** These analyses support AUC as the relevant predictor of tofacitinib clinical response and inform clinical development of an MR formulation of tofacitinib for QD dosing.

**References:**

[1] Lamba M et al. Ann Rheum Dis 2015; 74 (Suppl 2): 626.

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## THU0193 RESPONSE TO BARICITINIB AT 4 WEEKS PREDICTS RESPONSE AT 12 AND 24 WEEKS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM TWO PHASE 3 STUDIES

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**Background:** Baricitinib (bari), a JAK1 and JAK2 inhibitor, showed significant improvements across multiple measures of disease activity as early as week (wk) 1 that were maintained through wk 52 in ph 3 studies of patients (pts) with active RA.[1,2]

**Objectives:** To determine if, in bari-treated pts, early changes in disease activity predicted later achievement of low disease activity (LDA) or remission.

**Methods:** 1305 pts with inadequate response to methotrexate (MTX) were randomized in RA-BEAM (3:3:2, oral PBO/4 mg bari QD/SC injection adalimumab [ADA] Q2W, 52 wks); 584 MTX-naïve pts were randomized in RA-BEGIN (4:3:4, oral MTX QW/4 mg bari QD/4 mg bari QD+MTX QW, 52 wks). Improvement from baseline (BL) to wk 4 was used to predict LDA or remission defined by Disease Activity Score (DAS28) and Simplified Disease Activity Index (SDAI) at wks 12/24 (bari 4 mg arm, both studies). Early responder and early nonresponder were predefined as Clinical Disease Activity Index (CDAI) improvement ≥6 and <6, respectively, at wk 4.

**Results:** Compared to PBO or ADA (RA-BEAM) or MTX (RA-BEGIN), treatment with bari was associated with rapid decrease in DAS28 and CDAI from wk 1.[1,2] By wk 4, 86% (RA-BEAM) and 85% (RA-BEGIN) of bari pts had a CDAI decrease ≥6. In both studies, LDA/remission rates at wks 12/24 were higher in pts with CDAI improvement ≥6 compared to pts with CDAI improvement <6 from BL to wk 4 (Table). Negative predictive values (NPV) for remission at wks 12/24 associated with CDAI improvement <6 from BL to wk 4 exceeded 90%, indicating that pts with CDAI improvement <6 were highly unlikely to achieve remission; NPV for LDA exceeded 80%.

Table 1. LDA and remission After 12 and 24 weeks of 4 mg baricitinib treatment in RA-BEAM and RA-BEGIN

| Decrease from BL to Wk 4 | LDA (DAS28-ESR ≤3.2) | | Remission (DAS28-ESR <2.6) | |
|---|---|---|---|---|
| | Wk 12 | Wk 24 | Wk 12 | Wk 24 |
| CDAI | RA-BEAM | | | |
| <6 | 2/63 (3.2) | 7/61 (11.5) | 0/63 (0) | 3/61 (4.9) |
| NPV | 96.8 | 88.5 | 100 | 95.1 |
| ≥6 | 111/399 (27.8) | 143/382 (37.4) | 50/399 (12.5) | 81/382 (21.2) |
| CDAI | RA-BEGIN | | | |
| <6 | 0/24 (0) | 4/24 (16.7) | 0/24 (0) | 2/24 (8.3) |
| NPV | 100 | 83.3 | 100 | 91.7 |
| ≥6 | 34/129 (26.4) | 53/124 (42.7) | 21/129 (16.3) | 32/124 (25.8) |

Data are n/N (%) of patients achieving clinical outcome of interest except NPV. NPV = negative predictive value (%).

**Conclusions:** In RA-BEAM/RA-BEGIN, lack of early clinical response to bari 4 mg (failure to achieve CDAI improvement ≥6 at 4 wks) was associated with low rates of LDA/remission at wks 12/24. These results are consistent with similar analyses from previous ph 3 studies of bari.[3] The majority of bari pts had improvement in CDAI ≥6 at wk 4; these decreases were associated with improved clinical responses at wks 12/24. Early identification of pts (4 wks) who are not likely to achieve LDA/remission may be useful in tailoring therapy to individual pts.

**References:**

[1] Taylor PC et al. Arthritis Rheumatol. 2015; 67 (suppl 10).
[2] Fleischmann R et al. Arthritis Rheumatol. 2015; 67 (suppl 10).
[3] Kremer J et al. Arthritis Rheumatol. 2015; 67 (suppl 10).

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## THU0194 A NOVEL REVERSIBILE BRUTON'S TYROSINE KINASE (BTK) INHIBITOR (BMS-986142) PROVIDES FAVORABLE SAFETY, PHARMACOKINETIC, AND PHARMACODYNAMIC PROFILES IN HEALTHY SUBJECTS

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**Background:** BTK is an attractive, novel therapeutic target for autoimmune disease, based on the established mechanistic data via B cell receptor (BCR)-dependent and Fc receptors (FcR)-dependent pathways (Whang et al. Drug Discov Today, 2014;19:1200–4). BMS-986142, a new small molecule reversible inhibitor of BTK, is being developed for the treatment of rheumatoid arthritis (RA) and auto-immune diseases. To support clinical development of BMS-986142, it is important to demonstrate sufficient pharmacodynamic (PD) activity, acceptable pharmacokinetic (PK) profile, and low drug-drug interaction potential with methotrexate (MTX) prior to testing in patients.
**Objectives:** Here we present the outcomes from two phase 1 studies investigating safety, tolerability, PK, PD, and its effect on MTX PK following oral administration of BMS-986142 in healthy subjects.
**Methods:** In Study 1, healthy volunteers (18–50 y) were randomized to receive single doses of BMS-986142 (5 to 900 mg or placebo) or multiple doses of BMS-986142 (25 to 350 mg or placebo once daily [QD] for 14 days) to assess the safety, tolerability, PK, and PD (as measured by CD69 inhibition). In Study 2, safety and tolerability was assessed in healthy males (18–50 y) receiving single doses of MTX alone (7.5 mg) and in combination with BMS-986142 (350 mg QD) while assessing the effect of BMS-986142 on the PK of MTX.
**Results:** BMS-986142 was well tolerated in both studies. In Study 1, a grade 3 SAE (psychosis, 75 mg BMS-986142) not related to study drug was reported in 1 subject; 1 grade 3 AE (blood creatinine phosphokinase elevation, placebo) was also reported. Three drug related grade 1 AEs (headache-SAD, 900mg; back pain-MAD, 200 mg; cough-MAD, placebo) were reported in Study 1. There were no grade 3 AEs reported in Study 2. AEs reported at least twice among all dosing groups are presented in the table. BMS-986142 was rapidly absorbed with peak concentrations occurring within 2 hours and gradually eliminated with a half-life of up to 11 hours, enabling QD dosing in the patient studies. BMS-986142 showed linear PK following either a single- or multiple-dose administration. A dose- and concentration-dependent decrease in CD69 expression was observed following the administration of BMS-986142. Daily administration at 350 mg led to near complete coverage above the IC50 for CD69 inhibition throughout the dosing interval without time-dependent changes. BMS-986142 did not affect the PK of MTX, as the peak concentrations and total exposure were comparable when administered with and without BMS-986142 (adjusted geometric mean ratios [90% CI]: $C_{max}$, 1.046 [0.910, 1.202]; $AUC_{(0\text{-}T)}$, 1.041 [0.950, 1.139]).

| | Study 1 | | | | Study 2 |
|---|---|---|---|---|---|
| | SAD | | MAD | | |
| | Placebo n=12 | BMS-986142 n=36 | Placebo n=8 | BMS-986142 n=24 | BMS-986142 n=12 |
| Subjects with AEs | 2 | 8 | 4 | 8 | 4 |
| Dizziness | 0 | 1 | 0 | 0 | 2 |
| Headache/tension headache | 1 | 5 | 1 | 1 | 2 |
| Nausea | 0 | 1 | 0 | 0 | 2 |
| Diarrhea | 0 | 1 | 0 | 1 | 0 |
| Cough | 0 | 1 | 1 | 1 | 0 |
| Upper respiratory infection | 0 | 2 | 0 | 1 | 0 |
| Thermal burns | 0 | 1 | 0 | 1 | 0 |

**Conclusions:** BMS-986142 was found to be safe and well tolerated at the doses tested in two phase 1 studies in healthy subjects. It showed favorable PK/PD profile including lack of interaction with MTX and can be safely administered in RA patients that are on background MTX. Overall, BMS-986142 has the potential to show clinical activity in treating autoimmune diseases.
**Disclosure of Interest:** S. K. Lee Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, J. Xing Employee of: Bristol-Myers Squibb Company, I. Catlett Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, R. Adamczyk Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, A. Griffies Employee of: Bristol-Myers Squibb Company, A. Liu Employee of: Bristol-Myers Squibb Company, B. Murthy Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, M. Nowak Employee of: Bristol-Myers Squibb Company

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## THU0195 PREFERENTIAL INHIBITION OF IL-6 RELATIVE TO IL-7 SIGNALING PATHWAYS BY ABT-494: EXPOSURE-RESPONSE ANALYSIS OF EX-VIVO DATA FROM TWO PHASE 1 CLINICAL TRIALS AND COMPARISON TO TOFACITINIB

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**Background:** ABT-494 is a Janus activated kinase (JAK) inhibitor that demonstrated robust efficacy in Phase 2 clinical trials in rheumatoid arthritis and is currently being evaluated in Phase 3. ABT-494 has a higher in vitro potency against JAK1 compared to JAK2 and JAK3 isoforms. Selectivity of ABT-494 towards JAK1 has the potential to provide an improved safety profile compared to less selective JAK inhibitors.
**Objectives:** The objective of this work was to characterize the effects of ABT-494 on IL-6 and IL-7 signaling pathways and to compare the in-vivo potency of ABT-494 versus tofacitinib in inhibiting these different pathways in humans.
**Methods:** Data from two Phase 1 clinical studies of ABT-494 immediate-release capsules were included in this analysis. In the first study, single doses of ABT-494 (1, 3, 6, 12, 24, 36, and 48 mg) or placebo were administered to healthy subjects. In the second study, multiple doses of ABT-494 (3, 6, 12, and 24 mg), placebo, or tofacitinib (5 mg) were administered to healthy subjects twice daily for 14 days and multiple doses of ABT-494 (6, 12, and 24 mg) or placebo were administered twice daily to subjects with mild to moderate rheumatoid arthritis. Blood samples were collected to measure plasma concentrations of ABT-494 or tofacitinib and the degree of inhibition of IL-6-induced STAT3 phosphorylation (pSTAT3) and IL-7-induced STAT5 phosphorylation (p-STAT5) as measures of in-vivo inhibition of JAK1 and JAK1/JAK3, respectively, in whole blood. Non-linear mixed-effects modeling was conducted to characterize the relationships between ABT-494 or tofacitinib pharmacokinetics and ex-vivo IL-6-induced pSTAT3 and IL-7-induced pSTAT5. The dataset included 68 subjects who received ABT-494, 23 subjects who received placebo, and 9 subjects who received tofacitinib.
**Results:** Dose dependent inhibition of IL-6-induced pSTAT3 and IL-7-induced pSTAT5 relative to baseline was observed, with maximum inhibition occurring at 1 hour after ABT-494 dose administration. The relationships between ABT-494 or tofacitinib plasma concentrations and IL-6-induced pSTAT3 and IL-7-induced pSTAT5 were adequately described using direct $E_{max}$ models. The relationship between ABT-494 plasma concentrations and the ex-vivo pharmacodynamic effects were consistent in healthy volunteers and rheumatoid arthritis patients. The model-estimated plasma $EC_{50}$ [95% bootstrap confidence interval] values for inhibition of IL-6-induced pSTAT3 and inhibition of IL-7-induced pSTAT5 were 61 [48 to 77] nM and 125 [106 to 143] nM, respectively, for ABT-494 versus 119 [87 to 160] nM and 79 [69 to 91] nM, respectively, for tofacitinib.
**Conclusions:** ABT-494 is more potent than tofacitinib in inhibiting IL-6-induced pSTAT3 (mediated predominantly through JAK1) and is less potent than tofacitinib in inhibiting IL-7-induced pSTAT5 (mediated through JAK1 and JAK3). These results are consistent with higher in vitro potency of ABT-494 against JAK1 compared to JAK3. Results from the ongoing Phase 3 trials will determine whether the improved selectivity profile of ABT-494 will translate into improved benefit to risk profile compared to less selective JAK inhibitors.
**Disclosure of Interest:** M.-E. Mohamed Shareholder of: AbbVie, Employee of: AbbVie, D. Koenig Shareholder of: AbbVie, Employee of: AbbVie, H. Camp Shareholder of: AbbVie, Employee of: AbbVie, S. Jungerwirth Shareholder of: AbbVie, Employee of: AbbVie, A. Othman Shareholder of: AbbVie, Employee of: AbbVie

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## THU0196 GENOME-WIDE TRANS-ANCESTRY META-ANALYSIS OF HERPES ZOSTER IN RHEUMATOID ARTHRITIS AND PSORIASIS PATIENTS TREATED WITH TOFACITINIB

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of RA. Rates of HZ were higher than seen with other agents used to treat RA in the tofacitinib RA development programme, especially in Japan and Korea.[1] Higher than expected HZ rates were also noted in tofacitinib PsO studies in Japan. Thus, it is important to identify the mechanisms of increased risk of HZ infection for patients (pts) receiving tofacitinib.
**Objectives:** To determine if the increased risk of HZ infection with tofacitinib is associated with genetic risk factors, and whether such factors can inform the mechanisms of increased rate of HZ with tofacitinib and the variation of HZ infection rate across ethnicities.
**Methods:** We performed a trans-ethnic and trans-indication meta-analysis of a genome-wide association study in 5246 tofacitinib-treated pts in RA and PsO Phase 2, 3 and long-term extension (LTE) studies (data cut-off April 2014; LTE ongoing, database not locked), by evaluating ~8 million genetic variants on HZ

event (case vs control) and time to HZ event via logistic and Cox regressions, respectively.
**Results:** After adjusting for age, baseline absolute lymphocyte count, genetically defined ethnicity and concomitant methotrexate use (RA only), we identified 5 loci associated with either increased HZ event rate and/or shorter time to HZ event at a genome-wide significance ($p<5x10^{-8}$). Two associations were noteworthy based on biological plausibility. A SNP near CD83 (and LINC01108) was associated with increased risk of HZ events (meta-analysis OR=3.7, $p=2.1x10^{-8}$). Frequency of the risk allele was low (<3%) in Caucasian pts and rare (<0.1%) in Japanese pts. CD83 is expressed on multiple immune subsets, is a marker of dendritic cell maturation and B-cell activation and is down-regulated in dendritic cells by VZV infection, suggesting a plausible mechanism for increased HZ risk in pts treated with tofacitinib. The second SNP was near *IL-17RB* and was associated with faster rate of HZ onset (meta-analysis HR=3.6, $p=7.6x10^{-10}$); this was driven by a risk allele common in Japanese pts (~17% in general Japanese population) but occurring in <0.2% of Caucasian pts. *IL-17RB* is highly expressed on iNKT2 and iNKT17 cells, whereas iNKT1 cells are *IL-17RB* negative and dependent on JAK-dependent IL-15. iNKT cell deficiency with low production of IFN-gamma by iNKT cells was linked to disseminated VZV in response to vaccination in 2 case reports, despite generally intact immune systems. Overexpression of IL-25, the ligand for IL-17RB, also led to recurrence of VZV, suggesting that the ratio of iNKT1 to iNKT2 and 17 cells is important.
**Conclusions:** Genetic analysis of ~5300 pts treated with tofacitinib identified multiple loci associated with an increased risk of HZ. The risk allele of one SNP was significantly more prevalent in Japanese pts. A possible iNKT cell skewing mechanism was suggested and will be evaluated in future studies.
**References:**
[1] Winthrop K et al. Arthritis Rheumatol 2014; 66: 2675–2684.
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**Disclosure of Interest:** N. Bing Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Zhou Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, B. Zhang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Nagaoka Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Valdez Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Vincent Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Clark Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
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## THU0197 CONVENTIONAL DMARD THERAPY AND IMPROVEMENT OF DISEASE ACTIVITY IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS

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**Background:** Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA). This strategy is being used last years in Colombia. On the other hand a multidisciplinary care team (MCT) model was generated in order to improve outcomes.
**Objectives:** The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 24-month period in patients with conventional DMARD therapy in a large cohort of patients from a Colombian specialized in RA center with a MCT model.
**Methods:** A descriptive retrospective study was performed. Records of patients using conventional DMARD treatment from specialized in RA center were reviewed; those patients were followed-up under T2T standards. Clinical follow-up was according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it. A MCT model means that a patient should be seen by other specialties such as physiatrist, physical and occupational therapy, nutritionist and psychologist at least 3 times a year. We divided patients in three groups: low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission (REM). Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson's statistics.
**Results:** 767 patients were included in this study, 615 (80%) women and 152 (20%) men. Average age was 63 ± 11 years. Concerning to treatment of entire cohort, 76 (6.8%) patients were using Leflunomide alone, 47 (6%) and Metothrexate alone, 164 (21%) Leflunomide plus Metothrexate, 43 (6%), Leflunomide plus other DMARDs, 84 (11%), Metothrexate plus others DMARDs 168 (22%) and 261 (34%) "only" DMARDs without Leflunomide or Metothrexate. At 24 months was observed an increase in percentage of patients in remission/LDA (up to 85%) and a decrease in percentage of patients in MDA/SDA disease activity statistically significant. At beginning DAS28 was 4.07 ± 1.03 and after 24 months of follow-up DAS28 was 2.7 ± 0.72, showed improvement (p<0.00).

| ACTIVITY LEVEL | TIME 0 n (%) | 6 MONTHS n (%) | 12 MONTHS n (%) | 24 MONTHS n (%) |
|---|---|---|---|---|
| REM | - | 230 (29) | 397 (51) | 416 (54) |
| LDA | 194 (25) | 255 (33) | 200 (26) | 243 (31) |
| MDA | 438 (57) | 263 (34) | 163 (21) | 106 (14) |
| SDA | 135 (17) | 19 (2.5) | 7 (0.91) | 2(0.26) |

**Conclusions:** There is a global improvement of DAS28 in a cohort of RA patients receiving only conventional therapy, treated and followed under T2T strategy recommendations and a MCT model. We show real-world data on conventional DMARD utilization in patients with RA in a low income developing country, these observations could be used by decision makers in order to consider health decisions.
**Disclosure of Interest:** None declared
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## THU0198 BARICITINIB EFFECTS ON LIPID AND NMR-MEASURED LIPOPROTEIN PROFILES IN A PHASE 3 STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Baricitinib (bari), a JAK1 and JAK2 inhibitor, was efficacious compared to placebo (PBO) and adalimumab (ADA) in a 52-week (Wk) Ph 3 study in patients (pts) with active rheumatoid arthritis (RA) and an inadequate response (IR) to methotrexate (MTX)[1].
**Objectives:** To evaluate changes in lipid and lipoprotein profile over 52 wks of treatment with bari or ADA compared with PBO in the aforesaid study.
**Methods:** MTX-IR pts with active RA were randomized 3:3:2 to bari 4mg once daily (QD), PBO, or ADA 40mg biweekly. Lipid profile was evaluated at baseline and at Wks 12, 24, and 52 and nuclear magnetic resonance (NMR)-measured lipoprotein particle size and number at baseline and Wk 12.
**Results:** Treatment with both bari and ADA resulted in significant mean increases from baseline to Wk 12 in total cholesterol (PBO -0.2%, bari 15%, ADA 7%), triglycerides (PBO 1%, bari 17%, ADA 12%), LDL-C (PBO -0.6%, bari 16%, ADA 9%), and HDL-C (PBO 0.8%, bari 17%, ADA 8%). These increases persisted through Wk 52. The NMR lipoprotein profile revealed similar changes for bari and ADA relative to PBO regarding an increase in large LDL, a decrease of all types of small LDL, and increases in IDL, VLDL and subfractions, and total HDL as well as large and small HDL particles (Table 1). Significant increases in total LDL particle numbers were not observed with either bari or ADA.

NMR analyses (mean change from baseline ± SD)

| | Wk 12 | | |
|---|---|---|---|
| | PBO (N=488) | Bari (N=487) | ADA (N=330) |
| Total LDL particles† | –22.4±236.1 | 15.0±282.3 | –33.9±257.4* |
| Large LDL particles | –2.8±158.0 | 81.9±191.7*** | 42.2±182.2*** |
| Small LDL particles | –21.3±285.8 | –81.0±327.3*** | –82.7±349.7*** |
| Medium small LDL particles | –2.9±60.2 | –16.6±67.6*** | –15.5±74.4*** |
| Very Small LDL particles | –18.5±228.7 | –64.4±263.0*** | –67.2±278.6*** |
| Total HDL particles§ | –0.03±4.2 | 4.8±5.3*** | 2.0±4.6*** |
| Large HDL particles | 0.0±2.2 | 1.0±2.7*** | 0.4±2.2** |
| Medium HDL particles | 0.1±2.8 | 0.7±3.5*** | –0.4±3.1 |
| Small HDL particles | –0.2±4.1 | 3.1±5.2*** | 2.0±4.3*** |
| IDL particles† | 1.7±38.6 | 14.0±48.5*** | 6.6±40.4* |
| Total VLDL particles† | –1.7±24.7 | 12.0±28.8*** | 6.1±23.8*** |
| Large VLDL particles | –0.1±2.9 | 1.0±3.3*** | 0.5±2.7** |
| Medium VLDL particles | –0.8±15.7 | 5.5±18.2*** | 3.2±13.7*** |
| Small VLDL particles | –0.8±15.0 | 5.6±17.1*** | 2.3±17.2* |

†Values for LDL and VLDL particles are nmol/L; §Values for HDL particles are μmol/L; Within-treatment p-values, *p≤0.05, **p≤0.01, ***p≤0.001.

**Conclusions:** The increase in LDL-C and HDL-C with both bari and ADA is accompanied by an increase in large LDL, total HDL particles and a decrease in small LDL. The nature of these changes may potentially indicate a more atheroprotective profile than that of the PBO group.
**References:**
[1] Taylor et al. Arthritis Rheumatol 2015;67(suppl10). Abstract 2L.
**Disclosure of Interest:** P. Taylor Grant/research support from: UCB, Glaxo-SmithKline, Celgene, Consultant for: UCB, Eli Lilly & Company, Pfizer, Galapagos, Merck, GSK, AbbVie, Takeda, BMS, E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, F. Hoffman-La Roche Inc, Janssen, Eli Lilly & Company, Novartis, Pfizer, Sanofi-Aventis, Consultant for: Abbott, AstraZeneca, Biotest, BMS, F. Hoffmann-La Roche, Genentech, Janssen, Eli Lilly & Company, Merck, Pfizer, UCB, Speakers bureau: Abbott, Amgen, AstraZeneca, BMS

Canada, F. Hoffmann-La Roche, Janssen, Pfizer, UCB, Y. Tanaka Grant/research support from: Mistubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-Kirin, Abbvie, Bristol-Myers, Speakers bureau: Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, Santen, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Celgene, Daiichi, Eli Lilly & Company, Galapagos, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Employee of: Director Imaging Rheumatology BV, J. Zhong Employee of: Quintiles Transnational, Inc, S. Thanabalasundrum Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, G. Ruotolo Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, D. Schlichting Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, T. Rooney Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, W. Macias Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, S. Zuckerman Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, S. de Bono Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, M. Weinblatt Grant/research support from: Crescendo Bioscience, Consultant for: Eli Lilly & Company, Crescendo Bioscience, Pfizer, AbbVie

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## THU0199 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS: CHANGES IN LYMPHOCYTES AND LYMPHOCYTE SUBSET COUNTS AND REVERSIBILITY AFTER UP TO 8 YEARS OF TOFACITINIB TREATMENT

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**Background:** Tofacitinib is an oral Janus kinase (JAK) inhibitor for the treatment of rheumatoid arthritis (RA). Cytokines involved in lymphocyte development, function and homeostasis are known to signal through JAKs.
**Objectives:** To characterise the effects of tofacitinib treatment on absolute lymphocyte counts (ALCs) and lymphocyte subset counts (LSCs) and their reversibility after treatment discontinuation.
**Methods:** ALCs were collected as part of safety monitoring procedures throughout the tofacitinib RA clinical programme. Short-term (ST) changes were evaluated in five Phase (P) 2 studies (tofacitinib 1–30 mg twice daily [BID]; treatment duration 6 weeks–6 months). Long-term (LT) changes were assessed in an LT substudy (LSS) of NCT00413699 (study ongoing; database not locked) in which patients (pts) had received tofacitinib 5 or 10 mg BID for up to 8 years. Reversibility of changes in ALCs was evaluated in pts who permanently discontinued tofacitinib due to lymphopenia as defined by a confirmed ALC $<500$ cells/mm$^3$. Reversibility of changes in LSCs was evaluated in a P2 study (NCT00147498) through a 6-week withdrawal phase after 6 weeks' tofacitinib treatment and in the LSS during a 4 week temporary withdrawal phase in pts with an ALC $\leq$1000 cells/mm$^3$ and $\geq$40% decrease in ALC vs baseline (NCT00413699).
**Results:** In total, there were 1432 and 4867 pts from P2 and LT extension (LTE) studies, respectively. Approximately 1050 pts from LTE study NCT00413699 were enrolled into the LSS for evaluation of ALCs and LSCs (median tofacitinib exposure of 5 years). Pre-treatment baseline for natural killer (NK) cells, B cells, T cells (CD3+, CD4+ and CD8+) were available for 130, 133, 133, 52 and 52 pts, respectively. Effects of tofacitinib on ALCs and LSCs are summarised in Table 1. Tofacitinib treatment resulted in a transient increase in ALC at Month 1, followed by a gradual decline to stabilise below baseline levels by ~4 years. Magnitude and time course of changes in CD4+ and CD8+ T cells mirrored those of ALC. CD4+ and CD8+ cell counts were well correlated with ALC. LT treatment showed higher NK cell counts vs baseline, in contrast to decreases seen after ST dosing. B cell counts increased with ST treatment but returned toward baseline with LT treatment.

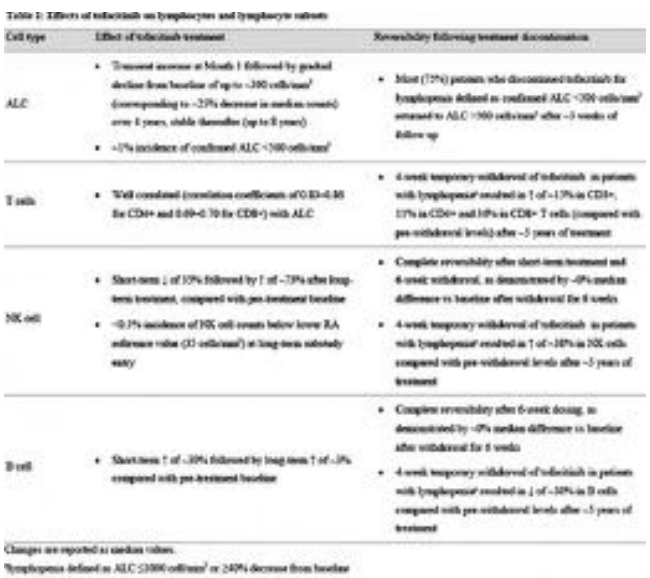


Table 1: Effects of tofacitinib on lymphocyte and lymphocyte subsets

| Cell type | Effect of tofacitinib treatment | Reversibility following treatment discontinuation |
|---|---|---|
| ALC | • Transient increase at Month 1 followed by gradual decline from baseline of up to ~300 cells/mm³ (corresponding to ~23% decrease in median count) over 4 years, stable thereafter (up to 8 years)<br>• ~1% incidence of confirmed ALC <500 cells/mm³ | • Most (75%) patients who discontinued tofacitinib for lymphopenia defined as confirmed ALC <500 cells/mm³ returned to ALC >500 cells/mm³ after ~3 weeks of follow up |
| T cells | • Well correlated (correlation coefficients of 0.83–0.86 for CD4+ and 0.69–0.70 for CD8+) with ALC | • 4-week temporary withdrawal of tofacitinib in patients with lymphopenia* resulted in ↑ of ~13% in CD3+, 15% in CD4+ and 10% in CD8+ T cells (compared with pre-withdrawal levels) after ~5 years of treatment |
| NK cell | • Short-term ↓ of 10% followed by ↑ of ~73% after long-term treatment, compared with pre-treatment baseline<br>• ~0.1% incidence of NK cell counts below lower RA reference value (33 cells/mm³) at long-term substudy entry | • Complete reversibility after short-term treatment and 4-week withdrawal, as demonstrated by ~0% median difference vs baseline after withdrawal for 8 weeks<br>• 4-week temporary withdrawal of tofacitinib in patients with lymphopenia* resulted in ↑ of ~38% in NK cells compared with pre-withdrawal levels after ~5 years of treatment |
| B cell | • Short-term ↑ of ~10% followed by long-term ↑ of ~5% compared with pre-treatment baseline | • Complete reversibility after 6-week dosing, as demonstrated by ~0% median difference vs baseline after withdrawal for 8 weeks<br>• 4-week temporary withdrawal of tofacitinib in patients with lymphopenia* resulted in ↓ of ~30% in B cells compared with pre-withdrawal levels after ~5 years of treatment |

Changes are reported as median values.
*Lymphopenia defined as ALC ≤1000 cells/mm³ or ≥40% decrease from baseline
ALC, absolute lymphocyte count; NK, natural killer; RA, rheumatoid arthritis

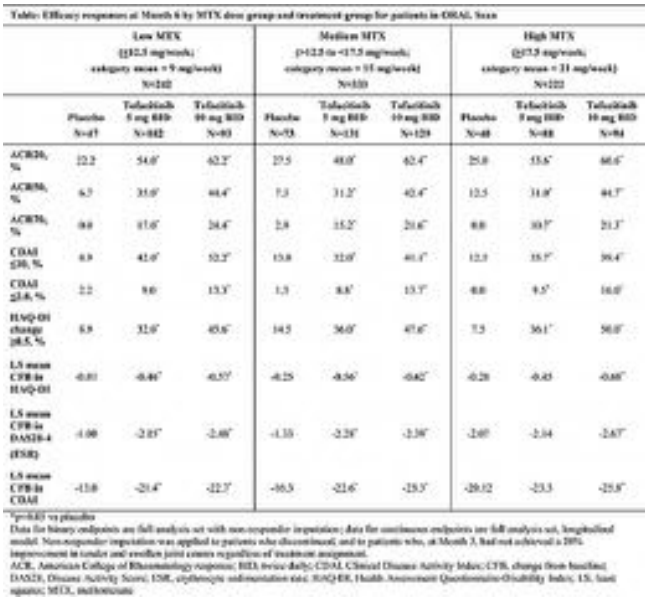
**Conclusions:** Tofacitinib treatment was associated with decreases in ALC. Changes in CD4+ and CD8+ T cell counts were reflected in ALC, while B cell and NK cell counts tended to return to or exceed baseline levels. Reversibility is observed following ST and LT dosing.
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**Disclosure of Interest:** R. van Vollenhoven Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, E. Choy Grant/research support from: Amgen, Boehringer Ingelheim, Chugai Pharma, Ferring Pharmaceuticals, Novimmune, Pfizer Inc, Roche, and UCB, Speakers bureau: Amgen, Boehringer Ingelheim, Chugai Pharma, Eli Lilly, Hospira, MSD, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis, and UCB, E. B. Lee Consultant for: Pfizer Inc, A. Hazra Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Anisfeld Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, I. Lazariciu Consultant for: Pfizer Inc, Employee of: Quintiles, P. Biswas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Lamba Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Hodge Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. D. Clark Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Krishnaswami Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

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## THU0200 EFFECT OF METHOTREXATE DOSE ON THE EFFICACY OF TOFACITINIB: TREATMENT OUTCOMES FROM A PHASE 3 CLINICAL TRIAL OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). ORAL Scan was a 2-year, randomised, Phase 3, clinical trial that evaluated tofacitinib therapy with background methotrexate (MTX) in patients (pts) with RA and an inadequate response (IR) to MTX.[1]
**Objectives:** To study the effect of MTX dose on tofacitinib efficacy in pts from the ORAL Scan study.
**Methods:** In ORAL Scan, MTX-IR pts with RA were randomised 4:4:1:1 to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, or placebo with advancement to 5 mg BID or to 10 mg BID at Month (Mo) 3 or Mo 6, in combination with background MTX. MTX dose was stable throughout the study and was categorised as Low ($\leq$12.5 mg/week), Medium ($>$12.5 to $<$17.5 mg/week), or High ($\geq$17.5 mg/week). Endpoints evaluated at Mo 6 included ACR response rates, proportion of pts achieving low disease activity measured by Clinical Disease Activity Index (CDAI $\leq$10), CDAI defined remission rate (CDAI $\leq$2.8), proportion of pts achieving an improvement $\geq$0.5 in Health Assessment Questionnaire-Disability Index (HAQ-DI), and least squares mean change from baseline in HAQ-DI, Disease Activity Score (DAS28-4[ESR]) and CDAI. Binary variables were evaluated with non-responder imputation, and continuous variables were analysed using a longitudinal model. Regression analyses were conducted to evaluate efficacy responses by MTX dose group and other covariates.
**Results:** 797 pts were randomised and treated (tofacitinib 5 mg BID, n=321; tofacitinib 10 mg BID, n=316; placebo, n=160). In total, 242 pts were included in the Low MTX (9 mg mean) dose group, 333 in the Medium MTX (15 mg mean) dose group, and 222 in the High MTX (21 mg mean) dose group. Baseline demographics and disease characteristics were generally similar across MTX dose groups, though weight, BMI, glucocorticoid (GC) use and CDAI were higher in the High MTX dose group. At Mo 6, greater efficacy was seen with tofacitinib compared with placebo for all endpoints across the 3 MTX dose groups (Table). Efficacy for placebo-treated pts was generally numerically greater in the Medium and High MTX dose groups than in the Low MTX dose group. Efficacy with tofacitinib appeared similar regardless of MTX dose group. Regression analyses demonstrated a lack of effect of BMI, GC use and MTX dose groups on efficacy assessments.
**Conclusions:** In this post-hoc analysis, clinical efficacy of tofacitinib at Mo 6 was greater than placebo, and appeared similar regardless of MTX dose, as in these pts, tofacitinib was added to patients that had an inadequate response to MTX. Higher MTX doses did not appear to result in additional efficacy to tofacitinib than



lower doses. A randomised clinical trial is needed in which different doses of MTX are added to tofacitinib in MTX-naïve pts in order to examine the effect of MTX dose on tofacitinib efficacy.

**References:**
[1] van der Heijde D et al. Arthritis Rheumatol 2013; 65: 559–570.

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## THU0201 WEAK CORRELATION BETWEEN A MULTI-BIOMARKER DISEASE ACTIVITY SCORE AND CLINICAL RESPONSE WITH BARICITINIB IN A PHASE 2B STUDY IN RHEUMATOID ARTHRITIS

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**Background:** Regular disease activity assessment should be a key component of rheumatoid arthritis (RA) care. In patients with moderate-to-severe RA and inadequate response to methotrexate (MTX-IR) treated with baricitinib (bari) 1, 2, 4, or 8 mg in a Phase 2b double-blind study, bari demonstrated clinically and statistically significant improvements at 12 wks including DAS28-CRP <2.6 for 1 (14%), 2 (15%), 4 (37%), and 8 (22%) mg versus placebo (4%; PBO).[1] (Elevated high-sensitivity C-reactive protein (hsCRP) >1.2xULN or erythrocyte sedimentation rate (ESR) >28 mm/h was required at study entry.[1]) In the same study, only modest, statistically significant improvements in a multi-biomarker disease activity score (MBDA)[2] were observed.[3]

**Objectives:** To investigate how MBDA correlates with clinical endpoints in the previously reported study.[3]

**Methods:** Post-hoc statistical analysis was conducted on combined bari 1, 2, 4, and 8 mg (n=189) and paired low (1, 2 mg; n=91) and high (4, 8 mg; n=98) doses using partial correlation analyses, which controls for effects of association with other variables, to assess the relationship between MBDA and absolute change from baseline in 13 disease activity measures.

**Results:** Mean MBDA improved from baseline to Wk 12 for each dose versus PBO,[3] but the two highest correlations were only of moderate strength: hsCRP [a component of MBDA] (r=0.60) and DAS28-CRP (r=0.43). For all other measures, associations with MBDA were significant ($p<0.05$) but of weak magnitude; swollen joint count (SJC) was not significant (Table). The low- and high-dose pairs had mostly weak correlations (not shown); the strongest correlation was with hsCRP (r=0.50, 0.68, respectively; both $p<0.001$).

| Disease activity measures | r† |
|---|---|
| hsCRP | 0.60** |
| DAS28-CRP | 0.43** |
| ESR | 0.32** |
| DAS28-ESR | 0.27** |
| SDAI | 0.27** |
| HAQ-DI | 0.24** |
| Patient's Global Assessment of Arthritis Pain | 0.23** |
| Physician's Global Assessment of Disease Activity | 0.23** |
| American College of Rheumatology Change from Baseline (ACR-N)‡ | –0.20* |
| Patient's Global Assessment of Disease Activity | 0.18* |
| TJC (68 joints) | 0.17* |
| CDAI | 0.16* |
| SJC (66 joints) | 0.04 |

†Pearson partial correlation coefficient (r) assessed relationship between MBDA score and absolute changes from baseline at Wk 12 in the combined dose group. **$p\leq0.001$, *$p<0.05$. P-value calculation based on Pearson correlation inference test. ‡ACR-N measures % improvement from baseline.

**Conclusions:** In MTX-IR patients treated with bari for 12 wks, significant changes in clinical response measures were seen but were not strongly correlated with MBDA. The highest correlations, although statistically significant, were of moderate strength. MBDA score changes did not have a strong correlation to clinical measures with bari. If these observations are corroborated they would suggest that caution is required when assessing clinical response to bari using the MBDA.

**References:**
[1] Keystone E et al. Ann Rheum Dis 2015;74(2):333–340.
[2] Segurado OG, Sasso EH. Clin Exp Rheumatol 2014;32(85):S29-S34.
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## THU0202 CLINICAL OUTCOMES OF RHEUMATOID ARTHRITIS PATIENTS RECEIVING TOFACITINIB MONOTHERAPY IN THE OPEN-LABEL LONG-TERM EXTENSION

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**Background:** Treatment options delivering sustained efficacy when given as monotherapy in RA are limited.[1] Tofacitinib is an oral JAK inhibitor for the treatment of RA. Tofacitinib monotherapy demonstrated efficacy in adult patients (pts) with RA in two Phase (P) 3 index studies (ORAL Solo[2] and ORAL Start[3]).

**Objectives:** To present data through Month 84 for safety and Month 60 for efficacy for pts who stayed on tofacitinib monotherapy in long-term extension (LTE) studies.

**Methods:** Data were pooled from two tofacitinib LTE studies (NCT00413699 [ongoing; database unlocked as of Mar 2015 data cut-off] and NCT00661661 [completed; Apr 2014]). Pts from P 1/2/3 tofacitinib index studies received tofacitinib 5 or 10 mg twice daily (BID) as monotherapy or with background conventional synthetic DMARDs in LTE. For tofacitinib and permitted concomitant RA medications, dose adjustments were allowed for inadequate efficacy or for safety reasons. In this analysis, pts were assigned to tofacitinib 5 or 10 mg BID groups based on average total daily dose in LTE (<15 mg/day or ≥15 mg/day, respectively). Monotherapy was defined as those pts who received tofacitinib

without other DMARDs throughout the LTE. Baseline values were those of the index studies for pts enrolling in LTE within 14 days of index study; for all others, baseline was start of LTE. Safety was evaluated through Month 84 and efficacy through Month 60 due to limited sample size.

**Results:** 1750 pts initiated LTE on tofacitinib monotherapy; 1552 (89%) stayed on monotherapy throughout LTE (495 on 5 mg BID; 1057 on 10 mg BID). For pts staying on monotherapy, mean (max) treatment duration was 1248 (2892) and 1011 (2377) days for 5 and 10 mg BID, respectively. Efficacy responses for tofacitinib monotherapy were stable through Month 60 (Table 1). In the 5 and 10 mg groups, 66% and 82% of pts, respectively, stayed on initial dose throughout LTE. The proportion of pts staying on steroids decreased from 56% to 40% and 41% to 35%, in the 5 and 10 mg groups respectively, from baseline to Month 60. Rates of discontinuation due to lack of efficacy and adverse events (AEs), and of serious infection and malignancy (excluding non-melanoma skin cancer) were low (Table 1).

Table 1: Efficacy responses over time and safety endpoints in patients receiving tofacitinib monotherapy

Efficacy responses

| | Tofacitinib 5 mg BID | | | | Tofacitinib 10 mg BID | | | |
|---|---|---|---|---|---|---|---|---|
| | ACR20 % (N) | ACR50 % (N) | Change from baseline in DAS28-4(ESR), mean (N) | Change from baseline in HAQ-DI, mean (N) | ACR20 % (N) | ACR50 % (N) | Change from baseline in DAS28-4(ESR), mean (N) | Change from baseline in HAQ-DI, mean (N) |
| Month 3 | 81.2 (474) | 58.2 (474) | -2.7 (444) | -0.63 (448) | 86.3 (1008) | 66.2 (1008) | -2.9 (991) | -0.76 (999) |
| Month 6 | 79.6 (460) | 58.5 (460) | -2.7 (446) | -0.64 (451) | 86.5 (982) | 67.0 (982) | -3.0 (967) | -0.76 (972) |
| Month 9 | 84.3 (440) | 61.8 (440) | -2.8 (433) | -0.67 (432) | 86.5 (949) | 68.4 (949) | -2.9 (935) | -0.78 (939) |
| Month 12 | 82.2 (428) | 62.2 (428) | -2.8 (423) | -0.67 (420) | 82.4 (908) | 62.0 (908) | -3.0 (891) | -0.77 (902) |
| Month 24 | 86.3 (380) | 68.2 (380) | -2.9 (374) | -0.69 (374) | 86.2 (799) | 62.0 (799) | -3.1 (787) | -0.79 (791) |
| Month 36 | 87.9 (322) | 66.2 (322) | -2.9 (317) | -0.63 (314) | 74.8 (630) | 54.3 (630) | -2.9 (627) | -0.66 (630) |
| Month 48 | 87.2 (187) | 69.5 (187) | -3.0 (180) | -0.67 (182) | 84.5 (304) | 66.2 (304) | -3.2 (302) | -0.69 (303) |
| Month 60 | 85.7 (119) | 67.2 (119) | -3.0 (117) | -0.64 (116) | 80.9 (110) | 54.0 (110) | -3.0 (108) | -0.7 (110) |

Safety endpoints in patients receiving tofacitinib monotherapy up to data cut-off

| | Tofacitinib 5 mg BID N=495 | Tofacitinib 10 mg BID N=1057 |
|---|---|---|
| Exposure, patient years | 1709 | 2957 |
| Discontinuations, n (%) | 223 (45.1) | 390 (36.9) |
| Due to lack of efficacy | 17 (3.4) | 22 (2.1) |
| Due to AEs | 112 (22.6) | 181 (17.1) |
| Discontinuations due to AEs, IR (95% CI) | 7.2 (6.3, 8.0) | 6.3 (5.4, 7.1) |
| Serious infection, IR (95% CI) | 2.5 (1.8, 3.4) | 2.4 (1.9, 3.0) |
| Malignancies (excluding NMSC), IR (95% CI) | 1.0 (0.4, 1.6) | 0.8 (0.5, 1.1) |

ACR, American College of Rheumatology response; AE, adverse event; BID, twice daily; CI, confidence interval; DAS28-4(ESR), disease activity score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, incidence rate (patients with event per 100 patient-years); N, number of evaluable patients; NMSC, non-melanoma skin cancer

**Conclusions:** In this analysis of pts receiving tofacitinib monotherapy in the LTE studies, nearly 90% of pts stayed on monotherapy, most did not have tofacitinib dose adjustments or add a DMARD and efficacy was sustained over 60 months, with low rates of discontinuation due to lack of efficacy or AEs. Safety was consistent with what has been reported previously.

**References:**

[1] Smolen JS et al. Ann Rheum Dis 2014; 73: 492–509.
[2] Fleischmann R et al. N Engl J Med 2012; 367: 495–507.
[3] Lee EB et al. N Engl J Med 2014; 370: 2377–2386.

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## THU0203 BARICITINIB TARGETS THE TYPE I IFN/STAT-MEDICATED ACTIVITIES OF HUMAN T CELLS AND DENDRITIC CELLS

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**Background:** The JAK/STAT pathway is a potent therapeutic target in autoimmune diseases. We previously reported that tofacitinib, a JAK1/3 inhibitor, suppressed pro-inflammatory cytokine production and co-stimulatory molecule expression on dendritic cells via suppression of IFN/STAT signal and directly inhibited lymphocyte proliferation. To date, baricitinib, a JAK1/2 inhibitor, has shown dramatic effect in the treatment of rheumatoid arthritis. However, the exact targets of the cells and cellular signaling by baricitinib remain unclear.

**Objectives:** To elucidate the mechanisms of action of baricitinib, we shed light on the JAK/STAT signal on human T cells and dendritic cells.

**Methods:** The effects of baricitinib and tofacitinib on the human $CD4^+$ T cells proliferation, phosphorylation of STAT, the maturation of human monocyte-derived dendritic cells, and the cytokine production of human plasmacytoid dendritic cells were investigated.

**Results:** Human T cells were proliferated after stimulation with anti-CD3 and anti-CD28 antibody. However, the T cell proliferation was significantly suppressed by the addition of baricitinib in a dose dependent manner. Both IFN-$\alpha$ and IL-6 induced phosphorylation of STAT1, STAT3 and STAT4 in human T cells. IL-12 induced phosphorylation of STAT4. IL-21 induced phosphorylation of STAT3 and STAT4. However, IL-23 did not induce the phosphorylation of STAT. Baricitinib, as well as tofacitinib, inhibited the phosphorylation of STAT1, STAT3 and STAT4 induced by IFN-$\alpha$, IL-6 and IL-21. Interestingly, the inhibition effect of baricitinib on phosphorylation of STAT4 which was induced by IFN-$\alpha$ was stronger than that of tofacitinib. On the other hand, CD80/CD86 and HLA-DR of human monocyte-derived dendritic cells (MoDCs) were significantly induced at 48 hour after lipopolysaccharide (LPS) stimulation. The CD80/CD86 expression in MoDCs was suppressed by the addition of baricitinib in a concentration-dependent manner, while the expression of HLA-DR was not affected. The induction of CD80/CD86 expression by LPS stimulation was also suppressed by tofacitinib. Moreover, the expression of CD80/CD86 which was induced by LPS was completely suppressed by the addition of an anti-type-I IFN receptor antibody. Baricitinib and tofacitinib suppressed the production of type-I IFN from plasmacytoid dendritic cells; however, it did not affect TNF-$\alpha$ production.

**Conclusions:** Tofacitinib and baricitinib inhibited not only lymphocyte proliferation but also T cell stimulatory capacity of human dendritic cells through suppression of type-I IFN and STATs signaling. Baricitinib characteristically inhibited the activation of IFN/STAT4 signal stronger than that of tofacitinib. Taken together, the different mode of action among JAK inhibitors may affect the clinical effects in patients not only with rheumatoid arthritis but other immune-mediated diseases.

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## THU0204 RETENTION RATE OF BIOLOGIC AGENTS AFTER REMISSION INDUCED WITH AND WITHOUT CONCOMITANT GLUCOCORTICOID TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROPENSITY SCORE MATCHED ANALYSIS

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**Background:** Concomitant glucocorticoids effectively increase remission rate in patients with early rheumatoid arthritis (RA) treated with synthetic DMARDs.[1] However, it remains unclear whether concomitant glucocorticoids have additive effects over biologic agents after achieving remission in the patients with RA. Given that drug retention reflects a good balance between effectiveness and tolerability, assessing the retention rate and reasons for discontinuation is important for drug evaluation.

**Objectives:** To compare retention rate of biologic agents for the patients who achieved clinical remission with and without concomitant glucocorticoid treatment [GC(+) and GC(–) groups, respectively], and investigate the predictors of drug discontinuation due to insufficiency in the GC(+) group.

**Methods:** A cohort study was performed using a multicentre registry. A total of 404 patients with RA achieved clinical remission defined as a DAS28-CRP $<2.6$ within the first year of treatment with the first biologic agents. Of all patients, 202 (50%) received concomitant glucocorticoids at achieving remission. Propensity score matching was performed given concerns of treatment-selection bias, and a total of 128 matched pairs of patients were identified. The first year follow-up time point after registration, which almost reflected the time of achieving remission, was considered the baseline in this study. The cumulative retention rate of the first biologic agents was estimated using Kaplan-Meier curves and compared with the log-rank test, and the impact of baseline characteristics on the drug discontinuation due to insufficiency in the GC(+) group was assessed with Cox proportional hazards models.

**Results:** There was good balance across all baseline characteristics after propensity score matching (Table 1). Six of the 128 patients (4.7%) in the GC(–) group discontinued the first biologic agents due to insufficiency during the follow-up period, while 31 of the 128 patients (24.2%) in the GC(+) group did so. According to Kaplan-Meier estimates, the discontinuation rate due to insufficiency for the GC(+) group was significantly higher than that for the GC(–) group (37% vs. 7%, respectively, at 5 years, $P<0.001$) (Fig. 1A). The number of patients who discontinued biologic agents due to adverse events (infection) during the follow-up period was 10 (6) and 11 (6) in the GC(–) and (+) group, respectively.

According to Kaplan-Meier estimates, there was no significant difference among the GC(–) and (+) group in the discontinuation rate due to adverse events (11% vs. 16%, respectively, at 5 years, *P*=0.676) (Fig. 1B). Multivariate analysis using Cox proportional hazards models revealed that Steinbrocker stage (III+IV vs. I+II) (HR: 3.37, 95% CI: 1.09–10.44, *P*=0.035) independently predicted drug discontinuation due to insufficiency in the GC(+) group.

**Table 1** Baseline characteristics of patients after propensity score matching

| Characteristics | GC (-) (n=128) | GC (+) (n=128) | P value |
|---|---|---|---|
| Age, median (IQR) years | 59 (49-66) | 59 (50-65) | 0.945 |
| Female, % | 84 | 83 | 1.000 |
| Disease duration, median (IQR) years | 7(3-16) | 7 (2-14) | 0.548 |
| RF positive, % | 82 | 81 | 0.867 |
| Steinbrocker stage III+IV, % | 63 | 63 | 1.000 |
| Steinbrocker class III+IV, % | 13 | 16 | 0.595 |
| DAS28-CRP, median (IQR) | 2.0 (1.4-2.3) | 2.0 (1.6-2.3) | 0.358 |
| TNF inhibitors, % | 87 | 88 | 0.850 |
| Concomitant MTX, % | 79 | 78 | 1.000 |
| MTX dosage, median (IQR) mg/week* | 8 (6-10) | 8 (6-8) | 0.964 |
| GC dosage, median (IQR) mg/day† | - | 4.0 (2.5-5.0) | - |

GC = glucocorticoid; IQR = interquartile range; RF = rheumatoid factor; DAS28-CRP = Disease Activity Score in 28 joints using the C-reactive protein; TNF = tumor necrosis factor; MTX = methotrexate. *Median among patients receiving the drug. †Prednisolone mg/day or equivalent. Median among patients receiving the drug.

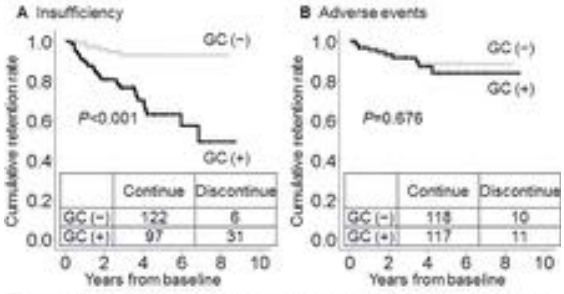



**Figure 1** Kaplan-Meier curves for time to discontinuation due to **A**, insufficiency, and **B**, adverse events stratified by use of glucocorticoids.

**Conclusions:** The patients who achieved remission with concomitant glucocorticoid treatment, especially with Joint destruction existing at achieving remission, had a high risk of subsequent discontinuation of biologic agents due to insufficiency.

**References:**

[1] Svensson B, et al. Arthritis Rheum 2005;52:3360–70.

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## THU0205 ASSOCIATION BETWEEN CONCURRENT METHOTREXATE AND TRIMETHOPRIM-SULFAMETHOXAZOLE USE AND THE RISK OF HOSPITALISATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE POPULATION STUDY

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**Background:** Concurrent use of methotrexate (MTX) and trimethoprim-sulfamethoxazole (TMP-SMX) has been linked to the development of cytopenia as a result of reduced renal clearance of MTX. However, the risk of adverse outcomes has not been estimated in a population setting.

**Objectives:** This study aimed to examine the risk for emergency department visits or hospitalisation after concurrent use of MEX and TMP-SMX in patients with rheumatoid arthritis (RA) in Taiwan using the National Health Insurance (NHI) data.

**Methods:** This was a retrospective cohort analysis of RA patients identified from the entire NHI database which contains essentially all residents in Taiwan. The case definition of RA was based on a rheumatologist diagnosis with a verification of expert panel commissioned by the Administration of National Health Insurance. Overall we identified 30,285 RA patients between 2000 and 2010. RA patients filled prescription for MTX in 453,114 person-quarters in which 9018 person-quarters they also filled a prescription for TMP-SMX. The main outcome measure was emergency department visit or hospital admission in person-quarters with concurrent fills of MTX and TMP-SMX compared with the rates in person-quarters with MTX prescription only. Multivariable logistic regression was used to adjust for age, sex, comorbidity, and socioeconomic status with a Generalised Estimating Equation (GEE) model to calculated the crude ORs (95% CIs) and adjusted ORs.

**Results:** Hospitalisations were more common in person-quarters with MTX and TMP-SMX use (688 events/8330 quarters) compared with quarters with MTX use alone (20,616 events/423,480 quarters) with a crude OR of 1.49 (95% confidence interval [CI], 1.36–1.62] and an adjusted OR of 1.45 (95% CI, 1.33–1.58). However, the risk for emergency department visits associated with MTX and TMP-SMX use (536 events/8,482 person-quarters) was not higher (21,115 events/422,981 person-quarters). The crude OR was 1.08 (95% CI, 0.97–1.19) for emergency department visits and the adjusted OR was 1.05 (95% CI 0.95–1.15]).

**Conclusions:** MTX use along with TMP-SMX is associated with an increased risk for hospitalisations which suggests a significant drug interaction between MTX and TMP-SMX in RA patients.

**Disclosure of Interest:** None declared

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## THU0206 POST-MARKETING SURVEILLANCE OF EFFICACY AND SAFETY OF TACROLIMUS ADD-ON THERAPY IN JAPANESE RHEUMATOID ARTHRITIS PATIENTS WITHOUT AN ADEQUATE RESPONSE TO BIOLOGICAL DMARDS

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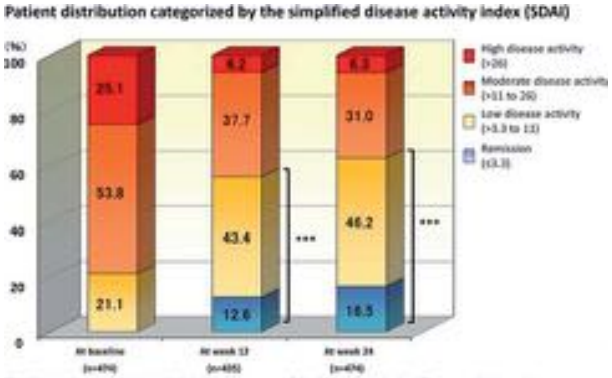
**Background:** Tacrolimus (TAC) is an immunosuppressive macrolide that blocks T-cell activation by specifically inhibiting calcineurin; it is widely administered after organ transplantation. TAC was approved in Japan for the treatment of rheumatoid arthritis (RA) in 2005. The emergence of biological disease–modifying anti-rheumatic drugs (DMARDs) has made remission an achievable goal for RA treatment. However, in some patients, biological DMARDs fail to achieve adequate suppression of disease activity or the efficacy of biological DMARDs is reduced. Therapeutic options for such patients include dose increases of biological DMARDs, switching to other biological DMARDs, and add-on use or dose increase of conventional anti-rheumatic drugs. The usage of add-on TAC has been reported in some studies [1,2].

**Objectives:** We report the results of post-marketing surveillance to evaluate the safety and efficacy of TAC add-on therapy with biological DMARDs in Japanese RA patients without an adequate response to biological DMARDs in a real clinical setting.

**Methods:** The observation period of this study was 24 weeks. Six hundred twenty-four patients were included in the safety population and 566 patients were included in the efficacy population. An inadequate response to biological DMARDs was defined as meeting all of the following conditions: Simplified Disease Activity Index (SDAI) >3.3 when TAC was started; both tender joint count and swollen joint count were the same or increased compared to those at 4 to 8 weeks prior to TAC; and biological DMARDs were used for at least 8 weeks prior to TAC. Efficacy was mainly evaluated using the SDAI and EULAR (European League Against Rheumatism) response criteria. SDAI improvement was defined as SDAI ≤11.

**Results:** Mean age was 61.9 years and mean disease duration was 10.5 years. The mean TAC dose was 1.3 mg during the observation period. Adverse drug

**Patient distribution categorized by the simplified disease activity index (SDAI)**




The SDAI analysis population included 474 patients out of the 566 patients in the efficacy population and excluded the patients who were missing baseline data and any week 12 and week 24 data (after tacrolimus administration).
Missing data at the final evaluation point of week 24 were input using the last observation carried forward.
***p<0.001 (McNemar test vs baseline).

reactions (ADRs) occurred in 94 patients and serious ADRs were observed in 11 patients. Infections occurred in 21 patients and serious infections were observed in 8 patients. SDAI remission rate was 16.5% at week 24, SDAI improvement rate was 62.7% at week 24, and the mean SDAI was decreased from 20.0 at baseline to 10.8 at week 24. Interestingly, 40 patients (33.6%) out of 119 patients with high disease activity at baseline achieved SDAI improvement at week 24. Based on EULAR response criteria, moderate to good response rate was 64.7% at week 24.

**Conclusions:** TAC is well tolerated and effective when used as an add-on to biological DMARDs in Japanese RA patients who do not achieve an adequate response to biological DMARDs in a real clinical setting.

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**Disclosure of Interest:** T. Takeuchi Grant/research support from: Astellas Pharma Inc., AbbVie GK, Asahikasei Pharma Corp., Bristol–Myers K.K., Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., Consultant for: AbbVie GK, Asahi Kasei Medical K.K., Astra Zeneca K.K., Bristol–Myers K.K., Daiichi Sankyo Co., Ltd., Eli Lilly Japan K.K., Mitsubishi Tanabe Pharma Co., Nipponkayaku Co., Ltd., Novartis Pharma K.K., Speakers bureau: AbbVie GK., Astellas Pharma Inc., Bristol–Myers K.K., Celtrion, Chugai Pharmaceutical Co., Ltd., Diaichi Sankyo Co., Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Nipponkayaku Co., Ltd., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., UCB., K. Ishida Employee of: Astellas Pharma Inc., K. Shiraki Employee of: Astellas Pharma Inc., T. Yoshiyasu Employee of: Astellas Pharma Inc.

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## THU0207 DIACEREIN IN COMBINATION WITH METHOTREXATE VERSUS METHOTREXATE ALONE IN THE TREATMENT OF EARLY RHEUMATOID ARTHRITIS

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**Background:** Diacerein is currently registered as a drug for the treatment of osteoarthritis. Evidence from in vitro studies and animal models of rheumatoid arthritis (RA) [1–3] suggest that it may also be a treatment option in early RA.

**Objectives:** To evaluate the efficacy and safety of diacerein in early RA patients with inadequate response to methotrexate (MTX).

**Methods:** Active early RA patients, according to the 1987 ACR revised criteria for RA, were invited to join this randomised, double-blind, placebo-controlled, multicentre phase II study. Inclusion criteria were insufficient response to MTX ($\geq$7.5 mg/week), $<$2 years disease duration, DAS28 $>$4.0, tender joint count $\geq$6/68 and swollen joint count $\geq$6/66. After a one-month run-in period on stable MTX therapy, eligible patients were randomised to receive either diacerein (DAR) 50 mg or matching placebo (PBO) twice daily in addition to MTX. Study assessments were scheduled at baseline (W0), then every 4 weeks through 24 weeks of treatment (W24). The primary endpoint was the ACR20 response criteria at W24. Secondary endpoints included EULAR response criteria for RA, MCII ($\geq$15 mm improvement in pain on VAS) and PASS ($<$41 mm of pain on VAS) response criteria.

**Results:** On 45 patients screened, 40 were randomised (ITT data set), and received at least one dose of study medication (safety data set). Five patients prematurely discontinued the study due to consent withdrawal (DAR: 2; PBO: 1) or unacceptable increase in disease activity (DAR: 2). Both groups were homogeneous at baseline for demographic and disease characteristics, except for a lower tender joint count in the DAR group (16.5±8.8 vs 24.6±13.2, p=0.0220). The efficacy analysis performed on the ITT data set showed that all parameters improved throughout the study in both groups. At W24, 13 patients in the DAR group and 9 patients in the PBO group responded to the ACR20 criteria (p=0.2036), while 15 patients in the DAR group reached a good or moderate EULAR response vs 5 patients in the PBO group (p=0.0016). The DAS28 improved from baseline by 1.26±1.37 and 0.85±1.17 in the DAR and PBO groups, respectively (p=0.1199). At W24, the MCII was met by 13 patients in the DAR group vs 9 patients in the PBO group (p=0.0388), while 16 and 10 patients reached the PASS, respectively (p=0.0014). Rescue medication consumption (paracetamol) was similar in both groups. The sensitivity analysis performed on the per protocol set (DAR: 19; PBO: 20) confirmed the results of the primary analysis. Thirty-one patients reported one or more adverse events (DAR: 16, PBO: 15). The most frequent adverse event (AE) was chromaturia (DAR: 8, PBO: 2), followed by diarrhoea (DAR: 4, PBO: 4) and upper respiratory tract infection (DAR: 2, PBO: 5). Gastrointestinal disorders accounted for 37.5% of all AEs (DAR: 8, PBO: 7). One serious AE was reported in each group (DAR: hip fracture; PBO: pharyngotonsillitis); both were not related to the study medication.

**Conclusions:** Diacerein 100 mg was shown to have efficacy in reducing RA signs and symptoms when combined with MTX. However, more powered clinical trials are needed to confirm these pilot findings.

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**Disclosure of Interest:** None declared

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## THU0208 EFFECT OF DOUBLE FILTRATION PLASMAPHERESIS ON MRI-BONE EROSION IN RA

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**Background:** The primary goal of treating the patient with rheumatoid arthritis (RA) is to maximise long-term health-related quality of life (1). The functional limitation caused by disease activity is reversible in RA patients, caused by joint structure damage is irreversible (2). The progressive structural damage contributes the life-long disability in RA patients (3).

**Objectives:** The current study was conducted to investigate whether the combination therapy of Double Filtration Plasmapheresis (DFPP), Leflunomide and Methotrexate improves bone erosion found through magnetic resonance imaging (MRI) in patients with long-standing rheumatoid arthritis (RA).

**Methods:** Seventy-two RA patients with high active disease of $>$3 years' duration were randomized to receive DFPP in combination with leflunomide and methotrexate (DFPP group), and leflunomide plus methotrexate (no-DFPP group). The primary end point was the improvement in MRI-detected bone erosion over 12 months. Secondary end points include subclinical remission by MRI and clinical remission in DAS44.

**Results:** The study achieved a significant improvement in MRI-detected bone erosion. Bone erosion score of the patients in DFPP group was 11.29±9.55 (mean±SD) at month 12, compared with 14.37±9.55 at baseline ($P<0.001$) and 16.88±8.33 at month12 of the patients in no-DFPP group ($P<0.001$). The patients with a decreased erosion score were reached 84.21% at month 12 in the DFPP group. This study showed significantly greater subclinical remission and clinical remission rates in the DFPP group than in the no-DFPP group ($P<0.001$). Patients with synovitis scores were 0 reached 65.79% of the patients in DFPP group, compared with 0 in no-DFPP group at month 12. The patients with 0 score in synovitis and bone edema reached 55.26% in the DFPP group at month 12. Clinical remission in DAS44 achieved 71.05% at month 12 of the patients in DFPP group, compared with 5.88% of the patients in no-DFPP group. A sustained DAS44 remission for at least 6 months reached 57.89% of the patients in DFPP group at month 12, compared with 0% of the patients in no-DFPP group.

**Conclusions:** The combination therapy of DFPP and DMARDs in long-standing RA patients achieved significant improvement in MRI bone erosion, repair of erosion. The DFPP combination therapy in RA patients had better responses in improving MRI bone erosion and reaching clinical remission and subclinical remission than DMARDs therapy.

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**Disclosure of Interest:** None declared

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## THU0209 CHARACTERIZATION OF CHANGES IN LYMPHOCYTE SUBSETS IN BARICITINIB-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS IN A PHASE 3 STUDY (RA-BEAM)

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**Background:** Baricitinib (bari; an oral JAK 1/JAK 2 inhibitor) is in development for patients (pts) with active RA. In healthy subjects, absolute lymphocyte counts (ALC) increased after bari administration, returning to baseline (BL) by 24 hrs.[1]

**Objectives:** To examine changes in ALC and lymphocyte (LYM) subsets in pts with active RA treated with bari (4 mg QD), placebo (PBO), or adalimumab (ADA, 40 mg Q2W).

**Abstract THU0209** – Table 1. ALC/LYM subsets at BL, Wks 4, 12, and 24 (Observed Mean Count)

| | PBO (N=488) | | | | Bari (N=487) | | | | ADA (N=330) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | BL | Wk 4 | Wk 12 | Wk 24 | BL | Wk 4 | Wk 12 | Wk 24 | BL | Wk 4 | Wk 12 Wk 24 |
| ALC, cells/μL | 1820 | 1750 | 1800 | 1800 | 1810 | 2160*** | 1860 | 1830 | 1810 | 2010*** | 2180*** 2140*** |
| T cells, cells/μL | 1300 | 1259 | 1309 | 1301 | 1294 | 1487*** | 1314 | 1286 | 1314 | 1426*** | 1533*** 1553*** |
| B cells, cells/μL | 215 | 208 | 215 | 212 | 209 | 316*** | 309*** | 296*** | 211 | 284*** | 303*** 306*** |
| NK cells, cells/μL | 214 | 215 | 215 | 211 | 223 | 290*** | 188*** | 191** | 211 | 220 | 230* 232* |

*p≤0.05, **p≤0.01, ***p≤0.001 vs PBO. Reference ranges: ALC = 800–4280; T cells = 603–2990; B cells = 107–698; NK cells = 95–640.

**Methods:** 1305 pts with active RA despite MTX treatment were randomized 3:3:2 to PBO, bari, or ADA. ALC, T, and B cell subsets (T: Th1, Th17, CD4, CD8, T reg, CD3+CD4+CD127-/loCD25+; B: switched/nonswitched memory, mature naive, immature transitional), and natural killer (NK) cells were quantified by flow cytometry at BL and wks 4, 12, and 24. Wk 4 phlebotomy was postdose bari or PBO; wks 12 and 24 were predose.

**Results:** ALC and T cells/subsets increased with bari and ADA at wk 4 (generally within normal ranges), returning to near BL at wks 12 and 24 in bari but remaining elevated in ADA (Table). B cells/subsets increased at wks 4 in bari and ADA and remained elevated through wk 24. NK cells were increased at wk 4 in bari and were below BL but within the normal range at wks 12 and 24; NK cells were increased at wks 12 and 24 in ADA. The percentages of pts with ≥1 low NK cell count were 20.5%, 32.6%, and 20.6% in PBO, bari, and ADA, respectively; percentage of pts with ALC CTCAE grade ≥2 were 14.1%, 9.9%, and 10.0%. Through wk 24, serious infection rates were 1.4%, 1.0%, and 0.6% for PBO, bari, and ADA; rates were 1.0%, 1.3%, and 0%, respectively, in pts with ≥1 low NK cell count and 2.9%, 4.2%, and 0% in pts with ≥1 ALC CTCAE Grade ≥2 value. Rates of herpes zoster (HZ) were 0.4%, 1.4%, and 1.2% for PBO, bari, and ADA; rates were 0%, 0.6%, and 0%, respectively, in pts with ≥1 low NK cell count and 1.4%, 2.1%, and 0% in pts with ≥1 ALC CTCAE Grade ≥2 value (no statistically significant differences between treatment groups).

**Conclusions:** Changes in ALC and subpopulations with bari in RA-BEAM were largely within normal ranges and are consistent with previous data.[2] Sustained increases in B cells were observed in bari and ADA. Sustained increases in ALC/T cells were only seen in ADA. A modest reduction in NK cells at wks 12 and 24 with bari was not associated with serious infection or HZ.

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**Disclosure of Interest:** Y. Tanaka Grant/research support from: Mistubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-Kirin, Abbvie, Bristol-Myers, Speakers bureau: Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, Santen, R. Fleischmann Grant/research support from: Pfizer, Inc, Eli Lilly and Company, Consultant for: Eli Lilly and Company, Pfizer, M. Schiff Grant/research support from: Eli Lilly and Company, Consultant for: Eli Lilly and Company, T. Takeuchi Grant/research support from: Chugai Pharmaceutical Co., Ltd, Eli Lilly and Company, Consultant for: Eli Lilly and Company, E. Keystone Grant/research support from: Abbott Laboratories, Amgen Inc., AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, Eli Lilly and Company, F. Hoffmann-La Roche Inc, Janssen Inc, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB., Consultant for: Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Eli Lilly and Company, F. Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Merck, Pfizer Pharmaceuticals, UCB, Speakers bureau: Abbott Laboratories, Astrazeneca LP, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Pfizer Pharmaceuticals, UCB, Amgen, M. Weinblatt Grant/research support from: Crescendo Bioscience, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, Crescendo Bioscience, S. Zuckerman Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, M. Issa Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Thanabalasundrum Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, B. Augendre-Ferrante Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. de Bono Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, D. Schlichting Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, T. Rooney Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, W. Macias Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Taylor Grant/research support from: Eli Lilly and Company, UCB, Consultant for: UCB, Eli Lilly and Company, Pfizer, Galapagos, Merck, GlaxoSmithKline, AbbVie, Takeda, Bristol-Myers Squibb

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## THU0210 MALIGNANCY DATA IN TOFACITINIB-TREATED JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS

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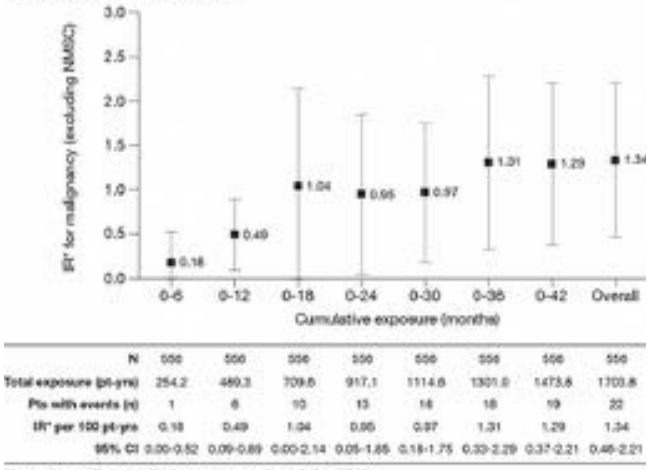
**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

**Objectives:** To evaluate age- and sex-standardised incidence rates (ASRs) for malignancy (excluding non-melanoma skin cancer [NMSC]) in Japanese RA (JRA) patients (pts) in the tofacitinib clinical programme.

**Methods:** Malignancy data were pooled from 2 Phase (P)2, 1 P3 and 1 open-label long-term extension RA studies conducted in Japan (April 2014 data-cut). Cumulative ASRs were calculated (6-month intervals). Crude incidence rates and standardised incidence ratios (SIRs) were calculated for tofacitinib clinical trials in Japan and Japan Medical Data Center (JMDC) RA sub-populations. General population data[1] were used to calculate ASRs and SIRs. Three sets of criteria for malignancy events (A, B and C) were defined for sensitivity analysis for the JMDC claims data. Compared with Malignancy criteria A, Malignancy criteria B and C included a more restricted definition of malignancy events in order to exclude possible false diagnoses of malignancy.

**Results:** Of 556 tofacitinib-treated JRA pts (1705 patient-years [pt-yrs] of exposure); 22 pts had malignancies. Overall, post-tofacitinib exposure in JRA pts, cumulative ASR (95% confidence interval [CI]) for malignancy (excluding NMSC) was 1.34 (0.46–2.21) pts with events/100 pt-yrs of exposure, and the SIR (95% CI) was 2.13 (1.33–3.22) which overlapped with the SIRs for several JMDC cohorts (Figure).

**Figure.** Cumulative incidence rate* for malignancy (excluding NMSC) for tofacitinib-treated RA patients in Japanese clinical trials




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| N | 556 | 556 | 556 | 556 | 556 | 556 | 556 | 556 |
| Total exposure (pt-yrs) | 254.2 | 469.3 | 709.6 | 917.1 | 1114.6 | 1301.0 | 1473.6 | 1705.8 |
| Pts with events (n) | 1 | 6 | 10 | 13 | 16 | 18 | 19 | 22 |
| IR* per 100 pt-yrs | 0.18 | 0.49 | 1.04 | 0.95 | 0.97 | 1.31 | 1.29 | 1.34 |
| 95% CI | 0.00-0.52 | 0.09-0.89 | 0.00-2.14 | 0.05-1.85 | 0.18-1.75 | 0.33-2.29 | 0.37-2.21 | 0.46-2.21 |

*Age and sex adjusted to the Japanese general population, 2010
CI, confidence interval; IR, incidence rate; NMSC, non-melanoma skin cancer; Pts, patients; pt-yrs, patient-years; RA, rheumatoid arthritis

**Conclusions:** SIRs for malignancies (excluding NMSC) in tofacitinib-treated JRA pts were comparable with JMDC RA sub-populations. Ongoing post-marketing surveillance will further evaluate malignancy among JRA pts treated with tofacitinib.

**References:**

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**Disclosure of Interest:** Y. Tanaka Consultant for: Mitsubishi-Tanabe Pharma Corporation, Abbott Japan, Eisai, Chugai Pharma, Janssen Pharma, Santen, Astellas Pharma, Daiichi-Sankyo, GlaxoSmithKline, Astra Zeneca, Actelion Pharma, Eli Lilly Japan, Nippon Kayaku, UCB Japan, Ono, and Novartis Pharma, Pfizer Inc, Speakers bureau: Mitsubishi-Tanabe Pharma Corporation, Abbott Japan, Eisai, Chugai Pharma, Janssen Pharma, Santen, Astellas Pharma, Daiichi-Sankyo, GlaxoSmithKline, Astra Zeneca, Actelion Pharma, Eli Lilly Japan, Nippon Kayaku, UCB Japan, Ono, and Novartis Pharma, Pfizer Inc, T. Takeuchi Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, H. Yamanaka Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, N. Sugiyama Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Yoshinaga Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Togo Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Geier Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Boy Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Connell Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

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THU0211 **THE COMBINATION OF CHINESE HERBAL PREPARATION ZHENG QING FENG TONG NING WITH METHOTREXATE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background:** Traditional Chinese Medicine (TCM) and TCM preparations for the treatment of rheumatoid arthritis (RA) present its unique advantages, which show the characteristics of overall adjustment, multi-level and multiple targets, and with fewer side effects. Base on its potent immunosuppressive and anti-inflammatory properties, Sinomenine (SIN) or its preparations are taken into consideration for the treatment of RA. A kind of SIN preparations Zheng Qing Feng Tong Ning (ZQFTN) tablet combined with methotrexate (MTX) which was used to treat active RA. And there are several clinical researches showed that ZQFTN plus MTX significantly improved symptoms and prevented disease progression compared to MTX monotherapy. Owning to minor species and inconsistent assessment methods, the results always are paradoxical.
**Objectives:** To assess the efficacy and safety of the combination of Chinese herbal preparation ZQFTN and MTX for the treatment of RA.
**Methods:** Randomized controlled trials (RCTs) data of traditional Chinese preparation ZQFTN combined with MTX versus MTX alone for the treatment of RA were collected by searching the Pubmed, Embase, SpringerLink, CNKI and Wanfang databases up to December 2015. Study selection, data extraction, data synthesis, and data analyses were performed according to the Cochrane standards.
**Results:** Ten RCTs involving 909 participants were included in this meta-analysis. Majority of the included RCTs had poor methodological quality. Compared with MTX, ZQFTN combined with MTX exhibited better therapeutic effects for the treatment of RA (OR=0.29; 95%CI: 0.17 to 0.50). In addition, ZQFTN combined with MTX caused more significant decrease in erythrocyte sedimentation rate (ESR) (MD=-7.40; 95%CI: -13.15 to -1.66), rheumatoid factor (RF) (MD=-14.02; 95%CI: -16.21 to -11.84), C reactive protein (CRP) (MD=-4.47; 95%CI: -7.17 to -1.78), and disease activity score in 28 joints (DAS28) (MD=-0.56; 95%CI: -0.74 to -0.37). Gastrointestinal discomfort and abnormal liver function were more frequently observed in RA patients treated with the combination of ZQFTN and MTX compared to MTX alone (OR=0.45; 95%CI: 0.22 to 1.01 for gastrointestinal discomfort; OR=0.24; 95%CI: 0.09 to 0.63 for abnormal liver function). No significant difference in low leucocyte account (OR=0.43; 95%CI: 0.17 to 1.11) was observed between the two groups. However, erythra with itching was more frequently reported in the MTX monotherapy group compared to the ZQFTN and MTX combination group (OR=4.43; 95%CI: 1.37 to 14.32). Additionally, publication bias was not identified based on the Begg's funnel plots and Egger's regression test.
**Conclusions:** Our study suggests that ZQFTN combined with MTX are more effective than MTX alone for the treatment of RA. However, the adverse effects of the combination of ZQFTN and MTX should be further assessed. Due to the poor methodological quality of included trials, well designed, multi-center, and large-scale RCTs are necessary to further confirm our conclusion.
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## Basic science in paediatric rheumatology

THU0212 **MODEL OF ARTHRITIS WITH THE TYPICAL SYSTEMIC MANIFESTATIONS IN WISTAR RATS**

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**Background:** Autoinflammatory component rather than autoimmune one is to be leading mechanism in the pathogenesis of the systemic juvenile idipathic arthritis (sJIA). Macrophage activation sydrome (MAS) ifatal complication of sJIA also is a result of a hyperactivation of monocytes/macrophages [1, 2]. Given those data, macrophage (M1 and M2) reprogramming becomes a very promising strategy to achieve remission of the disease. Existing animal models of arthritis (particularly collagen-induced arthritis) are not adequate for experimental implementation of this approach, because a key element of their pathogenesis is the formation of autoaggressive antibodies. For a long time, adjuvant arthritis in rats was meant to be the most close (but still not optimal) animal model to investigate the pathogenesis of rheumatoid arthritis and juvenile idiopathic arthritis [3].
**Objectives:** To create the model of arthritis with the typical systemic manifestations caused by the use of a macrophage M1 phenotype differentiation stimulus in Wistar rats.
**Methods:** Day 0: Rats (8 male Wistar rats, 8 month old) were injected intracutaneously (right footpads) with 0,1 ml of complete Freund's adjuvant (CFA, 5 mg/ml, DIFCO LABORATORIES, Michigan, USA) and injected intraperitoneally (i.p.) with 5 μg/kg body weight of lipopolysaccharide (LPS, 10 μg/ml, Medgamal, Russia). In control groups equivalent volumes of physiological 0.9% sodium chloride solution were used. Day 18: rats were reinjected i.p. with LPS (10 μg/kg body weight). Day 39: rats were reinjected intracutaneously (left footpads) with 0,1 ml of CFA and reinjected i.p. with LPS (10 μg per animal).
**Results:** The temperature over the hind paw joints was found to significantly increase ($p<0,05$) for at least 5 days in the group of LPS+CFA (main group) in comparison with the group of CFA only. This effect was confirmed to depend on the degree of inflammation in the joints as significant differences (p=0,019) were observed between left and right hind paws in the main group on the Day 42.
Metatarsal joint diameters were increased significantly ($p<0,05$) for at least 5 days (after Day 39) in the main group and remained increased (non-significantly) until the end of the study.
Pain assessment was performed by the method [4, 5], the severity of local changes in the region of inflamed joints [4]. More pronounced pain and arthritis symptoms after Day 39
**Conclusions:** Our novel animal model of arthritis (combined stimulation by M1 stimulus LPS and CFA) is cheap and easy to reproduce. The model allows to investigate systemic mechanisms of arthritis that pathogenetically are close to the systemic manifestations of arthritis in humans.
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## Paediatric rheumatology

THU0213 **ADALIMUMAB IN COMBINATION WITH METHOTREXATE FOR THE TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS: THE SYCAMORE TRIAL**

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**Background:** Uveitis associated with Juvenile Idiopathic Arthritis (JIA) is a major cause of morbidity with potentially sight-threatening complications. Despite current screening and (pre-biologic) therapeutic options, 10–15% of children develop bilateral visual impairment. Tumour necrosis factor alpha plays a pathogenic role in JIA-uveitis. No controlled trials have determined the impact of biologic therapy in JIA-associated uveitis.
**Objectives:** To compare the clinical effectiveness of adalimumab in combination with methotrexate (MTX) versus MTX alone, with regard to controlling disease activity in refractory uveitis associated with JIA.
**Methods:** Patients aged 2 to 18 years with active JIA-associated uveitis, despite stable methotrexate (MTX) treatment for at least 12 weeks, were randomly assigned to adalimumab or placebo in a ratio of 2:1. All patients were treated up to a maximum period of 18 months, with follow up of 2 years from randomisation. All patients received a stable dose of MTX and in addition either adalimumab (20 mg for patients weighing $<30$ kg or 40 mg for patients weighing $\geq 30$ kg, subcutaneous injection every 2 weeks) or placebo.
Primary endpoint was "time to treatment failure" defined by the "Standardisation of the Uveitis Nomenclature" criteria. Ten secondary efficacy endpoints were assessed including quality of life variables and arthritis disease activity measures. Adverse events from both arms were collected. Post-hoc analyses investigated "time to treatment response" and the proportion of responders, failures or those who had no change at three and six months. Statistical analysis of the primary outcome used the log rank test to compare treatment groups with a hazard ratio and 95% confidence interval also being reported.
**Results:** The trial was stopped early for reasons of efficacy after 90 patients had been randomised and the interim analysis met the pre-specified statistical stopping guidelines. The final analysis of the primary outcome showed a positive treatment effect in favour of adalimumab: hazard ratio (HR) 0.25 (95% CI 0.12–0.49); $p<0.0001$. Adverse events were experienced by 88.3% (53/60, 694 events) of patients in the adalimumab group and 90% (27/30, 144 events) of patients in the placebo group. Events were consistent with the known adalimumab profile. Post-hoc analyses showed significant differences showing favourable response to Adalimumab with respect to both the time to treatment response HR 3.15 (95% CI 1.42 to 7.00); $p<0.0027$ and the proportion of responders at both three and six months (p=0.0014 for each timepoint).
**Conclusions:** This trial, the largest of its kind to be conducted in JIA-associated

uveitis, provides evidence of efficacy of adalimumab treatment used in addition to methotrexate in this population. The safety profile of adalimumab was consistent with that previously reported for adalimumab.

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## THU0214 SAFETY OF ADALIMUMAB IN PEDIATRIC PATIENTS WITH POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS, ENTHESITIS-RELATED ARTHRITIS, PSORIASIS, AND CROHN'S DISEASE

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**Background:** Adalimumab (ADA) is a tumor necrosis factor (TNF) inhibitor used for treatment of chronic immune diseases. The safety of ADA treatment in pediatric patients (pts) is particularly important since prolonged treatment for these conditions is often required.
**Objectives:** To evaluate the safety of ADA, alone or in combination with concomitant therapy, in pediatric pts with polyarticular juvenile idiopathic arthritis (pJIA), enthesitis-related arthritis (ERA), psoriasis (Ps), and Crohn's disease (CD)
**Methods:** Safety data from 6 clinical trials and their open-label extension studies were analyzed. Pts treated for pJIA (NCT00048542, NCT00775437, and NCT00690573) and ERA (NCT01166282 [interim week-52 data]) received ADA 24 mg/m$^2$ body surface area every other week (eow) or 20 mg eow ($<$30 kg) to 40 mg eow ($\geq$30 kg). Pediatric pts treated for Ps (NCT01251614) received ADA 0.4 mg/kg (up to 20 mg) or 0.8 mg/kg (up to 40 mg) at week 0, then eow from week 1. Pediatric pts treated for CD (NCT00409682) received open-label ADA induction therapy (160 mg and 80 mg at weeks 0 and 2, respectively, if $\geq$40 kg; 80 mg and 40 mg if $<$40 kg), followed by double-blind maintenance dosing (high dose: 40 mg eow if $\geq$40 kg or 20 mg eow if $<$40 kg at week 4; low dose: 20 mg eow if $\geq$40 kg or 10 mg eow if $<$40 kg at week 4); weekly dosing was allowed for disease flare at week 12 or later; pts received high-dose eow or weekly ADA during an open-label extension (NCT00686374). Events (E) per 100 pt-years (PY) were calculated using adverse events (AEs) reported after the first ADA study dose through 70 days after the last study dose.
**Results:** The analysis included 577 pediatric pts, representing 1423.3 PY of ADA exposure (Table). Over 90% of pts across indications reported treatment-emergent AEs. Common AEs were headache (13.8, 46.9, and 23.8 E/100 PY for pJIA and ERA, Ps, and CD, respectively), nasopharyngitis (12.4, 57.6, and 14.1 E/100 PY, respectively), and upper respiratory tract infection (30.1, 24.7, and 14.9 E/100 PY, respectively). The rates of serious AEs (E/100 PY) were 13.4 for pts with pJIA and ERA, 7.4 for pts with Ps, and 32.3 for pts with CD. One death was reported from an accidental fall (pt with Ps). There were no reports of malignancies, demyelinating disorders, cardiovascular events, pulmonary embolism, reactivation of hepatitis B, Stevens-Johnson syndrome, or erythema multiforme.

Table. Treatment-Emergent Adverse Events Occurring in ≥1% of Patients in Pediatric Adalimumab Clinical Trials

| Treatment-Emergent Event | pJIA and ERA[a] N=216 Exposure, PYs=797.8 | | Pediatric Ps N=111 Exposure, PYs=313.5 | | Pediatric CD N=152 Exposure, PYs=184.4 | |
|---|---|---|---|---|---|---|
| | n (%) | E (events per 100 PY) | n (%) | E (events per 100 PY) | n (%) | E (events per 100 PY) |
| Any AE | 205 (94.9) | 420.8 (52.7) | 103 (92.8) | 328.8 (32.9) | 151 (99.3) | 2630 (82.0) |
| Serious AE | 57 (26.4) | 107 (13.4) | 8 (7.2) | 8 (7.4) | 32 (21.1) | 18.5 (10.0) |
| AE leading to discontinuation of ADA | 24 (11.1) | 33 (4.1) | 3 (2.7) | 3 (2.8) | 11 (7.2) | 7.6 (4.1) |
| Severe AE | 45 (20.8) | 66 (8.3) | 11 (9.9) | 24 (7.7) | 67 (44.1) | 17.6 (9.5) |
| Drug-related[b] AE | 200 (92.6) | 1530 (191.9) | 48 (43.2) | 176 (56.1) | 115 (75.7) | 809 (436.7) |
| Infection | 204 (94.4) | 1195 (149.9) | 82 (73.9) | 253 (80.7) | 144 (94.7) | 957 (516.2) |
| Serious infection | 30 (13.9) | 21 (2.6) | 5 (4.5) | 5 (1.6) | 25 (16.4) | 34 (18.3) |
| Opportunistic infection (excluding tuberculosis and oral candidiasis) | 0 | 0 | 0 | 0 | 6 (3.9) | 4 (2.1) |
| Oral candidiasis | 2 (0.9) | 2 (0.3) | 0 | 0 | 6 (3.9) | 4 (2.1) |
| Tuberculosis | 3 (1.4) | 3 (0.4) | 2 (1.8) | 2 (0.6) | 1 (0.7) | 1 (0.5) |
| Active | 1 (0.5) | 1 (0.1) | 0 | 0 | 0 | 0 |
| Latent | 2 (0.9) | 2 (0.3) | 2 (1.8) | 2 (0.6) | 1 (0.7) | 1 (0.5) |
| Parasitic infection | 2 (0.9) | 5 (0.6) | 0 | 0 | 1 (0.7) | 1 (0.5) |
| Allergic reaction[c,b] | 41 (19.0) | 62 (7.8) | 7 (6.3) | 9 (2.4) | 10 (6.6) | 24 (12.8) |
| Intestinal perforation | 0 | 0 | 0 | 0 | 1 (0.7) | 1 (0.5) |
| Intestinal stenosis | — | — | — | — | 5 (3.3) | 5 (2.7) |
| Worsening/new onset of psoriasis[d] | 5 (2.3) | 5 (0.6) | 10 (9.0) | 11 (3.1) | 6 (3.9) | 7 (3.8) |
| Hematology disorders[e] | 10 (4.6) | 16 (2.0) | 2 (1.8) | 3 (0.9) | 37 (24.3) | 36 (19.5) |
| Liver event[f] | 5 (2.3) | 5 (0.6) | 0 | 0 | 1 (0.7) | 1 (0.5) |
| Injection site reaction[g] | 101 (46.8) | 644 (80.8) | 11 (9.9) | 17 (4.9) | 47 (30.9) | 164 (88.9) |

—, analysis only in the CD population; ADA, adalimumab; AE, adverse event; CD, Crohn's disease; ERA, enthesitis-related arthritis; pJIA, polyarticular juvenile idiopathic arthritis; Ps, psoriasis; PYs, patient-years.
[a]The ERA study includes interim week-52 data.
[b]Investigator-assessed as possibly or probably related to study drug.
[c]Some were serious.
[d]Events included hypersensitivity (n=36), urticaria (n=27), asthma (n=16), eye pruritus (n=3), rash (n=3), bronchospasm (n=2), generalized pruritus (n=2), injection site urticaria (n=2), drug hypersensitivity (n=1), facial edema (n=1), generalized rash (n=1), and wheezing (n=1). One event of anaphylactic reaction was reported as an immune system disorder.
[e]Events included anemia (n=24), leukopenia (n=17), neutropenia (n=13), lymphopenia (n=11), macrocytic anemia (n=11), microcytic anemia (n=11), and pancytopenia (n=11). 13 events were serious (leukopenia, n=2 and neutropenia, n=2 [JIA]; anemia, n=9 [CD]).
[f]Events included liver disorder (n=2), hepatotoxicity (n=1), and hepatocellular injury (n=1) in the pJIA and ERA group, and 1 serious event of hepatitis in the CD group.

**Conclusions:** The safety profile of ADA in pediatric pts with pJIA, ERA, Ps, or CD was similar across indications, and no new safety signals specific to the pediatric population were identified.

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## THU0215 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA): 5-YEAR FOLLOW-UP OF AN OPEN-LABEL TRIAL

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**Background:** SJIA is a distinct and debilitating form of arthritis associated with elevated cytokine (interleukin [IL]-1 and IL-6) levels.[1] Studies have shown that biologics (IL-1 and IL-6 inhibitors), including canakinumab (CAN), a selective, human anti-IL-1β monoclonal antibody, are more effective than conventional medications (NSAIDs, corticosteroids, methotrexate) in the treatment of SJIA patients (pts).[1,2] However, little is known about long-term efficacy and safety of biologics in SJIA.
**Objectives:** To assess long-term efficacy and safety of CAN treatment in a 5-year (yr) follow-up of SJIA pts.
**Methods:** This was an open-label extension study of SJIA patients participating in the clinical trials of CAN, with details reported earlier.[3] Pts (age, 2–20 yrs) received subcutaneous (sc) CAN (4 mg/kg) every 4 wks. Baseline is defined as the starting point of the extension trial. Efficacy measurements were done every 3 months including adapted paediatric response criteria (aACR), clinical inactive disease, clinical remission on medication (12 months of continuous clinical inactive disease) and juvenile arthritis disease activity score (JADAS). Safety was assessed monthly.
**Results:** Overall, 147 pts had a median treatment duration of 3.2 yrs, and 82 (56%) were exposed to CAN for $>$3 yrs (total treatment exposure of $\sim$365 pt-yrs). At 3 month of CAN therapy, 50% of pts had inactive disease, increasing to 49% at last assessment. Of the 107 pts with an aACR 30 at entry to the extension, 61.7% had aACR 100, with 86.0%, 87.9% and 91.6% having aACR 70/50/30 responses, respectively at last assessment. Clinical remission on medication was achieved in 43.0% of pts. Median JADAS10-CRP at baseline was 8.2 (indicating moderate disease activity), and at last assessment, median change from baseline was –0.2, with a median score of 1.8, indicating low disease activity, with similar results noted for JADAS27-CRP. Most common adverse event (AE) was infection (2.0 infections/100 pyr) typically involving the upper respiratory tract. Overall, 47 (32.0%) pts had $>$1 serious AE (SAE; mostly infections, macrophage activation syndrome [MAS] or SJIA flare), 10 cases of MAS (43.8 events/100 pyr) were reported, and 18 (12.2%) pts discontinued due to an AE. No deaths were reported.
**Conclusions:** In patients previously treated with CAN in pivotal trials, response to treatment was sustained or improved during long-term treatment in the extension study. Safety profile of CAN was consistent with safety findings from previous studies.
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## THU0216 SAFETY AND EFFECTIVENESS OF ADALIMUMAB±METHOTREXATE FOR THE TREATMENT OF POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (PJIA): STRIVE REGISTRY

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**Background:** JIA is the most common chronic inflammatory rheumatic diseases of childhood. Due to their long-term safety and efficacy, biologic disease modifying antirheumatic drugs (DMARD) are commonly necessary for control of pJIA patients (pts).
**Objectives:** To evaluate 6-year (y) safety and 2 y effectiveness profile of Adalimumab with or without methotrexate (ADA±MTX) when used in current clinical practice for the treatment of moderately to severely active pJIA.
**Methods:** This is a 6 y interim analysis of an ongoing, multicenter, non-interventional, observational registry of pts with moderately to severely active pJIA with up to10 y safety follow-up. Included pts are treated with either ADA±MTX or MTX alone as part of their routine clinical care enrolled in the US, EU, and Australia. MedDRA observational adverse events (AEs) were recorded from the first day in the registry through last contact, irrespective of the duration of registry treatment. Effectiveness was assessed by 27-joint juvenile arthritis disease activity score (JADAS27), based on CRP.
**Results:** As of January 2014, enrollment was complete. As of June 1, 2015 cut-off date, 846 pts (543 in ADA±MTX and 303 in MTX groups) were treated in the registry. There were 39 pts who rolled over from the MTX to the ADA±MTX arm. At registry entry mean pJIA disease duration was 1.4 y and 3.7 y for MTX and ADA±MTX arms, respectively. At baseline (BL), mean AJC71 was 5.8 and 5.3 for MTX and ADA±MTX arms, respectively, and Childhood Health Assessment Questionnaire Disability Index (CHAQ-DI) was 0.6 for both arms. At data cutoff, the mean duration of study exposure was 1.81 y and 2.15 y for MTX and ADA±MTX arms, respectively. Overall, 206 pts (68%) in the MTX and 216 pts (39.8%) in the ADA±MTX arms discontinued registry drug through 6 y. The main reasons for registry drug discontinuation for the MTX arm: pts required additional therapy (32.3%), other (11.9%), lack of efficacy (10.9%), AEs (8.3%), or pts achieved JIA remission (7.6%), and for ADA±MTX arm: lack of efficacy (16%), lost to follow-up (7.2%), other (5.9%), and AEs (5.3%). Frequencies and rates of treatment-emergent AEs were similar to those reported for observational AEs (Table). There were no reports of deaths, malignancies, opportunistic infections, active TB, oral candidiasis, or CHF. Mean JADAS27 (CRP) improved from 12.2 at BL to 9.7, 5.2, 4.4, 3.5, 2.2 at months 1, 6, and 12, 18, 24 for pts in the MTX and from 11.8 at BL to 7.0, 4.-2, 4.2, 3.6, 3.9 in the ADA±MTX arms, respectively (observed data).
**Conclusions:** Overall, ADA±MTX was well-tolerated in these pts with pJIA with no new safety signals. Discontinuations from the registry drug were relatively high through 6 y, but greater in the MTX only arm.

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## THU0217 DKK-1 LEVELS ARE ELEVATED IN PATIENTS WITH ENTHESITIS RELATED ARTHRITIS WITHOUT SACROILIAC JOINT FUSION

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**Background:** Dkk-1 is an inhibitor of the Wnt signalling pathway and therefore plays an important role in bone remodelling. Studies in adults with ankylosing spondylitis have described lower levels of Dkk-1 compared to healthy controls although this is not consistent. Higher levels have been found in some cohorts and particularly in patients with no syndesmophyte formation, suggesting that Dkk-1 may be an important factor in bony ankylosis. There has been no description of Dkk-1 in a younger population with enthesitis related arthritis (ERA).
**Objectives:** To test serum Dkk-1 levels in adolescent and young adult patients with ERA and compare between different disease phenotypes and healthy controls.
**Methods:** Patients were recruited from the adolescent and young adult clinics at University College London Hospital. Serum samples were stored at -80℃ until use. Dkk-1 levels were measured by ELISA (Quantikine, R&D Systems, Minneapolis, MN) as per manufacturer's instructions, in duplicate and correlated with clinical features and MRI results.
**Results:** Serum from 78 patients with ERA (median age 17 years) and 20 age and gender matched healthy controls was tested. Dkk-1 levels were significantly higher in patients with ERA (median=2971pg/ml, IQR 2258–3511pg/ml) compared

to healthy controls (median=1806pg/ml, IQR 1307–2950pg/ml, p=0.0014) (Figure 1A). Patients with ERA who were HLA-B27 positive had higher Dkk-1 levels (median=3081pg/ml, IQR 2337–3680) than those who were HLA-B27 negative (median=2445pg/ml, IQR 1832–3365, p=0.0488) (Figure 1B). Interestingly, there was no significant difference in Dkk-1 levels between patients with axial and those with persistently peripheral ERA or between patients on TNF inhibitors versus those naïve to biologics. There was no correlation between Dkk-1 and CRP, ESR, patient age at date of sample or disease duration. Eleven patients with ERA of the 78 tested had already developed bony fusion of their sacroiliac joints (SIJs); in this group Dkk-1 levels were unexpectedly lower (median=2214pg/ml, IQR 2103–2618pg/ml) compared to those with ERA who had no evidence of bony fusion on MRI scan (median=3042pg/ml, IQR 2321–3607pg/ml, p=0.0355) (Figure 1C).

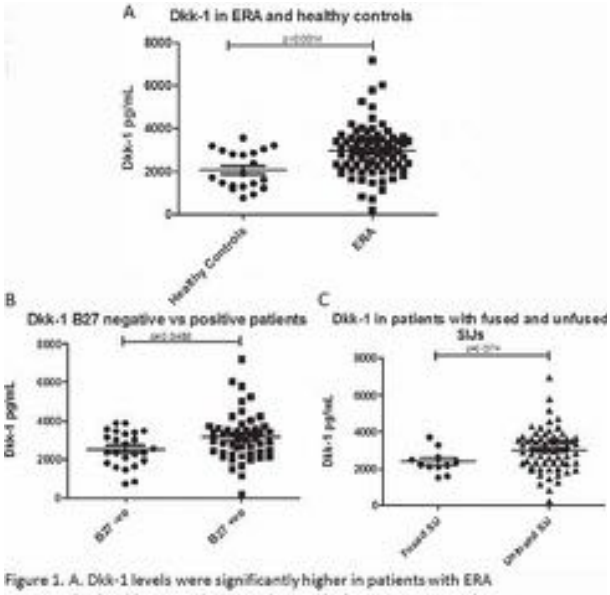



Figure 1. A. Dkk-1 levels were significantly higher in patients with ERA compared to healthy controls. B. Levels were higher in patients with ERA who were HLA-B27 positive compared to negative. C. Patients with SIJ bony fusion had significantly lower levels than those with no bony fusion.

**Conclusions:** In our study, patients with ERA had significantly higher serum levels of Dkk-1 compared to controls. Levels were even higher in those patients who were HLA-B27 positive but there was no correlation with axial disease, patient age, disease duration, CRP, ESR or TNF inhibition treatment. Patients with existing bony fusion of their SIJs had lower levels of Dkk-1, despite the numbers being relatively small. Dkk-1 levels appear elevated in ERA but may reduce with the occurrence of bony fusion. Further larger and longitudinal studies are needed to confirm these findings and to correlate changes in Dkk-1 levels with treatment and MRI findings over time.

**Disclosure of Interest:** None declared
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## THU0218 COW'S MILK ALLERGY IN INFANCY AND LATER DEVELOPMENT OF JUVENILE IDIOPATHIC ARTHRITIS: A REGISTER-BASED CASE-CONTROL STUDY

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**Background:** There is discursive information about the incidence of food allergies in juvenile idiopathic arthritis (JIA). In rheumatoid arthritis antibodies from proximal gut secretions against nutritional proteins including cow's milk have been detected (1). We have earlier found a low-grade mucosal inflammatory activation in JIA patients, which resembled the findings of delayed type food allergy (2–3). Also in some case reports, JIA has been linked to food allergy. In our earlier study, we found that exposure to antibiotics was associated with later diagnosis of JIA (4).
**Objectives:** Since there is discursive information about the relation between cow's milk allergy (CMA) and JIA, we wanted to study the association.
**Methods:** The material was collected from national registers (Special Reimbursement Register, Drug Purchase Register and Population Register Center) containing all children born between 2000 and 2010 in Finland and diagnosed with JIA (N=1,298) and age-, gender- and place of birth-matched controls (N=5,179). Altogether 235 children with CMA were identified and 66 of them had JIA. A conditional logistic regression analysis was performed to evaluate the association between CMA and JIA. Additive interaction between CMA and antibiotics for JIA was evaluated by relative excess risk due to interaction (RERI), the attributable proportion due to interaction and synergy index.
**Results:** In boys, a diagnosis of CMA and usage of hypoallergenic formula in infancy associated with later development of JIA (OR 2.4, 95% CI 1.6 to 3.6) whereas in girls with CMA such an association was not found (OR 1.1, 95% CI 0.7 to 1.7). Additionally, every 10-liter purchase of hypoallergenic formula increased the risk of JIA by 2% in boys (OR 1.02, 95% CI 1.01 to 1.03), but there was no increase in girls.
The association was most evident in those boys with diagnosis of JIA at less than three years of age (OR 3.8, 95% CI 1.9 to 7.6) and in those boys who had CMA with gastrointestinal symptoms (OR 4.4, 95% CI 1.9 to 9.9). In boys with both CMA and antibiotic exposure the risk of JIA was fourfold (OR 4.0, 95% CI 2.3 to 6.9) when compared to those without any such exposure. Nevertheless, no statistically significant additive interaction between CMA and antibiotic exposure was detected.
**Conclusions:** Current associations may reflect difficulty in the maturation of intestinal immunity in boys at risk of JIA. Environmental factors related to JIA pathogenesis seem to have sex disparity.
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## THU0219 PROSPECTIVE ANALYSIS OF THE IMMUNOGENIC RESPONSE IN JIA PATIENTS (PAEDIATRIC AND ADULT) ON ANTITNF TREATMENT

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**Background:** There is some evidence that clinical response in patients with chronic arthritis treated with antiTNF agents can be influenced by their immunogenicity. This particular has not been fully studied in patients with juvenile idiopathic arthritis (JIA)
**Objectives:** To evaluate the immunogenic response against antiTNF agents and its possible impact on treatment efficacy in patients with JIA
**Methods:** Seventy-three patients (40 children and 33 adults) fulfilling ILAR criteria of JIA were included. All of them were on treatment with Etanercept (ETN), Adalimumab (ADA) or Infliximab (IFX) +/– Methotrexate (MTX). Demographical and disease characteristics were recorded at baseline. Clinical outcome was prospectively assessed every 6 months (JADAS, patient or parents VAS, physician's VAS, CHAQ/HAQ, ESR, CRP, number of swollen, painful and limited joints). Patients were tested for the presence of both, serum drug levels and antidrug antibodies levels at baseline and every 6 months
**Results:** Thirty-one paediatric patients (77.5%) needed combined treatment (antiTNF + MTX) *vs* 18 patients (54.4%) in the adult group. Furthermore, paediatric patients followed an intensified antiTNF therapy protocol more frequently than adult patients (54% *vs* 39.33%; p=0.044). A total of 189 determinations for the assessment of immunogenic response against antiTNF therapy were analysed. No differences were found between children and adults in the prevalence of antidrug antibodies or in the circulating antiTNF levels. No antidrug antibodies were found neither in the 107 determinations of patients following ETN treatment nor in the 6 determinations of patients on IFX. Just 5 (17%) of the 29 patients on ADA treatment produced anti-ADA antibodies at least once during the follow-up period. Regarding the 77 ADA determinations, patients who were on monotherapy with ADA produced antidrug antibodies with a significant higher frequency than patients on combined treatment with MTX (37.5% *vs* 8.7% of them respectively; p=0.016). Patients on monotherapy with ADA also exhibit a significant reduced serum ADA levels than patients on ADA+MTX (4.73μg/mL *vs* 12.73μg/mL respectively; p=0.019). However, no significant differences were observed in the ETN concentration between patients on monotherapy or on ETN+MTX treatment (1.50μg/mL *vs* 1.77μg/mL respectively). No correlation was observed between drug levels or the presence of antidrug antibodies and any of the clinical or biological parameters
**Conclusions:** JIA paediatric patients needed intensified and combined with MTX antiTNF therapy more frequently than adults. In spite of this, no differences were found regarding antiTNF levels between children and adults. This fact suggest

that children need more therapy to maintain antiTNF concentrations to control the disease activity. No antibodies antiETN were detected in our patients. ADA in monotherapy seems to be more immunogenic than in combined therapy in JIA. We found no correlation between antiTNF levels or the presence of anti-antiTNF antibodies and the clinical outcome of JIA patients

**Disclosure of Interest:** None declared

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## THU0220 RETROSPECTIVE STUDY EVALUATING TREATMENT DECISION AND OUTCOME OF NON-JUVENILE IDIOPATHIC ARTHRITIS (JIA)-ASSOCIATED CHILDHOOD UVEITIS

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**Background:** Non-infectious uveitis is the most common cause of blindness in children. Most studies have evaluated diagnosis criteria and treatment of JIA-associated uveitis.

**Objectives:** We analyzed treatment and outcome of childhood uveitis related to other causes than JIA.

**Methods:** A retrospective chart review of pediatric uveitis in patients <16y-old seen between 2001 and 2015 at a university hospital in Paris. We excluded patients with JIA-associated uveitis. Clinical characteristics, treatment and ocular complications were collected. We used the SUN [1] (Standardization of Uveitis Nomenclature) for the classification of uveitis, disease activity (inactive uveitis: rare cells or less) and treatment endpoints, improvement: defined as a 2-step decrease in the inflammation level or a decrease to grade 0, worsening: defined as a 2-step increase in the inflammation level or an increase from grade 3+ to 4+, or remission (inactivity without treatment for ≥3 months).

**Results:** Thirty patients (SR: 0,5; 51 eyes) were enrolled. Mean age of diagnosis was 9.6±3.5 years (3 to 15 y). Mean follow-up was 4 ±3 years. Main diagnoses were: idiopathic (60%), Behçet's disease (BD) (13%), sarcoidosis (10%), Vogt-Koyanagi– Harada syndrome (3%), herpes simplex virus (3%) and tubulointerstitial nephritis and uveitis (TINU) syndrome (3%).

Among idiopathic uveitis (n=27 eyes), 44% were anterior uveitis. Twenty eyes (74%) received systemic corticosteroid as first-line therapy, inducing inactivity for 2 eyes (10%) and remission for 1 eye (5%) at 5 years. DMARDs were needed for 18 eyes (66.6%). Methotrexate was used as first-line therapy in 14 eyes (77%) with 7.1% (n=1 eye) remission at 4 months.

Infliximab was used as second-line treatment in 9 eyes (60%) with 78% of improvement and 78% of inactivity but no remissions. Ocular complications occurred in 67% of patients: posterior synechia (37%), macular edema (37%), severe vision loss (26%), cataract (22%), vasculitis (19%), and band keratopathy (16%). In BD uveitis (n=6 eyes), 83% had panuveitis. All BD patients received systemic corticosteroid therapy and azathioprine among those 50% responded with inactive uveitis. Infliximab was used as second-line therapy in 3 eyes with 100% of improvement. All BD patients developed complications: vasculitis (83%), posterior synechiae (83%), vitreous hemorrhage (50%), severe vision loss (33%) and macular edema (17%). Sarcoidosis affected 4 eyes, 75% were panuveitis and all patients received systemic corticosteroids and became steroid dependent. All of these patients received methotrexate, and 50% required infliximab as a second line with remission in 1 eye and inactivity in 3 eyes. Posterior synechiae developed in 3 eyes.

**Conclusions:** Idiopathic uveitis is the most common cause of non-JIA uveitis in children. BD and sarcoïdosis are thought to be the most severe ones, but idiopathic uveitis seems very difficult to treat as two third of patients have severe complications at the end of the treatment. Most patients were steroid dependent and required a DMARD in association with infliximab. Improvement and disease inactivity were frequently obtained but remission was rare.

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## THU0221 EFFICACY OF BIOLOGICAL AGENTS IN COLCHICINE RESISTANT CHILDREN WITH FMF

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**Background:** Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease diagnosed usually during childhood period. It is managed appropriately with colchicine. Hovewer, even though very rare, there are cases that can not be controlled by colchicine treatment. Ultimate goal of treatment is to control attacks and subside inflammation both during and in between attacks. There are some drugs offered for resistant cases. The anti IL-1 therapy is the most promising one.

**Objectives:** This study that is performed in two pediatric rheumatology centers in Turkey is aiming to collect and evaluate the data of children resistant to colcicine treatment and receving anti IL-1 treatment by means of eficacy and safety.

**Methods:** Two pediatric rheumatology centers had been involved to the study. The medical data were collected retrospectively. The children had been diagnosed as FMF according to the Tel-Hashomer criteria. Colchicine resistance was defined as having 3 or more attacks despite maximum dose of colchicine treatment regarding to age. The severity of the disease before and after biological treatment was performed by Pras and FMF 50 scores.

**Results:** From two pediatric rheumatology centers 26 children were enrolled to the study. The median age at onset of disease was 4 years [(IQR)2–5]. The consanguinity rate was 46.2%. Thirteen of the children had a family member with diagnosed FMF. Only 3 patients had a family history of amyloidosis. Abdominal pain (88.5%) was the most common symptom. The median number of attacks per year was 12 before colchicine treatment, the median attack number dropped to 11 per year after colchicine. The median dose of colchicine before biologic therapy was 1.5 g/day (range 1–1.5). The median duration of colchicine treatment before biologic therapy was 54 months (IQR 23.7–99 months). The median biologic treatment starting age was 11.5 years (range 8.7–16). As biological agent, nineteen patients were started with anakinra, 2 were with etanercept, 5 with canakinumab. The two patients who were under etanercept treatment were switched to anakinra due to lack of effectiveness. Of 19 patients who were commenced anakinra, 12 (63.1%) were switched to canakinumab due to painful injections, lack of effectiveness, allergy and patient's choice. There were no switches among canakinumab users. Pras scores had been changed from 10.17 to 6 in anakinra users, from 10 to 6 in canakinumab users. There was no difference of effectiveness between two drugs. The FMF 50 score showed improvement in 14 of 15 anakinra users, 15 of 15 canakinumab users. The difference of scores was not significant between both groups.

**Conclusions:** Although colchicine is the main treatment option in FMF, resistant children need additional medications. IL-1 is the major cytokine modulating inflammation in FMF. There are reports pointing out these agents as promising for resistant cases. Our study is the largest cohort of children with resistant FMF under biological treatment. Both anakinra and canakinumab had shown good and similar efficiacy in resistant cases. Long term efficacy and safety evaluations should be done with controlled trials.

**Disclosure of Interest:** None declared

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## THU0222 THE DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER FOLLOWING THE INITIAL PRESENTATION OF MONOARTHRITIS

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**Background:** Familial Mediterranean Fever (FMF) is the most common Mendelian autoinflammatory syndrome resulting from mutations in the MEFV gene [1]. Musculoskeletal involvement, mostly in the form of arthritis or arthralgia is the second common manifestation of FMF following periodic fever and abdominal pain [2,3]. The incidence and pattern of joint involvement is highly heterogeneous. Retrospective data suggest that arthritis may be the initial presentation of FMF in up to 15% of patients in certain populations [4,5].we aimed to examine whether certain "idiopathic monoarthritis" episodes are in fact the initial presentation of FMF.

**Objectives:** to prospectively investigate the prevalence of FMF in children admitted to our department with an acute episode of "idiopathic monoarthritis". In addition we aimed to identify risk factors that when associated with monoarthritis, will specifically indicate genetic testing of the MEFV gene.

**Methods:** A prospective study of 71 otherwise healthy children admitted to our pediatric department between 2010–2013 with a first episode of idiopathic monoarthritis. Demographic, clinical and laboratory data were documented and genetic assay of the five common mutations in our population of the MEFV gene were analyzed in the entire study population.

**Results:** Among the cohort 7 (10%) children harbored 2 pathogenic mutations in the MEFV gene, thus confirming diagnosis of FMF. This FMF induced arthritis group had a statistically significant female predominance compared with the idiopathic arthritis group 6 (86%) vs 19 (30%), respectively) (P=0.006, OR =14.2). In addition, associated abdominal pain during the attack 2 (28%) vs 2 (3%), respectively (P=0.04, OR=12.4) and a family history of FMF 2 (29%) vs 5 (8%), respectively (P=0.1 OR 4.7,) were more common in the FMF induced arthritis group

**Conclusions:** In Mediterranean populations where FMF is relatively common we recommend for every child with first episode of arthritis, without an identifying cause to strongly consider MEFV genetic testing of the common mutations in the relevant population.

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## THU0223 DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH JUVENILE SCLERODERMA-A SINGLE CENTER EXPERIENCE

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**Background:** Juvenile scleroderma (JS) is a rarely seen chronic connective tissue disorder. According to organ involvement, the disease is divided into two main forms: systemic and localized. Localized scleroderma (JLS) is characterized with sclerosis of the skin but internal organs involvement is not expected. Juvenile systemic sclerosis (JSS) is characterized by both cutaneous and internal organ involvement. Clinical features are insidious and it can take years until complete clinical picture develops.
**Objectives:** The aim of the study was to investigate main demographic and clinical characteristics of patients with JS, followed up at our department. Additionally, we aim to share our experience of this rare condition.
**Methods:** Patients with JS were included in cross-sectional study. Demographic data were taken from disease history of patients. Clinical features, laboratory results and treatment options were evaluated at last clinical visit.
**Results:** A totally of 46 patients were included in the study: 40 (86,9%) female, 6 (13%) male. The mean age of patients was 14±3 years, mean age at disease onset was 9,1±4,23 years and the mean age at diagnosis was 10,2±3,4 years. Twenty six patients (56,5%) were diagnosed with JSS and 20 (43,4%) had JLS. Skin involvement and peripheral vasculopathy were the most common clinical features. Musculoskeletal involvement takes a second place. Gastro-intestinal (GIS) involvement was present only in systemic sclerosis group. Six patients (13%) had lung fibrosis. Pulmonary hypertension was found in 6,5% of all JS patients but its percentage was higher among patients with JSS (11,5%). None of patients had neurological and renal involvement. All JSS patients were positive while 40% of JLS patients were negative for ANA. Anti Scl 70 antibody was positive only among patients with JSS. Combination of MTX+corticosteroids was used in 15 patients (32,6%). Vasoactive agent was added in therapy of 20 patients (43,5%) which all belong to JSS group. While 31 patients were in remission (67,4%), 15 (32,6%) had active disease in last visit. All patients with active disease belonged to systemic group.
**Conclusions:** Juvenile scleroderma is rarely seen multisystemic disease. Unlike adults, cardiovascular and pulmonary involvement is uncommon among children. Early diagnosis, regular follow up and appropriate treatment are of high importance in clinical course and disease prognosis.
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**Disclosure of Interest:** None declared
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## THU0224 PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH JUVENILE LUPUS ERYTHEMATOSUS

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**Background:** Juvenile systemic lupus erythematosus (jSLE) is a chronic autoimmune disease characterized with multisystemic involvement. Vital organ involvement is the most important morbidity and mortality factor. Early diagnosis of cardio-vascular and pulmonary involvement is shown to be relevant in term of reducing mortality.
**Objectives:** The aim of this study is to explore the frequency of pulmonary hypertension in patients with jSLE, using non-invasive methods (Doppler echocardiography).
**Methods:** Patients with diagnosis of jSLE followed up at our department were included in the study. Doppler echocardiography was performed at all included patients. Pulmonary arterial pressure was determineted by three different methods. Systolic pulmonary arterial pressure (SPAP) was estimated by measurement the maximal velocity of tricuspid insufficiency (TI). Diastolic pulmonary arterial pressure (DPAP) was estimated by velocity of pulmonary insufficiency at the end of diastole (PI). Mean pulmonary arterial pressure (MPAP) was determinated by pulmonary insufficiency acceleration time (AT) and the ration of AT to ejection time (ET). Systolic pulmonary arterial pressure was calculated by modified Bernoulli equation. Right atrial pressure was evaluated by measurement the right atrial volume, the degree of tricuspid regurgitation and contraction of vena cava inferior during inspiration
**Results:** A total of 38 jSLE patients were included in the study. Mean age of patient was 16±2,59 year, mean age at diagnosis was 10,6±3,5 year and mean disease duration was 57±33,6 month. Velocity of pulmonary insufficiency at the end of diastole (PI) was 1,469±0,295 m/sec and 1,214±0,128 m/sec in patients and control group, respectively. Maximal velocity of tricuspid insufficiency (TI) was 2,340±0,277 m/sec and 2,044±0,411 m/sec in patients and control group, respectively.The ration of pulmonary insufficiency acceleration time (AT) to ejection time (ET) was normal in both patients and in control group. Although estimated pulmonary arterial pressure was found to be in normal ranges (<25 mmHg) in all studies patients, it was statistical significantly higher comparing to control group. According to those results, there were no findings of pulmonary hypertension among patients with jSLE.
**Conclusions:** This study confirms that pulmonary hypertension is uncommon among patients with jSLE. Early diagnosis, regular follow up and proper therapy are thought to be important in reducing the risk of pulmonary hypertension.
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## THU0225 HYPOGONADOTROPIC HYPOGONADISM IN SYSTEMIC ARTHRITIS- AN INTERESTING CASE SERIES FROM A TERTIARY CARE CENTRE

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**Background:** The musculoskeletal, cardiac, pulmonary, hepatic, reticuloendothelial, hematological, neurological manifestations of systemic arthritis are very well known. Hormonal abnormalities of systemic arthritis have not been reported thus far
**Objectives:** To study hormone profile in systemic arthritis and identify abnormalities
**Methods:** We present a case series of abnormal hormone profile in 5 consecutive cases of Systemic arthritis admitted and evaluated at Institute Of Rheumatology, Madras Medical College during Februrary 2015. All patients had high systemic disease activity – elevated ESR, CRP, ferritin, fibrinogen, thrombocytosis.
Fasting serum hormone profile was done by chemiluminescence method – Adrenocorticotropin releasing hormone (ACTH), Thyroid stimulating hormone (TSH), Follicle stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin,

| Parameters | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
|---|---|---|---|---|---|
| AGE (years)/sex | 6/Male | 11/Male | 10/Male | 9/Male | 6/Male |
| Disease duration | 1 year | 4 years | 3 years | 1 year | 2 years |
| ESR mm/hr | 70 | 50 | 60 | 94 | 64 |
| CRP in dilutions | 48 | 24 | 48 | 48 | 24 |
| Platelet count, lakhs/cumm | 8 lakhs | 4 lakhs | 6 lakhs | 5.2 lakhs | 6 lakhs |
| Serum ferritn | 2150 | 540 | 2105 | 3578 | 2210 |
| Fibrinogen | 512 | 480 | 541 | 502 | 510 |
| Prednisolone | 10 mg | 10 mg | 15 mg | 7.5mg | 5mg |
| DMARDS | Methotrexate | Methotrexate | Methotrexate | Methotrexate | Methotrexate |
| Biologics | Tocilizumab | Tocilizumab | Tocilizumab | Nil | Tocilizumab |
| ACTH, pg/ml | 7.8 | 2.4 | 13.9 | 4.8 | 6.2 |
| TSH, μIU/ml | 2.1 | 0.7 | 4.9 | 2.4 | 2 |
| FSH, mIU/ml | 0.02* | 0.06* | 0.6* | 0.2* | 0.3* |
| LH, mIU/ml | 0.01* | 0.01* | 0.01* | 0.01* | 0.01* |
| Prolactin, ng/ml | 4 | 4 | 13 | 6 | 8 |
| Testosterone, ng/dl | <2.5* | <2.5* | <2.5* | <2.5* | <2.5* |
| IGF-1, ng/ml | 137 | 103* | 164 | 241 | 156 |
| GH, ng/ml | 2.6* | 0.1* | 0.5* | 0.1* | 0.5* |

Testosterone, Insulin like growth factor-1 (IGF-1), Growth hormone (GH) were estimated.

**Results:** All 5 patients had low serum FSH,LH,GH,Testosterone levels. All 5 patients had normal ACTH,TSH,prolactin levels. * indicates LOW VALUES

**Conclusions:**

– Hypogonadotrophic secondary hypogonadism was observed in 5 consecutive patients with systemic arthritis with high disease activity.
– We are presenting this case series as no studies have so far been reported on hormone profile of patients with systemic arthtritis to the best of our knowledge.
– Further studies with more number of cases are needed to find out whether the endocrine dysfunction is disease related or drug induced.

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**Disclosure of Interest:** None declared

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## THU0226 OUTCOMES OF TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS RELATED UVEITIS WITH TNF-ALPHA INHIBITORS

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**Background:** Uveitis is the inflammation of the uvea by definition, but for a rather long time the term "uveitis" was used to identify inflammation in any part of the eye (retinitis, chorioretinitis, scleritis, episcleritis). According to some authors one of the most common causes of uveitis in childhood is Juvenile Idiopathic Arthritis (JIA). Patients with JIA associated uveitis are usually asymptomatic at early stages. In 20–30% of cases uveitis may occur a few years before joint manifestation. As the result of those two factors we often see the delay in the treatment or not adequate treatment. Early and aggressive treatment of JIA associated uveitis can help better control inflammation and can help to eliminate inflammation before development of irreversible ophthalmic pathology.

**Objectives:** The goal of the study was to evaluate the efficacy of two anti-TNF-alpha biological agents: Adalimumab (ADA, humanized monoclonal anti-TNF-alpha antibody) and Infliximab (INF, chimeric monoclonal antibody that binds both circulating and membrane-bound TNF-alpha receptors) in the treatment of uveitis, associated with Juvenile idiopathic Arthritis (JIA). The incidence of eye involvement in JIA can be as high as 10–20%.

**Methods:** Thirty-seven children with aggressive forms of JIA with uveitis who failed immunosuppressive agents were enrolled in the study. The age of the patients at the beginning of anti-TNF-alpha treatment ranged from 5 to 17 years. All patients were divided into two groups: one group received ADA (40 mg sc every 2 weeks), and the other group was received INF (iv 5–6 mg/kg at week 0–2-6 and after every 8 weeks). Duration of treatment was 3–48 months. The efficacy of treatment was assessed by reduction of flare-ups, reduction of topical and systemic steroids, immunosuppressive drugs and reduction of activity of uveitis.

**Results:** In ADA group the remission was observed in 61% of cases, reduction of number of flare-ups was in 18% and in 14% we saw worsening of the disease due to discontinuation of non-biological drug. In INF group remission was in 78% and in 22% of the cases no improvement. The remission of uveitis was achieved in 0.5 - 4 months from the starting of ADA. Topical steroids was tapered within 1.5–3 months and none of the patient required regional injections of steroids. Therapy with ADA permitted to cease non-biological immunosuppressive agents, especially in children who received simultaneously 2 non-biological agents.

**Conclusions:** Our experience in ADA treatment of uveitis shows good result in control of uveitis independent from the severity of the disease and despite it was used as a first-, second- or third-line agent among the biologics. The speed of remission in patients with JIA associated uveitis treated with ADA and INF depends on the severity of uveitis, the time between the beginning of the disease and administration of immunosuppressive therapy. This study needs to be continued to enroll more patients and to increase the follow-up time to evaluate the long-term efficacy and safety of anti-TNF-alpha agents in JIA associated uveitis.

**Disclosure of Interest:** None declared

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## THU0227 ADOLESCENT AND YOUNG ADULT CARE IN ADULT RHEUMATOLOGY CLINICS

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**Background:** The importance of transitional care for young people from paediatric to adult rheumatology is well established. However, in most rheumatology departments there will be a significantly larger cohort of older adolescents and young adults (AYAs) that enter adult services de-novo than will have transitioned from paediatric services.

**Objectives:** Our aim was to evaluate AYA care within adult Rheumatology clinics, in particular focusing on use of the HEEADDSS psychosocial interview.

**Methods:** A review of clinical correspondence for patients aged 16–25yrs attending adult rheumatology clinics at University Hospital of South Manchester, between February 2015 and May 2015 was undertaken. Data collected included demographics, diagnosis and evaluation of documentation of the components of the HEEADDSS screen.

**Results:** 193 appointments were issued for 16–25yr olds, representing 5% of the total number of appointments. 103 were new referrals, with a majority from general practice. Age distribution was even, over two thirds were female. The "did not attend" rate was 10%.

36 had a confirmed inflammatory condition, 27 were under investigation for a possible inflammatory arthritis and 47 had a non inflammatory condition. Of the HEEADDSS criteria the most often documented was education/employment at 31%, with exercise at 19%.

**Conclusions:** The AYA group is well represented within this secondary care setting. Documentation of the HEEADDSS criteria was suboptimal. There may be wider implications of this on health outcomes.

The first step towards improving care for this cohort is to establish an awareness within the adult team of the particular needs of this patient group, AYA health is not just a concern for paediatric rheumatologists.

**Disclosure of Interest:** None declared

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## THU0228 EFFICACY COMPARISON WITH TOCILIZUMAB, INTERLEUKIN-1 INHIBITORS AND ETANERCEPT FOR TREATMENT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Since the approval of first biologics for JIA, such treatments in Germany are monitored prospectively by the BiKER registry.

**Methods:** sJIA pts documented in BIKER exposed to Etanercept (ETA), Tocilizumab (TOC) or IL-1inhibitors were identified. A 6-month therapy period was chosen as a meaningful time for early efficacy judgement. Intention to treat analysis (ITT) of JADAS10 was performed. Discontinuation due to inefficacy/intolerance was calculated as non-response.

**Results:** 205 sJIA patients (51% male) received 269 treatment courses with biologics (TOC 71, Anakina 36, Canakinumab 19, ETA 143). Median age and disease duration (ETA 3.3;TOC 3.3;IL-1i 3.0) were comparable. The choice of drug was influenced by the availability. ETA was started in 80% of pts before 2008 while in the TOC cohort all pts and in the IL-1i cohort 74% started therapy after 2008. Pre-treatment consisted of steroids in all pts, MTX in the ETA/TOC/IL-1i cohort in 88%/83%/76% and biologics preexposure was used in 2%/66%/86%. Concomitant treatment with systemic steroids was significantly less frequent with TOC (44%, $p<0,001$) and IL-1i (44%, $p<0.001$) compared to 83% with ETA. Concomitant MTX was used with ETA in 81% but significantly less frequent with TOC (64%; $p=0.004$) or IL-1i (44%; $p<0.0001$). Also other DMARDs were used less frequently with TOC (9%) and IL-1i (4%) compared to ETA (24%).

Systemic manifestations were present at baseline in: 8% ETA, 96% TOC and 38% IL-1i cohort. The mean±SD baseline JADAS was higher in the ETA cohort (20.7±9.1) than in the TOC cohort (16.2±10.6) or IL-1i cohort (7.8±8.9).

At month 6, a marked decrease of the JADAS was noted in all cohorts. ITT analysis revealed a significant advantage of TOC and Il-1i over ETA (table). Significantly more pts reached a JADAS-Remission (JADAS$\leq$1) upon TOC (OR/95CI 3.85/1.68–8.83/$p<0.001$) or upon IL-1i (OR/95CI 4.55/1.92–

| | | ETA (n=143) | TOC (n=71) | IL-1i (n=55) |
|---|---|---|---|---|
| Baseline | JADAS10 Median (IQR) | 8.2 (5.3–13.0) | 9.6 (4.9–13.3) | 8.2 (5.1–13.3) |
| Month 6 | JADAS10 Median (IQR) | 6.2 (1.1–15.6) | 0.8 (0.1–5.3) | 6.6 (0.2–2.0) |
| | JADAS MDA n (%) | 26 (29.5%) | 21 (61.8%) | 21 (65.6%) |
| | JADAS Remission n (%) | 16 (18.2%) | 15 (44.1%) | 16 (50%) |
| | Discontinuations (< Month 6) | | | |
| | Inefficacy | 23 (26.1%) | 4 (11.8%) | 7 (21.9%) |
| | Intolerance | | 1 (2.9%) | |
| | Remission | 1 (1.1%) | | |

10.77/p=0.003) than with ETA. Significantly more pts reached a JADAS-MDA (JADAS≤3.8) upon TOC (OR 3.55/1.49–8.46/p=0.003) or upon IL-1i (OR 4.5/1.87–10.84/p<0.0001) than with ETA. ETA was more often discontinued due to inefficacy before month 6 than TOC or IL-1i.
**Conclusions:** A high proportion of pts showed a significant response to treatment especially with TOC or with IL-1i. After 6 months on treatment JADAS remission criteria were reached by up to 50% of patients while 60% to 65% reached JADAS minimal disease activity desoite much less steroids and DMARD used with TOC or IL-1i. ETA has been used in earlier times but it is less effective and it's use in sJIA has markedly decreased in Germany.
**Disclosure of Interest:** None declared
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## THU0229 IS THERE A DIFFERENCE IN THE PRESENTATION OF DIFFUSE AND LIMITED SUBTYPE IN CHILDHOOD? RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

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**Background:** Juvenile systemic sclerosis (jSSc) is an orphan autoimmune disease. Several adult publications looked at the differences between limited (ljSSc) and diffuse subtype (djSSc). There is rarity of data regarding this topic in pediatric jSSc. The juvenile scleroderma inception cohort is a prospective standardized register for patients with jSSc.
**Objectives:** comparison of patients characteristic at the time of inclusion with ljSSc and djSSc
**Methods:** We compered the demographics and clinical characteristics of the ljSSc and djSSc.
**Results:** Up till now 74 patients were enrolled, 54 (76%) with djSSc and 18 with ljSSc (24%). 9% in djSSc and 25% in ljSSc showed overlap features. Disease duration at time of inclusion in the cohort was 3.7 years in the djSSc and 3.3 years in ljSSc. 82% in the djSSc and 78% in the ljSSc group were female. The mean age of the onset of Raynaud symptomatic was 9.0 years in the jdSSc and 9.9 years in ljSSc group and onset of the non-Raynaud symptomatic with 9.4 in djSSc and 10.6 ljSSc. At the time of inclusion the mean modified Rodnan Skin Score was 18.5 in the djSSc and 8,4 in ljSSc (p=0.0001). Anti-Scl 70 positivity was found in 31.5% of djSSc and 30.8% in ljSSc. Only 2 patient in the djSSc group and one in the ljSSc group was anticentromere positive. Capillary changes occurred in 60.7% in the djSSc and 50% in ljSSc, but 58.2% in djSSc and only 23.5% in ljSSc had already history of ulcerations (p=0.013) and 21.8% had active ulceration in the djSSc and 5.9% in the ljSSc. 33.3% of djSSc and 72.7% of ljSSc had cardiac involvement (p=0.027). pulmonary hypertension occurred in 57.1% djSSc and 18.2% in ljSSc. 63% in djSSc and 27.3% in ljSSc group had signs of interstitial lung disease on imaging (p=0.046). Renal involvement occurred in 7.1% djSSc and 5.6% in ljSSc. 39.3% of djSSc and 22.2% of ljSSc had gastrointestinal involvement. 56.4% in djSSc and 83.35 in ljSSc had musculoskeletal involvement (p=0.04).
**Conclusions:** Patients with djSSc have younger age at onset, have more often capillary changes and active ulcerations, pulmonary hypertension and less gastorintestinal and joint involvement and more disease damage. The characteristics of the pediatric subtypes differs from adults with SSc, especially the high proportion of patients with diffuse subtype.
**Disclosure of Interest:** None declared
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## THU0230 IS THERE A DIFFERENCE IN THE PRESENTATION OF MALE AND FEMALE PATIENTS WITH JUVENILE SYSTEMIC SCLEROSIS? RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

I. Foeldvari[1], J. Klotsche[2], O. Kasapcopur[3], A. Adrovic[3], M.T. Terreri[4], V. Stanevicha[5], M.M. Katsikas[6], E. Alexeeva[7], F. Sztajnbok[8], R. Cimaz[9], M. Kostik[10], W.A. Sifuentes-Giraldo[11], T. Lehman[12], D. Nemcova[13], M. Moll[14], M.J. Santos[15], T. Avcin[16], C. Battagliotti[17], J. Brunner[18], S. Nielsen[19], T. Kallinich[2], K. Minden[2], M. Janarthanan[20], L. Harel[21], Y. Uziel[22], D. Eleftheriou[23], K.S. Torok[24], N. Helmus[1]. *[1]Hamburg Center for Pediatric and Adolescent Rheumatology, Am Schön Klinik Eilbek, Hamburg; [2]Uni Child Hosp, Berlin, Germany; [3]Uni Child Hosp, Istanbul, Turkey; [4]Uni Child Hosp, São Paulo, Brazil; [5]Uni Child Hosp, Riga, Latvia; [6]Uni Child Hosp, Buenos Aires, Argentina; [7]Uni Child Hosp, Moscow, Russian Federation; [8]Uni Child Hosp, Rio de Janeiro, Brazil; [9]Uni Child Hosp, Firenze, Italy; [10]Uni Child Hosp, Saint-Petersburg, Russian Federation; [11]Uni Child Hosp, Madrid, Spain; [12]Uni Child Hosp, New York, United States; [13]Uni Child Hosp, Prague, Czech Republic; [14]Uni Child Hosp, Tuebingen, Germany; [15]Uni Child Hosp, Almada, Portugal; [16]Uni Child Hosp, Ljubljana, Slovenia; [17]Uni Child Hosp, Santa Fe, Argentina; [18]Uni Child Hosp, Innsbruck, Austria; [19]Uni Child Hosp, Copenhagen, Denmark; [20]Uni Child Hosp, Chennai, India; [21]Uni Child Hosp, Tel Aviv; [22]Uni Child Hosp, Kfar Saba, Israel; [23]Uni Child Hosp, London, United Kingdom; [24]Uni Child Hosp, Pittsburgh, United States*

**Background:** Juvenile systemic sclerosis (jSSc) is an orphan autoimmune disease. Several adult publications looked at the differences between male and female patients with Systemic Sclerosis. There is rarity of data regarding this topic in pediatric jSSc. The juvenile scleroderma inception cohort (www.juvenilescleroderma.com) is a prospective standardized register for patients with jSSc.
**Objectives:** comparison of patients characteristic at the time of inclusion in the registry who are male or female.
**Methods:** Patients with jSSc were included worldwide to the juvenile scleroderma inception cohort. We compered the demographics and clinical characteristics of the male and female patients.
**Results:** Up till now 74 patients were enrolled, 54 with djSSc (76%) and 18 with ljSSc (24%). 14 (19%) of the patients were male (M) and 60 female (F) (81%). The mean disease duration at the time of inclusion was 9.3 in M and 9.2 in F patients. 74.4% of the M and 76.7% of the F had diffuse subset. The mean age of the onset of Raynaud symptomatic was 9.3 in M and 9.2 years in the F patients and the non-Raynaud symptomatic with 9.1 in M and 9.9 in F patients. At the time of the inclusion the mean modified Rodnan Skin Score was 20 in M and 15.1 in F patients. Anti-Scl 70 positivity was found in 42.9% in M and 32.1% in F patients. Anticentromere positivity occurred in 16.7% in M and 3.3% in F patients (p=0.027). Capillary changes were present in 50% of the M and 60% of F patients, but 50% in M and F had already history of ulcerations, but 28.6% in M and 15.5% in F had active ulceration. 57.1% of the M and 50% of the F patients had cardiopulmonary involvement. Six patients had pulmonary hypertension, they were all F. 75% of M and 46.7% of F patients had signs of interstitial lung disease on imaging. Renal involvement was around 7% in both sexes. 21.4% in M and 38.3% in F patients had gastrointestinal involvement. 92.9% of M and 55.9% in M patients had musculoskeletal involvement.
**Conclusions:** We present the data on the first 74 patients with jSSc included in our cohort. Patients with male sex have a more severe disease similar to adult male patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2700

## THU0231 BELIMUMAB IN PAEDIATRIC SLE (THE PLUTO STUDY) – STUDY DESIGN AND PARTICIPATION

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**Background:** Belimumab, a fully human IgG1λ monoclonal antibody for B Lymphocyte Stimulator protein, was licensed in 2011 by the FDA and EMA for add-on therapy in adult patients with active systemic lupus erythematosus (SLE). As part of a paediatric investigational plan, a study of belimumab in paediatric SLE was designed and commenced in 2012 (BEL114055, ClinicalTrials.gov: NCT01649765).
**Objectives:** To outline the study design, study participation and rationale for subject selection.
**Methods:** The PLUTO study is a 52-week multi-centre, randomized parallel group, placebo-controlled double-blind study to evaluate the safety, efficacy, and pharmacokinetics (PK) of belimumab plus standard therapy in paediatric patients (5–17 yrs) with SLE. To be eligible to enrol patients need to have a clinical diagnosis of SLE according to the ACR criteria, be autoantibody positive and have a SELENA-SLEDAI score of ≥6. Patients who complete the double-blind phase (Part A), are eligible to join an open-label safety follow-up period of up to ten years (Part B). For subjects who withdraw from Part A or Part B, there is a long-term safety follow up phase (Part C).
Part A is divided into 3 Cohorts. Cohort 1 will consist of the first 12 subjects (12–17 yrs). Once the PK and safety profile of Cohort 1 is evaluated and any

potential dose adjustments are determined as a result of this analysis, additional subjects 12–17 yrs will then enrol in Cohort 3. Cohort 2 will enrol 12 patients (5–11 yrs) at the dose determined from the PK analysis of Cohort 1. Once the PK and safety profile of Cohort 2 is evaluated and any potential dose adjustments are determined as a result of this analysis, additional subjects 5–11 yrs will then enrol in Cohort 3. Cohorts 1 and 2 will be randomized in a 5:1 ratio, and Cohort 3 subjects will be randomized in a 1:1 ratio to receive belimumab or placebo on a background of standard therapy.
An Independent Data monitoring Committee (IDMC) will monitor unblinded safety, efficacy and PK data from the study.
**Results:** The study is currently enrolling and is active in the following countries: US, Canada, Argentina, Peru, Mexico, UK, Spain, Netherlands, Poland, Russia and Japan.
Subjects selected for study inclusion had active SLE indicated by skin/mucosa, musculoskeletal, haematologic, renal or CNS organ manifestations and were receiving standard concomitant SLE therapies including corticosteroids, anti-malarials and immunosuppressants. The profile of the trial population reflects a patient population who have active SLE but with an inadequate response to standard therapy and who therefore may benefit from an alternative treatment such as belimumab.
The ongoing IDMC reviews support the study continuation according to the current protocol.
**Conclusions:** The PLUTO study aims to address an area of unmet clinical need in which there are no licensed therapies. Please consider the eligibility of your paediatric SLE patients for this important study.
**Acknowledgement:** This study is funded by GSK.
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## THU0232 DOES THE TIME OF BDMARD START DETERMINE THE OUTCOME OF JIA IN ADULTHOOD?

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**Background:** Biological disease modifying antirheumatic drugs (bDMARD) had great impact on the medical management of patients with juvenile idiopathic arthritis (JIA). Many patients nowadays enter adulthood in clinical remission, with normal function and without long-term sequelae. There is little information to what extent the early use of bDMARDs affects the long-term outcome of patients with JIA.
**Objectives:** To investigate if the 10-year outcome after JIA onset is associated with the time lag between JIA disease onset and first bDMARD use.
**Methods:** Outcome variables were examined in patients prospectively observed in the national JIA biologic register BiKeR and its follow-up register JuMBO since initiation a bDMARD therapy. Analyses included patients with at least one visit in JuMBO. Assessed parameters were JADAS3–10, C-HAQ, joint surgery (replacements, synovectomies), eye surgery and patient-reported outcomes. To analyze the influence of the time lag between JIA onset and first use of bDMARD, patients were assigned to one of the following three groups (G1: $\leq$2 year = early therapy, G2: intermediate, G3: $\geq$5 years = late). A general propensity score was estimated to adjust for baseline differences between the three groups. Mixed models were used to determine the association of the three groups and outcomes. Surgeries were analyzed by Cox regression analyses.
**Results:** 609 patients were ever treated with a bDMARD and successfully transferred to JuMBO. Most (91%) patients were enrolled in BiKeR on etanercept followed by adalimumab (6%), 93% had previously received a conventional synthetic (cs) DMARD. 27.9% had RF negative polyarthritis and 19.5% enthesitis-related arthritis. The first csDMARD was started 0.4 years after disease onset in the early bDMARD group (n=142), and 1.2 and 3.1 years after JIA onset in the in-between group and late group (n=274), respectively. At their last follow-up (10.2±6.2 years after JIA onset), the patients' mean age was 21.2 years. The clinical outcome 10 years after disease onset could be investigated in 478 patients. Patients with early biologic treatment were significantly more often in drug-free JADAS remission (15%) for at least 12 months, had more often an inactive disease (JADAS3–10$\leq$1, 27.6%) and no functional limitations (58.6%) compared to late treatment start. There was no significant difference in the patient-reported outcome measures. Among all 609 patients, 35 (5.8%) patients had undergone joint replacement, 100 (16.4%) synovectomy and 19 (3.2%) eye surgery. Patients on bDMARD in follow-up had a lower likelihood for joint replacement (HR=0.25, p=0.003) or synovectomy (HR=0.26, p$<$0.001). Patients with late DMARD treatment had significantly more synovectomies (HR=4.9, p$<$0.001) than patients with early treatment.
**Conclusions:** Patients who started with cs and bDMARDs within the first two years of disease are significantly more often in drug-free remission in adulthood and have less sequelae than those who started later. The data emphasize the importance of a fast disease activity control and may support the idea of a window of opportunity for JIA.
**Disclosure of Interest:** None declared
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## THU0233 IMPACT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS/STILL'S DISEASE ON ADOLESCENTS AS EVIDENCED THROUGH SOCIAL MEDIA POSTING

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**Background:** Systemic juvenile idiopathic arthritis (SJIA)/Still's disease is a rare form of chronic arthritis in pediatrics. The patient perspective of living with the disease is not well understood, particularly among adolescent age patients.
**Objectives:** The objective was to understand the adolescent SJIA experience as shown by their own social media posts.
**Methods:** English posts from SJIA patients were reviewed on public social media sites.
**Results:** 71 posts with a date range of 2009–2015 on 15 sites were reviewed in Nov 2015. 24 unique authors were identified: 17 SJIA patients (40 posts) and 7 mothers of SJIA patients (12 posts). Patients were aged 13–20 years. Several patients posted about similar diagnostic experiences marked by 5 stages: (1) misunderstood with their pain and fatigue being overlooked until a crisis occurs, (2) dismissed as "fakers", where their initial misdiagnosis is often "growing pains" or "fake pains", (3) misdiagnosis, often as cancer, when the symptoms acutely worsen (4) testing stage that leads to an SJIA diagnosis, and (5) focus on the difficulties of dealing with a chronic invisible disease where they feel ashamed of their arthritis and distressed at being different from their peers. Many adolescent patients, looking back at the onset of the disease when they were children, describe themselves as a "sleeping child" rather than the typical active, playing child. Patients describe trying to hide their illness from friends, but express their concerns more openly online. Patients also describe anger directed at SJIA which is described as a powerful external enemy attacking their body, using terms like "bulldozer," "dragon", and "monster'.' Many posters used superhero language or imagery in their social media posts to help them "fight" the disease and their struggle. Mothers of SJIA patients also used warrior-child imagery and language in their posts. Some SJIA patients also posted about the risk of death, or shared stories about other SJIA patients who died which is a distinct difference from non-SJIA patients. Many patients also have adopted the term "spoonie" to describe themselves as living with a chronic disease, a term that originated in the autoimmune community to refer to how people with chronic conditions manage their energy throughout the day. Only the older teenagers used the term Still's.
**Conclusions:** Adolescent SJIA patients posted openly about the difficulties of their disease causing them to be different from their healthy friends, whereas in the real world they tried to minimize or hide the effects of their disease. They frequently used superhero words and images in posts in describing their fight for health. Physicians can use these insights when counseling adolescent SJIA patients to provide a narrative that meshes with the patients' worldview and perhaps, by speaking a similar language, could increase treatment adherence.
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## THU0234 CLINICAL EXPERIENCE AND DECISION MAKING IN RELATION TO THE USE OF BIOLOGICS IN ADULT JIA

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**Background:** Juvenile Idiopathic Arthritis (JIA) is the most common chronic inflammatory musculoskeletal disease of childhood in the UK. More than 30% of patients will continue to have active disease as adults, with some requiring a biologic for the first time after the age of 18 years. Prior to December 2015, there was no national UK approval for the use of biologics in this older population, albeit they were used in adults with JIA (British Society for Rheumatology Biologics Register BSRBR Data).
**Objectives:** This mixed methods study aimed to explore the clinical experience

and decision-making of health care professionals in relation to the use of biologics in adults with JIA.
**Methods:** An online survey of 205 healthcare professionals working in UK hospitals who have recruited adults with JIA to BSRBR-RA (response rate: 81 (39%) including rheumatology consultants (49), rheumatology specialist nurses (29), research nurses (2) and staff associates (1)), ascertained their experience in relation to four distinct areas: (1) Education, Training and Practice; (2) Factors Suggesting a Diagnosis of JIA, (3) Use and Choice of Biologics; and (4) Treatment Challenges. The survey data were analysed using descriptive statistics and free-text comments using qualitative techniques. This study had ethical approval with informed consent from all participants.
**Results:** Most (95%) survey participants currently treat adults with JIA and many (63%) also treat children. Most had not received any education or training in the specific management of adults with JIA (65%) although 56% had received some training in paediatrics (described as formal training programmes, attendance at meetings; in practice learning and colleague support). Many stated further need for training in JIA in adults (52%) and children (58%).
Participants reported using all currently approved biologics for either JIA in children or rheumatoid arthritis; etanercept, adalimumab and tocilizumab being the most common. Factors influencing choice included: National guidelines and funding; JIA disease-associated factors; patient previous treatment; previous experience of clinician; and patient choice. The challenges encountered in treating adults with JIA included: access to biologic therapy; JIA awareness and knowledge; access to support from colleagues and MDT; problems associated with transitional care services; and patient expectations. Potential improvements to aid the diagnosis and management of adults with JIA were offered and these included: Introduction of national guidelines; further education/training and support; and introduction or improvement of transition service links.
**Conclusions:** Improved access to education, training and treatment guidelines in JIA is likely to improve clinical experience and decision-making in relation to the management of adults with JIA. Future qualitative work will explore this further.
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## THU0235 ADJUVITE: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF ADALIMUMAB IN JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS

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**Background:** Juvenile idiopathic arthritis (JIA) patients may develop chronic, anterior uveitis. Topical steroids and methotrexate (MTX) often lack of efficacy.
**Objectives:** To asses safety and efficacty of adalimumab in patients with JIA-associated uveitis.
**Methods:** Elligible patients had chronic, "white eyes" uveitis with inadequate response to topical steroids and MTX, no previous anti-TNF antibody therapy and at least one assessable eye with inflammation quantified by laser flare photometry $\geq$30 photons/ms. Double-blind randomization at Day 1 (D1) into 2 equal groups, one treated with placebo and one with adalimumab (24 mg/m$^2$ in patients aged 4 to less than 13 years, 40 mg in patients $\geq$13), every other week subcutaneous injections. Primary objective: to demonstrate a higher response rate at Month 2 (M2) in the adalimumab arm versus the placebo arm. Response was defined as a 30% reduction of inflammation on laser flare photometry in the eye with the highest flare value at D1 and improvement or a stable appearance on slit lamp examination. From M2 to M12, all patients were allowed to receive adalimumab (open phase) (NCT01385826).
**Results:** 34 patients were screened and 31 received at least one injection of study treatment.

Table 1. Patients characteristics at study treatment onset

| | Ada (n=16) | Placebo (n=15) | All (n=31) |
|---|---|---|---|
| Female, n (%) | 15 (94) | 13 (87) | 28 (90) |
| Age, median value, years [ranges] | 10.8 [5.0–20.3] | 9.2 [4.9–29.1] | |
| Active joints, median n [ranges] | 0 [0–3] | 0 [0–4] | 0 [0–4] |
| Uveitis median duration, years [ranges] | 4.4 [0.4–18.9] | 4.8 [0.6–24.2] | |
| Laser flare (ph/ms), median [ranges] | 99 [23–322] | 70 [36–265] | |
| Bilateral uveitis, n (%) | 10 (63) | 14 (93) | 24 (78) |
| Ongoing treatments at D1 | | | |
| Oral steroids, patients n (%) | 7 (44) | 3 (20) | 10 (32) |
| Methotrexate, patients n (%) | 15 (94) | 11 (73) | 26 (84) |

At M2, in intention-to-treat (Primary objective), there were 9/16 responders in the adalimumab group and 3/15 in the placebo group ($p$=0.038, Chi-squared test; RR=2.81, CI95%=[0.94–8.45] with log-binomial model estimation). One patient stopped the trial at D14 (adalimumab group, uveitis worsening) and one at M9 (ocular hypertony). 29 patients reached M12 on adalimumab. There were 5 serious adverse events in 4 patients, all in the placebo group, 4 during the open-label phase, none related to study treatment (investigator assessment).
**Conclusions:** Adalimumab was effective in reducing ocular inflammation within 2 months and well tolerated over 12 months in patients with JIA-associated chronic uveitis and an inadequate response to topical steroids and MTX. Laser flare photometry is a valuable tool to assess early improvement.
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## THU0236 BONE METABOLIC INDEX AND CLINICAL PHENOTYPE IN JUVENILE-ONSET ANKYLOSING SPONDYLITIS (JAS)

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**Background:** Ankylosing spondylitis (AS) is a common inflammatory rheumatic disease which preferentially affects the axial structures causing spinal ankylosis, AS is more common in young adults aged 10–40, but the onset age can also be childhood. It was grouped according to onset age: those with onset symptoms before the age of 16 years were classified as Juvenile-onset Ankylosing Spondylitis (JAS), and patients with onset symptoms older than 16 at onset were classified as Adult-onset Ankylosing Spondylitis (AAS). Clinical phenotype and prognosis of JAS is different from AAS,but up to now scarce information about JAS was reported, especially the related bone metabolism mechanism.
**Objectives:** To analyse bone metabolic index (BMI) changes on patients with Juvenile-onset Ankylosing Spondylitis (JAS) and their relations with clinical index.
**Methods:** To collect the clinical data of JAS,such as C-reactive protein (CRP), blood sedimentation (ESR),the disease activity index (BASDAI),functional index (BASFI) and bone mineral density (BMD), detect the serum bone metabolism index,such as Wnt-3a, BMP-2, Dkk-1, 25 (OH) D and ICTP, then group these data and do statistical analysis.
**Results:** Osteopenia and VitD lack were widespread in JAS. Compared with controls, The elevated Wnt-3a and reduced Dkk-1 levels were not significant in JAS ($P>0.05$), and there was no significant correlation between the two indexes and other BMI, course, clinical inflammation index, BASDAI and BASFI. However,the serum ICTP and BMP-2 were increased significantly in JAS, and both the CRP and BMP-2 were positive related with serum Wnt-3a (r was 0.271 and 0.250 respectively, $P<0.05$).Correlation analysis shew there was positive correlation between serum 25 (OH) D and hip BMD in JAS (r=0.383, $P<0.01$), and there was negatively correlation between ICTP and BASDAI (r=-0.405 and -0.273 respectively, $P<0.05$).Besides,regression analysis shew that both serum 25 (OH) D and the disease course were independent prognostic factors of patients' hip BMD decreasing, where as CRP and ICTP were also independent prognostic factors of patients' BASDAI. BMI in JAS with different clinical phenotypes were compared, BMP-2 level was much higher in JAS with hip joint involvement than other groups (P=0.032), while there was no significant difference in serum 25(OH)D,ICTP,Wnt-3a and Dkk-1 level in all groups ($P<0.05$).
**Conclusions:** There is bone metabolism imbalance in JAS,and BMI can indirectly reflect the disease activity and bone loss,among which BMP pathway played an important role in the JAS with hip lesions and deserves further research.
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## THU0237 DISEASE ACTIVITY IN PATIENTS WITH JUVENILE SPONDYLOARTHROPATHY ON ANTI-TNF THERAPY AS MEASURED BY THE JUVENILE ARTHRITIS DISEASE ACTIVITY SCORE (JADAS)-10 AND THE JUVENILE SPONDYLOARTHRITIS DISEASE ACTIVITY INDEX (JSPADA)

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**Background:** Juvenile Spondyloarthropathy (jSpA) is SpA that starts during childhood and adolescence. Most children with jSpA fall into the categories of

enthesitis-related arthritis (ERA), psoriatic arthritis, and undifferentiated arthritis of the ILAR classification of Juvenile idiopathic arthritis (JIA). Several disease activity scores have been developed for adults with SpA and for children with JIA (such as the Juvenile Arthritis Disease Activity Score or JADAS). However, neither of these measures has been validated in jSpA. The Juvenile Spondyloarthritis Disease Activity Index (JSpADA) has been recently developed and retrospectively validated in jSPA (1).

**Objectives:** to assess disease activity in a cohort of patients with ERA on anti-TNF therapy using the JADAS-10 and the JSpADA.

**Methods:** retrospective review of prospectively collected data. Patients with ERA treated with anti-TNF agents for $\geq$1 year and complete records were included. Information was collected on visits 0 (immediately prior to anti-TNF therapy start), 1 month after start of therapy, and every 3 months thereafter (up to 36 months) on demographics, therapeutic agents used, and disease activity measures: active joints (AJ), active enthesitis (AE), pain score, wellbeing according to the patient (VASp), disease activity according to the physician (VASphy), JADAS-10, JSpADA, and ESR. Comparisons between visits were performed using paired t-test; correlations between outcome measures was done using Spearman's correlation test.

**Results:** 24 of 28 patients treated with anti-TNF agents fulfilled inclusion criteria. They were all male, 50% HLA-B27 positive; median age at entry 13 y, disease duration 4 y; median observation period was 21 months, 207 visits were recorded. Twenty-two (92%) children showed peripheral arthritis while 17 (71%) exhibited sacroiliitis on MRI/Xrays before starting therapy. Patients received etanercept (17, 2 were later switched to infliximab and adalimumab each), adalimumab (5), or infliximab (2). At baseline patients showed (medians): AJ 4.5, ESR 15 mm/h, VASphy 1, JSpADA 2, and JADAS 9.5. AE was present in 4 (17%) and lumbar limitation (LL) in 9 (37%) children. All patients showed JSpADA $>$0 and 95% children had JADAS $>$1. After 3 months JSpADA decreased to 1.25 and JADAS-10 to 6; 5 (21%) patients achieved inactive disease (ID, JADAS-10 $\leq$1). At visit 12 months: AJ 0 (p=0.0015), ESR 7 mm/h (p=0.06), VASphy 0.5 (p=0.005), JSpADA 1 (p=0.0004), and JADAS 1.75 (p=0.02); AE was present in 0 patients and LL in 6 (25%). JADAS-10 $\leq$1 was observed in 18 (75%) patients and JSpADA $\leq$1 in 21 (87%) children during follow-up. At baseline and at visit 12 months JSpADA showed high correlations with JADAS-10 (r=0.97, 0.75) and AJ (r=0.73, 0.77); JADAS-10 also correlated with AJ (r=0.92, 0.83).

**Conclusions:** in this retrospective cohort of ERA patients with peripheral and axial active involvement there was a marked and progressive reduction in disease activity after the initiation of anti-TNF therapy. Both JSpADA and JADAS-10 demonstrated to be sensitive, feasible and useful activity measures that could be used in clinical trials or a treat to target strategy for JSpA.

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**Disclosure of Interest:** None declared

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## THU0238 HOW TO DIAGNOSE AND PREVENT THE EPISODES OF PFAPA SYNDROME

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**Background:** Periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis (PFAPA) syndrome is the most frequent repetitive fever syndrome in childhood. It is characterized with fever episodes lasting for about three to six days, once every three to eight weeks.

**Objectives:** In this study, we aim to elucidate the clinical clues that will facilitate the identification of PFAPA which is a clinical diagnosis and the efficacy and safety of colchicine prophlaxis in a large cohort. Additionally, we intend to investigate the relation between MEFV gene mutations and clinical findings of PFAPA.

**Methods:** Clinical and laboratory data of 400 consecutive patients with PFAPA syndrome followed up at the department of Pediatric Immunology and Rheumatology Uludag University Faculty of Medicine, were collected from the medical records retrospectively.

**Results:** Four-hundred children (256 male, 144 female), the mean age at diagnosis was 4.2 ± 2.2 years, were involved in our study. During the episodes, the mean number of WBC was high (12724,7/mm$^3$) with predominantly neutrophils. The mean number of monocytes was found to be 1256.2/mm$^3$ and 90.2% of the patients had monocytosis. Serum amiloid A and C reactive protein levels were high in 84.6% and 77.8% of the patients, respectively. Procalcitonin was negative in 97.3% of the patients. MEFV gene heterozygous mutation was determined in 57 of the 231 patients (24.7%) tested. Colchicine prophylaxis was administered in 356 patients. The mean duration between episodes was prolonged from 18.8 to 49.5 days by prophylactic colchicine therapy. During the episodes, a single dose of 1 mg/kg methyl prednisolone was prescribed. Four patients underwent tonsillectomy.

**Conclusions:** Our study, include the largest number of patients with PFAPA syndrome in the literature. It is particularly important to assess and to demonstrate the high rate of response to colchicine prophylaxis in patients with PFAPA syndrome, especially those with MEFV variant. In blood screening neutrophilia associated with monocytosis and low procalcitonin level could contribute to diagnosis.

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## THU0239 PERFORMANCE OF DISEASE ACTIVITY MEASURES IN JUVENILE SPONDYLOARTHRITIS IN A PLACEBO CONTROLLED TRIAL WITH INFLIXIMAB

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**Background:** Several outcome measures in trials with juvenile-onset spondyloarthritis (Jo-SpA) have been borrowed from trials in juvenile idiopathic arthritis and from adult spondyloarthritis, but a proper psychometric analysis has never been conducted in patients with Jo-SpA.

**Objectives:** To assess discriminatory aspects of several disease activity outcome measures and response criteria for Jo-SpA.

**Methods:** Data from a previously reported 12-week RCT comparing infliximab (IFX) and placebo (PBO) in patients $<$18 years with Jo-SpA and onset $<$16 years of age were analyzed. The primary endpoint of the trial was the number of active joints (both swollen and tender). Several other disease activity measures and response criteria were also tested (Table). Statistics to determine how well disease activity measures could discriminate between IFX and PBO included "standardized mean difference" (SMD) and "Guyatt's effect size". Both statistics are standardized measures to compare change from baseline per group. For categorical response criteria, the chi-square test ($\chi^2$) was used. Higher numbers indicate better discriminatory capacity.

**Results:** Patients were randomised to IFX (n=12) and PBO (n=14). Of the continuous measures, the ASDAS showed the best and very good discrimination between IFX and PBO (SMD:1.98; Guyatt: 4.28) (Table). The physician's global, CRP, JADAS and JSpADA also discriminated well. The BASDAI (or its separate items), BASFI and spinal mobility measures performed worse. Of the response criteria ASAS40 and ACR Pedi 90 discriminated best between IFX and PBO (Table). ASDAS response criteria and ACR Pedi 30–70 also performed well.

**Table: Discrimination between patients on infliximab and placebo at week 12**

| CONTINUOUS OUTCOME MEASURES | | | | |
|---|---|---|---|---|
| | Infliximab mean change (SD) | PBO mean change (SD) | Guyatt's effect size | SMD |
| ASDAS | 2.4 (1.3) | 0.5 (0.6) | 4.28 | 1.98 |
| Physician's global assessment, 0-10 mm VAS | 5.2 (2.4) | 1.6 (2.2) | 2.34 | 1.56 |
| JADAS27 (0-57) | 12.7 (5.9) | 4.3 (5.7) | 2.22 | 1.46 |
| JSpADA (0-8) | 2.8 (1.2) | 0.5 (1.4) | 1.98 | 1.73 |
| CRP (mg/L) | 21.1 (8.4) | 2.3 (10.9) | 1.93 | 1.90 |
| Total enthesitis (0-51) | 8.5 (10.6) | 1.6 (5.0) | 1.71 | 0.85 |
| Patient's global assessment, 0-10 mm VAS | 4.3 (3.8) | 0.8 (2.8) | 1.55 | 1.08 |
| BASDAI total (0-10) | 3.3 (3.1) | 0.9 (2.3) | 1.41 | 0.90 |
| Pain, 0-10mm VAS | 3.3 (2.1) | -1.7 (3.2) | 1.03 | 1.80 |
| Active joint count (0-72) | 4.4 (1.7) | 2.6 (4.6) | 0.96 | 0.51 |
| | **Infliximab mean change (SD)** | **PBO mean change (SD)** | **Chi-square** | **p-value** |
| ACR Ped 90 | 8 (67%) | 1 (7%) | 10.12 | 0.001 |
| ASAS40 | 6 (55%) | 0 (0%) | 10.05 | 0.002 |
| ACR Ped 70 | 9 (75%) | 2 (14%) | 9.76 | 0.002 |
| BASDAI50 | 8 (73%) | 2 (14%) | 8.77 | 0.003 |
| ASDAS-MI | 5 (63%) | 0 (0%) | 8.65 | 0.003 |
| ACR Ped 50 | 11 (92%) | 5 (36%) | 8.55 | 0.003 |
| ASDAS-CII | 7 (88%) | 2 (20%) | 8.10 | 0.004 |
| ASDAS-ID | 7 (64%) | 1 (8%) | 7.74 | 0.005 |
| ACR Ped 30 | 11 (92%) | 6 (43%) | 6.80 | 0.009 |
| JADAS27 MDA (≤2) | 6 (50%) | 1 (7%) | 6.03 | 0.014 |
| JADAS27 inactive disease/remission (≤1) | 3 (25%) | 0 (0%) | 3.96 | 0.047 |
| ASAS20 | 7 (64%) | 4 (29%) | 3.07 | 0.080 |

**Conclusions:** Of all continuous measures tested in adult axial SpA the ASDAS discriminates best between active treatment and PBO in patients with Jo-SpA. But the child specific JSpADA also performs well.

Of all response criteria tested the child-specific ACR Pedi 30 to 90, as well as the adult ASAS40 and ASDAS response criteria work well. One of these measures should be used as primary endpoint in trials with Jo-SpA.
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**Disclosure of Interest:** None declared
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## SLE, Sjögren's and APS - etiology, pathogenesis and animal models

### THU0240 DYSREGULATIONS IN THE SPHINGOLIPID PATHWAY IN SLE PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease with a heterogeneous presentation of symptoms from joints, skin, kidneys, central nervous system, lungs, and the cardiovascular system. There is no cure for SLE and development of novel drugs and biomarkers of effective treatment is needed. Sphingolipids are bioactive signaling molecules involved in the regulation of cell growth, differentiation and apoptosis. Dysregulation of single sphingolipids has been described in several diseases with an inflammatory component and sphingosine-1-phosphate (S1P) agonist (Fingolimod) is investigated as treatment in SLE. Therefore, the sphingolipid pathway has arisen as very important compounds to study in respect to SLE pathogenesis.
The compounds of the sphingolipid pathway are highly correlated and simultaneous measure of several sphingolipids in an "omics" like analysis is expected to provide more information than compounds individually determined.
**Objectives:** Our objective is to screen the sphingolipid pathway in patients with SLE compared to healthy controls. In addition we aim to study if the altered sphingolipids will be normalized after treatment.
**Methods:** EDTA-plasma from 107 SLE female patients were screened for 34 different sphingolipids by liquid chromatography tandem mass spectrometry (LC-MS/MS) and compared to matched healthy population-based donors (n=23). In addition, female SLE patients (n=22) were analyzed before and after induction of remission treatment.
**Results:** SLE patients were found to exhibit an altered sphingolipid profile compared to controls. Significantly ($p<0.01$) increased levels of C16:0- and C24:1-ceramides, C16:0, C18:0 and C24:1-hexosylceramides and decreased levels of S1P were found in SLE patients compared to controls. The observed higher levels of ceramide to S1P ratios in SLE patients may reflect the blockage of the pathway that is controlled by ceramidase and can be inhibited by nitric oxide. These alterations were associated with SLAM and SLEDAI clinical scores and were normalized after induction of remission treatment.
**Conclusions:** This work shows the importance of performing a holistic approach targeting the different molecules of the sphingolipid pathway. Our results show dysregulations in circulating sphingolipids in patients with SLE and normalized after treatment, suggesting that sphingolipids may be useful markers of disease progression and possible drug targets.
**Disclosure of Interest:** None declared
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### THU0241 PRESENCE OF GERMINAL CENTERS IN DIAGNOSTIC BIOPSIES OF PRIMARY SJÖGREN'S SYNDROME PATIENTS IS NOT A RISK FACTOR FOR THE DEVELOPMENT OF PAROTID MALT LYMPHOMAS

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**Background:** B cell hyperactivity is a hallmark of primary Sjögren's syndrome (pSS) and plays a critical role in sustainment and progression of pSS.[1] Hyperactivity is reflected by the presence of germinal centers (GCs) in periductal lymphoid infiltrates in the salivary glands. Risselada et al[2] reviewed the presence of GCs in the salivary gland biopsies of pSS patients. On hematoxylin and eosin (HE) stained sections a mean weighted percentage of 25.1±5.0% (range 18.3–33%) of GCs positivity was present. On CD21 sections, staining follicular dendritic networks, this increased to 35.3±14.8% (range 19–58.8%).
A serious complication of pSS is the 5–10% lifetime risk of developing non-Hodgkin B cell lymphomas.[3] Most lymphomas associated with pSS are of the Mucosa Associated Lymphoid Tissue (MALT) type, which typically arise in parotid glands. Which pSS patients will develop non-Hodgkin's lymphomas is largely unknown, but several risk factors have been identified. Presence of GCs in minor salivary glands at diagnosis of pSS has been postulated as a risk factor. Theander et al[4] observed that six out of seven pSS patients that developed malignant lymphomas had GCs in their initial diagnostic minor salivary gland biopsy. However, a drawback of that study was that also lymphomas not characteristic for pSS such as follicular lymphoma and anaplastic T-cell lymphoma were included.[4]
**Objectives:** The aim of this study was to explore the possible role of GCs as risk factor for malignant lymphoma development in pSS restricting ourselves to lymphomas which are typically associated with pSS, namely parotid gland MALT lymphomas.
**Methods:** In a cohort of 56 pSS patients with parotid MALT lymphomas we were able to collect and reassess tissue sections from 14 salivary gland biopsies (11 minor, 3 parotid) taken at diagnosis of pSS, i.e. before diagnosis of MALT. Paraffin sections were analyzed for the presence of GCs on HE sections and, more sensitively, by B cell lymphoma 6 protein (BCL6) staining.
**Results:** HE stained sections of 11 diagnostic minor salivary gland biopsies revealed that GCs were present in 2/11 (18%) biopsies (Fig. 1a,c). BCL6 staining showed a small GC in one additional patient in the initial biopsy (Fig. 1b,d). Thus, GCs were present in 3/11 labial salivary gland biopsies (27%). Including diagnostic parotid gland biopsies, GCs were present in 4/14 (29%) HE stained sections and in 5/14 (36%) BCL6 stained sections. The mean interval between diagnosis of pSS and parotid MALT lymphoma was 6.0 yr (range 0.2–14.4 yr).

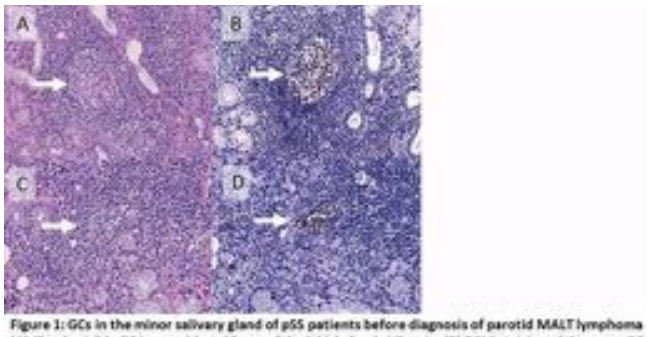


**Figure 1: GCs in the minor salivary gland of pSS patients before diagnosis of parotid MALT lymphoma**
(A) Clearly visible GC in a periductal focus of the labial gland, HE stain. (B) BCL6 staining of the same GC. (C) Conspicuous GC in a periductal focus of the labial gland, HE stain. (D) BCL6 staining shows a small GC. Arrows point to GCs.

**Conclusions:** In this study percentages of GCs in salivary gland biopsies prior to MALT lymphoma were comparable to the percentage of GCs positive biopsies in the general pSS population.[2] We therefore conclude that presence of GCs in diagnostic (minor) salivary gland biopsies is not predictive for developing pSS associated parotid gland MALT lymphomas.
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### THU0242 HIGH-THROUGPUT SCREENING DISCOVERS NOVEL AUTOANTIBODIES IN AUTOIMMUNE DISEASES: THE SEROTAG APPROACH IN SYSTEMIC LUPUS, SYSTEMIC SCLEROSIS AND RHEUMATOID ARTHRITIS

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**Background:** Diagnostic biomarkers are decision-making tools in clinical lab routine and are of growing importance for clinical management of patients. In autoimmune diseases, one class of biomarkers are autoantibodies (AAB) directed against human autoantigens. Apart from diagnostic antigens used in clinical routine, additional AAB reactivities to more than 100 human antigens are described in literature. Obviously, the autoimmune profile of humans covers a huge number of AABs, which display an enormous resource to identify novel marker candidates.
**Objectives:** Here we describe a new screening platform SeroTag for screening of novel AABs in autoimmune diseases. By offering thousands of human antigens to serum samples of several autoimmune diseases a comprehensive landscape shall be drawn to identify diseases and disease subgroups according to their intrinsic, highly differentiated autoantibody pattern.
**Methods:** SeroTag utilizes over 7,000 human proteins as antigen collection in bead-based suspension arrays (Luminex FlexMap 3D) to allow for high throughput serum sample processing with high accuracy, followed by standard and advanced data mining procedures. We screened over 4,000 serum samples from patients with autoimmune diseases such as SLE (n= >500), SSc (n= >250), RA (n= >500), and healthy individuals (n= >350) to confirm known and to discover novel autoantibodies. Recombinant antigens were covalently coupled to magnetic, color coaded beads and serum samples were incubated with 20 multiplex bead mixes

each representing hundreds of antigens. Univariate and multivariate statistical analyses were performed to reveal significant antigens and to define correlation of antigens with clinical parameters and amongst themselves.
**Results:** In SLE, SSc and RA novel autoantigens were discovered in independent discovery and validation studies. Antigens showing reproducible, significant reactivity compared to active and passive controls were selected in a stepwise marker refinement approach. Examples include BICD2 and KDM6B as novel antigens in SSc with 20–30% prevalence, TMPO and MVP in SLE with 15–25% prevalence, and several novel protein targets of anti-citrullinated peptide antibodies.
**Conclusions:** Discovery approaches for autoantigens in autoimmune diseases show great promise to further detail the autoimmune landscape. SeroTag screening is a valuable tool for "omics"-type biomarker discovery and verification. Novel autoantigens were discovered and validated in RA, SLE, SSc which show potential for improved and earlier diagnosis, differential diagnosis, and disease subgrouping.
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## THU0243 INTEGRATED ANALYSIS OF MICRORNA AND MRNA EXPRESSION PROFILES RELATED TO CARDIOVASCULAR DISEASE IN MONOCYTES FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** MicroRNAs (miRNAs) are endogenous small non-coding RNAs that regulate gene expression by interfering translation or stability of target transcripts. This interplay between miRNA and their mRNA might constitute an important mechanism in the regulation of the proatherothrombotic status of SLE patients.
**Objectives:** To investigate the contribution of deregulated miRNAs to the altered gene profile associated to cardiovascular disease in SLE.
**Methods:** Thirty three SLE patients and 27 healthy donors were included in the study. Gene Expression Microarray (44K, Agilent, one colour) and nCounter microRNA Expression Array (NanoString Technologies) were performed, respectively, to analyze mRNA and miRNA expression profiles on isolated monocytes. Target genes of the differentially expressed miRNAs were identified by using the Igenuity Pathway Analysis Software (IPA). To recognize the putative microRNA-mRNA target pairs and interaction networks, the subsets of miRNAs and mRNAs were characterized by the microRNA Target Filter tool of IPA. The resulting identified interactions were revalidated by RT-PCR on the whole cohort of SLE patients. The predicted microRNA-mRNA interactions were also tested by functional analyses using microRNA over expression experiments in monocytes purified from SLE patients
**Results:** Comparative analysis of the mRNA profiles showed significantly different expressions of 1222 genes in SLE monocytes in relation to healthy monocytes (658 up-regulated and 564 down-regulated). Functional analysis by using IPA showed that about 30% of altered genes were involved in inflammation and cardiovascular disease (CVD). Comparative analysis of the microRNA profiles showed significantly different expressions of 37 microRNAs in SLE monocytes (8 up-regulated and 29 down-regulated). Functional IPA analysis showed that microRNAs altered were mainly related to connective tissue disorders, inflammatory response and reproductive system disease. A total of 63 genes were inversely correlated, and predicted as CVD-related target genes of 23 differentially expressed microRNAs. Interaction networks of those genes and some microRNAs differentially expressed in SLE monocytes were also identified. Among them, we verified the overexpression of STAT3 and PPARg (which promote monocyte/macrophage differentiation and uptake of oxLDL) associated to inhibition of miR-130a-3p. Similarly, we demonstrated in our patients cohort the overexpression of CMKLR1 (chemokine receptor regulating the recruitment of inflammatory monocytes to sites of inflammation) associated with inhibition of miR-149–5p. The relationship between these identified target genes and specific miRNAs was further delineated in ex vivo studies.
**Conclusions:** We have identified novel microRNA-mRNA regulatory networks related to CVD in SLE, thus delineating a novel genetic control of the diverse biological processes and factors related to the cardiovascular pathology present in this autoimmune condition.
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## THU0244 NONINVASIVE ASSESSMENT OF MACROPHAGE ACTIVATION IN EXPERIMENTAL GLOMERULONEPHRITIS USING OPTICAL IMAGING WITH NEAR-INFRARED LIGHT SERVES AS A SURROGATE OF DISEASE ONSET

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**Background:** Glomerulonephritis (GN) represents a major cause of morbidity and mortality in many conditions such as systemic lupus erythematosus. The standard for diagnosing GN is through renal biopsy, but this is not performed uniformly across many centers. Furthermore, it is well established that early treatment of GN improves complication and survival outcomes (1,2). While proteinuria and/or hematuria is typically the first clinical sign of GN, immunologic changes in the kidney such as macrophage infiltration is observed well before. Thus, there is an unmet need to identify a noninvasive approach for recognizing GN, especially the preclinical stages. Recent advances in deep tissue imaging using probes detected by near-infrared (NIR) wavelengths have enabled the noninvasive probing of biologic activity. Activated macrophages that infiltrate the kidney early in GN express the papain-like cysteine protease cathepsin B (3). Thus, renal macrophage activation can be assessed using an NIR probe that becomes fluorescent upon cleavage by cathepsin B.
**Objectives:** We tested whether NIR optical imaging can assess renal macrophage activation as a noninvasive marker for early-stage GN.
**Methods:** GN was induced in 129 mice by nephrotoxic serum (NTS) delivered intravenously. Proteinuria was quantitated using albumin ELISA and chromogenic creatinine assay. Presence of renal macrophages was confirmed using FACS. NIR optical imaging of anesthetized mice was performed following intravenous administration of a cleavable sensor for cathepsin B and fluorescence intensity of kidney regions quantified using the Perkin Elmer FMT4000 fluorescence molecular tomography device.
**Results:** In mice with uninflamed kidneys, we confirmed the paucity of renal macrophages. Accordingly, there was minimal renal fluorescence signal as determined by fluorescent molecular imaging of cathepsin B activity. 3 days post-NTS administration, we observed a massive influx of macrophages into the kidney by flow cytometry, which correlated with a significant increase in renal fluorescence intensity signal in NTS mice compared to control mice. This was followed by the onset of proteinuria on days 5–7 in NTS mice.
**Conclusions:** Induction of GN by NTS caused significant macrophage infiltration, which could be detected noninvasively by a cathepsin B-activatable probe and NIR optical imaging. Importantly, detection of activated macrophages preceded the onset of proteinuria by several days. These data establish the proof-of-principle that NIR optical imaging may represent a translatable approach to detecting the preclinical stages of GN.
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## THU0245 INDIVIDUAL VERSUS COMBINED BLYS OR/AND APRIL NEUTRALIZATION REVEALS DEVELOPMENTAL PLASTICITY FOR PLASMA CELL SURVIVAL FACTOR REQUIREMENTS

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**Background:** The role of the TNF family cytokine APRIL (a proliferation inducing ligand) in the etiology and pathogenesis of autoimmunity is incompletely understood. The inhibition of B cell survival factors in the NZBWF1 mouse model of systemic lupus erythematosus (SLE) thus far revealed similar efficacy profiles for compounds that neutralize BLyS (B lymphocyte stimulator, also known as BAFF) only, or both BLyS and APRIL (1, 2). Strategies that exclusively target APRIL are sparse, mostly confined to genetic approaches and do not dissect its temporal requirements in disease progression.
**Objectives:** Comparison of single versus dual pharmacological inhibition of BLyS and APRIL in a mouse model for the human autoimmune disease SLE.
**Methods:** Reagents that neutralize either APRIL alone (an anti-APRIL antibody), BLyS alone (BAFFR-Fc), or both BLyS and APRIL (TACI-Fc), were administered to NZBWF1 mice after the onset of autoimmunity, but before nephritis occurred.
**Results:** The inhibition of APRIL alone was inefficient, in contrast to BLyS single antagonism, which instead delayed lupus symptoms, or to the dual inhibition of BLyS and APRIL, which arrested further disease development, autoantibody production, immune complex deposition in glomeruli and prevented onset of nephritis. While studying the plasma cell compartment over time in a T-dependent hapten/carrier immunization system, developmental plasticity in terms of survival factor requirements was observed. Moreover, a maturation window for plasma

cells was identified during which APRIL predominantly mediated survival. The results indicate that plasma cells are flexible in the use of APRIL or BLyS to support their survival in the bone marrow niche.

**Conclusions:** These results suggest that targeting plasma cells by neutralization of both BLyS and APRIL might be beneficial to prevent autoantibody-mediated damages in SLE.

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## THU0246 ROLE OF IGE IN THE PATHOGENESIS OF TUBULOINTERSTITIAL INFLAMMATION IN HUMAN LUPUS NEPHRITIS

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease, the most frequent severe manifestation of which is lupus nephritis (LuN). We have previously shown that tubulointerstitial inflammation (TII) is a usual feature of LuN with $T_{FH}$ cells participating in conjugates with B cells, and driving adaptive immune responses (1).

**Objectives:** To investigate the role of innate immune responses and plasmacytoid dendritic cells (pDCs) in LuN TII

**Methods:** We utilized multichannel immunofluorescent confocal microscopy, performed on 18 human biopsy samples of LuN and compared this to 7 cases of de-identified normal kidney (NK) biopsies. Control staining for Igk and IgE in addition to stains for CD20, BDCA2, IgE, and MxA (a protein, upregulated in IFN-a signature responses) were performed. To check for the presence of serum antibodies, matched human serum from 5 of the biopsies analyzed was assayed by means of ELISA for the presence of anti-dsDNA IgE antibodies.

**Results:** Control staining for Igk and IgE was performed with over 90% overlap between the two stains across NK and LuN samples. Stains for CD20, BDCA2, IgE, and MxA (a protein, upregulated in IFN-a signature responses) were performed and revealed the presence of activated $MxA^+$ pDCs in close association with IgE antibodies and $CD20^+$ cells in LuN but not NK tissue. IgE staining was present in the tubulointersititium in 16 of 18 LuN biopsies as compared to 1 out of 7 NK biopsies. Qualitative analysis indicated that tubulointerstitial staining was more prominent in all LuN cases as compared to the single NK case. Among the LuN biopsies studied, a germinal center was clearly present in one sample with the finding of IgE co-localized with B cells and surrounded by activated pDCs, similar to that seen in tonsil controls, raising the possibility of *in situ* production of IgE antibodies.

To check for the presence of serum antibodies, matched human serum from 5 of the biopsies analyzed was assayed by means of ELISA for the presence of anti-dsDNA IgE antibodies. 4 out of 5 (80%) of the samples had detectable levels of IgE anti-dsDNA antibody. Matched renal biopsies revealed interstitial staining with IgE in all of the cases.

**Conclusions:** Our data suggests that activated pDCs are present in a majority of LuN TII cases, and are closely associated with IgE antibodies and $CD20^+$ B cells. Furthermore, matched serum experiments showed the presence of detectable anti-dsDNA IgE antibodies in 4 of 5 cases. The finding of a germinal center in complex with IgE staining and activated pDCs raises the possibility of *in situ* production of IgE mediating LuN TII and participating in the pathogenesis of this disease, providing a link between the innate and adaptive immune responses and revealing a new role for IgE in autoimmunity.

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## THU0247 THE EFFECT OF HYDROXYCHLOROQUINE AND IRAK4 INHIBITION ON THE IFN-A AND TNF-A PRODUCTION INDUCED BY SLE RELATED IMMUNE COMPLEXES

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**Background:** Patients with systemic lupus erythematosus (SLE) have an ongoing interferon (IFN)-α production due to the stimulation of Toll-like receptors (TLR) 7 and 9 in plasmacytoid dendritic cells (pDCs) by immune complexes (ICs) containing self-derived nucleic acid. Such interferogenic ICs also trigger the production of TNF-α by several immune cells. Produced TNF-α in SLE contributes to organ inflammation such as nephritis and arthritis, but can also modulate the central autoimmune process as demonstrated by the induction of a lupus-like syndrome after anti- TNF-α treatment.

**Objectives:** To clarify the effect on IFN-α and TNF-α production by IC-stimulated immune cells from healthy individuals and SLE patients exposed to hydroxychloroquine (HCQ) and an IRAK4 inhibitor

**Methods:** pDC and NK cells were isolated from peripheral blood of healthy individuals and monocyte depleted PBMCs from SLE patients. Cells were stimulated with RNA-containing ICs (RNA-IC) comprised of SLE-IgG and U1snRNP particles in the presence or absence of HCQ, which blocks endosomal TLR7/9 activation, or a IL-1 receptor associated kinase (IRAK) 4 inhibitor (AZ13732754–004) acting downstream of TLR 7/9. IFN-α and TNF-α production was measured after 20 h by immunoassays or by intracellular staining using flow cytometry.

**Results:** RNA-IC induced IFN-α production selectively in pDC, whereas TNF-α was produced by both pDC and NK cells. Co-cultivation of pDC and NK cells enhanced the production of IFN-α (28-fold) and TNF-α (15-fold). TNF-α was rapidly produced by NK cells (5 h), but exhibited a delayed production in pDC (9 h). All IFN-α positive pDCs (13.6%) were TNF-α positive, whereas a fraction of pDCs (7.1%) were only TNF-α positive. HCQ completely inhibited the IFN-α and TNF-α production by pDCs, but did not affect TNF-α production by NK cells. Preliminary studies showed that cells from HCQ-treated SLE patients produced little IFN-α (mean 3 U/ml vs 27 U/ml in not HCQ-treated) in response to RNA-IC [NH1], whereas TNF-α production was maintained (mean 760 U/ml [NH2] vs 407 U/ml in not HCQ-treated). Inhibition of IRAK4 effectively blocked IFN-α production in both pDC (94%) and pDC-NK cell co-cultures (91%).

**Conclusions:** The IFN-α production induced by RNA-IC is completely blocked by HCQ and the IRAK4 inhibitor AZ13732754–004, suggesting that administration of an IRAK4 inhibitor could be an effective treatment strategy in SLE. The observation that HCQ inhibited the pDC derived TNF-α production, but not TNF-α released from other immune cells in SLE patients, may explain why HCQ treatment is only partially effective in SLE. In addition, our observation indicates that RNA-IC stimulated TNF-α production is induced by different mechanisms in pDC and NK cells. Further investigations are needed to clarify if IRAK4 inhibition has a broader inhibitory effect than HCQ on the production of proinflammatory cytokines, and if inhibition of IRAK4 should be explored as a therapeutic option in SLE.

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## THU0248 THERAPEUTIC INTEREST OF ANTI-CD3 AND ANTI-BAFF MONOCLONAL ANTIBODIES IN THE NOD MODEL OF SJÖGREN'S SYNDROME

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**Background:** BAFF is an essential cytokine for autoreactive B-cell activation, survival, and autoantibody secretion. Therapeutic interest of anti-BAFF therapy is under evaluation in primary Sjögren's syndrome (pSS) with encouraging data in an open clinical trial but it has not been evaluated in an animal model of the disease. In addition, T-lymphocytes, which represent the predominant cell population infiltrating salivary glands, also contribute to its pathogenesis. Targeting T-cells with anti-CD3 antibodies is efficacious to control diabetes in NOD mice, which also represent a relevant animal model of pSS, and in patients with type I diabetes.

**Objectives:** We aimed to evaluate the therapeutic effect of anti-CD3 and anti-BAFF antibodies and their potential synergy on dryness and salivary gland infiltrates in the NOD model of pSS.

**Methods:** Female NOD mice were studied between 10 and 20 weeks. 8 mice were treated with anti-BAFF antibodies, 8 with isotype control antibodies, 6 with the combination of anti-BAFF and anti-CD3 antibodies, 5 with anti-CD3 antibodies and 12 were not treated. Dryness was assessed by measuring the stimulated salivary flow at 10 and 20 weeks. Focus score was analysed at 20 weeks. Spleen, salivary glands and blood lymphocyte sub-populations were analysed using flow cytometry.

**Results:** Only anti-BAFF antibody therapy led to a significant increase in the salivary flow (10.4μL/20 minutes/g ±1.3 with anti-BAFF antibodies, 5.7±2.7 with isotype control antibodies, p=0.003, 5.5±1.7 in non-treated mice, p=0.002) and resulted in the decrease in salivary gland infiltrates (focus score of 1.75±0.5 with anti-BAFF antibodies, 4.0±0 with isotype control antibodies, p=0.028, 4.6±1.14 in non-treated mice, p=0.015). Inhibition of BAFF resulted in a marked decrease of blood, spleen and salivary B-cells (proportion of B-lymphocytes out of total number of lymphocytes in salivary glands: 1.0%±0.9 with anti-BAFF antibodies, 7.6%±2.6 with anti-CD3 antibodies, 0.3%±0.2 with combined treatment and 12.5%±2.3 with isotype control). With anti-BAFF and/or anti-CD3, an increase in salivary glands Foxp3+ regulatory T-cells was observed (proportion of FoxP3+ T cells among total number of CD4+ T cells: 28.7%±5.9 with anti-BAFF antibodies, 27.6%±1.8 with anti-CD3 antibodies, 27.7%±1.9 with combined treatment and 20.7%±1.0 with isotype control). In addition, salivary CD3+CD4-CD8- double negative T-cells markedly increased after anti-BAFF treatment (41.0%±5.5 with anti-BAFF antibodies, 26.4%±7.8 with anti-CD3 antibodies, 37.7%±8.9 with combined treatment and 24.8%±13.5 of T-lymphocytes CD3+ with isotype control). Salivary double negative CD4-CD8- T-cells were inversely correlated with the focus score, which suggests their protective role.
**Conclusions:** Anti-CD3 therapy was not efficacious nor synergic with anti-BAFF. Anti-BAFF therapy resulted in a marked improvement of dryness and salivary gland infiltrates in the NOD model of pSS. Interestingly, BAFF inhibition resulted in the increase of regulatory T-lymphocyte populations, which might contribute to the therapeutic effect of this strategy. This study strengthens the rationale to target BAFF in patients with pSS.
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## THU0249 FUNCTIONAL CLUSTERS OF AUTOANTIBODIES TARGETING TLR AND SMAD PATHWAYS DEFINE NEW SUBGROUPS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** The molecular targets of the vast majority of autoantibodies in systemic lupus erythematosus (SLE) are unknown. Multiple recent failures of new therapies in SLE clinical trials demonstrate the need for improved classification of SLE based on pathogenesis.
**Objectives:** To identify novel autoantibodies in SLE for the development of an improved assay for diagnosis and identification of autoantibody clusters for classification of SLE subgroups.
**Methods:** We used a baculovirus-insect cell expression system to create an advanced protein microarray with 1545 full-length human proteins. All proteins were expressed with a biotin carboxyl carrier protein (BCCP) folding tag, so that only correctly folded proteins were bound to the array. Sera were assayed from three independent cohorts of SLE individuals (total n=277) and age, gender and ancestry-matched controls (n=280).
**Results:** We confirmed 116 proteins (FDR<0.01) as autoantigens in SLE, of which 13 had been previously reported, hence we identified 103 novel SLE autoantigens. The 116 SLE autoantigens clustered into four distinct groups by unsupervised hierarchical clustering. The presence of these four clusters was confirmed by principal component analysis. Protein-protein interaction network analysis showed that the autoantigens in each of the four clusters were functionally linked. The original SLE autoantigens Ro60, La, and SMN1/Sm complex formed a distinct antigen cluster (SLE1a), extended by a second cluster (SLE1b) of proteins involved in RNA/DNA/chromatin processing. The largest two clusters of novel autoantigens revealed two networks of interconnected proteins: the receptor-regulated SMAD2, SMAD5 and proteins linked to TGF-β signalling (SLE2); and the TLR adaptor MyD88 and multiple key proteins involved in TLR signalling, regulation of NF-κB, and lymphocyte development (SLE3). ROC curve analysis of antibody biomarker panels showed improved diagnostic sensitivity/specificity compared to conventional anti-nuclear (ANA) and anti-dsDNA antibody tests. Of particular clinical importance, autoantibodies from cluster SLE1b and SLE3 enabled detection of SLE individuals who were negative for ANA or anti-dsDNA antibody tests.
**Conclusions:** Novel autoantibodies, especially from cluster SLE1b and SLE3, identified in this study may improve diagnosis of SLE, through identification of SLE patients who are negative for ANA or dsDNA antibodies. SLE patients clustered into four groups with autoantibody responses against networks of proteins with related cellular or immunological functions, suggesting that different pathogenic mechanisms underlie the four SLE subgroups. Thus the autoantigen clusters may be clinically useful for stratifying SLE patients for specific therapies: SLE patients with TLR signaling autoantigens might preferentially benefit from B cell targeting therapies; SLE patients with autoantibodies against SMAD2/5 and related pathway autoantigens might benefit from TGF-β targeting therapies.
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## THU0250 DYSREGULATION OF AUTOPHAGY IN SYSTEMIC LUPUS ERYTHEMATOSUS IS CORRELATED TO TRANSCRIPTIONAL INTERFERON SIGNATURES AND PROVIDES CANDIDATE BIOMARKERS

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**Background:** Autophagy, a lysosome-mediated catabolic process that allows cells to degrade unwanted cytoplasmic constituents and to recycle nutrients, is also involved in innate and adaptive immune responses. It is induced by different stress signals including cytokines such as interferons (IFN). In systemic lupus erythematosus (SLE), a pivotal role for IFN is supported by gene expression studies. A dysregulation of autophagy has been recently reported in SLE patients and hydroxychloroquine (HCQ), its main treatment, is an inhibitor of autophagy.
**Objectives:** The aim of this study was to evaluate autophagy pathways and identify autophagy-related (A-R) biomarkers in SLE patients.
**Methods:** After identification of A-R transcripts (PubMed, KEGG), candidate A-R transcripts were selected through a data-driven approach. Publicly available datasets related to "human/blood/SLE" gene expression profiles and restrained to types of platforms (illumina or affymetrix) as well as tissue (whole blood (WB) or PBMC) were retrieved from GEO database. Candidate A-R transcripts corresponded to those with a significant differential expression between SLE patients (n=157) and matched healthy controls (adjusted p-value <0.05) in the LUPUCE cohort dataset. Fold change (FC) analyses across multiple SLE datasets and interferon inducibility (interferome database) of these candidates allowed the selection of a final panel. Finally, the relative expression of this panel of A-R transcripts (ΔΔCT) was determined by RT-qPCR on WB samples from SLE patients (n=32) and their controls (n=14). Results were correlated with clinical (SLEDAI score) and biological (including IFN modular transcriptional signatures) characteristics as well as treatments of SLE patients (Brown-Mood test).
**Results:** Overall, 97 A-R transcripts were identified through the literature search and 12 SLE datasets from GEO database (WB n=8, PBMC n=4). Among SLE patients from the LUPUCE cohort study, 16 genes (corresponding to 23 A-R Transcripts) were differentially expressed, of which 9 with a significant FC (>1.3): 8 overexpressed (RGS19, MAP1LC3B, ATG7, RAB24, APP, TGM2, TNFSF10/TRAIL and STAT1) and 1 underexpressed (CASP8). The expression levels of a panel of 5 of these candidates (TRAIL, STAT1, CASP8, WIPI1, ATG7) were determined by PCR and only TRAIL and STAT1 exhibited significant overexpression in SLE patients compared to controls (p=0.0105 and 0.0001 respectively). For TRAIL, expression was significantly lower in patients with completely inactive disease (SLEDAI=0) compared to other SLE patients with moderate to important disease activity (p=0.0338). For these 2 genes, no clinical of biological differences were observed between high expressers (> mean ΔCT ± 2SD) and other SLE patients, except that high STAT1 and TRAIL expressers had significantly higher modular transcriptional type I and II IFN signatures, and a trend for being less treated by HCQ was observed for high STAT1 expressers (p=0.075).
**Conclusions:** An exploratory transcriptome data-driven approach identified autophagy-related transcripts as candidate biomarkers in SLE, and suggests that autophagy is induced by type I IFN via the JAK1-STAT1 pathway and may present a potential therapeutic target in this disease.
**Disclosure of Interest:** None declared
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## THU0251 ABSENCE OF CASPASE-ACTIVATED DNASE AFFECTS NETOSIS AND ITS MODULATION OF DENDRITIC CELL ACTIVATION IN A SEX-DEPENDENT MANNER

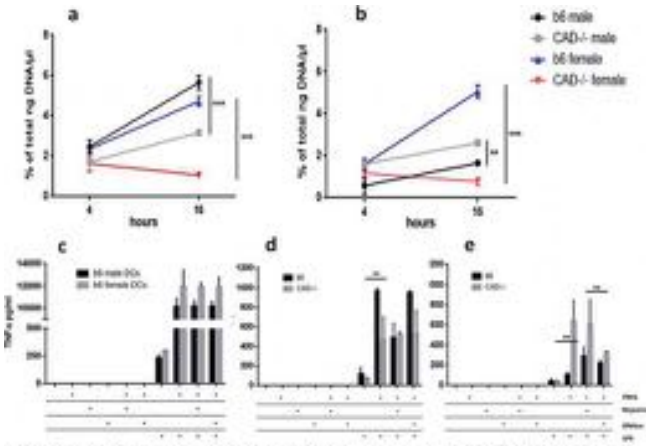
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**Background:** NETosis is an antimicrobial cell death program of neutrophils characterized by the release of Neutrophil Extracellular Traps (NETs). NETs consist of processed chromatin associated with cytoplasmic proteins and granules. NETs behave as alarmins and can directly activate Dendritic Cells (DCs) or modulate their LPS-mediated activation. Interestingly recent data demonstrate a role for NETosis in Systemic Lupus Erythematosus (SLE) and other autoimmune diseases. The underlying mechanisms are not completely clear, but defective NET-DNA degradation seems to be important. Caspase-activated DNAse (CAD) is an intracellular DNAse activated by caspases during apoptotic cell death whose absence leads to the lupus-like disease in genetically predisposed mice.
**Objectives:** Our aim was to determine the role of CAD in NETs release.

Specifically whether its absence may influence LPS-mediated DCs activation via NETs modulation. We also investigated weather NETosis in the absence of CAD was sex-biased. The latter in view of the relevance of sex in lupus

**Methods:** Neutrophils from the bone marrow of C57bl/6 (b6) and b6.CAD (CAD)–/– mice were treated with 50 nM phorbol myristate acetate (PMA) to induce NETosis. NET-DNA was detected in supernatants by spectrophotometry after 4 and 16 hours. Pretreatment with heparin (50 ug/ml) or physiological concentrations of DNAse (20 ng/ml) was used to respectively neutralize NET-histones and degrade NET-DNA. NETting neutrophils were also visualized and counted by Immunofluorescence. Bone marrow-derived Dendritic Cells (BMDCs) were co-cultured for 20 hours with neutrophils previously treated for 4 hours as mentioned before, in presence or absence of 25 ng/ml LPS. Neutrophils and BMDCs were also treated separately as controls. DCs activation was studied by quantifying TNF-alpha from supernatants by ELISA and by staining cells were stained for flow cytometry to detect CD11b+CD11c+CD86+ DCs.

**Results:** We found that in CAD–/–, NET-DNA was lower than b6 at 4 and 16 hours, and DNAse was not as effective as in b6 in degrading NET-DNA. NETting neutrophils didn't produce any detectable TNF-alpha. LPS-mediated DC activation was enhanced in the presence of NETting neutrophils from b6 males and CAD–/– males and females. Interestingly we found that for b6 females, heparin pretreatment increased the response. In contrast for CAD–/– females, the response was reduced by DNAse. Finally in males, NETs in the absence of CAD led to lower LPS-mediated DC activation. The latter showed decreased activation only with heparin pretreatment.




NET-DNA from $5x10^5$ neutrophils /well in 24-well plates after treatment with PMA 50 nM alone (a) and 30' pretreatment with DNAse 20 ng/ml (b). TNF-α detected from $5x10^5$ DCs cultured alone (c) and with $5x10^5$ pre-treated neutrophils in males (d) and females (e): neutrophils were treated for 4 hours with PMA 50 nM with or without heparin 50 µg/ml or DNAse 20 ng/ml; after 4 hrs pre-treatment, LPS 25 ng/ml was added and supernatants were processed after 20 hours.

**Conclusions:** We show that CAD activity is important for the proper release of NETs, its absence confers resistance to DNAse and its role is sex-biased. Indeed we show that NETs protect only b6 females from enhanced LPS-induced DC activation, and activation is significantly higher in absence of CAD and resistant to NET inhibition. Finally in males, histones seem to have a significant role in DC activation in b6, while in females the role of DNA seems to be more relevant in both strains. Further studies are needed to characterize the molecular features of these differences.

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## THU0252 DECREASED EXPRESSION OF IMMUNOREGULATORY PROTEIN PROGRAMMED DEATH LIGAND-1 (PD-L1) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PLACENTA

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**Background:** The increased rates of preeclampsia, pre-term birth, and intra-uterine growth restriction in SLE pregnancy are only partially explained by the vascular effects of anti-phospholipid antibodies. SLE patients themselves are on average born preterm, suggesting a heritable defect in maternal-fetal tolerance. PD-L1 is one candidate gene, in that it has been implicated in the both autoimmunity and maternal-fetal tolerance: PD-L1 is expressed on healthy antigen presenting cells to downregulate inflammatory responses, and also on placental trophoblasts at the maternal-fetal interface, where it inhibits alloreactive T cells. Peripheral blood antigen presenting cells from SLE patients are deficient in PD-L1 expression compared to remission or healthy controls. Little is known about placental costimulatory molecules in women with autoimmune diseases.

**Objectives:** This study tested the hypothesis that placental PD-L1 expression is abnormally regulated in SLE pregnancy.

**Methods:** Expression of PD-L1 was quantified by immunohistochemistry in placentas from 6 SLE patients, 7 rheumatoid arthritis patients (RA) and 9 healthy control women obtained from the Global Alliance for the Prevention of Prematurity and Stillbirth Repository. PD-L1 mRNA expression was assayed by RT-PCR and normalized to GAPDH expression. PD-L1 on peripheral CD14+/CD11c+ monocytes was assayed by flow cytometry. Significant differences between groups were tested by T-test.

**Results:** By immunostaining, PD-L1 expression in SLE placentas was low compared to control groups. PD-L1 mRNA expression correlated with protein expression, although the differences were not significant. A limited analysis of CD45 and CD43 co-expression suggested that a subset of maternal T lymphocytes expressed PDL-1 but that fetal cells did not. The mean gestational age was lower in SLE (27 weeks, range 18–39) compared to RA (38, range 29–40) and controls (34, range 19–40), but there was not a strong correlation between gestational age and PD-L1 expression ($R^2$ 0.18). Three SLE patients exhibited placental insufficiency, with relatively low PD-L1 expression (18 compared to 24 in healthy SLE). On peripheral blood monocytes, PD-L1 expression was low in juvenile SLE patients compared to healthy controls (55% of SLE monocytes v. 93% of healthy monocytes, p=0.001). Although in the normal range, mothers of SLE patients also had relatively low PD-L1 expression compared to control mothers (87% v. 94%, p=0.04).

Table 1. Relative mean PD-L1 expression in placenta

| | | Controls | SLE | P* | RA | P** |
|---|---|---|---|---|---|---|
| Protein | Mean | 39 | 21 | 0.012 | 37 | 0.63 |
| | Fetal | 39 | 16 | | 36 | |
| | Maternal | 41 | 23 | | 34 | |
| mRNA | | 109 | 72 | 0.21 | 300 | 0.08 |

*SLE versus controls; **RA versus controls.

**Conclusions:** Placental PD-L1 expression is dysregulated in women with SLE. Inadequate expression of PDL-1 in the placentas of patients with SLE could result in loss of maternal-fetal tolerance, *contributing to the high rate of pregnancy complications in SLE.*

**Disclosure of Interest:** None declared

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## THU0253 A POLYMORPHISM UPSTREAM MIR1279 GENE IS ASSOCIATED WITH PERICARDITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND CONTRIBUTES TO DEFINITION OF A GENETIC RISK MODEL PROFILE

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**Background:** MicroRNAs have emerged as important regulators of gene expression in post-transcriptional level. These are a class of small non-coding molecules, which could contribute to the pathogenesis of autoimmune diseases, including systemic lupus erythematosus (SLE). Recently, it has been demonstrated that the rs1463335 SNP in MIR1279 gene region was associated with decreased levels of TRAF3IP2 expression. We have previously demonstrated an association between TRAF3IP2 polymorphisms and SLE, especially with the development of pericarditis (1).

**Objectives:** Thus, we aimed to investigate the role of the MIR1279 rs1463335 SNP in SLE, with particular regards to pericarditis development. Furthermore, we aimed at constructing a pericarditis genetic risk profile for SLE patients considering others risk alleles that we had previously found associated with pericarditis development (1, 2).

**Methods:** We recruited 315 Italian SLE patients and 278 healthy controls. Rs1463335 SNP, located upstream MIR1279 gene, was analyzed by allelic discrimination assay. MIR1279 gene was further sequenced in 50 patients. Genotyping of rs7574865 (STAT4), rs2542151 (PTPN2), rs2241880 (ATG16L1) and rs33980500 (TRAF3IP2) SNPs were also performed. A case/control association study and a genotype/phenotype correlation analysis were performed and a risk profile model for pericarditis in SLE was built.

**Results:** The full sequencing of the MIR1279 gene in SLE patients did not reveal any novel or known variation. The variant allele of the rs1463335 SNP was significantly associated with susceptibility to pericarditis (P=0.017, OR=1.67). Patients carrying the A allele were more susceptible to develop the pericarditis with an allele-additive effect: patients carrying the variant homozygous genotype have a higher risk than patients carrying the heterozygous genotype (P=0.013, OR=3.28 vs P=0.06, OR=2.4, respectively). A risk profile model for pericarditis considering the risk alleles of MIR1279 and other three genes (STAT4, PTPN2 and TRAF3IP2) showed that patients with 4 or 5 risk alleles have a significantly higher risk to develop pericarditis (OR=4.09 with P=0.001 and OR=6.04 with P=0.04 respectively). Anti-Sm antibodies were the only parameter associated

with the development of pericarditis. A multivariate analysis by binary regression analysis, considering as dependent variable the presence/absence of pericarditis and as independent variables all the studied SNPs associated with pericarditis, was performed. In a stepwise approach including anti-Sm, MIR1279, STAT4, TRAF3IP2 and PTPN2 SNPs, this model explains about 25% ($R^2$ Cox &Snell) of the variability involved in the susceptibility to pericarditis.
**Conclusions:** We describe for the first time the contribution of a MIR1279 SNP in pericarditis development in SLE patients and a genetic risk profile model useful to identify patients more susceptible to develop pericarditis in SLE. This approach could help to improve the prediction and the management of this manifestation.
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## THU0254 IN VIVO UBIQUINOL (COQ10) SUPPLEMENTATION REDUCES THE ATHEROTHROMBOTIC STATUS OF ANTIPHOSPHOLIPID SYNDROME PATIENTS

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**Background:** Previous studies have demonstrated the presence of an oxidative perturbation in antiphospholipid syndrome (APS) patient's leukocytes, which was directly related to an inflammatory and proatherothrombotic status, and relied on alterations in mitocondrial dynamics and metabolism, which was prevented and/or reversed by in vitro treatment with coenzyme Q10 (CoQ10).
**Objectives:** 1) To investigate the beneficial effects of in vivo ubiquinol (Q, reduced form of CoQ10) supplementation on atherothrombosis prevention in APS patients, through the implementation of a prospective, randomized, double-masked, placebo-controlled study. 2) To characterize the cellular and molecular mechanism involved.
**Methods:** The study was conducted on 32 APS patients randomized to receive either Q (200 mg/day) or placebo for one month. Blood was drawn at time 0 and at the end of the treatment. Studies were performed in plasma and purified leukocyte subsets. Endothelial activity was evaluated by Laser-Doppler measurement of post ischemic reactive hyperemia. Carotid intimae media thickness (CIMT) was measured as atherosclerosis marker.
**Results:** Twenty nine out of the 32 APS patients completed the intervention, which increased significantly plasma Q levels. Endothelial function improved notably. Q treatment decreased expression of a number of protrombotic and proinflammatory mediators, and produced a reduction in both, the levels of peroxides and the percentage of monocytes with altered mitochondrial membrane potential ($\Delta\Psi m$). Electron Microscopy analyses indicated that Q treatment promoted an increase in monocytes' mitochondrial size. MiRNA profiling by Nanostring technology revealed 22 microRNAs reduced in APS patients. Among them, 10 were upregulated by effect of Q treatment. Functional classification of those miRNAs revealed a preponderance of target mRNAs involved in cardiovascular disease. Gene profiling showed differential expression of 33 atherosclerosis-related genes in APS patients, of which 16 were changed by effect of Q. Using bioinformatic tools, interaction networks of those genes and microRNAs were also identified (i.e. downregulation of PDGFB, IL-1A and SERPINE1 was associated to upregulation of miR150–5p; in parallel, downregulation of TGFB2 and MMP-1 was linked to the upregulation of miR-145–5p).
Correlation studies demonstrated that reduced expression prothrombotic and proinflammatory mediators, and increased miRNA expression, were related to the increased plasma Q levels and improved endothelial function. Q effects were particularly relevant in APS patients showing pathologic CIMT and thrombotic recurrences, who showed a better response to Q treatment.
**Conclusions:** 1) Q supplementation significantly improved endothelial function, and reduced mitochondrial dysfunction, oxidative stress and the expression of prothrombotic/proinflammatory proteins. 2) Underlying epigenetic mechanisms seem to be involved. Our results support the potential impact of Ubiquinol in the prevention of atherothrombosis in APS patients.
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**Disclosure of Interest:** None declared
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## THU0255 IDENTIFICATION OF NOVEL REGULATORY NETWORKS RELATED TO ATHEROTHROMBOSIS IN MONOCYTES FROM ANTIPHOSPHOLIPID SYNDROME THROUGH INTEGRATED ANALYSIS OF MICRORNA/MRNA/PROTEIN EXPRESSION PROFILES

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**Background:** MicroRNAs have a functional role in numerous physiological and pathological processes by regulating the expression of their target genes. A number of miRNAs have been involved in the pathogenesis of antiphospholipid sindrome (APS). However, the miRNA-mRNA regulatory network involved in the regulation of the proatherothrombotic status in APS patients is far from being fully understood.
**Objectives:** To identify and characterize novel regulatory miRNA/mRNA/protein networks related to atherothrombosis in monocytes from APS.
**Methods:** Twenty one APS patients and 27 healthy donors were included in the study. A multi-step approach combining microarray miRNA (Nanostring technology) and mRNA expression profile (44K, Agilent, one color) and bioinformatics analysis was adopted to identify the APS specific miRNA-mRNA regulatory networks. Target genes of the differentially expressed miRNAs were identified by using the Igenuity Pathway Analysis Software (IPA). To recognize the putative miRNA-mRNA target pairs and interaction networks, the subsets of miRNAs and mRNAs were characterized by the miRNA Target Filter tool of IPA. The resulting identified interactions were validated by RT-PCR and western blot on the whole cohort of APS patients and by functional analyses using miRNA overexpression experiments in monocytes purified from APS patients.
**Results:** Comparative analysis of the mRNA profiles showed significantly different expressions of 519 genes in APS monocytes (352 up-regulated and 167 down-regulated). Functional analysis by using IPA showed that about 33% of altered genes were involved in inflammation and cardiovascular disease (CVD). Comparative analysis of the miRNA profiles showed significantly different expressions of 22 miRNAs in APS monocytes (3 up-regulated and 19 down-regulated). Functional IPA analysis showed that miRNAs altered were mainly related to connective tissue disorders, inflammatory response and reproductive system disease. A total of 56 genes were inversely correlated, and predicted as CVD-related target genes of 19 differentially expressed miRNAs. An interaction network of those genes and miRNAs differentially expressed in APS monocytes were also identified. Interestingly, a few number of miRNAs (i.e. miR-30b, miR-145, miR-199, miR-17, miR-26a) regulate idependently multiple gene targets belonging to the cluster of genes related to inflammation and atherogenesis, (i.e. VEGF, TGFβ, LDLR, PPARD, IL1, IL2, IL12, VCAM1, ITGA, CACNB2, MMP3). Transfection assays validated regulatory relationships between those miRNAS and a number of targets at both RNA and protein levels.
**Conclusions:** Our system biology approach introduced and nominated 1) important deregulated miRNAs involved in atherothrombosis in monocytes from APS; 2) Significant and confident deregulated mRNAs which were anti-correlatively targeted by deregulated miRNAs; and 3) dysregulated proteins in association with deregulated miRNA-mRNAs interactions. These results introduce a possible mechanism of function of deregulated miRNAs and mRNAs in atherothrombosis-related APS that could be used as potential therapeutic targets.
**Acknowledgement:** Supported by FIS (PI01333/2015) and CTS-7940.
**Disclosure of Interest:** None declared
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## THU0256 COMPLEMENT C3 EXACERBATES TLR7-MEDIATED SKIN INFLAMMATION BUT NOT SYSTEMIC AUTOIMMUNITY

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**Background:** Short–term topical application of a Toll-like receptor 7 (TLR7) agonist, Imiquimod (IMQ), is a widely used murine model of psoriasis. Recently long–term epicutaneous application (4–8 weeks) of IMQ has been shown to elicit lupus-like manifestations. Importantly the topical application of IMQ induced more potent systemic effects than the intraperitoneal administration, indicating that activation of the TLR7-signalling in the skin plays a key role.
**Objectives:** Since complement activation is known to have a crucial role in the regulation of local inflammation and in the pathogenesis of lupus, we investigated whether C3 played a role in the induction of the cutaneous lesions as well as in the lupus-like syndrome triggered by IMQ
**Methods:** BALB/c wild-type (WT) and C3-deficient (BALB/c.$C3^{-/-}$) mice were treated with topical application of 5% IMQ cream for either 7 consecutive days (short-term) or 3 days /week for 11 weeks (long-term).
**Results:** After 7 days, skin thickening (ear thickness at day 7: WT 60.14 mm ± 1.625, n=7, vs BALB/c.$C3^{-/-}$ 50.88 mm ± 2.460, n=8, p value=0.0094) and local neutrophil recruitment (cell number at day 7: 52.3±6.736, n=7, vs BALB/c.$C3^{-/-}$ 30.33±4.192, n=7, p value=0.0170) were significantly reduced in

the absence of C3. The expansion of IL17$^+$ $\gamma\delta^+$ T cells in the draining lymph nodes was also significantly impaired (day 7: WT 59.06% ± 2.961, n=7, *vs* BALB/c.C3$^{-/-}$ 46.21% ± 2.023, n=8, p value=0.0029*)*. Long-term IMQ treatment resulted in the development of similar low titres of auto-antibodies in both groups of mice (anti-RNP: WT 29.75±11.33, n=5 *vs* BALB/c.C3$^{-/-}$ 97.28±41.53, n=5, p=0.1553; anti-ssDNA: WT 9.252±3.367, n=5, *vs* BALB/c.C3$^{-/-}$20.70±12.03, n=5, p=0.386; anti-chromatin: WT 12.59±7.001, n=5, *vs* BALB/c.C3$^{-/-}$ 16.72±12.60, n=5, p=0.781). In addition, the kidney histology scored by a trained histopathologist evidenced no difference in the glomerulonephritis severity.

**Conclusions:** Collectively, these data suggest that C3 acts as a potential mediator of IMQ-induced skin inflammation. However, the different local tissue response does not result in an altered autoimmune response in the C3-deficient mice. The study of the involvement of other complement components is currently in progress.

**Disclosure of Interest:** None declared

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## THU0257 DIAGNOSTIC ACCURACY OF MULTIPLEX BEAD-BASED IMMUNOASSAY FOR ANTINUCLEAR ANTIBODIES (ANA) TESTING IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** ANA are a large family of autoantibodies directed at various cellular constituents. The measurement of ANA is a useful tool to confirm the diagnosis of SLE. New automated bead-based arrays can simultaneously and rapidly determine a profile of multiple ANA. Clinical performance of multiplexed technologies for detection of ANA specificities in SLE is not validated.

**Objectives:** To evaluate the diagnostic accuracy of multiplex bead-based immunoassay for the detection of ANA profile in SLE.

**Methods:** We studied 94 patients (pts) (80 F, age 35.9 [16.0–65.0] years, disease duration 113.5 [2.0–576.0] months) with SLE (ACR criteria, 1997), 50 pts with other systemic autoimmune rheumatic diseases, 20 pts with non-autoimmune rheumatic diseases and 30 healthy controls. Serum samples were analyzed for SLE-associated ANA (anti-dsDNA, anti-Sm, anti-chromatin, anti-SS-A/Ro 52 kDa and 60 kDa, anti-SS-B/La, anti-RNP-70, anti-ribosomal P) using automated multiplex bead-based immunoassay system BioPlex® 2200 (ANA Screen; Bio-Rad Laboratories Inc., USA). The following ANA values were considered positive: anti-dsDNA≥10.0 IU/mL, other antigen-specific ANA ≥1.0 AI (Antibody Index).

**Results:** The detection of anti-dsDNA, anti-Sm, anti-ribosomal P antibodies by BioPlex assay demonstrated the highest overall specificity (0.95, 0.97, 0.99, respectively), and positive likelihood ratio (LR) (10.40, 9.67, 15.0, respectively) for diagnosis of SLE (Table 1). BioPlex assay for anti-RNP-70, anti-SS-A/Ro, anti-chromatin antibodies was a useful diagnostic test in SLE (positive LR 2.80, 2.31, 4.15, respectively). Anti-SS-B/La antibodies testing had no value in SLE diagnosis (positive LR 1.20). The frequency of 1 ANA in SLE pts was 79.8%,2 ANA – 28.7%, 3 ANA – 15.6%, 4 ANA – 10.6%, 5 ANA – 5.3%, 6 ANA – 1.1%. Simultaneous detection of ≥3 ANA increased the specificity of multiplex immunoassay up to 0.98–1.00, and positive LR – to a maximum value.

Table 1
Diagnostic accuracy of multiplex bead-base immunoassay for ANA detection in SLE (n=94)

| Antibody | Sensitivity | Specificity | Positive LR | Negative LR |
|---|---|---|---|---|
| anti-dsDNA | 0.52 | 0.95 | 10.40 | 0.51 |
| anti-Sm | 0.29 | 0.97 | 9.67 | 0.73 |
| anti-chromatin | 0.54 | 0.87 | 4.15 | 0.52 |
| anti-SS-A/Ro | 0.37 | 0.84 | 2.31 | 0.75 |
| anti-SS-B/La | 0.12 | 0.90 | 1.20 | 0.98 |
| anti-RNP-70 | 0.14 | 0.95 | 2.80 | 0.91 |
| anti-ribosomal P | 0.15 | 0.99 | 15.00 | 0.86 |

**Conclusions:** The detection of ANA profile by multiplex bead-based immunoassay has a high specificity and positive likelihood ratio for diagnosis of SLE. Additional investigations are required to evaluate the usefulness of multiplex ANA testing for monitoring disease activity and for determining prognosis of SLE.

**Disclosure of Interest:** None declared

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## THU0258 DRVVT AND APTT RATIOS FOR LABORATORY DETECTION OF LUPUS ANTICOAGULANT – TO NORMALIZE OR NOT TO NORMALIZE THAT IS THE QUESTION

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**Background:** The laboratory testing of lupus anticoagulant (LA) is based on the guidelines given by ISTH-SSC and CLSI. Both guidelines advocate using diluted Russel viper venom (dRVVT) test in combination with activated partial thromboplastin time (aPTT) assay and the results should be expressed as ratio to the pooled normal plasma (PNP). Since reagents used for testing may differ between lots as well as between manufacturers, those guidelines recommend normalization of the results. However some authors suggest not using the normalization step to decrease the complexity of already very complicated LA testing.

**Objectives:** To investigate how the normalization of dRVVT and aPTT-ratios based on PNP reference values affects the reference ranges and the number of positive and negative results for the presence of LA.

**Methods:** Double centrifuged plasma samples from healthy subjects (N=49) were analyzed on Behring Coagulation System BCS XP. All samples were analyzed with the dRVVT-based assay, using LA screen and LA confirm from Life Diagnostics, as well as with aPTT assays - PTT-LA from Diagnostica Stago as screen and Actin FS from Siemens Healthcare Diagnostics as the confirm step. Ratios were calculated for both dRVTT and aPTT before and after normalization using mean of run-specific PNP value. Our laboratory reports the dRVVT-ratio and aPTT–ratio as: negative <1.2, weakly positive 1.2–1.4, and positive >1.4. We also investigated 362 previously analyzed samples to figure out how the normalization step influences the results.

**Results:** Ratios for PNP were 1.06±0.01 and 1.26±0.02 for dRVVT and aPTT respectively. Out of 49 healthy subjects without the normalization step, 34 would have been reported as negative (15 as weakly positive) with dRVVT and 3 would have been reported as negative (8 as positive and 38 as weakly positive) with aPTT. After normalization 45 samples would have been reported as negative (3 and 1 as weakly positive with dRVVT and aPTT respectively). The normalization step led to a decrease in the amount of positive diagnosis (from 58% to 44% and 77% to 41% using dRVVT and aPTT respectively) and at the same time the number of samples tested negative increased (7% to 15% and 6% to 34% for dRVVT and aPTT respectively).

**Conclusions:** Our findings indicate that without the normalization step only 6% of healthy subjects would be reported as negative for the presence of LA. The introduction of the normalization step decreases the number of false positive results and this is particularly true for the aPTT based assay. Since false positive results lead not only to unnecessary patients' discomfort, but also generate an increased cost due to prolonged follow up of the patients, an additional step using normalization which is relatively simple and inexpensive is definitely justified for the laboratory diagnosis of LA.

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**Disclosure of Interest:** None declared

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## THU0259 INDUCTION OF APOPTOSIS AND AUTOPHAGY IN CIRCULATING PBMC BY MICROPARTICLES FROM PATIENTS WITH SYSTEMIC LUPUS ERYTEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by heterogeneous clinical manifestation and a complex pathogenesis. Lymphocytes from patients with SLE display multiple alterations, including increased cell activation, abnormal apoptosis and impairment of autophagic pathway. Recently, evidence from genetic, cell biology and animal models suggested that autophagy, a major pathway for organelle and protein turnover, may play a pivotal role in the occurrence and development of SLE. Some studies showed altered profile of circulating microparticles (MPs) in SLE patients. These MPs are released constitutively and may increase as a result of cellular activation and apoptosis. Originally considered as inert debris, MPs are now known to display diverse pro-inflammatory and pro-thrombotic activities, and they are implicated in the intercellular communications. MPs can influence the course of rheumatic and other immune-mediated diseases.

**Objectives:** The aim of our study was to evaluate the possible role of MPs purified from SLE patients on the modulation of apoptosis and autophagy in *peripheral blood mononuclear cells* (*PBMCs*) isolated from healthy donors.

**Methods:** PBMCs from healthy donors were isolated by Ficoll-Hypaque density-gradient centrifugation, cultured and treated with 0.5,2.5,5 *10$^6$ MPs purified by 10 sera of active SLE for 16 h. Apoptosis was measured using FITC-conjugated annexin V (AV) and a propidium iodide (PI) apoptosis detection kit. Acquisition was performed on a FACS Calibur. Autophagy was measured by Western blot for LC3II.

**Results:** MPs appeared capable of inducing apoptosis. Indeed, PBMCs showed significantly higher apoptosis if treated with MPs compared with untreated cells (percentage of apoptotic cells treated with 5, 2.5 and 0.5*10$^6$ MPs: 15, 10, 9 *vs.* 7%, *P*=0.0001, P=ns, P=ns, with respectively). Moreover, MPs increased autophagy in a dose response manner (LC3-II/β-actin ratio: 1.2, 1, 0,6 *vs.* 0.5, with 5, 2.5 and 0.5*10$^6$ MPs, respectively *P*=0.0001).

**Conclusions:** We demonstrated that MPs from SLE patients induce apoptosis in PBMCs, thereby possibly decreasing the number of circulating leucocytes. The mechanisms underlying such phenomena are not known. Some authors suggested that MPs, through the arachidonic acid pathway, may induce apoptosis.

Indeed, this pathway, together with the sphingomyelinic, increase the concentration of ceramide, thus leading into apoptosis mediated by the activation of caspase 8 and by the release of downstream pro-apoptotic factors. Moreover, available data do not exclude the possibility that components of MPs other than arachidonic acid, may also contribute to the ceramide-mediated apoptosis. Finally, this is the first study addressing the relations between MPs and autophagy, suggesting an increase of this cellular event after exposure to MPs. Since an augmented autophagy has been implicated in autoimmunity, it could be of interest to target MPs in order to re-balance the autophagic processes.

**Disclosure of Interest:** None declared

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## THU0260 IL-25 AXIS IS ACTIVATED AND ASSOCIATED WITH AN ILC2 AND M2 INFLAMMATORY STATE IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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**Background:** Type 2 innate lymphoid cells (ILC2) and M2 polarized macrophages are activated and produce cytokines in response to IL-25/IL-17RB, although the relevance of this axis to immune responses in primary Sjoren's syndrome (pSS) is unknown.

**Objectives:** We sought to investigate the role of the IL-25/IL-17RB axis and ILC2 and M2 macrophages in patients with pSS.

**Methods:** Expression analysis of IL-17B, IL-25, IL-33 and IL-17RB was performed by TaqMan real-time PCR and immunohistochemistry on salivary glands from 50 patients and 20 controls. Analysis of IL-17RB expression and the frequencies of natural type 2 innate lymphoid cells (nILC2), inflammatory ILC2 (iILC2), and M2-polarized macrophages were assessed by means of flow cytometry among salivary gland (SGMC) and peripheral blood (PBMC) mononuclear cells. Clusters of ILC2 cells and M2 macrophages were also studied by immunohistochemistry and confocal microscopy. The role of IL-25 on ILC2 was investigated in *ex vivo* studies.

**Results:** IL-25 and IL-17RB, but not IL-25, were significantly over-expressed in the MSG of pSS patients and correlated with the focus score and the degree of lymphoid organization. IL-17RB was mainly expressed by T lymphocytes, ILC2 cells and macrophages. No significant increased expression of IL-33 was observed in pSS. Significant increase in the frequency of iILC2, but not of nILC2, was observed in both PBMC and SGMC. Clusters of ILC2 cells, resembling fat associated lymphoid clusters (FLAC), and M2 polarization were also observed in pSS salivary glands and correlated with the focus score. IL-25 stimulation of isolated SGMC and PBMC resulted in the expansion of iILC2.

**Conclusions:** These findings suggest that IL-25 may promote, by interacting locally and sistemically with IL-17RB$^+$ cells, an iILC2 and M2 inflammatory state in pSS. Blockade of the IL-25 axis could be clinically relevant in pSS.

**Disclosure of Interest:** None declared

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## THU0261 T FOLLICULAR REGULATORY CELLS FROM PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME EXPRESS LOWER LEVELS OF CTLA-4

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**Background:** Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands. Within circulating CD4$^+$ T cells, the proportion of Tfh cells (CD45RA$^-$FoxP3$^-$CXCR5$^+$PD-1$^+$) is increased in pSS patients, compared with healthy controls (HCs). Increased levels of circulating Tfh cells are associated with higher systemic disease activity, as measured by serum IgG titers and the European League Against Rheumatism (EULAR) Sjögren's syndrome Disease Activity Index (ESSDAI). However, it is unknown if the proportion of T follicular regulatory (Tfr) cells is also altered. Tfr cells may play an important role in pSS pathogenesis, since the ratio between T follicular regulatory (Tfr) cells (CD45RA$^-$FoxP3$^+$CXCR5$^+$PD-1$^+$) and Tfh cells seems to dictate B cell responses.[1]

**Objectives:** To analyze the Tfr/Tfh ratio in pSS patients and HCs and to assess the functional suppressive capability of Tfr cells by means of their expression of the inhibitory immune receptor cytotoxic T-lymphocyte-associated protein 4 (CTLA-4).

**Methods:** Twenty-four pSS patients (23 female, mean age 44, median ESSDAI 8), diagnosed according to the revised AECG criteria, and 24 sex- and age-matched healthy controls were included. Cryopreserved peripheral blood mononuclear cells were analyzed by flow cytometry for expression of CD3, CD4, CD45RA, FoxP3, CXCR5, PD-1 and CTLA-4. Besides the frequency of positive cells, median expression levels per cell of CTLA-4 were measured using median fluorescence intensity. Statistical analysis were performed using the Mann–Whitney U or the Spearman's Rho test.

**Results:** In addition to the increase in Tfh cells, we found an increased proportion of Tfr cells within the pool of circulating CD4$^+$ T cells in pSS patients, compared with HCs ($p<0.001$). Unexpectedly, the Tfr/Tfh ratio was significantly higher in pSS patients, compared with HCs ($p<0.001$), pointing towards an immune suppressive equilibrium. However, expression levels of CTLA-4 on Tfr cells from pSS patients were significantly decreased ($p<0.001$), which suggests that Tfr cells from pSS patients have a lower suppressive capability. Furthermore, lower expression levels of CTLA-4 on Tfr cells were associated with an increase in the Tfh cell proportion ($r^2$=-0.382, p=0.066). CTLA-4 expression levels were also decreased on total Treg cells (CD45RA$^-$FoxP3$^+$) from pSS patients ($p<0.001$).

**Conclusions:** Although both the proportion of Tfr cells and the Tfr/Tfh ratio are increased in pSS patients, the decreased expression of CTLA-4 by Tfr cells suggests that Tfr cells from pSS patients have a lower suppressive capacity. This may contribute to the expansion of Tfh cells and consequently to hyperactivity of B cells in pSS. Limitation of Tfh cell expansion by immunomodulatory treatment may reduce this B cell hyperactivity.

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**Disclosure of Interest:** None declared

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## THU0262 IMPAIRED SUPPRESSIVE CAPACITY OF REGULATORY B CELLS IN PRIMARY SJOGREN'S SYNDROME

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**Background:** primary Sjogren's syndrome (pSS) is a chronic systemic autoimmune disorder that typically affects exocrine glands. B cell hyperactivity is a cardinal feature in pSS[1]. Besides the antibody-producing, regulatory B cells (Breg) has recently been shown to contribute to the maintenance of immunological tolerance[2,3]. The role of the Breg cells in pSS is not well understood.

**Objectives:** In this study, we investigated the levels of Breg cells in peripheral blood in patients with pSS, primary biliary cirrhosis (PBC) as well as in healthy controls (HC) and explore the characteristic and function of Breg cells in pSS patients.

**Methods:** Newly diagnosed pSS patients (n=70) were enrolled, 50 healthy volunteers and 25 PBC patients were recruited as healthy and disease controls. To analyze the percentages of Breg cells and the level of IL-10 secreted by Breg cells, PBMCs were surface and intracellular stained, and detected by flow cytometry. The expression of IL-10 in B cells were determined by real-time PCR. The function of Breg cells was tested by co-culturing isolated CD19$^+$CD24$^{hi}$CD38$^{hi}$ Breg cells with purified CD4$^+$CD25$^-$T cells (Teff cells) from pSS patients or HC at a ratio of 1:1. The cytokines in culture supernatants were measured by cytometric beads array.

**Results:** The frequency of circulating Breg cells in pSS patients was significantly increased, compared with PBC patients and HC (6.88 ± 2.48%, 1.95 ± 1.04%, and 1.52±0.65%, respectively; $p<0.0001$). The percentages of IL-10$^+$ Breg cells was much lower in pSS patients, compared to PBC and HC (16.04 ± 9.03%, 81.40 ± 21.00%, 31.00 ± 7.79%, respectively; $p<0.05$), while the expression of IL-10 in B cells was much higher in pSS patients than that in HC (13.48 ± 18.90, 3.55 ± 0.71, respectively; $p<0.05$). When autologous or heterologous Teff cells/Breg cells were co-cultured, IFN-$\gamma$, TNF-$\alpha$, IL-4, IL-17 in supernatants secreted by HC or pSS Teff cells significantly suppressed by healthy Breg cells, not by Breg cells in pSS patients ($p<0.05$).

**Conclusions:** This preliminary study showed that the frequency of Breg cells was significantly increased in pSS patients. Although the expresssion of IL-10 mRNA in B cells was much higher, the secretion of IL-10 of Breg cells from pSS patients was decreased and less effective in the control of Teff cell proliferation. Unlike HC, the suppressive capacity of Breg cells was impaired in pSS. The malfunctioning Breg cells may play an important role in pathogenesis of pSS.

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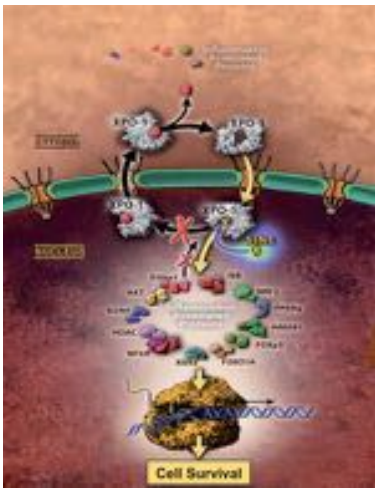
**Disclosure of Interest:** None declared

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## THU0263 KPT-350, A SELECTIVE INHIBITOR OF NUCLEAR EXPORT (SINE) COMPOUND, EFFECTIVELY REDUCES INTERFERON-ALPHA ACTIVATION AND AUTOREACTIVE PLASMA CELLS IN MURINE LUPUS

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**Background:** There is great interest in developing new treatment approaches for systemic lupus erythematosus (SLE), but the biologic therapies under investigation have yielded disappointing results. Recently the nuclear export protein XPO1 (Exportin 1/CRM1) has surfaced as an attractive target for the treatment of inflammatory disorders like SLE. Selective Inhibitor of Nuclear Export (SINE) compounds are potent, orally-available, and well-tolerated XPO1 (Exportin 1/CRM1) agonists. *In vitro* and *in vivo*, SINE compounds exert apoptotic and anti-inflammatory effects by mediating nuclear retention of important XPO1 cargos like the NFκB pathway regulatory protein, IκB (figure).
**Objectives:** This study evaluated the efficacy of the SINE compound KPT-350 on disease progression, interferon-α (IFN-α) production by plasmacytoid dendritic cells (pDCs) and autoantibody production by plasma cells (PCs) in a murine model of SLE.
**Methods:** Cohorts of nephritic NZB/W F1 lupus-prone female mice, with established disease (elevated anti-dsDNA antibody titer and proteinuria) were treated with low or high dose KPT-350 (5 or 7.5 mg/kg, respectively) or a vehicle control three times per week for 8 weeks (n=8/group). Proteinuria was monitored and kidney histology assessed. Spleen, bone marrow (BM) and kidney cells were harvested and analyzed by flow cytometry. Antibody secreting cells (ASCs) and germinal centers (GCs) were enumerated and measured by ELIspot and immunofluorescent staining. Serum samples and RNA were collected for Luminex assay and qPCR. Effects on pDC production of IFN-α were assessed using *in vitro* cultures of BM cells stimulated with CpG 2216 10ng/ml for 5 hours.
**Results:** Both high and low doses of KPT-350 prevented nephritis progression with a statistically significant reduction in urine protein levels in treated groups ($p<0.05$ beginning at 6 weeks). Moreover, nephritis was improved histologically (GN score: 3.3±1.2 vehicle vs. 1.0±-0 SINE; interstitial nephritis: 2±-1.1 vehicle vs. 0±-0 SINE; lipoid infiltrate score: 1.3±-0.6 vehicle vs. 0±-0 SINE). In the spleen, levels of GC B cells ($CD19^+PNA^+CD95^+$) and IgG and anti-DNA ASCs were dramatically reduced. ASCs were also reduced in the BM and became undetectable in the kidney. Importantly, serum anti-DNA antibodies decreased with treatment but total IgG levels remained intact. KPT-350 inhibited the production of IFN-α by pDCs in a strong, dose-dependent fashion (% of vehicle: 1 uM 88%, 10 uM 66%, 100 um 39%, and 1000 uM 0%). Additionally, IFN-α regulated chemokines in the serum of treated mice were decreased (MCP-1: 250±-90 pg/mL vehicle vs. 54±-26 pg/mL SINE, p=0.049), as were the renal mRNA levels of three PC survival factors: BAFF (38% of vehicle, $p<0.05$), APRIL (19% of vehicle, $p<0.05$) and IL6 (40% of vehicle).




**Conclusions:** SINE compounds influence the generation, survival and function of PCs and other immune cells through a multifactorial mechanism involving pDCs, GCs and ASCs. It is likely that a common process, namely inhibition of the canonical NFκB pathway, underlies KPT-350's effect. Collectively, our findings suggest that, by simultaneously modulating IFN-α activation and NFκB signaling, SINE compounds might slow disease progression in SLE.
**Disclosure of Interest:** J. Rangel-Moreno: None declared, W. Wang: None declared, T. Owen: None declared, J. Barnard: None declared, B. Klebanov Employee of: Karyopharm Therapeutics, Inc, Y. Landesman Employee of: Karyopharm Therapeutics, Inc, S. Tamir Employee of: Karyopharm Therapeutics, Inc, S. Shacham Shareholder of: Karyopharm Therapeutics, Inc, Employee of: Karyopharm Therapeutics, Inc, J. Anolik: None declared

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## THU0264 A SELECTIVE JAK1 INHIBITOR, FILGOTINIB SUPPRESSES LYMPHOCYTIC INFILTRATION IN SALIVARY GLAND OF NON OBESE DIABETIC MICE VIA SUPPRESSION OF BAFF PRODUCTION OF SALIVARY GLAND EPITHELIAL CELLS

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**Background:** Interferon (IFN) signatures are upregulated in patients with primary Sjogren's syndrome (pSS) and interferons are considered to play a pathogenic role in pSS. Therefore, Janus kinase (JAK) which mediates interferon signaling pathway may be a good therapeutic target
**Objectives:** We set out to investigate whether a selective JAK1 inhibitor, filgotinib would ameliorate disease-related parameters in non-obese diabetic (NOD) mice, an animal model SS
**Methods:** Filgotinib (1.5mg/kg) or vehicle (saline) was intraperitoneally injected three times per week from 8 weeks after birth. Salivary flow rate (SFR) was addressed on 8, 12, 16 and 20 weeks. Histologic analysis was performed on 20 weeks. The effect of filgotinib on the expressions of B cell activating factor (BAFF) and chemokines (CXCL10 [IP-10], CXCL3 [fractalkine], CCL-2 [MCP-1]) in human salivary gland epithelial cell (SGEC) line or primary epithelial cells of patients with pSS was determined *in vitro*.
**Results:** The SFR of NOD mice in both groups decreased over time. Of note, SFRs of filgotinib-treated mice were greater than those of controls. Histologic evaluation of the salivary gland revealed that the lymphocytic infiltration of salivary gland was markedly reduced in the mice treated with filgotinib. Filgotinib suppressed STAT1 phosphorylation in IFN-treated SGECs. In addition, IFN-induced BAFF and chemokine production of SGECs or primary epithelial cells were abrogated by filgotinib treatment.
**Conclusions:** Filgotinib suppresses SFR decrease and lymphocytic infiltration of salivary glands of NOD mice by inhibiting inhibiting IFN signaling pathway, thus suppressing BAFF and chemokine production of salivary gland epithelial cells. JAK inhibition may be a novel therapeutic approach for SS.
**Disclosure of Interest:** None declared
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## THU0265 B CELL PHENOTYPIC CHANGES IN ANTI-NUCLEAR ANTIBODY POSITIVE INDIVIDUALS PRIOR TO THE ONSET OF SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASE

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**Background:** Patients with systemic autoimmune rheumatic diseases (SARD) often have a prolonged pre-clinical phase during which they are anti-nuclear antibody $(ANA)^+$ but lack clinical symptoms. It has been proposed that progression from asymptomatic autoimmunity to clinical disease is accompanied by immunologic changes that could be used as predictors of disease development. Previous studies indicate that a number of B cell phenotypic changes are seen in SARD patients including changes in the proportions of various naïve and memory B cell subsets, increased B cell activation and elevated levels of plasmablasts/plasma cells.
**Objectives:** To determine whether $ANA^+$ individuals who lack sufficient symptoms for a SARD diagnosis have B cell phenotypic changes similar to those seen in SARD.
**Methods:** Healthy controls (HC) and $ANA^+$ individuals who: 1) lacked clinical symptoms of SARD (ANS); 2) had at least one clinical symptom of SARD (UCTD); or 3) had a recently diagnosed steroid and immunosuppressive naïve SARD (SLE, SS, SSc, MCTD, DM) were recruited. PBMCs were isolated over a Ficoll gradient, stained with various combinations of fluorescently labeled antibodies and analyzed by flow cytometry. Anti-nuclear antibodies were measured through the hospital laboratory. Whole blood IFN signature and BAFF RNA levels were measured by NanoString.
**Results:** B cell phenotypes were examined for 32 HC, 38 ANS, 28 UCTD, and 59 early SARD (24 SS, 26 SSc, 6 SLE, 2 MCTD, 1 DM) patients. Patients with early SARD had a number of changes in their naïve and memory B cell subsets, as previously reported for patients with established disease, including: increased proportions of mature naïve B cells (SSc); increased proportions of T1T2 cells (SLE and SS); and trends to decreased proportions of switched memory B cells ($CD27^+IgD^-$) in all SARD. Similar decreases in the proportion of switched memory B cells were seen in ANS and UCTD patients, and as seen for the SARD patients, these cells were activated with elevated levels of CD86 as compared to HC. Significantly increased activation of the $CD27^-IgD^-$ memory compartment was also seen in ANS, UCTD, SLE and SjD patients. Although significantly increased proportions of plasmablasts and/or $CD138^+$ plasma cells

were seen in all SARD patients (except those with SSc), these were not seen in ANS and UCTD patients. Nevertheless, in pre-SARD individuals (ANS + UCTD) there was a significant positive correlation between the size of these cell subsets, as well as the proportion of T1T2 cells, and ANA titer and the number of different anti-nuclear antibodies specificities. As observed for early SARD patients, there was a trend to increased BAFF levels as compared to HC in pre-SARD individuals, which achieved statistical significance in UCTD patients. However, there was no association between the levels of BAFF and any of the B cell phenotypes, whereas the IFN signature was positively associated with the proportion of T1T2 cells.

**Conclusions:** B cell phenotypic abnormalities precede the onset of clinical disease in ANA$^+$ individuals and have a pattern suggesting ongoing activation through T-B collaboration.

**Disclosure of Interest:** None declared

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## THU0266 CGAMP AND CGAS ARE EXPRESSED IN A SUBSET OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ASSOCIATE WITH DISEASE ACTIVITY

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**Background:** Type I interferon (IFN-I) is strongly implicated in the pathogenesis of Systemic Lupus Erythematosus (SLE) and "interferonopathies" such as Aicardi-Goutieres Syndrome (AGS). A recently discovered DNA-activated IFN-I pathway, cyclic GMP-AMP (cGAMP) synthase (cGAS), which is crucial in viral immunity, has been linked to AGS and mouse models of SLE. Whether this pathway plays a role in human SLE is unknown.

**Objectives:** Given the pivotal role played by interferon in the pathogenesis of SLE, our initial aim was to determine whether cGAS expression and subsequent cGAMP production contribute to IFN-I production in SLE. A further objective was to establish whether there is a specific disease phenotype associated with activation of this pathway.

**Methods:** There were three phases to this work. Initially, we evaluated cGAS mRNA expression by QPCR from stored cDNA in 51 SLE patients and 20 normal controls. Peripheral blood mononuclear cells (PBMC) were obtained from a second cohort comprising 17 SLE patients, 10 RA patients and 9 healthy volunteers. Extracts from these PBMC were tested for cGAMP by a Multiple Reaction Monitoring (MRM) assay developed on a mass spectrometer coupled with Ultra-Performance Liquid Chromatogram (UPLC). In a third cohort, cGAS and cGAMP were examined in the same SLE patients (n=31). Disease activity was determined by SELENA-SLEDAI and organ involvement, serology and medications recorded. Categorical variables were compared using Fischer's exact test, mean data was compared using a t-test or the Wilcoxon Sum-Rank test for normal or non-normally distributed data respectively.

**Results:** Phase 1 revealed that cGAS expression in PBMC was significantly higher in SLE patients (n=51) when compared to normal controls (n=20) (p=0.0045). cGAS expression positively correlated with IFN response gene (ISG) expression in SLE patients ($p=1.8 \times 10^{-5}$). When PBMC from healthy controls were incubated with IFN-I, cGAS mRNA increased in a dose response manner consistent with it being an IFN stimulated gene. Targeted measurement of cGAMP by mass spectrometery detected cGAMP in 14.6% (7/48) SLE patients but not in any of the normal (n=19) or RA (n=22) controls. Disease activity was significantly higher in SLE patients with cGAMP detected versus those in which it was not detected (SLEDAI=7.0, SD 5.09 versus 3.52, SD 2.78, p=0.0102).

**Conclusions:** Although cGAS appears to be a prominent cytosolic DNA sensor responsible for inducing IFN in response to infection, its role in human autoimmune diseases is unknown. Here, we describe for the first time, evidence of cGAS/cGAMP activation in human SLE. We demonstrated high disease activity associated with activation of this pathway. The inducing stimulus, cell type of production and overall importance in generating the IFN signature in SLE remain to be determined.

**Disclosure of Interest:** None declared

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## THU0267 THE OXIDATIVE STRESS MARKERS AS RISK FACTOR FOR ENDOTHELIAL DYSFUNCTION IN PRIMARY AND SECONDARY ANTIPHOSPHOLIPID SYNDROME

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**Background:** The oxidative stress markers as risk factor for endothelial dysfunction in primary and secondary antiphospholipid syndrome.

**Objectives:** Antiphospholipid syndrome (APS) may manifest as a primary (PAPS) or as a secondary disease (SAPS). It is featured by clinical manifestations in the presence of antiphospholipid antibodies (aPL). Antioxidant status has been evaluated in patients with SLE, with conflicting results.

**Methods:** The study involved 152 APS patients (95 PAPS, 57 SAPS) and 41 age/sex-matched controls. Brachial artery responses to reactive hyperaemia (endothelium-dependent dilatation) [FMD] and sublingual nitroglycerine (endothelium-independent dilatation) [NMD] were measured by using high-resolution vascular ultrasound. Markers of oxidative stress, including lipid hydroperoxydes (LOOH), advanced oxidation protein products (AOPP), total thyol groups and paraoxonase 1 activity (PON1) were determined by spectrophotometric method.

**Results:** FMD in patients with PAPS and SAPS was significantly lower than those of the controls ($p<0.001$ and $p<0.001$, respectively) without difference in NMD. FMD impairment was similar in both APS groups. Risk factors for endothelial impairment were age ($p<0.05$), obesity (p=0.048) and hypertension (p=0.020) but not aPL. We also found statistically significant difference in prevalence of FMD and NMD impairment in PAPS patients with longer disease duration. LOOH and AOPP concentrations were significantly higher and thyol groups lower in APS patients comparing to control group as the same relations between SAPS to PAPS groups. APS patients with fetal losses had higher AOPP (p=0.002) as well as patients diagnosed with thrombosis (p=0.011). Impairment of FMD was found in APS patients with higher LOOH and AOPP concentrations (p=0.044 and 0.015, respectively). There was no difference between impairment of FMD and NMD according to aPL category (except LA positivity to FMD impairment in PAPS group) or clinical APS manifestation.

**Conclusions:** Endothelial dysfunction is present in APS patients with marked oxidative imbalance. Oxidative stress is more prominent in SAPS than in PAPS group. Endothelial dysfunction is doubtlessly present in APS patients with oxidative imbalance as additional risk factor among other risk factors for clinical event. AOPP could be relevant prognostic factor for APS manifestations since it contribute to endothelial dysfunction and correlate to clinical APS manifestations.

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## THU0268 DECREASED EXPRESSION OF MIR-130A AND MIR-708 IN TYPE-1 CLASSICAL DENDRITIC CELLS OF SJÖGREN'S SYNDROME PATIENTS INDICATES THEIR DYSREGULATION

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**Background:** Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the salivary and lachrymal exocrine glands that leads to dryness of mouth and eyes. Type-1 classical dendritic cells (cDCs) are very potent antigen presenting cells known to induce strong T-cell proliferation and cytokine production. Despite the fact that especially cDC1s are candidate key players in the activation of local T and B-cells in pSS, they have rarely been studied in pSS.

**Objectives:** Considering the critical role of micro-RNAs (miRNAs) in regulation of gene expression, we investigated miRNA expression in isolated cDC1s of pSS patients.

**Methods:** Two independent cohorts (discovery and validation) were established including a total of 29 pSS patients. 17 healthy controls (HC) were included as control group. cD1c+CD19- cells were isolated from peripheral blood using MACS and we performed miRNA profiling of 758 miRNA targets using the OpenArray platform in the donors included in the discovery cohort. A selection of the miRNAs found to be differentially expressed in pSS versus HC was measured in the validation cohort. We performed pathway enrichment with the experimentally supported targets of the validated miRNAs.

**Results:** A total of 24 miRNAs were downregulated in pSS patients versus HC in the discovery cohort (all at least $p<0.05$ and 2log expression difference). Of these, 16 targets were selected to be validated in validation cohort. Two miRNAs, miR-130a and miR-708, were significantly downregulated in pSS patients in both cohorts ($p<0.05$). Pathway enrichment showed that the experimentally supported targets of these miRNAs are mainly involved in vesicle trafficking and a number of growth-factor signalling pathways ($p<0.05$, FDR corrected), including epidermal growth factor (EGF) signalling and endocytosis. We are currently linking the miRNA expression data to RNAseq data and performing functional experiments with primary DCs to dissect the effects of miRNA dysregulation in these cells.

**Conclusions:** We here for the first time show differentially expressed miRNAs in an isolated immune cell subset of pSS patients. In addition, this is the first evidence for dysregulation of primary peripheral blood type-1 cDCs in pSS. Considering threimportant role of miRNAs in cell function, this suggests that targeting aberrant miRNA expression may provide tools to modulate cDC activity.

**Disclosure of Interest:** None declared

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## THU0269 A MULTITUDE OF DOWNREGULATED MIRNAS IN PLASMACYTOID DCS OF SJÖGREN'S SYNDROME PATIENTS INDICATES NUMEROUS DYSREGULATED SIGNALLING PATHWAYS

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**Background:** Plasmacytoid dendritic cells (pDCs) are indicated to be key players in the pathogenesis of primary Sjögren's syndrome (pSS) and important producers of type-1 interferon (IFN). This is based on their increased presence in pSS salivary glands, potential role in experimental animal models and the presence of an IFN signature in pSS patients, which is associated with disease activity measures. MicroRNAs (miRNA) are key regulators of cellular function and may play a pivotal role in pDC function.
**Objectives:** To unravel the role of miRNAs in pDCs of pSS patients, we investigated the expression of miRNA in these cells in pSS patients.
**Methods:** Two independent cohorts (discovery and validation) were established including a total of 30 pSS patients. 15 healthy controls (HC) were included as control group and divided over the two cohorts. CD304-expressing pDCs were isolated from peripheral blood using MACS and profiling of 758 miRNA was performed using the OpenArray platform in the donors included in the discovery cohort. miRNAs found to be differentially expressed in the discovery cohort were subsequently measured in an independent validation cohort. Experimentally supported targets of validated miRNAs were used to perform pathway enrichment.
**Results:** A total of 24 miRNAs were significantly downregulated in pSS patients versus HC in the discovery cohort (all $p<0.05$ and $>2$log fold difference). 15 miRNAs were selected to be measured in the validation cohort, ten of these miRNAs were subsequently validated ($p<0.05$). Pathway enrichment indicated that these miRNAs are mainly involved in regulation of growth factor signalling and cell cycle (FDR corrected, $p<0.05$), including MTOR and PI-3K pathways. We are currently studying the involvement of these miRNAs in pDC function by linking miRNA expression to RNA sequencing data and *in vitro* functional assays.
**Conclusions:** We here for the first time show differential expression of miRNAs in isolated pDCs of pSS patients. Considering the strong potential of miRNAs in regulation of cell function, these data suggest a significant contribution to pDC function. Further analysis of the pathways in which these miRNAs are involved will expand our understanding on the role of pDCs in pSS.
**Disclosure of Interest:** None declared
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## THU0270 ACTIVATION OF PLASMACYTOID DENDRITIC CELLS BY APOPTOTIC PARTICLES - MECHANISM FOR THE LOSS OF IMMUNOLOGIC TOLERANCE IN ANDROGEN-DEPLETED SJÖGREN'S SYNDROME

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**Background:** Sjögren's syndrome (SS) is a common autoimmune disease targeting salivary and lacrimal glands. It is strongly female-dominant characterized by low estrogen (E) levels combined with a local intracrine dihydrotestosterone defect (DHT) [1, 2]. It is assumed that the primary effect in SS is the abnormal apoptosis of salivary gland cells, combined with increased production and abnormal handling of the apoptotic particles [3].
**Objectives:** The working hypothesis was that these hormonal defects lead to increased apoptosis of the epithelial cells and pro-inflammatory plasmacytoid dendritic cell (pDC) mediated host responses. Apoptosis induced particles contain SS autoantigens, which may affect immune cells.
**Methods:** Apoptotic particles were collected by different centrifugation steps. The expression and localization of SS autoantigens ($\alpha$-fodrin and SS-A) was analysed with flow cytometry. Isolated apoptotic particles were used to stimulate pDCs. The effect of the particles on TLR7/9 expression in pDCs was studied with qPCR and the elicited cytokine/interferon (IFN) profile with xMAP and ELISA measurements. To study the effects of sex steroids, pDCs were cultured without and with various concentrations of dehydroepiandrosterone (DHEA), DHT and 17-$\beta$-estradiol (E2).
**Results:** Apoptosis-induced apoptotic particles contained SS-autoantigens and hy1-RNA. These particles were internalized by pDCs, which stimulated the TLR expression and the production of proinflammatory cytokines TNF-$\alpha$, interleukin-6 (IL-6) and IL-8. On the contrary, type I IFN production was not induced. Androgens inhibited the particle-induced increase of TLR9 expression in pDCs.
**Conclusions:** Apoptosis of epithelial cells leads to translocation of SS-autoantigens and single-stranded hy1-RNA to apoptotic blebs and membrane particles. The apoptotic particles are internalized by pDCs, which in response mature and produce proinflammatory cytokines. Androgens affect to redistribution of autoantigens and diminish the particle-elicited increase of TLR expression in pDCs. Apoptosis of salivary gland cells lead to formation of apoptotic particles, which might affect immunotolerance, production of autoantibodies and onset of autoinflammation. This event might describe how the immunologic tolerance is broken in the early stages of SS.
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## THU0271 IMPAIRMENT OF GAS6/MERTK SYSTEM IN LUPUS NEPHRITIS

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**Background:** Growth Arrest-Specific 6 (Gas6) and its receptor MERTK have been involved in the regulation of inflammation and apoptosis.
**Objectives:** We evaluated if an impairment of Gas6/MERTK signalling system could be associated with Systemic Lupus Erythematosus (SLE) disease activity and, specifically, with kidney involvement.
**Methods:** Gas6 and the soluble, cleaved form of MERTK (sMER) plasma concentration were measured in 59 SLE patients and in 46 healthy controls. Clinical and laboratory data were collected.
**Results:** SLE patients had significantly higher plasma sMER concentrations (10,40 ng/ml [IQR 7,92–13,83] vs 2,65 ng/ml [2,38–3,23]) while healthy subjects showed only slightly higher plasma Gas6 concentrations than patients (22,8 ng/ml [IQR 19,2–24,7] vs 14,7 ng/ml [11,8–20,5]). Moreover, only sMER, but not Gas6, was significantly different being higher in SLE patients with renal involvement (11,3ng/mL [9,7–13,9ng/mL] vs 7,8 ng/mL [6,2–12,2ng/mL]). At univariate analysis sMER concentration was related to clinical and laboratory indexes of disease activity as SLEDAI, haemoglobin, ESR, proteinuria and creatinine plasma concentration but, at multiple regression analysis only 24 h urine protein concentration fitted the model (R=0,9751 F11,314; $p<0,002$).
**Conclusions:** An increased sMER concentration can be detected in SLE patients, particularly those who showed renal involvement. Interestingly sMER is directly related to the degree of proteinuria, This observation suggests an increased cleavage of MERTK; on this basis an impairment of MERTK-mediated apoptotic bodies clearance could be supposed.
**Disclosure of Interest:** None declared
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## THU0272 INCOMPLETE AND SYSTEMIC LUPUS ERYTHEMATOSUS REVEAL A DIFFERENT PATTERN OF INTERFERON-STIMULATED GENES UP-REGULATION

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**Background:** Type I interferons (IFN-I) play a central role in the pathogenesis systemic lupus erythematosus (SLE). IFN-I activity has been used as a biomarker by measuring interferon-stimulated gene (ISG) transcripts in the peripheral blood of SLE patients, but its relationship with clinical features still remains unclear. Incomplete lupus erythematosus (ILE) describes individuals with new onset of features suggestive of SLE, but do not fulfil diagnostic criteria. Up to 20% of these patients eventually progress to SLE.
**Objectives:** To investigate ISG expression in patients with ILE and explore possible qualitative differences between established and early stages of SLE.
**Methods:** A meta-analysis of known ISGs indicated 33 genes of importance [1]. The expression of 33 ISGs was measured using qPCR in PBMCs from individuals with SLE (n=54), ILE (n=27), and healthy controls (HC; n=14). SLE was defined using 2012 ACR/SLICC criteria. ILE was defined as ANA +ve, 1–2 clinical ACR/SLICC criteria, and symptom duration $<12$ months. Factor analysis (FA) was used to reduce expression data to a limited set of factors, which were compared between patient groups using ANCOVA test.
**Results:** FA on SLE patients indicated two factor scores explaining 80% of the data variance. The majority of variability was explained by Factor F1; however, Factor F2 appeared more relevant to the presence of fully established SLE. F1 and F2 were significantly different between patient groups; p=0.005 and p=0.044 respectively. F1 was similarly high in both SLE [SLE:HC=4.22 (1.80, 9.88), p=0.001] and ILE [ILE:HC=2.96 (1.20, 7.32), p=0.019]. In contrast, F2 was increased only in SLE [SLE:HC=1.38 (0.95, 2.00), p=0.086] but not in ILE [ILE:HC=1.02 (0.69, 1.51), p=0.917]; a significant difference was observed

between SLE and ILE patients [SLE:ILE=1.35 (1.04, 1.77), p=0.026].In total, 16 and 14 genes loaded onto F1 and F2 respectively. Most of the genes were involved in IFN signalling pathways. Genes related to apoptosis and ubiquitination were present in both F1 and F2. Additionally, F1 loaded genes were mainly associated with antiviral immunity, complement regulation, and Th2 responses; genes loaded onto F2 were associated with regulation of IFN-I, dsDNA binding, chemotaxis, and Th1 responses.

**Conclusions:** IFN-I activity is present in ILE. However, the majority of measured ISG expression (F1) cannot distinguish ILE and SLE. F1 represents genes that distinguish healthy individuals, but show little variation at different stages of disease development. We define a subset of ISGs (F2), the expression of which is only increased in patients with confirmed clinical SLE. ISG expression is not unidimensional: qualitative differences in expression of distinct ISGs can contribute to clinical progression after disease initiation.

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## THU0273 DECREASED INTERLEUKIN-35 IS ASSOCIATED WITH HIGHER RISK OF PREGNANCY MORBIDITY IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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**Background:** Antiphospholipid syndrome (APS) is an autoimmune disease characterized mainly by recurrent pregnancy failures and/or thrombosis [1]. Interleukin (IL)-35, a new member of IL-12 family, was demonstrated to play a role in the immunopathogenesis of several autoimmune diseases [2,3]. The expression of IL-35 was observed to be abnormal in idiopathic recurrent pregnancy loss [4].

**Objectives:** To determine the expression of IL-35 and assess its association with clinical /laboratory features in patients with APS.

**Methods:** Serum IL-35 was detected by the enzyme-linked immunosorbent assay (ELISA). 126 patients with APS, 38 patients with primary pregnancy morbidity, and 69 healthy controls were enrolled in the study. Clinical and laboratory features of APS patients were recorded. The Mann-Whitney U test was used to evaluate differences of non-normal distribution data and the Student's t test was used for normal distribution data. The differences in the frequency of clinical /laboratory characteristics were assessed by the Chi-square ($\chi^2$) test. The relevances between IL-35 and clinical/laboratory features were further analyzed by the Spearman test (measurement data) or Chi-square ($\chi^2$) test (qualitative data).

**Results:** Serum IL-35 was significantly decreased in APS patients (median 14.73, IQR 0–28.09 pg/ml) and patients with primary pregnancy morbidity (16.00, 10.56–25.00 pg/ml), compared to healthy controls (28.87, 20.16–47.47 pg/ml; all $p<0.001$). Female APS patients with decreased IL-35 had higher risk of pregnancy morbidity than those with normal IL-35, with an odds ratio (OR) of 2.565 (95% confidence interval (CI) 1.138–5.785, $p=0.022$), especially events of fetus death $\geq$ the 10th week (OR=6.545, 95% CI 6.03–21.101; $p<0.001$). In contrast, the frequency of thrombosis was significantly lower in APS patients with decreased IL-35 and the OR value was 0.382 (0.185- 0.789; $p=0.009$).

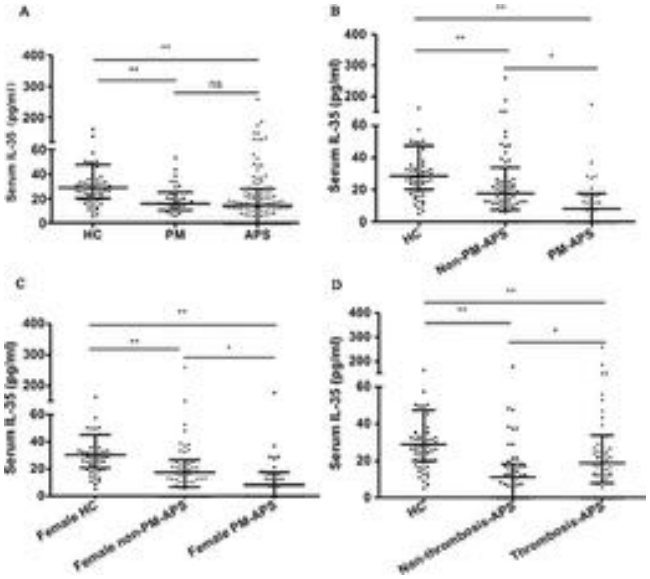



Figure 1

**Conclusions:** Serum IL-35 was decreased in APS patients and was associated with pregnancy morbidity and thrombosis, raising the hypothesis of its complicated pathogenic roles in APS.

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**Disclosure of Interest:** None declared

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## THU0274 UPREGULATION OF NOD2 INVOLVED IN THE INFLAMMATORY RESPONSE BY ACTIVATION OF MAPK SIGNALING PATHWAY IN LUPUS NEPHRITIS

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**Background:** Nucleotide-binding oligomerization domain (NOD) - containing 2 (NOD2) is a NOD - like receptors (NLRs) which plays important role in immune regulation and inflammatory response. There are increasing evidences to show that NOD2 may contribute to the development of numerous auto inflammatory and autoimmune disorders. However, their role in lupus nephritis (LN) is not known. Here, we explored the role of NOD2 in LN.

**Objectives:** However, their role in lupus nephritis (LN) is not known. Here, we explored the role of NOD2 in LN.

**Methods:** Immunohistochemistry was applied to observe the expression of NOD2 in renal biopsies. Real-time quantitative polymerase chain reaction (RT-qPCR) was used to detect the level of NOD2 mRNA in the biopsies. In vitro studies, HK-2 cells (renal tubular epithelial cell-line) were cultured with different inflammatory stimulation, western blot was used to investigate their expression of NOD2 and the following activation of MAPK pathway signals (ERK1/2, p38 and JNK), real-time qPCR was applied to observe the mRNA levels of downstream pro-inflammatory mediators (IL-1b, IL-8, MCP-1, TGF-b1, IL-6).

**Results:** (1) Immunohistochemistry staining demonstrated that the expression of NOD2 in LN is higher than that of normal control (P=0.002), and the mRNA level of NOD2 in renal tissue of LN patients was higher than that of normal control (P=0.001). (2) In vitro studies, the urine and serum from onset LN patients can significantly promote higher NOD2 expression in HK2 cells than that from healthy control ($P<0.001$). In addition, TGF-b1, LPS and muramyl dipeptide (MDP) can also induce higher NOD2 expression in HK2 cells ($P<0.001$, respectively). (3) The activation of NOD2 increased phosphorylation of ERK1/2, p38 and JNK. Moreover, the activation of NOD2 induced the release of pro-inflammatory mediators including IL-1b, IL-8, MCP-1, TGF-b1, IL-6.

**Conclusions:** Our study showed NOD2 expression was increased in LN patients. The activation of NOD2 can promote the activation of MAPK signaling pathway and release of downstream pro-inflammatory mediators. NOD2 may participate in the pathogenesis of LN.

**Disclosure of Interest:** None declared

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## THU0275 PHARMACODYNAMIC MODELING OF BTK OCCUPANCY VERSUS EFFICACY IN RA AND SLE MODELS USING THE NOVEL SPECIFIC BTK INHIBITOR M2951

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**Background:** Bruton's tyrosine kinase (BTK) is a clinically proven target in several hematological indications. Due to its role in mediating the signaling of both B cell receptors (BCR) and Fc receptors (FcR), BTK is also a potential target for the treatment of autoimmune disease such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), where B cell and innate immune cell activation are key drivers of pathology.

**Objectives:** We are developing M2951, a novel,highly selective BTK inhibitor that

is suitable for the treatment of chronic diseases. This work aimed at characterizing its efficacy in various cellular assays in vitro as well as in disease models for RA and SLE. Based on in vivo efficacy and target occupancy data, a PKPD model describing the correlation of BTK inhibition and disease severity reduction was built.
**Methods:** The BTK inhibitor M2951 was characterized in various biochemical and cellular assays to demonstrate its potency and specificity. To determine disease-modifying activity, M2951 was tested in NZB/W F1 mice which had been infected with e replication-deficient adenovirus expressing IFN-alpha in order to synchronize disease onset. Efficacy was determined by measuring proteinuria and histological kidney damage. Furthermore, M2951 was tested in a collagen-induced arthritis model (CIA) in the mouse. Paw scores were used to measure efficacy. A biochemical assay was developed that allowed to measure the degree of BTK occupancy in blood cells and splenocytes was developed. This assay was used to build a translational PKPD model linking target occupancy to efficacy.
**Results:** M2951 potently inhibits BCR- and FcR-mediated signaling and subsequent activation and function of B cells and certain myeloid cells. In mouse models of RA and SLE, M2951 displayed robust efficacy as demonstrated by a marked reduction of disease severity. In the NZB/W F1 IFN-α-accelerated SLE model, efficacy correlated with B cell inhibition, reduction of autoantibodies, and decreased circulating memory B and T cells. In addition to SLE, RA-like symptoms were inhibited in a collagen-induced arthritis model. In order to translate preclinical efficacious doses to humans, we determined the degree of target occupancy necessary to achieve disease reduction. Pharmacodynamic modeling showed that BTK occupancy of 60 and 80% was linked to 80% and near complete disease inhibition, respectively, in both the RA and SLE models.
**Conclusions:** In summary, these results demonstrate the potential of M2951 to treat autoimmune disease and may inform rational dose decisions as M2951 is advanced for development in rheumatologic diseases.
**Disclosure of Interest:** P. Haselmayer Employee of: Merck KGaA, M. Camps Employee of: Merck Serono, L. Liu-Bujalski Employee of: EMD Serono, F. Morandi Employee of: EMD Serono, J. Head Employee of: EMD Serono, S. Zimmerli Employee of: EMD Serono, L. Bruns Employee of: Merck KGaA, A. Bender Employee of: EMD Serono, P. Schroeder Employee of: EMD Serono, R. Grenningloh Employee of: EMD Serono
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## THU0276 INCREASED OXIDATIVE DNA DAMAGE AND IMPAIRED GENE REPAIRING PATHWAY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease and may affect multiple organs and systems. Definite etiology and pathogenesis of disease is unknown. Apoptosis, defective clearance of apoptotic materials, uncontrolled DNA damage related to oxidative stress play important roles in the pathogenesis of SLE.
**Objectives:** In this study we aimed to evaluate some parameters related to oxidative stress, apoptosis and gene repairing system in SLE and lupus nephritis (LN) patients.
**Methods:** The study included 10 patients with active SLE, 10 patients with active LN and 10 healthy controls. The demographical and clinical features of patients were obtained from medical charts. RNA isolation from peripheral blood was performed according to protocol of RNA kit. RT-PCR was used to analyze gene expressions of SOD, CAT, glutathione synthetase, survivin, BCL-2, CCN D1 and that of genes in the apoptotic pathway. To compare the features of study groups, one-way ANOVA test was performed and Duncan test was used as posthoc analysis.
**Results:** 8-hydroxy-deoxyguanosine (8-OHdG) which is the most common stable product of oxidative DNA damage caused by ROS is significantly higher in SLE (618±293) and LN groups (732±303) than in healthy controls (333±128) (p values $<0.01$). In addition, genomic template stability (GTS) in SLE and LN groups were significantly lower than in healthy controls (p values $<0.001$). Telomer length was used to assess overal biological aging. In our SLE and LN patients, telomer length is shortened than in healthy controls (p values $<0.01$).
We also evaluated the antioxidant system gene expression. We detected that main antioxidant system gene expression like SOD, SOD2, GS and GPX were significantly decreased in LN patients than in SLE and healthy controls. In the contrary, gene repair pathway related gene expression such as TDG, SMUG1 and RAD18 were significantly increased in SLE and especially in LN groups when compared to healthy controls (p values $<0.05$).
In LN patients, p53 gene was expressed significantly more than in SLE and controls. This gene was also expressed significantly more in SLE than in controls ($p<0.05$).
The expression of apoptosis associated genes like BAX, APAF, CYTC, CASPASE3 were elevated in LN than in SLE and healthy controls (p values $<0.01$). Apoptosis inhibitor genes like survivin, livin, XIAP and BCL2 were expressed signficantly higher in LN patients than in SLE and controls (p values $<0.01$). These genes were also expressed higher level in SLE patients than in controls ($p<0.05$).
**Conclusions:** In SLE patients, particularly in LN group, oxidative DNA damage is increased and antioxidant gene expression is decreased. Gene repair pathway is also impaired in SLE and LN. Although, genes related to inhibition of apoptosis is elevated, this elevation is not enough to eliminate the activation of apoptosis.
**Disclosure of Interest:** None declared
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## THU0277 EVALUATION OF POLYMORPHISMS OF STAT4, TRAF31P2 AND HCP5 IN SJÖGREN SYNDROME: ASSOCIATION WITH DISEASE SUSCEPTIBILITY AND CLINICAL ASPECTS

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**Background:** Primary Sjögren syndrome (pSS) is a systemic inflammatory condition characterized by lymphocytic infiltrates in exocrine glands. STAT4 is one of the genes involved in "interferon (IFN) signature" and a single nuclear polymorphism (SNP), rs7574865 has been found associated with pSS. Other SNPs in TRAF3IP2 (rs33980500 and rs13193677) and HCP5 (rs3099844) genes, have been previously associated with the susceptibility to systemic lupus erythematosus (SLE), and seem to influence the disease phenotype.
**Objectives:** To evaluate the association of different SNPs [STAT4 (rs7574865), TRAF3IP2 (rs33980500), HCP5 (rs3099844)] with the susceptibility to pSS and their role in modulation of clinical and laboratory features.
**Methods:** One hundred thirty-five consecutive patients with pSS (AECC) were enrolled and clinical and laboratory data collected. Three hundred age and sex-matched healthy subjects were used as controls. Genomic DNA was isolated from peripheral blood mononuclear cells (Qiagen blood DNA mini kit). Genotyping was performed by allelic discrimination assays (Applied Biosystems, Foster City, CA, USA).
**Results:** Clinical and laboratory features are reported in table.

| Clinical features | Number (%) | Laboratory features | Number (%) |
|---|---|---|---|
| Sex (M/F) | 5/130 | ANA | 116/135 (85.9) |
| Age (mean ± SD), yrs | 59±12.1 | Anti-Ro/SSA | 81/135 (60) |
| Age at diagnosis (mean ± SD), yrs | 53,2±12,2 | Anti-La/SSB | 56/135 (41.4) |
| Xerophthalmia | 124/135 (91.8) | Hypergammaglobulinemia | 44/135 (32.5) |
| Xerostomia | 124/135 (91.8) | Rheumatoid factor | 46/135 (34) |
| Glandular swelling | 27/135 (20) | Leucopenia | 28/135 (20.7) |
| Arhritis | 16/135 (11.8) | Hypocomplementemia | 11/135 (8.1) |
| Lymphoma | 4/135 (2.9) | Monoclonal component | 13/135 (9.6) |
| | | Cryoglobulinemia | 6/135 (4.4) |

Deviations from Hardy–Weinberg equilibrium were not observed. The SNPs rs7574865 of STAT4 and rs3099844 of HCP5 were found associated with pSS at both the genotypic and allelic level ($p<0.001$, OR=1.84, 95%CI=1.28–2.65 and $p<0.05$, OR=2.28, 95%CI=1–3.7, respectively) and the data was confirmed after adjustment for other variables. STAT4 was found associated with the presence of monoclonal component (p=0.021). HCP5 was associated with the presence of leukopenia (p=0.021, OR=2.91, 95%CI=1.15–7.38) and lymphoma ($p<0.001$).
**Conclusions:** This study confirms the association between the rs7574865 polymorphism of STAT4 and the susceptibility for pSS, and shows for the first time the association with a variant of HCP5. STAT4 was associated with monoclonal component supporting the role of IFN signature in autoantibodies production. Furthermore, HCP5 seem to be able to influence the disease phenotype predisposing to the development of leukopenia and lymphoma. These data need to be validated on larger cohorts of patients.
**Disclosure of Interest:** None declared
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## THU0278 INCREASED PLATELET AGGREGATION BY VON WILLEBRAND FACTOR ACTIVITY CORRELATES WITH ANTI-DSDNA ANTIBODY LEVELS AND ACUTE PHASE REACTANTS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Von Willebrand Factor (vWF) typically is released in response to endothelial damage or dysfunction to promote thrombus formation. In Systemic Lupus Erythematosus (SLE) patients vWF protein levels (vWF:Ag) predict cardiovascular events [1], but endothelial dysfunction in SLE is an incompletely understood multifactorial process [2].
**Objectives:** To investigate whether vWF functional activity (VWF:RCo) is related to clinical disease activity, markers of inflammation, vascular risk factors and events in SLE.
**Methods:** A cross sectional study in patients (n=90) that fulfilled ACR classification criteria for SLE and had detailed clinical information and serology collected at an extended outpatient visit. VWF functional activity was determined by ristocetin induced platelet aggregation (vWF:RCo), while vWF protein level was measured by turbidimetric assay (vWF:Ag). Variables included in this study were: SLEDAI2K;

SLICC-DI; immunosuppressive drug usage (n=33); anticoagulant therapy (n=33); antiphospholipid antibody status (aPL) and syndrome (APS) and levels for anti-dsDNA Ab, B-cell activating factor (BAFF), IL-6 and TNFα, acute phase reactants and plasma Factor VIII [3, 4].

**Results:** Platelet aggregation by vWF was significantly higher in SLE patients compared to healthy controls (n=10) (median vWF:RCo, 123% vs 78%, p=0.004) as were vWF:Ag levels (142% vs 107%, p=0.001). VWF:RCo correlated with levels of ESR (Rs 0.332, p=0.01), anti-dsDNA Ab (Rs 0.26, p=0.02), LDH (Rs 0.26, p=0.016), ceruloplasmin (Rs 0.367, $p<0.01$), C1-inhibitor (Rs 0.24, p=0.02), total cholesterol (Rs 0.23, p=0.03) and correlated inversely to transferrin (Rs -.317, $p<0.01$). VWF:RCo levels were unrelated to SLEDAI2K, CRP and IL-6 or TNFα levels and were not significantly different in patients with a previous cardiovascular event, vasculitis, antiphospholipid Ab, or in current smokers.

**Conclusions:** The association between vWF dependent platelet aggregation, acute phase proteins and increased anti-dsDNA antibody levels suggest that anti-dsDNA Ab mediated inflammation contributes to endothelial dysfunction in SLE.

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## THU0279 MSCS ALLEVIATE CLINICAL AND EXPERIMENTAL SJOGREN'S SYNDROME BY INHIBITING IL-12 PRODUCTION OF APCS

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**Background:** Mesenchymal stem cells (MSCs) have been demonstrated to be effective in treating clinical and experimental Sjogren's syndrome (SS). However, the underlying mechanisms of benefit effects of MSCs on pSS remain unclear. IL-12 was mainly generated from monocytes, dendritic cells (DCs) and macrophages, and regarded as a pro-inflammatory cytokine in autoimmune diseases, including SS.

**Objectives:** In this study we test whether the therapeutic effects of MSCs on SS is mediated by reducing IL-12 production.

**Methods:** $1\times10^6$ human umbilical cord derived MSCs were injected into NOD mice (experimental Sjogren's syndrome, ESS) via tail vein. 4 weeks later, the salivary flow rates were detected. Splenocytes were collected and CD11c+ and CD11b+ cells were sorted by magnetic beads. Lacrimal and salivary glands were collected for histologic analysis. Serum IL-12 was quantified by ELISA inprimary Sjogren's syndrome (pSS) patients and healthy controls. 5 patients with pSS received MSCs transplantations. Whole blood was collected before MSCs treatment and 4 weeks later. CD14+ cells from pSS patients and healthy controls were isolated by magnetic beads. The CD14+ cells were induced to generate DCs or macrophages. Expression of IL-12 was detected by RT-PCR. Human THP-1 cells were induced towards macrophage or DC. THP-1 cells, THP-1-induced macrophages and DCs were co-cultured with MSCs, respectively. IL-12 levels in supernatants were detected by ELISA. IL-12 gene expression was quantified by real-time PCR.

**Results:** MSCs transplantation improved salivary flow rates and decreased lymphocyte infiltrations in lacrimal and salivary glands, proving its effectiveness in alleviating symptoms of NOD mice. *In vivo* transplantation of MSCs into NOD mice also reduced serum IL-12 levels, and IL-12 mRNA in CD11c+ and CD11b+ cells. Serum IL-12 levels were significantly increased in pSS patients. MSCs transplantation also decreased IL-12 levels in pSS patients after 4 weeks. CD14+ monocytes, monocyte-derived DCs and macrophages from pSS patients generated significantly more IL-12 than that from healthy individuals. MSCs significantly reduced IL-12 production by human THP-1-induced DCs, macrophages or monocytes *in vitro*. Moreover, MSCs also decreased IL-12 production in mouse Raw246.7 cells (mouse macrophage), mouse CD11c+ cells and CD11b+ cells *in vitro*.

**Conclusions:** IL-12 over-production by APCs may contribute to the pathogenesis of pSS and ESS. MSCs may alleviate clinical and experimental Sjogren's syndrome through decreasing IL-12 production.

**Disclosure of Interest:** None declared

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## THU0280 IL-12 EXACERBATES SJOGREN'S SYNDROME THROUGH INDUCING LYMPHOCYTE INFILTRATIONS INTO SALIVARY GLANDS AND IMBALANCE OF LYMPHOCYTE SUBSETS

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**Background:** Primary Sjogren's syndrome (pSS) is characterized by inflammation of exocrine glands and functional impairment of the salivary and lacrimal glands, accompanied by the disorders of immune system, including increased pro-inflammatory cytokines, decreased anti-inflammatory cytokines, and turbulence of immune cell homeostasis. IL-12 is a pro-inflammatory cytokine relating to autoimmune diseases. However, the role of IL-12 in pSS and the underlying mechanism is still not fully understood.

**Objectives:** We aimed to explore the role of IL-12 in the pathogenesis of pSS.

**Methods:** Serum IL-12 was detected in pSS patients and healthy controls. The percentages of T cell subsets, B cells and plasma cells in peripheral blood were analyzed. NOD mice (experimental Sjogren's syndrome model, ESS) were treated with recombinant IL-12 protein, anti IL-12 MAb or same volume of saline, respectively. One week later, the salivary flow rate was detected. Histopathology of submandibular gland, lacrimal gland, lung and kidney were observed by HE staining. Immunochemistry was performed to identify the phenotype of the infiltrated lymphocytes. Flow cytometry was used to detect the proportion of lymphocyte subsets of splenocytes.

**Results:** IL-12 levels were significantly higher in pSS patients. Th1, Th17 and Tfh cell percentages were significantly higher in pSS, while Treg percentage was decreased. Th1/Th2 and Th17/Treg ratios were also higher in pSS patients. Besides, plasma cell percentages were also higher in pSS patients. All of the above data suggested the disturbance of both cellular and humoral immune balances in pSS patients. In vivo IL-12 treatment in NOD mice significantly increased salivary gland swollen severity, decreased salivary flow rates, and promoted lymphocyte infiltration in salivary glands, pulmonary interstitium and renal medulla. Immunochemistry staining showed that most of the infiltrated lymphocytes into the organs were CD4+, and a majority of the CD4+ cells were IL17A+, suggesting IL-12 induced Th17 cell infiltrations in multiple organs of NOD mice. On the other hand, anti IL-12 decreased the percentages of Th1, Th17 and Tfh cells, and corrected the imbalance of Th1/Th12 and Th17/Treg ratio. The anti IL-12 also reduced the salivary gland swollen and lymphocyte infiltration, whilst increased salivary flow rates.

**Conclusions:** IL-12 deteriorated the pathogenesis of ESS partially by promoting lymphocyte infiltration into the affected organs and disturbance of lymphocyte subsets. Targeting IL-12 may be a potential therapeutic strategy for SS patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2598

## THU0281 ARTESUNATE INHIBITS TYPE I INTERFERON INDUCED PRODUCTION OF MACROPHAGE MIGRATION INHIBITORY FACTOR IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Macrophage migration inhibitory factor (MIF) is a key regulator of both atherosclerosis and systemic lupus erythematosus (SLE), yet the factors participating in its production remain unclear.

**Objectives:** In this study, the relationship between type I interferon (IFN) and MIF levels in SLE patients were examined, and the effect as well as the mechanism of artesunate (ART), an anti-malarial agent extracted from Chinese herbs, on the regulation of MIF were explored.

**Methods:** Serum and peripheral blood cells from SLE patients and healthy controls were collected, with MIF levels measured by ELISA and type I IFN inducible gene expressions detected by real-time PCR. Associations between two factors were assessed by Spearman correlation analysis. ART at different concentrations was added to human umbilical vein endothelial cells (HUVECs) cultures with or without prior IFNα-1bstimulation and to SLE peripheral blood mononuclear cells (PBMC) cultures, with dexamethasone or fludarabine, a selective inhibitor of signal transducer and activator of transcription (STAT) 1, applied as positive treatment controls. Protein levels of STATs and phosphorylated (p-) STATs in HUVECs were determined by western blotting.

**Results:** Serum MIF levels were elevated in SLE patients and positively associated with disease activity ($r$ =0.86, $p$ <0.0001) and accumulated damage ($r$ =0.34, $p$ =0.048). Meanwhile, increased MIF levels were closely associated with IFN scores in SLE patients ($r$ =0.74, $p$ =0.0002). *In vitro* experiments showed that IFNα-1b had a direct impact on MIF production. ART could inhibit IFN inducible gene (LY6E and ISG15) expressions in HUVECs and PBMC cultures, and suppress IFNα-1b induced MIF production. Over-expression of p-STAT1, but not p-STAT3 or STAT5, was detected after IFNα-1b stimulation, which was completely reversed at the presence of ART.

**Conclusions:** MIF could be regulated by type I IFN in SLE patients. ART counteracts the effect of IFNα to inhibit MIF production by blocking STAT1 phosphorylation, thus may have therapeutic potential for SLE-associated atherosclerosis.

**Disclosure of Interest:** None declared
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## SLE, Sjögren's and APS - treatment

### THU0282 EXPOSURE-RESPONSE ANALYSES OF EFFECTS OF VENETOCLAX, A SELECTIVE BCL-2 INHIBITOR, ON B AND TOTAL LYMPHOCYTE COUNTS IN FEMALE SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** B-cell Lymphoma 2 (Bcl-2) is an anti-apoptotic protein that plays a critical role in hemostasis of auto reactive lymphocytes (B and T cells) thought to be involved in various autoimmune diseases such as SLE. Abnormalities in the Bcl-2 mediated lymphocyte apoptotic process have been implicated in development of these autoimmune diseases. Venetoclax is an orally bioavailable, selective Bcl-2 inhibitor currently under evaluation for treatment of SLE and several oncology indications.
**Objectives:** The objective of this work was to quantitatively characterize the relationship between venetoclax plasma concentrations and time course of the reduction in B and total lymphocyte counts following single and multiple dosing of venetoclax in female subjects with SLE
**Methods:** Serial pharmacokinetic and lymphocyte count data from a double-blind, randomized, placebo-controlled Phase 1 study of venetoclax (single doses of 10, 30, 90, 180, 300 and 500 mg or two cycles of 30, 60, 120, 240, 400 and 600 mg or matching placebo once daily for seven days followed by 21 day washout) in female subjects with SLE (N=98) were analyzed using non-linear mixed-effects modeling.
**Results:** Venetoclax plasma concentrations in subjects with SLE were characterized using a two-compartment pharmacokinetic model with first-order elimination. Venetoclax resulted in reduction of B and total lymphocytes and the effect was consistent between the two cycles of treatment for the multiple dose evaluation. An indirect response model with venetoclax stimulating B lymphocytes turnover was utilized to describe venetoclax exposure/ B lymphocytes relationship. The slope for stimulation of the first order rate constant of B lymphocytes turnover was estimated at 0.02 [95% CI: 0.01, 0.03] $day^{-1}$/(ng/mL) following multiple dosing. An $E_{max}$ model with an effect site (to introduce time-delay) was used to describe venetoclax effect on total lymphocytes. The maximum effect was estimated to be 60% relative to baseline with an estimated $EC_{50}$ of 225 [95% CI: 146 to 383] ng/mL. Baseline B and total lymphocytes were identified as covariates for venetoclax slope and $EC_{50}$, respectively. For the cyclic regimens of 120 and 600 mg, the model predicted typical reduction from baseline at day 7 of 26% and 77%, respectively, for B lymphocyte (for a baseline value of $0.18x10^9$ cells/L) and 15% and 37%, respectively, for total lymphocytes (for a baseline value of $1.7x10^9$ cells/L)
**Conclusions:** The current analyses demonstrate that B lymphocytes are more sensitive than total lymphocytes to the effects of venetoclax and these effects were quantitatively characterized in female subjects with SLE using an exposure-response modeling approach. The developed models will be utilized to guide the design of future trials of Bcl-2 inhibitors in subjects with SLE, including dose selection and assessment of cyclic versus continuous dosing.
**Disclosure of Interest:** M. Minocha Shareholder of: AbbVie, Employee of: AbbVie, A. Jones Shareholder of: AbbVie, Employee of: AbbVie, P. Lu Shareholder of: AbbVie, Employee of: AbbVie, A. Othman Shareholder of: AbbVie, Employee of: AbbVie
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### THU0283 ANTICOAGULATION AND LONG-TERM OUTCOMES IN PATIENTS WITH RENAL ARTERY STENOSIS AND ANTIPHOSPHOLIPID SYNDROME

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**Background:** Our previous data [1],[2],[3] showed that renal artery stenosis (RAS) is more prevalent in antiphospholipid syndrome (APS) (26%) compared to the general hypertensive population (8%),and anticoagulation with INR$\geq$3 was associated with initial reduction of chronic kidney disease (CKD) and hypertension.
**Objectives:** To characterise the long-term outcomes and associations with anticoagulant treatment for patients with renal artery stenosis and antiphospholipid syndrome.
**Methods:** We identified 37 patients with RAS and APS fulfilling Sapporo criteria [4]: anticardiolipin IgG/IgM titer$>$40 units or $>$99th percentile (or +lupus anticoagulant) on $\geq$2 occasions $\geq$6 weeks apart AND vascular thrombosis (or pregnancy morbidity). RAS was diagnosed by magnetic resonance angiography (MRA).
**Results:** 15 patients had APS alone and 22 APS associated with autoimmune conditions (13 lupus, 5 ANCA vasculitis, 4 mixed). Median age at RAS diagnosis was 48 years, 31/37 (83.8%) were female and median follow-up was 10.4 years. 25/37 (67.6%) had previous thrombosis. 7/37 (18.9%) had bilateral RAS, 3 artery occlusion. 6/37 (16.2%) had concurrent coeliac stenosis. Recanalization of RAS occurred after hydroxychloroquine in 3/37 and 9/37 (24.3%) underwent angioplasty +/– stenting. MRA was repeated in 11/37 (29.7%) after 2 years. 23/37 (62.2%) were anticoagulated, with 9/37 (24.3%) on antiplatelet therapy. 13/37 (35.1%) received hydroxychloroquine, 10/22 (45.5%) immunosuppressives and 18/37 (48.6%) antihypertensives. 9/37 (24.3%) died after a median of 10 years since RAS diagnosis. 21/37 (56.8%) developed CKD: 6 endstage renal failure (ESRD) and 15 with median eGFR 39 mls/min.

| Patient group | CKD (eGFR$<$60 mls/min) | ESRD | Death |
|---|---|---|---|
| Anticoagulant therapy (23) | 15/23 | 4/23 | 5/23 |
| No anticoagulation (14) | 6/14 | 2/14 | 4/14 |
| p value | 0.3 | 1.0 | 0.7 |
| APS alone (15) | 7/15 | 3/15 | 1/15 |
| APS+ autoimmune disease (22) | 14/22 | 3/22 | 5/22 |
| p value | 0.3 | 0.7 | 0.4 |
| Medical therapy (28) | 13/28 | 3/28 | 7/28 |
| Renal angioplasty (9) | 8/9 | 3/9 | 2/9 |
| P value | 0.05 | 0.14 | 1 |

**Conclusions:** The majority of patients with RAS and APS were female, developed CKD and did not benefit from renal angioplasty. Anticoagulation was not associated with longterm reduction of ESRD or death, suggesting a non-thrombotic pathogenic process underlying RAS, such as intimal hyperplasia. Treatment of associated vascular risk factors and autoimmune disease is paramount. Anticardiolipin antibodies and renal MRA are useful screening tests for lupus patients with difficult blood pressure control.
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**Disclosure of Interest:** None declared
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### THU0284 DYNAMICS OF B LYMPHOCYTE SUBSETS IN SLE PATIENTS TREATED WITH RITUXIMAB

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**Objectives:** to study B-cell subsets dynamics in SLE patients receiving rituximab (RTX) therapy with following 6 months observation.
**Methods:** The study included 16 SLE pts (1m/15f) with high (SLEDAI2K$>$10 - 13 pts.) and moderate (SLEDAI2K$<$10- 3 pts.) disease activity. Out of them 7 pts with lupus nephritis and 3 pts with neurolupus. RTX was administered to pts who failed to respond to glucocorticoids (GCs) and cytostatics (CTs). B-cells subsets were assessed before RTX administration (month 0), and at month 3 and month 6 of RTX therapy. RTX was administered at 500 to 2000 mg doses depending on disease activity. We investigated the absolute and relative number of CD19+ B cells, the total population of memory B cells (CD19+CD27+), "preswitch" (CD19+IgD+CD27+) and "postswitch" (CD19+IgD-CD27+) memory B cells, naive (CD19+IgD+CD27-) and transitional (CD19+IgD+CD10+CD38++CD27-) B cells, plasmablasts (CD19+CD38+++IgD-CD27+CD20-), short-lived plasma cells (CD19+CD38+), long-lived plasma cells (CD19+CD138+), and double-negative B-cells (CD19+CD27-IgD) were measured. All B cell subsets were analyzed by technique of multicolor flow cytofluorometry using panel of monoclonal antibodies to surface membrane markers of B-lymphocytes.
**Results:** Following initiation of RTX SLE clinical and lab activity indices have decreased in all 16 pts by month 3 and month 6 of follow up (SLEDAI-2K 0 month –Me 15 [11;19], 3 month -Me 7 [3;10], 6 month –Me 5 [4;9], $p$$<$0.05), as well as decrease of absolute count CD19 B-cell subpopulation (0 month – Me 0,11 [0,0741; 0,2], 3 month - Me 0,0017 [0; 0,003], 6 month - Me 0,0045 [0,0005; 0,01], $p$$<$0.05). B-cell repopulation by 6 month in 11 out of 16 pts was due to "naive" B-cells Me 0,00085 [0; 0,008], double negative Me 0,001 [0; 0,0025] and "postswitch" memory B-cells Me 0,0013 [0,0001; 0,003]. SLE exacerbation by 6 month was documented in 5 pts, in 3 out of them B-cell repopulation occurred. A correlation between baseline high SLE activity before RTX infusions (SLEDAI-2K 5 pts – Me 20 [18;24], 11 pts. Me 12 [8;12]) and SLE exacerbation at 6 month after initiation of RTM therapy ($p$$<$0,05, r=0,54) was found.
**Conclusions:** Decrease in clinical and lab SLE activity was documented in all 16 pts by 3 month after one course of RTM therapy. In 3 out of 5 exacerbated pts at 6 month B-cell repopulation was found, but without significant correlation with counts of B-cells subpopulations during the whole follow up period.
**Disclosure of Interest:** None declared
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## THU0285 DALAZATIDE, AN INHIBITOR OF THE KV1.3 CHANNEL ON ACTIVATED EFFECTOR MEMORY T CELLS, HAS IMMUNOTHERAPY POTENTIAL IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** T cell activation depends upon a calcium signaling cascade that is regulated by voltage-gated potassium channels. Effector memory T cells ($T_{EM}$), which are implicated in the immunopathogenesis of a panel of autoimmune diseases, express the potassium channel Kv1.3. Dalazatide is a potent peptide inhibitor of the Kv1.3 channel that has recently shown efficacy in a Phase 1b plaque psoriasis trial. Evidence suggests that inflammatory cytokine producing $T_{EM}$ cells might be involved in the immunopathology of lupus nephritis.
**Objectives:** Provide proof-of-principle *ex vivo* data for therapeutically targeting chronic T cell activation in systemic lupus erythematosus (SLE) by using dalazatide to block the Kv1.3 channel and to evaluate the effect of dalazatide on the *in vitro* inflammatory cytokine production of $T_{EM}$ cells from SLE patients.
**Methods:** Peripheral blood mononuclear cells from pediatric and adult SLE patients as well as healthy controls were studied. T lymphocyte subsets were assayed *ex vivo* for Kv1.3 expression by flow cytometry. The effect of dalazatide on phorbol myristate acetate (PMA)/ionomycin-induced inflammatory cytokine expression by $T_{EM}$ cells was evaluated by intracellular cytokine staining.
**Results:** Kv1.3 expression by $CD8^+$ $T_{EM}$ cells was significantly higher in patients with active lupus nephritis when compared to patients with inactive SLE or healthy controls. Dalazatide inhibited IFN-$\gamma$, IL-17 and TNF-$\alpha$ production by both $CD4^+$ and $CD8^+$ $T_{EM}$ cells from SLE patients in a dose-dependent manner. Higher levels of dalazatide-mediated inhibition were observed in IFN-$\gamma$ and TNF-$\alpha$-expressing $CD4^+$ $T_{EM}$ cells from patients with active SLE when compared to samples from SLE patients with inactive disease.
**Conclusions:** *Ex vivo* studies suggest that dalazatide inhibition of Kv1.3 may be a therapeutic target for SLE. In addition, Kv1.3 expression may be a useful biomarker of disease activity in SLE.
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## THU0286 THE EFFICACY AND THE LONG-TERM PROGNOSIS OF RITUXIMAB FOR REFRACTORY THROMBOTIC MICROANGIOPATHY ASSOCIATED WITH CONNECTIVE TISSUE DISEASES

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**Background:** Recently, it has been described in many reports that B cell has important roles in connective tissue disease (CTD). Rituximab (RTX), anti-CD20 monoclonal antibody is widely known as effective for patients with several autoimmune hematological disorders including thrombotic microangiopathy (TMA) through not only B cell depletion but reducing antigen-presenting cell function, complement hyperactivation, release of inflammatory cytokines and abnormal auto-reactive T cell response through co-stimulatory signals.[1)] TMA is developed in CTD occasionally. CTD-TMA especially with normal activity of von Willebrand factor cleaving protease, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member-13 (ADAMTS-13) is often resistant for plasma exchange (PE) conducted for thrombotic thrombocytopenic purpura with ADAMTS-13 inhibitor and lack of ADAMTS-13 activity as a first-line treatment.[2)] It has been reported that the autoantibodies other than ADAMTS-13 inhibitor, complement hyperactivation, and excessive inflammatory cytokines production associated with refractory TMA.[3)]
**Objectives:** We investigate the efficacy and the long-term prognosis of RTX treatment for refractory TMA associated with CTD.
**Methods:** We enrolled 7 CTD-TMA patients (SLE; 3, SS; 2, MCTD; 1, DM; 1) with refractory to PE treatment between 2006 and 2015. We examined the ADAMTS-13 activity, its inhibitor and ultra-large von Willebrand factor multimers (UL-VWFMs) at TMA onset. RTX was given 375mg/$m^2$ per a dose. We defined complete response (CR) as platelet counts $>150\times10^9$/l for more than 3 consecutive days, with normal levels of serum LDH and an absence of TMA-related symptoms. We considered CR continued more than 30 days after RTX treatment as remission. In addition, we investigated as follow subjects; duration from initial RTX treatment to CR, duration of sustained CR, relapse and adverse events.
**Results:** No abnormality of ADAMTS-13 activity was observed 6 patients. The thrombocytopenia was improved immediately within 2–3 weeks after the initiation of RTX and hemolytic anemia and neuropsychiatric manifestations were improved following after the recovery of thrombocytopenia, respectively. 6 patients could achieve CR. They who achieved CR all have sustained long-term remission by only 1 or 2 doses of RTX administration and there was no relapse. RTX was partial response for 1 patient with insufficient recovery of thrombocytopenia but detectable serum haptoglobin and she was reported with controllable bacterial pneumonia.
**Conclusions:** We suggest that RTX treatment has efficacy with high response rate and long-term remission for the refractory CTD-TMA patients. Moreover, RTX treatment can be the first-line treatment for CTD-TMA.
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**Disclosure of Interest:** None declared
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## THU0287 GLUCOCORTICOIDS WITHDRAWAL IN SYSTEMIC LUPUS ERYTHEMATOSUS: MYTH O REALITY?

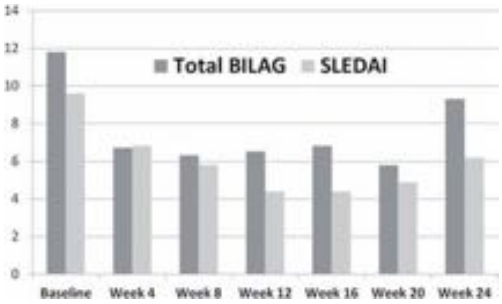
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**Background:** Glucocorticoids (GC) minimization is a pursued goal in the management of systemic lupus erythematosus (SLE) and is a target in patients (pts) management [1]. However, real-life data show that the vast majority of SLE pts are receiving long-term GC therapy despite being considered in clinical remission by their treating physician [2]. Few data are available on treatment discontinuation and tapering protocols in routine clinical practice.
**Objectives:** To analyze the clinical characteristics and the disease outcome of a group of GC free SLE pts
**Methods:** GC-free SLE pts were selected from the lupus clinic database; this is an electronic database where demographic, clinical and serological data, as well as therapies of patients referring to the clinic, are prospectively collected and regularly updated. Disease activity is defined by the clinician's judgement as well as by the SELENA-SLEDAI and the ECLAM scores, damage accrual is computed according to the SLICC-DI score.
**Results:** Out of 410 pts followed at the clinic, 210 had a regular follow-up (at least 3 yearly assessments) and were included in the study. Out of these,46 (21.9%) pts were GC free for at least 3 months and were included in the present analysis. Forty-one (89%)were female and the mean age at enrolment was 43.3±13; 16 pts had a history of lupus nephritis (35%). At the last visit, the median duration of GC withdrawal was 24 months (3–141 months) and 84% were GC free for at least 12 months. Thirty-eight pts (82.6%) were taking antimalarials,32 patients were also immunosuppressant free.At GC stopping, mean disease duration was 11.6±8 years (2 to 35), being less than 5 years in 17%; 21 patients (46%)were in clinical and serological remission, 23 (50%) had serological activity (low complement and/or anti-dsDNA), 2 (4%) had mild hematological abnormalities. Organ damage (SLICC$\geq$1) was present in 12 pts (26%). After GC withdrawal, disease flares were observed in 8 pts (17%): one severe flare (lupus nephritis onset),7 minor flares (3 articular, 2 cutaneous,2 hematological) requiring a short course of GC therapy. Additionally, shortly after GC stopping, fatigue was reported by 3 pts. Interestingly, only two pts (4.3%) accrued further damage during the follow-up (cancer and coronary artery disease) over a period of 60 and 72 and months respectively. No differences in patients' age, disease duration, disease activity or ongoing therapies at GC stopping were observed between pts who flared *vs* those without flares. Additionally, serological activity at GC withdrawal was not associated with an increased risk of disease flare.
**Conclusions:** In our cohort GC withdrawal was successfully attempted in 20% of cases. A severe flare was observed in only one patient; interestingly, a very low damage accrual was recorded. No clinical or serological variables predictive of disease flare after GC stopping were identified. Our data support that GC withdrawal is an achievable goal in SLE patients in routine clinical practice and represent a feasible target in the disease management.
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**Disclosure of Interest:** None declared
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## THU0288 IMMU-115 (HUMANIZED ANTI-CD74 ANTIBODY) FOR SUBCUTANEOUS (SC) ADMINISTRATION: A PHASE IB STUDY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** IMMU-115 (milatuzumab), a humanized antibody targeting the CD74 antigen present on antigen-presenting cells (APC), is being studied in hematological malignancies, but dysregulation of APCs may also occur in nonmalignant disorders. IMMU-115 could thus potentially help control underlying immune responses responsible for autoimmunity.
**Objectives:** To evaluate a weekly dosing regimen of SC IMMU-115 in patients with SLE and moderately active disease.
**Methods:** Phase I, open-label study of adults with SLE (ACR Revised Criteria) and positive ANA (titer $\geq$1:80) who have moderate disease activity but not severe flares (at least 2 BILAG B's, but no A's) despite standard SLE medications incuding at least 5 mg/day prednisone. Patients continued background lupus medications and received SC IMMU-115 administered for 4 consecutive weeks, with disease activity assessed by BILAG2004 and SELENA-SLEDAI every 4 weeks until week 24.
**Results:** Ten patients (9F/1M; median age, 37; median 7 years from diagnosis) have now received 250 mg SC IMMU-115 injections once-weekly for 4 weeks. They were on prednisone (5–20 mg/day, n=10), antimalarials (n=7), and immunosupressives (n=2) with mean SLEDAI 9.6 and BILAG-B activity in the musculoskeletal (n=10), mucocutaneous (n=9), cardiorespiratory (n=1), and renal (n=1) body systems. All patients showed improvement in at least one body system, having eliminated most muscoloskeletal B's (9/10, 90%) and mucocutaneous B's (7/9, 78%) by week 8, with the single cardiorespiratory B eliminated by week 20, and the renal B vacillating between B and C over the study. Four patients developed new B-level disease after treatment at weeks 8, 12 and 20 (all cardiorespiratory) and week 24 (neuropsychiatric). Overall, mean total BILAG (scored using B=5, C=1, D/E=0) decreased 43% with treatment, while mean SLEDAI decreased 54%, with both measures still decreased at week 24 (see Figure). Nine patients had adverse events, all Grade 1–2 (mild-moderate) and predominantly injection site (N=7) or constitutional/flu-like (N=9) reactions managed with supportive medication (steroids, antihistamines, anti-pyretics). Routine safety and other laboratories (B and T cells, monocytes, dendritic cells, serum immunoglobulins, cytokines, ANA and other autoantibodies, CRP, C3) were unremarkable. One patient developed anti-IMMU-115 antibodies (HAHA) of uncertain clinical significance, resolving within 3 months. IMMU-115 serum levels with the current assay were not detectable ($<$0.5 $\mu$g/mL).




**Conclusions:** SC IMMU-115 appeared safe with manageable toxicity in the first cohort of patients with SLE and moderately active disease, all of whom received 250 mg doses given weekly for 4 weeks. Already at this first planned dose level there was evidence of treatment efficacy with suppression of initial disease activity extending 24 weeks in most patients. As such, patients are currently being randomized in a double-blinded placebo-controlled expansion phase in order to confirm the activity of SC IMMU-115 in this population.
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## THU0289 LONG TERM USE OF HYDROXYCHLOROQUINE IN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: A RETROSPECTIVE COHORT STUDY

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**Background:** A potential role of hydroxychloroquine (HCQ) use in patients with antiphospholipid antibodies (aPL) has been suggested by some retrospective cohorts and in animal models based on its potential beneficial effects on autoantibody effect and titer, endothelial function and glucose or lipid metabolism [1–3].
**Objectives:** To evaluate the impact of HCQ on aPL titers, on glucose and cholesterol levels and its role in the prevention of thrombotic recurrences in Primary Antiphospholipid Syndrome (PAPS).
**Methods:** Patients with PAPS, diagnosed according to 2006 Classification Criteria without any Connective Tissue Disease, that received HCQ (HCQ+) but no immunosuppressive drugs, were matched with similar patients that did not received HCQ (HCQ-) according to the following characteristics: same gender, follow-up duration, disease onset, age at the beginning of the follow-up ±10 years and initial date of the follow-up ± 5 years.
**Results:** Seventy-two patients (36 HCQ+ and 36 HCQ-) with a mean follow-up of 77 (±SD 49) months between 1992 and 2015 were studied. No significant variations in demographical, clinical, serological features were observed between the two groups except for of anti-extractable nuclear antigen antibodies (19% in HCQ+ versus 0% in HCQ-,p:0.014). Anti-β2Glycoprotein I IgG titers were significantly lower in HCQ+ than in HCQ- patients at the end of the follow-up (Student t,p:0.018). The variations of all the aPL titers in the two groups are shown in Figure 1. No differences in glucose and cholesterol levels were detected. Eight percent of HCQ+ and 17% of HCQ- patients experienced a thrombosis during the follow-up. Among patients with a history of thrombosis the annual incidence of recurrences was lower (0,87%) in HCQ+ patients than in HCQ- (2,17%).

Table 1. Prevalence of medium-high titer antiphospholipid antibodies over follow-up

| Antiphospholipid antibodies medium-high titers | Variation between beginning and end of follow-up in HCQ+ (%) | Variation between beginning and end of follow-up in HCQ– (%) |
|---|---|---|
| Anticardiolipin IgG | –25% | –4% |
| Anticardiolipin IgM | –0% | +11% |
| Anti-β2 Glycoprotein IgG* | –30% | –7% |
| Anti-β2 Glycoprotein IgM | –28% | –6% |

*Statistically significant (p=0.04).

**Conclusions:** This study showed a strong reduction of aPL titers and of the incidence of recurrences in patients treated with HCQ, supporting a possible role of this drug in the treatment of patients with PAPS.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4186

## THU0290 TWELVE MONTHS SURVIVAL RATE AND CAUSES OF WITHDRAWAL OF BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS IN A REAL LIFE SETTING

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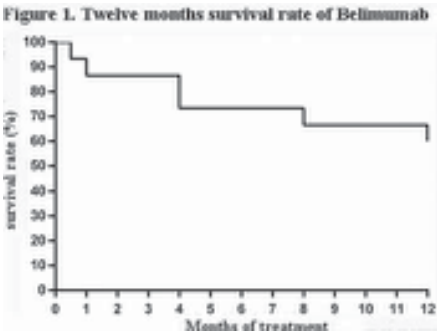
**Background:** Systemic Lupus Erythematosus (SLE) is a chronic disease requiring long-term treatment. Even though immunosuppresive therapy has significantly improved the survival, a great percentage of SLE patients exhibit a persistently active disease or deal with disease flares during the follow-up. Belimumab (BLM), an anti-*B Lymphocyte Stimulator* (BLyS), is currently the only biological drug approved for the treatment of active SLE patients not responding to standard of care, without active kidney or neuropsychiatric involvement.
**Objectives:** Aim of the study was to analyse 12 months survival of BLM treatment and causes of withdrawal in a monocentric cohort of SLE patients followed-up in a daily practice setting.
**Methods:** The study was proposed to all the patients who were due to start BLM. After the informed consent was obtained, demographic, clinical and serological data, indication to BLM and concomitant therapies were registered. At baseline and after 3, 6 and 12 months of follow-up, disease activity (SLE Disease Activity Index – SLADAI 2K), C3 and C4 levels, anti-dsDNA status and weekly dose of glucocorticoids were recorded. At each visit adverse events and causes of withdrawal were also evaluated. Data were expressed as mean±standard deviation; after 3, 6 and 12 months, difference in SLEDAI 2K, C3 and C4 and prednisone-equivalent dose compared to baseline were evaluated by Student t test. The treatment survival was evaluated by Kaplan-Meier analysis. P value $<$0.05 were considered significant.
**Results:** We enrolled to the study 15 Caucasian females with mean age of 41.3±10.1 years and mean disease duration of 19.2±9.2 years. Indication for starting BLM were: mucocutaneous involvement (n=5, 33.3%), arthritis (n=10, 66.7%) and lung involvement (1 patient, 6.7%). At baseline, all the patients were taking prednisone; 88.7% hydroxychloroquine, 33.3% mycophenolate mofetil, 20% azathioprine, 20% cyclosporine, 20% methotrexate and 6.7% thalidomide.

Table 1 summarizes the trend of SLEDAI 2K, C3 and C4, prednisone dose and percentage of patients positive for anti-dsDNA during the follow-up.
The Kaplan-Meier (Figure 1) shows a 12 months survival rate of 60%. In 13.3% of patients adverse events were the cause of BLM withdrawal (severe infection in one patient and acute infusion reaction in another one). In 2 patients (13.3%) BLM was discontinued for lack of efficacy on articular and skin manifestations, after 4 and 8 months respectively; one patient developed a severe neuropsychiatric flare after the second BLM infusion and was admitted in our hospital for depression and suicidal thoughts. The other patient was lost during the follow-up.

Table 1. SLEDAI 2K, C3 and C4, prednisone dose and anti-dsDNA status during the follow-up

| | T0 | T3 | T6 | T12 |
|---|---|---|---|---|
| N° of patients | 15 | 13 | 11 | 9 |
| PDN mg/sett[#] | 80.7±39.2 | 51±17.2* | 45±18,5* | 30.9±26.1* |
| SLEDAI 2K[#] | 7±2.8 | 5.9±2.7 | 5.6±2.7 | 3.7±3.1** |
| C3[#] | 71.7±18.5 | 71.2±16.8 | 70.9±12.1 | 73.3±18.3 |
| C4[#] | 16.4±6.6 | 12.4±5.8 | 9.9±4.3 | 12.3±8.5 |
| aDNA+ (%) | 100 | 41.6** | 30** | 28.5** |

[#] mean ± standard deviation; *p<0.05; **p<0.005.




**Conclusions:** In our monocentric cohort of SLE patients treated in a real life setting, the main causes of BLM withdrawal were the lack of efficacy or disease flare.
**Disclosure of Interest:** None declared
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## THU0291 ENDOTHELIAL PROGENITOR CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS: EFFECT OF B LYMPHOCYTE STIMULATOR AND ITS INHIBITION

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**Background:** Cardiovascualar disease is the main comorbidity in Systemic Lupus Erythematosus (SLE). Circulating endothelial progenitor cells (EPCs) are bone marrow-derived cells, able to differentiate into mature endothelial cells. Several studies demonstrated a reduction and functional impairment of EPCs in SLE patients, contributing to the endothelial dysfunction characterizing these patients. Belimumab (BLM), a human monoclonal antibody anti-B Lymphocyte Stimulator (BLyS) is the first biological drug approved for the treatment of SLE patients. In murine models of atherosclerosis, treatment with a BLyS inhibitor slowed the progression and reduced the size of atherosclerotic plaque.
**Objectives:** to evaluate the effect of BLyS inhibition on EPCs both *ex vivo* – in SLE patients receiving BLM– and *in vitro*.
**Methods:** We enrolled consecutive patients with SLE diagnosed according to 1997 ACR criteria. Patients with known cardiovascular disease were excluded. As control, we studied age and sex-matched healthy subjects. SLE disease activity was evaluated by SLEDAI 2K at baseline and after 4 and 12 weeks of BLM; blood samples were collected at the same time-point. Peripheral blood mononuclear cells (PBMC) isolated by Ficoll density-gradient centrifugation were incubated with fluorescein isothiocyanate-labeled anti-CD34 monoclonal antibodies and phycoerythrin-labeled anti VEGF-R2/KDR; acquisition was performed by flow cytometry: EPCs were defined as CD34/KDR double-positive cells. For *in vitro* studies, recovered cells isolated from healthy donors' PBMC were plated on dishes coated with human fibronectin. Apoptosis was investigated after 6, 12, 24 and 48 hours of incubation with BLyS at different concentration – 5, 20 and 100 ng/ml – and re-evaluated after 6 hours of co-incubation with BLM at 173 and 300 μg/ml. Kolmogorov-Smirnov showed the normal distribution of EPCs; data were expressed as mean±standard deviation. To test the hypothesis that BLM may increase EPCs number we used one-tailed T-test. A p value <0.05 was considered statistically significant.
**Results:** We enrolled 18 female patients (mean age 41.3±10.1 yrs, mean disease duration 19.2±9.2 yrs). Number of EPCs was significantly lower in SLE patients compared to NHS (p<0.0001). Of the 18 patients, 10 (mean age 44.9±9.6 yrs, mean disease duration 15.6±10.0 yrs) started BLM for refractory disease (mean baseline SLEDAI 2K 7.1±3.1). After 4 and 12 weeks, SLEDAI 2K tended to decrease (p=ns). Baseline EPC number was significantly lower compared to NHS (p=0.002). After 4 weeks, mean EPC number increased to 0.026±0.015 (p=0.038 vs baseline; p=n.s. vs NHS). At week 12 we observed a slight decrease of EPC number compared to week 4 (0.021±0.015 p=ns).
*In vitro* studies demonstrated that 20 ng/ml of BLyS induced apoptosis of EPC after 6 hours of incubation; this effect was reverted by the addiction of 173 and 300 μg/ml of BLM. BLM alone did not induce apoptosis of EPC.
**Conclusions:** This study confirms a reduction of EPCs number in SLE patients compared to NHS. Treatment with BLM significantly increased EPCs number. *In vitro* data suggest a direct role of BLM by demonstrating a pro-apoptotic effect of BLyS that was reverted by the addition of the human anti-BLyS in EPCs culture. These results furhter support a contribution of BLyS and B cells in the promotion of atherosclerosis.
**Disclosure of Interest:** None declared
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## THU0292 C-PEPTIDE AND MODIFIED HOMA-INDEX IN DIFFERENT CARBOHYDRATE METABOLISM DISTURBANCES DURING GLUCOCORTICOID THERAPY

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**Background:** Glucocorticoid administration can lead to profound metabolic side-effects, including peripheral insulin resistance (IR), impaired glucose tolerance (IGT) and hyperglycemia and diabetes mellitus (DM). Homeostatic model (HOMA) is a validated method of IR evaluation.
**Objectives:** To evaluate the role of C-peptide and modified HOMA-index in different carbohydrate metabolism disturbances (CMD) during glucocorticoid therapy.
**Methods:** 165 patients were included: 53 patients with systemic lupus erythematosus (LE), 35 - with systemic vasculitis (SV); 67 - with chronic glomerulonephritis (CGN). 98 patients received glucocorticoid pulse-therapy (GC-PT) (1 course of 3 sessions) and 67 received oral GC. All patients underwent standard clinical and laboratory tests, glucose tolerance test (GTT), C-peptide evaluation, also HOMA-IR was calculated.
**Results:** Oral GCT group revealed increased prevalence of CMD and DM – in 21 (31.1%) and 19 (28.4%) patients, respectively, compared to GC-PT group (p=0.038 and p=0.049, respectively). All patients receiving GC-PT (both with CMD and normoglycemia) demonstrated significant increase of C-peptide level and HOMA-IR index on during maximal blood glucose level, that is 4–6 hours after GC-PT (p<0.05). In patients with CMD HOMA-IR index normalization was insignificant; there were significant differences between the evaluated parameters before and after GC-PT, which indicates a more pronounced IR in these patients. C-peptide level in patients with DM, which developed after GC-PT, was significantly elevated compared to patients without CMD both at baseline (1050 vs. 410 pmol/l, respectively) and after GC-PT course (1796 vs. 1152 pmol/l, respectively) (p<0.05). During maximal blood glucose levels C-peptide was significantly elevated in patients with CMD, compared to patients without CMD (3170 vs. 2430 pmol/l; p<0.05), which substantiates the development of severe IR in patients with CMD and DM. HOMA-IR index in patients with DM was significantly elevated compared to patients without CMD at baseline (5.04 vs. 2.2; p<0.05), during maximal blood glucose level (15.2 vs. 5.84; p<0.05) and after GC-PT course (10.4 vs. 4; p<0.05) and in patients with IGT compared to patients without CMD – during maximal blood glucose levels (17.47 vs. 5.84; p<0.05) and after GC-PT course (9.67 vs. 4; p<0.05). C-peptide level was significantly elevated in patients receiving oral GC therapy and demonstrating impaired fasting glucose, IGT and DM compared to patients without CMD both at baseline (681.2, 877.9, 1106.1 vs. 384.7 pmol/l; p<0.05) and after OGTT (1411, 3296.7, 4981.7 vs. 839.2 pmol/l; p<0.05). C-peptide elevation after oral GTT was accompanied by a significant increase in HOMA-IR index compared to control group in patients with impaired fasting glucose, IGT and DM (6.37 vs. 9.04, 16.21, 19.84; p<0.05).
**Conclusions:** CMD is more prevalent after oral GC therapy compared to GC-PT. In both groups C-peptide levels and HOMA-IR index were elevated in patients with IGT and DM both at baseline and after oral GTT, compared to patients without CMD and fasting glucose impairment, which proposes a presence of IR in that group of patients. HOMA-IR index can be utilized for the prognosis and early diagnostics of profound CMD in patients receiving intensive GC therapy and prolonged oral GC therapy.
**Disclosure of Interest:** None declared
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## THU0293 SAFETY, PHARMACOKINETICS, ENZYME ACTIVITY, AND IMMUNOGENICITY OF RSLV-132, A NOVEL RNASE FUSION PROTEIN DEVELOPED TO REDUCE RNA-CONTAINING IMMUNE COMPLEXES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** RNA-associated with immune complexes (ICs) is recognized to

play a central role in driving interferon production and systemic inflammation in systemic lupus erythematosus (SLE). To date, therapeutic strategies which have sought to block interferon directly or to target various B-cell regulatory proteins have met with mixed success. Given the proximal point of nucleic acid-containing ICs in the inflammatory cascade, reduction in associated RNA is expected to render the ICs less pathogenic. RSLV-132 is a fully-human Fc fusion protein consisting of the Fc domain of IgG1 fused to human RNase 1 that is designed to enzymatically digest RNA-containing ICs.

**Objectives:** This multiple ascending dose study of RSLV-132 in SLE patients was carried out to assess the safety, pharmacokinetics (PK), serum enzyme activity, and immunogenicity of this novel biologic in SLE.

**Methods:** A phase 1b, multicenter, randomized, double-blind, placebo-controlled study evaluated 4 dose cohorts (0.3 – 10.0 mg/kg) administered by intravenous infusion. Each cohort consisted of 8 subjects (6 received RSLV-132 and 2 received placebo). Three to five doses were given over 29 days. Serum samples were collected and analyzed for PK analysis, anti-drug antibody (ADA) assessment, autoantibody profiles, and RNase catalytic activity assessment.

**Results:** A total of 61 adverse events (AEs) were recorded in the 32 subjects during the study. One grade 3 event (cholecystitis; unrelated) occurred in a subject in the 0.3 mg/kg group There were no deaths in the study. The PK analysis demonstrated a linear increase in serum RSLV-132 concentration with a terminal half-life of approximately 19 days. None of the subjects in the study were positive for ADA. RNase catalytic activity increased in a proportional manner up to approximately 100 ug/ml at $C_{max}$ in the 10 mg/kg dose cohort, and very closely paralleled the drug concentration curve detected by ELISA. SLEDAI scores were recorded during the study and of the evaluable subjects (SLEDAI $>0$) a greater proportion of RSLV-132-treated subjects (44%) saw a reduction in SLEDAI scores than in the placebo group (33%). Given the small size of the study this trend will need to be confirmed in larger studies.

**Conclusions:** RSLV-132 is a promising, novel biologic for the treatment of SLE. An excellent safety profile was observed in the current study. The PK profile showed good dose-proportionality and the observed half-life will support bi-weekly dosing going forward. High serum RNase activities were achieved and sustained over the entire course of the study with no evidence of an ADA response. The results of this study support continued development of RSLV-132 in SLE.

**Disclosure of Interest:** None declared

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## THU0294 AN INTERNATIONAL CONSENSUS EXERCISE TO CLASSIFY SLE DAMAGE ITEMS ACCORDING TO THEIR LIKELY ASSOCIATION WITH STEROIDS

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**Background:** Corticosteroids (CS) have been identified as a key factor associated with long term damage in systemic lupus erythematosus (SLE). The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) has been extensively validated and a previous analysis (Gladman et al J Rheumatol 2003;30:1955–9) suggested that SDI items can be grouped according to their likely association with CS.

**Objectives:** To generate international expert consensus opinion on which SDI items have an association with the use of CS.

**Methods:** We performed a Delphi exercise amongst SLICC members and associates. A survey requested expert opinions on how each SDI item was influenced by CS use on a Likert scale. The scale ranged from -3 to +3 where -3 = I believe that CS have a strong protective link with this item, 0 = I believe that CS have no effect on this item, +3 = I believe that CS have a strong causal link with this item. A second Delphi round presented each participant with their previous rating and the group median for that item, providing the opportunity for revision. A preliminary univariate analysis of CS exposure against damage was performed within the SLICC Inception Cohort to assess the appropriateness of these groupings and if any other items needed reclassifying.

**Results:** Of 43 members/associates, 36 respondents returned 26 complete forms (60.5%). All 26 completed the second round (100%) after which adequate consensus was reached. Four items (cataract, osteoporosis, avascular necrosis and diabetes mellitus) were assessed to be highly likely to be related to CS (median & mode =3, Table 1). Ten other items were "probably"/"possibly" CS related by expert opinion. The remaining items were felt not to be associated with CS. The univariate analysis supported these groupings and identified a significant association between CS exposure and the muscle atrophy/weakness item (e.g. OR (95% CI) 6.81 (1.91–24.27) if on steroids for all of intervening follow up period c.f. some or none of the period). It was agreed that muscle atrophy/weakness should be reclassified into the 'definite association' group.

**Conclusions:** A consensus exercise based on expert opinion and initial analysis in an international inception cohort has generated a preliminary classification of the 42 SDI items according to their likely association with CS. This classification system requires further validation but will facilitate studies examining the impact of CS exposure on SLE populations.

**Acknowledgement:** The Systemic Lupus International Collaborating Clinics (SLICC) acknowledge funding support of UCB Pharma for this study.

Table 1. Groupings of SLICC/ACR Damage Items (SDI) according to likely association with the use of CS (highly likely, probable and possible causative role groups shown only)

| CS have a causative association the SDI item | SDI item | Likert scale rating | |
|---|---|---|---|
| | | Median (range) | Mode (%) |
| Definite | Cataract | 3 (2,3) | 3 (69.23) |
| | Osteoporosis | 3 (2,3) | 3 (92.31) |
| | Avascular necrosis | 3 (2,3) | 3 (76.92) |
| | Diabetes | 3 (2,3) | 3 (76.92) |
| Definite (in final consensus) | Muscle atrophy or weakness | 2 (–2,3) | 2 (50.00) |
| Probable | Angina or coronary artery bypass | 2 (1,3) | 2 (46.15) |
| | Myocardial infarction | 2 (0,3) | 2 (50.00) |
| Possible | Cognitive impairment | 1 (–1,3) | 1 (42.31) |
| | Cerebrovascular accident | 1 (–3,3) | 1 (42.31) |
| | Claudication | 1 (–1,2) | 1 (46.15) |
| | Osteomyelitis | 1 (0,3) | 1 (65.38) |
| | Ruptured tendon | 1 (–1,3) | 1 (50.00) |
| | Major Psychosis | 1 (–2,3) | 2 (30.77) |

**Disclosure of Interest:** None declared

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## THU0295 ANIFROLUMAB REDUCES DISEASE ACTIVITY IN MULTIPLE ORGAN DOMAINS IN MODERATE TO SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** As reported elsewhere, anifrolumab was evaluated in a Phase IIb study of SLE patients with moderate to severe disease activity, in which 305 patients received intravenous infusions of anifrolumab (300 mg, 1000 mg) or placebo every 4 weeks for 1 year. Both doses demonstrated increased rates of reduction in global disease activity, although a more favorable risk-benefit profile was observed with the 300-mg dose.

**Objectives:** To compare the impact of anifrolumab on individual organ domains in patients with moderate to severe SLE who participated in the Phase IIb study.

**Methods:** At Week 52, changes from baseline in organs domain activity were assessed using the British Isles Lupus Assessment Group (BILAG) and SLE Disease Activity Index 2000 (SLEDAI-2K). Improvement in a BILAG organ domain was defined as the transitioning from "A" or "B" to a lower score. Improvement in a SLEDAI domain required a lower score at Day 365 compared with baseline in at least one of its components.

**Results:** The majority of patients had baseline involvement of the mucocutaneous and/or musculoskeletal domains of SLEDAI-2K and BILAG. Compared with placebo, a greater percentage of patients in the anifrolumab-treated group improved in these frequently involved organs: [Mucocutaneous: SLEDAI-2K: placebo 38/100 (38.0%) vs. 300 mg 61/99 (61.6%; $p<0.001$) vs. 1000 mg 51/102 (50.0%; $p=0.082$); BILAG: 24/87 (27.6%) vs. 49/84 (58.3%; $p<0.001$) vs. 33/82 (40.2%; $p=0.069$); Musculoskeletal: SLEDAI-2K: 42/99 (42.4%) vs. 55/97 (56.7%; $p=0.032$) vs. 50/98 (51.0%; $p=0.197$); BILAG: 47/95 (49.5%) vs. 64/94 (68.1%; $p=0.005$) vs. 54/91 (59.3%; $p=0.149$)]. Trends suggesting potential benefits were observed in most of the other less frequently active domains including SLEDAI-2K cardiorespiratory, vascular, hematological, and constitutional, and BILAG cardiorespiratory and constitutional domains. Of those patients who had involvement in the SLEDAI-2K immunological domain at baseline [positive anti-double-stranded-DNA (anti-dsDNA) and/or low complement level], a greater number of patients in the anifrolumab groups [placebo: 4/53 (7.5%); 300 mg: 9/43 (20.9%; $p=0.068$); 1000 mg: 18/59 (30.5%; $p=0.004$)] had lower scores at Day 365, representing a normalization of anti-dsDNA and/or hypocomplementemia. However, among patients who had a normal anti-dsDNA and/or normal complements at baseline a slightly greater number of patients treated with 300 mg anifrolumab had an increase in the score representing the development of a new anti-dsDNA or hypocomplementemia compared with baseline [placebo: 7/79 (8.9%); 300 mg: 11/82 (13.4%), 1000 mg: 6/79 (7.6%)].

**Conclusions:** Anifrolumab treatment resulted in greater rates of improvement than placebo in multiple organs, with greatest impact seen with 300 mg anifrolumab.

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## THU0296 LOW BM, LOW HDL CHOLESTEROL AND CURRENT STEROID DOSE MIGHT CONTRIBUTE TO SUBCLINICAL ATHEROSCLEROSIS IN SLE PATIENTS WITH LOW DISEASE ACTIVITY

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**Background:** Systemic lupus erythematosus (SLE) patients have increased risk of advanced atherosclerosis and cardiovascular disease. The mechanism of premature atherosclerosis in SLE is not completely understood, and systemic inflammation representing disease activity and traditional risk factors such as overweight and dyslipidemia have been regarded to contribute. Many SLE patients have low disease activity or sporadic occurrence of mild symptoms after a period of vigorous manifestations derived from autoimmune activation.
**Objectives:** Previously we evaluated subclinical atherosclerosis of SLE patients with mild disease activity by Doppler ultrasound 4 years ago[1]. This time we checked them again and assessed which features affects their changes.
**Methods:** We assessed carotid artery intima-media thickness (cIMT) and carotid plaque by Doppler ultrasonography among sixty-one female SLE patients who were enrolled in the previous work 4 years ago, and analyzed the changes with clinical characteristics.
**Results:** The SLE disease activity index of the participants was 4.2 ± 3.9, and 25(OH)$D_3$ level was elevated than previous study (25.7 ± 6.9 vs 12.7 ± 8.6 ng/mL, $p<0.001$), while other features were similar. The mean cIMT of SLE patients was 0.39 ± 0.09 mm and 11 patients had carotid plaques, which were not significantly different with previous study. Twenty one patients had the increased cIMT, while 35 patients had decreased cIMT. And new carotid plaque was developed in 7 SLE patients, while the carotid plaque of 10 SLE patients was resolved. The patients with increased cIMT had lower body mass index (BMI) (19.8 ± 1.8 vs 21.7 ± 3.1 kg/$m^2$, $p$=0.007), longer disease duration (102.0 ± 42.2 vs 74.8 ± 55.2 months, $p$=0.006) and higher total steroid dose (18.5 ± 21.6 vs 10.5 ± 22.9 g, $p<0.001$) compared with those not. The patients having new carotid plaque had lower high-density lipoprotein (HDL) cholesterol levels (41.6 ± 10.2 vs 55.6 ± 15.5 mg/dL, $p$=0.024) and were taking higher doses of current steroid (8.9±9.5 vs 3.6±4.5mg, $p$=0.008). On multiple regression analysis, BMI (0.62 [0.42–0.91], $p$=0.01) and HDL cholesterol (0.94 [0.89–1.0], $p$=0.02) were revealed to affect cIMT increment, and current steroid dose (1.14 [1.01–1.28], $p$=0.04) were revealed to affect plaque development.
**Conclusions:** BMI have been known to affect atherosclerosis and vitamin D deficiency has been known to associate with cardiovascular disease. In contrast of other studies, our data showed BMI contributed negatively cIMT increment. The result about BMI was regarded that very low BMI might have a harmful effect to atherosclerosis, considered that mean BMI was much lower (21.0 ± 2.8 kg/$m^2$) than other studies[2].The follow up study for SLE patients with low disease activity showed low BMI and HDL cholesterol might be a risk factor for subclinical atherosclerosis and current steroid dose could be associated with plaque development.
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## THU0297 PHYSICAL ACTIVITY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: EFFECTS ON FATIGUE AND DEPRESSIVE BEHAVIOR FOR IMPROVED QUALITY OF LIFE

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**Background:** Because of the fact that systemic lupus erythematosus (SLE) causes joint and muscle pain, fatigue, depression, the very thought of exercising can be a challenge for patients. Although exercise can be beneficial and can significantly improve the quality of life.
**Objectives:** The aim of the study is to determine the form of physical activity in SLE patients that could improve their quality of life. Although exercise can be beneficial and can significantly improve the quality of life.
**Methods:** This prospective study included 60 patients diagnosed with SLE in stable condition. A randomly selected group of 30 women had aerobic training on a bicycle ergometer for a period of 15 minutes, 3 times per week for 6 weeks, while the second group of 30 women did exercise for 30 minutes, 3 times per week during the same period. FSS (fatigue Severity Scale), Short Form 36 (SF36) questionnaire on the quality of life and Beck depression inventory (BDI) were analyzed at baseline and after 6 weeks.
**Results:** Fatigue was present in all patients (FSS score 53.8 ± 5.7; min 39, max 63) before starting the exercise. Fatigue was present in 11 patients (18.3%) after the physical activity while 49 (81.7%) patients did not experience it (FSS score 29.1 ± 7.8; min 18, max 45). Before starting the exercise the largest number of patients, 40 (66.67%) of them, was in a moderate depressed state, while after physical activities the greatest number of patients, 37 (61.66%), had a mild mood disturbance. There are high statistical differences ($p<0.001$) in values of all areas of quality of life questionnaire SF36 before and after the implementation of physical activity. Comparing the different types of physical activities there were not any statistically significant differences ($p>0.05$) in values of FSS and BDI questionnaire. A statistically significant difference was observed in terms of reducing the parameters of pain, general health and mental health in a group that had a physical activity on a bicycle ergometer evaluated by the SF36 questionnaire ($p<0.05$).
**Conclusions:** Our study has shown that a continuous physical activity in SLE patients significantly improves their quality of life by reducing fatigue and depressive reactions without negative impacts on the activity of their disease. The type of physical activity was not relevant.
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## THU0298 TYPE I INTERFERON PREDICTS BIOLOGICAL EFFECT OF BELIMUMAB ON RHEUMATOID FACTOR POSITIVE B-CELLS IN SJÖGREN'S SYNDROME: RESULTS FROM THE BELISS TRIAL

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**Background:** B-lymphocyte Stimulator (BLyS, or BAFF), a survival factor for B cells, has been previously implicated in the pathogenesis of Sjögren's syndrome (SS) and SS related lymphoproliferation (1–2). It has been also previously shown to be induced by both type I and II Interferons (IFNs) also implicated in the pathogenesis of SS (3). Belimumab, an anti-BAFF monoclonal antibody that targets BAFF, was recently found to be effective and safe in SS in the phase II BELISS trial (4–5).
**Objectives:** To explore the possible effect of belimumab on IFN-induced peripheral blood gene expression in the phase II BELISS trial. Additionally, to evaluate whether baseline IFN signature could serve as a predictor of clinical and serological responses following belimumab treatment.
**Methods:** Twelve patients who were enrolled in the phase II BELISS trial were studied for peripheral blood IFN signature at baseline, at w28 (10/12), and at w52 (4/12). Patients were all females, median 47.5 yrs (35–79), all positive for anti-SSA/SSB and for rheumatoid factor (RF), with a median ESSDAI score of 7 (2–27) at BELISS study entry. Peripheral blood mononuclear cells from all study participants were subjected to Real-Time PCR for 3 interferon inducible genes (MX-1, IFIT-1, IFI44) preferentially induced by type I IFN and 2 interferon inducible genes preferentially induced by type II IFN (MIG-1, GBP1). Both type I and II IFN scores were determined, as previously described.
**Results:** No statistically significant changes were observed between baseline and w28 or w52 type I IFN scores (mean±SE: 17.8±3.2 vs 19.9±3.7 vs 20.2±1.2, respectively, $p>0.05$ for all comparisons by paired sample t-tests). Baseline type I IFN scores were correlated with changes in rheumatoid factor from baseline to w52, baseline mental component score of SF-36 (r=0.7/p=0.007, and r=0.8/p=0.003, respectively, by Pearson's test). When patients were subdivided in two groups, i.e. low IFN score and high IFN score, based on the baseline mean of IFN score, a significant differences were found between low and high IFN score groups as regards baseline to w52 changes in IgG (p=0.004, by Mann-Whitney), IgA (p=0.004, by Mann-Whitney), IgM levels (p=0.03, by Mann-Whitney) in favour of high IFN score group, while changes in RF levels tended to be significant (p=0.08, by Mann-Whitney). No significant changes or associations with type II IFN scores were observed.
**Conclusions:** Type I IFN-induced peripheral blood gene expression may affect the magnitude of biological effect of belimumab in SS, and in particular on RF-positive B-cell clones. Patients showing higher IFN signature may be the optimal target for belimumab in SS.
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## THU0299 B CELL COMPARTMENT AND PHARMACODYNAMICS OF BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS: EARLY CLINICAL EFFICACY BY DEPLETION OF CD27- AND INCREASE OF CD27+ B CELLS

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**Background:** Belimumab, a human anti-BAFF monoclonal antibody that inhibits soluble BAFF, is effective in systemic lupus erythematosus (SLE), and leads to a partial B cell depletion. However, which subset of B cells may be the main therapeutic target of belimumab in SLE is still unclear.
**Objectives:** Primary objective of this study was to evaluate the effect of belimumab on the expression of BAFF receptor (BAFFR) on B cells through 12 months of belimumab treatment in SLE, and to correlate BAFFR expression with changes in B cell subsets.
**Methods:** Twelve consecutive patients with SLE (all female, age 44±7,8 yrs, 12,6±5,4 yrs of disease duration) undergoing belimumab therapy were studied. All patients received at least two immunosuppressors before belimumab. All patients were taking glucocorticoids at baseline [median (range): 7,5 (0–40) mg/day of prednisone or equivalent)], and 11/12 also at least one immunosuppressor. Median SLEDAI-2k score at baseline was 8,5 (range 8–15). Samples were collected and analysed at baseline (T0), month +3 (T3), +6 (T6), +9 (T9) and +12 (T12) for clinical and biological parameters. B cells subsets were characterized by multiparametric flowcytometry on a BD FACSCanto flowcytometer. The expression of BAFFR was also analysed as Mean Fluorescence Intensity (MFI). Parametric or non-parametric tests were used, as appropriate based on variable distribution. Data is reported as mean±standard error.
**Results:** A transient statistically significant increase of BAFFR MFI was observed from T0 to T3 (p=0,004) and from T0 to T6 (p=0,066) with a subsequent decrease until T12 (table 1). Interestingly, this course was similar to that observed in CD19+CD27+ cell subset (table 1), that showed a transient significant increase at T3 (p=0,014) and T6 (p=0,025) in 9/12 patients, with a subsequent slightly significant decrease from T6 to T12 (p=0,05) in all patients. Globally, a decrease of CD19+ cells was observed from T0 to T12 (p=0,19, table 1). This course is consistent with that observed in the CD27- B cell subset, that showed a decrease from T0 to T3 (p=0,14) and from T0 to T6 (p=0,14), and the decrease was persistent from T6 to T12 (p=0,6). SLEDAI-2k score decreased from T0 to T3 (p=0,007), to T6 (p=0,003) and to T12 (p=0,03) (table 1).
**Conclusions:** BAFF depletion differently acts on B cell subsets, CD19+27+ subset being able to increase BAFFR and transiently expand themselves, while CD19+27- being more sensitive to BAFF deprivation, and faster decreasing. Thus, early clinical response may be related to the changes in the CD27+/CD27- B cell ratio.
**Disclosure of Interest:** None declared
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## THU0300 RISK FACTORS FOR ADVERSE PREGNANCY OUTCOME IN FIRST-LINE TREATED PREGNANCIES IN ANTIPHOSPHOLIPID ANTIBODIES-POSITIVE WOMEN ACCORDING TO DIFFERENT TREATMENT STRATEGIES: RESULTS FROM OUR 30 YEARS'EXPERIENCE PREGNANCY CLINIC

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**Background:** Antiphospholipid antibodies (aPL) are risk factors for Adverse Pregnancy Outcome (APO). The therapeutic strategy to adopt in aPL patients during pregnancy should in fact consider different clinical and serological risk factors. In addition to conventional therapy, some recent evidences suggest a possible role of hydroxychloroquine.
**Objectives:** To review our approach in first-line treated pregnancies in aPL patients in our 30 years' experience Pregnancy Clinic (1985 -2015) to find out which clinical and serological risk factors have influenced the choice of treatments and which should be considered in the future for possible additional treatments.
**Methods:** We reviewed 120 first-treated pregnancies that were prospectively followed in our center by a multispecialistic team of Rheumatologists and Obstetricians. Patients were classified as Primary Antiphospholipid Syndrome (PAPS) according to revised criteria and as Incomplete PAPS or aPL carriers according to their clinical history or aPL status. Patients with concomitant systemic autoimmune diseases were excluded. aPL profile was defined as the combination of the 3 criteria tests for aPL (Lupus Anticoagulant, anti-cardiolipin, anti-Beta2 Glycoprotein I). APO was defined as at least one of the followings: miscarriage (<10th week), fetal death (≥10th week), severe preterm delivery (≤34th week) with or without preeclampsia (PE), HELLP syndrome or perinatal death.
**Results:** The type of therapy was divided in three main categories: combination therapy with low molecular weight heparin (LMWH) and LDA (68,57%), single therapy with low dose aspirin (LDA) (31,26%) and therapy with corticosteroids plus LDA (21,18%).
We collected 16 APO (13%): 11 (75%) in the category of LMWH+LDA. Analyzing APO vs. non-APO pregnancies we found no differences in variables that could predict an APO (history of thrombosis, a previous APO or a triple positive aPL profile) in any of the 3 categories (Table 1). Moreover, we found an increased rate of non criteria aPL manifestations in APO patients in LMWH+ASA category (31% vs. 4%, p:0.002; OR 2.19, 95%CI 2.20–61.6), but not in the other 2 categories of treatment.

| | Pregnancies with APO (n=16) | Pregnancies without APO (n=104) | P Value |
|---|---|---|---|
| **LDA+LMWH (n=68)** | **11 (69%)** | **57 (55%)** | |
| Obstetric PAPS (n=35) | 5 (31%) | 30 (29%) | |
| **Thrombotic ± Obstetric PAPS (n=12)*** | **2 (13%)** | **10 (10%)** | **0.662** |
| Non-criteria PAPS (n=13) | 1 (6%) | 12 (12%) | |
| aPL carriers (n=8) | 3 (19%) | 5 (5%) | |
| Single positive (n=54) | 4 (25%) | 30 (29%) | |
| Double positive (n=12) | 1 (6%) | 11 (11%) | |
| **Triple positive (n=22)*** | **6 (38%)** | **16 (15%)** | **0.075** |
| **Previous APO (n=52)*** | **7 (44%)** | **45 (43%)** | **1.000** |
| **Non-criteria aPL manifestations° (n=9)*** | **5 (31%)** | **4 (4%)** | **0.002** |
| **LDA in single therapy (n=31)** | **2 (13%)** | **29 (28%)** | |
| Obstetric PAPS (n=7) | 0 (0%) | 7 (7%) | |
| **Thrombotic ± Obstetric PAPS (n=0)*** | **0 (0%)** | **0 (0%)** | **1.000** |
| Non-criteria PAPS (n=11) | 0 (0%) | 11 (11%) | |
| aPL carriers (n=13) | 2 (13%) | 11 (11%) | |
| Single positive (n=24) | 1 (6%) | 23 (22%) | |
| Double positive (n=5) | 0 (0%) | 5 (5%) | |
| **Triple positive (n=2)*** | **1 (6%)** | **1 (1%)** | **0.250** |
| **Previous APO (n=19)*** | **0 (0%)** | **19 (18%)** | **0.072** |
| **Non-criteria aPL manifestations° (n=3)*** | **0 (0%)** | **3 (3%)** | **1.000** |
| **Corticosteroids + LDA (n=21)** | **3 (19%)** | **18 (17%)** | |
| Obstetric PAPS (n=9) | 2 (13%) | 7 (7%) | |
| **Thrombotic ± Obstetric PAPS (n=5)*** | **0 (0%)** | **5 (5%)** | **1.000** |
| Non-criteria PAPS (n6=) | 1 (6%) | 5 (5%) | |
| aPL carriers (n=1) | 0 (0%) | 1 (1%) | |
| Single positive (n=8) | 2 (13%) | 6 (6%) | |
| Double positive (n=13) | 1 (6%) | 12 (12%) | |
| **Triple positive (n=0)*** | **0 (0%)** | **0 (0%)** | **1.000** |
| **Previous APO (n=19)*** | **3 (19%)** | **16 (15%)** | **0.717** |
| **Non-criteria aPL manifestations° (n=5)*** | **1 (6%)** | **4 (4%)** | **0.517** |

**Table 1** *variables considered for univariate analysis with Fisher's exact test [p<0.05]
°non-criteria aPL manifestations were defined as the presence of at least one of the followings: (livedo reticularis, thrombocytopenia, headache, hemolytic anemia, cardiac valvulopathy, epilepsy).

**Conclusions:** Non-criteria aPL manifestations are a risk factor for APO ande can determine failure to conventional treatment with LMWH plus LDA during pregnancy in aPL patients regardless of clinical diagnosis, serological profile or obstetric history. These patients may represent a more severe phenotype of disease and may deserve an immunomodulatory treatment to increase the probability of success during pregnancy.
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**Abstract THU0299** – Table 1

| | CD19+/uL mean (SE) | CD19+27-/uL mean (SE) | CD19+27+/uL mean (SE) | Mean MFI BAFFR mean (SE) | SLEDAI median (range) | Patients with SLEDAI ≤5 (%) |
|---|---|---|---|---|---|---|
| T0 (N=12) | 188,6 (83,7) | 184,9 (88,5) | 16,7 (5,1) | 9,1 (1,3) | 8,5 (8–15) | 0 (0) |
| T3 (N=12) | 71,3 (20,4) | 52,5 (22,3) | 22,4 (6,0) | 13,4 (0,8) | 5,5 (4–8) | 6 (50) |
| T6 (N=11) | 72,4 (23,3) | 50,7 (25,6) | 25,5 (7,9) | 13,2 (1,5) | 4 (4–6) | 7 (63,6) |
| T12 (N=9) | 37,6 (7,5) | 25,7 (5,6) | 11,7 (3,0) | 10,3 (0,8) | 4 (0–6) | 7 (77,8) |

## THU0301 A PHASE II TRIAL OF RETINOIDS ON LUPUS NEPHRITIS IN A SINGLE CENTER

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**Background:** Although immunosuppressants such as corticosteroids or cyclophosphamide can suppress the progression of LN, a major manifestation of systemic lupus erythematosus (SLE), some cases are resistant to those agents, and severe adverse reactions (ARs) may occur. Therefore, development of new effective drugs with fewer ARs is important. Recently, all-trans retinoic acid (ATRA), one of natural retinoids, has been reported to differentiate regulatory T cells and suppress Th17 cells in the models of autoimmune diseases. We have reported that ATRA improved proteinuria, survival rate as well as renal pathology in lupus-prone mice (ref). On the other hand, AM80, a synthetic retinoid, has been reported to suppress the expression of inflammatory cytokines in collagen-induced arthritis and EAE.
**Objectives:** Effectiveness and safety of these retinoids for the treatment of LN were examined.
**Methods:** Twenty-three patients with LN who fulfilled the ACR's revised criteria for classification of SLE were enrolled. Those unable to prevent pregnancy for more than 2 years, and who had been newly given any immunosuppressants within 8 weeks before this study were excluded. ATRA (10 mg/day) was administered to 9 patients (group A) and AM80 (4 mg/day) to 14 (group B) for 6M. Six in group B dropped out due to ARs, and effectiveness was analyzed using data of 8 patients. Through the study, the dose of steroid was not increased but allowed to be reduced if the clinical course was improved. Urinary protein (UP), serum albumin (Alb) and creatinine (Cr) levels, titer of the serum anti-double-strand DNA antibody (ADNA), serum complement levels (C3, C4) and activity (CH50) were determined every month.
**Results:** In group A, Average of UP decreased at 6M after the treatment (3.2 to 0.4 g/g Cr, $p<0.05$), Alb tended to elevate (3.2 to 3.8 g/dl), and Cr did not change. ADNA tended to reduce from 23.5 to 15.5 IU/ml, and C3, C4 and CH50 tended to elevate. In group B, UP tended to reduce at 6M (2.3 to 1.3), while Alb and Cr did not change. ADNA reduced from 37.6 to 18.8 at 3M and kept the similar value at 6M. Serum C3, C4 and CH50 tended to elevate until 6M. In group A, ARs occurred in 3 cases (leucopenia, fatigue and myalgia), while skin rash occurred in 4, bone pain in 3, hair loss in 3, and faintness, hypertension and fever in one case each in group B. AM80 was discontinued in 6 cases due to bone pain, faintness, hypertension and fever within 2M. Dose of steroid tended to reduce at 6M (A:17.1 to 15.0, B:13.6 to 13.2 mg/day).
**Conclusions:** This is the first report of on effectiveness and safety of retinoids for LN. Although the difference did not reach significance due to lack of number, UP and ADNA tended to reduce, Alb elevate, and complements tended to elevate in the both groups. Dose of steroid was reduced in some cases. Number of the cases was not enough mainly because of the exclusion criteria of contraception. Bone pain occurred relatively frequently and caused dropout in AM80 group, although it was not so severe. These findings suggest that retinoids might have a role in improvement of LN resistant to conventional therapy, and ancillary role of retinoids to high-dose steroids or immunosuppressants should be also tested in future.
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## THU0302 VALIDATION OF HIGHLY SENSITIVE FLOW CYTOMETRY AS A BIOMARKER FOR RITUXIMAB IN SLE: A RATIONALE FOR MORE INTENSIVE TREATMENT TO IMPROVE CLINICAL OUTCOMES

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**Background:** Rituximab is effective for SLE in open label series however level of clinical response varies and was not superior to standard of care in randomised trials. We previously showed that clinical response was associated with the depth of initial B cell depletion and relapse was associated with early plasmablast repopulation [1].
**Objectives:** To validate B cell depletion as a predictor of response to rituximab in SLE as a basis to develop more effective B cell targeted therapy.
**Methods:** The published discovery cohort included 38 renal and extra-renal lupus patients. A validation cohort of 46 new patients was recruited. All patients received an initial cycle of 2 infusions of 1000mg rituximab, each preceded by 100mg methylprednisolone. Rituximab was repeated on clinical relapse. Concomitant therapy with cyclophosphamide was not used. Oral immunosuppressants were continued if used at baseline. Oral prednisolone doses varied. B cell depletion using a protocol optimized to detect low numbers of B cell subsets and plasmablasts was measured at baseline, after both infusions of rituximab (6 weeks) and at early B cell repopulation (6 months). Complete depletion was defined as total B cell count $<0.0001x10^9$/L
**Results:** Depletion and response data were available for 84/100 patients. Overall complete depletion rate was 54%.

| Cohort | Depletion | Non response | Response | p |
|---|---|---|---|---|
| Discovery (n=38) | Incomplete | 7/22 (32%) | 15/22 (68%) | 0.012 |
| | Complete | 0/16 (0%) | 16/16 (100%) | |
| Validation (n=46) | Incomplete | 6/17 (35%) | 11/17 (65%) | 0.014 |
| | Complete | 2/29 (7%) | 27/29 (93%) | |
| Combined (n=84) | Incomplete | 13/39 (33%) | 26/39 (67%) | 0.001 |
| | Complete | 2/45 (4%) | 43/45 (96%) | |

Incomplete depletion was predicted at baseline by low complement C4 (p=0.044) but not baseline BILAG score or immunosuppressant use. In original cohort there was a significant association between plasmablast repopulation ($>0.0008x10^9$/L) and time to relapse <18 months (p=0.024). Follow up for relapse was limited to 22/36 responders in the validation cohort at the time of analysis, with a trend to the same association (p=0.119).
**Conclusions:** We have validated depth of B cell depletion as a predictor of response to rituximab in SLE. Clinical trials using more intensive rituximab treatment regimens, or alternative CD20 molecules are likely to increase clinical response rates to B cell depletion in clinical trials. B cell subsets should be monitored in the routine care of SLE patients receiving rituximab and repeat infusions considered if early depletion is incomplete or plasmablast repopulation is detected at 6 months.
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## THU0303 LONGITUDINAL PATTERNS IN SLE RESPONSE TO STANDARD OF CARE THERAPY: IMPLICATIONS FOR SLE CLINICAL TRIAL DESIGN

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**Background:** Most clinical trials of new treatments for systemic lupus erythematosus (SLE) have shown weak discrimination between investigational agents and placebo when added to standard of care (SOC). Given that targeted biologics are unlikely to be effective in all patients, it is challenging for these experimental therapies to exceed the high response rates observed with SOC alone in placebo arms. The design of future SLE trials may be improved by considering strategies for reducing placebo response rates and obtaining a better understanding of the within-patient variability in disease activity during follow up.
**Objectives:** The goal of this study was to evaluate longitudinal patterns of response in SLE patients who received placebo plus SOC in two completed 52-week clinical trials. Baseline characteristics discriminating early and persistent responders from non-responders to SOC were also examined to identify patient populations who may benefit most from experimental therapies and could be targeted for enrollment in future trials.
**Methods:** Data was obtained from the Collective Data Analysis Initiative (CDAI) of the Lupus Foundation of America and included 147 patients from the placebo plus SOC arms of two randomized Phase II/III trials in moderately-to-severely active lupus patients without acute nephritis. A BILAG-based response was evaluated at weeks 12, 24, 36, 48, and 52. Both cross-sectional and longitudinal analyses of response patterns were performed. Clinical variables, including background medications and baseline factors associated with disease severity, that discriminated persistent responders from non-responders were identified using logistic regression.
**Results:** The cross-sectional response rates ranged from 37% - 46% between 12 - 52 weeks for patients treated with placebo plus SOC, similar to the placebo response rates estimated in most non-nephritis lupus trials. The response rate decreased to 14.3% (95% CI: 8.6% - 19.9%) when the criterion was complete response, i.e., response at all visits between 12 - 52 weeks. Agreement between response status at 12 weeks and 36–52 weeks was low (kappa =0.15 - 0.25); furthermore only 31% of initial 12 week responders maintained response at all subsequent visits. Factors contributing to non-response to SOC at all visits included more severe disease, as suggested by more organ systems active at baseline, and low C3 levels at baseline. Less aggressive immunosuppression was also associated with non-response.
**Conclusions:** An endpoint based on a sustained rather than cross-sectional response may reduce high placebo response rates in SLE trials that continue aggressive SOC and may improve discrimination between effective experimental

treatments and SOC. Although there is increasing interest in conducting efficient 12 or 24 week early phase trials, the observed lack of stability in response to SOC over time highlights a potential weakness with shorter studies that use an endpoint of improvement. Our data also confirm earlier reports that the likelihood of response in the placebo group depends on the severity of disease and the aggressiveness of background treatments.

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## THU0304 ADHERENCE TO HYDROXYCHLOROQUINE AS ASSESSED BY MEASUREMENTS OF DRUG AND METABOLITE BLOOD LEVELS IN AN INTERNATIONAL PROSPECTIVE STUDY OF SLE PATIENTS IN FLARE

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**Background:** Non-adherence to treatment, a major cause of continued lupus activity and flares, may be difficult to recognize.

**Objectives:** In this international prospective study, we evaluated adherence to hydroxychloroquine (HCQ) in SLE patients with flares (NCT01509989).

**Methods:** This study included 305 SLE patients (SLICC criteria) from 10 countries, all of whom had been prescribed HCQ for ≥2 months and were having a disease flare (SELENA-SLEDAI Flare Index). Adherence to HCQ was assessed by self-questionnaires (MASRI, Morisky), physician's assessment (VAS 0–100), and blood concentrations of HCQ and its main metabolite desethylchloroquine ([HCQ] and [DCQ]). Non-adherence was defined by MASRI <80%, Morisky<6, [HCQ] <200ng/ml and/or undetectable [DCQ].

**Results:** 305 patients (288 women; mean age 38 ± 12ys) met the inclusion criteria. The median SLE duration was 11ys [range 1–46]; 108 patients (35%) had a history of lupus nephritis.

At enrollment, the median SELENA-SLEDAI score was 8 [2–30] and the flare was considered severe in 43%. The HCQ dosage was 400mg/d in 72%, 200mg/d in 15%, or another dosage in 13%. The median [HCQ] was 718ng/ml [0–4345]. In addition, steroids were prescribed in 76%, and immunosuppressives in 46%.

Severe non-adherence defined by [HCQ] <200ng/ml was found in 44 patients (14.4%). 12 additional patients with very low median [HCQ] of 235ng/ml [210–343] had an undetectable [DCQ] indicating a very recent resumption of treatment. Thus, 56 patients (18.4%) were objectively defined as severely non-adherent. Table 1 shows that the treating physician believed that 75% of these non-adherent patients were taking at least 50% of their prescribed HCQ dose, strongly suggesting that doctors were often unaware of non-adherence. The median VAS evaluating the adherence from the doctor's point of view was 75 [0–98] in objectively non-adherent patients vs 87 [0–100] in other patients. The doctor's opinion, therefore, was poorly informative.

Good adherence to treatment with HCQ (MASRI ≥80%) was self-reported by 77% of the patients, including by 43% of those objectively severely non-adherent. On the other hand, the investigators felt that only 12% of patients took less than 50% of HCQ, with severe non-adherence confirmed in 39%. Conversely, while intake was estimated at ≥75% (65%), 15% of these patients were objectively severely non-adherent.

Non-adherent patients defined by self-questionnaires (MASRI<80% or Morisky <6) and/or drug blood levels, represented 47% of this cohort.

**Conclusions:** These data demonstrate that blood HCQ and DCQ measurements objectively identify significant non-adherence to HCQ in nearly 20% of SLE patients. Non-adherence was often unrecognized by the doctor, suggesting usefulness of blood assays to more accurately determine adherence.

| | Non-adherent (n = 56) | Others (n = 249)* | Total (n = 305)* |
|---|---|---|---|
| **Reported adherence by the patients** | | | |
| - Mean MASRI | 69 [0-75] | 90 [0-100] | 86 [0-100] |
| - N of patients with MASRI ≥ 80% | 24/56 (43%) | 205/243 (84%) | 229/299 (77%) |
| **Perceived adherence by physician on a VAS (0 to 100)** | | | |
| - Median VAS [range] | 75 [0-98] | 87 [0-100] | 85 [0-100] |
| - N of patients with VAS 0-24 | 9 (16%) | 5 (2%) | 14 (5%) |
| - N of patients with VAS 25-49 | 5 (9%) | 17 (7%) | 22 (7%) |
| - N of patients with VAS 50-74 | 12 (21%) | 60 (24%) | 72 (24%) |
| - N of patients with VAS 75-100 | 30 (54%) | 167 (67%) | 197 (65%) |

**Legends:** HCQ: hydroxychloroquine. DCQ: desethylchloroquine. N: number. MASRI is a self-questionnaire assessing adherence from the patient's point of view. A MASRI ≥80% is considered a good adherence to treatment. VAS: Visual Analogue Scale. This represents the rating of the patient's adherence from the physician's point of view. A VAS of 0 means that the physician believes that the patient did not take any HCQ tablet in the last month, and 100% means that he/she thinks that the patient never missed a single dose.
Non-adherence was defined by [HCQ] <200ng/ml and/or undetectable concentration of DCQ.
"Others" included patients perfectly adherent as well as less adherent patients with a blood level of HCQ >200 ng/ml and a measurable DCQ.
*: 1 missing data regarding [HCQ] and [DCQ]

## THU0305 PHARMACOKINETICS OF SWITCHING FROM INTRAVENOUS TO SUBCUTANEOUS BELIMUMAB FOR PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** The ability to self-administer subcutaneous (SC) belimumab would enhance treatment options for patients with SLE.

**Objectives:** The pharmacokinetics (PK) across the change in administration from monthly belimumab intravenous (IV; 10 mg/kg) to weekly self-administration of belimumab 200 mg SC was examined in patients with SLE.

**Methods:** Study 200339 (NCT02124798) enrolled adults with SLE who had received at least three monthly belimumab 10 mg/kg IV doses plus standard care, or who completed the open-label continuation phase of a randomised, controlled trial of belimumab SC (prefilled syringe). The target period between the last IV dose and first SC dose was 1 to 4 weeks. Open-label belimumab 200 mg SC (1 mL) was self-administered weekly (thigh or abdomen) using an autoinjector under clinic observation at Weeks 1, 2, 4, 8 and at home at Weeks 3, 5, 6, 7. PK samples were collected prior to SC administration at Weeks 1, 2, 4 and 8.

**Results:** 95 patients enrolled: 91 completed the study. All except two patients transitioned from belimumab IV administration. Overall, 94% (89/95) of patients successfully self-administered belimumab at Weeks 1 and 2. A total of 736 injections were attempted over the 8-week treatment period, and 720 (98%) were concluded to be successful. Median serum belimumab trough concentration at Week 8 was 113 μg/mL (Figure). Following the switch from IV to SC, steady-state trough belimumab levels were attained on average by Week 2 (Figure). Median % changes from Week 1 to Week 8 were -51%, -23%, 1% and -3% for subjects with investigator-reported IV to SC switching time intervals of ≤1.5 weeks, 1.5–2.5 weeks, 2.5–3.5 weeks and >3.5 weeks, respectively.

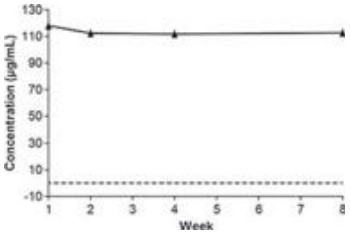



Figure 1. Median belimumab serum concentration. Dashed line: lower limit of quantification (0.1 μg/mL)

**Conclusions:** Patients with SLE successfully self-administered belimumab SC using a novel autoinjector. With a protocol-specified 1–4-week interval between

the last IV and the first SC administration, baseline (Week 1) belimumab concentrations were on average similar to their eventual steady-state concentration. Since bioequivalent exposures were previously demonstrated for belimumab SC administration with autoinjector and prefilled syringe[1], the pharmacokinetically stable transition from IV to SC administration demonstrated here, is also assumed to hold for belimumab SC administered with the prefilled syringe. The median Week 8 belimumab concentration of 113 μg/mL confirms that steady-state average concentrations over the dosing interval (CavgSS) for weekly belimumab 200 mg SC are similar to the CavgSS of 110 μg/mL for belimumab 10 mg/kg IV every 4 weeks[2]. The appropriate dosing interval between IV to SC dosing appears to be 1–4 weeks to start SC treatment when exposure is close to SC steady-state levels.

**References:**
[1] Struemper, H., et al., Clin Pharm Drug Dev, 2015, doi: 10.1002/cpdd.219.
[2] Struemper, H., Roth, D., Gordon, D. Arthritis Rheumatol 2014;66(Suppl 10): S292

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**Disclosure of Interest:** S. Sheikh: None declared, N. L. Fox Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, A. Hammer Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, H. Struemper Shareholder of: GlaxoSmithKline, Employee of: PAREXEL, J. Groark Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, D. Roth Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, D. Gordon Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline

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## THU0306 SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF THE BCL-2 INHIBITOR VENETOCLAX (ABT-199) IN A PHASE 1 SINGLE AND MULTIPLE ASCENDING DOSE STUDY IN FEMALE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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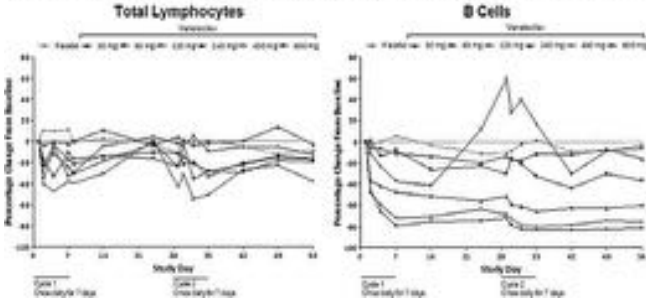
**Background:** Apoptosis eliminates auto-reactive T and B cells during immune responses; failure of elimination is important in development of systemic lupus erythematosus (SLE). Elevated Bcl-2 expression may contribute to cell death abnormalities for auto-reactive cells. Venetoclax (ABT-199) is a selective, small-molecule Bcl-2 inhibitor.

**Objectives:** To examine safety, tolerability, pharmacokinetics, and pharmacodynamics (PD) of venetoclax in female patients (pts) with SLE

**Methods:** This was a single and multiple ascending dose (MAD), double-blind, randomized, placebo (PBO)-controlled, phase 1 study (NCT01686555) in women aged 18–65 y with SLE for >6 mo, receiving stable SLE therapy. Twelve cohorts were planned (N=96); in each cohort, 6 pts received venetoclax and 2 received PBO. Pts in cohorts 1–6 received single doses of venetoclax 10, 30, 90, 180, 300, and 500 mg, respectively, or matching PBO. Pts in MAD arms (cohorts 7–12) received 2 cycles (once daily for 1 wk, then 3 wk off in each cycle) of venetoclax 30, 60, 120, 240, 400, and 600 mg, or matching PBO, beginning after safety evaluation of the single-dose venetoclax 90-mg cohort.

**Results:** In 98 enrolled pts, adverse events (AEs) were reported for 62% of pts receiving venetoclax and 48% receiving PBO; common AEs were headache (23% vs 24%, respectively) and gastrointestinal disorders (diarrhea [8% vs 4%], nausea [16% vs 12%], vomiting [8% vs 4%]). Most drug-related AEs were mild to moderate; no serious AE was reported with venetoclax. There were no deaths and no clinically relevant abnormalities of vital signs or electrocardiograms. Exposure to venetoclax was dose proportional, with a half-life of ~7–17 h after single doses. PD effects of Bcl-2 inhibition included dose-dependent reductions of total lymphocytes and B cells (Figure) after single and multiple venetoclax doses up to 600 mg. B cells were most sensitive to Bcl-2 inhibition, with up to 80% reduction from baseline in high-dose groups. Similar sensitivity was observed across B cell subsets. Total lymphocytes and T cells showed modest reduction; recovery of total lymphocytes occurred during the dosing interval of cyclic multiple dose regimens (Figure). Levels of neutrophils, platelets, reticulocytes, hemoglobin, and safety laboratory values showed no consistent patterns or marked changes across single- and multiple-dosing groups.

Figure. Percentage changes from baseline in total lymphocytes and B cells during multiple dosing of venetoclax




**Conclusions:** In female SLE pts, venetoclax was well tolerated in single and multiple doses; exposure appeared consistent with findings in cancer pts. PD assessments showed venetoclax-mediated reductions of lymphocytes and subsets.

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## THU0307 REPOSITORY CORTICOTROPIN INJECTION (RCI) ATTENUATES DISEASE ACTIVITY IN PATIENTS WITH PERSISTENTLY ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) REQUIRING CORTICOSTEROIDS: RESULTS FROM A 44-WEEK OPEN-LABEL EXTENSION STUDY

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**Background:** We recently reported results from a pilot 8-week randomized double-blind placebo (PBO)-controlled study of RCI in subjects with persistently active SLE involving skin and/or joints despite moderate dose corticosteroids for ≥4 weeks[a]. Although the primary endpoint of this study (resolution of disease active for SLEDAI rash or arthritis with no worsening of other organ systems by BILAG) was not met, RCI therapy (40U daily or 80U every other day SC) led to improvement in several measures of disease activity, including total hybrid SLEDAI (hSLEDAI), total BILAG, CLASI Activity scores, and Tender and swollen joint count, as compared with PBO.

**Objectives:** To describe the topline results of a 44-week open-label extension (OLE) of this study of RCI in persistently active SLE.

**Methods:** 33/38 subjects completed the double-blind phase of the study and opted to enroll in the OLE. Of these 33, 22 had received RCI and 11 PBO during the prior 8 weeks. The dose of RCI could be adjusted beginning at week 9, with the goal of achieving a stable dose (16, 40 or 80U SC, 1–3x/week) to control disease activity no later than Week 28. Beginning at Week 20, investigators were encouraged to taper background prednisone. Disease activity was assessed monthly by hSLEDAI, BILAG, CLASI, Tender & swollen joint counts, and physician's global assessment (PGA).

**Results:** 20 subjects completed the OLE, 13/22 from the RCI/RCI and 7/11 from the PBO/RCI groups. No unexpected adverse events were observed.

| | RCI/RCI (n=22) | PBO/RCI (n=11) |
|---|---|---|
| OLE baseline, mean (SD) | | |
| Total hSLEDAI | 5.8 (3.02) | 9.1 (3.42) |
| Total BILAG | 6.8 (4.31) | 13.5 (8.82) |
| PGA | 28.73 (21.05) | 39.09 (27.24) |
| CLASI activity (of those >0) | 4.8 (4.25) (n=17) | 7.0 (7.00) (n=9) |
| Tender & swollen joint count (of those >0) | 4.6 (1.67) (n=5) | 5.0 (2.94) (n=4) |
| Prednisone (mg/day) | 8.98 (1.67) | 16.36 (8.09) |
| Results, proportion (%) | | |
| SLEDAI rash or arthritis domain 0 & no new BILAG prior to steroid taper | 5/10 (50%) | 2/7 (28.6%) |
| SRI (week 52) | 10/13 (76.9%) | 6/7 (85.7%) |
| Prednisone to <7.5 mg/day (week 52) | 9/13 (69.2%) | 3/7 (42.9%) |
| Prednisone decreased >50% | 7/13 (53.8%) | 4/7 (57.1%) |
| Severe flares (SFI) (week 52) | 2/22 (9.1%) | 3/11 (27.3%) |
| Change from OLE baseline at week 52, mean (SD) | | |
| Total hSLEDAI | –1.5 (2.79) | –4.7 (3.77) |
| Total BILAG | –1.2 (5.58) | –7.0 (8.35) |
| PGA | –9.92 (16.02) | –14.14 (13.70) |
| CLASI Activity | –3.0 (4.92) | –2.8 (1.6) |
| Tender & swollen joint count | –2.0 (5.66) | –2.5 (4.95) |

**Conclusions:** These data demonstrate that subjects in the RCI/RCI group had a durable response to therapy over 52 weeks, whereas those in the PBO/RCI group experienced improvements in disease activity during the OLE that were generally comparable to the improvements seen with RCI treatment from the blinded phase of the trial.

**References:**
[1] Furie R, Das M, Li D, Smythe S, Mathura E, Becker P. Repository Corticotropin Injection (H.P. Acthar® Gel) Attenuates Disease Activity in Patients with Persistently Active Systemic Lupus Erythematosus (SLE) Requiring Corticosteroids [abstract]. Arthritis Rheumatol. 2015; 67 (suppl 10).

**Disclosure of Interest:** P. Becker Shareholder of: Mallinckrodt Pharmaceuticals

Inc, Employee of: Mallinckrodt Pharmaceuticals Inc, R. Furie: None declared, M. Mitrane Consultant for: Mallinckrodt Pharmaceuticals Inc, E. Zhao Employee of: Mallinckrodt Pharmaceuticals Inc
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## THU0308 HYDROXYCHLOROQUINE IMPROVES PREGNANCY OUTCOME IN WOMEN WITH ANTIPHOSPHOLIPID ANTIBODIES WITHOUT OTHER UNDERLYING CONNECTIVE TISSUE DISEASE

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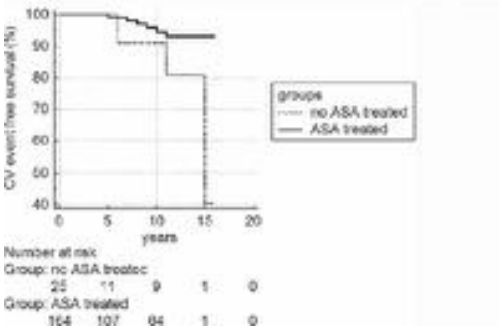
**Background:** Low-dose aspirin and/or heparins represent the treatment of choice for the management of pregnant women with antiphospholipid antibodies (aPL). However, despite these treatments, maternal, fetal, and neonatal complications related to the presence of aPL may still occur.
**Objectives:** To assess pregnancy outcome in women with aPL without other underlying connective tissue disease (CTD) who were treated with hydroxychloroquine (HCQ) in addition to conventional treatment during pregnancy.
**Methods:** Eighty-nine pregnancies in 48 women with persistent aPL were included in this observational, retrospective, cohort study: (group 1) 17 pregnancies that occurred in 13 women were treated with HCQ for at least 6 months before pregnancy, and the therapy continued throughout gestation; (group 2) 72 pregnancies that occurred in 35 women with aPL that were not treated with HCQ were included as controls. All the patients were tested positive for aPL in the absence of conclusive clinical signs/symptoms of CTD.
**Results:** HCQ-treatment was associated with a higher rate of live births (82% group A vs 58% group B; p=0.05). Placenta-mediated complications (pre-eclampsia and abruption placentae) were not observed in group 1 but occurred in 5 cases of group 2. Pregnancy duration was longer in group 1 than group 2 (36.4 [6–40] vs 33.5 [6–40] weeks; p=0.04).
**Conclusions:** Despite the limit of the small sample size, our observations support that HCQ may improve pregnancy outcome in women with aPL.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6118

## THU0309 LOW-DOSE ASPIRIN AS PRIMARY PROPHYLAXIS FOR CARDIOVASCULAR EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A LONG-TERM FOLLOW UP

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**Background:** Cardiovascular (CV) morbidity and mortality are significantly greater in Systemic Lupus Erythematosus (SLE) patients than in the general population. Acetylsalicylic acid (ASA) is known to be associated with a decrease in the incidence of CV events in high-risk patients from general population [1].
**Objectives:** We previously investigated ASA efficacy as primary prophylaxis in 167 SLE patients followed for 7 patient-years [2]. Here, we report data collected in 189 patients followed for 8,2 patient-years.
**Methods:** SLE patients consecutively admitted to a tertiary center, who, at admission, satisfied 1992 ACR and/or 2012 SLICC classification criteria for SLE and had not experienced any CV event, were enrolled into the study. Low-dose ASA (100 mg/day) was prescribed to each patient at first visit. Fourteen patients (7%) refused to take it. At each 6-monthly visit, ASA side effects, ASA discontinuation and occurred CV events were recorded.
**Results:** 189 consecutive SLE patients were followed-up for a median of 8 years (range 1–15). Among them, 164 regularly took the medication (ASA-treated) and 25 refused to take or discontinued it (non-ASA-treated patients). Six CV events occurred in the 164 ASA-treated (4.2/1000 person-years), 4 in the 25 non-ASA-treated patients (25.4/1000 person-years) (p=0.003). No relevant side effect related to ASA treatment was recorded.

**Figure 1**. Rate of CV events over time in ASA- and non-ASA treated patients.

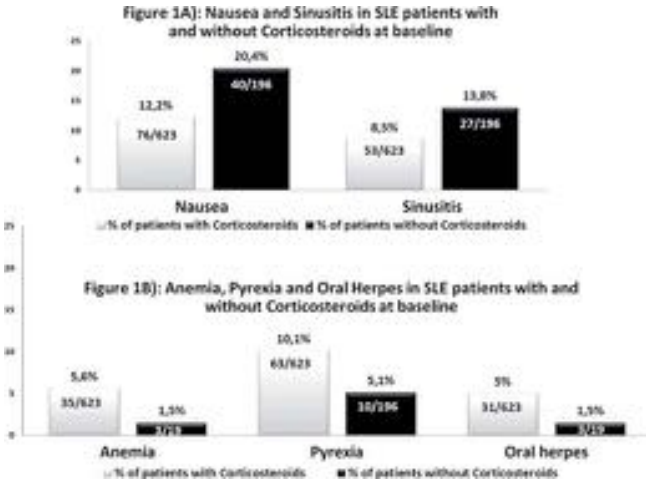



**Conclusions:** Present data further support the role of ASA in the primary prophylaxis of CV events in SLE patients.
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[1] Vandvik PO, Lincoff AM, Gore JM, et al. Primary and secondary prevention of cardiovascular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.Chest. 2012;141
[2] Iudici M, Fasano S, Gabriele Falcone L, et al. Low-dose Aspirin as Primary Prophylaxis for Cardiovascular Events in Systemic Lupus Erythematosus: A Long-Term Retrospective Cohort Study. Rheumatology (Oxford) Submitted for publication.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3613

## THU0310 RELATIONSHIP BETWEEN CORTICOSTEROIDS AND UNFAVORABLE MEDICAL EFFECTS. A STUDY UNDER THE SHARE SYSTEM BASED ON THE CLINICAL TRIAL BELIMUMAB IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (BLISS-76)

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**Background:** Corticosteroids (CSs) are used to control moderate to severe manifestations in Systemic Lupus Erythematosus (SLE) patients. CSs have rapid and strong favorable effects in controlling the disease manifestations but have very significant side-effects and long-term adverse consequences when used at high doses for prolonged periods of time. However, detailed quantitative information on the relationship between CS exposure (dosage and duration) and side-effects in the literature is limited.
**Objectives:** To obtain a better understanding of the exact relationship between exposures to CSs and possible adverse events (AEs).
**Methods:** Data from the BLISS-76 clinical trial, which are owned by the sponsor company GSK, were accessed through an agreement under the SHARE mechanism, whereby investigators are granted access for performing pre-specified analyses within the dataset [1]. We focused our analyses on AEs that were frequently reported or where a causal relationship with CSs could be suspected. We studied the relationship between AEs CSs at baseline (BL) as well as during the trial.
**Results:** Among the 819 patients included in BLISS-76, 623 (76.1%) were treated with CSs at BL. Significantly higher proportions of the following AEs: anemia, pyrexia and oral herpes were found in patients treated with CSs at BL compared to those who were not (5.6% vs. 1.5%, p=0.018; 10.1% vs. 5.1%, p=0.031; 5.0% vs. 1.5%, p=0.039, respectively). In contrast, the reverse was observed for nausea and sinusitis (12.2% vs. 20.4%, p=0.007; 8.5% vs. 13.8%, p=0.038, respectively) (Figure 1). The following AEs: cataract, glaucoma/ocular hypertension, osteopenia, musculoskeletal disorders, myalgia, cardiac disorders, hypertension, type 2 diabetes/hyperglycaemia, hypercholesterolaemia/hyperlipidaemia, peptic ulcer, skin ulcer and cushingoid, were numerically but not statistically more frequent in patients with CSs at BL compared to those without.




**Conclusions:** The SHARE mechanism is a useful tool for allowing detailed independent analyses of sponsored clinical trial data. Our results suggest that anemia, pyrexia and oral herpes are associated with CS-exposure in a large clinical trial of patients with SLE. Notably,the use of CSs was associated with reduced occurrence of nausea and sinusitis.
**References:**
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**Disclosure of Interest:** S. Emamikia: None declared, C. Gentline: None declared, M. Backheden: None declared, K. Chatzidionysiou: None declared, L. Arnaud Consultant for: L. Arnaud has received honoraria and invitations to international meetings from GSK, R. van Vollenhoven Grant/research support from: AbbVie, Amgen, BMS, GSK, Pfizer, Roche, UCB, Consultant for: AbbVie, Biotest, BMS, Crescendo, GSK, Janssen, Lilly, Merck, Pfizer, Roche, UCB, Vertex
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## THU0311 IL3R-ALPHA AS A NOVEL THERAPEUTIC TARGET IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Despite currently available therapies, a significant morbidity, and mortality remains in SLE. Major therapeutic targets have been the auto-antibody producing B cell, and more recently, type I IFN, which is produced by pDCs activated via TLR7 and TLR9 stimulation by SLE immune complexes. Alternate ways of reducing type I IFN, such as by modulating pDCs, are now emerging (1, 2). We have developed a novel mAb targeting the IL-3Rα, CSL362, which both depletes IL-3Rα expressing cells, and neutralizes signaling through IL-3.
**Objectives:** Our objective was to explore the potential utility of CSL362 as a therapeutic in SLE, via its effects on multiple pathogenic cell types and cytokines.
**Methods:** *In vitro* studies were undertaken in a heterogenous population of SLE donors, and healthy and autoimmune disease controls, and major findings confirmed *in vivo* in cynomolgus macaques. The effect of CSL362 on peripheral blood mononuclear cell types was evaluated by flow cytometry, on cytokine production by ELISA or Luminex assays, and on gene expression by qRT-PCR.
**Results:** CSL362 potently and specifically depleted $CD123^{hi}$ pDCs and basophils (average depletion 86.07%±2.07 (SEM), $p<0.05$, n=72 for pDCs, and 59.39%±3.57, $p<0.05$, n=71 for basophils). This occurred mainly through antibody-dependent cell-mediated cytotoxicity, although neutralization of IL-3 alone with the Fab fragment of CSL362 resulted in pDC, but not basophil, depletion at higher doses. Through pDC depletion, TLR7-, TLR9- and SLE serum- stimulated IFNα production, and IFN-inducible gene expression was markedly reduced (average reduction in TLR9-stimulated IFNα production 99.36%±0.39, $p<0.05$, n=29). Additionally, TLR7- and TLR9-induced plasmablast expansion was inhibited by CSL362. This depended upon depletion of pDCs by CSL362, which decreased not only IFNα, but IL-6, production that was required for plasmablast expansion. Importantly, we found that IFN-inducible gene expression and plasmablast expansion were more effectively inhibited by CSL362 than by IFNα blocking mAbs. This may be because pDC depletion by CSL362 reduced production of cytokines other than IFNα, such as IL-6, and interferon types other than type I. Indeed, CSL362 reduced production of type III IFN, a cytokine which has been postulated as a cause of ongoing disease activity despite type I IFN blockade (3). Administration of a single subcutaneous dose of CSL362 to cynomolgus macaques confirmed pDC and basophil depletion, correlating with a decrease in IFN-inducible gene expression, that lasted several weeks post dose, with no major adverse events observed.
**Conclusions:** The unique ability of CSL362 to affect the major pathogenic targets of type I IFN and the B cell, and newer targets such as the basophil (4), IL-3 (5) and type III IFN, presents a strong rationale for its therapeutic evaluation in SLE.
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**Disclosure of Interest:** S. Oon Grant/research support from: CSL Limited, H. Huynh Employee of: CSL Limited, T. Y. Tai Employee of: CSL Limited, M. Ng Employee of: CSL Limited, K. Monaghan Shareholder of: CSL Limited, Employee of: CSL Limited, M. Biondo Employee of: CSL Limited, G. Vairo Shareholder of: CSL Limited, Employee of: CSL Limited, E. Maraskovsky Shareholder of: CSL Limited, Employee of: CSL Limited, A. Nash Shareholder of: CSL Limited, Employee of: CSL Limited, N. Wilson Shareholder of: CSL Limited, Employee of: CSL Limited, I. Wicks Grant/research support from: CSL Limited
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## THU0312 PHYSICAL FATIGUE IS VERY IMPORTANT AS CLINICAL OUTCOME FOR IMPROVEMENT BY TREATMENT ACCORDING TO PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Besides ocular and oral dryness, fatigue is a prominent symptom in patients with primary Sjögren's syndrome (pSS).
**Objectives:** To investigate the importance of fatigue in relation to other symptoms and to evaluate the effect of rituximab treatment on fatigue in pSS patients with active disease.
**Methods:** The present analysis was based on data from our follow-up study of treatment with rituximab.(1) Twenty-eight pSS patients were treated with rituximab (1000 mg at days 1 and 15) and evaluated for 60 weeks. Subjective symptoms of dryness, physical fatigue, and limb pain were scored on a scale of 0–10 according to the ESSPRI. Mental fatigue was also scored on a scale of 0–10. Patients were asked to rank their symptoms of dryness, physical fatigue, pain, and mental fatigue in order of importance; from most to least eligible for improvement. In addition, the importance for improvement of each symptom was scored on a scale of 0–10. Fatigue was assessed in more detail with the Multidimensional Fatigue Inventory (MFI). Systemic disease activity was assessed with the ESSDAI.
**Results:** At baseline, 24 of the 28 (86%) pSS patients reported physical fatigue as most eligible for improvement, followed by pain and dryness. Mental fatigue was ranked as least eligible for improvement by 50% of the patients. However, for all these 4 domains, patients found it very important to get rid of their symptoms, reflected by median scores of importance of 8 or higher. The highest scores were given for physical fatigue (median 10, IQR 9–10).
Rituximab treatment resulted in a significant improvement in all clinical assessments. At 16 and 24 weeks of follow-up, physical fatigue showed 31% and 25% improvement in median values at group level, pain 36 and 29%, dryness 29% and 36%, and mental fatigue 36% and 9%, respectively. Regarding MFI domains, most improvement was reported in general (25% and 25%) and physical (19% and 16%) fatigue. In comparison, systemic disease activity assessed with ESSDAI improved 73% at group level. At 60 weeks of follow-up, all clinical assessments had returned to baseline values.
Before rituximab treatment, 18% of the patients had physical fatigue score $<5$, representing patient-acceptable symptom state (PASS). At 16–24 weeks, this proportion of patients increased to 21–36%. The proportion of patients with low disease activity according to ESSDAI increased from 29% at baseline to 75–79% at 16–24 weeks.
**Conclusions:** Fatigue is a very important symptom in pSS patients with active disease, which particularly concerns physical fatigue. Rituximab treatment resulted in a significant improvement of all patient-reported symptoms. However, the large majority of patients still experienced physical fatigue above the cut-off value for the PASS. Therefore, clinical attention for this prominent symptom is warranted in future clinical trials in pSS.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3932

## THU0313 DOUBLE-BLIND, RANDOMIZED STUDY OF VAY736 SINGLE DOSE TREATMENT IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME (PSS)

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**Background:** VAY736 is a novel, defucosylated, human IgG1 mAb targeting the receptor for B cell activating Factor of the TNF family (BAFF-R), providing both enhanced antibody-dependent cellular cytotoxicity (ADCC)-mediated depletion of B cells and blockade of BAFF:BAFF-R signaling that drives B cell differentiation, proliferation and survival.
**Objectives:** To clinically evaluate the clinical efficacy of the dual mechanisms of action of VAY736 in patients with pSS, a highly BAFF-driven, systemic autoimmune disease involving lymphocytic infiltration and progressive dysfunction of exocrine glands along with various extra-glandular manifestations.
**Methods:** A single center, randomized, parallel group, double-blind, placebo-controlled trial recruited 27 seropositive pSS patients with EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) $\geq 6$ and residual salivary flow over a 10-month period and randomized for treatment with intravenous VAY736 at either a single high dose, (n=12), a single lower dose (n=6), or with placebo (n=9). Outcomes were measured at baseline and at weeks 6, 12 and 24. The primary outcome was change in ESSDAI at week 12. Secondary outcomes included the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), Short Form-36 (SF-36), Multidimensional Fatigue Inventory (MFI) and global VAS assessments. Additional outcomes included salivary flow rates, Ocular Staining Score (OSS), high resolution salivary gland ultrasound (US) de Vita scores, serum markers of B cell hyperactivity and flow cytometry-determined lymphocyte subsets.
**Results:** Data analyses included all patients. VAY736 was safe and well-tolerated with no drug-related SAE, drop outs or discontinuations. Mean age was 50.5 years with 4 males, 2 in placebo and 1 in each treated arm. Baseline mean ESSDAI scores (range) were 11.5 (6–18), 14.5 (6–31) and 11.1 (6–19) in the high dose, lower dose and placebo arms, respectively. Rapid, profound depletion of circulating B cells was observed in all VAY736-treated patients. The primary endpoint of ESSDAI was reduced within 12 weeks but did not reach clinical or statistical significance. Improvements in VAY736-treated subjects were seen across the clinical secondary outcome measures, particularly for scores of patient and physician global assessments and SF-36 physical. Of note, the higher dose group had more sustained effects on clinical outcomes (e.g., ESSPRI, MFI) at

weeks 6 and 12, while maximal effects in the lower dose group were more evident at the earlier week 6 time point, suggesting reduced VAY736 tissue exposure in some patients by week 12. PD measurements (serum BAFF levels, circulating B cells) confirmed target engagement. A trend in improvement of US scores occurred in the high dose group. There were no consistent changes in salivary flow rate or OSS. Analyses of additional biomarkers are pending.

| | VAY736 | | Placebo | | VAY736 vs Placebo Change from baseline | |
|---|---|---|---|---|---|---|
| | Baseline | Change from baseline | Baseline | Change from baseline | Mean | 95% CI |
| **ESSDAI*** | 12.50 (6.38) | -2.28 (5.40) | 11.11 (4.07) | -0.89 (2.98) | -0.93 | (-4.98, 3.18) |
| **ESSPRI** | 6.56 (1.28) | -0.96 (1.65) | 6.37 (2.00) | -0.04 (1.60) | -0.88 | (-2.23, 0.47) |
| **MFI** | | | | | | |
| - Total | 67.50 (10.73) | -14.56 (21.18) | 63.00 (19.44) | -3.89 (5.35) | -10.52 | (-23.77, 2.73) |
| - General Fatigue Score | 16.28 (3.03) | -3.28 (4.31) | 14.00 (4.72) | -1.22 (1.64) | -1.95 | (-5.02, 1.12) |
| - Physical Fatigue Score | 14.67 (3.11) | -4.00 (5.25) | 12.89 (4.56) | -0.67 (1.32) | -2.72 | (-5.86, 0.43) |
| - Mental Fatigue Score | 11.39 (3.11) | -1.50 (4.45) | 12.44 (4.93) | -0.44 (2.40) | -2.12 | (-5.48, 1.23) |
| - Reduced Activity Score | 13.44 (3.40) | -3.33 (5.74) | 11.89 (4.78) | -0.22 (2.95) | -1.34 | (-4.19, 1.52) |
| - Reduced Motivation Score | 11.72 (2.44) | -2.67 (4.33) | 11.78 (2.86) | -1.33 (1.80) | -1.29 | (-4.13, 1.55) |
| **VAS** | | | | | | |
| - Physician VAS Score | 65.39 (13.41) | -18.72 (22.97) | 57.33 (17.73) | 2.44 (12.21) | -18.11 | (-32.54, -3.68) |
| - Patient VAS Score | 62.22 (19.22) | -20.33 (22.05) | 56.22 (24.86) | -1.00 (17.71) | -16.56 | (-32.04, -1.08) |
| **SF 36 Score** | | | | | | |
| - Mental Component | 43.59 (10.31) | 2.93 (13.16) | 36.91 (15.28) | 4.30 (5.33) | 0.32 | (-7.33, 7.98) |
| - Physical Component | 43.82 (8.50) | 3.12 (5.48) | 46.89 (6.39) | -2.10 (7.95) | 4.40 | (-0.62, 9.45) |

Baseline/Change from baseline at week 12 as Mean (SD); combined treatment arms represented by VAY736 data
ESSDAI/ESSPRI: EULAR Sjögren's Syndrome Disease Activity Index/ Patient Response Index
MFI: Multidimensional Fatigue Index
Phys/Pat VAS: Physician/Patient Global Visual Analog Scale
SF36: Short Form 36
*For ESSDAI: Bayesian 95% Credibility Interval was presented as CI

**Conclusions:** Despite a limited, single infusion, VAY736 achieved in this early phase trial trends in the primary outcome and across all secondary outcomes. Thus, this treatment was safe and suggests a positive therapeutic effect for this dual mechanisms of action in pSS that warrant further evaluation.
**Disclosure of Interest:** T. Dörner: None declared, M. Posch: None declared, F. Wagner: None declared, A. Hüser: None declared, T. Fischer: None declared, L. Mooney Employee of: Novartis Pharma AG, O. Petricoul Employee of: Novartis Pharma AG, P. Maguire Employee of: Novartis Pharma AG, P. Pal Employee of: Novartis Pharma AG, J. Doucet Employee of: Novartis Pharma AG, M. Cabanski Employee of: Novartis Pharma AG, E. Kamphausen Employee of: Novartis Pharma AG, S. Oliver Employee of: Novartis Pharma AG
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### THU0314 CLINICAL AND IMMUNOLOGICAL CONSEQUENCES OF TOTAL GLUCOSIDES OF PAEONY TREATMENT IN SJÖGREN'S SYNDROME: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Sjögren's syndrome (SS) is an autoimmune disease and the treatment of SS remains symptomatic. The total glucosides of paeony (TGP) is the active compound extracted from the roots of Paeonia lactiflora Pall. TGP can reduced production of IFN-γ, IL-6 and IL-12, and inhibited dendritic cells. Recently, TGP had been approved in the treatment of rheumatoid arthritis by China State Food and Drug Administration. However, the therapeutic effects of TGP on SS and the mechanisms behind were largely unknown.
**Objectives:** To investigate the clinical and immunological consequences of total glucosides of paeony (TGP) treatment in patients with Sjögren's syndrome (SS).
**Methods:** Forty-five patients with primary SS participated in a randomized, double-blinded, placebo-controlled clinical trial. Patients were assigned randomly to TGP or placebo group in a ratio of 2:1 and followed up for 24 weeks. Clinical assessment was performed by EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), stimulated and unstimulated salivary flow rate, and Schirmer test at week 4, 12, 18 and 24. The proportion of B cells and levels of serum IL-6, TNF-α, IFN-γ and BAFF were measured before and after treatment. This trial was registered on www.chictr.org, with the register number of ChiCTR-TRC-12002325.
**Results:** ESSPRI in the patients who got 3 to 6 score at baseline was significantly reduced in TGP group at 18- and 24-week changed from (4.81±0.60) to (4.15±1.27) ($P$=0.012) and (4.20±1.46) ($P$=0.027). Stimulated salivary flow rate increased at week 24 from (1.80±0.39) to (2.01±0.51) ($P$=0.031) and unstimulated salivary flow rate increased from (1.30±0.92) to (1.55±0.90) ($P$=0.011) in TGP group, but the placebo group showed no significant difference. Erythrocyte sedimentation rate (ESR) was decreased significantly compared to the placebo group at 12- and 24-week from (40.9±18.0) to (29.4±12.2) ($P$=0.003) and (30.4±17.3) ($P$=0.024). The percentage of naive B cells decreased in TGP group from (77.34±12.20)% to (64.59±15.60)% ($P$=0.005) while memory B cells increased at week 24 from (21.79±11.97)% to (34.21±15.48)% ($P$=0.006). The concentrations of TNF-α and IFN-γ decreased in TGP group at week 24 from (32.51±26.67) to (24.22±13.56) ($P$=0.017) and (10.71±8.94) to (6.55±4.88) ($P$=0.022), respectively.
**Conclusions:** TGP appears to improve the glandular secreting function and ameliorate the inflammatory process.
**Acknowledgement:** We thank the patients who participated in the study and Lansen Pharmaceutical Co. Ltd. (Shenzhen, China) which kindly provided drugs. This work was funded by a grant from the National Nature Science Foundation of China (No. 81373187) and the Clinical Research Special Foundation of Chinese Medical Association (12040730373).
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## SLE, Sjögren's and APS - clinical aspects (other than treatment)

### THU0315 SERUM PROTEIN PATTERN OF SYSTEMIC LUPUS ERYTHEMATOSUS USING PROXIMITY EXTENSION IMMUNOASSAY

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**Background:** Systemic lupus erythematosus (SLE) is a severe autoimmune connective tissue disorder. Current knowledge about the serum protein pattern associated with SLE is still limited.
**Objectives:** To identify SLE-associated serum protein signature using innovative multiplex Proximity Extension ImmunoAssay (PEA).
**Methods:** We investigated the serum levels of 92 inflammation-related proteins in 76 Czech patients with SLE and 24 age-matched healthy control subjects (C) using a highly sensitive multiplex PEA (Proseek Multiplex, Olink Bioscience, Sweden). Statistical tests (Student t-test, Benjamini-Hochberg correction, Principal component analysis (PCA)) were performed using GenEx (Sweden), $P$-value $<0.05$ was considered as significant.
**Results:** When comparing SLE to control subjects, serum levels of 30 proteins were deregulated ($P<0.05$ after multiple comparisons). PCA revealed three proteins distinguishing SLE and C: sirtuin 2 (SIRT2; SLE *vs* C fold change: 2.1, $P$=0.000005), interleukin 18 (IL18; 1.5, $P$=0.00002) and sulfotransferase 1A1 (ST1A1; 2.2, $P$=0.00007). Interestingly, SIRT2 and ST1A1 were not reported in SLE yet; from neuroinflammation there is evidence that SIRT2 regulates NFκB signalling and Toll-like receptors, ST1A1 contributes to resistance to anti-inflammatory treatment. Among other highly-deregulated proteins, we observed elevation of many inflammatory mediators (IL-18R1, CCL4, CSF1, SLAMF1, CD40 and TNFRSF9), and also of Caspase 8, a metalloprotease STAMBP and Axin-1, a modulator of Wnt-signalling pathway ($P<0.0005$) in SLE. Subanalysis of protein pattern in patient phenotypes is ongoing.
**Conclusions:** This first study using PEA identified SLE-associated serum signature, with many of novel proteins not yet reported in SLE. Their exact function and suitability as biomarkers in SLE deserves further investigation.
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### THU0316 ISCHEMIC HEART DISEASE AMONG SLE PATIENTS: A CASE-CONTROL STUDY

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**Background:** Ischemic heart disease (IHD) is a well identified cause of mortality in SLE patients due to accelerated premature atherosclerosis attributed to both traditional cardiovascular risk factors and to the inflammatory effect of SLE itself (1,2).
**Objectives:** To investigate the incidence and prevalence of IHD among Middle Eastern SLE patients derived from a large, national real-life database.
**Methods:** Using data from the largest HMO in Israel, the Clalit Health Services, we selected for patients with SLE. These patients were compared with age and sex matched controls with regards to the prevalence of IHD in a case-control study. Chi-square and t-tests were used for univariate analysis and a logistic regression model was used for multivariate analysis.
**Results:** The study included 5,018 patients with SLE and 25,090 age and

Logistic regression for IHD (n=30,108)

| Variable | OR | 95% CI | P-value |
|---|---|---|---|
| SLE | 3.774 | 3.344–4.260 | <0.001 |
| Age (per year) | 1.068 | 1.064–1.072 | <0.001 |
| Female | 0.344 | 0.304–0.391 | <0.001 |
| High SES vs. low | 0.893 | 0.783–1.018 | 0.090 |
| High SES vs. intermediate | 0.780 | 0.663–0.917 | 0.003 |

CI, confidence interval; OR, odds ratio; SES, socioeconomic status.

sex-frequency matched controls. The prevalence of IHD in patients with SLE was increased compared to controls (11.3% and 3.1%, respectively, P<0.001). In a multivariate analysis SLE was associated with IHD (OR 3.77, 95% confidence interval 3.34–4.26).

**Conclusions:** Our data supports that SLE is an independent risk factor for IHD. When evaluating by gender, the risk seems even more substantial in females.

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**Disclosure of Interest:** None declared

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## THU0317 TUBULOINSTERSTIAL DAMAGE IS AN INDEPENDENT PREDICTOR OF END STAGE RENAL DISEASE IN LUPUS NEPHRITIS PATIENTS WITH MILD TO MODERATE RENAL IMPAIRMENT

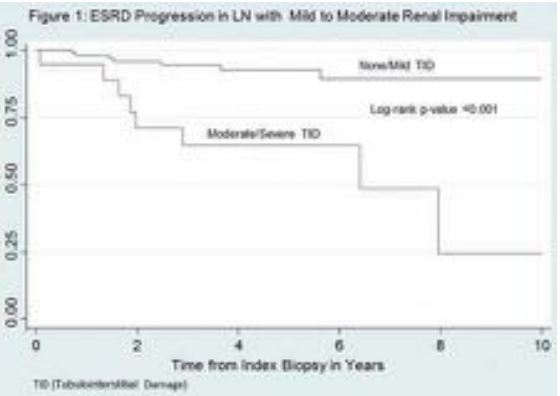
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**Background:** Tubulointerstitial damage (TID) is associated with progression to end stage renal disease (ESRD) in lupus nephritis (LN)[1,2]. However, it has not been established whether the association of TID and ESRD holds true in individuals with preserved or only moderately impaired renal function.

**Objectives:** To determine if TID predicts progression to ESRD in LN patients with mild to moderate renal impairment at the time of kidney biopsy.

**Methods:** We identified all adult and pediatric SLE patients (by ACR and/or SLICC criteria) who had an index biopsy consistent with LN between January 2005 and July 2015. Demographic data, comorbidities, medications, laboratory data, ESRD onset, and deaths through December 2015 were ascertained from medical chart reviews, the United States Renal Data Systemic Report, and National Death Index. Renal impairment was defined as mild (chronic kidney disease [CKD] stage 1 or 2, estimated glomerular filtration rate [eGFR] $\geq$60 mL/min/1.73m$^2$), or moderate (CKD stage 2, eGFR$\geq$30 and $<$60 mL/min/1.73m$^2$). TID was defined as the presence of moderate to severe tubular atrophy and/or interstitial fibrosis as reported on the renal biopsies in accordance with the 2003 ISN/RPS criteria. Time to ESRD onset was defined as time from the index biopsy date to incident ESRD date; non-ESRD patients were censored at time of death or the last visit. Kaplan-Meier survival curves and Cox proportional hazards models were used to evaluate whether TID was predictive of ESRD progression adjusting for eGFR (as a continuous variable) and LN class.

**Results:** Of the 131 LN patients with mild to moderate renal impairment (8 (6%) Class II, 58 (44%) Class III/IV, 38 (29%) Class V, and 27 (21%) mixed), 16 (12%) progressed to ESRD. Eighty six percent of ESRD progressors had proliferative or mixed LN vs. 51% of non-ESRD, p=0.02. There were no significant differences with respect to age, sex, race, comorbidity scores, complement levels, anti-dsDNA, or protein to creatinine ratio at index biopsy between ESRD and non-ESRD groups. Median (IQR) baseline eGFR was 65 (51, 75) mL/min/1.73m$^2$ in the ESRD group and 97 (69, 127) mL/min/1.73m$^2$ in the non-ESRD group, p=0.001. TID was present in 12% of biopsies with eGFR$\geq$60 mL/min/1.73m$^2$ and in 35% of biopsies with GFR between 30 and 60 mL/min/1.73m$^2$. Moderate to severe TID was associated with a high risk of ESRD progression (Figure 1, log-rank p-value$<$0.001), HR=8.3, 95% CI: (2.6, 27), p-value$<$0.001, adjusted for eGFR and proliferative or mixed LN. Similarly, TID remained a significant predictor when the analyses were limited to patients with a eGFR$>$60 mL/min/1.73m$^2$, HR=5.6, 95% CI: (1.3, 22.9), p=0.02, adjusted for eGFR.




**Conclusions:** TID was found in a significant proportion of clinically-indicated kidney biopsies in LN patients with mild to moderate renal impairment. The presence of TID was a strong predictor of ESRD progression in these patient independent of eGFR or biopsy class. Further studies are needed to identify factors associated with the presence of TID to develop effective prevention strategies.

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**Disclosure of Interest:** None declared

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## THU0318 THE PREGNANCY EXPERIENCE OF 85 WOMEN WITH SLE FOLLOWED IN A SPECIALIST LUPUS CLINIC COMPARED TO THE GENERAL POPULATION

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**Background:** SLE affects women of childbearing age. Research suggests that patients with SLE have similar rates of pregnancy as other women but a higher rate of pregnancy loss [1]. Parity may be reduced due to infertility eg. secondary to antiphospholipid syndrome, pregnancy loss or personal choice. Concerns over teratogenic medication, disability and child health have been cited as personal reasons [2].

**Objectives:** Our aim was to carry out a retrospective analysis of the pregnancy experience of women with SLE followed up for a mean of 18 years in a specialist clinic.

**Methods:** Pregnancy data were collected on 85 women with SLE via questionnaire between June and December 2015. Questions focused on parity, number of pregnancies, miscarriages, stillbirths, termination of pregnancy and number of live births. Questions related to pregnancy complications included pre-eclampsia, intrauterine growth retardation (IUGR), abruption placenta, gestational diabetes, caesarean sections (CS) and preterm labour $<$37 weeks. Data on smoking and serology were obtained from the medical records.

**Results:** Of 85 women with SLE, the mean age was 45 years and mean follow-up was 18±11 years. Ethnicity was 53% white, 10.5% Asian, 27% Afro-Caribbean and 9% other. 20% were current/previous smokers. 43.5% were anti-Ro positive. 14% were LA positive, 15% were aCL positive and 8% were anti-β2GPI positive. The questionnaire results are summarised in Table 1, with comparison to UK population figures where they are available.

Table 1

| | SLE (n=85) | UK population average |
|---|---|---|
| Never pregnant | 36.5% | Unknown |
| No children | 47% | 20% at age 45* |
| Miscarriage rate | 22% | 15–20% |
| Elective TOP | 20% | ≈36% by age 45 |
| Average family size (for the 45 who had children) | 1.5 | 1.82 children |
| Number with >3 children | 11% | 14.3%* |

*Office of National Statistics UK.

Among the 45 parous women, there were 83 live births. 80% (36/45) had 1–2 children. 15% had 3 (7/45) children and 4% (2/45) had 4 children. No patient had more than 4 children.

Miscarriages occurred in 22% (19/85); 18% (8/45) had preterm labour, 4.4% (2/45) had hypertension during pregnancy, 9% (4/45) had CS, 4.4% had low birth weight. Other adverse pregnancy outcomes included placental abruption (2.2%), ectopic pregnancy (2.2%), IUGR (2.2%) and stillbirth (twins) (2.2%).

**Conclusions:** The major finding of this study was that almost half the respondents had no children, more than double what one would expect in UK women of the same mean age. This was primarily due to never having been pregnant rather than increased rate of TOP or miscarriage. Further research into the social and/or medical reasons for this avoidance of pregnancy is required. Pregnancy morbidity amongst those who had been pregnant was common especially miscarriage and pre-term labour.

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**Disclosure of Interest:** None declared

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## THU0319 SUBOPTIMAL VITAMIN D LEVELS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a systemic autoimmune

disease that mainly affects women of childbearing age. Recent studies suggest a high prevalence of vitamin D insufficiency and deficiency in patients with SLE. Inadequate levels of vitamin D could determinate not only skeletal problems but also a potentiation of autoimmune activity in SLE.
**Objectives:** The purpose of this study was to determine the prevalence of vitamin D insufficiency and deficiency in SLE patients attended in a tertiary care center.
**Methods:** Consecutive patients with SLE seen in the Lupus Clinic of a Rheumatology Service belonging to a high complexity center in the Spanish Public Health System were included. Patients had to fulfill the 1997 ACR criteria for the classification of SLE. Different epidemiological, clinical, laboratory and serological variables were recorded. Levels of vitamin D and PTH, as well as serum levels of calcium, phosphorus, and alkaline phosphatase were systematically determined in all patients serum. Serum vitamin D levels at 25 nmol/L and 75 nmol/L were the cut-off values for vitamin D deficiency and vitamin D insufficiency, respectively. The local ethical committee authorized the study. Descriptive statistics was used to present the results; chi-square test, Student t test, and Mann-Whitney U test were used to establish statistical significance. A $p<0.05$ was considered significant. Statistical analyses were performed by using Stata v12.0.
**Results:** One hundred and twenty patients were included, with a mean age of 51 years. Eighty-nine percent were women and 89% were caucasian. The average time of disease evolution was 13 years. Seventy-six percent of patients were taking hydroxychloroquine, 42% were taking glucocorticoids, and 37% of them were taking calcium plus vitamin D supplements.
Nine percent of patients had vitamin D deficiency and 56% had vitamin D insufficiency. Elevated levels of PTH were detected in 18% of patients with vitamin D insufficiency and in 45% of patients with vitamin D deficiency. There were no statistically significant differences between them and patients with optimal levels of vitamin D. Likewise, no statistically significant association was observed between suboptimal vitamin D levels and skin involvement, photosensitivity, use of photoprotection, use of glucocorticoids, use of antimalarial or use of anticonvulsants.
**Conclusions:** Despite taking vitamin D and calcium supplements, vitamin D deficiency and insufficiency are common among SLE patients. Therefore, it might be advisable to monitor serum vitamin D levels in order to adjust the dose of vitamin D prescribed.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3508

## THU0320 CARDIOVASCULAR RISK PROFILES IN A LUPUS COHORT: THOSE THAT ARE MISSED

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**Background:** Risk prediction models for Cardiovascular Disease (CVD) are based on known risk factors and are used to guide therapy. Amongst these, the Framingham Risk Equation ("Framingham Score")[1] is perhaps most well-known and attempts to moderate risk by targeting ideal lipid and blood pressure levels in those identified as high-risk (defined as an estimated 10-year CVD risk>15%). Systemic Lupus Erythematosus (SLE) is associated with increased CVD risk despite these patients not conforming to conventional CVD risk profiles. Petri *et al* have described a novel SLE-specific cardiovascular risk equation ("SLE Score")[2] that incorporates SLE disease parameters in addition to conventional risk factors.
**Objectives:** To determine the prevalence of high CVD risk amongst a SLE cohort, and to assess the characteristics of patients who might be missed when using conventional CVD risk assessments.
**Methods:** Using data collected via the Monash Lupus Clinic, patients meeting ≥4/11 ACR diagnostic criteria for SLE were studied. A cross-sectional analysis using the most recent data for each patient was used to categorise patient risk via both the "Framingham Score" and "SLE Scores". The characteristics of patients identified as "high-risk" by the SLE Score only (termed the "missed group") were compared to those identified by the Framingham score (the "conventional group") using non-parametric tests (Mann-Whitney U test for continuous and Fisher's exact test for categorical variables).
**Results:** Of 184 patients screened, 146 (79%) had complete data for calculation of the CVD risk scores. Overall, 22 (15%) and 44 (30%) of patients were determined to be at "high-risk" based on the Framingham and SLE Scores respectively. Traditional risk factors such as smoking (18.5%), diabetes (2%) and hypertension (18.5%) were generally lower in this lupus cohort than similar age-matched population rates.[3] Using the SLE Score, 18% (n=27) of patients were newly assigned as high-risk. The "missed group" lacked traditional risk factors, being more likely to be female (81% vs 50%; p-value 0.03), younger (mean age 54 vs 69 years $p<0.01$), with lower blood pressure (systolic BP 132 vs 143; p=0.05) and body-mass index (24.1 vs 28.0 kg/m$^2$; p value 0.02). Of the 49 participants deemed high-risk via either score, 12 (25%) and 2 (4%) were appropriately treated to target BP and lipid targets respectively.
**Conclusions:** In this cross-sectional comparison between cardiovascular risk prediction models, a significant proportion of patients were re-classified as high-risk using a formula that incorporates SLE disease-related parameters. Females were underrepresented using the Framingham Risk Equation, and conventional risk factors were not increased in SLE patients- suggesting a disease specific CVD risk profile. Further evaluation of the disease-specific risk calculator is warranted in long-term prospective studies, including focus on appropriate blood pressure and lipid levels.
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**Disclosure of Interest:** None declared
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## THU0321 THE ASSOCIATION BETWEEN ECHOCARDIOGRAPHIC PARAMETERS AND MORTALITY IN PATIENTS WITH LUPUS NEPHRITIS

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**Background:** Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease that affects multiple organs, with a broad spectrum of manifestations and a clinical status marked by periods of exacerbation and remission, with a variable course and prognosis. Cardiac abnormalities are common in lupus patients even when clinically asymptomatic from cardiac aspect. Echocardiography is an excellent non-invasive tool for cardiac evaluation.
**Objectives:** The aim of this study is to investigate the relationship between echocardiographic parameters and mortality in lupus nephritis (LN) patients.
**Methods:** A total of 258 LN patients who underwent echocardiography during year 1998–2015 were enrolled into this study. In all patients a structural and functional cardiovascular alterations has been described. Association with all-cause and cardiac mortality were examined by the Cox proportional hazards model with adjustments for demographic factors, laboratory variables, medication use and echocardiographic parameters.
**Results:** The median duration of follow-up was 191,72 ± 82,54 months. The frequency of heart complications in LN patients is quite variable and depends on follow-up period. Among 258 LN patients, 94 (36,43%) died during the follow-up period. Of them, 44 patients (46,81%) died of cardiac disease. Disease duration of SLE and proteinuria were risk factors associated with the descent of E/A (E: the peak velocity at rapid left ventricular filling; A: the peak velocity during left atrial contraction) ratio ($p<0,05$). In the multivariate analysis, the presence of cardiac manifestation, high systolic blood pressure (SBP) and serum level of C-reactive protein (CRP), low serum level of albumin, low estimated glomerular filtration rate (eGFR) and decreased left ventricular ejection fraction (LVEF) ($p<0,05$) were independently associated with increased all-cause mortality. Meanwhile, factors correlated independently with an increase in cardiac mortality included the presence of cardiac manifestation, low eGFR, increased left ventricular mass index (LVMI) ($p<0,05$) and decreased LVEF ($p<0,05$).
**Conclusions:** Patients with LN have a higher risk of myocardial involvement, which can result in ventricular dysfunction. Decreased LVEF is associated with all-cause and cardiac mortality, whereas, increased LVMI is an independent risk factor for cardiac mortality in LN patients. These findings indicate the need for rigorous cardiac follow up in patients with LN.
**Disclosure of Interest:** None declared
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## THU0322 ALTERED QUALITY OF LIFE IS MAINLY ASSOCIATED WITH PATIENT REPORTED OUTCOMES IN PRIMARY SJÖGREN'S SYNDROME PATIENTS: DATA FROM A LARGE THERAPEUTIC TRIAL

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**Objectives:** To identify the main determinants of quality of life (QoL) alteration in patients with active primary Sjögren's syndrome (pSS) participating in a large therapeutic trial.
**Methods:** At the inclusion visit in the TEARS trial, 120 patients with active pSS completed the Short Form survey 36 (SF36), a validated tool measuring the level of QoL. The association of demographic data, patient-reported outcomes (including the EULAR SS Patient Reported Index (ESSPRI) score), objective measurements of dryness and autoimmunity, and the physician evaluation of systemic activity (using the EULAR SS Disease Activity Index (ESSDAI) score) with SF36 physical and mental components were assessed by univariate then multivariate linear regression analyses.

Table 1. Determinants of the Physical Component Summary (PCS) of the SF36 score

| | | Univariate | | Mutivariate model 1 | | Mutivariate model 2 | |
|---|---|---|---|---|---|---|---|
| | | Beta | P | Beta | P | Beta | P |
| General characteristics | Gender (male) | 2.963 | 0.410 | | | | |
| | Age | −0.017 | 0.792 | | | | |
| | BMI>25 | −3,917 | 0,027 | −1.661 | 0.249 | −2.217 | 0.143 |
| | Disease duration | −0,247 | 0,102 | | | | |
| PROs | ESSPRI | −0,301 | <0.001 | N/A | | −0.263 | <0.001 |
| | Global VAS | −0,17 | 0,001 | 0.015 | 0.763 | N/A | |
| | Pain VAS | −0,191 | <0.001 | −0.150 | <0.001 | N/A | |
| | Fatigue VAS | −0,196 | <0.001 | −0.069 | 0.105 | N/A | |
| | Global dryness VAS | −0.053 | 0.215 | | | | |
| | Oral dryness VAS | −0,092 | 0,011 | −0.025 | 0.444 | N/A | |
| | Ocular dryness VAS | −0,058 | 0,059 | −0.041 | 0.124 | N/A | |
| *Objective tests* | Schirmer's test ≤5 mm | 0.287 | 0.873 | | | | |
| | UWSF ≤0.01 mL/min | 3,32 | 0,064 | 1.481 | 0.333 | 1.998 | 0.20 |
| | Abnormal SG biopsy | −0.038 | 0.988 | | | | |
| | Anti-SSA/SSB | 0.307 | 0.889 | | | | |
| *Systemic activity* | Physician VAS | −0.036 | 0.239 | | | | |
| | ESSDAI | −0,335 | 0,007 | −0.161 | 0.128 | −0.185 | 0.10 |

**Results:** SF36 results showed a marked alteration of QoL in this population of patients with active pSS. The strongest predictors of a low QoL (for both physical and mental components, Table 1) were patient-reported symptoms, best assessed using the ESSPRI, with pain and ocular dryness intensity displaying independent association with QoL. Conversely, systemic activity level was not associated to QoL alteration, even in the subset of patients with moderate to high systemic activity as defined by the ESSDAI.
**Conclusions:** pSS cardinal symptoms (dryness, fatigue and pain) are the major predictors of QoL alteration and should be targeted in future therapeutic trials in addition to systemic involvement.
**Disclosure of Interest:** None declared
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## THU0323 PREDICTORS OF DISEASE SEVERITY, LYMPHOMA AND DEATH: PREVALENCE IN PATIENTS REGISTERED ON THE UNITED KINGDOM PRIMARY SJÖGREN'S SYNDROME REGISTRY

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**Background:** There has been much research aimed at elucidating key biological and clinical features which predict severity of disease and development of lymphoma in patients with primary Sjögren's syndrome (pSS). Key biological predictors identified include the presence of leukopenia or lymphopenia, hypocomplementaemia, cryoglobulinaemia, monoclonal gammopathy; key clinical predictors include younger age at time of symptom onset or diagnosis, peripheral neuropathy, salivary gland enlargement and skin involvement (particularly palpable purpura) [1–4]. The UK Primary Sjögren's Syndrome Registry (UKPSSR) is a MRC funded patient cohort, devised to facilitate research into pSS to improve understanding of the condition.
**Objectives:** Ascertain the prevalence of putative clinical predictors amongst UKPSSR patients. Explore the relationship between demographics, clinical parameters, disease severity and lymphoma development.
**Methods:** Patients were identified on the UKPSSR (n=868), those with insufficient data were excluded from analysis (n=36). Frequency of the predictors was calculated for remaining 832 patients. Patients were assigned a value for each predictor: 1 for present, 0 for absent. These values were then added to provide the prevalence of each predictor within the cohort, and a cumulative score for each patient. Each patient had 2 cumulative scores: one for disease severity and risk of death, the other for risk of lymphoma. Patients with a recorded age of pSS symptom onset (n=739) were analysed to investigate the relationship between age of onset and development of lymphoma. SPSS used for statistical analysis.
**Results:** Pearson Chi-squared analysis found a statistically significant (p=0.004) increased incidence of lymphoma in patients presenting with symptoms of pSS before the age of 35. Predictors of lymphoma development were more common in patients whose symptoms started between age 20–34 (p=0.05). Patients with diagnosed lymphoma had a higher cumulative lymphoma risk score than patients who did not have lymphoma (p=0.05). Predictors of severe disease were found to be more common in patients whose symptoms began before age 35 (p=0.05).
**Conclusions:** This analysis corroborates the findings of previous research showing an increased lymphoma prevalence in patients presenting with pSS at a younger age [4]. It also finds a statistically significant link between poor prognostic features and development of lymphoma as described in the literature [2,3]. Further statistical analysis will aim to establish the link between each predictor and the development of systemic manifestations of pSS, baseline and cumulative ESSDAI scores and lymphoma.

| Predictor of disease severity | Number | % |
|---|---|---|
| Cytopenia | 274 | 32.9 |
| Hypocomplementaemia (C3 or C4) | 133 | 16.0 |
| Cryoglobulinaemia | 8 | 1.0 |
| Peripheral neuropathy | 90 | 10.8 |
| ESSDAI score ≥14 | 46 | 5.5 |
| Renal involvement (Active nephritis) | 3 | 0.4 |
| Male | 56 | 6.7 |
| Altered parotid imaging | 42 | 5.1 |
| Lymphopenia | 156 | 18.8 |
| Anti-La | 509 | 61.2 |
| Monoclonal gammopathy | 41 | 4.9 |
| Highest available score in ≥2 ESSDAI domains | 15 | 1.8 |
| >1 laboratory abnormality | 587 | 70.6 |
| Any ESSDAI score in: Constitutional, Biological, Pulmonary, Lymphadenopathy, Haematological | 549 | 66.0 |
| **Predictor of lymphoma** | **Number** | **%** |
| Renal involvement (Active nephritis) | 3 | 0.4 |
| Past/Present salivary gland enlargement | 450 | 54.1 |
| Lymphadenopathy | 51 | 6.1 |
| Purpura | 15 | 1.8 |
| Peripheral neuropathy | 90 | 10.8 |
| Low C4 | 122 | 14.7 |
| Monoclonal gammopathy | 41 | 4.9 |
| Cryoglobulinaemia | 8 | 1.0 |
| Anti-La | 509 | 61.2 |
| Leukocytopenia / Lymphocytopenia | 240 | 28.9 |
| **Lymphoma diagnosis** | **41** | **4.9** |

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2522

## THU0324 OBESITY INTERFERES WITH THE INFLAMMATORY STATUS IN LUPUS PATIENTS

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**Background:** High frequency of obesity among SLE patients has been described, however, it is unknown whether obesity can modify the inflammatory status of those individuals.
**Objectives:** To analyze the profile of cytokines and evaluate whether obesity interferes with the inflammatory status of SLE patients.
**Methods:** Cross-sectional study included 189 women with SLE and 70 controls, older than 18 years, were included in the study. Data related to clinical and laboratory manifestations besides medication use were assessed. Disease activity was measured by SLEDAI-2K and irreversible cumulative damage by SLICC-ACR/DI. Nutritional status was assessed by body mass index (BMI). Serum concentrations of IL6, IL10, IL17, TNFα, soluble TNFα receptors 1 (sTNFR1) and 2 (sTNFR2) were analyzed using high sensitivity cytometric bead array and adipokines (leptin and adiponectin) by ELISA kits. Multiple linear regression method was performed for multivariate analysis. In order to adjust the multivariate models the following variables were included: age, menopause, disease activity, use of antimalarial drugs, immunosuppressive and current dose of corticosteroids.
**Results:** In lupus patients group, mean (SD) values of age and disease duration were, respectively, 37.5 (10.0) and 9.1 (6.3) years. Considering BMI, 72 (38.1%) patients were classified as eutrophic, 64 (33.9%) as overweight and 53 (28.0%) as obese. The mean (SD) cumulative dose of prednisone was 32.9 (26.1) g, and of the current daily dose of prednisone was 10.4 (12.9) mg. The median (IQR) disease activity and damage index scores were 2 (0–6) and 0 (0–1), respectively. Serum levels of cytokines were higher in lupus patients when compared to controls [IL6 ($p<0.001$), sTNFR1 (p=0.028), sTNFR2 (p=0.003), IL10 ($p<0.001$), leptin (p=0.044) and adiponectin ($p<0.001$)]. Only the IL17 levels (p=0.518) did not differ statistically between the two groups. Higher BMI correlated with age (rs =0.335; p = <0.001), age at diagnosis (rs=0.319; $p\leq0.001$) and with less years of education (rs= -0.204; p=0.005). No correlation was observed between BMI and disease activity (rs: 0.116 p=0.113) as well as with damage index (rs:-0.080 p=0.309). Higher concentrations of IL6 (rs=0.246, p=0.002), IL17 (rs=0.195, p=0.014) and leptin (rs=0.430; $p<0.001$) were positively and independently correlated with BMI.
**Conclusions:** This study showed higher serum levels of cytokines and adipokines in SLE patients. Also, higher BMI was correlated with higher concentrations of IL6, IL17 and leptin in the study group, suggesting that BMI could interfere, regardless of disease activity, with the inflammatory profile of women with SLE.
**Disclosure of Interest:** None declared
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## THU0325 LONG-TERM OUTCOME OF PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: A RETROSPECTIVE MULTICENTER STUDY

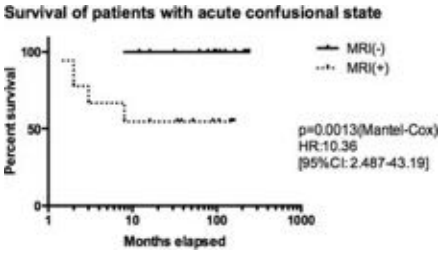
F. Dall'ara[1], M. Taraborelli[2], R. Reggia[1], M. Fredi[2], L. Andreoli[1], M. Gerosa[3], A. Hoxha[4], L. Massaro[5], M. Tonello[4], P. Cacoub[6], N. Costedoat-Chalumeau[7], F. Franceschini[2], P.L. Meroni[3], J.C. Piette[6], A. Ruffatti[4], G. Valesini[5], E.N. Harris[8], A. Tincani[1]. *[1]Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia; [2]Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia; [3]Division of Rheumatology, Department of Clinical Sciences and Community Health, Ospedale Gaetano Pini, University of Milan, Milan, Italy, Milan; [4]Rheumatology Unit, Department of Medicine - DIMED, University of Padua, Padua, Italy, Padua; [5]Internal Medicine and Medical Specialties Department, Policlinico Umberto I, "La Sapienza" University of Rome, Rome, Italy, rome, Italy; [6]Internal Medicine Department, Centre de référence maladies auto-immunes et systémiques rares, AP-HP, Hospital "Pitié-Salpêtrière", "Pierre et Marie Curie Paris VI" University, Paris, France; [7]Internal Medicine Department, Cochin Hospital, "René-Descartes Paris V" University, Paris, France, Paris, France; [8]Vice Chancellor Emeritus, University of the West Indies, Kingston 7, Jamaica, West Indies, Jamaica*

**Background:** Data on the long-term outcome in primary antiphospholipid syndrome (PAPS) patients are still very limited.
**Objectives:** To assess the long-term frequency of recurrences, organ damage, severe comorbidities, mortality and evolution in connective tissue disease (CTD) in PAPS patients.
**Methods:** Medical records of PAPS patients followed in 6 centers for ≥15 years were retrospectively reviewed. Chi square for categorical and Student t test for continuous variables were used. $P<0.05$ was considered significant.
**Results:** One hundred and fifteen patients (88% females) followed between 1983 and 2014 with a mean age at diagnosis of 33 (±10) years and mean follow-up of 19 (±3.5) years were studied. Fifty-one patients (44%) had at least a thrombotic event during follow-up for a total of 75 events and an annual incidence of 3.5%. Thromboses were more frequent in patients with previous thrombotic history (p:0.002,OR:4.8, 95%CI:1.6–14.7). There was a tendency towards anticoagulant treatment being not protective against recurrences (p:0.063). Six patients (5%) had a catastrophic event. Fifty-two women had 87 pregnancies, successful in 78% of cases. Twenty-nine percent of patients had functional damage. Damage was significantly associated with a thrombotic history (p:0.004,OR:13.9,95%CI:1.8–288.4) and to arterial events ($p<0.001$,OR:7.9,95%CI:2.7–24.3) especially stroke, but not to demographics, serology or treatment. Twenty-four major bleeding episodes were recorded in 18 patients, all on anticoagulants. Severe infections affected 6 patients (5%) with 1 fatality. A solid cancer was diagnosed in 8 patients (7%). One patient (1%) with a chronic bowel ischemia died for sepsis. Eleven percent of patients developed a CTD and 14% another autoimmune disease.
**Conclusions:** Despite therapy, a high proportion of patients experienced new thrombotic events,while pregnancy outcome was significantly improved. Organ damage developed in a significant proportion of patients and was associated with arterial events. The risk of evolution in CTD has to be considered.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3100

## THU0326 BRAIN MRI IN PATIENTS WITH ACUTE CONFUSIONAL STATE OF DIFFUSE PSYCHIATRIC/NEUROPSYCHOLOGICAL SYNDROMES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Neuropsychiatric systemic lupus erythematosus (NPSLE), especially diffuse psychiatric/neuropsychological syndromes (diffuse NPSLE), is one of the most difficult complications of the disease. For the evaluation and the diagnosis of central nervous system manifestations, including NPSLE, brain MRI is a very useful tool to detect the various abnormalities. We previously disclosed that patients with diffuse NPSLE and MRI abnormalities have more severe inflammation in the central nervous system compared with those without MRI abnormalities, as evidenced by poorer prognosis. Of note, acute confusional state (ACS) is the most recalcitrant manifestation in diffuse NPSLE. However, it remains unclear whether abnormalities in brain MRI still have any influences in patients with ACS.
**Objectives:** The aim of this study is to explore the differences in clinical characteristic between ACS patients with and without MRI abnormalities.
**Methods:** Thirty-six patients with ACS admitted to our University Hospitals from 1992 to 2015 were exhaustively enrolled in this study. Their medical charts and brain MRI scans were reviewed. The relationship of MRI abnormalities with various parameters was analyzed.
**Results:** As many as 19 of 36 patients (52.8%) had abnormal MRI findings. MRI findings improved after treatment in 14 of 19 patients for whom follow-up studies were available. Among the 5 patients without improvement of MRI findings, 4 patients died from active NPSLE itself. MRI abnormalities were not correlated with the age at the onset of ACS, the disease duration of SLE, the presence of anti-DNA antibody, anti-phospholipid antibodies, or anti-ribosomal P antibodies, and the levels of IL-6 in sera or cerebrospinal fluid. Notably, MRI abnormalities were significantly associated with the presence of serum anti-Sm antibodies (p=0.0005). Finally, the presence of MRI abnormalities in patients with ACS significantly increased the mortality (p=0.0013, HR=10.36 [95% CI: 2.487–43.19]) (figure).




**Conclusions:** These results demonstrate that patients with ACS of diffuse NPSLE with MRI abnormalities have more severe inflammation in the central nervous system, as evidenced by poorer prognosis. The data also indicate that anti-Sm in involved in the development of MRI abnormalities in ACS.
**Disclosure of Interest:** None declared
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## THU0327 COMPARISON OF IMMUNOENZYMATIC ASSAY AND CRITHIDIA IMMUNOFLUORESCENCE TEST FOR THE DETECTION OF ANTI-DOUBLE STRAND DNA ANTIBODIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Anti double strand DNA (dsDNA) antibodies are one of the immunologic hallmarks used to identify patients with systemic lupus erythematosus (SLE). However, they can be seen in patients with other connective tissue diseases (CTDs) on occasion. These auto-antibodies can also be drug-induced by medications such as anti-TNF$\alpha$ agents. Different methods are available for their detection. In the past, radioimmunoassays (RIA) and immunofluorescence by Crithidia (CLIFT) were commonly used. More recently, immunoenzymatic assays (ELISA) have been widely utilized.
ELISA assays are much faster, cheaper and easier to perform than other methods such as CLIFT and now are the most common method used by immunology laboratories.
The Crithidia test is still used in clinical practice, often for the purpose of confirmation after ELISA or further testing if ELISA is negative, but its real usefulness needs to be more clearly defined.
**Objectives:** Investigate the relation between dsDNA Abs measured by CLIFT and ELISA. Define the clinical role for CLIFT testing.
**Methods:** 1000 consecutive adult patients tested for anti dsDNA by ELISA in Mayo Clinic Rochester immunology lab from September to December 2015 had their sera tested also by CLIFT. Laboratory, clinical data and history were reviewed. For ELISA we used Quanta Lite dsDNA ELISA kit by Inova Diagnostic, taking as stated by the manufacturer for negative value below 30 IU/ml, for borderline between 30 and 75 IU/ml and for positive above 75 IU/ml. For CLIFT we used Crithidia Luciliae Kit by Kallestad, considering positive the samples with immunofluorescence signal from the kinetoplast or from both the kinetoplast and the nucleus.
**Results:** CLIFT showed a very high specificity (99%) but a low sensitivity (14%) for patients with SLE. ELISA had specificity close to CLIFT (92–95%) but with a substantially better sensitivity (36–47%). ELISA performed better considering borderline as negative (positive predictive value [PPV] with borderline as negative 68% vs 63% as positive).

Table 1. Samples by ELISA and CLIFT results, SLE samples out of total samples for each group, with percentage

| | ELISA | | | |
|---|---|---|---|---|
| | Negative | Borderline | Positive | Total |
| Crithidia | | | | |
| Negative | 119/817 (15%) | 26/49 (53%) | 57/93 (61%) | 202/959 (21%) |
| Positive | 4/7 (57%) | 1/3 (33%) | 27/31 (87%) | 32/41 (78%) |
| Total | 123/824 (15%) | 27/52 (52%) | 84/124 (68%) | 234/1000 (23%) |

**Conclusions:** CLIFT is very specific but its low sensitivity limits its usefulness.
New generation ELISA has good performance, with high specificity and good sensibility.
A negative test by ELISA is most of the time negative also by Crithidia, and among the rare ELISA-/CLIFT+ few patients have SLE, so there's no need to run Crithidia in ELISA negative patents.
Among the ELISA positive, Crithidia could add value for some patients with SLE, but always keeping in mind the limit of sensitivity.
**Disclosure of Interest:** None declared
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## THU0328 A COMPREHENSIVE EVALUATION OF SERUM AUTOANTIBODIES IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** Conventional antibodies are well described and studied in primary Sjögren syndrome, nevertheless patients can also present unconventional autoantibodies.
**Objectives:** The objective of this study was to investigate the prevalence of a large panel of conventional and unconventional autoantibodies (Ab) in a well-characterized population of patients with primary Sjögren's syndrome (pSS).
**Methods:** Two hundred and twenty six pSS patients benefiting from a comprehensive clinical and radiological assessment were recruited. A new technique based on chemiluminescence (ISYS-IDS) was selected, in 44 patients, to assay 17 autoantigens including SSA/Ro (52+60 kDa), SSB/La, dsDNA, centromere, Sm, U1-snRNP, Scl70, Jo1, cardiolipin, β2-GPI, CCP2, PR3, MPO, GBM, transglutaminase (IgA), and deaminated gliadin (IgA&IgG). If positive, the presence of Ab was validated by another technique. The study was completed by the search for anti-nuclear Ab (ANA) on HEp-2 cells and rheumatoid factors (RF) against human and rabbit IgG.
**Results:** Search for conventional Ab showed ANA (71.7% at 1:320), anti-SSA/Ro Ab (61.1%), anti-SSB/La Ab (31.0%, all anti-SSA+) and IgM RF (44.2%). The triple Ab association (ANA+SSA+RF) rather than the SSA/SSB association was associated with an earlier diagnosis, an active immunological profile (hypergammaglobulinemia, erythrocyte sedimentation rate) and a salivary gland involvement (lymphocyte infiltration, ultrasonography and enlargement). Three patients out of 44 (6.8%) had unintended Ab in current practice directed against centromere, Jo1, and dsDNA plus IgG deaminated gliadin Ab but without associated clinical signs.
**Conclusions:** The ability to combine a wide range of autoantibodies can lead to defining new subgroups of pSS patients for precise disease characterization, patient stratification and response prediction.
**Disclosure of Interest:** None declared
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## THU0329 RETROSPECTIVE ANALYSIS OF CLINICAL FEATURES, DISEASE COURSE AND OUTCOME OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN KYRGYZSTAN

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**Background:** Systemic lupus erythematosus (SLE) is a devastating disease affecting different organs, ultimately leading to organ failure and death. To date, there are no data regarding the real-life picture of SLE in Kyrgyzstan.
**Objectives:** To define retrospectively the pattern of clinical features, disease course and outcome of patients with SLE in Kyrgyzstan.
**Methods:** The retrospective study comprised of 107 consecutive patients with confirmed SLE, who underwent inpatient care in the department of rheumatology of the National Center of Cardiology and Internal Medicine (NCCIM) from 2001 to 2011. Subsequently enrolled patients were followed-up on a regular basis. Study protocol included clinical, instrumental, laboratory and immunological parameters obtained from specially designed registry database of NCCIM (BLIPS 8, ADS-Limathon). All patients fulfilled the revised ACR criteria for SLE. Age, gender, disease activity index (SLEDAI-2K), SLICC Damage Index (SDI) and other parameters obtained at the time of first hospitalization and subsequently in 75 cases out of 107 after 5 years of follow-up observation were included for the statistical analysis. Immunological analysis included determination of anti-dsDNA and anti-Sm antibodies "ANA-LIA-Max 17". Date and cause of death were determined according to the primary medical records.
**Results:** Vast majority of patients (79.4%) enrolled in this study were from the northern part of the country. The study included 91.5% women and 8.4% men with a mean age 30 years and mean disease duration - 2.0 years. It took from 6 months to 3 years since the onset of symptoms to the verification of the diagnosis. Majority of patients (49.5%) were with subacute variant of the disease. Based on disease activity index, patients with moderate and high grade of disease activity were 46.7% and 44%,respectively. Within 5-year follow-up observation of 75 out of 107 patients the remission was achieved in 3.7%, and the low grade disease activity in 6.4% patients. In all cases upon a significant decrease in disease activity, there was a statistically significant increase in SDI score for 1 or higher points. Various irreversible organ damages were found in almost half of the cases (47.6%) at a mean of 2.0 years from the onset of the disease. Majority of patients showed low (28.7%) and moderate (28.3%) SDI score. During observation 27 (36%) of 107 patients died. The main causes of death were active SLE and its complications involving different organ damages: kidney (29.6%), lung (22%) and combined central nerves system (CNS) and kidney (11%). Overall mortality from the concomitant infection was 18.7%, prominently from the infection of the respiratory system, among them 42.7% with severe pneumonia and progressive respiratory failure.
**Conclusions:** The study identified that progressive organ damages and infectious complications involving respiratory system were associated with poor prognosis and outcome of patients with SLE in Kyrgyzstan.
**Disclosure of Interest:** None declared
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## THU0330 VALIDIITY OF PROTEIN-TO-CREATININE RATIO IN AN UNTIMED URINE SPECIMEN AND ESTIMATED GLOMERULAR FILTRATION RATE AS MEASURES OF PROTEINURIA AND RENAL FUNCTION IN PATIENTS WITH LUPUS NEPHRITIS

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**Background:** In 2006, the American College of Rheumatology (ACR) Ad Hoc Committee on Systemic Lupus Erythematosus (SLE) recommended the urinary protein level in a spot (untimed) urine specimen (determined as urinary protein-to-urinary creatinine ratio; spot P/C ratio) over a 24-hour urine protein excretion. In addition, the committee stated that renal function refers to the estimated glomerular filtration rate (GFR) and selected the MDRD study equation. However, several subsequent reports suggested that the spot P/C ratio may be inaccurate in the assessment of the degree of proteinuria in lupus nephritis (LN). In addition, there is no consensus as to which estimating equation is preferred for estimated GFR in LN.
**Objectives:** We aimed to evaluate the validity of spot P/C ratio and estimated GFR by the modified MDRD study equation as measures of proteinuria and renal function in patients with LN.
**Methods:** A total of 61 patients with active LN who were admitted to our hospital from 2010 through 2015 were included. LN was pathologically confirmed in 51 patients and renal biopsy was not performed in the other 10 patients. In addition, 22 SLE patients without active LN in whom spot P/C ratio, 24-hour urine protein excretion, estimated GFR, and 24-hour urine creatinine clearance were measured were also included. All the patients met the revised ACR classification criteria for SLE. Clinical and laboratory data were retrospectively collected from the electronic medical records and statistically analyzed.
**Results:** The spot P/C ratio and the 24-hour urine protein excretion were moderately correlated (n=64, Pearson's $r$ =0.62). However, the Bland-Altman plot demonstrated proportional bias (progressive deviation with values). Agreement of the spot P/C ratio $\geq$0.5 and the 24-hour urine protein excretion $\geq$0.5 g was moderate (Cohen's $\kappa$ =0.56) whereas that of $\geq$0.2 was almost perfect ($\kappa$ =0.83). Measured 24-hour urine creatinine excretion ranged from 220 mg to 2120 mg; the mean and median values were 860 mg and 840 mg, respectively. Among the 10 patients in whom serial data could be obtained in more than 3 times, the spot P/C ratio and the 24-hour urine protein excretion were highly correlated ($r$ =0.87 to 0.99), except for 2 patients ($r$ = -0.30 and 0.68, respectively). In these serial samples derived from the 8 patients, there was substantial agreement between the spot P/C ratio and the 24-hour urine protein excretion about whether increased or decreased compared to previous data ($\kappa$ =0.65). The estimated GFR by the modified MDRD study equation and the body surface area (BSA) corrected 24-hour urine creatinine clearance were moderately correlated (n=81, $r$ =0.62). However, the Bland-Altman plot demonstrated both fixed and proportional bias. Agreement of the estimated GFR and the BSA-corrected 24-hour urine creatinine clearance $\geq$60 (ml/min/1.73 $m^2$) was moderate ($\kappa$ =0.48).
**Conclusions:** Our results supported the validity of spot P/C ratio and estimated GFR by the modified MDRD study equation as convenient screening and monitoring measures of proteinuria and renal function in patients with LN. However, agreement between these convenient measures and measures based on 24-hour urine collection is not always good. Spot P/C ratio and estimated GFR should be used with attention to their limitation.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1896

## THU0331 OUTCOME OF PREGNANCY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, PREVALENCE OF MATERNAL, OBSTETRIC, AND FETAL COMPLICATIONS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic disease affecting mainly women in childbearing age. Studies have shown that pregnancy in SLE women puts the mother and the fetus at risk of serious adverse events [1]. The prevalence of these events is under reported in the Arab countries. This study is to examine the pregnancy outcomes in patients with SLE.
**Methods:** We have retrospectively analyzed the medical files, and electronic medical records of all pregnant patients with SLE attended our Rheumatology Clinic between 2007 to 2014. All patients met ACR classification criteria for SLE. We have excluded patients diagnosed with DM, hypertension, chronic kidney disease before the onset of lupus.
We captured the following data: patient demographic number of pregnancies after the onset of SLE, pregnancy outcomes, maternal complications during and after pregnancy.
**Results:** We identified 150 pregnancies in 64 patients with lupus, and 57 (89%)

patients were Arabs. The total number of live birth was 105 (70%). An adverse fetal event was observed in 48 (32%) pregnancies. Total number of miscarriages was seen 43 (28.6%), six (4%) were induced abortions. Two died in utero (1%) and there was one neonatal death (1%). 44 (29%) were born below 2,500g, four were premature (less than 37 weeks) (3%), intrauterine growth retardation was observed in 19 (12.6%) and four born with malformation (3%). Obstetric complications occurred in 30 (20%) pregnancies, 5 (3%) had pre-eclampsia, 5 (3%) had gestational diabetes, and one had postpartum hemorrhage (1%). Maternal complications were detected in 20 (13.3%) pregnancies, lupus flare was observed in 18 (12%), five had thrombosis (3%), and no death.

**Conclusions:** Pregnancy in lupus is often associated with an adverse maternal and fetal outcome independent by disease activity.

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**Disclosure of Interest:** None declared

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## THU0332 THE PREDICTIVE RISK FACTORS AND PROGNOSES OF THROMBOTIC MICROANGIOPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS

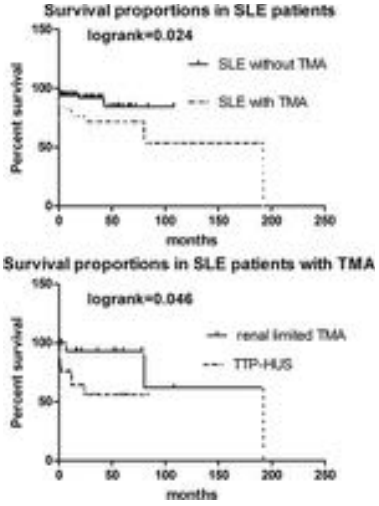
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**Background:** Systemic lupus erythematosus (SLE) with thrombotic microangiopathy (TMA) has been reported in numerous patients with high mortality and poor renal prognosis. The risk factors and prognoses of these patients remain unknown.

**Objectives:** The aim of this study is to investigate the predictive risk factors of TMA in SLE patients and analyze the prognoses.

**Methods:** Clinical and laboratory parameters of 42 patients (SLE with TMA) and 84 patients (active lupus patients without TMA) were retrospectively analyzed. Clinical and laboratory data was also compared between 17 patients with renal-limited TMA and 25 patients with TTP-HUS. Logistic regression and Kaplan-Meier survival curves were statistically tested with the logrank test. HRs and their 95% CIs were calculated using the multivariate Cox proportional-hazards model.

**Results:** SLE patients with TMA suffered more neurological and cardiac involvements, as well as poor renal function. More plasma was exchanged (42.9% vs. 2.4%) and infused (64.3% vs. 40.5%) in these patients. Serological creatinine and C-reactive protein were independent risk factors for TMA. TMA patients presented poorer outcome (P=0.024), while a longer survival was expected in renal-limited TMA patients (P=0.046). In lupus patients with TMA, serum creatinine value (hazard ratio=1.005, P=0.014) and C-reactive protein levels (hazard ratio=1.009, P=0.058) predicted poor outcome.




**Conclusions:** Serum creatinine value and C-reactive protein levels were predictive for lupus with TMA. Renal-limited TMA patients presented relatively better outcome than patients with TTP-HUS.

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**Disclosure of Interest:** None declared

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## THU0333 CHRONOLOGICAL ANALYSIS OF DAMAGE ACCRUAL IN SLE PATIENTS FROM THE SPANISH REGISTRY (RELESSER)

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**Background:** Mortality in SLE has improved over the last decades. Outcome measures as damage become more important.

**Objectives:** To study damage manifestations and the timing of their appearance.

**Methods:** In the 1st transverse phase of RELESSER, accumulated information on 400 variables per patient at the time of the last evaluation was collected. We evaluated damage manifestations in each system and the temporal relationship of their appearance with the time of SLE diagnosis.

Cumulative incidence function for damage was estimated.The impact on mortality was studied controlling for sex, race, age at diagnosis and delay of diagnosis of SLE by Cox regression.

**Results:** 2,662 SLE patients had the dates of presentation of each event of damage: 2,417 (91.0%) women, 2,402 (92.8%) Caucasian, mean age (±SD) 34.0 (±13.6) years at the time of diagnosis. The mean follow-up time was 115.6 (±50.8) months. 112 (4.2%) patients died.

At the time of the study 917 (34.4%) patients had at least 1 damage manifestation, the mean number of systems per patient with at least 1 damage manifestation was 0.54 (±0.92) and the mean SDI score was 0.65 (±1.2).

The systems more frequently damaged were musculoskeletal (MS) (11.9%), ophtalmic (7.8%) and cardiovascular (CV) (5.9%).In the 1st year after SLE diagnosis, the cumulative incidence (CI 95%) of damage in at least 1 system was 7.4% (6.4–8.4), at 5 years 18.9% (17.3–20.4) and after more than 10 years 29.2% (27.3–31.1).The systems damaged at earliest stages, 1 year after SLE diagnosis, were: MS 1.7% (1.2–2.2), neuropsychiatric 1.3% (0.8–1.7), renal 1.2% (0.8–1.6) and CV 0.9% (0.6–1.3).

The rate of increase of damage is significantly higher ($p<0.001$) short time after SLE diagnosis. The proportion of patients with damage in at least 1 system at 5 and 10 years was 18.9% (17.3–20.4) and 29.2% (27.3–31.1). While in the 1st year 7.4% of patients present damage in any system, only 2.9% per year do so since the 1st to the 5th year after diagnosis and, between the 5th and 10th year there was only an annual increase of damage of 2.1%.Risk of death is multiplied by 2.04 (1.7–2.3) at the time that a new system is damaged. Significant impact on neuropsychiatric, renal, pulmonary, CV systems and malignancy was found, with multiplicative risk factors of 2.0, 1.8, 2.8, 1.7 and 2.7 respectively.

**Conclusions:** Damage occurs already in early stages of the disease. It appears early in MS, neuropsychiatric and kidneys. The increase of damage is greater in the 1st year after SLE diagnosis. The accumulation of visceral damage increases the mortality rate.

**Disclosure of Interest:** J. Pego Grant/research support from: Spanish Society of Rheumatology, FIS/ISCIII (PI11/02857), BIOCAPS from the EU 7th Framework Programme/REGPOT-2012–2013.1 (316265),GSK, Roche, Novartis,UCB., A. Lois: None declared, C. Mouriño: None declared, F. L-Longo: None declared, M. Galindo: None declared, J. Calvo: None declared, J. Uña: None declared, V. Balboa: None declared, A. Olive: None declared, T. Otón: None declared, J. Ibañez: None declared, L. Horcada: None declared, A. Sánchez: None declared, C. Montilla: None declared, R. Melero: None declared, V. MTaboada: None declared, E. Diez: None declared, M. Fernandez: None declared, E. Ruiz: None declared, J. HBeriain: None declared, M. Gantes: None declared, B. HCruz: None declared, A. Pecondon: None declared, N. Lozano: None declared, G. Bonilla: None declared, V. Torrente: None declared, L. Silva: None declared, A. FNebro: None declared, I. Rua: None declared

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## THU0334 A LONGITUDINAL ANALYSIS OF CHANGE IN LUPUS NEPHRITIS IN AN INTERNATIONAL INCEPTION COHORT USING A MULTISTATE MARKOV MODEL APPROACH

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**Background:** Patients with lupus nephritis (LN) may have improvement or deterioration in renal status over time.

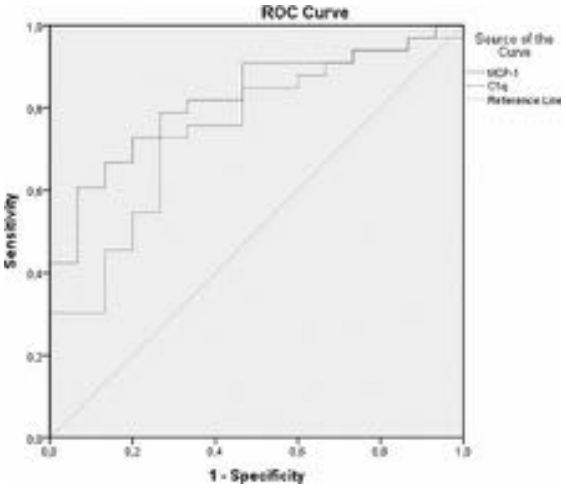
**Objectives:** To capture bidirectional change we used a reversible multistate

Markov model to study transitions in glomerular filtration rate (GFR) and proteinuria (PrU) in a prospective, international, inception cohort of SLE patients receiving standard of care.
**Methods:** Patients were evaluated at enrollment and annually. LN was identified from the ACR classification criteria and/or renal biopsy. Data included medications, estimated GFR (eGFR) and PrU (ePrU), disease activity (SLEDAI-2K), organ damage [(SLICC)/ACR damage index (SDI)] and lupus autoantibodies including IgG anticardiolipin (aCL) and lupus anticoagulant (LAC). GFR states were defined: state 1 (eGFR: >60 ml/min); state 2 (eGFR: 30–60 mL/min); and state 3 (eGFR: <30 ml/min). Similarly, PrU states were defined: state 1 (ePrU: <0.25 gr/day); state 2 (ePrU: 0.25–3.0 gr/day); and state 3 (ePrU: >3.0 gr/day). Multistate models were used to provide estimates of relative transition rates and state occupancy probabilities for various time periods.
**Results:** Of 1,826 SLE patients, 89% were female, 49.2% Caucasian with mean±SD age 35.1±13.3 years. The mean disease duration at enrollment was 0.5±0.3 years and follow-up was 4.6±3.4 years. LN occurred in 700/1,826 (38.3%) patients. There was no observed change in eGRF state for 2303/2430 (94.8%), 136/255 (53.3%) and 26/55 (47.3%) visits when the previous eGFR state was 1, 2 and 3 respectively. The corresponding values for ePrU states were 1167/1460 (79.9%), 547/983 (55.6%) and 59/205 (28.8%). For both outcomes the likelihood of improvement (states 2 to 1 and 3 to 2) was greater than deterioration (states 1 to 2 and 2 to 3). The transition from state 3 to ESRD was more likely with eGFR (54%) than ePrU (9%). Probability estimates of transitioning between eGFR and ePrU states, ESRD and death at 1, 2 and 5 years were determined. At year one the highest probability was for patients to remain in the initial eGFR (95%, 55%, 42%) or ePrU (81%, 56%, 31%) state. Following 2 and 5 years, the estimated probability for improvement in either eGFR or ePrU was higher than deterioration. Multivariate analysis identified older age ($p<0.001$), race/ethnicity (Hispanic, Asian and African ancestry) ($p<0.001$), higher ePrU state ($p<0.001$) and higher renal biopsy chronicity score (p=0.013) as predictors for deterioration in eGFR states and male sex (p=0.04) for improvement. For ePrU, multivariate analysis identified race/ethnicity (Hispanic, Asian and African ancestry) (p=0.009), earlier calendar year (p=0.017), SDI without renal variables (p=0.058) and higher renal biopsy chronicity score (p=0.015) as predictors for deterioration. Male sex (p=0.016), positive LAC (p=0.007) and ISN/RPN class V nephritis (p=0.012) and mycophenolic acid (p=0.003) were associated with lower improvement rate.
**Conclusions:** In lupus nephritis, the expected improvement and deterioration in renal outcomes can be estimated by multistate modeling and is predicated by identifiable risk factors. New therapeutic interventions for LN should meet or exceed these expectations.
**Acknowledgement:** The Systemic Lupus International Collaborating Clinics (SLICC) research network received funding for this study from Bristol-Myers Squibb.
**Disclosure of Interest:** None declared
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## THU0335 ANTI C1-Q ANTIBODIES AND URINARY MONOCYTE CHEMOATTRACTANT PROTEIN-1 LEVELS AS BIOMARKERS FOR RENAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Some previous studies in Caucasian, Asian, and African-american patients have shown that the anti-C1q antibodies and urine levels of MCP-1 (uMCP-1) were significantly greater in patients with LN. However, information in Mestizo and Afro-Latin American patients is very limited.
**Objectives:** Our aim was to evaluate diagnostic value of Anti-C1q and uMCP-1 as a potential markers for the diagnosis of LN in Colombian SLE patients
**Methods:** We examined serum levels of anti-C1q and uMCP-1 in 67 consecutive SLE patients (ACR criteria 1997) from Hospital San Vicente Fundación, at Medellín, Colombia. A fresh urine sample from each patient was collected in a sterile container. Serum Anti-C1q antibodies and uMCP-1 were measured by ELISA techniques (Inova, San Diego, and R&D system, Minneapolis, EEUU, respectively). Several clinical and serological features were analyzed as well as disease activity (SLEDAI). Descriptive statistics were used to describe data. Mann-Whitney tests were used to compare data and Spearman'srho for correlations. Additionally, ROC curves relating the specificity and sensitivity profiles of the 2 biomarkers were done
**Results:** 67 SLE patients were recruited (89% female) with median age of 33.5± 12.0 yrs and median disease duration of 6.76 ± 6.80 years. Mestizo (71%) and Afro-latin American (26%) were majority. Hematologic disease (89%), arthritis (86%), cutaneous involvement (80%), and renal disease (66%) were among most common manifestations. Sixty-three percent of patients were positive for anti-C1q and 56% had elevated levels of uMCP-1 (mean levels 1678 ±3722 pg/ml). Mean SLEDAI score was 10.0 ± 9.0. We found significant association between anti C1q antibodies and several clinical features including serositis, proteinuria, renal and hematological involvement and with several serological markers including anti-dsDNA, low complement and higher SLEDAI score. Patients with LN had higher levels of anti-C1q antibodies than patients without LN (mean levels of 91.3 ± 85.4 vs 31.7 ± 38.7, p value=0.002). uMCP-1 levels were significantly higher in patients with LN than in patients without LN (2399 ± 4566 vs 472 ± 596 pg/ml, p value=0.017) and in patients with proteinuria (2537 ± 4731 vs 553 ± 688, p value=0.025). There was no correlation between anti-C1q levels and uMCP-1. An ROC curve constructed for anti-C1q and uMCP-1 and renal in all SLE patients showed that uNGAL had a good level of sensitivity and specificity with an AUC of 0.74 for anti-C1q and 0.82for uMCP1 (see figure).



ROC curve on Anti-C1q and uMCP-1. Solid line for Anti-C1q, dotted line for MCP-1.

**Conclusions:** Although further confirmatory testing is underway, LN patients had almost 3 times and 5 times higher levels of Anti-C1q and uMCP-1, respectively than patients without LN. Anti-C1q antibodies and uMCP-1 may be a good biomarkers for LN in Mestizo and Afro-Latin american SLE patients, and can be a useful marker to identify patients with higher risk of renal involvement
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**Disclosure of Interest:** None declared
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## THU0336 OUTCOMES IN PATIENTS WITH ISCHEMIC STROKE REGARDING TITER AND PERSISTENCE OF ANTIPHOSPHOLIPID ANTIBODIES

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**Background:** Stroke and transient ischemic attack (TIA) are the most common neurologic manifestation of antiphospholipid syndrome (APS). The international consensus criteria for APS classification require persistent antiphospholipid antibodies (aPL) positivity (at least 12 weeks apart) and medium or high titer for anticardiolipin antibody (aCL) associated with clinical manifestations [1]. To confirm the diagnosis of a patient who comes with stroke/TIA and positive aPL as definite APS, we serially check the positivity of aPL in addition to titer of aCL. However, significance of persistence and moderate or high titer of aPL on the clinical relevance is not identified.
**Objectives:** To evaluate the effect of persistent and medium or high titer of aPL positivity on recurrence in patients with ischemic stroke/TIA.
**Methods:** We reviewed medical records of 99 patients with ischemic stroke/TIA who had at least one or more positive aPL (ie, positivity for anticardiolipin antibodies [aCL], $\beta_2$-glycoprotein I antibodies [$\beta_2$-GPI], lupus anticoagulant

| | aPL carriers (n=53) | Definite APS (n=46) | Total (n=99) | p-value |
|---|---|---|---|---|
| 1st attack age (years) | 43.2±13.8 | 44.0±13.0 | 43.6±13.4 | 0.758 |
| Female sex (%) | 19 (35.8% | 28 (60.9% | 47 (47.5%) | 0.013 |
| F/U duration (months) | 43.8±39.2 | 60.4±53.3 | 51.6±46.8 | 0.078 |
| HTN | 18 (34.0%) | 12 (26.1%) | 30 (30.3%) | 0.511 |
| DM | 11 (20.8%) | 2 (4.3%) | 13 (13.1%) | 0.016 |
| Smoking | 23 (43.4%) | 15 (32.6%) | 38 (38.4%) | 0.271 |
| (pack-years) | 9.9±16.1 | 7.7±13.2 | 8.9±14.8 | 0.458 |
| Prior CVD | 1 (1.9%) | 0 (0%) | 1 (1.0%) | 0.349 |
| Cardiac diseases | 13 (24.5%) | 6 (13.0%) | 19 (19.2%) | 0.148 |
| Abortion Hx. | 4 (7.5%) | 4 (8.78%) | 8 (8.1%) | 0.834 |
| T.chole | 183.1±45.1 | 175.5±43.8 | 179.6±44.5 | 0.400 |
| TG | 152.7±142.3 | 121.6±100.2 | 138.0±124.5 | 0.231 |
| HDL | 43.5±10.4 | 42.8±14.2 | 43.2±12.3 | 0.764 |
| LDL | 105.2±33.2 | 105.8±28.8 | 105.5±31.1 | 0.923 |
| Recurrence | 16 (30.2%) | 14 (30.4%) | 30 (30.3%) | 0.979 |
| Duration to recurrence (months) | 35.2±48.3 | 33.7±43.5 | 34.5±45.3 | 0.931 |

antibodies [LA]). We divided these patients into two groups according to the most recent revised classification (Sydney consensus conference), and designated as "definite APS" who fulfilled the laboratory criteria, and "aPL carriers" who had transient or low titer aPL. We compared the subsequent ischemic stroke/TIA events between the two groups.
**Results:** Of the 99 patients, 46 (46%) were classified as definite APS and 53 (54%) as aPL carriers. There was no increased risk of subsequent ischemic/TIA events in definite APS group compared with aPL carriers group. The overall event was 14 (30.4%) in APS group and 16 (30.2%) in aPL carriers group during 60.4 months and 43.8 months follow up period respectively. 38 patients were having anticoagulation for treatment and 60 patients were on anti-platelet treatment without anticoagulation, but there was no difference on recurrence events regarding the treatment. Among definite APS group, there was no difference in recurrence events according anticoagulation vs anti-platelet agent.
**Conclusions:** The persistence and medium or high titer of aPL enables to diagnose APS in ischemic stroke/TIA patients, but does not predict increased risk for subsequent ischemic stroke/TIA.
**References:**
[1] Rand JH. The antiphospholipid syndrome. Hematology Am Soc Hematol Educ Program 2007:136–142
**Disclosure of Interest:** None declared
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## THU0337 RAYNAUD PHENOMENON IS ASSOCIATED WITH MYOCARDIAL FIBROSIS IN PRIMARY SJÖGREN SYNDROME, ASSESSED BY A CARDIAC MAGNETIC RESONANCE APPROACH: A PROSPECTIVE PILOT STUDY AT A SINGLE CENTER

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**Background:** Primary Sjögren syndrome (pSS) shares many clinical, inflammatory, and immunological features with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Both SLE and RA are characterized by a high risk of cardiac involvement. However, there are limited data on the risk of overt cardiac involvement in pSS.
**Objectives:** We sought to use a cardiac magnetic resonance imaging (CMR) approach to assess cardiac involvement and determine its association with disease characteristics in pSS patients without cardiac symptoms.
**Methods:** Consecutive pSS patients, according to ACR classification criteria (2012), without a history or clinical findings of hypertension, cardiovascular disease, diabetes, or dyslipidemia underwent contrast CMR. Late gadolinium enhancement (LGE) was used for the assessment of myocardial fibrosis. Using a black-blood T2-weighted image (T2-WI), myocardial inflammation could be assessed. Sjögren syndrome disease activity index (ESSDAI) was determined. Eighty percent patients had documentation of a minor salivary gland biopsy. Salivary gland biopsy data were classified by focus score (FS). We investigated the patients in terms of prevalence of CMR abnormalities and explored possible associations between CMR abnormalities and pSS disease characteristics.
**Results:** Thirty-seven female pSS patients were enrolled (mean age: 55.5 ± 7.0 years). On an average, cardiovascular risk was low for the group, with patients demonstrating no ECG abnormalities, and the patients had generally low traditional cardiovascular risk factors, with a mean Framingham 10-year hard cardiovascular risk score of 4 ± 2%. The mean ESSDAI was 3.3 ± 2.1. Thirteen patients (35%) demonstrated myocardial abnormalities. Myocardial edema was seen in 5 patients (13%) on T2-WI. LGE was found in 11 patients (29%), 3 of whom demonstrated edema on T2-WI. The main finding observed in 7 among 11 LGE-positive patients (63%) was a linear LGE pattern without coronary distribution. A patchy nodular LGE pattern was observed in 4 among 11 patients (37%). The patients with CMR abnormalities showed no significant difference of ESSDAI, compared with those with no CMR abnormalities. Antibodies to La/SSB antigens were significantly higher in LGE-positive than LGE-negative patients (p=0.003). Raynaud phenomenon was significantly associated with LGE-positive and T2-WI-positive patients (p=0.001 and p=0.04, respectively). Other pSS characteristics such as disease duration, commodities, and cardiovascular risk factors were not significantly associated with myocardial abnormalities. The greatest relative difference between LGE-positive and -negative patients was observed in FS >3, with an adjusted odds ratio of 3.0. After adjusting for confounding by age, pSS duration, and anti-SSB antigen, the association of LGE with Reynaud phenomenon remained significant (p=0.02).
**Conclusions:** Subclinical myocardial involvement, as detected by CMR, was frequent in pSS patients without cardiac symptoms. Our results suggest that Raynaud phenomenon has a role in promoting cardiac involvements in patients with pSS.
**Disclosure of Interest:** None declared
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## THU0338 CYSTIC LUNG DISEASE IN SJÖGREN'S SYNDROME: AN OBSERVATIONAL STUDY

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**Background:** Assessments of the prevalence of pulmonary involvement in Sjögren's syndrome (SS) vary considerably in the literature. Moreover some publications found that lung involvement in SS is usually mild and stable while others describe a far more severe disease complication with a 5-year mortality of more than 15%. This is indicating that more studies of prevalence and severity of pulmonary involvement in SS are needed
**Objectives:** To analyze the prevalence, characteristics and outcome of cystic lung disease associated with Sjögren's syndrome (SS).
**Methods:** From June 2010 to February 2015, 90 SS patients (60.1±14.8 years; 88 (97.8%) female, 62 (68.9%) primary SS) had a systematic chest CT-scan. The presence of thin-walled cysts was analyzed by one experienced radiologist. Demographic data, clinical history, laboratory findings, and pulmonary function tests were extracted from medical records.
**Results:** Twenty-one (23.3%) patients had cysts on CT scan performed 40.5±54.5 months after SS diagnosis. Cysts number ranged from 1 to 25, were often bilateral (52.4%) and mostly located in the middle lung zone (76.2%). Cysts were isolated (n=6, 28.6%) or associated with other lesions including bronchiectasis (n=5, 23.8%), micronodules (n=5, 23.8%), ground-glass opacity (n=4, 19%) and/or air trapping (n=3, 14.3%). Most patients with cysts (57.1%) had no respiratory symptoms. When comparing SS patients with and without cysts, patients with cysts tended to be older (65.3±15.3 versus 58.5±14.4 years, p=0.06). Smoking habits were similar in both groups. Anti-SSB antibodies were more frequently detected in patients with cysts (57.1% vs 26.1%, p=0.02). Pulmonary function tests were normal in most cases (52.6%) or displayed only mild small airways obstruction and reduced diffusion capacity to carbon monoxide. Four (19%) patients with cysts had a past history of associated pulmonary disease including interstitial lung disease. During follow-up (25.1±17.7 months) no patient developed specific lung disease or lymphoproliferative disorders.
**Conclusions:** Cystic lung disease is frequent, benign, associated with anti-SSB/La antibodies and has no impact on outcome in SS
**Disclosure of Interest:** None declared
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## THU0339 NON-CALCIFIED CORONARY ARTERY PLAQUE ASSOCIATES WITH ADVERSE LIPOPROTEIN PROFILES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) associates with excess cardiovascular (CV) disease and related mortality. This is contributed to, but cannot be fully explained, by traditional CV risk factors, treatments and SLE-specific factors. Coronary artery calcium scores (CAC), by computed tomography (CT) have been shown to predict atherosclerotic burden and CV events. Non-calcified plaque (NCP), common in SLE, can also be quantified and may be more metabolically active and unstable. Routine lipids are unhelpful in distinguishing SLE patients with or without either CAC or NCP. Nuclear magnetic resonance (NMR) spectroscopy allows determination of the size and concentration of lipoprotein classes and subclasses.
**Objectives:** To determine whether differences in NMR lipoprotein parameters can distinguish SLE patients with and without CAC. An additional aim was to establish whether NMR parameters associate with quantified NCP or calcified plaque.
**Methods:** As part of a longitudinal lupus cohort, SLE patients had coronary CT angiography performed. The burden of atherosclerosis was evaluated (CAC, NCP). CAC scores were calculated according to the Agatston system. NCP was also categorized and scored for each patient. Lipoprotein particle numbers

| Biomarker | Calcified Plaque | | NCP | |
|---|---|---|---|---|
| | Correlation Coefficient | P-value | Correlation Coefficient | P-value |
| Medium VLDL (nmol/L) | 0.07 | 0.56 | –0.00 | 0.97 |
| Small VLDL (nmol/L) | 0.00 | 0.99 | –0.05 | 0.68 |
| LDL (nmol/L) | 0.14 | 0.26 | 0.26 | 0.034 |
| IDL (nmol/L) | 0.05 | 0.66 | –0.02 | 0.89 |
| Large LDL (nmol/L) | 0.09 | 0.44 | 0.15 | 0.22 |
| Small LDL (nmol/L) | 0.02 | 0.89 | 0.14 | 0.22 |
| HDL (total) (μmol/L) | 0.17 | 0.17 | 0.16 | 0.20 |
| Large HDL (μmol/L) | –0.04 | 0.75 | –0.03 | 0.83 |
| Large HDL (μmol/L) | 0.10 | 0.42 | –0.07 | 0.57 |
| Small HDL (μmol/L) | 0.11 | 0.36 | 0.21 | 0.086 |
| VLDL size (nm) | 0.21 | 0.082 | 0.25 | 0.038 |
| LDL size (nm) | 0.09 | 0.49 | –0.05 | 0.70 |
| HDL size (nm) | –0.08 | 0.50 | –0.13 | 0.30 |
| Triglyceride (mg/dL) | 0.24 | 0.043 | 0.20 | 0.10 |
| Lipoprotein Insulin Resistance Score | 0.21 | 0.080 | 0.24 | 0.044 |

and size were evaluated by NMR. The initial statistical analysis compared those with and without calcified and NCP using t-tests. Further evaluation involved the calculation of correlation coefficients to evaluate the relationship between lipoprotein abnormalities and the burden of calcified and NCP.
**Results:** 69 SLE patients were evaluated, 49 (71%) African-American and 20 (29%) Caucasian. Significant NCP was present in 41 (59%) and CAC in 14 (20%). Individuals with NCP had significantly larger VLDL particles (44.8 ±5.5 nm versus 47.7 ±6.1 nm, p=0.042). Considering the volume and extent of CAC and NCP; (Table 1) higher triglycerides were observed with increasing levels of CAC. Increasing volumes of NCP were associated with higher LDL particle number and larger VLDL size. The lipoprotein insulin resistance scores were also positively associated with NCP. Table 1:Spearman Correlation for lipoprotein parameters and quantified coronary artery plaque.
**Conclusions:** The mechanisms underlying atherosclerosis in SLE are poorly understood. NCP is highly prevalent in SLE and may be contributed to by differences in LDL, VLDL and insulin resistance measures, not evaluated in routine lipid profiles. Further longitudinal analysis will determine whether these abnormalities associate with progression of disease and can be considered prognostic markers.
**Disclosure of Interest:** None declared
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## THU0340 RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS EXHIBIT SIMILAR DEGREE OF SEVERITY OF SUBCLINICAL ATHEROSCLEROSIS. RESULTS FROM A CROSS-SECTIONAL STUDY IN A POPULATION OF NORTHWESTERN SPAIN

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**Background:** Chronic inflammation plays a central role in the development of atherosclerosis, being especially relevant in patients with rheumatic diseases. Patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are more prone to suffer cardiovascular events than the general population.
**Objectives:** Our aim was to study the prevalence of subclinical atherosclerosis in patients with RA and SLE and determine the differences between these conditions.
**Methods:** We evaluated 99 SLE patients and 206 sex- and age-matched RA patients without previous history of cardiovascular events. Subclinical atherosclerosis was defined by the presence of carotid plaque according to Manheim Consensus Conference criteria and/or intima-media thickness ≥0.90 mm. Carotid ultrasonography was performed by a MyLab 70 scanner (Esaote; Genoa, Italy), equipped with 7–12 MHz linear transducer and the *automated software guided technique radiofrequency – Quality Intima Media Thickness* in *real-time* (*QIMT*, *Esaote*, *Maastricht*, *Holland*). After the univariate analysis, multivariate regression models were fitted to adjust for potential confounders.
**Results:** The mean age was 52 ± 13 years in RA and 51±13years in SLE (p=0.77). Demographic data and traditional cardiovascular risk factors are summarized in table 1.
Regarding carotid plaques, there were no statistically significant differences. The frequency of carotid plaques was 40.2% among patients with RA and 44.4% in SLE patients. Bilateral plaques were present in 26% patients with RA and in 21.2% of those with SLE.
An IMT ≥0.90 mm was observed in 9.8% RA patients and in 6.3% of SLE patients (p= NS).
After adjusting for traditional cardiovascular risk factors and disease duration, there were no differences in the frequency of carotid plaques (OR SLE vs RA 1.52; CI 0.88–2.62) or in the frequency of IMT ≥0.90 mm (OR 0.75; CI 0.27–2.07).

| | SLE, % (n=99) | RA, % (n=206) | P |
|---|---|---|---|
| Female | 93.9 | 95.1 | 0.784 |
| Age (mean ± SD), years | 51.4±13.4 | 51.9±13.5 | 0.768 |
| Disease duration (mean ± SD), years | 11.1±8.5 | 8.6± 8.3 | 0.015 |
| Hypertension | 25.3 | 31.9 | 0.284 |
| Dyslipidemia | 19.2 | 42.2 | <0.001 |
| Diabetes | 1.0 | 8.3 | 0.009 |
| Smokers | 24.2 | 33.8 | 0.084 |
| Former smokers | 27.3 | 17.6 | |
| Family history of premature CV disease | 29.6 | 19.2 | 0.055 |
| Carotid plaque | 44.4 | 40.2 | 0.535 |
| Plaque unilateral | 23.2 | 13.7 | 0.104 |
| Plaque bilateral | 21.2 | 26.5 | |
| IMT ≥0.90 mm | 6.3 | 9.8 | 0.383 |

**Conclusions:** The frequency of subclinical atherosclerosis is similar in patients with SLE and RA after adjusting for traditional cardiovascular risk factors.
**Disclosure of Interest:** None declared
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## THU0341 CORRELATION BETWEEN ESSDAI AND CLINESSDAI IN A REAL-LIFE COHORT OF SJÖGREN'S SYNDROME PATIENTS

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**Background:** ClinESSDAI has been recently proposed as a valid tool for the assessment of disease activity in Sjögren's syndrome (SS) and it seems very close to the original ESSDAI (1, 2). The rationale of developing ClinESSDAI was to provide an accurate evaluation of disease activity independently of B-cell biomarkers, and it has been proposed to be used in biological/clinical studies to avoid data colinearity, in clinical trials, as secondary endpoint, to detect change independently of biological effect of the drug, and in clinical practice to assess disease activity for visits where immunological tests have not been done. However, validation in real-life cohorts is lacking, since 702 fictive vignettes derived from 96 real cases of primary SS of the ESSDAI development study were used.
**Objectives:** Primary objective of the study was to correlate ClinESSDAI and ESSDAI scores in large real-life cohorts of primary SS patients.
**Methods:** SS patients from 5 independent cohorts were studied. All patients fulfilled the American-European Consensus Group Criteria for primary SS. ESSDAI and ClinESSDAI scores were calculated at SS diagnosis. The whole population comprised 966 patients with primary SS (mean age 52±14, 95.4% female). Patients positive for anti-SSA antibodies were 684 (70.8%), for anti-SSB antibodies were 353 (46.5%), and negative for both anti-SSA/SSB antibodies were 271 (28.1%). Correlation between ClinESSDAI and ESSDAI scores was evaluated by Spearman's test.
**Results:** ClinESSDAI score significantly correlated with ESSDAI score in the first cohort (p<0.0001, r=0.972). Both ClinESDDAI and ESSDAI scores significantly correlated with all the single domains of the ClinESSDAI and ESSDAI, respectively, showing very similar results, even if the level of correlation was moderate to low in all the domains for both tools (table 1). Importantly, ClinESSDAI also significantly correlated with the biological domain of the ESSDAI score (table 1). Interestingly, focus score, available in 363/966 (37.6%) patients, did not correlate with both ClinESSDAI and ESSDAI scores (p=0.63, and p=0.426, respectively), while age at diagnosis inversely correlated with ClinESSDAI and ESSDAI scores (p<0.0001, r=-0.151, p<0.0001, r=-0.17, respectively).

Table 1

| ESSDAI Domain | ESSDAI | | ClinESSDAI | |
|---|---|---|---|---|
| | P | Spearman's rho | P | Spearman's rho |
| Constitutional | <0.0001 | 0.365 | <0.0001 | 0.386 |
| Lymphadenopathy | <0.0001 | 0.497 | <0.0001 | 0.498 |
| Glandular | <0.0001 | 0.323 | <0.0001 | 0.311 |
| Articular | <0.0001 | 0.393 | <0.0001 | 0.454 |
| Cutaneous | <0.0001 | 0.354 | <0.0001 | 0.346 |
| Pulmonary | <0.0001 | 0.276 | <0.0001 | 0.262 |
| Renal | <0.0001 | 0.183 | <0.0001 | 0.193 |
| Muscular | 0.031 | 0.069 | 0.014 | 0.079 |
| PNS | <0.0001 | 0.285 | <0.0001 | 0.291 |
| CNS | 0.0004 | 0.125 | <0.0001 | 0.136 |
| Hematological | <0.0001 | 0.391 | <0.0001 | 0.351 |
| Biological | <0.0001 | 0.327 | <0.0001 | 0.225 |

**Conclusions:** ClinESSDAI is a valid tool to assess systemic disease activity in primary SS.
**References:**
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**Disclosure of Interest:** None declared
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## THU0342 PREGNANCY OUTCOME IN JAPANESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE STUDY OF 134 PREGNANCIES

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**Background:** Most previous studies reported less successful fetal outcome and more frequent maternal obstetric complications in systemic lupus erythematosus (SLE) pregnancy, whereas the impact of pregnancy on SLE remains controversial. On the other hand, because there have been only a few small published studies focusing the pregnancy outcome in Japanese patients with SLE, available information is currently still insufficient for Japanese women and their partners.
**Objectives:** We aimed to investigate the pregnancy outcome in Japanese patients with SLE in more than twice larger size than previous reports.
**Methods:** The questionnaires about past pregnancies were delivered to all

the Japanese women with SLE seen at our university clinic in November and December 2013. All the patients met the revised ACR classification criteria for SLE. Respondents were asked to answer the questionnaires while referring to the Maternal and Child Health Handbook, which consists of records of pregnancy, delivery, child development, and healthcare, and is filled in by obstetricians, pediatricians, and public health nurses. Clinical and laboratory data were also retrospectively collected from the medical records. Integrated data were statistically analyzed and also compared to available corresponding data in general Japanese populations.

**Results:** A total of 77 patients answered about 134 pregnancies: 18, 7, and 109 pregnancies occurred before, concomitant with, and after SLE diagnosis, respectively. In cases with pregnancies after SLE diagnosis, SLE was clinically quiescent in 105 of 109 pregnancies. Of the 116 pregnancies concomitant with or after SLE diagnosis, 81 (70%) resulted in a live birth, 14 (12%) in induced abortion, 19 (16%) in spontaneous abortion, and 2 (2%) in stillbirth. Among the 81 live births, low birth weight (LBW), fetal growth restriction (FGR), and preterm birth occurred in 43 (53%), 9 (11%), and 27 (33%) pregnancies, respectively. In general Japanese populations, these incidences were reported to be 10%, 3 to13%, and 5 to 13%, respectively. Although immunosuppressants other than steroids, namely tacrolimus, cyclosporine, and azathioprine, were continued during 9 pregnancies, these incidences were not significantly different compared to those without immunosuppressants. Of the 7 live birth pregnancies before SLE diagnosis, there were no LBW, FGR, or preterm birth. Of all, there were 2 cases of neonatal lupus. Of the 116 pregnancies concomitant with or after SLE diagnosis, pregnancy-induced hypertension (PIH) occurred in 24 (21%) pregnancies, which reportedly occurred in 3 to 5% in general Japanese populations. Maternal obstetric complications (including PIH and excluding SLE flare) more frequently occurred in the pregnancies concomitant with or after SLE diagnosis than in the pregnancies before SLE diagnosis (49/116 vs. 3/18, $p$ =0.04). Of the 109 pregnancies after SLE diagnosis, 16 (15%) pregnancies were associated with SLE flares, but their predictors were not clarified.

**Conclusions:** The present study showed that LBW, preterm birth, and maternal obstetric complications such as PIH were associated with SLE pregnancies among Japanese women. Concurrent use of tacrolimus, cyclosporine, and azathioprine during pregnancy was not associated with poor fetal outcome. SLE flares occurred in 15% of the pregnancies, but their predictors were not clarified.

**Disclosure of Interest:** None declared

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## THU0343 RECURRENT THROMBOSIS IN YOUNG PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: THE RELEVANCE OF THE ANTIPHOSPHOLIPID ANTIBODY PROFILE

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**Background:** Recurrence of thrombosis in patients with Primary Antiphospholipid Syndrome (PAPS)is a major event yielding to poor prognosis.The identification of risk factors for recurrence is crucial to improve secondary prophylaxis strategies.

**Objectives:** To determine the risk factors for rethrombosis in patients with PAPS.

**Methods:** Retrospective analysis of a monocentric cohort of patients with thrombotic PAPS defined according to the updated Sapporo Criteria. aPL were determined by Lupus Anticoagulant (LA), anti-cardiolipin (aCL) IgG/IgM and anti-β2 glycoproteinI (anti-β2GPI) IgG/IgM. A positive result by all 3 assays was defined as triple positivity.Retrospective collection of serum samples was possible for 107 patients (66%).Ninety-two patients with positive anti-β2GPI IgG (57%) were selected for testing IgG against the domain I of β2GPI (anti-DI)using the chemiluminescence immunoassay in BIO-FLASH®system (INOVA Diagnostics, San Diego, CA, USA; cut-off 20CU). High titre anti-DI was defined as above 60CU.Patients were grouped by the number of events (single – S or recurrent – R). Comparisons between groups were performed using chi square and Mann-Whitney. Multivariate logistic regression was used to identify independent determinants of R events.Variables identified as having p-value $<0.1$ in univariate analysis were included. Anti-DI was not included because data were not available for the whole cohort. P-values $<0.05$ were considered statistically significant.

**Results:** The study included 162 PAPS patients (118 female, median age 48 years; venous thrombosis, VT – 103, arterial thrombosis, AT – 59). During the follow-up 70 recurrences were observed in 53 patients (VT – 36, AT – 34). Patients with rethrombosis more frequently had cardiac disease (hypertensive cardiopathy, valvular dysfunction, patent foramen ovale) (43% vs 21% p=0.007) and arterial hypertension (53% vs 33% p=0.01). Recurrent events were significantly associated with triple positivity (64% vs 44% p=0.01), LA (83% vs 62% p=0.008) and anti-β2GPI IgM (77% vs 60% p=0.03). Patients with rethrombosis less frequently received hydroxychloroquine (HCQ) (11% vs 41% $p<0.001$), OA (19% vs 46% p=0.009) and anti-platelet treatment (37% vs 59% $p<0.001$). The logistic regression analysis showed that triple positivity (OR 3.57 95%CI 1.32–9.65), cardiac dysfunction (OR 3.51 95%CI 1.35–9.15), HCQ (OR 0.22 95%CI 0.08–0.64), OA (OR 0.06 95%CI 0.02–0.24) and anti-platelet treatment (OR 0.01 95%CI 0.03–0.34) remained significant. Triple aPL positivity was more frequent in younger patients (under 50 years, n=118) who had recurrent events (71% vs 51% p=0.05), while no differences were found in terms of traditional cardiovascular risk factors. In the subgroup of anti-β2GPI IgG positive patients, recurrence was associated with the presence of high titre anti-DI in the whole cohort (80% vs 50% p=0.006) and in patients below the age of 50 (80% vs 55% p=0.03). Anti-DI levels were significantly higher in patients with recurrence (median 316CU vs 61CU p=0.02).

| | Single (n= 105) | Recurrent (n=53) | p |
|---|---|---|---|
| Demography | | | |
| Age at last visit, median (25th, 75th percentile) years | 47,8 (37,6 – 56,9) | 54,5 (42,7 – 65,7) | NS |
| Age at first event, median (25th, 75th percentile) years | 36,0 (24,0 – 45,5) | 42,0 (31,0 – 53,0) | NS |
| Sex, no.female | 79 (75%) | 39 (73%) | NS |
| Disease duration, median (25th, 75th percentile) months | 89,9 (42,2 – 169,9) | 108,5 (35,3 – 174,3) | NS |
| Clinical features | | | |
| Thrombosis (first event) | | | |
| Arterial | 39 (36%) | 20 (38%) | NS |
| Venous | 70 (64%) | 33 (62%) | NS |
| Thrombotic Risk Factors | | | |
| Cardiac disease | 23 (21%) | 23 (43%) | 0,007 |
| Arterial hypertension | 23 (21%) | 22 (42%) | 0,016 |
| - Untreated hypertension | 32 (29%) | 22 (42%) | NS |
| Diabetes mellitus | 3 (3%) | 4 (7%) | NS |
| Obesity | 23 (21%) | 13 (24%) | NS |
| Smoking | 37 (34%) | 13(25%) | NS |
| Hypercholesterolemia | 34 (31%) | 17 (32%) | NS |
| Hypertriglyceridemia | 10 (9%) | 6 (11%) | NS |
| Hyperhomocysteinemia | 26 (24%) | 12 (23%) | NS |
| Inherited thrombophilia | 36 (33%) | 16 (30%) | NS |
| Laboratory Profile | | | |
| LA | 68 (62%) | 44 (83%) | 0,008 |
| - Isolated LA | 6 (5%) | 4 (7%) | NS |
| aCL IgG | 72 (66%) | 36 (68%) | NS |
| aCL IgM | 82 (75%) | 38 ( 71%) | NS |
| β2GPI IgG | 82 (75%) | 38 ( 72%) | NS |
| β2GPI IgM | 66 (61%) | 41 (77%) | 0,034 |
| β2GPI IgG anti-DI (n=92) | 41 (56%) | 25 (83%) | NS |
| β2GPI IgG anti-DI: high-titer (>60 CU) (n=92) | 31 (50%) | 24 (80%) | 0,008 |
| Single positivity | 24 (22%) | 8 (15%) | NS |
| Double positivity | 36 (33%) | 11 (21%) | NS |
| Triple positivity | 48 (44%) | 34 (64%) | 0,016 |

**Conclusions:** Patients with thrombotic PAPS still develop recurrence despite treatment.Triple positivity and high titre anti-DI conferred an increased risk of rethrombosis irrespective of traditional risk factors.

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## THU0344 OSTEOPOROSIS AND VERTEBRAL FRACTURES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** Observational studies have indicated a high but heterogeneous prevalence of low bone mineral density (BMD) and vertebral fractures (VR) in patients with systemic lupus erythematosus (SLE).

**Objectives:** To evaluate the relationship between SLE and BMD, osteoporosis and the risk of vertebral fracture.

**Methods:** A systematic review and meta-regression analyses were carried out according to the Preferred Reporting Items for Systematic Meta-Analyses (PRISMA) guidelines. Articles were identified from electronic databases (PubMed, Embase, VHL, SciELO and the Cochrane Library). The search was conducted using MesH terms, Boolean operators and keywords, which included “systemic lupus erythematosus”, “osteoporosis”, “bone mineral density”, and “vertebral fractures”. Prospective longitudinal and cross-sectional studies were considered for review without language restrictions. Articles were screened for suitability. Those selected were evaluated by two investigators, who extracted information on study characteristics, outcomes of interest, and risk of bias, and summarized the strength of evidence. Data was extracted when studies met inclusion criteria and were of sufficient quality. BMD, reported as the mean ± standard deviation

evaluated by dual-energy X-ray absorptiometry (DXA), was analyzed including information on SLE cases and controls, treatment, menopausal status and fractures by meta-regression analysis adjusted by anatomical region. Data were analyzed using the Metafor package in R (3.0.2 version).
**Results:** In total 49 articles were identified and analyzed (12, 593 SLE cases/six anatomical regions and 14,235 controls/six anatomical regions). SLE women, but not SLE men, had a lower BMD than healthy controls ($p<0.0001$). When only SLE patients were analyzed, the BMD did not significantly differ between patients who had or had not received corticosteroid (CTS) therapy. Unsurprisingly, postmenopausal SLE patients had a lower BMD (lumbar spine and total hip) compared with premenopausal patients ($p<0.0001$). The BMD did not differ in patients with and without fractures.
**Conclusions:** This systematic review and meta-regression analysis shows that women with SLE had a higher risk of low BMD than healthy controls. The data did not show that CTS therapy had an impact on BMD.
**References:**
[1] Bultink IE. Osteoporosis and fractures in systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2012;64:2–8.
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## THU0345 PRESENCE OF IMMUNOGLOBULIN (IG) A ANTIBODIES AGAINST CARDIOLIPIN AND β2-GLYCOPROTEIN-I IN THE ABSENCE OF IGG AND IGM IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** The antiphospholipid (Hughes) syndrome (APS) is characterized by vascular thrombosis and/or pregnancy morbidity and twice repeated confirmed presence of anti-cardiolipin and/or anti-β2-glycoprotein-I antibodies of IgM/IgG isotype and/or a positive lupus anticoagulant test. These tests and isotypes are found in the 1997 update of the American College of Rheumatology (ACR) classification criteria for systemic lupus erythematosus (SLE). As antiphospholipid antibodies are associated with increased morbidity and mortality in SLE, it is of major concern to screen new patients early for these antibodies. Despite limited scientific evidence, however, IgA isotype was added as a formal laboratory criterion in the 2012 SLICC criteria.
**Objectives:** Herein, we thus evaluated a well-characterized Swedish SLE cohort with regard to the presence of IgM, IgA and IgG isotypes of anti-cardiolipin or anti-β2-glycoprotein-I antibodies in relation to disease phenotype, organ damage, smoking habits, medical treatment, APS and thromboembolic events. We aimed to define the frequency of each isotype separately in order to disclose if any specific features are associated with the presence of isolated IgA antiphospholipid antibodies.
**Methods:** Serum samples from 254 patients (88% women) of the "Clinical Lupus Register in Northeastern Gothia" were included. All cases had a clinical diagnosis of SLE and met the 1982 ACR classification criteria and/or the Fries' diagnostic principle (*i.e.* positive ANA + manifestations in $\geq$2 typical organ systems). 211 (83%) were prevalent cases, whereas 43 (17%) had a newly diagnosed SLE at the time for blood sampling. 200 healthy blood donors and 100 patients with early rheumatoid arthritis (RA) served as controls. Anti-cardiolipin and anti-β2-glycoprotein-I antibodies (IgM, IgA and IgG) were analyzed at Linköping Clinical immunology unit using a fluoroenzyme-immunoassay (Phadia-250 instrument, Thermo-Fisher Scientific Phadia AB, Uppsala, Sweden). Cut-off limits for positive antibody tests were set at $>$99th percentile of healthy blood donors.
**Results:** Among the SLE patients: 45 (18%) fulfilled APS classification; 69 (27%) were positive for at least one isotype (IgM/IgA/IgG) and 34 (13%) for IgA of either anti-cardiolipin or anti-β2-glycoprotein-I antibody. 24 (9%) SLE cases were positive for IgA anti-cardiolipin, 12 of whom were positive in the absence of IgM/IgG class antibodies. 28 (11%) SLE cases were positive for IgA anti-β2-glycoprotein-I, 13 of whom were positive in the absence of IgM/IgG. 7 (2.8%) SLE patients were positive for isolated IgA anti-cardiolipin and/or anti-β2-glycoprotein-I antibodies and fulfilled APS classification, whereas 9 SLE cases (3.5%) were positive for isolated IgA anti-cardiolipin and/or anti-β2-glycoprotein-I antibodies without meeting APS classification. 7% of the RA cases were positive with regard to at least one isotype of anti-cardiolipin or anti-β2-glycoprotein-I antibodies.
**Conclusions:** We demonstrate that IgA anti-cardiolipin and/or anti-β2-glycoprotein-I antibodies can be found in almost 1/7 of Swedish SLE patients, either in the absence of IgM/IgG (47%) or in combination with other isotypes (53%). In 7 of these cases, the presence of isolated IgA antiphospholipid antibodies was associated with APS. Analyses of associations with disease outcome, phenotype, drugs and smoking habits are ongoing.
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## THU0346 FURTHER VALIDATION OF SIMPLE INDEX AS A SIMPLE DISEASE ACTIVITY ASSESSMENT TOOL FOR SLE

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**Background:** An easy, quick tool, requiring minimal training or physician input for disease activity (DA) assessment in SLE, would have potentially greater uptake for routine use among rheumatologists and primary care physicians. Furthermore, integration into busy work flow processes would be easier for the same reason. Most DA tools for SLE are complex, require training and physician time; and are not performed during routine care visits for most SLE patients. SIMPLE (Simple Disease Assessment for People with Lupus Erythematosus) [1] is a numeric composite index based on patient reported questions and two laboratory values, and requires minimal input from health care provider which can be provided by nurse or a physician extender. Here, we prospectively evaluate the correlation of SIMPLE index with physician based DA measure.
**Objectives:** Prospectively validate SIMPLE index as a DA measure compared to traditional physician based DA assessment tools.
**Methods:** 72 consenting patients meeting ACR classification criteria for SLE were recruited from two academic center clinics. Primary outcome of interest was correlation between Simple Index (SI) and SELENA-SLEDAI (SS). Secondary outcome of interest was correlation between SI and Physician Global Assessment (PGA). Patients filled the self-reported components of SI in the waiting room prior to their visit. PGA and SS were assessed at the same visit by the physician. Descriptive and spearman correlational analyses were obtained. Stratified analysis by fibromyalgia status (FMS) was also conducted. P value of $\leq$0.05 was considered significant on two tailed tests. We considered correlation coefficient of $<$0.30, 0.30 to 0.49 and $>$0.50 as weak, moderate and strong correlation, respectively.
**Results:** Mean (SD) age was 40.8+12.4 yrs, and 87.5% participants were women. Ethnic background of the participants was as follows: 52.8% Blacks, 25% Whites, 8.3% Hispanic, 6.9% Asians and 6.9% others. Median (IQR) SI was 21.7 (17.2). Median (IQR) values of PGA and total SS were 0.5 (1.0) and 4.0 (6.0), respectively. Spearman correlation coefficient between SI and PGA and SS were 0.507 (p 0.001), 0.568 (p 0.001), respectively. In a sub analysis excluding fibromyalgia patients, these correlations were 0.538 (p 0.001, n=60), 0.633 (p 0.001, n=59) respectively.
**Conclusions:** SIMPLE index is strongly correlated with PGA and SS in SLE patients, and the correlation is even stronger in SLE patients without FMS. SIMPLE index is quick, easy and requires negligible health care team input, which can be from a physician extender or a nurse or any physician. SIMPLE Index has the potential to be widely used in varied health care access levels and systems in different parts of the world. SIMPLE Index can potentially serve as a quality of care measure. Larger and longitudinal studies that include patients with greater DA and to test its responsiveness are currently ongoing.
**References:**
[1] Simple Disease Assessment for People with Lupus Erythematosus. A&R. 2014; 66 (11):s312
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## THU0347 IS BALANCE AFFECTED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

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**Background:** Systemic Lupus Erythematosus (SLE) is a multisystem disease that has a broad range of manifestations. Balance as a complex task may be affected in SLE and this may cause postural instability and fall risk.
**Objectives:** The aim of this study was to determine the fall risk in cases with SLE with an objective computerized technique and to evaluate the potential related risk factors for falls in these cases.
**Methods:** Female patients with SLE (1997 ACR revised classification criteria for SLE) and female healty controls were included. Patients who were not able to tolerate posturography, with a history of orthopedic surgery and with known balance problems were excluded. The age, disease duration, anamnesis of falls, fear of falling and drugs used were recorded. Disease activity (with SLE disease activity index SELENA modification) and damage (with Systemic Lupus International Collaborating Clinics/ACR Damage Index) were evaluated. For the evaluation of fall efficacy, we used the Falls Efficacy Scale International (FES-I). Fall risk analysis was performed by Tetrax Interactive Balance System which is a computerized posturography device. By this method, fall risk is obtained as a numeric value (0–100) and as ranges indicating low, moderate or high risk of fall. We investigated age, disease duration, fall anamnesis, fear of falling, drug usage, FES-I, disease activity and damage as possibe related factors to fall risk. Mann–Whitney U, chi square and Spearman correlation tests were used for statistical analysis.
**Results:** 48 cases with SLE and 30 controls were included. The mean ages of the cases and controls were 37,8±12,6 and 39,1±15,7 years, respectively. Symptom duration of the cases was 6,1±4,2 months. 7 cases (15%) had anamnesis of

falls during the last 12 months, whereas only 1 control (3%) had this anamnesis ($p<0,05$). Fear of falling was reported by 40% of the cases and 30% of the controls ($p<0,05$). FES-I scores were found to be significantly higher in cases than controls (22±11 and 16±9 respectively; p=0,040). With the computerized system used, significantly higher fall risk results were recorded in patients with SLE than the controls (59,3±29,5 and 35,8±26,9, respectively; $p<0,001$). Low, moderate and high fall risks were recorded as 31%, 15% and 54% of the cases and 53%, 23% and 23% of the controls and this distribution was also significantly worse in cases than controls ($p<0,05$). No significant correlation was found between fall risk and other factors including age, disease duration, fall anamnesis, fear of falling, drug usage, disease activity and disease damage except FES-I which was significantly correlated both with fall risk assessment and fall risk category in cases ($p<0,05$).

**Conclusions:** With an objective computerized technique, fall risk was found to be higher in cases with SLE than controls in our study. The higher fall risk in these patients seems to be affected by the disease itself, rather than its other characteristics. An increased awareness of the potential fall risk and future studies investigating the possible coexisting balance problems in SLE may contribute to the management.

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## THU0348 ASSESSMENT OF SUBMANDIBULAR GLAND ULTRASONOGRAPHY IN EARLY-STAGE SJÖGREN'S SYNDROME

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**Background:** Sjögren's syndrome (SS) is a chronic inflammatory autoimmune disease characterized by lymphocyte infiltration in salivary and lacrimal glands. Recently, salivary gland ultrasonography proved valuable for the assessment of salivary gland involvement in SS and seemed to exhibit good diagnostic properties. We previously reported that submandibular gland ultrasonography (SGUS) is a useful noninvasive and inexpensive procedure for the evaluation of the structural changes of salivary gland involvement in SS patients (International Symposium on SS 2002, EULAR 2009, EULAR 2012, EULAR 2015). However, the usefulness of SGUS for the evaluation of early-stage SS patients with normal salivary flow was unknown.

**Objectives:** The aim of this study was to examine the usefulness of SGUS in early-stage SS patients with normal salivary flow.

**Methods:** We observed 9 non-SS patients with anti-SS-A antibodies sero-positive, 13 SS patients with low salivary flow (L/SS) and 16 SS patients with normal salivary flow (N/SS). SS was diagnosed according to the American College of Rheumatology (ACR) classification criteria for SS. SS was divided into two groups according to salivary flow using Gum test [L/SS ($\leq$10mL/10min) and N/SS ($>$10mL/10min)]. All patients were examined RF, FANA, anti-SS-A/SS-B antibodies in serum and labial salivary gland biopsies for the diagnosis of SS. All patients were performed US scans by a single examiner who was blinded to the clinical data and used an US with a 7.5-MHz liner array transducer (SSA-350A; Toshiba, Tokyo, Japan). US staging scores were assessed by glandular size, inhomogeneity and contrast of diagastric muscle (0: normal, 1: mild, 2: moderate, 3: severe structural damage). PD grading scores were graded by pulsed wave pattern in power Doppler US at the internal SG facial arteries (0: normal, 1: intermittent wave pattern, 2: disappearance of wave pattern).

**Results:** The whole salivary flow was significantly decreased in L/SS (4.4±2.8mL/10min) patients than in non-SS (19.0±7.6mL/10min, $p<0.001$) and N/SS (19.1±8.0mL/10min, $p<0.001$) patients. All patients were anti-SS-A antibodies sero-positive. There were no significant differences among non-SS, N/SS and L/SS patients in the frequency of sero-positive antibodies such as RF, FANA and anti-SS-B. However, the size of SG was significantly smaller in L/SS (216.1±59.7mm$^2$) than in non-SS (325.9±66.2mm$^2$, $p<0.005$) and N/SS (311.3±98.7 mm$^2$, $p<0.005$). US staging scores and PD grading scores were significantly higher in L/SS (2.85±0.38, 1.62±0.51) than in non-SS (0.89±1.05, 0.33±0.71, $p<0.001$) and N/SS (1.44±1.15, 0.44±0.51, $p<0.001$) patients.

**Conclusions:** SUSG findings reflect salivary gland functions and is useful for the diagnosis of SS with low salivary flow but not for early-stage of SS patients with normal salivary flow.

**Disclosure of Interest:** None declared

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## THU0349 EARLY SYMPTOMS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) RECALLED BY 337 SLE PATIENTS

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**Background:** EULAR and ACR have jointly funded a project to develop systemic lupus erythematosus (SLE) classification criteria, aiming at earlier and more accurate classification of the disease. This abstract reports on an early phase of that project, aimed at collecting potential candidate criteria. Since SLE patients usually experience the onset and diagnosis as a critical life event, memories of this time appear remarkably accurate.

**Objectives:** The objective of this study was to identify early symptoms of SLE from the patient perspective.

**Methods:** As approved by the local ethics committee, we conducted a cross-sectional survey of German SLE patients. An anonymous self-report questionnaire was published in the "Schmetterling" the quarterly journal of the "Lupus erythematodes Selbsthilfegemeinschaft", the German SLE patient association. Patients were asked for year of and age at their initial diagnosis. The questionnaire included typical organ manifestations, symptoms and autoantibodies. In addition, patients were asked to add additional symptoms in free text. For each symptom, boxes were provided to indicate the presence of the symptom before diagnosis, in the first year of diagnosis and at the time of completion of the questionnaire.

**Results:** 333 patient questionnaires were completed and mailed. Of the respondents, 93% were female. The respondents' mean age at diagnosis was 36 years, their mean disease duration was 17 years. 83% reported to be definitely ANA-positive. Joint, skin and kidney involvement were reported at 82%, 66% and 33%, respectively. 22% of patients reported fibromyalgia. For the time before and shortly after diagnosis, more than 50% of the patients reported fatigue (89%), joint pain (87%), sensitivity to sunlight (79%), myalgias (76%), rash (71%), fever (54%), Raynaud's (52%) and hair loss (51%). Approximately one third (37%) affirmed shortness of breath. Free text symptoms reported frequently before or early in diagnosis are listed in Table 1.

Table 1. Free text symptoms frequently present before or early in diagnosis

| | |
|---|---|
| Diarrhea/abdominal pain | n=33 (10%) |
| Headache/migraine | n=33 (10%) |
| Sicca symptoms | n=33 (10%) |
| Depression/mood disorder | n=26 (8%) |
| Cognitive impairment | n=25 (8%) |
| Dizziness/vertigo | n=20 (6%) |
| Serositis | n=18 (5%) |
| Polyneuropathy/paresthesias | n=16 (5%) |
| Sleep disturbance | n=12 (4%) |

**Conclusions:** For a Caucasian European SLE patient population, the overall characteristics suggested meaningful representation. While many symptoms were reported as expected, a significant number of patients volunteered gastrointestinal complaints and symptoms of the central and peripheral nervous system.
Solicitation of self reported information from the patient perspective has not been widely used in the development of classification criteria for SLE. These data add to the information on early SLE symptoms that may help improve classification of early SLE.

**Disclosure of Interest:** None declared

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## THU0350 MORPHOLOGICAL ALTERATION OF THE RETINAL POSTERIOR POLE AND FUNCTIONAL EYE IMPAIRMENT IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOUS AND SJÖGREN SYNDROME

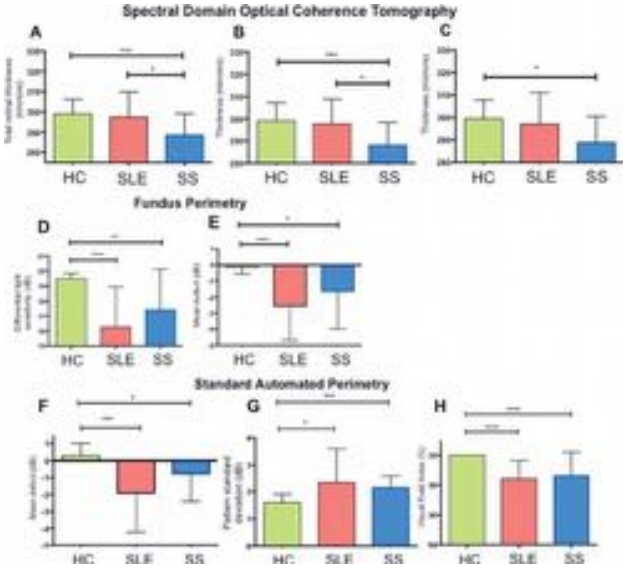
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**Background:** Systemic Lupus Erythematous (SLE) and Sjögren Syndrome (SS) are autoimmune diseases that may exhibit several manifestations including an ocular involvement. Ocular involvement may be underestimated or be subclinical since current treatments as hydroxycloroquine and steroid may exert both beneficial and side effects on eyes.

**Objectives:** To assess the eye involvement in patients affected by autoimmune diseases as SLE and SS.

**Methods:** 48 patients affected by autoimmune diseases (29 SLE, 19 SS) without an active eye involvement were prospectively and consecutively enrolled.

Morphological and functional eye assessment included: complete ophthalmogical examination, Spectral Domain Optical Coherence Tomography examination, fundus perimetry (FP), standard automated perimetry (SAP). 25 age and sex-matched healthy controls (HC) were also evaluated.
**Results:** SS patients displayed a reduction of mean retinal thickness in the posterior pole compared with HC and SLE (p=0.0003 and p=0.03, Fig.1A). This reduction was demonstrated in superior and inferior hemifield compared with HC (p=0.001 and p=0.007) and in superior hemifield compared with SLE (p=0.01) (Fig.1B-C). The FP mean differential sensitivity in SLE and SS patients was reduced compared with HC (p<0.0001 and p=0.001, Fig.1D). The FP mean defect values in SLE and SS patients were higher than HC (p<0.0001 and p=0.03, Fig.1E). A negative correlation was demonstrated in SLE between age and FP mean differential sensitivity (p=0.0005, r= -0.7). FP alteration in SLE was prevalent in those patients that were not on steroid treatment. In SS a higher proportion of patients with alteration in FP received a cumulative hydroxycloroquine dose higher than 1000g (p=0.02). The SAP demonstrated in SLE and SS patients a significant increase of the mean defect (MD) and the pattern standard deviation (PSD) compared with HC (MD: p=0.001 and p=0.01, PSD: p=0.02 and p=0.0002; Fig.1F-G). Visual field index (VFI) values were reduced in both SLE and SS patients compared with HC (p<0.0001 for both comparisons, Fig.1H). SLE patients with kidney involvement displayed a significant increase of the MD and the PSD compared with those without kidney involvement (p=0.04 and p=0.01, respectively). Likewise, VFI values were reduced in SLE with nephritis compared with that in patients without a kidney involvement (p=0.04).




**Conclusions:** In a small cohort of patients with autoimmune diseases without an overt active eye involvement a morphological alteration of the retinal posterior pole and functional impairment was demonstrated suggesting a subclinical involvement thatmight be concealed by the treatment.
**Disclosure of Interest:** None declared
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## THU0351 VITAMIN D INSUFFICENCY IS ASSOCIATED TO FATIGUE IN NON-SUPPLEMENTED WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN A MEDITERRANEAN REGION

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**Objectives:** It has been previously reported that vitamin D deficiency is more prevalent among SLE patients than in the general population. We sought to determine the prevalence of vitamin D insufficiency and deficiency and their related factors, its relationship to SLE symptoms and disease activity on a group of supplemented and non-supplemented female SLE patients from the Mediterranean region.
**Methods:** We performed a cross-sectional study including female SLE patients who regularly attended the outpatient Lupus Unit at Parc de Salut Mar-IMAS in Barcelona, from January 2012 and May 2014. Collected data were: sociodemographics; vitamin D supplementation; fatigue degree visual analog scale; pharmacological treatment; main SLE serological markers, Indexes, scales; and plasma levels of 25-hydroxy vitamin D
**Results:** One-hundred and two consecutive female SLE patients were included. Vitamin D overall insufficiency and deficiency were exhibited by 46% and 22.5% of patients, respectively. Vitamin D insufficiency was found in 50% of supplemented and 60% of non-supplemented patients. Among non-supplemented female SLE patients, it was found that patients with Vitamin D insufficiency showed more fatigue (p=0.009) and received more oral corticosteroids (p=0.02) than those with normal levels. Patients with Vitamin D insufficiency (supplemented and non-supplemented) received more oral corticosteroids than those without insufficiency (p=0.008).

| Variable | 25(OH)D <30 ng/mL (n=16) | 25(OH)D ≥30 ng/mL (n=24) | p-value |
|---|---|---|---|
| BMI (kg/m$^2$)* | 23.9 [21.3–29.2] | 23.7 [21.7–30.2] | 0.672 |
| Sun blocker** | 12 (75%) | 18 (75%) | 1.000 |
| Vitamin D diet intake | 14 (87.5%) | 18 (75%) | 0.439 |
| SLEDAI* | 3.3 [0–5.5] | 3.4 [0–7.5] | 0.967 |
| MHAQ* | 0.39 [0–0.68] | 0.33 [0–0.75] | 0.859 |
| VAS fatigue* | 63.5 [51.5–80.0] | 39.5 [20.0–59.7] | 0.009 |
| Anti-dsDNA UI/mL* | 208 [35–265.7] | 141 [30–176.2] | 0.318 |
| ESR (mm/h)* | 14 [4.2–23] | 14.7 [5.5–20.2] | 0.881 |
| CRP (mg/dl)* | 0.4 [0.2–0.4] | 0.3 [0.2–0.2] | 0.233 |
| Corticosteroids** | 9 (56.2%) | 5 (20.8%) | 0.021 |
| Mean Corticosteroids dosage* | 6.4 [0–10] | 0.9 [0–0] | 0.020 |
| Photosensitivity | 15 (93.8%) | 22 (91.7%) | 1.000 |

*N* (%)/Mean ± SD; Med [P25–P75]. *Comparisons performed with Mann-Whiney U test. **Comparisons performed with Chi-Square test or Fisher exact test.

**Conclusions:** Vitamin D insufficiency is highly prevalent among female SLE patients, even in southern regions. Non-supplemented female SLE patients showed more fatigue and received more oral corticosteroids than those with normal levels of Vitamin D. This data was not found in supplemented patients despite having a high prevalence of Vitamin D insufficiency (up to 50%). Further studies with longer follow-up and larger population are needed to confirm our observations.
**Disclosure of Interest:** None declared
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## THU0352 WORLDWIDE HETEROGENEOUS DIAGNOSTIC APPROACH TO PRIMARY SJÖGREN SYNDROME IN 8315 PATIENTS (EULAR-SS TASK FORCE BIG DATA SJÖGREN PROJECT)

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**Objectives:** To analyse the diagnostic approach used in the largest international cohort of patients with primary Sjögren syndrome (pSS)
**Methods:** The Big Data Sjögren Project is a multicentre registry formed in 2014 by experts participating in the EULAR-SS Task Force. By January 2016, the database included 8315 consecutive patients fulfilling the 2002 criteria. The main features at diagnosis/recruitment (time of criteria fulfilment) were collected and analysed
**Results:** The cohort included 7753 (93%) women (mean age at diagnosis 53 years). Sicca symptoms were reported in more than 90% of patients at diagnosis (92% for dry eye and 92.5% for dry mouth). The diagnostic tests used included the determination of anti-Ro/La antibodies in 8250 (99%) patients, Schirmer test in 6205 (75%), salivary gland biopsy in 5988 (72%), salivary flows in 4941 (59%), corneal stainings in 3304 (40%), scintigraphy in 2578 (31%) and sialography in 873 (10%) patients. The mean number of diagnostic tests included in the 2002 AE criteria was 4.85 ± 1.44 (of a maximum of 8 different tests), and was higher in patients with negative ANA (5.18 vs 4.80 in ANA+, p<0.001) or negative RF (5.06

vs 4.81 in RF+, $p<0.001$), and was also higher in American patients vs European or Asian patients (5.28 vs 4.83 and 4.63, respectively). A correlation was found between the number of tests carried out and the number of 2002 criteria finally fulfilled (R=0.48)

**Conclusions:** We found a heterogeneous diagnostic approach of pSS with respect to the number of 2002AE diagnostic tests carried out; the approach varied significantly according to geographic origin and baseline immunological profile

**Disclosure of Interest:** None declared

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## THU0353 SERUM TWEAK LEVELS IN PATIENTS WITH NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is autoimmune disease involving various organs including the nervous system. Neuropsychiatric SLE (NPSLE) occurs in 30 - 40% of SLE patients. One of the most common manifestations of NPSLE is cognitive dysfunction (CD) which occurs in 21 - 81% of SLE patients. TWEAK is a TNF family ligand that mediates pleotropic effects through its receptor Fn14, including the stimulation of inflammatory cytokine production and induction of neuronal death. Recent studies in animal models and human SLE patients suggest TWEAK as a potential mediator of NPSLE.

**Objectives:** To examine potential association between serum TWEAK levels and NPSLE, mainly cognitive dysfunction in patients with SLE, to determine a possible association with other types of organ involvement and specific autoantibodies (antineuronal, antiphospholipid, anti-dsDNA, antinuclear, anti-P protein, etc), and a correlation with disease activity.

**Methods:** The SLE patients (fulfilling ACR classification criteria for SLE) have undergone a complete neuropsychiatric examination for the presence NPSLE including brain MRI. CD has been assessed according to the ACR classification of NPSLE. The activity of the disease was evaluated using the diseases activity index (SLEDAI). Serum TWEAK levels were measured by ELISA.

**Results:** We analyzed 90 SLE patients. The neuropsychiatric involvement and cognitive dysfunction with moderate to severe disability was diagnosed in 58 (64.4%), 53 (58.8%) patients, resp. The headache, cranial neuropathy and epilepsy were the most frequent neurological manifestations. Active disease was present in 44 patients (48.8%). In contrast to recent studies no significant differences were found in the serum TWEAK levels between patients with and without NPSLE. There were also no differences in serum TWEK levels between patients with and without CD. We did not observe any association of serum TWEAK levels with different organ SLE manifestations, presence of antibodies or disease activity.

**Conclusions:** NPSLE and CD were found to be frequent SLE manifestations in our cohort. However, serum TWEAK levels do not seem to be a reliable biomarker for NPSLE or other manifestations in patients with SLE. Further studies in patients with new NPSLE manifestation prior to initiating therapy may be needed.

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## THU0354 THROMBOCYTOPENIA IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES: A PARADOXICAL THROMBOTIC RISK FACTOR

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**Background:** Thrombocytopenia is a non-criteria manifestation of antiphospholipid syndrome (APS). Antiphospholipid antibodies (aPL) have been shown to activate platelet through multiple mechanisms. In patients with idiopathic/immune thrombocytopenia, aPL have been shown to increase the risk of thrombosis. Conversely, it remains unclear whether thrombocytopenia increases the risk of thrombosis in patients who have aPL.

**Objectives:** To evaluate the relationship between thrombocytopenia and thrombosis in patients who have aPL.

**Methods:** A single center retrospective study comprising 670 consecutive patients who underwent testing for aPL including lupus anticoagulant, anticardiolipin antibodies (IgG and M), anti-β2-glycoprotein I antibodies (IgG and M), and phosphatidylserine-dependent antiprothrombin antibodies (IgG and M) between January 2004 and December 2006. Excluded were patients who had been followed-up for $\leq$1 year.

**Results:** Of 524 patients included in this study, 187 had systemic lupus erythematosus, 70 rheumatoid arthritis, and 33 primary APS. At least one of aPL was positive in 241 patients. The prevalence of thrombocytopenia was not different in aPL positive and negative patients (24% vs 18%, p=0.11). In aPL positive group, patients with thrombocytopenia experienced arterial thrombosis (46% vs. 17%, $p<0.001$), venous thrombosis (27% vs. 7%, $p<0.001$), and recurrent thrombosis (10% vs. 2%, p=0.006) more frequently than patients without thrombocytopenia. Lupus anticoagulant (56% vs. 35%, p=0.006) and phosphatidylserine-dependent antiprothrombin antibodies (57% vs 34%, p=0.001) were more prevalent in patients with thrombocytopenia than in those without. Higher aPL score (Otomo K, et al. Arthritis Rheum 2012), were detected higher (p=0.001) in patients with thrombocytopenia than in those without. In aPL negative group, conversely, patients with and without thrombocytopenia similarly experienced thrombosis (23% vs 16%, p=0.23).

**Conclusions:** Our data indicate that thrombocytopenia is associated with the risk of thrombosis in aPL positive patients providing new insight into the pathophysiology of aPL mediated platelet activation.

**Disclosure of Interest:** None declared

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## THU0355 CLINICAL TRIAL SIMULATION IDENTIFIES FACTORS FOR PATIENT ENGAGEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS TRIALS IN AFRICAN-AMERICANS

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**Background:** Clinical trials of patients with systemic lupus erythematosus (SLE) and lupus nephritis (LN) can be confounded by difficulties in engaging patients. Identifying factors of non-engagement informs strategies to increase involvement and compliance.

**Objectives:** We generated qualitative data on the engagement and experience of patients in clinical trials, which can be used to improve the design and conduct of future trials.

**Methods:** A unique approach was used simulating key study visits for an upcoming study involving patients with active SLE/LN and clinical staff from an indigent care hospital in Atlanta, GA. Patients underwent a consent procedure (30–45 minutes), simulated SLE/LN screening visit (2.5 hours), and simulated SLE/LN first dosing visit (4.5–5 hours). Patients and site staff were interviewed to obtain sentiments and perceptions relating to the simulated visits.

**Results:** *Demographics:* Six African-American patients (1 male, 5 female) aged 27–60 years with moderate to severe SLE/LN were recruited. Although the sample size was small, it provided value owing to its targeted clinical context. Patients differed in cognitive ability and health literacy. *Communication:* Patients expressed a preference for obtaining general disease and specific trial information from the Internet and stated that both strong online and community support were important. Patients valued help and support to discuss their conditions and options with family and friends. For support groups, the use of lupus community leaders was suggested for communicating the importance and relevance of clinical trial participation. Study sponsors were also advised to engage the lupus community through lupus community leaders. Despite completing full informed consent procedures, not all patients understood the degree of commitment at the time of study enrollment; in addition, a few patients thought the study might cure their disease. Patients suggested developing condensed and/or electronic versions of the informed consent form in text or audio format. Staff mentioned using electronic patient-reported outcome tools, which the patients found acceptable to complete. *Patient needs:* The extent of disruption to patients' lives due to study participation was cited as a major factor for potential study withdrawal. Limited flexibility in work schedules and inflexible commitments such as child care, leading to financial burden were raised as significant concerns. Although patients were generally happy with their current disease management, they were willing to consider changing their medications for a better outcome. Some patients were motivated by being part of developing a possible cure. The simulation also considered infusion visits, which required coordination between relevant parties, with post-infusion observation times potentially shortened. The duration of study visits (2+ hours) was a concern for patients and made them particularly sensitive to wait times between procedures.

**Conclusions:** Insights and techniques from this study at an urban indigent care lupus clinic with large numbers of African-Americans can be applied to the design of future clinical trials for patients with SLE/LN in high-risk populations to potentially improve recruitment, retention, compliance and advocacy.

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## THU0356 COMPARISON BETWEEN JUVENILE-, ADULT-, AND LATE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune, immune-complex, multi-system, chronic inflammatory disease of the connective tissue. Late onset SLE (LSLE) represents a specific sub-group of the disorder, beginning after 50 years of age.
**Objectives:** The objective of this study is to evaluate the association of clinical features and prognosis with age at disease onset in patients (pts) with SLE. This article discusses the prevalence, clinical course, serological features, prognosis and treatment of LSLE.
**Methods:** Medical records of 301 SLE consecutive pts were reviewed and classified into three groups according to their ages at disease presentation. Sociodemographic, clinical and laboratory data, concomitant diseases were found at the time of diagnosis of SLE. Categorical data were analyzed by chi-square test and potentially associated factors were tested by multinomial logistic regression.
**Results:** Among the pts studied, 33 (10,96%) were juvenile (J) onset ($\leq$18 years), 236 (78,41%) were adult (A) onset ($>$18 and $\leq$50 years) and 32 (10,63%) were LSLE ($>$50 years). The incidence of LSLE was significantly higher in women than in men ($p<0,001$), but the predominance of women among LSLE (4:1) was reduced when compared with that observed in JSLE or ASLE. JSLE were more likely to be untreated before admission ($p<0,001$) and have mucocutaneous manifestations ($p<0,001$), but musculoskeletal symptoms ($p<0,05$) and leukopenia ($p<0,05$) were less frequent, while comorbidities were much higher in pts with LSLE ($p<0,001$). Arthritis, fever, serositis, sicca symptoms, Raynaud's syndrome, Sjögren's syndrome, lung disease, neuropsychiatric symptoms, hemolytic anemia and thrombosis were more frequently found in LSLE, while malar rash, discoid lupus, photosensitivity, vasculitis and glomerulonephritis are less common in LSLE compared with JSLE or ASLE. Most LSLE pts have a positive anti-nuclear antibody test, but anti-double-stranded DNA, anti-C1q antibodies, anti-ribosomal antibodies, hypocomplementaemia and anti-Sm antibodies were found more frequently in JSLE and less frequently in than ASLE or LSLE. Rheumatoid factor, anti-Ro/SS A and anti-La/SSB are more often positive in LSLE.
The diagnosis of LSLE is often delayed and treatment is determined by the presence of concomitant diseases, NSAID's, antimalarials or low doses of glucocorticoids are used for the less severe forms. Immunosuppressives and higher doses of glucocorticoids are the treatments of choice for more severe organ involvements and complications.
The probability of survival was reduced in LSLE patients. With respect to this, the 10-year and 15-year survival probability were 78,2% and 58,4% in the LSLE group and 94,7% and 90,4% in patients with JSLE, respectively. Infections are the main cause of death in LSLE pts.
**Conclusions:** Our results indicate that SLE pts present with different clinical and serological manifestations according to age at disease onset. LSLE has specific features with misleading signs and symptoms, but its clinical course seems milder compared with that in younger pts. Considering that the LSLE pts had simultaneously easily controllable diseases and high incidence of comorbidities, a different treatment strategy from JSLE pts should be considered. Our data support the claim of a reduced probability of survival in the older age-group of SLE patients.
**Disclosure of Interest:** None declared
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## THU0357 DIFFUSE ALVEOLAR HEMORRHAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS - A SINGLE CENTER RETROSPECTIVE CLINICAL ANALYSIS FROM INDIA

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**Background:** Diffuse Alveolar hemorrhage (DAH) a rare life threatening manifestation of Systemic Lupus Erythematosus (SLE) with high mortality.[1,2]
**Objectives:** To characterize the profile of SLE patients with DAH in our cohort.
**Methods:** Medical charts of patients with SLE and DAH from 2008 to 2015 in our institute were reviewed. Clinical, laboratory, treatment, outcome details were noted. Statistical analysis carried out with SPSS software (version 21). Independent sample T test was done to compare survivors and non-survivors.
**Results:** Nineteen (1.32%) of 1438 SLE patients had DAH. Their mean age was 24.2±7.8 years, mean duration of hospital stay 16.1±7.5 days, mean SLE disease activity index (SLEDAI) (19.2 ±8.7). Seven had DAH at initial diagnosis of lupus, 4 had recurrent episodes of DAH. Ten (52.6%) patients died. Clinical manifestations included fever (84.2%), cough (78.9%), dyspnea (100%), hemoptysis (73.7%). Organ involvement include nephritis in (14/19) 73.7%, CNS involvement (6/19) 31.6%, arthritis (9/19) 47.4%, mucocutaneous (13/19) 68.4%, myocarditis (5/19) 26.3%, pulmonary arterial hypertension (7/19) 36.8%, serositis (8/19) 42.1%, renal failure (8/19) 42.1%, autoimmune hemolytic anemia in (2/19) 10.5% patients. Leucopenia (10/19) 52.6%, thrombocytopenia (11/19) 57.9%, low complements in 14/15 patients, dsDNA positive in (16/19) 84.2%, aCL antibody positivity in 4/14, raised serum procalcitonin in 3/14. Mean erythrocyte sedimentation rate (ESR) was 52.9±41.6 mm first hour, mean creatinine 1.6±1.5 mg/dl. Concomitant infection was seen in 7 (36.8%) patients. Respiratory tract infection was seen in 5 (4 had bacterial, 1 had strongyloides) and 2 had systemic infection. Eleven (57.9%) required mechanical ventilation. All patients received intravenous methylprednisolone pulses, cyclophosphamide in (16/19) 84.2%, IVIg in 2, Rituximab in 1, plasmapheresis in 1 patient. Median follow up of survivors is 33 months, 2 lost to follow up.
Univariate analysis showed age and high ESR as independent risk factors associated with DAH. Mortality was associated with requirement of mechanical ventilation.
**Conclusions:** DAH in SLE is rare, but associated with high mortality. It occurs in patients with high disease activity. Requirement of mechanical ventilation is associated with higher mortality.
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## THU0358 HIP JOINT AVASCULAR NECROSIS IN A MULTI-ETHNIC SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

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**Background:** Avascular necrosis of bone (AVN) is a well known complication in patients with systemic lupus erythematosus (SLE).
**Objectives:** To determine the prevalence of avascular necrosis (AVN) involving hip joint among SLE patients and its associated factors.
**Methods:** Consecutive SLE patients attending outpatient follow-up clinics in National University of Malaysia and Putrajaya Hospital, Malaysia from 2004 until 2014 with confirmed avascular necrosis of hip joint on magnetic resonance imaging (MRI) were reviewed. Demographics and disease characteristics of patients with AVN complications were compared with other lupus controls.
**Results:** A total of 300 patients were reviewed and majority of them were Malays (175, 58.3%) followed by Chinese (107, 35.7%), Indian (15, 5%) and others (3, 1%). Eighteen patients (6%) had hip joint AVN and more than two-thirds were bilateral (14 patients, 77.8%). The median onset of AVN was 3 (IQR 4.25) years from diagnosis of lupus. A higher proportion of patients who did not received hydroxychloroquine (HCQ) developed AVN compared to those receiving HCQ (50% vs 24.8%, p=0.02). On the other hand, prednisolone dose $\geq$60mg daily for at least 2 weeks were associated with a higher prevalence of AVN (55.6% vs 23.4%, p=0.005). Positive antiphospholipid antibody (aPL) was also associated with higher prevalence of AVN (55.6% vs 27%, p=0.01). Multivariable logistic regression analysis revealed that the independent predictors of AVN were prednisolone dose $\geq$60mg OD [OR 3.7 (95% CI 1.3–9.9)] and aPL positivity [OR3.1 (95% CI 1.1–8.3)]. HCQ use was independently associated with lower prevalence of AVN [OR 0.3 (95% CI 0.1–0.9)].
**Conclusions:** Hip joint AVN was significantly associated with positive aPL, prednisolone dose $\geq$60mg daily for at least 2 weeks while HCQ use was demonstrated to be associated with lower hip AVN prevalence.
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## THU0359 ANTI-B2GLYCOPROTEIN-1 IGA ANTIBODIES INDEPENDENTLY AND DIFFERENTIALLY CONTRIBUTE TO THROMBOTIC RISK IN SYSTEMIC LUPUS ERYTHEMATOSUS ABOVE AND BEYOND ACL AND LA: LESSONS FROM A CONTEMPORARY MULTIETHNIC PATIENT COHORT

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**Background:** Lupus anticoagulant (LA), IgM and IgG anticardiolipin (ACL), and anti-beta2 glycoprotein 1 (b2GPI) Ab, positive twice 12 weeks apart, constitute laboratory diagnostic criteria of the Antiphospholipid Syndrome (APLS) in patients with or without SLE. IgA ACL and b2GPI Ab subclasses are not included in this classification.
**Objectives:** We investigated the prevalence and contribution of various (sub)classes of APLs to thrombotic events in a multiethnic cohort of SLE patients. We further evaluated the independent contribution of a-b2GPI IgA to thrombotic events above and beyond criteria APL subclasses and clinical risk factors.

**Methods:** A total of 401 patients (232 latinos, 109 African Americans, 25 Caucasians and 35 Asians) fulfilling ≥4 1996 criteria for SLE, and follow-up in a single center between 2008 and 2015 were included. LA was assessed with both aPTT and DRVVT. ACL and a-b2GPI subclasses were tested using commercial ELISA kits and positivity was defined according to manufacturer specifications. Logistic regression models assessed incremental thrombotic risk by higher numbers of APL Abs. Hierarchical forward stepwise regression models evaluated incremental thrombotic risk by a-b2GPI IgA, after accounting for clinical factors (step 1, table 1), and other APL (sub)classes (step 2).
**Results:** Of 401 patients, 92 (23%) had 1 APL Ab class, 12 (3.1%) had 2, and 10 (2.7%) had 3 APLs; LA and a-b2GPI IgA were the most prevalent (14% and 13.7% respectively). Other ACL and a-b2GPI subclasses were uncommon (<2.8%). Sixty-nine (17.2%) subjects had 109 events (57 venous, 35 arterial, 14 obstetric, and 3 glomerular thrombosis); APLS was diagnosed in 34 (49.3%). Higher number of APLs yielded increased thrombotic risk compared to none [OR of 6.6, 9.9, and 27.8 for 1, 2, and 3 respectively, all with p<0.0001]; triple APL positivity bore higher event risk than single [OR=4.2, p=0.047]. In the final model (table 1), SLE duration and hypertension contributed to thrombotic risk (p<0.0001, and p=0.055 respectively), whereas age, gender, smoking, history of nephrotic syndrome, and oral contraceptives did not. Presence of ACL (IgG or IgM) and LA significantly raised risk in the entire cohort, with variation at the ethnic group level, whereas addition of a-b2GPI IgG and IgM did not; a-b2GPI IgA independently contributed an additional 3-fold risk (p=0.001), for the entire cohort, as well as all individual ethnic subgroups. Inclusion of a-b2GPI-IgA in the consensus criteria would have established an APLS diagnosis in an additional 12 subjects (+17.4%, p=0.0005).

**Table 1**: Contributions of clinical factors and various (sub)classes of APLs on thrombotic risk in patients with SLE

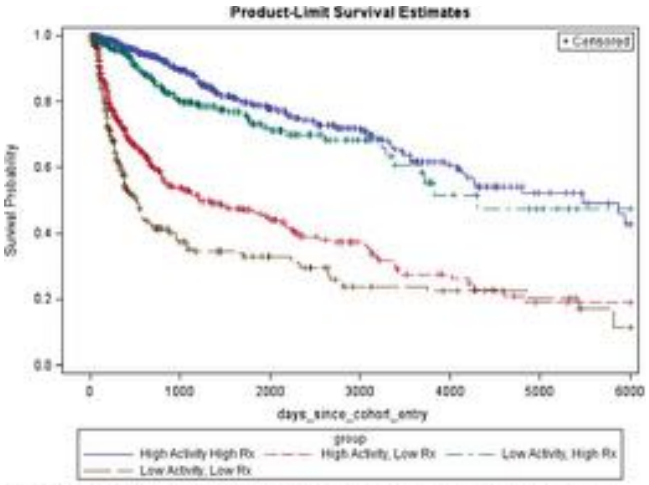
| | Factors | B | SE | Wald | OR | 95% CI | p-value |
|---|---|---|---|---|---|---|---|
| Step 1 | SLE Duration | 0.07 | 0.02 | 12.8 | 1.07 | 1.03-1.1 | *<0.0001* |
| | Gender | 0.78 | 0.38 | 4.3 | 2.20 | 1.04-4.54 | *0.038* |
| Step 2 | SLE duration | 0.07 | 0.02 | 10.9 | 1.07 | 1.03-1.20 | *0.001* |
| | Gender | 0.75 | 0.41 | 3.3 | 2.12 | 0.94-4.76 | 0.07 |
| | ACL IgG/IgM (+) | 1.90 | 0.64 | 8.9 | 6.70 | 1.90-23.21 | *0.003* |
| | LA (+) | 1.96 | 0.33 | 34.8 | 7.10 | 3.90-13.60 | *<0.0001* |
| Step 3 | SLE duration | 0.06 | 0.02 | 8.5 | 1.06 | 1.02-1.1 | ***0.004*** |
| | Gender | 0.75 | 0.42 | 3.1 | 2.12 | 0.92-4.80 | 0.08 |
| | ACL IgG/IgM (+) | 1.66 | 0.67 | 6.2 | 5.30 | 1.40-11.60 | ***0.013*** |
| | LA (+) | 2.03 | 0.34 | 35.2 | 7.62 | 3.90-14.90 | ***<0.0001*** |
| | a-b2GPI IgA (+) | 1.14 | .38 | 9.1 | 3.13 | 1.50-6.56 | ***0.003*** |

**Conclusions:** A-b2GPI IgA and LA were the most prevalent APLs in a contemporary multiethnic cohort of SLE patients. Higher numbers of APLs yielded higher thrombotic risk, and so did triple positivity compared to single. A-b2GPI IgA presence significantly enhanced event risk above and beyond clinical factors and all other APL subclasses.
**Disclosure of Interest:** None declared
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## THU0360 APPLICATION OF NEW DEFINITIONS OF REMISSION IN SLE: DURABLE REMISSION IS RARE

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**Background:** Remission is the ultimate goal in SLE. However, after more than 50 years of research on this topic, no agreement on the definition of remission has been widely accepted. Developing definition(s) of remission was one of the primary research recommendations of the treat-to-target (T2T/SLE) international task force. Definitions of remission were agreed on by an international collaboration from the DORIS working group [1].
**Objectives:** In this study, we applied four DORIS definitions of remission to a large cohort to determine the time to remission, duration of remission and predictors of remission.
**Methods:** The four DORIS definitions of remission are Clinical Remission, Complete Remission, Clinical ROT (remission on treatment) and Complete ROT. Any definition requires the clinical Systemic Lupus Disease Activity Index (cSLEDAI), meaning without serology, to be 0 and the Physician Global Assessment (PGA) to be <0.5 (0–3 VAS). For Remission, prednisone intake has to be 0 and immunosuppressives are not allowed. For ROT, prednisone intake has to be ≤5 mg per day and immunosuppressives are allowed. Clinical Remission and Clinical ROT are regardless of serology, whereas Complete Remission and Complete ROT require negative anti-ds DNA and normal complement. 2263 patients were included in our analyses. Patients entered the cohort from 1987 to 2014 and were seen at least quarterly. Patients not in remission at cohort entry were followed prospectively. We used the Kaplan-Meier approach to estimate the distribution of time to remission after cohort entry. Once remission was achieved, patients were followed prospectively until relapse occurred. The Kaplan-Meier approach was used to estimate the distribution of time from remission to relapse. Cox regression was used to identify baseline factors associated with time to remission, adjusting for baseline level of disease activity and baseline treatment.
**Results:** The median time to remission is 8.7, 11, 1.8 and 3.1 years for Clinical Remission, Complete Remission, Clinical ROT and Complete ROT, respectively. High baseline treatment is the major predictor of a longer time to remission, followed by high baseline activity (Figure). The median duration of remission is just three months. Surprisingly, this is quite similar for all the definitions. African-American ethnicity, baseline low C3 and baseline hematologic activity are negative predictors for time to remission for all definitions. Baseline anti-dsDNA and baseline low C4 are negative predictors for Complete Remission and for Complete ROT. Baseline low C4 is also a negative predictor for Clinical Remission. In multivariable models, income and education were not significant after controlling for race. Furthermore, we did not find a significant association for sex, age group and the use of hydroxychloroquine.




Kaplan-Meier Estimates of probability of not being in clinical remission, by time since cohort entry, stratified by baseline disease activity and treatment (High baseline disease activity defined as PGA ≥1 or SLEDAI ≥3. High baseline treatment defined as Prednisone >5 or Immunosuppressant use.)

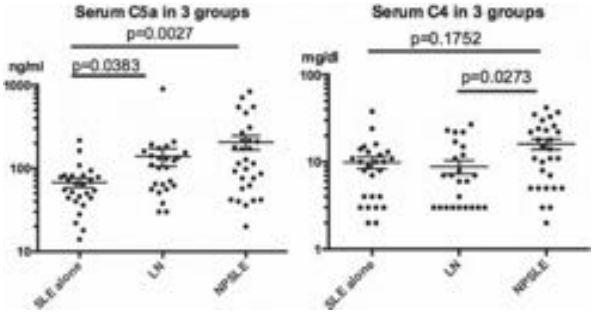
**Conclusions:** Our results provide further insights into the frequency and duration of remission in SLE and call attention to the major role of baseline activity and baseline treatment in predicting remission.
**References:**
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**Disclosure of Interest:** None declared
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## THU0361 SERUM C5A IS INCREASED IN LUPUS NEPHRITIS AS WELL AS IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS THROUGH DIFFERENT MECHANISMS

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**Background:** Neuropsychiatric manifestation in systemic lupus erythematosus (NPSLE) is one of the most serious complications of the disease. We have recently demonstrated that the breakdown of blood brain barrier (BBB) plays a crucial role in the development of diffuse psychiatric/neuropsychological manifestations (diffuse NPSLE), allowing influx of neuron-reactive autoantibodies from systemic circulation into the brain (ref). Notably, C5a, a split product of C5, has been recently shown to cause BBB damages. Moreover, association of C5a with some forms of glomerulonephritis has been implicated.
**Objectives:** The present study therefore explored the levels of C5a in sera from patients with NPSLE and lupus nephritis (LN).
**Methods:** Serum specimens were obtained from 29 patients with NPSLE including 18 patients with diffuse NPSLE and 9 patients with neurologic syndromes (focal NPSLE), 25 patients with LN, 26 patients without NPSLE or LN (SLE alone), and from 21 healthy individuals. Cerebrospinal fluid (CSF) specimens were obtained from 29 patients with NPSLE on the same day of the collection of serum specimens. The levels of C5a, C5, C3 and C4 were measured by enzyme-linked immunosorbent assay. The BBB function was evaluated by CSF /serum albumin ratio (Q albumin).
**Results:** Serum C5a was significantly increased in 80 SLE patients compared with that in healthy individuals. Serum C5a was significantly elevated in NPSLE as well as in LN compared with that in SLE alone (figure), whereas there were no significant differences in serum C5 among these 3 groups. Serum C4, but not serum C3, was significantly lower in LN than that in NPSLE (figure), indicating the activation of complement classical pathway in LN, but not in NPSLE. Q albumin was significantly elevated in diffuse NPSLE compared with that in focal NPSLE, whereas there were no significant differences in CSF C5a and in serum C5a between these 2 groups. Notably, Both CSF C5 and CSF C5a were significantly

correlated with Q albumin, whereas serum C5a, but not serum C5, was inversely correlated with Q albumin in NPSLE patients.




**Conclusions:** These results have disclosed that serum C5a was elevated in NPSLE as well as in LN through different mechanisms. Moreover, the data indicate that CSF C5a and C5 were elevated in NPSLE due to BBB damages. Finally, it is suggested that C5a might be consumed during the process of BBB damages.

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**Disclosure of Interest:** None declared

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## THU0362 ADVERSE PREGNANCY OUTCOMES AND ASSOCIATED FACTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Compared to the general population, pregnant women with systemic lupus erythematosus (SLE) tended to suffer a higher risk of adverse pregnancy outcomes (APOs). Since SLE often affected women of reproductive age, pregnancy outcomes and the associated factors had always been a major concern.

**Objectives:** To investigate the maternal and fetal outcomes among pregnant patients with SLE, and to evaluate the clinical predictors of adverse pregnancy outcomes.

**Methods:** We collected the clinical data from 251 SLE patients with 263 pregnancies between Jan 2001 to Dec 2015 and then conducted retrospective analysis. APOs included pregnancy loss (spontaneous or therapeutic abortion, fetal death, and neonatal death), adverse fetal outcomes [fetal malformation, preterm delivery, and neonatal lupus erythematosus (NLE)], obstetrical complications [pregnancy induced hypertension (PIH), intrauterine growth retardation (IUGR), and fetal distress]. Associated factors for APOs were analyzed by Logistic regression model.

**Results:** The mean age of patients was 28.6±3.9 yrs, apart from newly diagnosed ones, the mean duration was 5.8±4.0 yrs. Of all the 263 pregnancies, 188 were from previously diagnosed SLE patients and 75 were from newly diagnosed (during pregnancy or puerperium) patients. Successful delivery and pregnancy loss occurred in 71.5% (188/263) and 29.5% (75/263), respectively. Pregnancy loss included therapeutic abortion in 60 (22.8%), spontaneous abortion in 6 (2.3%), fetal death in 7 (2.7%), and neonatal death in 2 (0.8%). Adverse fetal outcomes included 4 cases (1.5%) with fetal malformation, 56 (21.3%) with premature and 12 (4.6%) with NLE. Obstetrical complications included 35 cases (13.3%) with PIH, 32 (12.2%) with IUGR, 21 (8.0%) with fetal distress. Pregnancy loss in newly diagnosed SLE patients was significantly higher than those in previously diagnosed ones (45.3% vs. 21.8%; $P<0.001$). In multivariate analysis, hypocomplementemia (OR=3.60, 95%CI 1.30–9.94, P=0.01), hypoproteinemia (OR=3.21, 95%CI 1.23–8.30, P=0.02), antiphospholipid antibodies positivity (OR=8.393, 95%CI 1.73–40.84, P=0.01), anti-DNP antibody positivity (OR=5.64, 95%CI 1.24–28.36, P=0.03), and hypertension (OR=14.597, 95%CI 1.51–141.60, P=0.02) were independent risk factors for APOs. Usage of hydroxychloroquine (OR=0.27, 95%CI 0.11–0.73, P=0.01) during pregnancy was a protective factor for APOs.

**Conclusions:** The rate of APOs is still high in SLE patients complicated with pregnancy. Pregnancy loss in newly diagnosed SLE patients is significantly higher than those in previously diagnosed ones. Hypocomplementemia, hypoproteinemia, antiphospholipid antibodies positivity, anti-DNP antibody positivity and hypertension are important risk factors for APOs. Usage of hydroxychloroquine during pregnancy is protective.

**Disclosure of Interest:** None declared

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# Spondyloarthritis - etiology, pathogenesis and animal models

## THU0363 POSITION 97 (P97) OF HLA-B, A RESIDUE IMPLICATED IN ANKYLOSING SPONDYLITIS PATHOGENESIS, PLAYS A KEY ROLE IN CELL SURFACE FREE HEAVY CHAIN EXPRESSION VIA INTERACTIONS WITH β2-MICROGLOBULIN

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**Background:** Polymorphisms of position 97 (P97) residue in HLA-B are strongly associated with Ankylosing Spondylitis (AS).[1] Position 97 residue locates in the α2 domain of HLA-B*27 and contributes to the C/F pocket that accommodates the C-terminal of peptide ligands.[2] Mutation of Asparagine (N) at P97 to Aspartic acid (D) has been reported to decrease HLA-B*27:04 cell surface expression.[3] We hypothesized that variations of residues at P97 might contribute to AS pathogenesis through altering cell surface HLA-B*27 expression.

**Objectives:** In this study, we studied the effect of P97 residue variants on cell surface expression of HLA-B*27.

**Methods:** Flow cytometry was used to measure surface expression of HLA-B*27 in C1R and HeLa cells expressing wildtype HLA-B*27 (N97) and six mutants at position 97 (N97T, N97S, N97V, N97R, N97W and N97D). TAP-deficient T2, Tapasin-deficient 220 cells, ERAP1-silenced and β2m-silenced C1R cells were used to identify protein interactions. β2m-deficient HCT15 cells and β2m-knockout HeLa cells were used to study the effect of P97 residues on HLA-B*27 expression in the absence of β2m. Surface expression of HLA-B*7/ HLA-B*51 and their P97 mutants in C1R and HeLa cells was also studied.

**Results:** Mutation of P97 to AS risk residue Threonine, but not to the protective residues (Serine and Valine) or the non-associated residues (Arginine and Tryptophan), increased surface free heavy chain (FHC) expression in C1R and HeLa cells. The HLA-B*27-N97D mutation significantly reduced both of HLA-B*27 FHC and classical complex expression on the surface of C1R and HeLa cells. Only β2m, not TAP, Tapasin or ERAP1, was essential for the reduction of cell surface HLA-B*27 FHC expression in HLA-B*27-N97D mutant. The expression of HLA-B*7 and HLA-B*51 was also affected by P97 residue mutations.

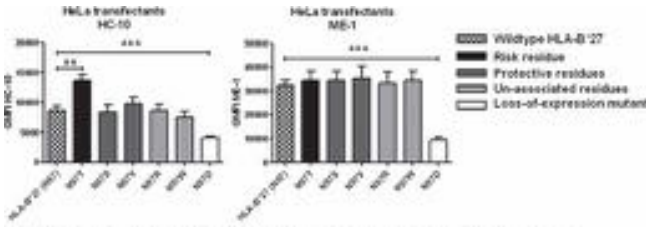



**Figure 1 P97 amino acid variants affect HLA-B*27 expression on the cell surface.** HeLa cells were transfected using lentivirus to express HLA-B*27(N97) and six mutants at position 97 (N97T, N97S, N97V, N97R, N97W and N97D). HLA-B*27 free heavy chain (HC-10 antibody) and classical HLA-B*27 complex (ME-1 antibody) cell surface expression is shown. All experiments were repeated three times. Results are expressed as mean and standard deviation. P value was determined using unpaired two-tailed t-test (** = P<0.01, *** = p<0.001).

**Conclusions:** The P97 residue affects HLA-B*27 free heavy chain and classical complex cell surface expression, in which β2m plays a key role. Cell surface expression of HLA-B*7 and HLA-B*51 is also affected by residue variations at P97. The association of P97 amino acid polymorphisms with AS is, at least in part, explained by its effect on HLA-B*27 free heavy chain cell surface expression.

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**Disclosure of Interest:** None declared

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## THU0364 RARE ERAP1 ALLOTYPE COMBINATIONS DO NOT EXPLAIN THE ERAP1 ASSOCIATION WITH ANKYLOSING SPONDYLITIS

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**Background:** Single nucleotide polymorphisms (SNPs) in *ERAP1* are strongly associated with ankylosing spondylitis (AS) (1,2). ERAP1 is an aminopeptidase involved in the generation of optimal peptide epitopes for presentation by T-cells in the context of major histocompatibility complex (MHC) class I molecules such

as HLA-B27. One small study (17 AS cases and 19 controls) suggested that the frequencies of functionally different *ERAP1* allotypes differ between patients and controls in AS (3,4). In this study 13 ERAP1 alleles were identified, many of which were rare and previously unreported; allotype *001 was reported in 44% of cases and 8% controls; allotype *002 in 3% of cases and 45% of controls; allotype *005 in 11% of cases and 29% of controls. The authors also reported that the frequencies of particular allotype combinations differed greatly between AS and controls. For example, the allotype combination *001+*005 was found in 53% of cases, but no controls. This allotype combination (and several other less common combinations) were reported exclusively in AS cases, and were shown in parallel *in vitro* experiments to be associated with poor processing of peptides and altered HLA class I expression. The results of these unexpected *ERAP1* associations clearly required verification in a larger population sample in view of their potentially dramatic implications for understanding one of the most enduring mysteries of the pathogenesis of AS, namely its association with HLA-B27.

**Objectives:** Our study was performed in a much larger sample to assess the veracity of previous suggestions that rare *ERAP1* alleles and allotype combinations are associated with AS.

**Methods:** We genotyped 213 AS families and 46 control families using KASP™ technology for 5 SNPs (M349V, K528R, D575N, R725Q, Q730E) to infer *ERAP1* allotypes. Allotype and genotype frequencies were compared.

**Results:** Several of the reported rare variants were not observed in our sample. We did not confirm the previously reported *ERAP1* associations with rare allotype combinations; the *001 allotype was seen in 17.1% of cases and 23.9% controls. Allotype *002 was seen in 34.7% of cases and 25% controls. The *005 allotype, which was common in the previous report among cases, was not seen in either of our AS cases or controls. The *001+*005 allotype combination, which was observed in 53% of cases in the previous small study was completely absent from both our larger sample of 213 cases and 46 controls.

**Conclusions:** We were unable to confirm the suggested association of AS with rare *ERAP1* allotype combinations in this much larger population study. We were also unable to confirm the diversity of *ERAP1* haplotypes previously suggested. Further investigation will be required to clarify the correlation of *ERAP1* allotype combinations with both functional effects and their potential association with AS.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2859

## THU0365 LIGHT RS1077667 G>A GENE POLYMORPHISM IS ASSOCIATED WITH SUSCEPTIBILITY TO ANKYLOSING SPONDYLITIS IN A CHINESE HAN POPULATION

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**Background:** Single-nucleotide polymorphisms (SNPs) are single base-pair changes which will lead to the structural changes of mRNA and get involved in the pathogenesis process of ankylosing spondylitis (AS). LIGHT is indicated to be a inflammatory mediator in AS. Meanwhile the SNP rs1077667 G>A, which was located on LIGHT, is associated with the expression of LIGHT.

**Objectives:** This study explored the relationship between AS and the SNP rs1077667 G>A in a Han Chinese population. Meanwhile we explored the relationship between the SNP and the laboratory characteristic of AS patients.

**Methods:** A case-control study with 497 subjects diagnosed AS and 387 healthy controls to compare their genotype and gene frequencies was delivered. SNP is identified by high-resolution melting methods (HRM). Clinical characteristics of patients with AS and controls were registered at the same time.

**Results:** Statistical significance was found in both co-dominant model (GG vs. GA vs. AA) (P=0.000004) and allele [p=4.59E-08, OR (95%CI) = 0.740 (0.663–0.827)] between LIGHT rs1077667 G>A and the risk of AS. However, no significant association was found between the SNP and the laboratory indexes.

**Conclusions:** This is the first study to address the association between the LIGHT rs1077667 G>A polymorphisms and AS, and it suggests a potential pathogenic factor for AS.

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**Acknowledgement:** We are grateful to the participating AS patients and their families. This research was sponsored by the National Natural Science Foundation of China (Nos. 81301496, and 81202354). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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## THU0366 ASSOCIATION OF CHROMOSOME 1Q32 WITH ANKYLOSING SPONDYLITIS IS INDEPENDENT OF BOWEL SYMPTOMS AND FAECAL CALPROTECTIN

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**Background:** Colonoscopic, endoscopic, and histological studies have demonstrated that intestinal inflammation, similar to the ileo-colitis seen in Crohn's disease (CD), is a common feature of ankylosing spondylitis (AS). More recently, the existence of a shared genetic basis to CD and AS has been demonstrated [1,2].

**Objectives:** To test whether the association of known CD risk loci with AS is primarily due to the presence of bowel inflammation in AS patients.

**Methods:** 286 Caucasian patients fulfilling the modified New York criteria for AS and with no history of inflammatory bowel disease were assessed non-invasively for bowel inflammation using faecal calprotectin and the Dudley Inflammatory Bowel Symptom Questionnaire (DISQ) [3]. All patients and 568 matched healthy controls were genotyped with TaqMan® SNP genotyping assays for the confirmed CD risk loci [2], 1q32 (rs11584383),*JAK2* (rs10758669), *CDKAL1* (rs6908425), *IL12B* (rs100454310), *ZPBP2* (rs2872507), *MUC19/LRRK2* (rs11175593), *STAT3* (rs744166), and *IL23R* (rs1343151, rs10489630, rs11209026). Chi square testing was used to test for association.

**Results:** Minor alleles of 1q32 SNP rs11584383 (p=0.002, OR=0.69, 95% CI 0.55–0.87), and *IL23R* SNPs rs11209026 (p=0.011, OR=0.53, 95% CI 0.32–0.87) and rs1343151 (p=0.027, OR=0.77, 95% CI 0.61–0.97) all conferred protection against AS. However, only the association of 1q32 SNP rs11584383 remained significant after Bonferroni correction for multiple testing (p=0.02). The Cochran's Q test found no significant difference between ORs after stratification of AS patients by DISQ score and faecal calprotectin ($P_{difference} > 0.09$).

**Conclusions:** Previously, the association of CD risk loci with susceptibility to AS has been attributed to the co-occurrence of asymptomatic intestinal inflammation which is well recognised and supports the concept that CD and AS are two extremes of a related genetic and phenotypic disease spectrum. However, our study provides preliminary evidence that the association of the confirmed CD risk locus 1q32 SNP rs11584383 with AS is independent of bowel inflammation.

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**Disclosure of Interest:** None declared

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## THU0367 IDENTIFICATION OF DIFFERENTIALLY METHYLATED GENES IN PURIFIED DISEASE-RELEVANT BLOOD CELL POPULATIONS IN PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** Spondyloarthritis (SpA) is a complex disease involving genetic, epigenetic and environmental contributions to disease risk. However, associated polymorphisms explain only 25% of SpA heritability suggesting that a significant inherited component of SpA is not being detected by screening genetic polymorphisms and suggests an important role for epigenetic factors such as DNA methylation. However, no comprehensive analysis of genome-wide DNA methylation in disease relevant blood cell populations has so far been performed in SpA allowing to experimentally verify this hypothesis.

**Objectives:** This study aimed to perform a genome-wide DNA methylation analysis in sorted CD4 and monocytes from SpA patients compared with controls.

**Methods:** In the exploratory cohort, 24 SpA patients and 16 age and sex-matched controls were analyzed. SpA patients were monocentrically recruited between October 2014 and May 2015 in the department of rheumatology (Cochin hospital). These patients had an active disease despite NSAIDs intake and were eligible for a TNF-blocker treatment. The mean BASDAI (± SD) was 53.2±23.7; ASDAS 3.2±1.1 and CRP 13±16.6. Among these patients, 23 fulfilled the ASAS classification criteria (imaging arm) with sacro-iliitis on X-rays (n=16) or objective signs of inflammation on MRI (n=21). Only one patient fulfilled the clinical arm. Genome-wide DNA methylation patterns were analyzed in cell-sorted (MACS)

monocytes and CD4 T-lymphocyte populations from SpA patients and controls using the Illumina 450K Infinium Human Methylation 450K BeadChip allowing the simultaneous quantitative monitoring of more than 480,000 CpG positions.
**Results:** In CD4 cells 122 CpGs in 82 promoter regions of genes were found to be differentially methylated using stringent quality thresholds including several genes involved in disease-relevant signaling cascades such as Wnt-signaling and genes in which genetic polymorphisms have previously been associated with susceptibility to SpA. With 158 CpGs located in 86 promoter regions, slightly more genes were found to be differentially methylated in monocytes. Differentially methylated loci included again genes in Wnt signaling and bone metabolism, osteoblast or chondrocyte-specific genes as well as genes that have previously been shown to be implicated in related diseases such as psoriasis. A single gene was found differentially methylated in both monocytes and T-lymphocytes underlining the importance to perform these epigenetic analyses in purified cell populations. Validation of these differentially methylated positions in 12 genes at single-nucleotide resolution is ongoing in monocytes and CD4 lymphocytes from 12 additional patients and 12 additional controls using the highly quantitative pyrosequencing technology.
**Conclusions:** This study is the first to analyze genome-wide DNA methylation in purified disease-relevant blood cell populations in SpA bringing into evidence a moderate number of promoters whose deregulation might contribute to the pathogenesis of SpA. Integration with RNA expression data will allow defining the functional impact of the DNA methylation patterns to better understand the molecular changes in SpA and potentially identify novel targets for therapeutic intervention.
**Disclosure of Interest:** None declared
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## THU0368 IL-22 IMPACT ON HUMAN BONE MARROW MESENCHYMAL STEM CELLS FUNCTIONS; A NOVEL PATHWAY THAT MAY CONTRIBUTE TO ABERRANT NEW BONE FORMATION IN HUMAN SPA

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**Background:** The spondyloarthropathies (SpAs) including ankylosing spondylitis (AS) show a propensity for florid new bone formation following bouts of inflammation. However, in other skeletal diseases such as rheumatoid arthritis, inflammation predictably leads to diffuse bone loss and periarticular erosion.[1] Anti-TNF therapies effectively alleviate spinal inflammation in SpA but fail to arrest the new bone formation.
SpAs are genetically and therapeutically linked to IL-23, which in turn regulates IL-22. it is a master regulator of stem cell niches in the intestine, liver, endometrium and skin[2] but to the best of our knowledge, no data on its influence upon human osteoprogenitors or MSCs has been described.
**Objectives:** We hypothesized that IL-22, a master regulator of stem cells in other niches, might also regulate mesenchymal stem cell (MSC) osteogenesis in an inflammation-dependent context.
**Methods:** Bone marrow samples were obtained after informed consent (n=10), and MSCs isolated and culture expanded for 2–4 passages. Cells were analysed using flowcytometry for ISCT criteria and expression IL-22R ±IFNG and TNFa stimulation. IL-22 effects were tested with and without inflammatory cytokines (IFNG and TNFa) on: MSC proliferation using colorimetric XTT assay, MSC migration using transwell migration assays, the expression of trascriptional factors of MSC adipo-, osteo- or chondro-genic potential using qRT-PCR, and on osteogenic differentiation assay evaluated by colorimetric calcium assay.
**Results:** Interestingly, IL-22R expression was detected in MSCs intracellularly and showed a mean 1.8±0.12 fold increase post IFNG and TNFa stimulation.
MSC stimulation with combined IL-22, IFNG and TNFa but not single cytokines increased MSC proliferation (p=0.008) and migration (p=0.037) compared to unstimulated MSCs.
Osteogenic, adipogenic but not chondrogenic transcription factors were upregulated by IL-22 ($p<0.05$). Moreover, Inflammatory stimuli (IFNG+TNFa±IL-22) did not affect the chondro- and adipogenic transcription factors but did temper the increase of pro-osteogenic *RUNX2*. Mature bone markers, particularly *BGLAP*/osteocalcin were rarely detectable in the presence of inflammation. The inflammatory milieu also downregulated all tested chondrogenic markers *ACAN*, *COL2A1* and *COL10A1* compared to unstimulated and IL-22 stimulated MSCs.
Notably, MSC osteogenesis was enhanced following IL-22 exposure (p=0.031 for calcium production). The combination of IFNG and TNFa with or without IL-22 suppressed MSC osteogenesis (p=0.0313 for both).
**Conclusions:** This is the first study to show that IL-22 is involved in MSC proliferation/migration in inflammatory environments with MSC osteogenesis occurring only in IFNG/TNFa absence. Given the genetic link with SpA, these physiological MSC bone responses need evaluation in pathological post-inflammation osteogenesis in human SpA.
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**Disclosure of Interest:** None declared
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## THU0369 IL-17A+ AND IL-22+ T CELLS INCREASE DURING ANTI-TNFα TREATMENT IN SPONDYLOARTHRITIS – A LINK TO RADIOGRAPHIC PROGRESSION?

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**Background:** The pro-inflammatory Th17 associated cytokines IL-17A and IL-22 have been proposed as important mediators in spondyloarthritis (SpA).
Treatment of SpA has been improved dramatically with the introduction of tumor necrosis factor (TNF)α inhibitors. Despite good clinical efficacy, anti-TNFα fail to affect bone formation and radiograpchic progression in SpA. Th17 cells and cytokines might be involved in this lack of response to anti TNF-α antibodies.
**Objectives:** To investigate the association of Th17 cells with changes in clinical and MRI activity in SpA patients treated with anti-TNFα. Furthermore, to investigate the involvement of the Th17 cytokines IL-17A and IL-22 on bone anabolic pathways in SpA.
**Methods:** Percentage of IL-17A and IL-22 producing T cells were assessed in peripheral blood mononuclear cells from 30 SpA patients at baseline, after 12 and 52 weeks of anti-TNFα therapy using intracellular flow cytometry. Clinical activity was evaluated using the Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). MRI grading was performed on the whole spine and in the sacroiliac joints (SIJ). Correlation analyses were performed to investigate the association between percentages of Th17 cells and disease progression during the course of treatment.
Normal human osteoblasts and fibroblast like synoviocytes (FLS) were stimulated with IL-17A, IL-22, TNFα and supernatants from CD4+CD45RO+CCR6+ cells to determine the bone modulatory activity of Th17 cytokines.
**Results:** Percentages of IL-17A producing and IL-22 producing, and CCR6 expressing CD4+CD45RO+ T cells were increased at baseline compared with healthy controls. These subsets increased during 52 weeks of anti-TNFα therapy, despite clinical response with the composite scores ASDAS decreasing from 3.6 (3.0–4.0) to 1 (0.5–1.9) and BASDAI decreasing from 63.50 (52–71) to 15 (3- 31). High baseline percentages of IL-17A and IL-22 producing CD4+CD45RO+ T cells correlated with greater improvement in ASDAS and BASDAI score. Both baseline percentages of IL-17A and IL-22 producing CD4+CD45RO+ T cells were associated with increased levels of chronic MRI changes at baseline (both $p<0.05$). Additionally, IL-17A producing CD4+CD45RO+ T cells at baseline were associated with chronic MRI changes in the SIJ at 12 months ($p<0.01$).
IL-17A, IL-22 and TNFα stimulation increased mineral deposition from normal human osteoblasts. IL-22 in combination with TNFα inhibited the secretion of Dkk-1 from SpA FLS, whereas neither TNFα nor IL-17A were able to affect Dkk-1 secretion from SpA FLS.
**Conclusions:** Th17 cells increased during anti-TNFα therapy, regardless of clinical improvement. Th17 cell percentages at baseline predict clinical response and are associated with chronic MRI changes at baseline and outcome at 52 weeks. Not only IL-17A, but also IL-22 are able to affect bone formation and bone remodelling pathways, but only IL-22 induce Dkk-1 in FLS.
Hereby, the consistently elevated percentages of Th17 cells, despite good disease control in this group of SpA patients, could provide a link to the ongoing ectopic bone formation seen in SpA.
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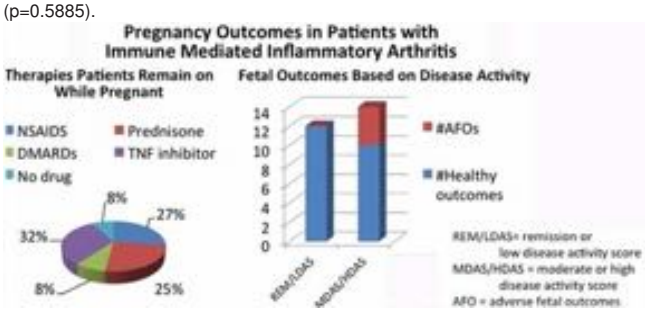
## THU0370 DISEASE ACTIVITY, NOT DRUG EXPOSURE, AFFECTS PREGNANCY OUTCOMES IN INFLAMMATORY ARTHRITIS

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**Background:** Pregnancy is commonly encountered in women who have immune mediated inflammatory arthritis such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), juvenile arthritis (JIA) or ankylosing spondylitis (AS). They are often diagnosed with these diseases during their fertile years; yet, data is scant on how disease activity and drug exposure affects maternal outcomes.
**Objectives:** Our goals were to chart medication use during pregnancy and to determine what is more likely to cause adverse fetal outcomes (AFOs): disease activity or drug exposure.
**Methods:** This is an observational study at a single clinic of females aged 18–45 years, diagnosed with RA, JIA, AS or PsA who had: 1) >12 months follow-up; 2) documented pregnancy during this period; and 3) clinic visits that qualified as being preconception (within 12 months of conception), pregnancy (1st, 2nd or 3rd

trimester) and post-partum (within 12 months after delivery). Drug exposure was classified as occurring preconception (PRE- ≥1 month before conception), at risk (RISK- 1st trimester plus 1 month preconception) or during 2nd and 3rd trimesters of pregnancy (PREG). Data collected included therapies (DMARDS, biologics, steroids, NSAIDS), modified health assessment questionnaire (mHAQ), tender joint count (TJC), swollen joint count (SJC), pain score, and global arthritis score (GAS) calculated from TJC (0–28) + pain (0–10) + mHAQ (0–24) where remission (REM) <3; low activity 3–7; mod activity 8–19; high activity >20 Maternal disease activity was further classified as flared or improved (defined: 20% change in TJC+SJC or >3 increase in joint count if PRE count <2). Fetal outcomes were classified as live births or AFOs: preterm labor, miscarriages, preeclampsia, fetal growth restrictions, or malformations. A $\chi^2$ test of homogeneity was calculated to determine if AFOs were more likely a result of drug exposure or maternal disease activity during pregnancy.

**Results:** 26 pregnancies (8 RA, 6 PsA, 4 AS, 8 JIA) were observed in 20 patients (7 RA, 5 PsA, 3 AS, 5 JIA). This number represents 7.5% of all clinic women who were fertile with these diagnoses. Mean age at delivery was 31.6 years and disease duration was 10.8 yrs. During PRE the most common drugs used were TNFi (62%), methotrexate (20%), other DMARDS (12%), other Biologics (8%), Prednisone (23%), and NSAIDs (81%). Drug use was relatively unchanged in PREG: TNFi (58% same), DMARDS (15% same), Prednisone (23% same), NSAIDs (31% less) and no drugs (15% more). Of the 10 PRE patients in REM, 5/10 stayed in REM or LDAS during PREG; 3/10 were in MDAS or HDAS POST pregnancy. Of the 16 PRE patients with GAS ≥4, only 4/16 improved to REM or stayed in LDAS during PREG; 10/16 were in MDAS or HDAS POST pregnancy. There were 4 AFOs (2 preterm, 2 miscarriage), but no malformations. The 4 AFOs occurred in women with high flare rates during pregnancy, and none of the women in remission or low disease activity states had an AFO (p=0.1422). There was no significant correlation between the different drug therapies and AFOs (p=0.5885).




**Conclusions:** These observational data show that during pregnancy, patients with inflammatory arthritis, the majority still require drugs to control their disease. Only 15% of women were able to get off of therapy. While fetal outcomes were primarily favorable, AFOs were seen in patients with the highest disease activity, and not by drug exposure.

**Disclosure of Interest:** None declared

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## THU0371 INCREASED FREQUENCY OF REGULATORY CD19+CD24HIGH CD38HIGH B CELLS IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS)

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**Background:** CD19+CD24$^{high}$CD38$^{high}$ B cells have been described to have a regulatory capacity and their frequency is altered in the peripheral blood of patients with various autoimmune diseases. The pathogenesis of AS is not well understood, and evidence suggesting the implication of either autoinflammatory or autoimmune mechanisms has been reported. In addition, increased frequencies of circulating B cells bearing a regulatory phenotype has recently been described in spondyloartrhitis (1).

**Objectives:** To study the frequency of circulating CD19+CD24$^{high}$ CD38$^{high}$ B cells (Breg) in patients with Ankylosing Spondylitis (AS), and test the regulatory capacity of this B cell subset.

**Methods:** Peripheral blood was drawn from AS patients naïve for TNF blockers (AS/nb) (n=37) and healthy controls (HC) (n=37), that were matched with patients for age and gender. After isolation by Ficoll-Hypaque gradient, PBMCs were stained with antibodies to CD3, CD4, CD19, CD24, and CD38, and examined by flow cytometry. For functional studies, total CD19+ B cells were isolated from PBMCs of 3 HC by magnetical sorting. Breg-depleted CD19+ B cells were obtained after total CD19+ B cells were depleted of CD19+CD24$^{high}$CD38$^{high}$ B cells by cytometry in a FacsVantage sorter (Beckton Dickinson). Total CD19+ B cells or Breg-depleted CD19+ B cells were established in culture and stimulated through their BCR. Secretion of IFNγ was determined by ELISA in culture supernatants.

**Results:** When compared with healthy controls, AS/nb patients demonstrated a significantly increased frequency of CD19+CD24$^{high}$CD38$^{high}$ B cells (Breg). The frequency of circulating Breg was increased not only in AS/nb patients with high or very high disease activity (ASDAS-CRP) >2.1 but also in AS patients with low activity or no activity (ASDAS-CRP<2.1). The frequency of circulating Breg cells did not correlate significantly with ASDAS-CRP, ASDAS-ESR, BASDAI, CRP or ESR values. Functional in vitro studies showed that the secretion of IFNγ was significantly higher in Breg-depleted CD19+ as compared with total CD19+ B cells, indicating that Breg have the capacity to downmodulate B cell pro-inflammatory cytokine secretion.

**Conclusions:** An increased frequency of circulating CD19+CD24$^{high}$CD38$^{high}$ B cells is observed in AS/nb patients, that is not related with disease activity. Functional in vitro studies confirmed that CD19+CD24$^{high}$CD38$^{high}$ B cells are able to downmodulate B cell pro-inflammatory cytokine secretion.

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**Disclosure of Interest:** None declared

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## THU0372 SUBCLINICAL JOINT INFLAMMATION IN PSORIASIS PATIENTS WITHOUT CONCOMITANT PSORIATIC ARTHRITIS- A CROSS-SECTIONAL AND LONGITUDINAL ANALYSIS

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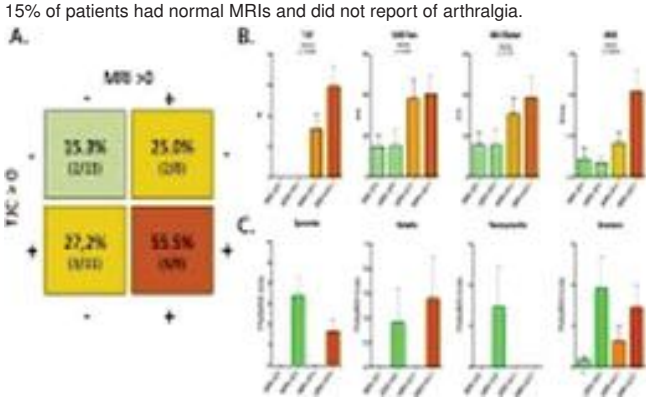
**Background:** Psoriasis is a chronic inflammatory disease affecting 2–3% of the population [1,2]. Up to 30% of psoriasis patients develop psoriatic arthritis (PsA), and usually musculoskeletal symptoms start after the onset of skin disease. Psoriatic skin disease has a higher prevalence than arthritis what raises the question whether psoriasis patients without PsA are indeed spared from joint inflammation [3].

Detecting subclinical joint inflammation could help identify which patients with skin disease would benefit of treatment covering both skin and musculoskeletal inflammation.

**Objectives:** To search for subclinical inflammatory joint disease in psoriasis patients without arthritis, and to determine whether such changes are associated with the later development of PsA.

**Methods:** Eighty-five subjects without arthritis (55 with psoriasis and 30 healthy controls) received high field magnetic resonance imaging (MRI) of the hand. MRI scans were scored according to the PSAMRIS method [4]. Psoriasis patients received complete clinical investigation, high-resolution peripheral quantitative computed tomography (HR-pQCT) to detect erosions and enthesiophytes and were followed up for at least one year for the development of PsA.

**Results:** 47% of psoriasis patients showed at least one inflammatory lesion on MRI. Synovitis was the most prevalent inflammatory lesion (38%), while osteitis (11%), tenosynovitis (4%) and periarticular inflammation (4%) were less frequent. The mean (±SD) PSAMRIS synovitis score was 3.0±2.5 units. Enthesiophytes and bone erosions were not different between psoriasis patients with or without inflammatory MRI changes. The risk for developing PsA was as high as 55% if patients had subclinical synovitis and symptoms related to arthralgia, but only 15% of patients had normal MRIs and did not report of arthralgia.




**Conclusions:** Prevalence of subclinical inflammatory lesions is high in patients with cutaneous psoriasis. Arthralgia associated with MRI synovitis constitutes a high-risk constellation for the development of PsA.

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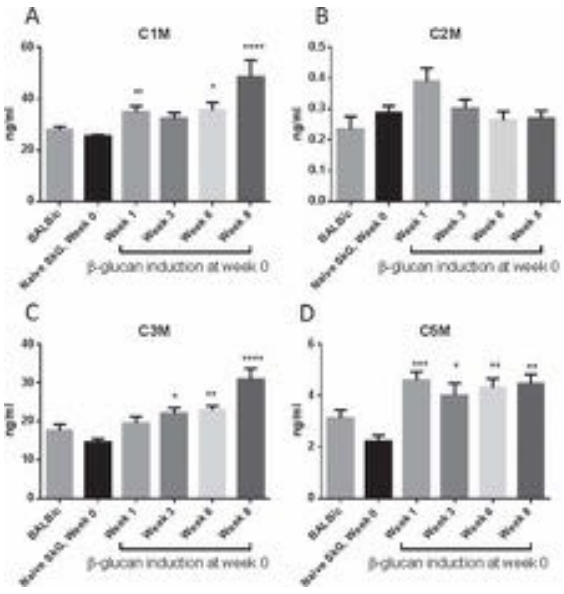
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**Acknowledgement:** This study was supported by the Deutsche Forschungsgemeinschaft (SPP1468, CRC1181), the Marie Curie project OSTEOIMMUNE, the Metarthros project of the German Ministry of Science and Education, the IMI-funded project BTCure and the Pfizer Competitive Grant Award Germany.
**Disclosure of Interest:** None declared
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## THU0373 DEGRADATION FRAGMENTS OF COLLAGEN I AND V ARE EARLY DISEASE MARKERS IN β-GLUCAN TRIGGERED SPONDYLOARTHRITIS IN SKG MICE

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**Background:** Spondyloarthritis (SpA) is a slowly progressing, chronic inflammatory disease predominately affecting the axial skeleton. It is caracterized by excessive extracellular matrix (ECM) remodeling of the affected tissues. It is proposed that serological biomarkers of ECM remodeling can be used in assessment of SpA progression, diagnosis and treatment efficacy.
**Objectives:** In this study we investigated the turnover of selected ECM proteins in a β-glucan triggered SpA SKG mouse model. Turnover of type I, II, III and V collagen were evaluated in serum by biomarkers reflecting MMP-derived degradation fragments of the collagens (C1M, C2M, C3M and C5M, respectively).
**Methods:** Fifty SKG mice were included in the study for the SpA model. Additionally ten BALB/c mice were included as a reference of regular healthy mice. The BALB/c mice and ten SKG mice were sacrificed at week 0. The remaining SKG mice (n=40) were induced with 3 mg/kg β-glucan at week 0. 10 animals were sacrificed each at week 1, 3, 6 and 8. All groups were observationally scored weekly for the development of arthritis and skin inflammation, and body weight. Blood was collected via cardiac puncture at termination. The biomarkers (C1M, C2M, C3M and C5M) were assessed by competitive ELISAs in serum. Differences between biomarker levels in Naive SKG mice compared to other groups were evaluated by Kruskal-Wallis multiple comparison test.
**Results:** Clinical scoring revealed that the disease progressed throughout the study, starting with mild manifestations at week 1 in the β-glucan induced SKG mice. The biomarkers of interstitial tissue C1M, C3M and C5M were in general elevated compared to naïve SKG mice (Fig. A, C, D). The C5M levels were increased from an average of 2.2ng/ml to 4.6ng/ml already one week after β-glucan induction ($p<0.001$) and the levels remained elevated in all β-glucan induced mice compared to SKG naïve mice throughout the study (Fig. D). C1M was significantly increased from an average of 25.6ng/ml to 34.7ng/ml at week 1. This level was further increased at week 8 of which the average level was 48.5ng/ml ($p<0.0001$; Fig. A). C3M levels were significantly increased from an average of 14.6ng/ml in SKG naïve mice to 22.7ng/ml three weeks after β-glucan induction ($p<0.01$) and they were further increased to an average of 30.9ng/ml after eight weeks ($p<0.0001$; Fig. C)). In contrast cartilage turnover reflected by C2M (Fig. B) did not change significantly after β-glucan induction at any time point. There were no significant differences between biomarker levels of BALB/c mice compared to the SKG naïve mice.




**Conclusions:** The turnover of type I, III and V was significantly altered in this mouse model of SpA. This indicates an unbalanced turnover of the interstitial tissue. Levels of C1M and C5M were significantly increased already at week 1 after β-glucan induction, while symptoms were still weak. This suggests that C1M and C5M may be useful to assist early diagnosing. In contrast levels of C2M reflecting cartilage degradation were unaltered upon β-glucan induction, suggesting that cartilage turnover was not significantly affected in this model.
**Disclosure of Interest:** None declared
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# Spondyloarthritis - clinical aspects (other than treatment)

## THU0374 A LONGITUDINAL STUDY OF GUT INFLAMMATION AND THE DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE IN ANKYLOSING SPONDYLITIS

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**Background:** Patients with ankylosing spondylitis (AS) have an increased risk of developing inflammatory bowel disease (IBD). There is however a lack of knowledge regarding the incidence of IBD in AS and what predicts the development from subclinical gut inflammation to IBD.
**Objectives:** To determine the intra-individual variation in fecal calprotectin (FC) over 5 years in relation to AS disease activity, disease manifestations and medication and to study the 5–year incidence of IBD in AS and identify predictors for its' development.
**Methods:** At baseline FC was assessed in 204 AS patients (NY-criteria) without diagnosed IBD. FC was then reexamined in 164 of the patients at the 5-year follow-up. The patients answered questionnaires regarding gastrointestinal symptoms, medication, physical function and disease activity. Ileocolonoscopy was performed at the 5-year follow-up if FC remained ≥200 mg/kg after 3 weeks NSAID-pause. The medical records were checked for colonoscopies, episodes of gut inflammation or diagnose of IBD during the follow-up period.
**Results:** The characteristics of the 164 AS patients [median (IQR)]: 74♀/90♂, age 54 (46–67) ys, symptom duration 27 (18–39) ys, BASDAI 3.2 (1.8–5.2), $ASDAS_{CRP}$ 2.1 (1.3–2.7), BASFI 2.3 (1.0–4.1) and BASMI 3.4 (2.4–4.6).
At the 5-year follow-up FC was elevated (>50 mg/kg) in 63% of the patients, but not associated with gastrointestinal symptoms. In 24% of the patients FC was >200 mg/kg. The intra-individual variation in FC during the 5-year follow-up was less than ±200 mg/mg in 80% (131/164) of the patients. FC was correlated with CRP ($r_S=0.219$; p=0.005), ESR ($r_S=0.172$; p=0.027), $ASDAS_{CRP}$ ($r_S=0.207$; p=0.008), hemoglobin ($r_S=-0.200$; p=0.01), BASMI ($r_S=0.207$; p=0.008) and BASFI ($r_S=0.154$; p=0.048).
Users of NSAIDs had higher FC than non-users [93 (44–215) vs. 40 (23–120) mg/kg; p=0.011], whereas DMARD users had lower FC than non-users [45 (29–87) vs. 110 (40–250) mg/kg; $p<0.001$]. Users of infliximab, adalimumab and golimumab had lower FC than non-users [48 (23–135) vs. 89 (40–210) mg/kg; p=0.022], whereas users of etanercept had higher FC [200 (93–555) mg/kg]. In linear regression DMARD-use (B= -111.6, SE=41.0, p=0.007) and BASMI (B=41.9, SE=10.7, $p<0.001$) remained independently associated with log-transformed FC.
Totally 1.5% (3/204) had been diagnosed with Crohns disease (CD) and 0.5% with lymphocytic colitis at the five-year follow-up. Furthermore 3% had demonstrated a picture of subclinical CD and 2% a picture of subclinical chronic colitis at ileocolonoscopy. A high FC and presence of mucus in diarrhea were the main predictors of the development of CD.
**Conclusions:** FC was elevated in approximately two-thirds of the patients both at baseline and at the five-year follow-up and positively associated with disease activity at both time points. The results supports a link between gut and joint disease in AS.
Use of NSAIDs and etanercept was associated with a higher FC, whereas use of other TNF-blockers and DMARDs was associated with a lower FC. The five-year incidence of CD was 1.5%, and an elevated FC was a main predictor thereof.
**Disclosure of Interest:** None declared
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## THU0375 ASDAS-BASED REMISSION WAS LESS FREQUENT THAN BASDAI-BASED REMISSION, AND BOTH WERE RELATED TO CRP AND SMOKING IN EARLY AXIAL SPONDYLOARTHRITIS. THE DESIR COHORT

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**Background:** Remission is the final goal for treat to target strategy in axial spondyloarthritis (axSpA). No clear definition is currently recognized, but ASDAS-CRP inactive state or BASDAI threshold (1) have been proposed. The frequency of remission using these definitions and factors associated with remission are unknown in early axSpA.
**Objectives:** To evaluate the percentage of patients in remission in early AxSpA, comparing different definitions of remission, and to evaluate factors associated with remission at inclusion in the DESIR cohort and after 24 months.
**Methods:** DESIR is a prospective observational cohort of patients with recent onset (less than 3 years) inflammatory back pain, beginning before 45 years, suggestive of axial SpA. For each of three definitions of remission (ASAS partial remission (PR), ASDAS-CRP less than 1.3 (ASDAS-R), BASDAI less than 3.6 (1) (BASDAI-R)), the ability to detect patients in remission according to the two other definitions was assessed using ROC curves and Areas Under the Curve (AUC). Data at baseline (M0) and M24 were analyzed, to look for factors (clinical, biological and imaging) associated with remission in uni and multivariate analysis by logistic regression.
**Results:** 706 patients were evaluated at M0 and 577 at M24. At M0, the percentage of patients in remission was 4% (PR), 8% (ASDAS) 34% (BASDAI), and at M24: 15%, 24% and 54% respectively, in the whole population and in Amor, ESSG and ASAS classified patients, but lower in mNY patients (data not shown). BASDAI less than 3.6 detected best patients in PR and ASDAS-R, with AUC of 0.84 and 0.86 respectively. In univariate analysis at M0, lower ESR and CRP, DKK-1, low BMI, male gender, absence of psoriasis, less smoking, HLA-B27 positivity, ASAS criteria fulfillment, positive sacro iliac imaging, less analgesics use and less subsequent use of anti TNF at M24 were associated with remission (ASDAS-R, BASDAI-R). No association was found with age, disease duration, enthesitis, uveitis, IBD, NSAID use, mSASSS. In multivariate analysis, remission was associated with lower ESR, less smoking, use of analgesics. At M24, low ESR and CRP, female gender, less smoking, less NSAID use, lower NSAID score, ASAS criteria fulfillment, lower biologics use and lower systemic steroid use were associated with remission in univariate analysis. In multivariate analysis, remission was associated with less smoking, less analgesics, ASAS clinical arm fulfillment, less NSAIDs (ASDAS-R), low CRP (ASDAS-R), low BMI (BASDAI-R) (Table 1).

Table 1

| Remission | ASDAS-R ASDAS <1.3 | r, p | BASDAI-R BASDAI <3.6 | r, p |
|---|---|---|---|---|
| M0 (N=706) | CRP | –0.59*** | ESR | –0.04* |
| | Smoking | –1.5** | Smoking | –0.93* |
| | Analgesics | 1.55*** | Analgesics | 1.39** |
| M24 (N=577) | CRP | –0.6*** | BMI | –0.14** |
| | Smoking | –1.08* | Smoking | –1.16** |
| | ASDAS clinical | 1.76* | ASAS clinical | 1.28* |
| | NSAIDs | –1.4** | | |
| | Analgesics | –2.02*** | Analgesics | –1.74*** |

**Conclusions:** In this population suggestive of early SpA, acute phase reactants and analgesics were associated with remission at baseline and M24, but smoking appears as a major marker of disease activity and remission in early AxSpA.
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**Acknowledgement:** The DESIR cohort is supported by an unrestricted grant from PFIZER France.
**Disclosure of Interest:** None declared
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## THU0376 PREVALENCE OF PERIPHERAL AND EXTRA-ARTICULAR DISEASE IN ANKYLOSING SPONDYLITIS VERSUS NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A META-ANALYSIS

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**Background:** Axial spondyloarthritis (axSpA) is a common chronic inflammatory disease with predominantly axial symptoms. Besides axial symptoms, the disease is characterized by peripheral (arthritis, enthesitis, dactylitis), and extra-articular (uveitis, psoriasis, inflammatory bowel disease (IBD)) disease manifestations. A much debated question is whether the radiographic form (defined as ankylosing spondylitis or AS) and the non-radiographic form (nr-axSpA) of axSpA represent subsets of the same disorder or if they are distinct disease entities (1–4). Hypothesizing that AS and nr-axSpA reflect subsets of a single disease entity and have similar disease burden, we performed a meta-analysis of published studies of axial SpA in order to assess if the prevalence of peripheral and extra-articular disease manifestations is similar in AS and nr-axSpA.
**Objectives:** The objective of this meta-analysis was to assess the prevalence of peripheral and extra-articular disease manifestations in AS and nr-axSpA.
**Methods:** We performed a systematic literature search to identify publications describing the prevalence of peripheral and extra-articular disease manifestations in patients with AS and nr-axSpA. We assessed the risk of bias, between-study heterogeneity and extracted data. Pooled prevalence and prevalence differences were calculated.
**Results:** Eight studies including 2236 AS patients and 1242 nr-axSpA patients were included. Seven out of 8 studies were longitudinal cohort studies. There was a male dominance in AS (70.4%; 95% CI 64.4–76.0%) but not in nr-axSpA (46.8%; 95% CI 41.7–51.9), which was independent from HLA-B27 prevalence. HLA-B27 prevalence was similar in AS (78.0%; 95% CI 73.9–81.9%) and nr-axSpA (77.4%; 95% CI 68.9–84.9%). The pooled prevalence of arthritis (29.7% (95% CI 22.4–37.4%) versus 27.9% (95% CI 16.0–41.6%)), enthesitis (30.4% (95% CI 3.7–65.8%) versus 34.1% (95% CI 4.7–71.0%)), dactylitis (6.0% (95% CI 4.7–7.5%) versus 6.0% (95% CI 1.9–12.0%)), psoriasis (10.2% (95% CI 7.5–13.2%) versus 10.9% (95% CI 9.1–13.0%)) and IBD (4.1% (95% CI 2.3–6.5%) versus 6.4% (95% CI 3.6–9.7%)) were similar in AS and nr-axSpA. The pooled uveitis prevalence was higher in AS (23.0% (95% CI 19.2–27.1%)) than in nr-axSpA (15.9% (95% CI 11.8–20.4%)).
**Conclusions:** Peripheral and extra-articular manifestations are equally prevalent in AS and nr-axSpA, except for uveitis, which is slightly more prevalent in AS. These data support the concept that AS and nr-axSpA belong to one pathogenic entity with similar disease manifestations.
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**Disclosure of Interest:** None declared
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## THU0377 ARE PATIENTS WITH ANKYLOSING SPONDYLITIS REALLY DIFFERENT FROM NON-RADIOGRAPHIC AXIAL SPA: RESULTS FROM CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS REGISTRY

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**Background:** Only a few european studies have shown that most of the clinical features and assessments of axial spondyloarthritis (ax-SpA) are similar in patients with/without radiographic changes[1]. However, some differences might be observed which might be prognostic factors of more severe disease.
**Objectives:** To describe the demographic, clinical, patient reported outcomes (PROs) and treatment characteristics of ax-SpA population in the Corrona registry, a large national cohort of psoriatic arthritis (PsA)/SpA patients in the US.
**Methods:** The study included ax-SpA patients enrolled in the registry between 3/2013–7/2015. Ax-SpA population was further stratified into two cohorts: ankylosing spondylitis (AS) and non-radiographic Axial SpA (nr-axSpA) based on the NY modified criteria for AS (1984) and ASAS criteria for ax-SpA without sacroiliac radiographic changes respectively. Descriptive analyses on patient characteristics (demographics, clinical, patient reported outcomes and treatment) were evaluated at enrollment into the registry. Chi-square and t-tests were used for continuous and categorical variables respectively to evaluate the differences.
**Results:** Of the 407 patients identified with ax-SpA, 310 were diagnosed with AS and 97 with nr-axSpA. Patients with AS were slightly older (mean: 49yrs vs 44 yrs) and mostly males (65% vs 57%) compared to patients with nr-axSpA respectively. Both cohorts had similar functional disability measured by health assessment questionnaire, HAQ (mean: 0.6 vs 0.6), quality of life measured by EQ-5D (mean: 0.7 vs 0.7) and mean percentage of overall activity impairment measured by WPAI (26.8% vs 31.6%). About 7.6% of AS patients had fibromyalgia compared to 9.7% of nr-axSpA (p-value: 0.5). While clinical features (BASDAI, BASFI, ASDAS) did not differ between the AS and nr-axSpA patients, signs of inflammation measured by acute phase reactants were significantly higher in patients with AS compared to nr-axSpA (mean ESR: 14.4 vs 8.9 respectively, $p<0.05$) (figure 1), which are consistent with other national cohorts (1). In addition, patients with nr-axSpA

**Figure 1: Clinical features in AS and nr-AxSpA patients in Corrona**




were more likely to have enthesitis (47.4% vs. 29.0%) and dactylitis (12.4% vs. 9.0%) respectively. Although there were some differences in the history of biologic use (65% and 74% resp.), current biologic use (61.3% and 63.9%) and use of prednisone (5.5% and 6.2%) was similar in both groups.

**Conclusions:** This is the first characterization of axial SpA patients from the US Corrona registry with stratification into ankylosing spondylitis and non-radiographic axial SpA. Patients with nr-axSpA were younger and more likely to be female compared to patients with AS. Both groups had similar clinical characteristics, quality of life, disability and work impairment.

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## THU0378 HOW FREQUENT WERE PATIENT REPORTED FLARES IN ANKYLOSING SPONDYLITIS PATIENTS BEFORE THE WIDE USE OF ANTITNF AND WHAT IS THE VALIDITY OF PATIENT REPORTED FLARES? A CROSS-SECTIONAL ANALYSIS OF 234 PATIENTS

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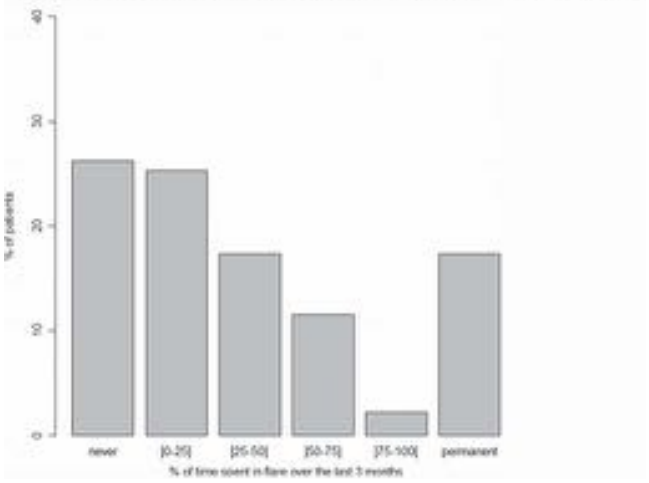
**Background:** Axial Spondyloarthritis (axSpA) is characterized by alternated periods of flares and remission. This fluctuating disease activity varies from one patient to another in terms of symptom intensity and flares frequency and may lead to poor outcomes.

**Objectives:** The objective of this study was to assess the frequency of patient reported flares, and the validity of this concept through their related factors and through the relation between time spent in flare and disease activity assessed by BASDAI.

**Methods:** This was a cross-sectional study in 2004 from the Canadian FOllow-up Research Cohort of Ankylosing SpondyliTis (FORCAST). Participants had definite Ankylosing spondylitis (AS) according to modified New-York criteria. Current flare status (yes/no), number of flares over the past 3 months and average duration of a flare (in weeks) were assessed by self-report. Disease activity was assessed by BASDAI and BASFI was also collected. Only patients with complete data for flare questions were included in this analysis. Descriptive statistics were performed and univariate and multivariate logistic regression analysis compared patients with at least 1 flare over 3 months to those without flares, for disease activity, treatment, and demographic characteristics. Association between disease activity and percentage of time spent in flare was assessed by Spearman correlation.

**Results:** 234 patients were analyzed including 169 (72.2%) men, with a mean age of 45.5 (±11.8) years and a mean disease duration of 21.7 (±11.7) years. Their mean BASDAI and BASFI (0–10) were respectively 4.4 (±2.3) and 3.4 (±2.6); 55 (23.5%) were taking conventional disease modifying drugs and 18 (7.69%) were taking antiTNF. Overall, 117 (50%) of patients were currently in flare and 174 (74.3%) reported at least one past flare. In those with flares, the median number of flares per patient over 3 months was 3 (interquartile range, 2, 4.5), their median duration was 2 weeks (1, 3) and the median time spent in flare was 25% (0, 66.7) over 3 months (figure). In multivariate analyses patients flaring had

**Distribution of patients according to the percentage of time spent in flare over the last 3 months**




a significantly higher BASDAI (OR=1.84, p<0.001), were more often treated by NSAIDs (OR=6.65, p=0.02) and less often by anti-TNF (OR=0.16, p<0.01) than the no flare group. Patients reporting only past flares also had higher BASDAI (OR=1.59, p<0.01) and were less often treated by anti-TNF (OR=0.14, p=0.01). There was a significant correlation between the percentage of time spent in flare and the BASDAI score (r=0.58, p-value <0.0001).

**Conclusions:** In this cross-sectional study assessment of patients in 2004 little treated with anti-TNF, flares were very frequent and long; patients reported spending a mean of 25% of their time in flare. As expected patients reporting at least one recent flare had higher disease activity, were more likely to be taking NSAIDs and were less likely to be taking anti-TNF. The time spent in flare was well-correlated with BASDAI. These results indicate the validity of the concept of flares as assessed by a single question in axSpA.

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## THU0379 CLINICAL DISEASE ACTIVITY MEASURES ARE ASSOCIATED WITH RADIOGRAPHIC SPINAL PROGRESSION IN EARLY AXIAL SPONDYLOARTHRITIS

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**Background:** It has been shown in the past that elevated C-reactive protein (CRP) [1] and the composite Ankylosing Spondylitis Disease Activity Score (ASDAS) [2,3] are associated with radiographic spinal progression in axial spondyloarthritis (axSpA). It is not clear, however, whether patient-reported measures of disease activity might also play a predictive role.

**Objectives:** To investigate the association between patient-reported measures of disease activity and radiographic spinal progression over two years in early axSpA.

**Methods:** Altogether 178 patients with definite axSpA (100 with ankylosing spondylitis and 78 with non-radiographic axSpA) from the German Spondyloarthritis Inception Cohort (GESPIC) were included in the current study. Spinal radiographs (cervical spine lateral views, lumbar spine lateral and anteroposterior views) were scored according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) system and for the presence of syndesmophytes. Clinical and lab data were collected at baseline and every 6 months thereafter. Time-averaged values (over 2 years) of the patient global assessment of disease activity (PG), BASDAI and its components, CRP and CRP-based ASDAS, were calculated.

**Results:** In the logistic regression analysis there was a significant association between time-averaged patient global and syndesmophyte formation (table): the adjusted odds ratio (OR) was 1.30 (1.01–1.69) meaning a 30% increase of the chance for new syndesmophytes formation over two years with an increase of PG by 1 point (on a 0–10 scale). The time-averaged BASDAI demonstrated no significant association with radiographic spinal progression, but duration and severity of morning stiffness were both significantly associated with syndesmophytes formation with a similar strength of association as the patient global (table). Similar trends although not always significant were observed for the mSASSS worsening by 2 points and more after two years. CRP and ASDAS did show an already known association with radiographic spinal progression in early axial SpA.

**Conclusions:** Higher patient global assessment of disease activity, duration and severity of morning stiffness are clinical parameters, which are associated with

**Table:** Crude and adjusted* odds ratios for the association between disease activity parameters and radiographic spinal progression in patients with early axial spondyloarthritis.

| Disease activity measure (time-averaged) | Crude OR (95% CI) | Adjusted OR (95% CI)* |
|---|---|---|
| *Outcome: syndesmophyte formation / progression over two years* | | |
| BASDAI, 0-10 | 1.24 (0.98-1.57) | 1.25 (0.94-1.65) |
| • Fatigue | 1.08 (0.87-1.34) | 1.11 (0.85-1.44) |
| • Back pain | 1.23 (0.98-1.54) | 1.22 (0.94-1.60) |
| • Arthralgia / arthritis | 1.12 (0.93-1.35) | 1.14 (0.91-1.43) |
| • Enthesitis | 1.19 (0.99-1.43) | 1.18 (0.95-1.46) |
| • Morning stiffness duration | **1.30 (1.05-1.64)** | **1.36 (1.00-1.85)** |
| • Morning stiffness severity | **1.27 (1.05-1.54)** | **1.25 (1.00-1.57)** |
| Patient global, 0-10 | **1.28 (1.03-1.57)** | **1.30 (1.01-1.69)** |
| CRP, mg/l | **1.07 (1.02-1.11)** | **1.07 (1.01-1.13)** |
| $ASDAS_{CRP}$ | **2.62 (1.46-4.68)** | **2.45 (1.26-4.77)** |
| *Outcome: mSASSS progression by 22 points over two years* | | |
| BASDAI, 0-10 | 1.04 (0.85-1.29) | 1.12 (0.87-1.45) |
| • Fatigue | 0.94 (0.78-1.14) | 0.99 (0.79-1.24) |
| • Back pain | 1.07 (0.88-1.29) | 1.13 (0.90-1.43) |
| • Arthralgia / arthritis | 0.98 (0.82-1.16) | 1.05 (0.85-1.29) |
| • Enthesitis | 1.03 (0.88-1.22) | 1.06 (0.87-1.29) |
| • Morning stiffness duration | **1.19 (0.96-1.47)** | **1.33 (1.02-1.74)** |
| • Morning stiffness severity | 1.16 (0.98-1.37) | 1.21 (0.99-1.48) |
| Patient global, 0-10 | 1.12 (0.93-1.34) | 1.21 (0.97-1.51) |
| CRP, mg/l | **1.05 (1.01-1.09)** | 1.04 (0.99-1.08) |
| $ASDAS_{CRP}$ | **1.64 (1.03-2.62)** | **1.80 (1.04-3.13)** |

*Adjusted for the presence of syndesmophytes at baseline, smoking status and NSAIDs intake score over 2 years.

more radiographic spinal progression (syndesmophytes formation) in patients with early axial spondyloarthritis.

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**Disclosure of Interest:** None declared

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## THU0380 A SINGLE DETERMINATION OF C-REACTIVE PROTEIN DOES NOT SUFFICE TO DECLARE A PATIENT WITH A DIAGNOSIS OF AXIAL SPA "CRP-NEGATIVE"

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**Background:** Four TNF-inhibiting biologicals (TNFi) have been approved by European regulatory authorities for active non-radiographic (nr) and radiographic (r; also termed ankylosing spondylitis) axial (ax) SpA.[1–4] To be eligible to receive TNFi treatment, nr-axSpA patients (pts) must have either a positive MRI showing inflammation of the sacroiliac joints or a positive CRP assessment (CRP >upper limit of normal [ULN]). CRP is also considered a predictor of treatment response in axSpA.[5] However, many axSpA pts are classed as CRP-negative despite levels close to the ULN.

**Objectives:** These analyses investigated the reproducibility of negative CRP test results in pts with active axSpA who were intolerant to or had insufficient response to NSAID treatment.

**Methods:** The 204-week (wk) phase 3 RAPID-axSpA trial (NCT01087762) evaluated the efficacy and safety of certolizumab pegol (CZP) in axSpA pts, and was double-blind and placebo (PBO)-controlled for the initial 24 wks. At screening, pts were either MRI or CRP (>ULN [7.9mg/L]) positive. PBO-treated pts continued on stable conventional medication and were re-randomized to CZP at Wk16 (ASAS20 non-responders) or Wk24 (ASAS20 responders). These analyses considered CRP data for all PBO-randomized (n=107) pts up until re-randomization to CZP (Wk16 or Wk24). CRP was assessed at screening, baseline and at 9 time points to Wk24. Descriptive methods and linear mixed models (LMM) were used to investigate time trends and variability of CRP, and empirical best linear unbiased prediction (EBLUP) to estimate prediction limits of CRP. Log(CRP+1) transformation was used for modelling.

**Results:** Of 106 pts with baseline CRP assessments, 26 (25%) had negative CRP tests at baseline, of whom 13 (50%) had ≥1 positive CRP test to Wk16 (Table). Of the 80/106 (75%) pts with positive CRP at baseline, 25 (31%) had ≥1 negative CRP test to Wk16.

LMM did not reveal statistically significant changes in mean CRP to Wk24 in pts randomized to PBO. EBLUP analysis showed that even for a pt with a CRP score of 2mg/L at a single evaluation, the 80% prediction interval for the next assessment (4 wks apart from the first) included 7.9mg/L, indicating that there was >10% chance of a positive CRP test upon re-evaluation. The 4-wk interval prior to re-evaluation was selected because residual autocorrelation was observed between assessments at shorter intervals.

The EBLUP result was supported by descriptive evaluations, with 10.8% of CRP assessments ≤3mg/L testing positive (>7.9mg/L) at their subsequent assessment (4 wks apart from the first). This increased to 53.1% when the original CRP assessment was between ≥6 and ≤7.9mg/L.

**Table:** Likelihood of finding positive CRP tests after an initial negative CRP test

| Proportion of subsequent* CRP-tests positive | Screening CRP test negative (n=26) | Baseline CRP test negative (n=26) |
|---|---|---|
| 0% | 42% | 50% |
| >0–20% | 0% | 4% |
| >20–40% | 23% | 15% |
| >40–60% | 12% | 15% |
| >60–80% | 8% | 4% |
| >80–<100% | 4% | 8% |
| 100% | 12% | 4% |

*CRP was assessed at screening, baseline and at 6 time points post-baseline to Wk16.
16 patients had negative CRP tests at both screening and baseline assessments.
Positive: CRP >7.9mg/L; Negative: CRP ≤7.9mg/L.

**Conclusions:** In axSpA pts with a clinical indication to initiate TNFi treatment, but with a negative CRP test (<ULN), the CRP test should be repeated at least once after a number of weeks, since there is a substantial chance of finding a positive result at subsequent testing.

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## THU0381 THE INCIDENCE OF HERPES ZOSTER INFECTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: ANALYSIS FROM KOREAN NATIONAL HEALTH INSURANCE SERVICE–COHORT SAMPLE DATABASE

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**Background:** Herpes zoster (HZ) infection occurs more commonly in patients with underlying autoimmune disease, partially due to immunosuppressive treatment. However, little is known about the incidence of HZ in patients with ankylosing spondylitis (AS), especially who were treated with conventional disease modifying anti-rheumatic drugs (cDMARDs) or TNF inhibitors.

**Objectives:** The aims of our study were to investigate the incidence of HZ in AS patients and to determine whether use of cDMARDs or TNF inhibitors could increase the risk of HZ infection in AS patients.

**Methods:** We used database of the Korean National Health Insurance Service–Cohort Sample (1,025,340 individuals) from 2002 to 2013, which was age-, gender-, district- and income stratified random sample. We evaluated HZ incidence among three groups (non-DMARD users, cDMARDs [sulfasalazine, methotrexate] users and TNF inhibitor users) based on drug exposure episodes. Cox proportional hazard analysis was performed to investigate the association between treatment group and HZ infection.

**Results:** Among 1,079 patients with AS, we identified 54 HZ infections. Crude incidence rates were 11.0 per 1000 patient-years (95% CI, 8.2–14.3) in all AS patients; 9.1 (95% CI, 6.2–12.8) in non-DMARD users, 16.7 (95% CI, 9.1–28.0) in

Table 1. Hazard ratio of herpes zoster in ankylosing spondylitis patients according to the treatment regimens

| Exposures | Crude hazard ratio (95% CI) | Adjusted hazard ratio (95% CI)[a] |
|---|---|---|
| Non-DMARD | 1.00 [Reference] | 1.00 [Reference] |
| Conventional DMARD | 3.11 (1.47–6.58) | 3.70 (1.68–8.14) |
| TNF inhibitors | 2.60 (1.09–6.19) | 3.52 (1.37–9.01) |
| Etanercept | 2.57 (0.84–7.91) | 3.93 (1.21–12.76) |
| Infliximab | 1.71 (0.23–12.75) | 2.00 (0.27–15.04) |
| Adalimumab | 2.53 (0.56–11.39) | 3.40 (0.66–17.53) |
| Switching | 6.43 (0.82–50.40) | 6.27 (0.72–54.77) |

[a]Adjusted for gender, age and baseline corticosteroid use.

cDMARDs users and 14.1 (95% CI, 6.1–27.8) in TNF inhibitor users, respectively. Adjusted hazard ratio (HR) of HZ infection was higher in cDMARDs users and TNF inhibitor users than in non-DMARD users (Table). In subgroup analysis, TNF inhibitor increased the risk of HZ infection more significantly in female (adjusted HR =8.01; 95% CI, 1.97–32.54) and patients older than 50-yr (adjusted HR =7.29; 95% CI, 1.88–28.21), but not in patients exposed to baseline corticosteroid (95% CI, 0.53–32.84) compared to non-DMARD users.

**Conclusions:** The incidence of HZ in AS patients was 11.0 per 1000 patient-years which is similar to the previously reported incidence in general Korean population. cDMARDs or TNF inhibitors increased the risk of HZ infection in AS patients, especially in female and older patients, which can be considered as target of HZ vaccination in AS population.

**Disclosure of Interest:** None declared

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## THU0382 DEVELOPMENT OF SPA-FEATURES IN PATIENTS WITH CHRONIC BACK PAIN OVER A ONE-YEAR COURSE: DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE)-COHORT

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**Background:** Little is known on the development of SpA-features over time in patients with recent onset chronic back pain (CBP).

**Objectives:** To explore whether patients with suspicion of axial spondyloarthritis (axSpA) develop spondyloarthritis (SpA)-features over time in the SPACE-cohort, and to study the effect of gaining features on the clinical diagnosis and classification according to the Assessment of SpondyloArthritis international Society (ASAS)-criteria for axSpA.

**Methods:** SPACE is an inception cohort study in which CBP pts (≥3 months, ≤2 years, onset <45 years) from various rheumatology centres across Europe are included. Baseline (BL) and one-year (FU) data were used for this study. Pts underwent a full diagnostic work-up consisting of MRI and radiographs of the sacroiliac joints (MRI-SI and X-SI), acute phase reactants, HLA-B27, and assessment of all other SpA-features. For the purpose of this study positive SpA-features were accumulated according to the principle of "once a feature always a feature" meaning pts were not able to "lose" features over time. Total number of SpA-features was calculated excluding sacroiliac imaging and HLA-B27 status. Clinical diagnosis (axSpA yes/no) of pts was provided by the treating rheumatologist with use of local reading and the ASAS-criteria for axSpA (based on central scoring and agreement of 2/3 readers) were used for classification.

**Results:** A total of 270 pts with CBP with both baseline and one-year follow-up visits were included: 36.7% were male, mean age (SD) at inclusion was 31.2 (8.0) years, mean number of SpA-features (SD) at BL and one-year FU were 2.8 (1.5) and 3.5 (1.6), respectively. After one year 49.3% of pts had gained one or more features. Most common features were IBP (BL: 77.0%, FU: 88.2%), good response to NSAIDs (BL: 48.5%, FU: 70.6%), elevated CRP/ESR (BL: 29.5%, FU: 43.3%), and positive family history for SpA (BL: 48.9%, FU: 52.6%).

For 16 out of the 270 pts information on diagnosis at either BL or FU was missing. In the remaining 254 patients, rheumatologists diagnosed 150 (59.1%) and 66 (26.0%) patients with axSpA and no axSpA at both time points, respectively. In 15.0% (38/254) of patients the diagnosis changed; 16 patients with no axSpA diagnosis at BL were diagnosed with axSpA at FU of which 11/16 (68.8%) had acquired one or more features. In 22 patients with axSpA at BL rheumatologists reconsidered their diagnosis at FU. In the 150 patients diagnosed with axSpA, 108/150 (72%) of patients already fulfilled the ASAS-criteria at BL and 79 (52.7%) patients gained a minimum of one feature, which led to a new the axSpA classification for 9 patients at FU.

**Figure 1.** Number of acquired SpA-features (after medical history taking, physical examination and measurement of acute phase reactants; excluding sacroiliac imaging and HLA-B27 status) at one-year follow-up (FU) in patients with and without axSpA diagnosis.

| Diagnosis | Number of features gained after one year | | | | | |
|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | >3 | Total |
| AxSpA baseline and FU | 71 | 50 | 18 | 9 | 2 | 150 |
| AxSpA only at FU | 5 | 9 | 2 | - | - | 16 |
| AxSpA only at BL | 11 | 8 | 2 | 1 | - | 22 |
| No AxSpA baseline and FU | 40 | 23 | 2 | 1 | - | 66 |
| Total | 127 | 90 | 24 | 11 | 2 | 254 |

**Conclusions:** In patients with CBP of short duration almost half developed at least one new SpA-feature within one year, however the impact on diagnosis and classification was limited.

**Disclosure of Interest:** None declared

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## THU0383 DOES CHANGE IN DISEASE ACTIVITY OVER ONE YEAR RESULT IN CHANGE IN HEALTH-RELATED QUALITY OF LIFE IN AXIAL SPONDYLOARTHRITIS PATIENTS?

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**Background:** Treatment target of patients with axial Spondyloarthritis (axSpA) is based on assessment of disease activity (remission) while the ultimate goal is improvement of Health Related Quality of Life (HRQoL). Therefore it is important to know if a change in disease activity is indeed related to a change in HRQoL.

**Objectives:** To assess the association between the change in disease activity and change in HRQoL between baseline and one year in patients with early axSpA.

**Methods:** The Spondyloarthritis Caught Early (SPACE) study is a prospective cohort study in patients with chronic back pain (≥3 months, ≤2 years, onset <45 years) recruited from various rheumatology centres across Europe. The 36-item Short-Form (SF-36) was completed by patients to assess HRQoL at baseline and 1 year. After recoding and recalibration, raw scale scores were converted in scale scores ranging from 0 (worst) to 100 (best). Physical (PCS) and Mental Component Summary (MCS) scores were calculated by adjusting converted scale scores for country, gender, and age, and were compared to the general population mean of 50 with a standard deviation (SD) of 10. The Ankylosing Spondylitis Disease Activity Score (CRP based; ASDAS) was calculated to assess disease activity. Linear regression models were made with change of ASDAS between baseline and 1 year (ΔASDAS) as a determinant and the change of PCS (ΔPCS) or MCS (ΔMCS) as an outcome. The models were adjusted for age. Fulfilment of the imaging or clinical arm and gender were tested for interaction.

**Results:** A total of 86 patients fulfilled the ASAS axSpA criteria; 50 patients fulfilled the clinical arm and 36 patients the imaging arm. Mean age was 29.3 years (SD 7.7), 48.8% was male, and mean duration of back complaints was 13.8 months (SD 7.4). Patients had a mean PCS of 27.0 (SD 15.8, IQR 17.8–38.1), mean MCS of 49.3 (SD 13.0, IQR 40.0–59.4), and mean ASDAS of 2.4 (SD 1.0, IQR 1.6–3.0) at baseline. At 1 year the mean PCS increased to 36.0 (SD 13.9) and the MCS remained stable at 49.7 (SD 12.1), and mean ASDAS decreased to 2.0 (SD 0.8). As the MCS was not different from the general population, only the effect of ASDAS on PCS was determined. In the univariable model (Figure 1), a decrease of 1 unit of ASDAS between baseline and 1 year resulted in an increase of 9.7 (SE 1.5) in the PCS score over 1 year. Fulfilment of the clinical or imaging arm and gender were effect modifiers (2-way interaction) in the model for PCS ($p=0.10, R^2=38.6\%$). Results were stratified for these variables. The effect of ΔASDAS on ΔPCS was most pronounced in men (fulfilling the imaging arm (-15.8; SE 2.7) and fulfilling the clinical arm (-11.8; SE 4.0)). It was still significant but to a lesser extent in women fulfilling the clinical arm (-6.9; SE 2.1) but not in women fulfilling the imaging arm (-1.2; SE 4.8).

**Figure 1:** Association between the change in ASDAS and the change in Physical (PCS) at baseline and 1 year among axial Spondyloarthritis patients in the SPACE cohort (n=86)

| | n | Coefficient | Standard error | P-value |
|---|---|---|---|---|
| **ΔPCS** | | | | |
| **Univariable model** | | | | |
| ΔASDAS | 86 | -9.7 | 1.5 | <0.001 |
| **Model for gender and ASAS classification** | | | | |
| *Men fulfilling the clinical arm* | | | | |
| ΔASDAS | 18 | -11.8 | 4.0 | 0.010 |
| *Men fulfilling the imaging arm* | | | | |
| ΔASDAS | 24 | -15.8 | 2.7 | <0.001 |
| *Women fulfilling the clinical arm* | | | | |
| ΔASDAS | 32 | -6.9 | 2.1 | 0.002 |
| *Women fulfilling the imaging arm* | | | | |
| ΔASDAS | 12 | -1.2 | 4.8 | 0.815 |

Abbreviations: Physical Component Summary (PCS), Ankylosing Spondylitis Disease Activity Score, CRP-based (ASDAS)

**Conclusions:** Although improvement in ASDAS is correlated to improvement in the physical component of HRQoL, the impact of this correlation largely depends on gender and arm of the ASAS criteria: impact is highest in men fulfilling the imaging arm.

**Disclosure of Interest:** None declared

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## THU0384 PERFORMANCE OF THE ASAS CLASSIFICATION CRITERIA FOR AXIAL AND PERIPHERAL SPONDYLOARTHRITIS – A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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**Background:** The Assessment of SpondyloArthritis international Society (ASAS) has developed and validated classification criteria for axial spondyloarthritis (axSpA) and peripheral SpA (pSpA). Following their release, the ASAS criteria

have been "challenged" in different cohorts, thus warranting a review of the so-far accumulated evidence on the criteria validity and applicability.
**Objectives:** To summarize the evidence on the performance of the ASAS classification criteria for axSpA (also imaging and clinical arm separately), pSpA and the entire set of SpA, when tested against the Rheumatologist's diagnosis ("reference standard").
**Methods:** A systematic literature review was performed to identify eligible studies. Only studies with full-text available were included and, thereafter, raw data was obtained from the authors of the selected publications. A meta-analysis was performed to obtain pooled estimates for sensitivity, specificity, positive (LR+) and negative (LR-) likelihood ratios, by fitting random effects models. With a series of sensitivity analyses we assessed the possible effects of: i) target population (original validation study inclusion criteria *vs* different inclusion criteria); iii) setting (hospital *vs* community); and iii) disease duration (<2 years *vs* ≥2 years).
**Results:** Of the 1,647 retrieved articles, 8 fulfilled the inclusion criteria (N=5,042 patients). The entire set of the ASAS SpA criteria yielded a high pooled sensitivity (73%) and specificity (88%), but with limited available data (Table). Similarly good results were found for the axSpA criteria (sensitivity: 82%; specificity: 88%) in a larger number of studies. Splitting the axSpA criteria in "imaging arm only" and "clinical arm only" resulted in much lower sensitivity (30% and 23% respectively) but retaining very high specificity (97% and 94% respectively). The "imaging arm only" compared to the "clinical arm only" had a much higher LR+ (9.6 *vs* 4.5, respectively). The pSpA criteria were less tested than the axSpA and have shown a similarly high pooled specificity (87%) but lower sensitivity (63%). Sensitivity analyses yielded consistently good results for the axSpA criteria (sensitivity (range): 78% - 86%; specificity (range): 86% - 93%). For pSpA there were few studies therefore hampering sensitivity analyses.

**Table.** Results of the meta-analysis

| | Number of studies | Number of patients | LR+ (95% CI) | LR− (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| ASAS SpA criteria | 2 | 1,750 | 6.3 (3.2; 12.4) | 0.31 (0.13; 0.70) | 0.73 (0.47; 0.89) | 0.88 (0.81; 0.93) |
| ASAS pSpA criteria | 1 | 749 | 4.7 (3.5; 6.3) | 0.43 (0.30; 0.62) | 0.62 (0.47; 0.76) | 0.87 (0.81; 0.91) |
| ASAS axSpA criteria | 6 | 4,293 | 8.9 (3.8; 12.4) | 0.19 (0.15; 0.27) | 0.82 (0.76; 0.87) | 0.88 (0.79; 0.94) |
| axSpA criteria (imaging arm +/- clinical arm) | 5 | 3,426 | 13.6 (4.8; 38.7) | 0.45 (0.37; 0.56) | 0.57 (0.47; 0.66) | 0.96 (0.88; 0.99) |
| axSpA criteria (clinical arm +/- imaging arm) | 5 | 3,426 | 6.0 (2.9; 12.4) | 0.56 (0.43; 0.72) | 0.49 (0.34; 0.64) | 0.92 (0.82; 0.96) |
| axSpA criteria (imaging arm only) | 5 | 3,426 | 9.8 (4.4; 20.7) | 0.72 (0.59; 0.88) | 0.26 (0.16; 0.40) | 0.97 (0.94; 0.99) |
| axSpA criteria (clinical arm only) | 5 | 3,426 | 4.5 (2.3; 8.8) | 0.81 (0.72; 0.91) | 0.23 (0.17; 0.29) | 0.94 (0.89; 0.96) |

**Conclusions:** Accumulated evidence from more than 5,000 patients confirms the good performance of the various ASAS SpA criteria as tested against the Rheumatologist's diagnosis. The clinical and imaging arm have high specificity but lack sensitivity if applied separately, indicating that the full set of axSpA criteria is the preferred set.
**Disclosure of Interest:** None declared
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## THU0385 PATIENT AND PHYSICIAN AGREEMENT IN ALL BATH ANKYLOSING SPONDYLITIS DISEASE ACTIVITY INDEX QUESTIONS IS EXCELLENT EXCEPT FOR ENTHESITIS

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**Background:** The BASDAI is a validated and widely used instrument to assess disease activity in SpA. Despite being a self-administered questionnaire, in daily practice, physicians often ask the questions themselves to the patients. To the authors best knowledge no data has been reported evaluating the agreement between patient and physician for the BASDAI.
**Objectives:** To assess the agreement between patients and physicians reported BASDAI in axial SpA patients in daily practice.
**Methods:** Patients with axial SpA according to the treating rheumatologist were included. First, patients were asked to fill out the BASDAI questionnaire in the waiting room. Thereafter, and being unaware of the results reported by the patients, the rheumatologist collected another BASDAI by reading out loud the questions to the patient and giving explanations if needed. Agreement for the total score and for each question was calculated by the intraclass correlation coefficient and its 95%CI. Evaluation of the agreement for the axial BASDAI (i.e. removing questions 3 and 4) was performed identically.
**Results:** Fifty patients were included, aged 44 (±10) y and 32 (64%) males. Mean disease duration was 15 (±10) y and among them 34 (69,4%) had a radiographic sacroiliitis.
Agreement between patient and physician was excellent both for the BASDAI and axial BASDAI: ICC 0.91 [95% CI, 0.84–0.95] and ICC 0.94 [95% CI, 0.90–0.97], respectively. The lowest agreement was found for question 4 (i.e. referring to enthesitis) with an ICC [95%CI] =0.51 [0.28 – 0.69].
**Conclusions:** An excellent agreement was found between patients and physicians for the BASDAI and its axial version. However, the question for enthesitis yielded only a moderate agreement, even in a group of patients with long-standing disease, and therefore used to fill this questionnaire. This should encourage physicians to use BASDAI as a self-administered questionnaire.
**Acknowledgement:** This research was conducted while the first author Liana Ghukasyan was an ARTICULUM Fellow.
**Disclosure of Interest:** None declared
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## THU0386 THE ASSOCIATION OF SERUM TRAIL LEVELS AND METABOLIC PARAMETERS IN PATIENTS WITH AS AND PSA

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**Background:** Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL), is a pro-apoptotic, multi-functional cytokine.Several studies have suggested that autoimmun diseases, diabetes mellitus, hyperlipidemia and cardiovascular diseases were associated with circulating TRAIL concentrations.
**Objectives:** The aim of this study was to investigate, whether TRAIL levels were associated with metabolic features in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA).
**Methods:** We compared the relationship between the serum levels of TRAIL with body mass index, waist circumference, fasting plasma glucose, insulin, HOMA, hemoglobin A1C, cholesterol levels in 53 patients with AS, 42 patients with PsA and 53 healthy controls. We also analysed the association ofTRAIL with inflammatory parameters (CRP, ESR, TNF-α)and disease acitivity (BASDAI, BASFI, DAS28-ESR). None of the patients included in this study had diabetes mellitus or CVD.
**Results:** Serum levels of TRAIL were not different in patients with PsA (5,06±3,23 pg/ml), AS (4,36±2,49 pg/ml) and HC (3,85±2,2 pg/ml, *p=0,155*).Serum TRAIL had a direct and significant correlation with waist circumference (*p=0,005*), TNF-α (*p=0,000*) and CRP (*p=0,021*).When we analysed the results in patients with AS;serum TRAIL levels directly correlated with TNF-α (*p=0,003*),LDL (*p=0,041*) and total cholesterol (*p=0,026*).Serum TRAIL levels were higher in HLAB-27 positive patients than negative patients (*p=0,001*). TNF-α levels were higher in AS than PsA and healthy controls (*p=0,038*).TNF-α was inversely associated with BASDAI (*p=0,029*) and BASFI (*p=0,046*).

Table 1

| | AS (n=53) | PsA (n=42) | Healthy controls (n=53) | *p* |
|---|---|---|---|---|
| Age (mean ± SD) | 31.8±6.8 | 44±11.8 | 31.4±5 | 0.00 |
| Sex , M/F (ratio, %) | 41/12 (77.4%) | 12/30 (28.6%) | 38/15 (71.7%) | 0.00 |
| Waist circumference, cm (mean ± SD) | 89.6±13.3 | 97±12 | 84.4±10.6 | 0.00 |
| BMI, kg/m$^2$ (mean ± SD) | 26.3±5.2 | 30±5.7 | 24.3±2.9 | 0.00 |
| Fasting glucose, mg/dl (mean ± SD) | 89.2±12.5 | 95.86±21.8 | 82.13±6.9 | 0.00 |
| Insulin, IU/ml (mean ± SD) | 12.9±9.2 | 14±9.4 | 9.4±5.5 | 0.002 |
| HOMA (mean ± SD) | 2.9±2.24 | 3.65±4.2 | 1.9±1.2 | 0.00 |
| Hemoglobin A1C (mean ± SD) | 5.6±0.98 | 6.1±0.97 | 5.38±0.49 | 0.00 |
| Total cholesterol, mg/dl (mean ± SD) | 182.7±37 | 204±52.9 | 179.94±28.4 | 0.008 |
| LDL-cholesterol, mg/dl (mean ± SD) | 111±30.2 | 129±42.4 | 110.8±26.8 | 0.015 |
| HDL-cholesterol, mg/dl (mean ± SD) | 44.35±12.3 | 48.4±12.6 | 47.9±12 | 0.057 |
| Trigliserid, mg/dl (mean ± SD) | 136.2±82.2 | 148±113 | 106±62.4 | 0.042 |
| CRP, mg/dl (mean ± SD) | 0.63±0.9 | 2.1±10.9 | 0.038±0.2 | 0.00 |
| ESR, mm/h (mean ± SD) | 13.8±11.2 | 17.7±14.2 | 5.5±4.7 | 0.00 |
| TNF-α, pg/ml (mean ± SD) | 31.27±9.33 | 17.59±9.34 | 12.9±5.7 | 0.038 |
| TRAIL, pg/ml (mean ± SD) | 4.36±2.49 | 5.06±3.23 | 3.85±2.2 | 0.155 |
| BASDAI/BASFI (mean, ± SD) | 2.9±2.1/2.2±1.7 | – | – | |
| DAS28-ESR | – | 2.54±1.08 | – | |

**Conclusions:** Our results showed that, serum TRAIL levels were associated with TNF-α, LDL-cholesterol and total cholesterol in patients with AS.Serum TRAIL concentrations were higher in HLAB-27 positive patients.Further studies are needed to clarify the underlying basis, because it seems there is a complex interaction between inflammatory processes and metabolic disorders.
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## THU0387 SERUM LEVELS OF TNF ALPHA AND VEGF AS MARKERS OF DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

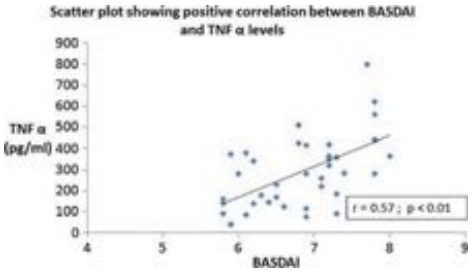
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**Background:** Monitoring of disease activity in axial spondyloarthritis is difficult due to lack of specific markers of inflammation. Conventional markers of inflammation namely ESR and CRP, seldom correlates with disease activity. To help in the early diagnosis and monitoring of axial spondyloarthritis, there has been a growing need for new biomarkers of disease activity.
**Objectives:** To investigate the role of serum vascular endothelial growth factor (VEGF) and tumor necrosis factor alpha (TNF α) as markers of disease activity in patients with Axial Spondyloarthritis (axSpA).
**Methods:** 40 patients with axSpA (28 with Ankylosing Spondylitis and 12 with non-radiological axSpA; mean age 29 years, mean duration 5 months) were included in this study. ESR, CRP, BASDAI/BASFI, serum TNF α and VEGF levels were assessed at baseline and after 12 weeks of therapy with either etanercept or NSAIDs (20 patients in each group). 20 healthy age and sex matched controls were also recruited for the study.
**Results:** Patients with axSpA had higher levels of serum TNF α (mean 341pg/ml) and VEGF (mean 797pg/ml) when compared with healthy controls (mean 72.5 pg/ml, $p<0.001$ and mean 269 pg/ml, $p<0.001$). There was significant reduction in serum TNF α and VEGF levels after 12 weeks of treatment with etanercept (mean 161pg/ml, $p<0.001$ and mean 442 pg/ml, $p<0.001$ respectively) but not with NSAID (p=0.29, p=0.25). Both TNF α and VEGF had a positive correlation with BASDAI (r=0.57, $p<0.01$ and r=0.44, $p<0.01$) and BASFI (r=0.61, $p<0.01$ and r=0.33, p=0.03) at baseline. The levels of TNF α and VEGF showed no correlation with ESR and CRP (p=0.48, p=0.07 and p=0.21, p=0.06 respectively)at baseline. There was no correlation between BASDAI and levels of ESR, CRP (p=0.27 and p=0.49 respectively).

Table 1. Comparison of parameters in Etanercept group (Before and after treatment)

| Parameter | Healthy control | Etanercept group (before treatment) (N=20) | Etanercept group (after treatment) | P value paired data | P value between control and before treatment group |
|---|---|---|---|---|---|
| Age (yrs) | 26 (6.1) | 27.3 (7.5) | 27.5 (7.5) | NA | 0.55 |
| BASDAI | – | 7.0 (0.6) | 3.9 (0.6) | <0.001[a] | NA |
| BASFI | – | 6.9 (0.5) | 3.8 (0.5) | <0.001[a] | NA |
| ESR (mm/hr) | – | 27.6 (16.8) | 11.4 (6.9) | <0.001[a] | NA |
| CRP (mg/L) | – | 5.5 (2.5) | 4.2 (1.2) | 0.04[a] | NA |
| TNF α (pg/ml) | 72.5 | 341.25 (142.8) | 169.5 (125.1) | <0.001[a] | <0.001[a] |
| VEGF (pg/ml) | 269.7 (142.6) | 791 (287.7) | 442.5 (208.5) | <0.001[a] | <0.001[a] |

[a]Statistically significant.




**Conclusions:** Serum levels of TNF α and VEGF serve as better markers of disease activity when compared with ESR and CRP in axSpA. Significant reduction in VEGF levels with treatment makes it a potentially new therapeutic target in axSpA

**References:**

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**Disclosure of Interest:** None declared
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## THU0388 THE ASSOCIATIONS BETWEEN AGE WITH THE CLINICAL AND RADIOLOGICAL ACTIVITY IN SPONDYLOARTHRITIS

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**Background:** Spondyloarthritis (SpA) is an umbrella term which includes several inflammatory arthritides sharing common clinical features, such as sacroiliitis, spondylitis, peripheral arthritis/enthesitis and other extra-articular manifestations. Although typically presenting at a young age, SpA is often a relentlessly progressive disease even in this new era of biologics.
In the last few years, much research has been generating on discovering new and more sensitive modalities in the use of magnetic resonance imaging (MRI) for assessing SpA. The advent of MRI has enabled clinicians to detect objective features of active inflammation, thereby allowing earlier diagnosis and more quantitative assessment of disease severity.
Despite these rapid advancements, there have been few reports on examining the association between age and disease activity in SpA, especially with the use of these various new modalities of imaging. In this cross-sectional analysis, we examine the associations between age and the clinical and radiological disease activities in axial SpA using radiographs as well as different modalities of MRI.
**Methods:** One hundred and twenty one patients fulfilling the Assessment of SpondyloArthritis International Society Classification Criteria for axial SpA were included in analyses. Patient demographics, disease activity and radiographic scores, as well as magnetic resonance imaging (MRI) with diffusion weighted imaging derived apparent diffusion coefficient values ((DWI(ADC)), were compared between patients older than and younger/equal to 40 years of age at a cross-sectional level. Variables with significant differences in univariate analyses were used as dependent variables in multivariate linear regression models adjusted for potential confounding/contributing factors.
**Results:** Multivariate analysis showed that increasing age was significantly associated with higher Bath Ankylosing Spondylitis Functional Index (B=0.04, $p<0.01$) and Bath Ankylosing Spondylitis Metrology Index scores (B=0.03, $p<0.01$); as well as higher modified Stoke Ankylosing Spondylitis Spine Score (B=0.57, $p<0.01$). On MRI, increasing age was associated with a lower SpondyloArthritis Research Consortium of Canada MRI index (B=(-0.2), p=0.01) and DWI(ADC) (B=(-0.01), $p<0.01$) of the SI joints, but higher DWI(ADC) values of the axial spine (B=0.01, p=0.01).
**Conclusions:** Increasing age in SpA was associated with greater functional impairment and structural damage, more inflammation of the axial spine, but less inflammation of the SI joints. Our findings are consistent with the traditional belief of SpA being an "ascending disease" and highlights the importance of different modalities of MRI in the diagnosis and disease monitoring of SpA.

**Disclosure of Interest:** None declared
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## THU0389 COMPARING DIFFUSION WEIGHTED IMAGING (DWI) WITH CLINICAL PARAMETERS AND SHORT TAU INVERSION RECOVERY (STIR) SEQUENCE IN DETECTING SPINAL AND SACROILIIAC (SI) JOINTS INFLAMATION IN SPONDYLOARTHRITIS (SPA)

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**Background:** DWI has been proposed for SpA diagnosis and disease monitoring1,2. The clinical correlation and effectiveness of this imaging when compared to the traditional STIR sequence is still under evaluation.
**Objectives:** To compare DWI with with clinical features, and traditional STIR sequence in detecting spinal and SI joints inflamation in SpA patients.
**Methods:** One hundred and ten patients fulfilled ASAS Axial SpA criteria were recruited consecutively from two rheumatology centers in Hong Kong. Clinical, radiological and blood parameters were collected. DWI and STIR MRI were performed simultaneously and results were scored according to the Spondyloarthritis Research Consortium of Canada (SPARCC) for comparison. The Apparent Diffusion Coefficient (ADC) values were also calculated.
**Results:** DWI showed no correlation with clinical features. When compare with STIR sequence, it correlated well with STIR sequence at the SI joints level (CC 0.76, $p<0.001$), but weakly at the spinal level (CC 0.23, p=0.02). At SI joints level, presence of inflammation by both STIR sequence and DWI were associated with increase in maximum (B=0.24, p=0.02 in STIR; B=0.37, $p<0.001$ in DWI) and mean ADC values (B=0.17, p=0.003 in STIR; B=0.15, p=0.01 in DWI). Maximum (B=0.19, p=0.04) and mean spinal ADC values (B=0.18, p=0.01) were also positively associated with DWI detected spinal inflammation. STIR sequence had no association with ADC values. Presenec of Modic lesion showed positive correlation with STIR (B=7.12, p=0.01) but not spinal ADC values.
**Conclusions:** Both STIR sequence and DWI perform similiarily in detecting active sacroiliitis. At spinal level, ADC values appear to be independent of other imaging/clinical assessment and are not affected by degenerations.

**References:**

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**Disclosure of Interest:** None declared
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## THU0390 CLINICAL CHARACTERISTICS OF SPONDYLOARTHRITIS IN JAPANESE PATIENTS

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**Background:** Spondyloarthritis (SpA) has been considered relatively rare in Japan, with an estimated incidence rate of 0.48/100,000 person-years and an estimated population prevalence of less than 0.01%. However, in daily practice, we have diagnosed SpA more frequently after recent increase in awareness of this disease entity, suggesting presence of potentially severe under-diagnosis in the previous time periods. Further improvement of awareness of this disease entity is necessary to allow patients to receive appropriate treatments. In this study, we aim to characterize distinguishing clinical features of SpA in Japanese patients, which should then allow us to improve both under-diagnosis and misdiagnosis of this increasingly treatable disease entity.
**Objectives:** To evaluate clinical characteristics commonly manifested in Japanese SpA patients in COMOSPA database.
**Methods:** Descriptive statistics of patient demographics and clinical characteristics of SpA were provided in the Japanese subgroup comparing with those in rest of Asian countries and non-Asian countries. Prevalence of characteristics were compared across regions using ANOVA (continuous variables) or $\chi^2$ test (categorical variables) to identify clinical features that were more characteristic of Japanese SpA patients. These analyses were conducted using the COMOSPA database.
**Results:** 161 Japanese patients, 933 non-Japanese Asian patients, and 2890 non-Asian patients were included in the study. Mean age and male percentage for Japanese patients were 48.9 years old and 59.3%, respectively. As a baseline characteristic, Japanese patients weighed less than other groups (65.0 vs. 66.6 vs. 78.3kg, $p<0.001$). Radiographic axial SpA patients were significantly fewer in Japanese patients (50.9 vs. 76.4 vs. 61.1%, $p<0.001$). Percentage of the patients with inflammatory back pain was lower in Japanese patients (71.9 vs. 88.6 vs. 85.1%, $p<0.001$) as well. In contrast, peripheral arthritis consistent with SpA was more common in Japanese patients (75.0 vs. 46.2 vs. 63.6%, $p<0.001$), as well as dactylitis (26.9 vs. 7.2 vs. 17.6%, $p<0.001$), enthesitis (48.1 vs. 23.5 vs. 42.1%, $p<0.001$) and nail involvements (25.5 vs. 3.3 vs. 13.5%, $P<0.001$). Psoriasis was also more common in Japanese patients (38.5 vs. 6.2 vs. 20.0%, $p<0.001$). HLA-B27 was less frequently positive in Japanese patients (29.2 vs. 80.0 vs. 49.9%, $p<0.001$). Functional status measured by BASFI (Bath Ankylosing Spondylitis Functional Index) and disease activity measured by BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) tended to be lower in Japanese patients compared to non-Asian patients.
**Conclusions:** Japanese SpA patients demonstrated unique clinical pictures compared to other Asian and non-Asian countries. These results allow us to improve both under-diagnosis and misdiagnosis of the disease.
**Disclosure of Interest:** C. Min Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, K. Yoshida Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, Y. Haji Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, H. Inoue Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, Y. Kaneko Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, T. Kawasaki Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, K. Matsui Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, M. Morita Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, K. Tada Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, N. Takizawa Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, N. Tamura Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, N. Ichikawa Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, Y. Taniguchi Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, S. Tsuji Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, M. Okada Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, S. Kobayashi Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, T. Tomita Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, M. Kishimoto Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None
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## THU0391 AXIAL DISEASE IN PSORIATIC ARTHRITIS (ADIPSA) STUDY: SERUM-SOLUBLE BONE-TURNOVER BIOMARKERS OF PSORIATIC ARTHRITIS PHENOTYPES

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**Background:** Psoriatic spondyloarthritis (PsSpA), peripheral-only psoriatic arthritis (pPsA) and ankylosing spondylitis (AS) are characterised by differing patterns of osteoproliferation and bone resorption, which may be reflected by levels of serum-soluble bone-turnover biomarkers.
**Objectives:** To investigate four such potential biomarkers (Dkk-1, M-CSF, MMP-3 and OPG) as predictors of: (i) PsSpA occurrence; (ii) axial radiographic severity; (iii) psoriatic arthritis mutilans (PAM) occurrence.
**Methods:** A prospective single-centre cross-sectional study (ADIPSA) recruited pPsA (n=127; fulfilling CASPAR criteria), PsSpA (n=118; psoriasis with radiographic sacroiliitis and/or spondylitis) and AS (n=157; fulfilling modified New York criteria) cases, and assessed them clinically, radiographically, and in terms of serum biomarkers. Serum was obtained from two other centres of clinically characterised psoriasis-only (PsC; n=200) cases, and sex/age-matched healthy controls (HC; n=50). ELISA was used to measure serum Dkk-1, M-CSF, MMP-3 and OPG concentrations. Multivariable regression analyses compared serum concentrations across disease groups.
**Results:** OPG is a biomarker of axial disease in spondyloarthritis (SpA) cases; concentrations were significantly lower in SpA cases with axial disease (RAD) than in those without (non-RAD) (adjusted odds ratio, $OR_{adj}$ 0.20 per ng/ml increase in concentration; 95%CI 0.05, 0.80; p=0.02), independently of having psoriasis.
Dkk-1 is a biomarker of axial disease in SpA cases, with a pattern for increasing concentration along a spectrum of increasing axial involvement. Dkk-1 concentrations were significantly higher in SpA cases with axial disease than in those without ($OR_{adj}$ 1.22; 95%CI 1.05, 1.42; p=0.01), independently of having psoriasis, and significantly lower in PsSpA than AS cases ($OR_{adj}$ 0.85; 95%CI 0.74, 0.98; p=0.02).
M-CSF is a biomarker of arthritis. Compared with HC, M-CSF concentrations were significantly lower in pPsA ($OR_{adj}$ 0.14; 95%CI 0.06, 0.32; $p<1x10^{-5}$), PsSpA

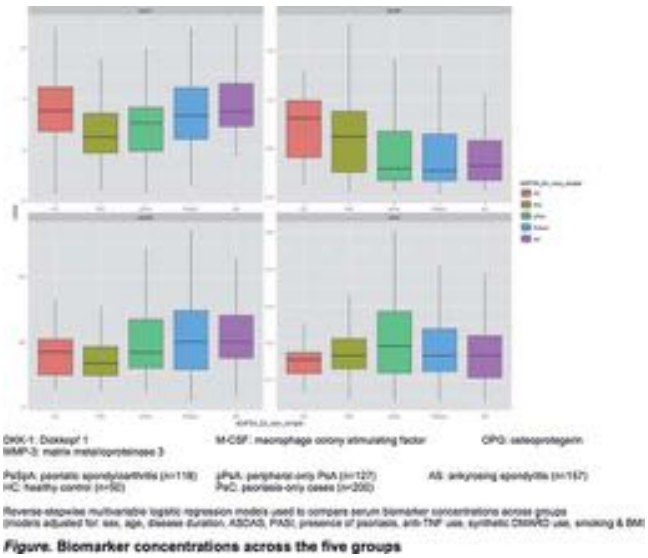



**Figure. Biomarker concentrations across the five groups**

($OR_{adj}$ 0.07; 95%CI 0.03, 0.17; $p<1x10^{-8}$), and AS ($OR_{adj}$ 0.37; 95%CI 0.16, 0.85; $p<1x10^{-7}$). Similarly, M-CSF concentrations were significantly lower in PsA than PsC cases ($OR_{adj}$ 0.44; 95%CI 0.24, 0.82; p=0.01).
MMP-3 is a biomarker of arthritis. Compared with HC, MMP-3 concentrations were significantly higher in pPsA ($OR_{adj}$ 1.06; 95%CI 1.01, 1.10; p=0.02), PsSpA ($OR_{adj}$ 1.06; 95%CI 1.01, 1.11; p=0.02), and AS ($OR_{adj}$ 1.06; 95%CI 1.01, 1.11; p=0.01). Similarly, MMP-3 concentrations were significantly higher in PsA than PsC cases ($OR_{adj}$ 1.02; 95%CI 1.01, 1.03; p=0.0004).
There were no significant associations between biomarkers and either morphology or radiographic severity (mSASSS or PASRI).
Biomarker levels were no different in PsA cases with/without PAM.
**Conclusions:** OPG and Dkk-1 appear to be biomarkers of axial disease in SpA patients (pPsA, PsSpA, AS), independently of cutaneous psoriasis status. M-CSF and MMP-3 appear to be biomarkers of arthritis, but don't differentiate SpA phenotypes. No biomarkers for PAM occurrence in PsA were found. The high concentration of Dkk-1 in AS and PsSpA, supports previous evidence that Dkk-1 is dysfunctional in axial SpA.
**Disclosure of Interest:** None declared
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## THU0392 BONE MINERAL DENSITY CHANGES IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS

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**Background:** Bone loss in patients (pts) with early axial spondyloarthritis is insufficiently studied.
**Objectives:** To assess 1-year bone mineral density (BMD) changes at the femoral neck (FN) and lumbar spine (LS) in pts with early axial spondyloarthritis (axSpA).
**Methods:** 47 pts (20 men and 27 women) with axSpA and <5 years duration of inflammatory back pain (ASAS 2009 criteria) of the Russian CORSAR cohort were observed. Pts included had baseline and 1-year-visit BMD measurements. Pts matched the ASAS criteria and were observed according to ASAS guidelines. At baseline, the median age was 27.0 (24.0–31.0) years, disease duration 22.0 (10.0–34.0) months. 90% of pts were HLA-B27 positive. 46% of pts alongside inflammatory back pain also had peripheral arthritis. Median BASDAI was 3.5 (2.1–5.2), ASDASCRP 2.3 (1.4–3.2), ESR 9.0 (5.0–24.5) mm/h, CRP 3.9 (1.0–19.7) mg/L. Femoral neck (FN) and lumbar spine (LS) (L2–4) BMD were measured in all pts using dual-energy x-ray absorptiometry (DXA). Low BMD was defined as Z score ≤-2 SD (at least in one investigated site). MRI of sacroiliac joints (SIJs), LS and hip joints (HJs) (in case of hip joint involvement) were performed using Signa Ovation 0.35 T scanner (matrix 288x192).
**Results:** In all 47 pts, baseline median Z-score was -0.6 (-1.3 – 0.2) SD for the FN and -0.7 (-1.8 – 0.3) SD for the LS. Z-score for the FN was significantly lower in women: -1.0 (-1.5 – -0.3) SD and 0.0 (-0.75 – 0.4) SD, respectively, p=0.0065. At baseline examination low BMD at least in one of the sites was evidenced in 8 (17%) pts (4 men and 4 women). While all 8 pts had low LS BMD, 3 of them had also low FN BMD. At baseline examination of the 47 pts association between lumbar spine MRI-spondylitis and low BMD was revealed. MRI-spondylitis was evidenced in 8 (17%) pts: 3 (62.5%) of them had low FN and/or LS BMD, while 5 (62.5%) pts of this group had normal BMD values. In contrast, within the group of pts without the LS MRI inflammation (n=39) nobody had low BMD (p=0.0006). Initially, there was found a relationship between high ASDAS activity and low BMD: 11.5% of pts with high ASDASCRP values had low BMD. In contrast, within the group of pts with low or moderate ASDASCRP values nobody had low BMD (p=0.054).
Among the 8 pts with low baseline BMD, 1-year BMD normalized in 3 pts (all women and all initially had low LS BMD). In one patient (male) with normal baseline BMD values low LS BMD at the 1-year visit was observed. Therefore, at 1-year visit fewer pts had low BMD than at baseline examination (n=8, 17% vs n=6, 12.8%, respectively). In males the lowering of LS BMD at 1-year visit was evidenced with much higher confidence than in females (5 among 20 pts, 25%, vs 1 among 27 pts, 3.8%, respectively; p=0.043).
Neither at baseline examination nor at 1-year visit any correlation was detected between low BMD and disease duration, high disease activity according to BASDAI, raised CRP or ESR levels, the presence of MRI-sacroiliitis or MRI-coxitis.
**Conclusions:** In the Russian cohort of axSpA pts there was found an association between active MRI-spondylitis of the LS and BMD reduction in LS and/or FN. The findings corroborate the hypothesis that low BMD in pts with early axSpA is a result of inflammation. Males more often than females had lowered LS BMD after 1 year of observation.
**Disclosure of Interest:** None declared
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## THU0393 INCREASED 18F-FLUORIDE UPTAKE LESIONS AT VERTEBRAL CORNERS ON POSITRON EMISSION TOMOGRAPHY PREDICT NEW SYNDESMOPHYTES DEVELOPMENT IN ANKYLOSING SPONDYLITIS

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**Background:** 18F-fluoride uptake on positron emission tomography (PET) represents osteoblastic activity. Previous cross-sectional studies showed that increased 18F-fluoride uptake lesions at vertebral corners were associated with both inflammation and structural changes on magnetic resonance imaging (MRI) and radiography, respectively, in patients with ankylosing spondylitis (AS) [1,2]. But, longitudinal studies that investigated the association between increased 18F-fluoride uptake lesions and future syndesmophytes formation are lacking.
**Objectives:** We aimed to demonstrate that increased 18F-fluoride uptake lesions on PET predict the development of new syndesmophytes.
**Methods:** In 12 patients with AS, 18F-fluoride PET-MRI (Philips Healthcare, Cleveland, OH, USA) was performed at baseline and radiography was performed at baseline and 2 years. We recorded 18F-fluoride uptake lesions on PET, acute (type A) and advanced (type B) corner inflammatory lesions (CILs) and fat lesions on MRI and syndesmophytes on radiography. An increased 18F-fluoride uptake lesion was defined as an uptake greater than the uptake in the adjacent normal vertebral body (Figure 1).

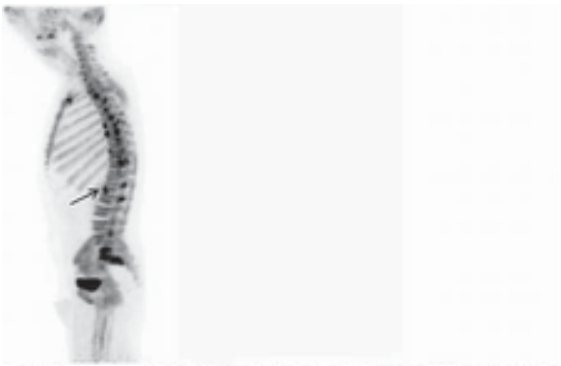


Figure 1. Increased 18F-fluoride uptake lesions at L1 lower and L2 upper anterior vertebral corners (arrow) on positron emission tomography in a 43-year old patient with ankylosing spondylitis

**Results:** Of 231 anterior vertebral corners without syndesmophyte at baseline, 13 type A CILs (5.5%), 2 type B CILs (0.9%) and 20 fat lesions (8.7%) on MRI and 6 increased fluoride uptake lesions (2.6%) on PET were observed. After 2 years, 16 new syndesmophytes (6.9%) in 8 AS patients (66.7%) occurred. New syndesmophytes developed significantly more frequently in anterior vertebral corners with increased 18F-fluoride uptake lesions (50%) or fat lesions (25%) at baseline, as compared with those without either feature (5.8% and 5.2%, respectively). In generalised linear latent mixed models after adjusting within-patient correlation, baseline increased 18F-fluoride uptake lesion significantly predicted the development of new syndesmophytes (OR=20.6, 95% CI=2.7–156.1, p=0.003). Fat lesions were also associated with new syndesmophytes development (OR=9.3, 95% CI=2.1–40.2, p=0.003), but this association was not observed in CILs.
**Conclusions:** Our findings indicate that increased 18F-fluoride uptake lesions can predict future new syndesmophytes formation in patients with AS. 18F-fluoride PET may be used to estimate structural damage in these patients.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1875

## THU0394 MRI ASSESSMENT OF AXIAL INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE-RELATED SPA: AGE AT DISEASE DIAGNOSIS, NOT EXTENT AND SEVERITY OF AXIAL DISEASE, RELATES TO HLA-B27

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**Background:** Up to 20% of inflammatory bowel diseases (IBD) cases may have an associated form of Spondyloarthropathy (SpA). Axial disease in SpA may vary from sporadic back pain to advanced spinal fusion, undistinguishable from Ankylosing Spondylitis (AS). Magnetic resonance imaging (MRI) is well established in the assessment of spinal disease in SpA, but axial MRI data in IBD are still sparse. In AS and axial Psoriatic Arthritis (PsA), it has previously been shown that the extent and severity of inflammatory changes of bone marrow oedema (BMO) on MRI is related to HLA-B27.
**Objectives:** The aims of this study were to describe the prevalence and extent of BMO lesions and their relationship with HLA-B27 status in IBD-related SpA with axial symptoms.
**Methods:** Consecutive MRI scans [thoracic spine (TS), lumbar spine (LS) and sacroiliac joints (SIJs)], from patients attending the Leeds Combined Rheumatology and Gastroenterology service between 2005–2015, were assessed retrospectively. Scans had been performed as part of clinical assessment for inflammatory back pain. All subjects had histological diagnosis of IBD and fulfilled ASAS classification criteria for SpA, HLA-B27 status and demographics were also collected. MRI scans were scored by consensus by two expert readers, blinded to the clinical characteristics of the patients. We used the semiquantitative (0–3) Leeds MRI Scoring System for BMO lesions representative of inflammation in the spine and SIJs, whereby a lesion graded as moderate (grade 2) is considered clinically significant. Concordant data from the two readers were used to report on definite lesions.
**Results:** MRI scans from 43 patients were available for analysis; mean age 43.4 yrs (SD 13.2, range 18.1–80.9), 25 were females (58.1%). Mean age at SpA diagnosis was 37.1 yrs (SD 11.9, range 17.1–63). HLA-B27 was positive in 15 subjects (34.9%) and was associated with younger age at SpA diagnosis (p=0.015). The median MRI score and number of BMO lesions were 2 (IQR 0–7 and 0–5, respectively), 13 patients (30.2%) scored zero, 14 subjects (32.6%) showed at least 1 clinically relevant lesion (grade $\geq$2). Gender, current age or age at MRI scan were not associated with HLA-B27. MRI total (whole axial skeleton) and partial (TS, LS and SIJs single analysis) score, number of BMO lesions and severe lesions (total axial skeleton and TS-LS-SIJs single analysis) were not different according to HLA B27 status.
**Conclusions:** Although the majority of IBD-related SpA do not carry HLA B27, diagnosis at a younger age was related to HLA-B27 status. Axial BMO lesions in IBD disease showed the whole spectrum of changes noted in AS. Unlike AS and axial PsA, no association was found between the extent and severity of MRI-determined axial disease and HLA-B27.
**Disclosure of Interest:** None declared
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## THU0395 THE PREVALENCE OF INFLAMMATORY AND STRUCTURAL LESIONS ON MRI OF THE SACROILIAC JOINTS IN PATIENTS WITH VERY EARLY PERIPHERAL SPONDYLOARTHRITIS

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**Objectives:** To assess the prevalence of inflammatory and structural lesions on MRI of the sacroiliacal joints (SIJ) in patients with peripheral spondyloarthritis (PSpA) in a very early stage of the disease.
**Methods:** Baseline data originated from the double-blind RCT with golimumab in 60 patients (CRESPA), who were diagnosed with PSpA and had a symptom duration <3 months. MRI SIJ was performed at baseline. Peripheral arthritis, dactylitis or enthesitis combined with $\geq$1 SpA feature (uveitis, psoriasis, IBD, preceding infection, HLAB27 or sacroiliitis on imaging) was necessary for inclusion. However, all patients already fulfilled the classification criteria without data on imaging of the SIJ. Bone marrow edema (BME) of the SIJ was quantified using the Spondyloarthritis Research Consortium of Canada (SPARCC) scoring system. Besides BME of the SIJ, all MRIs were also scored for other inflammatory lesions such as enthesitis and capsulitis. Structural MRI lesions of the SIJ such as subchondral sclerosis, erosions, periarticular fat and ankylosis were also assessed. Hip evaluation consisted of the presence of joint effusion, BME, enthesitis and cortical aberrations.
**Results:** Although not the reason for encounter, 7 out of 60 patients reported ever having inflammatory back pain (IBP) at inclusion or in the past, with median Visual analogue scores (VAS) of 2.0 (range 0.0- 9.0) for back pain. Overall, 35% of patients (21/60) exhibited BME of the SIJ and fulfilled the definition of a positive MRI by ASAS, with median SPARCC score of 8.0 (range 2.0–37.0). Only 3 out of 7 patients with IBP exhibited BME on MRI SIJ. Therefore, almost 86% of patients (18/21) with active sacroiliitis did not exhibit symptoms of IBP. Median VAS back pain in patients with sacroiliitis compared to patients without sacroiliitis respectively reached 2.0 and 1.0 (P=NS). Pelvic enthesitis was present in 23.8% (5/21) of patients with an ASAS positive MRI SIJ and in 10.3% (4/39) of patients with negative MRI. None of the patients exhibited enthesitis of the L5 spinous process, iliac crest, anterior superior iliac spine or ramus pubis. The MRI features of PSpA patients are presented in Table 1.

Table 1

| | ASAS MRI+ (n=21) | | ASAS MRI– (n=39) | |
|---|---|---|---|---|
| | Unilateral | Bilateral | Unilateral | Bilateral |
| Inflammatory lesions of the SIJ, n (%) | | | | |
| BME | 16 (76.2) | 5 (23.8) | 1 (2.6) | 0 |
| Capsulitis | 7 (33.3) | 0 | 0 | 0 |
| Retroarticular enthesitis | 5 (23.8) | 1 (4.8) | 1 (2.6) | 0 |
| Chronic lesions of the SIJ, n (%) | | | | |
| Sclerosis | 1 (4.8) | 2 (9.5) | 0 | 0 |
| Fat metaplasia | 2 (9.5) | 4 (19.0) | 1 (2.6) | 0 |
| Erosions | 3 (14.3) | 8 (38.1) | 4 (10.3) | 0 |
| Ankylosis | 2 (9.5) | 0 | 0 | 0 |
| Pelvic enthesitis, n (%) | | | | |
| Symphysis | 1 (4.8) | | 1 (2.6) | |
| Ischial tuberosity | 2 (9.5) | 0 | 1 (2.6) | 2 (5.4) |
| Posterior superior iliac spine | 3 (14.3) | 0 | 0 | 0 |
| Greater trochanter | 0 | 1 (4.8) | 0 | 2 (5.4) |
| Gluteus posterior | 1 (4.8) | 0 | 0 | 0 |
| Hip, n (%) | | | | |
| Joint effusion/ BME | 4 (19.0)/ 1 (4.8) | 0/0 | 4 (10.3)/ 1 (2.6) | 1 (4.8)/0 |
| Bony changes of the cortex | 1 (4.8) | 1 (4.8) | 2 (5.4) | 0 |

**Conclusions:** Even in early diagnosed peripheral SpA patients, over 1/3 exhibited BME suggestive of acute sacroiliitis and structural lesions of the SI joints. Our findings underscore the importance of sacroiliitis as the cornerstone feature within the SpA-concept, even in asymptomatic patients.
**Disclosure of Interest:** None declared
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## THU0396 VISCERAL ADIPOSE TISSUE AND CARDIOVASCULAR RISK IN SPONDYLOARTHRITIS: RESULTS FROM THE DESIR AND COMOSPA COHORTS

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**Background:** Spondyloarthritis (SpA) is associated with an increased cardiovascular risk. Abdominal adiposity, especially visceral adipose tissue (VAT) is emerging as a independent cardio-metabolic risk factor.
**Objectives:** Our study aimed at assessing association between VAT and cardiovascular risk factors in patients with early or long-standing SpA.
**Methods:** This study was performed in patients recruited from 2 cohorts of SpA: COMOSPA (long-standing SpA) and DESIR (early SpA).
VAT was measured by total body dual energy X-ray absorptiometry in patients with SpA, at baseline in the COMOSPA cohort; at baseline and after 2 years of follow-up in the DESIR cohort. We also collected the following items: demographic data, disease characteristics, current treatment, inflammation biomarkers, cardiovascular risks (BMI, smoking status, hypertension, diabetes, hypercholesterolemia and hypertriglyceridemia) and cardiovascular events (history of ischemic cardiovascular disease).
We, first, compared VAT values in these 2 groups of patients, then, searched for an association between VAT and cardiovascular risks, and finally, studied 2-year VAT variations for patients in the DESIR cohort.
**Results:** 82 patients and 129 patients from COMOSPA and DESIR cohorts were included respectively. In COMOSPA, patients were mostly males (68.3% vs. 55.6%), older (46.3±12.8 vs. 33.0±8.6 years old), with a longer duration of disease (12.0±11.2 vs. 1.5±0.9 years), and received more frequently TNF-blockers (64.6% vs. 30.2%), as compared to DESIR cohort (all p<0.02).
SpA patients of COMOSPA cohort had more frequently hypertension (34.1% vs. 3.1%, p<0.01), dyslipidemia (43.9% vs. 7.0%, p<0.01), current smoking (34.1% vs. 32.6%, p<0.01) and tended to have a higher BMI (26.5±5.4 vs. 23.7±3.5 kg/m$^2$, p=0.06) than patients from the DESIR cohort.
Mean VAT was higher in patients of COMOSPA cohort than in DESIR cohort (140.6±75.2 vs. 79.2±44.0 cm$^2$, p<0.01) after adjustment for age.
In patients of COMOSPA cohort, VAT was significantly associated with the presence of dyslipidemia (p=0.02) and high level of LDL cholesterol (p<0.01), after adjustment for age, gender and BMI, in univariate analysis.
In patients of DESIR cohort, baseline VAT was significantly associated with high level of CRP (p=0.04), high consumption of NSAIDs (assessed by NSAIDs score) (p=0.04) and presence of hypertension (p=0.05), after adjustment for age, gender and BMI, in univariate analysis. In patients of DESIR cohort, VAT tended to increase over 2 years from baseline (79.2 vs 82.6 cm$^2$, +1.8%, p=0.054); this variation was significantly associated with SpA responding to

ASAS criteria (p=0.01), presence of hypercholesterolemia (p<0.01), presence of hypertriglyceridemia (p<0.01) and 2-year changes of BMI (p<0.01). 2-year VAT variation was similar in patients receiving TNF-blockers or not.
**Conclusions:** This study shows that VAT is higher in patients with long–standing SpA than with early SpA. VAT is associated with to the presence of cardiovascular risk factors, after adjusting on age and BMI in both settings. In addition to BMI, assessing VAT could be a complimentary tool for the assessment of cardiovascular risk in SpA patients.
**Disclosure of Interest:** None declared
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## THU0397 SAFETY OF TUMOR NECROSIS FACTOR INHIBITOR IN ANKYLOSING SPONDYLITIS PATIENTS WITH OCCULT HEPATITIS B VIRUS INFECTION

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**Background:** Tumor necrosis factor inhibitors (TNFi) are being widely used for treatment of ankylosing spondylitis (AS). It is known to increase the risk of hepatitis B virus (HBV) reactivation in hepatitis B surface antigen (HBsAg)-positive patients and possibly also in patients with occult HBV infection (HBsAg-negative/hepatitis B core antibody (HBcAb)-positve).
**Objectives:** The aim of this study was to evaluate the effects of TNFi therapy on HBV reactivation in AS patients with occult HBV infection.
**Methods:** AS patients treated with TNFi at our institution were retrospectively reviewed. Clinical datas before and after using TNFi including 3 serologic markers for HBV: HBsAg, HBcAb and hepatitis B surface antibody (HBsAb), type and duration of TNFi, and liver function tests. Definite HBV reactivation was defined as reappearance of HBsAg in a previously HBsAb-negative individual and possible HBV reactivation was defined as serum alanine aminotransaminase (ALT) elevation (>2 times upper normal limit) in patients with occult HBV infection.
**Results:** A total 295 of AS patients on TNFi therapy were assessed excluding 7 (2.4%) patients who were HBsAg-positive. Fifty-seven (19.8%) patients who were HBcAb-positive (occult HBV infection) and 231 (80.2%) patients who were HBcAb-negative were analyzed. The mean age of patients with occult HBV infection was 48.96 ± 11.26 years, which was significantly higher than patients who were HBcAb-negative (35.86 ± 9.61). Duration of TNFi therapy, type and number of TNFi used, proportion of patients with abnormal liver function test, and HLA-B27 positivity did not differ significantly between the 2 groups. None of the patients showed definite HBV reactivation during TNFi therapy. However, 5 (2.2%) HBcAb-negative patients converted to HBcAb-positive after TNFi therapy. Their follow up ALT levels remained within normal ranges. Two (3.5%) of the 57 patients with occult HBV infection showed possible HBV reactivation with elevation in ALT levels. One of these patients had also on methotrexate and liver function normalized with discontinuation of methotrexate.
**Conclusions:** TNFi therapy was safe in AS patients with occult HBV infection. Nevertheless, close monitoring is necessary for detection of HBV reactivation in patients with occult HBV infection.
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**Disclosure of Interest:** None declared
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## THU0398 OBSERVATIONAL STUDY ON THE QUALITY OF LIFE OF ITALIAN AXIAL SPONDYLOARTHRITIS PATIENTS (QUASAR): BASELINE DATA

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**Background:** Quality of Life (QoL) is reduced in patients (pts) with axial spondyloarthritis (axSpA) who suffer from pain, stiffness and fatigue in their most productive years of life. Currently, data on QoL and impact on daily activities in axSpA pts classified according to the ASAS criteria are limited. No medical research in Italy has been conducted in AxSpA pts
**Objectives:** To assess the evolution of QoL in pts suffering from axSpA over a 12-month period and disease impact on daily life activities
**Methods:** QUASAR is a multicenter, longitudinal, observational study on adult axSpA pts in Italy. This interim analysis reports baseline data. Inclusion criteria were diagnosis of axSpA (either non radiographic [nr-axSpA] or ankylosing spondylitis [AS]) based on the ASAS classification criteria and ability to understand and complete the questionnaires. The following clinical parameters were recorded: CRP, HLA-B27, pain, stiffness, disease activity (BASDAI and ASDAS), Patient and Physician Global Assessment (PtGA/PGA), comorbidities and treatment. Subjects were asked to complete the ASQoL, WPAI, MARS, EQ-5D questionnaires and a VAS on satisfaction with the treatment during routine visits. Descriptive statistics (mean±Standard Deviation [SD] or frequencies) are presented for baseline clinical characteristics, disease activity and QoL. Mann-Whitney test, t-test, $\chi^2$ were used to calculate differences between pts groups
**Results:** A total of 512 pts (mean age 47.8±13.1 years; males 62.1%) were enrolled. 19% had a family history of SpA and 21% of psoriasis. 97 pts (18.9%) had a diagnosis of nr-axSpA. 246 (61.5%) subjects out of the 400 typed were HLA-B27 positive (48.7% and 62.7% of nr-axSpA and AS pts, respectively). Time to diagnosis since symptom onset was 5.4±2.9yrs for all pts, 3.8±3.1yrs for nr-axSpA and 5.8±2.8yrs for AS pts. 59.8% of nr-axSpA and 58.3% of AS pts had pain at the first visit. Low back pain was the most frequent type (73.3% of all pts) followed by cervical pain (35%) and dorsal pain (23.3%). 52.6% of nr-axSpA and 56.1% AS pts had morning stiffness. The following table shows the baseline demographic and characteristics of the pts involved in QUASAR:

Table 1

| | Overall | Nr-axSpA | AS | p-value |
|---|---|---|---|---|
| Age (years) | 47.8±13.1 | 42.5±13.5 | 49.0±12.6 | <0.001 |
| Male gender | 62.1% | 52.6% | 64.3% | 0.032 |
| HLA-B27 | 61.5% | 48.7% | 62.7% | 0.237 |
| CRP | 0.8±2.2 | 0.7±1.3 | 0.8±2.3 | 0.669 |
| Pain | 58.6% | 59.8% | 58.3% | 0.789 |
| PGA | 2.8±2.7 | 2.8±2.6 | 2.7±2.7 | 0.627 |
| PtGA | 3.6±2.7 | 4.1±2.6 | 3.6±2.7 | 0.545 |
| BASDAI | 3.2±2.5 | 3.6±2.5 | 3.2±2.4 | 0.861 |
| ASDAS | 13.2±9.0 | 14.4±9.0 | 12.9±9.0 | 0.138 |
| ASQoL | 5.8±5.5 | 6.2±5.6 | 5.7±5.4 | 0.429 |
| EQ-5D VAS | 66.3±21.8 | 64.0±23.1 | 66.9±21.4 | 0.926 |

Values reported are mean ± SD, if not indicated otherwise; p value refers to comparison between nr-axSpA and AS pts.

Extra Articular Manifestations (EAM) were as follows: psoriasis 17.6%, uveitis 15.8%, ulcerative colitis (UC) 4.1% and Crohn's disease 6.5%. EAMs were present in 24.7% and 15.9% (psoriasis), 15.5% and 15.9% (uveitis), 5.2% and 3.9% (UC), 4.1% and 7.0% (Crohn's disease) of nr-axSpA and AS pts
**Conclusions:** QUASAR is the first prospective Italian study with a large sample size that reports an overall similar burden of disease in nr-axSpA and AS patients, documented by pain, CRP, PGA/PtGA, BASDAI, ASDAS, ASQOL, and EQ-5D VAS. Our data support the importance of early diagnosis and treatment of axSpA
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## THU0399 THE ANKYLOSING SPONDYLITIS DISEASE ACTIVITY INDEX (ASDAS) TO ASSESS DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) belongs to the spondyloarthritides and disease activity can be evaluated by the Disease Activity Index for Psoriatic Arthritis (DAPSA) and the Composite Psoriatic Disease Activity Index (CPDAI) [1]. The Ankylosing Spondylitis Disease Activity Score (ASDAS) is a composite disease activity score for ankylosing spondylitis covering peripheral involvement in both versions selected by ASAS international society ($ASDAS_{CRP}$ and $ASDAS_{ESR}$)[2].
**Objectives:** To evaluate the possible importance of $ASDAS_{CRP}$ and $ASDAS_{ESR}$ to assess disease activity in PsA.
**Methods:** In a cross-sectional study patients attending our outpatient clinic and fulfilling CASPAR criteria of PsA underwent a complete rheumatologic assessment to calculate the disease activity score CPDAI and DAPSA for PsA as well as the $ASDAS_{CRP}$ and $ASDAS_{ESR}$ after informed consent was obtained. On the same day a rheumatologist unaware of the clinical status of the patients performed B-mode and power Doppler (PD) sonography of peripheral joints, of tendon sheets and entheses according to the MASEI, and of perisynovial tissue of finger joints. Results were graded semi-quantitatively and sum scores were calculated for PD signals and for pathological B-mode and PD findings together (GLUS, range 0–832). Descriptive statistics were used to summarise the data and correlations were analysed by the Spearman's rank correlation test.
**Results:** 67 of 84 included patients (49 male, 18 female; mean age 51 (SD 12) years; median disease duration 7 years (IQR 4–18) could be evaluated. We found a strong correlation of the DAPSA and CPDAI score and a low but significant

Table 1. Correlation of the PsA composite and ultrasound scores with the ASDAS

| | $ASDAS_{CRP}$ (r, 95% CI) | $ASDAS_{ESR}$ (r, 95% CI) |
|---|---|---|
| CPDAI | 0.67 (0.51–0.79)*** | 0.58 (0.38–0.72)*** |
| DAPSA | 0.74 (0.60–0.83)*** | 0.71 (0.56–0.81)*** |
| PD sum score | 0.24 (–0.01–0.46)* | 0.29 (0.05–0.50)* |
| GLUS | 0.30 (0.06–0.51)* | 0.37 (0.13–0.56)** |

*p<0.05; **p<0.005; ***p<0.0001. r: correlation coefficient; CI: confidence interval; PD sum score: semi-quantitative score of joints, entheses, tendons and perisynovial tissue with power Doppler signals; GLUS: global ultrasound score.

correlation of the GLUS and the PD sum score with the $ASDAS_{ESR}$ and $ASDAS_{CRP}$ (table). We observed only a moderate association of the DAPSA with the GLUS (r=0.52, 95%CI 0.32–0.68) and the association of the CPDAI with the GLUS and the PD sum score (r=0.25, 95%CI 0.003–0.47 and r=0.19, 95%CI -0.06–0.42, respectively) was even lower than the correlation of the GLUS and the PD sum score with the $ASDAS_{ESR}$ and the $ASDAS_{CRP}$. In PsA-patients with clinically defined remission 25.0% of the patients fulfilled the CPDAI and 29.1% the DAPSA remission criteria. However, in patients with clinically defined remission 50.0% and 54.2% fulfilled the $ASDAS_{ESR}$ and $ASDAS_{CRP}$ criteria for inactive disease.

**Conclusions:** This cross-sectional study shows that the ASDAS might also be a valuable tool to measure disease activity and to define clinical remission in PsA.

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**Disclosure of Interest:** None declared

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## THU0400 RELATIONSHIP BETWEEN HEALTH QUALITY OF LIFE AND OTHER INDICATORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Axial spondyloarthritis (AxSpA) is an inflammatory disease that mainly affects the spine. As the disease progresses, there is a reduction of quality of life (QOL) in patients due to loss of mobility and function, and also by episodes of inflammation and stiffness (disease activity).

**Objectives:** To Analyze relationship between QOL of patients with AxSpA and other commonly used indicators in assessing these patients.

**Methods:** 100 patients with AxSpA (67% male, age 48.38±11.05, disease duration 14.37±10.74, HLAB27 + 85%) were included. QOL of patients was assessed by the Ankylosing Spondylitis Quality of Life index (ASQoL). Mobility was evaluated by conventional metrology and by a new motion capture system (UCOTrack) and UCOASMI as its metrological index [1]. PRO questionnaries were completed to evaluate activity, function and overall status. Structural damage was scored by mSASSS index. To analyze relationship, Spearman tests, ANOVA and multiple linear regression were performed.

**Results:** ASQoL showed statistically significant correlations with BASFI, BAS-G, ASDAS and UCOASMI. No significant correlations between QOL and structural damage, neither B27+, or having nr-AxSpA were found. Table shows results groupped by sex, B27, duration, nr-AxSpA (mSASSS <5 Duration>5 years) high activity level and poor mobility with statistical significance. Variables that were independently associated with ASQOL, in a multivariable linear regresion, were gender (p=0.027), BASDAI (p=0.008) and BASFI (p<0.001) $R^2$ =0.676. Repeating this analysis, but including mobility measures obtained by motion capture, variables that were independently associated with ASQoL were BASDAI (p=0.000) lateral flexion defined by the position of shoulders and hips (p=0.004) and tilt of C7-L4 (p=0.023) $R^2$ =0.609.

**Conclusions:** QOL in AxSpA is influenced by the activity of the disease, and by decreased mobility. Women perceive a lower QOL. The best measure related to QOL is lateral bending. Improving patient mobility through exercise and finding appropriate treatment to decrease disease activity, you can improve QOL of patients with AxSpA.

**References:**

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**Disclosure of Interest:** None declared

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## THU0401 SEVERE BONE MARROW EDEMA ON SACROILIAC JOINT MRI INCREASES THE RISK OF LOW BMD IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Patients with axSpA have an increased risk of low bone mass. AS patients have a high prevalence of osteoporosis, which is observed in both early and advanced cases. A recent study showed that nr-axSpA patients show significantly greater bone loss than patients with mechanical back pain.

**Objectives:** To determine the association between inflammatory and structural lesions on sacroiliac joint (SIJ) MRI and BMD and to identify risk factors for low BMD in patients with axial spondyloarthritis (axSpA).

**Methods:** Seventy-six patients who fulfilled the ASAS axSpA criteria were enrolled. All underwent SIJ MRI and BMD measurement at the lumbar spine, femoral neck, and total hip. Inflammatory and structural lesions on SIJ MRI were scored. Laboratory tests and assessment of radiographic and disease activity were performed at the time of MRI. The association between SIJ MRI findings and BMD was evaluated.

**Results:** Among the 76 patients, 14 (18%) had low BMD. Patients with low BMD showed significantly higher bone marrow edema (BME) and deep BME scores on MRI than those with normal BMD (p<0.047 and 0.007, respectively). Inflammatory lesions on SIJ MRI correlated with BMD at the femoral neck and total hip. Multivariate analysis identified the presence of deep BME on SIJ MRI, increased CRP, and sacroiliitis on X-ray as risk factors for low BMD (OR: 5.6, 14.6, and 2.5, respectively).

**Conclusions:** The presence of deep BME on SIJ MRI, increased CRP levels, and severity of sacroiliitis on X-ray were independent risk factors for low BMD.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.1021

## THU0402 RADIOGRAPHIC PROGRESSION IS ASSOCIATED WITH INCREASED CARDIOVASCULAR RISK IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** A recent study showed that patients with chronic inflammatory arthritis have an increased risk of cardiovascular disease (CVD). Axial sponayloarthritis (axSpA) is also thought to carry an increased cardiovascular (CV) risk, but it is unclear whether axSpA patients have a higher risk of CVD than the general population.

**Objectives:** To compare the cardiovascular disease (CVD) risk between axial spondyloarthritis (axSpA) patients and matched controls, and to identify factors associated with increased CVD risk in axSpA patients.

**Methods:** This cross-sectional study enrolled 185 axSpA patients who fulfilled the ASAS criteria and 925 ageand sex-matched controls. None of the subjects had a previous history of CVD or diabetes mellitus. Traditional CVD risk factors were assessed and the 10 year CVD risk was calculated using the Framingham risk score (FRS). Estimated 10 year CVD risk was compared between axSpA patients and matched controls. Disease activity and radiographic progression in the sacroiliac joint and spine of axSpA patients were evaluated at the time of CVD risk assessment.

**Results:** HDL cholesterol levels were lower in axSpA patients than in matched controls (p=0.004); however, systolic blood pressure was higher (p<0.001). The FRS was 5.0 ± 6.6% for controls and 6.3 ± 8.7% for axSpA patients (p=0.046). Both the grade of sacroiliitis on X-ray and the number of syndesmophytes correlated with the FRS (p=0.009 and p=0.001, respectively), but disease activity variables did not. The FRS was significantly higher in axSpA patients with a greater number of syndesmophytes (p=0.035). Multivariate analysis identified the grade of sacroiliitis and number of syndesmophytes as being independently associated with the FRS (p=0.003 and p=0.042, respectively).

**Conclusions:** The FRS was higher in axSpA patients than in a matched general population. Radiographic progression in the spine and sacroiliac joints was associated with a high estimated 10 year CVD risk.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.1022

**Abstract THU0400** – Table 1

| | Total | Male/Female | B27+/B27– | Duration >10/Duration <10 | AxSpA/nr-AxSpA | ASDAS >2.1/ASDAS <2.1 | UCOASMI >4/UCOASMI <4 |
|---|---|---|---|---|---|---|---|
| Patients (n) | 100 | 67/33 | 85/15 | 60/40 | 72/28 | 66/34 | 58/42 |
| ASQoL | 4.0 (2.8) | 3.6 (2.8)/4.8 (2.7)* | 3.8 (2.7)/4.8 (3.4) | 4.0 (2.65)/3.8 (3.12) | 4.0 (2.7)/3.9 (2.9) | 5.2 (2.6)/1.9 (1.9)** | 5.0 (2.6)/2.6 (2.3)** |
| ASDAS | 2.6 (1.0) | 2.5 (1.0)/2.8 (1.1) | 2.5 (1.0)/2.9 (1.2) | 2.7 (1.01)/2.5 (1.20) | 2.6 (1.0)/2.4 (1.0) | 3.2 (0.7)/1.4 (0.4)** | 3.0 (1.0)/1.8 (0.7)** |
| BASFI | 3.8 (2.8) | 3.7 (3.0)/4.0 (2.6) | 3.7 (2.8)/4.3 (3.3) | 4.0 (2.94)/3.3 (2.86) | 4.0 (2.8)/3.3 (2.9) | 5.2 (2.6)/1.6 (1.6)** | 5.3 (2.6)/1.8 (1.7)** |
| BASG | 4.7 (2.6) | 4.3 (2.5)/5.3 (2.7) | 4.7 (2.6)/4.6 (2.5) | 4.6 (2.5)/4.6 (2.8) | 4.7 (2.6)/4.5 (2.5) | 6.1 (2.0)/1.9 (1.2)** | 5.5 (2.4)/3.6 (2.4)** |
| UCOASMI | 4.7 (1.8) | 4.8 (2.0)/4.6 (1.4) | 4.7 (1.8)/4.5 (2.0) | 5.1 (1.9)/3.9 (1.4)** | 5.0 (1.9)/3.8 (1.3)** | 5.3 (1.6)/4.1 (1.9)* | 5.9 (1.5)/3.1 (0.6)** |
| mSASSS | 14.4 (16.3) | 18.1 (18.7)/6.9 (3.9)** | 14.4 (16.6)/14.7 (15.9) | 17.3 (17.7)/8.3 (7.6)** | 18.7 (17.4)/3.3 (1.5)** | 16.2 (17.3)/16.7 (19.2) | 19.6 (19.5)/7.2 (5.1)** |

* p<0.05, ** p<0.001.

## THU0403 PERFORMANCE OF MODIFIED MINIMAL DISEASE ACTIVITY (MDA) CRITERIA IN PATIENTS WITH PERIPHERAL SPONDYLOARTHRITIS: POST-HOC ANALYSIS OF ABILITY-2

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**Background:** Due to lack of validated outcome measures in non-psoriatic peripheral spondyloarthritis (pSpA), recent studies in this patient (pt) population have used varying endpoints [1]. Thus, developing new pSpA-specific indices may be worthwhile. Minimal Disease Activity (MDA) has been validated in psoriatic arthritis but not in pSpA.

**Objectives:** To evaluate the performance of a modification of the MDA criteria (excluding psoriasis) in pSpA patients (pts) from the ABILITY-2 study [2].

**Methods:** This post-hoc analysis evaluated the validity of a modified MDA (mMDA) in pSpA. ABILITY-2 was a 12-week trial comparing adalimumab (ADA) with placebo (PBO) in pSpA followed by a 144 week extension. The mMDA for pSpA was defined as achieving at least 4 or 5 out of the following 6 criteria: (1) tender joint count (TJC, 78 joints) $\leq$1; (2) swollen joint count (SJC, 76 joints) $\leq$1; (3) pt pain visual analog scale (VAS) $\leq$15 of 100 mm; (4) pt global activity (PtGA) VAS $\leq$20 of 100 mm; (5) health assessment questionnaire–disability index (HAQ-DI)$\leq$0.5; and (6) tender entheseal points $\leq$1. Enthesitis was assessed by the Leeds Enthesitis Index (LEI) or the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index for this analysis. The proportion of pts achieving the 4 different versions of mMDA were evaluated (either 4 or 5 of 6 using LEI and either 4 or 5 of 6 using SPARCC). The correlations between mMDA and the novel pSpA response criteria [PSpARC] remission from ABILITY-2 and Ankylosing Spondylitis Disease Activity Score Inactive Disease [ASDAS ID] were evaluated by tetrachoric correlation ($r_{tet}$).

**Results:** Of the 163 pts (82 ADA, 81 PBO) who completed wk 12, significantly greater proportion of pts receiving ADA achieved mMDA (regardless of the definition) compared with PBO (P<0.001 for all comparisons, Table 1a). The proportion of mMDA responders at yrs 1, 2, and 3 was numerically higher in pts initially randomized to ADA. The mMDA response showed a stronger positive correlation with PSpARC remission ($r_{tet}$>0.9) than ASDAS ID ($r_{tet}$>0.75) at wk 12, and yrs 1–3. Among pts who fulfilled the 4/6 criteria (LEI or SPARCC), approximately 20–30% of pts did not meet TJC and SJC criterion (Table 1b). However, the 5/6 criteria (LEI or SPARCC) were more stringent with approximately 5% and 13% not meeting the TJC and SJC criterion, respectively.

Table 1a. Proportion of patients achieving modified MDA*

| Modified MDA | Week 12 (DB) | | Year 1 (OLE) | | Year 2 (OLE) | | Year 3 (OLE) | |
|---|---|---|---|---|---|---|---|---|
| | ADA (n=82) | PBO (n=81) | ADA (n=71) | PBO>ADA (n=74) | ADA (n=62) | PBO>ADA (n=68) | ADA (n=54) | PBO>ADA (n=58) |
| 4/6 LEI | 33 (40.2) | 11 (13.6) *** | 44 (62.0) | 35 (47.3) | 44 (71.0) * | 34 (50.0) | 37 (68.5) * | 29 (50.0) |
| 5/6 LEI | 23 (28.0) | 4 (4.9) *** | 30 (42.3) | 30 (40.5) | 37 (59.7) | 29 (42.6) | 29 (53.7) | 37 (46.6) |
| 4/6 SPARCC | 29 (35.4) | 10 (12.3) *** | 43 (60.6) | 34 (45.9) * | 43 (69.4) | 33 (48.5) * | 35 (64.8) | 28 (48.3) |
| 5/6 SPARCC | 22 (26.8) | 4 (4.9) *** | 30 (42.3) | 29 (39.2) | 36 (58.1) * | 27 (39.7) | 29 (53.7) | 27 (46.6) |

P-values for difference between ADA and PBO treatment groups: ***, P<0.001; **, P<0.01; *, P<0.05.

Table 1b. Criteria not met in modified MDA responders receiving ADA at week 12*

| Modified MDA | Modified MDA criterion | | | | | |
|---|---|---|---|---|---|---|
| | TJC78 > 1 | SJC76 > 1 | Pt Pain VAS > 15 | PtGA VAS > 20 | HAQ-DI > 0.5 | Enthesitis Index > 1 |
| 4/6 LEI (n=33) | 9 (27.3) | 10 (30.3) | 2 (6.1) | 3 (9.1) | 3 (9.1) | 0 (0.0) |
| 5/6 LEI (n=23) | 1 (4.3) | 3 (13.0) | 0 (0.0) | 1 (4.3) | 2 (8.7) | 0 (0.0) |
| 4/6 SPARCC (n=29) | 6 (20.7) | 7 (24.1) | 1 (3.4) | 2 (6.9) | 3 (10.3) | 3 (10.3) |
| 5/6 SPARCC (n=22) | 1 (4.5) | 3 (13.6) | 0 (0.0) | 1 (4.5) | 1 (4.5) | 2 (9.1) |

*n (%)

Abbreviations: MDA=Minimal Disease Activity; DB=double-blind period; OLE=Open-Label Extension; ADA=Adalimumab; PBO=Placebo; LEI=Leeds Enthesitis Index; SPARCC=Spondyloarthritis Research Consortium of Canada; TJC78=Tender Joint Count (78 joints); SJC76=Swollen Joint Count (76 joints); Pt Pain=Patient global assessment of Pain; VAS=Visual Analog Scale; PtGA=Patient Global assessment of disease Activity; HAQ-DI=Health Assessment Questionnaire-Disability Index based on 20 questions.

**Conclusions:** All 4 versions of mMDA discriminated between ADA and PBO treatment groups; both entheseal indices performed similarly. The mMDA (particularly the 5/6 versions which closely represents the concept of MDA) could be an appropriate treatment target in pSpA pts.

**References:**

[1] Turina, M.C., et al., Ann Rheum Dis, 2015. (doi: 10.1136/annrheumdis-2014-207235).

[2] Mease, P., et al., Arthritis Rheumatol, 2015. 67(4): p. 914–23.

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## THU0404 THE PREVALENCE OF AXIAL AND PERIPHERAL SPONDYLOARTHRITIS IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW & META-ANALYSIS

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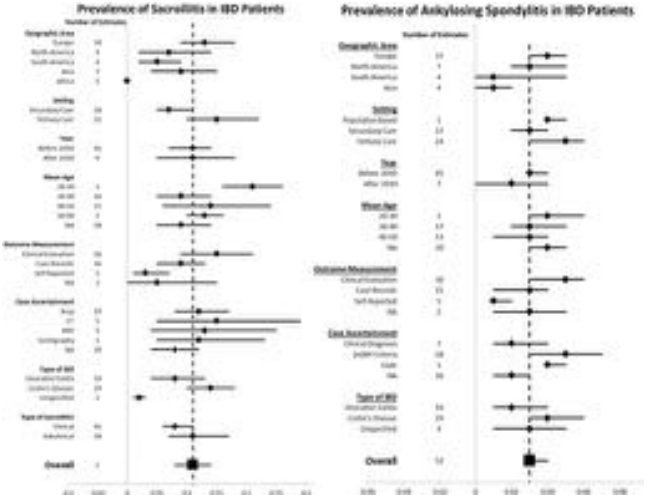
**Background:** Inflammatory Bowel Disease (IBD) is a chronic disease that affects up to 0.5% of the population, comprising both Crohn's Disease (CD) and ulcerative colitis (UC). Various extra-intestinal manifestations can occur, among which spondyloarthritis (SpA). SpA can manifest with both axial and peripheral manifestations, but prevalence estimates of these manifestations differ widely.

**Objectives:** To provide a pooled estimate of the prevalence of axial and peripheral manifestations of SpA in patients with IBD and to identify factors that might influence the prevalence estimates.

**Methods:** We systematically searched Embase, Pubmed, OvidSP, Scopus and Web-of-science databases from inception to May 2014. All articles addressing the prevalence of axial and/or peripheral manifestations of spondyloarthritis in adult IBD patients were included. Risk of bias was assessed using a quality assessment tool including items on selection bias, non-response bias, sample size and misclassification of SpA diagnosis.

**Results:** Out of 4846 studies, 60 studies were included. Sample size varied from 9 to 4454. Methodological quality of the included studies was moderate, with only a slight majority scoring positively on the individual items of the quality assessment tool. With regard to axial manifestations, the pooled prevalence of sacroiliitis was 0.11 (95% CI 0.08–0.014), whereas the pooled prevalence for ankylosing spondylitis was 0.03 (95% CI 0.03–0.04). For peripheral arthritis the pooled prevalence was 0.14 (95% CI 0.12–0.16). Few estimates were available for the prevalence of enthesitis (range from 0.01 to 0.54) and dactylitis (range from 0 to 0.04). For both axial and peripheral manifestations, the prevalence was higher in patients with CD than in patients with UC.

Heterogeneity between studies was large, which might be explained by methodological quality as well as difference in geographic area, clinical setting and the use of criteria for case ascertainment as shown in figure 1 for the prevalence of SI and AS.




**Conclusions:** Spondyloarthritis is a common extraintestinal manifestation in IBD. Peripheral arthritis is slightly more common with a pooled prevalence of 0.14 than axial manifestations as sacroiliitis (pooled prevalence 0.11) and ankylosing spondylitis (pooled prevalence 0.03). For both axial and peripheral manifestations, the prevalence is higher in patients with CD than in patients with UC.

**Disclosure of Interest:** None declared

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## THU0405 ABILITY OF GENERAL PRACTITIONERS TO DISTINGUISH BETWEEN INFLAMMATORY AND NON-INFLAMMATORY SYMPTOMS IN PATIENTS AT RISK OF SPONDYLOARTHRITIS: THE APPSPA STUDY

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**Background:** Over the last couple of years early arthritis clinics provided quick access for patients with inflammatory arthritis. However, although early access to specialized care is now available, adequate referrals are also required to shorten the doctors' delay. Therefore, general practitioners (GPs), the ones who refer, should be aware of symptoms distinguishing between inflammatory and non-inflammatory disease in patients at risk for spondyloarthritis (SpA).
**Objectives:** To describe GP's ability to recognize symptoms suggestive of spondyloarthritis.
**Methods:** The AppSpA study was set up, a cross-sectional study focusing on awareness and knowledge of SpA in GPs and patients at risk for SpA. For the present study a single survey was developed and send out to GPs in various regions of the Netherlands. This survey was based on a study by Jois et al, which looked into recognition of symptoms of inflammatory back pain. Since we were also interested in the ability of GPs to recognize peripheral manifestations of SpA, we added some extra questions.
**Results:** 183 of the 950 GPs completed the survey, leading to a participation rate of 19.3%. Of the participating GPs the mean age was 47.2 years (SD 10.3) and 47.5% were male. Mean time working as a GP was 15.4 years (SD 13.5).
Almost all GPs (94.5%) indicated to be familiar with the term SpA, but 55.5% associated it only with axial manifestations. Up to one third of the GPs associated the term SpA with psoriatic arthritis (23.7%) and Inflammatory Bowel Disease (33.5%).
With regard to the recognition of signs of inflammatory pain, especially morning stiffness and pain relieve by NSAIDs were recognized (Table 1), whereas pain improvement with exercise was recognized in less than 25% of cases. When we focus on the peripheral manifestations of SpA; out of six signs for inflammatory peripheral disease, only 43.2% of GPs recognized at least three of these symptoms. For the eight axial signs, 60.6% recognized at least four symptoms.
If GPs thought about inflammatory symptoms, the majority asked for the presence of psoriasis (83.6%) and inflammatory bowel disease (72.1%). GPs less often ask about other SpA related symptoms such as uveitis (61.8%), enthesitis (19.1%) and dactylitis (19.1%).

**Table 1. Proportion of GPs who identified correct signs of inflammatory joint and back pain (n=183)**

| Signs of inflammatory disease | Peripheral | Axial |
|---|---|---|
| Insidious onset of complaints, n (%) | 53 (29.0) | 90 (49.2) |
| Symptom duration>3 months, n (%) | 57 (31.2) | 93 (50.8) |
| Pain improved with exercise, n (%) | 25 (13.7) | 38 (21.3) |
| Pain not relieved by rest, n (% | 30 (16.4) | 40 (21.9) |
| Pain relieved by NSAIDs, n (%) | 160 (87.4) | 150 (82.0) |
| Morning Stiffness>30min, n (%) | 141 (77.1) | 138 (75.4) |
| Nocturnal Pain, n (%) | Not Asked | 143 (78.1) |
| Alternating Buttock Pain, n (%) | Not Asked | 37 (20.2) |

**Conclusions:** Overall, recognition of inflammatory disease by GPs is suboptimal, where GPs are more aware of axial manifestations compared to peripheral manifestations. The recognition of these signs and symptoms of SpA in primary care needs improvement in order to facilitate the necessary referrals to rheumatologists.
**Acknowledgement:** This survey is part of initiative to develop a communication platform which was financially supported by AbbVie.
**Disclosure of Interest:** None declared
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## THU0406 LACK OF INFORMATION FOR PATIENTS AT RISK FOR SPONDYLOARTHRITIS: THE APPSPA STUDY

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**Background:** Patients with psoriasis (PSO) and inflammatory bowel disease (IBD) are at risk for developing spondyloarthritis (SpA). To overcome diagnostic delay, physicians treating patients with these conditions should be aware of this increased risk to minimize doctors' delay in referring patients to specialized care. However, as patients' delay could also be an issue, patients themselves should also be aware of their risk to develop SpA. Since the need to empower patients in order to effectively manage their disease has recently been included in several guidelines for rheumatic diseases, involving patients in their disease becomes more and more important.
**Objectives:** To assess whether patients with PSO or IBD are aware of the risk of developing SpA and if so how they became aware.
**Methods:** A cross-sectional study was set up including PSO and IBD patients between 18 and 55 years of age. Patients were invited to participate either by their GP or by the patient organizations for PSO and IBD. Patients willing to participate completed a set of questionnaires regarding their disease, level of awareness and presence of musculoskeletal complaints.
**Results:** 552 PSO patients completed the questionnaires, of which 43.1% indicated to be aware of the possibility of developing a rheumatic condition already before the study-invitation. Of these 238 patients, 34% indicated to have gained this knowledge by themselves. Another 13.5% was informed by their GP and 24.4% by their medical specialist, while 18.5% learned from family or neighbors. Of the IBD patients, 344 completed the questionnaires, of which 41.9% was aware of the possibility of developing a rheumatic condition before the invitation for the study. The majority of patients was informed by their medical specialist (40.3%) or gained this knowledge by themselves (39.6%). Only 1.4% was informed by their GP and 9.7% learned from family or neighbors. For both PSO and IBD, patients who were recruited via the patient organizations were significantly more aware than patients recruited via the GPs.

**Table 1. Level of Awareness in Patients with Psoriasis or IBD**

| | Psoriasis (n=552) | IBD (n=344) |
|---|---|---|
| % Awareness | 43.1 | 41.9 |
| % Informed by GP | 13.5 | 1.4 |
| % Informed by medical specialist | 24.4 | 40.3 |
| % Via surroundings | 18.5 | 9.7 |
| % Looked it up themselves | 34.0 | 39.6 |
| % Patient organization | 8.4 | 2.8 |
| % Other | 1.3 | 6.3 |

**Conclusions:** Less than half of the patients with psoriasis or IBD are aware of the possibility of developing a rheumatic condition. If patients are aware, the majority gained this knowledge by themselves and 60% were not informed by a medical professional. More awareness could be achieved if medical professionals like the GP or the medical specialist would have more knowledge about symptoms of SpA and are trained in informing their patients about the increased risk of developing SpA. Public awareness campaigns to inform patients at risk could also be beneficial in minimizing patients' delay. Patient organizations could play a role in this awareness campaigns, since they already seem to inform their patients well.
**Acknowledgement:** This survey is part of initiative to develop a communication platform which was financially supported by AbbVie.
**Disclosure of Interest:** None declared
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## THU0407 BASELINE RESULTS FROM PROOF – A 5-YEAR OBSERVATIONAL STUDY OF LONG-TERM DISEASE OUTCOME IN AXIAL SPONDYLOARTHRITIS

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**Background:** Axial spondyloarthritis (axSpA), encompassing ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) without advanced structural lesions in the sacroiliac joints (SIJ), is a relatively new disease concept. The natural disease course of axSpA, including progression of structural damage over time, has not yet been systematically studied in large patient (pt) groups.
**Objectives:** To report the baseline data of PROOF, a large study currently being conducted in 29 countries across the world, evaluating long-term outcomes in pts with axSpA classified by ASAS criteria.
**Methods:** PROOF is a multi-country prospective observational study evaluating axSpA pts in rheumatology clinical practice over 5 years. Pts with axSpA fulfilling ASAS classification criteria were eligible, if diagnosed $\leq$12 months prior to study enrolment. Investigator's confidence with the diagnosis of axSpA is ascertained on a numeric rating scale (NRS 0–10) at enrolment and end of follow-up. Assessments of disease activity (BASDAI, ASDAS-CRP), physical function (BASFI), quality of life (SF-12v2), productivity (WPAI-SHP), and pelvic X-ray are scheduled at yearly follow-up visits. X-rays are graded according to NY criteria by local and central readers.
**Results:** 2084 pts with axSpA fulfilling ASAS criteria have been enrolled in PROOF study, 1259 pts with AS (60%) and 825 pts with nr-axSpA (40%) according to the investigators. The level of confidence with the diagnosis of axSpA was 8.7±1.8. The imaging criterion was fulfilled by 85% of pts (40% MRI, 51% X-ray, 9% both), 15% of pts were classified through the clinical arm. HLA-B27 was tested in 85% of pts and found to be positive in 68% of cases (70% with AS and 60% with nr-axSpA). Overall, pts were in their mid-thirties, had a long delay in referral to rheumatologist and recently diagnosed axSpA. Comparison of demographic and clinical characteristics between pts with AS and nr-axSpA is shown in Table 1. Pelvic x-rays were reportedly done in 1635 (78%) pts within 6 months of the baseline visit; to date both local and central readers have scored x-rays of 1344 pts (82% of available). Of the 1344 pts, 83.3% retained their classification (AS or nr-axSpA) after the central reading,

**Table 1.** Baseline demographics and disease characteristics of patients in PROOF study

| Characteristic, measure | AS | nr-axSpA | P-value[a] |
|---|---|---|---|
| Subdiagnosis by investigators, *n (%)* | 1259 (60.4) | 825 (39.6) | NA |
| Age, years, *mean ± SD* | 34.9 ± 10.9 | 34.2 ± 9.8 | 0.4 |
| Gender, *male : female*, % | 68.5 : 31.5 | 48.7 : 51.3 | <0.0001 |
| HLA-B27 positive[b], % | 89.8 | 59.6 | 0.0001 |
| Time from onset of back pain, months, *mean ± SD* | 64.8 ± 89.7 | 50.0 ± 71.0 | <0.0001 |
| Time from first physician visit for back pain, months, *mean ± SD* | 55.5 ± 78.2 | 45.7 ± 66.1 | 0.0008 |
| Time from first physician visit for back pain to first referral to rheumatologist, months, *mean ± SD* | 46.0 ±72.4 | 38.0 ± 63.3 | 0.003 |
| Time from diagnosis of axSpA, months, *mean ± SD* | 3.1 ± 3.4 | 2.6 ± 3.2 | 0.004 |
| CRP, mg/L, *mean ± SD* | 17.4 ± 23.5 | 11.6 ± 20.0 | <0.0001 |
| ESR, mm/h, *mean ± SD* | 23.9 ± 20.6 | 16.5 ± 17.5 | <0.0001 |
| BASDAI, *mean ± SD* | 4.4 ± 2.3 | 4.7 ± 2.3 | 0.01 |
| ASDAS-CRP, *mean ± SD* | 3.0 ± 1.1 | 2.8 ± 1.1 | <0.0001 |
| BASFI, *mean ± SD* | 3.4 ± 2.5 | 3.2 ± 2.4 | 0.35 |
| HRQoL based on SF-12v2, PCS, *mean ± SD* | 40.8 ± 8.7 | 41.5 ± 8.9 | 0.14 |
| HRQoL based on SF-12v2, MCS, *mean ± SD* | 43.7 ± 10.3 | 43.0 ± 10.6 | 0.27 |
| WPAI-SHP, Total activity impairment, %, *mean ± SD* | 44.0 ± 27.6 | 43.3 ± 27.9 | 0.65 |
| Subdiagnosis based on local x-ray reading, *n (%)*[c] | 1035 (62.6) | 618 (37.4) | NA |
| Subdiagnosis based on central x-ray reading, *n(%)*[d] | 902 (67.1) | 442 (32.9) | NA |

[a]Baseline characteristics and disease measures were compared using Wilcoxon test for quantitative variables and Chi-square test for qualitative variables.
[b]HLA-B27 test was done in 85% of all patients.
[c]Missing n=291/1635 (currently being queried), [d]Missing n=73/1617 (in progress).
Abbreviations: AS=Ankylosing spondylitis; nr-axSpA=non-radiographic axial spondyloarthritis; NA=Not Applicable; CRP=C-reactive protein; ESR=Erythrocyte sedimentation rate; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP=Ankylosing Spondylitis Disease Activity Score containing CRP; BASFI=Bath Ankylosing Spondylitis Functional Index, HRQoL=Health-related quality of life; SF-12v2=Short form 12-item health survey; PCS=Physical component summary score; MCS=Mental component summary score. WPAI-SHP=Work productivity impairment Questionnaire-specific health problem.

while 16.7% were classified differently. Based on the kappa value, there was a substantial agreement on the grading of x-rays between the local and central readers: kappa=0.63 (95% CI, 0.59–0.68).
**Conclusions:** PROOF is the largest observational study in pts with axSpA classified by ASAS criteria so far. It provides insights into the clinical practice worldwide and aims to assess long-term outcomes of axSpA. Baseline results confirmed comparable clinical features and disease burden between AS and nr-axSpA, highlighted a long delay in referral to rheumatologists, and showed a good agreement between the SIJ x-ray grading by local and central readers.
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## THU0408 PREVALENCE OF RENAL IMPAIRMENT IN PATIENTS WITH SPONDYLOARTHRITIS: RESULTS FROM THE INTERNATIONAL COMOSPA STUDY

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**Background:** Renal impairement in spondyloarthritis (SpA), although uncommon, may include secondary renal amyloidosis (AA type), non-steroidal anti-inflammatory drug (NSAID) nephropathy, and glomerulonephritis. Data on the prevalence of renal impairement in SpA are relatively rare and usually come from small or retrospective studies.
**Objectives:** To assess the prevalence and associations of renal dysfunction in patients with SpA.
**Methods:** COMOSPA was an international (22 participating countries from four continents) multicentric study on comorbidities in SpA. Renal function was assessed from the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) equation. SpA characteristics, risk factors for renal impairment were collected. NSAID use was assessed by the currently (last 3 months) intake. Logistic regression models were constructed from variables which were significantly associated with an eGFR of $<$60ml/min/1.73m$^2$ or clinically relevant.
**Results:** Of the 3984 recruited patients, after excluding of outliers and patients for whom eGFR was not available, 2098 (52.6%) were analysed (male gender: 63.5%; age: 45.3 years; disease duration: 8.6 years; HLAB27+: 53.7%; BASDAI: 3.6/10). A total of 153 patients (5.2%, mean age 53.6 years) had an eGFR $<$60 ml/min/m$^2$. In univariate analysis, renal impairment was associated with age ($p<0.001$), HLAB27 positivity ($p<0.001$), several cardiovascular risk factors (history of hypertension [$p<0.001$], systolic blood pressure [p=0.03], diabetes [p=0.005] and the Framingham Risk score [$p<0.001$]), disease activity scores (BASDAI [p=0.001], ASDAS-CRP [$p<0.001$]), functionnal parameters (BASFI [$p<0.001$], HAQ [$p<0.001$]), inflammatory biomarkers (ESR and CRP, both $p<0.001$), but not with disease duration, disease sevrity (bamboo spine, hip replacement) or NSAID current intake.
**Conclusions:** Renal impairment is not rare in SpA and is associated with age, disease severity and inflammation but not with cardiovascular risk factors or NSAID currently use.
**Disclosure of Interest:** None declared
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## THU0409 IS DISEASE ACTIVITY ASSOCIATED WITH WORK PRODUCTIVITY LOSS, PRESENTEEISM, AND ABSENTEEISM IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS? RESULTS FROM THE SPACE COHORT

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**Background:** Disease activity has an important impact on work productivity in patients with Ankylosing Spondylitis (AS). However, knowledge is limited if this impact exists in early axial Spondyloarthritis (axSpA) patients and if it is similar in different subgroups of patients such as male vs. female patients.
**Objectives:** To investigate if the impact of disease activity, assessed by ASDAS (AS Disease Activity Score, CRP based), on work productivity is similar according to gender, age, medication use, profession, HLA-B27 positivity, and duration of back pain at baseline in early axSpA patients.
**Methods:** The SPACE-cohort includes patients (chronic back pain $\geq$3 months, $\leq$2 years, onset $<$45 years) recruited from 5 European centres. Patients who fulfilled the ASAS criteria for axSpA were included in this analysis. Work Productivity and Activity Impairment questionnaire (WPAI) was completed by patients at baseline to assess the impact of axSpA on Work Productivity Loss (WPL; i.e. total work impairment due to disease), presenteeism (i.e. decreased functionality at work due to disease), and absenteeism (i.e. absence at work due to disease) in the past 7 days. Higher scores indicate greater impairment (ranged 0–100). ASDAS was used to assess disease activity. Gender, age, medication use, profession, HLA-B27 positivity, and duration of back pain were tested for effect modification (cut-off of $p<0.20$) one by one in a linear regression model. Continuous variables were split by their median.
**Results:** In total, 87 axSpA patients working at baseline were included; 53 patients of them fulfilled the clinical arm and 34 patients the imaging arm of the ASAS axSpA criteria. Patients were on average 30.8 years old (SD 7.6), 52.9% was male, and had a mean duration of back pain of 13 months (SD 7.1). They worked on average 29.5 (SD 15.8) hours and missed 3.0 (SD 8.0) hours per week at work due to axSpA. Mean WPL, presenteeism, and absenteeism were 34.3% (SD 28.5), 31.4% (SD 25.3), and 8.2% (SD 20.1) respectively. Patients had a mean ASDAS of 2.3 (SD 0.9). The univariable model (Figure 1) shows that one point increase in ASDAS resulted in an increase of 19.3%, 16.9%, 8.7% in WPL, presenteeism, and absenteeism, respectively. Fulfilment of the clinical or imaging arm was not an effect modifier (not shown). Gender and duration of

**Figure 1:** Association between ASDAS and Work Productivity Loss, presenteeism, absenteeism and stratified for its related effect modifiers at baseline among axial Spondyloarthritis patients who performed paid work in the SPACE cohort (n=87)

| | WPL | | Presenteeism | | Absenteeism | |
|---|---|---|---|---|---|---|
| | *Coefficient (SE)* | *p-value* | *Coefficient (SE)* | *p-value* | *Coefficient (SE)* | *p-value* |
| **Univariable model (n=87)** | | | | | | |
| ASDAS | 19.3 (2.6) | <0.001 | 16.9 (2.3) | <0.001 | 8.7 (2.1) | <0.001 |
| **Model for gender** | | | | | | |
| *Men (n=46)* | | | | | | |
| ASDAS | 14.3 (3.5) | <0.001 | 12.1 (2.8) | <0.001 | 4.4 (2.5) | 0.086 |
| *Women (n=42)* | | | | | | |
| ASDAS | 22.0 (3.7) | <0.001 | 19.3 (3.3) | <0.001 | 12.6 (3.5) | 0.001 |
| **Model for duration of back complaints** | | | | | | |
| *<21 months (n=43)* | | | | | | |
| ASDAS | 13.5 (4.3) | 0.003 | 12.5 (3.9) | 0.003 | 5.0 (3.9) | 0.207 |
| *≥21 months (n=44)* | | | | | | |
| ASDAS | 21.4 (2.9) | <0.001 | 18.3 (2.6) | <0.001 | 11.0 (2.3) | <0.001 |

*Abbreviations: Standard Error (SE), Ankylosing Spondylitis Disease Activity Score, CRP based (ASDAS)*

back pain were effect modifiers in the associations between ASDAS and WPL, presenteeism, and, absenteeism. Results were stratified for these variables. The associations remained statistically significant in all stratified models, except in the model of absenteeism for males (p=0.207).
**Conclusions:** Disease activity is positively associated with WPL, presenteeism, and absenteeism in early axSpA patients. The same level of disease activity seems to have more adverse impact on work productivity in women than in men, and irrespective of that, in patients with relatively long disease duration. In addition to disease activity, gender, and disease duration are relevant contextual factors in explaining WPL in patients with early axSpA.
**Disclosure of Interest:** None declared
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## THU0410 THE ASSOCIATION BETWEEN DISEASE ACTIVITY AND IILLNESS PERCEPTIONS IN EARLY AXIAL SPONDYLOARTHRITIS PATIENTS IN THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE)-COHORT

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**Background:** Studies in patients with rheumatic diseases report that negative views of illness are associated with poorer disease outcomes, such as more disability and pain. Little is known about illness perceptions in patients with early axial Spondyloarthritis (axSpA).
**Objectives:** To describe illness perceptions and to explore the association between illness perceptions and disease activity in patients with early axSpA at baseline.
**Methods:** The Spondyloarthritis Caught Early (SPACE) cohort includes patients (chronic back pain ≥3 months, ≤2 years, onset <45 years) recruited from 5 participating centres in Europe. Patients completed the Revised Illness Perception Questionnaire (IPQ-R). The illness identity dimension asked patients if they have experienced a certain symptom (15 in total) and if they believed these symptoms are related to axSpA. The other illness perception dimensions and causal attributions (15 causes) used 5-point Likert scales to score all items ranging from 1 (strongly disagree) to 5 (strongly agree). For the IPQ-R dimensions, see Figure 1. Disease activity was assessed by ASDAS (Ankylosing Spondylitis Disease Activity Score, CRP based). Univariable linear regression models were built for each IPQ-R dimension as dependent and ASDAS as independent variable adjusted for age and gender. Results were stratified when gender was an effect modifier (p<0.10). P-values <0.05 were considered to be statistically significant.
**Results:** Only patients fulfilling the ASAS classification for axSpA (n=119) were included. These patients had a mean age of 29.7 (SD 7.9) years and 50.4% was male. The mean disease duration was 13.0 (SD 7.3) months and the mean ASDAS 2.4 (SD 1.0). Patients reported 4.2 (SD 2.3) symptoms to be associated with axSpA on average, see Figure 1. Pain, joint stiffness, fatigue, and sleeping problems were the most reported symptoms according to patients in the illness identity dimension. All other dimensions showed a mean of approximately 3, except psychological attributions, risk factors, immunity and accident of the causal section, which had a mean of approximately 2. Patients with axSpA attributed their complaints mostly to heredity, chance or bad luck, or stress and worries. Six dimensions of the IPQ-R were associated with ASDAS. A stronger illness identity (β=0.63, p=0.003), stronger beliefs in severe consequences (β=0.32, p<0.001), less illness coherence (β=-0.24, p=0.003), more negative emotions towards their complaints (β=0.22, p=0.003), stronger beliefs of psychological attributions as a cause only in men (β=0.22, p=0.034), and the belief of immunity as a cause (β=0.17, p=0.010) were statistically significantly associated with a higher ASDAS.
**Conclusions:** Negative illness perceptions, such as experiencing more symptoms, believing in severe consequences, less illness coherence, and negative emotions towards axSpA, are associated with disease activity in patients with early axSpA.
**Disclosure of Interest:** None declared
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**Figure 1:** Baseline characteristics of the Revised Illness Perception Questionnaire (IPQ-R) and linear regression models of ASDAS and subscales of the IPQ-R at baseline adjusted for age and gender (n=119)

| Baseline characteristics | | | Linear regression models with ASDAS (independent variable) | | |
|---|---|---|---|---|---|
| Scale | Range | Mean (SD) | Coefficient (β) | Standard error | p-value |
| *Illness identity (n=115)* | | | | | |
| Identity | 0-15 | 4.2 (2.3) | 0.63 | 0.21 | 0.003* |
| *Illness perceptions (n=119)* | | | | | |
| Consequences | 1-5 | 2.9 (0.8) | 0.32 | 0.07 | <0.001* |
| Timeline (acute/chronic) | 1-5 | 3.7 (0.7) | 0.01 | 0.06 | 0.863 |
| Personal control | 1-5 | 3.2 (0.6) | -0.10 | 0.06 | 0.086 |
| Treatment control | 1-5 | 3.4 (0.5) | -0.07 | 0.04 | 0.095 |
| Illness coherence | 1-5 | 3.3 (0.8) | -0.24 | 0.08 | 0.003* |
| Timeline (cyclical) | 1-5 | 3.6 (0.8) | -0.04 | 0.07 | 0.634 |
| Emotional representation | 1-5 | 2.7 (0.8) | 0.22 | 0.07 | 0.003* |
| *Causal attributions(n=119)* | | | | | |
| Psychological attributions | 1-5 | 2.0 (0.8) | Men 0.22<br>Women 0.03 | 0.10<br>0.12 | 0.034*<br>0.796 |
| Risk factors | 1-5 | 2.2 (0.6) | 0.08 | 0.05 | 0.133 |
| Immunity | 1-5 | 2.2 (0.7) | 0.17 | 0.07 | 0.010* |
| Accident | 1-5 | 1.8 (1.0) | 0.07 | 0.09 | 0.405 |
| Chance | 1-5 | 3.3 (1.1) | 0.12 | 0.10 | 0.248 |

** Statistically significant (p<0.05)*

## THU0411 FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND LOW VITALITY IN THOSE WITH PSORIATIC ARTHRITIS: RESULTS FROM A LARGE REAL-WORLD SURVEY IN EUROPE AND THE USA

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**Background:** Many patients diagnosed with AS or PsA experience chronic fatigue or low energy which can persist during treatment and affect health related quality of life (HRQOL) and the ability to work.
**Objectives:** To assess self-reported fatigue in patients with AS and vitality in those with PsA, HRQOL and employment status.
**Methods:** In this fatigue and HRQOL study of a cross-sectional survey from 5 European countries and the USA, physicians with 3–30 years' experience were eligible if treating patients with AS or PsA. Inclusion of patients was not restricted by treatment. Patients reported HRQOL (EQ-5D and SF-36), Work Productivity and Activity Impairment Questionnaire (WPAI) as well as other items. AS patients rated their fatigue using BASDAI (BASDAI-Fatigue). In PsA the SF-36 vitality domain (VT) was used to assess fatigue. Fatigue was classified in AS as non-severe (BASDAI-Fatigue <5) to severe (BASDAI-Fatigue ≥5). In PsA tertiles using SF-36 VT were applied to stratify fatigue: low (>65 to 100), moderate (45 to 65) high (0 to <45).
**Results:** Results are presented from 910 patients with AS (613 EU/297 USA) and 1136 with PsA (762/374) who completed questionnaires.
Among AS patients who answered the BASDAI-Fatigue item, 42.0% [373/889] reported severe and 58.0% [516/889] non-severe fatigue. Tertiles of fatigue in PsA were defined based on responses from 1108 patients, who answered the SF-36 VT as: 33.6% [372/1108] low, 35.4% [392/1108] moderate and 31.0% [344/1108] high fatigue.
AS patients reporting severe fatigue had significantly worse HRQOL than those with non-severe fatigue: EQ-5D utility (0.64 vs 0.89); SF-36 physical component summary (PCS) (52.7 vs 82.3); mental component summary (MCS) (54.4 vs 75.9) scores. All SF-36 domains were also significantly lower (all $p$ <0.0001).
PsA patients with high fatigue reported significantly worse HRQOL than those with low or moderate fatigue: EQ-5D (0.60 vs 0.93 and 0.81 respectively); SF-36 PCS (49.7 vs 90.2 vs. 74.1); SF-36 MCS (48.4 vs 84.4 vs. 67.3). All SF-36 domains were significantly worse, omitting VT as this was used for PsA fatigue classification. (all $p$ <0.0001)
Patients with AS reporting severe fatigue had significantly greater overall work impairment due to their disease than those with non-severe fatigue (WPAI (mean): 41.7% vs 13.7%; $p$ <0.0001). Similar significant associations were evident with PsA patients with high, low, moderate fatigue: 43.1% vs 8.9% and 20.0% respectively ($p$ <0.0001).
Among 156 AS patients reporting additional information on retirement or unemployment, 98 had severe and 58 non-severe fatigue. Those with severe fatigue had significantly higher rates of retirement or unemployment due to AS (49.0% vs. 22.4%; p=0.0012).
**Conclusions:** This large analysis of patient-reported data shows that fatigue is common in AS and PsA with a substantial number reporting high/severe fatigue. Fatigue significantly affects HRQOL, social functioning, work productivity and therefore impacts patients' daily life as well as societal costs.
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## THU0412 MASES CORRELATES LINEARLY WITH DISEASE ACTIVITY AND INVERSELY WITH PATIENT RELATED OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS WITHIN THE SCQM COHORT

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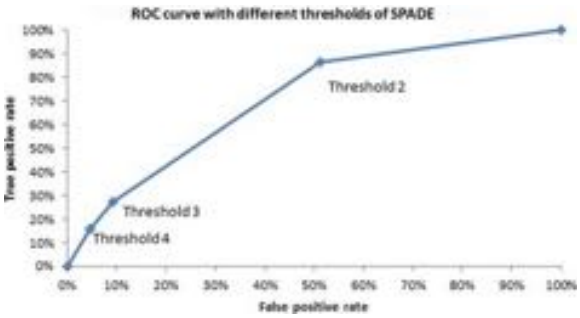
**Background:** Enthesitis is one of the potential extra-axial manifestations found in patients with spondyloarthritis (SpA). Enthesitis can be quantified using the MASES (Maastrich Ankylosing Spondylitis Enthesitis *Score*), consisting 13 predefined entheses assessed for tenderness. There are few data on the MASES outside of RCTs. To better understand the impact of enthesitis real live data are needed.
**Objectives:** To analyse (i) cross-sectionally the correlation of enthesitis with clinical, personal outcome parameters and (ii) longitudinally the development of enthesitis under treatment in patients with axial spondyloarthritis.
**Methods:** We included all patients from the Swiss national registry SCQM with axial spondyloarthritis and valid MASES at baseline. Patients were analysed for demographics at baseline, physical assessments (BASMI, BASFI, BASDAI) and patient centered outcomes (SF36). Continuous variables were compared using a Student's T-test, categorical variables with $\chi^2$ test. Spearman's Rho or linear regression were employed for correlational analyses. Patients were analysed for changes in MASES depending on the initial MASES scores and the therapeutic strategy employed: synthetical DMARDs vs. TNF antagonists.
**Results:** 3241 patients were included into the study. 45.9% of the patient had no entheseal affection at baseline (MASES =0). 59.7% of the patients were HLA B27 pos. and 60.5% of the patients were suffering from axial disease as defined by the New York criteria. The frequency of patients achieving higher MASES scores decreased linearly ($R^2$: 0.4823, p=0.0058). Moderate associations were found for BASDAI, BASFI, patient's and physician's assessments of disease activity patients assessment of pain, the SF 36 mental and physical component score (Spearman's Rho: 0.403, 0.328, 0.326, 0.381, 0.352, -0.215, -0.326, respectively). The average response of MASES after 1 year increases linearly with higher average MASES scores (slope -0.41, $R^2$ =0.78). Patient with a MASES of zero at baseline developed an increase of MASES during follow up (average after 12 month: 0.48). Patients treated with TNF antagonists or DMARDs had a mean change of -1.15 and -1.03 at 12 months, respectively (p=0.967).
**Conclusions:** Almost half of the axial SpA patients suffered from entheseal involvement. Half of the patients with a MASES of zero at baseline developed an entheseal involvement during follow up. Higher MASES scores correlate with parameters indicative of disease activity and patient related outcomes. In those with MASES over 1 the score decreased under treatment during follow up. However, changes of MASES under TNF antagonist or DMARD treatment did not differ in our cohort. In conclusion, a focussed analysis on enthesitis and its therapeutic strategy in SpA is needed.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1985

## THU0413 UTILITY OF THE SPADE TOOL TO IDENTIFY AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH CHRONIC BACKPAIN

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**Background:** Many referral strategies have been devised to optimize the early diagnosis of axial spondyloarthritis (AxSpA). These result in the diagnosis of AxSpA in 30 to 40% of patients. Strategies to reduce the delay in diagnosis of AxSpA and optimise the appropriateness of referrals to secondary care should be explored. The Spondyloarthritis Diagnosis Evaluation (SPADE) tool (www.spadetool.co.uk) has been designed to assist healthcare professionals define the probability of axial spondyloarthritis (AxSpA) in patients <45 years of age with chronic back pain and no definite changes on radiographs. The probability of AxSpA derived from the 'SPADE Tool' is displayed on a chart with clear instructions for the user on what action should be taken next.
**Objectives:** To assess the performance of the SPADE tool in the secondary care setting.
**Methods:** The RNHRD runs a weekly Early Back Pain (EBP) clinic. Data on all patients (AxSpA and Mechanical back pain) has been collected. The SPADE tool which consists of questions pertaining to clinical features, CRP, HLA-B27 and MRI findings was applied on all EBP patients utilizing data they were referred with (before Specialist advised investigations- MRI scan results) to obtain the probability of SpA as one of the 4 categories: Category 1-improbable, category 2-additional tests needed (HLA-B27 or MRI, consider referral to a specialist), category 3 (probable SpA) and category 4 (definitive SpA). A physicians diagnosis of AxSpA was used as the gold standard. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were estimated using observed ratios of patient numbers from this sample. 95% CIs on the NPV were generated by assuming a binomial model for x, where x is the number of patients with SpA who are not referred at a given SPADE threshold.
**Results:** N=87 (49 males); 44 (50.5%) had SpA subsequently diagnosed; 6/27 in category 1, 26/44 in category 2, 5/7 in category 3 and 7/9 in category 4. Estimates of PPV, NPV, sensitivity and specificity obtained by using each of the SPADE categories as a threshold for referral are given in the table.

| Threshold | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| 1 | 100 | 0 | 51 | |
| 2 | 86 | 49 | 63 | 78 [95% CI: 58, 91%] |
| 3 | 27 | 91 | 75 | 55 [95% CI: 43, 67%] |
| 4 | 16 | 95 | 78 | 53 |




**Conclusions:** The SPADE tool is a valuable resource to assist clinicians define the probability of SpA in patients with chronic back pain. The high NPV, especially with the referral threshold set at 2 or 3, implies that the test is most useful in ruling out SpA. Note that the prevalence of AxSpA in this sample is likely to be higher than in the target population (primary care), meaning that these estimates of NPV are likely to be underestimates. The tool needs to be validated in a primary care setting.
**Acknowledgement:** The funding for the SPADE tool was provided through a Medical Education grant from Abviee
**Disclosure of Interest:** None declared
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## THU0414 INTER SPA: SENSITIVITY AND SPECIFITY OF AUTOANTIBODIES AGAINST CD74 IN EARLY AXIAL SPONDYLOARTHRITIS

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**Background:** Making the diagnosis of axial spondyloarthritis (axSpA) may be difficult. Antibodies against CD74 have been shown to be present in 2/3 of patients with long established axial SpA.
**Objectives:** InterSpA is an international multicenter study, conducted to compare the sensitivity and specificity of anti-CD74 and HLA-B27 in patients with axSpA of recent onset.
**Methods:** Patients between 18 and 45 years suffering from inflammatory back pain (IBP) for maximally 2 years were recruited. The presence of ankylosing spondylitis, additional inflammatory rheumatic disorders and biologic therapy were exclusion criteria. MRI of sacroiliac joint was performed in all patients; HLA-B27 was detected by genotyping and anti-CD74 using a CE certified kit of Aesku Diagnostics (Wendelsheim, Germany). The sensitivity of anti-CD74 and HLA-B27 were calculated in patients fulfilling the imaging arm of ASAS criteria, in all patients fulfilling ASAS criteria and in 100 blood donors. Both the MRI reading as well as the laboratory procedures were performed blinded.
**Results:** 205 patients suffering from IBP were recruited. There were 40 recruiting failures. The remaining 165 patients had a mean age of 29.4 years, a mean duration of IBP of 12.6 months, 50% of the patients were female. Sacroiliitis was diagnosed by the local and an independent expert reader in 71/123 (57.7%). So far complete data sets are available of 91 patients. Of these, 16 fulfilled the ASAS criteria of axSpA by a pathologic MRI only, 40 by both MRI and presence of HLA-B27 and 20 by HLA-B27 only. The sensitivities of IgA anti-CD74, IgG anti-CD74 and HLA-B27 were 71.4%, 26.8% and 75% in the 56 axSpA patients with a pathologic MRI, 73.7%, 23.7% and 81.6% in all 76 patients fulfilling ASAS criteria, and 3%, 5% and 8% in the blood donors. The likelihood ratios are 23.8

(IgA anti-CD74), 5.4 (IgG anti-CD74) and 9.4 (HLA-B27) when considering the patients with a pathologic MRI only, and 24.6 (IgA anti-CD74), 4.7 (IgG anti-CD74) and 10.2 (HLA-B27) when considering all patients fulfilling ASAS criteria.
**Conclusions:** Considering their specificity and sensitivity, IgA anti-CD74 is a useful addition to our diagnostic tools for axSpA.
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## THU0415 THE EFFECT OF SMOKING ON CLINICAL AND STRUCTURAL DAMAGE IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Although it has been widely accepted that smoking has a negative effect on AS and aSpA patients, the findings were limited by small sample size and conflicting data.
**Objectives:** To examine the impact of smoking on clinical and structural damage in patients with AS and aSpA.
**Methods:** A systematic literature review was performed by 2 reviewers, a librarian and a methodologist. Studies were identified by a sensitive search strategies in the main bibliographic databases (Medline, Embase and Cochrane Library) up to November 2014. We selected articles that analysed, in AS and aSpA patients, the smoking impact on disease activity, structural damage, functional status and quality of life. Any type of study except case series or case reports was eligible. Two reviewers (VVG and TCI) screened the titles and abstracts of the retrieved articles independently. VVG reviewed the selected articles in detail and collected the data from the studies included by using *ad hoc* standard forms. A hand research was completed by reviewing the included studies references. The evidence level was assessed with the Oxford Centre for Evidence-based Medicine Levels of Evidence.
**Results:** Of 341 studies identified, 13 were selected for inclusion: 7 case-control and 6 cohort studies. These studies provided data from over 4.163 patients. All studies evaluated patients with AS and only two evaluated patients with AS and aSpA, being the quality of the studies moderate-low. Current smokers with AS, had a higher disease activity (BASDAI $>4$) [OR=1.83; IC95% 1.13 a 2.98; p=0.015], poorer quality of life (ASQoL$>7$) [OR=2.00, IC95% 1.25 a 3.22, p=0.004] and more pain (numerical scale NRS) [OR=2.00, IC95% 1.23 a 3.27, p=0.005], independently of age, sex, duration of the disease and social support. Smoking was significantly associated with progression of functional disability in patients with AS for less than ten years of disease duration (HAQ-S increased 0.0545 units/yr among smokers compared to nonsmokers, p=0.004).In patients with aSpA, smoking was associated with an earlier onset of inflammatory back pain [regression coefficient (B)= -1.46; IC 95% -2.87 a -0.06, p=0.04], higher disease activity (ASDAS-PCR B=0.20; IC95% 0.02 a 0.38; p=0.03; BASDAI B=0.50; IC95% 0.17 a 0.83; p=0.003), worse functional status (BASFI B=0.38; IC95% 0.07 a 0.69; p=0.02), more frequent inflammation and more structural damage in MRI (OR=1.91; IC95% 1.34 a 2.72, p$<$0.001) and plain radiography (OR=1.56; IC95% 1.08 a 2.26, p=0.02), and poorer quality of life (Euro-QoL) [B=1.38; IC95% 0.69 a 2.07, p$<$0.001].
**Conclusions:** Smoking cessation should be recommended in AS and aSpA patients, not only at the disease onset, but also along the follow-up. However, the available evidence is insufficient and limits the recommendation strength (NE 4, GR C). Larger-scale studies with longitudinal follow-up in disease activity, functional ability and structural damage in AS and aSpA patients, are necessary. This systematic literature review was performed to inform the aSpA and psoriatic arthritis guideline (ESPOGUIA) of the Spanish Society of Rheumatology.
**Disclosure of Interest:** None declared
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## THU0416 PREVALENCE OF COMORBIDITIES AND RISK FACTORS IN SPONDYLOARTHRITIS IN LATIN AMERICA: A COMPARATIVE STUDY WITH GENERAL POPULATION: DATA FROM THE MULTINATIONAL ASAS-COMOSPA STUDY

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**Background:** Increased risk of some comorbidities has been reported in spondyloarthritis (SpA). Knowledge about the prevalence and data related to these comorbidities and risk factors in Latin America is limited.
**Objectives:** To determine the prevalence of several comorbidities and risk factors for these comorbidities in patients with SpA in three Latin American countries, and to compare this prevalence with the rates in the general population investigating whether the prevalence is increased.
**Methods:** Data of 390 consecutive patients with SpA enrolled in the international cross-sectional ASAS-COMOSPA study from Argentina, Colombia and Mexico were analysed. The prevalence rates (95% CI) of arterial hypertension (AHT), tuberculosis (TB), and malignancies (colon, melanoma, lung, lymphoma, prostate, cervix and breast) were estimated with continuity correction according to the method described by Wilson. The data from Colombian general population (adjusted per gender and age group) were obtained from the CARMELA study for AHT, from the National Health Surveillance Public System for TB and HBV and from the GLOBOCAN project for malignancies. The prevalence (95% IC) in SpA patients was compared with the prevalence rates in the Colombian general population by calculating age and gender-specific prevalences for AHT, TB and HBV, and calculating gender-specific prevalences for malignancies. SPSS Statistics 22 was used to perform the statistical analysis.
**Results:** In total 64% were male, mean age of 45 (14.7) years and disease duration of 7.0 (8.1) years. The most common comorbidities were AHT (25.3%), hypercholesterolemia (21.8%), osteoporosis (9.4%) and gastrointestinal ulcer (7.8%). The prevalence of AHT was 25.3% (95% CI 21.2 to 29.4) and was significantly higher compared with the general population 13.4% (95% CI 11.5 to 15.2). The overall prevalence of TB was 3.33% (95% CI 1.8 to 5.7) and the prevalence of HBV infection was 1.03% (95% IC 0.3 to 2.7), both increased as compared with the general population (0.03% and 0.01% respectively). There was not an increased prevalence of cancers compared with general population.
**Conclusions:** In patients with SpA, we found a higher prevalence of hypertension, tuberculosis and hepatitis B infections in three Latin America countries as compared with general population data. A systematic evaluation and screening of these comorbidities and risk factors may help to properly monitor and detect these conditions in SpA patients.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1814

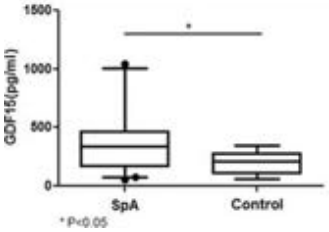
## THU0417 SERUM LEVELS OF GDF15 ARE ELEVATED IN SPONDYLOARTHRITIS, AND NEGATIVELY LINKED WITH BONE EROSION

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**Background:** In order to assess disease activity and predict outcomes of patients with spondyloarthritis (SpA), it is necessary to discover useful serum biomarker reflecting inflammation, fat deposition, erosion and ankylosis [1]. GDF15 was previously fond related to inflammation [2] and worked as a protective factor in inflammatory pathology. In rheumatology arthritis patients, serum level of GDF15 could predict the presence of joint erosions [3].
**Objectives:** The objective was to assess associations between GDF15 and radiographic features, including X-ray and MRI of the sacroiliac joint in SpA patients.
**Methods:** SpA was defined according to 2009 ASAS criteria. Sera from 53 patients with SpA and 18 healthy controls were measured GDF15 levels using ELISA. Inflammation was assessed by ESR, CRP and MRI of the SIJ, using the Spondyloarthritis Research Consortium of Canada (SPARCC) score and a method of dichotomy to assess fat deposition, bone erosion and ankylosis. Radiographs of the pelvis were scored by using the modified New York (mNY) score.
**Results:** Serum GDF15 levels were higher in SpA patients in comparison with controls (208.4 ± 173.7 vs 339.2 ± 295.0 pg/ml and P=0.005 Figure). Among

SpA, patients who suffered from bone erosion on MRI had lower levels of GDF15 (423.4± 288.1 vs 284.3± 275.6 pg/ml and P=0.022).In addition, correlation analysis showed there was a negative correlation between serum GDF15 and bone erosion (r= -0.433, p=0.007) in SpA patients whose X-rays were 0-III according to mNY criteria. Moreover, GDF15 levels of those patients were related to CRP levels ((r=0.328, p=0.044). No significant correlations were found between SPARCC score, fat deposition and ankylosis and GDF15 levels, but CRP and ESR levels were significantly correlated with SPARCC score (r=0.291, p=0.036 and r=0.474, p=0.0004) in SpA.

Figure1 Serum GDF15 levels in SpA patients and Controls




**Conclusions:** Our study suggested that serum GDF15 levels were higher in SpA patients than healthy controls.GDF15 was correlated with CRP which was correlated with SPARCC score, suggesting GDF15 may not directly related to bone edema in SpA. GDF15 was negatively related to bone erosion, which may play a protective role in process of bone erosion.

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**Disclosure of Interest:** None declared

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## Psoriatic arthritis

### THU0418 OBESITY IMPAIRS THE RESPONSE TO TUMOUR NECROSIS FACTOR-ALPHA INHIBITORS IN PSORIATIC ARTHRITIS: RESULTS FROM THE DANBIO AND ICEBIO REGISTRIES

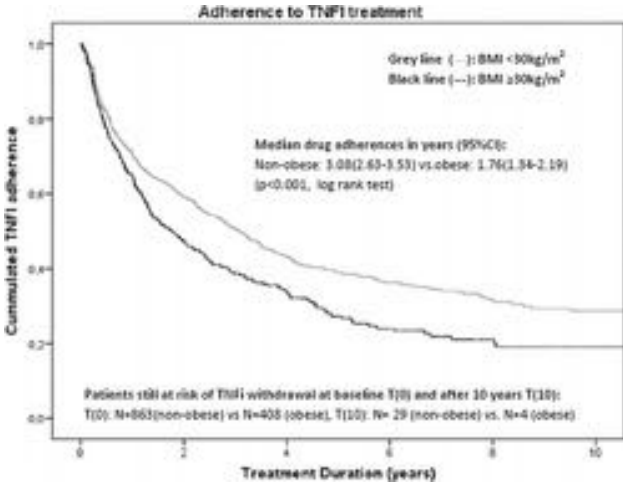
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**Background:** TNF-α inhibitor (TNFI) treatment fails among half of patients with psoriatic arthritis (PsA) treated in routine care. Obesity is a frequent, pro-inflammatory condition in PsA that may affect pharmacokinetics, immunological processes and patient-reported outcomes.

**Objectives:** To investigate the impact of obesity on disease activity, treatment response and drug adherence among PsA patients initiating their first TNFI treatment course in routine care.

**Methods:** Observational cohort-study based on the Danish (DANBIO) and Icelandic (ICEBIO) registries. Kaplan-Meier plots, Cox regression and logistic regression analyses studied the impact of obesity (body mass index (BMI) $\geq$30kg/m$^2$) on drug adherence and TNFI response. Six-month response was defined according to ACR20/50/70 and EULAR criteria. Sub-analyses stratified according to gender and TNFI (adalimumab/etanercept/infliximab) were performed.

**Results:** Among 1943 patients (1750 Danish, 193 Icelandic) included in the study, 1271 (65%) had available BMI and 408 (32%) of these were obese (327 (80%) Danish, 81 (20%) Icelandic). Prescription rates were: adalimumab (39%), etanercept (26%), infliximab (24%), golimumab (7%) and certolizumab (4%). Median follow-up-time was 1.5 years, IQR: 0.5–3.9. At baseline obese patients smoked less (23% vs 30%), were older (49±12 vs 47±13 years, (mean (SD)) and had higher disease activity measured as DAS28 (4.6±1.2 vs 4.4±1.2), tender joint count (6 (3–13) vs 5 (2–11); median, (IQR)), C-reactive protein (9 (5–19) vs 7 (3–18)), HAQ score (1.1 (0.8–1.6) vs 0.9 (0.5–1.4)), Visual-Analogue-Scale (VAS) patient global (72 (54–87) vs 65 (50–80)) and VAS pain (66 (48–76) vs 60 (38–74)), compared with non-obese (all $p<0.05$). Obese patients had shorter treatment adherence than non-obese (Figure 1), especially among men (5.9 (4.1–7.7) vs 2.5 (1.7–3.2)); median years (95%CI), ($p<0.01$). Similar results were found when Icelandic and Danish patients were analyzed separately. Obesity was an independent predictor of TNFI withdrawal both overall: HR 1.6 (95%CI 1.3–2.0), in men: HR 1.8 (1.3–2.5), women: HR 1.5 (1.1–2.0) and for every TNFI:




adalimumab: HR 1.6 (1.2–2.2), etanercept: HR 2.0 (1.3–3.3), infliximab: HR 1.6 (1.1–2.5). The EULAR good-or-moderate response rate was significantly lower in obese than non-obese (55% vs 65%), (p=0.02). In men, obesity reduced the chance of both EULAR good response: OR 0.5 (95%CI 0.3–0.9) and EULAR good-or-moderate, ACR20 and ACR50 responses (all OR 0.4 (0.2–0.8)). Obesity also predicted a poorer EULAR good-or-moderate response overall (OR 0.6 (0.4–0.9)), in women (OR 0.5 (0.3–0.9)) and for all TNFI types (data not shown).

**Conclusions:** Obesity is associated with increased disease activity and attenuates response and adherence to TNFIs in PsA.

**Acknowledgement:** Thank you to Elinborg Stefansdottir who assisted in the achievement of Icelandic data, to Niels Steen Krogh from Zitelab for extraction of data and to Peder Frederiksen and Robin Christensen for statistical advises. Thanks to all Danish and Icelandic Departments of Rheumatology for providing data to DANBIO and ICEBIO.

**Disclosure of Interest:** None declared

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### THU0419 RAPID3 PERFORMS WELL IDENTIFYING TREATMENT EFFECT IN THE TIGHT CONTROL OF PSORIATIC ARTHRITIS STUDY

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**Background:** RAPID3 is a patient completed outcome measure assessing disease activity in inflammatory arthritis consisting of the health assessment questionnaire (HAQ) and two VAS scales. It is feasible for use in clinical practice and has been well validated in rheumatoid arthritis (RA) and other conditions, but there is little data on its use in psoriatic arthritis (PsA).

**Objectives:** To investigate the responsiveness and discrimination of RAPID3 and a modified version with skin VAS in the Tight Control of Psoriatic Arthritis (TICOPA) trial.

**Methods:** Data from the TICOPA trial were used to assess the performance of the RAPID3 index. RAPID3 was calculated using the HAQ-DI, patient completed pain VAS and global disease activity VAS. Due to concerns about skin involvement in PsA, we also calculated a novel RAPID3Ps score which also included a skin activity VAS to see if performance was superior.

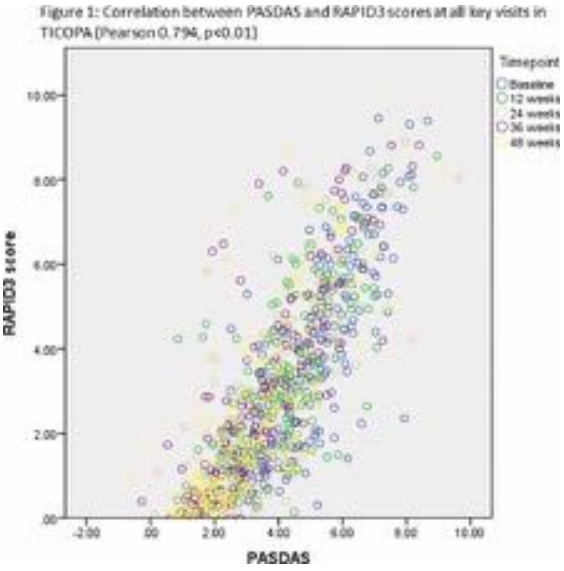
Results from the RAPID3 measures were correlated with the PsA disease activity score (PASDAS) a composite disease activity score already validated by GRAPPA. Change in the RAPID3 measures and other outcome measures were compared between the tight control arm and the standard care arm of the TICOPA study using t-test for continuous variables and chi-squared for categorical measures of disease state.

**Results:** RAPID3 scores strongly correlated with PASDAS (Pearson correlation 0.794, $p<0.01$) at all baseline and follow up visits. The change in score at follow up was also moderately correlated with the change in PASDAS (0.636, $p<0.01$). Correlation was similar for the RAPID3Ps at 0.831.

When looking at differentiation between treatment groups, change in RAPID3 score at 48 weeks was highly discriminant (t value -3.43, $p<0.001$) and was higher than all other PsA measures (DAPSA and other individual outcome measures) except for PASDAS (t value -3.75, $p<0.001$) as shown in the table.

Looking at specific cutpoints, RAPID3 “near remission” was also highly discriminant between treatment groups (chi squared 7.48, p=0.006) although with a lower value than the minimal disease activity criteria for PsA (chi squared 10.11, p=0.001).

| Measure | Tight Control | | | | Standard Care | | | | T value | p |
|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | Mean change | SRM | ES | Baseline | Mean change | SRM | ES | | |
| PASDAS | 5.27 | –2.49 | –1.45 | –1.77 | 4.96 | –1.38 | –0.83 | –1.09 | –3.75 | 0.00 |
| RAPID3 | 4.18 | –2.16 | –1.07 | –1.06 | 3.59 | –1.01 | –0.47 | –0.52 | –3.43 | 0.00 |
| Phy Global | 44.10 | –32.26 | –1.57 | –1.62 | 40.80 | –19.83 | –0.86 | –1.27 | –3.34 | 0.00 |
| Pt Global | 56.15 | –33.60 | –1.05 | –1.20 | 51.54 | –18.64 | –0.56 | –0.69 | –3.12 | 0.00 |
| pain VAS | 53.42 | –31.92 | –1.05 | –1.18 | 47.33 | –17.79 | –0.56 | –0.68 | –2.82 | 0.01 |
| DAPSA | 31.24 | –19.01 | –1.08 | –0.94 | 30.04 | –11.45 | –0.69 | –0.53 | –2.61 | 0.01 |
| fatigue | 48.85 | –21.44 | –0.73 | –0.78 | 46.39 | –13.20 | –0.46 | –0.46 | –1.84 | 0.07 |
| TJC | 12.33 | –6.62 | –0.65 | –0.56 | 13.22 | –3.34 | –0.28 | –0.24 | –1.57 | 0.12 |
| SJC | 7.57 | –6.27 | –0.96 | –0.97 | 6.82 | –4.50 | –0.57 | –0.58 | –1.22 | 0.22 |




**Conclusions:** RAPID3 shows good correlation with other validated measures of disease activity in PsA and addition of a psoriasis measure does not seem necessary in this population. The RAPID3 score and "near remission" definition are able to effectively discriminate between two active treatment groups in an interventional trial.

**Acknowledgement:** We acknowledge all collaborators and participants in the TICOPA trial.

**Disclosure of Interest:** None declared

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## THU0420 APREMILAST, AN ORAL PHOSPHODIESTERASE 4 INHIBITOR, IS ASSOCIATED WITH LONG-TERM (52-WEEK) IMPROVEMENTS IN BASDAI IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED RESULTS FROM 3 PHASE III, RANDOMIZED, CONTROLLED TRIALS

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**Background:** In the PALACE psoriatic arthritis (PsA) trials, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score was obtained as an exploratory measure in a subset of patients (pts) considered by investigators to have axial involvement, although PsA spondylitis was not confirmed by more objective measures such as MRI.

**Objectives:** Assess the impact of apremilast 30 mg BID (APR) on BASDAI over 52 wks using PALACE 1 (NCT01172938), 2 (NCT01212757), and 3 (NCT01212770) pooled data of pts with active PsA despite prior conventional DMARDs and/or biologics.

**Methods:** APR was evaluated in a subset of pts with baseline (BL) BASDAI ≥4 ("subset") over 16, 24, and 52 wks.

**Results:** BL BASDAI ≥4 was reported in 454/1493 (30%) pts. Mean PsA duration was similar between the subset and the rest of the PALACE 1–3 population (BL BASDAI <4: n=1039). Slightly higher percentages of the subset had a history of palmoplantar, nail, scalp, or plaque psoriasis; mean BL psoriasis BSA and % with BSA ≥3% were slightly increased. The subset had higher mean BL values for CRP (1.12 vs 0.93), pain VAS (63.6 vs 53.8), pt's global disease assessment (62.2 vs 53.5), and physician's global disease assessment (PhGA) (59.0 vs 53.0) and markedly worse mean HAQ-DI (1.41 vs 1.08), SF-36v2 PF (30.6 vs 35.8), and FACIT-F (25.7 vs 31.8); TJC was higher (25.1 vs 19.1) and SJC (12.4 vs 10.9) was less differentiated. DAS-28 scores were comparable. Despite disease activity differences, BL concomitant oral DMARDs were similar in both groups: 1 in 61.0% and 2 in 5.5% (subset) vs 1 in 57.8% and 2 in 6.4% (rest of PALACE 1–3 population); MTX was the most common DMARD. In the subset, 73.6% had only been treated with oral DMARDs pre-study and 44.9% with only 1 DMARD; 25.1% had prior biologic use and 9% prior biologic failure, slightly higher percentages vs the other group. Small increases in BL NSAID and analgesic use were noted in the subset. Mean BL BASDAI scores in the subset were 6.6 in APR and 6.4 in placebo (PBO)pts. APR resulted in a greater mean decrease in BASDAI score vs PBO at Wk 16 (–1.53 vs –0.91; *P*=0.0173) and Wk 24 (–1.64 vs –0.74; *P*=0.0002); other disease measures significantly improved, including marked HAQ-DI, PhGA, and fatigue improvements (Table). Long-term improvement was seen across measures, with mean Wk 52 BASDAI reduction of –2.18 (Table) and mean HAQ-DI improvement of –0.464.

**Outcomes at Wk 24 and Wk 52 in Pts With BASDAI ≥4 at BL**

| | Wk 24 (LOCF) | | Wk 52 (Data as Observed) |
|---|---|---|---|
| | APR 30 mg BID n=156 | PBO n=151 | APR 30 mg BID n=125 |
| BASDAI score, mean BL | 6.6 | 6.4 | 6.6 |
| BASDAI score, mean change from BL | –1.64* | –0.74 | –2.18 |
| SJC, mean change | –5.5* | –2.4 | –8.5 |
| HAQ-DI, mean change | –0.301* | –0.117 | –0.464 |
| SF-36v2 PF, mean change | 4.98* | 1.76 | 7.06 |
| Pain VAS, mean change | –12.6* | –7.9 | –22.1 |
| FACIT-F, mean change | 4.38* | 1.29 | 6.77 |
| Pt's global assessment, mean change | –10.9 | –5.7 | –19.8 |
| Physician's global assessment, mean change | –22.1* | –7.4 | –34.3 |

*P≤0.05; †P≤0.0001 vs PBO; based on an analysis of covariance model for the change from BL, with treatment group, BL DMARD use, and study as factors, and BL value as the covariate. Pt's global assessment of pain APR30 vs PBO at Wk 24, P=0.0590. At Wk 24, missing values were handled using LOCF; Wk 16 data were carried forwarded to Wk 24 for pts who early escaped at Wk 16; the n represents the number of pts randomized at BL and with a BL BASDAI value ≥4. For Wk 52, the n represents the number of pts randomized to APR30 at BL and with a BL BASDAI value ≥4 and an outcome measure at Wk 52; the n may vary slightly for each end point. LOCF=last observation carried forward; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; SJC=swollen joint count; HAQ-DI=Health Assessment Questionnaire-Disability Index; SF-36v2 PF=36-item Short-Form Health Survey version 2 Physical Functioning domain score; VAS=visual analog scale; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue.

**Conclusions:** In this post-hoc analysis, pts reporting BASDAI ≥4 appear to have added disease burden, with greater disability, pain, fatigue, and global disease ratings; this may not be captured by some disease activity measures, and effective treatment strategies may not have been available. APR resulted in long-term improvements in BASDAI scores and other measures. Further evaluation objectively assessing presence of inflammatory spine disease in PsA and its response to APR is warranted.

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## THU0421 SERUM-BASED SOLUBLE MARKERS MAY DIFFERENTIATE PSORIATIC ARTHRITIS FROM OSTEOARTHRITIS

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**Background:** It is often difficult to differentiate psoriatic arthritis (PsA) from osteoarthritis (OA) in clinical practice.

**Objectives:** To aid clinical diagnosis, we aimed to identify soluble biomarkers that differentiate PsA from OA.

**Methods:** Serum samples from 201 patients with OA (mean age 65 years, 43.3% males, no history of inflammatory disease), 77 patients with PsA satisfying CASPAR criteria (mean age 45 years, 54.5% males) and 76 healthy controls (mean age 37 years, 50% males) were obtained from the respective biobanks of the Arthritis Program, University Health Network, and the University of Toronto PsA Program. Samples were obtained at the time of joint replacement surgery (OA) or at the time of clinical assessment (PsA, healthy controls), and stored at -80°C until laboratory assays were conducted. Soluble markers of cartilage metabolism (COMP, hyaluronan), metabolic syndrome (adiponectin, adipsin, resistin, HGF,

insulin, leptin) and inflammation/immune response (CRP, IL-1b, -6, -8, TNF-α, MCP-1, NGF) were assayed in the samples using Luminex multiplex assay. Marker levels in serum were compared across the 3 groups using the Kruskal-Wallis test. Pair-wise comparisons were made with Wilcoxon rank sum test. To identify markers that differentiate PsA from OA, multivariate logistic regression analyses with backward elimination, adjusted for age and sex, were constructed using markers determined to be significant at a $p \leq 0.1$ from univariate analyses. Discriminative ability was assessed by way of receiver operating characteristic (ROC) curves based on findings from multivariate models. The final model was further validated in an independent set of 73 PsA and 75 OA samples using predicted probabilities estimated using coefficients from the model developed on the training set.

**Results:** Univariate analyses revealed the following markers significantly differed across groups ($p<0.001$): COMP, hyaluronan; resistin, HGF, insulin, leptin; CRP, IL -6, -8, TNF-α, MCP-1, NGF. When comparing PsA to OA, the following markers significantly differed ($p<0.001$): COMP, hyaluronan; resistin, HGF, insulin; CRP, IL-6, -8, TNF-α, MCP-1, NGF. Multivariate analysis demonstrated that COMP (OR 1.24, 95% CI 1.06, 1.46), resistin (OR 1.26, 95% CI 1.07, 1.48), MCP-1 (OR 1.10, 95% CI 0.07, 1.48) and NGF (OR $<0.001$, 95% CI $<0.001$, 0.25) were independently associated with PsA vs. OA. The area under the ROC curve (AUROC) for this model was 0.99. Internal cross-validation of the model consistently identified MCP-1 as a PsA marker. Further validation of the model including COMP, resistin, MCP-1 and NGF showed an AUROC of 0.98.

**Conclusions:** A panel of 4 biomarkers (COMP, resistin, MCP-1, NGF) may distinguish PsA from OA. Clinical utility of these markers will need to be determined in prospective studies.

**Disclosure of Interest:** None declared

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## THU0422 APREMILAST MONOTHERAPY AS THE FIRST SYSTEMIC TREATMENT IN DMARD-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: 3-YEAR TREATMENT RESULTS

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**Background:** Apremilast (APR) is an oral phosphodiesterase 4 inhibitor that helps regulate the immune response that causes joint inflammation and other manifestations of psoriatic arthritis (PsA), including skin disease. Primary findings from the PALACE 4 study (NCT01307423) demonstrated greater efficacy with APR vs. placebo in DMARD-naive patients with active PsA.[1,2]

**Objectives:** Describe the long-term efficacy and safety of APR monotherapy in DMARD-naïve patients in PALACE 4 for up to 156 weeks.

**Methods:** Patients were randomized (1:1:1) to placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20). Patients whose swollen joint count (SJC) and tender joint counts (TJC) had not improved by ≥20% at Week 16 were considered non-responders and required to be re-randomized (1:1) to APR30 or APR20 if they were initially randomized to placebo, or continued on their initial APR dose. At Week 24, all patients remaining on placebo were re-randomized to APR30 or APR20. Double-blind treatment continued to Week 52 with open-label APR for up to 4 additional years.

**Results:** A total of 527 patients were randomized and received ≥1 dose of placebo (n=176), APR30 (n=176), and APR20 (n=175). Of the patients entering the third year of therapy, 88.0% (272/309) completed the Week 156 visit. At Week 52, 58.0% (119/205) of patients receiving APR30 and 55.4% (107/193) receiving APR20 achieved a 20% improvement in modified American College of Rheumatology (ACR20) response (Table). At Week 156, rates of improvement in PsA signs and symptoms and physical function were sustained, as shown by modified ACR20/ACR50/ACR70 responses, mean percent change in SJC/TJC, mean change in Health Assessment Questionnaire-Disability Index (HAQ-DI) score, proportion of patients with HAQ-DI exceeding the minimal clinically important differences (MCID) ≥0.30 threshold, achievement of Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) of 0 and dactylitis count of 0, and 75% and 50% reduction from baseline Psoriasis Area and Severity Index (PASI-75 and PASI-50) responses (Table). During Weeks >104 to ≤156, the most common adverse events (AEs) among APR-exposed patients were upper respiratory tract infection (3.2%) and nasopharyngitis (3.9%); serious AEs occurred in 5.2% of APR patients, and no opportunistic infections occurred. In general, no change in the types of AEs and no increase in the incidence and severity of AEs were seen with longer-term exposure.

| | Outcomes at Weeks 52 and 156 | | | |
|---|---|---|---|---|
| | Week 52 | | Week 156 | |
| | APR30 n=207* | APR20 n=194* | APR30 n=143* | APR20 n=133* |
| ACR20, n/m† (%) | 119/205 (58.0) | 107/193 (55.4) | 84/141 (59.6) | 79/131 (60.3) |
| ACR50, n/m† (%) | 61/205 (29.8) | 54/191 (28.3) | 50/141 (35.5) | 51/131 (38.9) |
| ACR70, n/m† (%) | 32/206 (15.5) | 23/192 (12.0) | 33/143 (23.1) | 26/130 (20.0) |
| SJC, mean % change | −76.1 | −70.5 | −84.3 | −78.1 |
| TJC, mean % change | −59.4 | −52.4 | −65.7 | −63.6 |
| HAQ-DI (0-3), mean change | −0.35 | −0.28 | −0.38 | −0.35 |
| HAQ-DI MCID ≥0.30†, n/m (%) | 98/207 (47.3) | 89/194 (45.9) | 69/143 (48.3) | 66/133 (49.6) |
| MASES of 0, n/m (%)† | 65/127 (51.2) | 52/132 (39.4) | 50/79 (63.3) | 55/91 (60.4) |
| Dactylitis count of 0, n/m (%)† | 74/102 (72.5) | 72/102 (70.6) | 60/71 (84.5) | 65/73 (89.0) |
| PASI-75, n/m (%)† | 34/119 (28.6) | 42/112 (37.5) | 32/82 (39.0) | 33/77 (42.9) |
| PASI-50, n/m (%)† | 64/119 (53.8) | 65/112 (58.0) | 46/82 (56.1) | 46/77 (59.7) |

*Data as observed; n/m=number of responders/number of patients with sufficient data for evaluation. *The n reflects the number of patients treated with APR30 and APR20 regardless of when patients started taking APR (Baseline, Week 16, or Week 24) and who had data available at the specific time point; actual number of patients available for each end point may vary. †Denominators vary slightly due to availability of sufficient data for each level of ACR response assessment. ‡Pre-specified MCID threshold, based on the literature (Mease PJ, et al. Ann Rheum Dis. 2004;63(Suppl 1):391) at the time of protocol development and definition of analysis. §Examined among patients with enthesitis at baseline and data at the specific time point. Mean MASES at baseline were 3.5 (APR30) and 4.1 (APR20). ¶Examined among patients with dactylitis at baseline and data at the specific time point. Dactylitis mean counts at baseline were 3.6 (APR30) and 3.1 (APR20). #Examined among patients with psoriasis involvement of the body surface area ≥3% at baseline and data at the specific time point.

**Conclusions:** Over 156 weeks, APR monotherapy demonstrated sustained response and improvements in PsA signs and symptoms, including SJC, TJC, enthesitis, dactylitis, physical function, and psoriasis. APR continued to demonstrate an acceptable safety profile and was generally well tolerated.

**References:**

[1] Edwards et al. Arthritis Rheum. 2014;66(11 Suppl)S694–5. Abstract 1572.

[2] Wells et al. Arthritis Rheum. 2014;66(11 Suppl)S264–5. Abstract 602.

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## THU0423 TIME TO REBOUND IN JOINT SYMPTOMS FOLLOWING DISCONTINUATION OF TNFI THERAPY AFTER ACHIEVING LOW DISEASE ACTIVITY OR REMISSION IN PSORIATIC ARTHRITIS PATIENTS ENROLLED IN THE US CORRONA REGISTRY

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**Background:** The treatment goal for patients (pts) with psoriatic arthritis (PsA) is to suppress disease activity. Little is known about clinical outcomes in pts who stop TNFi therapy after achieving low disease activity (LDA) during routine care.

**Objectives:** We evaluated time to rebound (i.e., increase in joint symptoms after therapy discontinuation) in pts with PsA who achieved LDA prior to stopping TNFi therapy as well as changes in measures of disease activity at the first visit following TNFi discontinuation.

**Methods:** In the Corrona registry, we identified pts with PsA who initiated a TNFi (adalimumab, etanercept, infliximab, golimumab), achieved LDA based on Clinical Disease Activity Index (CDAI) ≤10 on TNFi therapy, discontinued TNFi altogether while still in LDA (persistence on conventional disease modifying medication was allowed) and had at least 1 follow-up visit while off TNFi. Demographic and clinical characteristics were assessed at discontinuation date (index date). To assess time to rebound, pts were followed until earliest of the following events: rebound of symptoms (CDAI >10), initiation of another biologic/small molecule or last follow-up visit. Kaplan-Meier curves were generated for time to rebound (CDAI >10). To assess impact of TNFi discontinuation, change in disease activity measures including CDAI, modified Health Assessment Questionnaire (mHAQ), pt and physician global assessments, and pt pain were assessed between discontinuation and first post-index visit.

**Results:** There were 94 pts (57% female, 51% biologic-experienced at TNFi initiation) who met study criteria. At TNFi discontinuation, mean (standard deviation [SD]) age and disease duration were 52.6 (12.7) and 9.8 (7.4) years, respectively. Over time, 67 (73%) pts had a rebound in symptoms, with median time to rebound of 8 months (95% CI 6–12). At first post-index visit, there was a significant mean increase in all measures of disease activity except mHAQ (Table).

Table 1. Disease activity measures at index (TNFi discontinuation), first post-index visit, and change during interval

| Disease activity measure | Index: Mean (SD) | Follow-up visit: Mean (SD) | Mean change (SD) | p-value |
|---|---|---|---|---|
| CDAI | 4.3 (3.1) | 7.5 (7.7) | –3.2 (6.9) | *<0.0001* |
| mHAQ | 0.24 (0.35) | 0.27 (0.38) | –0.03 (0.26) | 0.328 |
| Physician Global | 9.9 (10) | 14.7 (14.9) | –4.8 (15.4) | 0.003 |
| Pt. Global | 23.2 (21.4) | 29.6 (25.6) | –6.5 (23.7) | 0.01 |
| Pt. Pain | 26.4 (24.9) | 32.1 (26.7) | –5.6 (20.7) | 0.01 |

**Conclusions:** Rebound of symptoms in PsA patients occurred frequently with the majority of patients having worsening of disease activity by the next visit after TNFi discontinuation. These results suggest careful consideration before stopping these agents after achievement of low disease activity.
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## THU0424 TREATMENT WITH TNF ALPHA BLOCKERS IS ASSOCIATED WITH REDUCED PROGRESSION OF ATHEROSCLEROTIC PLAQUES IN PATIENTS WITH PSORIATIC DISEASE – A PROSPECTIVE STUDY

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**Background:** Patients with psoriatic disease are at high risk for cardiovascular morbidity. The strong link between inflammation and atherosclerosis highlights the role of suppression of inflammation as a potential strategy for prevention of cardiovascular events.
**Objectives:** To assess whether the use of TNFα blockers is associated with reduced rate of progression of atherosclerotic plaques in psoriatic disease patients.
**Methods:** Patients with psoriasis only (PsC) or psoriatic arthritis (PsA) from a large psoriatic disease cohort were enrolled. Baseline evaluation included clinical assessment of cardiovascular risk factors, joint and skin disease activity and medication use. Patients were followed every 6–12 months according to a standard protocol. Treatment with any TNFα blocker for at least 50% of the follow-up period was defined as the primary predictor. Ultrasound assessment of the carotid arteries was performed and Total Plaque Area (TPA) was measured at baseline and after 2–3 years. The average annual change in TPA was calculated by subtracting the baseline from the follow-up TPA divided by the number of years between the visits. This measure represented the annual progression rate of atherosclerosis and was considered the outcome of interest. The association between treatment with a TNFα blocker and progression of atherosclerosis was assessed by multivariate linear regression analysis after adjusting for cardiovascular risk factors, statin therapy and treatment with Disease Modifying Anti Rheumatic Drugs (DMARDs).
**Results:** A total of 319 patients with psoriatic disease (66.4% PsA, 33.6% PsC) were included in the analysis. Their mean age was 54.5±11.8 years and 56.3% were men. The mean duration of follow up was 2.9 years. 61.7% of the patients had at least one atherosclerotic plaque at baseline. Progression in atherosclerosis was observed in 46% of the patients, while in the remaining 54% no change/regression in atherosclerosis was found. Men had a significantly higher annual progression rate of atherosclerosis compared with women (annual TPA 2.4 vs. 0.6 $mm^2$, $p<0.001$, respectively). Since a statistically significant interaction between sex and several of the co-variates, including TNFα blocker therapy, was found, separate regression models were constructed for men and women. In men, TNFα blocker therapy was associated with a reduced adjusted rate of atherosclerosis progression (β=-2.25 95% Confidence Interval (CI) -3.45, -1.05, $p<0.001$). Additional predictors of atherosclerosis progression in men were baseline TPA (β =5.72, 95% CI 3.81, 7.62), current smoking (β=1.86, 95% CI 0.19, 3.54) and LDL cholesterol level (β=0.81, 95% CI 0.07, 1.56). In contrast, neither TNFα blocker therapy ($p=0.71$) nor any of the cardiovascular risk factors assessed predicted progression rate of atherosclerosis in women. No difference was found in atherosclerosis progression between PsA and PsC ($p=0.73$).
**Conclusions:** TNFα blocker therapy is associated with reduced progression rate of atherosclerosis in patients with psoriatic disease. The lack of association in women may be explained by reduced power due to minimal progression of atherosclerotic plaques in women in general or by alternative underlying mechanisms of cardiovascular morbidity in women.
**Disclosure of Interest:** L. Eder Grant/research support from: Abbvie, V. Chandran Grant/research support from: Abbvie, Consultant for: Abbvie, Amgen, Celgene, Janssen, Novartis, UCB, R. Cook: None declared, D. Gladman Grant/research support from: Abbvie, Eli Lilly, Pfizer, Amgen, Celgene, Janssen, Novartis, UCB, Consultant for: Abbvie, Eli Lilly, Pfizer, Amgen, Celgene, Janssen, Novartis, UCB
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## THU0425 THE EARLY DIAGNOSIS OF PSORIATIC ARTHRITIS: STANDARDIZED EVALUATION OF SPECIFIC ENTHESES, TENDONS AND CAPILLARIES IN PATIENTS WITH FRESH DIAGNOSED PSORIASIS

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**Background:** Early diagnosis of psoriatic arthritis (PsA) is a challenging topic. PsA is not a mild disease. Untreated it is to compare with rheumatoid arthritis. PsA leads in a high percentage to joint damage, to a poor functional status and to a reduced quality of life. Due to cardiovascular complications patients with PsA die earlier than the general population. Today effective treatment can be started earlier but early diagnosis is still a big problem.We have classification criteria (Caspar, Gepard) and the enthesitis-synovial concept is part oft he international ASAS classification criteria, but we have no early- disease-diagnostic criteria. The fact that skin lesions normally precedes the manifestation of PsA (80%) makes the cooperation between dermatologists and rheumatologists crucial.
**Objectives:** Our hypothesis is that tendonitis and enthesitis of the feet and capillary abnormalities in early PsA can be diagnosed in a very early stage of the disease long before joints involvement is occurring.
**Methods:** We investigated 51 consecutive patients with psoriasis diagnosed and referred by the collaborating dermatologists, without joint problems. Psoriasis must be diagnosed for the first time and should not last longer than 2 years. (All dermatologists in the area participated). No specific dermatological treatment should be started except topics. We performed PW-doppler ultrasound examination of the peronaeus tendons, the tibialis posterior muscle tendons, the tibialis anterior tendons and the attachement oft he Achillles tendons on both sides as well as nailfold capillaroscopy oft he 2.-4.finger of the right hand. A control group of 10 healthy controls was examined.
**Results:** Demographic data and specific assessments (Caspar, Gepard, PASI, DLQI, DAS28) were obtained from the psoriasis group. 20% of the study group had a nail psoriasis, more than 50% were suffering from psoriasis capitis. Our data reveal a large number of grade 1 (75%) and 2 (35%) (range grade1–3) tendonitis abnormalities in the peronaeus- and tib. posterior tendons. Joint effusions could be mostly seen in the talo-tibial joint, whereas the Achilles tendons and the bursa achillea were not often affected. Capillaroskopy results showed torsions/twist-signs in 18% in psoriasis- patients/nail psoriasis -patients which did not differ from the results of the control group. Hair-Pin capillaries occurred significantly more often in the control-group. No dactylitis could be detected in these early cases.
**Conclusions:** Tendonitis of the foot-ankle region occurs strikingly more often than expected in early stages of psoriasis. Ultrasonic of the ankle region is easy to perform in rheumatologic practises. Capillaroscopy is more time consuming and should be reserved for special diagnostic questions.
We have a simple tool to modify the natural course of PsA by early diagnosis. But that works only in a tight interdisciplinary setting (tight junction) between rheumatologists and dermatologists.
**Acknowledgement:** The study was supported by a research grant from Pfizer
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## THU0426 ACHILLES ENTHESITIS DEFINED BY ULTRASOUND IS NOT ASSOCIATED TO CLINICAL ENTHESITIS IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Clinical examination may overestimate Achilles enthesitis. Ultrasonography (US) is a valuable tool for assessment of musculoskeletal inflammation including subclinical enthesitis.
**Objectives:** The aim of our study was to compare clinical and US evaluation of Achilles enthesitis in patients with psoriatic arthritis (PsA).
**Methods:** Patients with PsA were included consecutively in a clinical setting during 1.5 years. The Achilles insertion was examined by clinical assessment of tenderness by a trained nurse, and an experienced ultrasonographer performed US evaluation of 1) inflammatory activity defined as power Doppler (PD) signal, tendon thickening, hypoechogenicity and bursal swelling as well as 2) structural damage defined as erosions at tendon insertion, calcifications and enthesophytes. US sum scores of inflammatory activity and structural damage were assessed. Demographic variables and US scores were assessed by descriptive statistics. Proportions were analysed by Chi-Square test. Correlations were assessed by Spearman's rank correlation test (non-parametric distribution of the data).
**Results:** A total of 141 PsA patients were included. They all fulfilled the CASPAR criteria. Mean (SD) age was 52.4 (10.2) years, disease duration 9.5

(6.6) years, BMI 28.3 (4.3) kg/m$^2$, 50.4% were females, 10.6% used steroids, 57.4% conventional synthetic disease modifying drugs (csDMARDs), 32.6% tumor necrosis factor inhibitors (TNFi) and 20.6% both TNFi and csDMARDs.
Of 282 Achilles tendons, 88 (33.2%) were tender on palpation. By US, 6 (17%) had hypoechogenicity, 37 (13.1%) thickening, 2 (0.8%) PD activity, 14 (5%) bursal swelling, 112 (39.7%) calcifications, 77 (27.3%) enthesophytes and 4 (1.4%) erosions at tendon insertion. Inflammatory activity was found in 55 (19.5%) of the examined Achilles tendons and 148 (52.5%) had structural damage on US sum scores. No significant correlation was found between US sum scores and tenderness on palpation. 36 (18.6%) of the Achilles tendons showed subclinical inflammation on US. No significant difference of percentages of patients with Achilles inflammatory activity or structural damage was found when comparing patients currently treated or not with TNFi, csDMARDs and steroids.
**Conclusions:** We report lack of association between palpation tenderness and US signs of Achilles enthesitis in PsA. US showed structural damage in 52.5% and subclinical inflammation in 18.6% of the examined Achilles tendons.
**Disclosure of Interest:** B. Michelsen: None declared, A. Diamantopoulos Consultant for: Pfizer, Novartis, Speakers bureau: Abbvie, UCB, Pfizer, D. Soldal: None declared, H. Hammer Speakers bureau: AbbVie, Pfizer, Roche, UCB and BMS, A. Kavanaugh: None declared, G. Haugeberg: None declared
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## THU0427 STUDY OF PREVALENCE AND PREDICTORS OF MINIMAL DISEASE ACTIVITY (MDA) STATE IN A SPANISH POPULATION WITH PSORIATIC ARTHRITIS. MAAPS STUDY

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**Background:** Biological therapies have greatly improved the management of psoriatic arthritis (PsA). Minimal disease activity (MDA) has become the optimal target in the treatment of PsA, waiting for a standardized definition of remission. Knowing the proportion of PsA patients in the MDA state could inform on the quality of management of these patients.
**Objectives:** To determine the prevalence of MDA (Coates et al.) in patients with PsA in Spain as well as its potential predictors. To evaluate the association between MDA and the impact of disease, as evaluated by the PsA Impact of Disease questionnaire (PsAID).
**Methods:** This was a non-interventional, cross-sectional, multicenter study, which aimed to evaluate the prevalence of MDA in a Spanish population with PsA. The study was carried out at 25 rheumatology outpatient clinics between May/2014 and Feb/2015. A total of 238 adult patients diagnosed with PsA (CASPAR criteria) with at least one year disease duration and treated with biological and non-biological *DMARDS* were included. Finally, 227 were considered evaluable. Clinical, demographic, treatment data, physical function (HAQ) and quality of life (PsAID) were obtained. According to the latter, the patient acceptable symptoms state (PASS) has been defined as a PsAID value $<4$. All patients gave informed consent. An Ethics committee board approved the final version of this study.
**Results:** Overall, 133 out of 227 (58.6%) subjects achieved MDA at study entry. Seventy-seven (37.9%) and 137 (64.4%) patients reached joint and skin remission, respectively. However, a fair relationship between MDA and joint remission (k=0.390) and a slight relationship between MDA and skin remission (k=0.178) were observed. Patients in MDA state had better functional capacity by HAQ (0.35 ± 0.47) vs non-MDA patients (0.79 ± 0.63), $p<0.001$. These patients also had a significantly lower impact of the disease as measured by PsAID: MDA patients (3.34 ± 3.05) vs non-MDA patients (7.13 ± 5.21), $p<0.001$. In multivariate logistic regression analysis, male gender (OR 2.74, p=0.001), sedentary lifestyle (OR 3.13, p=0.002), familial history of PsA (OR 0.38, p=0.036), CRP level (OR 0.92, p=0.010) and use of corticoids (OR 0.33 p=0.007) were predictors of MDA. Painful entheses count $\leq 1$ was the MDA criterion met by the highest proportion of patients (80.5%), whereas reaching a global disease activity VAS score $\leq 20$ was achieved by only 43.2% of them.
**Conclusions:** MDA was achieved by nearly 60% of patients in this study reflecting clinical practice in agreement with results from earlier studies. These patients had better functional state and most of them reached an acceptable symptoms state according to the PsAID. Our results of predictors to achive MDA should be confirmed in further prospective studies.
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## THU0428 PSORIASIS ARTHRITIS IS ASSOCIATED WITH PERIARTICULAR BONE LOSS OF THE METACARPALS

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**Background:** The BoneXpert is a new Digital X-ray Radiogrammetry method measures the cortical bone thickness of the metacarpals.
**Objectives:** The aim of this study was to quantify cortical bone loss in patients with Psoriasis Arthritis (PsA) and to compare these findings with the PsA modified van der Heijde Sharp Score.
**Methods:** The study includes 104 PsA patients. The BoneXpert method was used to measure the Metacarpal Index ($MCI_{BX}$) at the metacarpal bones (II to IV). Additionally, the T-Score of the MCI ($T\text{-}Score_{MCI}$) was calculated. Radiographic severity was evaluated by the PsA modified van der Heijde Sharp Score (Joint Space Narrowing Score and Erosion Score).
**Results:** For the total PsA study cohort the $T\text{-}Score_{MCI}$ was significantly reduced with -1.289 ± 1.313 SD. The MCI presented a negative correlation to the Joint Space Narrowing Score ($r = -0.558$; $p<0.001$) and Erosion Score ($r = -0.714$; $p<0.001$) of the PsA modified van der Heijde Sharp Score. In this context, a severity dependent and PsA-related periarticular demineralization as measured by the $MCI_{BX}$ was quantified. The highest reduction was observed for the $MCI_{BX}$ with -28.5% ($p<0.01$) regarding to the Erosion Score and with -21.1% ($p<0.01$) for the Joint Space Narrowing Score.
**Conclusions:** Patients with PsA presented also periarticular demineralisation and severity dependent bone loss as measured by the BX using the $MCI_{BX}$. The BX-parameters seem to function as surrogate marker of radiographic progression in PsA and potentially differentiate between different stages of disease manifestation affecting bone structures.
**Disclosure of Interest:** None declared
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## THU0429 THE RISK OF INCIDENT LIVER DISEASE AMONG PATIENTS WITH PSORIASIS, PSORIATIC ARTHRITIS, AND RHEUMATOID ARTHRITIS

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**Background:** Cross-sectional studies have suggested that psoriasis, psoriatic arthritis (PsA), and rheumatoid arthritis (RA) are associated with liver disease. Little is known about the risk for incident liver disease among patients with these diseases from a population-based perspective.
**Objectives:** To examine the risk for incident liver disease among patients with psoriasis, PsA, and RA compared to the general population
**Methods:** We conducted a population-based cohort study in the United Kingdom using The Health Improvement Network (THIN) data from 1994–2014. Patients age 18–89 with codes for PsA, RA, or psoriasis were matched to up to 5 controls from the general population on practice and start date in the practice. Patients with prior liver disease were excluded. Cox proportional hazards models were used to estimate hazard ratios (HR) with 95% confidence intervals (CI). A priori we hypothesized an interaction with disease modifying antirheumatic drug (DMARD) use. Patients with psoriasis who received a DMARD or phototherapy were identified as having "severe" psoriasis.
**Results:** Among patients with PsA (N=12,308) RA (N=54,251), psoriasis (N=197,130) and controls (N=1,279,754), 10,415 incident cases of liver dis-

**Abstract THU0429** – Table 1

| | | N | Incident liver disease diagnosis | Mean cohort time | Person years (PY) | Incidence (per 10,000 PY) | Age/Sex adjusted HR (95% CI) | Fully adjusted HR (95% CI) |
|---|---|---|---|---|---|---|---|---|
| Control | | 1,279,754 | 8,140 | 6.50 | 8,319,520 | 9.78 | Ref | Ref |
| PsA | No DMARD | 5,786 | 64 | 6.12 | 35,390 | 18.08 | 1.80 (1.40–2.30) | 1.37 (1.02–1.85) |
| | DMARD | 6,522 | 70 | 5.83 | 38,018 | 18.41 | 1.87 (1.48–2.37) | 1.66 (1.29–2.14) |
| RA | No DMARD | 21,396 | 189 | 5.71 | 122,204 | 15.47 | 1.60 (1.39–1.85) | 1.50 (1.27–1.77) |
| | DMARD | 32,855 | 227 | 6.13 | 201,351 | 11.27 | 1.19 (1.04–1.36) | 0.97 (0.83–1.13) |
| Psoriasis | Mild | 186,006 | 1,593 | 6.21 | 1,155,765 | 13.78 | 1.40 (1.33–1.48) | 1.37 (1.29–1.46) |
| | Severe | 11,124 | 132 | 5.31 | 59,018 | 22.37 | 2.32 (1.95–2.75) | 1.94 (1.61–2.35) |

ease were identified. After adjusting for age, sex, body mass index, drinking, smoking, NSAID use, systemic glucocorticoid use, and diabetes, the HR were significantly elevated for all groups except patients with RA who received a DMARD: PsA without a DMARD 1.37 (95%CI: 1.02–1.85), PsA with a DMARD 1.66 (95%CI: 1.29–2.14), RA without a DMARD 1.50 (1.27–1.77), RA with a DMARD 0.97 (0.83–1.13), psoriasis without a DMARD 1.37 (1.29–1.46), and severe psoriasis 1.94 (1.61–2.35). Among all patients, 38% of new liver disease was attributed to fatty liver disease, 19% was alcoholic liver disease, and 8% was viral mediated liver disease. Among patients with PsA prescribed a DMARD and patients with severe psoriasis, fatty liver disease accounted for more than half of new diagnoses of liver disease.

**Conclusions:** Patients with PsA, RA, and psoriasis have a significantly increased risk for development of liver disease even after accounting for risk factors and among patients not prescribed a DMARD. These results suggest systemic inflammation may play a role in the development of liver disease beyond the relationship with treatment-related toxicity.

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## THU0430 IXEKIZUMAB PROVIDES IMPROVEMENTS THROUGH 52 WEEKS IN PHYSICAL FUNCTION, QUALITY OF LIFE, AND WORK PRODUCTIVITY IN BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG-NAIVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease associated with psoriasis, peripheral arthritis, enthesitis, dactylitis, and spondylitis. PsA has a negative impact on patients' quality of life, physical function, and work productivity. Ixekizumab (IXE) is an IgG4 monoclonal antibody that binds with high affinity and specificity to the proinflammatory cytokine IL-17A. In this phase 3 trial (SPIRIT-P1), previously reported results showed that IXE treatment resulted in significant improvements (compared with placebo [PBO]) at Week [Wk] 24 in the patient-reported outcome (PRO) measures of Health Assessment Questionnaire – Disability Index (HAQ-DI), Short Form-36 Health Survey Physical Component Summary (SF-36 PCS), European Quality of Life 5 Dimensions Visual Analog Scale (EQ-5D VAS), and Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP; presenteeism, work productivity, activity impairment).

**Objectives:** To evaluate whether an effect of IXE on improvement of PROs is also observed at Wk 52.

**Methods:** A total of 417 biologic disease-modifying antirheumatic drug (bDMARD)-naive patients with active PsA were randomly assigned 1:1:1:1 to subcutaneous administration of 80-mg IXE every 4 wks (Q4W) or 2 wks (Q2W), each with a 160-mg starting dose at Wk 0; adalimumab (ADA) 40 mg Q2W (active comparator); or PBO in the Double-Blind Treatment Period (DBTP; Wks 0 through 24). Of these patients, 381 continued into the Extension Period (EP; Wks 24 through 52). PBO- and ADA-treated patients were randomly re-assigned (1:1) to 80 mg IXEQ4W or IXEQ2W at Wk 16 (inadequate responders) or Wk 24; ADA-treated patients started IXE after an 8-wk wash-out period at Wk 24 (inadequate responders) or Wk 32. Investigators were blinded as to criteria for inadequate response. Analyses for the EP were conducted on the EP Population, defined as all patients who received at least 1 dose of study drug during the EP.



Missing values were imputed by nonresponder imputation for categorical data and modified baseline observation carried forward for continuous data.

**Results:** Baseline demographics and clinical characteristics were generally similar between treatment groups; population mean baseline (Wk 0) scores for HAQ-DI, SF-36 PCS, and EQ-5D VAS (Table) indicated impaired physical function and quality of life. Physician-assessed clinical efficacy was shown by 69% of patients treated with IXE for 52 wks achieving American College of Rheumatology (ACR) 20 response. Patients receiving IXE (Q4W or Q2W) for 52 wks reported similar improvements in HAQ-DI, SF-36, EQ-5D VAS, and WPAI-SHP (presenteeism, work productivity, activity impairment) (Table) to Wk 24 results, and the percentage of IXE patients with improvement from baseline HAQ-DI score $\geq$0.35 achieving minimally clinically important difference for HAQ-DI was sustained at Wk 52 (Table) compared with Wk 24. At Wk 52, patients receiving ADA/IXE also showed similar improvements in ACR20 response and most PRO measures (Table) to Wk 24 results.

**Conclusions:** IXE provided sustained improvement through 52 wks in physical function, quality of life, and work productivity in bDMARD-naive patients with active PsA.

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## THU0431 SUSTAINED IMPROVEMENTS IN SKIN SYMPTOMS, PHYSICAL FUNCTIONING, AND QUALITY OF LIFE WITH SECUKINUMAB VERSUS USTEKINUMAB IN PATIENTS WITH MODERATE-TO-SEVERE PSORIASIS AND CONCOMITANT PSORIATIC ARTHRITIS: 52 WEEK RESULTS FROM THE CLEAR STUDY

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**Background:** Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis.[1] In the prospective, randomised, double-blind CLEAR study (NCT02074982), secukinumab, a human anti-interleukin (IL)-17A monoclonal antibody, demonstrated superior efficacy (Psoriasis Area and Severity Index [PASI] 90) over ustekinumab (an IL-12/23 inhibitor) in patients with moderate-to-severe plaque psoriasis.[2] We previously reported that secukinumab improved skin symptoms and physical functioning at 16 weeks (wks) in the subgroup with concomitant PsA.[3]

**Objectives:** To report 52 wk results in the subgroup with concomitant PsA.

**Methods:** Patients were randomised 1:1 to receive subcutaneous (s.c.) secukinumab 300 mg or ustekinumab (patients $\leq$100 kg, 45 mg sc; $>$100 kg, 90 mg s.c.). Secukinumab administered at baseline (BL), Wks 1, 2, and 3, and every 4 wks from Wk 4 and ustekinumab at BL, Wk 4, and every 12 wks from Wk 16. The primary endpoint was the proportion of patients achieving $\geq$90% reduction from BL in PASI score at Wk 16. PASI 75, PASI 90, PASI 100, and IGA mod 2011 responses over time, and changes from BL in the HAQ-DI, WPAI, and DLQI were analysed in the subgroup with concomitant PsA. Analyses used non-responder imputation for efficacy assessments and observed data for PROs.

**Results:** Of the total 676 patients randomised, 610 (93.7%) completed 52 wks of study (secukinumab group, 312 [94.8%]; ustekinumab group, 298 [92.5%]). In overall population, the PASI 90 response was achieved by 79.0% vs. 57.6% ($P<0.0001$) and 74.9% vs. 60.6% ($P=0.0001$) patients receiving secukinumab vs. ustekinumab at Wk 16 and Wk 52, respectively. Concomitant PsA was reported in 69/337 (20.5%) and 54/339 (15.9%) patients in the secukinumab and ustekinumab groups, respectively. In the subgroup with concomitant PsA, a higher proportion of patients in the secukinumab group achieved a PASI 90 response at Wk 52 vs. ustekinumab; 77.6% vs. 63.5% ($P<0.05$), respectively. The mean change from baseline in HAQ-DI at Wk 52 was –0.30 with secukinumab vs. –0.13 with ustekinumab. A higher proportion of patients receiving secukinumab achieved HAQ-DI response (minimum clinically important difference) vs. ustekinumab at Wk 52 (39.4% vs. 23.5%, respectively). Greater improvements were observed in other parameters with secukinumab vs. ustekinumab in the PsA subgroup (Table).

**Conclusions:** The significant efficacy of secukinumab vs. ustekinumab in clearing psoriasis was sustained through 52 wks in patients with moderate-to-

**Table. Clinical Response and PROs with Secukinumab in the PsA Subgroup at Wk 52**

| | Secukinumab N = 68 | Ustekinumab N = 54 |
|---|---|---|
| PASI 75 response, n (%) | 61 (91.0)* | 39 (75.0) |
| PASI 100 response, n (%) | 30 (44.8) | 21 (40.4) |
| IGA 0/1 response, n (%) | 49 (73.1)** | 29 (55.8) |
| DLQI 0/1 response, n (%)* | 39 (58.4) | 24 (50.0) |
| DLQI total score, change from baseline, mean ± SD | −12.3 ± 7.68 | −9.0 ± 7.44 |
| Assessment for pain, itching and scaling, change from baseline, mean ± SD | | |
| *Pain assessment* | −4.0 ± 2.80 | −3.0 ± 2.94 |
| *Itching assessment* | −5.2 ± 3.05 | −3.9 ± 2.55 |
| *Scaling assessment* | −5.2 ± 3.12 | −4.6 ± 2.54 |
| WPAI, change from baseline, mean ± SD | | |
| *Percent work time missed due to psoriasis* | −0.4 ± 15.12 | 0.8 ± 24.89 |
| *Percent impairment while working due to psoriasis* | −27.3 ± 26.81 | −15.0 ± 22.90 |
| *Percent overall work impairment due to psoriasis* | −20.4 ± 23.74 | −18.4 ± 25.42 |
| *Percent activity impairment due to psoriasis* | −35.4 ± 27.46 | −24.3 ± 24.77 |

*P <0.01; **P <0.05 vs ustekinumab. Percentages calculated using patients with both baseline and post-baseline assessment. †Observed data presented from 57 and 40 patients in secukinumab and ustekinumab groups respectively. N = total number of randomised patients with PsA at baseline; n = number of patients with response.

DLQI, dermatology life quality index; IGA, investigator's global assessment modified 2011; PASI, psoriasis area and severity index; WPAI, work productivity and activity impairment-psoriasis.

severe plaque psoriasis. In the subgroup with concomitant PsA, secukinumab was associated with greater improvements in skin symptoms, physical functioning, quality of life, and work productivity compared with ustekinumab through 52 wks.

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## THU0432 APREMILAST, AN ORAL PHOSPHODIESTERASE 4 INHIBITOR, IS ASSOCIATED WITH LONG-TERM (104-WEEK) IMPROVEMENT IN FATIGUE IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED RESULTS FROM 3 PHASE III, RANDOMIZED, CONTROLLED TRIALS

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**Background:** Fatigue, a common symptom affecting individuals with psoriatic arthritis (PsA), is associated with decreased quality of life and loss of work productivity.[1] The 2014 OMERACT PsA Working Group identified fatigue measurement as an important outcome to consider including in PsA core assessments.[2] The PALACE 1 (NCT01172938), 2 (NCT01212757), and 3 (NCT01212770) studies compared apremilast (APR) efficacy/safety, including fatigue level, with placebo (PBO) in patients (pts) with active PsA despite prior conventional DMARDs and/or biologics.

**Objectives:** Report APR treatment impact on fatigue over 104 wks in a pooled analysis of the PALACE 1–3 studies.

**Methods:** Pts were randomized (1:1:1) to PBO, APR 30 mg BID (APR30), or APR 20 mg BID (APR20) stratified by baseline DMARD use. The PBO-controlled phase continued to Wk 24, with a Wk 16 early escape option. At Wk 24, all remaining PBO pts were re-randomized to APR30 or APR20. Double-blind APR treatment continued to Wk 52; pts could then continue to receive open-label APR up to an additional 4 years. Fatigue was assessed using FACIT-F v4 and SF-36v2 Vitality domain (VT).[3] Total FACIT-F scores range from 0–52; lower scores denote higher fatigue levels. As a point of reference, mean fatigue scores of 40.1–43.6 in the general population,[4,5] 35.8 in PsA pts,[6] and 23.9 in anemic cancer pts[5] have been reported, and FACIT-F MCID in PsA has not been determined; this analysis used FACIT-F MCID in rheumatoid arthritis pts (3–4).[7] SF-36v2 VT, a subscale of SF-36v2, measures physical and mental impact of fatigue on individuals.[8] Scores are norm-based; group values <47 represent a below-average range vs the general population.[9]

**Results:** Baseline mean FACIT-F (29.4–30.9) and SF-36v2 VT (40.6–40.8) scores were below population norms. Long-term improvement in fatigue was seen in APR pts at Wks 52 and 104 (mean FACIT-F=35.0), marking a shift toward population FACIT-F norms (Table). APR30 mean change was 5.6, with 50.9% of pts achieving FACIT-F MCID. Similarly, improvements in SF-36v2 VT scores were observed at Wks 52 and 104 with ≈60% of pts achieving MCID. Over 104 wks, most AEs were mild/moderate; in general, no increase was seen in AE incidence/severity with longer term exposure.

| | FACIT-F v4 and SF-36v2 VT at Wks 52 and 104 | | | |
|---|---|---|---|---|
| | Wk 52 | | Wk 104 | |
| | APR30 n=559* | APR20 n=541* | APR30 n=454* | APR20 n=430* |
| **FACIT-F v4** | | | | |
| Baseline score, mean | 29.2 | 31.2 | 29.5 | 31.2 |
| Mean score at time point | 34.8 | 35.1 | 35.0 | 35.7 |
| Mean change from baseline score | 4.8 | 3.9 | 5.6 | 4.5 |
| Mean % change from baseline score | 35.4 | 21.5 | 44.5 | 26.1 |
| Pts achieving MCID, % | 50.6 | 48.0 | 50.9 | 50.5 |
| **SF-36v2 VT** | | | | |
| Baseline score, mean | 40.6 | 41.6 | 40.8 | 41.5 |
| Mean score at time point | 45.3 | 45.9 | 46.5 | 46.3 |
| Mean change from baseline score | 4.7 | 4.3 | 5.6 | 4.8 |

Data as observed. *The n represents the number of pts who completed 52 wks and 104 wks of treatment, respectively, regardless of when apremilast was started (baseline, Wk 16, or Wk 24), with a baseline value and value at the specific time point.

**Conclusions:** APR-treated pts experienced improvements in fatigue, as measured by FACIT-F and SF-36 VT scores. Over 104 wks, clinically meaningful improvements were maintained. APR demonstrated an acceptable safety profile and was generally well tolerated up to 104 wks.

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## THU0433 PERSISTENCY WITH TNFI IN BIOLOGIC EXPERIENCED VERSUS BIOLOGIC NATIVE PSA PATIENTS ENROLLED IN CORRONA REGISTRY

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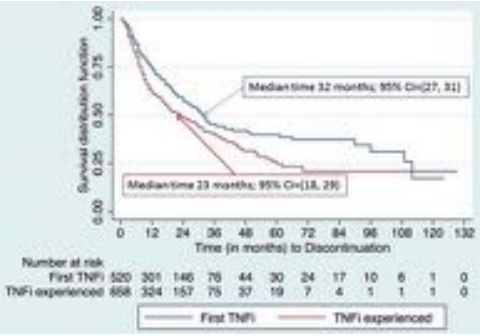
**Background:** Little is known about the long-term use of TNFi for the management of PsA in routine clinical practice in the US.

**Objectives:** To assess overall persistence with TNFi and evaluate differences based on patients' prior use or non-use of TNFi in the US Corrona registry.

**Methods:** We identified all PsA initiators of a TNFi (adalimumab, etanercept, infliximab, golimumab) with at least 1 follow-up visit from October 2002 to December 2014. Patients were followed until the earliest of: discontinuation of the TNFi, initiation of another biologic or small molecule therapy or last follow-up

visit. Patient characteristics (demographic and clinical characteristics) at the index date (TNFi initiation) were evaluated. Kaplan-Meier curves were used to describe time to discontinuation, with censoring for all patients with a ≥1year gap between office visits. The log rank test was used to assess for differences in persistence (defined as remained on index TNFi) based on prior TNFi use.

**Results:** A total of 1241 patients initiated a TNFi during the study period, with mean (standard deviation [SD]) age and disease duration of 50.7 (12.1) years and 8.3 (8.5) years, respectively. The mean (SD) swollen and tender joint counts were 3.3 (4.8) and 4.7 (6.4). Forty-four percent of patients (n=549) were TNFi-naïve at initiation. Overall, 46% of patients (n=572) discontinued TNFi during follow-up with 83.2%, 66.9%, 52.4%, 40.6% and 36.1% of patients persistent at 6, 12, 24, 36 and 48 months respectively; median time to discontinuation was 27 months (95% CI: 24, 31). Based on the log rank test, persistence was greater in patients on their first TNFi –than in patients with prior TNFi use (Figure).




**Conclusions:** Over half of all PsA patients included in this study were persistent to TNFi at 24 months post-initiation. TNFi-naïve patients had greater persistence compared to TNFi–experienced patients.

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## THU0434 SERIOUS INFECTIONS IN PSORIASIS PATIENTS WITH PSORIATIC ARTHRITIS IN THE PSORIASIS LONGITUDINAL ASSESSMENT AND REGISTRY STUDY

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**Objectives:** To describe the rates of serious infections (SI) in psoriasis (PsO) patients with psoriatic arthritis (PsA) from PSOLAR.

**Methods:** PSOLAR is an international, disease-based, observational study in which patients eligible for, or receiving conventional systemic & biologic agents for the treatment of PsO are followed prospectively. The characteristics & cumulative incidence rates of SIs occurring within 91 days of biologic administration, for patients who reported PsA,including a subset with PsA confirmed by a joint-specialist are summarized. Cohorts were defined as & attribution was based on treatment exposure in the following order (regardless of sequence & duration): (1) ustekinumab (UST) (2) other sponsor biologic (primarily infliximab [IFX]) (3) non-sponsor biologic (primarily adalimumab/etanercept [ADA/ETN]), & (4) non-biologic therapies (NB) (including immunodulators [eg MTX, cyclosporine], phototherapy, & topical therapy). Exposure to any therapy higher in the order precluded inclusion in the lower cohorts. Multivariate analyses using Cox hazard regression were used to identify predictors of time to first SI (using exposure within 91 days for biologics [compared to no biologic use] & for immunomodulators [compared to no immunomodulator use]).

**Results:** As of Aug 23, 2014, PSOLAR was fully enrolled with 12093 patients (40388 total patient-years [PY] of follow-up).Number of patients with reported PsA was overall 4316: 1489 UST, 776 IFX, 1680 ADA/ETN, 371 NB; of these patients, 1719 had confirmed PsA (664 UST, 356 IFX, 576 ADA/ETN, 123 NB). Baseline demographics & medical history were generally balanced across cohorts & were comparable to confirmed PsA subset; however, in overall PsA sub-group, more patients in NB cohort were ≥65yrs of age (UST 9.9%, IFX 13.9%, ADA/ETN 12.5%, NB 25.6%)& had a medical history of cancer (UST 3.3%, IFX 3.5%, ADA/ETN 3.9%, NB 8.4%).In the overall PsA subgroup (15 029 PY of follow-up), rates of SIs/100 PY were: UST 1.12, IFX 3.36, ADA/ETN 2.49, and NB 2.20. Among the confirmed PsA subset, rates/100 PY were: UST 1.06, IFX 2.83, ADA/ETN 2.58, NB 1.63. In the overall PsA sub-group, increasing age, male gender, current/prior smoking, history of significant infection, diabetes, & use of biologics (other than UST as a combined group) were associated with increased risk for SI; no increased risk was observed with UST & immunomodulators. In patients with confirmed PsA, diabetes, history of significant infection, more severe skin PsO, & use of biologics other than UST (as a combined group) were significantly associated with increased infection risk; UST & immunomodulators were not associated.

Inherent bias with respect to observational data may apply. Variability in size & clinical features was noted among treatment groups.Incidence rates are not adjusted for differences. Individual biologics beyond UST were not evaluated individually in statistical analyses.

**Conclusions:** Results suggest a higher risk of SIs with biologics (as a combined group), other than UST, in comparison with no biologic usage; increased risk was not observed with UST or immunomodulators.

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## THU0435 DAS-28 REMISSION AND IMPROVEMENTS IN SKIN DISEASE OVER 3 YEARS OF TREATMENT WITH APREMILAST: RESULTS FROM THE PALACE 3 STUDY IN DMARD/BIOLOGIC-EXPERIENCED ACTIVE PSA PATIENTS

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**Background:** Treatment goals for active psoriatic arthritis (PsA) include long-term control of both skin and joint symptoms. Achievement of remission in 28-joint count Disease Activity Score (DAS-28) using C-reactive protein (CRP), clinically important changes in DAS-28 (CRP), reduction in swollen joint count (SJC), or decrease in skin disease may be used as goals of treatment.[1] PALACE 3 (NCT01212770) included PsA patients with active joint disease with an active skin lesion at the time of enrollment.

**Objectives:** Assess long-term treatment responses across PsA manifestations in patients treated with apremilast (APR) for 3 years.

**Methods:** Patients were stratified by baseline DMARD use (yes/no) and psoriasis involvement of the body surface area (<3%/≥3%) and randomized (1:1:1) to placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID (APR20). After a PBO-controlled phase of 24 wks, all patients were treated with APR30 or APR20 and could enroll in long-term follow-up. Efficacy assessments in years 2 and 3 were conducted at Wks 65, 78, 91, 104, 117, 130, 143, and 156.

**Results:** 505 patients were randomized and received ≥1 dose of study medication (PBO: n=169; APR30: n=167; APR20: n=169). A total of 89% (249/281) of patients starting the third year of APR therapy completed the Wk 156 visit. Patients treated with APR30 demonstrated sustained decreases in disease activity at Wk 156, as shown by mean decreases in DAS-28 (CRP) of –1.58; 79.1% achieved a good/moderate EULAR response and 41.0% achieved DAS-28

| | Outcomes at Wk 156 | |
|---|---|---|
| | APR30 n=140* | APR20 n=114* |
| DAS-28 (CRP), mean change | −1.58 | −1.54 |
| DAS-28 (CRP) <2.6, n/m (%) | 57/139 (41.0) | 51/113 (45.1) |
| SJC, mean % change | −78.3 | −76.4 |
| TJC, mean % change | −65.0 | −65.3 |
| HAQ-DI (0-3), mean change | −0.39 | −0.41 |
| HAQ-DI MCID, ≥0.30, n/m (%) | 65/140 (46.4) | 61/114 (53.5) |
| ACR20, n/m† (%) | 89/138 (64.5) | 72/112 (64.3) |
| ACR50, n/m† (%) | 56/137 (40.9) | 52/113 (46.0) |
| ACR70, n/m† (%) | 29/137 (21.2) | 26/113 (23.0) |
| PASI-75, n/m (%)‡ | 33/68 (48.5) | 22/58 (37.9) |
| PASI-50, n/m (%)‡ | 46/68 (67.6) | 34/58 (58.6) |

Data as observed. n/m=number of responders/number of patients with sufficient data for evaluation.
*The *n* reflects the number of patients treated with APR30 and APR20, regardless of when APR was started (baseline, Wk 16, or Wk 24), and who had data available at Wk 156; actual number of patients available for each end point may vary. †Denominators vary slightly due to availability of sufficient data for each level of ACR response assessment. ‡Examined among patients with psoriasis involvement of ≥3% of the body surface area at baseline and having data at Wk 156.

(CRP) remission. Sustained relief across PsA manifestations, including SJC, a marker of inflammation, was also demonstrated (Table); at Wk 156, APR30 resulted in a mean 78.3% decrease in SJC, 65.5% of patients had a swollen joint count of 0 or 1. Decreases in disability and maintenance of functionality were demonstrated by sustained decreases in HAQ-DI scores (Table). Continued effect on skin disease was shown by decreases in skin involvement, as measured by the PASI; 54.7% of APR30 patients had a baseline PASI >5 and 27.3% had a baseline PASI >10; at 156 wks, 64.7% had a PASI <3, and 83.8% had a PASI of ≤5. PASI-75 and PASI-50 also signified clinically significant relief (Table). No new safety concerns were identified after 156 wks of APR treatment. During Wks >104 to ≤156 of APR exposure, adverse events (AEs) occurring in ≥5% of patients were nasopharyngitis and urinary tract infection; most AEs were mild or moderate in severity. Serious AEs occurred in 7.8% of APR patients during Wks >104 to ≤156, similar to rates seen for the earlier study periods; few discontinuations due to AEs (2.1%) occurred over Wks >104 to ≤156.

**Conclusions:** Over 156 wks, among patients continuing in the study, APR demonstrated sustained and clinically important improvements in PsA signs/symptoms, including physical function and associated psoriasis. APR was generally well tolerated and continued to demonstrate an acceptable safety profile with long-term use.

**References:**

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## THU0436 A RETROSPECTIVE NON-INTERVENTIONAL MULTI-CENTRE STUDY EVALUATING TREATMENT REGIMENS USED IN PSORIATIC ARTHRITIS PATIENTS IN AUSTRALIA- THE PSA REAL STUDY

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**Background:** Psoriatic arthritis (PsA) is a spondyloarthritis spectrum disease with prominent involvement of skin and joints. The management of PsA patients is often complex and there is no uniformity across the medical profession. The majority of PsA studies have been prospective clinical trials involving a homogenous and restricted patient population. This may not reflect real clinical practice where patients have co-morbidities and other clinical characteristics that preclude them from participating in clinical trials.

**Objectives:** To provide a cross sectional analysis of disease activity and management of PsA patients in the Australian population.

**Methods:** This was a retrospective non-interventional multi-centre study using the Audit4 clinical audit program, with de-identified and routinely collected clinical data sourced from participating rheumatology practices in the OPAL consortium (Optimising Patient outcomes in Australian rheumatoLogy) across Australia during November 2015[1]. Data collected included baseline characteristics, prevalence and duration of cDMARD and bDMARD treatments, DAS28-CRP results, and reasons for stopping therapy.

**Results:** A total of 3422 clinician diagnosed PsA patients were included in this study: 60% were female, mean age 54 years (±14) and mean disease duration 10 years (±9). Of patients with a valid treatment record (n=2948), 46% were on cDMARD monotherapy, 19% on bDMARD monotherapy, 13% on combination bDMARD and cDMARD therapy, 11% on combination cDMARD therapy and 10% were on no DMARDs. Of those with DAS28 CRP results (n=494), the highest mean DAS 28 CRP was 3.32 (±1.57) on combination cDMARD therapy, and the lowest DAS 28 CRP was 2.19 (±0.89) on bDMARD monotherapy. The most common reasons for cessation of cDMARD monotherapy was adverse reactions (41%), for bDMARD monotherapy lack of efficacy (26%) and combination bDMARD and cDMARD therapy either completed treatment or drug no longer required (37%).

**Conclusions:** Cross sectional analysis of this large cohort managed in rheumatology clinical practice suggests most are receiving DMARD therapies with less disease activity on bDMARD monotherapy. Adverse reactions and lack of efficacy remain common reasons for cessation of cDMARD and bDMARD monotherapy in PsA.

**References:**

[1] Tymms K, Littlejohn G. Optimising Patient Outcomes in Australian Rheumatology (OPAL): a clinician driven point of care observational data management consortium. Clin Exp Rheumatol 2014;32(85): S150-S152.

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**Disclosure of Interest:** None declared

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## THU0437 SECUKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS LICENSED BIOLOGICS AND APREMILAST FROM A NETWORK META-ANALYSIS

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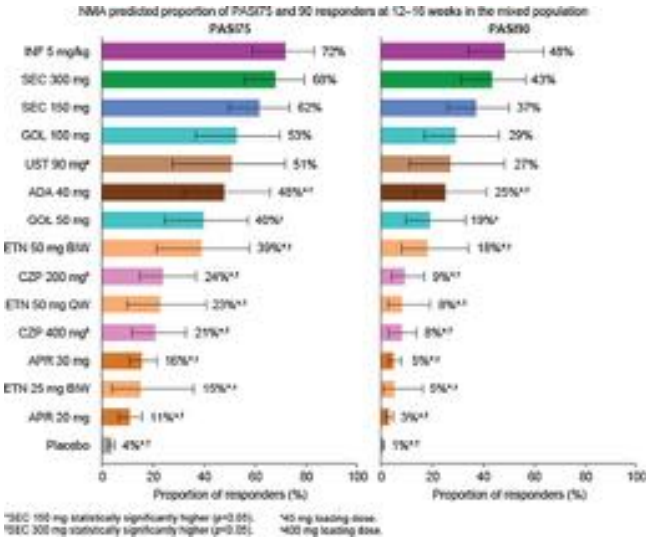
**Background:** Secukinumab (SEC) is approved for the treatment of active PsA in adults who have responded inadequately to DMARD therapy. The FUTURE 1 and 2 RCTs which included biologic-naïve and biologic-experienced patients, demonstrated superiority of SEC 150 mg and 300 mg over placebo. As no direct trial comparisons are yet available there is a need for comparative effectiveness assessment.

**Objectives:** Comparative assessment of SEC via network meta-analysis (NMA) vs. licensed biologics and apremilast in adults with active PsA who had failed conventional DMARD therapy.

**Methods:** A systematic review of the literature (November 2015) identified 20 relevant RCTs. NMAs were conducted following health technology assessment guidance using Bayesian fixed-effects models. PASI and ACR responses and their credible intervals (CrIs), which can be interpreted similarly to CIs, were modelled using a conditional binomial likelihood NMA with probit link function. The results of pairwise comparisons are presented for SEC using relative risks (RRs) [95%CrI]. Non-responder imputation data were used for all comparators except golimumab QM (GOL) and infliximab 5 mg/kg Q2M (INF) for which only last observation carried forward data were available. Analyses were performed in biologic-naïve, biologic-experienced, and mixed populations at week 16 for ACR and at weeks 12–16 for PASI.

**Results:** At week 16 in the biologic-naïve population, ACR20 responses were statistically significantly higher for SEC 150 mg (61%) and 300 mg (58%) than for ustekinumab QM (UST) 45 mg (RR 1.95 [1.29–2.86] and RR 1.84 [1.21–2.74], respectively), and for SEC 150 mg vs UST 90 mg (RR 1.52 [1.03–2.16]). ACR20 responses were statistically significantly higher for SEC 150 and 300 mg vs. apremilast BID (APR) 20 mg (RR 2.51 [1.52–4.29] and RR 2.37 [1.39–4.12] respectively), and for SEC 150 mg vs. APR 30 mg (RR 1.72 [1.09–2.71]). Comparisons between SEC and anti-TNFs did not show statisticall significance. For ACR50 and 70, both SEC doses showed the same pattern of significance as for ACR20. Sensitivity analyses using the mixed population were in general agreement with these observations.

For PASI50, 75, and 90 at weeks 12–16 in the biologic-naïve population, only a small evidence network with SEC, GOL 50/100mg, adalimumab 40 mg (ADA) and INF was available and there were no statistically significant differences between SEC and these comparators. In the mixed population, SEC was statistically significantly superior to ADA, APR 20/30 mg, certolizumab pegol (CZP) 200/400 mg, etanercept (ETN) 25/50 mg BIW and 50 mg QW, and (SEC 300 mg only) GOL 50 mg.



**Conclusions:** SEC shows statistically significantly higher results vs. UST and APR in ACR20, 50 and 70, with at least comparable response rates across all ACR and PASI endpoints vs. all therapies included in this NMA. For PASI50, 75, and 90 responses, SEC had high response rates with statistically significant results vs. ADA, APR, CZP, ETN, and (SEC 300 mg only) GOL 50 mg.
**Disclosure of Interest:** I. McInnes Consultant for: Novartis, Janssen, Abbvie, Pfizer and UCB, P. Nash Grant/research support from: Novartis, Consultant for: Novartis, C. Ritchlin Grant/research support from: Abbvie, Amgen, UCB, Consultant for: Amgen, Abbvie, Jannsen, Novartis, Sun Pharma, Sanofi, UCB, Boeringer Ingelheim, H. Thom Consultant for: Novartis Pharma AG and for a short time in 2015 for Eli Lilly, S. Kanters Consultant for: Novartis, E. Palaka Employee of: Novartis employee, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, S. Mpofu Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
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## THU0438 ENTHESITIS IN PSORIATIC ARTHRITIS AND NEED FOR BIOLOGICAL THERAPY

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**Background:** Psoriatic arthritis (PsA) is a potentially destructive inflammatory chronic arthropathy, with a wide range of clinical manifestations. Currently, biological therapy (BT) is the second step of treatment after an inadequate response to conventional disease-modifying anti-inflammatory drugs.
**Objectives:** The goal of our study was to identify baseline characteristics of patients with PsA associated with the need for BT use during the follow-up.
**Methods:** This is a single-centre, case-control study. Unselected PsA patients diagnosed after December 31st, 1999 and fulfilling CASPAR classification criteria were included. Reviewing medical records identified epidemiological, clinical, analytical and imaging features. The main outcome was the need of BT during the follow-up. The local ethical committee authorized the study. Chi-square, Student t test, and Mann-Whitney U test were used to establish statistical significance in the univariate analysis. Logistic regression was used for the multivariate analysis. A $p<0.05$ was considered significant.
**Results:** One hundred and fifty-nine patients were included (75 women and 84 men), with a mean age of 48 years. During the follow-up, 66 patients (41%) needed BT (BT+ patients). No significant differences in age, sex, race, presence of cardiovascular risk factors, smoking, alcohol consumption, initial joint pattern, presence of dactylitis, presence of onychopathy, HLA B27 positivity, presence of radiographic erosions, presence of axial radiographic involvement, mean C-reactive protein, or mean erythrocyte sedimentation rate were found in BT+ patients when compared with BT negative (BT–) patients. Twenty per cent of BT– patients had enthesitis at the beginning, compared with 39% of BT+ patients [Odds ratio 2.53 (CI 95%: 1.25–5.12); p=0.009]. Mean time from the onset of symptoms to the first appointment with a rheumatologist was significantly associated with the need for further use of BT (20 weeks in BT– patients versus 108 weeks in BT+ patients; $p<0.001$). Multivariate analysis showed that the delay in rheumatology consultation and presence of enthesitis were independent factors significantly associated with the need for BT.
**Conclusions:** In PsA patients, the initial presence of enthesitis is an independent risk factor associated with the need for biological therapy during the follow-up.
**Disclosure of Interest:** None declared
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## THU0439 52-WEEK EFFICACY AND SAFETY OF APREMILAST AND SWITCH FROM ETANERCEPT IN PATIENTS WITH MODERATE TO SEVERE PSORIASIS: RESULTS FROM THE LIBERATE STUDY

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**Background:** Psoriasis is a chronic systemic inflammatory disease often treated with conventional systemic and biologic drugs that may variously be ineffective, inaccessible, or pose significant safety and tolerability risks.
**Objectives:** The phase IIIb LIBERATE (Evaluation in a Placebo-Controlled Study of Oral Apremilast and Etanercept in Plaque Psoriasis) study (NCT01690299) evaluated the efficacy and safety of apremilast or etanercept vs. placebo in biologic-naive patients (pts) with moderate to severe plaque psoriasis.
**Methods:** In this double-blind, double-dummy study, pts were randomized (1:1:1) to placebo (PBO), apremilast 30 mg BID (APR), or etanercept 50 mg QW (ETN) through Wk16; thereafter, all pts switched to or continued APR (PBO/APR, ETN/APR, APR/APR). The primary endpoint was achievement of a ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI) score (PASI-75) at Wk16 with APR vs. PBO; secondary endpoint was PASI-75 achievement at Wk16 with ETN vs. PBO. Additional physician global assessments (PGA) of disease activity were conducted using the static (sPGA), lattice system (LS-PGA), and scalp (ScPGA) instruments; nail disease was also evaluated (Nail Psoriasis Severity Index [NAPSI]). Responses were assessed at Wks16 and 52 using the last-observation-carried-forward (LOCF) methodology.
**Results:** 250 pts received ≥1 dose of study drug, had both baseline PASI and ≥1 post-treatment PASI evaluations, and were included in the analysis set (PBO n=84; APR n=83; ETN n=83). At baseline, 166 (66.4%; PBO n=58; APR n=54; ETN n=54) pts had an ScPGA score ≥3 (moderate to very severe) and 148 (59.2%; PBO n=46; APR n=52; ETN n=50) had a NAPSI score ≥1. At Wk16, PASI-75 achievement was significantly greater ($P<0.0001$) with APR (39.8%) or ETN (48.2%) vs. PBO (11.9%). Although this study was not designed/powered for APR vs. ETN comparisons, Wk16 PASI-75 achievement was not significantly different between APR and ETN ($P=0.2565$, post hoc). At Wk16, APR and ETN produced significantly greater achievement of 0 or 1 ratings (clear or almost clear) vs. PBO in sPGA and LS-PGA and in ScPGA (clear or minimal) (Table). Improvements in nail psoriasis were also achieved with APR and ETN at Wk16 (Table). At Wk52, PASI-75 response was sustained in APR/APR (50.6%) and ETN/APR (55.4%) pts; PASI-75 response was 46.4% in PBO/APR pts (Table). sPGA, LS-PGA, and ScPGA responses achieved at Wk16 were generally sustained through Wk52 with APR (Table). Continued APR treatment over 52wks resulted in further improvements in nail psoriasis (Table). Adverse events were consistent with known safety profiles of APR and ETN.

**LIBERATE Efficacy Outcomes**

| Pts Achieving Response, % (LOCF) | PBO n=84 | APR n=83 | ETN n=83 |
|---|---|---|---|
| **Wk16** | | | |
| PASI-75 | 11.9 | 39.8* | 48.2* |
| sPGA 0 or 1[‡] | 3.6 | 21.7* | 28.9* |
| LS-PGA 0 or 1[‡] | 6.0 | 24.1* | 22.9* |
| ScPGA 0 or 1[¶] | 25.9 | 44.4* | 50.0* |
| NAPSI-50[#] | 10.9 | 25.0** | 48.0* |
| **Wk52** | **PBO/APR n=84** | **APR/APR n=83** | **ETN/APR n=83** |
| PASI-75 | 46.4 | 50.6 | 55.4 |
| sPGA 0 or 1[‡] | 31.0 | 24.1 | 25.3 |
| LS-PGA 0 or 1[‡] | 22.6 | 27.7 | 24.1 |
| ScPGA 0 or 1[¶] | 46.6 | 50.0 | 61.1 |
| NAPSI-50[#] | 41.3 | 46.2 | 68.0 |

APR=apremilast 30 mg BID; ETN=etanercept 50 mg QW; LOCF=last observation carried forward; LS-PGA=Lattice System Physician Global Assessment; NAPSI=Nail Psoriasis Severity Index; NAPSI-50=50% or greater reduction from baseline in NAPSI score; PASI=Psoriasis Area and Severity Index; PASI-75=75% or greater reduction from baseline in PASI score; PBO=placebo; ScPGA=Scalp Physician Global Assessment; sPGA=static Physician Global Assessment.
*P<0.0001; †P=0.0005; ‡P≤0.0021; §P≤0.0458; **P=0.0701 vs. PBO (LOCF). Italics indicate values are nominally significant due to hierarchical testing of study endpoints.
¶With ≥2-point reduction from baseline.
‡All pts had LS-PGA ≥4 (moderate to very severe) at baseline.
¶In pts with ScPGA ≥3 (moderate to very severe) at baseline (exploratory): PBO n=58; APR n=54; ETN n=54.
#In pts with NAPSI ≥1 at baseline: PBO n=46; APR n=52; ETN n=50

**Conclusions:** APR demonstrated significant efficacy vs. PBO at Wk16; with continued APR treatment, therapeutic responses were generally sustained at Wk52. Efficacy was maintained in ETN pts who switched to APR.
**Disclosure of Interest:** K. Reich Grant/research support from: Abbott, AbbVie, Amgen, Basilea, Biogen-Idec, Celgene, Centocor, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD (Essex Pharma, Schering-Plough), Novartis, Ocean Pharma, Pfizer (Wyeth), UCB, Consultant for: Abbott, AbbVie, Amgen, Basilea, Biogen-Idec, Celgene, Centocor, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD (Essex Pharma, Schering-Plough), Novartis, Ocean Pharma, Pfizer (Wyeth), UCB, Speakers bureau: Abbott, AbbVie, Amgen, Basilea, Biogen-Idec, Celgene, Centocor, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD (Essex Pharma, Schering-Plough), Novartis, Ocean Pharma, Pfizer (Wyeth), UCB, J. Soung Grant/research support from: Celgene, Amgen,Novartis, Galderma, Pfizer, Jannsen, Merz, Speakers bureau: Celgene, Amgen, AbbVie, M. Gooderham Grant/research support from: AbbVie, Allergan, Celgene, Eli Lilly, Galderma, Kythera, Leo Pharma, Merck, Novartis, Pfizer, Speakers bureau: AbbVie, Amgen, Astellas, Galderma, Janssen, Leo Pharma, Novartis, Pfizer, Z. Zhang Employee of: Celgene Corporation, K. Nograles Employee of: Celgene Corporation, R. Day Employee of: Celgene Corporation, L. Ferris Grant/research support from: Celgene Corporation, M. Goodfield Grant/research support from: Celgene Corporation
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## THU0440 IXEKIZUMAB PROVIDES SUSTAINED IMPROVEMENT UP TO 52 WEEKS OF DISEASE ACTIVITY AS ASSESSED BY COMPOSITE MEASURE SCORES IN BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG (BDMARD)-NAIVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory

disease associated with psoriasis, peripheral arthritis, enthesitis, dactylitis, and spondylitis. PsA can be progressive and destructive, resulting in physical deformities, impaired function, decreased quality of life, and increased mortality. Ixekizumab (IXE) is an IgG4 monoclonal antibody that binds with high affinity and specificity to the proinflammatory cytokine IL-17A. Results are presented from a phase 3 trial (SPIRIT-P1; NCT01695239) with IXE in patients with active PsA.

**Objectives:** To explore the impact of IXE, as assessed by disease activity composite measures, up to 52 weeks (wks).

**Methods:** A total of 417 bDMARD-naive adult patients with active PSA, were randomly assigned 1:1:1:1 to subcutaneous administration of either 80-mg IXE every 4 wks (Q4W) or every 2 wks (Q2W), each with a 160-mg starting dose at Wk 0; adalimumab (ADA) 40 mg Q2W (active comparator); or placebo (PBO) in the Double-Blind Treatment Period (DBTP; Wks 0 through 24). Of these patients, 381 continued into the Extension Period (EP; Wks 24 through 52). PBO- and ADA-treated patients were randomly re-assigned (1:1) to 80 mg IXEQ4W or IXEQ2W at Wk 16 (inadequate responders) or Wk 24; ADA-treated patients started IXE, after an 8-wk wash-out period, at Wk 24 (inadequate responders) or Wk 32. Investigators were blinded as to the criteria for inadequate response. Disease activity was measured at Wks 24 and 52 by composite measures including the following: minimum disease activity (MDA) as measured with the Psoriasis Area and Severity Index ($MDA_{PASI}$) and with the static Physician Global Assessment of psoriasis ($MDA_{sPGA}$), and modified Composite Psoriatic Disease Activity Indices (CPDAI-12 and CPDAI-14 [see Table 1 footnote]). Analyses for the DBTP were conducted on the Intent-to-Treat Population, defined as all randomly assigned patients; analyses for the EP were conducted on the EP Population, defined as all patients who received at least 1 dose of study drug during the EP. In the DBTP, treatment comparisons were made by a logistic regression model for categorical data with missing values imputed by nonresponder imputation; a mixed model for repeated measures analysis was used for continuous data.

**Results:** At Wk 24, CPDAI-12 and CPDAI-14 total scores (assesses domains of peripheral arthritis, skin disease, enthesitis, dactylitis [and spinal disease for CPDAI-14 only]) for patients receiving IXEQ4W, IXEQ2W, or ADA, were significantly improved compared with results for patients receiving PBO (Table 1). Similarly, at Wk 24, significantly more patients receiving IXEQ4W, IXEQ2W, or ADA achieved $MDA_{sPGA}$ and $MDA_{PASI}$ compared with patients receiving PBO (Table 1), and percentages of patients receiving IXEQ4W or IXEQ2W who achieved $MDA_{sPGA}$ and $MDA_{PASI}$ were sustained through Wk 52 (Table 2). Results for $MDA_{sPGA}$ were similar to results for $MDA_{PASI}$ within each treatment group.

**Table 1: Improvement in Composite Outcome Measures at Week 24 (Double-Blind Treatment Period)**

| Assessment | PBO N=106 | ADA N=101 | IXEQ4W N=107 | IXEQ2W N=103 |
|---|---|---|---|---|
| NRI: | | | | |
| $MDA_{sPGA}$, n (%) | 16 (15.1) | 35 (34.7)*** | 31 (29.0)* | 39 (37.9)*** |
| $MDA_{PASI}$, n (%) | 16 (15.1) | 32 (31.7)** | 32 (29.9)** | 43 (41.7)*** |
| Change from baseline: | | | | |
| **CPDAI-14[†] Total Score**, LSM (SE) | -1.32 (0.29) | -2.51 (0.26)*** | -3.41 (0.26)*** | -3.66 (0.26)*** |
| **CPDAI-12[‡] Total Score**, LSM (SE) | -1.12 (0.26) | -2.13 (0.23)** | -2.94 (0.24)*** | -3.21 (0.23)*** |

Abbreviations: ADA=adalimumab; ASQoL= Ankylosing Spondylitis Quality of Life; CPDAI=Composite Psoriatic Disease Activity Index; IXE=ixekizumab; LSM=least square mean; MDA=minimum disease activity; $MDA_{PASI}$=MDA measured by Psoriasis Area and Severity Index; $MDA_{sPGA}$=MDA measured by static Physician Global Assessment of psoriasis; N,n=number of patients; NRI=nonresponder imputation; p=p-value; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SE=standard error.

[†] CPDAI-14 is modified from CPDAI (Mumtaz A, Gallagher P, Brian K, et al. Development of a preliminary composite disease activity index in psoriatic arthritis. *Ann Rheum Dis*. 2011;70:272-7); this modified index does not include ASQoL questionnaire and has a possible total score of 14.

[‡] CPDAI-12 is modified from CPDAI (Mumtaz et al. 2011); this modified index does not include the ASQoL or the BASDAI, and has a possible total score of 12.

* p<.05; ** p≤.01; *** p≤.001; MDA p-values for are from a logistic regression model; CPDAI p-values are from a repeated measures mixed model.

**Table 2: Improvements in Composite Outcome Measures at Week 52 (Extension Period)**

| Assessment | PBO/ IXEQ4W N=45 | PBO/ IXEQ2W N=46 | ADA/ IXEQ4W N=49 | ADA/ IXEQ2W N=48 | IXEQ4W/ IXEQ4W N=97 | IXEQ2W/ IXEQ2W N=96 | Total IXEQ4W N=191 | Total IXEQ2W N=190 |
|---|---|---|---|---|---|---|---|---|
| NRI: | | | | | | | | |
| $MDA_{sPGA}$, n (%) | 15 (33.3) | 19 (41.3) | 20 (40.8) | 15 (31.3) | 42 (43.3) | 38 (39.6) | 77 (40.3) | 72 (37.9) |
| $MDA_{PASI}$, n (%) | 15 (33.3) | 19 (41.3) | 20 (40.8) | 15 (31.3) | 42 (43.3) | 38 (39.6) | 77 (40.3) | 72 (37.9) |

Abbreviations: ADA=adalimumab; IXE=ixekizumab; MDA=minimum disease activity; $MDA_{PASI}$=MDA measured by Psoriasis Area and Severity Index; $MDA_{sPGA}$=MDA measured by static Physician Global Assessment of psoriasis; N,n=number of patients; NRI=nonresponder imputation; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks.

**Conclusions:** IXE provides sustained improvement of disease activity, as measured by various composite measures, for up to 52 wks in bDMARD-naive patients with active PsA.

**Disclosure of Interest:** L. Coates Consultant for: Lilly, M. E. Husni Consultant for: Lilly, Novartis, AbbVie, Celgene, Bristol Myers Squibb, Amgen, Janssen, UCB Pharma, C. Shuler Shareholder of: Lilly, Employee of: Eli Lilly and Company, H. Carlier Shareholder of: Lilly, Employee of: Eli Lilly and Company, C.-Y. Lin Employee of: Eli Lilly and Company, J. Mou Shareholder of: Lilly, Employee of: Eli Lilly and Company, C. Lee Shareholder of: Lilly, Employee of: Eli Lilly and Company, P. Mease Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB Pharma, Consultant for: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Covagen, Crescendo, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Lilly, Pfizer, UCB Pharma

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## THU0441 EFFECT OF CONCOMITANT CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CDMARDS) ON THE EFFICACY AND SAFETY OF IXEKIZUMAB IN BIOLOGIC DMARD-NAIVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease associated with psoriasis, peripheral arthritis, enthesitis, dactylitis, and spondylitis. Ixekizumab (IXE) is an IgG4 monoclonal antibody that binds with high affinity and specificity to the proinflammatory cytokine IL-17A. Results are presented for the phase 3 trial (SPIRIT-P1) with IXE treatment of patients with active PsA.

**Objectives:** To evaluate the efficacy and safety of IXE when used alone or in combination with concomitant conventional DMARDs (cDMARDs).

**Methods:** A total of 417 bDMARD-naive adult patients were randomly assigned 1:1:1:1 to subcutaneous administration of 80-mg IXE every 4 wks (Q4W) or every 2 wks (Q2W), each starting with a 160-mg dose at Wk 0; adalimumab (ADA) 40 mg Q2W (active comparator); or placebo (PBO) during the Double-Blind Treatment Period (DBTP; Wks 0 through 24). Of these patients, 267 were receiving a concomitant cDMARD at baseline, 149 were not, and 1 did not receive study drug; patients were stratified by cDMARD use, and were to remain on their cDMARD through the DBTP. At Wk 24, efficacy was evaluated by American College of Rheumatology (ACR) response; and progression of structural damage was assessed by the modified Total Sharp Score (mTSS). Safety assessments included the percentage of patients experiencing treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and discontinuations due to adverse events (AEs). Efficacy analyses were conducted on the Intent-to-Treat Population, defined as all randomly assigned patients; safety analyses were conducted on the Safety Population, defined as all randomly assigned patients who received at least 1 dose of study drug. Fisher's test was used for treatment comparisons in ACR and AE data, and an analysis of covariance model was used for mTSS data. Missing values were imputed by nonresponder imputation for ACR data and by linear extrapolation for mTSS data.

**Results:** At Wk 24, compared with patients receiving PBO, significantly more patients receiving IXEQ4W or IXEQ2W (with/without concomitant cDMARD) achieved ACR20/50/70 responses (see Table for ADA results). Patients receiving IXEQ2W (with/without concomitant cDMARD) or IXEQ4W or ADA (with concomitant cDMARD) showed significantly less progression in mTSS from baseline compared with patients receiving PBO (Table). No treatment-by-subgroup effects were observed for ACR20/50/70 or mTSS (Table footnotes). In patients receiving concomitant cDMARDs, significantly more patients receiving IXE or ADA experienced ≥1 TEAE, compared with patients receiving PBO; the percentages of patients with SAEs or discontinuations due to an AE were comparable among treatment groups (Table).

**Table: Effect of Concurrent Use of Conventional DMARDs on Efficacy and Safety of Ixekizumab**

| Baseline use of cDMARD? | Placebo N=106 Yes n=69 | Placebo N=106 No n=37 | ADA/Q2W N=101 Yes n=67 | ADA/Q2W N=101 No n=34 | IXEQ4W N=107 Yes n=68 | IXEQ4W N=107 No n=39 | IXEQ2W N=103 Yes n=63 | IXEQ2W N=103 No n=40 |
|---|---|---|---|---|---|---|---|---|
| **Efficacy Outcomes at Week 24** | | | | | | | | |
| ACR20*, NRI, n (%) | 22 (31.9) | 10 (27.0) | 43 (64.2)*** | 15 (44.1) | 38 (55.9)** | 24 (61.5)** | 39 (61.9)*** | 25 (62.5)** |
| ACR50*, NRI, n (%) | 13 (18.8) | 3 (8.1) | 28 (41.8)** | 11 (32.4)* | 26 (38.2)* | 17 (43.6)*** | 30 (47.6)*** | 18 (45.0)*** |
| ACR70*, NRI, n (%) | 6 (8.7) | 0 (0.0) | 19 (28.4)** | 7 (20.6)** | 16 (23.5)* | 9 (23.1)** | 20 (31.7)*** | 15 (37.5)*** |
| mTSS[†], change from baseline, LSM (SE) | 0.44 (0.101) | 0.56 (0.161) | 0.11 (0.095)* | 0.11 (0.171) | 0.13 (0.098)* | 0.26 (0.156) | 0.11 (0.099)* | 0.03 (0.154)* |
| | Placebo N=106 | | ADA/Q2W N=101 | | IXEQ4W N=107 | | IXEQ2W N=103 | |
| Baseline use of cDMARD? | Yes n=69 | No n=37 | Yes n=67 | No n=34 | Yes n=68 | No n=39 | Yes n=63 | No n=40 |
| **Safety Outcomes at Week 24** | | | | | | | | |
| TEAEs[‡,§], n (%) | 30 (43.5) | 20 (54.1) | 45 (67.2)** | 20 (58.8) | 42 (61.8)* | 29 (74.4) | 40 (63.5)* | 27 (69.2) |
| SAEs[‡,§], n (%) | 2 (2.9) | 0 (0.0) | 5 (7.5) | 0 (0.0) | 3 (4.4) | 3 (7.7) | 0 (0.0) | 3 (7.7) |
| AEs leading to discontinuation[‡,§], n (%) | 2 (2.9) | 0 (0.0) | 1 (1.5) | 1 (2.9) | 1 (1.5) | 1 (2.6) | 4 (6.3) | 0 (0.0) |

Abbreviations: ACR=American College of Rheumatology; ACR20=at least 20% improvement in ACR assessments from baseline; ACR50=at least 50% improvement in ACR assessments from baseline; ACR70=at least 70% improvement in ACR assessments from baseline; ADA=adalimumab; AE=adverse events; ANCOVA=analysis of covariance; cDMARD=conventional disease-modifying antirheumatic drug; IXE=ixekizumab; LSM=least squares mean; N,n=number of patients; NRI = nonresponder imputation; mTSS=modified Total Sharp Score; SAEs=serious adverse events; SE=standard error; TEAEs=treatment-emergent adverse events.

* Treatment-by-subgroup interaction p-values are .321 (ACR20), .454 (ACR50), and NA (ACR70, because 0 PBO patients without cDMARD achieved ACR70). Treatment-by-subgroup interaction p-values are based on a logistic regression model with effect of treatment, subgroup, and the treatment-by-subgroup interaction, and are tested at the significance level of 0.10.

† Treatment-by-subgroup interaction p-value is .727. Treatment-by-subgroup interaction p-value is from an ANCOVA model with treatment, baseline score, subgroup, and interaction of treatment by subgroup included as factors.

‡ Patients with ≥1 event.

§ Statistical analyses presented are for the baseline use of cDMARD – "yes" or "no" subgroup within each treatment group, and the respective baseline use of cDMARD – "yes" or "no" subgroup within the placebo group.

* p< .05; ** p≤.01; *** p≤.001; p-values for ACR20/50/70 and AEs are based on Fisher's exact test; p-values for mTSS are from an ANCOVA model with treatment and baseline scores.

**Conclusions:** IXE demonstrated efficacy in improvement of PsA signs and

symptoms and structural inhibition in bDMARD-naive patients with/without concomitant cDMARD use. With concomitant cDMARD use, although significantly more patients receiving IXE or ADA experienced ≥1 TEAE, compared with patients receiving PBO, the frequency of SAEs and discontinuations due to an AE were comparable among all treatment groups.

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## THU0442 REDUCTION IN FATIGUE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS ARE SUSTAINED OVER 2 YEARS: LONG-TERM RESULTS OF TWO PHASE 3 STUDIES WITH SECUKINUMAB

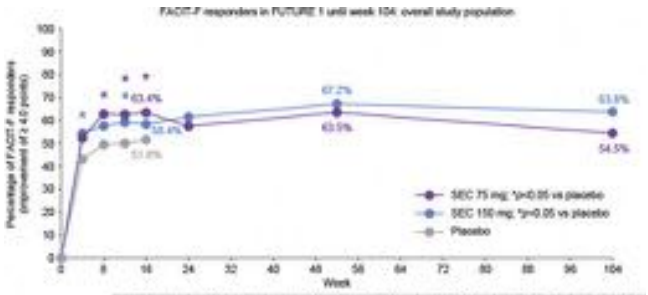
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**Background:** Fatigue is an important symptom associated with active psoriatic arthritis (PsA) and can impact on health-related quality of life (HRQoL) and social functioning. Secukinumab (SEC) has resulted in rapid improvements in signs and symptoms, physical functioning and HRQoL in patients with active PsA vs placebo (PBO) in the FUTURE 1 (F1) and FUTURE 2 (F2) studies. Rapid improvements in fatigue were reported in F2.

**Objectives:** To assess 1- and 2-year data on the effects of SEC on fatigue in patients with PsA, including both biologic-naïve patients and those with an inadequate response to TNF therapy (TNF-IR) and to investigate correlations between fatigue and baseline characteristics or clinical endpoints.

**Methods:** Patients with active PsA (F1, N=606; F2, N=397) received SEC or PBO every 4 weeks. Patients receiving PBO who did not meet predefined response criteria at week 16 were re-randomized at week 24 to active treatment. Fatigue was assessed at baseline and weeks 4, 8, 12, 16, 24, 52 and 104 using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale. A change in FACIT-F score of ≥4 from baseline was used to define fatigue response. Logistic regression was used to explore the relationship between fatigue response (weeks 16 and 52) and baseline characteristics and clinical response criteria. The FACIT-F response analyses were based on observed data with no imputation; the FACIT-F score analyses used mixed-effect model repeated measure imputation.

**Results:** Improvements in fatigue compared with PBO were observed for all SEC doses in from week 4 onwards. A fatigue response at week 16 was achieved by 58.4% (F1) and 70.0% (F2) of patients receiving SEC 150 mg, compared with 51.6% (F1) and 43.2% (F2) of those receiving PBO (see figure for F1 data). For SEC 300 mg, a 16 week response was achieved by 50.5% (F2). Responses were sustained at week 52 for 150 mg (F1, 67.2%; F2, 68.5%) and 300 mg (F2, 60.2%) and at week 104 for 150 mg (F1, 63.8%). Sustained responses were also seen in both biologic-naïve (F1, n=425; F2, n=258) and TNF-IR patients (F1, n=181; F2, n=104). Logistic regression analyses of pooled data from F1 and F2 found age and baseline HAQ-DI scores were associated with fatigue response (weeks 16 and 52). Achieving a fatigue response was moderately to strongly correlated with clinical response criteria (including ACR, HAQ-DI and PASI scores at weeks 16 and 52).




| | Week 4 | Week 8 | Week 12 | Week 16 | Week 24 | Week 52 | Week 104 |
|---|---|---|---|---|---|---|---|
| SEC 75 mg, n/m | 99/189 | 120/191 | 119/190 | 123/194 | 111/193 | 113/178 | 79/143 |
| SEC 150 mg, n/m | 105/193 | 110/191 | 113/191 | 111/190 | 116/192 | 123/183 | 97/152 |
| Placebo, n/m | 65/197 | 96/194 | 91/192 | 97/188 | .. | .. | .. |

n, number of patients with sufficient data for evaluation; m, number of responders.

**Conclusions:** SEC provided rapid and sustained improvements in fatigue for up to 104 weeks in patients with active PsA, regardless of prior biologic exposure. Achieving a fatigue response was moderately to strongly correlated with improvement in clinical response criteria, indicating a relationship between fatigue and PsA disease activity. SEC-induced sustained improvements in fatigue may be important for improving HRQoL in patients with PsA. Analysis of factors predictive of fatigue response may help to clarify the drivers of fatigue; this study highlights the importance of age and physical functioning.

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## THU0443 UNMET NEEDS IN PSORIATIC ARTHRITIS: ONE THIRD OF THE PATIENTS WITH QUIESCENT DISEASE ACCORDING TO THE RHEUMATOLOGIST'S OPINION DO NOT ACHIEVE MINIMAL DISEASE ACTIVITY

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**Background:** Several new drugs, including ustekinumab, apremilast, and secukinumab, became available for the treatment of psoriatic arthritis (PsA) over the last years, broadening our possibilities to treat the disease effectively. The new therapeutic modalities open a new perspective for patients not responding to conventional DMARDs and TNF inhibitors (TNFi). As achieving the lowest possible level of disease activity in all domains of disease is associated with better long-term outcomes, the new therapeutic modalities may potentially also benefit patients with partial but not full disease control with cDMARDs and/or TNFi.[1] Therefore, defining an acceptable disease state in routine clinical practice is becoming increasingly important to identify who could potentially benefit from treatment adjustment.

**Objectives:** The aim of the study was to assess how many patients with quiescent disease according to the treating rheumatologist have an acceptable disease state defined as minimal disease activity.

**Methods:** This cross-sectional study was performed in 2 rheumatology outpatient clinics and included a total of 250 PsA patients between Feb 2013 and June 2015. Key inclusion criteria were fulfillment of the CASPAR criteria and quiescent disease in the opinion of the treating rheumatologists, defined by the fact that the rheumatologist did not consider to modify the current treatment. Patients were systematically evaluated by an independent research physician for current disease activity including clinical assessments and patient reported outcomes (PRO). Minimal disease activity (MDA) was defined as the fulfillment of ≥5 of the following: TJC68≤1, SJC68≤1, PASI≤1, VASpain≤15mm, VASptglobal≤20mm, HAQ≤0.5, tender entheseal points≤1.

**Results:** One third (88/250) of the PsA patients with quiescent disease according

Table 1

| | All pts | MDA+ | MDA- | p-value (<0.05 = sign.) |
|---|---|---|---|---|
| N | 250 | 162 | 88 | |
| Patient characteristics mean (SD) | | | | |
| Age | 55 (11) | 53 (12) | 59 (10) | 0.000 |
| Gender (%♀) | 33% | 50% | 26% | 0.002 |
| Age at arthritis onset | 43 (12) | 41 (12) | 45 (11) | 0.021 |
| PRO scores median (IQR) | | | | |
| HAQ | 0.25 (0–0.63) | 0.0 (0–0.38) | 0.75 (0.5–1.38) | 0.000 |
| DLQI | 1 (0–3) | 0 (0–1) | 2 (0–5) | 0.000 |
| SF-36 PCS | 46 (39–54) | 51 (46–54) | 38 (31–43) | 0.000 |
| VAS pt global (mm) | 10 (3–29) | 6 (1–11) | 37 (23–56) | 0.000 |
| WPAI (daily activities) | 1 (0–4) | 1 (0–2) | 4 (2–7) | 0.000 |
| Laboratory median (IQR) | | | | |
| ESR (mm/hr) | 6 (4–11) | 5 (3–9) | 8 (5–16) | 0.000 |

to the treating rheumatologist did not fulfill MDA criteria (MDA-). A high TJC, VASpain and VASptglobal were the items most frequently contributing to the failure to achieve MDA (not achieved in 83%, 82% and 80%). However, also objective signs of disease activity were higher in MDA- vs MDA+ patients: a SJC>1 occurred in 35% vs 7% (p=0.000), enthesitis>1 in 14% vs 3% (p=0.002), and PASI>1 in 43% vs 26% (p=0.002). There was no difference in treatment use (including cDMARD and TNFi) between MDA- and MDA+. See table 1 for additional patient characteristics.

**Conclusions:** One third of the PsA patients with quiescent disease according to the treating rheumatologist do not achieve the MDA criteria. These patients have higher disease activity both on subjective and objective disease activity measurements. As this is associated with worse PROs, further research should evaluate if treatment adjustments may be beneficial for this patient group with residual disease activity.

**References:**

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## THU0444 SUBCLINICAL ULTRASONOGRAPHIC ENTHESITIS IN PATIENTS WITH PSORIASIS IS ASSOCIATED WITH RISK MARKERS FOR PSORIATIC ARTHRITIS

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**Background:** Enthesitis is considered a primary feature of psoriatic arthritis (PsA). PsA has a period of pre-clinical disease in which enthesitis can be detected in patients with psoriasis only by sensitive imaging modalities such as ultrasound. In this study we consider the presence of subclinical enthesitis detected by ultrasound in psoriasis patients as a proxy for PsA-risk.

**Objectives:** We aimed to estimate the prevalence of subclinical enthesitis in patients with psoriasis without clinical arthritis and to assess their relation with known risk markers for PsA.

**Methods:** 178 patients with a diagnosis of psoriasis confirmed by a dermatologist were enrolled. Patients with clinical signs suggestive of PsA were excluded. Information about demographics, co-morbid conditions and psoriasis phenotype was recorded. Musculoskeletal ultrasound assessment of 12 entheseal sites was performed according to a standard protocol. Enthesis thickness, structure, calcification/bone proliferation, erosion, bursa and power Doppler signal in the cortical bone profile, tendon and bursa were scored according to the MAdrid Sonographic Enthesitis Index (MASEI). A cut-off of ≥20 was used to define "subclinical enthesitis". The association between the presence of subclinical enthesitis and patients' characteristics was assessed using logistic regression analysis adjusting for age.

**Results:** A total of 19 of 178 patients (10.7%) were found to have subclinical enthesitis on ultrasound (MASEI≥20). The most frequently affected sites were the attachments of the distal patellar tendon (46.7%), Achilles tendon (44.1%) and plantar fascia (38%). 37 patients (20.8%) had one or more entheseal sites with positive power Doppler signal. Patients with subclinical enthesitis were more likely to be older (p=0.002), obese (p=0.01), diabetic (p=0.005), have nail pitting (p=0.006) and work in physically demanding occupations (p=0.01). Moreover, patients with subclinical enthesitis were more likely to report morning stiffness (p=0.008); however, no association was found with other musculoskeletal symptoms or patient reported outcomes estimating the degree of pain, function, fatigue and quality of life. On multivariate analysis the presence of ultrasonographic enthesitis was associated with obesity (Odds Ratio (OR) 14.3, 95% Confidence Interval (CI) 1.7, 118, p=0.01), current smoking (OR 5.1, 95% CI 1.3, 19.4, p=0.02), physically-demanding occupation (OR 4.3, 95% CI 1.3, 13.8, p=0.01), diabetes mellitus (OR 5.5, 95% CI, 1.1, 28.1, p=0.04) and psoriatic nail pitting (OR 4.3, 95% CI 1.5, 11.9, p=0.006).

**Conclusions:** The presence of subclinical enthesitis is associated with known risk markers of PsA including: nail pitting, obesity and occupation-related mechanical stress. These findings reinforce the use of ultrasound for investigation of pre-clinical PsA in patients with psoriasis.

**Disclosure of Interest:** None declared

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## THU0445 VALIDATION OF THE CONTEST QUESTIONNAIRES TO SCREEN FOR PSORIATIC ARTHRITIS IN PRIMARY CARE PSORIASIS PATIENTS

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**Background:** Various screening tools have been developed and validated over the years in order to enhance early recognition of psoriatic arthritis (PsA) among psoriasis patients, but their performance remains suboptimal. In 2014 the CONTEST-group developed a new screening tool consisting of the most discriminating questions from 3 existing tools (PEST, PASE, TOPAS) which was externally validated in 2 psoriasis cohorts from dermatology. Validation in a primary care setting has yet to be performed.

**Objectives:** To externally validate the CONTEST questionnaire in psoriasis patients in primary care.

**Methods:** Data from the SENSOR study was used, a cross-sectional study in adult psoriasis patients with regular spells of musculoskeletal complaints from primary care. In this study, patients completed the PEST and PASE screening-questionnaires before clinical evaluation. Within CONTEST 3 TOPAS questions are used that were not included in our study. These questions were therefore replaced by similar questions: ToPAS 2A was replaced by PEST 3, ToPAS 2B by nail assessment by a dermatologist and ToPAS 7 by data from the manikin in the PEST. We calculated sensitivity, specificity and area under the curve (AUC) for the CONTEST with a cutoff of 4, as well as the CONTEST-w (weighted version, cutoff of 8) and the CONTEST-jt (including the PEST manikin, cutoff of 5). Performance was also calculated selecting the patients in the same way as the CONTEST study, i.e. only inviting patients with a positive PEST and/or PASE questionnaire for clinical evaluation. As a reference standard we used a clinical diagnosis of PsA made by a rheumatologist and enthesitis confirmed by ultrasound (presence of Power Doppler). Results from our dataset were compared with data from the development cohort and with the performance of the PEST.

**Results:** For this analysis 473 psoriasis patients at risk for PsA were available. Compared with the development cohort sensitivity was considerably lower in our dataset (0.30–0.51) than in the development of the CONTEST (0.86). Specificity was higher in our dataset (0.75–0.87) compared with the CONTEST development (0.35–0.48). While AUCs were around 0.7 for all three versions, comparable with the AUCs found in the development of CONTEST. Comparing these results with the performance of the PEST in our population, it shows that the sensitivity is lower for the CONTEST (0.30–0.51) than for the PEST (0.68), while the specificity is slightly higher (0.75–0.87 vs 0.71).

**Table 1. Performance (AUC, Sensitivity and Specificity) of the CONTEST questionnaires in the development study and in the SENSOR dataset**

| | AUC | | | Sensitivity | | | Specificity | | |
|---|---|---|---|---|---|---|---|---|---|
| | Development | SENSOR | SENSOR selection* | Development | SENSOR | SENSOR selection* | Development | SENSOR | SENSOR selection* |
| CONTEST | 0.69 | 0.69 | 0.60 | 0.86 | 0.53 | 0.64 | 0.35 | 0.75 | 0.5 |
| CONTEST-w | 0.74 | 0.67 | 0.60 | 0.86 | 0.30 | 0.36 | 0.48 | 0.87 | 0.73 |
| CONTEST-jt | 0.70 | 0.69 | 0.60 | 0.86 | 0.51 | 0.62 | 0.37 | 0.78 | 0.55 |
| PEST | 0.91 | 0.71 | NA | 0.92 | 0.68 | NA | 0.78 | 0.71 | NA |

* Only selecting patients with a positive PEST and/or PASE questionnaire

**Conclusions:** External validation of the CONTEST questionnaire in primary care psoriasis patients with regular spells of musculoskeletal symptoms resulted in lower sensitivity and higher specificity compared to the development cohort, while AUCs were comparable. When only selecting patients with at least one positive screeningtool, the sensitivity slightly increases while the specificity slightly decreases. However, the performance of the CONTEST questionnaires does not seem to exceed the performance of the PEST in a primary care setting.

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## THU0446 MANAGEMENT OF PSORIATIC ARTHRITIS IN EAST OF ENGLAND

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**Background:** Currently there are many guidelines for the management of psoriatic arthritis which advocate the use of DMARDs (Disease Modifying Anti-Rheumatic Drugs) such as the EULAR (2011) and the BSR (2012) guidelines. These guidelines are based on systematic reviews comparing DMARD to placebo rather than head to head trials.

**Objectives:** The purpose of the survey is firstly to establish whether clinicians in our region were managing psoriatic arthritis in line with recommendations, and secondly, to explore the reasons behind choice of DMARDs or biologic agent.

**Methods:** An anonymous regional survey of 25 clinicians was conducted based around the diagnosis, classification and management of psoriatic arthritis.

**Results:** The most popular classification for PsA is the Moll and Wright's

criteria (39%). Methotrexate is the first choice DMARD in oligoarthritis (77%) and polyarthritis (96%). The reasons being: evidence based (31%) prior experience (31%) and to manage the skin condition (38%). The majority favour leflunomide (60%) over sulphasalazine (32%) as second line DMARD. Factors influencing this choice consisted of: evidence (52%); prior experience (28%); safety (12%); likelihood of improving the skin condition (8%). Of the 76% of clinicians who stated they regularly use outcome measures, 67% used PsARC of which 50% use it sometime, 43% always, and 7% rarely. DAS is used by 19% while 14% noted tender or swollen joint counts. Only few clinicians actively subcategorise dactlitis (17%) and enthesitis (36%). The majority (83%) didn't distinguish between PsA and Ankylosing Spondylitis. Popular first choice biologic agents were adalimumab (58%): golimumab (13%): certolizumab (13%). The reasons being: prior experience (37%), articular efficacy (21%), and extra-articular efficacy (16%).

**Conclusions:** The majority of clinicians use PsARC for outcome measurement although not many use it frequently. This may be due to a relatively small cohort of patients on biologic treatment who would need this score to meet criteria to continue biologic therapy. The majority of clinicians didn't distinguish between PsA and Ankylosing Spondylitis which may affect management.There is a general consensus in the East of England region regarding first line DMARD therapy as Methotrexate despite the lack of evidence. There are only few randomised controlled trials showing articular efficacy of DMARDs in psoriatic arthritis but they do show symptomatic benefit. Over half of clinicians use Adalimumab as the first line biologic agent. BSR guidelines (2012) recommend the use of an anti TNF monoclonocal antibody in those who require rapid control of skin psoriasis. Other suggested considerations included cost effectiveness and patient preference which were not stipulated in this survey. The reasons for biologic choice vary but at least a third of all clinicians rely on their prior experience.

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## THU0447 MEASURING OUTCOME IN PSORIATIC ARTHRITIS: CORRELATION BETWEEN DIFFERENT SKIN SCORES

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**Background:** Psoriatic arthritis (PsA) is a heterogeneous disease that includes features of peripheral arthritis, spondylitis, dactylitis, enthesitis, and skin and nail disease. PsA affects about 30% of patients with psoriasis (PsO).[1]

Measuring outcome in psoriatic arthritis (MOPsA) is a web-based tool, freely available to use (see https://mopsa.ie), that collects clinical information about all domains affected in PsA including skin disease and patient reported outcome measures (PROMs). MOPsA also calculates the composite psoriatic disease activity index (CPDAI) and minimal disease activity (MDA).[2,3]

Assessment of skin disease in rheumatology clinics can be challenging. Availability of patient self-assessment questionnaires that correlate with, and possibly can replace, physical examination would address this challenge.

**Objectives:** Our aim was to correlate skin-related patient self-assessment questionnaires and skin sores assessed by physicians using MOPsA.

**Methods:** 189 patients with PsA, fulfilling CASPAR criteria, were recruited in this study. 137 patients from rheumatology clinic and 52 patients from dermatology clinic. We calculated the following skin scores: Dermatology Quality of Life Index (DLQI), Psoriasis Symptom Inventory (PSI), Body Surface Area (BSA) and Psoriasis Area Severity Index (PASI). GraphPad Prism version 6 was used for statistical analysis.

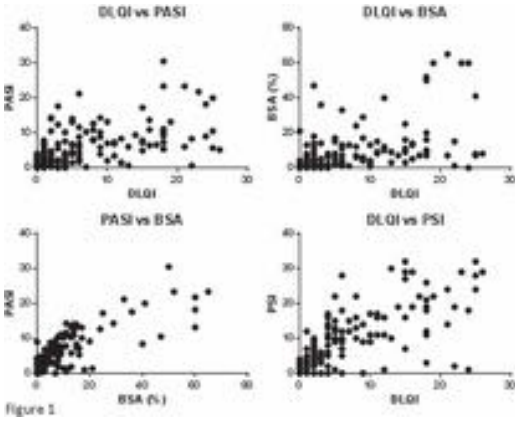



Figure 1

**Results:** Data from 189 patients with skin scores were included in this analysis. Mean ± SD age of 44.61 (± 12.54), 99 (52%) patients were males. 96 (51%) patients had nail involvement. Mean ± SD DLQI was 5.57 (± 6.93), PSI 7.36 (±8.68), BSA 7.27 (± 12.17), and PASI 4.57 (± 5.56).

There was strong correlation between PASI and BSA (r=0.8502, P<0.0001) and between PASI and DLQI (r=0.7256, P<0.0001), but moderate correlation between PASI and PSI (r=0.5812, P<0.0001). There was strong correlation between BSA and DLQI (r=0.7048, P<0.0001) but moderate correlation between BSA and PSI (r=0.6246, P<0.0001 respectively). Finally, there was strong correlation between DLQI and PSI (r=0.7873, P<0.0001).

**Conclusions:** Our analysis confirms the correlation between PASI and DLQI. The strongest correlation was between PASI and BSA. DLQI correlates very well with all three parameters (PASI, BSA and PSI). These preliminary results suggest that the combination of BSA and DLQI might work equally well to PASI and DLQI when accurately accessing skin involvement in rheumatology clinics.

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**Disclosure of Interest:** M. Elmamoun: None declared, C. Loftus: None declared, A. Szentpetery: None declared, P. Gallagher: None declared, L. Barnes: None declared, O. FitzGerald Grant/research support from: Pfizer, AbbVie, BMS, UCB, Consultant for: Pfizer, AbbVie, Janssen, MSD, Cellgene, Novartis, Speakers bureau: Pfizer, AbbVie, Janssen, Cellgene

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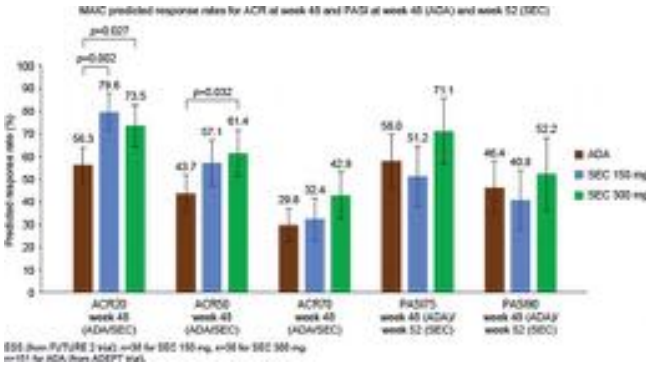
## THU0448 SECUKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS ADALIMUMAB UP TO 48 WEEKS USING A MATCHING-ADJUSTED INDIRECT COMPARISON

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**Background:** Secukinumab (SEC) is approved for the treatment of active PsA in adults with inadequate response to DMARDs. The FUTURE 2 (F2) trial showed superiority of SEC 150 mg and 300 mg over placebo for the primary outcome of ACR20 response at week 24 and for multiple secondary outcomes, with efficacy sustained to week 52. The ADEPT trial compared adalimumab 40 mg (ADA) with placebo in biologic-naïve patients. In F2, patients could switch from placebo (from week 16); for both trials all had switched after week 24. In the absence of direct comparison or a continuous common placebo arm, matching-adjusted indirect comparison (MAIC) can assess relative efficacy. MAIC adjusts for differences in patient characteristics at baseline, reducing the effective sample size (ESS) for the therapy arm in one trial, but matching this with the population of the therapy arm from another trial, thus simulating head-to-head comparison.

**Objectives:** To assess the relative efficacy of SEC 150 mg and 300 mg vs. ADA using F2 and the published ADEPT trial.

**Methods:** Patient-level data from the SEC arms of the F2 trial (n=200 across SEC doses) were weighted to match patient baseline characteristics for the ADA arm of ADEPT (n=151). Logistic regression was used to determine weights for age, body weight, sex, race, methotrexate use, presence of psoriasis (≥3% body surface area), mean PASI score, dactylitis, enthesitis, mean HAQ-DI and previous biologic therapy. Weighted outcomes from F2 (ESS: n=36 for SEC 150 mg; n=38 for SEC 300 mg) were compared with data from ADEPT (both trials used non-responder imputation). Pairwise comparisons using relative risks (RRs) were



performed and results are presented as RR (95% CI) and probability of response (95% CI) for ACR20, 50 and 70 at week 48. For PASI75 and 90, ADA week 48 results are compared with SEC week 52 data (the nearest data point).
**Results:** In the MAIC, both SEC doses had higher mean ACR20, 50 and 70 responses than ADA, with statistical significance for SEC 150 mg (RR: 1.41 [1.14–1.76], $p$=0.002) and SEC 300 mg (RR: 1.31 [1.03–1.66], $p$=0.027) at ACR20 and for SEC 300 mg (RR: 1.41 [1.03–1.92], $p$=0.032) at ACR50. The ACR20, 50 and 70 response rates were 79.6% (72–88), 57.1% (47–67) and 32.4% (23–42) respectively for SEC 150 mg; 73.5% (64–83), 61.4% (51–71) and 42.9% (33–53) for SEC 300 mg; and 56.3% (48–64), 43.7% (36–52) and 29.8% (23–37) for ADA. Findings were consistent across sensitivity analyses which also showed significance for SEC 300 mg at ACR70.
PASI 75 and 90 response rates were numerically better for SEC 300 mg: 71.1% (57–86) and 52.2% (36–68) than ADA: 58.0% (46–70) and 46.4% (35–58). SEC 150 mg rates were 51.2% (38–64) and 40.8% (28–54) respectively.
**Conclusions:** When adjusted for patient baseline characteristics, SEC was associated with numerically higher response rates for joint and skin outcomes with statistically significantly higher responses vs. ADA for ACR endpoints at week 48. The next level of evidence will be a head-to-head to substantiate these findings.
**Disclosure of Interest:** P. Nash Grant/research support from: Novartis, Consultant for: Novartis, I. McInnes Consultant for: Novartis, Janssen, Abbvie, Pfizer and UCB, P. Mease Grant/research support from: Corrona, Speakers bureau: Corrona, Merck and Novartis, H. Thom Consultant for: Novartis Pharma AG and for a short time in 2015 for Eli Lilly, S. Cure: None declared, E. Palaka Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, S. Mpofu Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
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## THU0449 ASSESSMENT OF DISABILITY LEVELS IN A COHORT OF 1,489 PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS, AND THE EFFECT OF APREMILAST TREATMENT: POOLED DATA FROM 3 PHASE III, RANDOMIZED, CONTROLLED TRIALS

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**Background:** Psoriatic arthritis (PsA) reduces physical function and QoL; a treatment goal is to improve/maintain functionality. PALACE 1 (NCT01172938), 2 (NCT01212757), and 3 (NCT01212770) compared apremilast (APR) efficacy/safety with placebo (PBO) in patients (pts) with active PsA despite prior conventional DMARDs and/or biologics, providing one of the largest databases (N=1,489) examining physical disability in pts with moderate/severe PsA.
**Objectives:** Assess APR 30 mg BID (APR30) treatment impact on disability using the HAQ-DI over 104 wks with PALACE 1–3 pooled data.
**Methods:** Pts were randomized (1:1:1) to PBO, APR30, or APR 20 mg BID (APR20) stratified by baseline (BL) DMARD use (yes/no). At Wk 24, all remaining PBO pts were re-randomized to APR30 or APR20. HAQ-DI scores were collected at BL and Wks 16, 24, 40, 52 65, 78, 91, and 104. Mean change, proportion reaching MCID, and disability levels were calculated; HAQ-DI cutoff levels were ≤1.0 (clinically significant disability[1]), ≤0.5 (MDA criteria[2]), and ≤0.25. Score shift categories were examined in 0.25 increments to clarify pt disability level. Wk 16 data, compared with PBO, are analyzed by intent-to-treat/LOCF methodology. Other data shown are as observed to Wk 104. Mean change and MCID outcomes are for all pts receiving treatment with APR30 at any time during the study; for disability level and category shift assessments, data are shown for pts randomized to APR at BL.
**Results:** Pts exhibited significant BL physical disability (mean HAQ-DI=1.2); 60% of APR30 pts had a score >1.0, and 31% >1.5, noting marked difficulty/need for assistive devices in performing activities of daily living. Major disability was noted in 19% with BL HAQ-DI >1.75. As early as Wk 16, physical function improved with APR30; pts exhibited a mean HAQ-DI change of –0.23 (vs –0.08 PBO; $P$<0.0001), 56% achieved HAQ-DI ≤1.0 at Wk 16 (vs 48% PBO pts), and 29% achieved HAQ-DI ≤0.5 (vs 25% PBO pts). Fewer PBO vs APR30 pts reached the MCID of –0.13 (prespecified analysis; 37% vs 47%; $P$<0.005) or –0.30 (prespecified analysis)/–0.35[3] (post hoc analysis) (26% vs 36% for both; $P$<0.005). At Wk 52, decreases in disability were maintained (APR30 mean change in HAQ-DI=–0.33); 48% of APR30 pts achieved MCID –0.30 and –0.35. Importantly, at Wk 52, 58% of all APR30 pts achieved HAQ-DI ≤1.0, 34% ≤0.5, and 24% ≤0.25 (Table). Among pts with greater BL disability (HAQ-DI ≥1.5), 64% improved by ≥1 shift category and 47% by ≥2. At Wk 104, 50% of APR30 pts achieved MCID of –0.30 and –0.35, with 64% achieving HAQ-DI ≤1.0, 38% ≤0.5, and 28% ≤0.25; LOCF analysis confirmed Wk 104 results.

| Pts Achieving Improvement in Physical Function by HAQ-DI Level | | |
|---|---|---|
| Pts Achieving HAQ-DI Disability Threshold, % | Wk 52* APR30 n=377 | Wk 104* APR30 n=306 |
| ≤1.0 | 58 | 64 |
| ≤0.5 | 34 | 38 |
| ≤0.25 | 24 | 28 |
| **Pts Achieving HAQ-DI MCID Levels, %** | **APR30 n=567** | **APR30 n=456** |
| ≥0.30 | 48 | 50 |
| ≥0.35 | 48 | 50 |

Health Assessment Questionnaire-Disability Index (HAQ-DI) ≤1.0=disability not clinically significant; ≤0.5=disability remission.
*Wk 52 and Wk 104 were based on data as observed.

**Conclusions:** In APR30 pts, physical function improved at Wk 16 and was sustained with long-term treatment. Most pts achieved HAQ-DI MCID –0.30 or –0.35 and HAQ-DI scores ≤1.0, with many obtaining HAQ-DI ≤0.5, defined as minimal disease in recent criteria. These data indicate improvement and long-term maintenance of functionality with APR treatment.
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[1] Arthritis Rheum. 2003;48:59–63.
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**Disclosure of Interest:** P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, Bristol-Myers Squibb, Genentech, Janssen, Eli Lilly, Pfizer Inc, UCB, Celgene Corporation, Novartis, Roche, Consultant for: Abbott, Amgen, Biogen Idec, Bristol-Myers Squibb, Genentech, Janssen, Eli Lilly, Pfizer Inc, UCB, Celgene Corporation, Novartis, Roche, J. Wollenhaupt Grant/research support from: Abbott, Bristol-Myers Squibb, MSD, Pfizer Inc, and UCB, Consultant for: Abbott, Bristol-Myers Squibb, MSD, Pfizer Inc, and UCB, S. Hall Grant/research support from: Celgene Corporation, Pfizer, UCB, Bristol-Myers Squibb, Glaxo-Smith Kline, Roche, Janssen, Novartis, Merck, Consultant for: Celgene Corporation, Pfizer, UCB, Bristol-Myers Squibb, Glaxo-Smith Kline, Roche, Janssen, Novartis, Merck, F. Van den Bosch Grant/research support from: Celgene Corporation, E. Lespessailles Grant/research support from: Amgen, Celgene, Eli Lilly, Novartis, and Servier, Speakers bureau: Amgen, Eli Lilly, Novartis, and Servier, M. McIlraith Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, C. Edwards Grant/research support from: Celgene Corporation, Pfizer Inc, Roche, Samsung, Consultant for: Celgene Corporation, Pfizer Inc, Roche, Samsung, Speakers bureau: Abbott, Glaxo-SmithKline, Pfizer Inc, Roche
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## THU0450 ALL-CAUSE MORTALITY AND MALIGNANCIES IN PSORIASIS PATIENTS WITH PSORIATIC ARTHRITIS IN THE PSORIASIS LONGITUDINAL ASSESSMENT AND REGISTRY STUDY

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**Objectives:** To describe characteristics&incidence rates of all-cause mortality & malignancies (excluding NMSC) in PsO patients with PsA from PSOLAR.
**Methods:** PSOLAR,an international, disease-based, observational study in which patients eligible for, or receiving conventional systemic & biologic agents for PsO are followed prospectively.Characteristics & safety for patients who reported PsA, including a narrower subset with PsA confirmed by a joint-specialist,are summarized. Cohorts were defined as & attribution was based on treatment exposure prior to/during registry, in the following order (regardless of sequence & duration): (1) ustekinumab (UST) (2) other sponsor biologic (primarily infliximab [IFX]) (3) non-sponsor biologic (primarily adalimumab/etanercept [ADA/ETN]),& (4) non-biologic therapies (NB) (including immunomodulators {IMM} [eg. MTX, CsA], phototherapy, & topical therapy). Exposure to any therapy higher in the order precluded inclusion in the lower cohorts. Multivariate analyses using Cox hazard regression were used to identify predictors of time to first malignancy & mortality [compared to no biologic use] & for IMM [compared to no IMM use].
**Results:** As of Aug 23, 2014, PSOLAR is fully enrolled with 12093 patients (40388 total patient-years [PY] of follow-up).Number of patients with reported PsA overall was 4316: 1489 UST, 776 IFX, 1680 ADA/ETN, 371 NB; of these patients, 1719 had confirmed PsA (664 UST, 356 IFX, 576 ADA/ETN, 123 NB). Baseline demographics & medical history were generally balanced across cohorts; however, in overall PsA sub-group, more patients in the NB cohort were ≥65 yrs of age (UST 9.9%, IFX 13.9%, ADA/ETN 12.5%, NB 25.6%) & had a medical history of cancer (UST 3.3%, IFX 3.5%, ADA/ETN 3.9%, NB 8.4%). In the overall PsA subgroup, cumulative incidence rates/100PY for all-cause mortality were UST 0.28, IFX 0.30, ADA/ETN 0.52, NB 0.70; age, obesity, history of cardiovascular disease (CVD), history of diabetes& smoking were predictors of time to mortality. Cumulative incidence rates/100PY for malignancy were UST 0.57, IFX 0.67, ADA/ETN 0.64, & NB 1.01; age & history of malignancy were predictors of time to first malignancy. Biologic & IMM use were not predictors for mortality or malignancy. Among the confirmed PsA subset, cumulative incidence rates per 100PY for all-cause mortality UST 0.21, IFX 0.36, ADA/ETN 0.38, NB 0.25 & for malignancy UST 0.52, IFX 0.54, ADA/ETN 1.02, NB 1.25. Inherent bias with observational data may apply. Variability in size & clinical features was noted among groups. Incidence rates are not adjusted for differences (adjustment for

key factors are included in statistical analyses). Small numbers of patients in the confirmed PsA subset precluded assessment of risk factors.
**Conclusions:** Unadjusted rates of all-cause mortality&malignancies for biologics were generally comparable among both PsA subsets. Advanced age, history of malignancy were predictors of time to first malignancy & age, obesity, CVD history, diabetes history & smoking were predictors for time to mortality based on overall PsA subset; biologics & IMM were not predictors for mortality or malignancy.
**Disclosure of Interest:** None declared
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## THU0451 COMPARING FOUR SCREENING TOOLS FOR PSORIATIC ARTHRITIS AMONG SUBJECTS DIAGNOSED WITH PSORIASIS

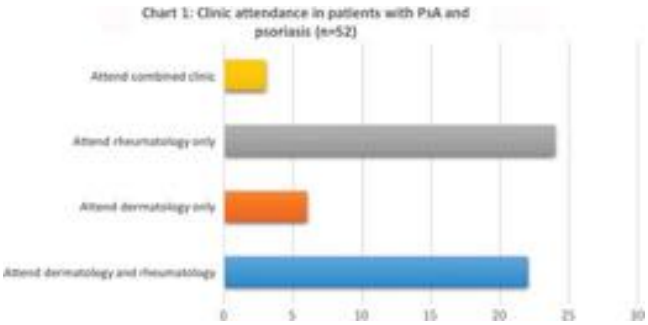
R.M. Baddoura[1], R. Tomb[2], A. Ghanem[2], E. Halaby[2], N. Mansour[3], N. Ayoub[3], F. Stephan[3], B. Soutou[3], F. El Sayed[3], A. Ammoury[3], H. Megarbane[3], J. Helou[3]. *[1]Rheumatology; [2]Dermatology; [3]St Joseph University, Beirut, Lebanon*

**Background:** Screening psoriatic arthritis remains a challenge. A few dedicated tools have been developed in different settings however direct comparative data is limited.
**Objectives:** To compare screening properties of a new instrument [PsoQ], inspired by both ASAS recommendations for early diagnosis of spondyloarthritis and ACR criteria for rheumatoid arthritis, to three others developed in the setting of dermatology practice [PAQ, PASE and PEST].
**Methods:** Consecutive subjects diagnosed with psoriasis by the dermatologist were submitted the four questionnaires. Subjects with scores above the reported threshold values and a set value for the new instrument, designated as screened positive, were offered rheumatological assessment to search for psoriatic arthritis. Screening properties of the four tools were compared.
**Results:** 371 patients with a mean (SD) age of 39.1 (16.9) were included [204 women (54.9%)]. Predominant psoriasis phenotype was psoriasis vulgaris (78%); prevalence of nail involvement was 15.6% and of scalp lesions 33.7%.
103 patients (27.0%) were screened positive using either of the four questionnaires: 25 (6.8%) using the PAQ questionnaire, 55 (14.8%) with the PASE questionnaire and 41 (11.1%) by the PEST questionnaire. 52 (14.0%) reported features of inflammatory back pain and 32 (8.6%) reported features of inflammatory peripheral arthritis and accordingly 68 (18.3%) were screened positive by the PsoQ. In total, 10 patients were identified as psoriatic arthritis (prevalence 2.7% (95%CI: 1.1%; 4.3%). Predominantly axial phenotype was present in 5 subjects and peripheral arthritis phenotype in five.
Sensitivities (SE) and specificities (SP) of the four questionnaires ranged between 70% and 100% for SE and between 83.9% and 94.4% for SP. SE was the highest using PsoQ (100%) while SP was the highest using PAQ7 (94.4%).
Positive predictive values (PPV) were low, between 12.7% and 20.0% while negative predictive values (NPV) were high, between 98.6% and 100.0%. The highest PPV was achieved with PAQ7 (20%) and the highest NPV (100%) was obtained with PsoQ.
Positive likelihood ratios (PLR) were moderate ranging from 5.3 to 8.8 and negative likelihood ratios (NLR) ranged between 1.9 and 4.5.
**Conclusions:** The four tools showed similar screening properties. Subjects with scores above threshold values need referral for rheumatological assessment.
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**Acknowledgement:** St Joseph University Council for scientific research for main funding of the study
Abbvie pharmaceuticals for partial funding of the study
**Disclosure of Interest:** None declared
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## THU0452 PSORIATIC ARTHRITIS AND PSORIASIS: THE ONGOING NEED FOR A MULTIDISCIPLINARY APPROACH TO MANAGEMENT

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**Background:** Psoriasis is a common inflammatory condition of the skin, associated with significant morbidity. Around 20% of patients with psoriasis suffer from psoriatic arthritis (PsA) (1). SIGN guidelines recommend a multidisciplinary approach in the assessment and management of patients with PsA or psoriasis. There is currently a combined clinic in Glasgow for review of patients with severe psoriasis and PsA, whilst most patients continue to attend separate dermatologist or rheumatologist led clinics.
**Objectives:** To review the population groups attending separate dermatologist and rheumatologist led clinics, to establish adherence to SIGN guidelines with regards to management, and to gauge the potential unmet demand for patients who may benefit from review in a combined clinic.
**Methods:** All patients attending tertiary PsA or psoriasis clinics in March 2015 were invited to complete a questionnaire on their disease, demographics and clinic attendance. Patients attending the PsA clinic completed a DLQI (Dermatology Life Quality Index), those attending the psoriasis clinic completed a PEST (Psoriasis Epidemiology Screening Tool) score.
**Results:** 48 patients attending the PsA clinic and 34 patients attending the psoriasis clinic were included (n=82). 63% (n=52) had both PsA and psoriasis. 14 (17%) patients saw their GP for annual review.
38% (n=18) and 21% (n=10) of patients attending the PsA clinic had been offered referral to physiotherapy and occupational therapy respectively. 22 (42%) of the 52 patients with psoriasis and PsA attended both rheumatology and dermatology, with 4% (n=3) attending the combined clinic (chart 1). 87% (n=45) of patients with a diagnosis of both psoriasis and PsA would find a combined clinic useful.
A PEST score of $\geq$3 is considered positive, and referral to a rheumatologist is recommended (1). 50% of patients attending the psoriasis clinic had a PEST score $\geq$3. 59% of these patients had been referred to, or were currently attending, a rheumatology clinic. 10 patients attending the PsA clinic had a DLQI $\geq$6, these patients should be referred to a dermatologist (1). 60% of these patients had seen a dermatologist.
Leflunomide is the recommended systemic drug of choice in patients with PsA. 1 patient in the PsA group was receiving leflunomide. Methotrexate was the most commonly used systemic therapy in 20 patients in the PsA group and 6 patients in the psoriasis group.
Adalimumab was the most commonly used biologic in both groups (n=17).




**Conclusions:** Currently there are multiple rheumatology and dermatology clinics for the management of PsA and psoriasis throughout Greater Glasgow and Clyde, with only one combined clinic.
Despite clear recommendations for a multidisciplinary approach to the management of psoriasis and PsA, only 4% of our patients attend a combined clinic, fewer than a third have been reviewed by a physiotherapist or occupational therapist and only 17% have an annual GP review. 41% of patients attending the psoriasis clinic with a positive PEST score had not seen a rheumatologist while 40% of patients with a DLQI $\geq$6 attending the PsA clinic had not seen a dermatologist. This audit suggests the need to consider greater access to combined clinics, to allow a multidisciplinary approach to management.
**References:**
[1] SIGN Guideline 121, Diagnosis and management of psoriasis and psoriatic arthritis in adults; a national clinical guideline, Oct 2010
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1184

## THU0453 HIGH PREVALENCE OF PSORIATIC ARTHRITIS MISDIAGNOSES IN PSORIASIS PATIENTS IN RUSSIAN DERMATOLOGICAL CLINICS BASED ON PSORIASIS EPIDEMIOLOGY SCREENING TOOL (PEST), RHEUMATOLOGICAL EVALUATION AND THE CASPAR CRITERIA

M. Chamurlieva, T. Korotaeva, E. Loginova. *Research Institute of Rheumatology named after V.A. Nasonova, Moscow, Russian Federation*

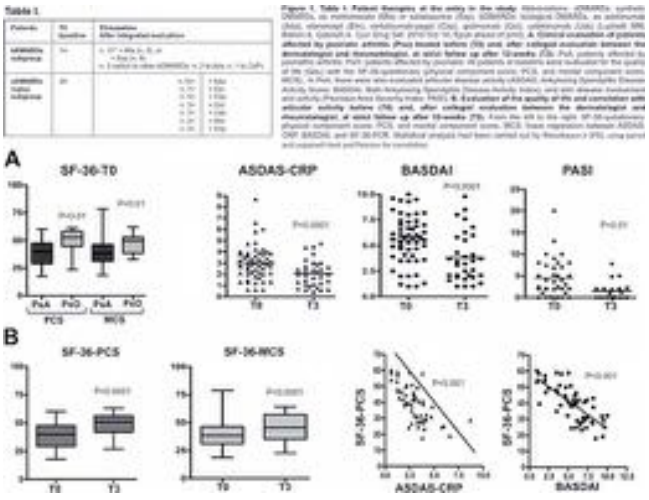
**Background:** According to official Russian Federation statistics the mean annual incidence of psoriatic arthritis (PsA) in patients (pts) with psoriasis (PsO) is 2.5%. Lower estimates may reflect a missed diagnosis of PsA. The efficiency of PsA screening approach in PsO pts in Russian dermatological clinics remains unknown.
**Objectives:** to evaluate the prevalence and misdianosis of PsA in PsO pts in dermatological clinics according to the PEST questionnaire, rheumatological evaluation and the CASPAR criteria.
**Methods:** 103 consecitive unselected pts (male-47/female-56) with plaque PsO mean age 44±13.69 years (yrs.), BSA 9.32±13.55%, PASI 15.39 ± 12.51, DQLI 9.42±6.8 with no known diagnosis of inflammatory arthritis were included. All pts completed the PEST questionnaire before being consulted by a dermatologist. A total score PEST$\geq$3 is indicative of PsA, PEST$<$3 is non-PsA. All pts were subsequently evaluated by a rheumatologist to confirm/exclude PsA. The CASPAR criteria are considered to be the "gold standard" for the diagnosis of PsA. The sensitivity (Sen.) and the specificity (Sp.) of the PEST, (%) were calculated.

**Results:** 60 out of 103 pts (58.2%) had PEST≥3 but after rheumatological assessment according to the CASPAR criteria PsA confirmed in significantly fewer cases – in 47 out of 60 pts (78.3%) and in 13 out of 60 pts (21.6%) PsA was overdiagnosed (false-positive). 43 out of 103 pts (63.4%) had PEST<3 but even so in 14 out of 43 pts (32.5%) PsA was undiagnosed and then confirmed after rheumatological assessment according to the CASPAR criteria (false-negative). So finally the prevalence of PsA in a series of 103 plaque PsO pts was 59.2% (61 pts). PsA was misdiagnosed in 27 out of 103 pts (26.2%). PEST Sen./Sp. were 77%/69% accordingly.
**Conclusions:** In dermatological clinics the PEST questionnaire is a proper approach that is available for PsA screening. But PEST alone is limited due to high amounts of misdiagnoses. All pts should follow up with a rheumatologist and the CASPAR criteria despite the PEST results. For proper diagnosis of PsA among PsO pts need interdisciplinary collaboration with rheumatologists.
**Disclosure of Interest:** None declared
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## THU0454 THE MULTIDISCIPLINARY APPROACH IS THE BEST OPTION TO ACHIEVE THE IMPROVEMENT OF DISEASE ACTIVITY AND QUALITY OF LIFE IN PATIENTS AFFECTED BY PSORIATIC ARTHRITIS: PRELIMINARY RESULTS OF A MONOCENTRIC STUDY

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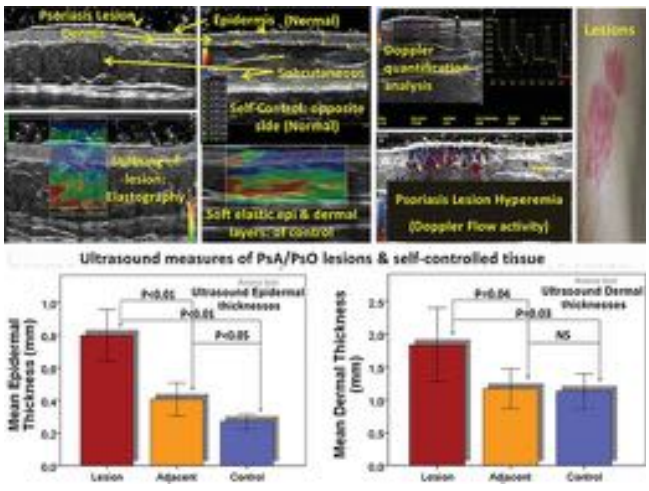
**Background:** Psoriatic arthritis (PsA) is a chronic arthritis, included in the spondyloarthritis group, characterized by the coexistence of skin and joint inflammation. The delayed diagnosis and therapy may result in an increased rate of progression of clinical damage, affecting significantly the quality of life (QoL) (1). An integrated clinical examination of PsA patients, carried out by the dermatologist and rheumatologist, is actually considered the optimal approach to manage the PsA disease.
**Objectives:** Evaluation of the effect of the multidisciplinary integrated approach, performed by dermatologist and rheumatologist, in: a) the early diagnosis of PsA, and b) the quality of life before and after therapeutic integrated approach.
**Methods:** Since January 2015, we examined 145 consecutive patients complaining articular symptoms and/or psoriasis in the outpatient clinics and in the clinical ward of the dermatology and internal medicine departments. Among them, 53 patients were diagnosed as PsA and 21 by psoriasis (Pso). At baseline, after collegial evaluation, the treatment strategy was planned depending on articular activity-involvement (peripheral or axial), systemic inflammation (C-reactive protein, CRP, and erythrocyte-sedimentation rate, ESR, levels), and skin involvement. Moreover, at baseline and after 12-weeks, articular disease was assessed by Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), following ASAS (Assessment of SpondyloArthritis international Society) indications, and skin disease by the Psoriasis Area Severity Index (PASI). QoL was assessed using the Short Form-36 questionnaire (SF-36).
**Results:** At baseline, QoL was significantly worse in PsA than Pso patients, as assessed by mean SF-36 (physical component score, PCS, and mental component score, MCS) (Fig.1A). Female patients had significantly worse SF-36 MCS than male patients globally considered (37.4±8.4 vs 46.1±12.3, p=0.03), also in the PsA patient's group alone (35.8±8.1 vs 44±13.7, p=0.01). After the integrated evaluation in: a) 33 PsA naïve patients a biological drug was prescribed; b) 3 patients switched to another biological drug; c) 11 patients assuming already a biological drug a synthetic DMARD was added; d) 6 a synthetic DMARD alone was prescribed (Fig. 1, Table I). At 12 weeks, 33 patients had been evaluated at follow-up. It was observed a significant improvement in articular disease as well as skin disease activity (Fig. 1). Consistently, a significant improvement was obtained also in QoL (Fig. 1) and a significant statistical correlation resulted between articular activity and QoL. In fact, a significant correlation between ASDAS-CRP and BASDAI with SF-36 PCS was observed (Fig. 1).
**Conclusions:** In our work, we demonstrate that the multidisciplinary treatment and follow-up approach in patients with PsA has achieved a significant and, most importantly, fast improvement in disease activity and patient reported QoL after 12 weeks. Thus this reinforces the importance of a shared choice of the therapy and it encourages further studies to assess the long-term outcomes and feasibility.
**References:**
[1] Betteridge N. et al. JEADV, 16 Sep2015.
**Disclosure of Interest:** None declared
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## THU0455 EVALUATING PSORIATIC SKIN LESIONS IN PSORIASIS AND PSORIATIC ARTHRITIS: ULTRASOUND AS A COMPLEMENTARY MEASURE

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**Background:** Currently, the diagnosis and assessment of psoriatic arthritis (PsA) and psoriasis (PsO) skin lesions are mostly done by visual inspections, and when in doubt, supplemented by biopsies. Although PsA is primarily assessed by physical examination, the utility of ultrasound (US) is beneficial.
**Objectives:** The aim of this proof of concept study was to determine the performance of ultrasound (using advanced imaging software applications) in assessing skin lesions and inflammation in selected PsA and PsO patients.
**Methods:** A rheumatologist and dermatologist assessed the PsA and PsO patients respectively. PsA examination included the standard clinical joint assessments, and we thereafter evaluated the hands & wrists and symptomatic joints with US for synovitis & tenosynovitis (including nail beds & tendons). Blinded by the clinical results and treatment plans, the epidermal, dermal and subcutaneous tissue thicknesses of 2 of the most affected psoriasis lesions were US scanned using high frequency B-Mode, automated Color Doppler quantification (CDQ; measured over 4 seconds) and elastography applications (measuring lesion size, depth, hyperemia and tissue elasticity). The skin tissue adjacent to the psoriasis lesions, as well as the unaffected skin on the contralateral side (self-control) was measured.
**Results:** A total of 270 skin depth measurements (2 of the most affected lesions, 3 intervals apart, at 3 different sites described above) of 5 PsA/PsO patients were analyzed. Epidermal thickness differed significantly between the adjacent and control tissue layers [F (2,27) =30.95, MSE =0.76, p<0.001]. Similar findings were evident for dermal thickness differences [F (2,27) =5.05, MSE =1.59, p=0.014]. In contrast and as expected, subcutaneous tissue thicknesses showed no significant differences. US using color Doppler revealed the presence of hyperemia in 80% of the examined lesions by CDQ resulted in flow averages ranging from 0.016–0.655 for minimum ratios to 0.103–0.241 for maximum ratios. Of these Doppler active lesions, 60% were echogenic (some with acoustic shadowing). Contrary, 20% of the psoriasis lesions showed no obvious Doppler activity, displaying reduced tissue stiffening on elastography (suggesting healed lesions). Two of 10 (20%) lesions showed no abnormal findings (soft on elastography) having no acoustic shadows, and low-level CDQ activity (minimum 0.016:0.034 and maximum 0.103:0.135 ratios). Ultrasound displayed the presence of synovitis, tenosynovitis, and nail-bed hyperemia together with altered microcirculation & hand psoriasis skin perfusion in PsA patients.



**Conclusions:** Ultrasound metrics of skin tissue (plaque characteristics, tissue depth & elasticity, and Doppler activity quantification) has potential as a complementary measure for the clinical assessment of PsA and PsO.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2484

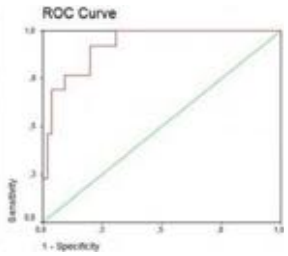
## Osteoporosis

### THU0456 MAJOR RISK FACTORS OF FEMORAL NECK OSTEOPOROSIS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Osteoporosis (OP) is 2–3 times more frequent in rheumatoid arthritis (RA) patients as compared to general population with associated 1,5–2,5 – fold increased risk of fractures. Femoral neck fracture is the most unfavorable prognosis and outcome in these patients, compromising their quality of life.
**Objectives:** To identify major risk factors of femoral neck OP in female RA patients.
**Methods:** The study included 206 female RA patients (ACR criteria), aged 20–75 years (mean age 56,6±11,2 years). An individual patient's file contained social and demographic data, anthropometric parameters, case history, clinical examination and lab findings, traditional OP risk factors, patient's joint status and comorbidities. Hand and distal feet X-ray was taken in each case. Van der Heijde modified Sharp method was used to score the erosions and joint space narrowing in hands and feet. Axial bone mineral density (BMD) was measured using DEXA scan. DEXA T-score was used in post-menopausal women, and Z-score – in menstruating women.
**Results:** Femoral neck OP was diagnosed in 68 patients (33%), while in 138 (67%) no OP was found. Patients with and without OP were of comparable age (58,7 ± 12,3 vs 55,5 ± 10,2 years, $p$=0,06), but differed in disease duration (12 (7; 22) vs 11 (7; 15) years, $p$=0,04) and total Sharp score (181,5 (92; 267) vs 112 (59; 173), $p$=0,006). OP patients were taking higher average daily dose of glucocorticosteroids (GC) during the previous year (5 (2,5; 7,5) vs 2,5 (1,3; 5) mg/day, $p$=0,03) and were prescribed greater number of intra-articular (i/a) GC injections vs patients without OP (8 (3; 18) vs 6 (2; 10), $p$=0,04, respectively). Analysis of traditional OP risk factors identified lower body weight in OP patients (62,8 ± 11,4 vs 69,6 ± 12,4 kg, $p$<0,001) and post-menopause status in the majority of them (89,7 vs 74,6%, RR =1,2, 95% CI 1,06–1,36, $p$=0,007). Higher incidence of femoral neck fractures within the immediate family members was found in OP patients family history (16,4 vs 2,9%, RR =5,57, 95% CI 1,82–17,07, $p$=0,001). Multifactorial analysis identified the following major femoral neck OP risk factors: total Sharp score, average daily GC dose during the previous year, total number of intra-articular GC injections, and menopause; the contribution of these variables in OP development was assessed (discriminant function coefficients: 0,006; 0,37; 0,07; 2,91, respectively) to suggest a model (with the area under the ROC curve equal to 0,926), allowing prediction of femoral neck OP with high accuracy, equal to 89,7%.

| Factors | Discriminant function coefficient |
|---|---|
| Total Sharp score | 0,006 |
| Total number of i/a GC injections | 0,07 |
| Average daily GC dose in the previous year | 0,37 |
| Menopause | 2,91 |
| Weight | -0,09 |
| Constant | 3,73 |




**Conclusions:** The degree of erosive joint destruction in hand and feet (based on total Sharp score), average daily GC dose during the previous year, total number of intra-articular GC injections, and menopause are major risk factors of femoral neck OP in female patients with RA.
**Disclosure of Interest:** None declared
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### THU0457 COMPREHENSIVE DISEASE CONTROL WITH LESS RELAPSE AND RADIOGRAPHIC PROGRESSION AT ONE YEAR BY INTENSIVE THERAPY WITH ADDITIONAL SHORT-COURSE OF TOCILIZUMAB: A REAL-WORLD, PROSPECTIVE COHORT STUDY IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Tocilizumab (TCZ) was the first approved non-TNFα bDMARD for rheumatoid arthritis (RA) in China since November 2013. However, the mean course of TCZ for most Chinese RA patients is about 3–6 months because of self-paid and expensive price, similar to the situation of other biological originator DMARDs or their biosimilar.
**Objectives:** To investigate the efficacy and safety of additional short-course of TCZ combined with csDMARDs on disease activity and 1-year radiographic progression of RA patients.
**Methods:** One hundred and ten RA patients with moderate to high disease activity were treated with csDMARDs and followed up regularly at baseline, week 4, 12, 24 and 52. Thirty-seven of them were willing to receive additional 3–6 consecutive doses of intravenous TCZ 8 mg/kg every 4 weeks. One-year radiographic progression was defined as mTSS≥0.5. Comprehensive disease control (CDC) was defined as DAS28(4)-CRP<2.6, health assessment questionnaire (HAQ)<0.5 and mTSS<0.5. Relapse was defined as leaving DAS28 theraputic target corresponding to a DAS28(4)-ESR score of >3.2.
**Results:** Seventy-four RA patients who have finished 52 weeks follow-up were qualified for statistics. Patients in TCZ+csDMARDs group (n=23) were with significant higher disease activity by DAS28(4)-ESR than those in csDMARDs group (n=51) at baseline ($p$<0.05, Table 1), and there was no significant difference of other baseline characteristics and csDMARDs therapy during follow-up between two groups (all $p$<0.05). There was 35% patients in TCZ+csDMARDs group reached remission at week 4 which was significantly greater than those in csDMARDs group (8%, $p$=0.006), and the rates of patients reached therapeutic target (DAS28[4]-ESR<3.2), remission (DAS28[4]-ESR<2.6) or deep remission (DAS28[4]-ESR<1.98) at week 12 in TCZ+csDMARDs group were also significantly higher (Fig. 1). The ratio of patients with EULAR good response at week 12 in TCZ+csDMARDs group was significantly higher than that in csDMARDs group (74% vs. 35%, $p$=0.010), consistent at week 24 (87% vs. 49%, $p$=0.002) and week 52 (70% vs. 43%, $p$=0.046). For patients who have reached therapeutic target during follow-up, 65% (22/34) of them in csDMARDs group and 33% (7/21) in TCZ+csDMARDs group relapsed within 52 weeks ($p$=0.029).The one-year radiographic progression rate at week 52 in TCZ+csDMARDs group was significantly lower than those in csDMARDs group (13% vs. 49%, $p$<0.05) and 52% patients in TCZ+csDMARDs group achieved CDC at week 52 which was significantly greater than those in csDMARDs group (24%, $p$=0.030). No significant difference of adverse events during follow-up was found between two groups (all $p$<0.05).

**Table 1** The baseline characteristics, treatments and adverse effects between TCZ+csDMARDs group and csDMARDs group

| | TCZ+csDMARDs group (n=23) | csDMARDs group (n=51) | P |
|---|---|---|---|
| **Baseline characteristics** | | | |
| Female, n (%) | 18 (78) | 40 (78) | 1.000 |
| Age (years) | 53 (37-65) | 50 (39-57) | 0.629 |
| Disease duration (months) | 20 (5-96) | 36 (12-84) | 0.259 |
| Positive RF, n (%) | 18 (78) | 41 (80) | 1.000 |
| Positive anti-CCP antibody, n (%) | 19 (83) | 42 (82) | 0.752 |
| DAS28 (4)-CRP, median (IQR) | 5.0 (4.6-6.4) | 4.7 (4.0-5.7) | 0.079 |
| DAS28 (4)-ESR, median (IQR) | 6.0 (5.5-7.0) | 5.4 (4.6-6.4) | **0.045** |
| **csDMARDs therapy during follow-up** | | | |
| MTX+LEF, n (%) | 20 (87) | 40 (78) | 0.527 |
| MTX+HCQ, n (%) | 2 (9) | 6 (12) | 1.000 |
| MTX+HCQ+SASP, n (%) | 1 (4) | 1 (2) | 1.000 |
| Glucocorticoid, n (%) | 10 (43) | 30 (59) | 0.184 |
| Others, n (%) | 0 (0) | 4 (8)* | - |
| **Adverse effects** | | | |
| Upper respiratory tract infection, n (%) | 3 (13) | 4 (8) | 0.670 |
| Elevated aminotransferase (1~2 folds of ULN), n (%) | 6 (26) | 7 (14) | 0.206 |
| Elevated aminotransferase (over 2 folds of ULN), n (%) | 1 (4) | 3 (6) | 1.000 |
| Neutropenia, n (%) | 2 (9) | 4 (8) | 1.000 |

*Four patients with MTX intolerance due to gastrointestinal discomfort were treated with LEF+HCQ (n=2), LEF+SASP and HCQ+SASP, respectively. ULN, upper limit of normal range.

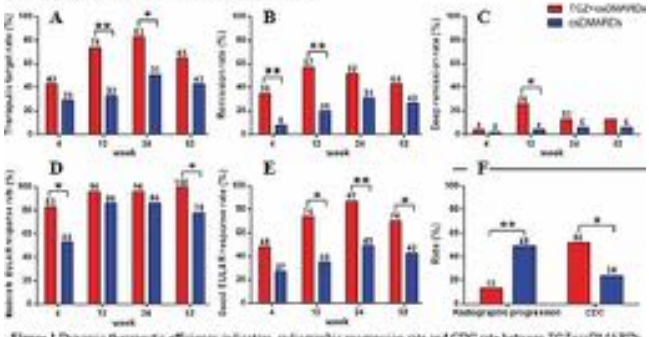



**Figure 1** Dynamic therapeutic efficiency indicators, radiographic progression rate and CDC rate between TCZ+csDMARDs group and csDMARDs group. *$p$<0.05, **$p$<0.01. Therapeutic target, remission and deep remission were defined as DAS28 (4)-ESR<3.2, 2.6 and 1.98, respectively

**Conclusions:** Intensive therapy with additional short-course of TCZ combined with csDMARDs could induce more CDC with less relapse and radiographic progression at one year which implies an alternative cost-effective strategy of biologics for RA patients especially in developing countries.
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**Disclosure of Interest:** None declared
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## THU0458 INFLUENCE OF ORAL PREDNISOLONE ON EFFECT OF DENOSUMAB ON OSTEOPOROSIS IN PATIENTS WITH JAPANESE RHEUMATOID ARTHRITIS; 12 MONTHS OF FOLLOW-UP – A MULTICENTER REGISTRY STUDY

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**Background:** Denosumab (DMB) is a fully human monoclonal antibody to the receptor activator of nuclear factor-kappaB ligand (RANKL) that blocks its binding RANK, inhibiting the development and activity of osteoclasts, decreasing bone resorption, increasing bone density and reducing fracture risk. Osteoporosis (OP) is more frequent in patients with rheumatoid arthritis (RA) than in the general population due to active systemic inflammation as well as the use of glucocorticoid and immobility. However efficacy of denosmab is not clear in patirnts with glucocorticoid- induced OP in RA. Therefore we investigated the influence of oral prednisolone on effect of DMB in patients with Japanese RA from initiation to 12 months at this time.
**Objectives:** This prospective study investigated the efficacy of DMB for 12 months on glucocorticoid- induced OP in RA patients.
**Methods:** Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria who had been prescribed DMB from Tsurumai Biologics Communication Registry (TBCR)-BONE between October 2013 and October 2014 were enrolled. The final study cohort of 67 patients received continuous DMB therapy more than 12 months. The DMB dose was 60mg at once every 6 months. In all cases native or activated vitamin D has been used. We reviewed the results for 6 and 12 months about the increase and decrease of bone mineral density (BMD) of lumbar spine (LS) and total hip (TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen (PINP) and tartrate-resistant acid phopshatate form 5b (TRACP-5b)
**Results:** In the patients receiving oral prednisolone group (n=26, R-PSL) and not receiving group (n=41, N-PSL), the number of female was each 24 (92%) and 40 (98%) cases (p=0.555). The mean age was 68.5 ± 7.9 and 69.9 ± 7.2 years old (p=0.657); disease duration was 16.3 ± 9.9 and 16.0 ± 13.3 years (p=0.532); the body mass index was 19.9 ± 3.5 and 19.6 ± 2.9 (p=0.852) and the FRAX was 32.7 ± 18.3 and 21.6 ± 13.5 (p=0.007). Clinical findings related to RA and OP at baseline were as follows; CRP 1.1 ± 1.3 and 0.4 ± 1.0 mg/dl (p=0.017); DAS-CRP 3.20 ± 1.13 and 2.39 ± 1.22 (p=0.003); m-HAQ 1.20 ± 0.83 and 0.73 ± 0.72 (p=0.026); PINP 60.4 ± 37.0 and 55.0 ± 32.7 μg/l (p=0.433); TRACP-5b 502 ± 245 and 488 ± 206 mU/dL (p=0.852); LS-BMD 0.86 ± 0.18 and 0.83 ± 0.17 g/cm$^2$(p=0.296) and TH-BMD 0.60 ± 0.11 and 0.60 ± 0.08 g/cm$^2$ (p=0.892). The rate of decreased PINP from baseline to 6 and 12 months were each -29.4% vs -40.2% (p=0.289) at 6 month and -13.7% vs -41.4% (p=0.118) at 12month and TRAC-5b were -28.5% vs -35.1% (p=0.849) at 6 month and -21.4% vs -31.6% (p=0.401) at 12month in the R-PSL group vs N-PSL group. The rate of increased LS-BMD from baseline to 6 and 12 months were each 3.4% vs 4.5% (p=0.305) at 6 month and 4.7% vs 6.8% (p=0.175) at 12month and TH-BMD were 3.0% vs 3.0% (p=0.816) at 6 month and 3.9% vs 3.9% (p=0.898) at 12month in the R-PSL group vs N-PSL group (Fig. 1). The rate of patients who did not increase LS-BMD and TH-BMD for 12 months were each 17.4% vs 15.4% (p=0.836) and 17.4% vs 5.0% (p=0.179) in the R-PSL group vs N-PSL group (Fig. 2).

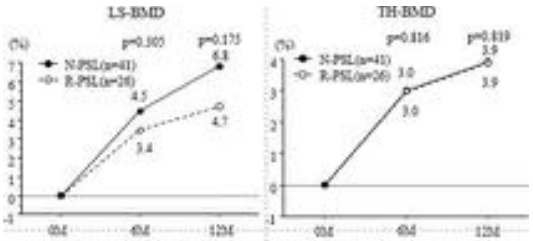


Figure 1: The rate of increased LS-BMD and TH-BMD from baseline to 6 and 12 month

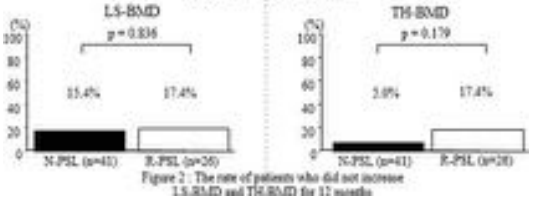


Figure 2 : The rate of patients who did not increase LS-BMD and TH-BMD for 12 months

**Conclusions:** DMB was effective in OP of RA patients. Oral prednisolone use did not influence the efficacy of DMB in the short period of 6 and 12 months.
**Disclosure of Interest:** Y. Kanayama: None declared, Y. Hirano Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, and Bristol-Myers Squibb., N. Takahashi Speakers bureau: Abbvie Japan Co. Ltd, Eisai Co. Ltd, UCB Japan Co. Ltd, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Company Ltd, Pfizer Co. Ltd, Chugai Pharmaceutical Co. Ltd, Janssen Pharmaceutical K.K., and Bristol-Myers Squibb Co. Ltd., S. Asai: None declared, N. Ishiguro Grant/research support from: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, ChugaiPharmaceutical, Mitsubishi Tanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan, Speakers bureau: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai Pharmaceutical, MitsubishiTanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan., T. Kojima Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, AbbVie, Bristol-Myers Squibb, and Pfizer, Janssenn Pharmaceutical Companies, Astellas Pharma and Chugai Pharma.
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## THU0459 COMPARISON BETWEEN THE AMERICAN RECOMMENDATIONS AND THE JAPANESE GUIDELINES FOR GLUCOCORTICOID-INDUCED OSTEOPOROSIS IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** In 2014, the Japanese Society for Bone and Mineral Research (JSBMR) updated their guidelines for the management and treatment of glucocorticoid-induced osteoporosis (GIO) and incorporated a new scoring method that does not use the Fracture Risk Assessment Tool (FRAX®).
**Objectives:** In this study, using the JSBMR guidelines (1) and the American College of Rheumatology (ACR) 2010 recommendations (2) for the prevention and treatment of GIO, we compared our evaluations of Japanese patients with rheumatoid arthritis (RA) who were treated with glucocorticoids.
**Methods:** The Institute of Rheumatology Rheumatoid Arthritis (IORRA) study, which began in 2000, was a prospective cohort study of RA patients conducted at the Institute of Rheumatology, Tokyo Women's Medical University (Tokyo, Japan). Applying ACR recommendations and JSBMR guidelines, we evaluated 1,752 of these Japanese patients who were over the age of 50 years (mean age 63 years) and had been treated with glucocorticoids. The ACR recommendation is to prescribe osteoporosis treatments for patients treated with ≥7.5 mg/day prednisolone or whose 10-year risk of major osteoporotic fractures is >10%. The Japanese GIO guidelines identify age, glucocorticoid dose, lumbar bone mineral density, and prior fragility fractures as factors predictive of bone fracture, and the fracture risk for an individual can be calculated as the sum of the scores for each risk factor with a score of 3 representing the optimal cut-off score for pharmacological intervention.
**Results:** Among the female RA patients older than 50 years who were treated with glucocorticoids (n=1,438), in accordance with the ACR recommendations and the Japanese guidelines, 1,183 (82%) and 1,119 (78%) patients, respectively, should have received osteoporosis treatments (Table). Among the male RA patients older than 50 years who were treated with glucocorticoids (n=314), the ACR recommendations and the Japanese guidelines propose that 217 (69%) and 267 (85%) patients, respectively, should have received osteoporosis treatments (Table). Among the male patients, the Japanese guidelines would recommend significantly more patients receive osteoporosis treatments compared with the ACR recommendations ($P<0.0001$).

| Recommendations/guidelines | Female (n=1,438) | Male (n=314) |
|---|---|---|
| ACR | 182 (12.7%) | 3 (1.0%) |
| JSBMR | 118 (8.2%) | 53 (16.9%) |
| ACR and JSBMR | 1001 (69.6%) | 214 (68.2%) |
| None | 137 (9.5%) | 44 (14.0%) |

**Conclusions:** The updated Japanese GIO guideline appears to be a simple and useful tool to use when treating Japanese RA patients with glucocorticoids. The ACR recommendations may have underestimated the need for osteoporosis treatment in male patients with RA compared with the Japanese guideline, although prospective studies are necessary to conclude.
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## THU0460 WHAT IS THE BEST LUMBAR SPINE VERTEBRAE COMBINATION TO PREDICT MAJOR OSTEOPOROTIC FRACTURE? THE OSTEOLAUS COHORT STUDY

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**Background:** The international guidelines recommend to use the average bone mineral density (BMD) over L1 to L4 in the management of osteoporosis and prediction of fracture. Exclusion of certain vertebrae is recommended according to specific rules (ISCD position). The spine Trabecular Bone score (TBS), a surrogate of bone micro-architecture, has been newly introduced into international guidelines and the FRAX® tool for clinical use in conjunction with BMD and clinical risk factors.

**Objectives:** The aim of this study is to test several TBS vertebrae combinations in regard to major osteoporotic fracture prediction.

**Methods:** The osteoLaus cohort (Lausanne, Switzerland) included 1500 woman 50 to 80 years old. All women had a detailed questionnaire related to clinical risk factors and treatment known to influence bone metabolism, BMD measurement (hip, spine and whole body), vertebral fracture assessment and TBS. The primary outcome was the prevalence of major osteoporotic fracture (MOF) according to TBS per-vertebral combination. Appropriate statistics and necessary adjustment for confounding factors were performed. L1-L4 TBS was used as reference value.

**Results:** Out of 1'466 women included in the study (mean age 64.5±7.6 years, BMI 25.7±4.4), 12.7% suffered from MOF. The odd ratios per standard deviation decreased (OR) were 1.53 (1.29 – 1.80) and 1.80 (1.50 – 2.15) for the spine and total femur BMD respectively. Adjusted (age & glucocorticoids status) OR and area under the curve of different combination of vertebrae can be found in the following table for TBS.

| | OR (95% CI) | AUC (95% CI) | p<0.05 vs L14TBS | p<0.05 vs L12TBS |
|---|---|---|---|---|
| **L1–2 TBS** | **2.16 (1.80–2.58)** | **0.73 (0.69–0.76)** | ns | – |
| L1–3 TBS | 2.09 (1.74–2.50) | 0.72 (0.68–0.75) | ns | ns |
| *L1–4 TBS* | *1.98 (1.65–2.36)* | *0.71 (0.67–0.75)* | – | *ns* |
| L2–3 TBS | 1.92 (1.61–2.29) | 0.70 (0.66–0.74) | ns | 0.04 |
| L2–4 TBS | 1.81 (1.52–2.17) | 0.69 (0.65–0.73) | 0.001 | 0.001 |
| L3–4 TBS | 1.53 (1.29–1.82) | 0.68 (0.65–0.72) | 0.0002 | 0.0002 |

**Conclusions:** It seems that excluding L4 tends to improve the fracture risk prediction. TBS is very sensitive to vertebra positioning (e.g. projection). To compensate for the natural lordosis of the spine, one has to lift the legs of the patient. L4 is often still angled which could explained such results. Further prospective studies are needed to confirm these results.

**Disclosure of Interest:** None declared

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## THU0461 REBOUND-ASSOCIATED VERTEBRAL FRACTURES AFTER DENOSUMAB DISCONTINUATION: A SERIES OF 8 WOMEN WITH 35 SPONTANEOUS VERTEBRAL FRACTURES

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**Background:** Osteoporosis (OP) treatments are given for a limited period of time because of a risk/benefice balance. Reversibility of OP treatment is observed by the measurements of bone markers turnover (BMTs) and bone mineral density (BMD). The effect on vertebral fracture (VFx) is difficult to evaluate. The OP treatment discontinuation is associated with an increase of BMTs and a more or less rapid decrease of BMD. Denosumab (Dmab) discontinuation is associated with a severe rebound effect on BTMs and BMD for near 24 months. A recent publication suggests an increase of VFx [1].

**Methods:** We report the cases of 8 postmenopausal women. They received Dmab 60mg every 6 months for 2 to 8 doses. The 8 women were on calcium and vitamin D. A wide biological assessment excluded a secondary cause of OP. VFx were documented by MRI.

**Results:** Five OP women without any prior fragility fracture were treated every 6 months with 4 to 6 Dmab doses. Dmab was stopped because there was no more OP on BMD (3 women 55, 56 and 59 y old), the aromatase inhibitors were stopped (77y old) and according to the wish of the patient (77y old). 9 to 16 months after Dmab discontinuation, they presented respectively 5 (D11, D12, L2-L4), 7 (D9, D12-L5), 2 (D11 and D12), 3 (D12-L2) and 9 (D5-D9 and D11-L2) symptomatic spontaneous (SS) VFx.

A 65 y old woman with osteoporosis and 3 prevalent VFx was treated every 6 months with 8 Dmab doses. Ten months after Dmab discontinuation she presented 2 SSVFx (D12, L3).

These 62 y old woman (osteopenia, treated with *aromatase* inhibitors) received 2 Dmab doses every 6 months. The subsequent Dmab dose was forgotten. Twelve months after the last Dmab dose she presented a D10 SSFx.

A 71 y old woman (one prevalent VFx and one hip fracture) received 2 Dmab doses with a delay of 11 months because of a lack of compliance. Eleven months after the last Dmab dose she presented 5 SSVFx (D12, L2-L5).

**Conclusions:** These 8 cases show a severe increased risk of vertebral fractures in the 9 to 16 months after the last injection of Dmab. The occurrence of these fractures can be explained by the severe rebound effect observed after denosumab discontinuation. It is urgent to: 1) inform the health authorities and patients of this risk; 2) determine treatment regimens before or at the time of denosumab discontinuation.

**References:**

[1] Aubry-Rozier B, Gonzalez-Rodriguez E, Stoll D, Lamy O. Severe vertebral fractures after denosumab discontinuation: 3 cases reports. Osteoporos Int. 2015 Oct 28.

**Disclosure of Interest:** None declared

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## THU0462 THE PREDICTORS OF FRACTURE IN PATIENTS WITH COELIAC DISEASE: AN OBSERVATIONAL STUDY

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**Background:** Coeliac disease and other malabsorptive diseases have been associated with a low bone mineral density secondary to a variety of factors including calcium absorption. We have previously shown that there is a fivefold propensity for having Osteoporosis (OP) compared to controls with a predilection for spinal osteoporosis (1). However this does not translate completely to predicting fragility fractures. The FRAX™ tool uses the femoral neck to predict fractures on a population basis and ignores the lumbar spine.

**Objectives:** We set out to determine the predictors of fragility fractures in a large observational cohort. Specifically we set out to determine if the lumbar spine bone mineral density (BMD) is a predictor for fragility fractures.

**Methods:** Patients referred for bone mineral density (BMD) estimation in a scanner in the North west of England between 2004 and 2014 with a history of coeliac disease were identified from a dual X-ray absorptiometry (DEXA) database. Demographics and other risk factors were also recorded. Initially those that sustained a fracture were compared ot those that had not sustained a fracture using the chi squared test for categorical variables and Students T test for continuous variables. Fragility fractures were also recorded. Initially univariate logistic regression models were modelled predicting fractures in the cohort and a multivariate model was subsequently fitted. Variables included age at scan, gender, body mass index (BMI), family history of fracture, alcohol, smoking, glucocorticoid exposure, rheumatoid arthritis in addition to BMD in the lumbar spine (L1-L4) and the femoral neck.

**Results:** 788 patients were scanned in the referral period. Mean age at scan was 55.4 year (SD 14.4), 576 (73.1%) were female, 159 (20.2%) had sustained a fracture. Patients who had sustained a fracture were more likely to be female 127/576 (22%) vs 32/212 (15%) (p=0.03), older 59.2 years (SD14) vs 54 years (SD 14) (p<0.001) and have concomitant rheumatoid arthritis 5/159 (3%) vs 6/629 (1%) (p=0.04). They also had lower BMD in both the lumbar spine and the femoral neck. Results of the univariate analysis are shown in table 1. Significant predictors are denoted with an asterisk (*).

Table 1

| Predictor | Odds ratio | 95% CI |
|---|---|---|
| Age at scan in decades | 1.27 | 1.18, 1.44* |
| Female gender | 1.59 | 1.04, 2.43* |
| Lumbar spine BMD | 0.06 | 0.02, 0.15* |
| Femoral neck BMD | 0.05 | 0.01, 0.17* |
| Rheumatoid arthritis | 3.37 | 1.02, 11,2* |
| smoking | 1.10 | 0.76, 1.62 |
| Excess alcohol | 1.50 | 0.71, 3.16 |
| Family history of fracture | 0.92 | 0.54, 1.56 |
| Steroid exposure | 1.18 | 0.78, 1.79 |
| Body mass index kg/m$^2$ | 0.98 | 0.96, 1.02 |

In the multivariate model, the only variables that predicted fractures in this cohort were the BMD in the lumbar spine (OR 0.09 95%CI 0.03,0.25) and age at scan OR 1.19 (95%CI 1.04,1.37) per decade.

**Conclusions:** In univariate analysis, many risk factors are associated with fracture in this cohort, but in multivariate analysis, the best predictor of fracture was the BMD in the lumbar spine. This is not included in the FRAX™ tool and would make estimating the fracture risk in this cohort difficult. Further modelling in other cohorts is needed to validate this finding.

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**Disclosure of Interest:** None declared

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## THU0463 VIEWPOINTS OF DENTAL SURGEONS ON THE USE OF BISPHOSPHONATES IN RHEUMATOLOGY PATIENTS

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**Background:** While typically prescribed in oncology, bisphosphonates (BP) are also used in rheumatology, particularly in osteoporosis treatment. The most serious complication of BP is osteonecrosis of the jaw (ONJ). In the 2012 guidelines for good clinical practices, the French Society of Stomatology and Maxillofacial Surgery reported a much lower incidence of ONJ in BP-treated patients for rheumatologic diseases (0.001–0.1%) than in oncology (1–10%).
**Objectives:** We recorded the viewpoints of dental surgeons in the Auvergne region of France on these treatments.
**Methods:** A questionnaire was sent to 880 dental surgeons. This questionnaire comprised four independent sections:
– characteristics of the participating dental surgeons;
– evaluation of everyday practice during dental surgery consultations;
– evaluation of practices for patients already treated with BP for rheumatologic indications;
– evaluation of practices for patients meant to start BP treatment for rheumatologic indications.
**Results:** We obtained 382 responses (43.4%), finally analyzing 376 respondents with available data. Of these, 58.7% were men ($n$=221) and 198 were aged between 46 and 65 years (52.6%). In total, 156 had attended an in-service training course (ISTC) on the topic (41.5%).
Our results demonstrated that 237 dental surgeons systematically asked their patients if they were treated with BPs (63.0%); this percentage was higher among those who had been practicing for less than 10 years ($p<0.004$), who worked in a group practice (71.3%, $p<0.001$) or who had attended an ISTC on the topic (71.6%, $p<0.001$).
For patients on BPs, 84.5% of the practitioners felt uncomfortable about performing dental surgery ($n$=318) and 11% about non-surgical dental care ($n$=41). These results did not differ significantly according to overall practice experience or practice structure, nor for practice location. Of the respondents, 67% stated that their practice differed depending on the BP administration (*per os* or i.v.) route. Dental panoramic radiography was systematically performed prior to all work by 55.3% of dentists ($n$ =208). 81.6% did not discontinue BP *per os* prior to dental surgery ($n$ =307).
Of the practitioners, 53.7% felt uncomfortable when a rheumatologist asked whether the patient's dental status allowed for BP prescription ($n$=202). This percentage was higher among those who had not attended any ISTC (62.6% *vs.* 50.7%; $p<0.03$). On completion of dental work, 27.4% of the practitioners waited 1–3 months before approving the initiation of BP treatment ($n$ =103).
In all, 71 practitioners reported at least one case of dental complication under BP treatment (18.8%), consisting of 49 ONJs, 12 healing problems, and three bone sequestrae. Four dental surgeons stated the complications arose in patients under treatment for cancer.
**Conclusions:** This original study reveals that dental surgeons are uncomfortable about giving dental care to patients receiving BPs. Closer collaboration and better information-sharing between rheumatologists and dental surgeons appears necessary to facilitate the use of BPs in rheumatology.
**Disclosure of Interest:** None declared
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## THU0464 OSTEOPOROSIS, NOT OSTEOARTHRITIS, COULD PREDICT THE OCCURRENCE OF SARCOPENIA IN THE NEAR FUTURE: A 4-YEAR FOLLOW-UP OF THE ROAD STUDY

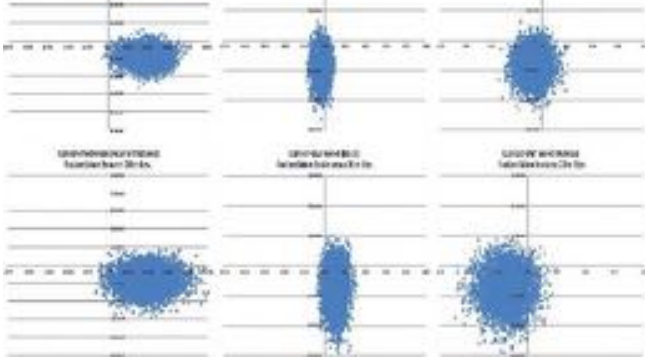
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**Objectives:** The present 4-year follow-up study of the general population was conducted to clarify whether the presence of musculoskeletal diseases, such as, osteoporosis (OP), knee osteoarthritis (KOA), and lumbar spondylosis (LS) could predict the occurrence of sarcopenia (SP) in the near future.
**Methods:** The second survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study, a large-scale population-based cohort study, was conducted between 2008 and 2010. We enrolled 1,099 participants (aged ≥60 years; 377 men and 722 women) from the second survey of the ROAD study who had completed assessments of handgrip strength, gait speed, skeletal muscle mass by using bioimpedance analysis, and bone mineral density by using dual X-ray absorptiometry. The third survey was conducted between 2012 and 2013. Of the 1,099 individuals who were enrolled from the second survey, 767 (69.8%; 253 men and 514 women) had completed assessments identical to those in the second survey. SP was defined as per the algorithm of the Asian Working Group for Sarcopenia, while OP at the lumbar spine L2–4 and/or femoral neck was defined according to the World Health Organization criteria. KOA and LS were diagnosed as grade 3 or higher of the Kellgren-Lawrence scale.
**Results:** Among the 767 subjects who completed both the second and third surveys of the ROAD study, the prevalence rates of OP, KOA, and LS in the second survey were 20.5% (men, 3.6%; women, 28.9%), 32.7% (men, 23.1%; women, 37.4%), and 49.8% (men, 46.0%; women, 51.7%), respectively. The cumulative incidence of SP during the 4-year period between the second and third surveys was 2.0%/yr (men, 2.2%/yr; women, 1.9%/yr). After adjustment for confounding factors such as age (yr), gender (0: men, 1: women), regional differences (0: mountainous area, 1: coastal area), and body build (0: normal; body mass index (BMI) ≥18.5 and ≤27.5 kg/m$^2$, 1: emaciation; BMI <18.5 kg/m$^2$, 2: obesity; BMI >27.5 kg/m$^2$), a logistic regression analysis using the occurrence of SP as the objective variable and the presence of OP as the explanatory variable indicated that the presence of OP was significantly associated with the occurrence of SP (odds ratio, 2.51; 95% confidence interval, 1.23–5.11; $p$ =0.011). By contrast, the presence of KOA, and LS was not significantly associated with the occurrence of SP (KOA: 1.32, 0.72–2.41, $p$ =0.369; LS: 1.08, 0.60–1.94, $p$ =0.792).
**Conclusions:** This prospective study suggests that the presence of OP could predict the incidence of SP in the near future, but KOA and LS could not. Treatment of OP might reduce the risk not only of osteoporotic fracture but also of SP.
**Disclosure of Interest:** None declared
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## THU0465 FRACTURE LIAISON SERVICE REDUCES RE-FRACTURE RATE, COST-EFFECTIVE AND COST SAVING IN WESTERN AUSTRALIA

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**Background:** Osteoporotic fractures impose significant morbidity, mortality and economic burden (1). Earlier research showed low rates of secondary prevention for patients discharged from Emergency Department (ED) with a fracture (2). The Fracture Liaison Service (FLS) aimed to identify, review and then manage these patients following their discharge from the ED.
**Objectives:** Determine the economic benefits of a FLS in a Western Australian hospital.
**Methods:** Patients aged >50yrs whom presented to the Emergency Department at Sir Charles Gairdner Hospital (SCGH) after a fracture were invited to the FLS. A retrospective control group from SCGH and a prospective control group from Fremantle Hospital were the comparators.
A health economic analysis from the Payer's Perspective (WA Health) examined recurrent fracture rates and quality of life (EQ-5D). Bottom-up costing included medications, investigations, GP visits and the cost of fracture determined by the literature or the AR-DRG 2013/14 prices for hospital presentation and admission. The mean incremental cost effectiveness ratios were bootstrapped (5000 iterations). Cost-effectiveness acceptability curves were generated and the willingness-to-pay was $50,000AUD.
**Results:** This FLS reduced the rate of re-fracture compared to the retrospective cohort and other tertiary centre by 9.2 - 10.2%, equating to cost savings of approximately $750,168 - $810,400/1,000 patient-years in the first year compared to control cohorts. There was no difference in the QALYs gained across groups over 12 months.
The FLS compared to SCGH retrospective cohort had a mean incremental cost of $6,168 (95CI $133, $18,626) per 1% reduction in the 12 month recurrent fracture risk. The FLS compared to other sites had a mean incremental cost of $6,782 (95CI -$2,562, $25,686) per 1% reduction in the 12 month recurrent fracture risk. The FLS compared to SCGH retrospective cohort had a mean incremental cost of



$859 (95CI -$4,074, $4,864) per QALY gained at 12 months. The FLS compared to other sites had a mean incremental cost of -$119 (95CI -$1,665, $700) per QALY gained at 12 months.
Figure 1 demonstrates that the FLS is cost-effective in delivering a reduction in the fracture rate at 12 months. However, the QALY gained (EQ-5D) was no different at 12 months between the study groups.
**Conclusions:** This FLS demonstrated to be effective in reducing rates or recurrent fracture(s) and resulted in significant cost effectiveness and cost-saving.
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## THU0466 OSTEOPOROSIS-RELATED ANKLE FRACTURE: SHOULD WE CONSIDER IT?

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**Background:** Osteoporosis is defined as a systemic skeletal disease characterized by low mineral density and microarchitectural changes in the bone which increase its fragility and fracture risk. Ankle fracture is one of the most common fractures; however the relation with osteoporosis is still being debated. The diagnosis and treatment of osteoporosis is not always adequate.
**Objectives:** To determine the relation of ankle fractures to osteoporosis
**Methods:** Retrospective study 2008–2014. Center: Tertiary academic hospital with a referral area of 850,000 inhabitants. The medical charts, bone mineral density (BMD), radiographs and electronic data bases of patients with ankle fracture were reviewed. Demographic data (age, gender), BMD, mechanism of injury (high or low energy trauma), fracture pattern (single malleolus, bimaleollar and trimalleolar fracture) and treatment of fracture and osteoporosis were collected. Patients were divided into younger age ($\leq$60years) and older age ($>$60 years) groups.
**Results:** A total of 299 patients with ankle fractures were included. The mean age was 49.5 years (DS 26.5). There were 131 (43.8%) male and 168 (56.2%) female patients. Among these patients, 84 (28.1%) were in the older age group (74% female and 26% male) and 216 (72.2%) were in the younger age group (51% male and 49% female). Bimaleolar fracture was the most common pattern in both groups (62.7% and 50.5%). Proportion of low energy trauma and conservative treatment was higher in elderly group compared to younger group (63.9% vs 38%, p 0.002/20.5% vs 8.3%; p 0.003). Of note 34 (11.7%) of patients underwent a dual-energy X-ray absorptiometry (DXA): 17 (50%) in the elderly group and 17 (50%) in younger (82% were older than 50 years). In the older group only 1 (5.9%) patient had a normal BMD, 8 (47.1%) had osteopenia and 8 (47.1%) had osteoporosis. Compared with younger patients, osteoporosis was more frequent in older group (10.8% vs 1.4%; p$<$0.005). Older patients had a higher proportion of new fractures than younger (23.8% vs 12.6%; p 0.016), between 3 and 60 months after the ankle fracture. The new fractures were: 9 Colles', 4 vertebral, 4 hip and 3 in other location.
**Conclusions:** Ankle fracture was more common in females in the older group. DXA was performed in a very low percentage of cases. The features of ankle fractures and the higher ratio of new fractures in the older group suggest a possible link with osteoporosis. Patients with ankle fracture should be studied in order to diagnose osteoporosis. These patients may have a benefit of treatment.
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## THU0467 OSTEOPOROSIS AND CELIAC DISEASE IN PATIENTS WITH DISTAL RADIUS AND ANKLE FRACTURES

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**Background:** Patients suffering a distal radial fracture have a high prevalence of osteoporosis [1]. Ankle fractures have traditionally not been considered to be an osteoporotic fracture, however more recent studies suggest otherwise [2, 3]. Patients with celiac disease (CD) have low bone mineral bone density (BMD), and overall findings indicate an increased risk of fracture [4, 5].
**Objectives:** To investigate and compare the prevalence of osteoporosis in patients with acute distal radius or ankle fracture and describe risk factors for osteoporosis in the two groups.
**Methods:** 400 consecutive patients over the age of 40 with acute distal radius or ankle fracture were included in this study after referral from the orthopedic department at Forde General Hospital in Sogn og Fjordane county, Norway. BMD of the hips and spine was measured and history of previous fracture, comorbidities, medication, physical activity, smoking habits, body mass index (BMI) and nutritional factors were registered. Serum analysis to detect secondary osteoporosis including IgA tissue transglutaminase was performed.
**Results:** The prevalence of osteoporosis was 44.7% in the patients with distal radius fracture (n=293) compared to 23.4% in the ankle fracture group (n=107). Significant risk factors for having osteoporosis when having suffered a distal radius fracture were older age, female gender, lower BMI, and celiac disease (defined as either known celiac disease AND/OR positive IgA tissue transglutaminase). Elevated PTH or low vitamin D was not significant. The patients with radius fracture and osteoporosis had a higher prevalence of celiac disease (7.6%) than the ones with radius fracture and osteopenia or normal BMD (0.6%). In the ankle fracture patients with osteoporosis there were no celiac disease cases, versus 3.7% in the ankle fracture patients with osteopenia/normal BMD. In the ankle fracture group, low BMI was a significant risk factor for being osteoporotic, but no other significant risk factors were found.
**Conclusions:** The prevalence of osteoporosis was higher among persons suffering a distal radius fracture than among those with acute ankle fracture. Several well-known risk factors for osteoporosis were associated with being osteoporotic among subjects suffering a distal radius fracture, but only BMI was associated with osteoporosis in the ankle fracture group.
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**Disclosure of Interest:** None declared
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## THU0468 OSTEOPOROSIS AND OSTEOCALCIN LEVELS IN PATIENTS WITH GOUT

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**Background:** Gout is a rheumatic disease characterized by the deposition of monosodium urate crystals in the joints and surrounding tissues. Gout is the most common inflammatory arthritis in men. It affects 1–2% of the adult population. Comorbid conditions and drugs used in gout are thought to increase the risk of osteoporosis but unlike some other forms of rheumatic diseases, gout is not believed to cause osteoporosis.
**Objectives:** In our study, we aimed to investigate the osteoporosis and osteocalsin levels in patients with gout.
**Methods:** 70 patients diagnosed with gout and 53 age-sex match controls were included in the study. Cardiovascular diseases, chronic renal disease, diabetes mellitus, hypertension, thyroid disease, bone disorders, eating disorders, gastrointestinal surgery or disease history, steroid use, alcohol use, patients with family history of osteoporotic fracture were excluded. The t and z scores from lumbar spine (L2-L4) and femur (neck, ward, trochanter, total) were determined by Dual energy X-ray absorptiometry (DEXA). Osteocalcin levels was measured by electrochemiluminescent immunoassay (ECLIA).
**Results:** Osteoporosis according to t- scores of lumbar vertebrae L2-L4 was found to be significantly higher in patients with gout compare to control group (p=0.02). There was no correlation between osteoporosis and the frequency of gout attacts, tophi and disease duration. Osteocalcin levels were detected to be significantly increased in the gout patients compare to control group (p=0.004). Vitamin D levels were similar in gout and control group (p=0.14). Alkaline phosphatase, parathyroid hormone levels were found to be significantly lower in control group compare to gout group (p=0.001).

Table 1. Gout patients and control group results

| Parameter | Gout (n=70) | Control (n=53) | p |
|---|---|---|---|
| Osteoporosis , n (%) | 16 (22.9%) | 5 (9.4%) | 0.02* |
| Osteopenia, n (%) | 35 (50%) | 23 (43.4%) | NS |
| Osteocalcin (ng/ml) | 26.6 (14.9–53.8) | 18 (14.2–25.2) | 0.004* |
| Vitamin D (ng/ml) | 20.3 (13.2–25.6) | 16 (11–25) | NS |
| Parathyroid hormone (pg/ml) | 57.9 (42–86) | 43.7 (33.8–55) | 0.001* |
| Alkaline phosphatase (U/L) | 76 (63.2–92.5) | 62 (48–76.5) | 0.001* |

Values are presented as median (25–75 interquartile ranges. *P$<$0.05, NS: non significant.

**Conclusions:** Gout may increase the risk of osteoporosis and serum osteocalcin

levels in clinical practice may be a useful biomarker for osteoporosis. Long-term randomized controlled prospective studies with larger populations are required for the clarification of the relationship between gout and osteoporosis.
**Disclosure of Interest:** None declared
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## THU0469 COMPARISON OF DORSAL AND LUMBAR PAIN IN PATIENTS WITH AND WITHOUT NON-ACUTE VERTEBRAL FRACTURES IN TERMS OF THERAPEUTIC APPROACH AND URGENT CARE BURDEN

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**Background:** Among people over 65 years old, many circumstances increase the frequency and intensity of back pain including osteoarthritis, less muscle mass and kyphosis. Acute vertebral fracture (VF) is also a cause of intense spine pain and a relevant cause of consultation due to its locomotive impairment and need of potent pharmacological analgesia.
**Objectives:** To compare the frequency of healthcare demand and intensity of analgesic treatment of patients with lumbar or dorsal pain according to the existence or not of a vertebral fracture excluding the acute event.
**Methods:** A retrospective comparative study was conducted. Registries of patients who consulted in our A&E department by lumbar or dorsal pain, older than 65 years old from November 2013 to November 2015 were identified and grouped according to the presence or absence of a known VF. Records of patients who were diagnosed by the first time of vertebral fracture during the medical attention were excluded. Main outcome variables were number of consultations/year and type of treatment according to the WHO pain ladder.
**Results:** The inclusion criteria were achieved in 1528 registries. Among them, 76 registries were incomplete or unavailable. Of the remaining 1452 registries, 168 (11.5%) presented a previously documented vertebral fracture (PDVF) and the remaining did not (nVF). Average age in the PDVF and nVF group was 75.9 SD 3.3 and 73.6 SD 4.2 years old, respectively ($P$=0.0001). Average number of consultations was 1.58 SD 0.23 consultations/year in PDVF group and 1.02 SD 0.11 consultations/year in nVF group (95%CI of difference 0.5391–0.5809; $P$=0.0001; T Student's test). Among patients with PDVF, MD group had an average of 1.60 SD 0.26 consultations/year and CRVF group had an average of 1.60 SD 0.32 ($P$=0.29). The odds ratio of to require a further consultation within a month of first assessment was 2.24 when PDVF group was compared with nVF group (CI95% 1.54–3.26; $P$<0.0001). At discharge, 42 (25.0%) patients of PDVF group and 652 (50.7%) of nVF group were sent to primary care units and 98 (58.3%) patients of PDVF group and 210 (16.3%) of nVF group were sent to secondary care units ($P$=0.0001 for both comparison, Fisher's exact test). The odds ratio of be discharged without need of further follow up was 0.40 when compared PDVF and nVF group (CI95% 0.26–0.62; $P$<0.0001). 53.5% of PDVF patients and 23.4% of nVF patients were treated at discharge with 2º scale WHO-pain ladder drugs ($P$=0.0001). 29.1% of PDVF group and 23.4% of nVF group were treated with 3rd scale WHO-pain ladder drugs ($P$=0.0001). The odds ratio of be treated with major opiods at discharge was 78.02 when compared PDVF with nVF group (CI95% 38.57–161.86; $P$<0.0001). Among patients with PDVF, 21.3% of patients of the MD group and 41.5% of patients of the CRVF were treated with drugs of the 3rd scale WHO-pain ladder (OR 2.61; 95%CI 1.32–5.17, $P$=0.0057)
**Conclusions:** Patients with non-acute vertebral fractures have a higher index of urgent consultations per year, are more probably to be treated with major opiods and generates a higher burden of primary or secondary care appointments. As far as we know, this is the very first study which measures the impact of VF in an urgency environment.
**Disclosure of Interest:** None declared
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## THU0470 HOSPITAL UTILISATION AND MORTALITY OF TRAUMATIC HIP AND NON-HIP FRACTURES IN PATIENTS WITH OSTEOPOROSIS IN WESTERN AUSTRALIA: A TEN-YEAR STUDY USING LINKED ADMINISTRATIVE DATA

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**Background:** Osteoporosis is common. Traumatic fracture is more likely in those with osteoporosis at significant cost. Given the burden of the osteoporotic fracture and need to prioritise fracture prevention and management initiatives in WA, we sought to further investigate the 10-year linked data from the previous study to examine hospital utilisation and mortality associated with traumatic fractures in those with osteoporosis.[1]
**Objectives:** To compare hospital utilisation and mortality outcomes of "traumatic" hip with non-hip fractures in patients with osteoporosis in Western Australia (WA) over 10 years.
**Methods:** *Design:* Retrospective cohort study (2002 to 2011).
*Setting:* Population-based data linkage of the WA Hospital Morbidity Data System and Mortality Registry.
*Participants:* WA residents aged ≥50 years hospitalised with an index "traumatic" fracture and osteoporosis. Index fractures sites included hip, spine, pelvic, rib or "other" fracture sites.
*Main outcome measures:* Index hospitalisations, hospital readmission due to any subsequent fractures, length of stay (LOS), admission costs, characteristics of hospital stay and mortality.
**Results:** Specific fracture sites for index cases were identified in 974 patients (18% of all index cases) due to coding inconsistencies. Index hip and spine fractures were the most common fractures requiring hospitalisations, with index hip being the most expensive to treat ($40,570 per person on average) and the cost accounted for 65% of total cost of index cases. Non-hip fractures accounted for 68% of admissions and have similar hospital utilisation as hip fracture in terms of LOS (30 days on average), requirement for hospital transportation (over 60%) and rate of readmission. The risk of readmission following index spine fracture was 1.5-fold higher (95%CI=1.14–1.98) than index hip fractures. No significant mortality difference was found between hospitalised hip and non-hip cases. The 1 year, 5 years and 10 years cumulative probability of death for hip fracture was 21%, 61% and 84%, respectively.
**Conclusions:** Fracture prevention strategies need to target all with osteoporosis (marker of frailty) to reduce incidence of first fracture (including traumatic). Although mortality and readmission were similar for hospitalised hip and non-hip fracture patients, hip fracture accounted for 32% of index fractures and 65% of costs. Better coding system of osteoporotic fracture in the hospital data in Australia is required to monitor the disease progression in the aging population.
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**Disclosure of Interest:** None declared
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## THU0471 AN OPPORTUNITY TO BREAK THE FRAGILITY FRACTURE CYCLE: 10 MONTHS OF A FRACTURE LIAISON SERVICE

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**Background:** A Geriatric Trauma Unit (GTU) was created in our hospital to optimize the acute treatment of patients with fragility fractures. The rheumatology department assists in subsequente evaluation of these.
**Objectives:** To report the results of the evaluation after 10 months of a fracture liaison service (FLS).
**Methods:** All patients over 65 years-old admitted to the GTU with a fragility hip fracture were systematically identified on a daily, prospective basis. The protocol was first implemented on March 2015 and we describe all patients included until December 2015. After a first evaluation during the hospital admission, patients are referred to the outpatient clinic for further characterization, generally within 3 months. The investigations included were dual-energy x-ray absortiometry (DXA, GE-Lunar), FRAX® including DXA and laboratory blood tests. A descriptive study was performed.
**Results:** 208 cases of fragility hip fracture in patients above 65 years were identified, 78.9% women. Mean age (sd) of 83 years old (7.6). The most frequently affected segment of the hip was the trochanteric region (n=109, 52.4%), followed by the femoral neck (n=75, 36.1%). Most patients (68.8%) underwent surgical intervention within the first 48 hours. Regarding risk factors for osteoporosis (OP), there was a high prevalence of selective serotonin reuptake inhibitor consumption (n=40, 20.1%) as well as antiepileptics (n=10, 5%) and corticosteroids (n=9, 4.5%). Another highly prevalent risk factor was diabetes (n=49, 23.5%). Regarding the body mass index we found that the majority of patients (42.3%) had values within normal limits. Benzodiazepines use, clearly associated with falls, was reported by 44% of patients (n=91). In our analysis only 13.5% (n=28) of the patients had past or current use of bisphosphonates (BP) and only 5.8% of those reporting previous fragility fracture were ever treated for OP. The prevalence of previous fragility fracture was 25.3% (n=47), most commonly hip fracture (n=19, 10.2%). Prior to fracture, 62.5% of patients were independent for daily activities. However, within 3 months after the fracture, only 32% of these patients regain their autonomy. We have recorded 22 deaths, 12 cases during hospitalization.
Full assessment of bone health was conducted in 44 patients. In 34% (15/44) of the cases, the densitometric criteria for OP were not met and 20 (45.5%) patients had radiographic signs of vertebral fragility fracture. Only 9 patients had 25-OH vitamin D levels above 30 ng/mL and 19 (43%) patients had deficiency levels. Using the FRAX toll, the absolute risk of major osteoporotic fracture was higher than 20% in 8 (18%) patients and the absolute risk of hip fracture was higher than 3% in 30 (68%) patients. Regarding treatment implementation, all patients received calcium and vitamin D supplementation and 35 (84%) patients started anti-osteoporotic treatment (33 BP and 2 denosumab).
**Conclusions:** FLS are key pieces in the secondary fracture prevention as they facilitate patient care by automatically including all patients with a fragility fracture

within a health-care system able to implement the adequate strategies to prevent future fractures as well as fracture-related complications.
**Disclosure of Interest:** None declared
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## THU0472 EVALUATION OF TRABECULAR BONE SCORE IN PATIENTS WITH A DISTAL RADIUS FRACTURE

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**Background:** Studies have shown that trabecular bone score (TBS) is associated with vertebral and non-vertebral fractures in postmenopausal women, and it may have value for assessing microarchitectural deterioration other than low bone mass. There are limited data on the TBS in patients with a distal radius fracture (DRF), which often occurs in the osteopenic or even normal bone mineral density (BMD) ranges.
**Objectives:** The purpose of this study was to compare BMD and TBS in patients with a DRF and propensity score-matched control patients.
**Methods:** We compared BMD and TBS in 269 women with a DRF older than 50 years of age with age- and body mass index (BMI)-matched control patients who had no history of fractures. BMD was measured at the lumbar spine and at the femur using a GE Lunar Prodigy scanner. TBS was calculated on the same spine image. The differences of BMD and TBS between the two groups were assessed. A multivariate logistic regression analysis was used to analyze the odds ratio for the occurrence of DRF for variables such as age, BMI, lumbar or total femur BMD, and the TBS.
**Results:** Patients with a DRF had significantly lower BMDs at the femur (neck, trochanter and total) than control patients ($p$=0.004, 0.001 and 0.010, respectively). However, BMDs at the lumbar spine and TBS were not significantly different between the groups ($p$=0.367 and 0.708, respectively). Multivariate analysis indicated that only total femur BMD was significantly associated with the occurrence of DRF (odds ratio, 0.102; 95% confidence interval, 0.018 – 0.569; $p$=0.009).
**Conclusions:** TBS is not different between women with a distal radius fracture and those without a history of fractures. This result suggests that the TBS measured at the lumbar spine, which is mainly trabecular, may not reflect early microarchitectural changes in the distal radius, which is mainly cortical. BMD at the femur is the reliable evaluation of bone frailty in patients with a DRF.
**Disclosure of Interest:** None declared
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## THU0473 CORRELATION BETWEEN METACARPAL CORTICAL BONE MINERAL DENSITY MEASURED BY DUAL X-RAY DENSITOMETRY AND RADIOGRAMMETRY ON EARLY ARTHRITIS PATIENTS

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**Background:** Low bone mass at metacarpal (MC) diaphysis measured by radiogrammetry (DXR) has been described as a poor prognostic factor in rheumatoid arthritis (RA). However, this technique is not available in our environment. Our group has previously described the measurement of bone mineral density (BMD) at metacarpophalangeal joints (MCP) by dual X-ray absorptiometry (DXA). This measurement showed an acceptable correlation with the DXR at MC bones. However, DXR at MC bones mainly assesses cortical bone, whereas DXA at MCP mainly analyzes trabecular bone. Therefore, we have developed a procedure to evaluate MC's (2nd to 4th) bone mass of the nondominant hand through DXA.
**Objectives:** To study the correlation between BMD at 2nd to 4th MC of the nondominant hand measured by DXA with data obtained by DXR.
**Methods:** We studied 171 patients belonging to the Princesa Early Arthritis Register Longitudinal (PEARL) Study (84% women, 55.4 years at symptoms onset; 56.7% fulfilled RA 2010 criteria; 52% RF+ and 43.5% ACPA+). Demographic, clinical and laboratory data were collected per protocol. Hand X-rays were performed at baseline and after one year of follow-up, as well as nondominant hand BMD assessment by DXA (Hologic© QDR4500, Elite).
The standard Hologic© software allows to design regions of interest (ROI) tailored to the researcher needs. In order to develop ROIs in DXA similar to that in DXR, the ROI generator was placed on every MC mid third of the diaphysis (aprox 17x17 mm). The ROI was rotated to be aligned to the MC longitudinal axis, avoiding overlap between adjacent ROIs.
The BMD by DXA was the average of 3 successive measurements. The BMD by DXR was measured with standardized software Sectra (Linköping, Sweden) on hand digital X-ray (GE© DX Definium 8000).
Statistical analysis was performed using Stata 12 for Windows, including linear correlations according to the Spearman test between the BMD values of MC by DXA and DXR and BMD by DXA at global hand and MCP joints. In addition, a multivariate analysis was performed to determine which variables accounted for the differences between MC bone mass measured by DXR and DXA.

**Results:** 248 BMD measurements (154 at baseline and 94 at second visit) of the 3 regions described whose values are shown in Table 1.

| | MC-DXR | MC DXA | Total Hand DXA | MCP DXA |
|---|---|---|---|---|
| BMD (g/cm$^2$; mean ± SD) | 0.529±0.074 | 0.427±0.060 | 0.327±0.041 | 0.265±0.040 |
| Difference with MC-DXR | – | 0.104±0.074* | 0.206±0.060* | 0.268±0.053* |
| Correlation with MC-DXR | – | 0.865* | 0.824* | 0.717* |

MC: metacarpal bone; DXR: bone radiogrammetry; DXA: dual X-ray absorptiometry; MCP: metacarpophalangeal joints. *p<0.0001.

**Conclusions:** As shown in table 1, MC bone mass measured by DXA shows the lowest absolute difference and the best correlation with MC bone mass by DXR. Female gender (beta coefficient =0.013; p=0.039), patients older than 65 years (beta coefficient =0.014; p=0.019) and patients with higher body mass index (beta coefficient =0.002 by kg/m$^2$; p=0.019) were significantly associated with lower differences between the values of MC by DXA and DXR.
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## THU0474 THE INFLUENCE OF OSTEOPOROTIC HIP FRACTURE AFTER TOTAL KNEE ARTHROPLASTY: A PROPENSITY-MATCHED COHORT STUDY

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**Background:** Total knee arthroplasty (TKA) is an effective treatment for end stage knee osteoarthritis but the postoperative rehabilitaion period can be as long as one year[1]. During this period, patients may have increased risk of osteoporotic hip fracture after a fall[2]. Currently, there is a lack of literature reporting the effect of hip fracture on functional outcome in TKA.
**Objectives:** This study aims to investigate: 1) the incidence of osteoporotic hip fracture within one year after undergoing TKA; and 2) the influence of hip fracture on functional outcome in TKA.
**Methods:** Between March 1999 and February 2012, 2456 male patients and 10,452 female patients underwent a primary TKA at a tertiary hospital. Within one year after TKA, 25 patients had an ipsilateral hip fracture after a fall. A propensity score matching algorithm was used to select a 3:1 control group without hip fracture, with adjustment for potential confounders of functional outcome in TKA such as patients' age, gender and Body Mass Index. The operated knee was assessed using the Knee Society Function Score (KSFS), Knee Society Knee Score (KSKS) and Oxford Knee Score (OKS) at two years after TKA; while the general health of the patients was evaluated using the Physical Component Score (PCS) and Mental Component Score (MCS) of SF-36®. The Student's unpaired t-test was used to compare the two groups for continuous variables.
**Results:** The incidence of hip fracture within one year after undergoing TKA was 0.16% (4 out of 2456) among male patients and 0.20% (21 out of 10,452) for female patients. The average age of these 25 patients was 71 ± 8 years old. There were 15 patients with neck of femur fractures and 10 patients with intertrochanteric fractures. Among them, 7 had a fall within 3 months after TKA and 6 each between 4–6 months, 7–9 months as well as 10–12 months after TKA. At two years after TKA, the KSFS was 50 ± 24 in the hip fracture group versus 68 ± 21 in the control group (p=0.002); while the KSKS was 83 ± 12 and 87 ± 8 respectively (p=0.090). Similarly, the OKS was 36 ± 7 in the hip fracture group versus 41 ± 5 in the control group (p<0.001). The PCS was 37 ± 12 in the hip fracture group versus 47 ± 11 in the control group (p<0.001); while the MCS was 55 ± 10 and 54 ± 11 respectively (p=0.662).
**Conclusions:** In the country where the authors practise, the incidence of hip fracture after a fall was 0.16% for males and 0.44% for females among the general population. The incidence of hip fracture within one year after undergoing TKA among male patients was comparable to the general population, however it was two fold lower than the general population for female patients. Nonetheless, those patients who had an osteoporotic hip fracture during the rehabilitation period after TKA had poorer function at two years follow up, with significantly lower KSFS, OKS and PCS. The authors recommend additional caution against hip fracture within one year after TKA.
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## THU0475 INCOMPLETE AND INCONSISTENT: INVESTIGATION OF OSTEOPOROSIS IN A DISTRICT GENERAL HOSPITAL

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**Background:** Osteoporosis is a disease of low bone density, micro-architectural destruction, increased bone fragility and susceptibility to low trauma fractures1, leading to increased morbidity and mortality with a 2–3 fold increased risk of further fractures[1–2]. Prompt diagnosis and optimal management of osteoporosis prevents further fractures[1–2]. The aim of screening is to identify those with greatest risk of sustaining a low trauma fracture who would benefit from intervention, as well as identifying other pathology including malignancy, presenting similarly. It is well documented that the majority of patients presenting with fragility fractures are neither appropriately assessed nor treated for osteoporosis[3–4].
**Objectives:** To assess compliance in screening for secondary causes of osteoporosis in all patients admitted with Neck of femur (NOF) fracture, comparing this to local CCG (Clinical Commissioning Group) guidelines.
**Methods:** Retrospective data collection from electronic records of all patients admitted from May- July 2015 who sustained a NOF fracture. Data was collected re: screening for myeloma, hyperparathyroidism, coeliac and thyroid disease, with baseline full blood count, liver function tests, renal function, Vitamin D, bone profile and testosterone within 48hours of admission.
**Results:** A total of 85 patients were identified as having sustained a NOF fracture during this period. 68% were female. The majority were postmenopausal (mean age: 85yrs; range: 73–99 yrs). Full blood count and renal function were performed in all, liver function tests in 64% and bone profile and vitamin D in 36% and 34% respectively. C-reactive protein was performed in 40% vs ESR in 1.2%. Only 3 and 4 patients were assessed for parathyroid and thyroid dysfunction respectively. No patient was fully screened for myeloma or coeliac disease. Of the 27 male patients all were over 70years old and none had their testosterone levels checked.
**Conclusions:** Overall, recommended screening tests for osteoporosis were inconsistent and incomplete, which is in keeping with the current literature. Patients that were cared for in the orthopaedic and geriatric setting who have sustained a NOF fracture should have the above baseline tests.
We have recommended a single tick box to encompass the above "osteoporosis bloods" on our electronic requesting system. All patients with a confirmed fracture should also be referred to our fracture liaison nurse for further evaluation and instigation of treatment. Junior doctors undergoing an orthopaedic rotation should have training in evaluating for secondary causes of osteoporosis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3045

## THU0476 EFFICACY OF DENOSUMAB FOR THE TREATMENT OF OSTEOPOROSIS IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Recent studies have reported that RA patient with osteoporosis administered Denosumab (DMAB) was associated with significant increases of low bone mineral density (BMD) at lumbar spine and femoral neck.
DMAB increases cortical bone more effective than any other drug for treatment of osteoporosis.
**Objectives:** Therefore, we investigated efficacy of DMAB in the patient with RA for 12 months at lumbar spine, femoral neck, and radius.
**Methods:** Sixty RA patients with osteoporosis were administered DMAB between April 2014 and October 2015, 45 patients were evaluated for 12 months in our institute. The following items were examined just before administered and at the time of 6 months and 12 months after administration: BMD of lumbar/femur/radius, Biomarker (total P1NP, TRACP-5b), radiograph of the hand.
Also, comparisons were performed on the basis of efficacy of DMAB at the time of 12 months in radius between the patients with the poorly effected group (NR group), and the patients with the well-effected group (R group).
**Results:** After treatment of DMAB at 12 months, 5.2 percent increase of BMD at the lumbar spine was obtained, 4.2 percent increase at the femoral neck.
However, there was not significant change at the distal third of the radius.
Comparing the NR group to the R group, there was statistically significant difference in Larsen grade at the wrist.
**Conclusions:** DMAB significantly increases bone mineral density in the patient with RA.
However, in the patient with severe joint destruction, DMAB could not increase BMD at the radius.
**Disclosure of Interest:** None declared
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## THU0477 EFFECT OF RECENT SPINAL CORD INJURY ON THE OPG/RANKL SYSTEM AND ITS RELATIONSHIP WITH BONE LOSS AND ANTIOSTEOPOROTIC RESPONSE TO DENOSUMAB THERAPY. PRELIMINARY RESULTS

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**Background:** Spinal cord injury (SCI) has been associated with a marked increase in bone loss and bone remodeling, especially short-term after injury. However, the pathogenesis and clinical management of this process remain unclear, as well as the role of the key regulators of bone remodeling, the OPG/RANKL system.
**Objectives:** To analyze the role of the regulators of bone remodeling, OPG and RANKL, in the bone loss associated with recent SCI as well as the effect of antiosteoporotic therapy with denosumab in these bone regulators in a prospective study.
**Methods:** Twenty-three male patients (aged 18 - 67 years [mean 36 ± 16 years]) with recent (<6 months) complete SCI were prospectively included (43.5% paraplegic, 56.5% tetraplegic). Patients were followed every 6 months. All patients received calcium and vitamin D supplementation. Antiosteoporotic therapy with denosumab was recommended when patients developed densitometric osteoporosis during follow-up. Serum levels of OPG and RANKL (Biomedica, Vienna, Austria), bone turnover markers (PINP, bone ALP, sCTX) and bone mineral density (BMD) at the lumbar spine and total hip were assessed at baseline (99±30 days after SCI), prior to initiating antiosteoporotic treatment (14±4 months post-SCI) and during antiosteoporotic therapy with denosumab (6 months after initiating treatment). The results were compared with a healthy control group.
**Results:** At baseline, SCI patients showed a significant increase in RANKL serum levels compared to controls (3.4±1.7 vs. 2.3±1.6 pg/mL, p=0.022) which correlated with days-since-SCI (r=0.589, p=0.005) and became undetectable after denosumab treatment in 67% of the patients (p=0.001). OPG serum levels were similar to controls at baseline (87.7±38.7 vs. 71.7±25.4, p=0.1) and did not change with denosumab treatment. No differences were observed in RANKL and OPG levels on comparing tetraplegic vs. paraplegic patients. Neither were RANKL or OPG levels related to the increase in bone loss and bone turnover markers after SCI. Patients with undetectable RANKL serum levels after denosumab treatment did not present further sublesional bone loss but increased total hip BMD (+2.5±1.3%, p=0.005), and bone markers markedly decreased (PINP: -53%, p=0.007; sCTX: -68%, p=0.005).
**Conclusions:** This study shows that short-term after SCI there is an increase in RANKL serum levels which become undetectable after denosumab treatment. The preventive effect of denosumab on sublesional bone loss further suggests a contributory role of RANKL in this clinical process.
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## THU0478 ASSESSING COMPLIANCE WITH ROYAL COLLEGE OF PHYSICIANS GUIDELINES IN GCA/PMR PATIENTS WITH GLUCOCORTICOID INDUCED OSTEOPOROSIS

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**Background:** The Royal college of physicians (RCP) guidelines recommend that all patients placed on long term glucocorticoids (GCs) are at risk of osteoporosis, especially when the dose exceeds ≥10mg of Prednisolone or equivalent for >3months[1]. Patients with Giant cell arteritis (GCA) and Polymyalgia Rheumatica (PMR) are particularly at risk.
**Objectives:** To assess our departmental compliance with the RCP guidelines for glucocorticoid induced osteoporosis (GIO) published in 2002. Following review of the International Osteoporosis Foundation and the European Calcified Tissue Society and American college of Rheumatology (ACR) guidelines for GIO, we also looked into use of FRAX tool for risk assessment.

**Methods:** Retrospective data collection of 50 patients diagnosed with either GCA or PMR was selected at random since 2010. Documentation of smoking history, alcohol intake, height and weight, history of falls and started dose of GCs were also noted. Data regarding DXA results, other imaging e.g. spinal x-rays, biochemistry and the use of the FRAX assessment tool were obtained. The use of bisphosphonate, calcium/vitamin D supplementation and steroid sparing agents were also recorded.
**Results:** The majority of the patients were postmenopausal (mean age 75.2years, Range: 59–92) females (68%) with a diagnosis of PMR (72%). Ninety percent were over the age of 65years. The modal starting dose was 60mg of prednisolone in GCA patients and 15mg in those with PMR. Nine patients (18%) were identified as having an additional risk factor for osteoporosis such as thyrotoxicosis or premature menopause. History of falls was documented in 22%. Fourteen percent had a prior history of fragility fracture, of those 2% were <65years of age. Steroid sparing agent (Methotrexate (18%) and azathioprine (10%)) was commenced in 28%. None of the patients had a baseline FRAX assessment. Calcium and vitamin D supplementation was prescribed in 90%, of which 78% had this checked prior to administration. Adherence for bone protection was documented in 44%.
**Conclusions:** The documentation of risk factors and DXA requests was inconsistent for various age groups. Bone protection was commenced in the majority of patients; especially calcium and vitamin D were prescribed in almost all patients. Based on the RCP guidelines, International Osteoporosis Foundation and the European Calcified Tissue Society and ACR guidelines for GIO, local departmental guidelines have been designed to ensure appropriate investigations and bone protection is considered all these patients. There is a need for new national guidelines incorporating FRAX tool.
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## THU0479 PILOT STUDY OF BONE MASS IN HEART TRANSPLANT RECIPIENTS

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**Objectives:** Our objective was to describe changes in bone mineral density (BMD), incidence of fractures and levels of bone remodeling markers in the first year post-heart transplant (postHTX).
**Methods:** We included patients aged ≥18 years with heart transplant performed in our institution from 01.01.2013 to 31.07.2015, excluding those on antiresorptive or bone forming treatment and pregnant women. Before heart transplant (preHTX) and in the one year postHTX visit, the following data were registered: body mass index, risk factors for osteoporosis, biochemical parameters of bone metabolism, presence of osteopenia or osteoporosis in the densitometric analysis of lumbar spine and femoral neck, presence of fractures in the X-ray of the spine and echocardiographic left ventricular ejection fraction (LVEF).
**Results:** All 17 patients (age 48±16 years, 12 male) included in the study were treated with calcineurin inhibitors and steroids (mean dose 15 mg/day). At the preTX visit, body mass index was 24,7±3,8 kg/m$^2$, obesity was present in 4 patients, DM in 1, kidney stones in 3, excessive alcohol consumption in 1, and 11 patients were ex-smokers. Low BMD was present in 14/17 patients (82%) in the preTX visit: 12 osteopenia (8 men and 4 women) and 2 osteoporosis (1 man and 1 woman); and 15/17 patients (88%) in the one year postTX visit: 9 osteopenia (6 men and 3 women) and 6 osteoporosis (3 men and 3 women). One patient died before the first year postHTX visit. Twelve patients (80%) had a vitamin D blood level <20 ng/ml at the one year postHTX visit. A man presented a spinal fracture in the follow-up. Mean LVEF was 25±6% (preHTX) and 75±8% (postHTX).
**Conclusions:** In this pilot study, 82% of heart transplant recipients had a low BMD preHTX and 88% at the one year postHTX visit. Moreover, 80% of patients had a vitamin D deficiency at the one year postHTX visit. Larger studies are required to fully evaluate this morbidity and describe clinical predictors.
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## THU0480 COMPARATIVE EFFECTIVENESS OF EDUCATIONAL PROGRAMS FOR OSTEOPOROSIS

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**Background:** Educational programs may be beneficial in a variety of important factors for the prevention, treatment and management of osteoporosis.
**Objectives:** To evaluate the influence of the three different educational interventions on knowledge, dietary calcium, physical activities and adherence to treatment of osteoporosis.
**Methods:** 117 patients (middle age 63.3 ± 8.1 years old, 95.7% are women) with osteoporosis have been included in this study. All patients were randomized to three groups. The patients of intervention group (n=39) had an osteoporosis school program (4 lessons with using interactive methods in groups of sevens to tens). The patients of the control group (n=38) received brochures with general information about osteoporosis. The patients of the comparison group (n=40) received lecture (1 x 1.5 h) about osteoporosis. Average changes from baseline in knowledge, dietary calcium, physical activities and time of physical exercises was evaluated in 3, 6 and 12 months. Adherence to treatment was evaluated in 12 months.
**Results:** After educational programs level of knowledge was increased in patients of the intervention group in 3, 6 and 12 months by 23,8%, 22,9%, 21,1%, in the group of brochures – by 0.5%, 1.8%, 4.7%, correspondingly, $p<0.01$. In the group received lecture level of knowledge was increased by 18.0%, 15.8%, 14.6% ($p<0.05$ when compared with the brochure at visits 3 and 6 months). The use of dietary calcium was increased in 3, 6 and 12 months in the intervention group by 188.5 mg, 211.8 mg and 238.1 mg, in group received lecture by 146.8 mg, 106.4 mg, 84.4 mg, in control group received brochures by 66.0 mg, 80.4 mg and 68.3 mg ($p<0.05$ when compared intervention group with the control group at visits 3 months). Physical activity was increased in 3, 6 and 12 months in intervention group by 1.7, 1.9, 0.9 scores and was significantly higher, than in group received lecture (0.2, 0.2, 0.1 scores) and in control group received brochures (0.1, 0.2, 0 scores). Time of physical exercises was increased by 45.1, 54.2 and 49.9 min in week in the intervention group and was significantly more than in the groups received lecture or brochures. Adherence to pathogenetic osteoporosis treatment was higher in the intervention group: 56.4% of intervention group, and 30.0% of the group received lecture, and 13.2% of group received brochures took pathogenetic medication regularly during the year ($p<0.01$ when compared the intervention group with the control group).
**Conclusions:** Educational program with using interactive methods in small groups increases knowledge about of osteoporosis, dietary calcium, physical activities and increases adherence to treatment of pathogenetic medication more than brochure and lecture.
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## THU0481 PREVALENCE OF ASYMPTOMATIC MORPHOMETRIC VERTEBRAL DEFORMITIES IN HIV-INFECTED PATIENTS

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**Background:** Patients infected with the human immunodeficiency virus (HIV) have a high rate of low bone mineral density (BMD) of multifactorial origin, that involve traditional risk factors, activity of the infection and highly active antiretroviral therapy (HAART). An increased risk of fractures has been reported in these patients but few studies have estimated the true prevalence of asymptomatic morphometric vertebral deformities (MVD).
**Objectives:** To determine the prevalence of MVD in HIV-infected patients followed in a Spanish tertiary center, taking into account both traditional risk factors as those associated with their underlying disease.
**Methods:** We performed a cross-sectional study in HIV-infected patients with age 50 years treated in our center during the period 2014–2015. Demographics and traditional risk factors were collected through a specific survey. BMD was determined by X-ray absorptiometry dual-energy (DXA) at the lumbar spine and hip. Blood and urine samples were collected for biochemical analysis of bone metabolism. WHO definitions were used to classify DXA results. MVD were assessed on lateral X-rays of thoracic and lumbar spine using the Genant's semiquantitative method: 1) reduction of any height of the vertebral body between 20–25%: grade I (mild); 2) between 26–40%: grade II (moderate); and 3) >40%: grade III (severe).
**Results:** A total of 75 patients were included, 54 males (72%), with a mean age of 54.8 years (range: 50–70). MVD was detected in 15 cases (20%): 4 grade I, 6 grade II and 5 grade III. All patients received HAART during the study period. Femoral neck BMD was normal in 39%, 52% were in range of osteopenia and 9% osteoporosis. Variables independently associated with development of MVD were female gender (13% vs 31%, p=0.13), daily calcium intake (490 mg/d vs 594 mg/d, p=0.16), serum phosphorus (2.79 mg/dL vs 3.17 mg/dL, p=0.02) and low BMD in total hip (0.69 vs 0.75, p=0.05) (Table 1). Significant association was also found with disease duration (mean time in patients with MVD: 264.7 months,

p=0.09). No correlation was found with age, a fact that can be attributed to limited sample size and age of patients (50–70 years).

Table 1. Comparison of the characteristics of HIV-infected patients with and without MVD

| | VMD (n=15) | Non-VMD (n=60) | p-value |
|---|---|---|---|
| Mean age (years) | 53,5 | 51,4 | 0,24 |
| Female gender | 13% | 31% | 0,13* |
| Body mass index | 24,3 | 23,9 | 0,93 |
| Nadir CD4+ level | 254 | 191 | 0,12 |
| Duration of HIV infection | 264,7 | 227,2 | 0,09* |
| Total length of HAART | 206,3 | 184 | 0,32 |
| BMD total hip | 0,69 | 0,75 | 0,05* |
| T-score femoral neck | –1,63 | –1,1 | 0,03* |
| Osteopenia/osteoporosis femoral neck | 85% | 55% | 0,02* |
| BMD lumbar spine | 0,88 | 0,89 | 0,48 |
| T-score lumbar spine | –1,8 | –1,6 | 0,63 |
| Osteopenia/osteoporosis lumbar spine | 85% | 59% | 0,08* |
| Vitamin D3 level | 33,4 | 32,6 | 0,81 |
| Parathormone level | 52,7 | 51,8 | 0,82 |
| Serum phosphorous level | 2,79 | 3,17 | 0,02* |
| Serum calcium level | 9,71 | 9,53 | 0,54 |
| Daily calcium intake | 490 | 594 | 0,16* |
| Previous peripheral fractures | 27% | 35% | 0,76 |
| Family history of hip fracture | 7% | 10% | 0,69 |

**Conclusions:** We found a high prevalence of asymptomatic MVD in our series (20%). X-rays of thoracic and lumbar spine should be performed as a screening method in HIV-infected patients with risk factors, such as long-term infection, low calcium intake, low serum phosphorus levels and female gender.
**Disclosure of Interest:** None declared
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## THU0482 PREDICTORS OF FRACTURES IN PATIENTS WITH UNTREATED EARLY MENOPAUSE: AN OBSERVATIONAL STUDY

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**Background:** A previous case-control study demonstrated that untreated early menopause (menopause before 45 years of age) predisposes to a lower bone mineral density (BMD) at the femoral neck and the lumbar spine and that the condition increases ten year risk of sustaining a major osteoporotic fracture (1). However, less has been published on the predictors of fractures within this group of patients.
**Objectives:** This study aims to investigate the predictors of fractures in patients with untreated early menopause.
**Methods:** A cohort of patients attending for a DEXA scan in the North-West of England between June 2004 and July 2013 who were diagnosed with untreated early menopause was identified. These patients were divided into two groups: women with a history of post-menopausal fragility fracture and women with no history of fragility fracture. Characteristics of these two groups were compared using the chi squared test for categorical variables and stduents T test for continuous variables. Logistic models were used to describe the associations between known risk factors of fracture (FRAX risk factors and BMD, adjusting for the time from menopause).
**Results:** A total of 2,171 females with untreated early menopause were included in the study. The mean age was 63.56 (±SD12.57). The mean age at menopause was 41.12 (±SD3.85) and the mean years from menopause was 22.44 (±SD12.54). Of those women, 1308 (60.25%) had no fractures and 863 (39.75%) had a fracture. The age at scan of patients with a fracture (66.79±11.50) was significantly different from the age of patients without a fracture (61.43±12.70), p-value 0.000. The mean years from menopause was significantly different in the fracture group (25.84±11.70) as compared to the group without fractures (20.19±12.58), p-value 0.000. The body mass index, age at menopause, history of smoking, rheumatoid arthritis as well as alcohol use were not significantly different between the two groups. The mean femoral neck BMD was significantly lower in females with fracture than those with no fracture: 0.79g/cm$^2$ vs. 0.84g/cm$^3$, respectively, p-value 0.000. The mean lumbar BMD was significantly lower in fracture patients as compared to patients without fractures: 0.97g/cm$^2$ vs. 1.04g/cm$^2$, respectively, p-value 0.000. Prevalence of steroid use was relatively higher in patients without fractures as compared to those with fractures: 22.63% and 17.61% respectively, p-value 0.005. Logistic regression analysis, adjusted for age at scan and years from menopause, revealed a significant association between having a fracture and steroid use OR0.70 (95% CI 0.55, 0.88) as well as between having a fracture and having lower BMD in the lumbar spine OR 0.24 (95% CI 0.13, 0.47).
**Conclusions:** This study demonstrates that steroid use and low lumbar BMD, but not other FRAX predictors, are associated with fracture in patients with an early untreated menopause. These observations can guide measures on enhancing bone health in this patient group.
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## THU0483 INCREASED INFECTION RISK WITH CONCOMITANT USE OF RANKL-INHIBITOR, DENOSUMAB AND TNF-INHIBITORS OR OTHER BIOLOGICS: FACT OR FICTION?

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**Background:** Patients with autoimmune diseases are at increased risk of early onset osteoporosis because of prolonged exposure to corticosteroids. RA patients may also develop early-onset osteoporosis secondary to the disease process itself. Same patients are more likely to be on TNF inhibitors or other biologics which cause them to be at an increased risk of infections. Denosumab is an anti-RANK ligand inhibitor used to treat osteoporosis. Receptor activator of nuclear factor kappa-B ligand (RANKL) is also expressed on activated T and B lymphocytes. Therefore, a RANKL inhibitor such as denosumab may increase the risk of infections.(1) In the Freedom Trial, the denosumab group reported more serious infections leading to hospitalization than in the placebo group.(1) It is unknown if biologic agents will increase the risk of infections when denosumab is used concomitantly.
**Objectives:** To determine rate of infections in patients on combination therapy with denosumab and either TNF inhibitors or other biologics.
**Methods:** We identified 40 patients in the rheumatology clinic on denosumab and either a TNF inhibitor or a biologic agent for 1 to 4 years. A retrospective chart review was conducted at the Keck Medical Center of USC to record if the patients developed infections.
**Results:** The mean age of the population was 65 ± 20 years, among which 98% were females. 75% had Rheumatoid Arthritis (RA), 10% Systemic lupus erythematosus (SLE), 2.5% SLE and Sjogren's, 2.5% SLE with Antiphospholipid Syndrome (APLS), 2.5% RA and SLE, 2.5% Microscopic Polyangiitis, 2.5% Psoriatic arthritis, and 2.5% Neurologic Behcet's disease. Prior to initiation of denosumab, patients either failed bisphosphonate therapy or became intolerant. The addition of denosumab showed a trend of improvement of T scores in lumbar spine and hip. 40% of our patients developed some infection, which is lower than 52.9% in the FREEDOM trial.(1) 70% (28/40) patients were on TNF inhibitors. 35% of these developed infections. 30% (12/40) patients were on other biologic agents. 50% of these patients developed infections. Urinary tract infection (UTI) accounted for the most common infection (12%). 12% of our patients required hospitalization for infections, compared to 4% in the Freedom trial. 17.5% of these had developed infections before denosumab. 9% had been hospitalized before denosumab for infections.

| Infections | Infection rate x/n (%) | Average time to develop infections (months) |
|---|---|---|
| Overall rate | 16/40 (40%) | |
| UTI | 5/40 (12.5%) | 15 |
| Bronchitis/Pneumonia | 4/40 (10%) | 16 |
| Wound infection | 3/40 (7.5%) | 16 |
| Sialadenitis | 1/40 (2.5%) | 28 |
| Herpes Zoster/HSV-II | 3/40 (7.5%) | 17 |

**Conclusions:** In conclusion, data from this study demonstrates that 40% patients developed infections. However, 17.5% of patients who developed infections in our study had developed infections before starting denosumab. It is therefore unclear weather the overall infection rate can be attributed solely to the combination of denosumab and biologics. Since we did not see any infections within the first year, there may be a cumulative effect of increased infection risk, if any. Antibiotic prophylaxis, while on denosumab and biologics, may be considered in patients with recurrent infections in the past.
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## THU0484 ZOLEDRONIC ACID INFUSION AND EFFECT ON RENAL FUNCTION AND CALCIUM IN OSTEOPOROSIS

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**Background:** Zoledronic acid is a commonly used intravenous bisphosphonate. Predominantly it is excreted through the kidney. Use of zoledronic acid is contra-indicated in patients with eGFR of <30. Effect of zoledronic acid on kidney function after repeated infusions in a real life scenario is not well described. Zoledronic acid related hypocalcaemia is well recognized. But frequency of this complication in real life and its link to renal function has not been studied.
**Objectives:** The aim of our study was to assess the effect of zoledronic acid on

the renal function, calcium level and link between renal function and calcium level in patients treated with yearly zoledronic acid infusion for primary or secondary prevention of fractures in osteoporosis.

**Methods:** A retrospective review of patients receiving zoledronic acid infusions between August 2008 and August 2015 was carried out. Patients receiving the treatment for osteoporosis and who had received at least one infusion were included. All the patients had calcium level and renal function measured before and a week after the infusion. Calcium level >2.5 mMol/L was considered elevated and <2.1 as low. The e GFR measures were classified into categories of >60 (normal), 45–59 (mild impairment) and 30–44 (moderate impairment). Pre and post infusion calcium values were matched to assess the effect on the calcium. Parametric analysis was carried out to compare the means.

**Results:** 200 patients were identified on the database. 175 patients were analysed based on our inclusion criteria. 175 patients received 354 infusions. Baseline eGFR, calcium and post infusion eGFR and calcium levels are detailed in the table below. There was no significant difference between pre and post infusion eGFR or calcium levels. We also did not find any significant correlation between baseline eGFR and post infusion calcium level.

| | eGFR | | Calcium (mmol/L) | | p |
|---|---|---|---|---|---|
| | Pre infusion | Post infusion | Pre infusion | Post infusion | |
| 1st infusion (n=175) | 60.505 (41.7–90) | 60.326 (36.6–90) | 2.399 (1.98–2.75) | 2.342 (1.91–2.88) | >0.5 |
| 2nd infusion (n=103) | 58.09 (36.6–76.5) | 60.129 (28.4–90) | 2.386 (2.21–2.74) | 2.369 (2.1–2.88) | >0.5 |
| 3rd infusion (n=76) | 60.187 (35.5–88.5) | 58.808 (37.8–83.6) | 2.380 (2.16–2.7) | 2.360 (2.13–2.66) | >0.5 |

**Conclusions:** 1. Only one patient's post infusion eGFR dropped to 28.4 after the second infusion. This improved to baseline a week later.

2. Only one patient had calcium below 2.1 post infusion (1.91). The post infusion calcium returned to normal after a week.

3. There was no significant drop in post infusion eGFR compared to baseline particularly in those who had mild or moderate renal impairment.

4. Calcium level did not come down significantly following zoledronic acid infusion.

5. Baseline eGFR had no significant effect on post-infusion calcium level.

6. This real life experience reinforces the safety of zoledronic acid infusion outside trial environment.

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## THU0485 AN ADVANCED ECHOSOUND APPROACH FOR FEMORAL NECK DENSITOMETRY

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**Background:** Dual X-ray absorptiometry (DXA) currently represents the most common method for osteoporosis diagnosis and it is considered the gold standard for bone mineral density (BMD) measurements. However, DXA has also some important limitations that prevent its use for population screenings and this has led to the investigation of alternative ultrasound (US) approaches. In this context, we have recently introduced a new US methodology for osteoporosis diagnosis, which is based on a closely integrated processing of echographic images and corresponding "raw" radiofrequency (RF) signals ("echosound approach" [1]). The basic idea underlying this approach is that the RF signals acquired during an echographic scan of the investigated bone district can be employed to assess the bone health status through comparisons with previously derived reference spectral models. The implemented RF signal analysis method is also integrated with echographic imaging, which provides both the identification of the regions of interest and the simultaneous acquisition of a statistically significant number of US signals for each frame.

**Objectives:** To assess the accuracy of an advanced echosound approach, which was specifically tailored and optimized for femoral neck densitometry.

**Methods:** A total of 289 female patients (55–80 y) underwent both a femoral DXA and an echographic scan of proximal femur. Specific attention was paid to ensure adherence to correctness criteria for DXA scanning and data analysis as reported in the guidelines of the International Society for Clinical Densitometry [2]. The algorithm adopted for US data analysis was based on the echosound approach and included an additional dedicated signal compensation, which was specifically implemented to better account for the physiological variability in soft tissue thickness and corresponding US attenuation. The diagnostic agreement between DXA and US was assessed by accuracy calculation, Cohen's *k*, Pearson correlation coefficient (*r*), root mean square error (*RMSE*), and Bland-Altman analysis, whereas the method precision was assessed by the root mean square (*RMS*) average of the *SD* (*RMS-SD*) of repeated measurements, the root mean square coefficient of variation (*RMS-CV*), and the least significant change for a 95% confidence level (*LSC95*).

**Results:** By assuming DXA output as the gold standard reference, the overall US accuracy in patient classification was 93.1% ($k$ =0.882, $p<0.0001$). A strong correlation was also found between US-estimated BMD values and DXA-measured ones ($r$ =0.86, $p<0.001$), with a low residual error (*RMSE* =0.044 g/cm$^2$). The average difference between paired BMD measurements was -0.002 ± 0.089 g/cm$^2$ (bias ± 2 SDs). US method precision, expressed as *RMS-SD*, resulted to be 0.003 g/cm$^2$ (*RMS-CV* =0.29%; *LSC95* =0.008 g/cm$^2$).

**Conclusions:** The proposed echosound approach for femoral neck densitometry showed an excellent agreement with corresponding DXA diagnoses and an optimal measurement reproducibility, indicating a potential for an effective clinical routine adoption.

**References:**

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**Disclosure of Interest:** M. Muratore: None declared, F. Conversano Shareholder of: Echolight srl, a National Research Council spin-off that may or may not benefit from the results of this study, M. Peccarisi: None declared, P. Pisani: None declared, T. De Marco: None declared, R. Franchini: None declared, E. Casciaro Shareholder of: Echolight srl, a National Research Council spin-off that may or may not benefit from the results of this study, E. Quarta: None declared, L. Quarta: None declared, O. E. Casilli: None declared, S. Casciaro Shareholder of: Echolight srl, a National Research Council spin-off that may or may not benefit from the results of this study

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## THU0486 PERSISTENCE WITH ANTI-OSTEOPOROTIC THERAPY IN PATIENTS WITH RHEUMATIC DISEASE

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**Background:** Osteoporotic fragility fractures decrease physical performance and disability-free life expectancy. Patients with rheumatic disease develop osteoporosis due to local cytokine production, low levels of physical activity, and glucocorticoid therapy. Rheumatologists need to proactively manage osteoporosis in patients with rheumatic disease to extend their healthy and disability-free life years. While studies have reported that approximately 50% of postmenopausal patients with osteoporosis discontinue anti-osteoporotic therapy within 1 year, there is a paucity of data on treatment continuation and discontinuation in patients with rheumatic disease.

We conducted a retrospective analysis of the status of oral anti-osteoporotic therapy in patients with rheumatic disease using the prescription database at a single rheumatology specialty center from June 2007 to May 2010, a period before teriparatide, a recombinant form of parathyroid hormone, and denosumab, a monoclonal antibody to receptor activator of nuclear factor kappa B ligand, were approved for clinical use.

**Objectives:** To estimate persistence with oral anti-osteoporotic therapy in patients with rheumatic disease and identify factors influencing the persistence and reasons for discontinuation.

**Methods:** Based on prescription database, we identified patients who started treatment with alendronate, risedronate, or selective estrogen receptor modulators during the study period. Patients who continued treatment after June 1, 2010, were "censored". Patients who did not receive a prescription for 190 or more days during the study period were classified as "discontinued". Persistence were estimated using Kaplan-Meier survival analysis. Multivariate Cox proportional hazard analysis was carried out to identify factors influencing the persistence. Reasons for discontinuation were abstracted from medical charts.

**Results:** Analysis of prescription database identified 557 patients (477 females and 80 males). Of these, 378 had rheumatoid arthritis, and 112 had systemic lupus erythematosus, dermatomyositis, systemic sclerosis, vasculitis syndrome, or other connective tissue diseases. Mean age at the start of anti-osteoporotic therapy was 62.1 years, and 481 patients (86.4%) received a mean prednisolone dose of 8.4 mg/day. Persistence with anti-osteoporotic therapy was 71.9%, 61.1%, 50.1% after 1, 2, and 3 years, respectively. Factors associated with persistence were the diagnosis of connective tissue disease and use of glucocorticoids. Among patients who discontinued therapy, the most frequent reason for discontinuation of anti-osteoporotic therapy was onset of adverse events (32.4%).

**Conclusions:** Patients with rheumatic disease receiving anti-osteoporotic therapy had a higher persistence than postmenopausal patients with osteoporosis. These results suggest that rheumatologists should take a proactive stance on managing osteoporosis in patients with rheumatic disease.

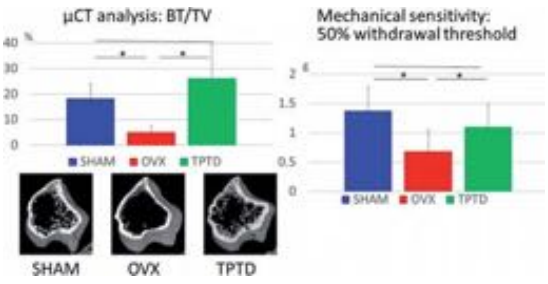
**Disclosure of Interest:** None declared

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## THU0487 TERIPARATIDE IMPROVED BONE LOSS AND HYPERALGESIA IN A MOUSE MODEL OF OSTEOPOROSIS

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**Background:** Osteoporosis may cause not only fractures but also chronic back pain in elderly women. Bente reported that postmenopausal women with severe osteoporosis who were prescribed teriparatide (TPTD) in standard clinical practice had a reduction in back pain. However, there have been no reports regarding the effect of TPTD on pain in animal models of osteoporosis.
**Objectives:** The objective of the current study was to investigate the effect of TPTD on pain-related behavior in ovariectomized (OVX) mice.
**Methods:** Female ddY mice (8 weeks old) were ovariectomized and assigned to 3groups; SHAM-operated mice treated with vehicle (SHAM), OVX mice treated with vehicle (OVX), OVX mice treated with TPTD (TPTD).
Starting immediately after surgery, vehicle or 40μg/kg TPTD was injected subcutaneously 5 times a week for 4 weeks.
The proximal tibial metaphysis were analyzed three-dimensionally by μCT 4 weeks after surgery (each group; 8 mice).
Mechanical sensitivity was tested using von Frey filaments 4 weeks after surgery. To evaluate the withdrawal threshold, each von Frey filaments was applied once, starting with 0.008g and increasing until a withdrawal response was reached, which was considered a positive response. The lowest force producing a response was considered the withdrawal threshold. To evaluate the 50% withdrawal threshold, seven von Frey filaments were applied to the middle of the plantar surface. Testing was initiated with the 0.6g filament. In the absence of a clear paw withdrawal response, increasingly stronger filaments were presented consecutively, until one of them was found to elicit such a response. If the 0.6 g filament elicited a response, filaments with decreasing strength were presented until determination of the first one which failed to cause paw withdrawal. Data was collected using the up-down method.
To identify osteoclasts in hindlimb bone, we used the tartrate-resistant acid phosphatase (TRAP) method. TRAP-positive multinucleated cells were scored as osteoclasts. Measurements were made within an area the proximal tibial metaphysis starting immediately below the growth plate. Histomorphometry was conducted to quantify the number of osteoclasts.
**Results:** μCT analysis of the proximal tibial metaphysis showed that bone volume/tissue volume (BV/TV) and trabecular number (Tb.N) were significantly less in the OVX group than in the SHAM group, whereas trabecular separation (Tb.Sp) was significantly greater in the OVX group than in the SHAM group. In the TPTD group, BV/TV and Tb.N were significantly greater than in the OVX group, whereas Tb.Sp was significantly less than in the OVX group.
The withdrawal threshold was significantly lower in the OVX group than in the SHAM group, and it was significantly higher in the TPTD group than in the OVX group. Similarly, the 50% withdrawal threshold was significantly lower in the OVX group than in the SHAM group, and it was significantly higher in the TPTD group than in the OVX group.
The number of osteoclasts was significantly higher in the OVX group than in the SHAM group, whereas it was higher in the TPTD group than in the OVX group, but there were no significantly changes.




**Conclusions:** TPTD prevented ovariectomy-induced bone loss. In addition, mechanical hyperalgesia in hindlimbs significantly improved in OVX group compared with TPTD group. The results suggest that TPTD prevented postmenopausal osteoporotic pain.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3809

## THU0488 NEW ZOLEDRONATE DATABASE SIGNIFICANTLY IMPROVES PRE-ASSESSMENTS AND WAITING TIMES TO REPEAT INFUSIONS – RESULTS FROM A QUALITY IMPROVEMENT PROJECT

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**Background:** IV Zoledronate is used to treat osteoporosis patients who failed an oral bisphosphonate. Checking adjusted calcium (Ca), serum creatinine (Cr), estimated GFR, vitamin D and PTH before infusion can help optimise treatment outcomes. Previous audit demonstrated that our department was failing to reach 100% pre-infusion assessment (92% had Ca, Cr and eGFR; 85% Vitamin D and 74% PTH). Our previous zoledronate data was on an MS Excel spreadsheet with no audit or next due date functionality (service target: to deliver annual infusions within a month of due date). A database with these functionalities is not commercially available.
**Objectives:** We aimed to develop such a database, and demonstrate its Quality Improvement/audit functionality through analysis of waiting times to repeat infusions, and re-audit of pre-infusion assessments.
**Methods:** The new database was created in MS Access 2010 and introduced in Oct 14. Fields included Ca, Cr, eGFR, vit D and PTH. Functions were created to automatically generate next due date, and to view a list of patients in order of next due date. Waiting times were compared for repeat infusions before and after database was introduced. A proportion of all consecutive patients receiving infusions (first and repeat) since database started were selected for analysis of pre-infusion assessment. Biochemistry laboratory ranges were used for interpreting Ca (2.20–2.60mmol/l) and PTH (1.1–7.4 pmol/L); and to stratify total 25 hydroxy vit D (nmol/L; as used in previous audit: <25 = deficiency; 26–50 = insufficiency; 51–75 = adequate; 76–250 = optimal). EGFR (ml/min) was stratified according to the Chronic Kidney Disease stage (>90 = 1; 60–89=2; 30–59=3; 15–29=4; <15=5). Data were transferred to MS Excel 2010 for processing and descriptive statistics.
**Results:** 68 consecutive patients before Oct 14 and 65 consecutive patients from Oct 14 to Jan 16 who received repeat infusions were eligible for comparison. Improvements included more receiving infusion within target date (23.5% v 35.4%); and reduced waiting time (days) beyond target (mean 62.6 v 38.2; median 31 v 18). 35 consecutive patients who received zoledronate between Oct 14 and Feb 15 were identified for analysis of pre-assessments (27 women, 8 men; mean age 76.6±9.4yrs, range 52–91yrs). 35 (100%) had Cr and eGFR, 34 (97%) had Ca and vit D, and 25 (71%) had PTH. Mean Ca was 2.34±0.1mmol/l (range 2.2–2.59); Cr 88.5±17.4umol/l (59–122); eGFR 67.1±13.5ml/min (41–90); Vit D 77.2±30.5 (32–203) and PTH 5.1±2.3pmol/L (2–9.9). Vit D was deficient in 0, insufficient in 3 (8.8%), adequate in 15 (44.1%) and optimal in 14 (41.2%) (1 insufficient sample). eGFR was normal in 8 (22.8%); CKD2 in 19 (54.3%); CKD3 in 8 (22.9%) and none in CKD4 or 5.
**Conclusions:** Introduction of the purpose-built new database has achieved significant reduction in waiting times, and improvements in pre-infusion assessment (100% Cr and eGFR, and 97% Ca and Vit D compared to previous audit's 92% for Cr, eGFR and Ca and 85% for Vit D). The re-audit also confirmed overall improvement in Vit D levels (85% v 46% adequate or optimal), and 100% safety with respect to acceptable Ca and eGFR pre-infusion. We expect further improvements in waiting times for repeat infusions on a later re-audit when all patients entered on the database for first infusion complete a repeat infusion.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4744

## THU0489 DAILY TERIPARATIDE TREATMENT AFTER BISPHOSPHONATE THERAPY IN OSTEOPOROSIS OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Ithough medication of rheumatoid arthritis (RA) has been improved by early intensive treatment using MTX and biological DMARDs for decades, treatment of concomitant disease in RA patients, such as osteoporosis (OP), will be more important to improve activity of daily living of RA patients. We reported efficacy of daily teriparatide (TPTD) on OP in RA patients in EULAR 2014[1)] and EULAR 2015[2)]. Although many drugs for OP treatment can be used in clinical practice, information of effect of switching drugs are lacking and needed. Better switching strategy in OP treatment are not well understood.
**Objectives:** This study investigated the efficacy of TPTD after bisphosphonate (BP) treatment in OP of RA patients (RA-OP).
**Methods:** 49 females with RA-OP were included in this study. 2 years had passed after the initiation of TPTD. 32 cases were treated using BP before TPTD (BP-G) and 17 cases were treatment-naïve or treated using only activated-vitamin D3 (N-G). Bone mineral density of lumbar spine (LSBMD) and total hip (THBMD) were measured every 6 month. Bone turnover markers (BTMs) were measured every 6 month (BAP, P1NP, NTX, TRACP-5b). Data were compared between BP-G and N-G.
**Results:** There were no significant differences in most of baseline characteristics between two groups except for CRP value at baseline (0.52mg/dl in BP-G and 0.68mg/dl in N-G).Used BPs were risedronate in 26 cases, alendronate in 4 cases and minodronate in 2 cases. There were no significant differences in LSBMD and THBMD at baseline between 2 groups. Baseline BAP in BP-G were significantly low compared with that in N-G (15.1μg/l vs. 18.6μg/l). Baseline NTX in BP-G were also significantly low compared with that in N-G (15.2 nmolBCE/L vs. 21.6 nmolBCE/L). P1NP and TRACP-5b were comparable between two groups. Mean LSBMD and THBMD in both group were significantly increased during TPTD treatment (Fig1). %increase of LSBMD and THBMD were compared between two groups and there were no significant differences (Fig2). Four BTMs

were increased during TPTD treatment in both group. Although there were no significant differences in % increase of BAP, P1NP and TRACP-5b during TPTD treatment, %increase of NTX in BP-G was significantly high compared with that in N-G (84.3% in BP-G and 57.4% in N-G at 6 month).

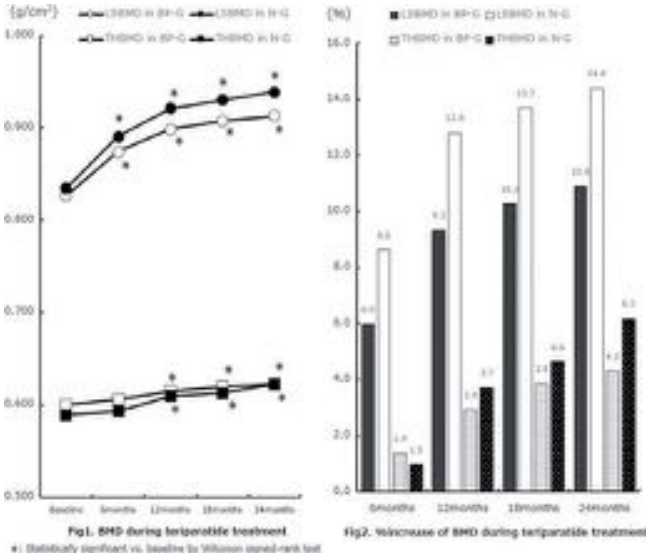


Fig1. BMD during teriparatide treatment

Fig2. %increase of BMD during teriparatide treatment

**Conclusions:** TPTD was effective in not only N-G but also BP-G. Although bone turnover was slightly inhibited and slow in BP-G, TPTD upregulated bone turnover preferably and resulted in increase of BMD in not only N-G but also in BP-G. This study suggested that TPTD was one of options after BP treatment in RA-OP.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2508

## Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

### THU0490 ASYMPTOMATIC GOUT IN CHRONIC KIDNEY DISEASE: PREVALENCE STUDY USING DUAL ENERGY CT AND ULTRASOUND

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**Background:** Gout is a metabolic disorder of purine metabolism with primary manifestations of acute and chronic arthritis and tophus formation. Asymptomatic gout is defined as tophus formation without any clinical symptoms of arthritis. Detection of asymptomatic gout may be important, as it can cause bone erosions and joint destruction. Reduced kidney function is an important risk factor for gout[1]. The prevalence of hyperuricemia and gout increases with decreasing estimated glomerular filtration rate (eGFR) independent of other risk factors for gout[1]. Dual Energy CT (DECT) and ultrasound (US) are novel radiological techniques to detect monosodium urate (MSU) crystals.

**Objectives:** The aim of this study was to assess the prevalence of asymptomatic gout in patients with chronic kidney disease (CKD) stages 4 or 5, this is an eGFR $<30mL/min/1.73m^2$.

**Methods:** Patients with CKD stages 4 or 5 were recruited from a nephrology outpatient clinic in a university hospital. Exclusion criteria were a history of arthritis or gout, the use of urate lowering drugs and the use of more than 7.5 mg prednisone/day. The joints of the feet, ankles and knees were examined with US and DECT. The OMERACT criteria for gout lesions on US were used: tophi, MSU deposits and double contour sign[2]. A DECT was scored positive if at least one tophus was present[3].

**Results:** Twenty-five patients were included. Patients were recruited from a population of 387 patients with CKD stages 4 or 5, 208 were excluded because they did not meet the in-/exclusion criteria, 58 were not treated at the outpatient clinic anymore at time of inclusion and the rest declined participation. The mean (SD) age of the participants was 65 (12), 18 were man and the mean (SD) duration of CKD was 5.3 (3.8) years.

| | | US: Double contour | | US: MSU depositions | | US: Tophi | | Positive DECT | | Any gout sign on US or DECT | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | NO | YES | NO | YES | NO | YES | NO | YES | NO | YES |
| Serum uric acid groups | <0.42 | 4 | 1 | 3 | 2 | 5 | 0 | 4 | 1 | 3 | 2 |
| | ≥0.42 | 13 | 5 | 11 | 7 | 15 | 3 | 16 | 2 | 9 | 9 |
| Total N (%) | | 17 (74) | 6 (26) | 14 (61) | 9 (39) | 20 (87) | 3 (13) | 20 (87) | 3 (13) | 12 (52) | 11 (48) |

Table 1. Findings on ultrasound and DECT compared for uric acid group. Serum uric acid is in mmol/L, <0.42 is a normal serum uric acid, ≥0.42 is a high serum uric acid.

Twelve out of 25 patients (48%) had any sign of gout on DECT or US, nine patients (36%) had MSU depositions, four (16%) had a tophus, seven (28%) had a double contour sign and three patients (13%) had a positive DECT. Patients with MSU depositions were older (73 vs. 60 years, p=0.007). Gout signs were far more common in the high uric acid group, this is an uric acid of 0.42 or higher (table 1), although this did not reached a statistical significance.

**Conclusions:** Our study shows a high prevalence of gout in patients with CKD. To our knowledge this is the first study that assessed the prevalence of asymptomatic gout in patients with CKD stages 4 or 5. Radiological signs of gout were more frequently found in patients with higher uric acid. The relevance of these findings needs further research.

**References:**

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2678

### THU0491 A NOVEL METHOD OF ESTIMATING EXTRA-RENAL CLEARANCE OF URIC ACID

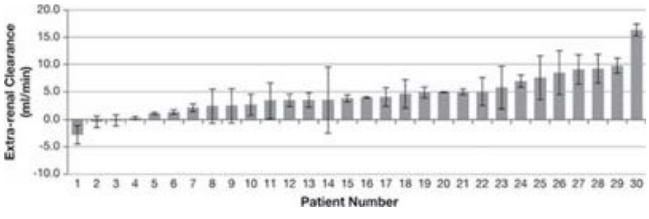
D. Hyndman, S. Liu, J. Hall, J.N. Miner. *Ardea Biosciences, Inc., San Diego, United States*

**Background:** Serum uric Acid (sUA) concentration is a function of uric acid production and both renal and extra-renal clearance. Decreased renal clearance is well understood as a contributing factor in gout. Extra-renal clearance, however, has not been as well characterized. Estimating extra-renal clearance would allow the classification of patients with gout as having high or low extra-renal clearance. Additionally, since production must equal the sum of urinary excretion and extra-renal elimination, determining the amount of extra-renal elimination would allow estimation of the rate of uric acid production. With this information, subjects could be characterized by all three parameters that determine sUA levels.

**Objectives:** To estimate the extra-renal uric acid clearance of patients with gout.

**Methods:** sUA and 24-hour urinary uric acid excretion (24hrUUE) were measured in 30 patients with gout in the absence and presence of a specific URAT1 inhibitor that lowers uric acid by increasing renal uric acid excretion. In these patients, at least a 1 mg/dl decrease in sUA was achieved with the URAT1 inhibitor at steady state. Extra-renal clearance was calculated by dividing the drug-induced increase in 24hrUUE by the drug-induced decrease in sUA and adjusting units to yield ml/min. This calculation was performed twice for each patient as two sets of measurements for each patient were taken. The two calculated clearance values were then averaged.

**Results:** The average estimated extra-renal clearance of the 30 patients with gout was 4.4 ml/min. Maximum extra-renal clearance was 16 ml/min, while some patients apparently had no measurable extra-renal elimination (Figure).




**Conclusions:** Estimated extra-renal elimination varies greatly among patients with gout. Some patients have very low estimated extra-renal clearance which likely contributes to high sUA concentration.

**Acknowledgement:** Research sponsored by Ardea Biosciences/AstraZeneca. Editorial support was provided by PAREXEL and funded by AstraZeneca.

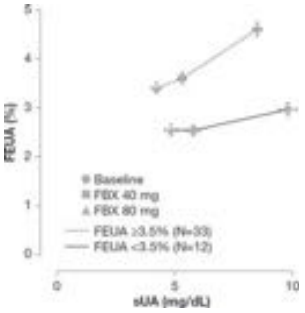
**Disclosure of Interest:** D. Hyndman Employee of: Ardea Biosciences, Inc., S. Liu Employee of: Ardea Biosciences, Inc., J. Hall Employee of: Ardea Biosciences, Inc., J. Miner Employee of: Ardea Biosciences, Inc.

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## THU0492 URIC ACID TRANSPORT KINETICS IN THE KIDNEY: DETECTION OF RENAL SECRETION AND THE MECHANISM OF LOW FEUA

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**Background:** Approximately 70% of urate is excreted by the kidney. Renal excretion is governed by reabsorption and secretion in the proximal convoluted tubule. However, there is little direct evidence that renal uric acid secretion occurs in humans, and it is unknown if higher renal uric acid reabsorption or low renal uric acid secretion contributes to the low fractional excretion of uric acid (FEUA) observed in patients with gout.
**Objectives:** The objectives of the study were to test the hypothesis that uric acid secretion occurs in humans, to distinguish uric acid secretion from incomplete reabsorption, and to determine if insufficient secretion and/or enhanced reabsorption are responsible for low FEUA.
**Methods:** Patients with gout in a Phase II study were treated once daily with 40 and 80 mg of febuxostat (FBX), with each treatment lasting 1 week. FBX is a xanthine oxidase inhibitor that reduces uric acid production and lowers serum uric acid (sUA). sUA and FEUA were measured at baseline and at the end of each treatment. sUA (X-axis) and FEUA (Y-axis) were plotted to evaluate the kinetics of renal uric acid handling (Figure).
**Results:** Forty-five male patients with gout, with a mean (SD) age of 49±9.3 years and BMI of 32±3.9 kg/m$^2$, participated in this study. As has been observed in previous publications, decreasing sUA led to a decrease in FEUA. However, this effect reached a plateau at low sUA levels for those who had low (<3.5%) baseline FEUA; the FEUA did not decrease further when the FBX dosage was increased from 40 mg to 80 mg (Figure). The FEUA response to decreasing sUA reaches a plateau at an FEUA of ~ 2.5%. In contrast, the curve for fractional excretion of glucose reaches zero at lower plasma glucose levels.[1] Since a prominent difference in renal handling of uric acid and glucose is that glucose is not secreted while uric acid is believed to be secreted, we suggest that the plateauing of the FEUA curve at the lower sUA range is due to renal uric acid secretion. Preliminary modeling of transporter kinetics also suggests that the observed relationship between sUA and FEUA requires secretion. In addition, the sUA level at which the FEUA begins to rise (equivalent to the renal glucose threshold) is higher for those whose baseline FEUA was low, and this observation is consistent with the hypothesis that patients with gout with low FEUA have higher reabsorption capacity. To determine the ultimate contribution of secretion to low FEUA, sUA will need to be lowered even further.




**Conclusions:** We provide direct evidence for renal uric acid secretion occurring in humans. This method can also be used to determine the relative importance of candidate renal secretory transporters in the secretion of uric acid. Higher reabsorption capacity appears to contribute to low baseline FEUA.
**References:**
[1] DeFronzo RA, et al. Diabetes Care. 2013;36:3169–3176.
**Acknowledgement:** Research sponsored by Ardea Biosciences/AstraZeneca. Editorial support was provided by PAREXEL and funded by AstraZeneca.
**Disclosure of Interest:** S. Liu Employee of: Ardea Biosciences, Inc., D. Hyndman Employee of: Ardea Biosciences, Inc., J. Miner Employee of: Ardea Biosciences, Inc.
**DOI:** 10.1136/annrheumdis-2016-eular.1798

## THU0493 RACIAL DISPARITIES IN THE RISK OF STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS AS URATE-LOWERING DRUG ADVERSE EVENTS IN THE US

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**Background:** Although uncommon, the most feared adverse event of urate-lowering drugs (ULDs) is allopurinol hypersensitivity syndrome (AHS), primarily manifesting as Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). *HLA-B*5801* allele carriage (a strong determinant of AHS) varies substantially among races, which may lead to major racial disparities in the risk of SJS/TEN in the context of ULD adverse events (ULDAEs). Such information could immediately help risk stratification to prevent these severe ULDAEs.
**Objectives:** To examine potential racial disparities in the risk of SJS/TEN in the context of ULDAEs in a large, racially diverse, and generalizable population.
**Methods:** Using the Nationwide Inpatient Sample (NIS, 2009–2013), a database representative of all US hospitalizations, we examined the racial distribution of hospitalized SJS/TEN (principal discharge diagnosis) as ULDAEs (ICD-9-CM Classification of External Causes); this combination implicates allopurinol, which is the only ULD established to cause SJS/TEN. Our reference groups were the US Census population, US allopurinol users (from the NHANES), and ULDAE hospitalizations without SJS/TEN (from the NIS).
**Results:** We identified 606 patients hospitalized for SJS/TEN as ULDAEs meeting our criteria between 2009–2013 (mean age, 68 years; 44% male). Of these 606 patients, there was a substantial over-representation of Asians (27%) and Blacks (26%), and an under-representation of Whites (29%) and Hispanics (% too-low-to-report), compared with the US Census population (5%, 12%, 67%, and 15%, respectively). The hospitalization rate ratios for SJS/TEN among Asians, Blacks, and Whites were 11.9, 5.0, and 1.0 (referent), respectively. These associations persisted using other national referents (allopurinol users and ULDAE cases without SJS/TEN).



| Race | White | Black | Asian |
|---|---|---|---|
| **Among US Adults According to Race** | | | |
| Hospitalizations, N | 175 | 155 | 143 |
| Hospitalizations per 1,000,000 US adults | 0.22 | 1.30 | 2.84 |
| Hospitalization rate ratio (95% CI) | 1.0 (ref) | 5.0 (4.0 to 6.2) | 11.9 (9.6 to 14.8) |
| **Among US Allopurinol Users According to Race** | | | |
| US adults with allopurinol use, N | 1,840,829 | 283,564 | 52,936 |
| Hospitalizations, N | 175 | 155 | 143 |
| Hospitalizations per 1,000,000 with allopurinol users | 19.0 | 106.3 | 638.5 |
| Hospitalization rate ratio (95% CI) | 1.0 (ref) | 5.7 (4.8 to 7.1) | 32.6 (26.3 to 40.4) |
| **Among NIS Hospitalizations for ULDAE According to Race*** | | | |
| Hospitalizations for ULDAE with SJS/TEN, N (%) | 175 (29) | 155 (26) | 163 (27) |
| Hospitalizations for ULDAE without SJS/TEN, N (%) | 10,012 (60) | 2,840 (18) | 985 (6) |
| Crude OR (95% CI) | 1.00 (Ref) | 2.9 (2.5 to 4.7) | 8.3 (5.0 to 13.7) |
| Age-Sex-Adjusted OR (95% CI) | 1.00 (Ref) | 2.6 (1.7 to 4.6) | 8.5 (5.1 to 14.0) |
| Age-Sex-CAD-CKD-Diabetes-Adjusted OR (95% CI) | 1.00 (Ref) | 2.8 (1.7 to 4.5) | 8.1 (5.0 to 13.3) |

SJS/TEN = Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis; ULDAE = Urate-Lowering Drug Adverse Event
CAD = coronary artery disease; CKD = chronic kidney disease
*Hispanics, other races, and those with missing race data are not reported as their unweighted cell size was 10 or fewer, in which case individual group reporting is not allowed according to the Healthcare Cost and Utilization Project Data Use Agreement.

**Conclusions:** These national data indicate that Asians and Blacks have a substantially higher risk of SJS/TEN as ULDAEs than Whites (or Hispanics), correlating well with corresponding frequencies of *HLA-B*5801* in the US population (i.e.,7.4%, 4%, 1%, and 1% among Asians, Blacks, and Whites, Hispanics, respectively). As no other ULDs available in the US have been established to cause SJS/TEN, these findings support the use of vigilance in these minorities when considering allopurinol.
**Disclosure of Interest:** None declared
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## THU0494 SKIN EVENTS WITH FEBUXOSTAT IN GOUT PATIENTS WITH PREVIOUS SKIN REACTIONS TO ALLOPURINOL. A RETROSPECTIVE REVIEW

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**Background:** Allopurinol is the most used urate-lowering agent for patients with gout. However, 10% of patients show intolerance to this drug, often at skin, which can be severe. Febuxostat is a novel non-purine selective xanthine oxidase inhibitor that has been proposed for allopurinol-intolerant patients due to its different structure. However, data regarding safety in those with previous skin reactions to allopurinol is still limited (1,2).
**Objectives:** To assess the cutaneous safety of febuxostat when used in patients with previous skin reactions to allopurinol.
**Methods:** Retrospective review of patients with crystal-proven gout treated with febuxostat in our Unit until December 2015. Those with previous skin reaction to allopurinol were selected. We registered epidemiological (age, gender), clinical (skin events) and laboratory variables (serum uric acid, glomerular filtration rate). The primary study variable was the rate of patients also presenting skin reactions with febuxostat. A descriptive analysis with estimation of the 95% confidence interval (95%CI) was performed.
**Results:** Out 102 gout patients treated with febuxostat in our Unit, we identified 24 patients with prior allopurinol-related skin events. The median age was 68.5 years (p25-p75 53.7–71.0), being 18 males (75%). Most used starting dose of febuxostat was 80mg/d (n=16), others were 5mg/d (n=1), 40mg/d (n=4) or 120mg/d (n=3). Median glomerular filtration rate at that time was 77.2 mL/min (62.7–68.6). We have identified five patients (20.8%; 95%CI 3–38%) who also

Characteristics of patients developing skin reactions with both allopurinol and febuxostat (5/24)

| Gender | Age | Allopurinol start | | Febuxostat start | | Rash with febuxostat | Outcome with benzbromarone |
|---|---|---|---|---|---|---|---|
| | | Dosage (mg/d) | GFR (mL/min) | Dosage (mg/d) | GFR (mL/min) | | |
| Female | 70 | 50 | 78 | 120 | 77.2 | Nonspecific | No rash |
| Male | 69 | N/A | 90 | 40 | 90.5 | SJS | No rash |
| Female | 68 | 100 | 52 | 80 | 80.3 | Nonspecific | No rash |
| Male | 45 | 50 | 90 | 80 | 90.9 | Nonspecific | No rash |
| Female | 41 | 300 | 40 | 5 | 40.9 | Nonspecific | No rash |

GFR: glomerular filtration rate; SSJ: Stevens-Johnson syndrome.

developed skin reactions with febuxostat (see table): in four cases a nonspecific rash, but one suffered from a Stevens-Johnson syndrome. None of these patients presented skin reactions to benzbromarone.

**Conclusions:** In our series, one out five patients with previous skin reaction to allopurinol also developed after febuxostat. Larger studies are needed to confirm these results, but this finding strengths caution when using febuxostat in this subgroup of patients.

**References:**
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**Disclosure of Interest:** None declared

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## THU0495 EXAMINATION OF SERUM URIC ACID (SUA) LOWERING AND SAFETY WITH EXTENDED TREATMENT WITH LESINURAD AND ALLOPURINOL IN SUBJECTS WITH GOUT

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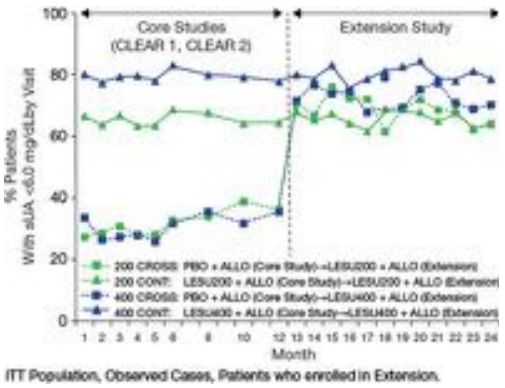
**Background:** Two replicate, randomized, core Phase III trials (CLEAR 1 and 2) reported significantly more subjects treated with lesinurad 200 mg (LESU200) or 400 mg (LESU400) combined with allopurinol (ALLO) achieved target sUA <6.0 mg/dL at 6 and 12 months than ALLO+placebo (PBO) ($P<0.0001$). The safety profile of LESU200+ALLO was comparable to ALLO+placebo, except for higher rates of predominantly reversible serum creatinine (sCr) elevation.

**Objectives:** Assess long-term safety and efficacy of LESU+ALLO therapy in subjects enrolled in the CLEAR 1and 2 extension study (NCT01808131).

**Methods:** Efficacy was assessed for those completing the core study and either 1) continuing core LESU+ALLO treatment (200CONT, 400CONT) or 2) crossing over from core ALLO+PBO to either ALLO+LESU200 (200CROSS) or LESU400 (400CROSS). Core LESU200+ALLO or LESU400+ALLO subjects and 200CONT and 400CONT extension groups are reported for safety. Efficacy endpoints included proportions of subjects with target sUA <6.0 mg/dL and mean sUA levels (ITT–observed cases). Treatment-emergent adverse events (TEAEs) were calculated as exposure-adjusted incidence rates (EAIRs; events per 100 person-years [100-PY]).

**Results:** For efficacy, the 200CONT (n=239) and 400CONT (n=232) groups receiving treatment for up to 24 months, and 200CROSS (n=121) and 400CROSS (n=122) groups, receiving treatment for up to 12 months, were analyzed. Proportions of subjects with sUA <6.0 mg/dL during core and extension are shown (Figure). Mean (SD) sUA (mg/dL) for 200CONT, 200CROSS, 400CONT and 400CROSS groups, respectively, were 6.96 (1.14), 6.92 (1.33), 6.80 (1.20) and 6.99 (1.14) at baseline of the core studies, and 5.71 (1.80), 6.68 (1.57), 5.06 (1.94) and 6.68 (1.38) at the end of the 12-month core studies. After 12 months in the extension study when all patients received lesinurad, mean (SD) sUA was 5.75 (1.77), 5.78 (1.92), 5.01 (1.95), and 5.25 (1.77), respectively.

For safety, pooled analysis on a total of 405 and 401 subjects (LESU200, LESU400 respectively), from the core studies and 239 and 232 (200CONT, 400CONT, respectively) from the extension studies, was conducted. EAIRs (per 100-PY) of TEAEs and serious TEAEs at any time during core or extension studies were 54.2 and 5.8 for LESU200 and 57.2 and 8.3 for LESU400. EAIRs of renal-related TEAEs and serious renal-related TEAEs were 7.4 and 0.5 for LESU200 and 14.2 and 0.8 for LESU400. EAIRs of kidney stone incidence rates were 0.5 and 2.0 per 100-PY for LESU200 and LESU400, respectively. EAIRs of sCr elevations ≥1.5x baseline was 7.8 and 17.0 per 100-PY for LESU200 and LESU400, respectively; resolution of sCr elevations by analysis cutoff occurred in 91.7% and 87.8% of cases, respectively.




ITT Population, Observed Cases, Patients who enrolled in Extension.

**Conclusions:** Subjects treated with LESU+ALLO therapy through 2 years continued to be at sUA target; those crossing over from ALLO monotherapy had increased proportions reach target. Safety during continued treatment was consistent throughout the core and extension studies.

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## THU0496 ASSOCIATIONS OF PLASMA URIC ACID AND PURINE METABOLITES WITH BLOOD PRESSURE IN CHILDREN: THE KOALA BIRTH COHORT STUDY

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**Background:** Elevated uric acid concentrations have been associated with high blood pressure (BP) in adults and children. An increased production of uric acid by the enzyme xanthine oxidoreductase (XOR), which is accompanied by the generation of reactive oxygen species, is a putative underlying mechanism that has so far scarcely been studied. We hypothesize that a higher XOR activity leads to increased concentrations of downstream purine metabolites, resulting in higher ratios of xanthine/hypoxanthine, uric acid/xanthine, and uric acid/hypoxanthine (figure 1).

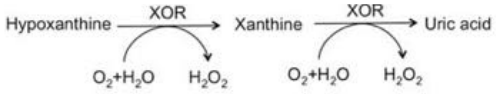



**Figure 1. Purine metabolism**
During the final stage of the purine metabolism, xanthine oxidoreductase (XOR) breaks down hypoxanthine to xanthine, and xanthine to uric acid, while reactive oxygen species are formed. These free radicals inactivate the vasodilator nitric oxide.

**Objectives:** The objectives were therefore to study the association between (i) the purine metabolites uric acid, hypoxanthine, and xanthine and (ii) the ratios of the three different purine metabolites as proxy measures for uric acid production, with systolic (SBP) and diastolic blood pressure (DBP).

**Methods:** Cross-sectional analyses were performed in a subset of 246 children from the Dutch Koala Birth Cohort Study. This cohort originates from two recruitment groups: pregnant women with either a conventional lifestyle or recruited through alternative channels. During a home visit, a nurse collected a venous blood sample and measured BP three times after a 5-minute rest, with an automated BP monitor. Furthermore, parents were in instructed to measure their child's BP on three consecutive days, in the morning and evening, using the same monitor. Purine metabolites were determined with UPLC-MS/MS. Data were analysed using a multivariable generalized estimating equations model, including repeated BP measurements, with an exchangeable correlation structure. Analyses were adjusted for sex, age, BMI, recruitment group, place and mode of delivery (hospital *vs.* at home; natural *vs.* caesarean section), maternal smoking during pregnancy (active and passive), total physical activity, and dietary intake at four years of age (total energy intake [kcal], energy from carbohydrates and protein [%] and fibre intake [grams]).

**Results:** At a mean age of 7.1 yrs, mean plasma concentrations were 202.8 μmol/L (SD 37.7) for uric acid, 4.60 μmol/L (SD 6.93) for hypoxanthine, and 0.53 μmol/L (SD 0.17) for xanthine. Average BP was 104.3 mm Hg (SD 10.0) systolic and 63.4 mm Hg (SD 10.6) diastolic. Higher ratios of uric acid/xanthine and xanthine/hypoxanthine were associated with higher DBP (adj. β 0.01 mm Hg; 95%CI 0.00 to 0.02; $P$=0.03; and adj. β 0.11 mm Hg; 95%CI 0.01 to 0.21; $P$=0.03), respectively, but not with SBP. Uric acid, xanthine, and hypoxanthine concentrations and the ratio uric acid/hypoxanthine were not associated with SBP nor DBP ($P\geq0.05$).

**Conclusions:** In multivariable-adjusted analyses, DBP in children was significantly associated with the ratios of uric acid/xanthine and xanthine/hypoxanthine, and might, as hypothesized, be proxies for uric acid production. The ratio uric acid/hypoxanthine was not associated with BP, may be explained by differential excretion or autofeedback (of non XOR metabolism).
**Disclosure of Interest:** None declared
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## THU0497 ULTRASOUND IN GOUT: WHICH JOINTS SHOULD BE EVALUATED CONCERNING DIFFERENCES BETWEEN THE EARLY AND LATE GOUT?

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**Background:** The sensitivity of ultrasound (US) signs of monosodium urate (MSU) deposition in symptomatic joints is only 60% with negative predictive value of 62% while multiple joins examination gives better sensitivity and better negative predictive value with less specificity though [1]. The 12 sites' combination assessment has been proposed by Naredo and colleagues with 84, 6% sensitivity and 83, 3% specificity in late gout [2]. Does it fit in the early gout?
**Objectives:** To compare the frequencies and specificity of US dual contour sign (DC), tophus (T) in early versus late gout using multiple investigation of joints and tendons, most often affected by gout, in order to define the most suitable test for diagnosis of both early and late stage of the disease.
**Methods:** Prospective single centre case - control study was performed. Crystal - proven gout compared according healthy controls. Systematic US assessment of 36 joints and 4 tendons (patellar and triceps) was done by rheumatologist, blinded to study group and clinical findings. The reliability of the US assessment was checked in a web – based exercise, evaluated by kappa coefficient. The early (symptoms $\leq$2 years) and rest gout was compared according frequency of DC and T in different anatomical sites using chi – square test. The specificity and sensitivity of T and DC in total investigated sites, in 10, 6 and 4 anatomical areas has been compared.
**Results:** 50 patients with gout (16 early, 34 late gout) and 36 age matched healthy controls were investigated. In late gout US T sign was most often found in I MTF (79,4%), patellar tendon (39,7%), triceps tendon (38,2%), wrist (33,8%), II MCP, II MTF joint; DC sign - in I MTF (45,6%), knees (38,2%), ankles (35,2%), II MCP (27%), II MTP, III MTP. In early gout the most often T was in I MTF (65, 7%) and wrist (21,9%), DC – in I MTF (25%), ankles (22%), II MTF. There were no T found in II MCP and PIP joints, 0,6% in the rest MCP, less T found in m. triceps and patellar tendons than in late gout ($p<0,001$ and $p<0,01$ accordingly). There were less DC found in total MCP, II MCP, total PIP and knees joints in early than in late gout with $p<0,001$; $<0,05$; $<0,01$; $<0,01$ accordingly. The best balance between sensitivity (91%) and specificity (81%) has been noticed with 6 US abnormalities in 4 joints. The intrareader reliability was good (mean kappa 0,712).
**Conclusions:** Our results suggest, that US signs of urate deposition in metacarpophalangeal and proximal interphalangeal joints, m. triceps and patellar tendons are very seldom found in gout with symptoms duration up to two years and might be the symptoms of late disease. Bilateral assessment of first metatarsophalangeal joint for tophus, dual contour sign and knee femoral cartilage for dual contour sign shows best balance between sensitivity and specificity diagnosing both early and late gout.
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## THU0498 GENDER DIFFERENCES IN THE PHENOTYPE OF GOUT AND ITS EFFECT ON CLASSIFICATION USING THE ACR-EULAR CRITERIA

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**Background:** Gout is a quite prevalent disorder in affluent countries, with the prevalence in males being 3–4 times higher than in females [1]. In practice, gout may be perceived as a "males" disorder and it has been suggested that the phenotype of gout differs between males and females, due to selection bias or by nature of the disease.
**Objectives:** To analyse whether there are differences between males and females in the phenotype of gout and in the performance of the ACR-EULAR classification criteria.
**Methods:** We used the multi-country SUGAR data set in which the ACR-EULAR classification criteria were constructed and validated [2]. In SUGAR, patients with at least one swollen joint or subcutaneous tophus conceivably being due to gout were consecutively included. Presence of MSU crystals in synovial fluid or tophus aspirate was the gold standard for gout, as assessed at inclusion, using microscopy by certified examiners in all included patients. Gout manifestations were standardly assessed without knowing the results of the microscopy. Gout manifestations included in the ACR-EULAR classification criteria were compared between male and female MSU positives. Sensitivity and specificity of the ACR-EULAR criteria, calculated without MSU results, were compared between males and females. To preserve power, the development and validation data sets of SUGAR were combined.
**Results:** There were 983 subjects included (71% male), of whom 52% (509/983) were MSU crystal-positive. Sixty-three percent (440/702) of the males and 25% (69/281) of the females were MSU crystal-positive, respectively ($p<0.0001$). There were no large ($>10\%$) or significant ($p<0.05$) differences between male and female MSU positives regarding: previous or current involvement of MTP1, mono/oligo/poly-arthritis, joint erythema, painfulness for touch, tophus, largest pain increase within 24 hours, highest level of Serum Uric Acid (SUA) level without treatment, current level of SUA, occurrence of erosions on X-ray, or double contour sign on ultrasound. Male MSU positives more frequently reported: disablement (98% versus 87%; $p<0.0001$), symptom resolution within 14 days (84% versus 65%; p=0.0002), complete resolution (86% versus 70%; p=0.0004). In the complete sample of 983 subjects, the classification system lead to a median (P25-P75) score of 5 (2–8) in females and 9 (6–14) in males ($p<0.0001$). Sensitivity and specificity of the classification system to detect MSU crystal positivity were 86% and 79% in the complete sample, and 87% and 89% for females and 85% and 70% for males.
**Conclusions:** Male and female gout patients are similar on most important aspects of the gout phenotype. The ACR-EULAR classification criteria perform well in both males and females; sensitivity is the same in males and females, while specificity was better in females.
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**Acknowledgement:** We are grateful for the contributions of all investigators who submitted subjects in the SUGAR study.
**Disclosure of Interest:** None declared
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## THU0499 NEUTROPHIL EXTRACELLULAR TRAPS (NETS): A SHARED FEATURE OF ACUTE MICROCRYSTALLINE ARTHRITIS

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**Background:** Neutrophil extracellular traps (NETs) are web-like structures, composed of nucleic acids, histones and granular enzymes, including myeloperoxidase and elastase, that have a physiological crucial role in innate immunity response by trapping microbes. In addition, NETs have been identified as regulators of many inflammatory and autoimmune disorders, including crystal-induced arthritis.[1,2] In particular, a key role in the pathogenesis of gout flares has been postulated for NETs. During gout attacks, NET aggregates should package MSU crystals with a concomitant degradation of proinflammatory cytokines, leading to the rapid resolution of the inflammatory phase.[3]
**Objectives:** To evaluate NET expression in synovial fluid from acute CPPD arthritis and to compare NET release between acute MSU and CPPD arthritis.
**Methods:** Synovial fluid was collected from patients with active gout or pseudogout attack (n=5 for each group) and immediately centrifuged (805 rad) to separate cells from supernatant.
*Polymorphonuclear leukocytes* were counted and immediately processed for morphological evaluation under transmission electron microscopy (Zeiss EM 109; 4000x). NET expression was evaluated by fluorescence microscopy using SYTOX Green (Life Technologies) and neutrophil elastase specific antibody (ABCAM). Fluorometric quantification of NET components, DNA and neutrophil elastase, was performed in supernatant (Cary Eclipse Varian; exc/em 503/526). Results were normalized to cells/mm$^3$. Peripheral blood neutrophils from healthy donors stimulated with PMA were used as positive controls whereas PMA-untreated neutrophils were used as negative ones.
All the experiments were performed according with Helsinki guidelines.
**Results:** Extracellular material morphologically compatible with NETs was observed by electron microscopy in samples from both acute MSU and CPPD arthritis. NET structures were confirmed by the presence of extracellular DNA and neutrophil elastase at immunofluorescence.
Fluorometric quantification of extracellular DNA and neutrophil elastase showed an increased NET release in both gout and pseudogout samples compared

with negative controls ($p<0.01$). No significant differences in NET release were measured between acute MSU and CPPD arthritis samples.
**Conclusions:** Beyond confirming NETs in acute MSU arthritis, we have evidence of NET release in synovial fluid from acute CPPD arthritis. Our preliminary data suggest that the release of NETs could be a common physiophatological pathway to both crystral induced arthropaties.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3928

## THU0500 FREQUENCY OF IL-1 GENE CLUSTER POLYMORPHISM AND ITS RELATIONSHIP WITH CLINICAL FINDINGS IN PATIENTS WITH GOUT

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**Background:** IL-1β has role in promotion of acute gout inflammation. The relationship of IL-1 with comorbid conditions and many other disorders has been investigated previously. Gout is an auto-inflammatory disease. Activation of IL-1 gene can contribute to pathogenesis.
**Methods:** The study included 70 patients with gout and 106 age- and sex-matched healthy volunteers. By using genomic DNA isolated from patients and healthy volunteers, 5 polymorphic gene regions (rs16944, rs2234650, rs1800587, rs1143634 and rs315952) were analyzed by using PCR. Genotyping was performed by using Melting Curve Genotyping analysis.
**Results:** Mean age was 57.73 ± 10.2 years in the patient group and 57.42 ± 8.53 years in the control group. The frequency of IL1 rs16944 gene polymorphism of heterozygous (AG) genotype was found to be increased in the patient group compared to controls (61.4% vs. 40.6%; p=0.01). Genotype distribution of remaining gene polymorphisms was similar in both groups. When each gene polymorphism was assessed regarding allele frequency, no significant difference was detected between patient and control groups ($p>0.05$). It was seen that CRP values (p=0.011) and number of attacks per year (p=0.035) were higher in patients with rs2234650 wild type (CC).The haplotype analysis was performed for rs2234650, rs1143634 and rs315952 which could have significant association with disease. Similar haplotype distribution was observed in both groups.

Table 1. Mean laboratory and clinical values according to polymorphisms

| Polymorphism | | CRP | LDL | PLT | BMI | Number of attack per year |
|---|---|---|---|---|---|---|
| | | mg/dl | mg/dl | K/uL | kg/cm$^2$ | |
| rs16944 | Wild | 0.52±0.85 | 121±24.8 | 259.5±94.8 | 29.5±1.9 | 2±0.8 |
| | Heterozygous | 2.62±14.58 | 112.6±46.6 | 254.4±83.6 | 28.7±3.8 | 1.7±0.7 |
| | Mutant | 0.66±1.43 | 111±47 | 228.2±58.4 | 29.2±3.6 | 1.7±0.7 |
| rs1143634 | Wild | 0.40±0.46 | 105.7±38.5 | 254.4±85.2 | 29.2±3.8 | 1.8±0.7 |
| | Heterozygous | 5.72±21.91 | 117.7±49.2 | 221.4±56.3 | 28.2±3.7 | 1.6±0.6 |
| | Mutant | 0.41±0.39 | **165.7±70.3** *p=0.045* | 279.2±36.0 | 29.5±2.8 | 1.5±0.5 |
| rs1800587 | Wild | 0.40±0.48 | 106.1±36.8 | 246.7±78.8 | 28.9±3.4 | 1.7±0.7 |
| | Heterozygous | 5.44±21.36 | 114.4±51.8 | 274.7±84.5 | 29.6±4.4 | 1.9±0.8 |
| | Mutant | 0.43±0.46 | 145.2±62 | 244.5±50.9 | 27.7±3.0 | 1.4±0.5 |
| rs2234650 | Wild | **4.83±20.36** *p=0.011* | 99.3±35.4 | 262.6±101 | 28.9±2.8 | **2±0.75** *p=0.035* |
| | Heterozygous | 0.37±0.54 | 123.06±50.9 | 233.7±54.6 | 27.6±4.20 | 1.6±0.7 |
| | Mutant | 0.55±1.23 | 122.05±49.8 | 235.5±48.8 | 30.1±4.2 | 1.5±0.7 |
| rs315952 | Wild | 2.60±13.95 | 116.5±50.2 | 254.8±82.5 | 29.3±3.7 | 1.8±0.7 |
| | Heterozygous | 0.28±0.42 | 102.24±31.1 | **215.4±61.3** *p=0.014* | **27.8±3.7** *p=0.049* | 1.4±0.6 |
| | Mutant | 0.38±0.35 | 111±34.7 | 283±17.9 | 30±2.44 | 0.95±0.5 |

**Conclusions:** Although there was no significant difference in the distribution of IL-1 gene polymorphism, it is seen that the presence of some genotypes could affect clinical course of gout.
**Disclosure of Interest:** None declared
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## THU0501 ZOLEDRONIC ACID TREATMENT IN BONE MARROW EDEMA SYNDROME

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**Background:** Bone marrow edema (BME) syndrome describes a clinic-radiological entity in which transient subacute or chronic joint pain is associated with characteristic MRI findings (Thiryayi et al.). The etiology remains unknown and can result in significant disability (Guerra et al). Recently, it has been shown that biphosphonates can be used to achieve a reduction in BME (Ringe et al).
**Objectives:** Our objective was to review the cases of patients diagnosed with BME syndrome in the last 6 years which had also received at least one dose of zoledronic acid
**Methods:** We accessed the hospital's Pharmacy database to obtain the zoledronic acid prescriptions from January 2010 to December 2015. Subsequently we selected all the patients with diagnosis of BME syndrome (chronic joint pain AND hypointense on T1-weighted and hyperintense on T2 or STIR sequences). Pain intensity (grade 0: No pain, grade 1: Mild, grade 2: Moderate and grade 3: severe) was measured at baseline, and at 3 and 12 months after treatment with zoledronic acid. MRI changes in bone edema were assessed according to the following scale: Grade 0: No change in edema, Grade 1: Decrease <50% of the initial edema, grade 2: Decrease in >50% of the initial edema, grade 3: Disappearance of bone edema. Functionality was assessed based on whether the patient had returned to his/her daily activities. Finally, complete response was defined as patient fulfilling the following characteristics: Disappearance of pain, or recovery of daily life activities and >50% decrease on bone edema from baseline on MRI.
**Results:** 17 patients met the inclusion criteria (8 male/9 female), with a mean age of 54 years. Most commonly affected site was the ankle 9 cases (52.9%), followed by the hip: 5 cases (29.4%). 16/17 patients had baseline moderate to severe pain, and 12 months after treatment pain disappeared in 13/17. In those patients with post treatment MRI in the first 3 months (8/17), bone edema had disappeared in 5 patients (62%) and the rest of the MRIs showed a reduction of edema greater than 50%. Finally, 13 of 17 patients (76.4%) had a complete response.

Table 1. Evolution of pain, edema on MRI and functionality of patients

| | All (n=17) | Male (n=8) | Female (n=9) | Ankle (n=9) | Hip (n=5) | Knee (n=1) | Foot (n=2) |
|---|---|---|---|---|---|---|---|
| Pain (grades): Basal | | | | | | | |
| G 0: No pain | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| G 1: Mild | 1 (5.8%) | 0 | 0 | 1 | 0 | 0 | 0 |
| G 2: Moderate | 13 (76.4%) | 7 | 6 | 6 | 4 | 1 | 2 |
| G 3: Severe | 3 (17.7%) | 1 | 2 | 2 | 1 | 0 | 0 |
| 3 months | | | | | | | |
| G 0: No pain | 7 (41%) | 3 | 4 | 5 | 1 | 1 | 0 |
| G 1: Mild pain | 8 (47%) | 4 | 4 | 3 | 3 | 0 | 2 |
| G 2: Moderate | 2 (11.6%) | 1 | 1 | 1 | 1 | 0 | 0 |
| G 3: Severe | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12 months | | | | | | | |
| G 0: No pain | 13 (76.4%) | 7 | 6 | 7 | 4 | 1 | 1 |
| G 1: Mild pain | 3 (17.7%) | 1 | 2 | 2 | 0 | 0 | 1 |
| G 2: Moderate | 1 (5.8%) | 0 | 1 | 0 | 1 | 0 | 0 |
| G 3: Severe | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MRI control (change in bone edema) | (n=8) | (n=3) | (n=5) | (n=2) | (n=5) | (n=0) | (n=1) |
| No changes | 0 (0%) | 0 | 0 | 0 | 0 | 0 | 0 |
| Decreased <50% | 0 (0%) | 0 | 0 | 0 | 0 | 0 | 0 |
| Decreased >50% | 3 (37.5%) | 2 | 1 | 1 | 1 | 0 | 1 |
| Disappearance of edema | 5 (62.5%) | 1 | 4 | 1 | 4 | 0 | 0 |
| Complete response | | | | | | | |
| 12 months | 13/17 (76.4%) | 5/8 | 8/9 | 7/9 | 4/5 | 1/1 | 1/2 |

**Conclusions:** The present study shows that zoledronic acid may be a reasonable therapeutic option in bone marrow edema syndrome, as >75% of the treated patients had a complete response. This is the largest series of patients with bone marrow edema treated with zoledronic acid, but more prospective studies are needed.
**Disclosure of Interest:** None declared
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## THU0502 COMPARISON OF LOW DOSES OF SYSTEMIC CORTICOSTEROIDS THERAPY IN DIABETIC PATIENTS WITH OLIGOARTICULAR OR POLYARTICULAR GOUT FLARES: AN OBSERVATIONAL RETROSPECTIVE STUDY

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**Background:** ACR and EULAR recommendations in management of gout flares with oligoarticular involvement points that systemic corticosteroids should be strongly considered in patients with oligoarticular gout flares. However, some considerations must be taking into account before been used, especially in diabetic patients with an unstable glycemic control of with history of hyperglycaemic states after corticoids administration. Instead of avoiding its use, some clinicians use doses lesser than recommended in such patients with different results.
**Objectives:** To compare the effectiveness of different doses of corticoids in diabetic patients with acute oligoarticular gout flares fixed to weight and colchicine doses.
**Methods:** An observational retrospective study was performed. Electronic charts of diabetic patients who consulted to our A&E department from 2013 and 2015 and were diagnosed by oligoarticular gout flare were identified and revised. Registries included patients with oligoarticular gout flares who were not treated with parenteral corticoids or joint infiltrations. They were grouped according to the corticoids dose received fixed by weight and colchicine treatment. Main outcome variables were: need of further consultation before 14th day, VAS-pain score at 7th and 14th day, hyperglucemic states and time off work, where applied. Treatments with systemic corticoids were classified in two arbitrary groups: up to 0.30mg/kg/day (Group I) and 0.31 to 0.49mg/kg/day (Group II). Patients who were treated with higher doses were considered regular doses and were excluded.

**Results:** During the period of observation, 81 registries of diabetic patients diagnosed by gout flares with more than a joint involved were detected. Among them, only 62 had complete registries of weight (diabetic control at primary care facility) and complete follow up assessment after gout flare. 29 and 32 patients were included in groups I and II, respectively. Table 1, summarizes the results of the study.

| Variable | Group I <0.31mg/Kg/day | Group II 0.31-0.49mg/Kg/day | Statistics |
|---|---|---|---|
| Age and SD | 55.0 SD 8.1 | 57 SD 6.4 | *P*=0.286 |
| Male proportion | 27/29 (93.1%) | 31/32 (96.9%) | *P*=0.600 |
| Time after tappering | | | |
| • <7 days | 2 | 2 | |
| • 7-30 days | 22 | 24 | *P*=1.000 |
| • >30 days | 5 | 6 | |
| Colchicine therapy | | | |
| • None | 1 | 2 | |
| • 0.5mg/day | 9 | 8 | |
| • 1mg/day | 11 | 13 | *P*=1.000 |
| • 2mg/day | 8 | 9 | |
| Proportion of patients who asked for medical assessment before 14th day | 13 (44.8%) | 8 (25.0%) | *P*=0.068 |
| VAS pain score and SD at 7th day | 4,3 SD 2,2 | 3,1 SD 1,9 | *P*=0.025 |
| VAS pain score and SD at 14th day | 4,1 SD 2,5 | 2,0 SD 0,5 | *P*=0.0001 |
| Hyperglucemic state during treatment | 1 (3.45%) | 1 (3.13%) | N.A. |
| Time off work (where corresponds) | 6.3 SD 2.6 d/patient | 5.1 SD 1.9 d/patient | *P*=0.051 |

Table 1. Demographic data and results according to doses of prednisone per Kg/day.

**Conclusions:** In diabetic patients with oligoarticular or polyarticular gout flares the therapeutic approach with prednisone doses higher than 0.3mg/kg/day seems to be associated with a lower tendency of need of new clinical assessment, and a better pain control without a higher frequency of hyperglucemic states.
**Disclosure of Interest:** None declared
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## THU0503 MAJOR CARDIOVASCULAR EVENTS IN PATIENTS WITH RECURRENT GOUT, CARDIOVASCULAR AND CHRONIC KIDNEY DISEASE, INITIATING ON ALLOPURINOL OR FEBUXOSTAT

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**Background:** Chronic management of hyperuricemia with xanthine oxidase inhibitors has been shown to reduce long term incidence of gout flares, but their resultant impact in highly comorbid populations is unclear.
**Objectives:** To compare major cardiovascular event (MCE) rates in patients with gout, moderate to severe chronic kidney disease (CKD), and cardiovascular disease (CVD) after initiation of uric-lowering therapy (ULT), with allopurinol (ALO) or febuxostat (FBX).
**Methods:** Gout patients (ICD-9-CM 274.xx), aged ≥18, with a baseline diagnosis of stage 3/4 CKD, CVD [coronary artery disease (CAD), cerebrovascular disease (CBV), peripheral vascular disease (PVD)] and/or heart failure (HF), and ≥2 baseline gout flares were selected from the MarketScan® database (January 2009-June 2013) after initiating ULT with either ALO or FBX. Patients were followed until disenrollment, discontinuation of the qualifying ULT or initiation of the alternate study agent. MCE included myocardial infarction, stroke, transient ischemic attack, non-traumatic lower extremity (LE) amputation, and coronary, cerebrovascular, or LE revascularization. Cox proportional hazard models assessed MCE risk as a function of demographics, CVD and HF history, including CVD hospitalization, gout severity, resource intensivity and history of arrhythmia/conduction disorder.
**Results:** A total of 352 patients (148 FBX, 204 ALO) met eligibility criteria (69% male; mean age 71).A majority of patients (74%) had stage 3 CKD and, by definition, all patients had CVD (68% CAD, 15% CBV, and 23% PVD) and/or HF (53%) with no significant differences between cohorts. Mean daily dose was 51 mg in FBX and 198 mg in ALO cohorts. Mean baseline flares per patient were significantly higher in the FBX cohort (2.5 vs. 2.3, p=0.005). A total of 28 MCE occurred in 5.4% and 9.8% of FBX and ALO patients respectively. A total of 15 patients (4.3%) had a CAD-specific MCE, 4 (1.1%) a CBV-specific MCE, and 10 (2.8%) a PVD-specific MCE. The MCE rate per 1000 PY (95% CI) was 75.8 (33–149) in the FBX cohort vs. 128.1 (78–198) in the ALO cohort. Cox model results suggest significantly lower MCE risk in patients initiating on FBX (hazard ratio (HR) 0.4; 95% confidence interval (CI) 0.1–0.9, p=0.035) and those with a HF history (HR 0.4, 95% CI 0.16–0.93, p=0.034). Model results suggest increased risk associated with PVD history (HR 5.3; 95% CI 2.3–12.0, p<0.0001), baseline CVD/HF hospitalization (HR 3.2; 95% CI 1.4–8.0, p=0.008), residing in the western US (HR 4.3; 95% CI 1.4–13.8, p=0.013) and higher baseline expenditure (HR 1.1; 95% CI 1.0–1.1, p=0.006).
**Conclusions:** Patients with recurrent gout, moderate to severe CKD and CVD/HF initiating on FBX had a significantly lower rate of MCE than patients initiating on ALO. It is unclear if this is due to a selective prescribing of drugs from the same therapeutic class to patients with different prognostic characteristics (channeling bias) greater clinical effectiveness of FBX or due to ALO under-dosing in renally impaired patients.
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**Disclosure of Interest:** J. Foody Consultant for: Outcomes Research Solutions, Inc., R. Turpin Shareholder of: Takeda Pharmaceuticals U.S.A., Inc., Employee of: Takeda Pharmaceuticals U.S.A., Inc., B. Tidwell Consultant for: Takeda Pharmaceuticals U.S.A., Inc., D. Eisenberg Lawrence Shareholder of: Takeda Pharmaceuticals U.S.A., Inc., Employee of: Takeda Pharmaceuticals U.S.A., Inc., K. Schulman Consultant for: Takeda Pharmaceuticals U.S.A., Inc.
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## THU0504 COMORBIDITIES AND THE EFFECTIVENESS OF CORTICOSTEROIDS IN PATIENTS WITH GOUTY ARTHRITIS

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**Background:** The choice of an optimal anti-inflammatory therapy (AIT) targeting to cut a gouty attack in the shortest terms is based on the assessment of the severity of gouty arthritis (GA), which involves a visual analog scale (VAS) for pain, number of inflamed joints (NIJ) and their sizes, the time since the onset of a gout attack till the beginning of an AIT.
**Objectives:** To determine the influence of comorbidities on the effectiveness of corticosteroids (CS) in patients with GA inadequately responding to previous AIT.
**Methods:** 220 patients with GA were included into the study. The diagnosis was based on GA criteria (ACR, 1977). 88.2% of patients were males. The mean age was 54.5 ± 9.4 years, the mean duration of disease – 8.2 ± 6.8 years. At the beginning, the patients received either NSAIDs or Colchicine with the mean duration of 10.7 ± 5.7. Because of their non-effectiveness, the treatment with CS i.v. or i.m., excepting long-acting CS, was started in clinical setting. The effectiveness of the CS was evaluated after 5 days: 47.3% (n=104) of patients had no signs of inflammation in the joints, and 52.7% (n=116) of them retained the signs of active arthritis. 28 patients continued the same CS, and 88 patients were added a long-acting CS i.m., i.a. or CS per os. Comorbidities included: eGFR <60 ml/min, cardiovascular (CV) pathologies (hypertension (HT), chronic heart failure II-III FC (CHF), ischemic heart disease (IHD), including coronary disease and arrhythmias), diabetes mellitus (DM), elevation of hepatic enzymes, infections.
**Results:** The patients with a little effect of CS as compared to the group of patients with the satisfactory effect had the longer duration of the previous AIT (p<0.001), higher VAS scores (p<0.005), greater NIJ (p<0.000) and the prevalence of polyarthritis ($\chi^2$ =15.21; p=0.0001).
Among the patients without a significant effect of CS, as opposed to the patients who responded positively to the CS treatment, more cases of eGFR <60 ml /min. were detected (52.6% and 29.8%; OR - 2.71; 95% CI, 2.11 – 3.48; p=0.0004). In the same group, we noted the prevalence of CV pathologies in general (86.2% and 75%; OR - 2.08; 95% CI, 1.39 – 3.13; p=0.035), in particular, CHF (24.1% and 9.6%; OR =2.99, 95% CI 2.35 - 3.81, p=0.004) and IHD (41.4% and 23.1%; OR =2.02, 95% CI 1.58 - 2.58, p=0.004), but not HT (p>0.05). No statistically significant difference in the number of patients with DM between the groups was found (23.3% and 13.5%; $\chi^2$ =3.42; p=0.062). At the same time, elevation of hepatic enzymes by more than 2-fold was observed more frequently in patients with a good effect of CS ($\chi^2$ =5.70, p=0.017). The proportions of patients with the presence of infections were distributed quite equally in both groups (7.4% and 6.1%; p>0.05).
**Conclusions:** Refractoriness to anti-inflammatory drugs in patients with gout along with the parameters of GA severity may also be due to comorbid disorders, such as kidney failure and CV disease (CHF, IHD). Therefore, the assessment of the GA severity for the optimal anti-inflammatory approach might include the assessment of these comorbidities. Their presence should be an indication to an early use of either a monotherapy or combinations of CS that would meet the targets of treatment.
**Disclosure of Interest:** None declared
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## THU0505 THE DEVELOPMENT OF A NEW EUROPEAN REGULATORY GUIDELINE ON THE CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS FOR THE TREATMENT OF GOUT

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**Background:** The EMA's Committee for Medicinal Products for Human Use (CHMP) prepares scientific guidelines in consultation with regulatory authorities in the EU Member States, to help applicants prepare marketing-authorisation applications for human medicines, including in the domain of rheumatology. These guidelines are developed by the Rheumatology/Immunology Working Party (RIWP), which is composed of European experts selected from or associated with national agencies.

**Objectives:** There is a need of new and safe treatment options for the prevention and treatment of gout attacks, and several are under development. Moreover, the EULAR an ACR have updated their recommendations for the diagnosis and treatment of gout. Imaging techniques become increasingly important in diagnosing and monitoring of gout. Therefore, a CHMP guidance is developed to promote drug development and European consensus on the choice of the endpoints and design of the studies.
**Methods:** Development and release for consultation of the concept paper by the RIWP. The draft guideline will be open for public consultation during the EULAR 2016 Congress (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline).
**Results:** The development plan and endpoints will mainly be related to the mode of action of the drug. This may either urate lowering therapy (ULT), or anti-inflammatory drugs. For ULT products, serum uric acid (SUA) could serve as a surrogate endpoint. The primary endpoint is defined as SUA levels below a target level of 6 mg/dl, for a period of 3 consecutive months. For tophaceous gout patients SUA levels <5 mg/dl are considered a more appropriate primary endpoint. Tophi can be included as secondary endpoint. At present, imaging of tophi by e.g. ultrasound is considered as supportive evidence, since it's validation has been limited thus far to case series of selected patients. The treatment goal of anti-inflammatory drugs could be the acute treatment of flares. The primary endpoint should reflect a clinically relevant reduction in pain, in a relatively short time frame of 12–24 hrs. A specific goal of anti-inflammatory drugs could be the prophylaxis of flares upon initiation of ULT. The primary endpoint should be the mean number of flares within 3–6 months after the start of ULT. In general, parallel, randomised, double-blind, active-controlled trials should be performed for both ULT and anti-inflammatory drugs.
In addition, long-term anti-inflammatory treatment options may be developed for refractory gout patients with chronic gouty arthropathy, without symptom-free intervals. A suitable primary endpoint could be the reduction of pain, with the improvement of function (e.g. measured by HAQ-DI or Patient's Global Assessment) as co-primary endpoint.
The development of treatment options for *asymptomatic* hyperuricaemia is beyond the scope of this guideline.
**Conclusions:** A European regulatory guideline for the development of new treatment options of gout is under development. The guideline is open for public consultation.
**References:**
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**Disclosure of Interest:** None declared
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## THU0506 CARDIOVASCULAR RISK AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH GOUT: EXPERIENCE IN A MULTIHOSPITAL SPANISH GROUP

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**Background:** Several reports have shown the relationship between gout and increased cardiovascular risk (CVR). There is a lack of research in Spain about endothelial and cardiac dysfunction in gout
**Objectives:** Analyze CVR factors in gouty patients in our sample with vascular assessment, cardiological tests and laboratory parameters
**Methods:** Prospective cohort study with collection of clinical data, family history (FH) of gout and cardiovascular disease (CVD), and treatments received (calcium channel antagonists [CCA], ACE inhibitors [ACE-i], angiotensin receptor blokers [ARB], beta blockers [BB] or thiazides. A history of hypertension, diabetes (DM), dyslipidemia (DL), smoking, thrombotic events, ischemic heart disease (IHD) were also collected. Body mass index (BMI), serum uric acid (SUA), sedimentation rate (ESR), conventional/ultrasensitive RCP [cRCP, hsCRP], ferritin, total cholesterol (CHOL) and subtypes (HDLc, LDLc), triglycerides (TG), vitamin D and homocysteine were measured. Patients were referred to Vascular Surgery Department for ultrasound examination with search of carotid plaques and study of intima-media thickness (IMT), and also were to Cardiology Department for echocardiogram (ECHO-CG) and electrocardiogram (ECG)
**Results:** 150 patients, 97% men and 3% women. Average age at time of study and diagnosis: 56 (23–92) and 47 years (15–79), respectively. Age at symptoms onset: 45 years (15–77). 22.5% had tophi and 11.3% urate stones. FH: 42% had gout history and 41% CVD history. Classical CVR factors: hypertension 47.3%; DM-2 4.6%, glucose intolerance 0.6%; DL 56.7% (CHOL: 37, TG: 15, both: 33); smokers 20.6% and quitters 37.6%, 21 pack/year (1–90); 1 patient had suffered stroke; 4 thrombosis; 17 IHD (11 angina, 6 myocardial infarction). 75% overweight/obesity, BMI 28 (19–40). Analytical parameters: ESR 10 mm/h (1–68), hs-CRP 2.7 mg/dL (0.1–57.7), c-CRP 2.3 mg/L (0–14.8); SUA 6.9 mg/dL (2.4–11.8); ferritin 259 ng/ml (11–2000); COL-t: 187 mg/dL (102–321, 6 not collected [NC]), HDLc 47 mg/dL (15–88; 22 NC), LDLc 113 mg/dL (15–248) TG 145 mg/dL (53–603); vitamin D 24.7 ng/mL (5.6–23.6; 28.6% <20); homocysteine 24.7 mmol/L (4–40; 32% >15 mmol/L). ECHO-CG: 6 valvular disease, 13 left ventricular hypertrophy, 45 had >1 finding, 5 NC. ECG was normal in 79 patients; 9 right bundle branch block (BBB), 1 left BBB, 4 IHD signs, 2 repolarization abnormalities and 6 arrhythmia; 13 had ≥2 findings, 9 showed other findings, 54 NC. Vascular examination: carotid IMT greater than corresponding adjusted by age group in 75% and 79% of patients (right and left, respectively); both: 65%. Carotid plaques 23%. Treatments: ACA 2.6%, ACE-i 2%, ARB 4.6%, BB 2%, thiazides 3.3%
**Conclusions:** 75% of our patients have overweight/obesity. High percentage of subjects with hyperhomocysteinemia and/or vitamin D deficiency. Marked prevalence of increased IMT and carotid plaques, and outstanding number of cardiac abnormalities in ECHO-G/ECG. Further statistical studies will quantify the value of these early findings, that seem very relevant
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**Disclosure of Interest:** None declared
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## THU0507 EVIDENCE OF THE USE OF COLCHICINE ARE MORE NUMEROUS IN CARDIOLOGY AND HEPATO-GASTROENTEROLOGY THAN IN RHEUMATOLOGY: A SYSTEMATIC LITERATURE REVIEW OF CLINICAL TRIALS

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**Background:** Colchicine has been used for millennia to treat acute gout flare, but numerous other conditions have been proposed for the use of this "*eau médicinale*", including familial Mediterranean fever, Behçet's disease and pericarditis.
**Objectives:** To investigate the efficacy and safety of colchicine whatever the indication.
**Methods:** A literature search of MEDLINE, EMBASE and Cochrane library databases was performed for human studies without language restriction from inception to January 2016, using the followings key-words: "colchicine", "clinical trial", "clinical controlled trials", "randomized controlled trials". We did not impose any date or language restrictions in the search. We also handsearched reference lists of identified studies.
**Results:** The process of selection of studies is presented in Figure 1. Of the 477 articles reviewed, 106 were analyzed including 77 randomized controlled trials, 2 nonrandomized controlled trials and 27 open studies. The subjects studied were chronic liver disease (n=13), primary biliary cirrhosis (n=11), post cardiac surgery syndromes (n=11), pericarditis (n=9), coronary syndromes and other heart disease (n=6), Familial Mediterranean fever (n=5), Behçet's disease

Table 1. Main clinical trials with colchicine and their efficacy

| | Diseases | RCT available YES/NO | Efficacy YES/NO |
|---|---|---|---|
| Rheumatology | Gout | YES | YES |
| | Familial Mediterranean fever | YES | YES |
| | Behçet's disease | YES | YES |
| | Knee osteoarthritis | YES | Mixed |
| Cardiology | Acute and recurrent pericarditis | YES | YES |
| | Post cardiac surgery syndromes | YES | YES |
| | Coronary heart disease | YES | Mixed |
| Hepatology and gastroenterology | Primary biliary cirrhosis | YES | YES |
| | Primary sclerosing cholangitis | YES | NO |
| | Other chronic liver diseases | YES | Mixed |
| | Constipation | YES | YES |
| Pneumology | Lung fibrosis | YES | NO |
| | Asthma | YES | NO |
| Dermatology | Psoriasis | YES | NO |
| Others | Amyloidosis | YES | YES |

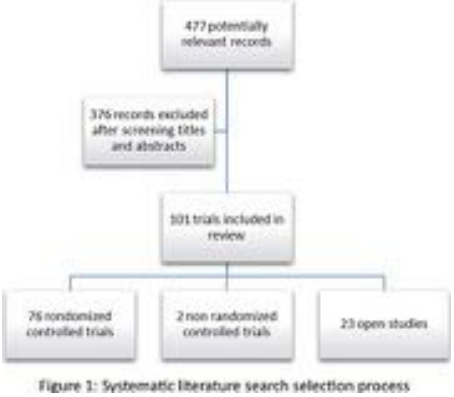


Figure 1: Systematic literature search selection process

(n=5), amyloidosis (n=4), gout (n=3), knee osteoarthritis (n=3), constipation (n=3), lung fibrosis (n=3), psoriasis and psoriatic arthritis (n=3), asthma (n=3), primary sclerosing cholangitis (n=2), low back pain (n=2), proliferative vitreoretinopathy (n=2), recurrent aphthous stomatitis (n=2). Other indications have been evaluated in one clinical trial (Graves' ophthalmopathy, oral mucositis during hematological malignancies, Peyronie's disease, hidradinitis suppurativa, acne vulgaris, chronic bullous dermatosis, actinic keratosis, cutaneous leukocytoclastic vasculitis, finger clubbing and hypertrophic osteoarthropathy, pustulosis palmaris and plantaris, scleroderma, penile condylomata acuminate, mixed cryoglobulinemia, allergic rhinitis, delayed urticaria). Table 1 summarizes the main directions of colchicine in clinical trials. The most common adverse events were gastrointestinal intolerance.
**Conclusions:** Although acute gout is the major indication for use of colchicine, only 3 clinical trials are available for gout and no for other crystal-induced arthritis. Evidence are limited for knee osteoarthritis, low back pain and psoriatic arthritis. Clinical trials published are dominated by the treatement of heart diseases (especially pericarditis), systemic diseases (primary biliary cirrhosis, Familial Mediterranean fever, Behçet's disease) and others chronic liver diseases.
**Disclosure of Interest:** None declared
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## THU0508 IMPROVEMENT IN TREAT TO TARGET SERUM URATE LEVELS: RESULTS FROM A COMPARISON BETWEEN THE GEMA AND THE GEMA-II AUDITS

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**Background:** The prior GEMA (1) audit included patients before the EULAR 2006 recommendations were published (2), showing poor adherence to the EULAR recomendations in both crystal-based diagnosis and target urate levels.
**Objectives:** 1) assess the current quality of care in gout patients in Spain and 2) compare the current management with previous audit data.
**Methods:** The GEMA-II study included patients from EULAR 2006 to ACR 2012 guidelines. Agreement on diagnosis and treatment of gout with the EULAR 2006 recommendations was assessed. The selection of patient's files for review was performed selecting a stratified 2-stage sampling of centers according to national population statistics. A random sample in each unit with a diagnosis code of gout (ICD, R9) was centrally selected. The sample size was estimated according to previous results and expected outcomes. The main co-principal variables were >50% improvement in the rate of gold-standard diagnosis and >50% improvement in the rate of patients at target serum urate levels.
**Results:** Data from 511 randomly selected clinical records from 38 units were included. Out of the 38 units, 93% reported having a polarized microscopy facility at the office. sUA at final visit was available in 479/511 (93.7%). Samples from the two audits (GEMA and GEMA-II) did not differ in age, sex distribution or time from onset to first visit.
Crystal-based diagnosis was performed in 209/803 (26.0%) and 162/511 (31.7%) in the GEMA and GEMA-II studies (p=0,030, 5.7% improvement, not reaching endpoint >50%). By contrast, the pre-defined improvement >50% for the rate of patients achieving target serum urate (<6 mg/dl) was achieved (Table) for the overall population, independently of the aprioristic perception of the rate of target sUA or the presence of gold-standard diagnosis. A post-hoc analysis showed that in the subgroup of patients on urate-lowering medications, the improvement in the rate of patients achieving sA target was 49.31%, very close to the >50% improvement (Table).
Both crystal based diagnosis and rate of sUa in target were higher in Units with dedicated crystal-arthritis office and also in those that had presented the EULAR 2006 recommendations at least once.

Table 1

| All patients | | | Patients on urate-lowering treatment | | |
|---|---|---|---|---|---|
| sUA (mg/dl) | <6 mg | ≥6 mg | sUA (mg/dl) | <6 mg | ≥6 mg |
| GEMA (N=701) | 286 (40.8) | 415 (59.2) | GEMA (N=642) | 274 (42.7) | 368 (57.3) |
| GEMA-II (N=479) | 294 (61.4) | 185 (38.6) | GEMA-II (N=450) | 285 (63.3) | 165 (37.7) |

**Conclusions:** Overall the improvement in the rate of patients achieving target serum urate over a 6-year period exceeded 50%. The rate of gold-standard diagnosis improved, but did not reach the expected outcome. Interest in recommendations and dedicated crystal arthritis offices were associated with best results.
These preliminary data show for the first time that substantial improvement has been achieved in treat to target serum urate levels strategy for gout in the Rheumatology community.
**References:**
[1] Perez-Ruiz F, et al. J Clin rheumatol 2011.
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**Acknowledgement:** Funded by the Spanish Foundation for Rheumatology through an unrestricted grant from Menarini Spain
**Disclosure of Interest:** None declared
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## THU0509 OPTICAL COHERENCE TOMOGRAPHY DESCRIPTION OF TOPHI IN GOUT SHOWS THAT IRREGULAR TOPHUS MORPHOLOGY, OEDEMA AND ABSENCE OF CAPSULE ARE ASSOCIATED WITH SYMPTOMATIC DISEASE

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**Background:** The basis as to why chronic gout related tophi may be completely asymptomatic is not understood. In experimental settings coating of gouty crystals may be associated with the prevention of inflammatory responses (1).
**Objectives:** We used optical coherence tomography (OCT) in patients with gout to test the hypothesis that tophus related pain was due to the disruption of tophus capsule.
**Methods:** Eight consecutive patients with tophaceous gout were recruited. Each patient received detailed clinical assessment by a Rheumatologist including physical examination, history, current therapy, presence, number and site of tophi and whether or not each tophus was symptomatic. Tophi were photographed and scanned using Vivosight OCT scan (Michelson Diagnostics, Kent, UK). OCT of corresponding regions of the opposite side were undertaken for comparison and for subclinical tophi evaluation. One hundred slices OCT scans allowed post-processing 3D reconstructions of the visualized superficial tophus morphology (smooth or irregular) and presence or absence of tophus capsule were assessed. VAS pain scores for individual tophi were subsequently collected and correlated with imaging.
**Results:** Thirty seven tophi from eight patients with tophaceous gout were scanned. Four patients had tophi located at fingers, one at toes, two at both sites. Two patients of the third group had additional sites involved in form of multiple aggregates located at knees, heels, elbows. VAS score ranged from 0 to 9 (median=2). Eleven of the 37 tophi were symptomatic (VAS score range: 4–9), the remaining 26 were mildly or not symptomatic (VAS score 0–3). Most of the tophi (28/37) had a smooth border, 9 had an irregular aspect. Tophi with smooth border seemed to be surrounded by a "pseudo-capsule" ($p<0.05$). Tophi with irregular aspect were associated with optical density changes possibly consistent with oedema ($p<0.05$). A relationship between irregular tophi and pain was evident (p=0.0025). On the contrary, presence of smooth tophi with capsules were not associated with significant pain.
**Conclusions:** These findings suggest that non-painful tophi in patients with tophaceous gout have a different morphology and a capsule which provides support for the idea that a capsule prevents pain and inflammation. Capsular disruption is linked to flares and the hypothesis that initial serum urate lowering therapy may lead to capsule disruption should be further investigated.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5161

## THU0510 A LONGITUDINAL DUAL ENERGY COMPUTED TOMOGRAPHY STUDY ON THE EFFECT OF URATE LOWERING THERAPIES ON THE REDUCTION OF TOPHUS BURDEN IN PATIENTS WITH CHRONIC GOUT

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**Background:** Dual energy computed tomography (DECT) allows reliably detecting and quantifying tophus burden in patients with chronic gout. Longitudinal studies on the effect of uric acid lowering drug therapy on tophus burden assessed by DECT are currently lacking with the exception of a small study performed in patients treated with pegloticase (1)
**Objectives:** To assess the effects of uric acid lowering drug therapy to reduce tophus volume in patients with chronic gout
**Methods:** Follow-up DECT scans were performed in 94 patients with DECT+ chronic gout receiving stable treatment with either allopurinol, febuxostat, benzbromaron or pegloticase, or had life-style intervention only with no concomitant uric acid lowering drug therapy. Baseline and follow-up scans of both feet captured tophus volume by *Syngo DE Gout* software (Siemens). Artefacts were manually excluded. Changes in tophus volume were calculated in a descriptive (tophus volume at baseline minus tophus volume at follow-up) and inferential way (Wilcoxon signed-rank test). Demographic data, medication and blood values (CRP, creatinine, serum urate) were recorded at the time of DECT scan.

**Results:** 94 patients (75 men and 19 women) were analyzed. Mean disease duration until the first DECT examination was 3.3 years and mean interval between both DECT examinations was 1.5 years. The overall baseline serum uric acid level decreased from 7.3 ± 2.5 mg/dl to 5.9 ± 2.8 mg/dl at follow up. Baseline tophus volume decreased by 77% with allopurinol ($p<0.001$, r=-0.50), 35% with febuxostat (p=0.001, r=-0.51) and 90% with pegloticase (p=0.005, r=-0.58). Only 2 patients were treated with benzbromaron showing numerical decrease of tophus volume at a similar range as seen with allopurinol (-75%). Life-style intervention also led to a moderate (-31%), though significant (p=0.007, r=-0.40), decrease in tophus burden.

| Parameters | No therapy N = 20 | Allopurinol N = 28 | Febuxostat N = 25 | Pegloticase N = 12 | Uricosurics N = 2 | Discontinuation N = 6 |
|---|---|---|---|---|---|---|
| Disease duration* | 0,7 ± 2,1 | 2,0 ± 6,4 | 4,8 ± 8,5 | 8,7 ± 8,0 | n.a. | 4,3 ± 6,7 |
| Interval* | 21 ± 11 | 17 ± 10 | 13 ± 6 | 10 ± 8 | 11 ± 7 | 27 ± 16 |
| Serum urate | | | | | | |
| Baseline (mg/dl) | 7,1 ± 1,8 | 6,6 ± 1,5 | 7,7 ± 3,0 | 8,3 ± 4,2 | 5,9 ± 1,1 | 7,1 ± 1,0 |
| Follow up (mg/dl) | 6,8 ± 1,8 | 5,3 ± 1,9 | 4,9 ± 2,6 | 6,9 ± 5,0 | 4,5 ± 0,8 | 7,5 ± 2,4 |
| Urate volume | | | | | | |
| Baseline (mm³) | 78 ± 89 | 86 ± 111 | 924 ± 2749 | 5779 ± 9756 | 140 ± 184 | 132 ± 142 |
| Follow up (mm³) | 51 ± 157 | 20 ± 36 | 607 ± 2046 | 623 ± 1047 | 35 ± 35 | 85 ± 139 |
| Urate reduction | | | | | | |
| Absolute (mm³) | 24 ± 90 | 65 ± 102 | 318 ± 710 | 5156 ± 9881 | 105 ± 149 | 47 ± 70 |
| Relative* | 0.31 | 0.76 | 0.34 | 0.89 | 0.75 | 0.35 |
| p- value# | 0.007 | <0.001 | 0.001 | 0.005 | 0.317 | 0.093 |

Results are mean ± SD for continuous and n/N for categorical variables. SD, standard deviation.
* Disease duration until first DECT in years
† Interval between DECT1 and DECT2 in months, corresponds the application period
‡ Absolute urate reduction/Baseline urate volume
# Asymptotic significance

**Conclusions:** Sustained uric acid lowering drug therapy leads to significant reduction of DECT tophus burden in chronic gout patients. Tophus reduction depends on initial tophus volume.

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## THU0511 FACTORS ASSOCIATED WITH PRECLINICAL ATHEROSCLEROTIC CHANGES IN CAROTID ARTERY IN MEN WITH GOUT

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**Background:** Although a number of studies have reported that hyperuricemia and gout are independent risk factors for the development of cardiovascular disease (CVD), little is known about the relationship between hyperuricemia or gout and arterial stiffness.

**Objectives:** This study sought to compare carotid arterial stiffness in gout patients and healthy controls, and evaluate the predictive factors for arterial stiffness in male patients with gout using carotid ultrasonography.

**Methods:** In this cross-sectional study, 69 male gout patients and 64 male healthy controls without any known CVD were prospectively analyzed. Carotid artery stiffness index β (β-index) and the intima-media thickness (IMT) were measured as surrogate markers of preclinical atherosclerosis. We also measured serum uric acid, high sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), lipid profiles, and renal function. Adjusted comparison of the β-index and cIMT in both groups and their associations with clinical parameters were investigated.

**Results:** The gout group showed higher ESR, Cr, prevalence of HT and DM than the control group ($p<0.05$). However, HDL was higher in the control group ($p<0.05$). β-index and cIMT were higher in the gout group, but only β-index showed a statistically significant difference (11.12 ± 5.19 vs 8.68 ± 3.67, p=0.002). Multiple regression analyses showed that duration of gout was significantly associated with increased β-index and cIMT in the gout group (Table 1).

Table 1) Multiple regression analyses of clinical factors possibly affecting the β-index and cIMT in gout group

| | β-index | | cIMT | |
|---|---|---|---|---|
| | β ± SE | p | β ± SE | p |
| Age | 0.122 ± 0.070 | 0.087 | 0.002 ± 0.002 | 0.296 |
| PY of smoking | -0.051 ± 0.040 | 0.210 | -0.001 ± 0.001 | 0.579 |
| Duration of gout | 0.222 ± 0.110 | 0.049 | 0.009 ± 0.003 | 0.004 |
| Uric acid | 0.287 ± 0.366 | 0.435 | -0.004 ± 0.010 | 0.689 |
| ESR | -0.002 ± 0.041 | 0.954 | 0.000 ± 0.001 | 0.707 |
| hs-CRP | -0.112 ± 0.410 | 0.787 | -0.003 ± 0.011 | 0.770 |
| NLR | -0.354 ± 0.547 | 0.520 | 0.007 ± 0.015 | 0.661 |
| BUN | -0.084 ± 0.097 | 0.389 | 0.003 ± 0.003 | 0.310 |
| Cr | 2.014 ± 1.646 | 0.226 | -0.033 ± 0.044 | 0.463 |
| | ($R^2$=0.152 , adjusted $R^2$= 0.022) | | ($R^2$=0.194 , adjusted $R^2$= 0.071) | |

β-index, arterial stiffness index beta; BUN, blood urea nitrogen; cIMT, carotid intima-media thickness; Cr, creatinine; ESR, erythrocyte sedimentation rate; hs-CRP, high-sensitivity C-reactive protein; NLR, neutrophil lymphocyte ratio; PY, pack-year; SE, standard error.

**Results:** The gout group showed higher ESR, Cr, prevalence of HT and DM than the control group ($p<0.05$). However, HDL was higher in the control group ($p<0.05$). β-index and cIMT were higher in the gout group, but only β-index showed a statistically significant difference (11.12 ± 5.19 vs 8.68 ± 3.67, p=0.002). Multiple regression analyses showed that duration of gout was significantly associated with increased β-index and cIMT in the gout group (Table 1).

**Conclusions:** Patients with gout had increased carotid arterial stiffness, which was significantly related to gout duration rather than serum uric acid level or status of inflammation.

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## THU0512 INSULIN RESISTANCE AS AN INDEPENDENT PREDICTOR OF SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH GOUT

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**Background:** Gout is linked with metabolic disorders those are important risk factors of cardiovascular diseases.

**Objectives:** The aim of the present study was to identify independent predictor of subclinical atherosclerosis in patients with gout by measuring presence of atherosclerotic plaque and prevalence of erectile dysfunction (ED).

**Methods:** We analyzed 80 patients with gout and 70 healthy controls. Carotid plaque and ED were assessed by using ultrasound measurement of carotid plaque and the five-item version of the International Index of Erectile Function questionnaire in participants, respectively. Logistic regression analysis was performed to estimate the effect of variables on presences of carotid plaque or ED on all of the study subjects and patients with gout.

**Results:** Gout patients had more ED (55.3% vs. 41.4%, $p<0.047$) and carotid plaque (59.2% vs. 17.1%, $p<0.007$) compared to controls. After adjustment of compounding factors, only HOMA-IR was significantly associated with ED (OR: 1.82, 95% CI: 1.05–3.15) whereas was not with carotid plaque (OR: 1.02, 95% CI: 0.99–1.47). Gout showed significant association with carotid plaque after multivariate analysis (OR: 13.39, CI: 1.93–92.88). Older age ($p<0.001$), higher HOMA-IR (p=0.048) and lower GFR (p=0.038) were observed in patients with presence of ED than without ED in gout patients. And gout patients with carotid plaque were older (p=0.003) and had higher insulin level (p=0.035) and HOMA-IR (p=0.039) than without plaque. Logistic regression analysis showed that HOMA-IR was an independent predictor for the presence of both ED (OR: 1.62, 95% CI: 1.03–2.82) and carotid plaque (OR: 1.40, 95% CI: 1.04–1.63).

**Conclusions:** In our study, insulin resistance was an independent predictor of subclinical atherosclerosis in patients with gout.

**Disclosure of Interest:** None declared

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## THU0513 DETECTION OF SUBCLINICAL TOPHI IN PATIENTS WITH GOUTY ARTHRITIS: A DUAL-ENERGY COMPUTED TOMOGRAPHY STUDY

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**Background:** Tophi are generally considered as manifestations of chronic gout, but subclinical tophi in intra- and extra-articular structures have been shown to occur in early gout and asymptomatic hyperuricemia. Since occurrence of tophi is linked to joint destruction, it is important to detect tophi early before clinical detection.

**Objectives:** The aim of our study was to evaluate the utility of dual-energy CT (DECT) in detecting subclinical tophi in patients with gouty arthritis.

**Methods:** DECT scans of feet in 65 patients with gout without apparent clinical tophi were evaluated for presence of tophi. Plain X-ray of feet, clinical and laboratory data were obtained simultaneously at the time of the DECT evaluation. Total volumes of tophi in both feet were quantified using an automated software program of DECT.

**Results:** Subclinical tophi were detected in 63 (96.9%) patients and in 341 (18.7%) joints, and median 3 (1 to 22) joints per patient were positive for tophi. The most common sites for tophi were first metatarsophalangeal joints (17.6%), followed by ankle joints (10.9%). Tophi in Achilles tendons were present in 10.8% of patients. Patients with early gout (disease duration <2 years) had tophi in 99 (13.6%) joints. Mean number of tophi was significantly lower in patients with early gout compared to those with chronic gout (3.8 versus 6.2, p=0.038). Mean volume of tophi was not significantly different between early gout and chronic gout.
**Conclusions:** Tophi frequently occur in both intra- and extra-articular structures of gouty arthritis patients despite absence of clinically apparent tophi. DECT is an excellent imaging modality for detecting subclinical tophi.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5399

## THU0514 SEASONAL VARIATIONS OF EPISODES OF ACUTE GOUTY ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** Acute gouty arthritis is the inflammatory arthritis with abrupt and intermittent nature of attack.
**Objectives:** The aim of this study was to analyze the seasonal variations of episodes of acute gouty arthritis.
**Methods:** We searched MEDLINE, EMBASE, the Cochrane library, and KoreaMed for all articles published before November 2015. Studies with quantitative data on episodes of acute gouty arthritis by months and/or seasons were included. Meta-analysis for episodes of acute gouty arthritis was done by seasons and months. Subgroup analyses by the confirmatory methods of acute gouty arthritis were done by seasons.
**Results:** Ten studies published between 1920 and 2015 were included, containing a total of 29,863 subjects. Plotting of episodes of acute gouty arthritis by months showed higher episodes during the period from March to July than other months. The risk ratio of episodes of acute gouty arthritis in spring was 1.21 (95% CI: 0.95 to 1.55, $I^2$=86%; $p$=0.12), 1.32 (95% CI: 0.98 to 1.78, $I^2$=90%; $p$=0.07), 1.27 (95% CI: 1.02 to 1.59, $I^2$=81%; $p$=0.03) when compared to summer, fall and winter, respectively. Therefore, spring had significantly higher episodes of acute gouty arthritis than winter. Subgroup analyses by confirmatory methods of episodes of acute gouty arthritis were as follows: 1) The risk ratio of acute gouty arthritis confirmed by the presence of monosodium urate in synovial fluid in spring was 1.46 (95% CI: 1.22 to 1.76, $I^2$=0%; $p$<0.0001), 1.28 (95% CI: 1.07 to 1.54, $I^2$=7%; $p$=0.007), 1.24 (95% CI: 0.93 to 1.65, $I^2$=59%; $p$=0.15) when compared to summer, fall and winter, showing that spring had significantly higher episodes of acute gouty arthritis than summer and fall; 2) The risk ratio of acute gouty arthritis confirmed by the presence of inflammation in synovial fluid was 1.53 (95% CI: 1.31 to 1.80, $I^2$=0%; $p$<0.00001), 1.44 (95% CI: 1.07 to 1.93, $I^2$=69%; $p$=0.02), 1.28 (95% CI: 1.05 to 1.55, $I^2$=40%; $p$=0.01) when compared to summer, fall and winter, showing that spring had significantly higher episodes of acute gouty arthritis than 3 other seasons.
**Conclusions:** This seems to be the first systematic review and meta-analysis on seasonal variations of acute gouty arthritis. Based on our study, the acute gouty arthritis might be developed more frequently during the period from spring. Increase in physical activity, dehydration, and seasonal variation of cortisol level could be related with this seasonal variation of episodes of acute gouty arthritis.
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**Disclosure of Interest:** None declared
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## THU0515 INCREASED CAROTID INTIMA-MEDIA THICKNESS WAS RELATED WITH ELEVATED SERUM HOMOCYSTEINE LEVEL IN PATIENTS WITH HYPERURICEMIA

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**Background:** Hyperuricemia is known to be associated with metabolic syndrome and cardiovascular disease (CVD). It was reported that elevated level of homocysteine (Hcy) in patients with gout was related with decreased renal function. A high level of Hcy is regarded as a risk factor for CVD, since Hcy is related with endothelial cell damage, which can lead to inflammation in the blood vessels and atherosclerosis. However, there was no report about the relationship between Hcy and atherosclerosis in patients with hyperuricemia.
**Objectives:** In this study, we investigated whether or not carotid intima-media thickness (IMT) was increased in patients with hyperuricemia. We also evaluated the correlation between serum Hcy level and carotid IMT in hyperuricemic patients.
**Methods:** This study includes 1,228 patients who visited the Health Promotion Center of Chung-Ang University Hospital from January 2013 to August 2015. Serum Hcy, uric acid, fasting glucose, blood urea nitrogen (BUN) and creatinine (Cr), cholesterol profiles, C-reactive protein (CRP) and other laboratory findings were tested. Serum Hcy level was measured by a competitive immunoassay using direct chemiluminescent (Siemens Centaur Immunoassay Systems, USA). Carotid IMT was measured by B-mode carotid ultrasonography. Hyperuricemia was defined as the serum uric acid above 7.0 mg/dL, and hyperhomocysteinemia was defined as the serum Hcy above 15.0 μmol/L.
**Results:** The mean ages of hyperuricemic and normouricemic patients were not significantly different (51.19 ± 15.08 vs. 51.57 ± 17.01, $p$=0.833), however, the male ratio in hyperuricemia group was higher than that in normouricemia group (160/167, 96% vs. 732/1,061, 69%, $p$ <0.001). Patients with hyperuricemia showed significantly higher levels in serum Hcy than normouricemic individuals (13.65 ± 4.47 μmol/L vs 11.68 ± 3.65 μmol/L, $p$<0.001). Carotid IMT in hyperuricemia group was significantly thicker than that in normouricemia group (1.13 ± 0.66 mm vs 1.03 ± 0.53, $p$ =0.029). In patients with hyperuricemia, carotid IMT was correlated with serum Hcy level ($\gamma$=0.209, $p$=0.007), estimated glomerular filtration rate (eGFR), serum BUN and Cr levels ($\gamma$= -0.318, $p$<0.001; $\gamma$=0.229, $p$=0.003; $\gamma$=0.311, $p$<0.001, respectively), however, it was not correlated with serum uric acid level, glucose level and cholesterol profiles. It was shown that serum Hcy level was correlated with eGFR, serum BUN and Cr levels in hyperuricemic patients ($r$= -0.490, $p$<0.001; $r$=0.369, $p$<0.001; $r$=0.487, $p$<0.001, respectively), whereas it was uncorrelated with cholesterol profiles. The patients with high serum Hcy showed higher level of IMT than the patients with low serum Hcy (1.18 ± 0.68 mm vs 1.02 ± 0.52 mm, $p$<0.001). In multiple linear analyses, carotid IMT was affected by eGFR ($\beta$= -0.289, $p$=0.001), however, it was not influenced by glucose level and cholesterol profiles in patients with hyperuricema.
**Conclusions:** Carotid IMT was higher in patients with hyperuricemia than in those with normouricemia, and it was correlated with serum Hcy level in patients with hyperuricemia. This study suggests that decreased renal function in patients with hyperuricemia leads to elevated serum Hcy level, which in turn leads to atherosclerosis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4806

## THU0516 SERUM URIC ACID IS POSITIVELY ASSOCIATED WITH PULMONARY FUNCTION IN KOREAN HEALTH SCREENING EXAMINEES: A CROSS-SECTIONAL STUDY

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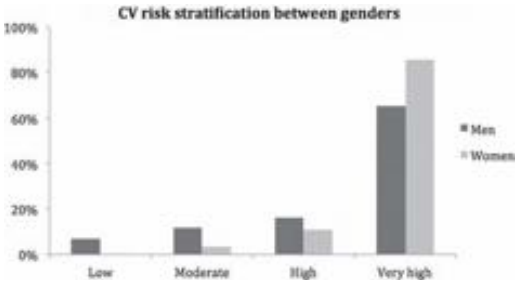
**Background:** Serum uric acid (SUA) is an end product from the action of xanthine oxidase on purine or purine-containing compounds. Recently, much attention has been paid to the role of uric acid in disease modification. A recent study supports the view that hyperuricemia may be an independent risk factor for impaired pulmonary function in the general population. On the other hand, in view of its antioxidant properties, uric acid potentially has important beneficial effects within the respiratory system. The double-edged characteristics of SUA and mixed results from previous studies have complicated determination of whether SUA plays a pulmonary-protective or pulmonary-destructive role.
**Objectives:** The aim of this study was to determine whether level of SUA, a potent antioxidant, is linked to pulmonary function in health screening examinees without overt clinical disease.
**Methods:** We performed a cross-sectional study on 69,928 Koreans without overt medical conditions who underwent a health examination in 2010.
**Results:** A total of 30,572 male (43.7%) and 39,356 female eligible subjects were enrolled in our study. The overall prevalence of hyperuricemia among Korean health screening examinees was 25.5% in males and 8.5% in females. The median age of subjects was 40 (range 35–46) years. Increasing age was positively associated with SUA level. In sex-stratified analyses of SUA level, mean SUA level was positively associated with a quartile increase in FVC% and FEV1% in both genders ($P$ <0.001). There were also a significant positive correlation between SUA level and spirometric measures (FEV1% or FVC%) in both genders (FVC%, $r$ =0.361; FEV1% $r$ =0.314 in men and FVC%, $r$ =0.413; FEV1%, $r$ =0.382 in women). Multiple regression analysis was performed to assess whether FEV1% and FVC% were independently associated with the prevalence of hyperuricemia. The adjusted ORs for hyperuricemia comparing quartiles 2, 3, and 4 to quartile 1 (the reference group, highest quartile) of FVC% in men were 0.876 (95% CI, 0.809–0.949), 0.631 (0.574–0.695), and 0.311 (0.278–0.349), respectively. The adjusted ORs for hyperuricemia comparing quartiles 2, 3, and 4 to quartile 1 of FEV1% in men were 0.791 (95% CI, 0.729–0.859), 0.565 (0.513–0.623), and 0.302 (0.270–0.337), respectively ($p$ for trend <0.001). Similarly, the adjusted ORs of hyperuricemia in women decreased significantly across quartiles 2 to 4 of FEV1% and FVC % compared with the highest quartile as the reference group ($P$ for trend <0.001).
**Conclusions:** SUA was positively associated with FVC% and FEV1% in a healthy Korean population. This finding has important implications for the hypothesis that hyperuricemia might have a favorable effect on lung function. Longitudinal follow-

up studies and prospective interventional studies are required to confirm this positive association between SUA and lung function.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2855

## THU0517 WOMEN WITH GOUT SHOW A POORER CARDIOVASCULAR PROFILE AFTER STRUCTURED ASSESSMENT

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**Background:** Cardiovascular (CV) disease affects gout patients. This is thought to result from a combination of an increase in CV risk factors and crystal-led inflammation. Despite being more prevalent in men, gout also has an impact on the CV risk of women (1). To date, few studies have focused on gender differences on gout, especially in terms of CV assessment.
**Methods:** Observational, cross-sectional study. Consecutive newly-diagnosed crystal-proven gout patients seen in a tertiary hospital underwent a structured CV assessment which included risk prediction tools, carotid ultrasound and CV risk stratification according to current European guidelines. Gout features were also registered. A gender comparison in the different variables was performed, employing chi-2 tests for binary variables, and Student's t or Mann-Whitney's tests for quantitative variables.
**Results:** A total of 199 patients - 28 (14.1%) women and 171 (85.9%) men - were analyzed. Women were significantly older than men (72.7± 11.1 years in women vs 62± 13.0 in men, $p<0.001$). In terms of CV risk factors, women had more commonly high blood pressure (89.3% vs 64.9%, p=0.01), diabetes (53.6% vs 18.7%, $p<0.001$), diuretic use (78.6% vs 38.2%, $p<0.001$), and chronic kidney disease (71.4% vs 21.3%, $p<0.001$). Smoking background was more frequent in men (20% vs 66%, $p<0.001$), and dyslipidemia rates were similar. Uric acid levels at diagnosis were higher (8.97 vs 7.82 mg/dL, p=0.001) in women. Regarding gout features, men showed longer disease duration (median (p25–75) 1 year (0–3.0) in women and 5 years (2.0–15.0) in men, p=0.005) and reported more gout attacks (2 attacks (1.0–3.5) in women and 5 (3.0–20.0) in men, p=0.001), with no differences between genders in the proportion of patients with tophi. No significant differences in carotid plaques were noted (50% in women and 33.6% in men, p=0.32), but ultrasound was often deemed unnecessary in women because they already presented a very high CV risk at assessment (64.3% of women and 33.7% of men, p=0.002). At final CV risk stratification, women tended to show higher CV risk than men (Figure 1).

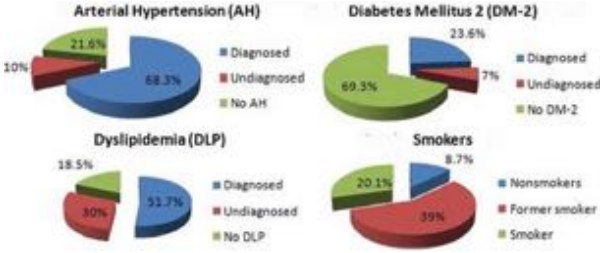



**Conclusions:** The CV profile of women with gout seems worse than male patients in this series. Differences in gout pathogenesis between genders likely explain these results. This finding highlights the need for an optimal CV management when dealing with female gout patients.
**References:**
[1] De Vera MA. Ann Rheum Dis 2010;69:1162
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4279

## THU0518 NEW CARDIOVASCULAR RISK FACTORS SCREENING IN PATIENTS WITH GOUT

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**Background:** Gout is a disease triggered by the crystallization of uric acid in the joints secondary to persistent hyperuricemia, that leads to chronic inflammation. Patients with gout frequently have comorbidities including cardiovascular (CV) disease, kidney failure, diabetes mellitus etc. In fact, some these can increase the levels of uric acid and contribute to develop gout, and also deteriorate the CV profile of these patients. Therefore, their control and identification is essential for a proper management.
**Objectives:** To assess the prevalence of unknown cardiovascular risk factors (CVRF) in patients with gout.
**Methods:** Cross-sectional analysis of a inception cohort of gout patients recruited by consecutive sampling in our rheumatology unit. Gout was diagnosed by visualization of monosodium urate crystals in synovial fluid or tophus sample. A structured CV assessment included CVRF, measurement of blood pressure, anthropometry and lab tests. Arterial Hypertension (AH) was defined by previous diagnosis, blood pressure ≥140/90mmHg and/or use of antihypertensive agents. Type 2 Diabetes Mellitus (DM-2) was defined by previous diagnosis, fasting blood glucose ≥126 mg/dL, glycosylated hemoglobin ≥6.5%; presence of microangiopathic complications was also registered. Dyslipidemia (DLP) was defined by previous diagnosis, use of hypolipidemic agents, or total cholesterol>200 mg/dL and/or triglycerides >150 mg/dL. A descriptive analysis of the results is presented.
**Results:** The study involved 199 patients. The mean age was 63.4 (SD ±13.2) years, with 171 (85.9%) men. At inclusion the prevalence of CVRF was: AH in 136 patients (68.3%), DLP in 13 (51.8%), and DM-2 in 47 (23.6%). Seventy-six (38.6%) were found obese, smoking background was present in 40 (20.1%), use of diuretics (loop and/or thiazide) in 87 (43.7%), and chronic renal failure in 57 (28.6%). After structured assessment, the following undiagnosed CVRF were found: DLP in 59 patients (29.6%), AH in 20 (10.1%) and DM-2 in 14 (7%). New CVRF were found in 94 (46.7%) patients, among them 52 (26.1%) had one CVRF, 13 (6.5%) had 2 CVRF, and even 3 CVRF were identified in 2 cases (1.0%). The final prevalence of CVRF in included gout patients is shown in the Figure.




**Conclusions:** Half of our patients showed at least one unknown CVRF, mostly DLP followed by hypertension and DM-2. This finding highlights the need for active screening for new CVRF in patients diagnosed with gout, due to the potential impact on the proper CV management.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5647

## THU0519 XANTHINE OXIDASE GENE VARIANTS AND THEIR ASSOCIATION WITH BLOOD PRESSURE AND INCIDENT HYPERTENSION: A POPULATION STUDY

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**Background:** Uric acid has been associated with blood pressure and hypertension. During the final stage of purine metabolism xanthine oxidoreductase (XOR) produces uric acid, while at the same time reactive oxygen species are formed. We hypothesized that uric acid production, as assessed indirectly from *XOR* variants, is associated with hypertension (figure 1).
**Objectives:** The aim of the present study is to investigate the association of variants in the *XOR* gene with blood pressure and the development of hypertension.
**Methods:** Analyses were conducted in the prospective Flemish FLEMENGHO and European EPOGH study. Among 2769 participants (48.3% men; mean age

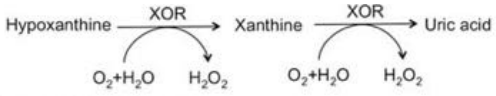



**Figure 1. Purine metabolism**
During the final stage of the purine metabolism, xanthine oxidoreductase (XOR) breaks down hypoxanthine to xanthine, and xanthine to uric acid, while reactive oxygen species are formed. These free radicals inactivate the vasodilator nitric oxide.

40.7 years) we genotyped 25 *XOR* SNPs and measured blood pressure at baseline and follow-up (median 8.8 years). The relation between variants of the *XOR* gene with changes in pulse pressure and mean arterial pressure over time; and incidence of hypertension, were analysed using multivariable mixed models and cox-regression, respectively.

**Results:** Compared with major allele homozygotes, pulse pressure increased approximately 2 mm Hg more in minor allele carriers of rs11904439 (*P*=value 0.01), whereas mean arterial pressure and diastolic blood pressure increased approximately 1 mm Hg less in minor allele carriers of rs2043013 (*P*=0.01). In 2050 participants normotensive at baseline, hazard ratios contrasting risk of hypertension in minor allele carriers *vs.* major allele homozygotes was 1.31 (95% confidence interval [CI] 1.03–1.68) for rs11904439 and 1.69 (95% CI 1.11–2.57) for rs148756340. With the false discovery rate set at 0.25, the aforementioned associations retained significance. The changes in systolic blood pressure from baseline to follow-up and the serum levels of uric acid at baseline (n=1949) were not associated with *XOR*.

**Conclusions:** In conclusion, pending confirmation in appropriately powered cohort studies, our findings suggest that variation in uric acid production, as captured by genetic variation in *XOR*, might be a predictor of changes in pulse pressure, mean arterial pressure and in the risk of hypertension.

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**Disclosure of Interest:** None declared

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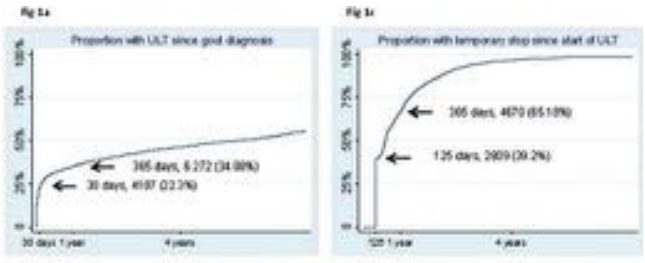
## THU0520 TREATMENT OF GOUT – FACTORS AFFECTING INITIATION AND PERSISTENCE OF URATE LOWERING THERAPY

M.I. Dehlin[1], E. Hoxha Ekström[2], M. Petzold[3], U. Strömberg[2], G. Telg[4], L. Jacobsson[5]. *[1]Dept of rheumatology and inflammation research, Institution of Medicine, Sahlgrenska Academy, University of Gothenburg; [2]Gothia Forum; [3]Health Metrics & Swedish National Data Service, University of Gothenburg, Gothenburg; [4]AstraZeneca, Södertälje; [5]Dept of rhaumatology and inflammation research, Institution of medicine, Sahlgrenska academy, University of Gothenburg, Gothenburg, Sweden*

**Background:** Gout is the most common inflammatory arthritic disease. Treatment has been available since the 1950's and studies from different countries have demonstrated insufficient treatment with urate lowering therapy (ULT); however, contemporary data are scarce.

**Objectives:** The aims of the present observational registry study were to determine; 1) the proportion of patients receiving ULT after gout diagnosis and predictors thereof, and 2) the proportion of patients stopping ULT temporarily and predictors thereof.

**Methods:** All incident cases of patients with gout in the Western Swedish Health Care Region (WSHCR) during 2005–2013, age ≥18 years, were identified in the healthcare consumption database VEGA. WSHCR covers approximately 20% of the total Swedish population. Incident case of gout was defined as a visit with gout diagnosis (ICD-10-CM M10, M14.0–14.1), not preceded by a gout diagnosis during the previous 12 months. First dispense of ULT (allopurinol, febuxostat and probenecid) was identified in the Swedish Prescribed Drug Register. Age, comorbidities (ischemic heart disease, cardiac arrhythmias, congestive heart failure, peripheral vascular disease, cerebrovascular disease, COPD and diabetes), renal disease and renal function (calculated eGFR based on demographics and serum-creatinine), at time of gout diagnosis and at time of first ULT dispensation, were identified in VEGA. Temporary ULT stop was defined as no collection of ULT within 125 days from last dispense. Two binary outcomes were addressed: (i) receiving ULT within 30 days since diagnosis and (ii) temporary ULT stop 125 days after first ULT dispensation. The effects of sex, age, comorbidity, renal disease and renal function, respectively, were estimated by logistic regression. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.




| | Predictors of receiving ULT treatment within 30 days post gout diagnosis | | | Predictors of temporary ULT treatment stop within 125 days after treatment start | | |
|---|---|---|---|---|---|---|
| | % of total (n= 18404) for * | OR | 95% CI | % of total (n = 7,165) for * | OR | 95% CI |
| Female*/ Male | 26.99% | 1.39 | 1.33 - 1.28 | 25.25% | 1.03 | 1.01 - 1.26 |
| Age | 30.55% | 1.44 | 1.33 - 1.56 | 26.45% | 0.59 | 0.59 - 0.65 |
| <60*/ >60 | | | | | | |
| **eGFR reduced kidney function 0*/1 | 62.46% | 1.82 | 1.67 - 1.97 | 88.22% | 0.68 | 0.62 - 0.76 |
| Renal disease 0*/1 | 89.98% | 1.51 | 1.36 - 1.68 | 53.96% | 0.74 | 0.63 - 0.86 |
| Comorbidity 0*/>= 1 | 54.54% | 1.60 | 1.49 - 1.72 | 49.05% | 0.82 | 0.56 - 0.68 |

* Reference group
** eGFR ULT n = 12,094, temp stop n = 3,078

Figure 1a-d. 1a) proportion of patients with ULT dispense post gout diagnosis, 1b) predictors of receiving ULT treatment within 30 days post gout diagnosis, 1c) proportion of patients with temporary ULT treatment stop at 125 days since start of ULT, 1d) predictors of temporary ULT treatment stop within 125 days after treatment start.

**Results:** In total, 18 404 incident cases of gout were identified, whereof 4107 (22.3%) and 6272 (34.08%) received ULT within 30 days and 365 days post-diagnosis, respectively (Fig 1a-b). Male sex, age ≥60, reduced kidney function by eGFR, presence of renal disease and presence of ≥1 comorbidities all moderately but significantly ($p<0.05$) predicted receiving ULT within 30 days (Fig 1a-b). 7165 (39%) of the cases were followed-up after their first ULT dispense (not necessarily within 30 days since diagnosis) and 2809 (39.2%) and 4670 (65.18%) had a temporary stop in the ULT treatment after 125 and 365 days, respectively (Fig 1c-d). The odds of a temporary stop was significantly ($p<0.05$) but moderately predicted by male sex, age <60, normal kidney function by eGFR, non-presence of renal disease and total lack of comorbidities (Fig 1c-d). The likelihood of starting or temporary stopping ULT did not significantly change during the study period (data not shown)

**Conclusions:** We found that only a minority of patients started ULT within one year after gout diagnosis, and the majority of these stopped therapy within one year. Age, renal disease and other comorbidities only moderately improved these results. Thus, there is still room for considerable improvement with regard to ULT in the treatment of gout.

Sponsor: AstraZeneca

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2046

## THU0521 PREVALENCE OF GOUT AND ULT TREATMENT IN WESTERN SWEDEN – A REGISTER STUDY

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**Background:** Gout is the most common inflammatory arthritic disease worldwide. The prevalence varies due to cultural, ethnical and genetic differences in populations, which emphasizes the need for national/regional data on occurrence. There are major insights in the pathogenesis and effective treatments have been available for decades. Despite this several earlier reports state sub-optimal treatment with urate lowering therapy (ULT) of this common and severe disease. Contemporary data on whether this has improved recently are overall few and completely lacking from the Nordic countries.

**Objectives:** In the present study we measured the prevalence of gout in western Sweden and the proportion thereof treated with ULT.

**Methods:** We identified all individuals with one or more ICD-10 diagnosis of gout (M10, M14) in the Western Swedish Health Care Region (WSHCR), Sweden, 2002-01-01 to 2012-12-31 through VEGA, a diagnosis register entailing all visits to physicians in primary and secondary care and hospitalizations in the region with diagnosis according to the Swedish version of ICD-10. WSHCR has 1 600 000 inhabitants, roughly 20% of the population of Sweden and is representative for the country as a whole with regard to demographics and health status. All cases were linked to Statistics Sweden (for death and possible emigration before Dec 2012) and the National Drug Prescription Register (for dispensation of ULT prescriptions during 2012). The point prevalence of gout Dec 2012 was calculated using the number of people aged 20 and above fulfilling our case definitions for gout who were alive and living in WSHCR 2012-12-31 as the numerator and the total population aged 20 and above of WSHCR by 2012–12–31 as the denominator. Dispensation of ULT prescriptions during 2012 were identified for allopurinol, febuxostat and probenecid. The presence of ≥1 dispensation was regarded as ULT treatment in 2012.

**Results:** The prevalence of gout in the Swedish population aged 20 years and above was 1,7% overall and increased with age and male sex (Fig 1), and was more than 3% in males above 50 years of age. Only 43% of the patients received

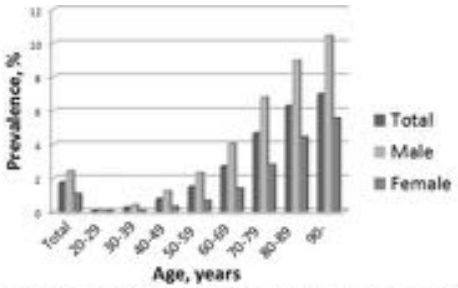



Fig 1 Prevalence of gout i WSHCR by 2012-12-31, age above 20 years in total and by age and sex

treatment with ULT in 2012, almost exclusively allopurinol (99%). Of these 43%, the majority (59%) received a dose of only 100 mg allopurinol daily.
**Conclusions:** Gout is the most common inflammatory arthritic disease in Sweden with an overall prevalence of 1.7%. Treatment with ULT is still in 2012 insufficient with low a low proportion being treated and those treated receiving low doses.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3916

## THU0522 INCREASING INCIDENCE OF GOUT IN WESTERN SWEDEN – A REGISTER STUDY

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**Background:** Gout is the most common inflammatory arthritic disease worldwide. The prevalence varies due to cultural, ethnical and genetic differences in populations, which emphasizes the need for national/regional data on occurrence. While there are several studies on the prevalence of gout only few have addressed the incidence of gout and there are no contemporary studies in Sweden and the neighbouring Nordic countries.
**Objectives:** In the present study we measured the incidence of gout in 2012 and its trends from 2004 to 2012 in the Western Swedish Health Care Region (WSHCR) in Sweden.
**Methods:** We identified all incident cases of gout from 2004 through 2012 through VEGA, a diagnosis register covering all visits to physicians in primary and secondary care and hospitalizations in WSHCR. WSHCR has 1 600 000 inhabitants, roughly 20% of the population of Sweden, and is representative for the country as a whole with regard to demographics and health status.
For the analyses of incidence trends an incident case of gout was defined as having a visit with a first ICD-10 diagnosis of gout (M10, M14) not preceded by a diagnosis of gout for the three calendar years before. Cumulative incidence per year was calculated using the number of incident gout cases aged 20 and above by calendar year (from 2004 to 2012) as the numerator and the total person-years aged 20 and above of WSHCR by the end of each year as the denominator. We calculated standardized estimates (direct method) using the whole Swedish population aged $\geq$20 years in 2012 as standard population Calculation of incidence trend was performed using logistic regression. Incidence in 2012 was based on cases with their first diagnosis of gout 2012 without any such diagnosis during the12 preceding years (2000–2011). All cases were linked to Statistics Sweden (for death and possible emigration before Dec 2012).
**Results:** The incidence of gout increased steadily and significantly (p for trend $<$0.001) from 2004 to 2012 with a 50% increase in the total population. The male to female ratio of gout incidence was consistently two to three fold from 2004 to 2012 (Fig. 1). The incidence of gout in Sweden 2012 was 190 cases per 100 000 person-years.

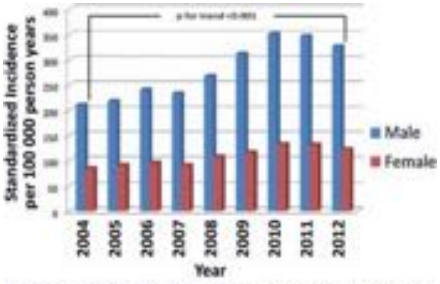


Fig 1 The standardized incidence of gout in the population aged 20 years and above by sex in western Sweden from 2004 to 2012

**Conclusions:** Gout is an increasing health care problem all over the world and also in western Sweden where the incidence of gout increased significantly over the last decade being approximately three times higher than that for rheumatoid arthritis. This increase might reflect changes in the disease panoramic and cultural changes.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3926

## THU0523 COMORBIDITY PATTERN AT THE TIME OF GOUT DIAGNOSIS: A POPULATION- AND REGISTER-BASED CASE-CONTROL STUDY FROM WESTERN SWEDEN

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**Background:** Gout is the most common form of inflammatory arthritis and is linked with an increased occurrence of several comorbidities that impair quality of life and influence mortality. Population based data from European countries are scarce and the majority of them include limited categories of comorbidities without specifically addressing them to the time of gout diagnosis.
**Objectives:** To examine the occurrence of comorbidities possibly related to gout at the time of first gout diagnosis compared with matched controls from the general population.
**Methods:** Using the regional population-based health care data base in Västra Götaland region in western Sweden, the National prescribed drugs register and the census register, we identified all patients who attended any inpatient, outpatient or primary care clinic in the region and received at least one ICD10-coded diagnosis (M10, M14.0, M14.1) corresponding to gout during 2000 through 2012. In this study, we included only incident cases with first ICD-coded diagnosis of gout between January 1st 2006 and December 31st 2012 (N=14.137, mean age 66.5, 66.3% men). Each case was matched by year of birth, sex and county to 5 general population comparators, alive and without gout at the date of the index patients' first gout diagnosis, identified in the population register (N=65.899). Comorbidities (previously suggested to be related to gout) were defined by at least one visit to a physician in primary or specialized care with corresponding ICD-coded diagnosis or having dispensed a prescription for a medication strongly supporting such diagnosis prior to the index date in cases and controls respectively. The treatment with diuretics and cyclosporine was defined by having dispensed a prescription of these agents within 6 months prior to gout diagnosis. Comorbidities were grouped as "possibly causal", "metabolic" and "cardiovascular" (CVD) (table).
**Results:** Among "possibly causal" comorbidities, exposure to diuretics (thiazide, loop and potassium-sparing) (48,1%) and renal disease (11,6%) were the overall most frequent and 1,5 to 2,5-fold more common in gout at diagnosis vs controls, whereas diagnosis of psoriasis was not (table).
Among "metabolic", diagnosis of diabetes or obesity was only modestly more frequent in gout vs controls, whereas hyperlipidemia and hypertension were both very frequent in gout (33,9% and 64,9% respectively) and more common, probably reflecting a high CVD comorbidity in gout (table).
Among "CVD comorbidities", different aspects of cardiovascular disease were all common (>5%) and highly associated with gout at diagnosis with exception of thromboembolism (table).

| Comorbidities | Gout Cases Prevalence, % | Controls Prevalence,% | Prevalence Ratio | 95% Confidence interval |
|---|---|---|---|---|
| **Possibly causal** | **52,6** | **30,0** | **1,76** | **1,71-1,8** |
| Psoriasis | 0,7 | 2,7 | 0,28 | 0,23-0,34 |
| Organ transplantation | 0,9 | 0,4 | 2,16 | 1,75-2,67 |
| Use of cyclosporine | 0,4 | 0,1 | 6,18 | 4,22-9,07 |
| Renal impairment | 11,6 | 7,9 | 1,48 | 1,4-1,57 |
| Use of diuretics | 48,1 | 21,3 | 3,26 | 3,2-3,33 |
| Alcoholism | 2,4 | 2,2 | 1,09 | 1,0-1,22 |
| **Metabolic** | **68,7** | **49,8** | **1,38** | **1,35-1,41** |
| Diabetes | 10,6 | 9,2 | 1,15 | 1,0-1,22 |
| Hypertension | 64,9 | 44,3 | 1,47 | 1,43-1,50 |
| Obesity | 4,1 | 3,9 | 1,04 | 1,0-1,14 |
| Hyperlipidemia | 33,9 | 22,7 | 1,5 | 1,44-1,54 |
| **Cardiovascular** | **35,0** | **25,9** | **1,35** | **1,31-1,39** |
| Ischemic heart disease | 19,0 | 13,0 | 1,46 | 1,40-1,53 |
| Heart failure | 13,7 | 4,3 | 3,2 | 3,06-3,4 |
| Atrial fibrillation | 15,8 | 7,8 | 2,09 | 2,0-2,19 |
| Stroke | 8,6 | 7,2 | 1,2 | 1,13-1,28 |
| Thromboembolism | 5,5 | 6,0 | 0,91 | 0,84-1,0 |

**Conclusions:** The majority of gout patients has at least one comorbidity at the time of gout diagnosis and compared to the general population, a higher prevalence of a wide range of comorbidities, such as renal impairment, organ transplantation, cardiovascular diseases and the diseases reflecting the metabolic syndrome.
**Disclosure of Interest:** None declared
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## THU0524 THE EFFECTIVENESS OF METHOTREXATE IN PATIENTS WITH RESISTANT CHRONIC CALCIUM PYROPHOSPHATE CRYSTAL ARTHRITIS

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**Background:** Calcium pyrophosphate deposition (CPPD) disease is a chronic arthropathy caused by calcium pyrophosphate (CPP) crystal formation and deposition in joints (1). It can be divided into different clinical subtypes: asymptomatic CPPD, osteoarthritis with CPPD, acute CPP crystal arthritis, and chronic CPP crystal inflammatory arthritis (2). In this latter form, colchicine (Co), nonsteroidal anti-inflammatory drugs (NSAIDs), and glucocorticoids (GCs) are commonly used with good effects.Some unresponsive cases, however, need alternative pharmacological treatments. Some authors suggested that methotrexate (MTX) could represent a good option in refractory patients (3).

**Objectives:** The aim of this study was to evaluate the effectiveness of MTX in patients with severe chronic CPP polyarthritis, who did not respond to NSAIDs and/or Co and GCs.
**Methods:** Twenty one outpatients (11 male; mean age 63.38 ±5.27) with resistant chronic CPP arthritis, were treated with MTX in dose between 7.5–12.5 mg/week. All patients fulfilled the EULAR diagnostic criteria for CPPD (2). Tender (TJC) and swollen joints count (SJC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were assessed at baseline, before MTX initiation (M0), and at three, six and nine months (M3, M6, M9). Clinical and biologic side effects of MTX were evaluated. The statistical analysis was performed using Friedman with Dunn's Multiple Comparison Test.
**Results:** At M0 the mean of TJC and SJC were 18.00±3.41 and 10.38±1.96, respectively. These parameters decreased considerably at M3 (TJC=9.62±2.52; SJC=7.95±2.84), reaching a significance at M6 (TJC=4.62±1.88; SJC=3.05±2.06) and at M9 (TJC=1.38±1.28;SJC=0.67±0.66) with respect to M0 ($p<0.0001$). These clinical features were associated to a significant improvement of ESR and CRP levels. The ESR decreased from 52.38±11.47 (M0) to 18.38±12.64 (M9) mm/hour ($p<0.001$) while CRP levels decreased from 3.00±1.27 (M0) to 0.28±0.22 (M9) mg/dl ($p<0.0001$). No relevant side biological and clinical effects were reported. No patients interrupted or reduced the dose of MTX.
**Conclusions:** This study confirms that MTX is a valid therapeutic alternative in severe chronic CPP arthritis patients, refractory to previous conventional drugs. According to this study, we observed an excellent response, with a good safety profile. Further additional studies are necessary to expanding the knowledge and identifying the patients in which MTX could be effective.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5201

## THU0525 COUNTING SYNOVIAL FLUID MONOSODIUM URATE CRYSTALS MAY BE USEFUL IN THE MANAGEMENT OF PATIENTS WITH GOUT

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**Background:** Gout is the most common form of arthritis, and its prevalence is increasing. The mainstay of its diagnosis is the identification of monosodium urate (MSU) crystals in the synovial fluid (SF) (1,2). In a recent study we tested a feasible and reliable technique for counting MSU crystals in the SF (3). This method could provide useful information for the management of patients with gout.
**Objectives:** To investigate correlations between MSU crystals count in SF and clinical characteristics of gout patients.
**Methods:** Forty-four consecutive patients (6 women) affected by gout diagnosed according to the ACR preliminary criteria were studied. Their SFs were examined: for crystal count, 20 ml of fresh SF were placed on a microscope slide and examined by compensated polarized microscopy (400x). The slide was divided into 4 equal parts drawing a cross with a pencil. Crystal count was obtained by continued viewing and in each quadrant the crystals were counted up to a maximum of 400 (maximum number of crystals/patient was 1600). Clinical information included: acute inflammation at the time of SF aspiration, disease duration, number of attacks, number of affected joints, presence of radiographic erosions, presence of tophi, chronic renal failure, type of antiinflammatory and urate lowering treatment (ULT), ESR, CRP, creatinine and serum uric acid (SUA). In five patients, crystal count was repeated after ULT.
**Results:** Mean age was 65.5±11.7 yrs and median disease duration was 6 years (range 0.1–35 years). Aspirated joints were the knee (40 SFs), elbow (1 SF), 1st metatarsophalangeal joint (2 SFs), and ankle (1 SF). Median crystal count was 273 (range 3–1600). Joints with recent (<1 week) inflammation tended to have a higher SF crystal count than the asymptomatic ones (491 [range 3–1600] vs. 100 [range 4–1600]; p=0.1). The number of crystals in the SF correlated with SUA (p=0.04), but not with ESR and CRP. No correlations were found with clinical features. In the 5 patients on ULT, mean MSU crystals count decreased from 871 to 473 (p=0.05).
**Conclusions:** SF MSU crystals count is not associated with the clinical features of gout, correlates with SUA, and decreases with ULT.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3116

## THU0526 EFFICACY AND SAFETY OF FEBUXOSTAT IN 73 GOUTY PATIENTS WITH STAGE 4/5 CHRONIC KIDNEY DISEASE: RESULT FROM A RETROSPECTIVE 9 MULTICENTER STUDY

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**Background:** Although allopurinol reminds the first urate lowering therapy (ULT), its limited dosage in gouty patients with stage 4 or 5 chronic kidney disease (CKD 4/5) prevents to achieve serum uric acid (sUA) level target (<60 mg/l). Febuxostat is a nonpurine xanthine oxidase inhibitor with predominant hepatic metabolism and can be used without dosage adaptation in gouty patients with CKD. However, its safety and efficacy in advanced CKD have been reported in only one study and no data was available in patients with kidney transplantation.
**Methods:** In this retrospective 9 multicenter study, clinical records of all gouty patients with estimated glomerular filtration rate (eGRF) ≤30 ml/min/1.73 $m^2$ (MDRD formula) at febuxostat initiation and at least 3 month-long follow-up period were selected. Items to collect (demographic data, co-morbidity, renal disease, gout history and former treatments, increasing serum urate drugs, laboratory data and any adverse effects-AEs) were approved by all participant centers. Analysis variables were: sUA level at initiation and last available sUA level; variation of eGFR; the percentage of patients who achieved sUA level <60 mg/l and 50 mg/l; and all AEs with specific attention to cardiovascular events.
**Results:** Seventy-three gouty patients (mean age 70.19 ± 11.84, 61 men) from 9 french different rheumatology and nephrology departments were included. 31 patients (41.47%) suffered from vascular CKD and 18 patients (24.66%) had had renal transplant. Mean duration of gout was 6 years. 32 patients (43.48%) had tophi, 28 (38.36%) gout arthropathies. Diuretics were used in 57 patients (78.08%). Cardiac dysfunction was present in 9 patients (16.4%). 72 patients had hypertension, 22 diabetes melitus, 48 dyslipidemia, 28 (38.36%) had past history of vascular events (stroke, heart infraction). Mean sUA level and eGFR at febuxostat initiation were 98.6 ± 28.5 mg/L and 21.5 ± 6.2 ml/min (6–30ml/min), respectively. Febuxostat initiation dosage was 80 mg daily for 47 patients (68.12%), 80mg every 2 days for 17 patients (24.64%) and 120 mg daily for 5 patients (7.25%). At the last visit (mean follow-up was 68.4 weeks (12–260)) mean sUA level was 50.5 mg/L ± 23.3. Forty-seven patients (64.38%) achieved sUA level target <60 mg/L and 42 (57.53%) had sUA level ≤50 mg/L. Renal function improved in 16 patients (23.88%), was unchanged in 20 (29.85%) and worsened in 31 (46.27%). 18 patients experienced flares under febuxostat treatment. AE was observed in 1 patient who had suffered from limb edema. No cardiovascular event was reported during the time of the febuxostat treatment.
**Conclusions:** Febuxostat appears efficient in gouty patents with stage 4/5 CKD or renal transplants. However, safety data is not clear regarding renal function. Further studies with larger sample are warrant to assess this point.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4817

## THU0527 LESINURAD, A SELECTIVE URIC ACID REABSORPTION INHIBITOR, IN COMBINATION WITH XANTHANE OXIDASE INHIBITORS: SUA AND FLARES COMPOSITE ENDPOINT FROM PHASE III STUDIES IN GOUT PATIENTS (CLEAR 1, CLEAR 2 AND CRYSTAL)

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**Background:** Lesinurad (RDEA594) is a selective uric acid reabsorption inhibitor (SURI) investigated for treatment of gout in combination with xanthine oxidase inhibitors (XOI).
**Objectives:** Investigate efficacy as assessed by a composite endpoint of serum uric acid (sUA) target and no flares in gout patients with inadequate response to XOIs alone from three Phase 3 clinical trials examining treatment with lesinurad in combination with allopurinol (ALLO) or febuxostat (FBX).
**Methods:** CLEAR 1 (NCT01510158), CLEAR 2 (NCT01493531) and CRYSTAL (NCT01510769) were 12-month, randomized, double-blind, Phase III trials to evaluate lesinurad (LESU; 200 mg or 400 mg oral, qd) in combination with ALLO vs ALLO + placebo (PBO) (CLEAR 1 and 2) or in combination with FBX vs FBX+PBO (CRYSTAL). A post-hoc composite endpoint defined as the proportion of patients reaching target sUA level (<6 mg/dL in CLEAR 1 and CLEAR 2 and <5 mg/dL in CRYSTAL) and no gout flares was assessed monthly starting at month 7 (after flare prophylaxis was to be discontinued) in each study and in a pooled analysis.
**Results:** CLEAR 1 (N=603), CLEAR 2 (N=610), and CRYSTAL (N=324) patients, respectively, were primarily male (94.0%, 96.2%, and 95.4%); mean ± SD age was 51.9 ± 11.3, 51.2 ± 10.9, and 54.1 ± 11.0 years and duration since gout diagnosis was 11.8 ± 9.4, 11.5 ± 9.3, and 14.7 ± 10.9 years. Most CLEAR 1 and CLEAR 2 patients (90.5% and 84.1%) received ALLO 300 mg daily (range: 200–600 mg and 200–900 mg, respectively). For CLEAR 1 and CLEAR 2,

LESU at both doses in combination with ALLO significantly increased proportions of patients achieving the composite endpoint (sUA target <6.0 mg/dL and no flares) vs ALLO+PBO at all visits, with approximately twice as many LESU patients achieving the composite endpoint ($p<0.001$). For CRYSTAL, LESU at both doses in combination with FBX increased proportions of patients achieving the composite endpoint (sUA target <5.0 mg/dL and no flares) vs FBX+PBO at all visits, with approximately 40% more LESU patients achieving the composite endpoint (p=0.374 to p=0.002). A pooled analysis of LESU at both doses in combination with ALLO or FBX significantly increased proportions of patients achieving the composite endpoint sUA target vs ALLO+PBO or FBX+PBO at all visits, with approximately twice as many LESU patients achieving the composite endpoint ($p<0.001$). Sensitivity analysis comparing gout flares requiring treatment (rather than all flares) and sustained achievement of composite endpoint were also carried out.

**Conclusions:** Significantly greater proportions of patients responded to the combination of lesinurad (200 or 400 mg) + XOI, with approximately twice as many achieving the composite endpoint of sUA target and no flares compared with patients treated with XOI+PBO. Combination therapy with lesinurad + XOI represents an option for gout patients who warrant additional therapy

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## THU0528 HOW KIDNEYS, HEART AND LIVER CHANGE WHEN TOPHI ARE PRESENT?

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**Background:** Gout is related to metabolic, cardiovascular and renal disorders. Whether pathological changes in the main substrate – kidneys, heart and liver are more pronounced in the presence of tophi is still unknown.

**Objectives:** To determine ultrasonographic parameters of the kidneys, heart and liver echogenicity.

**Methods:** A total of 132 gout patients (pts) were examined cross-sectionally and were divided into two groups: 78 gouty arthritis without tophi, 63 males and 15 females aged 56.46±12.38 years and 54 gouty tophi, 53 males and 1 female aged 58.83±11.46 years. All pts underwent a complex multimodal ultrasonography done by one investigator, who was unaware with clinical data. The following parameters were measured: renal length and resistive index (RRI) – an indicator of renal blood flow, thickness of the interventricular septum (IVS) and posterior wall (PW) of the left ventricle in end-diastolic phase, left ventricular muscle mass (LVMM), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), stroke volume (SV), ejection fraction (EF), fraction of shortening (FS), left atrium (LA), aortic (Ao) root and liver echogenicity. Data were analyzed by Kolmogorov-Smirnov, t-test, chi-square tests and multiple logistic regression.

**Results:** Pts were age matched (p=0.267) and had similar mean serum levels of uric acid (p=0.078). Also, in the groups no significant difference in the proportion of pts with flare was estimated – 20 (25.6%) of gouty arthritis without tophi and 22 (40.7%) of gouty tophi (p=0.067), but gouty tophi were with higher CRP (mean±SD; 24.35±34.86 vs 12.11±20.43 mg/l, p=0.002), lower Hb (p=0.001), Hct (p=0.015) and serum albumin ($p<0.001$). Further, we did not establish difference in renal length (p=0.553), but gouty tophi were with higher RRI (mean±SD; 0.68±0.06 vs 0.65±0.05, p=0.003). Comparing gouty tophi to gout without no difference was found in IVS (mean±SD; 12.57±1.84 vs 12.27±1.84 mm, p=0.366), PW (mean±SD; 12.49±1.90 vs 12.13±1.84 mm, p=0.277), LVMM (p=0.292), Ao root (p=0.786) and SV (p=0.070), but a tendency of significantly reduced FS was observed (mean±SD; 37.22±4.26 vs 38.61±3.52%, p=0.050). Gouty tophi were with larger LA (mean±SD; 40.84±5.93 vs 37.96±4.90 mm, p=0.003), higher LVEDV (mean±SD; 55.77±22.40 vs 44.76±24.83 ml/m$^2$, p=0.012), higher LVESV (mean±SD; 17.69±9.98 vs 13.78±8.33 ml/m$^2$, p=0.018) and lower EF (mean±SD; 66.93±5.85 vs 68.94±4.16%, p=0.024). In both groups the proportion of pts with hepatic steatosis was large – 55 (74.3%) of gouty arthritis without tophi and 38 (76%) of gouty tophi (p=0.832). We conducted a multiple logistic regression in which LA, LVEDV, LVESV and EF were included. The factor for development of tophi was LA. Its increase by 1 mm raised the subject's risk of having tophi with an OR=1.102 (95% CI; 1.026–1.184, p=0.008).

**Conclusions:** When tophi were present renal blood flow was reduced and LA was larger. Furthermore, LA was independently associated with the development of tophi. In gouty tophi higher LVEDV and LVESV with the lack of significant difference in SV can be explained with the activation of compensatory mechanisms. Probably, chronic inflammation is one of the causes for the pathological alterations.

**Disclosure of Interest:** None declared

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## THU0529 IMPACT OF AN EDUCATIONAL PROGRAM FOR THE MANAGEMENT OF GOUT DIRECTED TO PRIMARY CARE PHYSICIANS

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**Background:** Gout is the most frequent inflammatory arthritis in males, and therefore a common cause for consultation in both primary care and specialist settings. Despite its frequency, the diagnosis and treatment for this condition are far from desirable (1, 2). There is evidence of gout management improvement through educational programs targeted at primary care physicians (3).

**Objectives:** To measure the impact in diagnostic and therapeutic attitudes towards patients with gout, in primary care physicians, before and after performing an educational intervention based on a clinical case.

**Methods:** Through a training program aimed at general physicians with interest in musculo-skeletal diseases, an initiative of the Sociedad Española de Reumatología [Spanish Rheumatology Society] and the Sociedad Española de Médicos de Atención Primaria [Spanish Society for Primary Care Physicians], sessions were held in 6 Spanish locations. In the sessions, a general physician presented a clinical case about a patient with hyperuricaemia, intermittent arthritis, condrocalcinosis in knee joints and several associated comorbidities. In first place, 5 questions with multiple-choice answers were formulated, regarding the diagnosis and treatment deemed appropriate. Later, the case was evaluated and discussed by a rheumatologist, and the same questions were repeated.

Answers were recorded by electronic means.

**Results:** A total of 195 physicians, divided in 6 locations, attended the sessions. Statistically significant results for each evaluated area are summarized below:

Diagnosis: initially 21.8% of the attendants deemed arthrocentesis necessary for the diagnosis, but complementary investigations appeared to be more important (67.3%). Afterwards, a significant increase in the need for arthrocentesis was observed (46.7%).

Comorbidities: 52.6% of the attendants decided to prescribe a non-steroidal anti-inflammatory drug (NSAID) to the fictional patient, with chronic kidney disease. After the discussion, the broad majority of assistants opted for alternatives such as steroids (41.23%) and only 4.74% still preferred NSAIDs.

Initial complexity for diagnosis: a small percentage (12.7%) considered that a solid diagnosis was not possible without a sample of synovial fluid. This percentage rose up to 55.5% after the intervention.

Prophylaxis: Colchicine-based prophylaxis was prescribed initially by 57.4% of physicians, and after the session, by most of them (71.6%).

Urate lowering drugs: A change was observed in the use of urate lowering medications, from an initial 64.7%, up to 85.1% after the discussion.

There was a reduction in the number of referrals to specialists, but it was not statistically significant.

**Conclusions:** Through educational initiatives for primary care physicians it is possible to optimize the perception of diagnosis and treatment of patients with gout.

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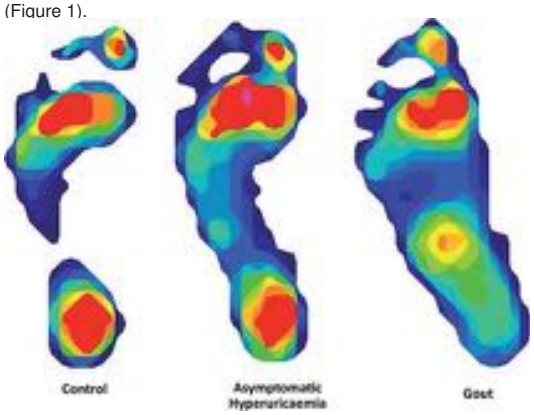
**DOI:** 10.1136/annrheumdis-2016-eular.4337

## THU0530 SPATIOTEMPORAL GAIT PARAMETERS AND PLANTAR PRESSURE DISTRIBUTION DURING BAREFOOT WALKING IN PEOPLE WITH GOUT AND ASYMPTOMATIC HYPERURICAEMIA: A CROSS-SECTIONAL OBSERVATIONAL STUDY

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**Background:** Chronic foot- and lower limb-related impairment are frequently reported by people with gout who also demonstrate altered gait and plantar pressure patterns when assessed during shod walking [1]. The impact of gout on plantar pressure distribution without the confounding effect of footwear is unknown. People with asymptomatic hyperuricaemia, who lack any symptoms or

clinical features of gouty arthritis also report disabling foot pain and lower limb disability compared to normouricaemic controls [2]. However, it unclear whether their gait and plantar pressure patterns also differ from healthy individuals.
**Objectives:** To identify spatiotemporal gait parameters and plantar pressure distribution during barefoot walking in people with gout and people with asymptomatic hyperuricaemia by comparing them to normouricaemic controls.
**Methods:** A total of 87 participants were included: 24 with gout, 29 with asymptomatic hyperuricaemia and 34 age- and sex-matched controls. Spatiotemporal parameters of gait were assessed during level barefoot walking using a GAITRite® walkway. Peak plantar pressure and pressure time integrals were recorded using a TekScan MatScan®. Results were adjusted for age and body mass index.
**Results:** Compared to controls, participants with gout demonstrated increased step time (0.60 vs. 0.64 s, *P*=0.022) and stance time (0.74 vs. 0.80 s, *P*=0.022), and reduced velocity (1.03 vs. 0.91 m/s, *P*=0.050). Participants with gout also walked with decreased peak pressure at the heel (294.3 vs. 268.2 kPa, *P*=0.012) and hallux (233.3 vs. 208.4 kPa, *P*=0.036) and increased peak pressure (95.4 vs. 130.8 kPa, $P<0.001$) and pressure time integrals (23.5 vs. 32.7 kPa*s, *P*=0.005) at the midfoot (Figure 1). Compared to controls, participants with asymptomatic hyperuricaemia demonstrated increased support base (0.08 vs. 0.11 cm, *P*=0.002), double support time (0.16 vs. 0.26 s, $P<0.001$) and cadence (101 vs. 107 steps/min, *P*=0.028) and reduced swing time (0.46 vs. 0.43 s, *P*=0.019) and single support time (0.46 vs. 0.43 s, *P*=0.020) as well as increased pressure at the midfoot (95.4 v 120.1 kPa, *P*=0.013), first metatarsal (211.5 vs. 239.7 kPa, *P*=0.015) and second metatarsal (292.6 vs. 321.3 kPa, P=0.007) (Figure 1).




**Conclusions:** During barefoot walking, people with gout walk slower with plantar pressure patterns suggestive of apropulsive and antalgic gait strategies. Individuals with asymptomatic hyperuricaemia also demonstrate altered barefoot gait patterns when compared to normouricaemic controls. Clinicians may consider dynamic gait outcomes when assessing and managing foot and lower limb related pain and disability in individuals with gout and asymptomatic hyperuricaemia.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2027

## THU0531 NOD2/CARD15 GENE MUTATIONS IN PATIENTS WITH GOUTY ARTHRITIS

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**Background:** Gouty arthritis is a chronic erosive autoinflammatory disease. NOD2/CARD15 molecule has been shown to play important roles in the etiopathogenesis of many inflammatory diseases, resulting in predisposition to the diseases. NOD2/CARD15 is a cytoplasmic molecule which plays a role in controlling apoptosis as well as inflammatory processes by recognizing some microbial components.
**Objectives:** The aim of this study was to identify the frequency of NOD2/CARD15 gene mutation in gouty arthritis patients and determine its possible correlation with disease phenotype.
**Methods:** The study included 93 patients with gouty arthritis and 51 healthy controls matched for age, gender and ethnicity. NOD2/CARD15 gene mutations (R702W and G908R, 3020insC) were studied by PCR method.
**Results:** Of the 93 patients included in the study, 72 were male and 21 were female. The mean patient age was 54.2±14.2 years, mean duration of the disease was 3.1 ± 2.9 years. In the clinical and laboratory evaluations of gouty arthritis patients; first MTP joint involvement was detected in 72 (77.4%), ankle arthritis in 43 (46.2%), knee arthritis in 20 (21.5%), finger joint involvement in 18 (19.5%) patients, increased serum levels of uric acid in 76 (81.7%) and CRP in 42 (45.2%) patients, and elevated ESR in 45 (48.4%) patients. Totally 4 (9%) heterozygous mutations were detected in the NOD2/CARD15 G908R and NOD2/CARD15 R702W genes, while no mutation was detected in the NOD2/CARD15 C3020ins gene. When compared with the control group, statistically significant difference was not detected for each of three regions (908,702,3020ins) (p=0.452, p=0.583 and p=0.350, respectively). In the patient group, statistically significant correlations were not detected in clinical and laboratory findings (first MTP arthritis, ankle arthritis, increased serum uric acid, ESR and CRP values) of the patients with and without mutations for each of the three regions ($p>0.05$)
**Conclusions:** Similar frequency of NOD2/CARD15 gene mutations was detected in patients with gouty arthritis in comparison to healthy control group. Again, no correlation was observed between clinical as well as laboratory findings and NOD2/CARD15 gene mutation. Prospective studies with large series of patients are needed to be carried out on this topic.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1652

## THU0532 GENETIC ANALYSIS FOR P2X7R RS3751142 AND CARD8 RS2043211 POLYMORPHISMS FOR SUSCEPTIBILITY OF GOUT IN MALE KOREAN POPULATION

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**Background:** The NLRP3 inflammasome, a member of the NLR family, is a key player in the production of uric acid-mediated IL-1β and is an important cytoplasmic protein complex involved in gouty inflammation. Recent single-nucleotide polymorphism (SNP) studies suggested that genetic alternations of several target molecules such as CARD8 and P2X7R contribute to the process of NLRP3 inflammasome activation.
**Objectives:** The aim of this study was to determine the association between P2X7R rs3751142 and CARD8 rs2043211 polymorphisms and gout susceptibility in male Korean subjects.
**Methods:** This study enrolled a total 242 male patients with gout and 280 healthy controls. The polymorphisms of two individual genes including rs3751142 (C>A) in the P2X7R gene and rs2043211 (A>T) in the CARD8 gene were assessed using Taq-Man analysis. Statistical analyses were performed using the Chi-square test, Kruskal-Wallis test, and logistic regression analyses.
**Results:** A difference in genotypic frequency of the P2X7R rs3751142 and CARD8 rs2043211 genes was not detected between gout and control patients. Clinical parameters including age, onset age, disease duration, body mass index, and serum uric acid levels were not different among the three genotypes for either P2X7R or CARD8 ($p>0.05$ for all). A pair-wise comparison of P2X7R rs3751142 and CARD8 rs2043211 genotype combinations revealed a protective effect of P2X7R/CARD8 AA/AA against gout susceptibility (OR=0.023, 95% CI 0.874–0.999).
**Conclusions:** This study revealed that genetic variability of the P2X7R rs3751142 and CARD8 rs2043211 genes might, in part, be associated with susceptibility for gout.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2814

## THU0533 COMPARATIVE EFFICACY OF METHOTREXATE AND COLCHICINE IN CPPD AND CHRONIC ARTHRITIS PATIENTS

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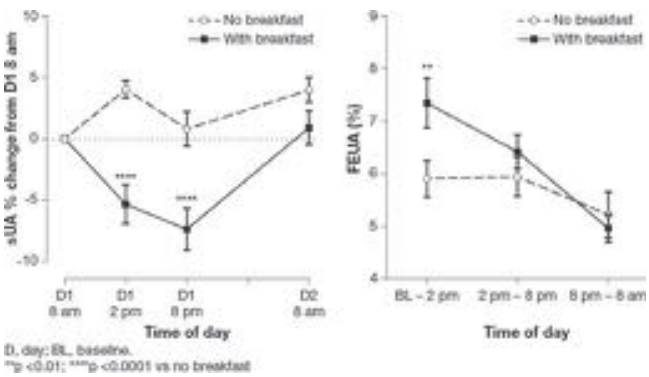
**Background:** Methotrexate is commonly used in patients with calcium pyrophosphate deposition (CPPD) condition, although data on methotrexate use for chronic arthritis in CPPD pts are controversial [1], and it's not clear yet, whether methotrexate can be used as an alternative to colchicine in this group of pts.
**Objectives:** The comparison of efficacy of methotrexate and colchicine in CPPD pts with chronic arthritis, in whom colchicine monotherapy was not sufficient

**Methods:** Results of controlled prospective crossover observational study, including 10 pts (8 females and 2 males) with chronic arthritis associated with CPPD are presented. The inclusion criteria were: age >18 y., the diagnosis of CPPD (by Ryan/*McCarty criteria*), chronic arthritis and low efficacy of NSAIDs. All patients were initially prescribed colchicine 1 mg/day for 3 months with a 1 month "wash-out" period before prescription of methotrexate s/c 20 mg/week for another 3 months. Pts' mean age was 62.5±11.5 y. Average disease duration was 12.4±12.0 y. For evaluation and monitoring was used to measure disease activity scores based on 44 joints (DAS44), together with the count of swollen and tender joints, pain intensity by VAS, health assessment by HAQ, and serum hsCRP at baseline, after first 3 mo of treatment, after 1 mo of "wash-out" period and after the second 3 mo treatment period. Statistica 10.0 package and Biostatistics were used for statistical processing of data. *P* values <0.05 were considered statistically significant.
**Results:** At baseline average DAS44 score was 2.47±0.27, swollen joints – 2.0±0.6, tender joints – 2.4±1.1, pain by VAS – 55.2±12.3 mm, serum level of hsCRP – 3.89±3.82 mg/L, HAQ score – 1.1±0.3. After 3 mo of colchicine therapy average DAS44 score was 1.76±0.28 ($p$=0.004), swollen joints– 1.4±0.5 ($p$=0.048), tender joints – 1.6±1.35 ($p$=0.023), pain by VAS – 42.0±13.2 mm ($p$=0.023), serum level of hsCRP – 3.13±2.85 mg/L ($p$=0.75), HAQ score – 0.95±0.3 ($p$=0.041). After 3 mo of colchicines monotherapy good results were documented in 7 pts (4 pts did not have arthritis, 3 patients showed significant reduction in disease activity (by DAS44) and intensity of pain. Insufficient efficacy was obvious in 3 pts. After 1 mo "wash-out" phase DAS44 score was 2.08±0.26, swollen joints – 1.6±0.5, tender joints – 1.7±1.4, pain by VAS – 46.5±9.8 mm, level of hsCRP – 3.38±1.74 mg/L, HAQ score – 1.3±0.34. After 3 mo of methotrexate therapy DAS44 score was 1.39±0.45 ($p$=0.027), swollen joints – 0.7±0.5 ($p$=0.023), tender joints – 0.6±0.5 ($p$=0.007), pain by VAS – 26.0±18.97 mm ($p$=0.045), serum level of hsCRP – 2.87±2.06 mg/L ($p$=0.75), HAQ score – 0.8±0,6 ($p$=0.045). In 2 out of 3 pts with insufficient colchicine efficacy the arthritis was resolved by methotrexate therapy. Meanwhile 2 pts with favorable outcome after colchicine therapy developed exacerbation after methotrexate phase.
**Conclusions:** Colchicine 1 mg/day and methotrexate 20mg/week demonstrate comparable efficacy. Methotrexate 20mg/week should be viewed as first-line choice in chronic arthritis pts associated with CPPD when colchicines efficacy is insufficient
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3464

## THU0534 SKIPPING BREAKFAST INCREASES SERUM URIC ACID LEVELS

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**Background:** Lifestyle intervention is an important component in uricemic control. Diets with low purine and fructose content, as well as limited alcohol consumption, are recommended for people with hyperuricemia/gout.[1] It has been reported that a 2-day fast can lead to higher serum uric acid (sUA) levels, with a concomitant decrease in urinary uric acid excretion.[2] This work explores whether a shorter fast, such as simply skipping breakfast, affects sUA levels.
**Objectives:** To study the effect on sUA of skipping breakfast.
**Methods:** Two successive experiments were conducted with the same group of healthy subjects (N=30). In the first experiment the subjects consumed all three meals during the day, whereas in the second experiment the subjects did not eat breakfast but had the other two meals as usual. sUA and fractional excretion of uric acid (FEUA) were measured throughout the 24 hr experiment period. In addition, corresponding sUA levels were simulated based on the measured FEUA in order to evaluate the contribution of FEUA to the effects of breakfast on measured sUA.
**Results:** At 6, 12 and 24 hr after breakfast (~8 am), the mean±SE change from baseline (pre-breakfast) in sUA was -0.3±0.09, -0.4±0.1 and +0.1±0.09 mg/dL, respectively, when the group ate breakfast (Figure). These changes average to a decrease in sUA of 0.2±0.08 mg/dL over 24 hrs. In comparison, the change in sUA from baseline was +0.3±0.05, +0.1±0.09 and +0.3±0.07 mg/dL at 6, 12 and 24 hr when they did not eat breakfast. These changes average to an elevation in sUA of 0.2±0.05 mg/dL over 24 hrs. As a result, the difference in sUA (no breakfast - breakfast) was +0.4±0.09 mg/dL ($p<0.0001$). In the first 6 hrs after breakfast, FEUA were 7.3±0.45 with breakfast and 5.7±0.33 without breakfast (Figure, $p<0.01$). However, when sUA levels are simulated based on the observed FEUA, the difference in FEUA between breakfast and no breakfast cannot fully explain the difference in their observed sUA.



D, day; BL, baseline.
**p <0.01; ****p <0.0001 vs no breakfast

**Conclusions:** Skipping breakfast leads to a 0.4 mg/dL elevation in sUA over 24 hr. A decreased FEUA is partially responsible for the difference in sUA; however, there are likely other mechanisms involved as well. Routinely skipping breakfast might lead to even higher elevations in sUA.
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**Disclosure of Interest:** S. Liu Employee of: Ardea Biosciences, Inc., J. Miner Employee of: Ardea Biosciences, Inc.
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## THU0535 QUALITY OF LIFE IN PATIENTS WITH GOUT IN SOUTH WESTERN SYDNEY

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**Background:** Gout is the most common type of inflammatory arthritis in men, with an Australian population prevalence of 0.39% (1, 2). Due to ageing and rising obesity, the global burden of gout is increasing. Global disability adjusted life years (DALYs) for gout rose from 76 000 in 1990 to 114 000 in 2010 (2). Patients with severe gout are known to have low health-related quality of life (HRQOL), especially in regards to physical function (3).
**Objectives:** To determine HRQOL in gout patients of South Western Sydney, and the utility of the Gout Impact Scale (GIS). To compare GIS in patients with acute versus non-acute gout, and high frequency of gout attacks versus low frequency of gout attacks. To compare Short Form 36 version 2 (SF36v2) in our gout cohort with normals and other chronic diseases.
**Methods:** Postal cross-sectional survey study of adult patients diagnosed with gout recruited from 3 public hospitals and a private clinic. SPSS software facilitated analysis.
**Results:** 133/184 patients recruited with a 72.3% response rate. The overall impact of gout on their life was 5.9/10, higher in acute gout vs non-acute gout, mean 6.8 vs 5.2, $p<0.02$. Of patients with gout attack in the last 3 months, the severity of pain was 6.8/10. Patients with more frequent attacks of gout had higher overall severity of gout than those with less frequent attacks, mean 7.5 vs 5.2, $p<0.002$.
Patients with acute gout had higher mean scores for gout concern overall (GCO), gout medication side effects (GMSE), unmet gout treatment need (UGTN), well being during attack (WBDA) and gout concern during attack (GCDA), compared to non-acute gout, $p<0.02$. There was a moderate correlation between GCDA and GCO ($\tau_b$ =0.566, $p<0.0001$) and GCDA and WBDA ($\tau_b$=0.508, $p<0.0001$)
Patients with more frequent attacks had higher mean scores for GCO, GMSE, UGTN, WBDA and GCDA, compared to those with less frequent attacks, $p<0.002$.
Gout patients scored significantly lower in all 8 domains of SF36v2 compared to Australian normative data and diabetics. There was a moderate correlation between WBDA and the mental component summary of SF36v2 ($\tau_b$ =-0.406, $p<0.0001$).




**Conclusions:** Results of the Gout Impact Scale made sense with greater impact of gout in patients with acute gout or more frequent attacks in all 5 scales, suggesting it is a robust instrument in the diverse gout population. The impact of gout was not confined to just physical domains, but had a significant negative impact on psychological health.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1931

## THU0536 REMISSION AND RE-TREATMENT OF PATIENTS WITH PAGET'S DISEASE OF BONE TREATED WITH ZOLENDRONIC ACID – A SINGLE CENTER 10 YEAR EXPERIENCE

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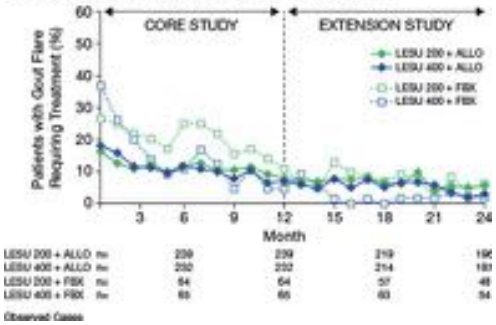
**Background:** Treatment of Paget's Disease of Bone (PDB) has been revolutionized by the use of zolendronic acid (ZA). Patients usually have a dramatic response to treatment with normalization serum alkaline phosphataise (ALP) levels and a longer period of clinical remission, compared with other class agents. Data from long-term use are scarse.
**Objectives:** Evaluate the effectiveness and safety of ZA in PDB patients, as well as remission, re-treatment rates and side effects in our outpatient population since 2005.
**Methods:** A retrospective study of PDB patients treated with 5 mg ZA intravenous infusion at our day-care center. Follow up time, demographic and clinical characteristics, previous therapeutic agents, rate of response, number and reasons of re-treatment(s) and rates of adverse events were collected. A descriptive statistic analysis was made.
**Results:** 48 patients, 60% female, mean age of 75 years, with a median time since the diagnosis of 12.3 years. The disease was poliostotic in 73% of the patients and pelvis (65%), skull (29%) and spine (27%) were the most common pagetic localizations. Deafness was present in 12.5% and 65% had hip involvement. 44% patients had been treated with another biphosphonate agent previously. Response rates were 97.9% at 1 year, 87.2% after 2 years and 95.1% after 3 years. The mean ALP levels before ZA infusion was 290 UI/L and after 112 UI/L. Sixteen patients needed a re-treatment in the period of follow up, minimum of 1 year after the ZA infusion and maximum of 8 years after. 56.3% due to raised of ALP levels and 43.8% due pain/ hip involvement. Four patients needed a third infusion due to hip involvement, and 2 of them a forth infusion due to the same reason. All of the patients re-treated due to hip involvement had severe hip involvement at time of diagnosis. In our population, 2 patients achieved 10 years remission, 5 patients 9 years remission and 10 patients 8 years remission with a single ZA infusion. Recording adverse effects were: 14.6% *Flu like* symptoms (7 patients), 2% assintomatic hypocalcemia (1 patient) and no reports of osteonecrosis or fractures. All of these effects were reported after the first ZA infusion.
**Conclusions:** In our population, we find high long-term sustained remission rate. Only sixteen patients needed re-treatment. Patients maintained sustained remission up to 10 years of a single ZA infusion. Incidence of adverse events was similar to the reported in the literature.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6083

## THU0537 CLINICAL RESPONSE OF TOPHUS AND FLARES TO EXTENDED USE OF LESINURAD IN COMBINATION WITH A XANTHINE OXIDASE INHIBITOR IN PATIENTS WITH GOUT

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**Background:** Three randomized, double-blind, Phase III trials reported that greater proportions of patients treated with lesinurad 200 mg (LESU200) or 400 mg (LESU400), combined with the xanthine oxidase inhibitor (XOI) allopurinol (ALLO; CLEAR 1 and 2) or febuxostat (FBX; CRYSTAL), achieved serum uric acid (sUA) targets at 6 months versus xanthine oxidase inhibitor (XOI) + placebo (PBO).
**Objectives:** To evaluate the impact of long-term treatment with lesinurad + XOI on tophus and flares for at least 1 year and up to 2 years.
**Methods:** Patients completing 12 months in the core CLEAR and CRYSTAL studies could enroll in respective uncontrolled, open-label extension studies (NCT01808131; NCT01808144). Patients randomized to LESU200 + XOI or LESU400 + XOI in the core studies who continued on combination therapy in the extension studies were analyzed. Efficacy endpoints included: (1) proportions of patients with complete resolution (CR) of ≥1 target tophus (i.e. measurable tophus on hands/wrists and/or feet/ankles 5–20 mm in longest diameter), (2) percent reductions in the total area of all target tophi, and (3) proportions of patients experiencing gout flares requiring treatment (GFRT).
**Results:** A total of 239 (LESU200+ALLO) and 232 (LESU400+ALLO) patients continued in the CLEAR extension; 64 (LESU200+FBX) and 65 (LESU400+FBX) patients continued in the CRYSTAL extension. Proportions of patients with CR of ≥1 target tophus increased from end of core study (1 year) to 2 years: from 25.0% to 43.8% in LESU200+ALLO and 30.3% to 36.4% in LESU400+ALLO, and from 26.6% to 53.1% in LESU200+FBX and 35.4% to 58.5% in LESU400+FBX (LOCF). Percent reduction in the total area of all target tophi versus baseline changed from end of core study to 2 years: from 11.6% to 41.8% in LESU200+ALLO and 42.7% to 49.3% in LESU400+ALLO, and from 54.8% to 68.3% in LESU200+FBX and 58.6% to 72.4% in LESU400+FBX (LOCF). Proportions of subjects with a GFRT per month decreased during continued combination treatment in both extension studies (Figure).The proportions of patients with a GFRT during Months 1, 12, and 24 were, respectively, 16.3, 7.9, and 5.6 in LESU200+ALLO; 18.1, 6.9, and 3.0 in LESU400+ALLO; 26.6, 10.9, 6.3 in LESU200+FBX; and 36.9, 4.6, 1.9 in LESU400+FBX. Extended treatment with LESU + XOI did not result in increased exposure-adjusted incidence rates of adverse events (AEs), AEs leading to discontinuation of lesinurad, serious AEs, or clinical laboratory abnormalities.

Figure. Patients With Gout Flares Requiring Treatment (GFRT) During Core Study and Extended Treatment With Lesinurad + XOI




**Conclusions:** The CLEAR and CRYSTAL extension studies showed that patients treated with lesinurad + XOI for up to 2 years exhibited continued increases in the rate of complete resolution of tophi and reduction in tophus area, as well as decreased rates of GFRT.
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## THU0538 DECREASING URIC ACID LEVEL IS ASSOCIATED WITH IMPROVING GLOMERULAR FILTRATION RATE IN CHRONIC KIDNEY DISEASE PATIENTS WITH/WITHOUT GOUT

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**Background:** Hyperuricemia was a risk factor for hypertension, metabolic syndrome, type 2 diabetes mellitus, cardiovascular disease, and chronic kidney disease. Uric acid lowering therapy was indicated when hyperuricemic patients with established diagnosis of gout. Clinical trials have demonstrated that xanthine oxidase inhibitor decreased the progression of chronic kidney disease in gout patients. Uric acid lowering therapy was not suggested in asymptomatic hyperuricemic patients due to lack of evidence.

**Objectives:** To evaluate the association between the change of uric acid level and renal function in chronic kidney disease patients with/without gout.
**Methods:** This is a retrospective cohort study. The data source was the electronic records of National Taiwan University Hospital and its branch Hospital during 2011 to 2015. Patients were included if they have chronic kidney disease stage 2, 3, and 4 according to K-DOQI staging and receive follow-up for more than 6 months. Multiple variables linear regression models were applied for evaluating the association between the change of uric acid level and eGFR. The variables including age, gender, hypertension, type 2 diabetes mellitus, dyslipidemia, gout, and initial uric acid level were analyzed. We performed a subgroup analysis of the patients with decreasing uric acid level.
**Results:** Total 272 patients were included. There were 154 (56.6%) females and 118 (43.4%) males. The mean age was 57.9±14.7 (SD) years. The mean uric acid level was 6.5±1.9 (SD) mg/dL. The mean duration of follow-up was 128.7 ±55.3 (SD) weeks. 52 (19%) patients had the diagnosis of gout. In multivariable linear regression models, the change of eGFR was affected by the change of uric acid level (β= -0.249, $P$ <0.001). In the subgroup analysis of the patients with decreasing uric acid level, the change of eGFR was also affected by the change of uric acid level (β= -0.214, $P$ =0.011).
**Conclusions:** The decreasing uric acid level is associated with increasing eGFR in chronic kidney disease patients even after adjusting the status of gout. The causal relationship between the uric acid level and renal function should be interpreted carefully.
**References:**
[1] Richette P, Perez-Ruiz F, Doherty M, et al. Improving cardiovascular and renal outcomes in gout: what should we target? Nature Reviews Rheumatology 2014;10(11):654–61.
**Disclosure of Interest:** None declared
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## THU0539 POPULATION-SPECIFIC RESEQUENCING REVEALS ASSOCIATION OF THE ABCC4/MRP4 GENE WITH GOUT IN NEW ZEALAND MĀORI AND PACIFIC MEN

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**Background:** Genetic variants in uric acid transporters that control serum urate levels have been identified in Europeans by genome-wide association studies [1]. However there is no evidence for association with serum urate (or gout) with the organic anion transporters (OAT) 1–3 (*SLC22A6, SLC22A7* and *SLC22A8*) and multi-drug resistance protein 4 (MRP4) encoded by *ABCC4*; all four transporters have been implicated in uric acid secretion [2]. The Māori and Pacific (Polynesian) population of New Zealand (NZ) has the highest prevalence of gout worldwide and exhibits lower fractional excretion of uric acid (FEUA) than Europeans.
**Objectives:** To identify any Polynesian population-specific genetic variants in the *SLC22A6–8* and *ABCC4* genes associated with gout.
**Methods:** All participants had ≥3 self-reported Māori and/or Pacific grandparents. From the total sample set of 1808 individuals, 191 hyperuricaemic (highest urate levels) and 202 normouricaemic (lowest urate levels) individuals were selected and resequenced over a total of 24.3 kb of promoter, exon and 3' and 5' untranslated region DNA within the four genes. Replication genotyping for *rs4148500* was done using Taqman over the remaining 1415 individuals. Logistic regression association analysis with gout or hyperuricaemia (≥0.36 mmol/L in women, ≥0.42 mmol/L in men) as outcome, or linear regression with FEUA or serum urate as outcome, was performed adjusting by age, sex and Polynesian ancestry.
**Results:** A total of 39 common variants were detected with one in *ABCC4* (*rs4148500*) significantly associated with hyperuricaemia and gout. There were substantial differences in allele frequency between Western (Samoan, Tongan, Niuean, Tokelaun) and Eastern (NZ and Cook Island Māori) Polynesian samples – adjusting for ancestry revealed evidence for association with gout in the resequenced samples (OR=1.62, $P$=0.012 for *rs4148500*). The association of *rs4148500* with gout was replicated (OR=1.25, $P$=0.033) and was restricted to males ($OR_{Males}$=1.43, $P$=0.001; $OR_{Females}$=0.98, $P$=0.89). The gout risk allele was associated with FEUA in males (b=-0.570, $P$=0.01) and there was a trend towards association with serum urate in the male controls (b=0.013, $P$=0.07). The Ensembl database revealed that the variant was monomorphic (for the protective major allele) in Europeans.
**Conclusions:** This is the first report of a genetic factor specifically contributing to the increased risk of gout in men of Māori and Pacific ancestry in NZ. Association of *ABCC4* with gout and FEUA is consistent with the established role of MRP4 as a unidirectional urinary uric acid efflux pump of uric acid [3].
**References:**
[1] Kottgen et al. Nat Genet 2013;45:145
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[3] Van Aubel et al. Am J Physiol 2005;288:F327
**Acknowledgement:** The New Zealand Health Research Council, Lottery Health New Zealand, Arthritis New Zealand and the National Institute of Health (United States) are thanked for funding this study.
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## THU0540 AUTOLOGOUS OSTEOBLASTIC CELLS VERSUS CONCENTRATED BONE MARROW IMPLANTATION IN OSTEONECROSIS OF THE FEMORAL HEAD: A RANDOMIZED CONTROLLED SINGLE BLIND STUDY

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**Background:** Non traumatic osteonecrosis (ON) of the femoral head is characterized by epiphyseal necrosis leading to femoral head collapse and hip replacement. ON can be seen as a vascular, mesenchymal and bone cells disease. Indeed, it was shown that implantation of bone marrow concentrate (BMC) containing mesenchymal stem cells (MSC) could delay ON progression and improve symptoms. Then, the possibility was raised that a cell-based medicinal product consisting in a population of autologous osteoblastic cells (OB) could be more efficacious than BMC in early stages ON of the femoral head.
**Objectives:** This study was undertaken to evaluate the efficacy of OB cells implantation in a randomized comparison with BMC implantation in early stages (prefractural ARCO stage 1 or 2) ON of the femoral head.
**Methods:** Patients with stage 1 or 2 ON were included in a randomized controlled single blind trial. Hips were randomized to receive a core decompression procedure followed by BMC or OB cells implantation. In the BMC group, 410.6±84.9 ml of BM was harvested from the iliac crest and concentrated to 41.8±10.9 ml. In the OB group, MSC were isolated from BM aspirate (48.8±17.7 ml), expanded and differentiated *ex vivo* under autologous conditions to obtain a population of OB cells (18.6±4.3x$10^6$ cells). Hip pain, WOMAC score and X-Rays were assessed at 3, 6, 12, 24 and 36 months. The primary endpoint was the proportion of responders at 24 months. A responder was defined as the absence of progression to a fractural stage (stage 3 or 4) and a clinically significant pain improvement.
**Results:** From 72 hips randomized, 60 hips (30 hips per group) were analyzed as the ITT efficacy cohort (50.6±11.8 years). Baseline demographic data, risk factors, location and size of ON and symptoms were not statistically different between groups. At 24 months, 70% versus 40% of hips ($p$<0.05) and at 36 months, 60% versus 33% of hips ($p$<0.05) in OB and BMC groups respectively were considered as responders. The rate of progression to stage 3 or 4 was in favor of the OB group. At 24 months, 20% versus 40% of hips (NS) and at 36 months, 20% versus 47% of hips ($p$<0.05) in OB and BMC groups respectively progressed to stage 3 or 4. A decrease in hip pain was observed in the OB group compared to the BMC group at 24 months (NS) and 36 months ($p$<0.05). Finally, patients treated with OB cells demonstrated a decrease in joint symptoms at 24 and 36 months according to the WOMAC score. Overall, 117 SAE (47 in the BMC group and 70 in the OB group) were reported of which 4% (5 SAE) were possibly related to the procedure or the cell therapy products.
**Conclusions:** This study showed that OB cells implantation in ON lesion could be more efficacious than BMC treatment to delay the evolution to subchondral fracture and to reduce pain in ON of the femoral head.
**Disclosure of Interest:** V. Gangji Consultant for: Bone Therapeutics, M. Toungouz: None declared, C. Lechanteur: None declared, Y. Beguin: None declared, E. Baudoux: None declared, V. De maertelaer: None declared, S. Pather: None declared, R. Katz: None declared, J. Ino Employee of: Bone Therapeutics, D. Egrise: None declared, M. Malaise: None declared, J.-P. Hauzeur Consultant for: Bone Therapeutics
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## Fibromyalgia

### THU0541 PAIN FROM STRUCTURAL PATHOLOGY IS A RISK FACTOR FOR LATER GENERALIZED PAIN: A POPULATION BASED COHORT STUDY

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**Background:** Generalized pain in the form of chronic widespread pain (CWP) and fibromyalgia is common in the general population [1] and is also a frequent comorbidity in several diseases. Chronic pain from structural pathology (e.g. inflammation or injury) has been proposed as a mechanism behind generalization of pain, likely through the mechanism of central sensitization [2].
**Objectives:** The aim was to study if patients with rheumatoid arthritis (RA), endometriosis or inflammatory bowel disease (IBD), diseases with a known component of pain from structural pathology and with diverse etiology, have an increased risk of later developing generalized pain.
**Methods:** This prospective cohort study used the Skåne Healthcare Register, covering routinely collected data on all types of care in the region of Skåne, southern Sweden (population approx. 1.3 million). The cohort included all patients in specialized and primary care between 2004 and 2014. The primary outcome, later generalized pain, was defined as a diagnosis of *pain, unspecified* (ICD-10 R52.9) or *fibromyalgia* (ICD-10 M79.7) which follows the stricter ACR-10 criteria. We used Poisson regression to calculate the incidence rate ratio (IRR), we adjusted for sex and age at study inclusion.
**Results:** During the study period 696,539 eligible individuals aged 18 or older living in the Skåne region and consulting health care at least once during the period were included in the study. After excluding patients with prevalent pain (n=1264) 695,275 individuals remained. Generalized pain was more common in women than in men (71% female). Out of 10,165 patients exposed to RA 5% later developed generalized pain, for endometriosis and IBD the corresponding percentage was 5% and 3% respectively. Among the 673,040 unexposed participants 2% developed generalized pain during the study period.

Incidence rate ratios for developing generalized pain

| | N (%) exposed cases | IRR (95% CI) | |
|---|---|---|---|
| | | Crude | Adjusted* |
| Rheumatoid arthritis | 518 (5.1%) | 3.0 (2.8–3.3) | 2.5 (2.3–2.7) |
| Endometriosis | 185 (5.2%) | 2.4 (2.0–2.7) | 2.4 (2.0–2.7) |
| IBD | 273 (2.4%) | 1.7 (1.5–1.9) | 1.7 (1.5–1.9) |

*For sex and age at inclusion.

The IRR for later generalized pain in patients with RA was 2.5 (95% CI: 2.3 - 2.7) compared to the unexposed, for endometriosis patients the IRR was 2.4 (95% CI: 2.0 - 2.7) and for IBD-patients 1.7 (95% CI: 1.5 - 1.9) when adjusted for age and sex. Restricting the outcome to only the patients with fibromyalgia, rendered equal or higher IRR for all studied diseases.
**Conclusions:** This study shows that pain from structural pathology, caused by diverse etiological factors, may predispose for later generalized pain. The understudied disease of endometriosis is a risk factor of almost equal magnitude as RA, which has, to the best of our knowledge not been shown before. These results have implications for both clinical practice, underlining the importance of optimizing pain control, and further research regarding the etiology of generalized pain and fibromyalgia.
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**Disclosure of Interest:** None declared
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### THU0542 PAIN CATASTROPHIZING AND SELF-EFFICACY AS DETERMINANTS OF SUBJECTIVE AND OBJECTIVE PHYSICAL FUNCTION IN WOMEN WITH FIBROMYALGIA: THE AL-ÁNDALUS PROJECT

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**Background:** A discrepancy between subjective (i.e., patients' perceptions) and objective (i.e., clinical observations) of physical function (PF) has been reported in fibromyalgia (FM). This discordance, with a worse subjective PF than objective PF, may have negative consequences for health-related outcomes such as the ability to pursue valued activities in daily life. Therefore, it seems important to find modifiable factors associated with this discrepancy between objective and subjective PF in FM.
**Objectives:** The present cross-sectional study examined 1) the existence of discordance between subjective and objective PF, 2) the independent association of catastrophizing and self-efficacy with subjective and objective PF, and 3) the independent association of catastrophizing and self-efficacy with the discrepancy between subjective and objective PF.
**Methods:** A total of 427 FM women filled out the Pain Catastrophizing Scale, Chronic Pain Self-efficacy Scale, and PF subscales of the SF-36 (SF-36-PF) and of the Revised FM Impact Questionnaire (FIQ-R-PF). Objective PF was measured by performance-based tests: the Senior Physical Fitness Test Battery plus handgrip strength test. Subjective and objective PF were transformed to standardized z-scores ([value-mean]/standard deviation; using means and standard deviations of a general population sample, *n*=230). These scores reflect the deviation of FM patients from the general population in standard deviation units.
**Results:** In one-way analysis of variance (ANOVA), subjective PF was poorer than objective PF ($P<.001$). Linear regression analysis (adjusted by age, body mass index, years since FM diagnosis, and educational level) showed that high pain catastrophizing and low self-efficacy were independently associated with high subjective and objective PF. Linear regression analysis revealed that high pain catastrophizing (for SF-36-PF and FIQ-R-PF) and low self-efficacy (for the SF-36-PF) were associated with a greater discrepancy between subjective and objective PF.
**Conclusions:** Subjective PF is worse than objective PF in FM. High catastrophizing and low self-efficacy are not only independently associated with low subjective and objective PF but also with a greater discordance between subjective and objective PF in FM. Our findings suggest that clinical trials that combine cognitive therapy (focused on increasing subjective PF and self-efficacy and reducing catastrophizing) and physical exercise (focused on enhancing objective PF) have potential to be effective in FM.
**References:**
[1] Hidding A, et al. J Rheumatol 1994;21(5),818–23.
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### THU0543 EVALUATION OF THE FIBROMYALGIA RAPID SCREENING TOOL (FIRST) QUESTIONNAIRE TO SCREEN FIBROMYALGIA ASSOCIATED WITH INFLAMMATORY RHEUMATIC DISEASE

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**Background:** Fibromyalgia (FM) is prevalent in patients with chronic inflammatory rheumatic diseases (CIRd), where it hampers diagnosis and activity assessment. No tool for screening FM associated with CIRd has ever been evaluated. The Fibromyalgia Rapid Screening Tool (FiRST) is a brief and simple self-complete questionnaire that has been validated for screening FM in patients with diffuse chronic pain.
**Objectives:** The purpose of this study was to evaluate how well FiRST performs on screening for FM associated with CIRd.
**Methods:** This single-center cross-sectional study was conducted between September 2014 and April 2015 on all patients with chronic pain presenting for rheumatoid arthritis (RA), spondyloarthritis (SpA), and connective tissue disease (Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), scleroderma (Scl), myositis). Diagnosis of FM was based on ACR–90 classification criteria (to minimize interfering overlap between rheumatic disease-related pain and FM-related pain) and expert opinion.
**Results:** The population included 605 patients: 279 RA, 271 SpA (52 psoriatic arthritis, 126 radiographic axial SpA, 64 non-radiographic axial SpA, 29 peripheral SpA), 57 connective tissue disease. In total, 51 patients had FM meeting the ACR–90 criteria, and 93 patients were given a diagnosis of FM by the expert. When tested against the ACR–90 classification criteria, FiRST demonstrated a sensitivity of 74.5%, a specificity of 80.4%, a positive predictive value of 26.6% and a negative predictive value of 97.1%. Specificity was significantly weaker

in the connective tissue disease group (RA: 84.4%, SpA: 80.2%, connective tissue disease: 59.6%; $p<0.001$). When tested against expert opinion, FiRST demonstrated a sensitivity of 75.8%, a specificity of 85.1%, a positive predictive value of 48.3% and a negative predictive value of 95%. FiRST underperformed on sensitivity in the SpA group compared to the connective tissue disease group (66% *vs* 94.4%; $p=0.004$). Performances varied according to item in the self-complete questionnaire.

**Conclusions:** The FiRST self-questionnaire performs less well in inflammatory rheumatic diseases than in primary fibromyalgia, but nevertheless it remains a simple and rapid tool to help rheumatologist and general practitioner detects fibromyalgia associated with inflammatory rheumatic disease.

**Disclosure of Interest:** None declared

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## THU0544 IMPAIRED PULMONARY DIFFUSING CAPACITY IN PATIENTS WITH FIBROMYALGIA

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**Background:** Fibromyalgia syndrome (FM) is a chronic pain disorder characterised by symptoms of morning stiffness, fatigue, depression, non-restorative sleep and reduced cognitive performance, some of which are worsened by emotional distress, meteorological changes, insomnia and strenuous activity.Some of the patients' symptoms, as well as their physical and psychological characteristics, can be attributed to autonomic nervous system (ANS) dysfunction. It has been demonstrated that ANS dysfunction in patients with type 1 diabetes mellits can induce functional alterations in the regulation of pulmonary microvascular tone and the distribution of pulmonary blood filling.

**Objectives:** The aim of this study was to evaluate whether pulmonary diffusing capacity is impaired in patients with FM as it is in those with other diseases characterised by ANS dysfunction such as type 1 diabetes.

**Methods:** Forty-five consecutive anti-nuclear antibody (ANA)-negative female Caucasian patients aged 50.1±5.6 years with FM and compared with 45 healthy female control volunteers matched in terms of age and body mass index (BMI). The autonomic function have been evaluated by means of standard electrocardiography (ECG), finger blood pressure respiration, and muscle sympathetic nerve activity (MSNA) at rest and during a stepwise tilt test up to 75°. Their autonomic profiles were drawn up on the basis of MSNA, plasma catecholamine levels, and spectral indices of cardiac sympathetic and vagal modulation, and sympathetic vasomotor control computed by means of the spectrum analysis of RR and systolic arterial pressure (SAP) variability. Lung volumes and dynamic spirometry parameters were assessed by means of plethysmography. All the patients were clinical evaluated and completed the fibromyalgia impact questionnaire (FQI) and Compositive Autonomic Symptom Score (COMPASS) questionnarie.The number of tender points (TPs) was counted using Wolfe's protocol, which gives a total score of 0–18, and the intensity of somatic pain was assessed using a 100 mm visual analogue scale (VAS).The severity of Raynaud's phenomenon was evaluated using the Raynaud's Condition Score (RCS), an ordinal scale ranging from zero to10 that measures the level of difficulty experienced by patients.

**Results:** There was no difference in lung volumes between the FM patients and healthy controls, but the carbon monoxide diffusion capacity of the lung (DLCO) (83±4 *vs.* 96±5; $p<0.001$), Kco (84±5 *vs* 98±5; $p<0.001$), alveolar-capillary membrane (DM) (12.7±2.4 *vs* 13.6±1.8; $p<0.05$) and pulmonary capillary blood volume (Vc) (48±3.9 *vs* 65±7; $p<0.001$) were significantly reduced in the patients.The COMPASS-31, RCS and pain VAS scores significantly correlated with DLCO, alveolar-capillary membrane (Kco) and Vc with the correlation being particularly close in the case of Vc. Furthermore, univariate Cox proportional hazard analysis showed that the three scores were all significantly associated with an increased risk of impaired DLCO (respectively, $\chi^2$ 16.21, $p<0.0005$; $\chi^2$ 7.09, $p<0.005$; $\chi^2$ 6.37, $p<0.01$).

**Conclusions:** FM impairs DLCO mainly as a result of a reduction in Vc, and that this defect is inversely proportional to the severity of the dysfunction suggestiong a relationship between impaired DLCO and autonomic nerve dysfunction.

**Disclosure of Interest:** None declared

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## THU0545 COMPARATIVE EFFICACY AND TOLERABILITY OF DULOXETINE, PREGABALIN, AND MILNACIPRAN FOR THE TREATMENT OF FIBROMYALGIA: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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**Background:** Duloxetine, milnacipran, and pregabalin are the only drugs approved by the Food and Drug Administration (FDA) for fibromyalgia. The recommended dosages are duloxetine 60 mg once a day, milnacipran 100 mg/day in two divided doses; may be increased to 200 mg/day, and pregabalin 150 to 300 mg/day in two divided doses. However, data on the relative efficacy and safety of the drugs approved by the FDA with different dosages are limited, because it is difficult to integrate information regarding the relative efficacy and safety of all tested drugs at different doses due to the lack of multiple comparisons in classical meta-analysis.

**Objectives:** The aim of this study was to assess the relative efficacy and tolerability of duloxetine, pregabalin, and milnacipran at the recommended doses in patients with fibromyalgia.

**Methods:** Randomized controlled trials (RCTs) examining the efficacy and safety of duloxetine 60 mg, pregabalin 300 mg, pregabalin 150 mg, milnacipran 200 mg, and milnacipran 100 mg compared to placebo in patients with fibromyalgia were included in this Bayesian network meta-analysis.

**Results:** Nine RCTs including 5,140 patients met the inclusion criteria. The proportion of patients with >30% improvement from baseline in pain was significantly higher in the duloxetine 60 mg, pregabalin 300 mg, milnacipran 100 mg, and milnacipran 200 mg groups than in the placebo group (pairwise odds ratio (OR) 2.33, 95% credible interval (CrI) 1.50–3.67; OR 1.68, 95% CrI 1.25–2.28; OR 1.62, 95% CrI 1.16–2.25; and OR 1.61; 95% CrI 1.15–2.24, respectively). Ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that duloxetine 60 mg had the highest probability of being the best treatment for achieving the response level (SUCRA =0.9431), followed by pregabalin 300 mg (SUCRA =0.6300), milnacipran 100 mg (SUCRA =0.5680), milnacipran 200 mg (SUCRA =0.5617), pregabalin 150 mg (SUCRA =0.2392), and placebo (SUCRA =0.0580). The risk of withdrawal due to adverse events was lower in the placebo group than in the pregabalin 300 mg, duloxetine 60 mg, milnacipran 100 mg, and milnacipran 200 mg groups. However, there was no significant difference in the efficacy and tolerability between the medications at the recommended doses.

**Conclusions:** Duloxetine 60 mg, pregabalin 300 mg, milnacipran 100 mg, and milnacipran 200 mg were more efficacious than placebo. However, there was no significant difference in the efficacy and tolerability between the medications at the recommended doses.

**References:**

[1] None

**Disclosure of Interest:** None declared

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## THU0546 CROSS-SECTIONAL ANALYSIS OF THE ASSOCIATIONS BETWEEN FIBROMYALGIA AND OTHER CHRONIC CO MORBIDITIES

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**Background:** The Fibromyalgia syndrome (FMS) has been linked to chronic organic and psychiatric conditions, however large population studies that systematically investigated this claim are scarce (1).

**Objectives:** To evaluate the association of FMS with other common chronic diseases such as psychiatric, rheumatic, cardiovascular, pulmonary and malignant disorders.

**Methods:** Utilizing the database of "Clalit" health services, the largest health maintenance organization (HMO) in Israel serving roughly 4,000,000 members, we carried out a cross-sectional study. Fibromyalgia patients were compared to age- and sex- matched controls regarding the coexistence of other chronic diseases. Chi-square and t-tests were used for univariate analysis and a logistic regression model was used for multivariate analysis.

**Results:** The study included 14,296 patients with Fibromyalgia and 71,324 age-

Table 1. Logistic regression for grouped diagnoses ($n$ = 85,620)

| | Psychiatric diseases | Rheumatic diseases |
|---|---|---|
| Age | 1.04 (1.03, 1.04) | 1.03 (1.03, 1.03) |
| Male | 0.67 (0.59, 0.76) | 0.72 (0.57, 0.87) |
| SES – Medium vs. low | 0.99 (0.94, 1.03) | 1.02 (0.95, 1.10) |
| SES - High vs. low | 0.90 (0.84, 0.95) | 1.08 (0.99, 1.17) |
| Smoking | 1.64 (1.60, 1.68) | 1.29 (1.22, 1.36) |
| BMI | 1.01 (1.01, 1.01) | 1.02 (1.01, 1.02) |
| Having co morbid Fibromyalgia | 3.17 (3.13, 3.21) | 3.72 (3.65, 3.79) |

Notes:
SES=Socioeconomic status ; BMI= body mass index
P<0.01

and sex- matched controls. The proportion of psychiatric disorders (anxiety, bipolar disease, depression, psychoses.) in patients with FMS was significantly higher compared with their proportion in controls (30.1% vs. 12.2% respectively, $p<0.001$, OR =3.09, 95% CI: 2.96–3.22). The proportion of rheumatic disorders was also significantly higher in FMS patients compared to controls (10.8% and 3.15% respectively, $p<0.001$, OR =3.73, 95% CI: 3.49–3.99). A multivariate logistic regression model demonstrated that FMS was significantly associated with psychiatric disorders and rheumatic diseases after controlling for confounders, including age, sex, socioeconomic status (SES) and BMI (psychiatric multivariate OR =3.17, $p<0.01$ 95% CI: 3.13–3.21; rheumatic multivariate OR =3.72, $p<0.01$ 95% CI: 3.65–3.79). In contrast, 1365 (1145 controls, 220 FMS) chronic heart failure patients and 1970 (1668 controls, 302 FMS) chronic renal failure patients were not found to be significantly associated with FMS (CHF: OR =0.96, $p<0.566$ 95% CI: 0.83–1.11; CRF: OR =0.90, $p<0.098$ 95% CI: 0.80–1.02).

**Conclusions:** Patients with the FMS have a greater proportion of psychiatric and rheumatic disorders than matched controls. Consequently, physicians treating patients with chronic illnesses in general and rheumatic or psychiatric conditions in particular, should be aware of this high co morbidity rate.

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**Disclosure of Interest:** None declared

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## THU0547 IS PAIN CATASTROPHISING ASSOCIATED WITH IMPAIRED CONDITIONED PAIN MODULATION IN PEOPLE WITH CHRONIC WIDESPREAD PAIN?

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**Background:** Fibromyalgia (FM) may be considered part of a clinical continuum with chronic widespread pain, which is its cardinal symptom [1]. These conditions are associated with abnormal nociceptive system processing, which is characterised by central sensitisation and signs of allodynia and hyperalgesia [2, 3]. Deficient endogenous pain inhibition has been implicated in the aetiology of FM [4], which may be measured by assessing conditioned pain modulation (CPM). Psychological factors such as pain catastrophising may also play a role in the heightened pain experience in FM. There is evidence that pain catastrophising may be associated with reduced CPM efficacy [5]. However, it is not yet known whether the CPM dysfunction in FM occurs at a spinal or supraspinal level and if this is related to pain catastrophising.

**Objectives:** The aims of the present study were to: (1) compare the function of the CPM response in healthy controls and individuals with chronic widespread pain; (2) to explore the relationship between pain catastrophizing and CPM efficacy; and (3) to examine the level of the nervous system where CPM dysfunction may occur in individuals with chronic widespread pain.

**Methods:** Twenty-three people with chronic widespread pain (19 of which met the criteria for FM) and 22 age- and gender-matched healthy control participants took part. Pain beliefs and depression were assessed using the Pain Catastrophising Scale (PCS) and the Depression, Anxiety, and Stress Scale (DASS), respectively. CPM efficacy was assessed by comparing the nociceptive flexion reflex (NFR) area and pain ratings elicited by electrostimulation of the dominant foot (the test stimulus) before and during a cold pressor test applied to the contralateral hand (the conditioning stimulus).

**Results:** The chronic widespread pain group had significantly higher scores in the PCS and DASS ($P<0.05$). In the chronic widespread pain group, test and conditioned reflex areas ($P=0.06$) and verbal pain ratings ($P=0.09$) were not significantly different. In contrast, the control group had a significantly smaller reflex area ($P=0.001$) and a lower verbal pain rating ($P=0.02$) during conditioning compared to the test stimulus alone. There were no significant correlations between catastrophising and CPM efficacy using either VAS or nociceptive NFR measures in either the widespread pain or control group ($P>0.05$).

**Conclusions:** This study suggests that, compared to healthy controls, people with chronic widespread pain have a dysfunctional CPM response and therefore, impaired endogenous pain inhibition. However, there was no evidence of a relationship between pain catastrophising and CPM efficacy at either spinal or supraspinal levels.

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## THU0548 SLEEP ARCHITECTURE AND CLINICAL PARAMETERS IN FIBROMYALGIA AND OSTEOARTHRITIS

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**Background:** Non restorative sleep (NRS) is a characteristic symptom of fibromyalgia (FM). A number of studies have reported abnormalities of sleep architecture on polysomnography (PSG) including alpha wave intrusion (AWI) during delta wave sleep (DWS). However, AWI in DWS has also been reported in other conditions including depression or in chronic fatigue. We have compared FM patients with patients who had sleep disturbance from osteoarthritis (OA) and a group of normal healthy control subjects (NHC) to determine if there are specific abnormalities of sleep architecture in FM related to clinical parameters.

**Methods:** We studied 19 newly diagnosed FM patients (mean age 41yrs, range 19–58yrs), 17 with OA (mean age 46yrs, range 19–63yrs) with localized pain and sleep disturbance, and ten NHC (mean age 38yrs, range 23–61yrs). All participants were female. The diagnosis was confirmed by a consultant rheumatologist. None were being treated for anxiety or depression or had taken antidepressant, psychoactive or sedative drugs for at least 2 weeks prior to analysis. All completed pain score (VAS), Brief Pain Inventory (BPI), Fatigue Severity Scale (FSS), Epworth Sleepiness Scale (EPS), Pittsburgh Sleep Quality Index (PSQI), Centre for Epidemiologic Studies Depression Scale (CESD), State and Trait Anxiety Scale (STAS), Multidimensional Scales of Health Locus of Control and Perceived Social Support (HLC), and 2 weeks actigraphy and 2 consecutive nights of polysomnography (PSG) at home, scored by a trained sleep researcher. Each frequency band was decomposed and power averaged using spectral analysis.

**Results:** Sleep efficiency was significantly worse in FM and OA ($p=0.025$). Sleep stage transitions (SST) were significantly increased in FM and OA ($p=0.019$) with a marked increase in SST per hour ($p=0.002$) compared with NHC with no significant difference between FM and OA. Alpha waves were increased during stage 3 sleep (DWS) in both FM and OA compared with NHC but also with no difference between FM and OA. There was a numerical increase in spindle frequency during non REM sleep compared with NHC, more in FM than OA but with wide variation ($1.12 \pm 0.8$; $0.98 \pm 0.39$; $0.61 \pm 0.27$ mpl). Pain scores in FM and OA groups were significantly different to NHC; mean difference in BPI of 6.07 and 4.83 respectively ($p<.001$). FM had significantly greater fatigue and EPS than OA (M diff14.41, $p<.001$; 3.42, $p=.033$) and NHC (M diff=29.87, $p<.001$; 3.99, $p=0.34$). PSQI was significantly greater than HC in both FM and OA (10.19 and 7.18, $p<.001$). The difference between FM and OA was significant ($p=.023$). There were highly significant differences between the 3 groups for CESD (FM 23.11; OA16.06; NHC4.8, $p<0.001$), STAS (49.6; 39.8; 31.9, $p<0.001$), HLC ($p<0.001$), and neuroticism (15.7; 13.5; 9.3 $p<0.01$).

**Conclusions:** Patients with FM had a similar duration of sleep to this group of OA patients but had a significant difference in subjective sleep quality, with significantly increased fatigue and sleepiness. They also had more anxiety, depression and neuroticism. AWI in DWS in FM is not specific and is similar in disturbed sleep from OA, but increased spindle frequency may be a feature of FM. We hypothesise that psychological factors in FM are linked to both sleep quality and fatigue and NRS may result from an increased rate of SST with frequent fluctuation between light and deep sleep.

**Disclosure of Interest:** None declared

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## THU0549 FATIGUE AND THE ROLE OF SLEEP IN FIBROMYALGIA: OBJECTIVE AND SUBJECTIVE MEASURES

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**Background:** Fibromyalgia (FM) is a chronic widespread pain syndrome associated with symptoms such as sleep disorders, fatigue, depression, anxiety and cognitive alterations with a severe impairment of the life quality.

**Objectives:** The aim of this study is to examine the relationship between subjective and objective assessment of sleep quality and to analyze the predictors of fatigue in an Italian cohort of FM patients.

**Methods:** Adult outpatients diagnosed with FM, fulfilling both ACR/EULAR 1990 and 2010 criteria were enrolled (1,2). The objective measure of sleep was assessed through an actigraph (AMI Motionlogger Watch), a device which records the parameters of sleep based on electronic measure of the continuous motion detected by an accelerometer. During the study period the patients were invited to wear the actigraph on the non-dominant wrist for one week and concurrently to complete a sleep diary. After seven days the patients returned the actigraph and answered a structured interview conducted by a trained junior psychologist. Subjective quality of sleep was assessed by the Sleep Disorder Questionnaire (SDQ) (3) and the patients filled out psychometric scales as the Brief Symptom Inventory (BSI) for anxiety and depression (4) and the Checklist of Individual Strength (CIS20) for perceived fatigue (5). Both pharmacological and not pharmacological treatments were not changed 1 month before and during the study.

**Results:** Twenty-one female patients completed the study, mean age of 46.9 years (range 32–68) and mean disease duration of 7.5 years (range 1–27). The majority of 21 FM patients interviewed (76.2%) described their sleep quality as poor or very poor (mean value 3.10 ±0.89 SD on 4 point Likert scale). All patients (100%) reported insomnia complaints, and 18 (81%) met the DSM V (Diagnostic and Statistical Manual of Mental Disorders) criteria for a diagnosis of Difficulties Initiating and Maintaining Sleep (DIMS). The patients' perception about the number of slept hours (M=5.7) was significantly lower (t=3.292, $p<0.005$) than the actigraphic data (M=6.8). Total Sleep Time (TST) measured through actigraphy was directly correlated with the intensity of perceived fatigue (r=.481; $p<0.05$). A multiple regression analysis considering TST, Total Time in Bed (TTB), depression, and type of fatigue self management, showed TST as the variable that gave a major and unique contribute to the prediction of perceived fatigue. Mean values of TST and TTB both negatively correlated with FM duration (respectively r=-.589, $p<0.005$; r=-.565, $p<0.008$).
**Conclusions:** These findings confirm the high prevalence of sleep disturbances in FM and suggest that sleep quality and duration could play an important role in the perceived fatigue severity. Intervention programs for FM should include sleep regulation.
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## THU0550 EARLY MULTIDISCIPLINARY INTERVENTIONS TO PROMOTE WORK PARTICIPATION IN PEOPLE WITH REGIONAL MUSCULOSKELETAL PAIN: A SYSTEMATIC REVIEW

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**Background:** Musculoskeletal disorders are amongst the leading causes of disability in the working age population. Whilst there is a growing body of evidence suggesting that early targeted multidisciplinary interventions can promote work retention and prevent disability, the evidence is far from conclusive as to which interventions are the most effective.
**Objectives:** To review randomised controlled trials evaluating the effectiveness of early interventions in promoting work participation in adults with regional musculoskeletal pain (RMSKP).
**Methods:** CENTRAL, MEDLINE, EMBASE, Scopus, PEDro and OT Seeker (1990 to April 2015) were searched. Reference lists of identified articles and reviews were hand searched. Only RCTs reporting on work-related outcomes were eligible for inclusion. The intervention had to include two or more elements of the biopsychosocial model delivered as an integrated programme. Participants were either experiencing difficulties at work or had less than three months sick leave as a result of their RMSKP at enrolment. Each RCT was assessed independently by two reviewers for risk of bias. Results were analysed by hazard ratios for return to work data, while continuous outcomes were analysed as mean difference (MD) with 95% confidence intervals.
**Results:** 19 RCTS were included; the considerable variation in the components employed in the interventions limited the option to pool the data statistically using meta-analysis. There was some evidence that programmes involving a stepped care approach (4 studies) increased the probability of return to work at the 12-month follow-up [HR 1.29 (95% CI, 1.03 to 1.61), p=0.03]. However, preliminary analyses indicate a lack of consistent evidence for effects on reducing sickness absences, pain reduction and functional improvement across the intervention types.
**Conclusions:** The lack of agreement as to what constitutes "early" in the context of treating RMSKP may have contributed to the rather ambiguous findings. In addition, the different health and social insurance systems across the trials have made it difficult to generalise the results. There remains a need to establish the active components that promote work retention in this population, and to identify the patients who are most likely to benefit from an integrated and cost-effective intervention.
**Disclosure of Interest:** None declared
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## THU0551 NOVEL SJÖGREN'S AUTOANTIBODIES FOUND IN FIBROMYALGIA PATIENTS WITH SICCA AND/OR XEROSTOMIA

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**Background:** A significant proportion of patients with fibromyalgia complain of dry eyes and mouth. The 2010 preliminary criteria for fibromyalgia even includes dry eyes and mouth as part of the somatic symptoms severity complex used to diagnose this condition. A significant proportion of Sjögren's (Sjö) patients also complain of fibromyalgia symptoms and there is literature that questions the interplay of these two disorders. Recently, novel autoantibodies, SP-1, CA6, and PSP, have been described in early Sjögren's syndrome (SS). These early markers present themselves before the classic autoantibodies, such as Ro, La, ANA, and RF. A recent paper found that 76% of patients with idiopathic xerostomia and exophthalmia for less than 2 years were positive for the early markers, while only 31% had antibodies to Ro and La. The authors concluded that SP-1, CA6, and PSP may be useful markers for identifying patients with SS at an early stage of the disease.
**Objectives:** This study aims to examine the relationship between SS and fibromyalgia by testing patients with fibromyalgia, that also complain of xerostomia and sicca symptoms, for Sjö markers Ro, La, SP-1, CA6, and PSP.
**Methods:** Beginning in April 2013, a cohort of patients was identified that presented with symptoms of fibromyalgia, meeting both the 1990 and 2010 preliminary criteria. These patients were further questioned about xerostomia and sicca symptoms. Patients that admitted to using artificial tears at least biweekly, drinking water excessively, or have previously experienced a blocked tear duct, but did not meet the strict diagnostic criteria for SS and did not have elevated inflammatory markers ESR or CRP, were selected for this study. Serum from study patients was sent to a tertiary lab, Immco Diagnostics, for testing of the classic (Ro, La) and early Sjö (SP-1, CA6, PSP) markers. Patients testing positive for the Sjö markers were provided with literature on the disease and offered appropriate treatment options, such as hydroxychloroquine.
**Results:** As of January 2016, 210 patients were selected for this study and tested for the Sjö markers. 91.0% of the patients were female and 8.6% of the patients were male. The average patient age was 56.5. 171 of the study patients were tested for both the early and classic markers, while 39 were tested for only the early markers. Of the patients that were evaluated for both the early and classic Sjö markers, 29.8% (51) tested positive for SS. 39 (22.8%) of the patients were positive for the early Sjö markers, 9.4% (16) were positive for the classic Sjö markers, and 2.3% (4) were positive for both the early and late Sjö markers. Further analysis of all the patients that tested positive for the early Sjö markers (n=47), found 74.5% (35) were positive for SP-1, 8.5% (4) were positive for CA6 and 44.7% (21) were positive for PSP. 68.1% (32) of these patients were positive for only one of the early markers and 15 (31.9%) were positive for more than one early marker.
**Conclusions:** In this cohort of fibromyalgia patients, about 1/3 of patients that were tested for both the early and classic Sjö markers tested positive for SS, with the majority of those patients being positive for one or more of the early Sjö markers. This suggests that autoimmunity, specifically early Sjögren's syndrome, may be a confounding variable in the pathophysiology of fibromyalgia.
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## THU0552 HAPLOTYPES OF VITAMIN D RECEPTOR GENE: BOTH RISKY AND PROTECTIVE FOR FIBROMIYALGIA (FMS)

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**Background:** Clinical observations suggest that vitamin D may influence fibromyalgia etiology. FMS and vitamin D deficiency share a similar symptom profile; the relationship between these conditions is unclear. Vitamin D receptor is a crucial mediator of the symptoms of vitamin D deficiency. Thus, vitamin D receptor gene polymorphisms or haplotypes may contribute to vitamin D resistance.
**Objectives:** This study evaluated the clinical relationship between FMS and vitamin D gene among Turkish FMS patients.
**Methods:** 73 patients with FMS were diagnosed according to the ACR 2010 criteria; the control group included 61 healthy unrelated volunteers. The rs2228570 (Fok I), rs1544410 (Bsm I), rs7975232 (Apa I) and (rs731236) Taq I polymorphisms were examined using PCR-RFLP.
**Results:** In individual SNP analyses, none of the snps have been found to be associated with FMS (p values are 0.491, 0.477, 0.207, and 0.736 respectively). However, it has been detected that there is a strong association between haplotypes of VDR gene polymorphisms and FMS. As a result of this study, the effect of haplotypes is shown to be both risky and protective. P value of risk haplotypes ATC (rs2228570, rs1544410, rs7975232) is 0,015 (26,5%) and

TTT is 0,0068 (12,8%). The p value of collected risk haplotypes (ATC, TTT) is 0,006 (39,3%) and (ATC, TGT, and TTT) 0,000009 (58,7%). Frequent protective haplotype TTC is 0,0385 (6,8%). The p value of collected protective haplotypes (ATT, TCG, and TTC) is 0,008 (38%).

Table 1. Haplotype analysis of VDR gene polymoprhisms (1 = Bsm1, 2 = Fok1, 3 = Taq1)

| Haplo No. | Haplotype Bsm1-Apa1-Fok1 | Control (%) | Case (%) | P | OR (95% CI) | RR (95% CI) | Risk/Protective |
|---|---|---|---|---|---|---|---|
| 1 | ATT | 31.7 | 38.4 | 0.327 | 0.74 (1.33–0.42) | 0.83 (1.21–0.56) | R |
| 2 | ATC | 26.5 | 14.5 | 0.015 | 2.37 (4.82–1.17) | 2.01 (3.59–1.13) | P |
| 3 | TGT | 19.4 | 10.5 | 0.077 | 2.05 (4.61–0.91) | 1.85 (3.71–0.92) | P |
| 4 | TTT | 12.8 | 2.6 | 0.0068 | 5.50 (21.52–1.41) | 4.92 (18.4–1.34) | P |
| 5 | TGC | 5.2 | 12.3 | 0.075 | 0.39 (1.14–0.13) | 0.39 (1.13–0.16) | R |
| 6 | TTC | 1.1 | 6.8 | 0.0385 | 0.15 (1.17–0.02) | 0.16 (1.19–0.02) | R |
| 2+4 | ATC+TTT | 39.3 | 17.1 | 0.006 | 3.1 (5.99–1.61) | 2.28 (3.73–1.39) | P |
| 2+3+4 | ATC+TGT+TTT | 58.7 | 27.6 | 0.000009 | 3.73 (6.74–2.06) | 2.13 (3.04–1.49) | P |
| 1+5+6 | ATT+TGC+TTC | 38 | 57.5 | 0.0008 | 0.39 (0.68–0.22) | 0.60 (0.82–0.44) | R |

**Conclusions:** The present study is the first study evaluating VDR gene in patients with FMS. Our results suggest that haplotypes in VDR are strongly associated with fibromyalgia expressing both risk and protective effect. Our findings may help guide future research needed to define the role of vitamin D in FMS.
**Disclosure of Interest:** None declared
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## THU0553 RELATIONSHIP BETWEEN ACTIVE DISEASE AND FIBROMYALGIA IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an inflammatory disease characterized by erosive synovitis. Fibromyalgia syndrome (FMS) known with widespread pain, fatigue, sleep disturbances and mood disorders. FMS frequency increased in patients with RA.
**Objectives:** This study aimed to assess the prevalence of FMS in patients with RA and to analyse the relationship between disease activity and FMS.
**Methods:** The study included 151 RA patients and 77 controls without inflammatory rheumatic diseases. RA patients and the control group were evaluated with 2010 ACR criteria for FMS. Participants were divided into 4 groups according to presence of RA and FMS (Group 1: RA+, FMS+; Group 2: RA+, FMS-; Group 3: RA-, FMS+; Group 4: RA-, FMS-). Demographic characteristics, laboratory results, VAS pain, DAS 28, and HAQ scores were compared between 4 groups. RA patients were classified as in remission or without according to the DAS 28 score (DAS 28$\leq$2.6 and$>$2.6 respectively) and FMS evaluated.
**Results:** The mean age and sex distribution were similar between the RA patients and controls. FMS was found in 35.1% of RA patients and 19.5% of controls ($p<0.05$). The highest VAS pain and DAS 28 scores were in the group 1 and group 3 between the sub-groups (Table 1). FMS were compared between controls, RA patients in remission and active disease. FMS ratio was 19.5%; 8.1%; 53.9% respectively ($p<0.05$). Four parameters (ESR, tender joints, swollen joints, patient global assessment) of DAS 28 were higher in RA patients with active disease ($p<0.05$).

Table 1. The evaluation of disease activity and pain in patients who were divided into four groups according to the presence rheumatoid arthritis and fibromyalgia

| | VAS pain | DAS 28 | HAQ |
|---|---|---|---|
| Group 1 (RA+, FMS+), n=53 | 6,2±2* | 4,4±1* | 1,63±0,68* |
| Group 2 (RA+, FMS–), n=98 | 2,3±2,1 | 2,6±1 | 0,62±0,64 |
| Group 3 (RA–, FMS+) n=15 | 7±1,7* | 3,4±1* | 0,72±0,60 |
| Group 4 (RA–, FMS–) n=62 | 2±2 | 1,7±0,5 | 0,32±0,44 |

VAS: Visual Analog Scale, DAS 28: Disease Activity Index 28, HAQ: Health Assessment Questionnaire, RA: rheumatoid arthritis, FMS: Fibromiyalgia Syndrome. *P<0.05.

**Conclusions:** FMS is more common in the patients with RA than the general population therewithal FMS found more common in the patients with active RA. When DAS 28 parameters are analyzed, objective values (ESH; swollen joint) were higher as subjective values (pain) in this group. In conclusion increased widespread pain and disruption of the sleep quality because of inflammation may facilitate the diagnosis of FMS.
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## THU0554 POLYMORPHISMS OF TRANSIENT RECEPTOR POTENTIAL VANILLOID (TRPV) 2 AND TRPV3 GENE POLYMORPHISMS WERE ASSOCIATED WITH FIBROMYALGIA IN A KOREAN POPULATION

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**Objectives:** Researchers continue to gather evidence that transient receptor potential vanilloid (*TRPV*) channels contribute towards pain signaling pathways. However, it is unknown whether polymorphisms of the *TRPV* gene are associated with fibromyalgia (FM). For the first time, we investigated the association between the polymorphisms of the *TRPV2* and *TRPV3* genes with FM susceptibility and the severity of the symptoms.
**Methods:** A total of 409 patients with FM and 423 controls were enrolled from 10 medical centers that participated in the Korean nationwide FM survey. The alleles and genotypes at three positions [rs3813768 (C>G), rs8121 (C>T), and rs1129235 (C>A)] in the *TRPV2* gene, and two positions [rs7216486 (G>A) and rs395357 (C>T)] in the *TRPV3* gene, were genotyped.
**Results:** The frequencies of the alleles and genotypes of individual *TRPV2* and *TRPV3* genes were not significantly associated with FM susceptibility. However, the GTA haplotype of *TRPV2* showed a defense against FM susceptibility ($P$=0.035). In addition, polymorphisms of *TRPV3* were associated with symptom severity in FM patients. The single nucleotide polymorphism (SNP) rs395357 of *TRPV3* was associated with the scores of the Brief Fatigue Inventory (BFI) ($P$=0.017) in FM patients. Furthermore, haplotypes of *TRPV3* were associated with the BFI and the SF-36 mental health summary scores ($P$=0.036, respectively)
**Conclusions:** This study was the first to evaluate the associations of *TRPV* gene polymorphisms with FM. Our results suggest that certain *TRPV2* haplotypes may have a protective role against FM, and also that some genotypes and haplotypes of *TRPV3* contribute towards the symptoms of FM.
**Disclosure of Interest:** None declared
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## THU0555 NEGATIVE AFFECT IN CHRONIC PAIN: THE HEART OF THE MATTER

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**Background:** A large body of studies supports the concept of a frequent comorbidity between chronic pain conditions and psychological distress/disorders, especially depression. However, most of the studies have focused on specific chronic pain conditions and not on the potential differences or similarities between them.
**Objectives:** We aimed to explore the prevalence and severity of depressive symptoms, tension/anxiety (TA), anger/hostility (AH) and fatigue/inertia (FI) among fibromyalgia (FM) and rheumatoid arthritis (RA) patients and healthy controls (HC).
**Methods:** Participants were recruited at rheumatology and gynecology practices in Coimbra and all met the classification criteria for FM and RA or, in the case of HC, the pre-established criteria of a zero score in the London Fibromyalgia Epidemiological Study Screening. The Portuguese versions of the following measures were completed by all participants: Beck Depression Inventory (BDI-II) and Profile of Mood States (PoMs). The samples' characteristics were examined. Descriptive analyses were performed in order to explore the severity of depressive symptoms across samples according with the recommended cut-off points. Differences between samples with respect to depressive symptoms and mood states was tested for significance via Fisher's Exact test and one-way independent ANOVA.
**Results:** 302 participants composed the total sample [103 FM (34.11%), 98 RA (32.45%) and 101 HC (33.44%)]. Differences between samples were found regarding age ($F=30.598$; $p<.001$) and education years ($F=25.883$; $p<.001$). 17.5% of FM patients reported severe depressive symptomatology against 3.3%

of RA patients and 2.1% of HC. Similarly the percentage of FM patients with moderate depressive symptoms (24.8%) was substantially greater than the percentage of RA patients and HC (7.7% and 4.3% respectively). Both FM and RA patients reported higher levels of mild depressive symptoms (24.7% and 11%), when compared to HC (just 3.2%). The majority of HC (90.4%) reported minimal depressive symptoms, a percentage relatively close to RA patients (78%) but considerably different from FM patients (33%). Fischer's Exact test pointed to significant differences between samples regarding the prevalence of depressive symptoms ($p<.001$). Further analyses revealed that FM, RA and HC differed significantly in the mean scores of BDI-II and its dimensions, with FM patients scoring higher than RA and HC. No significant differences were found between the latter two, except for the somatic/anxiety dimension, with RA patients scoring higher than controls. Significant differences between samples were also found for TA, AH and FI. In all of these dimensions, FM patients scored significantly higher than RA and HC. Once more, RA patients and HC did not differ significantly in the mean scores of PoMS dimensions.

**Conclusions:** Results revealed that FM participants not only evidenced more depressive symptoms than RA patients and HC but also greater levels of TA, AH and FI. In turn, RA patients present scores that are, overall, similar to those of HC. Such findings reinforce not only the extreme emotional suffering that FM patients experience but also the need for interventions designed to manage depressive/anxious symptoms and emotion regulation difficulties.

**Disclosure of Interest:** None declared

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## THU0556 ASSESSMENT OF PERIPHERAL SMALL FIBER NERVE IN FIBROMYALGIA

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**Background:** Fibromyalgia (FM) is related to the features of small fiber neuropathy (SFN). Sudoscan is a non-invasive device measures sweat gland dysfunction employing electrochemical skin conductance (ESC) and is useful for assessing peripheral small fiber nerve function. Little is known about the dysfunction of peripheral small fiber nerve in patients with FM.

**Objectives:** The aim of this study was to evaluate the prevalence and characteristics of SFN in patients with FM compared with a control group and to identify factors associated with SFN in FM.

**Methods:** 66 patients with FM (age: 53 ± 9 years old) to meet 2010 ACR preliminary diagnostic criteria and 66 healthy controls were enrolled. Each FM patient was required to fast 8 to 10 hours before blood samples. Serum fasting glucose, fasting insulin, Serum 25-(OH) D and the 75-gram two-hour oral Glucose tolerance test (GTT) were measured. Height and weight were measured and used to calculate Body mass index (BMI). Overt diabetes patients were excluded using their past and medication history. The small fiber neuropathy Symptoms Inventory Questionnaire (SFN-SIQ) was used to record neuropathic symptoms. Clinical assessments included fibromyalgia impact questionnaire (FIQ), Beck Depression Inventory (BDI), and The State-Trait Anxiety Inventory (STAI). All subjects underwent the examination of Sudoscan.

**Results:** The mean feet and hands ESC were significantly lower in the FM group than the control group.(table 1).

Table 1. Comparison of Mean feet and hands ESC between FM and control group

| | FM (n=66) | Control (n=66) | p-value |
|---|---|---|---|
| Mean feet ESC (μS) | 62.2±17.9 | 72.2±13.0 | <0.001 |
| Mean hands ESC (μS) | 54.3±19.6 | 65.63±15.4 | <0.001 |

Values are expressed as mean ± SD for 66 subjects in each group.

Mean Hands ESC was irrelevant to age, BMI, SFN-SIQ, FIQ, fasting glucose, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), and vitamin D and 2 hour GTT glucose level. However, Mean feet ESC showed significant correlation with fasting insulin ($r= -0.34$, $p<0.01$) and HOMA-IR ($r= -0.37$, $p<0.01$).

**Conclusions:** Sudomotor function was significantly lower in patients with FM than the control group. Mean feet ESC was correlated with hyperinsulinemia and HOMR-IR in patients with FM, which implies that SFN associated with insulin resistance may play an important role in FM pain.

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## THU0557 RELIABILITY AND VALIDITY OF TURKISH VERSION OF THE FIBROMYALGIA RAPID SCREENING TOOL (FIRST)

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**Background:** Fibromyalgia is a challenging chronic pain condition accompanied by several comorbidites. Since patients are encountered in various health care settings, there is a need for short, easy to use, psychometrically validated screening tool

**Objectives:** This study aims to evaluate reliability and validity of Turkish version of Fibromyalgia Rapid Screening Tool (FiRST) by correlating this tool with 2013 American College of Rheumatology alternative diagnostic criteria (ACR AltCr) and Hospital Anxiety and Depression Scale (HADS).

**Methods:** A convenience sample of 269 subjects recruited from outpatient Physical Medicine and Rehabilitation clinics were included in the study. Patients were asked to complete the questionnaire including FiRST (twice), 2013 AltCr and HADS. The reliability of the FiRST scale was examined by test-retest method. For criterion validity of FiRST scale, we used ACR 2013AltCr for comparison. The concordance between ACRAltCr and FiRST and the relationships between variables were evaluated. The sensitivity, specificity, positive and negative likelihood ratios of FiRST was calculated according to ACR 2013 AltCr criteria. Logistic regression analysis was carried out to find the confounding effect of HADS on FiRST to discriminate the patients with FMS

**Results:** The test-retest reliability coefficient of FiRST scale was r=0.875. FiRST was similar to ACR 2013 AltCr in defining patients with FMS. FiRST score was correlated with subscores of ACR 2013AltCr. Each point increase in FiRST global score increased odds of suffering FM approximately 10 times compared to HADS

**Conclusions:** Turkish version of FiRST is a reliable instrument for identifying patients with FMS

**Disclosure of Interest:** None declared

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## THU0558 FIBROMYALGIA SYMPTOMS IN A SAMPLE OF LEBANESE NURSES: PREVALENCE AND PREDICTIVE FACTORS

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**Background:** Nurses work in a physically and emotionnally stressful envirnment, which could lead to increased fibromyalgia symptoms.

**Objectives:** To estimate the prevalence of fibromyalgia symptoms in nurses from Hotel Dieu de France and North Center Hospitals and to determine predictive factors.

**Methods:** The study was conducted using a questionnaire distributed to all registered nurses working in the two hospitals in November 2014. For fibromyalgia screening, we used the validated French version of London fibromyalgia epidemiology study screening questionnaire (LFESSQ). The screening was considered positive if a subject met four criteria of pain and two criteria of fatigue items (LFESSQ-6). To estimate the positive predictive value of LFESSQ-6, a sample of nurses screened positive were then examined by a rheumatologist to clinically confirm the diagnosis of fibromyalgia. The prevalence of fibromyalgia in nursing was estimated by applying the positive predictive value to LFESSQ-positive subjects detected by the questionnaire. They were also asked about their demographics, their work environment, personal and family history, as well as the frequency of episodes of depressed mood through the Patient's Health Questionnaire-2 (PHQ-2). The statistical analysis was based on a logistic regression model used for the multivariate analysis to identify predictive factors of fibromyalgia.

**Results:** 485 questionnaires were distributed, with a response rate of 76.3%. 16.8% of the study sample met the criteria of LFESSQ-6. The subsequent rheumatology consultation confirmed the diagnosis of fibromyalgia in 57.14% of positively screened. Applying the positive predicted value in the nursing population, the prevalence of fibromyalgia was estimated of 9.6% using the screening by the LFESSQ -6. The factors that were significantly associated with a positive screening fibromyalgia were: the number of children and sports activities as protective factors on the one hand, and dissatisfaction with salary, lack of group cohesion, and the frequency of episodes of depressed mood as risk factors on the other hand

**Conclusions:** Our results suggest that fibromyalgia is prevalent in the nursing population. Some risk factors are modifiable: depression measured by the PHQ-2, dissatisfaction with salary and a lack of group cohesion. Protective factors were the number of children and the sports activities.

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Nursing administration. Centre Hospitalier du Nord. Lebanon.
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## THU0559 FREQUENCY OF FIBROMYALGIA SYNDROME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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**Background:** Fibromyalgia Syndrome (FS) is a chronic condition with widespread pain. Increased FS prevalence was observed in patients with Diabetes Mellitus (DM) in several of former studies.[1,2]
**Objectives:** The aim of this study is to assess the frequency of FS in patients with Type 2 DM. Additionally; we aimed to evaluate the association of pain severity with disease control of DM.
**Methods:** Patients with Type 2 DM who were followed in Endocrinology Clinic of Cukurova University Hospital were included in the study. FS was diagnosed according to 2013 Alternative Criteria set by American College of Rheumatology. Patients with anemia, hyper- and hypothyroidism, malignancy, pregnancy and rheumatologic conditions were excluded. Patients' pain during morning and sleep was evaluated by Visual Analog Scale (VAS). Fasting blood glucose and Hba1c levels were measured to assess disease control of DM.
**Results:** Ninety-two patients (61 female, 31 male) with Type 2 DM were included in the study. Mean age of the patients was 57.84 ± 10.01 years. FS was diagnosed in 4.3% of the patients. No significant difference was observed between Hba1c levels of Type 2 DM patients with and without FS ($P$=0.87). Mean VAS scores of the patients during morning and sleep were detected as 2.97±2.96 and 2.51±2.73 respectively. There was a weak negative correlation between VAS morning scores and Hba1c levels in diabetic patients (r=-0.24, $P$=0.04). There were no correlations of VAS sleep scores with fasting glucose and Hba1c levels ($P$=0.54, $P$=0.34 respectively).
**Conclusions:** According to the results of the present study, when diagnosis is based on 2013 alternative criteria of ACR, FS frequency in patients with Type 2 DM is found to be similar to that of among healthy populations. Yet, better control of blood glucose levels might decrease daily pain in diabetic patients.
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## THU0560 TNX-102 SL FOR THE TREATMENT OF FIBROMYALGIA: COMPARISON OF 30% PAIN RESPONDER ANALYSIS WITH OMERACT DRAFT COMPOSITE RESPONDER ENDPOINT ANALYSES

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**Background:** Novel responder definitions for fibromyalgia (FM) clinical trials have been proposed by the Outcome Measures in Rheumatology (OMERACT) FM subcommittee. These definitions include key symptom and functional domains relevant to FM patients, and were validated using outcome data from 12 previous registration trials of 4 other medications (Arnold L et al, Arth Rheum 64:885, 2012.) TNX-102 SL* is a proprietary sublingual formulation of cyclobenzaprine designed for rapid absorption and bedtime use. It showed improvements in pain and other symptoms in a Phase 2B study. This study was a 12-week, randomized, double-blind, placebo-controlled trial conducted at 17 US sites, designed to evaluate TNX as a potential treatment for FM. 205 participants were randomized (TNX=103; placebo=102).
**Objectives:** This current presentation is a retrospective analysis of the trial results using the two preferred response definitions proposed by the OMERACT committee.
**Methods:** The two OMERACT responder definitions are: the FM30 Short, which defines a responder as ≥30% reduction in pain, ≥10% improvement in physical function plus a ≥30% improvement in either sleep or fatigue, and the FM30 Long, which defines a responder as ≥30% reduction in pain, ≥10% improvement in physical function plus ≥30% improvement in any two of the following measures: sleep, fatigue, depression, anxiety or cognition.
**Results:** TNX improved multiple domains of FM. The table below compares a pain responder analysis (≥30% improvement in pain based on daily diary) to the alternative composite responder definitions proposed by OMERACT.

| Responder definition/Result (pain based on diary) | Physical function measure | Additional symptom measures | Result |
|---|---|---|---|
| 30% Pain responder | None | None | 34.0% vs. 20.6%; p=0.033 |
| FM30 Short Ver 1 | SF-36 physical function | 1 | 23.3% vs. 11.8%; p=0.038 |
| FM30 Short Ver 2 | SF-36 PCS score | 1 | 25.2% vs. 11.8%; p=0.015 |
| FM30 Long Ver 1 | SF-36 physical function | 2 | 21.4% vs. 9.8%; p=0.031 |
| FM30 Long Ver 2 | SF-36 PCS score | 2 | 23.3% vs. 9.8%; p=0.011 |

1: either FIQ sleep or FIQ energy; 2: any 2 out of FIQ sleep, FIQ energy, FIQ depression or FIQ anxiety.

Additional improvements noted over placebo included: FIQ-R total score (-17.2 vs. -9.1, p=0.015),PGIC response rate (30.1% vs. 16.7%, p=0.025), PROMIS sleep (-9.5 vs -6.1, p=0.004), sleep based on daily diary (change from baseline to week-12, 1.9 vs. -1.0; p<0.001) and FIQ-R sleep item (-2.9 vs. -1.2; p<0.0001). Systemic adverse events reported were similar to placebo. The most common local adverse event was transient tongue or mouth numbness occurring in 44% of TNX patients.
**Conclusions:** Bedtime TNX improved multiple domains of FM. Analysis by composite responder criteria developed by OMERACT suggests that the improvements in FM symptoms seen with TNX are not limited to an analgesic response, since these composite criteria all require improvement in other somatic and functional symptoms.
*TNX-102 SL is an Investigational New Drug and has not been approved for any indication.
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# Other orphan diseases

## THU0561 ADALIMUMAB IN PATIENTS WITH ACTIVE AND INACTIVE, NON-INFECTIOUS UVEITIS: VISUAL I AND VISUAL II TRIALS

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**Background:** Uveitis causes an estimated 10–15% of cases of blindness in western countries and there is an unmet need for effective therapies for patients (pts) with non-infectious uveitis who are at risk for long-term side effects from chronic corticosteroid use.
**Objectives:** To assess adalimumab (ADA) efficacy and safety in patients with active and inactive, non-infectious uveitis.
**Methods:** Adults with non-infectious intermediate, posterior, or panuveitis were enrolled in two global phase 3, double-masked trials, VISUAL I (pts with active uveitis despite ≥2 weeks (wks) of prednisone (PS), 10–60 mg/d) and VISUAL II (pts with inactive disease dependent on 10–35 mg/d of PS, to maintain inactivity). Pts were randomized 1:1 to receive placebo (PBO) or ADA subcutaneously (80 mg wk 0, followed by 40 mg every other wk from wk 1 up to 80 wks). In VISUAL I, all pts received a PS burst followed by taper to 0 mg by wk 15. In VISUAL II, PS taper to 0 mg was mandatory by wk 19. Integrated data (main study and Japan sub-study) from VISUAL I and VISUAL II trials are reported. The primary endpoint was time to treatment failure (TF) at or after wk 6 for VISUAL I or at or after wk 2 for VISUAL II. Nine ranked secondary endpoints were assessed and adverse events (AEs) were monitored.
**Results:** The intent-to-treat (ITT) analyses included 233 (217 main study, 16 Japan sub-study) and 258 (226 main study, 32 Japan sub-study) pts from VISUAL I and VISUAL II, respectively (VISUAL I and VISUAL II: female: 58% and 61%; mean age, 43.2 years (y) and 43.1 y; mean duration of uveitis, 46 months (mt) and 59 mt). Risk of TF was reduced by 44% (VISUAL I) and 48% (VISUAL II) in ADA-treated pts compared to PBO group (VISUAL I: HR=0.56, 95% CI, 0.40–0.76,

$P<0.001$; VISUAL II: HR=0.52, 95% CI, 0.37–0.74, $P<0.001$). Median time to TF was 3 mt for PBO, 4.8 mt for ADA (VISUAL I) and 5.6 mt for PBO, not estimable for ADA (>18 mt, as more than half of the pts did not achieve TF by wk 80; VISUAL II). ADA-treated pts had fewer TF criteria than PBO in both studies and treatment effects were numerically in favor of ADA for most of the secondary efficacy variables (Table). ADA and PBO AE rates were similar (VISUAL I: 1063 vs 960 events/100 pt-y, VISUAL II: 854 vs 884 events/100 pt-y) in both studies, respectively.

Table. Summary of Ranked Secondary Efficacy variables (Intent -to-treat population)

| | VISUAL I | | VISUAL II | |
|---|---|---|---|---|
| Ranked Secondary endpoints[a] | Placebo N=114 | Adalimumab N=115 | Placebo N=107 | Adalimumab N=131 |
| 1. Change in SC inflammation Left eye / Right eye | 0.56 / 0.65 | 0.55 / 0.56 | 0.63 / 0.63 | 0.66 / 0.64 |
| Difference, mean (95% CI) | -0.23 (-0.46, -0.00), P=0.053[b] | | -0.15 (-0.36, 0.06), P=0.164[b] | |
| 2. Change in VH grade Left eye / Right eye | 0.34 / 0.46 | 0.11 / 0.26 | 0.55 / 0.56 | 0.18 / 0.28 |
| Difference, mean (95% CI) | -0.28 (-0.45, -0.12), P=0.001[b] | | -0.17 (-0.32, -0.03), P=0.019[b] | |
| 3. Change in BCVA, logMAR Left eye / Right eye | 0.11 / 0.13 | 0.07 / 0.05 | 0.07 / 0.04 | 0.02 / 0.00 |
| Difference, mean (95% CI) | -0.06 (-0.10, -0.02), P=0.003[b] | | -0.04 (-0.09, 0.00), P=0.044[b] | |
| 4. Time to OCT evidence of macular edema [Pre-specified analysis (only in patients without macular edema at baseline)] | | | | |
| Median | 5.7 | 9.2 | NE | NE |
| Hazard ratio (95% CI) | 0.48 (0.30, 1.22), P=0.013[b] | | 0.40 (0.28, 1.20), P=0.007[b] | |
| 5. Percent change in central retinal thickness Left eye / Right eye | 19.2 / 21.7 | 12.9 / 14.3 | 4.3 / 8.0 | 3.2 / 5.8 |
| Difference, mean (95% CI) | -6.1 (-11.7, -0.5), P=0.032[b] | | -3.9 (-9.1, 1.4), P=0.150[b] | |
| 6. Change in VFQ-25 total score | -0.54 | -1.68 | 1.9 | 2.79 |
| Difference, mean (95% CI) | 1.47 (0.42, 2.71), P=0.010[b] | | 1.71 (-0.07, 4.33), P=0.207[b] | |
| 7. Change in VFQ-25 subscore (distance vision) | -0.72 | -4.42 | 0.60 | 2.96 |
| Difference, mean (95% CI) | 3.31 (-0.47, 7.09), P=0.086[b] | | 2.36 (-1.78, 6.47), P=0.236[b] | |
| 8. Change in VFQ-25 subscore (near vision) | -7.95 | -8.51 | 3.79 | 2.89 |
| Difference, mean (95% CI) | -0.24 (-5.43, 5.72), P=0.917[b] | | -0.87 (-5.28, 3.79), P=0.734[b] | |
| 9. Change in VFQ-25 subscore (ocular pain) | -12.29 | -5.56 | 2.60 | 2.15 |
| Difference, mean (95% CI) | 6.93 (1.89, 11.79), P=0.011[b] | | -0.46 (-5.32, 4.34), P=0.842[b] | |

AE=adverse event; BCVA=best corrected visual acuity; CI=confidence interval; OCT=optical coherence tomography; VFQ=Visual Function Questionnaire

*With the exception of analysis of time to OCT evidence of ME, which was on or after 6 months for VISUAL I and on or after week 24 for VISUAL II, mean/median changes from baseline were observed prior to week 8 in the final early termination visit for VISUAL I and change from baseline to final early termination visit for VISUAL II.

a. Those ranked for VISUAL I with treatment and figure 1 vs ex. - figure is the p-value adjusted for Cochran-Mantel-Haenszel.

b. RR of adalimumab vs placebo from proportional hazards regression with treatment - ex and figure vs ex. Figure ex factors.

c. Those ranked for VISUAL I with treatment, type of OCT machine and figure vs ex. - figure ex Simon adjusted for treatment stratification.

d. From ANCOVA with treatment and figure vs ex. - figure as for ex

**Conclusions:** ADA lowered the risk of uveitic flare or visual acuity loss in pts with active and inactive disease when off PS. The safety profile was consistent with the known safety profile across the approved ADA indications.

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## THU0562 A SURVEY OF RESISTANCE TO COLCHICINE TREATMENT IN FRENCH PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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**Background:** Colchicine is the standard treatment of FMF, preventing attacks and inflammatory complications in more than 90% of cases. Some patients, especially those carrying 2 M694V mutations in *MEFV* gene, may require doses higher than recommended overcoming disease manifestations. True resistance to colchicine may be exceptional but is still not defined on a consensus basis.
IL 1 targeting drugs are effective but are expensive alternative treatments requiring rigorous indications in FMF.

**Objectives:** To survey when and how physicians consider resistance to colchicine in FMF patients and to report how they handle this situation in their practise.

**Methods:** We performed a retrospective chart review of patients identified through reference centers and networks of inflammatory diseases expert physicians. We asked them to report their patients with a clinical diagnosis of FMF and at least one pathogenic *MEFV* mutation, in whom they considered resistance to colchicine. Patients with concomitant SPA or Crohn's disease were excluded. We collected their clinical data, genotypes, and more detailed information on colchicine treatment dose adjustment and compliance. Finally we tried to analyse the reason(s) to consider their patients as resistant to treatment and we collected the alternative attitudes treatments used.

**Results:** We identified 42 patients from 7 to 86 years old (mean age (±SD): 28,2 ± 22.1 years old) recruited from 10 centers. Thirty six of them could be fully analysed and consisted of 14 males and 22 females with a clinical diagnosis of FMF and, in whom 15 were children before 16 years. Sephardim Jews were the most represented. (n=23, 64%). All patients carried pathogenic mutations in the exon 10 of the *MEFV* gene except one girl and a woman with a complex allele including *MEFV* deletion. The mean (±SD) maximal dose of colchicine given in adult patients was 1.8± 0.65 mg, and it was 1.7 ± 0.6 mg (0.1 ± 0.01 mg/kg) in paediatric patients. The level of CRP in between attacks was evaluated in 40 patients and reached a mean of 35,8 mg/L. Fourty percent of patients declared to be fully observant to colchicine treatment. The main reasons to consider resistance to colchicine treatment were: >6 attacks/year (44%), >4 attacks in the last 6 months (20%), persistent inflammation (41%) and other reasons (44%). Twenty percent of patients were intolerant to an increase of colchicine dose. Concomitant treatments to overcome FMF symptoms were essentially NSAIDS, steroids, and analgesics. Sixty five percent of these patients are currently treated with IL-1 targeted drugs including anakinra (48%) and canakinumab (17%).

**Conclusions:** Our study has confirmed that resistance to colchicine treatment is rare (0–10% of patients, per investigating center) and more likely observed in patients carrying severe *MEFV* genotypes. In most cases the mean reasons to consider resistance to treatment were severe clinical symptoms and persistent subclinical inflammation, however low compliance to high doses of colchicine seems to play a major role. Patient's education and additional behavioural approaches preventing disease flares could probably reduce the use of biologics.

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## THU0563 CHARACTERIZATION OF A GROUP OF 6 PATIENTS WITH MEVALONATE KINASE DEFICIENCY: SYMPTOMS AND TREATMENT WITH IL-1 INHIBITORS

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**Background:** Mevalonate kinase deficiency (MKD) is a rare autosomal recessive autoinflammatory disease caused by mutations in MVK gene. MKD patients typically have an early onset of symptoms including recurrent episodes of high fever, abdominal pain, diarrhea and vomiting, arthralgia and lymphadenopathy. However not all patients have typical clinical picture of MKD.

**Methods:** We conducted a retrospective analysis of clinical features of six patients (4 females, 2 males) with MKD (confirmed by identification of MVK gene mutations). Four patients received therapy with inhibitors of IL-1 (Anakinra and/or Canakinumab). One of the patients died from amyloidosis and macrophage activation syndrome (MAS) prior to treatment initiation, her diagnosis was verified *post mortem*.

**Results:** All patients had the first symptoms of disease within the first 6 months of life. During the course of the disease all patients had periodic fever and peripheral lymphadenopathy (mainly cervical group), as well as abdominal pain, nausea/vomiting. Five patients had diarrhea, sometimes with blood, one patient suffered from severe constipation. Rash was seen in five patients, myalgia, artralgia were observed only in four. Oral ulcers were noted in two children. Two patients had neurological involvement. Interestingly, five out of six patients had rhinitis during attacks. One patient during the attack had periorbital edema and hyperemia, which; to our knowledge, have not been reported previously in MKD. One patient developed amyloidosis and MAS before treatment initiation, which led to her death. In patients receiving anti-IL-1 therapy AIDAI index decreased from 49.5±14,6 before to 1,75±1,3 after 6 month of therapy (p=0.003).

**Conclusions:** MKD symptoms can be variable and sometimes atypical, which requires physician's awareness. In our small cohort of MKD patients anti IL-1 therapy was highly effective.

**Disclosure of Interest:** None declared

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## THU0564 TREATMENT OF FAMILIAL MEDITERRANEAN FEVER WITH ANAKINRA IN PATIENTS UNRESPONSIVE TO COLCHICINE

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**Background:** Familial Mediterranean fever (FMF) is a hereditary autoinflammatory disease, characterized by self-limiting periodic fever attacks with typical clinical features and oversecretion of proinflammatory cytokines as interleukin-1 (IL1).
**Objectives:** The standard of care since the early 1970s is oral colchicine, which can help to prevent attacks. Unfortunately, 5–10% of the patients are unresponsive. In these cases there is no further approved treatment. MEFV, the underlying gene mutated in FMF, encodes pyrin, which takes part in the process of IL1 secretion. In this report we analyzed the benefit of anakinra, an IL1 receptor antagonist, in patients who were unresponsive to colchicine.
**Methods:** This is a single center retrospective case series of 13 patients. Anakinra was applied subcutaneously at a standard dose of 100mg per day. There are no defined criteria for responders as well as non-responders to a certain treatment in FMF. We therefore defined colchicine resistance in analogy to other studies (1) as increasing frequency of attacks (>1/month and/or >1.5-fold of the time of best response) or as increasing inflammatory proteins i.e. CRP and SAA (>1.5-fold from upper limit). Disease activity was evaluated by laboratory parameters and clinical symptoms based on patient's and physician's assessment. Complete response (CR) was defined as no attacks and acute phase reactants below the upper limit. Partial response (PR) was defined as FMF-50 response, meaning reducing the attack rate by 50% and/or decreasing acute phase reactants, i.e. CRP or SAA, by 50%.
This retrospective case series was approved by the ethics committee of Eberhard-Karls-university, Tübingen.
**Results:** All results presented in mean±SD.
13 patients were included, median age at starting anakinra was 30.5±8.5 years, six patients were female. Nine patients had homozygous exon ten mutation, three patients had heterozygous exon 10 mutations of the MEFV-gene, one patient showed no detectable mutation. All patients were taking therapeutic oral doses of colchicine before starting treatment with anakinra. During treatment the attack rate declined from 15.8±13.1 per year to 4.1±6.6 (p=0.047). This was also the case for laboratory parameters: SAA decreased from 287.1 ± 428.4 mg/l to 10.9±12.0 mg/l (p=0.006) after three months and to 53.8±73.4 mg/l (p=0.125) after six months of treatment. CRP decreased from 6.8±7.7 mg/dl to 0.8±0.8 (p=0.005) after three months, respectively 0.7±0.9 (p=0.029) after six months. We didn't observe any major complications.
**Conclusions:** This report, to our knowledge, analyses the largest group of adults with FMF, treated with anakinra after failure of colchicine. All 13 patients of our case series responded to anakinra, four of them with CR. Interestingly, all of them showed a homozygous MEFV exon 10 mutation, which goes along with higher IL1 rates and more often are not responsive to colchicine (2). Here we could show, that anakinra is an effective treatment option for patients with FMF. Still, further prospective studies should be performed to evaluate the dosage and long-term efficacy as well as safety of anakinra.
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## THU0565 CLINICAL RELEVANCE OF TREATMENT FAILURE AS ASSESSED BY THE 25-ITEM VISUAL FUNCTIONING QUESTIONNAIRE IN PATIENTS WITH INTERMEDIATE-, POSTERIOR- AND PAN-UVEITIS: RESULTS FROM THE VISUAL-1 TRIAL

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**Background:** Time to treatment failure is the primary endpoint in the VISUAL-1 clinical trial (NCT01138657) of patients with non-infectious intermediate-, posterior- and pan-uveitis (NIIPPU); however, the relationship between the treatment failure (TF) criteria and patient-reported outcome of visual functioning is not well understood.
**Objectives:** To examine the relationship between TF and vision-related quality of life (QoL) as assessed by the Visual Functioning Questionnaire 25 (VFQ-25) among patients with NIIPPU.
**Methods:** The VISUAL-1 clinical trial was a randomized, placebo-controlled, 80-week study designed to investigate the efficacy and safety of adalimumab in patients with active NIIPPU. Patients were examined at scheduled study visits for TF at and after week 6. TF was assessed using 4 criteria: presence of inflammatory, chorioretinal, and/or inflammatory retinal vascular lesions, anterior chamber (AC) cell grade, vitreous haze (VH) grade, and visual acuity (VA). Patients with TF due to 1, 2, 3, and 4 of these components met 1 of 4 criteria, 2 of 4 criteria, 3 of 4 criteria, and all 4 criteria, respectively. The VFQ-25 measures 12 health domains (11 vision-related; 1 general health–related) and was used to assess the effect of ocular disease on vision-related QoL from the patient's perspective. VFQ-25 total score was the mean of 11 vision-related domains. Scores ranged from 0 (worst vision) to 100 (best vision). Analyses were conducted for patients with 1, 2, 3, and 4 components, and for patients with no component (non-failure). Changes in VFQ-25 total and subdomain scores from best state prior to week 6 to final visit were calculated for each component, at least 1 component, and no component (non-failure). Analysis of covariance (adjusting for best state prior to week 6) was used to assess the association between VFQ-25 score and 1, 2, 3, or 4 components. Missing data were imputed using last observation carried forward.
**Results:** Data from 203 patients were analyzed. Unadjusted mean change in VFQ 25 total score was -4.92 for at least 1 component compared with 0.19 for non-failure; unadjusted mean change was –3.90, –5.09, –11.1, and –13.88, for 1, 2, 3, and 4 components, respectively. Adjusted change in VFQ-25 score from best state prior to week 6 to final visit was –3.9 ($P<.0001$) for each additional component. When assessing patients by component, the greatest change in VFQ-25 total score was seen for VA (–7.99) followed by VH grade (–3.29), AC cell grade (–2.8), and retinal vascular lesion (–2.76). In general, results were similar for the VFQ-25 subdomain scores.
**Conclusions:** Clinically meaningful decreases in VFQ-25 scores among patients experiencing TF were substantial[1] supporting TF as a relevant outcome from the patient perspective. Among causes for TF, the loss of VA had the greatest impact on the QoL, the other causes for TF had a lesser effect.
**References:**
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## THU0566 ADALIMUMAB OPTIMIZATION IN BEHCET'S SYNDROME REFRACTORY UVEITIS ONCE OBTAINED REMISSION

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**Background:** In non-infectious no anterior uveitis, adalimumab (ADA) is the only biologic that has shown efficacy in phase III randomized, double blind studies, such as VISUAL I and VISUAL II. (Brezin AP et al Arthritis Rheumatol 2015;67 (suppl 10): 2038 & Nguyen QD et al Arthritis Rheumatol 2015; 67 (suppl 10): 1388).
After a 80 mg loading dose, maintenance dose is the standard for other indications, 40 mg/sc/2 weeks.
**Objectives:** Our objective is to test a series of Behcet's síndrome uveítis, and proving if once remission was obtained, it was posible to "optimize" the maintenance dose.
**Methods:** Multicenter study of 174 patients with Behcet's síndrome refractory uveitis. All of them had insufficient response or intolerance to conventional treatment with corticosteroids and at least 1 systemic immunosuppressive drug. 71 patients started treatment with ADA and once remission was achieved, it was optimized in 23 of them.
The degree of ocular inflammation was assessed by "the Standardization of Uveitis Nomenclature (SUN) Working Group" (Am J Ophthalmol 2005; 140: 509–516), and macular thickness by optical coherence tomography (OCT). A comparison was made between the first visit before initializing ADA at standard dose, the start of the optimization of the drug, and the final visit.
The results are expressed as mean ± 1 SD for variables with a normal distribution, and as median [IQR 25–75] (range) when it is not normal. Comparison of continuous variables was performed using the Wilcoxon test.
**Results:** 23 patients/42 affected eyes (15 men/8 women) who had a dose optimization were studied, the median age was 37.2 ± 13.4 years (range 10–62). HLA-B51 was positive in 60.8%. Prior to ADA, and as systemic treatment besides oral steroids, they had received intravenous methylprednisolone bolus (n=7), cyclosporin A (CyA) (n=20), methotrexate (MTX) (n=11) and azathioprine (AZA) (n=11).
ADA monotherapy was used in 5 cases and also in combination with immunosuppressants: CyA (n=12), MTX (n=4) and AZA (n=2). The average remission before

optimization of the dose was 15.3 ± 9 months. In 23 patients the interval dose of adalimumab was progressively increased to 3 weeks (n=6), 4 weeks (n=13), 5 weeks (n=1), 6 weeks (n=1) and 8 weeks (n=2).
Only 2 patients had to return to the standard dose of ADA due to serious outbreak after optimizing the drug, reaching again remission of uveitis. It was also posible to suspend ADA in 4 patients after 35.2 ± 9.3 months in remission, not presenting a new outbreak after a mean of 20 ± 6.9 months following the suspension. There were not serious side effects during a mean follow-up of 34.7 ± 13.3 months after starting ADA.

TABLE 1.

| | At onset of ADA | At on set of ADA Optimization | Last Visit |
|---|---|---|---|
| VA (median [IQR]) | 0,8 [0,3-1] | 1 [0,8-1] * | 1 [0,9-1] * |
| anterior chamber cell (median [IQR]) | 0 [0-2] | 0 [0-0] * | 0 [0-0] * |
| Vitritis (median [IQR]) | 1 [0-2] | 0 [0-0] * | 0 [0-0] * |
| Retinal vasculitis (% affected eyes) | 41,8% | 10,8% * | 0% * |
| OCT (µ) (mean±SD) | 308,7±122,9 | 253±20 * | 250,5±17,9 * |

* p< 0,05 Between At onset of ADA, At onset of ADA optimization and last visit (Wilcoxon test)
Abreviatures: VA= Visual Acuicity, ADA= adalimumab

**Conclusions:** Optimizing ADA therapy, once remission is achieved, seems feasible in Behcet's síndrome uveítis refractory to systemic treatment.
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## THU0567 COMPARATIVE PERFORMANCE OF FAUTREL AND YAMAGUCHI CRITERIA FOR THE CLASSIFICATION OF PATIENTS WITH ADULT ONSET STILL DISEASE: PRELIMINARY RESULTS

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**Objectives:** To validate Fautrel criteria set for classification of adult onset Still's disease (AOSD), and to establish its discriminative performance to that of the Yamaguchi's set.
**Methods:** We retrospectively reviewed the medical charts of 344 patients who had ferritin and glycosylated ferritin measured at the biochemistry laboratory of Bichat Hospital. Medical informations were extracted via a standardized form. All clinical, biological, imaging features were collected, as well as elements in favor of an alternative diagnosis, specifically symptoms suggestive of other immune-mediated inflammatory diseases (IMID) or active infections. Patients were classified as AOSD or control group, according to a predefined procedure including a review by a group of experts for difficult cases. Algorithms corresponding to Fautrel's and Yamaguchi's classification criteria sets were applied for each patient.
**Results:** 49 AOSD and 229 control patients were included. Fautrel's set displayed a sensitivity of 89.8%, a specificity of 97.8%, and positive and negative predictive values of 89.8% and 97.8% respectively. 5 AOSD diagnoses were missed, and accurately classified as AOSD by standard Yamaguchi's set. The standard Yamaguchi's set – without strict application of exclusion criteria – produced a sensitivity of 95.9%, a specificity of 99.6%, and positive and negative predictive values of 97.9% and 99.1% respectively. 2 AOSD diagnoses were missed and correctly classified with the Fautrel's set. If we applied a stricter definition of exclusion criteria, the sensitivity of Yamaguchi's set decreased to 30.6% ($p<0.0001$). 34 AOSD diagnoses were also missed. These different sets showed excellent performance, although the differences did not reach statistical significance.

| Criteria sets | AOSD (n=49) | Control (n=229) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---|---|---|---|---|---|---|---|
| Fautrel | 44 | 5 | 89.8[a] | 97.8[b] | 89.8 | 97.8 | 96.4 |
| Standard Yamaguchi | 47 | 1 | 95.9 | 99.6 | 97.9 | 99.1 | 98.9 |
| Strict Yamaguchi | 15 | 0 | 30.6[c] | 100.0 | 100.0 | 87.1 | 87.8 |

PPV = positive predictive value; NPV = negative predictive value; exclusion criteria defined on the referring physician's word in the classification called "standard", and defined more on a performance of predefined diagnostic investigations in the classification called "strict". [a]p=0.26, [b]p=0.10, [c]p<0.0001.

**Conclusions:** Both criteria display high discrimination power in a new cohort of cases and controls. The Fautrel criteria set includes glycosylated ferritin and does not require exclusion criteria. The Yamaguchi criteria set is highly impacted by the way the satisfaction of exclusion criteria were performed.
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## THU0568 ULTRASONOGRAPHY OF SALIVARY GLANDS FOR DIAGNOSE OF IGG4-RELATED MIKULICZ'S DISEASE

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**Background:** Immunoglobulin 4-related Mikulicz'sdisease (IgG4-MD) is a subtype of IgG4-related diseases with the future of swollen bilateral salivary glands and highly responsive to gluccocorticoids (GCs) therapy. It has the similar ultrasonography (US) features as primary sjogren's syndrome (pSS) including multiply hypoechoic zone, hyperechogenic reflections, inhomogeity and echogeneity appearance of the parotid and submandibular glands. Our study tried to distinct IgG4-MD from pSS by US.
**Objectives:** Our study tried to distinct IgG4-MD from pSS by US.
**Methods:** 7 cases of IgG4-MD with parotid involvement and 28 cases of pSS first diagnosed without treatment before were observed by ultrasonography (US) of bilateral parotid and submandibular glands. Parameters includes parotid gland depth, submandibular size were recorded, and the extent of nodal hypoechoic areas, hyperchogenic reflections, inhomogeity, echogeneity, border clearness were scored according to the pSS US scoring system designed by Hocevar. Afterward, 7 IgG4-MD and 28 pSS patients were given 16mg Methylprednisolone and then tapered 4mg per month and followed up by US after 3 months.
**Results:** 1) The parotid gland depth of IgG4-MD were significantly larger than of pSS (38±7mm: 11±5mm, $p<0.01$).
2) The scores of hypoechoic areas, hyperchogenic reflections, inhomogeity of IgG4-MD cases by Hocevar's method were significantly higher than of pSS cases repectively (mean scores=9.1: 6.3, 11.1: 3.6, 11.8: 5.9, $p<0.01$), border clearness and echogeneity were not significantly difference.
3) It is shown depth of bilateral parotid glands (38±7mm: 14±3mm) and the score of hypoechoic areas (9.1: 3.7, $p<0.01$) in IgG4-MD cases remarkably decreased after 3 month follow-up, however, no too much difference of the depth of bilateral parotid glands (11±5mm: 10±6mm) and the score of hypoechoic areas (6.3: 5.3) in pSS cases.
**Conclusions:** Ultrasound could be used for distinguish IgG4-MD salivary involvement from pSS for monitoring the depth of parotid and scoring hypoechoic areas especially during the GCs therapy.
**Disclosure of Interest:** None declared
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## THU0569 PHARMACOKINETICS AND PHARMACODYNAMICS OF CANAKINUMAB IN PATIENTS WITH AUTOINFLAMMATORY PERIODIC FEVER SYNDROMES (COLCHICINE RESISTANT FMF, HIDS/MKD AND TRAPS)

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**Background:** Periodic fever syndromes are a group of rare autoinflammatory conditions that includes, among others, cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and TNF receptor-associated periodic syndrome

(TRAPS). The pharmacokinetics (PK) of canakinumab (CAN) and total interleukin (IL)-1β kinetics have been well characterised in CAPS patients (pts).[1] Here we present the PK and pharmacodynamics (PD) of CAN in colchicine resistant/intolerant (crFMF), HIDS/MKD and TRAPS pts.

**Objectives:** To evaluate the PK and PD of CAN (solution for injection-liquid in vial [LIVI]) from the phase III study in crFMF, HIDS/MKD and TRAPS pts at Week 16.

**Methods:** The study (NCT02059291) comprised of 3 disease cohorts (crFMF, HIDS/MKD and TRAPS). Each cohort followed the same study design across 4 epochs (screening epoch [up to 12 weeks], randomised treatment epoch [16 weeks], randomised withdrawal epoch [24 weeks] and open-label treatment epoch [72 weeks]). Pts (age, ≥2 years) with crFMF, HIDS/MKD or TRAPS who had a flare during Epoch 1 were randomised (1:1) in Epoch 2 to receive subcutaneous (sc) CAN 150 mg (or 2 mg/kg for pts weighing ≤40 kg) every 4 weeks (q4w) or placebo. Blinded uptitration (up to 300 mg) was allowed for pts not resolving the index flare by day15. Samples for CAN concentrations and total IL-1β were collected at baseline (Day 1), and trough samples at weeks 2, 4, 8, 12 and 16.

**Results:** In crFMF, HIDS/MKD and TRAPS pts, the serum clearance and steady-state volume of distribution of CAN varied according to body weight and were estimated to be 0.14±0.04 L/day and 4.96±1.35 L, respectively. The estimated half-life of CAN was 25.6±6.4 days. CAN minimal concentration at Week 16 following 150 mg sc q4w dosing was estimated to be 15.3±6.6 μg/mL. The estimated steady state area under the serum concentration-time curve from time zero to the end of the dosing interval tau ($AUC_{tau}$) was 648±202 μg.day/mL. Similar results were obtained in 3 diseases. CAN binding to circulating IL-1β was demonstrated by increase in total IL-1β following CAN dosing in all 3 diseases. In pts requiring up titration to 300 mg, levels of total IL-1β were higher suggesting higher production of IL-1β.

**Conclusions:** This was first study to evaluate the PK characteristics of canakinumab given in the LIVI form. The results observed in crFMF, HIDS/MKD and TRAPS patients were similar to those observed in other indications (CAPS and SJIA) using the lyophilisate form. These data suggested that new formulation did not affect PK/PD of the drug and similarly to CAPS, patients with higher levels of IL-1β may require canakinumab up-titration to have an optimal disease control.

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## THU0570 USE OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN A COHORT OF PATIENTS WITH IGG4-RELATED DISEASE

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**Background:** The use of non-biologic disease-modifying anti-rheumatic drugs (DMARDs) has been scarcely explored in patients with IgG4-related disease (IgG4-RD). There is only one small series reporting the use of methotrexate.

**Objectives:** This paper aims to describe the use of DMARDs in a monocentric cohort, the characteristics of the patients and the outcomes.

**Methods:** This is an observational study. Diagnoses were made according to the international 2012 criteria. Patients were divided into histologically highly suggestive and histologically probable IgG4-RD. Subjects with insufficient IgG4-RD pathological features were excluded. Medical records including baseline characteristics, treatments and outcomes were reviewed.

**Results:** Twenty-five patients were included, 8 of which (32%) were women. The median age at diagnosis was 50.5 years (IQR 14). Thirteen patients (52%) were assigned to the group of highly suggestive histological IgG4-RD and 12 (48%) in the probable group. Nine patients (36%) had systemic IgG4-RD (>1 organ affected). The most frequently involved organs were: retroperitoneum 8 (32%), orbitary pseudotumor 5 (20%) and aorta 3 (12%). Regarding treatments, 3 patients did not receive treatment (because of reluctance to treatment, minimal extension and new diagnosis, respectively). The reported use of DMARDs was: azathioprine 4 patients (16%, 50–200mg/day), mycophenolate mofetil 2 (8%, 2g/day), methotrexate 1 (4%, 15mg/day) and cyclosporin A 1 (4%, 200mg/day). The first time patients were treated, nineteen patients (76%) received corticosteroids, in 3 cases (12%) together with DMARDs. Seven patients (28%) underwent resective surgery. The response to the first treatment scheme was complete (no symptoms, >50% fibrotic mass reduction) in 12 patients (48%) and partial (no symptoms, <50% fibrotic mass reduction) in 10 (40%). Nine patients (36%) had treatment failure or relapses, always in the same organ involved at diagnosis. One of them had been treated with corticosteroids plus DMARDs. Within patients that required to be treated for a second time (treatment failure or relapses), 7 patients (77.7%) received corticosteroids. Of those, 2 individuals were given corticosteroids alone (25%) and five (62.5%) were given corticosteroids plus DMARDs. One patient received directly rituximab and another underwent surgery. Six patients (66.7%) had a complete response, 2 (22.2%) had a partial response and one was lost during follow-up. Among the five patients who received DMARDs, two had a partial response and three had a complete response. One patient was still refractory to treatment and was rescued successfully adding rituximab to the scheme. After a median follow-up of 2.5years (IQR 5.25), while no patients died.

**Conclusions:** This is the second largest single-center cohort reported in Europe. Corticosteroids seem the basis of any treatment done so far, although flares are common. The combined use of corticosteroids with DMARDs seemed effective in our series. DMARDs were more frequently used when treating flares. Although rituximab is a promising treatment, non-biological DMARDs could have a role in IgG4-RD treatment. Larger cohorts and randomized studies are required to make advances in this field.

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## THU0571 PRELIMINARY RESPONSE TO JANUS KINASE INHIBITION WITH BARICITINIB IN CHRONIC ATYPICAL NEUTROPHILIC DERMATOSIS WITH LIPODYSTROPHY AND ELEVATED TEMPERATURES (CANDLE)

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**Background:** Elevated serum IP-10 (CXCL10) levels and gene expression studies showing a prominent "interferon (IFN) signature" suggested modulation of IFN signaling might be a therapeutic option in CANDLE patients.

**Objectives:** The objective of this compassionate use program is to provide baricitinib (JAK1/JAK2 inhibitor) to CANDLE patients who have no other comparable or satisfactory treatment options. Potential efficacy of treatment was assessed by a reduction in mean Autoinflammatory Diary Scores (ADS) to <0.5 and reduction of steroid doses by at least 50% in patients receiving steroids at baseline.

**Methods:** Paired t-test was used to compare mean ADS and prednisone doses at the last NIH clinic visit to baseline data.

**Results:** Between October 2011 and January 1st, 2016, 11 CANDLE patients have been treated (mean duration 2.5 years (SD±1)). 9 of 11 patients achieved an ADS of <0.5 at the time of their last visit (mean ADS decreased from 1.3 ± 0.8 at baseline to 0.2 ± 0.3) ($p<0.005$), 8 of 10 patients achieved a reduction in steroids doses > than 50% from baseline (mean total prednisone dose decreased from 0.8 mg/kg/day (0.2–1.8) to 0.2 mg/kg/day (0–1.1)) ($p<0.005$), 4 patients discontinued prednisone completely. The mean dose of baricitinib at the last patient visit was 6.9 ± 2.8 mg/day. 7 patients reported at least 1 serious adverse event (SAE), infection being the most common. 2 patients have been discontinued due to SAEs (avascular necrosis; BK viremia and azotemia). 1 patient required temporary interruption of baricitinib due to neutropenia, and 3 other patients had their dose electively reduced after testing positive for BK viremia: patients were asymptomatic. The most common adverse events were upper respiratory infections, cough, and BK viruria (baseline BK virus screening was not performed).1 patient died due to worsening interstitial lung disease with development of respiratory failure 4 months after discontinuation of baricitinib and initiation of another JAK inhibitor.

**Conclusions:** Preliminary efficacy data in 11 CANDLE patients treated with baricitinib are encouraging and suggest that targeting IFN signaling with a JAK1/JAK2 inhibitor may be a successful therapeutic strategy. Monitoring BK viral titers in blood and urine, in addition to other measures of safety and efficacy, may be important in dose selection and the benefit-risk assessment of baricitinib for CANDLE patients.

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Hadigan: None declared, T. Heller: None declared, M. Waldman: None declared, K. Rother: None declared, R. Goldbach-Mansky: None declared
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## THU0572 RELATIONSHIP BETWEEN MENSTRUATION AND SYMPTOMS OF BEHÇET'S SYNDROME

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**Background:** It is well known that menstruation triggers several conditions such as migraine, recurrent aphtous stomatitis and acne vulgaris in otherwise healthy individuals (1). It may exacerbate chronic autoimmune diseases and familial Mediterranean fever (FMF) (2–4). There is also one study that briefly mentions menstruation causes activation in Behçet's syndrome (BS) (4).
**Objectives:** We investigated the relationship between menstruation and specifically the skin-mucosa lesions of BS. As controls, we studied FMF patients.
**Methods:** Premenopausal women with BS and FMF seen consecutively at the outpatient clinic of Cerrahpasa Medical Faculty at Istanbul, were interviewed. BS patients were asked whether they experienced increased skin-mucosa lesions during the menstrual period. A similar questionnaire assessing this time the frequency of serositis and fever attacks was given to the patients with FMF. As a control the participants were also asked whether they experienced headaches during the same period as well.
**Results:** A total of 140 BS patients with a mean age of 36±8 and mean disease duration of 9±6 years were studied. While 21 (15%) were off treatment, 103 (74%) were using colchicine and the remaining were using other immunosuppressive agents. As shown in the Table, among BS patients, 78 (56%) associated at least one symptom with menstruation. The most commonly reported symptom related with menstruation was the papulopustular involvement (50%), followed by oral (30%) and genital ulcers (21%) and nodular lesions (21%).
We also studied 185 patients with FMF. Their mean age was 32±8 and mean disease duration was 12±8 years. All patients were using colchicine for a mean duration of 8±7 years. A total of 138 patients (75%) reported that their attacks overlapped with menstruation. These attacks included mostly peritonitis in 126 patients (68%), pleuritis in 102 (55%), and fever in 73 (40%).
Among both BS and FMF patients, similar number of patients (41% and 41%, respectively) reported that menstruation triggered headaches.

| | Yes | No | do not remember |
|---|---|---|---|
| Behçet syndrome (n=140) | | | |
| Oral ulcer, n (%) | 42 (30) | 45 (32) | 53 (38) |
| Genital ulcer, n (%) | 30 (21) | 94 (67) | 16 (11) |
| Papulopustular lesions, n (%) | 70 (50) | 56 (40) | 14 (10) |
| Nodular lesions, n (%) | 30 (21) | 90 (64) | 20 (14) |
| At least one BS symptom, n (%) | 78 (55) | – | – |
| Headache, n (%) | 58 (41) | 45 (33) | 37 (26) |
| Familial Mediterranean fever (n=185) | | | |
| Peritonitis, n (%) | 126 (68) | 51 (28) | 8 (4) |
| Pleuritis, n (%) | 102 (55) | 74 (40) | 9 (5) |
| Fever, n (%) | 73 (39) | 100 (54) | 12 (6) |
| At least one FMF symptom, n (%) | 138 (75) | – | – |
| Headache, n (%) | 76 (41) | 77 (42) | 32 (17) |

**Conclusions:** This survey showed that, in about half of the patients with BS at least one skin mucosa lesion is exacerbated with menstruation. Most commonly reported were the papulopustular lesions. Menstruation had a stronger effect on FMF, triggering at least one symptom in about ¾ patients. The main limitation of the study was the self-reported assessment methodology, rather than a prospective diary assessment. Our findings provide further evidence that papulopustular lesions of BS and acne vulgaris are pathologically related (5).
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## THU0573 SEMEN ANALYSIS IN ADOLESCENT WITH FAMILIAL MEDITERRANIAN FEVER

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**Background:** Familial Mediterranean Fever (FMF) is a genetic disease that has characteristics like fever, sterile peritonitis, pleurisy, joint pain and rashes that are similar to erysipelas. In male patients, scrotal involvement is seen especially in children and adolescents with the frequency being below 5%.[1] Colchicine is an agent which regulates microtubules in cell's structure, pauses metaphase stage in cell division and stops microtubule dependent cell movement[2]. Colchicine is principal for treatment of FMF. Colchicine has a negative effect on sperm count and motility as it effects microtubules.
**Objectives:** We aimed to observe the relationship between sperm count and function with disease activity and colchicine usage in adolescent male patients with FMF.
**Methods:** Male patients between the age of 14–19 years old with FMF investigated retrospectively. Tel Hashomer and Turkish FMF Pediatric Criteria were used for diagnosis of FMF. Genetic screening was performed in all patients at the time of diagnosis. Sperm analysis was performed in 19 patients on treatment with colchicine. Demographic and clinical parameters of patients were analyzed.
**Results:** Mean age at the diagnosis was 11.13±3.82 years old, mean age at the study was 14.50±0.70 and mean follow-up period was 4.68±3.94 years. Homozygote, compound heterozygote and heterozygote mutations were found in eight, seven and one patients, respectively; no mutations in 3 patients. Mean colchicine dose was 1.16 mg/day at the start of treatment and 1.47 mg/day when sperm samples were collected. Mean sperm concentration was found as 66.26±41.02 million/ml (N>15), sperm count 113.42±132.39 million (N>35) and motility %51.78±23.70 (N>50%). Only 8 patients out of 19 had normal sperm parameters. Sperm concentration was reduced in two cases; sperm count was reduced in four patients whereas motility was reduced in nine cases. No relation was determined between sperm volume, count, concentration and motility results with age at diagnosis, follow-up period, symptoms on admission and inflammatory markers (CRP and erythrocyte sedimentation rate). Patients that had sedimentation values above 30 mm/hour during follow-up had sperm count below <35 million, with a specificity of 100% and sensitivity of 73.3% (AUC=0.858, p=0.032). It was found that patients who had FMF attacks during treatment had low sperm count and motility than patients without attacks (p: 0.034 and p: 0.02, respectively). There was an inverse relationship between the dose of colchicine with sperm motility (p: 0.025).
**Conclusions:** A high number of adolescents with FMF had abnormal sperm parameters, mostly sperm motility. It seems that both colchicine and uncontrollable attacks of FMF may be the reason of abnormal sperm parameters. We suggest that all adolescents with FMF should be screened for semen analysis.
**Disclosure of Interest:** None declared
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## THU0574 CHARACTERIZATION OF EYE SARCOIDOSIS WITH OR WITHOUT SYSTEMIC INVOLVEMENT:APPLICATION OF IWOS CRITERIA IN AN UVEITIS UNIT

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**Background:** Sarcoidosis (Sa) eye involvement is the most common extrapulmonary manifestation and is the initial presentation in 5–20% of cases. The definitive diagnosis is histopathological.The sensitivity (S) of the conjunctival biopsy is low,so Ocular Sa (OSa) diagnostic criteria (C) were proposed: IWOS (First International Workshop on Ocular Sarcoidosis), with high S and specificity (1/0.95). However, they have been poorly validated
**Objectives:** To apply the IWOS C. and to analyze their consistency with the suspected diagnosis of OSa.To discuss differential features between patients with OSa and those with systemic involvement
**Methods:** Observational cross-sectional study.Clinical records from patients with (presumed) Sa diagnosis who had been followed during the last 10 years in a multidisciplinar Uveitis Unit of a 3rd level hospital (Ophthalmology/Rheumatology) were reviewed.Clinical variables and complementary tests results were analyzed.IWOS C. were applied if OSa was suspected.For statistical analysis we use:Chi-square test and Kappa coefficient
**Results:** 71 patients were included:47 OSa,13 with ocular-systemic involvement (OS-Sa) and 11 with systemic involvement (SSa). Women/Men 57%/43%, mean follow-up time 9.42 years (±8.55), with no intergroup differences.Significant differences between patients with OSa vs. OS-Sa/SSa were observed:mean age at diagnosis (40.23±18.18 vs. 57.54±17.65/48.27 ±17 years, p=0.01); mean ESR (16.74±12.73 vs. 26.38±15./19.4±31.55 mm/h, p=0.01); mean CRP (3.58±4.29 vs. 8.12±8.11/10.24±14.37 mg/L, p=0.03); CT abnormalities (16.6% vs. 90%/92%, p=0.001); positive biopsy (0% vs. 88/100%, p=0.002); general, joint, respiratory and skin symptoms (OSa 6–12% vs SSa 15–50%, p=0.002). ACE was increased in 74.6%, with a mean value of 71.98±33.59 U/L, with no intergroup differences. Altered lacrimal scintigraphy was more often found in the OSa subset (26.7%) vs. OS-Sa/SSa (23.1%/0%), without statistical significance. Comparing OSa vs. OS-Sa patients, ocular involvement was as follows: anterior segment involvement 48% vs 61.5%, intermediate segment 21.3% vs. 15.4%, posterior segment 8.5% vs 0%, panuveitis 10.6% vs. 7.7%, mixed involvement 10.6% vs. 15.4% (p=0.001). If OSa, bilateral involvement was present in 60% of patients, unilateral involvement was more frecuent in OS-Sa (76%), p=0.06.There were no significant differences regarding uveitis's presentation, course and number of crisis and specific intraocular findings. Applying IWOS Criteria and comparing OSa vs OS-Sa we can classify: Definite OSa 0% vs. 69.2%, Presumed OSa 23.4% vs. 7.7%, Probable OSa 14.9% vs. 15.4% and Possible OSa 2.1% vs. 0%; not fulfilling criteria: 59.6% vs. 7.7% (p=0.001). The kappa coefficient between suspicion of OSa/OS-Sa and not fulfilling/fulfilling criteria was 0.30 (p=0.003).

**Conclusions:** We could classify as Presumed OSa in 25% and as Probable OSa in 15% of patients with suspected OSa but who hadn't undergo a biopsy. We excluded the diagnosis in 60%. There wasn't a good consistency between the suspected diagnosis/IWOS C. fulfillment,nevertheless they are a useful tool in clinical practice.OSa patients were younger and had lower ESR/CRP levels. Involvement of the anterior ocular segment was the most frequent one, bilateral in OSa and unilateral in OS-Sa
**Disclosure of Interest:** None declared
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## THU0575 TOCILIZUMAB IS SIGNIFICANTLY STEROID-SPARING COMPARED WITH METHOTREXATE IN POLYMYALGIA RHEUMATICA: A MULTICENTER RETROSPECTIVE STUDY (NTMC-KEIO PMR STUDY)

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**Background:** We have recently reported the effectiveness of tocilizumab (TCZ) against polymyalgia rheumatica (PMR) in a case series.
**Objectives:** Here, we aimed to investigate the efficacy of TCZ on the steroid-sparing effect in the treatment of PMR as compared with methotrexate (MTX).
**Methods:** We retrospectively studied all consecutive patients with PMR, diagnosed according to Bird's criteria and/or the 2012 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) provisional classification criteria, who had been treated at Keio University Hospital or National Tokyo Medical Center for at least 6 months between November 2005 and November 2015. The patients were divided into 3 groups based on the treatment at the last follow-up: prednisolone (PSL) monotherapy (PSL group), MTX+PSL (MTX group) and TCZ+PSL combination therapies (TCZ group). We evaluated the PSL dose in each therapy group at the last follow-up. TCZ was infused at 8 mg/kg every 4 weeks. 3 patients treated with both MTX and TCZ were excluded.
**Results:** Of 220 patients, 173 were in the PSL group, 32 in the MTX group, and 15 in the TCZ group. No difference was found in the proportion of women, mean age and the initial PSL dose among the PSL, MTX, and TCZ group (female, 72.8%, 78.1%, 73.3%; mean age, 73.1, 72.5, 74.1 years; initial PSL dose, 14.2, 16.2, 16.1 mg/day, respectively). The disease duration at the last follow-up in the PSL, MTX, and TCZ groups was 80.5, 60.4, and 43.3 months, respectively. The duration of MTX/TCZ use in combination with PSL was not different between the MTX and TCZ groups (30.2 vs 22.3 months, P=0.56). The PSL dose at the last follow-up in the TCZ group was much lower than the PSL and MTX groups (0.3, 3.2, 4.0 mg/day, $P<0.0001$). The patients in the TCZ group could discontinued PSL more frequently than the PSL and MTX groups (80.0%, 28.3%, 18.8%, $P<0.0001$ between the PSL and TCZ groups; $P<0.0001$ between the MTX and TCZ groups). The reduction in daily PSL dose at 6 months from the initiation of MTX/TCZ was much higher in the TCZ group than in the MTX group (-74.7% vs -29.6%, $P<0.0001$). Two patients discontinued MTX treatment because of adverse events (pneumonia and nausea) while none discontinued TCZ treatment.
**Conclusions:** TCZ is significantly steroid-sparing compared with MTX in the treatment of PMR. TCZ but not MTX may serve as an effective therapeutic option for patients who require quick reduction or discontinuation of PSL.
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## THU0576 TOCILIZUMAB MONO-THERAPY FOR POLYMYALGIA RHEUMATICA ~ A SINGLE-CENTER, OPEN, SINGLE-ARM TRIAL

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**Background:** Polymyalgia rheumatica (PMR) is a chronic inflammatory rheumatic disease that mainly affects the elderly. Corticosteroids (CSs) are a definite mainstay for the treatment of PMR; however, their use is associated with severe, serious clinical complications, such as osteoporotic fractures, diabetes, hyperlipidemia, cardio-cerebral vascular events, and glaucoma. Therefore, CS-free treatment strategies may be necessary for some patients with PMR. Interleukin-6 (IL-6) may be involved in the pathogenesis of PMR; furthermore, some case reports have already shown the efficacy of tocilizumab (TCZ), an anti-IL-6 receptor antibody, in the treatment of patients with PMR who had been intolerant or refractory to glucocorticoids [1, 2, 3].
**Objectives:** To assess the efficacy and safety of TCZ monotherapy for PMR
**Methods:** Thirteen PMR patients (3 males, 10 females) diagnosed by the 2012 ACR/EULAR classification criteria between Jan 2013 and Feb 2015 were enrolled after obtaining a written informed consent. TCZ (8 mg/kg) was administered biweekly for the first 2 months (5 infusions) and every 4 weeks for subsequent 24 weeks. ESR, CRP, visual analog scale (VAS) assessment of the patient's global health, and PMR activity score were prospectively measured every 4 weeks and were evaluated at week 24 and 52. Remission was defined as a PMR activity score less than 1.5 as proposed by Leeb [4].
**Results:** Baseline patient characteristics revealed various comorbidities in 11 of the patients; hypertension in seven, hyperlipidemia in five, diabetes mellitus in three, osteoporotic vertebral fractures in two, history of angina pectoris in one, history of brain infarction in one, history of hematemesis due to NSAID ulcer in one, and glaucoma in one patient. At week 24, nine patients achieved low disease activity as per the PMR activity score criteria, including three in remission. Two patients discontinued TCZ because of no response: one at week 6 and the other at week 16. Two patients discontinued TCZ due to adverse events [Editor 1]; pulmonary infiltrate at week 8, pemphigoid at week 50. The nine remaining patients achieved remission at week 52. There were no serious adverse events [Editor 2] except for pemphigoid during the 52-week treatment period.
**Conclusions:** TCZ monotherapy was effective in most (nine out of 13 [Editor 1]) PMR patients, although the response was not as rapid as that to CSs. TCZ monotherapy may be a good alternative therapy to CSs for the elderly with various comorbidities.
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**Disclosure of Interest:** K. Chino: None declared, A. Shibata: None declared, A. Okuyama: None declared, T. Kondo: None declared, J. Kikuchi: None declared, R. Sakai: None declared, H. Takei: None declared, K. Amano Grant/research support from: Chugai Pharmaceutical Co. Ltd.
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## THU0577 MUSCULOSKELETAL SARCOIDOSIS- DEMOGRAPHICS, CLINICAL CHARACTERISTICS, AND TREATMENT EXPERIENCE FROM A TERTIARY CARE CENTER IN THE UNITED STATES

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**Background:** Sarcoidosis, a systemic disease characterized by non-caseating granulomas within affected organs, typically targets the lungs. However, approximately 10–25% of cases manifest musculoskeletal (MSK) involvement of joints, muscles and bone tissue. Literature on the efficacy and safety of TNF-alpha inhibitors (TNFi) for treatment of MSK sarcoidosis is limited.
**Objectives:** Thus, we examined our experience with treatment of MSK sarcoidosis with TNFi.
**Methods:** We conducted an IRB-approved, retrospective EMR search using ICD-9 codes followed by EMR review of individual records to identify patients with MSK sarcoid seen in the Rheumatology clinic at the University of Iowa Hospitals and Clinics and the Iowa City Veterans Affairs Medical Center between January 1, 2000 and December 31, 2014. The diagnosis of MSK sarcoidosis was confirmed based on the presence of Löfgren's syndrome triad or positive pathology on biopsy of MSK tissue. We extracted from cases of MSK sarcoidosis variables on demographics, clinical manifestations, type and length of treatment, treatment response, relapse and adverse events.
**Results:** Retrospective chart review of 340 patients with sarcoidosis yielded 26 cases with MSK involvement, 7 fulfilling Löfgren's syndrome triad (27%) and 19 with biopsy-proven MSK sarcoid (73%). The mean age was 50 yrs and majority were females. 19 patients presented with arthritis (7 Lofgren's and 13 chronic, oligoarticular), 2 with sarcoid myopathy, and 4 with osseous sarcoid. MSK sarcoid symptoms were controlled in 69% of patients with maintenance methotrexate and/or hydroxychloroquine. 8 patients received TNFi due to failure of DMARDs. Long-term efficacy of TNFi was low (Table 1).

Table 1. Clinical outcomes of TNFi treatment of MSK sarcoidosis

| Age/Sex | Condition | Drug | Total therapy | Outcome | Side effect |
|---|---|---|---|---|---|
| 54/M | Osseous sarcoidosis | Infliximab | 8 yrs | Intolerance | Serum sickness |
| 65/F | Osseous sarcoidosis | Infliximab | 6 mo | Ineffective | None |
| 69/M | Myopathy | Infliximab | 8 yrs | Ineffective | None |
| 54/F | Chronic arthritis | Infliximab | 9 yrs | Relapsed | None |
| 57/F | Chronic arthritis | Adalimumab | 7 yrs | Ineffective | None |
| 50/F | Chronic arthritis | Adalimumab | 10 yrs | Effective | None |
| 54/M | Osseous sarcoidosis | Adalimumab | 2 yrs | Relapse | None |
| 54/M | Osseous sarcoidosis | Etanercept | 1 yr | Effective | Oral ulcers |

**Conclusions:** To our best knowledge, this study represents the largest case series of MSK sarcoidosis in North America since 1985. We also present data on outcomes of TNFi use in different forms of MSK sarcoid. In most patients standard DMARD therapy controlled symptoms of MSK sarcoid. TNFi benefited a few patients long term who failed oral DMARDs. Our case series underscores the need for identifying novel targets of treatment for the nearly one-third of patients with MSK sarcoid who fail standard DMARD treatment.

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## THU0578 FACTORS ASSOCIATED WITH EARLY DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER

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**Background:** Familial Mediterranean fever (FMF) is characterized by recurrent attacks of polyserositis. Delay in treatment may lead to recurrent attacks and amyloidosis.
**Objectives:** In this study, we aimed to evaluate clinical features of patients diagnosed early and compared to those diagnosed late
**Methods:** We enrolled 143 FMF patients over the age of 18 who met Tel-Hashomer Criterias into the study. Demographic features of the patients, duration of education, smoking habits, family history of FMF disease and amyloidosis,; features, duration and frequency of FMF attacks; age at first FMF attack; age at first admittance to a specialist, time between first FMF attack to first admittance to a specialist and which medical specialities patients admitted for their symptoms were recorded with face to face survey method. Else, MEFV gene mutations of the patients, time between first admittance to a specialist to diagnosis, clinical decision and judgement of the specialists at the time of diagnosis were obtained from hospital's medical recording system. Early diagnosis was defined as within three years after the first symptom.
**Results:** Mean diagnostic delay was 12.03±10.43 years. Age at first FMF attack (p=0.020), time between first FMF attack to first admittance to a specialist (p=0.003) and first admittance to a specialist after year 2000 (p=0.001) were found statistically important related with early diagnosis in a regression model. MEFV mutation was the only method that had an influence on the decision making of doctors in the diagnosis of FMF especially after year 2000.
**Conclusions:** Instead of demographic, clinical and genetic differences, early diagnosis may related with increased patient awareness about the disease. Furthermore, availability of MEFV mutation may influence doctors' decision making positively for facilitating early diagnosis of FMF and may replace clinical features. But, this may lead to failures in diagnosis in gene-negative FMF cases.
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## THU0579 TREATING TO TARGET WITH CANAKINUMAB IN PATIENTS WITH ACTIVE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM THE LONG-TERM EXTENSION THE PHASE III PIVOTAL TRIAL

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**Background:** The main therapeutic goals that can determine success of biologic treatment in systemic juvenile idiopathic arthritis (SJIA) include achieving and maintaining clinical remission, controlling disease activity and tapering corticosteroids (CS). Canakinumab (CAN) has been shown to improve several of these parameters in previous studies[1]. However, little is known about SJIA patients (pts) using CAN long-term.
**Objectives:** To evaluate the efficacy, safety and long-term treatment response of CAN treatment-naïve pts with active SJIA.
**Methods:** This was an open-label, non-comparative study (NCT00891046) of CAN-naïve SJIA pts (age ≥2 - <20 yrs) receiving CAN 4 mg/kg by s.c. q4w. Efficacy was assessed by the adapted pediatric ACR (aACR 30/50/70/90/100) responses compared to baseline (BL); inactive disease (ID) or clinical remission (ID for >6 Mo) and changes in JADAS-CRP (Juvenile Arthritis Disease Activity Score- C-reactive protein) scores over time. Safety was assessed by adverse events (AEs) and serious AEs (SAEs) reports.
**Results:** A total of 123 pts with active SJIA were enrolled of whom 70 (57%) pts had fever and 71 (57.7%) pts used CS at BL. Mean CRP was 117.8 mg/L (normal: 0–10mg/L) and, on average, pts had, 9.9 active joints and 8.9 joints with limited motion. A rapid response was observed at Day 15, 59 (51%) with aACR ≥70 responses and 27 (26%) having aACR 100 responses. These responses increased and were maintained at subsequent time points (Table). Overall, 73.0% of pts had ID on at least 1 visit. At 6th month, clinical remission was achieved in 52 (42.3%) pts and 33 (26.8%) pts had clinical remission for at least 12 consecutive months. At BL, the median JADAS10-CRP score was 22.3 (indicating high disease activity), with median changes from BL of -12.0 at Day 15 and -16.8 at last assessment indicating moderate and low disease activity, respectively. At the last assessment, 59 (48.4%) pts were rated as ID (JADAS <1); 14 (11.5%) with low active disease activity (JADAS >1 and <3.8); while 14 (11.5%) had moderate and 35 (28.7%) with high disease activity. 24 (33.8%) pts were steroid-free at last assessment. A total of 53 (43.4%) pts had at least 1 AE. Overall rate of AEs was 2.25 events/ 100 patient-days and SAEs was 0.15/ 100 patient-days. 40 (32.5%) pts had SAEs and the most commonly reported were disease flares or worsening of SJIA in 13 (10.6%) pts, macrophage activation syndrome in 6 (4.9%) pts, and pyrexia in 4 (3.3%) pts. No deaths were reported in this study.

**Table. ACR responses achieved in the cohort : Summary statistics, by time point**

| Time point | CAN N=123 | | |
|---|---|---|---|
| | Minimum adapted ACR pediatric response | n (n/m%) | Patients with inactive disease (n/m)% |
| Month 12 | m | 85 | (1/1) 100 |
| | Non-Responders | 4 (4.7) | |
| | aACR ≥30 | 81 (95.3) | |
| | aACR ≥50 | 77 (90.6) | |
| | aACR ≥70 | 73 (85.9) | |
| | aACR ≥90 | 58 (68.2) | |
| | aACR 100 | 49 (57.6) | |
| Month 30 | m | 29 | (1/1) 100 |
| | Non-Responders | 1 (3.4) | |
| | aACR ≥30 | 28 (96.6) | |
| | aACR ≥50 | 28 (96.6) | |
| | aACR ≥70 | 26 (89.7) | |
| | aACR ≥90 | 23 (79.3) | |
| | aACR 100 | 19 (65.5) | |
| Last Assessment | m | 121 | (62/122) 50.8 |
| | Non-Responders | 28 (23.1) | |
| | aACR ≥30 | 93 (76.9) | |
| | aACR ≥50 | 89 (73.6) | |
| | aACR ≥70 | 81 (66.9) | |
| | aACR ≥90 | 74 (61.2) | |
| | aACR 100 | 62 (51.2) | |

n = number of patients who satisfy the criteria, m = number of patients with an assessment in the time period.

**Conclusions:** In this long-term study, CAN treatment was associated with rapid response and sustained therapeutic effect over the long-term in the naïve pts with active SJIA. The safety profile is consistent with other CAN studies.
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## THU0580 PANNICULITIS IN RHEUMATOLOGY PRACTICE: RESULTS OF LONG-TERM FOLLOW UP

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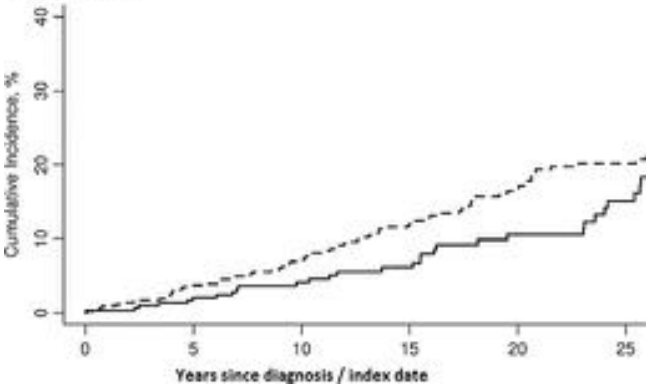
**Background:** Panniculitis (Pn) is a group of heterogeneous inflammatory diseases characterized by involvement of the subcutaneous fat (SF), musculoskeletal system and internal organs.
**Objectives:** to evaluate the clinical course and outcomes of Pn in a prospective study.
**Methods:** 73 pts (F-64, M-9) aged 19 - 77 y., referred for examination and treatment to V.A. Nasonova Research Institute of Rheumatology with referral diagnoses of "erythema nodosum" (EN) and "panniculitis", disease duration from 1 week to 13 years, were followed up. Patient evaluation included physical examination, lab tests (serum levels of $\alpha$1-antitrypsin, amylase, lipase, ferritin, creatine phosphokinase (CPK), rheumatoid factor) (RF), ANF, anti-DNA, ANCA), bacteriological and serological tests, radiological examination (chest CT scan), ultrasound examinations of skin and SF around the nodules, tuberculin skin test and histopathology of nodular skin samples. Patients were re-tested during the follow up (FUP) when necessary. The FUP period lasted from 3 to 5 years.
**Results:** based on clinical, lab and instrumental findings the following diagnoses were verified: EN, associated with infection (22 pts – Group1), lipodermatosclerosis (LDS) (15 pts – Group 2), Weber-Christian's Pn (11 pts – Group 3), Lőfgren syndrome (25 pts – Group 4). In Group 1 EN recurrences were documented in 10 (45%) pts during the FUP, presumably caused by: common cold (4), exacerbation of chronic tonsillitis (1), acute respiratory viral infection (ARVI) (1), stress (1), rapid down of dose of GCs (1), unknown cause (2). In Group 2 recurrences occurred in 9 (60%) pts due to stress (4), failure to observe anti-inflammatory therapy (hydroxychloroquine) (2), trauma (2), weight lifting (1). There were no recurrences in 3 pts from Group 2, nevertheless they failed to reach complete regression of the nodi, most probably due to poor compliance with treatment. 10 relapses (90,9%) registered in Group 3 were associated with absence/discontinuation of anti-inflammatory therapy (6), insufficient efficacy of administered anti-inflammatory therapy (2), and common cold (2). Relapse of nodules in 6 (24%) pts from Group 4 had the following plausible explanation: common cold /ARVI (5), GCs discontinuation (1). Two (2/7%) death were documented during the FUP: in 1 patient with LDS due to acute heart failure, and in 1 patient with Weber- Christian disease due to chronic cardio-pulmonary failure.
**Conclusions:** common cold and viral infections were the leading causes of relapses in pts with EN associated with infection and with Lőfgren syndrome, while stress and absence/insufficient efficacy of anti-inflammatory therapy were the major causes of recurrence in pts with Weber-Christian Pn and LDS. In this Pn case series mortality was 2,7% during the FUP.
**Disclosure of Interest:** None declared
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## THU0581 RISK OF MALIGNANCY AMONG PATIENTS WITH SARCOIDOSIS: A POPULATION-BASED COHORT STUDY

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**Background:** Previous studies on the association between sarcoidosis and malignancy yielded conflicting results.
**Objectives:** This study was aimed to investigate the risk of malignancy in patients with sarcoidosis in a population-based cohort.
**Methods:** An inception cohort of patients with incident sarcoidosis in 1976–2013 in a geographically well-defined population was identified based on comprehensive individual medical record review. Inclusion required physician diagnosis supported by histopathologic evidence of non-caseating granuloma, radiographic evidence of intrathoracic sarcoidosis, compatible clinical presentation, and exclusion of other granulomatous diseases. For each sarcoidosis subject, two sex and aged-matched comparator subjects without sarcoidosis were randomly selected. Cases and comparators were then cross-indexed with the Cancer Registry of the institution, which collected data on every type of malignancy except for non-melanoma skin cancer, for malignancy ascertainment.
**Results:** 345 incident cases of sarcoidosis and 690 comparators were identified. The median duration of follow-up was 12 years. There was no difference in the prevalence of malignancy at sarcoidosis incidence/index date between the 2 groups (14 cases, 3.8% among cases and 30 cases, 4.3% among comparators, *P*=0.87) compared to non-sarcoidosis subjects. During follow-up, 37 patients with sarcoidosis and 91 subjects without sarcoidosis developed malignancy with a cumulative incidence at 10 years of 4.1% and 7.1%, respectively. The difference corresponded to a hazard ratio of 0.74 (95% confidence interval (CI), 0.50 -1.09). The cumulative incidences at 10 years for individual types of malignancy were also similar between patients with sarcoidosis and non –sarcoidosis comparators, with non-significant hazard ratios. However, subgroup analysis found that cases with extra-thoracic involvement were at higher risk of incident hematologic malignancy compared with cases without extra-thoracic involvement (HR 1.87; 95% CI 1.09–3.22)

Figure. Cumulative Incidence of Any Cancer excluding non-melanoma skin cancers (Sarcoidosis solid line; Non-Sarcoidosis dashed line)




**Conclusions:** Risk of malignancy was similar among patients with sarcoidosis compared to non-sarcoidosis subjects. However, the risk of incident hematologic malignancy was significantly higher among patients with sarcoidosis with extra-thoracic involvement compared to patients without extra-thoracic disease.
**Disclosure of Interest:** None declared
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## THU0582 PROGNOSTIC FACTORS OF MACROPHAGE ACTIVATION SYNDROME IN ADULTS: ANALYSIS OF 40 CASES IN 2 TERTIARY REFERRAL CENTERS

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**Background:** Macrophage activation syndrome (MAS) is a rare, life-threatening disease in which early diagnosis and aggressive therapeutic strategy may improve the outcome [1]. Due to its rarity, epidemiologic data are still lacking. Hyperferritinemia is frequently associated with MAS and might modulate the cytokines storm the latter contributing to the development of multi-organ failure [2].
**Objectives:** In the current study, we aimed to investigate clinical data, treatments, and outcome of adult MAS patients secondary to autoimmune rheumatic disease.
**Methods:** We retrospectively investigated clinical data, treatments, and outcome of 40 adult MAS patients secondary to autoimmune rheumatic disease. For all the MAS patients, the following clinical characteristics were recorded: age, gender, values of serum ferritin, erythsedimentation rate (ESR) and C-reactive protein (CRP), treatments, concomitant comorbidities, time of observation and outcome. Furthermore, we evaluated the correlations among these clinical features and MAS-associated death.
**Results:** Forty consecutive MAS patients, 15 men (37.5%) and 25 women (62.5%), whose mean age at diagnosis was 48.20±14.10 (mean±SD) were enrolled. Thirty out of 40 enrolled patients reported an history of adult onset Still's disease (AOSD) (75%), 8 patients an history of systemic lupus erythematosus (20%), 1 patient an history of systemic sclerosis (2.5%), and 1 an history of ankilosing spondylitis (2.5%). Twenty-four out of enrolled patients (60%) did not show any comorbidity, and MAS was diagnosed during an AOSD flare. A severe

infections was associated with MAS in the other patients. The laboratory data (mean±SD) reported a strong increase of inflammatory markers: i. serum ferritin 6842.70±7569.70 ng/mL; ii. ESR 63.87±30.19 mm/hr; iii. CRP 51.59±46.92. All the patients were treated with pulsed high dosage of methylprednisolone (1000 mg/daily for a maximum of 6 cycles) and 16 patients (16, 40%) received a combination therapy with: cyclosporin (13, 32.5%); methotrexate (6, 15%); intravenous immunoglobulin therapy (3, 7.5%); anakinra (3, 7.5%); tocilizumab (1, 2.5%). MAS-associated death occurred in 17 patients (42.5%). By using Cox regression proportional hazard model of survival of enrolled MAS patients, we observed that: older age [p=0.017, EXP(B): 1.305, 95%CI: 1.006–1.365], increased serum ferritin levels [p=0.001, EXP(B): 1.776, 95%CI: 1.030–2.728], increased CRP levels [p=0.029, EXP(B): 1.511, 95CI%: 1.021–1.651], higher number of comorbidities [p=0.01, EXP(B): 1.751, 95%CI: 1.142–2.2686], and the use biologics [p=0.015, EXP(B): 2.915, 95%CI: 1.233–6892] were significantly associated with MAS-associated death.

**Conclusions:** Adult MAS is still associated with higher mortality rate. Some clinical features at diagnosis, such as older age, increased serum ferritin and CRP levels and higher number of comorbiditis, may be associated with MAS-associated death.

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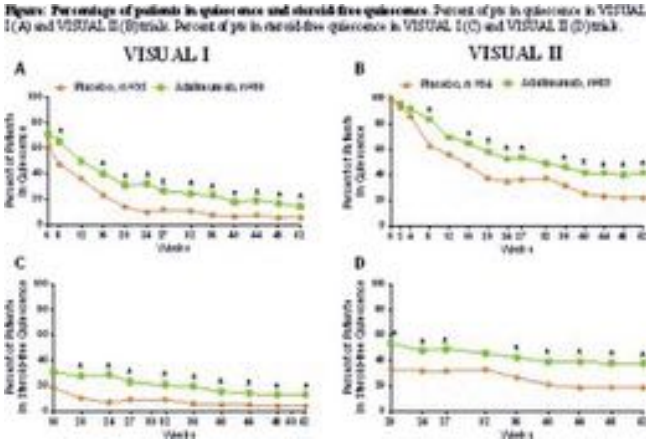
## THU0583 QUIESCENCE IN ACTIVE AND INACTIVE NON-INFECTIOUS, INTERMEDIATE, POSTERIOR, OR PANUVEITIS IN PATIENTS TREATED WITH ADALIMUMAB: VISUAL I AND VISUAL II TRIALS

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**Background:** There is an unmet need for effective therapies for patients (pts) with non-infectious intermediate, posterior, or panuveitis who are at risk for long-term side effects from chronic corticosteroid use. The therapeutic goal in uveitis is to achieve quiescence and adalimumab (ADA) has been shown to lower uveitic flare or vision loss in pts with active (VISUAL I) and inactive (VISUAL II) uveitis[1,2]. As 40–50% of uveitis pts have accompanying extra-ocular rheumatic associations such as Behcet's disease, sarcoidosis, understanding ocular quiescence will not only aid ophthalmologists but also rheumatologists in the overall management of the pt[3].

**Objectives:** To assess the control of inflammation over time in pts treated with ADA in the VISUAL I and II trials.

**Methods:** Adults with non-infectious intermediate, posterior, or panuveitis were enrolled in 2 global phase 3, double-masked trials: VISUAL I (pts with active uveitis despite ≥2 weeks [wk] of prednisone [PS] 10–60 mg/d) and VISUAL II (pts with inactive disease dependent on 10–35 mg/d of PS to maintain inactivity). Pts were randomized 1:1 to receive placebo (PBO) or ADA (80mg wk0, followed by 40mg every other wk from wk1 up to 80wks). In VISUAL I, all pts received a PS burst followed by taper to 0mg by wk15. In VISUAL II, PS taper to 0mg was mandatory by wk19. Quiescence as a pre-specified endpoint was defined as no new active inflammatory lesions and anterior chamber cell grade and vitreous haze grade ≤0.5+. Steroid free quiescence at each visit was additionally reported from wks16–52 for VISUAL I and from wk20- 52 for VISUAL II. Non-responder imputation was used for missing data. Statistical comparison between PBO and ADA was based on Chi-square test. Adverse events (AEs) were monitored.




**Results:** A greater proportion of pts in the ADA group than the PBO group achieved quiescence at each visit in both VISUAL I and VISUAL II. Statistically significance between ADA and PBO groups were observed at each visit from wks6–52 for VISUAL I, excluding wks6 and 12 and from wks8–52, excluding wks12 and 32 for VISUAL II (Fig. A,B).Similar results were observed for pts in steroid-free quiescence. Statistically significant differences between ADA and PBO groups occurred at each visit from wks20–52 for VISUAL I and from wks20–52, except wk32 for VISUAL II (Fig. C,D).Safety data from the VISUAL I and II trials have previously been reported[1,2]. Rates of AEs were similar between ADA and PBO groups.

**Conclusions:** Pts with non-infectious, intermediate, posterior, or panuveitis achieved significantly higher rates of quiescence and steroid-free quiescence with ADA treatment than PBO in the VISUAL I and II trials. The safety profile of ADA was consistent with the known safety profile across the approved ADA indications.

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## THU0584 CLINICAL CHARACTERISTICS OF SARCOID ARTHROPATHY

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**Background:** Sarcoidosis is known as a Th1-mediated disease which can mimic many primary rheumatologic diseases or can sometimes co-exist with them. Clinical characteristics of sarcoid arthropathy are not well described as only referral-based studies have been reported.

**Objectives:** The aim of this study were to evaluate the incidence and clinical characteristics of sarcoid arthropathy.

**Methods:** We used an inception cohort of sarcoidosis patients seen between July 2011 and August 2015. A total of 114 (32 male) sarcoidosis patients, who admitted to our clinic were included in the study. Clinical, demographical, laboratory, radiological and histological data of these patients obtained during 4-year follow-up and treatment period were compiled and analyzed.

**Results:** The mean patient age was 48.1 years (20–82 years), and the mean disease duration was 40.5 months (1–300 months). Sarcoid arthritis was observed in 71 (62.3%), and arthralgia in 106 (92.9%) patients. Out of the 71 patients with arthritis, 61 (85.9%) had involvement of ankle, 7 (9.8%) knee, two (2.8%) wrist, MCP and PIP joints, and one (1.4%) had shoulder periarthritis. Oligoarthritis (two to four joints) was the most common pattern followed by monoarthritis and polyarthritis. When the correlation between clinical findings were considered, erythema nodosum and arthritis and female gender were found to be correlated (p=0.03, p=0.001, respectively). Again in patients with arthritis, even higher levels of CRP/ESR as well as ANA and RF positivity were observed (p=0.03, p=0.01, p=0.01 and p=0.02, respectively). Eleven patients had another rheumatic pathology concurrent with sarcoidosis (1SjS, 3RA, 1Still disease, 1 Scleroderma, 4AS, 1FMF).

**Conclusions:** Inflammatory arthritis occurs in a majority of patients with sarcoidosis. Acute arthritis with bilateral ankles involvement was the most common pattern of sarcoid arthropathy. Sarcoidosis can mimic many primary rheumatic disease and/or may coexist. Sarcoidosis should be considered not only as a mimicker but also as a Th1-mediated primary rheumatologic pathology.

**Disclosure of Interest:** None declared

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## THU0585 DISTINCT CLINICAL FEATURES DISTINGUISHING IGG4-RELATED DISEASE AND MULTICENTRIC CASTLESMAN'S DISEASE

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**Background:** IgG4-related disease (IgG4-RD) is a fibro-inflammatory disease with multiple-organ involvement characterized by infiltration of $IgG4^+$plasma cells and elevated serum IgG4 concentrations. However, similar findings are observed in multicentric Castleman's disease (MCD)[1], thereby making it difficult to differentiate one disease from the other.
**Objectives:** The aim of this study was to clarify the differences of clinical characteristics and laboratory findings in IgG4-RD and MCD for differential diagnosis.
**Methods:** All consecutive patients with IgG4-RD and MCD who visited the Rheumatology or Hematology department in our institutes from January 2000 to November 2015 were retrospectively reviewed. Patient characteristics and laboratory data at the time of diagnosis were compared.
**Results:** Forty-nine patients with IgG4-RD and 48 patients with MCD were included. Patients with IgG4-RD were older compared to MCD (57.4 vs 47.3 years, $p<0.0001$) and there was no difference in gender distribution. While lymph nodes were affected less frequently in IgG4-RD compared to MCD (49% vs 100%, $p<0.0001$), lacrimal glands, salivary glands and pancreas were affected only in IgG4-RD. The levels of serum IgG, IgA and IgM were significantly lower in patients with IgG4-RD compared to MCD (IgG: 1945.6 mg/dl vs 4317.5 mg/dl, $p<0.0001$, IgA: 172 mg/dl vs 669 mg/dl, $p<0.0001$, IgM: 83 mg/dl vs 279 mg/dl, $p<0.0001$), whereas no difference was observed in serum IgE levels. Although level of serum IgG4 was also equivalent between IgG4-RD and MCD (607 mg/dl vs 353 mg/dl, $p=0.211$), IgG4/IgG ratio was significantly higher in IgG4-RD compared to MCD (0.30 vs 0.09, $p<0.0001$). In addition, atopic history was more frequent (71.4% vs 16.7%, $p<0.0001$), and the proportion of eosinophils (6.4% vs 2.7%, $p<0.0001$) was significantly higher in IgG4-RD compared to MCD. The level of serum C-reactive protein (0.3 mg/dl vs 5.4 mg/dl, $p<0.0001$) and erythrocyte sedimentation rate (35.9 mm/hr vs 110.7 mm/hr, $p<0.0001$), the prevalence of anemia (10.2% vs 50.0%, $p<0.0001$) and thrombocytosis (2.0% vs 31.3%, $p<0.0001$) were significantly higher in MCD compared to IgG4-RD.
**Conclusions:** The involvement of lacrimal gland, salivary gland and pancreas was unique for IgG4-RD. While allergic reaction such as hypereosinophilia and atopic history was more frequently observed in IgG4-RD, intense inflammation was the distinct characteristics for MCD. The distribution of organ involvement and marked inflammatory reaction represented by elevated serum CRP, anemia and thrombocytosis were important features to distinguish between IgG4-RD and MCD.
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## THU0586 AGREEMENT OF PATIENT AND PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN ADULT ONSET STILL'S DISEASE

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**Background:** There is not valid outcome measures for assessment Adult onset Still's disease (AOSD) activity. The patients or physicians global view is relevant way to assess this kind of complex diseases. However, it is well known that there is discordance between patient and physician perspective for disease activity in different inflammatory diseases.
**Objectives:** Objective of this study was to evaluate agreement of patient and physician perspective in AOSD patients.
**Methods:** We conducted a cross-sectional, multicenter study for assessment of disease activity in AOSD patients. All AOSD patients were fulfilled Yamaguchi criteria. For every center, at least 20% of AOSD patients had to be an active state according to physician assessment. Age, sex, disease duration, current disease symptoms was recorded. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), leucocyte, and ferritin level also recorded. Visual analog scale (VAS) (0–10 cm) used for physician and patient global assessment of disease activity. Disease activity status were also assessed by likert scale (as remission, low, moderate, severe, and more severe disease activity) for both patients and physician perspective. Patient global assessment VAS and physician global assessment were correlated by correlation coefficient (r). Agreement of disease activity level for patient and physician perspective were calculated with kappa. Kappa $>0.6$ was accepted as significant.
**Results:** One hundred thirty (83, 63.4% female) AOSD patients were enrolled. Mean age was 38 (14) years old and median disease duration was 3 years (0–29). Currently AOSD symptoms followed; fever 34 (26.2%), rash 28 (21.5%), arthritis 31 (23.8%), arthralgia 60 (46.2%), sore throat 28 (21.5), myalgia 42 (32.3), lympadenopathy 12 (9.2%), splenomegaly 17 (13.1%), hepatomegaly 7 (5.4%), pleuritic 3 (2.3%), hemophagocytic syndrome 2 (1.5%). ESR 47.7%, CRP 43.8%, ferritin 27.0%, and leucocyte 43.1% were higher than upper limit. Mean patient global assessment VAS was 3.53 (3.25), and mean physician global assessment VAS was 2.71 (2.95). Correlation coefficient (r) of patient and physican global VAS was 0.89. There was excellent agreement according to severe/more severe disease activity at patient and physician level (kappa 0.88 (CI 95% 0.79–0.98). There was also good to excellent agreement according to low disease activity/remission at patient and physician level (kappa 0.74 (CI 95% 0.62–0.86).
**Conclusions:** Although, features of AOSD seems more complex with constitutional symptoms, joint or reticuloendothelial system involvement, patients and physicians assess level of disease activity similarly. We thought, this results will be helpful for procedure of new composite index in AOSD.
**Disclosure of Interest:** None declared
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## THU0587 CLINICAL CHARACTERIZATION OF CASTLEMAN'S DISEASE IN A GROUP OF PEDIATRIC PATIENTS

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**Background:** Castleman's disease (CD) is a rare lymphoprolipherative mostly benign disorder presenting in two major forms: localized (unicentric) and systemic (multicentric). Based on pathomorphological finding it is classified as hyaline-vascular, plasma cell or mixed type. The age of onset can differ greatly from infancy to adulthood. Except for lymph node hyperplasia, patients with CD can also develop such symptoms as anemia, fatigue, hepatosplenomegaly, low-grade fevers and other systemic symptoms.
**Objectives:** Analysis of clinical manifestations, pathomorphology and treatment efficiency in a group of pediatric patients.
**Methods:** We conducted a retrospective analysis of 12 patients (11 boys and 1 girl) with histologically confirmed cases of Castleman's disease.
**Results:** Age of onset varied from the moment of birth to 16 years (median 8,5 years) 8 patients had unicentric form of disease, 3 had multicentric form and one patient had two groups of lymph nodes affected, thus could not be precisely classified. The majority of the patients (9 patients) had hyaline-vascular variant of CD, one patient had plasma-cell type and two patients had the mixed pathomorphological type. The reason for seeking medical attention in three patients was visible unilateral enlargement of neck lymph nodes, four patients initially presented with anemia, fatigue, fever and laboratory signs of inflammation, and in 4 patients enlarged lymph nodes were incidentally visualized during control X-ray, and no other symptoms of CD were present. Interestingly, of 3 patients with multicentric form of CD, two had underlying primary immunodeficiency – Wiskott-Aldrich syndrome (WAS). They presented with plasma cell type and mixed type of CD, respectively. No immunodeficiency has been proven in other patients. We have conducted tests to indicate HHV VIII in affected lymph node biopsies and blood samples via PCR in half of the patients and none occurred to be positive.
*Treatment:* The affected lymph nodes were completely excised surgically in 7 patients with unicentric form, with no relapse of the disease on follow-up. Both patients with WAS received rituximab treatment followed by bone marrow transplantation, which was originally planned as a treatment of WAS, with remission on follow-up at 3 month and 2 years, respectively. Third patient with multicentric form received several courses of anti-cytokine and immunosuppressive treatment including tocilizumab, cyclophosphamide, vincristine and prednisolone (total of 5 blocks), rituximab (6 infusions) with partial effect, then surgical excision of large conglomerates of lymph nodes followed by bortezomib and bendamustine (total of 6 blocks) with positive effect. However at the one year follow-up patients demonstrated enlarged lymph nodes again, so she was started on JAK tyrosine kinase inhibitor ruxolitinib. Follow-up results are pending.
**Conclusions:** Our analysis of a group of pediatric patients demonstrates great variability in symptoms and severity of the disease. Castleman's disease is a disorder with poorly studied pathogenesis. Based on our experience, the role of primary defects of immune system in development of CD requires further investigation.

**Disclosure of Interest:** None declared
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## THU0588 IGG4-RELATED DISEASE: FEATURES AND TREATMENT RESPONSE IN AN ASIAN COHORT

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**Background:** Most descriptions of IgG4-related disease (IgG4-RD) have been from Japanese and Caucasian populations.
**Objectives:** To describe the clinical, laboratory, histological features and treatment outcomes of IgG4-RD in multi-ethnic Asian patients in Singapore.
**Methods:** Patients diagnosed with IgG4-RD were identified from a Rheumatology and Gastroenterology patient database in a tertiary hospital. Demographics, clinical manifestations, laboratory results, disease activity, clinical outcomes and therapeutics used were derived from medical records. Disease activity was assessed by the IgG4-RD Responder Index.
**Results:** 42 patients (76% male) were included; all had a diagnosis of IgG4-RD made by a rheumatologist or gastroenterologist experienced in IgG4-RD. 79% and 17% fulfilled the 2011 comprehensive diagnostic criteria for IgG4-RD[1] for definite and probable IgG4-RD respectively. 81% were Chinese and 19% were Malays. Mean age of the cohort was 62.7 ± 13.1 years. Mean age of diagnosis was 57.5 ± 12.8 years. Mean duration of disease was 4.5 ± 3.5 years. Common initial manifestations included jaundice (52%), abdominal pain (36%), swollen salivary glands (26%) and constitutional symptoms (21%). Only 36% had a history of allergy. 83% had $\geq$1 organ involvement, including autoimmune pancreatitis (67%), lymphadenopathy (45%), sclerosing cholangitis (43%), sialadenitis (31%) and dacryoadenitis (21%). 86% (6/7) of patients with isolated lesions involved only the pancreas. There was no gender difference in type of organ involvement. Erythrocyte sedimentation rate (ESR), IgG1, IgG2, IgG3, IgG4 levels were elevated in 83%, 22%, 74%, 37%, 41% of patients respectively. IgG4 levels did not correlate with ESR, age, disease duration, IgE levels and number of organs involved. The most common histopathological feature was that of $>$10 IgG4+ cells per high power field (66%), followed by lymphocytic infiltration (51%) and storiform fibrosis (51%). Only 7% had obliterative phlebitis. 94% (34/36) of patients were treated with moderate to high doses of glucocorticoids, including 17 patients with combination immunosuppressants. Of these, all patients responded to therapy by 3 months. With a mean follow-up of 4.8 ± 3.1 years, 69% (25/36) needed low dose of glucocorticoids to maintain disease remission. 26% had relapse of disease, of which 82% had disease recurrence in the same organs.
**Conclusions:** Pancreatitis, lymphadenopathy and cholangitis were the commonest manifestations in Asians with IgG4-RD. All patients responded to glucocorticoid therapy by 3 months, two-thirds required maintenance therapy with glucocorticoids, and one-quarter developed relapse of disease.
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## THU0589 INFLIXIMAB THERAPY FOR NEURO-, VASCULAR, AND INTESTINAL BEHÇET'S DISEASE: EFFICACY, SAFETY, AND PHARMACOKINETICS IN A MULTICENTER PROSPECTIVE STUDY

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**Background:** Behçet's disease (BD) is a multisystem disease characterized by mucocutaneous, ocular, neurologic, vascular, or gastrointestinal manifestations. Involvement of the neuronal (NBD) and vascular (VBD) systems and intestinal tract (intestinal BD) is rare, although such cases tend to have a poor prognosis.
**Objectives:** We conducted a prospective multicenter clinical trial to determine the efficacy, safety, and pharmacokinetics of infliximab (IFX) in BD patients with these serious complications who had displayed poor response or intolerance to conventional therapy (ClinicalTrials.gov, NCT01532570).
**Methods:** IFX at 5 mg/kg was administered to 18 patients (3 NBD [2 acute and 1 chronic progressive], 4 VBD, and 11 intestinal BD) at Weeks 0, 2, and 6 and every 8 weeks thereafter until Week 46. In patients who showed inadequate responses to IFX after Week 30, the dose was increased to 10 mg/kg. We then calculated the percentage of complete responders according to the predefined criteria depending on the symptoms and results of examinations (ileocolonoscopy, brain MRI, CT angiography, positron emission tomography, cerebrospinal fluid, CRP, or ESR), exploring the percentage of complete responders at Week 30 as the primary endpoint.
**Results:** The percentage of complete responders was 61% (11/18) at both Weeks 14 and 30 and remained the same until Week 54. By BD type, the percentage of complete responders at Week 30 was 33% (1/3) among NBD patients, 100% (4/4) among VBD patients, and 55% (6/11) among intestinal BD patients. In acute NBD patients, IFX lowered the cell count and IL-6 concentrations in the cerebrospinal fluid and inhibited the onset of attacks. In a chronic progressive NBD patient, IFX lowered cerebrospinal fluid IL-6 concentrations along with inhibition of progression of clinical symptoms and brainstem atrophy. VBD patients showed improvement in clinical symptoms at an early stage (Week 2) with reductions in serum CRP levels and ESR. Accordingly, positron emission tomography/CT imaging studies showed reversal of inflammatory changes in three of the four VBD patients. Intestinal BD patients also showed improvements in clinical symptoms along with decrease in serum CRP levels after Week 2. Consistently, scarring or healing of the principal intestinal ulcer in each patient was found in more than 80% of these patients after Week 14. Irrespective of the type of BD, all patients achieved improvements in visual analogue scale and Short Form 36 scores, leading to the dose reduction or complete withdrawal of steroids. IFX dose was increased to 10 mg/kg in three intestinal BD patients, resulting in improvement of clinical symptoms, CRP level, and visual analogue scale score. Safety and pharmacokinetics profiles were comparable to those in patients with rheumatoid arthritis or Crohn's disease.

Table: Proportion of complete responders

| | Complete responders | | | | | |
|---|---|---|---|---|---|---|
| | | NBD | | | | |
| | All three types | All NBD | Acute NBD | Chronic progressive NBD | VBD | Intestinal BD |
| Week 14 | 61% (11/18) | 33% (1/3) | 0% (0/2) | 100% (1/1) | 100% (4/4) | 55% (6/11) |
| Week 30 (Primary endpoint) | 61% (11/18) | 33% (1/3) | 0% (0/2) | 100% (1/1) | 100% (4/4) | 55% (6/11) |
| Week 54 | 69% (11/16) | 50% (1/2) | 0% (0/1) | 100% (1/1) | 100% (4/4) | 60% (6/10) |
| Final point of 5 mg/kg therapy | 67% (12/18) | 33% (1/3) | 0% (0/2) | 100% (1/1) | 100% (4/4) | 64% (7/11) |

NBD, neuro-Behçet's disease; VBD, vascular Behçet's disease; intestinal BD, intestinal Behçet's disease

**Conclusions:** The results demonstrate that IFX is effective and well tolerated in the treatment of recalcitrant NBD, VBD, and intestinal BD with poor response or intolerance to conventional therapy. IFX may therefore represent a promising new therapeutic option for use in BD patients with these serious complications.
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## THU0590 RISK FACTORS FOR CYTOMEGALOVIRUS REACTIVATION IN PATIENTS WITH CONNECTIVE-TISSUE DISEASES

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**Background:** Intensive immunosuppressive treatment for remission induction in connective tissue diseases (CTDs) sometimes causes serious infection. Cytomegalovirus (CMV) is a herpesvirus remaining latent after primary mild or asymptomatic infection, and the reactivation of CMV is one of the problematic opportunistic infections in immunocompromised patients. However, little is known

about risk factors for CMV reactivation, therefore, identifying patients at risk for CMV reactivation is of importance.
**Objectives:** To investigate risk factors relevant with CMV reactivation in patients with CTD during remission induction therapy.
**Methods:** All hospitalized patients with CTD who started immunosuppressive agents as induction therapy from 2012 until 2015 were retrospectively reviewed. Clinical information were collected from their medical charts. CMV reactivation was defined by the detection of CMV PP65 antigen in polymorphonuclear leukocytes from peripheral blood. Risk factors for CMV reactivation were statistically analyzed.
**Results:** A total of 170 CTD cases with CMV pp65 measured during the induction therapy were enrolled in the analysis. Mean age was 56.9±16.9 years old and the female ratio was 68.8%. The CTDs were 43 systemic lupus erythematosus (25.3%), 35 antineutrophil cytoplasmic antibody -associated vasculitis (20.6%), 21 polymyositis/dermatomyositis (12.4%), 20 rheumatoid arthritis (11.8%), 10 adult-onset Still's disease 10 (5.9%), and 41 others 41 (24.1%). 112 cases (65.9%) were new-onset. All cases were treated with moderate to high dose of glucocorticoid (mean prednisolone (PSL) dose, 50.1±10.8 mg/day). Methylprednisolone (mPSL) pulse therapy was conducted in 56 (33.9%), and concomitant immunosuppressants were used in 113 (68.5%).
CMV was reactivated in 64 (37.6%) including 16 CMV infection (bone marrow suppression 12, pericarditis 2, liver injury 1, retinitis 1). Multivariate logistic analysis identified initial PSL dose (p=0.003, OR 1.066) and lower baseline serum albumin level (p=0.023, OR 1.946) as an independent risk factor for CMV reactivation. Among 34 patients who were observed without antiviral treatment, 11 required ganciclovir during the course owing to the exacerbation of CMV disease. The lymphocyte count at 2 week after the initiation of immunosuppressive therapy in those 11 cases was significantly less than the 23 cases in whom CMV disappeared spontaneously (710±709/μl vs 1116±766/μl, p=0.016).
**Conclusions:** The study demonstrates the risk factors for CMV reactivation in CTD patients treated with intensive immunosuppressive therapy. The results lead us to improve the management of opportunistic infection in immunosuppressed patients with CTD.
**References:**
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**Disclosure of Interest:** None declared
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### THU0591 CLINICAL FEATURES OF ERYTHEMA NODOSUM IN SARCOIDOSIS

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**Background:** Erythema nodosum (EN) is a type of septal panniculitis with multiple underlying etiological trigger factors. Combination of EN with involvement of ankle joints, fever and intra-thoracic lymphatic nodes (ITLN) is known as the Lőfgren syndrome. This syndrome is associated with acute clinical course of sarcoidosis, which usually does not require a morphological confirmation.
**Objectives:** To analyze specific clinical features of EN in sarcoidosis patients.
**Methods:** 125 EN patients (M-21,F-104), aged 18 - 69 years associated with sarcoidosis were examined. All patients were subjected to standard diagnostic clinical examination and lab procedures, including chest computed tomography (CT).
**Results:** Mean age of patients was 42±12 years. Disease duration up to 1 month was documented in 35% patients, 1- 3 months – in 41%, >3 months – in 20%. Range of complaints included cough – in 24% patients, and fatigue – in 10%. Dyspnea, sweating, myalgia, and sore throat were found in 5% of patients each, respectively. Skin lesions typically occurred on the lower leg (96%), but also on the thighs (35%), the upper limbs (24%), and on the trunk (3%). Average number of nodules was 15±13. More than 10 nodules in number were documented in 64% of cases. Dense aggregation of nodules was found in 46% patients. The VAS score was 45±28 mm. Acute EN course was documented in 20% of cases, subacute - in 62%, and chronic – in 18% of patients. Distribution of joints involved looks as follows: ankles – 92%, shoulder – 11%, small joints in the hand and feet– 3%. CT findings included enlarged ITLN in 65% of cases, ground glass opacity (GGO) pulmonary lesions- in 35%. GGO pulmonary lesions predominated in male patients (30%), ($p$=0,004 R=0,25), demonstrating nodule-aggregation pattern in the majority of cases ($p$=0,0009 R=0,29). In patients with isolated ITLN involvement, cough ($p$=0,0048 R=0,25), and subacute course ($p$=0,016 R=0,22) were the special clinical features of the disease.
**Conclusions:** combination of ankle joints involvement, fever, and EN necessitates thoracic CT, as in 1/3 of such patients lungs would inevitably be involved. Male gender and EN aggregation pattern are most likely indicative of the emergence of GGO-symptom.
**Disclosure of Interest:** None declared
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## Epidemiology, health services and outcome research

### THU0593 VALIDITY OF THE BRISTOL RA FATIGUE MULTI-DIMENSIONAL QUESTIONNAIRE (BRAF-MDQ) AND RHEUMATOID ARTHRITIS IMPACT OF DISEASE (RAID) SCALE ACROSS 6 EUROPEAN COUNTRIES

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**Background:** The BRAF-MDQ[1,2] and RAID[3] are patient-reported outcome measures derived from the patient perspective. The 20 item BRAF-MDQ has 4 factors (physical, cognitive, emotional fatigue, living with fatigue) and the 7 item RAID is uni-dimensional. The BRAF-MDQ properties have not been tested outside the UK, nor the validity of the new Swedish RAID examined.
**Objectives:** To test the structure, construct and criterion validity of the BRAF-MDQ and the RAID in 6 EU countries.
**Methods:** Survey of RA clinic patients in clinics in France, Germany, Netherlands, Spain, Sweden and UK (F, G, N, Sp, Sw, UK), using BRAF-MDQ, RAID and SF-36. Factor structure examined by Confirmatory Factor Analysis and internal consistency by Cronbach's Alpha. Criterion validity for the BRAF-MDQ evaluated by internal Spearman's correlations, and for BRAF-MDQ and RAID fatigue item by correlation with each other and SF-36 Vitality subscale. Construct validity of BRAF-MDQ and RAID evaluated by Spearman's Correlation with each other, HAQ, and SF-36 domains. Analysis conducted overall and by individual country and for BRAF-MDQ by total and subscales.
**Results:** 1276 patients participated: F 206, G 216, N 317, Sp 157, Sw 170, UK 210. Disease duration <5 yrs for 25%, 76% female, median HAQ 1.0 (IQR 0.375–1.5). Mean total BRAF-MDQ was 26/70 (SD 26) with subscales physical fatigue 11.38/22 (SD 5.77), living with fatigue 6.46/21 (SD 5.4), cognitive 4.28/15 (SD 8.7) and emotional fatigue 3.41/12 (SD 3.22). Mean RAID was 4.15/10 (SD 2.31).
Confirmatory factor analysis: BRAF-MDQ original UK 4 factor structure was confirmed in each country, demonstrating one factor for each set of variables, with high factor loadings (0.71–0.96). Bootstrapping (4 sets of analyses on 20 random samples of 50% of patients/country), found the structure held true in at least 19/20 sets per country. RAID single factor structure was confirmed in all countries (0.75–0.95). Internal consistency ranged from 0.75–0.96 for the BRAF-MDQ (total and subscales) and the RAID ranged from 0.93–0.96 (overall and by country).
Criterion validity overall and by country: The BRAF-MDQ correlated internally and with the SF-36 Vitality and RAID fatigue items (0.6–0.93). Construct validity: BRAF-MDQ and RAID correlatied with each other, the HAQ, and remaining 8 SF36 domains (0.46–0.86).
**Conclusions:** The BRAF-MDQ and RAID demonstrate strong, consistent factor structure and internal consistency, with moderate-good criterion and construct validity across 6 EU countries, reflecting their robust methods of development. This indicates no specific country scoring is necessary, and strengthens the case for measuring both fatigue and impact in multi-country studies.
**References:**
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[3] Gossec et al, Ann Rheum Dis 2009;68:1680–5
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**Disclosure of Interest:** None declared
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### THU0594 TOWARDS DEVELOPMENT OF A MINIMUM CORE DATASET AND STANDARDS OF DATA COLLECTION FOR OBSERVATIONAL RHEUMATOID ARTHRITIS RESEARCH – A EULAR INITIATIVE

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**Background:** Collaborative research is compromised by heterogeneity of data collection in observational rheumatoid arthritis (RA) databases. Therefore a EULAR taskforce has been convened to develop a minimum core dataset (MCD) to 1) harmonize future data collection 2) act as a common data model existing databases can be mapped to 3) serve as a template for standardized data collection for RA research in clinical practice.
**Objectives:** To identify data items (i.e. "what to collect") and instruments (i.e. "how to collect") for inclusion in a MCD using an online survey.

**Abstract THU0594** – Table 1. Frequency of rating importance of items/instruments to include in a MCD from 1 (not important) to 9 (very important)

| ITEM | Rate 1–3 | Rate 7–9 | ITEM | Rate 1–3 | Rate 7–9 | ITEM | Rate 1–3 | Rate 7–9 |
|---|---|---|---|---|---|---|---|---|
| Diagnosis of RA | 0% | 100% | Quality of life | 3% | 95% | MSK ultrasound | 22% | 66% |
| Composite Score | 0% | 100% | selected comorbidities | 4% | 93% | BMI | 5% | 65% |
| Tender joint count | 0% | 100% | x-ray hand /feet | 4% | 92% | Occupational therapy | 21% | 64% |
| Swollen joint count | 0% | 100% | NSAIDs | 8% | 90% | Chest-xray | 26% | 63% |
| Patient global | 0% | 99% | Smoking | 0% | 89% | Treatment not related to RA | 22% | 63% |
| Physical function | 1% | 99% | Symptom duration | 7% | 86% | Physiotherapy | 21% | 63% |
| Acute phase reactants | 0% | 99% | Extra-articular manifestation | 6% | 86% | Psychological /Emotional therapy | 19% | 61% |
| Current DMARD | 0% | 99% | Work productivity | 4% | 82% | Physical exercise | 12% | 57% |
| Steroids | 0% | 99% | Joint surgery | 13% | 82% | Grip strength | 21% | 57% |
| Disease duration | 0% | 97% | Fatigue | 3% | 81% | Charlson comorbidity index | 18% | 54% |
| Evaluator global | 0% | 97% | Morning stiffness | 3% | 81% | Podiatry | 29% | 51% |
| Serology | 0% | 97% | Adverse events | 13% | 81% | MRI of joints | 28% | 49% |
| DMARD history | 1% | 97% | Family history | 14% | 79% | Alcohol intake | 7% | 47% |
| Gender | 2% | 96% | Ethnicity | 12% | 69% | Sexual life | 18% | 46% |
| Pain | 1% | 96% | Vaccination | 14% | 68% | Martial status | 41% | 31% |
| Age | 0% | 95% | Socio-economic status | 9% | 67% | Diet | 35% | 27% |

**Methods:** First we performed a hierarchical literature review to identify data items and instruments of existing RA cohorts/registers. Extracted data presented in a separate abstract were used to develop an online survey to gather information from an expert panel involving Presidents of National Societies and selected representatives from each European country, patients, rheumatologists, other health professionals, and researchers. Experts were asked to rate importance of 48 different items and their instruments for possible inclusion in a MCD on a scale from 1 (not important) to 9 (very important). For analyses ratings of 1–3 (NO inclusion) and of 7–9 (INCLUSION) were combined and percentages of responses calculated.
**Results:** 90 experts from 28 different European countries (patients 18%, health professionals 18%, physicians 55%, researchers 10%) participated in the survey. 27/48 items were regarded to be important for inclusion in a MCD by >80% of responders. Highest level of agreement to INCLUDE an item was found for: diagnosis of RA, composite scores, tender and swollen joint count (100%; table). Discrepancies of rating were observed for instruments: 24/126 instruments were rated as important for inclusion by >80% of responders.
**Conclusions:** Based on expert ratings the majority of items were considered appropriate for inclusion into a MCD, leading to an extensive template. For most instruments no consensus was achieved. Results of the survey were moved forward onto the next phase of the project.
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## THU0595 IMPACT OF PHYSICIAN-PATIENT INTERACTIONS ON DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Physician-patient interactions can influence both quality of care and patient self-management decisions, which in turn can impact patients' health outcomes.
**Objectives:** Examine the influence of physician-patient interactions on disease activity in a sample of SLE patients at high risk for poor outcomes.
**Methods:** The Georgians Organized Against Lupus (GOAL) is a predominantly African-American (AA) cohort largely drawn from a population-based registry of patients with SLE in Atlanta, GA, US. A subset of 125 GOAL participants from the most recent survey collection were provided two validated patient-reported multidimensional surveys to complete. The Interpersonal Processes of Care (IPC) was used to assess patient perceptions of their interactions with physicians within 3 domains: Communication, Shared Decision Making and Interpersonal Style. The Systemic Lupus Activity Questionnaire (SLAQ) was used to measure disease activity and SLAQ scores were adjusted for age, disease duration, sex, race, education, and insurance.
**Results:** 97 (78.2%) participants were AA, 19 (15.3%) Caucasian, and 8 (6.5%) of other races. The IPC survey results indicate that patient perceptions were associated with the extent of their SLE disease activity (see table below; p-values <0.05 are starred).
**Conclusions:** Higher IPC scores indicating hurried communication were associated with higher disease activity, while higher IPC scores indicating effective and compassionate patient-centered interactions were associated with lower disease activity. Our findings highlight the potential impact of physician-patient interaction on SLE outcomes as perceived by the patient.
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Linear trend association between disease activity (SLAQ score) and IPC domains

| IPC characteristic | SLAQ: 0–10 (N=34) | SLAQ: 11–16 (N=25) | SLAQ: >17 (N=66) |
|---|---|---|---|
| Communication | | | |
| Hurried communication (–)* | 1.55 (1.18–1.93) | 1.62 (1.18–2.06) | 2.04 (1.72–2.37) |
| Elicited concerns, responded (+)* | 4.43 (3.99–4.87) | 4.35 (3.84–4.86) | 3.99 (3.62–4.37) |
| Explained results, medications (+)* | 4.01 (3.52–4.51) | 3.98 (3.40–4.57) | 3.34 (2.91–3.77) |
| Shared decision making | | | |
| Patient-centered decision making (+) | 3.35 (2.67–4.02) | 3.47 (2.67–4.26) | 2.95 (2.37–3.53) |
| Interpersonal style | | | |
| Compassionate, respectful (+)* | 4.38 (3.92–4.85) | 4.36 (3.81–4.90) | 3.71 (3.31–4.10) |
| Discriminated (–) | 1.47 (1.15–1.78) | 1.41 (1.04–1.78) | 1.64 (1.36–1.91) |

## THU0596 PHYSICIAN'S GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS, REFLECTS SOLELY OBJECTIVE MEASURES AND DISREGARDS PATIENT REPORTED OUTCOMES

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**Background:** Physician's global assessment of disease activity (PhGA) has been shown to be a determinant factor for therapeutic decisions in Rheumatoid Arthritis (RA). The adequacy of this assessment is, therefore crucial, to assure that the best options are taken in the perspective of the patient's interest.
**Objectives:** To evaluate the determinants of PhGA, including clinical variables and patient reported outcomes.
**Methods:** Consecutive RA patients followed in a Tertiary Rheumatology Department were included in this cross-sectional study. Patient demographics and clinical assessments were collected through a standardized protocol which included age, gender, disease duration, DAS(28)4v-CRP (and its individual measures), DAS(28)4v, pain (VAS 0–100mm), Patient Global Assessment (PGA) of disease activity (VAS 0–100mm) and function (Health Assessment Questionnaire (HAQ)). From physicians were collected PhGA (VAS 0–100 mm), summary score of the patient's mobility and deformity (VAS 0–100mm).
To identify independent predictors of PhGA, Pearson's Correlation Coefficient was used to select variables ($p<0.05$) to subsequent inclusion in multivariable linear regression (stepwise model).
**Results:** 311 patients were included: 81.7% females, 60±12 years, 11±9 years of disease duration, 8±5 years of formal education and a mean DAS(28)4v-CRP=2.9±1.2. PhGA was statistically and strongly associated only with swollen joint count (SJC28) (r=0.71). Moderate correlations were observed with tender joint count (TJC28) (r=0.41), DAS(28)3v–CRP (r=0.655) and DAS(28)3v (r=0.550). Weak correlations ($r<0.4$) were observed with pain, PGA, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and HAQ, as well as with mobility and deformity in the physician's perspective. In multivariable analysis, SJC28 ($\beta$=5.02, 95%CI: 4.29;5.73, $p<0.001$) and CRP ($\beta$=3.0, 95%CI: 1.56;4.46,

Table 1. Multivariable linear regression (stepwise model) to explain PhGA in RA patients

| Variable | Adjusted R-Squared | p-value | β | p-value | 95% CI for β | |
|---|---|---|---|---|---|---|
| | | | | | Lower bound | Upper bound |
| SJC28 | 0.747 | <0.001 | 5.02 | <0.001 | 4.29 | 5.73 |
| CRP (mg/dl) | | | 3.0 | <0.001 | 1.56 | 4.46 |
| PhGA mobility | | | 0.085 | 0.04 | 0.027 | 0.14 |

p<0.001) were the most significant predictors of PhGA, with a small contribution of the physicians assessment of patient mobility.
**Conclusions:** Physicians consider objective measures when assessing disease activity, apparently disregarding pain and the PGA. This may lead to suboptimal management approaches from the patient's perspective, especially regarding disease dimensions that are not directly affected by immunosuppressive therapy.
**Disclosure of Interest:** None declared
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## THU0597 COMPARAISON OF SELF ASSESSMENT OF DISEASE ACTIVITY TO DAS28 IN RHEUMATOID ARTHRITIS: DATA FROM THE RANDOMIZED "ROC" TRIAL

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**Background:** In rheumatoid arthritis (RA), self assessment of disease activity by patients could be useful in clinical practice. Data in literature regarding the relevance of self-assessment remain limited. We therefore addressed this issue in the Rotation Or Change of biologics (ROC) trial.
**Objectives:** To compare self-assessment of disease activity by patients to assessment of disease activity by physicians in RA.
**Methods:** The ROC trial randomized patients with an insufficient response to a 1st anti-TNF to receive either a second anti-TNF or a non-TNF targeted biologic. At enrollment in the trial, a very brief oral information on self assessment of disease activity, along with a short written reminder, was provided to patients. Within 2 weeks of enrollment and at 6 months, patients received a phone call by a clinical research technician to collect the self-DAS28 (patient-derived DAS28). The clinical research technician was unaware of the arm of randomization and of the result of the DAS28. The concordance between self-DAS28 and DAS-28-ESR assessed by the physician was analyzed using the Bland and Altmann method.
**Results:** At enrollment, self-DAS28 was collected in 97 patients treated with a non TNF-targeted biologic and in 94 patients treated with a second anti-TNF. Mean (SD) self-DAS28 was 4.97 (1.46) and mean DAS28-ESR assessed by the physician was 5.06 (1.10). The systematic difference between self DAS-28 and DAS28 (statistically significant if the confidence interval does not include 0) was -0.11 [-0.29; 0.07]. Thus, self-DAS28 at enrollment sligthly but not significantly underestimated DAS28 assessed by the physician.
At 6 months, self-DAS28 was collected in 91 patients treated with a non TNF-targeted biologic and in 84 patients treated with a second anti-TNF. Mean (SD) self-DAS28 was 3.82 (1.56) and mean DAS28-ESR assessed by the physician was 3.53 (1.40). The systematic difference between self DAS-28 and DAS28 was 0.29 [0.09; 0.46]. Thus, self-DAS28 sligthly but not significantly overestimated DAS28 at 6 months.
**Conclusions:** Self-assessment of disease activity by patients, even without a long period of training, provides a correct appreciation of genuine disease activity in RA. Self-assessment of disease activity could be helpful for patients to have a better perception of disease activity between times of referrals to their rheumatologist, and might therefore contribute to optimize disease control in RA.
**Disclosure of Interest:** None declared
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## THU0598 VARIATIONS IN POLICIES AND SOCIAL SECURITY REGULATIONS FOR PATIENTS WITH RHEUMATOID ARTHRITIS THAT EXPERIENCE RESTRICTIONS IN WORK PARTICIPATION: RESULTS FROM A SURVEY ACROSS 44 COUNTRIES OF THE EUROPEAN REGION

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**Background:** Despite important influence of country of residence on labour force participation among patients with RA, no attempt has been made to understand the role of national policies and social security (SS) systems. We hypothesized that: 1) access to SS depends on the type of SS system; 2) wealthier countries offer more facilities to maintain work but also easier access to income compensation; 3) work retention and SS policies have an impact on sick leave (SL) and long-term work disability (WD).
**Objectives:** To explore regulations in SS including availability of work support facilities to maintain paid employment and income substitution in relation to SL and WD.
**Methods:** A survey was conducted among countries of the European WHO Region (n=50). One rheumatologist per country completed a questionnaire about regulations related to SS for RA patients, including efforts to support employment, criteria for eligibility as well as level and duration of income compensation. To investigate whether the regulations differed by the type of SS system (Anglo-Saxon, Bismarckian, Mediterranean, Post-Communist, and Scandinavian), country's wealth (Gross Domestic Product (GDP)) or national disability/employment rates, correlations or subgroup comparisons were done with t-test/Mann-Whitney and chi-square/Fisher's test, as appropriate.
**Results:** Forty-four (28 EU and 16 non-EU member states) countries (88%) provided data. While all countries had arrangements to support patients with restrictions to work, large heterogeneity was observed in all specific regulations (Table). Twenty-nine (66%) and 26 (59%) countries had a requirement for employment history or social insurance contributions to be eligible for SL or WD compensation, respectively. Maximum SL length before transition to WD varied from 3 to 36 months (mean (SD) 13 (9)). Compensation for SL and WD varied from 25 to 100% and 18% to 100% of previous income, respectively. Although the majority of countries had facilities to support patients with RA in paid employment (n=33, 75%), only in a quarter of countries rehabilitation efforts were obligatory to qualify for WD. No relationship was found between any of these regulations and the type of SS system, GDP or rates of disability and employment.
The table shows the regulations related to sick leave in 44 countries of the European region.

| Regulation | N (%) |
|---|---|
| Rheumatologist authorized to certify sick leave | 33 (75%) |
| Minimal income compensation for sick leave, <70% | 15 (34%) |
| First 1-3 days of sick leave unpaid | 11 (25%) |
| Obligatory rehabilitation before work disability assessment | 11 (25%) |
| Minimum duration SL before work disability assessment | 22 (50%) |
| Factors accounted for in work disability assessment: | |
| Profession | 25 (57%) |
| Diagnosis | 31 (70%) |
| Physical disability | 33 (75%) |
| Physical ability | 18 (41%) |
| Earning capacity | 12 (27%) |
| Age and/or Sex | 19 (43%) |
| Income compensation | |
| In case of moderate (50%) work disability, <70% | 23 (74%) |
| In case of severe (75%) work disability, <70% | 16 (52%) |

**Conclusions:** Three quarters of countries had facilities to support employment while all countries had income compensation schemes. Large heterogeneity was observed in most regulations including income compensation. Differences in SL and WD in RA patients seem not to be explained by differences in work retention facilities nor social by security system. Inequalities in support and income compensation call for a platform to harmonize policies for patients with RA who experience restrictions in work participation.
**Disclosure of Interest:** None declared
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## THU0599 KEY DRIVERS IN BIOSIMILAR PRESCRIPTION IN INFLAMMATORY AUTOIMMUNE DISEASES INDICATIONS IN GERMANY

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**Background:** There is currently limited evidence relating to, and thus understanding of, physician views on prescribing biosimilars in the real world.
**Objectives:** Our aim is to address this lack of understanding, specifically by describing rheumatologists' motivations to prescribe, and perceptions of, biosimilars for Rheumatoid Arthritis (RA), Axial Spondyloarthritis (AxSpA) and Psoriatic Arthritis (PsA).
**Methods:** The Adelphi Biosimilars Therapy Insight Programme uses a well-established methodology, similar to that used in over 100 separate projects, and contains real-world, cross-sectional survey data from 50 German rheumatologists who currently prescribe biosimilars, collected in Q4 2015 - Q1 2016 in RA, AxSpA and PsA. Rheumatologists report their use of current therapies, therapy preferences, as well as experiences with prescribing biosimilars, including their reasons for prescribing them.
**Results:** Rheumatologists reported that in the absence of restrictions or guidelines for 1st and 2nd line biologics their preference would be to prescribe bio-originator; only 8%, 18% and 20% stated a biosimilar would be their preferred 3rd line option for Ra, AxSpA and PsA respectively. However, despite these data on rheumatologist preference it was shown that when biosimilars were prescribed, it was in place of a 1st and 2nd line biologic in 88% and 69% of cases respectively. Key reasons for biosimilars prescribing were non-clinical with 77% of rheumatologists indicating cost related issues and 73% reported a desire to gain experience with biosimilars. Only 60% stated they prescribed biosimilars because they were convinced of equivalent efficacy with bio-originators. Respondents indicated that with increased discounts they would be more likely to prescribe biosimilars in stable patients. However, in patients where the bio-originator has failed, 18%

of rheumatologists would be motivated to prescribe the biosimilar if it was 10% cheaper than bio-originator. Rheumatologists (86%) said that they would consider using a biosimilar once they had decided to prescribe that therapy, but the availability of a biosimilar was unlikely to affect the choice of therapy prescribed.
**Conclusions:** The results clearly indicate that the main drivers for biosimilar use are cost and desire for experience. It is possible that the desire to gain experience in prescribing biosimilars is a consequence of physicians anticipating payer pressure to prescribe biosimilars in future, even in well controlled bio-originator patients. Physician preference is to prescribe bio-originators but cost savings are leading to their use, mainly in place of the bio-originator of the same therapy. We observed that the majority of rheumatologists are not convinced of the interchangeability of biosimilars as they preferred not to switch (and were unlikely to switch) well managed patients from bio-originators to biosimilars. Given the economic pressures towards prescribing biosimilars, it is critical that the impact of non-clinical switches be fully understood to ensure patients are not put at undue risk for economic reasons. Given that German physicians are responsible for drug prescribing budgets these data may help provide insights into modeling in other markets where clinicians have to work with other budget holders to decide on appropriate use of drugs.
**Disclosure of Interest:** E. Sullivan Employee of: Adelphi Real World, J. Piercy Employee of: Adelphi Real World, J. Waller Employee of: Adelphi Real World, C. Black Shareholder of: Merck, Employee of: Merck, S. Kachroo Shareholder of: Merck, Employee of: Merck
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## THU0600 PATIENTS' PERCEPTION AND SATISFACTION OF WAITING TIME AT MEDICAL OUTPATIENTS

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**Background:** Patient satisfaction is an important determinant of health care quality. Decreasing waiting time is imperative in achieving patient satisfaction.
**Objectives:** The aim of this study was to determine the mean waiting time at medical outpatients and to assess waiting time satisfaction. A further aim was to identify factors that affect the patients' perceived waiting time.
**Methods:** Data was collected through questionnaire responses from 190 patients attending medical outpatients between 20th March and 9th April 2013. This included demographic data, waiting time and service satisfaction, expected and perceived waiting time, level of boredom and comfort while waiting. Moreover the actual waiting time was noted by the observer. The relationship between expected and perceived waiting time; and between actual and perceived waiting time were in turn analyzed using scatter plots and correlation coefficients. Approval to carry out this study was obtained from the University Research and Ethics Committee.
**Results:** The participants had a mean age of 53 (range 19 to 86), of which 59% were females. On a 10-point Likert scale, the mean waiting time satisfaction was 7.1, while the mean service satisfaction was 9.3. The mean expected waiting time was 65 minutes and the mean perceived waiting time was 55 minutes. The mean actual waiting time was 51 minutes.This study revealed that as perceived waiting time increased, patient satisfaction tended to decrease consistently and significantly ($p<0.001$). On the other hand, regression analysis revealed that perceived waiting time has a positive and significant linear relationship with the actual waiting time ($p<0.001$) and the boredom levels of patients ($p<0.001$). Patients seated comfortably had a significantly lower perceived waiting time that those who were not ($p<0.001$). Perceived waiting time was not influenced by whether the patient was accompanied ($p=0.313$) or being seen for the first time ($p=0.712$). The patients reported that the provision of free tea or coffee, magazines or television, could help reduce boredom and divert their attention, thus reducing perceived waiting time and in turn enhancing satisfaction. 11% (21 patients) suggested that the operation of free wireless internet in the waiting areas would also reduce the level of their boredom during their wait.
**Conclusions:** Overall service satisfaction was extremely positive, while waiting time satisfaction was moderate. Although reducing the actual waiting time may be difficult, altering patients' perceived waiting time may be beneficial to increase their satisfaction. This could be done by increasing their comfort and decreasing their boredom while waiting.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1912

## THU0601 WORK PARTICIPATION AFTER TWO YEARS IS EXCELLENT IN EARLY RA PATIENTS TREATED ACCORDING TO A TIGHT CONTROL STRATEGY, AND IMPROVED COMPARED TO PREVIOUS CLINICAL PRACTICE

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**Background:** Rheumatoid arthritis (RA) is a known cause of work productivity loss. Participation in work-related activities is defined as part of the primary goal of RA treatment in the 2015 treat to target recommendations (1).
**Objectives:** The objectives of the current study were to assess changes between baseline and 24 months in work participation in early RA treated according to a tight control treat to target strategy, and to compare sick leave rates to a cohort of early RA patients followed without treat to target.
**Methods:** We used data from two studies: the ARCTIC study (inclusion Oct 2010 – April 2013, RA patients fulfilling the 2010 ACR/EULAR classification criteria, symptom duration<2 years, DMARD-naïve with indication for DMARD) and the NOR-VEAC study (inclusion Oct 2004 – Aug 2010, patients included in the analyses fulfilled 2010 criteria for RA, had symptom duration <16 weeks and were DMARD-naïve). Data collection included patient reported outcomes with identical questions on work participation in both studies, clinical examination and laboratory assessment. In addition, the Work Productivity and Activity Impairment Questionnaire (WPAI) was recorded in ARCTIC. Absenteeism (work time missed) and presenteeism (impairment while at work) were calculated in ARCTIC at baseline and study completion, 24 months. We compared the proportion of patients reporting sick leave (among patients not reporting retirement or disability pension) across studies at baseline, 8 and 16 months, the time points with most data available in both cohorts, by chi-square test.
**Results:** The mean (SD) age for the 229 patients in ARCTIC was 51.4 (13.7) years, disease duration 7.1 (5.4) months, DAS28 4.4 (1.2), 61.1% were female and 86.2% seropositive. The 259 NOR-VEAC patients had shorter mean (SD) disease duration (2.0 (1.0) months, p-value <0.001), higher DAS28 (5.3 (1.3), p-value<0.001) and lower seropositivity rate (74.0, p-value <0.001). NOR-VEAC patients had comparable age (52.7 (14.1) years) and gender distribution (63.9% females) to ARCTIC. In ARCTIC, levels of presenteeism and absenteeism at 2 years were overall very low, with substantial improvement from baseline (figure). While 30.9% of employed patients reported 100% absenteeism at baseline, the corresponding number at 24 months was 3.7%. When comparing the cohorts after 16 months 14.5% of patients in ARCTIC and 26.1% of patients in NOR-VEAC reported sick leave (p-value 0.01). No difference in sick-leave was found between ARCTIC and NOR-VEAC at baseline (34% vs. 40%, p-value 0.24) but a trend was observed at 8 months (19.0 vs. 28.4%, p-value 0.06).

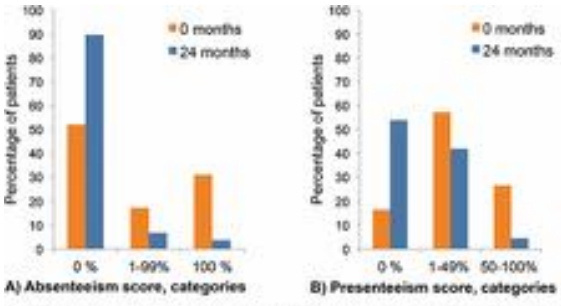



**Figure:** Absenteeism and presenteeism in ARCTIC patients at baseline and after 24 months. **A)** Absenteeism, results in employed patients. **B)** Presenteeism, results in patients with work attendance.

**Conclusions:** Patients with early RA participating in a tight control treat-to-target study reported very little work productivity loss after two years. After treatment, sick-leave rates with treat to target were significantly lower than in a previous cohort of early RA patients followed without implementation of such principles. The results support that patient care based on modern treatment strategies improves participation in work-related activities, a defined goal for RA treatment.
**References:**
[1] Smolen et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. ARD 2015
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3485

## THU0602 PATIENT GLOBAL ASSESSMENT IN RHEUMATOID ARTHRITIS CONVEYS A VARIABLE BLEND OF DISEASE ACTIVITY AND DISEASE IMPACT: A CROSS-SECTIONAL STUDY WITH 311 PATIENTS

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**Background:** Patient global assessment (PGA) is a key outcome measure in rheumatoid arthritis (RA) and the sole patient-reported outcome included in measures currently used to guide treat-to-target (T2T) strategies. However, it is still not clear which concepts it conveys and how appropriate they are to guide therapy.
**Objectives:** to explore the meaning of PGA in RA patients, namely the influence of disease activity, disease impact, comorbidities, and psychological aspects.
**Methods:** This was an observational, cross-sectional study including consecutive RA patients (ACR/EULAR 2010 or ACR 1987 criteria) followed in a tertiary rheumatology outpatient department. Data collection included PGA (100mm VAS), pain and fatigue (0–10 NRS), Health Assessment Questionnaire (HAQ),

Functional Assessment of Chronic Illness Therapy (FACIT), Hospital Anxiety and Depression Scale (HADS), Happiness Subjective Scale (HSS), and Ten Item Personality Inventory (TIPI). Demographic data, comorbidities, and disease activity [tender joint (TJC28) and swollen joint counts (SJC28), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)] were also collected. Disease activity categories were defined as: 1) remission (ACR/EULAR 2011 boolean-based definition), 2) near-remission (only PGA>1), and 3) non-remission. Univariate (Pearson correlation, student's *t* test and One Way ANOVA) and multivariable analysis (linear regression, with stepwise methods and assessment of multicolinearity) were performed to explain PGA.

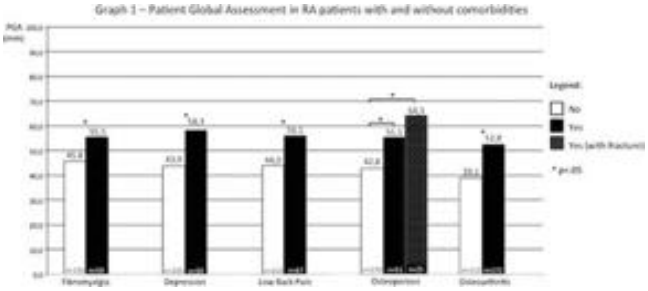
**Results:** 311 patients were included (82% females, 60±12 years, 11±9 years of disease duration, 8±5 years of formal education and a mean DAS(28)CRP4v = 2.9±1.2). All comorbidities assessed were associated with statistically ($p<0.05$) higher PGA than RA alone (Graph 1).

PGA was statistically correlated with all predictor variables, except for the personality domain "agreeableness". In multivariable analysis, PGA was explained ($R^2_{adj.}=0.58$) by pain ($\beta=0.33$), fatigue ($\beta=0.23$), function ($\beta=0.21$), anxiety ($\beta=0.13$), and SJC28 ($\beta=0.09$). The predictors of PGA were different between disease activity categories (Table 1).

Table 1. Multivariable linear regression models (stepwise-backward method) to explain PGA in RA patients

| Variable | Patients (β adjusted*) | | | |
|---|---|---|---|---|
| | All (n=281) | Remission (n=120) | Near-misses (n=19) | Non-remission (n=152) |
| Pain | 0.33 | 0.35 | | 0.28 |
| Fatigue | 0.23 | 0.44 | 0.72 | |
| HAQ | 0.21 | | | 0.30 |
| HADS-Anxiety | 0.13 | | | 0.19 |
| SJC28 | 0.09 | | | 0.12 |
| TJC28 | | 0.20 | 0.45 | |
| CRP | | | –0.31 | |
| $R^2$ adj. | 0.58 | 0.57 | 0.78 | 0.55 |

*All with $p<0.05$.




**Conclusions:** PGA does not only convey the inflammatory activity of the disease but also pain (of whatever musculoskeletal origin), fatigue, functional capacity, and psychological variables. These predictors present different relative impacts in different disease activity categories. In near-misses, the group where PGA is decisive for T2T, PGA is determined by fatigue, TJC28 and negatively associated with CRP.

Including PGA in composite indices drifts these measures away from strict disease activity representation. This may negatively affect the adequacy of target-driven decisions regarding immunosuppressive therapy, inherently designed to control inflammation.

**Disclosure of Interest:** None declared

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## THU0603 PERFORMANCE OF THE 2013 AMERICAN COLLEGE OF RHEUMATOLOGY/EUROPEAN LEAGUE AGAINST RHEUMATISM SYSTEMIC SCLEROSIS CLASSIFICATION CRITERIA

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**Background:** Systemic sclerosis (ScS) is a polymorphic autoimmune disease, with increased morbidity and mortality, often diagnosed in advanced stages. The recently published 2013 American College Of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for SSc were developed to increase the identification of early/mild SSc patients.

**Objectives:** To compare the sensitivity and specificity of the 2013 ACR/EULAR criteria with 1980 ACR criteria in a single-centre cohort of patients with SSc, diagnosed according to expert oppinion.

**Methods:** Data of SSc patients evaluated in our EUSTAR centre between 2004–2015 have been retrospectively analyzed. The control cohort included patients with Raynaud's phenomenon of other ethiology than SSc, evaluated between 2009–2015. The sensitivity and specificity of the 2013 ACR/EULAR and 1980 ACR criteria were tested using the McNemar test for correlated proportions.

**Results:** One hundred and fifty one patients with SSc (90.1% women, mean±SD age 58.4±13.2 years) and 65 controls (87.7% women, mean±SD age 43.7±14.6 years) were included. The sensitivity of the 2013 ACR/EULAR and 1980 ACR criteria were 94.7% and 84.4%, respectively ($p<0.001$). The specificity of the 2013 ACR/EULAR and 1980 ACR criteria were 86.2% and 96.9%, respectively ($p=0.01$). Patients missclassified according to the new 2013 ACR/EULAR criteria were 17, whereas according to the old 1980 ACR criteria were 32. The sensitivity of the 2013ACR/EULAR was significantly better than the 1980 ACR criteria in the limited cutaneous SSc patients (93.1 vs. 82.2%, $p<0.001$).

**Conclusions:** The 2013 ACR/EULAR criteria have a better sensitivity and missclassify fewer patients than the 1980 ACR criteria. Their excelent performance is close to the gold standard of diagnosis in SSc (expert opinion).

**Acknowledgement:** *This abstract was realized as part of the "Development of a computer-based nailfold videocapillaroscopy (NVC) system for longitudinal evaluation of patients with systemic sclerosis" (QUANTICAP) project, financed by the UEFIS-CDI PN-II-PT-PCCA-2013–4-1589 grant.

**Disclosure of Interest:** None declared

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## THU0604 DISEASE ACTIVITY AND BIOLOGIC USE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS IN THE PAST 10 YEARS: RESULTS FROM THE CORRONA REGISTRY

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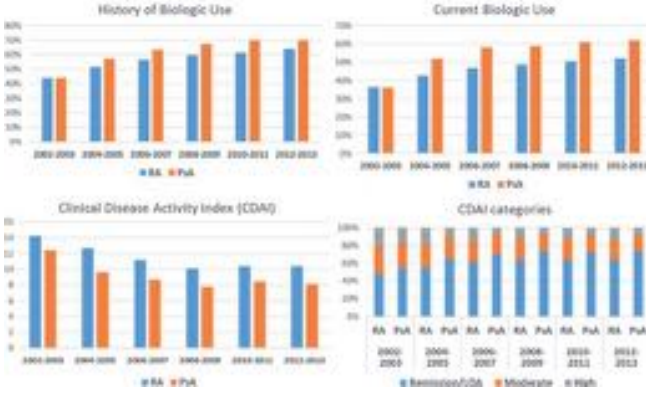
**Background:** While some treatment options for psoriatic arthritis (PsA) are similar to those initially developed for rheumatoid arthritis (RA), their introduction to the clinic has generally increased in the recent years. Also, there has been a perception among some that RA is perhaps associated with greater disease burden compared to PsA.

**Objectives:** The objective of this study was to determine and compare the disease activity related to peripheral arthritis and biologic use in patients with RA and PsA over the past 10 years in Corrona registry.

**Methods:** All patients between 01/2002 – 03/2013 were included and patients were grouped in 2 year intervals 2002–2003, 2004–2005, 2006–2007, 2008–2009, 2010–2011, 2012–2013. Within each time period, standardized differences were used to identify patient characteristics that were different between PsA and RA patients. Logistic regression models evaluated the likelihood of being in moderate/high clinical disease activity index (CDAI) and use of biologics in PsA patients compared to patients with RA, adjusting for covariates within each time period. Random effects logistic regression models were also considered to account for site random effects.

**Results:** A total of 20982 and 2552 RA and PsA patients respectively were studied over the six time intervals. The mean age was 59 yrs and 53 yrs for RA and PsA patients respectively. Mean CDAI and percentage of patients in moderate/severe disease activity were significantly higher in RA and PsA over the years; disease activity generally decreased over time for both (Figure). History of biologic use was similar between the two groups in 2002–03 (44% in RA vs 42.5% in PsA), however there was an upward trend in biologic use in both groups with higher use among PsA patients over the past years (figure). Similarly current biologic use also increased from 36.3% vs 36.1% in RA vs PsA in 2002–03 to 52.1% vs 62% in 2012–2013 respectively. Adjusted models showed that PsA patients were significantly less likely to be in moderate/severe disease activity defined by CDAI (OR (95% CI): 0.79 (0.72, 0.88)) over the past years and more

**Figure 1: Disease activity and biologic use in RA and PsA patients at different time intervals**



likely to be on a biologic compared to RA patients in 2012–13 (Odds ratio (95% CI): 1.37 (1.25, 1.49)).
**Conclusions:** Although disease activity has generally decreased while biologic therapy use has increased over recent years, there continues to be a significant proportion of PsA and RA patients with moderate/severe disease. Joint burden among PsA patients is slightly lower in comparison to RA, although biologic use was higher in the PsA population. Future research should evaluate the correlation in disease activity and biologic use over time.
**Acknowledgement:** This study is sponsored by Corrona, LLC. The Corrona, LLC. RA registry has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, Astra Zeneca, BMS, Crescendo, Genentech, Horizon Pharma USA, Janssen, Eli Lilly, Novartis, Pfizer, and UCB. The design, study conduct, and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.
**Disclosure of Interest:** A. Kavanaugh Grant/research support from: Amgen Abbvie Jannsen Pfizer Novartis, J. Griffith Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., C. Karki Employee of: Corrona, LLC, C. Etzel Consultant for: Merk, Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie, Amgen, BMS, Genentech, GSK, Lilly, Medimmune, Pfizer, Sanofi, Employee of: Corrona, LLC, Speakers bureau: Genentech (for non-branded talk only), J. Greenberg Shareholder of: Corrona, LLC, Consultant for: AstraZeneca, Celgene, Genentech, Janssen, Novartis and Pfizer, Employee of: Corrona, LLC, A. Ganguli Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc.
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## THU0605 OMEGA-3 FATTY ACIDS ASSOCIATES WITH DECREASED PAIN, INDEPENDENT OF INFLAMMATION, IN MTX TREATED EARLY RA PATIENTS

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**Background:** Dietary intake of omega-3 fatty acids (FA) may play a role in etiology of RA [1] and has also been shown to be anti-inflammatory in RA [2]. Increased intake of omega-6 FA as well as omega-6:3 FA ratio are associated with inflammation in RA [3]. However, little is known about how omega-3 FA may affect pain in RA.
**Objectives:** To study the association between omega-3, omega-6, omega-6:3 FA ratio and pain, despite inflammatory control, after three months of MTX treatment in early RA patients.
**Methods:** We included newly diagnosed RA patients with MTX monotherapy from Epidemiological Investigation of Rheumatoid Arthritis (EIRA) study linked to clinical data from Swedish Rheumatology Quality register (SRQ). Data on omega-3, omega-6, and omega-6:3 FA ratio (dietary questionnaires) were linked with data on self-assessed pain after three months of MTX treatment. Pain despite inflammatory control (Remaining Pain) was defined based on the Patient Acceptance Symptom Scale (PASS)[4] together with low systemic inflammation (VAS pain >40mm and CRP<10mg/L). Statistical analysis: logistic regression adjusted for age, sex, smoking, education, BMI, energy intake and omega-3 FA supplementation.
**Results:** We included 591 patients (median age: 55 years; females: 70.6%; ACPA+: 67.9%). Mean values for clinical measures at baseline were: DAS28 5.2±1.3, VAS pain 53.9±24.7 and HAQ 1.1±0.6. Mean BMI was 25.8±4.7 kg/m$^2$. Omega-3 FA supplements were used by 19.5% of the patients. After three months, 92 patients (15.6%) had Remaining Pain. These patients had lower intake of omega-3 FA compared to those without Remaining Pain (0.6±0.4 vs. 0.7±0.3 g/day, p=0.004). Omega-3 FA intake was inversely associated with Remaining Pain (OR=0.5 [95% CI 0.3–0.9]), after adjustment. Omega-6:3 FA ratio but not omega-6 FA alone was directly associated with remaining pain (OR=2.3 [95% CI 1.3–4.2]). Similar ORs were found after adjustment for ACPA and physical activity. Omega-3 FA was not associated with CRP or EULAR response at the follow-up.
**Conclusions:** Omega-3 FA was inversely associated with Remaining Pain and omega-6:3 FA ratio was directly associated with Remaining Pain. These associations were independent of inflammation. Our data suggest that dietary omega-3 FA may dampen the development of chronic pain in early RA.
**References:**
[1] Di Giuseppe, D., et al., Long-term intake of dietary long-chain n-3 polyunsaturated fatty acids and risk of rheumatoid arthritis: a prospective cohort study of women. Ann Rheum Dis, 2014. 73(11): p. 1949–53.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1598

## THU0606 INCIDENCE AND PREVALENCE OF CARDIOVASCULAR RISK FACTORS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIASIS, OR PSORIATIC ARTHRITIS

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**Background:** Studies have suggested that the chronic inflammatory nature of rheumatic conditions (rheumatoid arthritis (RA) and psoriatic arthritis (PsA)) as well as psoriasis (PsO) may predispose patients to cardiovascular (CV) disease and metabolic disorders. However, the individual impact of RA, PsA, and PsO on traditional CV risk factors is not well understood.
**Objectives:** We estimated the incidence and prevalence of traditional CV risk factors - hypertension, diabetes mellitus (DM), hyperlipidemia, and obesity - among three separate cohorts of patients with RA, PsA, or PsO.
**Methods:** Patients with RA, PsA, and PsO between January 1, 2002 and June 30, 2014 were identified (and included in three separate cohorts) in the Truven Health MarketScan Commercial and Medicare Supplemental databases. Index date was defined as the date of RA, PsA or PsO diagnosis. Patients were required to be continuously enrolled for 12 months prior to the index date. Follow-up time for the identification of the CV risk factors began on the day after index date and continued until disenrollment from MarketScan, or the end of the study. The primary outcome was the first occurrence of the CV risk factors during the follow-up period. Incidence rates (IR) per 1,000 patient-years (PY) with 95% confidence intervals (CI) were calculated. The prevalence (number of cases/total population) of CV risk factors prior to the index date was also calculated.
**Results:** We identified 266,167 patients with RA, 35,050 with PsA, and 301,593 with PsO. Mean age at index date was similar for both PsO and PsA patients (51 yrs), but RA patients were older (58 yrs). Mean follow-up time ranged from 2.3 years to 2.5 years. Prevalence of the CV risk factors ranged as follows: hypertension 24.7% in PsO to 34.6% in RA; DM 8.2% in PsO to 10.4% in RA; Hyperlipidemia 16.5% in PsO to 18.2% in RA; and Obesity 5.1% in PsO to 6.7% in PsA. The pattern of CV risk factors development after RA, PsA, and PsO diagnosis was similar as prior to diagnosis. The RA cohort demonstrated the highest incidence of hypertension and hyperlipidemia whereas PsA cohort demonstrated the highest incidence of DM and obesity. All risk factors were lowest in the PsO cohort (Table 1).

Table 1. Incidence rate (per 1,000 person-years) of CV risk Factors among RA, PsA, and PsO patients

| CV risk factors | Events | Person-years | IR [95% CI] | IR ratio |
|---|---|---|---|---|
| Hypertension | | | | |
| RA | 39,887 | 340,946 | 117.0 [115.8, 118.1] | 1.52 |
| PsA | 4,432 | 48,167 | 92.0 [89.3, 94.8] | 1.20 |
| PsO | 35,447 | 461,152 | 76.9 [76.1, 77.7] | Ref |
| Diabetes mellitus | | | | |
| RA | 9,768 | 585,435 | 16.7 [16.4, 17.0] | 1.08 |
| PsA | 1,312 | 70,031 | 18.7 [17.7, 19.8] | 1.22 |
| PsO | 10,052 | 652,719 | 15.4 [15.1, 15.7] | Ref |
| Hyperlipidemia | | | | |
| RA | 33,543 | 476,658 | 70.4 [69.6, 71.1] | 1.13 |
| PsA | 4,025 | 58,231 | 69.1 [67.0, 71.3] | 1.11 |
| PsO | 33,023 | 532,193 | 62.1 [61.4, 62.7] | Ref |
| Obesity | | | | |
| RA | 18,522 | 619,621 | 29.9 [29.5, 30.3] | 1.03 |
| PsA | 2,602 | 73,138 | 35.6 [34.2, 37.0] | 1.23 |
| PsO | 19,665 | 678,401 | 29.0 [28.6, 29.4] | Ref |

**Conclusions:** The incidence rates of hypertension, hyperlipidemia, DM, and obesity are higher among patients with RA and PsA compared to patients with PsO. Differences in levels of systemic inflammation may underpin differences in rates of risk factors. Different treatment strategies may be useful in preventing these comorbidities. The results highlight the importance of close monitoring and managing CV risk factors in patients with RA, PsA and PsO.
**Disclosure of Interest:** D. Solomon Consultant for: Amgen Inc and received a research contract to assist with these analyses, T. Lesperance Employee of: Amgen Inc, H. Radner Consultant for: Amgen Inc and received a research contract to assist with these analyses, N. Accortt Employee of: Amgen Inc
**DOI:** 10.1136/annrheumdis-2016-eular.2094

## THU0607 EFFECTIVENESS AND PERSISTENCE OF GOLIMUMAB ACROSS RHEUMATIC DISEASE INDICATIONS IN CLINICAL PRACTICE: RESULTS FROM THE NATIONAL SWEDISH REGISTER

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**Background:** Real life evidence regarding the effectiveness and discontinuation of golimumab across indications is limited.

**Abstract THU0607** – Table 1. Baseline characteristics of the golimumab treated population, stratified by indication. Reported numbers are median and interquartile range in parenthesis

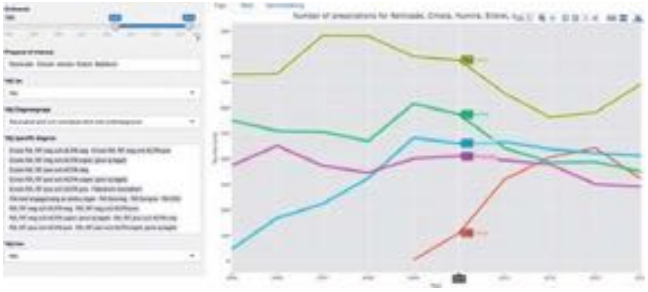
| | All (n=2984) | RA (n=1366) | PsA (n=655) | AS (n=499) | SpA (n=464) |
|---|---|---|---|---|---|
| Symptom duration (years) | 6 (1–15) | 3 (1–13) | 6 (2–14) | 12 (5–23) | 7 (2–13) |
| Concurrent therapy | | | | | |
| NSAID | 989 (38.98%) | 441 (36.78%) | 182 (45.16%) | 209 (37.06%) | 157 (42.32%) |
| MTX | 1252 (49.35%) | 793 (66.14%) | 71 (17.62%) | 271 (48.05%) | 117 (31.54%) |
| Non-MTX DMARD | 310 (12.22%) | 184 (15.35%) | 21 (5.21%) | 64 (11.35%) | 41 (11.05%) |
| Percentage bionaïve | 47% | 48% | 47% | 46% | 48% |
| Among patients switching from previous biological therapy: | | | | | |
| Time from start of first biologic (months) | 41 (15–80) | 48 (16–93) | 35 (14–69) | 42 (19–72) | 30 (13–67) |
| Number of biologics before golimumab | 1 (1–2) | 1 (1–2) | 2 (1–2) | 1 (1–2) | 2 (1–2) |
| Difference between start of treatment and the 6 months visits: | | | | | |
| ΔDAS28 | | −1.41 (−2.33; −0.48) | −1.38 (−2.41; −0.53) | NA | NA |
| ΔHAQ | | −0.13 (−0.50; 0) | −0.13 (−0.50; −0) | NA | NA |
| ΔTJC | | −3 (−6; −1) | −3 (−6; 0) | NA | NA |
| ΔSJC | | −3 (−6; 0) | −1 (−4; 0) | NA | NA |
| ΔPatient global assessment (VAS) | | −16 (−39; 0) | −20 (−40; 2) | −22 (−43; −3) | −23 (−47; −8) |
| ΔPain in general (VAS) | | −18 (−37; 0) | −18 (−40; 3) | −28 (−48; −2) | −26 (−49; −7) |
| ΔEQ-5D | | 0.04 (0; 0.26) | 0.07 (0; 0.23) | 0.09 (0; 0.38) | 0.17 (0; 0.5) |
| ΔCRP | | −2 (−10; 0) | −1.40 (−8.60; 0) | −6 (−14.1; 0) | −1.40 (−10.40; 0) |
| ΔSR | | −4 (−12; 1) | −3 (−13; 0) | −7 (−19; −1) | −4 (−15; 0) |

**Objectives:** To describe the effectiveness and persistence of golimumab in a real-life setting, in rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), and other spondyloarthropathies (SpA), in relation to disease activity at treatment initiation.
**Methods:** The national Swedish Rheumatology Quality Register (SRQ) was used to identify patients starting treatment with golimumab between 2009 and 2014. Effectiveness was assessed using the difference between start of treatment and at the 6 months visits (defined as 110–240 days from start of treatment) of different measures of disease activity. Persistence was evaluated using Kaplan Meier curves and Cox proportional hazard model.
**Results:** A total of 2984 patients (1366 RA (69% were RF positive), 655 PsA, 499 AS and 464 SpA) started treatment with golimumab. The percentage of bionaïve patients was similar across indications (from 46% in AS to 48% in RA). There was positive response at 6 months across all indications, according to DAS28, HAQ, tender and swollen joint counts (TJC and SJC), patient global health, pain, EQ-5D, CRP and SR (Table 1). Proportion of persistence was highest in AS (69% at 1 year, 56% at 2, and 50% at 3), and was lowest in PsA (60%, 49%, and 42%). Across all indications, the hazard ratio of discontinuation was higher among women, lower among bionaïve compared to non-bionaïve patients, and 34% higher among RA patients >65 years old compared to RA patients 56–65 years old. There was no association between age and discontinuation among patients with other indications, and between DAS28 and HAQ and discontinuation in RA and SpA.
**Conclusions:** In this real-life national cohort, patients on golimumab experienced clinical improvement. Persistence is dependent on contextual factors rather than disease activity at start, and is better in AS than in RA.
**Disclosure of Interest:** None declared
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## THU0608 VISUALIZATION AND ANALYSIS PLATFORM IN THE SWEDISH RHEUMATOLOGY REGISTER FOR REAL-TIME DATA FEEDBACK

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**Background:** The Swedish Rheumatology Quality register (SRQ) started in 1995 and is one of the largest register collecting data on rheumatoid arthritis and other rheumatic diseases in the world. The aim of the register has always been to support health care along with collect data for research. The national coverage is 82.7% in rheumatoid arthritis. However, the extraction of useful real-time data in every day practice have been so far only limited.
**Objectives:** To design and implement a tool connected to the SRQ that allows users to monitoring their local data and results of care in comparison to national data.
**Methods:** We designed a Visualization and Analysis Platform (VAP) based on R language, using the web framework of Shiny (© RStudio, Inc.). The platform is based on predefined types of analyses such as flexible tabular presentations, cross-sectional and longitudinal comparisons. A user interface with reactive programming was implemented to control the appearance of interactive graphs and tables, and to explore the changes in outcome measures.
**Results:** A web-based platform for live visualization of data was developed and linked to the SRQ, a register containing ca. 75,000 patients and 500,000 registered visits, as long as 60,000 prescriptions of biological treatments. The users is able to control the specifics of the data analysis using a flexible interface, and it can visualize the results in a graph as long as in a table, that can easily be download. An explanation of the graph is included, to support the user in the understanding of what is represented. The VAP tool has been used to visualize data on the so called Open Comparison diagrams, 5 quality indicators that have been discussed at national level and that have been used to evaluate performances of care across counties in Sweden. We also applied this tool to the analysis of use of biological treatments in Stockholm (Fig.1). The user is therefore able to visualize how many times a specific biological treatment has been prescribed in his unit and compare it to the national value, as long as select different periods of time of interest and different diagnosis.



**Conclusions:** The VAP offers a flexible tool for visualization and analysis of real-time SRQ's data and it is aimed to satisfy the growing request of data by clinicians, patients, researchers, care providers and pharma companies. Moreover, the VAP tool by its nature allows the possibility of fast changes in this structure, following the changes in everyday rheumatology care in real-time.
**Disclosure of Interest:** None declared
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## THU0609 PATIENT-REPORTED OUTCOMES FROM A PHASE 3 STUDY OF BARICITINIB VERSUS PLACEBO OR ADALIMUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO BACKGROUND METHOTREXATE THERAPY

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**Background:** Baricitinib (bari), an oral JAK1 and JAK2 inhibitor, was efficacious in a Ph 3 study (RA-BEAM) in RA patients (pts) with active disease and an inadequate response (IR) to MTX.[1]
**Objectives:** To evaluate patient-reported outcomes (PROs) from RA-BEAM.
**Methods:** Pts on stable background MTX were randomized to placebo (PBO), bari 4 mg QD, or adalimumab (ADA) 40 mg Q2W. PROs listed in the table and the Work Productivity and Activity Impairment-Rheumatoid Arthritis (WPAI-RA) were collected on electronic tablets during study visits. Bari vs. PBO and bari vs. ADA were assessed with ANCOVA and logistic regression models.
**Results:** 1305 pts were randomized. Functional disability at baseline (mean HAQ-DI) was: 1.55, 1.57, 1.59 for PBO, bari, and ADA, respectively. Compared to PBO, bari was superior in physical function, Pt's Global Assessment of Disease Activity (PtGDA), pain, fatigue and quality of life (physical component score [PCS]), at Wk 12 and 24. Compared to ADA, bari was superior in physical function, PtGDA, and pain at Wks 12, 24 and 52. Compared to PBO, a similar proportion of bari and ADA pts were employed throughout the study. Statistically significant improvements in all components of the WPAI-RA (absenteeism, presenteeism, work productivity loss and activity impairment) were seen in the bari pts compared

**Abstract THU0609** – Table 1. PRO measures, LSM change from baseline (unless noted)

| | Wk 12 | | | Wk 24 | | | Wk 52 | |
|---|---|---|---|---|---|---|---|---|
| | PBO (N=488) | Bari 4 mg (N=487) | ADA (N=330) | PBO (N=488) | Bari 4 mg (N=487) | ADA (N=330) | Bari 4 mg (N=487) | ADA (N=330) |
| Physical function (HAQ-DI) [% with MCID ≥0.22] | –0.34 [58] | –0.65$^{***+++}$ [75$^{***}$] | –0.55$^{***}$ [71$^{***}$] | –0.34 [45] | –0.72$^{***+++}$ [73$^{***+}$] | –0.61$^{***}$ [64$^{***}$] | –0.73$^{+}$ [68$^{++}$] | –0.64 [58] |
| Pt's Global Assessment of Disease Activity | –16.7 | –31.2$^{***++}$ | –26.6$^{***}$ | –17.0 | –33.1$^{***+}$ | –29.1$^{***}$ | –36.3$^{+++}$ | –30.3 |
| Pt's Assessment of Pain | –17.1 | –31.5$^{***++}$ | –26.4$^{***}$ | –17.5 | –33.6$^{***++}$ | –28.8$^{***}$ | –36.1$^{+++}$ | –30.3 |
| Fatigue (FACIT-F) [% with MCID ≥3.56] | 6.7 [59] | 9.1$^{***}$ [66$^{*}$] | 8.7$^{***}$ [68$^{**}$] | 6.5 [43] | 10.0$^{***}$ [65$^{****}$] | 9.3$^{***}$ [59$^{***}$] | 10.7$^{+}$ [60] | 9.3 [54] |
| QoL: SF-36 PCS [% with MCID ≥5]; | 4.2 [40]; | 8.7$^{***++}$ [65$^{****}$]; | 7.2$^{***}$ [56$^{***}$]; | 4.6 [36]; | 9.7$^{***++}$ [65$^{***}$]; | 7.9$^{***}$ [57$^{***}$]; | 10.4$^{++}$ [60$^{+}$]; | 8.6 [52]; |
| MCS [% with MCID ≥5] | 3.1 [33] | 3.4 [37] | 3.3 [37] | 2.2 [28] | 3.8$^{**}$ [38$^{**}$] | 3.3 [34] | 4.3 [34] | 3.4 [29] |

LSM: least-squares mean; MCID: minimum clinically important difference; MCS: mental component score; $^{*}p\leq0.05$, $^{**}p\leq0.01$, $^{***}p\leq0.001$ vs. PBO; $^{+}p\leq0.05$, $^{++}p\leq0.01$, $^{+++}p\leq0.001$ vs. ADA.

to PBO at Wk 12; statistically significant improvements were seen for work loss and activity impairment for bari pts compared to ADA at Wk 12.

**Conclusions:** In this Ph 3 study of RA patients with an IR to MTX, treatment with bari resulted in significant improvement in most PROs compared with PBO or ADA, including functional disability, pain, and fatigue.

**References:**

[1] Taylor et al. Arthritis Rheumatol 2015;67(S10)

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## THU0610 THE SPONDYLOARTHRITIS IN SUB-SAHARAN AFRICA IN THE ERA OF ASAS CLASSIFICATION CRITERIA FOR AXIAL AND PERIPHERAL SPONDYLOARTHRITIS

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**Background:** The ASAS classification criteria for axial and peripheral spondyloarthritis have revolutionized the management of patients with suspicion of spondyloarthritis (1,2). These criteria have not been validated in sub-Saharan Africans. Moreover, the application of these new criteria on a population of sub-Saharan Africa with spondyloarthritis has not yet been published.

**Objectives:** To classify sub-Saharan Africans followed for spondyloarthritis according to the new ASAS classification criteria for axial spondyloarthritis and peripheral spondyloarthritis (1,2).

**Methods:** We performed a cross-sectional study among 6804 patients seen in the Rheumatology Unit of the Douala General Hospital, a tertiary healthcare centre in Cameroon, between January 2004 and December 2013. All patients followed for spondyloarthritis according to the Amor and/or ESSG criteria were collected to classify them according to the ASAS classification criteria for axial spondyloarthritis and peripheral spondyloarthritis.

**Results:** Seventy two (27 men and 45 women) patients fulfilled Amor and/or ESSG criteria. The mean age of these patients was 34 ± 13.9 years. The diagnosis was made primarily on the basis of clinical examination and X-rays of the spine and pelvis. No patient achieved a magnetic resonance imaging (MRI). The HLA B27 was negative in all patients tested. Ankylosing spondylitis was the most common spondyloarthritis, followed by reactive arthritis. The distribution of patients according to nosological entities and the predominant topography, axial and/or peripheral are respectively shown in Table 1 and Table 2. Two patients were not classified according to the ASAS criteria.

Table 1, Distribution of patients according to disease entities

| | n (%) | Mean age ± SD | Sex (M/F) |
|---|---|---|---|
| Ankylosing spondylitis | 36 (50.0) | 46±13.6 | 19/17 |
| Reactive arthritis | 29 (40.2) | 38±8.2 | 7/22 |
| Psoriatic arthritis | 3 (4.2) | 34±7.0 | 0/3 |
| Spondyloarthritis associated to inflammatory bowel diseases | 2 (2.8) | 32±3.8 | 1/1 |
| Undifferentiated spondyloarthritis | 2 (2.8) | 21±15.7 | 0/2 |

Table 2. Distribution of patients according to ASAS classification

| | n (%) | Mean age ± SD | Sex (M/F) |
|---|---|---|---|
| Spondyloarthritis (all the patients) | 72 (100) | 36±13.9 | 27/45 |
| Axial Spondyloarthritis | 40 (55.5) | 39±12.6 | 11/29 |
| Peripheral Spondyloarthritis | 29 (40.3) | 34±16.7 | 14/15 |
| "Unclassified Spondyloarthritis" according to ASAS classification | 3 (4.2) | 27±11.5 | 1/1 |

**Conclusions:** The ASAS criteria have not changed the epidemiology of spondyloarthritis in Cameroon (prevalence 1.05%), and probably in all the sub-Saharan Africa. The diagnosis is difficult because of the lack of biological markers (HLA B27 negative) and limited access to MRI (available since 2014 in our hospital). Improving the performance of the ASAS criteria for axial and peripheral spondyloarthritis will require numerous other modifications.

**References:**

[1] Rudwaleit M. Ann Rheum Dis. 2009 Jun;68(6):777–83.
[2] Rudwaleit M. Ann Rheum Dis. 2011 Jan;70(1):25–31.

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**Disclosure of Interest:** None declared

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## THU0611 SUBJECTIVE WELL-BEING OF JAPANESE RA PATIENTS WHO REACH TREATMENT TARGET IS HIGHER THAN THE JAPANESE AVERAGE

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**Background:** Subjective Well-Being (SWB) refers to a construct which includes one's emotional responses, domain satisfactions, and global judgments of life satisfaction. Many variables such as age, sex, income, employment and marital status are related to SWB. Being healthy is also an important factor of SWB. RA is a chronic illness which is considered to influence SWB. However, little is known about the impact of RA on SWB.

**Objectives:** To evaluate the SWB of Japanese RA patients and identify factors that associate with SWB.

**Methods:** This study was done in cooperation with the Cabinet Office Government of Japan Economic and Social Research Institute. This institute had previously conducted the "Well-being studies 2014" surveying the SWB of randomly selected Japanese citizens. In this survey, SWB was determined by having the participants rate their happiness between 10 (Very happy) and 0 (very unhappy). The Well-being studies 2014 also included a questionnaire consisting of 56 questions covering topics closely associated with well-being such as socioeconomic and health status. The same survey was done for RA patients at Kobe University Hospital and clinical data including disease duration, stage, class, disease activity, HAQ, complications and the therapeutic drug was also collected at the same time.

**Results:** Multivariate analysis on data including RA patients (n=339) and Japanese controls (n=7690) revealed that RA patients with high or moderate disease activity had similar SWB scores as Japanese controls. However, the SWB of RA patients with remission or low disease activity were higher than Japanese controls. Age, sex, marital status, presence of child, household income, financial

| | Value | Std.Error | p-value | |
|---|---|---|---|---|
| DAS28-CRP≤2.7 (Remission/Low disease activity) | 0.32 | 0.12 | 0.0099 | ** |
| DAS28-CRP≥2.7 (Moderate/High disease activity) | 0.04 | 0.2 | 0.853 | |
| Age | -0.01 | 0.0017 | <0.00001 | ** |
| Sex (Male) | -0.12 | 0.04 | 0.0011 | ** |
| Presence of spouse (Yes) | 0.43 | 0.07 | <0.00001 | ** |
| Presence of child(ren) (Yes) | 0.35 | 0.079 | <0.00001 | ** |
| Presence of family living with (Yes) | -0.09 | 0.13 | 0.48 | |
| Presence of relatives one see regularly (Yes) | 0.46 | 0.26 | 0.0778 | |
| Presence of anyone can help one in case (Yes) | 0.56 | 0.17 | 0.0009 | ** |
| Working status (Yes) | -0.15 | 0.046 | 0.0008 | ** |
| Household income | 0.03 | 0.0091 | 0.001 | ** |
| Leeway in living cost | 0.47 | 0.029 | <0.00001 | ** |
| Leeway in housing cost | 0.06 | 0.027 | 0.0255 | * |
| Psychological distress (Kessler 6 scale) | -0.13 | 0.0048 | <0.00001 | ** |
| Self assessment of health | -0.27 | 0.021 | <0.00001 | ** |

leeway, working status, psychological distress (Kessler 6 scale), self-assessment of health, and social connection were all associated with SWB.
**Conclusions:** Japanese RA patients may be able to get higher SWB than Japanese controls by achieving treatment target.
**Disclosure of Interest:** None declared
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## THU0612 DEVELOPMENT AND VALIDATION OF AN ACCURATE AND PRECISE NATURAL LANGUAGE PROCESSING SYSTEM TO CAPTURE RHEUMATOID ARTHRITIS DISEASE ACTIVITY MEASURES

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**Background:** Systems to electronically retrieve disease activity measures in medical records would significantly aid rheumatoid arthritis (RA) management and enhance epidemiologic research. As part of the national VA rheumatoid arthritis (VARA) registry our clinic measures 28 joint disease activity score (DAS28) by manual extraction (ManEx).
**Objectives:** 1. To develop a natural language processing (NLP) system to extract core measures from patient clinic note text and erythrocyte sedimentation rate (ESR) from the laboratory data to calculate DAS28.
2. To compare the accuracy and precision of the NLP DAS28 with ManEx DAS28.
3. To validate these findings in a second RA cohort.
**Methods:** An NLP application used clinical notes between January 1, 2015 and September 30, 2015 for RA patients in VARA (n=207) at our single site to extract tender joint count (TJC), swollen joint count (SJC), and patient global assessment (PtGA) from note text. The ESR value within 2 weeks closest to the clinic visit was combined with TJC, SJC, and PtGA to calculate DAS28. During the same observation period, ManEx of DAS28 observations were also identified. Discrepancies between ManEx and NLP were resolved by investigator review of the clinic notes. An analysis of all notes identified either by ManEx or NLP were evaluated for accuracy (% of values correctly detected in all notes) and precision (% of retrieved values by either ManEx or NLP correctly identified by that specific method). The NLP system was validated in a second cohort of RA patients in VARA (n=214) at our site between April 1, 2014 to December 31, 2014.
**Results:** The derivation set contained a total of 472 notes; 440 (93%) identified by both ManEx and NLP; 20 (4%) by ManEx alone and 12 (3%) notes by NLP alone. The accuracy and precision for TJC, SJC, PtGA, ESR and DAS28 are as noted in the table. Failure of NLP to detect core measures was because of use of incorrect note template (n=5, 1.0%) and template modification (n=18, 3.8%); however, when detected NLP precision was near 100%. Failure of ManEx was a result of missed notes (n=19, 4.0%) and data entry errors (n=13, 2.8%). Similar results were seen in the validations set of notes (n=484).

Table 1

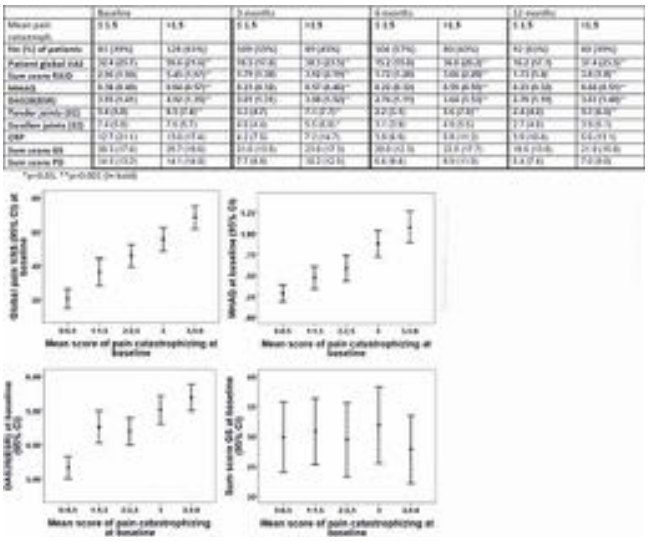
| | | Derivation set | | | Validation set | |
|---|---|---|---|---|---|---|
| | | Accuracy | Precision | | Accuracy | Precision |
| ManEx | TJC | 459/472 (97.2%) | 459/459 (100%) | TJC | 467/484 (96.5%) | 467/468 (99,8%) |
| | SJC | 459/472 (97.2%) | 459/459 (100%) | SJC | 465/484 (96.1%) | 465/467 (99.6%) |
| | PtGA | 445/472 (94.3%) | 445/450 (98.9%) | PtGA | 462/484 (95.5%) | 463/465 (99.5%) |
| | ESR | 439/472 (93.0%) | 439/451 (97.3%) | ESR | 442/484 (91.3%) | 442/456 (94.2%) |
| | DAS28 | 433/472 (91.7%) | 433/441 (98.2%) | DAS28 | 434/484 (89.7%) | 434/452 (96.0%) |
| NLP | TJC | 437/472 (92.6%) | 437/437 (100%) | TJC | 450/484 (93.0%) | 450/450 (100%) |
| | SJC | 439/472 (93.0%) | 439/439 (100%) | SJC | 446/484 (92.1%) | 446/446 (100%) |
| | PtGA | 434/472 (91.9%) | 434/434 (100%) | PtGA | 445/484 92.1%) | 445/446 (99,8%) |
| | ESR | 435/472 (92.2%) | 435/435 (100%) | ESR | 438/484 (91.8%) | 438/443 (98.9%) |
| | DAS28 | 415/472 (87.9%) | 415/415 (100%) | DAS28 | 416/484 (87.0%) | 416/421 (98.8%) |

**Conclusions:** This accurate and precise NLP system can retrieve DAS28 from clinic notes to aid in clinical care and research activities. This method can be implemented at other VARA sites and other research networks to collect RA outcomes.
**Disclosure of Interest:** None declared
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## THU0613 PAIN CATASTROPHIZING HAS A MAJOR IMPACT ON BOTH SUBJECTIVE AND COMPOSITE OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS; RESULTS FROM A LONGITUDINAL STUDY OF PATIENTS STARTING BDMARDS

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**Background:** Patient reported outcomes (PROs) are important for the evaluation of treatment response in patients with rheumatoid arthritis (RA). The degree of pain catastrophizing (conceptualized as a negative cognitive–affective response to anticipated or actual pain) may influence the patient's scoring of disease activity. Ultrasound (US) is a sensitive method for assessing inflammation, including grey scale synovitis (GS) and vascularization (power Doppler (PD)).
**Objectives:** To explore the impact of pain catastrophizing on subjective outcomes and composite scores in comparison with objective outcomes, such as US-defined synovitis, during one-year follow-up of patients with RA starting treatment with biologic DMARDs (bDMARDs).
**Methods:** A total of 209 patients with RA (mean (SD) age 53 (13) years, disease duration 10 (9) years, 81% women, 79% anti-CCP positive) were included when starting bDMARD. The patients were assessed at baseline and after 1, 2, 3, 6 and 12 months with PROs (joint pain VAS, patient's global disease activity VAS, Rheumatoid Arthritis (RA) Impact of Disease (RAID) score, MHAQ), clinical examination (assessor's disease activity VAS, tender and swollen joint counts (SJC) of 32 joints, performed by a study nurse) and laboratory variables (ESR and CRP). DAS28(ESR) and CDAI were calculated. Pain catastrophizing was assessed by the mean of two questions (each score 0–6) from the Coping Strategies Questionnaire (CSQ); "When I have pain, it's terrible and I think it's never going to get any better" and "When I have pain, I feel I can't stand it anymore". All US examinations (semi-quantitative scoring (0–3)) of GS and PD (PIP 2–3, MCP 1–5, wrist (RC, IC, RU), elbow, knee, talo-crural, MTP 1–5 and extensor carpi ulnaris/tibialis posterior tendons bilaterally) were performed by one rheumatologist (HBH) (Siemens Acuson Antares, excellence version, 5–13 MHz probe). Correlations were explored by use of Spearman's, Wilcoxon explored changes from baseline and Mann-Whitney examined for differences between two independent groups.
**Results:** 209 patients were included and 152 patients (72.7%) continued their bDMARD for the whole 12 months study. All variables, including pain catastrophizing, decreased significantly ($p<0.001$) during follow-up. Pain catastrophizing was highly correlated with patient reported outcomes (r=0.51–0.65, $p<0.001$), moderate with DAS28/CDAI (0.43/0.32, $p<0.001$) but not with CRP (r=0.1), SJC (r=-0.01) or GS (r=–0.06)/PD (r=-0.04) scores. All the subjective and composite scores were much higher ($p<0.001$) in patients with higher levels of pain catastrophizing (cut-off 1.5) (4 time points shown below), while there were no differences for CRP, SJC or US scores. All subjective and composite scores had increasing levels with increased quintiles of pain catastrophizing ($p<0.001$), while this was not found for CRP, SJC or US (some variables illustrated).



**Conclusions:** It is generally assumed that the tendency to catastrophize plays a causal role in the pain experience which may influence the PROs. Pain catastrophizing was presently found to have a major impact on all the subjective as well as composite scores, but not on inflammatory variables like CRP, SJC or US assessments. This emphasises the importance of taking into account the degree of pain catastrophizing when evaluating disease activity in RA patients.
**Disclosure of Interest:** None declared
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## THU0614 FOREWARNED IS FOREARMED? RISK COMMUNICATION DURING THE COMMENCEMENT OF METHOTREXATE; PRESENTING THE CLINICIANS' & PATIENTS' PERSPECTIVES

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**Background:** Methotrexate (MTX) is the first-line treatment for rheumatoid arthritis (RA). Previously, we have shown that patient concerns about side effects were associated with early MTX non-adherence. The first opportunity to address these concerns is during the initial clinical consultation. A crucial factor in determining

if a patient initiates and adheres to MTX could be if side effects are adequately addressed in the initial clinical consultation.
**Objectives:** The aims of this research were to evaluate from a patient's and rheumatologist's perspective i) the extent to which MTX risks are addressed during consultation and ii) possible factors constraining discussion of side effects
**Methods:** This is a mixed methods study. To evaluate the patient's perspective an online survey was co-constructed with the National Rheumatoid Arthritis Society in the UK. The survey gathered basic demographic information and included items relevant to risk communication during the initial consultation, including the extent to which side effects were discussed. The responses of patients who reported commencing methotrexate were selected for descriptive analyses.
To evaluate the rheumatologist's perspective interviews were conducted with rheumatologists. A sampling strategy ensured the views of senior and junior clinicians from different clinical settings across the UK were represented. The semi-structured topic guide contained questions about the MTX commencement consultation, including key information patients should have, how this was communicated and barriers to communication. The interviews were audio-recorded, transcribed and analysed qualitatively using Framework Analysis.
**Results:** Overall 648 people with RA completed the online survey, (83% female & 63% aged between 46 and 65 years). Eleven rheumatologists with one to 25 years experience as consultants and four trainees consented to be interviewed. The majority of respondents to the patient survey (62%) reported their initial consultation was less than 30 minutes. Of the 587 respondents who reported commencing methotrexate 16% reported they discussed side effects very little and 16% did not discuss side effects with their rheumatologist at all. Rheumatologists reported that patients should be informed about the side effects of methotrexate, however clinicians (n=9) were concerned about overloading the patient with information. Particular barriers to discussing side effects included; limited consultation time and concurrent diagnosis of RA and methotrexate commencement. These barriers were perceived as particularly acute when patients were unprepared for the diagnosis or had pre-existing negative beliefs about methotrexate.
**Conclusions:** Patients and rheumatologists separately reported side effects were not always discussed when commencing methotrexate, and barriers to communication were identified. Given that suspected side effects are a reason for non-adherence to methotrexate these need to be addressed. The development of new tools acceptable to patients and clinicians that facilitate the discussion of side effects, without extending the clinical consultation, may improve patient understanding and adherence.
**Disclosure of Interest:** None declared
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## THU0615 COST PER RESPONSE FOR ABATACEPT COMPARED WITH ADALIMUMAB IN THE TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON ANTI-CITRULLINATED PROTEIN ANTIBODY TITRES IN ITALY, SPAIN AND CANADA

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**Background:** RA is a chronic inflammatory disorder leading to disability and reduced quality of life. Effective treatment with biologic DMARDs poses a significant economic burden. The Abatacept versus Adalimumab Comparison in Biologic-Naive RA Subjects with Background Methotrexate (AMPLE) trial was a head-to-head, randomized study comparing SC abatacept with SC adalimumab.[1] Recent subgroup analyses showed improved efficacy for abatacept in serum anti-citrullinated protein antibody (ACPA)-positive patients, with increasing efficacy across ACPA quartile levels.[2]
**Objectives:** To evaluate the cost per response of abatacept relative to adalimumab in ACPA-positive patients with RA from the Italian, Spanish and Canadian societal perspectives.
**Methods:** A decision tree was designed to compare the cost per response of abatacept with adalimumab in a cohort of 1000 ACPA-positive patients (Q1: 28–235 AU/mL, Q2: 236–609 AU/mL, Q3: 613–1046 AU/mL, Q4: 1060–4894 AU/mL) over 2 years. Clinical inputs were based on the AMPLE trial, and response was based on ACR20/50/70/90 and HAQ-DI. Unit costs for direct medical costs of AEs were based on local tariffs for disease-related groups and the ex-manufacturer's price, including mandatory reductions, payback and transparent discounts for drugs. Societal costs included patient costs, indirect costs of work absence and early retirement, according to HAQ functional capacity categories.
**Results:** The cost per response in ACPA-positive patients favoured SC abatacept compared with SC adalimumab for ACR20, ACR70, ACR90 and HAQ-DI across all countries (Table 1). When evaluating across ACPA quartiles, cost per ACR20, ACR50 and ACR70 favoured SC abatacept with increasing stringency of response criteria and serum ACPA levels. Cost per ACR90 and HAQ-DI response consistently favoured SC abatacept across all ACPA subgroups and countries. In terms of cost per remission across all countries, cost per DAS28 favoured SC abatacept in ACPA-negative patients, while cost per CDAI and SDAI favoured SC abatacept in ACPA-positive patients.SC abatacept was consistently favoured in ACPA-Q4 patients across all outcomes and countries.

**Table.** Differences in costs per outcome (abatacept versus adalimumab) according to ACPA status across Italy, Spain and Canada

| | | Italy | Spain | Canada | | | Italy | Spain | Canada |
|---|---|---|---|---|---|---|---|---|---|
| | | Difference in costs per outcome (abatacept minus adalimumab) | | | | | Difference in costs per outcome (abatacept minus adalimumab) | | |
| Monthly cost per responding patient – ACPA-negative | ACR20 | -€244 | €266 | $35 | Monthly cost per responding patient – ACPA-positive | ACR20 | -€154 | -€76 | -$83 |
| | ACR50 | -€534 | -€81 | -$200 | | ACR50 | -€33 | €340 | $111 |
| | ACR70 | €1301 | €4.794 | $2430 | | ACR70 | -€644 | -€1072 | -$899 |
| | ACR90 | -€7052 | -€11.675 | -$7243 | | ACR90 | -€6426 | -€15.399 | -$8083 |
| | HAQ-DI | -€1976 | -€3552 | -$2109 | | HAQ-DI | -€281 | -€366 | -$254 |
| Monthly cost per remission – ACPA-negative | DAS28 | -€442 | -€137 | -$156 | Monthly cost per remission – ACPA-positive | DAS28 | €27 | €469 | $199 |
| | CDAI | €744 | €2247 | $1607 | | CDAI | -€848 | -€1612 | -$951 |
| | SDAI | €1313 | €4837 | $2371 | | SDAI | -€419 | -€678 | -$353 |
| Monthly cost per responding patient – ACPA-Q1 | ACR20 | €118 | €183 | $108 | Monthly cost per responding patient – ACPA-Q4 | ACR20 | -€380 | -€379 | -$288 |
| | ACR50 | €518 | €1130 | $631 | | ACR50 | -€461 | -€506 | -$376 |
| | ACR70 | €1264 | €2841 | $1615 | | ACR70 | -€808 | -€1431 | -$914 |
| | ACR90 | -€3997 | -€10.998 | -$5712 | | ACR90 | -€4277 | -€8598 | -$4827 |
| | HAQ-DI | -€10 | -€106 | -$73 | | HAQ-DI | -€521 | -€760 | -$495 |
| Monthly cost per remission – ACPA-Q1 | DAS28 | €333 | €867 | $394 | Monthly cost per remission – ACPA-Q4 | DAS28 | -€302 | -€186 | -$164 |
| | CDAI | €396 | €721 | $435 | | CDAI | -€1960 | -€4225 | -$2370 |
| | SDAI | €942 | €2149 | $1188 | | SDAI | -€1333 | -€2573 | -$1495 |

**Conclusions:** The costs per responder were lower for SC abatacept than SC adalimumab in ACPA-Q4 patients across all countries. Cost savings were greater when more stringent response criteria were applied and also with increasing ACPA levels, which could lead to a lower overall healthcare budget impact with abatacept compared with adalimumab in Italy, Spain and Canada.
**References:**
[1] Schiff M, et al. Ann Rheum Dis 2014;73:86–94.
[2] Sokolove J, et al. Ann Rheum Dis. 2015 Sep 10. doi: 10.1136/annrheumdis-2015-207942.
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## THU0616 TREATMENT ADHERENCE AND ATTITUDES TOWARDS SYSTEMIC MEDICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN DIFFERENT GEOGRAPHICAL REGIONS

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**Background:** Adherence to systemic medication may vary between patients (pts) from different geographic areas.
**Objectives:** To explore differences in self-reported adherence and attitudes to systemic medications in different geographical regions, and identify factors associated with high adherence in pts with rheumatoid arthritis (RA) from the ALIGN study.
**Methods:** ALIGN was a global, cross-sectional, non-interventional study in adult pts with 6 inflammatory diseases, including RA. Clinical data were collected and validated pt questionnaires, including 4-item Morisky Medication Adherence Scale (© MMAS-4) and Beliefs About Medicines Questionnaire (BMQ), were administered at a routine visit. Results were compared between the following regions: West, including 16 countries from Western Europe, Canada, Australia and New Zealand; Eastern Europe (EE), including 6 countries; Middle East (ME), including Saudi Arabia and Lebanon; Latin America (LA), including 4 countries; Asia, including Korea and Taiwan. Associations between various factors, including geographic location, and medication adherence were assessed by multiple regression analysis.
**Results:** Data from 1943 pts [West, 1011 pts; EE, 322 pts; ME, 109 pts; LA, 367 pts; Asia, 134 pts; overall mean±SD age: 54.8±13.5 years (y); mean±SD disease duration, 9.2 ± 8.8 y] were analysed. 38.3–51.7% of pts had completely responded to current RA treatment. Duration of current treatment was longest in West region pts and shortest in Asian pts (6.1±5.6 y vs 2.3±2.0 y, $P<.0001$). Significantly more pts in the West region were highly adherent to their medication vs pts in other regions, with the fewest fully adherent pts in Asia and LA (Table). In general, similar observations were made across various treatment groups (Table). Depending on region, 17–60% of pts reported ever forgetting to take their RA medication; 24.6% of LA pts admitted having problems remembering to take their medication (Table). All groups had similar treatment necessity scores; however, Asian pts reported significantly lower necessity scores, but higher treatment concerns vs pts in all other regions (all $P<.05$). West region pts reported significantly lower concerns scores vs pts in other regions except EE pts (Table). In multiple regression analysis, higher treatment necessity beliefs were

associated with higher medication adherence, and higher treatment concerns with less adherence.

**Table. Patient-Reported Medication Adherence, Medication Necessity Beliefs and Concerns**

| | West pts (n=1051) | EE pts (n=322) | ME pts (n=309) | LA pts (n=367) | Asian pts (n=194) | P Value* |
|---|---|---|---|---|---|---|
| High adherence[a] across medications | | | | | | |
| % (n) | 72.0 (n=1578) | 64.1 (n=498) | 65.0 (n=183) | 53.2 (n=605) | 36.8 (n=253) | <.0001 |
| OR[d] | 1.00 | 0.54* | 1.13 | 0.32*** | 0.11*** | n.a. |
| High adherence[a] by treatment regimen, % (n) | | | | | | |
| csDMARD mono (±GC) | 66.9 (n=531) | 59.5 (n=195) | 61.1* (n=72) | 42.6*** (n=216) | 28.1*** (n=89) | <.0001 |
| TNFi mono (±GC) | 76.3 (n=114) | 66.7 (n=18) | 87.5** (n=8) | 67.4** (n=34) | 0 | 513 |
| csDMARD-TNFi comb (±GC) (csDMARD rating) | 73.4 (n=335) | 60.4* (n=101) | 66.7 (n=27) | 58.4** (n=113) | 47.7** (n=44) | .0007 |
| csDMARD-TNFi comb (±GC) (TNFi rating) | 80.9 (n=330) | 80.4** (n=102) | 85.5 (n=27) | 69.0** (n=113) | 48.9*** (n=45) | <.0001 |
| Pts responding "yes" to the following [b] MMAS-4 questions, % (n) | | | | | | |
| Do you ever forget to take your medication? | 18.9 (n=1578) | 16.7 (n=498) | 24.6* (n=183) | 35.2*** (n=605) | 59.7*** (n=253) | <.0001 |
| Do you ever have problems remembering to take your medication? | 11.3 (n=1578) | 14.1 (n=498) | 20.2** (n=183) | 34.6*** (n=605) | 14.6 (n=253) | <.0001 |
| When you feel better do you sometimes stop taking your medication? | 8.7 (n=1578) | 11.0 (n=498) | 10.9 (n=183) | 17.5*** (n=605) | 21.3*** (n=253) | <.0001 |
| Sometimes if you feel worse when you take your medication, do you stop taking it? | 6.1 (n=1578) | 15.9*** (n=498) | 6.0 (n=183) | 13.4*** (n=605) | 5.1 (n=253) | <.0001 |
| Treatment Beliefs | | | | | | |
| Adj mean±SD BMQ-Specific Necessity score[e] | 19.8±0.12 | 19.8±0.19 | 19.2±0.33 | 19.8±0.18 | 18.2±0.29*** | n.a. |
| Adj mean±SD BMQ-Specific Concerns score[e] | 14.0±0.14 | 14.3±0.23 | 14.8±0.39* | 14.7±0.22* | 16.1±0.35*** | n.a. |

Adj, adjusted; BMQ, Beliefs About Medicines Questionnaire; EE, Eastern Europe; GC, glucocorticoid; LA, Latin America(n); ME, Middle East; [b]MMAS-4, 4-item Morisky Medication Adherence Scale; OR, odds ratio; West, includes Western Europe, Canada, Australia and New Zealand; a. *P* value for comparison of all regions; b. High/full adherence: [a]MMAS-4 score = 4; c. n = no. of available questionnaire results: patients receiving multiple treatments rated their adherence to each treatment; d. OR from multiple regression analysis; e. Adjusted for age, gender, disease duration, current and prior disease severity, no. of comorbidities, cumulative treatment duration, response to current treatment, prior TNFi therapy, duration of formal education, and current primary occupation using analysis of covariance (ANCOVA); *Pr ≤ 05, **Pr ≤ 001, ***Pr ≤ 0001 for comparison vs West (reference) according to chi-square test ([a]MMAS-4); regression analysis ([b]MMAS-4) or ANCOVA (BMQ-Specific).

**Conclusions:** There were more RA pts reporting high medication adherence in the West vs other regions, with the fewest in LA and Asia. Asian pts may be less adherent to RA medication due to higher concerns and lower necessity beliefs towards systemic medication. Reasons for the low adherence rate in LA pts need to be explored further.

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## THU0617 WORK PRODUCTIVITY AND DAILY ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN FOUR PHASE III RANDOMIZED CLINICAL TRIALS OF BARICITINIB

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**Background:** Baricitinib (bari), an oral JAK1 and JAK2 inhibitor, was efficacious in Ph 3 studies in patients (pts) with active RA.[1–4]

**Objectives:** To assess effects of bari on workplace and daily activity with the Work Productivity and Activity Impairment-Rheumatoid Arthritis (WPAI-RA) questionnaire in adult RA pts.

**Methods:** In 4 Ph 3 trials (table), pts completed the WPAI-RA at baseline and ~every 4 wks. Least-squares mean (LSM) of change from baseline was compared with ANCOVA.

**Results:** Across studies, bari pts tended to have less absenteeism, presenteeism, and impairment in work productivity and daily activities at primary and final timepoints vs pts from comparator groups.

**Conclusions:** Across 4 Ph 3 studies, bari treatment improved workplace and daily activities in RA pts.

**References:**

[1] Dougados et al. Ann Rheum Dis 2015;
[2] Genovese et al. Ann Rheum Dis 2015;
[3] Taylor et al. Arthritis Rheumatol 2015;
[4] Fleischmann et al. Arthritis Rheumatol 2015

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## THU0618 DISEASE ACTIVITY DURING AND AFTER PREGNANCY IN WOMEN WITH JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM A PROSPECTIVE MULTICENTER STUDY

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**Background:** Studies from the 1990s have demonstrated that the majority of women with juvenile idiopathic arthritis (JIA) experience decreased disease activity during pregnancy while about 50% flare post partum (1–3). However, these studies were retrospective studies without validated disease activity measures. DAS28 is a validated disease activity measure in women with JIA, and DAS28-CRP-3 is a validated disease activity measure during pregnancy in women with rheumatoid arthritis (4).

**Objectives:** The aim of this project was to prospectively study disease activity in women with JIA during pregnancy and until one year post partum with DAS28-CRP-3 as disease activity measure.

**Methods:** RevNatus is a Norwegian national research database, designed for the follow-up of women with inflammatory rheumatic diseases during and after pregnancy. The women have 6 or 7 visits at a rheumatology unit; before conception

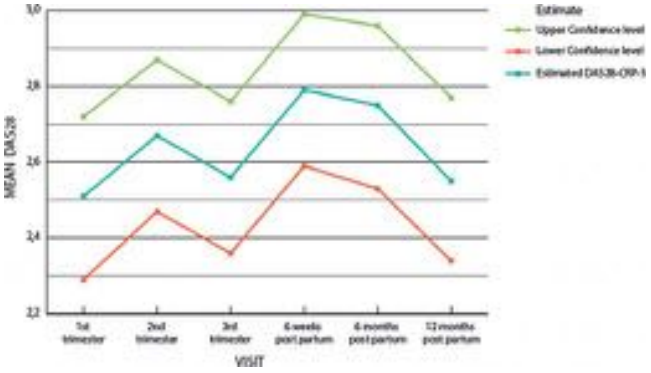
**Abstract THU0617** – Table 1

| Bari study | Employment | | Absenteeism, % of work-time missed | | Presenteeism, % of work-time impaired | | Work productivity loss, % of overall work impairment | | Activity impairment, % regular activity impairment | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline, n (%) | Employed at baseline & at Primary/ Final Timepoint, n (%) | Baseline, mean (SD) | Primary/Final Timepoint, LSM change from baseline | Baseline, mean (SD) | Primary/Final Timepoint, LSM change from baseline | Baseline, mean (SD) | Primary/Final Timepoint, LSM change from baseline | Baseline, mean (SD) | Primary/Final Timepoint, LSM change from baseline |
| Naïve (RA-BEGIN): Primary: Wk 24; Final Study Timepoint: Wk 52 | | | | | | | | | | |
| MTX (N=210) | 94 (45) | 80 (94)/57 (85) | 18.9 (31.0) | –2.4/–3.2 | 49 (28) | –20/–26 | 52.6 (29.0) | –18.4/–23.3 | 61 (26) | –25/–29 |
| Bari 4 mg (N=159) | 67 (42) | 59 (94)/55 (95) | 14.3 (29) | –10.2§/–7.5 | 49 (26) | –29§/–29 | 51.3 (26.8) | –29.4§/–29.9 | 62 (25) | –37§§§/–35§ |
| Bari 4 mg + MTX (N=215) | 117 (55) | 94 (90)/80 (83) | 14.7 (24.8) | –8.6#/–7.8 | 50 (26) | –31##/–31 | 54.5 (26.7) | –29.9##/–32.4# | 59 (25) | –33###/–38### |
| csDMARD-IR (RA-BUILD): Primary: Wk 12; Final Study Timepoint: Wk 24 | | | | | | | | | | |
| PBO (N=228) | 90 (40) | 78 (94)/48 (87) | 8.0 (20.1) | 4.2/–3.7 | 43 (24) | –8/–18 | 45.0 (25.3) | –3.0/–18.0 | 57 (23) | –13/–20 |
| Bari 2 mg (N=229) | 88 (38) | 80 (94)/67 (92) | 18.7 (30.2) | –1.0/1.1 | 46 (26) | –14/–20 | 51.4 (27.9) | –13.3*/–18.0 | 58 (25) | –19**/–23 |
| Bari 4 mg (N=227) | 76 (34) | 70 (96)/61 (92) | 9.4 (23.3) | 2.2/0.8 | 42 (24) | –16*/–22 | 44.2 (24.9) | –11.3*/–19.4 | 56 (23) | –20**/–23 |
| MTX-IR (RA-BEAM): Primary: Wk 12; Final Study Timepoint: Wk 24 for PBO and Wk 52 for Bari 4 mg and ADA | | | | | | | | | | |
| PBO (N=488 | 206 (42) | 175 (90)/126 (89) | 12.4 (26.9) | 1.3/1.0 | 42 (25) | –10/–10 | 44.5 (26.1) | –8.4/–8.2 | 56 (25) | –12/–16 |
| Bari 4 mg (N=487) | 199 (41) | 176 (92)/128 (82) | 13.0 (26.1) | –3.1*/–4.1 | 46 (25) | –18***/–24 | 48.9 (26.4) | –17.9***†/–23.5 | 58 (24) | –24***/–30 |
| ADA (N=330) | 140 (43) | 127 (93)/101 (89) | 11.9 (25.8) | 0.4/–3.9 | 44 (25) | –14/–23 | 46.6 (26.4) | –11.3/–23.0 | 58 (26) | –19+++‡/–28 |
| TNF-IR (RA-BEACON): Primary: Wk 12; Final Study Timepoint: Wk 24 | | | | | | | | | | |
| PBO (N=176) | 53 (30) | 42 (91)/22 (82) | 10.2 (23.3) | 2.1/8.0 | 47.6 (26.2) | 0.8/–3.2 | 49.7 (26.7) | –0.1/–0.6 | 66.5 (21.4) | –9.5/–15.2 |
| Bari 2 mg (N=174) | 69 (40) | 61 (94)/38 (86) | 13.7 (24.9) | –3.6/5.7 | 47.6 (21.3) | –8.1/–7.6 | 52.3 (22.8) | –9.3/–6.3 | 64.0 (19.6) | –16.7**/–22.2* |
| Bari 4 mg (N=177) | 60 (34) | 51 (90)/42 (89) | 19.0 (29.7) | –1.9/6.0 | 44.6 (29.1) | –7.9/–11.7 | 49.1 (30.1) | –9.4/–8.4 | 64.6 (23.1) | –18.1***/–26.3*** |

ADA: adalimumab; IR: inadequate response; *p≤0.05, **p≤0.01, ***p≤0.001 for bari vs PBO; +++p≤0.001 for ADA vs. PBO; †p≤0.05, ‡p≤0.01 for bari vs. ADA; §p≤0.05, §§p≤0.01, §§§p≤0.001 for bari 4 mg vs. MTX; #p<0.05, ##p≤0.01, ###p≤0.001 for bari 4 mg + MTX vs. MTX.

if possible (visit 0), in each trimester (visit 1–3), and 6 weeks, 6 months and 12 months post partum (visit 4–6). RevNatus included 135 fullterm pregnancies in 114 women with JIA between 2006 and 2015. To explore disease activity throughout pregnancy and until one year post partum, DAS28-CRP-3-values registrered at each visit were analyzed in a three level linear mixed model.

**Results:** Analyzing DAS28-CRP-3-values from 6 time points throughout and after pregnancy in 135 pregnancies in 114 women with JIA, we found that disease activity 6 weeks post partum was significantly higher than disease activity in first trimester (p=0,004), in third trimester (p=0,011) and 12 months post partum (p=0,015). Results are displayed in figure shown below.




**Conclusions:** In 135 pregnancies in women with JIA disease activity increased significantly from pregnancy to 6 weeks post partum, and then decreased significantly between 6 weeks and 12 months post partum. The results call for tight follow-up of women with JIA in the first weeks after delievery.

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## THU0619 LIFESTYLE BELIEFS OF 672 PATIENTS WITH RHEUMATOID ARTHRITIS OR AXIAL SPONDYLOARTHRITIS

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**Background:** In rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA), lifestyle factors such as physical exercise and smoking cessation are beneficial, whereas the impact of dietary factors is debatable. Is there a gap between what is known scientifically and what patients (pts) believe?

**Objectives:** To describe the most frequent lifestyle beliefs of pts with RA or axSpA, and identify the factors associated with erroneous lifestyle beliefs.

**Methods:** In this national cross-sectional study conducted in 2014–2015 in France, pts with RA (ACR/EULAR criteria) or axSpA (ASAS criteria) completed the self-reported "Opinions and fears of pts with chronic inflammatory rheumatism" (QOC-RIC) questionnaire,[1] which assessed pt beliefs through 19 questions. Of these, 11 questions were on lifestyle beliefs; each question was scored between 0–10, with 10 indicating "totally agree". For each lifestyle belief, descriptive analysis reported the percentage of pts with scores ≥7/10 in both RA and axSpA subpopulations. A multiple linear regression model with imputation of missing data explored the association between high levels of beliefs (≥7/10) and pt characteristics (including demographics, social and economic characteristics, disease status, and anxiety/depression levels through the Hospital Anxiety and Depression [HAD] and Arthritis Helplessness Index [AHI] scores).

**Results:** Overall, 672 pts recruited by 100 rheumatologists were analyzed: 432 with RA, 240 with axSpA. For RA and axSpA pts, respectively, 74.0% and 45.2% were female, average age was 58.3 (±13.1) and 47.0 (±13.2) years, and 77.3% and 72.7% were treated with biologics. Mean Disease Activity Score 28 (DAS28[ESR]) was 2.64 (±1.24) in RA pts and mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was 3.3 (±2.2) in axSpA pts. The belief (Table) of physical effort triggering flares (P2) was associated with higher anxiety levels (OR=1.80, p=0.005), whereas the opposite belief (P1) was associated with low depression levels (OR=0.56, p=0.007). Beliefs on alcohol (D3) were associated with underprivileged backgrounds (i.e. eligible for minimum social benefits; OR=4.27, p=0.027), whereas the belief on diet (D1) was associated with female gender (OR=2.17, p=0.014).

**Table:** Beliefs of RA and axSpA patients (% of patients that scored the belief ≥7/10)

| Lifestyle factors | Beliefs | RA | axSpA |
|---|---|---|---|
| Physical Lifestyle | P1 "I think that doing sport or a physical activity reduces my flares" | 31.4% | 45.8% |
| | P2 "I think that my flares are triggered by physical effort" | 31.1% | 43.3% |
| | P3 "I think that my disease was triggered by physically overdoing it" | 17.9% | 19.7% |
| Dietary Lifestyle | D1 "I think that eating certain foodstuffs can reduce my flares" | 10.5% | 9.7% |
| | D2 "I think that eating certain foodstuffs can trigger flares" | 10.3% | 9.7% |
| | D3 "I think that drinking alcohol (even in moderation) triggered my disease" | 6.2% | 0.8% |
| Other Lifestyle Factors | O1 "I think that smoking (even in moderation) or being exposed to passive smoking triggered my disease" | 6.2% | 1.7% |
| | O2 "I think that my disease was triggered by an environmental factor such as pollution" | 5.9% | 5.9% |
| | O3 "I think that my disease was triggered by a vaccination" | 8.3% | 8.4% |

**Conclusions:** Beliefs about physical activity are varied. Erroneous pt beliefs regarding physical activity were associated with anxiety, indicating that some beliefs may mirror psychological distress. Risks related to smoking were rarely perceived in this population of long-standing pts, and erroneous dietary beliefs were more frequent in female pts and those with underprivileged backgrounds. Physicians need to account for pt beliefs and pursue their educational efforts towards lifestyle modifications.

**References:**

[1] Gossec L. Ann Rheum Dis 2015;74(S2):323

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## THU0620 GENDER, DISEASE ACTIVITY, ANXIETY AND DEPRESSION LEVELS ARE RELATED TO THE LEVELS OF FEARS OF PATIENTS WITH RHEUMATOID ARTHRITIS OR AXIAL SPONDYLOARTHRITIS: A CROSS-SECTIONAL STUDY OF 672 PATIENTS

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**Background:** Patients (pts) with rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) have personal fears related to their disease which can impact therapeutic strategy.[1] We previously reported high levels of fears in RA and axSpA pts in a French multicenter survey.[2]

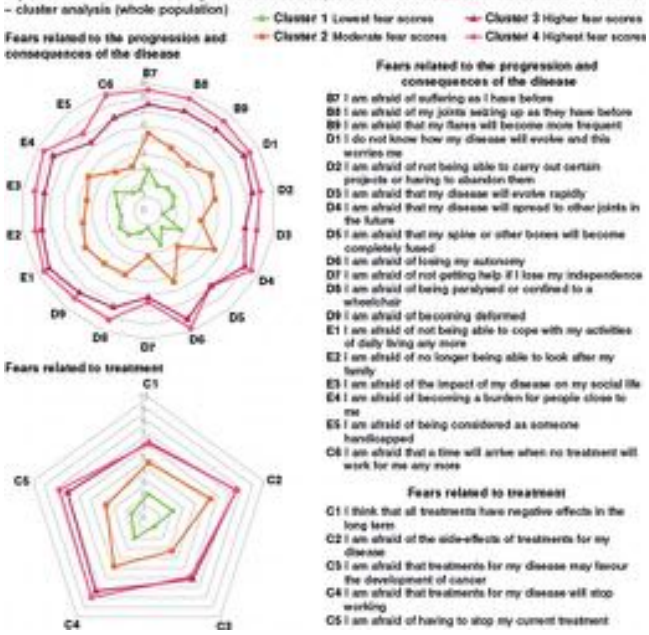
**Objectives:** To identify factors associated with high levels of fears in RA and axSpA pts.

**Methods:** This national cross-sectional study was performed in 2014–2015 in France.[2] Rheumatologists recruited 6–20 pts with RA (ACR/EULAR criteria) or axSpA (ASAS criteria). Pts self-completed the "Opinions and fears of pts with chronic inflammatory rheumatism" (QOC-RIC) questionnaire[2] comprising 44 items including 23 questions on pt fears; each scored between 0–10 (10 = "totally agree"). Eighteen questions related to progression and consequences of the disease and 5 questions related to treatment. For each fear, descriptive analysis explored the percentage of pts with scores ≥7/10. A cluster analysis was run on the whole population to identify homogeneous groups (clusters) of pts according to their fears and beliefs (hierarchical ascendant classification). A multivariate multinomial logistic regression model using backward selection and multiple missing data imputation explored the variables (eg. epidemiological, socioeconomic, clinical) with $p<0.05$ on differences between clusters.

**Results:** Overall, 672 pts recruited by 100 rheumatologists were analyzed (432 RA, 240 axSpA). For RA and axSpA pts respectively, 74.0% and 45.2% were

female, average age was 58.3 (±13.1) and 47.0 (±13.2) years, and 77.3% and 72.7% were treated with biologics. Mean Disease Activity Score 28 (DAS28[ESR]) in RA pts was 2.64 (±1.24) and mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in axSpA pts was 3.3 (±2.2).
Four pt clusters were identified corresponding to very high (31.6%), high (21.9%), moderate (32.7%) or low (13.8%) levels of fears (Figure). Variables related to the highest fear cluster were gender (female vs male; OR=2.38, p=0.013), high Pt Global Assessment of Disease Activity (PtGA [VAS]; >60 vs ≤30; OR=3.03, p=0.029), anxiety (HADS, anxiety score; >10 vs <8; OR=4.55, p<0.001) and depression (HADS, depression score; ≥8 vs <8; OR=3.23, p=0.011). Socioprofessional and family status did not have an associated p value <0.05 between populations with lowest and highest fears.

Figure: Fears related to the progression and consequences of the disease and fears related to treatment – cluster analysis (whole population)




**Conclusions:** Pts with the highest fears were most likely to be women with higher PtGA and anxiety/depression scores. Fears may reflect overall psychological distress in this population of pts and interventions to decrease these fears should be further assessed.
**References:**
[1] Nestoriuc Y. Arthritis Care Res 2010;62:791–9;
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**Acknowledgement:** The authors acknowledge Costello Medical Consulting, funded by UCB Pharma, for writing and editorial assistance. This study was funded by UCB Pharma and Arthritis Foundation Olivier Courtin.
**Disclosure of Interest:** L. Gossec: None declared, P. Chauvin: None declared, C. Hudry: None declared, M. Poussière: None declared, T. de Chalus Employee of: UCB Pharma, V. Saulot: None declared, F. Russo-Marie: None declared, J. Joubert Employee of: UCB Pharma, A. Saraux: None declared, F. Berenbaum: None declared
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## THU0621 ONE THIRD OF PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS (RA) ARE CORRECTLY VACCINATED AGAINST INFLUENZA AND PNEUMOCOCCUS AND THIS IS INCREASING: 3 YEAR LONGITUDINAL ASSESSMENT OF 776 PATIENTS

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**Background:** Influenza and pneumococcal vaccinations are recommended in all patients with RA. However, it is well known that a gap exists between recommendations and their implementation in real life.
**Objectives:** As EULAR recommendations for vaccinations are now widely disseminated, we took the opportunity of assessing vaccination rates of the patients who participated in the COMEDRA study [1], both at study entry and 3 years after the trial ended, to assess the progression of vaccination rate in this long-standing RA population undergoing a nurse-led program.
**Methods:** This was an open long term (3 years) extension of the COMEDRA 6 month randomized controlled trial in which patients with definite, stable RA were visiting a nurse for comorbidity counselling. Vaccination status was assessed during the RCT and nurses provided advice on vaccinations, and again 3 years later, during a face-to-face interview with a nurse. Agreement with the vaccination recommendations was defined as (a) influenza vaccination performed within the last 12 months and (b) pneumococcal vaccination performed within the last 5 years. The proportion of patients in accordance with the recommendations was compared between baseline and 3-year assessment using a McNemar test for paired data. The probability to be in accordance with recommendations was assessed by logistic mixed models including in the model the patient as random effect and as fixed effects: age, gender, disease duration, DAS28, educational level, work status, any biologic at baseline, and trial group and centre.
**Results:** Of the 970 recruited patients, 776 (80%) were followed up at 2–4 years and 759 (78%) had available data regarding both influenza and pneumococcal vaccination status: mean (±sd) age 61 (±11) years, median [IQR] disease duration 15 [10–23] years; 607 (80%) were women and 81% had ever received a biologic. The mean baseline and 3-year DAS28 scores were respectively 2.99±1.30 and 2.83±1.34.
At baseline, 337 (44.4%), 459 (60.5%) and 252 (33.2%) patients were in agreement with recommendations for influenza, pneumococcal and both vaccinations, respectively. After 3 years, this agreement increased for both vaccinations, to 420 (55.3%), 499 (65.7%) and 317 (41.8%) respectively (Table 1).
Having ever received a biologic (odds ratio, OR=4.73 [95% CI: 2.62- 8.52]), centre size (OR=2.8 [1.04–1.7]), university education (OR=1.79 [1.11–2.89]) and higher age (OR=1.07 [1.04–1.10]), were independently associated with being in accordance with both vaccinations recommendations.

Table 1. Adherence to vaccination recommendations

| | COMEDRA RCT study baseline* (month 0 for group I and month 6 for group II) | Follow-up at 3 years* | *p* value between baseline and follow up date |
|---|---|---|---|
| Influenza | 337 (44.4) | 420 (55.3) | p<0.0001 |
| Pneumococcus | 459 (60.5) | 499 (65.7) | p<0.01 |
| Both | 252 (33.2) | 317 (41.8) | p<0.0001 |

*N (% of 759).

**Conclusions:** The agreement with the EULAR vaccination recommendations is moderate but has increased in patients who had participated in a nurse-led program aiming at checking systematically for vaccination status.
**References:**
[1] Dougados M, Soubrier M, et al. Ann Rheum Dis. 2015;74(9):1725–33.
**Acknowledgement:** grant from the French National Research Program (PHRC AOM 12072).
**Disclosure of Interest:** None declared
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## THU0622 EPIDEMIOLOGY AND OUTCOME OF DERMATOMYOSITIS IN NORTHWESTERN THRACE REGION IN TURKEY

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**Background:** Dermatomyositis (DM) is a rare disease that may affect the skeletal muscles and the skin. Literature data on its incidence and prevalence are limited. There is no data on its incidence or prevalence in Turkey.
**Objectives:** In our study, we determined the epidemiology, general clinical features and outcomes of DM based on hospital-based data in Thrace region, which is in northwestern Turkey.
**Methods:** Patients diagnosed with DM at the Trakya University Medical Faculty, Department of Rheumatology November 2004 and November 2014 were reviewed retrospectively. Patients' clinical features, laboratory measurements, demographics, treatments, follow-up durations, disease courses, outcomes and complications were evaluated. As a tertiary care center for rheumatologic diseases, our hospital serves approximately 620,447 adults (306,036 females and 314,411 males) from both rural and urban areas. The population number was obtained from the 2012 census data of the Turkish Statistical Institution, and this population remained stable during 2004–2014. Pediatric patients (<16 years) were not included. Edirne city is located in Thrace region, in northwestern part of Turkey; and it makes borders with Greece and Bulgaria. Our hospital is the only tertiary care reference center for rheumatic diseases for both Edirne and Kırklareli, another city to the north of Edirne.
**Results:** Our study included 23 patients with dermatomyositis. Of them, 14 (60.9%) were females and 9 (39.1%) were males (female to male ratio: 1.55). Over the course of the study, the annual incidence of dermatomyositis was 3.7/1,000,000 (95%CI: 0–18.8); and the overall prevalence was 32.2/1,000,000 (95%CI: 18.1–46.3). Incidence in women was higher 4.6/1,000,000 (95%CI: 0–28.6) compared to men 2.9/1,000,000 (95%CI: 0–21.6). Heliotrope rash (82.6%), gottron papules (87%), proximal myopathy (78.3%) and facial erythema (60.9%). As the first-line treatment, the classic dm patients were given steroid 18 (100%), hydroxychloroquine 16 (88.6%), methotrexate 11 (61.1%) or azathioprine 4 (22.2%) treatment and the amyopathic dm patients were given steroid 3 (60%), hydroxychloroquine 5 (100%) or azathioprine 1 (20%) treatment. The median duration of follow-up in all DM patients was 60 months (range 3–132 months). We observed recurrence in 7 patients during follow-up. We increased the dose of the steroid upon recurrence in all our recurring patients. We added a combination of hydroxychloroquine and methotrexate to treatment upon recurrence in 2 patients receiving steroid alone; and in 3 patients receiving a combination of steroid and

hydroxychloroquine at baseline, we added methotrexate upon recurrence and we added azathioprine to treatment in one patient with interstitial pulmonary disease upon recurrence. One patients who did not respond to current therapies, whose condition recurred frequently or had was given cyclosporine and intravenous immunoglobulin.
**Conclusions:** In conclusion, in our hospital-based study on DM for which very limited epidemiological data is available, we observed lower frequency than in North American studies. Female gender was more common in our series. Data in this study is the first epidemiological data on DM reported from Turkey.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1625

## THU0623 PATIENT-REPORTED OUTCOMES FROM A PHASE 3 STUDY OF BARICITINIB IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS WHO HAD RECEIVED LIMITED OR NO TREATMENT WITH DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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**Background:** Baricitinib (bari), an oral JAK1 and JAK2 inhibitor, was efficacious in a Ph 3 study (RA-BEGIN) in RA patients (pts) who had limited or no exposure to methotrexate (MTX) and who were naïve to other csDMARDs and bDMARDs.[1]
**Objectives:** To evaluate patient-reported outcomes (PROs) from RA-BEGIN.
**Methods:** Pts were randomized to MTX QW, bari 4 mg QD, or bari 4 mg QD+MTX QW. PROs listed in the table and the Work Productivity and Activity Impairment-Rheumatoid Arthritis (WPAI-RA) questionnaire were collected on electronic tablets during study visits. Bari vs. MTX and bari+MTX vs. MTX were assessed with ANCOVA and logistic regression models.
**Results:** 584 pts were randomized. Mean baseline PROs for MTX, bari, and bari+MTX, respectively, were HAQ-DI:1.67, 1.64, 1.58; Pt's Global Assessment of Disease Activity (PtGDA):65.6, 65.0, 63.1; pt assessment of pain:65.2, 64.1, 62.6. Compared to MTX, bari and bari+MTX were superior in physical function, PtGDA, pain, and fatigue at Wks 24 and 52. Statistically significant improvements in all components of the WPAI-RA (absenteeism, presenteeism, work productivity loss and activity impairment) were seen in the bari and bari+MTX pts vs. MTX at Wk 24; statistically significant improvements were seen for work loss for bari+MTX vs. MTX at Wk 52 and for activity impairment for bari and bari+MTX vs MTX at Wk 52.
**Conclusions:** In this Ph 3 study of pts with early active RA, bari alone or with MTX was associated with significant improvements at 24 and 52 wks compared to MTX in most PROs.
**References:**
[1] Fleischmann et al. Arthritis Rheumatol 2015;67(S10)
**Disclosure of Interest:** M. Schiff Consultant for: AbbVie, Amgen, BMS, Eli Lilly & Company, JNJ, UCB, T. Takeuchi Consultant for: AbbVie GK; Asahi Kasei Medical K.K., Astellas Pharma, Astra Zeneca K.K., Bristol–Myers K.K., Celtrion, Chugai Pharmaceutical Co. Ltd, Daiichi Sankyo Co. Ltd, Eisai Co. Ltd, Eli Lilly Japan K.K., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Nipponkayaku Co. Ltd, Novartis Pharma K.K., Pfizer Japan Inc, Santen Pharmaceutical Co. Ltd, SymBio Pharmaceuticals Ltd, Taisho Toyama Pharmaceutical Co. Ltd, Takeda Pharmaceutical Co. Ltd, Teijin Pharma Ltd, C. Gaich Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, A. DeLozier Employee of: Eli Lilly and Company, D. Schlichting Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, W.-L. Kuo Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Durez Consultant for: Eli Lilly and Company, T. Carmack: None declared, J.-E. Won Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, R. Fleischmann Grant/research support from: AbbVie, Akros, Amgen, Ardea, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Genentech, Janssen, Eli Lilly & Company, Novartis, Pfizer, Regeneron, Resolve, Roche, Sanofi-Aventis, UCB, Consultant for: AbbVie, Akros, Amgen, Ardea, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Genentech, Janssen, Eli Lilly & Company, Novartis, Pfizer, Regeneron, Resolve, Roche, Sanofi-Aventis, UCB
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## THU0624 SLEEP QUALITY IN PATIENTS WITH SEVERE KNEE OSTEROARTHRITIS

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**Background:** Sleep disturbance is closely related to chronic musculoskeletal diseases. Reports suggest 55% of patients aged >55 years sleep <6 hours (15%) with deficient or poor quality sleep (29%), insomnia (56%) and diagnosed sleep disorders (18%). Osteoarthritis (OA) is one of the most prevalent of these diseases. Older adults with OA have poorer health, worse sleep quality, more limitations in activities of daily living and more pain compared with persons without OA. The prevalence of night joint pain and sleep problems increase with the severity of OA, which negatively impacts the quality of life.
**Objectives:** To determine whether sleep quality is associated with the health status in patients with severe knee OA.
**Methods:** Cross-sectional observational study. Consecutive patients with severe knee OA on a waiting list for arthroplasty were included. Sociodemographic and clinical variables were determined. Patients were asked the number of hours they usually sleep and about sleep quality (whether sleep was restorative) in the previous ≥6 months, using the question: How do you usually sleep? (by Likert scale: 1=good, 2=fair, 3=poor and 4=with medication). The health status was assessed using specific and generic health-related quality of life questionnaires (HRQOL) (WOMAC and SF-36, respectively). *Data analysis:* Multiple linear regression models were used to analyse the association between health and sleep quality (dichotomized as 1: reparative sleep (RS)=1 and non-reparative sleep (NRS)=2,3,4). Dependent variables were: total WOMAC scores (TW), SF-36 physical component (PC) and mental component (MC). Independent variables were: sleep quality, age, gender, BMI, severity OA number of comorbidities and depression/anxiety.
**Results:** 142 patients, (84% female, mean age 68.5 (SD 8.6), mean BMI 33.9 (SD 4.1), mean comorbidities 5.1 (SD 3.6) were included. The most-frequent comorbidities were hypertension 63.8%, back pain 47.5%, depression/anxiety 38.6%. Patients with RS (27%) slept a mean of 7.6 (SD 1) hours vs 6.6 (SD 1.4) hours in those with NRS ($p<0.001$). There was no association with the MC. Mean TW scores were 49.8 (SD 16.1) for patients with RS vs. 59.3 (SD 16.4) for patients with NRS (p=0.003). Mean PC scores were 36.1 (SD 9.5) for RS and 31.8 (SD 8.4) for NRS (p=0.009). Mean MC scores were 46.2 (SD 13.1) and 43.8 (SD 13.6) (p=0.343) for RS vs. NRS, respectively. Separate regression models showed RS was associated with better TW scores (p=0.002), with other variables not being significant, and that RS was associated with better PC scores (p=0.012) and female sex, the number of comorbidities and anxiety/depression were associated with worse PC scores (p=0.013 and p=0.004, respectively).
**Conclusions:** Reparative sleep is associated with a better health status in OA patients on a waiting list for TKA.
**References:**
[1] Parmelee PA et al. Sleep disturbance in osteoarthritis: linkages with pain, disability and depressive symptoms. Arthritis Care Res 2015;67(3):358
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**Disclosure of Interest:** None declared
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## THU0625 HEALTHCARE PROFESSIONALS' PERSPECTIVES ON THE DESIGN AND IMPLEMENTATION OF AN EARLY INTEGRATED CARE INTERVENTION FOR MUSCULOSKELETAL PAIN IN THE IRISH HEALTHCARE SETTING: A QUALITATIVE STUDY

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**Background:** Musculoskeletal disorders are amongst the leading causes of disability in the working age population. Growing evidence suggests early screening and targeted interventions during the acute phase can promote work retention and prevent disability.

**Abstract THU0623** – Table 1. PRO measures, Least Squares Mean change from baseline (unless noted)

| | Wk 24 | | | Wk 52 | | |
|---|---|---|---|---|---|---|
| | MTX (N=210) | Bari 4 mg (N=159) | Bari 4 mg + MTX (N=215) | MTX (N=210) | Bari 4 mg (N=159) | Bari 4 mg + MTX (N=215) |
| Physical function (HAQ-DI) [% with MCID ≥0.22] | −0.72 [70] | −1.00*** [81*] | −0.95*** [79*] | −0.66 [57] | −0.88** [68*] | −0.94*** [72***] |
| PtGDA | −30.5 | −41.1*** | −39.9*** | −29.0 | −40.4*** | −42.6*** |
| Pt Assessment of Pain | −30.0 | −40.8*** | −41.2*** | −30.7 | −40.3*** | −43.4*** |
| Fatigue (FACIT-F) [% with MCID ≥3.56] | 8.9 [65] | 13.3*** [76*] | 12.2*** [71] | 8.9 [54] | 11.7** [62] | 12.6*** [62] |
| QoL: SF-36 PCS [% with MCID ≥5]; | 10.0 [62]; | 13.8*** [71]; | 13.6*** [74*]; | 11.1 [48]; | 13.0 [65**]; | 14.5*** [65***]; |
| MCS [% with MCID ≥5] | 3.8 [32] | 5.4 [41] | 4.7 [41] | 3.5 [29] | 5.1 [33] | 5.3 [37] |

MCID, minimum clinically important difference; M/PCS, mental/physical component score; VAS, visual analog scale; *p≤0.05, **p≤0.01, ***p≤0.001 vs. MTX.

**Objectives:** This study aims to develop and feasibility test an early, case manager-led intervention focusing on work as a clinical outcome. Here we report qualitative findings from focus groups and interviews conducted to consider issues of content, delivery and optimal timing, and to explore key priorities and potential challenges in service delivery.
**Methods:** Two focus groups and three individual interviews were conducted, involving 17 experts representing the multidisciplinary team. Thematic analysis was used to summarise the views and ideas expressed.
**Results:** Participants highlighted the importance of early access to diagnosis, relevant investigations and referral to specialists as necessary in reducing the risk of long term disability; noting the critical importance of GPs in facilitating early access. The need to provide reassurance and education about the patient's condition was highlighted, as was the importance of screening for psychosocial risk factors. Patients most likely to benefit from the intervention were identified as those highly motivated to maintain their current work roles. Ready access to the MDT and the skill set of the case manager were noted as critical concerns, resource constraints pose considerable challenges.
**Conclusions:** Introduction of an early integrated care intervention that targets risk of work disability is warranted. Considerable "buy-in" is required from all stakeholders involved. The data will help to inform the planned feasibility study.
**Acknowledgement:** We would like to thank all of the individuals who participated in the interviews and focus groups.
**Disclosure of Interest:** None declared
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## THU0626 DRUG ADHERENCE IMPACT ON SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS HEALTH

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**Background:** Poor adherence to therapeutic regimens is a common and expensive problem in patients with chronic diseases including SLE and is associated with a higher risk of flares, morbidity, hospitalizations and poor renal outcome.
**Objectives:** To measure the prevalence of adherence to drug treatment and analyze its associations with medications prescribed, disease characteristics, health professionals performance and services, and socio-demographic issues in patients with SLE to improve patients' outcome and quality of service.
**Methods:** 100 SLE patients (with disease duration $\geq$1year) fulfilled the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria recruited from the outpatient clinic and inpatient unit of Rheumatology & Internal Medicine Department at Ain Shams University Hospitals. After consent all patients subjected to detailed history taking and full clinical examination, ANA, Anti-dsDNA titers, urine analysis, CBC, ESR, assessment of disease activity by SLEDAI and assessment of disease damage using the SLICC/ACR damage Index. All patients completed the screening adherence survey questionnaire for assessment of adherence to SLE medications (in the previous 6 months).
**Results:** The prevalence of adherence to drug treatment was 76%. The cause of adherence in 44.74% of adherent patients was their fear of disease worsening if medications were stopped, while feeling of moral obligation and responsibility to others (family members) was the cause of adherence in 28.95%. The reasons for non-adherence were forgetfulness (66.66%), high medications cost and difficulty to obtain medications (54%), then the large number of tablets prescribed (50%). 8.3% of our non-adherent patients stopped taking their drugs when they felt better. Source of getting medications was a highly statistically significant factor in adherence ($P<0.001$) as 86.83% of the adherent patients were taking their medications at governmental expense, while 89.47% of non-adherent patients couldn't afford. The non-adherent group had statistically significant higher disease duration (7.71 Vs 5.7 years) (P=0.032), higher prevalence of development of side effects (especially gastritis and peptic ulcer) (P=0.047) and higher SLEDAI (36.92 ±11.93 Vs 6.8±1.9) & DI score (6.67±2.5 Vs 0.21±0.47) ($P<0.001$) than the adherent group. 87.5% of non-adherent patients didn't regularly attend the clinic (P=0.068); the median of number of drugs was 5.33 which was higher than that of adherent group 4.6 (P=0.015). 61% of our patients were satisfied with the standards of care at the clinic ($P<0.001$).
**Conclusions:** Longer disease duration, higher drug cost, forgetfulness and the large number of prescribed drugs are risk factors for SLE patients non adherence.
**References:**
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## THU0627 DIFFERENCES IN DAS28-CRP AND DAS28-ESR INFLUENCE DISEASE ACTIVITY STRATIFICATION IN RHEUMATOID ARTHRITIS AND COULD INFLUENCE USE OF BIOLOGICS, TREATMENT EFFICACY EVALUATIONS AND DECISIONS REGARDING TREAT-TO-TARGET: AN ANALYSIS USING THE BSRBR-RA

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**Background:** Disease activity in rheumatoid arthritis (RA) has traditionally been measured using the 28-joint count disease activity score (DAS28) using ESR. Use of DAS28 using C-reactive protein (CRP) in place of ESR is increasing. This study investigates the level of agreement between the DAS28-ESR and DAS28-CRP scores across different disease activity thresholds and identifies how patient characteristics may influence agreement.
**Objectives:** To identify the interscore agreement between the DAS28-ESR and DAS28-CRP scores and identify if gender or body mass index (BMI) influence the level of agreement.
**Methods:** Patients with concurrent measures of ESR and CRP were identified from the BSRBR-RA, enabling paired calculation of DAS28-ESR and DAS28-CRP. Paired scores were stratified by patients' baseline BMI and gender. Agreement between the scores was compared using Bland-Altman statistics and agreement matrices.
**Results:** 5457 patients (mean age 56 yrs, 76% female) with 31,084 data entries were identified where paired DAS28-ESR/DAS28-CRP scores could be calculated. Mean DAS28-ESR was 0.3 points (95% CI -0.8 - 1.4) greater than DAS28-CRP (4.4 (SD 1.7) and 4.1 (SD 1.6) respectively). Men had a lower mean difference between the two scores compared with women (DAS28-ESR $>$ DAS28-CRP by 0.2 points (95% CI -1.0 – 1.3) vs. 0.4 points (95% CI -0.7 – 1.4) respectively). The results stratified by BMI were similar to the overall mean difference. Agreement between the two scores according to disease activity thresholds are shown in Table 1.

Table 1. Overall agreement between DAS28-ESR and DAS28-CRP scores

| | DAS28-CRP | | | | |
|---|---|---|---|---|---|
| | Remission ($<$2.6) | LDA (2.6 to $\leq$3.2) | MDA (3.2 to $\leq$5.2) | HDA $>$5.2 | Totals |
| DAS28-ESR | | | | | |
| Remission ($<$2.6) | 4041 (66.7%) | 646 (15.8%) | 170 (1.4%) | 0 | 4857 (15.6%) |
| LDA (2.6 to $\leq$3.2) | 1541 (25.4%) | 1303 (32.0%) | 591 (4.9%) | 5 (0.1%) | 3440 (11.1%) |
| MDA (3.2 to $\leq$5.2) | 481 (7.9%) | 2128 (52.2%) | 8881 (73.7%) | 320 (3.6%) | 11810 (38.0%) |
| HDA $>$5.2 | 0 | 0 | 2414 (20.0%) | 8563 (96.3%) | 10977 (35.3%) |
| Totals | 6063 (19.5%) | 4077 (13.1%) | 12056 (38.8%) | 8888 (28.6%) | 31084 |

LDA, low disease activity; MDA, moderate disease activity; HDA, high disease activity.

**Conclusions:** Overall, the DAS28-ESR classifies fewer patients in remission (15.6% vs. 19.5%) giving a score, on average 0.3 points greater than the DAS28-CRP, with women having a greater difference between the two scores than men. When categorising scores by disease activity thresholds, the DAS28-ESR/DAS28-CRP have lowest agreement at LDA. 54.4% of DAS28-ESR scores were classified as MDA when the paired DAS28-CRP was LDA, which could influence results in clinical trial reporting. Conversely, 20% of patients were classified as being in MDA by DAS28-CRP when the paired DAS28-ESR demonstrated HDA. This is of importance given NICE biologics guidelines, and shows that up to 20% of patients may not satisfy the criteria for biologic therapy if DAS28-CRP were used instead of DAS28-ESR. These results highlight the impact of using the DAS28-ESR or DAS28-CRP interchangeably, and the importance of using a consistent version of the DAS28.
**Disclosure of Interest:** None declared
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## THU0628 SOCIO-ECONOMICALLY DEPRIVED PATIENTS HAVE A HIGHER LIKELIHOOD FOR HAVING ANY TYPE OF RHEUMATIC AND MUSCULOSKELETAL DISEASES AND HAVE HIGHER HEALTHCARE COSTS - RESULTS FROM A POPULATION-BASED ADMINISTRATIVE DATABASE INCLUDING 1.9 MILLION PERSONS (BASQUE COUNTRY, SPAIN)

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**Background:** Rheumatic and musculoskeletal diseases (RMDs) are prevalent and have a strong impact on health care costs. Some evidence in specific diseases

indicates that patients with lower socio-economic background are at higher risk to have the disease and incur more healthcare costs. However, knowledge whether these effects of socio-economic status are comparable across all RMDs is lacking.
**Objectives:** To compare the impact of socio-economic deprivation on occurrence of different RMDs and associated health care costs.
**Methods:** An administrative dataset linking clinical (based on ICD codes), socio-demographics (age, gender and deprivation index) and health care utilization costs information of the entire adult (≥18 y.o.) population of the Basque Country, Spain was used. Deprivation index was based on area employment and education status, and included five categories (1 to 5 (most deprived)). Costs included primary and specialist care, planned and acute hospital admissions, and ambulatory drug prescriptions. Thirty-six individual diseases were grouped into seven larger diagnostic groups: Rheumatoid Arthritis, Crystal Arthropathies, Osteoarthritis, Soft tissue diseases, Connective Tissue Diseases, and Vasculitis. Logistic and Poisson regression models were computed to explore the relation between the deprivation index and the occurrence of the disease (separately and grouped) and health care utilization costs, respectively. Models were adjusted for age, gender, and models with costs were also adjusted for comorbities, computed with the Rheumatic Diseases Comorbidity Index.
**Results:** In total, data from 1,923,156 individuals were analyzed. Mean age was 49.9 (SD18.4) years, 49% were males. Soft tissue diseases were the most prevalent (5.5%), third most costly in terms of health care utilization costs after vasculitis and rheumatoid arthritis. Socio-economic deprivation was associated with higher likelihood to have any of the RMDs, and gradients were of comparable magnitude. The strongest socio-economic gradient was seen for the occurrence of soft tissue diseases (OR 1.82 [95%CI 1.78;1.85], most vs. least deprived) (Figure). Deprivation was also associated with higher costs across the majority of the conditions, but a somewhat different pattern across diseases was seen. The strongest gradients were observed in patients with Spondyloarthritis (in particular. with Ankylosing spondylitis) and Vasculitis.

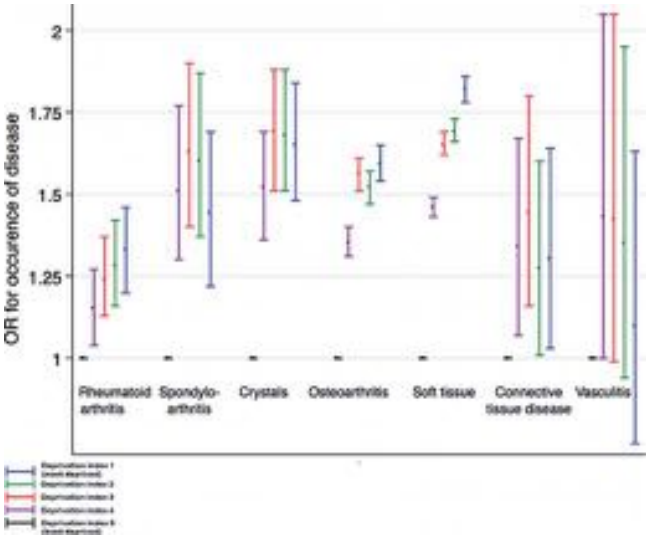



Figure 1. Association of the occurrence of rheumatic diseases with the socio-economic deprivation.

**Conclusions:** Socio-economic deprivation was consistently associated with higher occurrence and higher costs across most of the RMDs. Among major RMDs, the group of soft tissue diseases (comprising chronic low back and neck pain, fibromyalgia, and soft tissue disease), was the most prevalent and costly for the society, and occurred more often in individuals with lower socio-economic status.
**Disclosure of Interest:** None declared
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## THU0629 THE COST-EFFECTIVENESS OF GOLIMUMAB AS AN ADD-ON TO CONVENTIONAL CARE COMPARED TO CC FOR THE TREATMENT OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN SCOTLAND

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**Background:** Golimumab (Gol) has been approved by the Scottish Medicines Consortium in the treatment of adults with severe active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation, as indicated by elevated C-reactive protein and/or magnetic resonance imaging evidence, who have had an inadequate response to or are intolerant to nonsteroidal anti-inflammatory drugs.
**Objectives:** To evaluate the cost-effectiveness (CE) of Golimumab (Gol) in addition to conventional care (CC) in the treatment of nr-axSpA, in Scotland, from an NHS perspective.
**Methods:** We built a Markov model to assess CE in nr-axSpA patients over their lifetimes. Among the treated population, disease progression through 60 weeks was based on the GO-AHEAD trial. Post-week 60, BASDAI/BASFI scores were held constant until week 260, when assumed the disease deterioration rate to be 50% of CC. At week 12, patients were responders if they had a ≥50% improvement from baseline BASDAI scores, otherwise they discontinued. We applied a fixed discontinuation rate, post-week 12. Patients reached equivalent health states to those on CC 24 weeks, post-discontinuation. Utilities were linked to BASDAI/BASFI scores based on trial data. We used a published equation using BASFI scores to estimate long term health care costs. Discounting was applied at 3.5%/year. Uncertainty was explored through sensitivity analyses.
**Results:** The average baseline values for age, BASFI and BASDAI scores (based on GO-AHEAD data) was 31 years, 5.01 and 6.49, respectively. GoI when added to CC, led to an increase of 2.06 QALYs (8.98 vs. 6.92) per patient at an additional net cost of £39,770 (£146,908 vs. £107,138) compared with CC alone. GoI resulted in an incremental cost-effectiveness ratio (ICER) of £19,280/QALY. The ICER was sensitive to the correlation between BASDAI/BASFI and health-care costs and utilities in sensitivity analyses.
**Conclusions:** GoI+CC is cost-effective compared with CC alone for the treatment of nr-axSpA in Scotland.
**Disclosure of Interest:** R. Borse Employee of: Merck & Co., Inc, E. McCann Employee of: Merck & Co., Inc, O. McGill Employee of: Merck & Co., Inc, C. Black Employee of: Merck & Co., Inc, S. Kachroo Employee of: Merck & Co., Inc, R. Insinga Employee of: Merck & Co., Inc
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## THU0630 TREATMENT FAILURE, TREATMENT SWITCHING AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS OR PSORIATIC ARTHRITIS: RESULTS FROM A LARGE MULTINATIONAL REAL-WORLD SAMPLE IN EUROPE AND THE USA

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**Background:** Many patients with ankylosing spondylitis (AS) or psoriatic arthritis (PsA) do not receive advanced therapy (AT; a biologic or apremilast) or their first experience of AT is inadequate owing to lack of efficacy, intolerance or loss of benefit over time.
**Objectives:** To describe use of AT, treatment failure and switching, and assess implications of failure.
**Methods:** In this cross-sectional survey from five European countries and the USA, physicians with 3–30 years' experience were eligible if currently treating patients with AS or PsA. Physician-completed record forms included reasons for switching AT, including "primary lack of efficacy (PLE, initial non-response)" and "secondary lack of efficacy (SLE, loss of response over time)". Patients reported HRQoL (EQ-5D and SF-36), work productivity and activity impairment (WPAI) and HAQ-DI (PsA only). At analysis, current AT was assessed as "failed" if, after ≥3 months, disease severity had worsened since AT initiation or had remained severe, or if the physician was dissatisfied with disease control, perceived disease activity as "unstable" or "deteriorating", or did not consider treatment a "success".
**Results:** Data are presented from 599 physicians (457 EU/142 USA), 2018 patients with AS (1520/498) and 2436 with PsA (1839/597). Of 1889 AS patients with full treatment data, 33.5% had never received AT, 57.1% were receiving their first, 6.9% their second and 2.5% their third or later AT. Of the 2278 patients with PsA and full treatment data, the proportions were 40.8%, 48.0%, 7.9% and 3.2%, respectively.
Of the 190 AS patients with known reasons for switching from first AT, 15.8% switched owing to PLE and 46.8% to SLE. Of the 245 PsA patients, the proportions

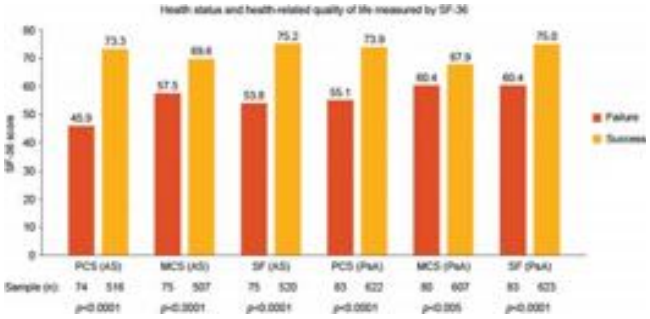



Figure 1

were 22.0% and 44.9%. Despite PLE, patients continued on first-line AT for a mean 12.1 months (AS, n=30) and 9.5 months (PsA, n=52).
The "failure" rate increased with successive ATs: 10.8% (116/1079) of AS patients on their first AT, 16.2% (21/130) on their second and 22.9% (11/48) on their third. For PsA, the rates were 11.0% (120/1094), 13.3% (24/181) and 19.2% (14/73).
AS patients failing AT had significantly worse EQ-5D utilities (0.55 vs 0.82) and SF-36 physical component summary (PCS; 45.9 vs 73.3), mental component summary (MCS; 57.5 vs 69.6) and social function scale (SF; 53.8 vs 75.2) scores than those not failing (all $p<0.0001$). PsA patients failing AT also had significantly worse EQ-5D (0.63 vs 0.80, $p<0.0001$), PCS (55.1 vs 73.9, $p<0.0001$), MCS (60.4 vs 67.9, $p=0.0024$) and SF (60.4 vs 75.0, $p<0.0001$) scores than those not failing. For AS failure, WPAI (44.0% vs 21.7%, $p<0.0001$) was higher, and for PsA failure, WPAI (29.7% vs 21.0%, $p=0.0112$) and HAQ-DI (0.96 vs 0.55, $p<0.0001$) were higher than non-failure.
**Conclusions:** This large multinational survey in AS and PsA showed that the main reason for switching AT is lack of efficacy. Failure of AT has significant negative effects on HRQoL and work productivity.
**Disclosure of Interest:** R. Alten Grant/research support from: Novartis, Speakers bureau: Novartis, V. Strand Consultant for: Abbvie, Amgen Corporation, AstraZeneca, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, GlaxoSmithKline, Janssen, Jazz Pharmaceuticals, Lilly, Novartis, Pfizer, Regeneron, Sandoz, Sanofi and UCB, P. Conaghan Speakers bureau: Abbvie, Janssen, Lilly, Novartis, Pfizer and Roche, A. Deodhar Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer and UCB, Consultant for: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer and UCB, E. Sullivan Consultant for: Novartis, S. Blackburn Consultant for: Novartis, H. Tian Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
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## THU0631 INCIDENCE OF SERIOUS ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS EXPOSED TO BIOLOGIC THERAPIES. RESULTS FROM BIOBADABRASIL REGISTRY

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**Background:** The safety profile of biologic drugs might have substantial regional differences. Since 2009, the Brazilian Society of Rheumatology runs BiobadaBrasil, a registry for monitoring of biologic therapies in rheumatic diseases, in collaboration with other Latin America countries (BiobadaAmerica) and with Biobadaser
**Objectives:** To report the incidence of serious adverse events (SAE) in Rheumatoid Arthritis (RA) patients exposed to biologic drugs in Brazil
**Methods:** BiobadaBrasil counts on thirty two centers, from almost all Brazilian states, that prospectively include patients with active rheumatic diseases who started a biologic drug or a synthetic DMARD as a parallel control group. A constant three level monitory of data quality is maintained (online, by phone and "in situ"). This study focuses on SAE (for definition: Protocolo 1.1 at https://biobadaser.ser.es/biobadamerica/Brasil/cgi-bin/upload/documentacion.aspx) in RA patients exposed to biologics from January 2009 to June 2015. Time of exposure was set from start of the drug to the date of last administration or censorship. Continuous variables were expressed as mean with standard deviation (SD). SAE incidence rate was calculated per 1000 patient/years with 95%CI
**Results:** Out of a total of 1649 subjects with RA, 1121 were exposed to biologics (4735 p/y), 91% a-TNFs, follow-up 2.8 (2.2) yrs, 85% females, at baseline: age 50 (14) yrs, disease duration 9 (8) yrs, DAS28 5.4 (1.4). Controls were 528 (1971 p/y), follow-up 3.6 (2.2) yrs, 86% females, at baseline: age 54 (13) yrs, disease duration 6 (8) yrs, DAS28 5.1 (3.1). The incidence rates of SAE in the biologics and control groups were 86 [78, 94] vs 34 [27, 44] (ratio 2.5 [1.9, 3.3], $p<0.001$). There was no statistical difference in SAE incidence between a-TNFs and non-a-TNF biologics. Among a-TNFs, Adalimumab was associated with less SAE (64 [53,79]) compared with Etanercept (93 [77,113] $p<0.01$) and Infliximab (102 [86,122] p=0.0003). SAE were more frequent with subsequent a-TNF than with the first, 107 [87, 132] vs 79 [70, 90] (ratio 1.4 [1.1, 1.7] p=0.0078). Among SAEs with biologics, serious infections account for half of the events (43 [37–49])
**Conclusions:** In the BiobadaBrasil registry the incidence of SAE is 2 fold higher with biologics than with synthetic DMARDs, and higher with subsequent a-TNF than with the first
**Acknowledgement:** for data monitoring P Cabral, for contributing to BiobadaBrasil registry, L.Barbosa, W.Chahade, A.Hayata, A.Kakehasi, M.Pinheiro, A.Ranzolin, M.Scheinberg, F.Sztajnbok, I.Silveira
**Disclosure of Interest:** None declared
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## THU0632 RETROSPECTIVE ANALYSIS OF THE ASSOCIATION BETWEEN ANTI-CYCLIC CITRULLINATED PEPTIDE POSITIVITY AND HEALTHCARE COSTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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**Background:** A recent retrospective analysis of US insurance claims data suggested that, among patients newly diagnosed with RA, those who were anti-cyclic citrullinated peptide (anti-CCP) and/or rheumatoid factor (RF) positive (+) had increased RA-related healthcare costs over a 6-month post-diagnosis period compared with those who were anti-CCP/RF negative (–).[1] Identification and treatment of this poor prognostic factor in the realm of RA diagnosis per the ACR guidelines appear to be of value.
**Objectives:** To investigate the potential role of anti-CCP status in association with clinical outcomes and healthcare costs in conventional (c)DMARD-naïve patients with RA using real-world data.
**Methods:** This was a retrospective, observational cohort study using the MarketScan® US administrative commercial claims and laboratory results databases. Patients included in this study had initiated cDMARD therapy between 1 January 2006 and 1 July 2014 (initiation=index), were aged ≥18 years at index, were continuously enrolled for 12 months before (baseline) and 12 months after (follow-up) index, did not receive cDMARDs or biologics during baseline, had an anti-CCP test result and had ≥2 medical claims with diagnoses of RA during baseline to 3 months after index. Patients were designated anti-CCP+ if their anti-CCP laboratory value was ≥20 IgG Ab units/mL. The study outcomes were all-cause and RA-related (i.e. medical claims with a diagnosis of RA or claims for cDMARDs and biologics) healthcare costs measured over the 12-month follow-up period. Generalized estimating equations were used to estimate the difference in healthcare costs from baseline to follow-up between anti-CCP+ and anti-CCP– patients (i.e. difference-in-difference [DiD]).
**Results:** The study included 635 patients: 391 anti-CCP+ (mean age 52 years; 81% female); 244 anti-CCP– (mean age 52 years, 80% female). Anti-CCP+ and anti-CCP– patients differed substantially with respect to baseline all-cause healthcare costs (mean [SD] anti-CCP+: $7650 [$12,901], anti-CCP–: $12,591 [$23,922]; p<0.001), but not RA-specific costs (mean [SD] anti-CCP+: $809 [$2683], anti-CCP–: $891 [$2629]; p=0.239). In the DiD analysis, which adjusts for baseline differences between groups, anti-CCP+ patients experienced increases in all-cause total healthcare costs that were $2756 greater (p<0.001) than those of anti-CCP– patients; this result was primarily driven by greater increases in outpatient costs ($2274; p<0.001; Table). Analyses of RA-related healthcare costs were directionally consistent across the categories.

| All-cause healthcare cost category | Difference-in-difference* |
|---|---|
| Total | $2756; p<0.001 |
| Inpatient medical | $(–234); p=0.089 |
| Outpatient medical | $2274; p<0.001 |
| Pharmacy† | $716; p=0.010 |

*Positive value indicates that anti-CCP+ patients' healthcare costs increased more than those of anti-CCP– patients from baseline to follow-up
†Includes outpatient pharmacy and infused biologics

**Conclusions:** After accounting for baseline differences between anti-CCP+ and anti-CCP– patients, anti-CCP+ patients' healthcare costs increased substantially more than anti-CCP– patients over a 12-month follow-up period. Among patients with RA who are newly initiating cDMARDs, anti-CCP positivity may serve as an identifiable predictor for markedly increased future healthcare costs, therefore establishing a need for a more appropriate treatment for cost reduction.
**References:**
[1] Johnston S, et al. J Manag Care Pharm 2015;21(Suppl. 10a):S69.
**Disclosure of Interest:** S. Johnston Employee of: Truven Health Analytics; Truven Health Analytics was paid by Bristol-Myers Squibb to conduct this study, C. Patel Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, K. Wilson Employee of: Truven Health Analytics, which was contracted by BMS to conduct this study, D. Spencer Grant/research support from: Bristol-Myers Squibb, L. Rosenblatt Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb
**DOI:** 10.1136/annrheumdis-2016-eular.1323

## THU0633 THE REVISED BRISTOL RA FATIGUE NRS, CONTAINING NEW NRS-COPING ANCHORS (BRAF-NRS V2 REVISED): VALIDITY ACROSS 6 EUROPEAN COUNTRIES

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**Background:** BRAF-NRS are a trio of items for fatigue severity, impact and coping. At development, patients wanted the NRS-Severity & Impact anchors to read 0=No fatigue/effect, 10=Totally exhausted/Great deal of effect, but the NRS-Coping to read 0=Not at all well, 10=Very well.[1] Construct and criterion validity of the NRS-Coping-NRS are less strong than NRS-Severity and Impact;[2] cognitive interviewing shows patient confusion over Coping anchors.[3]
**Objectives:** Test construct and criterion validity of BRAF-NRS V2, which has Revised NRS-Coping anchors of 0=Very well, 10=Not at all well (NRS-Severity and Impact unchanged), in 6 EU countries.
**Methods:** RA patients from France, Germany, Netherlands, Spain, Sweden and UK completed the BRAF-NRS V2 Revised, BRAF-NRS Original, BRAF-MDQ, RAID, SF-36. Spearman's correlations assessed criterion and construct validity.
**Results:** Of 1276 patients 76% were female, median HAQ 1.0 (IQR 0.375–1.5). Mean BRAF-NRS-Coping Revised 4.0 (SD 2.66) vs Original 5.95 (SD 2.57), NRS-Severity 4.86 (SD 2.56), NRS-Impact 4.61 (SD 2.69). BRAF-NRS-Severity and Impact had appropriate validity with all 18 variables, overall and by country (r=0.46–0.96). Table shows BRAF-NRS-Coping Revised had better validity than NRS-Coping Original in all variables overall (stronger correlations bolded), and for 15–18/18 variables in all countrie except Spain (3/18). The difference in strength of correlations between the versions was large for the total sample, but minimal for Spain.

Table 1

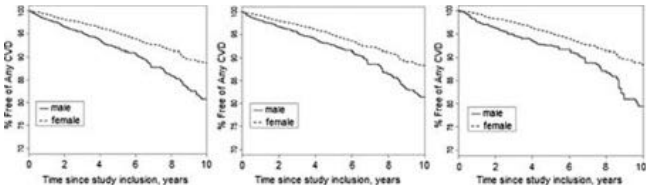
| | BRAF-NRS Coping | | | |
|---|---|---|---|---|
| | Original Not – Very well | V2 Revised Very – Not well | Original Spain Not – Very well | V2 Revised Spain Very – Not well |
| BRAF Cope NRS Original | | –0.299 | | –0.082 |
| BRAF Severity NRS | –0.280 | **0.739** | 0.445 | 0.390 |
| BRAF Impact NRS | –0.313 | **0.768** | 0.438 | 0.366 |
| BRAF-MDQ Total | –0.342 | **0.719** | –0.029 | **0.744** |
| BRAF-MDQ Physical | –0.293 | **0.718** | 0.478 | 0.350 |
| BRAF-MDQ Living | –0.329 | **0.658** | 0.348 | 0.214 |
| BRAF-MDQ Cognitive | –0.278 | **0.555** | 0.242 | **0.296** |
| BRAF-MDQ Emotional | –0.315 | **0.602** | 0.289 | 0.287 |
| RAID coping item 7 | –0.104 | **0.503** | 0.369 | 0.291 |
| SF36 Vitality | 0.34 | **–0.616** | –0.311 | –0.258 |
| RAID | –0.288 | **0.749** | 0.396 | 0.344 |
| HAQ | –0.219 | **0.495** | 0.304 | 0.163 |
| SF36 Physical function | 0.236 | **–0.497** | –0.314 | –0.136 |
| SF36 Physical role | 0.298 | **–0.537** | –0.252 | –0.209 |
| SF36 Emotional role | 0.277 | **–0.471** | –0.085 | **–0.186** |
| SF36 Social function | 0.319 | **–0.592** | –0.202 | **–0.325** |
| SF36 Pain | 0.276 | **–0.576** | –0.315 | –0.265 |
| SF36 Mental health | 0.335 | **–0.531** | –0.104 | **–0.270** |
| SF36 General health | 0.266 | **–0.511** | –0.135 | **–0.153** |

**Conclusions:** BRAF-NRS V2 Revised has construct and criterion validity across 6 EU countries. Whilst the BRAF-NRS-Coping Original is acceptable, the BRAF-NRS-Coping Revised has greater validity. In Spain, the validity of both versions is lower but similar to each other. Further exploration of the concept and wording of "coping" in the Spanish population is warranted.
**References:**
[1] Nicklin et al 2010a;
[2] Nicklin et al 2010b;
[3] Hewlett et al 2016 in press
**Acknowledgement:** EULAR project grant EP1009
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2277

## THU0634 SEX DIFFERENCES IN CARDIOVASCULAR RISK FACTORS AND EVENT RATES IN PATIENTS WITH RHEUMATOID ARTHRITIS - DATA FROM 13 RHEUMATOLOGY CENTERS

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**Background:** In the general population it is well documented that females have their CVD diagnosed at a later stage compared to males. Wether this is true also for rheumatoid arthritis (RA) patients is not known.
**Objectives:** To evaluate if cardiovascular disease (CVD) risk prediction and event rates differed between the sexes, and if adjustments for traditional and RA specific risk factors were of importance.
**Methods:** RA cohorts from 13 rheumatology centers were compared. Data on CVD risk factors and RA characteristics were collected at baseline; CVD outcomes were collected using standardized definitions. Standardized incidence ratios (SIR) were calculated with respect to sex using the following risk calculators FRS, SCORE, ACC/AHA and QRISK II.
**Results:** 5638 patients with RA and no prior CVD were included (mean age: 55.3 [SD: 14.0] years, 76% female). During a mean follow-up of 5.8 (SD: 4.4) years, 437 patients developed CVD events. SIRs (95% CI) using the various CVD risk calculators were for females and males: FRS: 1.02 (0.80, 1.31) and 0.86 (0.67, 1.12) (p=0.19), SCORE: 0.34 (0.17, 0.67) and 0.25 (0.11, 0.58) (p=0.98), ACC/AHA: 0.72 (0.50, 1.04) and 0.56 (0.36, 0.88) (p=0.74) and QRISKII 0.61 (0.47, 0.79) and 0.52 (0.35, 0.79) (p=0.42). The 10 year CVD-free survival differed significantly between the sexes, when adjusting for a) age, b) age and CVD risk factors and c) age, CVD risk factors and RA disease characteristics (Females [mean %±SD] 88.3±0.3, males 79.4±0.4), p<0.001 for all (Figure).



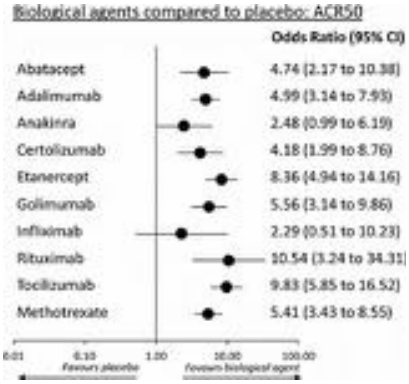

**Conclusions:** In a large international cohort of patients with RA, there was no sex difference in the ability of the various risk calculators to predict CVD. CVD-free survival was significantly higher in females, even after adjustments for both traditional and RA specific risk factors.
**Acknowledgement:** ATACC-RA collaborators: T.K. Kvien (Diakonhjemmet hospital, Oslo, Norway), E.L. Matteson (Mayo Clinic, Rochester, United States), K. Douglas and A. Sandoo (Dudley Group NHS Foundation Trust, West Midlands, United Kingdom), E. Arts and J. Fransen (Radboud University Medical Centre, Nijmegen, Netherlands), P.P. Sfikakis and E. Zampeli (University of Athens, Athens, Greece), S. Rantapää-Dahlqvist and S. Wållberg-Jonsson and L. Innala (University of Umeå, Umeå, Sweden), G. Karpouzas (Harbor UCLA Medical Center RHU, Torrance, United States), D. Solomon and K. Liao (Harvard Medical School Brigham and Women's Hospital, Boston, United States), M.A. Gonzalez-Gay and A. Corrales (Hospital Universitario Marques de Valdecilla, Santander (Cantabria), Spain), P.H. Dessein and L. Tsang (University of Witwatersrand, Johannesburg, South Africa), H. El-Gabalawy and C. Hitchon (University of Manitoba, Winnipeg, Manitoba, Canada), V.P. Ramos and I.C. Yáñez (Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City, Mexico), M. van de Laar and H. Vonkeman and I. Meek (Hospital Medisch Spectrum Twente, Enschede, Netherlands), E. Husni and R. Overman (Cleveland Clinic, Cleveland, United States), I. Colunga and D. Galarza (Hospital Universitario "Dr. José E. González", Monterrey, Mexico)
**Disclosure of Interest:** None declared
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## THU0635 DEFINING THE OPTIMAL BIOLOGICAL MONOTHERAPY IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF RANDOMISED TRIALS

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**Background:** Many rheumatoid arthritis (RA) patients might not tolerate or adhere to conventional synthetic DMARDs, it is therefore important to evaluate use of biological agents as monotherapy.

**Objectives:** To summarise and compare the benefits and harms of biological agents used as monotherapy for RA.
**Methods:** We searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials and other sources for randomised trials that compared biological monotherapy with MTX, placebo, or other biological monotherapies. Primary outcomes were ACR50 and the number of patients who discontinued due to adverse events. Our network meta-analysis was based on mixed-effects logistic regression, including both direct and indirect comparisons of the treatment effects, whilst preserving the randomised comparisons within each trial.
**Results:** The analysis comprises 28 trials (8,602 patients), including all nine biological agents approved for RA. Of the included trials, 8 (29%) included "DMARD-naïve", and 20 (71%) "DMARD-Inadequate responder" (DMARD-IR) patients. All agents except anakinra and infliximab were superior to placebo with regard to ACR50 (Figure). Etanercept and rituximab were superior to anakinra. Tocilizumab was superior to adalimumab, anakinra, certolizumab, and golimumab. When including only DMARD-IR trials, the same statistical pattern emerged, complemented with superiority of etanercept and tocilizumab compared with abatacept. Focusing on recommended doses, both etanercept and tocilizumab were superior to adalimumab and certolizumab. No differences in benefit among etanercept, tocilizumab, and rituximab were found. However, because rituximab was evaluated in just 40 patients, our confidence in the estimates is limited, No statistically significant differences among biological agents were found with respect to harm.



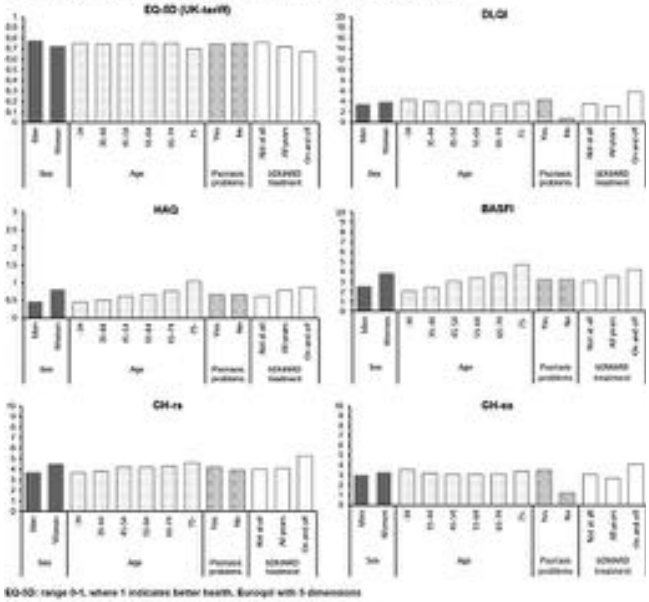

**Conclusions:** This study suggests there are differences in effectiveness but not in harm among biological agents applied as monotherapy in RA. Patient-important benefits such as ACR50 occurred more frequently with etanercept or tocilizumab monotherapy than with other biological agents. Further, in recommended dose, both etanercept and tocilizumab were superior to adalimumab and certolizumab pegol. Despite no differences between rituximab and etanercept or tocilizumab were found, our confidence in these findings were limited. In conclusion evidence suggests etanercept or tocilizumab to be the most appropriate choice for RA patients treated with biological monotherapy.
**References:**
[1] PROSPERO: CRD42012002800
**Acknowledgement:** The Parker Institute is supported by grants from the Oak Foundation.
**Funding:** This study, including the protocol, was supported by a grant from Roche, Denmark; the grant was provided as an unrestricted grant to Musculoskeletal Statistics Unit, The Parker Institute. The sponsor of the study had no role in data collection, data analysis, data interpretation, or writing of the abstract. The corresponding author had full access to all the data in the study and had the final responsibility for the decision to submit for publication.
**Disclosure of Interest:** S. Tarp Grant/research support from: AbbVie, Roche, Speakers bureau: Pfizer, MSD, D. Furst Grant/research support from: Abbott, Amgen, BMS, Janssen, Pfizer, Roche/Genentech, UCB, Speakers bureau: Abbott and UCB (CME only), A. Døssing: None declared, M. Østergaard Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Janssen, Merck, Mundipharma, Novartis, Novo, Pfizer, Schering-Plough, Roche, Takeda, UCB, Wyeth, T. Lorenzen Consultant for: Pfizer and Roche, M. Hansen Consultant for: Roche, J. Singh Grant/research support from: Takeda, Savient, Consultant for: Savient, Takeda, Regeneron, Iroko, Merz, Bioiberica, Crealta, Allergan pharmaceuticals, E. Choy Grant/research support from: Abbott Laboratories, Allergan, Amgen, AstraZeneca, Biogen, BMS, Boehringer Ingelheim, Celgene, Chugai Pharma, Daiichi Sankyo, Eli Lilly, Ferring Pharmacuetical, GSK, Hospira, ISIS, Jazz Pharmaceuticals, Jenssen, MedImmune, Merrimack Pharmaceutical, MSD, Napp, Novimmune, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, Synovate, Tonix, and UCB., M. Boers Consultant for: Pfizer, BMS, Novartis, Takeda, M. Suarez-Almazor Grant/research support from: Pfizer, Consultant for: Abbvie, L. Kristensen: None declared, H. Bliddal Grant/research support from: Abbott, Bristol-Myers Squibb, Lilly, MSD, Pfizer, Roche, UCB, Wyeth, R. Christensen Grant/research support from: Abbvie, MSD, Mundipharma/Norpharma, Novartis, Roche, Consultant for: Abbvie, Bristol-Myers Squibb, Eli Lilly, Hospira, MSD, Novartis, Pfizer, Roche
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## THU0636 ASSESSMENT OF FUNCTIONAL STATUS AND HEALTH-RELATED QUALITY OF LIFE INSTRUMENTS IN A POPULATION-BASED COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** In addition to reduce joint destruction progress and pain, one goal in psoriatic arthritis (PsA) treatment is to improve functional status (FS) and health-related quality of life (HRQoL). Demand for data on patient-reported outcomes is partly driven by the needs of cost-effectiveness analyses for reimbursement decisions. Several outcome measures are used for assessing the complex impact of PsA, but there is need for more information from studies with parallel assessment of FS and HRQoL measures.
**Objectives:** To assess patient-reported functional status by HAQ (health assessment questionnaire) and by BASFI (Bath Ankylosing Spondylitis Functional Index), health-related quality of life by EQ-5D (EuroQol-five dimensions), by DLQI (Dermatology Life Quality Index) and by GH (general health) across sex, age, presence of psoriasis and drug treatment to explore trends of similarities.
**Methods:** A sub cohort of PsA patients from the Swedish SpAScania cohort (age≥15 years, spondyloarthritis between 2003 and 2007 in the Skåne region) was used. 1181/2003 eligible PsA patients (diagnosed with PsA once by rheumatologist/internist or at least twice by other physician) responded to a questionnaire in 2009. Sex, age, disease duration, presence of psoriasis, HAQ, BASFI, EQ-5D, DLQI, and GH regarding joint (GH-rs) and skin symptoms (GH-ss) were assessed. Information about biologic disease modifying antirheumatic drugs (bDMARDs) treatment during 2008–2011 was collected from the Swedish Prescribed Drug Register and from the Southern Swedish Arthritis Treatment Group Register. Differences between groups were tested by chi-squared test for categorical data and Students t-test for continuous data.
**Results:** Out of 1181 patients 43% were men. The mean age (standard deviation) was 58 (13) and 57 (17) years for men and women respectively. Mean disease duration was 13 (11) years. 77% of the patients reported psoriasis. bDMARD treatment during all 4 years was reported by 17% of the patients; 74% reported no use at all during the same period. Women reported significantly worse health across all six health status measures compared to men (Figure 1). Patients with irregular use of bDMARDs during the 4-year period reported significantly worse health compared to patients with use during the whole period or no use at all. There was a significant association between worse health and older age for HAQ, BASFI and GH-rs. Patients with psoriasis reported significantly worse health measured by DLQI and GH-ss.

Figure 1. Statistics of functional status, health-related quality of life and general health across sex, age, psoriasis problems and bDMARD treatment for PsA patients. Cross-sectional survey in 2009.




EQ-5D: range 0-1, where 1 indicates better health, Europol with 5 dimensions
DLQI: range 0-20, where 0 indicates better health, Dermatology Life Quality Index
HAQ: range 0-3, where 0 indicates better health, Health Assessment Questionnaire
BASFI: range 0-10, where 0 indicates better health, Bath Ankylosing Spondylitis Functional Index
GH-rs and GH-ss: range 0-10, where 0 indicates better health.

**Conclusions:** While all outcome measures seemed to capture differences in patient perceptions by treatment not all were sensitive to expected differences as to reporting psoriasis or age. This highlight the value of letting the choice of instrument match the decision problem. For reimbursement decisions, measures picking up differences by treatment group and direct disease related aspects such as skin problems seem important. This is also important knowledge in

cost-effectiveness analyses where choice of effectiveness measure may have large impact on the ratio between costs and effects. The finding that patients with irregular bDMARD treatment seem to have worse health than those with long-term regular or no bDMARD treatment at all will be further investigated.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2243

## THU0637 IMPACT OF PSORIATIC ARTHRITIS: LINKING THE DOMAINS OF HEALTH WHICH ARE IMPORTANT FOR PATIENTS WITH PSORIATIC ARTHRITIS TO THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH

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**Background:** The impact of psoriatic arthritis (PsA) is wide-reaching and covers various aspects of life, e.g., physical, psychological and social. This impact could be categorised using a universally accepted, standardized reference system: the International Classification of Functioning, Disability and Health (ICF).
**Objectives:** The objective was to assess how the impact of PsA from the patient's perspective mapped to the ICF.
**Methods:** Data sources: Publications with dimensions of health important for PsA patients were identified through a systematic literature review using the following terms: ("psoriatic arthritis") AND ("quality of life" OR "impact"). Only studies related to impact from the patient's perspective, i.e., studies using qualitative methodology (e.g., focus groups, individual interviews) or instruments that were patient derived (patients included in the development task force, development based on qualitative methods) were included. Data extraction and interpretation: Domains of health important for patients were identified. Meaningful concepts were extracted from the publications and linked to the ICF categories, according to the updated linking rules [1] by 2 persons. The number of concepts linked to each ICF category and to each ICF level was calculated. The number of concepts not linkable was also calculated. Descriptive statistics were used.
**Results:** Eleven studies (13 articles) were included in the analysis, corresponding to 2893 patients (of whom 623 assessed qualitatively); two studies did not precisely define the population involved in their qualitative phases. Eight studies were exclusively on PsA and the other 5 included also patients with only psoriasis; only 5 studies were qualitative *per se.* Twenty-five domains of health were cited, of which Ability to work/volunteer and Social participation were most cited (both by 10 studies). In total 258 concepts were identified, of which 217 (84.1%) could be linked to 136 different ICF categories; 41 concepts (15.9%), mostly personal factors, namely coping with the disease (21 concepts; 51.21%) could not be linked. The most represented ICF component was Activities and Participation (42.6%) rather than Body functions (29.4%) or Body structures (10.3%). Ten studies (90.9%) reported impairments in Ability to work/volunteer and Social participation; 7 (63.6%) reported Leisure activities, Family and intimacy, Pain, Skin problems and Body image.
**Conclusions:** PsA widely impacts all aspects of patients' lives, in particular regarding activities and participation, reflecting the functional limitations, but also the psycho-social and societal burden of PsA. The ICF is a useful approach for the systematic classification of disease impact.
**References:**
[1] Cieza A, Geyh S, Chatterji S et al. ICF linking rules: an update based on lessons learned. J Rehabil Med 2005;37:212–8.
**Acknowledgement:** Dr. Gudu's work was supported by a scientific training bursary of the European League Against Rheumatism.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2662

## THU0638 LEG LENGTH INEQUALITY AS A RISK FACTOR FOR DISABILITY IN A COMMUNITY-BASED LONGITUDINAL STUDY

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**Background:** Leg length inequality (LLI), a condition in which one limb is longer than the other, is associated with osteoarthritis (OA) and pain of the knee and hip. OA is a leading cause of disability, but it is not known whether LLI is a risk factor for disability when accounting for OA.
**Objectives:** This longitudinal analysis examined the hazard of incident and progressive disability by LLI in a large, bi-racial (African American and Caucasian) community-based study in the United States of men and women 45+ years old with and without OA.
**Methods:** Participants were enrolled from 1991–1997 (original cohort) or 2003–2004 (enrichment cohort); 2369 participants had complete baseline LLI and baseline and follow-up (1999–2003 or 2006–2010) disability data available for analyses. With the participant supine, right and left lower extremity lengths were measured by trained examiners using a tape measure from anterior superior iliac spine to distal medial malleolus. LLI was defined as a difference between limbs $\geq$2 cm at baseline. Self-reported disability was assessed with the Stanford Health Assessment Questionnaire (HAQ) Disability Index, which assesses 20 functions covering 8 domains (dressing, arising, eating, walking, reaching, gripping, chores, hygiene) scored on a scale of 0–3 (no difficulty to unable). HAQ scores were calculated by averaging the scores of the 8 domains. Incident Disability was present if baseline HAQ =0 and follow-up HAQ >0, and Progression of Disability was present if baseline HAQ < follow-up HAQ. Separate parametric Weibull time-to-event models estimated hazard ratios of the association of LLI and disability outcomes, adjusting for time of LLI assessment (1991–1997 or 1999–2004), age, sex, race, body mass index (BMI), radiographic knee or hip OA, knee or hip problems (injury, surgery, fracture, or congenital anomaly), and knee or hip symptoms (pain, aching, stiffness on most days). Interactions between LLI and covariates were examined ($p<0.05$ considered statistically significant).
**Results:** Characteristics of the total sample were: mean ± standard deviation (SD) baseline age 60 ± 9.7 years; 66% women; 31% African American; mean ± SD baseline BMI 30 ± 6.2 kg/m$^2$; 23% knee OA; 26% hip OA; 21% knee problems; 8% hip problems; 44% knee symptoms; 36% hip symptoms; median follow up time 7.6 years, range 3.6–17.8 years. 154 participants (6.5%) had a LLI $\geq$2 cm. Compared to those without LLI, the adjusted hazard of Incident Disability was 39% higher among participants with LLI (adjusted hazard ratio [aHR] 1.39, 95% confidence interval [CI] 1.002, 1.93). For the model with Progression of Disability, a statistically significant interaction was noted between baseline LLI and time of baseline LLI assessment; thus, results were stratified by time of assessment. Among participants with baseline LLI collected during 1999–2004, the adjusted hazard for Progression of Disability was 60% higher among participant with LLI vs. no LLI (aHR 1.60, 95% CI 1.12, 2.28).

Table. Adjusted* Hazard Ratio (HR) and 95% Confidence Interval (CI) of Baseline Leg Length Inequality (LLI) and Disability Outcomes.

| Disability Outcome | Sample | HR | 95% CI |
|---|---|---|---|
| Incident disability (baseline HAQ=0, follow-up HAQ >0) (n=1297) | Overall | **1.39** | **1.002, 1.928** |
| | Baseline LLI Assessment 1991-1997 | 0.96 | 0.73, 1.27 |
| Progression of disability (baseline HAQ < follow-up HAQ) (n=2369) | Baseline LLI Assessment 1999-2004 | **1.60** | **1.12, 2.28** |

*Adjusted for time of baseline LLI assessment, age, sex, race, body mass index, knee osteoarthritis (OA), hip OA, knee problems (injury, surgery, fracture, congenital anomaly), hip problems, knee symptoms (pain, aching, stiffness), hip symptoms

**Conclusions:** LLI appears to be a modifiable risk factor for incident and progressive disability outcomes when accounting for OA. Treatment for LLI, such as shoe lift therapy, should be examined as an approach to prevent disability progression.
**Disclosure of Interest:** None declared
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## Cytokines and inflammatory mediators

### FRI0001 TREATING EXPERIMENTAL ARTHRITIS WITH THE INNATE IMMUNE INHIBITOR IL-37 REDUCES JOINT AND SYSTEMIC INFLAMMATION

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**Background:** Recently characterized as a fundamental inhibitor of innate and adaptive immune responses, IL-1 family member IL-37 curbs excessive inflammation and prevents tissue damage by suppressing the production of pro-inflammatory cytokines (1).
**Objectives:** We investigated the effects of recombinant IL-37 on joint and systemic inflammation and joint pathology in a mouse model of arthritis. In addition, we explored the potential for therapeutic use in human joint inflammation.
**Methods:** Wild-type (WT) mice were treated systemically with a recombinant form of the naturally occurring human IL-37, and then arthritis was induced via instillation of streptococcal cell wall (SCW) fragments in the knee joints; joint inflammation, histology, and synovial and systemic cytokine levels were evaluated after 24 hours. Mice deficient in IL-1 family decoy receptor IL-1R8 were similarly treated. The effects of IL-37 treatment were also assessed in a model of SCW-induced peritonitis. Changes in circulating and bone marrow neutrophils were evaluated. Gene expression of IL-37 and IL-1R8 was determined in the synovia of patients with rheumatoid arthritis (RA).
**Results:** In WT mice, low doses (40 $\mu$g/kg) of IL-37 suppressed joint inflammation by 51.7% ($p<0.001$). In the synovial extracts of IL-37-treated mice, IL-1$\beta$ was reduced by 84% ($p<0.001$), IL-6 by 73% ($p=0.002$), TNF$\alpha$ by 33% ($p<0.001$). These reductions were associated with a lower recruitment of neutrophils into the joint, as also demonstrated by a 60% reduction in synovial levels of the neutrophil enzyme MPO ($p<0.001$). Consistently, IL-37 treatment was associated with a decrease in circulating and an increase in bone marrow neutrophils. Mechanistically, mice treated with IL-37 exhibited a marked decrease in synovial levels of main neutrophil chemo-attractants KC, CCL3/MIP1$\alpha$, and IL-1$\alpha$, and of circulating G-CSF. We show that the anti-inflammatory effects of IL-37 require the IL-1 family decoy receptor IL-1R8, as protective effects were abrogated in mice deficient for this receptor. These results were confirmed in a model of SCW-induced systemic inflammation, that is, peritonitis. We found that gene expression of IL-1R8, but not IL-37, is markedly increased in the synovia of patients with RA.
**Conclusions:** The present study demonstrates that by curbing excessive inflammation IL-37 exerts a protective role against arthritis. Short-term, low-dose treatment with recombinant IL-37 suppressed joint inflammation, reduced cell influx, and lowered histologic scores by more than 50%. These effects were associated with suppression of synovial and systemic inflammatory cytokines and chemokines, leading to a reduced recruitment of neutrophils to the joint. We also demonstrate that IL-37 is scarcely expressed in the diseased synovia of patients with RA, but expression of IL-1R8, the receptor transducing the anti inflammatory effects of IL-37, is elevated. Thus, while levels of endogenous IL-37 are too low to contain the overwhelming inflammatory reaction in the synovia of RA patients, exogenous administration may suppress the pathological process.
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[1] Nold MF, et al. IL-37 is a fundamental inhibitor of innate immunity. Nat Immunol. 2010
**Disclosure of Interest:** None declared
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### FRI0002 SPINAL MICROGLIAL ACTIVATION IN A MURINE SURGICAL MODEL OF KNEE OSTEOARTHRITIS

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**Background:** Microglial cells are the resident macrophages of the central nervous system (CNS). Their activation (termed "microgliosis") is thought to modulate synaptic transmission in the dorsal horn, thereby promoting chronic pain. Fractalkine derived from the central termini of primary sensory afferents has been shown to contribute to microgliosis.
**Objectives:** The primary aim of this study was to document the temporal profile of dorsal horn microgliosis after destabilization of the medial meniscus (DMM) in the mouse. Further, we assessed fractalkine release from dorsal root ganglia (DRG) after DMM surgery. We evaluated these pathological events in the pain pathway in three strains of mice: wildtypes (WT), which develop slowly progressive osteoarthritis following DMM surgery, associated with sustained pain-related behaviours during the 16-week follow-up period[1]; *Ccr2* null mice, which are protected from persistent pain in spite of joint damage[1]; and *Adamts5* null mice, which are protected from joint damage and associated pain-related behaviours after DMM surgery[2].
**Methods:** DMM or sham surgery was performed in the right knee of 10-week old male wild type (WT), *Ccr2* null or *Adamts5* null C57BL/6 mice. Mechanical allodynia in the hindpaw was monitored using von Frey fibers. L4 dorsal horn microgliosis was assessed 4, 8 and 16 weeks after surgery, based on the morphology of Iba1-immunoreactive (ir) microglia: Iba1-ir cells were classified as "resting" if their process length was more than double the soma diameter, and as "activated" if their process length was less than double the soma diameter[3]. The observer was blinded to the treatment groups. DRG cells (L3-L5) from DMM, sham or naïve control mice were cultured and supernatants collected for fractalkine ELISA.
**Results:** Four weeks after surgery in WT mice, the number of activated microglia in the L4 dorsal horn was not different between naïve and DMM mice. In contrast, 8 weeks after DMM, there was a significant increase in the number of activated microglia compared to shams. By 16 weeks after DMM, activated microglia were increased compared to age-matched naïve controls. DRG cultures from WT mice showed increased fractalkine release 8 and 16 weeks, but not 4 weeks, after DMM. In contrast, DRG cultures from *Ccr2* null and *Adamts5* null mice did not release increased fractalkine and L4 dorsal horn microgliosis was absent in these mice.
**Conclusions:** DMM surgery leads to late stage dorsal horn microgliosis, 8–16 weeks after surgery. This suggests that involvement of the CNS is a late event in this experimental model. Further, the temporal correlation with fractalkine release by DRG cells suggests that fractalkine may contribute to microglial activation. Finally, reduced microgliosis in *Ccr2* null and *Adamts5* null mice, both of which fail to display persistent pain behaviors after DMM, suggests that microgliosis is associated with the persistence of OA pain. Joint protection and prevention of peripheral sensitization may attenuate one aspect of central sensitization.
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[3] Thakur M et al. PLoS One 2012.
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### FRI0003 SYNOVIAL FLUID BIOMARKERS OF THE ACUTE KNEE INJURY RESPONSE ARE ASSOCIATED WITH EARLY CLINICAL OUTCOMES

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**Background:** Acute knee joint injury is the single greatest risk factor for development of knee osteoarthritis, but only half of these individuals will develop symptomatic disease. Identifying biomarkers of an individual's joint injury response at the outset which are associated with patient relevant outcomes over both the short and long term may allow us to stratify and target therapies at those at highest risk. In a surgical mouse model, where meniscal destabilisation leads to osteoarthritis, we previously identified several molecules which are strongly upregulated in the joint tissues immediately after knee injury, 7 of which were likely to be secreted and detectable in human synovial fluids in clinical translational studies.
**Objectives:** We investigated whether molecules which were up-regulated within hours of surgical joint destabilisation in the mouse were also elevated in the analogous human setting of acute knee injury, how this molecular response varied between individuals, and whether it related to patient-reported outcome measures in the 3 months following injury.
**Methods:** 150 participants were recruited to the Knee Injury Cohort @ Kennedy (KICK), who had recent structural knee injury (<8 weeks from injury). Blood and synovial fluid (SF) at baseline visit, and where available, at 14 days and 3 months following baseline visit were analysed for the 7 candidate molecules. Knee injury and Osteoarthritis Outcome Score (KOOS) was collected at baseline and 3 months, and the summary $KOOS_4$ score analysed. Assays were by MesoScale Discovery™platform or ELISA, and compared for blood and synovial fluid with uninjured control samples.
**Results:** Median age of KICK participants was 25, median time from injury to baseline visit was 17 days and there was substantial pain and impairment by KOOS at baseline visit. 6/7 molecules were significantly elevated in human synovial fluid immediately after injury: IL-6, MCP-1, MMP-3, TIMP-1, activin A and TSG-6. 3/6 molecules were significantly associated with baseline $KOOS_4$ (those individuals with higher SF IL-6, TIMP-1 or TSG-6 had lower $KOOS_4$). These 3 molecules, MMP-3 and activin A were all significantly associated with greater improvement in $KOOS_4$ over 3 months, adjusting for relevant, pre-defined factors including time from injury to sampling, extent of injury, age and presence of heavy blood staining of synovial fluid. When these 5 synovial fluid biomarkers were included in a linear regression model, only synovial fluid IL-6 was independently

associated with either baseline $KOOS_4$ (Coeff.-4.0 (-5.92,-2.08), P<0.001), or difference in $KOOS_4$ over 3 months (Coeff.2.80 (0.89,5.52), P=0.043).
**Conclusions:** Our findings validate relevant human biomarkers of joint injury identified from a mouse model. The response, represented best by synovial fluid IL-6, is associated with clinically-relevant outcomes over this early period: a greater inflammatory response soon after the injury is associated with increased impairment and pain by $KOOS_4$ at that time, but does not appear to be an adverse prognostic factor, at least in the short-term, and in this predominantly surgically-managed cohort. Longitudinal outcomes will determine if these molecules are biomarkers of subsequent disease risk.
**Disclosure of Interest:** None declared
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## FRI0004 INHIBITION OF PHOSPHODIESTERASE 4 (PDE4) REDUCES DERMAL FIBROSIS BY INTERFERING WITH THE RELEASE OF PRO-FIBROTIC CYTOKINES FROM M2-MACROPHAGES

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**Background:** PDE4 catalyses the breakdown of cAMP and cGMP to modulate intracellular effects. PDE4 is mainly expressed in inflammatory cells, and its inhibition leads to reduced inflammatory cell activity. Activation of the cellular immune system and autoimmunity are hallmarks of the pathogenesis of systemic sclerosis (SSc).
**Objectives:** To study the disease-modifying, anti-fibrotic effects of PDE4 inhibition in preclinical models of SSc.
**Methods:** The effects of the PDE4-specific inhibitors rolipram and apremilast were studied in the models of bleomycin-induced skin fibrosis and sclerodermatous chronic graft versus host disease (sclGvHD), reflecting local and systemic inflammatory fibrotic disease. To better understand the disease-modifying activity of PDE4 blockade in preclinical SSc, we investigated fibrosis relevant genes and cytokines in fibroblasts and macrophages from healthy individuals and patients suffering from diffuse-cutaneous SSc upon blockade of PDE4.
**Results:** We first studied PDE4 inhibition by rolipram in a preventive bleomycin model. In this model, rolipram reduced skin thickening by 33% ($p$ <0.001), the amount of fibrotic tissue assessed by histomorphometry by 38% ($p$ =0.016) and the number of α-SMA-positive myofibroblasts by 45% ($p$ <0.001). We then wondered if the clinically approved PDE inhibitor apremilast did also show significant anti-fibrotic activity, and if PDE inhibition did not only prevent but also treat fibrosis once it was established. In a modified bleomycin model of established fibrosis, apremilast reduced skin thickness by 26% (p=0.001) the amount of fibrotic tissue by 21% (p=0.037) and the number of myofibroblasts by 73% (p=0.001). Taking advantage of a model of cGvHD, we investigated if PDE4 blockade could also reduce fibrosis in a model for systemic fibrotic disease. Indeed, rolipram reduced skin thickness by 33% ($p$ =0.002), the amount of fibrotic tissue by 35% (p=0.016) and of the number of α-SMA-positive myofibroblasts by 46% ($p$ =0.002).
In line with the general mode of action of PDE4 blockade, we observed significantly reduced leukocytic infiltration in the fibrotic skin of all three animal models. We further demonstrated that fibroblasts were not the direct targets of the anti-fibrotic effects of PDE4 blockage. By contrast, PDE4 inhibition decreased the release of pro-fibrotic cytokines interleukin-6 and 13 (IL-6, IL-13) and, transforming growth factor β1 and β2 (TGFβ1, TGFβ2) and fibronectin-1 (FN-1) from activated M2 macrophages obtained from both healthy volunteers and SSc patients, resulting in reduced fibroblast activation and collagen release.
**Conclusions:** PDE4 inhibition reduces inflammatory cell activity and the release of pro-fibrotic cytokines from M2 macrophages, which leads to decreased fibroblast activation and collagen release. Importantly, apremilast is already approved by the FDA and the EMA for the treatment of psoriatic arthritis. Therefore, our preclinical results might prompt the use of PDE4 inhibitors in clinical studies with patients suffering from SSc. Our findings suggest that particularly patients with inflammation-driven fibrosis might benefit from PDE4 blockade.
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**Disclosure of Interest:** None declared
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## FRI0005 A DISTINCT PROFILE OF SERUM FREE FATTY ACIDS IS ASSOCIATED WITH CLINICAL FEATURES AND SKEWED TH1 RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** largely considered as mere sources of energy, metabolomics have revealed a role for lipid species in a number of biological processes. Among them, free fatty acids (FFA) are known to modulate cytokine transcription, expression of adhesion molecules and are involved in the production of proinflammatory and pro-resolving lipid compounds, such as prostaglandins and leukotrienes or protectins and resolvins, respectively. Recently, FFA were reported to modulate the function of CD4+ T-cells and macrophages in osteoarthritis. Thus, we hypothesize that altered FFA levels may underlie the initiation or perpetuation of pathogenic mechanisms in immune-mediated rheumatic diseases.
**Objectives:** to evaluate whether altered FFA levels can be found in RA patients linked to clinical features as well as CD4+ T-cell response.
**Methods:** serum levels of FFA (palmitic, stearic, palmitoleic, oleic, linoleic, γ-linoleic, arachidonic –AA–, linolenic, eicosapentaenoic –EPA– and docosahexaenoic –DHA–) were quantified by LC-MS/MS after methyl-tert-butylether (MTBE)-extraction in 124 RA patients and 56 healthy controls (HC). Total FFA serum levels were quantified by means of a colorimetric assay. CD4+ phenotype was studied by flow cytometry. TNFα, IL-8, VEGF, GM-CSF, IFNγ, IL-17, MCP-1, IP-10, leptin and resistin serum levels were quantified by immunoassays. The effect of FFA on IFNγ production by PBMC was evaluated in vitro.
**Results:** lower levels of palmitic (p<0.0001), palmitoleic (p=0.002), oleic (p=0.010), arachidonic (p=0.027), EPA (p<0.0001) and DHA (p<0.0001) were found in RA patients, some FFA being altered in patients at disease onset (n=18). Altered FFA exhibited distinct chemical properties, leading us to think that individual FFA within a given class followed distinct patterns and similar patterns were found among different groups of FFA. Total FFA levels did not differ between patients and controls (p=0.157), thereby supporting the existence of different profiles within the FFA pool. Cluster analysis identified a FFA profile (hallmarked by increased stearic and decreased EPA and DHA) overrepresented in RA patients compared to HC (p=0.002), being associated with clinical features (RF: p=0.029, shared epitope (2 copies): p<0.001 and erosions: p=0.003), increased IFNγ expression in CD4+ T-cells (p=0.002) and a Th1-biased serum milieu (IFNγ: p<0.001, MCP-1: p<0.0001 and IP-10: p=0.006). No associations with regulatory T cells or Th17 subsets were found. In vitro assays demonstrated that stearic/DHA/EPA-imbalanced FFA could underlie IFNγ production by CD4+ T-cells, in both resting and PHA-stimulated conditions. Finally, changes on FFA levels were associated with clinical response and CD4+ Th1 shift upon TNFα-blockade.
**Conclusions:** an altered FFA profile can be found in RA patients associated with clinical characteristics of aggressive disease, Th1-skewed response and poor clinical outcome upon TNFa-blockade. These results support the relevance of lipidomic studies in RA and provide a rationale for new therapeutic targets as well as for FA supplementation and stratification in RA.
**Disclosure of Interest:** None declared
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## FRI0006 CLASS 3 SEMAPHORINS MODULATE THE INVASIVE CAPACITY OF RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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**Background:** The semaphorin family is a large group of proteins initially described in axon guidance. However, semaphorins also play a role in other processes such as the regulation of immunity, angiogenesis, apoptosis and cell migration and invasion. Moreover, semaphorins have been related with the pathogenesis of multiple sclerosis, myocarditis, atherosclerosis and cancer. However, the potential role of class 3 semaphorins in rheumatoid arthritis (RA) remains unknown.
**Objectives:** The aim of this study was to analyze the role of class 3 semaphorins in the pathology of RA.
**Methods:** mRNA expression of class 3 semaphorins in the synovial tissue of early, DMARD-naive arthritis patients was analyzed by (q)uantitative PCR. RA FLS were stimulated for 4h with IL-1β, TNF or LPS. and mRNA and expression of class 3 semaphorins was analyzed by qPCR. RA FLS were stimulated with Sema3A, Sema3B or Sema3F in the presence or absence of PDGF. Cell migration and invasion were determined using wound closure motility and transwell invasion assays, respectively. Matrix metalloproteinase mRNA and protein expression was determined by qPCR array and luminex. PlexinA1 and neuropilin-1 expression were knocked-down by siRNA-mediated silencing. ERK and Rac1 activation were determined by immunoblot.
**Results:** mRNA expression of class 3 semaphorins in the synovial tissue of early arthritis patients negatively and significantly correlated with the mRNA expression of inflammatory mediators and the disease activity parameters of these patients. Moreover, Sema3B, Sema3C, Sema3F and Sema3G mRNA expression were significantly lower in early arthritis patients who developed persistent disease compared with patients with self-limiting disease after 2 years follow-up. Sema3F and Sema3B expression were significantly lower in patients that developed RA after 2 years of follow-up compared to those who remained as undifferentiated arthritis patients. FLS expression of Sema3A was significantly induced after IL-1, TNF or LPS stimulation, while the expression of Sema3B and Sema3F was down-regulated. Functional assays showed that Sema3A significantly induced the migration and invasion of FLS. In contrast, Sema3B and Sema3F reduced spontaneous FLS migration and PDGF-induced cell invasion. These effects were

associated withthe differential regulation of MMP-1, MMP-3 and MMP-8 by these semaphorins, and were mediated by the receptor PlexinA1 and the co-receptor NRP-1. Finally, we observed that class 3 semaphorins reduced the PDGF-induced ERK and Rac1 activation.

**Conclusions:** Our data demonstrate that class 3 semaphorins are differentially expressed in the synovium of early patients depending on the severity and the progression of the disease and that Sema3A, Sema3B and Sema3F play an important role in the invasive capacity of RA FLS. Together, class 3 semaphorins and their receptors could be useful biomarkers and promising therapeutic targets for the treatment of RA.

**Disclosure of Interest:** None declared

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## FRI0007 EFFECT OF TYPE 1 AND 2 INTERFERONS ON NEUTROPHIL APOPTOSIS IN NAÏVE AND TNF ALPHA PRIMED NEUTROPHILS

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**Background:** Juvenile-onset Systemic Lupus Erythematosus (JSLE) is a multisystem autoimmune disease characterised by the presence of autoantigens. These may result from increased numbers of apoptotic neutrophils and dysregulated clearance of these neutrophils by phagocytes. Serum from JSLE patients contains high levels of type 1 ($\alpha$ and $\beta$) and 2 ($\gamma$) interferons (IFN). In the context of JSLE being an inflammatory condition, JSLE neutrophils are likely to be more activated in comparison to healthy, non-inflammatory control neutrophils. Tumour necrosis factor (TNF)-$\alpha$ can prime neutrophils (demonstrated by CD62L shedding), and provides an inflammatory setting for neutrophils as seen in JSLE. Gene expression analysis has shown an IFN and granulocyte signature within SLE; however the interaction between IFN and neutrophils in regards to apoptosis, and the pathogenesis of JSLE, is yet to be elucidated.

**Objectives:** To investigate the effect of type 1 and 2 IFNs on neutrophil apoptosis of naïve and primed neutrophils

**Methods:** Neutrophils isolated from healthy control adult donors (n=5) were either unstimulated or primed with TNF-$\alpha$ (1$\mu$g/ml) for 30 mins. The neutrophils were subsequently incubated with IFN-$\alpha$ (10$\mu$g/ml), IFN-$\gamma$ (1$\mu$g/ml) or IFN-$\beta$ (1$\mu$g/ml) for 6hrs. The expression of CD62L after 30 min TNF-$\alpha$ incubation was measured using flow cytometry using CD62L-APC (DREG-56) antibody staining with IgG-APC isotype control. The percentage of apoptotic neutrophils were measured after 6hr IFN incubation using flow cytometry via annexin V FITC staining.

**Results:** CD62L expression was reduced in neutrophils exposed to TNF-$\alpha$ compared with unstimulated neutrophils (geometric mean: 1.61 ± 0.30 vs 11.43 ± 1.44). Apoptosis (% ± SEM) was significantly reduced upon IFN-$\alpha$ (6.57 ± 1.18%, p=0.04) and IFN-$\gamma$ (10.79 ± 1.92%, p=0.04) incubation compared to unstimulated (22.01 ± 3.18%), although IFN-$\beta$ (20.30 ± 5.10%, p=0.35) and TNF-$\alpha$ alone (26.40 ± 4.30%, p=0.50) had little effect. In neutrophils pre-treated with TNF-$\alpha$, there was significant increase in apoptosis when subsequently exposed to either IFN-$\alpha$ (48.91 ± 4.84%, p=0.04), IFN-$\gamma$ (43.09 ± 2.99%, p=0.04) or IFN-$\beta$ (39.41 ± 3.23%, p=0.04) compared to unstimulated neutrophils.

**Conclusions:** There is evidence that both type 1 and 2 IFNs contribute to the development of JSLE. Here we show a differential effect between IFNs on neutrophil apoptosis indicating a potential pro-apoptotic effect of IFNs on neutrophils in a JSLE environment through the pre-incubation with TNF-$\alpha$. IFNs may contribute to the increase in neutrophil apoptosis in JSLE and lead to an increase in autoantigens that are fundamental to JSLE pathogenesis.

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**Disclosure of Interest:** None declared

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## FRI0008 MOBILIZATION OF LYMPHATIC ENDOTHELIAL PRECURSORS CELLS AND LYMPHATIC NEOVASCULARIZATION IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** Lymphatic neovascularisation is a key feature of chronic inflammation but is almost unexplored in primary Sjögren's syndrome (pSS). The two available studies that focused on lymphatic neovascularization in pSS minor salivary glands (MSGs) were limited to the assessment of glandular mature lymphatic endothelial cells and yielded conflicting results. A recent study in an experimental model of inflammation revealed that the pro-inflammatory cytokine IL-17 also displays a pro-lymphangiogenic function. IL-17 is a leading actor in the pathogenesis of pSS as it is involved in several steps of disease development and perpetuation

**Objectives:** On this basis, aims of this study were: i. investigation of lymphangiogenic mediators and characterization of lymphatic vasculature in pSS; ii. Identification of the possible association of IL-17 and lymphatic neovascularization in this disease.

**Methods:** Circulating lymphatic endothelial precursor cells (LEPCs) and Th17 cells were enumerated in 15 pSS and 15 healthy females. VEGF-C and IL-17 were assessed in paired serum samples by ELISA. Lymphatic vasculature, VEGF-C, VEGFR3 and IL-17 were evaluated by either immunofluorescence or immunohistochemistry in MSGs from 18 pSS MSGs compared to 8 non-specific chronic sialadenitis (NSCS) MSGs and 8 normal MSGs.

**Results:** Circulating LEPCs were increased in pSS ($p<0.0001$) and were directly correlated to Th17 cell percentage, serum IL-17 and serum VEGF-C concentration (Spearman's rho=0.6; 0.6 and 0.5 respectively, all $p<0.05$). In pSS MSGs, a newly formed lymphatic capillary network was found within periductal inflammatory foci and the number of lymphatic vessels within the interlobular connective tissue was significantly increased compared to normal and NSCS MSGs ($p<0.05$). A strong expression of VEGF-C was detected in pSS ductal epithelial cells, microvessels and periductal inflammatory cells, while VEGF-C was barely detectable in ductal epithelial cells and microvessels of normal and NSCS MSGs. The expression of VEGFR-3 was strongly increased in lymphatic capillaries of pSS MSGs with respect to normal and NSCS MSGs. Numerous VEGFR-3$^+$ infiltrating mononuclear cells were exclusively observed in pSS MSGs. IL-17$^+$ inflammatory cells were often observed closely to lymphatic vessels in pSS MSGs, while no IL-17 expression could be detected in normal or NSCS MSGs.

**Conclusions:** In this study, we investigated for the first time lymphvasculogenesis and lymphangiogenic mediators in pSS and demonstrated that they are associated to IL-17 axis in this disease. In addition, we reported increased and anatomically aberrant lymphatic neovascularization in pSS-MSGs. Our results suggest another pathogenic role of IL-17 in pSS, further supporting its therapeutic targeting in this disorder.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2453

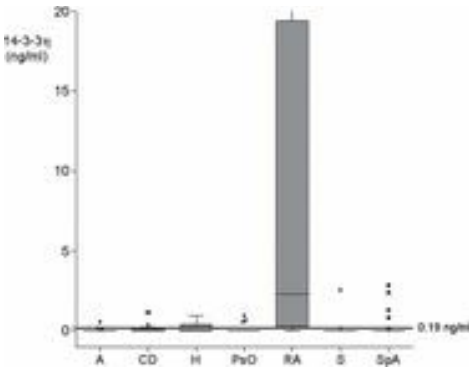
## FRI0009 SERUM 14-3-3 ETA IS AN RA SPECIFIC MECHANISTIC MARKER

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**Background:** 14–3-3$\eta$ is an emerging soluble Rheumatoid Arthritis (RA) biomarker that activates intracellular pathways that lead to the upregulation of inflammatory and joint damage factors. It is reported to be highly specific and sensitive for RA as a diagnostic marker, higher levels are associated with greater joint damage progression risk and 14–3-3$\eta$'s modulation with treatment suggests a role in disease monitoring.

**Objectives:** In this study, we examine the specificity of 14–3-3$\eta$ in an independent, clinically well-characterized cohort of moderate to severe RA and disease control subjects.

**Methods:** Serum 14–3-3$\eta$ levels were measured in a total of 147 patients using the Augurex 14–3-3$\eta$ ELISA. The patient set comprised 36 with RA and 111 controls consisting of 20 with asthma (A), 20 with Crohn's Disease (CD), 12 presumed healthy (H), 16 with psoriasis (PsO), 20 with sarcoid arthritis (S),

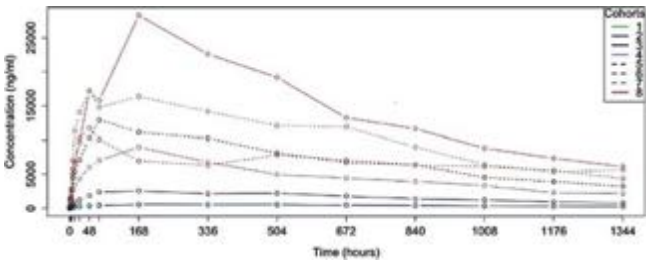


and 23 with spondylarthropathies (SpA). Sample testing was done independently of Augurex. Mann-Whitney testing together with Kruskal-Wallis analysis with the post-hoc Dunn's multiple comparison test was performed to assess group differences. Receiver operator characteristic curve (ROC) analysis was performed to assess the specificity of 14–3-3η for RA.
**Results:** Median (IQR) serum 14–3-3η levels were significantly higher in RA [2.35ng/ml (0.28–19.41)] than all controls [0 (0–0)], $p<0.0001$. ROC curve analysis further underscored this differential expression yielding a significant area under the curve (AUC) of 0.86, $p<0.0001$. At the diagnostic positivity cut-off of $\geq$0.19 ng/ml, the ROC curve delivered a sensitivity of 81% with a corresponding specificity of 84%. Kruskal-Wallis testing revealed that serum 14–3-3η levels were significantly higher in RA in comparison to all other diseases, $p<0.0001$.
**Conclusions:** Serum 14–3-3η is a highly specific RA biomarker. As a novel mechanistic disease factor, 14–3-3η is expected to provide new insights and approaches to RA management and clinical studies.
**References:**
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[2] J Rheumatol 2014; 41(11):2104.
**Disclosure of Interest:** B. Dasgupta Employee of: Janssen R & D, LLC, Y. Cherkas Employee of: Janssen R & D, LLC, S. Lamberth Employee of: Janssen R & D, LLC, K. Hayden Employee of: Janssen R & D, LLC, C. Brodmerkel Employee of: Janssen R & D, LLC, A. Marotta Grant/research support from: Janssen R & D, LLC, M. Curran Employee of: Janssen R & D, LLC
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## FRI0010 PHARMACOKINETICS, SAFETY AND TOLERANCE OF BCD-085, A NOVEL IL-17 INHIBITOR, BASED ON THE RESULTS OF PHASE 1 CLINICAL STUDY IN HEALTHY VOLUNTEERS

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**Background:** BCD-085 is an innovative humanized monoclonal antibody against interleukin-17 with genetically modified Fc- and CDR-regions, aimed to improve treatment outcomes in patients with several autoimmune disorders.
**Objectives:** To study pharmacokinetics and safety of a single SC injection of BCD-085 in ascending doses in healthy male volunteers.
**Methods:** A standard "3+3" first-in-human dose escalation phase 1 clinical study design was used. Different cohorts of healthy male volunteers 18 to 45 years of age received a single subcutaneous injection of BCD-085 in ascending doses (0.05 mg/kg, 0.025 mg/kg, 0.0825 mg/kg, 1.25 mg/kg, 1.75 mg/kg, 2.25 mg/kg and 3.0 mg/kg). After injection all participants underwent 57 days of observation which included assessment of the tolerance, safety, pharmacokinetics and immunogenicity of the studied medicine.
**Results:** 22 healthy male volunteers received a single SC injection of BCD-085. *Pharmacokinetics:* Pharmacokinetic data were available from 21 volunteers with median body weights of 73.6 kg (range; 65.2–84.8). 1 volunteer withdrew from the study due to SAE that was not related to study drug (car accident). Regardless of the cohort changes of BCD-085 concentration were linear: after SC injection it slowly increased and reached the maximum value at the end of the first week. Thus, dose dependency was observed, while the half-life was not dependent on the dose and was 15–22 days. Mean $C_{max}$ of BCD-085 amounted to 12,232.5 ng/ml (median – 10937.0 ng/ml), $T_{max}$ – 156.6 hours (median 168.0), $AUC_{0-t}$ – 8780483.5 (ng/ml)*h (median – 8169096.2 (ng/ml)*hr), $AUC_{0-inf}$ – 4786108616.7 (ng/ml)*h (median – 4275500952.5 (ng/ml)*h), the half-life – 387.9 hours (median – 383.7 hours). *Safety:* In total, 6 adverse events were registered during the study, the toxicity in all these cases was mild (grade 1 in accordance with CTCAE v.4.03). Transaminases increase was more common (9.09%); grade 1 neutropenia occurred just in one volunteer. Single SC injections of BCD-085 were well tolerated with no signs of any local reactions. Immunogenicity assessment did not detect occurrence of anti-drug antibodies.



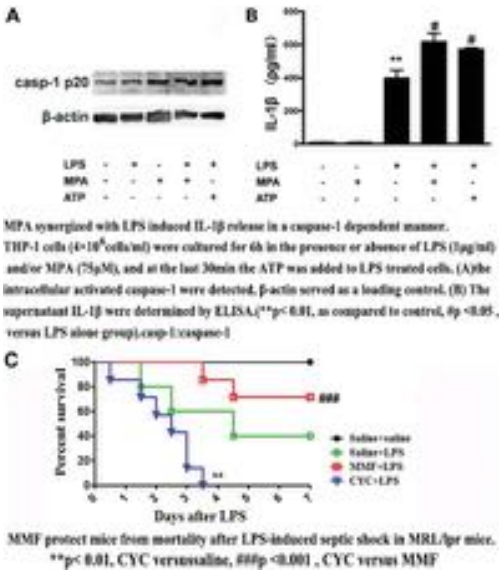
Figgure 1

**Conclusions:** BCD-085 is safe when administered SC in a wide range of doses from 0.05 to 3.0 mg/kg. Pharmacokinetics of a novel IL-17 blocker is standard for therapeutic monoclonal antibodies. Further clinical evaluation of BCD-085 is underway.
**References:**
[1] final study report on phase 1 clinical study of BCD-085 in healthy volunteers.
**Disclosure of Interest:** E. Chernyaeva Employee of: BIOCAD, A. Eremeeva Employee of: BIOCAD, A. Galustyan Grant/research support from: BIOCAD, R. Ivanov Employee of: BIOCAD
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## FRI0011 MYCOPHENOLIC ACID SYNERGIZES WITH LIPOPOLYSACCHARIDE TO INDUCE INTERLEUKIN (IL)-1β RELEASE VIA ACTIVATION OF CASPASE-1 AND PROTECTS MRL/LPR MICE AGAINST MORTALITY INDUCED BY ENDOTOXEMIA

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**Background:** Mycophenolate mofetil (MMF), which inhibits T and B lymphocyte proliferation, is widely used to treat a variety of autoimmune diseases, such as systemic lupus erythematosus (SLE) and lupus nephritis (LN)[1]. Several studies have reported that in lupus nephritis induction therapy, MMF was more effective than intravenous cyclophosphamide (CYC) with a more safety profile [2], but the mechanism is still unclear. We are the first to show that mycophenolic acid (MPA), the active metabolite of MMF, in association with lipopolysaccharide (LPS), is able to promote the secretion of interleukin (IL)-1β[3], which contradicts the traditional conception that immunosuppressants inhibit the secretion of inflammatory factors. This may be related to patients who are treated with MMF exhibiting better clinical outcomes and a lower incidence of infection than patients treated with CYC.
**Objectives:** To investigate the mechanism and significance of MPA synergizing with LPS to induce IL-1β release.
**Methods:** Undiluted human blood, THP-1 cells or monocytes was stimulated with LPS and treated with or without MPA, and the supernatant IL-1β was detected by ELISA. The intracellular protein levels of THP-1cells were measured by Western blot. MRL/lpr mice were treated with saline, MMF or CYC for 2 months, then given an intraperitoneal (i.p.) injection of LPS or saline, the effect, survival and cytokines were observed.
**Results:** We found that MPA alone failed to induce IL-1β, whereas MPA synergized with LPS to increase IL-1β in a dose-dependent manner. MPA did not affect the intracellular p-p65 and pro-IL-1β protein levels. However, MPA augmented LPS-induced IL-1β release by activation of NLRP3 inflammasome (Fig. 1A,B). Ac-YVAD-cmk, the inhibitor of caspase-1, blocked the activation of caspase-1 and subsequently attenuated IL-1β secretion. Both MMF and CYC can prevent the development of LN in MRL/lpr mice. Only MMF can protect mice from mortality after LPS-induced septic shock (Fig. 1C).



MPA synergized with LPS induced IL-1β release in a caspase-1 dependent manner. THP-1 cells ($4\times10^6$cells/ml) were cultured for 6h in the presence or absence of LPS (1μg/ml) and/or MPA (75μM), and at the last 30min the ATP was added to LPS treated cells. (A)the intracellular activated caspase-1 were detected. β-actin served as a loading control. (B) The supernatant IL-1β were determined by ELISA.(**p< 0.01, as compared to control, #p <0.05 , versus LPS alone group).casp-1:caspase-1

MMF protect mice from mortality after LPS-induced septic shock in MRL/lpr mice. **p< 0.01, CYC versussaline, ###p <0.001 , CYC versus MMF
Figure 1

**Conclusions:** MPA synergizes with LPS to induce IL-1β release depended on the activation of caspase-1 rather than the enhanced production of pro-IL-1β. MMF protects mice against mortality induced by LPS. These findings suggest that patients immunosupressed with MMF may have overly activated caspase-1, which causes a more sensitive host defense response to invading germs by promoting the induction of IL-1β.
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**Acknowledgement:** This work was supported by National Natural Science Foundation of China(81501417).
Xuechan Huang and Yi He contribute equally to this study. Corresponding author is Erwei Sun.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5552

## FRI0012 IL-17 IN RHEUMATOID ARTHRITIS BONE MARROW. NOT ONLY TH-17 CELLS

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**Background:** Inflammatory process in bone marrow (BM) observed on MRI scans of rheumatoid arthritis (RA) patients (called bone marrow oedema) together with autoantibodies production was shown to proceed joint destruction in RA. Our previous studies supported the concept that BM actively participate in the pathogenesis of RA by TLR triggered B cell activity (1) and increased number of activated T cells (2).
**Objectives:** In the present study we investigated IL-17 producers in BM.
**Methods:** BM and peripheral blood (PB) samples were obtained from RA and osteoarthritis (OA) patients during total hip replacement surgery. Levels of IL-17AF, IL-17FF, IL-17AA, GMCSF and IL-21 in bone marrow plasma were determined by specific ELISA. Th1/Th2/Th17 proportions were evaluated by flow cytometry. To confirm production of IL-17 in BM immunohistochemistry examination was done. Comparison between the groups of patients were analysed by two-tailed Mann-Whitney U test.
**Results:** We observed increased level of IL-17AF (147±104 pg/ml vs 115±74pg/ml, $p<0,05$) in bone marrow plasma from RA in comparison to OA. In contrast similar levels of IL-17FF were detected in RA BM (94± 115pg/ml) and OA BM plasma (44±66pg/ml). IL-17AA was not detected. Concentrations of both IL-17AF and IL-17FF were higher in BM than in PB. Surprisingly there were no differences between RA BM and OA BM levels of Th-17 related cytokines such IL-21 and GMCSF. We did not observe any statistically significant differences in percentage of IL-17, IFNγ or IL-4 producing lymphocytes in RA BM and OA BM. Immunohistological staining confirmed higher expression of IL-17 in RA BM in comparison to OA BM. We also observed strong IL-17 staining in granulocytes.
**Conclusions:** IL-17AF is overproduced in RA bone marrow. There are two main sources of these cytokine in RA BM: T cells and granulocytes
**References:**
[1] W Rudnicka et al.: Eur J Immunol 2009; 1211–20
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**Acknowledgement:** This work was sponsored by by grant No UMO-2011/03/B/NZ6/05035 from National Science Centre
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4378

## FRI0013 IL-22 INDUCES AN INCREASE IN SFP3 EXPRESSION BY SYNOVIAL FIBROBLASTS IN INFLAMMATORY JOINT DISEASES

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**Background:** Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS) are inflammatory joint diseases (IJD) with different joint remodeling patterns [1]. TNFalfa, IL17 and IL22 indirectly through signaling pathways such as Wnt may play a role in these phenotypes distinctiveness [2,3]. Fibroblast-like synoviocytes (FLS) have been considered an innate immunity component implicated in the switch of an acute and reparable to a chronic and persistent inflammatory process with irreversible tissue damage in that diseases [4].
**Objectives:** The aim of this study was to evaluate the expression of two Wnt pathway extracellular modulators (sFRP3 and DKK1) by FLS of patients with different IJD, in response to IL17, IL22 or TNFalfa. Additionally, we analyze the concentrations of all these proteins directly in the synovial fluid of inflamed peripheral joints.
**Methods:** 25 patients with an IJD diagnosis and the indication of joint infiltration for disease activity, was selected, regardless their systemic treatment. FLS were cultivated from synovial fluid and this were also used to measure the concentrations of DKK1, sFRP3, TNFalfa, IL17 and IL22 by ELISA. DKK1 and sFRP3 levels were dosed in the supernatant of cell cultures after pro-inflammatory stimulation.
**Results:** The concentrations of IL22 and sFRP3 were positively correlated ($r=0.76$; $p<0.01$) in synovial fluid and the highest levels were observed among TNFalfa inhibitors users ($p=0.01$). sFRP3 and DKK1 are constitutively expressed by FLS. Lower values of DKK1 were detected in PsA ($p<0.01$) as well as sFRP3 in AS ($p=0.01$). IL22 was the only cytokine able to increase sFRP3 production by these cells ($p<0.01$). No cytokine was efficient in increasing the expression of DKK1 in this study.

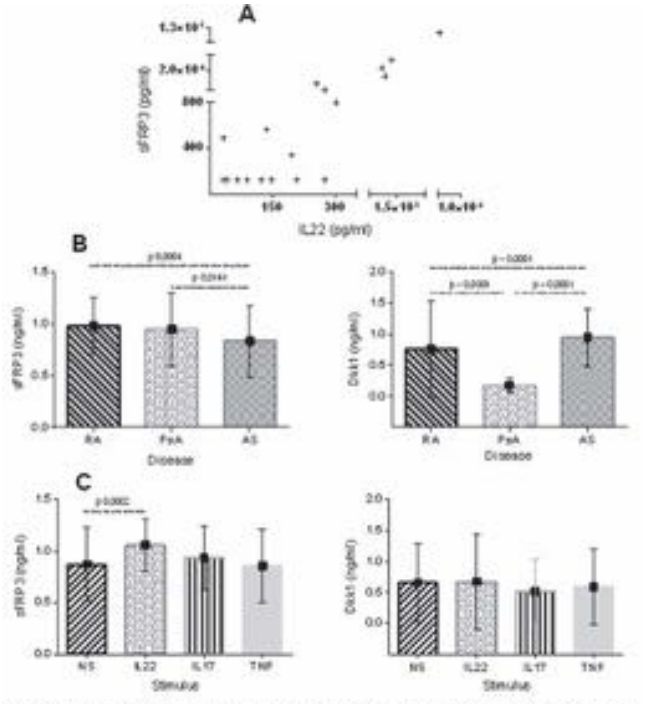



Fig 1 - Correlation between IL-22 and sFRP3 concentrations measured in synovial fluid (A). Concentrations in cell supernatant grouped by different diseases (B). Concentrations in cell supernatant grouped by different stimuli. NS - not stimulated (C). All values are presented as means with their standard deviations.

**Conclusions:** The high positive correlation between IL22 and sFRP3 in the synovial fluid of inflamed joints may be explained by the fact of that cytokine was capable of increasing this modulator production by FLS, in this experiment. Since sFRP3 is a canonical Wnt inhibitor and it blocks the osteoblastogenesis, different responses to IL22 may imply in different patterns of structural damage and joint remodeling.
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**Acknowledgement:** to Research Support Fund of Brazilian Society of Rheumatology
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3053

## FRI0014 MULTIPLEX SCREENING OF CYTOKINES IN THE SEARCH FOR DISEASE ACTIVITY MARKERS OF SLE

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**Background:** There is presently no consensus on how to best measure disease activity in systemic lupus erythematosus (SLE). Available validated measures, such as SLE Disease Activity Index (SLEDAI) and SLE Activity Measure (SLAM), are composite scores that in addition to laboratory tests require investigation by a physician. These scores are insensitive to change and have failed to differentiate treatment responses in clinical trials. It would be an important step forward, for clinical practice and for clinical trials, if one or several biomarkers could be used as proxies for disease activity in SLE.
**Objectives:** Our objective is to evaluate cytokines, in combination with basic laboratory tests, as potential disease activity biomarkers.
**Methods:** In a cross-sectional setting we examined 433 patients with SLE

(fulfilling four or more of the 1982 revised ACR criteria) and 322 age and gender matched population controls. Disease activity was assessed according to both SLEDAI and SLAM by a rheumatologist. Basic laboratory tests and analyses on MSD 30-plex cytokine assay (Mesoscale Discovery, K15054D) were performed on fasting blood samples (total >50 potential biomarkers). The discriminatory power for investigated biomarkers was tested between patients and controls. Spearman correlations with SLAM/SLEDAI scores were calculated among patients.
**Results:** Many potential biomarkers discriminated between patients and controls. Best discriminatory power was observed for TNF-α ($p=7x10^{-63}$), IL-6 ($p=2.5x10^{-40}$), orosomucoid ($p=7.1x10^{-38}$), plasma (P)-albumin ($p=1.6x10^{-36}$) and sedimentation rate (SR) ($p=5.6x10^{-34}$). The strongest correlations with SLEDAI/SLAM were observed for TNF-α (Spearman $\rho=0.32$, $p=6.0x10^{-12}$ for SLEDAI and Spearman $\rho=0.34$, $p=5.0x10^{-13}$ for SLAM), and for P-albumin (Spearman $\rho=-0.33$, $p=9.0x10^{-13}$ for SLEDAI and Spearman $\rho=-0.31$, $p=5.0x10^{-11}$ for SLAM). As SR is part of SLAM, expected positive correlations were observed (Spearman $\rho=0.27$, $p=7.7x10^{-9}$ for SLEDAI and Spearman $\rho=0.48$, $p=4.0x10^{-25}$ for SLAM).
**Conclusions:** Of more than 50 investigated biomarkers TNF-α was the best discriminator between SLE patients and controls. Furthermore TNF-α was the biomarker, which correlated best with disease activity. These correlations were further improved by the ratio between TNF-α and P-albumin. We propose that the TNF-α/P-albumin ratio merits further investigations as a clinically useful biomarker for diagnostic and surveillance purposes in SLE.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3563

## FRI0015 LEUCINE RICH ALPHA-2 GLYCOPROTEIN (LRG) IS INVOLVED IN PULMONARY FIBROSIS BY ENHANCING TGF-β SIGNALING IN FIBROBLASTS

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**Background:** Lung diseases related to collagen disorder are often accompanied by fibrosis and TGF-β is one of the essential mediators in tissue fibrosis. Leucine rich alpha-2 glycoprotein (LRG) is a novel serum protein that is increased in patients with inflammatory diseases, such as rheumatoid arthritis. LRG expression is increased in inflamed tissues, suggesting that the molecule is involved in the pathogenesis of the diseases. Since LRG has recently been reported as a modulator of TGF-β signals [1] [2], LRG may play a role in tissue fibrosis.
**Objectives:** In this study, we aimed to investigate the involvement of LRG in a murine model of lung fibrosis.
**Methods:** Wild type mice and LRG knockout (KO) mice were intratrachally treated with bleomycin and fibrosis were evaluated 21 days after the treatment. At the time of sacrifice, the lungs were harvested and processed for histological examination using hematoxylin and eosin staining, detection of collagen fibers using azan staining, and immunohistochemistry. Furthermore, the effect of LRG on TGF-β signaling was investigated using L929 mouse fibroblast cell line.
**Results:** Intratracheal administration of bleomycin increased LRG protein levels in bronchial alveolar lavage fluids (BALF) and lung tissues. When compared to wild type mice, fibrosis was markedly inhibited in LRG knockout (KO) mice, as evalulated by azan staining and by hydroxyproline assay. Although there was no significant difference in BALF TGF-β levels between WT and LRG KO mice, phosphorylation and nuclear translocation of Smad2 protein were attenuated in the lung of LRG KO mice. In vitro experiments using L929 revealed that LRG enhanced TGF-β-induced Smad2 phosphorylation and the expression of downstream genes, such as plasminogen activator inhibitor-1 (PAI-1) and alpha smooth muscle actin (SMA). Furthermore, TGF-β-induced Smad2 phosphorylation was enhanced by exogenous LRG protein in a dose-dependent manner. Although LRG has been reported to interact with endoglin, an accessory receptor of TGF-β, knockdown of endoglin showed no effect on LRG-induced enhancement of Smad2 activation.
**Conclusions:** These data demonstrate that LRG enhances TGF-β-induced activation of Smad2 cascade in fibroblasts leading to promote fibrosis in murine model of lung fibrosis.
**References:**
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[2] Oncotarget 2015 May 10; 6 (13):11009–22
**Acknowledgement:** We wish to thank K. Omori and Y. Maeda for their advice and expertise, E. Harada and R. Nishi for their technical assistance and the staff of Animal Bioscience Department of the Nagahama Institute of Bio-Science and Technology for their help in histopathological evaluation.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4508

## FRI0016 REGULATION OF OSTEOCLAST DIFFERENTIATION BY ARGINASE I

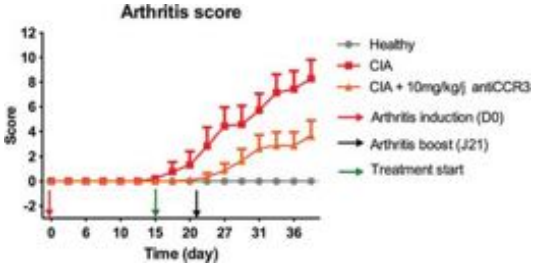
J. Brunner[1], M. Hofamann[2], V. Saferding[2], K. Redlich[2], J.S. Smolen[2], G. Schabbauer[1], S. Blüml[2]. *[1]Institute for Physiology; [2]Rheumatology, Medical University Vienna, Vienna, Austria*

**Background:** Osteoclasts are giant, multi-nucleated cells that derive from the monocyte-macrophage linage and are involved in bone turnover. They are further known as the main effector cells for development of age-related osteoporosis.
**Objectives:** While the role of Arginase I within certain myeloid lineages such as macrophages is well appreciated, its role within osteoclasts is relatively unknown. Our aim was therefore to investigate the importance of the enzyme in the context of osteoclastogenesis.
**Methods:** We analyzed osteoclastogenesis of C57BL/6J or BALB/c wildtype cells in vitro in the presence and absence of recombinant Arginase I (recARG1) and its inhibitor nor-NOHA. This was complemented via qPCR analysis of marker genes. We further investigated the potential of the enzyme to induce cell death via flow cytometry analysis of 7-AAD and Annexin V.
**Results:** In osteoclast differentiation assays, we show that Arginase I is strongly downregulated during osteoclastogenesis, suggesting involvement of this enzyme in OC differentiation. We further show that addition of recArgI completely abolishes osteoclast formation without inducing cell death. The inhibitory effect of recArgI on osteoclastogenesis was completely dependent on the enzymatic function, as no decrease in osteoclast formation could be observed during combined addition of recArgI and its specific inhibitor nor-NOHA. We further demonstrate that recArgI specifically inhibits RANKL-mediated terminal differentiation of OCs, but has no effect on MCSF dependent generation of OC precursors. In line, we could show that addition of recombinant Arginase I negatively regulated the expression of classic RANKL induced osteoclastic marker genes such as TRAP and Cathepsin K.
**Conclusions:** We propose that recArgI might be a potent inhibitor of osteoclastogenesis and could prove itself to be useful for the treatment of osteoclast driven diseases, such as osteoporosis.
**Disclosure of Interest:** None declared
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## FRI0017 PHARMACOLOGICAL BLOCKADE OF CCR3 REDUCES COLLAGEN-INDUCED ARTHRITIS SEVERITY

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**Background:** Chemokines are key pathophysiological mediators in the early phase of arthritis. Eotaxin-1 (Paquet and al., 2012) and its receptor, CCR-3 (CC Chemokine Receptor 3) (Haas and al., 2005), were previously shown to be highly expressed in the course of experimental arthritis. In human, CCR-3 positive monocytes are more abundant in the synovial fluid of arthritic patients than in healthy ones (Katschke and al., 2001). Moreover, RANTES, another chemokine with pathophysiological relevance to arthritis, is also a ligand of CCR-3, further suggesting that CCR-3 could be a potential therapeutic target for joint diseases.
**Objectives:** The main obective of this project was to study consequences of CCR-3 inactivation by a pharmacological antagonist in collagen-induced arthritis.
**Methods:** CIA was induced in 20 DBA/1J mice by intradermal injection of 100mg of bovine type II collagen in CFA at the basis of the tail, with a booster injection of 50mg by day 21. From day 15, mice were administered daily with antagonist of CCR-3 at a concentration of 10 mg/kg/day (i.p). Mice were regularly weighed and evaluated for the severity of arthritis with an arthritic score and by measuring hindpaw oedema by plethysmography. Mice were sacrificed at day 41, and histological analysis was performed on ankle joints after HES and safranin-O fast green staining. At that time, serum levels of IL-6 and IL-17F were measured by the multiplex technology.
**Results:** The clinical parameters showed that mice treated with a specific antagonist of CCR-3 develop less severe arthritis (respective clinical score 3.89 ± 1.25 vs 8.57 ± 1.63). Histological analyzes indicated that antagonist reduced the intensity of inflammatory process and limits cartilage degradation in arthritic joints. Blood level of IL-6 and IL-17F cytokines were reduced in mice treated with antagonist of CCR-3 compared to untreated arthritic mice.




**Conclusions:** Thus, our study shows that CCR-3 has an important role in arthritis development and designates it as a potential therapeutic target.

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## FRI0018 SP1 INTERFERENCE PREVENTS JOINT DESTRUCTION OF RA THROUGH INHIBITORY EFFECTS OF GLIOSTATIN AND MATRIX METALLOPROTEINASE-3

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**Background:** Gliostatin (GLS) has angiogenic and arthritogenic activities, which plays an important role in joint destruction as well as matrix metalloproteinase (MMP)- 3 in rheumatoid arthritis (RA). We previously reported that the expression of GLS in serum from RA patients was significantly correlated with disease activity, and that the expression of MMP-3 was induced by GLS in RA fibroblast-like synoviocytes (FLSs). The human GLS and MMP-3 gene promoter contains consensus binding sites for the DNA binding protein Sp1. Here we examined whether Sp1 was necessary for GLS and MMP-3 productions in RA.
**Objectives:** The purpose of this study was to investigate whether the effect of Sp1 interference using the Sp1 inhibitor mithramycin and RNA interference on GLS and MMP-3 productions in FLSs derived from patients with RA.
**Methods:** FLSs were cultured from synovial specimens obtained from 10 RA patients during total knee arthroplasty, and were stimulated by tumour necrosis factor (TNF)-α with or without treatment of mithramycin. The gene and protein expressions of GLS and MMP-3 were studied using the quantitative reverse-transcription polymerase chain reaction (RT-PCR) and an enzyme immunoassay. Intracellular signalling pathway activation was determined by a small interfering RNA (siRNA) transfection.
**Results:** GLS and MMP-3 productions were suppressed in FLSs by siRNA against Sp1 transfection. TNF-α (1 ng/ml) significantly increased GLS and MMP-3 expressions in RA FLSs; these effects were reduced by pre-treatment with mithramycin (300 nM).
**Conclusions:** Our results showed that pretreatment of mithramycin and Sp1 silencing resulted in a significant suppression of GLS and MMP-3 productions in TNF-α-stimulated FLSs compared to controls. The present study indicates that expression of the GLS and MMP-3 gene is mediated, in part, through the transcription factor Sp1.As physiological concentrations of mithramycin can regulate GLS and MMP-3 productions in RA, mithramycin is a promising candidate for anti-rheumatic therapy.
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## FRI0019 DIVERGENT EFFECTS OF FREE FATTY ACIDS ON CELLS OF BONE METABOLISM

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**Background:** Adipose tissue secretes numerous bioactive substances, which contribute to inflammation. Chronically elevated free fatty acid (FFA) levels are known to be associated with numerous inflammatory cardiovascular and metabolic diseases such as atherosclerosis, coronary heart diseases and type 2 diabetes. Conversely, inflammation can contribute to bone loss. FFA may therefore be a contributing factor in bone loss in osteoarthritis (OA) and/or rheumatoid arthritis (RA). Interestingly, obesity is associated with a higher risk of OA also in non-weight bearing joints and increased amounts of visceral fat are associated with lower bone density.
**Objectives:** To test the hypothesis that FFA affect cells of bone metabolism in the context of rheumatic diseases in a way that promotes bone loss.
**Methods:** Primary osteoblasts (OB) were isolated from cancellous bone of OA and RA patients undergoing knee joint surgery. Osteoclasts (OC) were differentiated from peripheral blood mononuclear cells (PBMC). OB and OC were stimulated with the saturated FFA palmitic acid (PA) and the unsaturated FFA linoleic acid (LA). Immunoassays were used to quantify protein secretion. mRNA expression levels were quantified by real-time PCR. Mineralization activity was quantified using Alizarin Red S staining, differentiated OC were quantified by counting TRAP-positive multinuclear cells. Toll-like receptor (TLR) 4 and TLR2 were blocked by neutralizing antibodies.
**Results:** Both PA and LA increased the secretion of the proinflammatory cytokine IL-6 (up to 9-fold) and the chemokines IL-8 (up to 221-fold), GRO-a (from below detection level to detectable levels) and MCP-1 (up to 16-fold). The degree of response was highly dependent upon the patient. RANKL as well as OPG, important regulators of osteoclastogenesis and OC activity, remained unaffected by FFA on protein and mRNA level. OB activity markers alkaline phosphatase (ALP) and collagen type I as well as markers of OB differentiation (e.g. osteocalcin) also remained unchanged after FFA stimulation. PA-induced IL-8 secretion by OB could be significantly reduced by TLR4 blockade (by 93%), while blocking TLR2 had no effect. Upon stimulation with PA and LA, secretion of IL-8 by RA OC was increased and MMP-9 reduced and the number of TRAP positive multinuclear cells decreased (by around 50%). Further markers of osteoclast activity (CLCN7, CTSK, TCIRG) remained unchanged.
**Conclusions:** The effect of FFA on cells of bone metabolism appears to be divergent: While FFA promote a pro-inflammatory phenotype in OB and may thus indirectly contribute to bone loss, the effects on OC mainly suggest an inhibitory effect on bone resorption.
**Disclosure of Interest:** None declared
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## FRI0020 BMP-2 AND TGF-B INHIBIT IL-34 EXPRESSION IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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**Background:** Interleukin-34 (IL-34) is a pro-osteoclastogenic cytokine, up-regulated by pro inflammatory cytokines, with a recently described role in rheumatoid arthritis (RA). TGF-b and BMP-2 are two members of the TGF-b family, whith an opposit role to the pro-inflammatory cytokines and that are also involved in rheumatoid synovitis.
**Objectives:** The present study aimed to assess the IL-34 expression in response to two members of the TGF-b family, TGF-b1 and BMP-2, in synovial fibroblasts from RA patients.
**Methods:** The IL-34, TGF-β1 and BMP-2 productions were measured in synovial fluids by ELISA. The IL-34 mRNA levels were quantified by qPCR in human synovial fibroblasts and murine mesenchymal stem cells (MSCs). Pharmacological inhibitions were used to determine the involvement of ALK1 and ALK5 downstream TGF-b1 and BMP-2.
**Results:** IL-34, TGF-b1 and BMP-2 were expressed in synovial fluids from RA patients. We found a significant correlation between IL-34 and TGF-b1 expressions. Levels of both IL-34 and TGF-b1 were thus correlated with the total leukocyte counts in the synovial fluids. TGF-b1 and BMP-2 decreased Il-34 expression in the synovial fibroblasts or in mMSC in a dose/time dependent manner through respectively ALK5 and ALK1 pathways. In addition, TGF-b1 antagonized TNFa-induced IL-34 gene expression.
**Conclusions:** This work identifies TGF-b1 and BMP-2 as potent inhibitors of IL-34 expression in RA synovial fibroblasts. These cytokines, as upstream inhibitors of IL-34, may thus contribute to antagonize inflammation and bone erosions in RA.
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## FRI0021 CALPROTECTIN LEVELS CORRELATE WITH INFLAMMATION IN EARLY RA BEFORE DMARD TREATMENT AND AFTER 12 MONTHS OF TREATMENT

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**Background:** Calprotectin (MRP8/MRP14, S100A8/A9) is a major leukocyte protein previously shown to be associated with disease activity in patients with established rheumatoid arthritis (RA), and some studies indicate that it may be a more accurate measure of joint inflammation than erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP).
**Objectives:** To compare the associations of calprotectin, ESR and CRP to clinical and ultrasound measures of inflammation in patients with early RA, both before and after 12 months of aggressive disease-modifying antirheumatic drug (DMARD) treatment.
**Methods:** RA-patients (n=238) who fulfilled the 2010 ACR/EULAR classification criteria were recruited to the ARCTIC trial between 2010 and 2013. All patients had symptom duration from first swollen joint <2 years and were DMARD-naïve with indication for DMARD treatment. Calprotectin in plasma was analyzed in 217 patients at baseline and 166 patients at 12 months by ELISA. Ultrasound (US) inflammation was evaluated using a standardized protocol with semi-quantitative scoring 0–3 for grey-scale (GS) and power Doppler (PD) in 32 joints (1). Clinical inflammation was assessed by 44 swollen joint count (SJC44), Ritchie Articular Index (RAI), ESR and CRP. Disease activity score (DAS) was calculated. Cross-sectional relationships were assessed by Spearman's correlations.
**Results:** A total of 217 patients were included: 61% female, 71% RF positive, 82% ACPA positive, mean (SD) age 53.5 (13.7) years, mean DAS 3.46 (1.17), median [25, 75 percentile] disease duration 5.7 [2.8, 10.4] months. At 12 months mean DAS was 1.25 (0.72); 74% were in remission according to DAS, 17% low, 9% moderate and 0% high DAS. The median baseline/12 month calprotectin was 1028 [567, 2158]/485 [293, 802] μg/L, ESR 19 [11, 31]/9 [5, 14] mm/h and CRP 7 [3, 18]/3 [1, 5] mg/L. Calprotectin was significantly correlated to clinical, laboratory and US measures of inflammation before treatment onset (table). After 12 months of treatment, calprotectin had a weaker, but statistically significant correlation to US scores, while no association between ESR/CRP and US scores was found.

Table 1. Spearman's correlation coefficients

| | Baseline (n=217) | | | 12 months (n=166) | | |
|---|---|---|---|---|---|---|
| | Calprotectin | CRP | ESR | Calprotectin | CRP | ESR |
| Calprotectin, μg/L | NA | 0.66** | 0.51** | NA | 0.33** | 0.43** |
| CRP, mg/L | 0.66** | NA | 0.63* | 0.33** | NA | 0.26** |
| ESR, mm/h | 0.51** | 0.63** | NA | 0.43** | 0.26** | NA |
| SJC44 (0–44) | 0.30** | 0.37** | 0.24** | 0.10 | 0.12 | 0.11 |
| RAI (0–78) | 0.21* | 0.32** | 0.16* | 0.10 | 0.16* | 0.12 |
| Ultrasound GS-score | 0.45** | 0.41** | 0.29** | 0.20* | 0.08 | –0.01 |
| Ultrasound PD-score | 0.42** | 0.35** | 0.35** | 0.26** | –0.02 | 0.03 |
| Ultrasound total score | 0.46** | 0.40** | 0.33** | 0.22* | 0.07 | 0.00 |

*p<0.05, **p<0.001.

**Conclusions:** Calprotectin was correlated to inflammation assessed by ultrasound before onset of DMARD treatment, and the association was also present after 12 months of DMARD treatment. The data support that calprotectin might be of interest when assessing disease activity in different stages of RA.
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## FRI0022 INFLAMMATORY STATUS AND SERUM URIC ACID LEVELS DETERMINE HIGH-DENSITY LIPOPROTEIN–CHOLESTEROL LEVELS IN A NON-RHEUMATIC POPULATION

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**Background:** In inflammatory disorders, highest incidence of cardiovascular (CV) events paradoxically occurs at lower lipid levels (1), especially in the case of high-density lipoprotein cholesterol (HDLc). Current data in general, non-inflammatory population suggest a similar but milder phenomenon (2). Serum uric acid (SUA) levels appear to determine the inflammatory status of the subjects, even in normouricemia (3).
**Objectives:** To assess whether inflammatory status and SUA levels associate with HDLc levels in a hypertensive population aged 65 years or older.
**Methods:** Retrospective analysis of the FAPRES study (cross-sectional study aimed at determining the prevalence of atrial fibrillation in hypertensive patients aged 65 years or older). Inflammatory status was considered based on serum leukocytes levels. A comparison between serum lipids levels (HDLc, low-density lipoprotein-cholesterol [LDL], total cholesterol [TCh], triglycerides [TG]) and different tertiles of leukocytes and SUA has been performed using ANOVA. In case of statistically significant differences, a multivariate linear regression model was built for each lipid parameter in order to adjust for potential confounders.
**Results:** A total of 1,003 patients were recruited, mean aged 72.9 years (SD±5.8), 52.5% females. In the sample median (±SD) leukocytes, SUA and HDLc were 6,719.6/mm$^3$ (±1773.1), 5.2 mg/dL (±1.1), and 52.8 mg/dL (±13.1), respectively. Table shows the distribution of lipids across leukocytes and SUA tertiles: lower HDLc and higher TG levels were found in upper tertiles of both leukocytes and SUA, with no differences on TCh and LDLc. After adjusting for potential confounder (age, gender, CV risk factors, renal failure, body mass index, use of diuretics or statins), an independent, inverse association of both leukocytes (β=-0.001, p=0.02) and SUA (β=-1.054, p=0.03) with HDLc levels was confirmed. For TG levels, an independent, direct association with SUA (β=8.254, p=0.004) was also found, as well as a trend for leukocytes (β=0.003, p=0.06).

Table 1

| Mean (±SD) | TCh | p | HDLc | p | LDLc | p | TG | p |
|---|---|---|---|---|---|---|---|---|
| Leukocytes | | | | | | | | |
| <5900 | 197.8 (±41.3) | 0.15 | 54.3 (±13.2) | 0.006 | 121.1 (±35.9) | 0.20 | 115.2 (±48.6) | 0.03 |
| 5900–7200 | 195.6 (±35.0) | | 53.1 (±12.7) | | 118.7 (±29.9) | | 132.7 (±88.3) | |
| >7200 | 191.7 (±41.7) | | 50.8 (±12.6) | | 116.1 (±34.7) | | 129.0 (±54.8) | |
| SUA | | | | | | | | |
| <4.7 | 198.1 (±40.5) | 0.32 | 56.6 (±13.8) | <0.001 | 119.6 (±36.6) | 0.60 | 111.6 (±47.9) | 0.001 |
| 4.7–5.8 | 194.3 (±36.3) | | 54.8 (±12.9) | | 117.5 (±32.5) | | 117.5 (±47.0) | |
| >5.8 | 191.7 (±37.1) | | 49.7 (±10.8) | | 116.6 (±31.3) | | 135.6 (±90.7) | |

**Conclusions:** In a non-rheumatic, hypertensive population aged 65 years or older, both inflammatory status and SUA levels showed an inverse, independent association with HDLc, following current data on patients with inflammatory disorders. This phenomenon might help to define a pro-atherogenic profile on the general population.
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## FRI0023 EFFECTS OF IL-33/ST2 AXIS ON CYTOKINE GENE EXPRESSION AT THE SITE OF ACUTE INFLAMMATION

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**Background:** Acute inflammation is an early response to a cell injury. Interleukin (IL)-33 is a new member of IL-1 cytokine family. It was discovered that IL-33 and its receptor ST2 have a role not only in Th2 mediated diseases, as firstly reported, but also in other diseases, such as rheumatoid arthritis, autoimmune uveitis, and squamous cell carcinoma. Effects of IL-33/ST2 axis in acute inflammation are still not completely understood.
**Objectives:** The aim of this study was to examine effects of IL-33/ST2 axis on cytokine gene expression at the site of acute inflammation.
**Methods:** Male mice were divided in groups: wild-type control group (WT-C), wild-type inflammatory group (WT-I), ST2 knockout control group (KO-C), and ST2 knockout inflammatory group (KO-I). Acute inflammation was induced in WT-I and KO-I by intramuscular injection of turpentine oil, whereas animals in

WT-C and KO-C were injected with saline. Mice were euthanized after 12 hours, and the treated tissue was collected for histopathological analysis, and gene expression determination (qRT-PCR) of IL-33, ST2 receptor, tumor necrosis factor alpha (TNF-alpha), IL-12p35, IL-23p19, and transforming growth factor-beta (TGF-beta). All experimental procedures were approved by the University of Belgrade School of Medicine Ethics Committee.
**Results:** Acute inflammation was histopathologicaly confirmed in WT-I and KO-I. IL-33 in the treated tissue was significantly higher in inflammatory groups, WT-I and KO-I, when compared to WT-C and KO-C, respectively. However, IL-33 was significantly higher in KO-I than in WT-I. ST2 significantly increased in inflamed tissue of wild-type mice, in comparison to WT-C. TNF-alpha, IL-12p35, and IL-23p19 in the treated tissue significantly increased in WT-I and KO-I, when compared to their corresponding control groups WT-C and KO-C. TGF-beta in the treated tissue was significantly higher in KO-I than in WT-I, whereas it did not significantly differ between WT-C and KO-C.
**Conclusions:** Results of this study indicated that IL-33/ST2-axis affected gene expression of cytokines at the site of acute inflammation, i.e. gene expression of IL-33, and anti-inflammatory cytokine TGF-beta. ST2 gene expression increased in acutely inflamed tissue, indicating importance of IL-33/ST2 axis in acute inflammation.
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## FRI0024 OLIVE-DERIVED OLEUROPEIN AS A POTENTIAL TREATMENT FOR BONE AND CARTILAGE AGE-RELATED DISORDERS

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**Background:** Oleuropein is the major glycoside component in olives and is well known to have several beneficial effects on human health [1]. However, the mechanisms associated with its potential pharmacological properties are not clear yet. Human bone marrow mesenchymal stem cells (hMSCs) exhibit an age-dependent reduction in osteogenesis and an increased propensity toward adipocyte differentiation. This switch has been associated with different bone disorders characterized by reduced bone formation and increased bone marrow fat accumulation [2,3]. Connexin 43 (Cx43) is an integral membrane protein that forms gap junction channels (GJs) and it is implicated in multiple cellular functions including cellular differentiation and control of bone and cartilage remodelling.
**Objectives:** The aim of this study was to test if oleuropein could act as an adipogenic suppressor in order to promote cartilage and bone regeneration through a Cx43-dependent mechanism.
**Methods:** Human mesenchymal stem cells were obtained from bone marrow donors. Cells were grown in α-minimum essential medium (MEM) and differentiation was initiated before achieving confluence with specific differentiation media in the presence of different concentrations of oleuropein. Adipogenesis and osteogenesis was held in culture chambers for 21 days; chondrogenesis was performed as a micromass culture for 30 days. Cellular differentiation was evaluated using histological stains: Oil Red O for adipogenesis; Alizarin Red for osteogenesis; Toluidine Blue and Safranin O/Fast Green for chondrogenesis. Scrape loading assays and lucifer yellow were used to study the cellular communication through gap junction (GJ) and hemichannels formed by Cx43. Western-blot and immunohistochemistry (IHC) assays were performed to study the levels of Cx43 protein.
**Results:** hMSCs treated with oleuropein showed a two-folded decrease in adipogenic differentiation, while osteogenesis was significantly increased. Micromasses cultured in chondrogenic medium using 10 μM of oleuropein showed a more intense toluidine blue and Safranin O stain, suggesting an increase in chondrogenesis. Real-Time qPCR, western blot analysis and scrape loading assays showed changes in the levels of Cx43 and dye transference through GJ channels when the hMSCs were grown in the presence of oleuropein.
**Conclusions:** Our results suggest that oleuropein via Cx43 and GJ intercellular communication increases the propensity towards osteogenesis and chondrogenesis, reducing adipocyte differentiation. Our preliminary assay indicates that oleuropein may represent a potential therapeutic target for cartilage and bone age-related disorders such as osteoarthritis in order to promote cartilage and bone regeneration.
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## FRI0025 NO REACTIVATION OF DORMANT MYCOBACTERIUM TUBERCULOSIS IN HUMAN IN VITRO GRANULOMA MODEL AFTER ANTI-IL-17A TREATMENT, IN CONTRAST TO ANTI-TNFα TREATMENT

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**Background:** IL-17A inhibition has shown significant efficacy in the treatment of psoriasis, psoriatic arthritis and ankylosing spondylitis. Blocking critical mediators of innate and adaptive immunity may carry the risk of an increased susceptibility to infections. While *Mycobacterium tuberculosis* infections can be an important complication of anti-TNFα therapies, the role of the Th17/IL-17 pathway in host resistance to this intracellular pathogen is less clear. A comparison of tool antibodies neutralizing TNFα or IL-17A in an acute murine *M. tuberculosis* infection model, confirmed the importance of TNFα in host resistance to *M. tuberculosis*, and highlighted that anti-IL-17A treatment for four weeks *in vivo* does not impair immunity to this intracellular pathogen[1].
**Objectives:** To investigate the effect of adalimumab (anti-TNFα antibody) and secukinumab (anti-IL-17A antibody) on *M. tuberculosis* dormancy and reactivation, we utilized a novel *in vitro* human 3D microgranuloma model[2].
**Methods:** Human peripheral blood mononuclear cells were infected with *M. tuberculosis*. Dormant mycobacteria exhibited the following characteristics: (1) loss of acid-fastness, (2) accumulation of lipid bodies, (3) development of rifampicin-tolerance, and (4) gene expression changes[2]. We measured Auramine-O and Nile red staining indicative of *M. tuberculosis* membrane acid fastness and accumulating lipid bodies, respectively, and also investigated rifampicin resistance. In this *in vitro* human 3D microgranuloma model we studied the anti-TNFα antibody adalimumab at 10 ng/ml, and the IL-17A antibody secukinumab at 10, 100, and 1000 ng/ml.
**Results:** *M. tuberculosis* from granulomas treated with anti-TNFα antibody (adalimumab) showed increased staining for Auramine-O, decreased Nile red staining, and decreased rifampicin resistance, indicating *M. tuberculosis* reactivation. In contrast, anti-IL-17A antibody (secukinumab) treatment was comparable to control treatment indicating that the drug did not trigger *M. tuberculosis* reactivation in human microgranuloma *in vitro*.
**Conclusions:** Overall, these results confirm the importance of TNFα in host resistance to *M. tuberculosis* infection, and highlight that anti-IL-17A treatment *in vitro* does not reverse *M. tuberculosis* dormancy in this human granuloma model, in accordance with available clinical data[3,4].
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## FRI0026 A CYTOKINE-MEDIATED BIOLOGICAL BASIS FOR FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

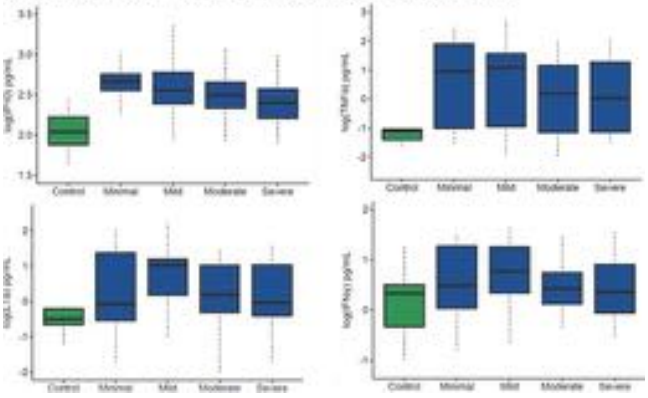
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**Background:** Fatigue is a common and problematic symptom in many chronic diseases including primary Sjögren's Syndrome (pSS).[1,2] Although the pathophysiological basis of fatigue is not fully understood and no biomarkers have yet been identified, emerging data implicates inflammatory pathways and immune dysregulation as potential mechanistic components.[3,4]
**Objectives:** The aim of this study is to investigate the relationship between cytokine levels and patient-reported levels of fatigue, using pSS as an example of a chronic immunological condition.
**Methods:** Blood levels of 22 cytokines were measured in 161 patients with pSS from the UK Primary Sjögren's Syndrome Registry (UKPSSR) and 28 healthy non-fatigued controls.[5] Differences between cytokines in cases and controls were evaluated using Wilcoxon test. Patient-reported scores for fatigue were evaluated,

classified according to severity, and compared with cytokine levels using ANOVA. Logistic regression was used to determine the most important predictors of fatigue levels.

**Results:** 13 cytokines were significantly higher in pSS patients compared to healthy controls, with a $p \leq 0.0001$ for 8 of these. Levels of four pro-inflammatory cytokines IP-10 (p=0.019), TNF-$\alpha$ (p=0.046), LT-$\alpha$ (p=0.034) and INF-$\gamma$ (p=0.022) decreased with increasing fatigue in the pSS cases. Serum levels of IFN-$\gamma$ and IP-10, and pain and depression scores were the best predictors of fatigue level with correct predictions of fatigue level in 67% of cases when these 4 parameters were used.

**Fig. 1a-d. Box-plot showing median cytokine levels and interquartile ranges for a) IP-10, b) TNF-α, c) LT-α, and d) IFN-γ in controls and pSS fatigue groups.** In all four cases the levels of anti-inflammatory cytokines are significantly higher in pSS patients. In addition, all four show an inverse relationship between fatigue severity and cytokine levels. Fatigue levels fall with increasing levels of the four cytokines.



**Conclusions:** 4 pro-inflammatory cytokines decrease as fatigue level increases in pSS patients. Research into anti-inflammatory pathways and cytokines may be insightful in understanding the pathophysiological basis of fatigue. Cytokines, pain and depression appear to be the most powerful predictors of fatigue. Further study is required to characterise the complex biochemical cascades underlying fatigue in pSS and other chronic conditions, as well as the influence of potential clinical confounding factors such as pain and depression

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## FRI0027 THE INFLAMMATORY PATHOLOGY OF LUPUS NEPHRITIS IS SIGNIFICANTLY INDUCED WITH PSYCHOSOCIAL STRESS, SUPPRESSED WITH EXERCISE, AND CORRELATES WITH TNF-ALPHA AND MCP-1 EXPRESSION IN A MURINE MODEL

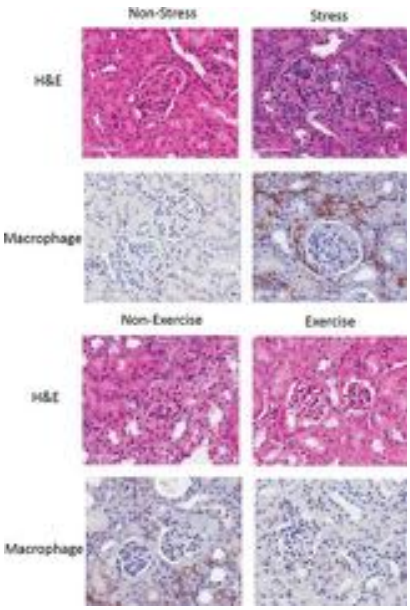
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**Background:** Studies incorporating either regular exercise or stress modification programs have been efficacious in influencing the clinical disease course of systemic lupus erythematosus (SLE). We have previously demonstrated in mice that daily, moderate exercise limits inflammation systemically and that repeated social stress stimulates proinflammatory responses.

**Objectives:** To determine if daily moderate exercise (DME) or psychosocial stress can significantly affect chronic autoimmune-mediated inflammation, we examined the NZM2410 mouse model of lupus nephritis, which spontaneously develops severe, early-onset glomerulonephritis at 22–40 weeks of age.

**Methods:** All mice were removed from the study when experimental removal criteria was reached [blood urea nitrogen (BUN)>50 $\mu$g/mL; weight loss>20%]. The DME protocol consisted of daily 45 min treadmill walks at moderate intensity (8 m/min) beginning at 18 weeks of age. To disturb the social order within an established social hierarchy, an aggressive intruder was introduced to induce repeated social disruption stress (SDR). SDR was performed daily for 6 consecutive days beginning at 20 weeks of age. When SDR mice met experimental removal criteria, an age-matched control counterpart was selected at random for comparative analysis. Kidney tissue and serum were collected at experimental endpoint. Multi-plex ELISA measurements of cytokine expression were performed on serum samples.

**Results:** Glomerulonephritis was enhanced with SDR, but significantly improved with DME, as indicated by IgG and C3 complex deposition. Histopathological examination of renal tissue showed glomerular hypercellularity and hyperplasia of the Bowman's capsule. Furthermore, BUN and weight measurements showed a 42% improvement with DME at 43 weeks of age. Immunohistochemical analysis and digital image quantitation of macrophage-mediated inflammatory responses in the kidney revealed a significant induction with SDR and suppression with DME. Additionally, serum cytokine analysis showed up-regulation of IL-5, IL-6, IL-10, and TNF-$\alpha$ with SDR and in older NZM2410 mice relative to younger mice and wild-type controls. While levels of IL-6 were not reduced, expression of IL-5, IL-10, and TNF-$\alpha$ was suppressed with DME. Since TNF-$\alpha$ induces monocyte chemoattractant protein-1 (MCP-1) secretion, MCP-1 expression was measured and demonstrated a reduction with DME and enhancement following SDR.




**Conclusions:** Our data suggests that renal histopathology can be modified via exercise and stress reduction by suppressing TNF-$\alpha$ induction and expression of MCP-1. Thus, stress reduction and moderate exercise could be used therapeutically in adjunct to pharmacological therapy to help control the chronic inflammation associated with lupus nephritis and other autoimmune diseases.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4813

## FRI0028 VASCULAR ENDOTHELIAL GROWTH FACTOR AS AN AID TO DIAGNOSIS OF GIANT CELL ARTERITIS

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**Background:** Giant Cell Arteritis (GCA) is a common vasculitis with significant risk of blindness. Although temporal artery biopsy (TAB) is currently performed for diagnosis, the sensitivity can be as low as 39%; ultrasound is emerging as a more effective and cheaper test. Vascular endothelial growth factor (VEGF) is present in inflamed arterial wall in GCA and elevated circulating levels have been reported in GCA compared to controls. Measurement of VEGF is less invasive than TAB, and cheaper than TAB or ultrasound.

**Objectives:** 1) Analyse performance of VEGF as a diagnostic marker for GCA

2) Combine VEGF with ESR and CRP to assess performance
3) Assess local expression of VEGF in TAB

**Methods:** We used samples from patients recruited to a large multi-centre study comparing temporal artery biopsy with ultrasound for diagnosis of suspected giant cell arteritis. We randomly selected 26 patients with TAB-positive GCA and 26 controls (negative TAB and final diagnosis not GCA). Most patients were receiving high doses of glucocorticoid therapy at recruitment. Serum VEGF concentration was measured at weeks 0, 2 and 26 by ELISA (Quantikine R&D systems). Week 0 values were plotted on a Receiver Operating Characteristic (ROC) curve to identify the most effective cut-off for an abnormal result. Sections of TAB were stained by immunohistochemistry for VEGF expression (Polyclonal Rabbit anti-human VEGF, AbCAM).

**Results:** Patients were significantly older than controls (mean age 76 SD 7.3 vs 66 SD 11.3, p=0.003). but had similar gender (62% females each). The mean (95% CI) baseline VEGF concentration was 873 pg/ml (631–1110) in GCA vs 476 pg/ml [328–625] in controls (p=0.017). This difference between groups was not observed at any other timepoint. The area under the ROC curve for VEGF concentration at week 0 was 0.73. The optimal cut off was 713pg/ml, providing a sensitivity of 65% and a specificity of 88%. These values compare favourably with reported performance of other available tests such as ESR and CRP (sensitivity 86% and 84%; specificity 30% and 29% respectively), TAB (sensitivity 40%, specificity 100%), and ultrasound (sensitivity 54%, specificity 81%).

VEGF concentration was combined with ESR and CRP values to assess if this improved its performance. High ESR was defined as ≥22 in men, ≥29 in women, and high CRP was ≥8. These results are summarised in Figure 1. ESR+CRP LOW had a 94% Negative predictive value to exclude GCA. ESR/CRP High + VEGF High had 95% Positive predictive value to diagnose GCA. For 27% of patients a further diagnostic test is needed.

VEGF expression by immunohistochemistry in TAB sections from 3 patients with GCA was higher than 2 controls, implying that VEGF is upregulated in GCA and may signal locally to drive the vasculitic process. Furthermore, serum concentration appears to reflect local concentration in the temporal artery; therefore measuring serum VEGF concentration is a valid surrogate for local inflammation.

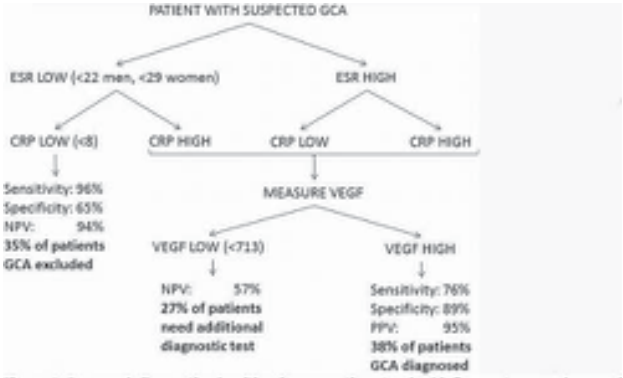



**Figure 1.** Proposed diagnostic algorithm incorporating standard inflammatory markers and VEGF. NPV = Negative Predictive Value, PPV = Positive Predictive Value, CRP = C-reactive protein, ESR = Erythrocyte Sedimentation Rate

**Conclusions:** In this study, serum VEGF was a useful test to support a diagnosis of GCA and potentially avoid the cost of TAB or ultrasound in over 60% of patients. Further studies will evaluate this in a larger cohort of suspected cases of GCA. Furthermore, VEGF could potentially be effective as a prognostic marker, or as a therapeutic target.

**Disclosure of Interest:** None declared

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## FRI0029 HUMAN CD40L DEFICIENCY DYSREGULATES THE MACROPHAGE TRANSCRIPTOME CAUSING FUNCTIONAL DEFECTS THAT ARE IMPROVED BY EXOGENOUS IFN-GAMMA

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**Background:** CD40 ligand (CD40L) deficiency predisposes to opportunistic infections including those caused by fungi and intracellular bacteria. Studies of CD40L-deficient patients reveal the critical role of CD40L-CD40 interaction for the function of T, B, and dendritic cells. However, the consequences of CD40L deficiency on macrophage function remain poorly understood.

**Objectives:** To analzye the role of CD40L-CD40 interaction in macrophages immune response.

**Methods:** MDMs were challenged with *Paracoccidioides brasiliensis* (Pb18, a highly virulent isolate) and the microbicidal activity determined by counting colony forming units (CFU). MDMs oxidative burst was measured by luminol-dependent chemiluminescence (LDCL). Supernatants of macrophages treated or untreated with rhIFN-γ or sCD40L were harvested 48 hours after *P. brasiliensis* or *M. tuberculosis* incubation and the Cytokine levels were evaluated by luminex. The analysis of *M. tuberculosis* (H37Rv strain) phagocytosis and proliferation control by MDMs were carried out by CFU counting. Macrophage transcriptome profiles from three CD40L deficient patients and three healthy controls were analyzed by RNAseq. All the experiments were performed before and after IFN-gamma *in vitro* treatment.

**Results:** Here we show that macrophages from CD40L-deficient patients exhibit defective fungicidal activity and reduced oxidative burst, which improved in the presence of IFN-γ but not soluble CD40L (sCD40L). In contrast, both IFN-γ and sCD40L ameliorate impaired production of multiple inflammatory cytokines. Comparing the gene expression signature of macrophages from CD40L-deficient patients to that of controls, we identified 109 differentially expressed genes (DEGs). *In vitro* treatment of macrophages with IFN-γ decreased the number of DEGs to only 11, and similarly affected the expression of 528 non-DEGs (140 genes down-regulated and 388 up-regulated) comparing patients and healthy controls. Finally, the addition of IFN-γ reversed defective control of *M. tuberculosis* proliferation by patient macrophages.

**Conclusions:** Our findings demonstrate that absence of CD40L impairs macrophage development and function. In addition, the improvement of macrophage immune responses by IFN-γ suggests this cytokine as a potential new therapeutic option for patients with CD40L deficiency.

**Disclosure of Interest:** None declared

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## FRI0030 ANTI-TNF-α ANTIBODY TARGETED TO INFLAMED SYNOVIAL TISSUE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

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**Background:** TNF-α neutralizing molecules represent one of the most efficient therapeutic approaches to control inflammation in rheumatoid arthritis (RA). The widespread distribution in the body induces the inhibition of TNF-α in all the tissues, requesting the use of high dose of this expensive drug. Another problem that has not yet been solved in the management of RA patients is how to reduce and possibly avoid the side effects, particularly the increased risk of common and opportunistic infections, which may be associated with long-term administration of these therapeutic drugs.

**Objectives:** The aim of the present investigation was to show that a recombinant protein obtained by fusing a synovial targeting peptide to an anti-TNF-α neutralizing antibody has a distinctive homing property for inflamed synovium and is effective in controlling joint inflammation in experimental models of arthritis.

**Methods:** The modified anti-TNF-α antibody specific for the synovial tissue (MC13) was generated by cloning the sequence for a synovial homing peptide (CKSTHDRLC) downstream of the cDNA for the variable regions of anti- TNF-α antibody adalimumab in the context of a miniantibody (scFv-Hinge-CH2-CH3 domains). Immunofluorescence technique was used to initially assess the ability of fluorescent-MC13 to target only inflamed synovial tissue. The biodistribution and the efficacy of the treatment with MC13 were evaluated in a rat model of antigen-induced arthritis (AIA).

**Results:** In vitro studies have shown that adalimumab and MC13 maintain the ability to neutralize human TNF-α and bind to rat and mouse TNF-α. Based on these findings, we used a rat model of arthritis to evaluate their in vivo therapeutic effect. The ability of MC13 to selectively target inflamed synovial tissues was evaluated by immunofluorescence analysis. A rat model of antigen-induced mono-arthritis was used to analyse the in vivo distribution of MC13 labelled with the near-infrared probe cyanine 5.5 using time-domain near infrared optical imaging. The results showed that the labeled-MC13 preferentially localized in the inflamed synovium with a peak at 4 days and persisted for more than 3 weeks, while failing to bind to healthy synovial tissue.

MC13 was able to prevent inflammation in the rat model of antigen-induced arthritis, as evaluated by the measurement of joint swelling, the count of PMN number and the level of IL6 in synovial tissue and the histologic assessment of tissue damage.

Intravenous injection of MC13 prevents acute inflammation in all the animals while the same dose of adalimumab was almost ineffective. MC13, administred i.v. 4 days after arthritis induction, was also able to cure joints analysed 7 days after the induction of inflammation.

**Conclusions:** Our results demonstrated that MC13 can selectively target inflamed and abrogate the inflammation in a model of antigen-induced arthritis with no sign of toxicity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6006

## FRI0031 TARGETING SIALIC ACID-MODIFIED RECEPTORS AS A POTENTIAL THERAPY FOR OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) is one of the most common diseases worldwide. Its prevalence and severity increase with age, but treatments only provide symptomatic relief. The articular cartilage consists of a collagen-proteoglycan matrix containing highly glycosylated proteins synthesized by chondrocytes. A notable shift from glycoproteins containing a-2,6-linked sialic acids to those containing a-2,3-linked sialic acids has been associated with progressive cartilage degeneration and with the onset of disorders such as rheumatoid arthritis (RA) and OA[1–3]. However, the pathophysiology of a-2,3-sialylation in cartilage has not yet been elucidated.
**Objectives:** Lectins recognize specific terminal aspects of glycan chains and the *Maackia amurensis* seed lectin (MASL) is a plant lectin that can bind to sialylated glycoproteins. Here, we study the effects of the lectin MASL on chondrocytes and cartilage integrity from healthy donors, OA patients and animal models of arthritis.
**Methods:** Cell viability, cell adhesion and growth were performed using commercial kits. Reactive oxygen species (ROS) levels were measured by DCFH-DA and by Flow Cytometry. Gene expression was analyzed by quantitative real-time PCR. Staining methods were used to study cartilage integrity. Oligomycin and LPS were used to induce cartilage degeneration *in vitro* and *in vivo* (human cartilage and mouse model, *Mus musculus* BALC/c).
**Results:** he expression of the a-2,3-sialylated transmembrane mucin receptor podoplanin (PDPN) is induced in cartilage from osteoarthritic patients. Co-immunofluorescence technique showed that MASL can be used to target PDPN. Nanomolar concentrations of MASL protected primary chondrocytes and prevented cartilage breakdown in human tissue from OA patients *ex vivo* and in an animal model of OA initiated by ROS, inflammatory cytokines, and metalloproteinases. Besides, the increased levels of the $\alpha$-2,3 sialyltransferase isoforms and the corresponding increase in the levels of a-2,3-sialylated glycoproteins in osteoarthritic chondrocytes may shed mechanistic light on the pathophysiology of OA. These findings based on various experimental models of arthritis reveal that specific lectins that target a-2,3-sialylated transmembrane receptors, such as PDPN on chondrocytes, may effectively inhibit cartilage destruction in the face of various arthritic insults. We also provide a three-dimensional molecular model for such an interaction.
**Conclusions:** The ability of MASL to target a-2,3-sialylated glycoproteins, such as PDPN, and to protect chondrocytes from insults leading to cartilage degradation might offer further possibilities for therapeutic interventions and novel arthritis treatments that may include the regulation of sialylation during acute disease stages.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1688

## FRI0032 RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS ADHESION TO ENDOTHELIAL CELLS IS CHANGED BY STIMULATION WITH ADIPOKINES

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**Background:** Rheumatoid arthritis (RA) is a chronic polyarticular inflammatory disease, in which RA synovial fibroblasts (SF) play a key role. These cells are able to migrate long distances *in vivo* via the vasculature as previously shown in our SCID mouse migration model. Adipose tissue, as an endocrine organ, plays an important role in inflammatory processes. Some of its effects may be mediated by adipokines, which can also act as immunomodulatory factors. In RA, these adipokines have been shown to affect RASF and endothelial cells (EC). The interaction between RASF and EC may be a crucial process in the migration of RASF through the vasculature.
**Objectives:** To investigate whether adipokines affect the adhesion of RASF to EC under flow conditions simulating the *in vivo* situation in blood vessels and to identify relevant adhesion molecules whose expression is altered by adipokines, glucocorticoids and methotrexate.
**Methods:** RASF adhesion to EC was studied under flow conditions (flow rates: 18.4/30.5/60.5 ml/h) in a dynamic adhesion assay as flow conditions are required for selectins to be obtain their active conformation. The expression of selected adhesion molecules from RASF and EC was analyzed by real-time PCR. For this purpose, primary RASF and EC were stimulated with adiponectin (10 $\mu$g/ml), visfatin (100 ng/ml) and resistin (20 ng/ml), and "therapeutically" with methotrexate (1.5 $\mu$M) and the glucocorticoids prednisolone (1 $\mu$M) and dexamethasone (1 $\mu$M).
**Results:** Using the dynamic adhesion assay to simulate the blood flow *in vivo*, RASF showed an increased adhesion to EC after stimulation with visfatin (+156%/+87%/+89%) and TNF-$\alpha$ (+61%/+18%+19%). Dexamethasone (-9%/-39%/-53%) and prednisolone (-31%/-64%/-53%) on the other hand decreased the adhesion of RASF to EC. The expression of integrin $\alpha$2 was upregulated after stimulation with resistin (2.8-fold; n=7) and TNF-$\alpha$ (13-fold; n=6). Only TNF-$\alpha$ increased the expression of ICAM-1 (40-fold; n=5) in RASF, while both visfatin (2.9-fold; n=10) and TNF-$\alpha$ (59-fold; n=9) increased the expression of VCAM-1 in RASF. In EC, TNF-$\alpha$ upregulated the expression of ICAM-1 (47-fold; n=9), while adiponectin decreased it (-2.9-fold; n=5). The expression of VCAM-1 was slightly decreased after stimulation with adiponectin (-1.3-fold; n=5) in EC, whereas TNF-$\alpha$ led to a strong upregulation (235-fold; n=7). P- Selectin was down-regulated after stimulation with TNF-$\alpha$ (-8.6-fold; n=7) in EC.
**Conclusions:** Under dynamic flow conditions, adipokines increase the adhesion of RASF to EC. Adhesion of RASF to EC most likely plays a role in the migration of RASF *in vivo*. The influence of adipokines on adhesion molecules and their strengthening effect on adhesion of RASF to EC could therefore enhance the migration of RASF and thus the spreading of RA to different joints. Glucocorticoids showed the opposite effect, which could explain some of the benefits observed in patients. The expression of adhesion molecules is influenced by adipokines. Yet, how they influence these expressions appears to differ between RASF and EC.
**Disclosure of Interest:** None declared
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## FRI0033 TNFALPHA PRODUCTION IN CULTURED HUMAN MACROPHAGES AFTER CTLA4-IG (ABATACEPT) IN VITRO TREATMENT

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**Background:** Proinflammatory cytokines and particularly tumor necrosis factor alpha (TNFalpha) are abundantly expressed in rheumatoid arthritis (RA) synovitis. Our recent data showed that CTLA4-Ig (abatacept), by interacting with the CD86 molecule on RA synovial macrophages, may induce reverse signaling with anti-inflammatory effects, involving NFkB intracellular pathway [1–4].
**Objectives:** We investigated the expression and production of TNFalpha on cultured human activated macrophages before and after *in vitro* CTLA4-Ig treatment.
**Methods:** THP-1 human monocytes, differentiated with phorbol myristate acetate (0.05 $\mu$g/ml for 24 hrs) into activated macrophages, were cultured in multiwells bottoms or flexiperm slides for 3, 24 and 48 hrs, in the absence (cells untreated) and in the presence of CTLA4-Ig (500 $\mu$g/ml). TNFalpha gene expression was investigated by quantitative real time polymerase chain reaction (qRTPCR), after 3 and 24 hrs from CTLA4-Ig treatment. Intracytoplasmatic TNFalpha protein expression was investigated by immunocytochemistry (ICC) analysis after 24 and 48 hrs from treatment. Extracellular TNFalpha production was evaluated in the culture surnatants, by immunoassay (ELISA) analysis, after 24 hrs from treatment. Experiments were done in triplicate.
**Results:** Interestingly, at gene level, qRTPCR showed already after 3 hrs (and 24 hrs) from CTLA4-Ig treatment a significant downregulation of TNFalpha gene expression ($p<0.05$ for both 3 and 24 hrs), compared to the untreated cells. ICC analysis showed that TNFalpha production resulted decreased (not significant) both after 24 hrs and 48 hrs from CTLA4-Ig (500 mg/ml) treatment, compared to the untreated cells. Extracellular evaluation by ELISA at 24 hrs, also demonstrated a reduction (not significant) of TNFalpha levels, compared to the untreated condition.
**Conclusions:** In cultured activated macrophages TNFalpha production was significantly reduced by CTLA4-Ig *in vitro* treatment at gene level, already after 3 hrs and still evident at 24 hrs. Regarding the protein synthesis, as expected, a trend for their reduction was observed on longer time (24–48 hrs).
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**Disclosure of Interest:** R. Brizzolara: None declared, P. Montagna: None declared, S. Soldano: None declared, A. C. Trombetta: None declared, S. Paolino: None declared, C. Pizzorni: None declared, A. Sulli: None declared, B. Ruaro: None declared, D. Camellino: None declared, V. Tomatis: None declared, M. Cutolo Grant/research support from: Research grant by Bristol Myers Squibb

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## FRI0034 RAGE ACTIVITY INFLUENCES CO-DEVELOPMENT OF JOINT AND VASCULAR DISEASE IN RA

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**Background:** RAGE is expressed by many cells in blood and joints of RA and interacts with a variety of pro-inflammatory ligands, especially HMGB1 that are enriched in inflamed joint. The RAGE-ligand interaction leads to a sustained inflammatory response. Soluble RAGE (sRAGE) lacks the transmembrane and cytoplasmic domain of the cell surface full-length RAGE (flRAGE) and function as a decoy for RAGE ligand. Relatively little is known about factors that regulate sRAGE levels in human subjects and whether circulating levels reflect tissue RAGE expression and activity is unclear. The relationship between the up-regulation of flRAGE/HMGB1 and the level of "protective" sRAGE levels in RA is of obvious clinical interest.
**Objectives:** To elucidate the balance between the expression of flRAGE on peripheral blood monocyte and dendritic cell (DC), and the plasma concentration of sRAGE and HMGB1 in patients with active RA compare to controls; To ascertain whether flRAGE expression profiles, plasma sRAGE and HMGB1 level correlated with disease activity or inflammatory markers in RA patients.
**Methods:** 40 consecutive patients attending the rheumatology clinic at Prince of Wales Hospital, who fulfilled the 2010 ACR/RULAR classification criteria with active RA (28 joint disease activity score 28–4 [CRP] (DAS28)>3.2) and 40 age- and sex-matched healthy volunteers were recruited for this cross-sectional study. The expression profile of cellular transmembrane RAGE on peripheral blood monocyte ($ILT3^+CD123^-$), total DC ($ILT3^+CD14^-CD16^-$), myeloid DC ($ILT3^+CD14^-CD16^-CD123^-$) and plasmacytoid DC ($ILT3^+CD14^-CD16^-CD123^+$), plasma levels of HMGB1 and soluble RAGE in all RA patients and healthy controls were measured at baseline using flow cytometry and ELISA. In RA patients, associations with disease activity and severity variables were analyzed by simple and multiple linear regressions.
**Results:** Protein expression of flRAGE on peripheral blood monocytes ($ILT3^+CD123^-$), total DCs ($ILT3^+CD14^-CD16^-$) and myeloid DCs ($ILT3^+CD14^-CD16^-CD123^-$) were significant increased in RA patients with active disese compared with control subjects (all $p<0.01$) (no enough cells for flRAGE detection on plasmacytoid $ILT3^+CD14^-CD16^-CD123^+$DCs). Also, the flRAGE was more common in patients with cardiac affection. There was no statistically significant difference of the plasma level of HMGB1 from active RA patients as compared healthy controls ($p>0.05$). The plasma sRAGE level was significantly lower in patients compared to healthy controls ($p<0.001$), which correlated negatively with serum levels of CRP, ESR, DAS28 and high-density lipoprotein (HDL) (all $p<0.05$). Linear regrssion analysis detected CRP as significant predictors for sRAGE level.
**Conclusions:** Autoimmunity-mediated inflammation might induce aberrant expression and activation of flRAGE while decreasing the plasma level of sRAGE in RA patients, subsequently leading to the augmented inflammatory response. Moreover, membrance flRAGE and sRAGE were associated not just with RA inflammation and autoantibody protein, but also with classical vascular risk factors for end-organ damage. These data suggest that RAGE activity influences co-development of joint and vascular disease in RA patients.
**Disclosure of Interest:** None declared
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## FRI0035 JOINT INFLAMMATION AND CARTILAGE DESTRUCTION IN EXPERIMENTAL OSTEOARTHRITIS IS NOT MEDIATED BY INTERLEUKIN-1

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**Background:** Osteoarthritis (OA) is a degenerative disease of the joint characterized by severe cartilage destruction, with a putative role for synovial macrophages. Up to 50% of the patients also show low grade joint inflammation reflected by a thickened synovial lining and elevated release of macrophage-derived mediators like interleukin-1 (IL-1) and S100A8/A9. The deteriorating role of S100A8/A9 in OA has been studied extensively (1), but the contribution of IL-1 to OA pathology is still unclear. IL-1 mediates cartilage destruction by degrading existing proteoglycans through stimulating degradative enzyme production, and by inhibiting new formation of proteoglycans. However, treatment of OA patients with IL-1 inhibitors has so far been disappointing.
**Objectives:** To investigate the role of IL-1$\alpha/\beta$ in synovitis and cartilage destruction during experimental collagenase-induced OA (CiOA).
**Methods:** Experimental OA was induced by intra-articular injection of collagenase into WT and IL-1$\alpha\beta^{-/-}$ mice. At day 7 and 42 after CiOA induction, total knee joints were stained with haematoxylin/eosin (H&E) to score synovial activation (arbitrary score from 0–3). Cartilage destruction was determined in knee sections stained with safranin O/fast green using a modified Pritzker score. Gene expression in inflamed synovium was analyzed using qPCR with primers for several cytokines. Serum protein levels of inflammatory mediators were measured with Luminex.
**Results:** At early stage (day 7) of CiOA, gene expression of IL-1 within inflamed synovium of knee joints was elevated 65 times compared to synovium of naïve control knees. However in later stages (day 21 and 42), IL-1 expression levels were reduced to basal levels. This is in contrast to pro-inflammatory mediators like S100A8 and S100A9 which remained elevated at day 21 and 42 (30–35-fold and 66–69-fold, respectively). Histological examination of knee joints showed a moderate synovitis at day 7 which waned thereafter but was still significant at day 21 and 42.
Remarkably, synovial inflammation at day 7 in IL-1$\alpha\beta^{-/-}$ mice was not different from WT controls (2.89±0.15 vs. 2.71±0.44), suggesting that IL-1 does not aggravate synovitis. Absence of IL-1$\alpha/\beta$ had no effect on the synovial gene expression levels of pro-inflammatory factors KC, S100A8 and S100A9. IL-6 mRNA levels, however, were significantly decreased in the synovium of IL-1$\alpha\beta^{-/-}$ mice (3-fold reduction). The lack of IL-1$\alpha/\beta$ also did not affect gene expression of anti-inflammatory cytokines IL-10, TGF$\beta$ and iNOS. Moreover, serum protein levels of KC, IL-6, MCP-1, IL-10 and S100A8/A9 at day 7 of CiOA in IL-1$\alpha\beta^{-/-}$ mice were not different compared to WT mice. Cartilage destruction in CiOA clearly aggravated over time, but we found no significant differences between IL-1$\alpha\beta^{-/-}$ mice and WT controls. No difference in cartilage damage was measured at day 42 of CiOA when compared to WT (medial femur (95.3±42.0 vs. 65.5±54.5), medial tibia (84.5±36.6 vs. 55.1±38.9), lateral femur (69.6±43.9 vs. 60.8±35.8), and lateral tibia (49.8±26.3 vs. 55.4±17.1)).
**Conclusions:** IL-1 does not affect synovial inflammation and cartilage destruction during collagenase-induced osteoarthritis, implicating that other macrophage-derived mediators such as S100A8/A9 are responsible for the joint damage.
**References:**
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**Disclosure of Interest:** None declared
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## FRI0036 META-IMMUNOLOGICAL PROFILING OF PATIENTS WITH BEHÇET'S DISEASE REVEALS NOVEL BIOMARKERS OF DISEASE ACTIVITY, PROGRESSION AND RESPONSE TO THERAPY

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**Background:** Behçet's disease (BD) is a rare and poorly understood condition characterised by systemic inflammation. Current biomarkers are still largely insensitive and unable to predict disease progression and response to treatment in BD patients.
**Objectives:** The specific aims of this study were i) to explore serum levels of soluble CD40L (sCD40L), soluble intracellular-adhesion-molecule (sICAM-1), monocyte-chemoattractant-protein-1 (MCP-1), myeloperoxidase (MPO), leptin, resistin, osteoprotegerin (OPG), soluble-type 1 tumour-necrosis-factor-receptor (sTNFR), interleukin-6 (IL-6) and serum-amyloid-A (SAA); ii) to evaluate potential correlations between the putative circulating biomarkers with the demographic profile, disease activity, organ involvement, genetical background, and different therapeutic regimes.
**Methods:** 57 serum samples were collected from 27 BD patients and 35 healthy controls (HC) after written consent. Demographic and clinical data are summarized in Table 1. Adipocytokines were analyzed using the bead-based-analyte-detection-system. Data were acquired by flow-cytometry. SAA serum concentration was determined with a enzyme linked-immunosorbent assay (ELISA). We used ANOVA test to identify statistical differences. $P<0.05$ was considered statistically significant.
**Results:** BD patients showed higher levels of circulating sTNFR (p=0.008), leptin (p=0.0011), sCD40L (<0.0001), and IL-6 (p=0.0154) than HC while no difference was found in MCP-1, MPO, sICAM, and resistin serum levels. Patients HLA-B51- had higher sTNFR and sICAM-1 serum levels than HC (p=0.0034, p=0.0037, respectively), while sICAM levels were significantly higher in patients HLA-B51- than in patients HLAB51+ (p=0.0010) as well as leptin was significantly higher in both HLA-B51+ and HLA-B51- BD patients than in HC (p=0.0183, p=0.0303, respectively). Patients treated with biologic-agents showed significantly higher sTNFR and leptin serum levels when compared to DMARDs-treated-patients (p=0.0246,p=0.0023, respectively). Moreover, sTNFR was found higher in patients with inactive disease and in patients over 40 years than HC (p=0.0104, p=0.0329, respectively).
**Conclusions:** The identification of a specific meta-immunological profile associated with disease status and response to therapy may contribute to our

Table 1. Demographic and clinical data of BD patients

| | BD patients | BD serum samples |
|---|---|---|
| Males/females | 12/15 | 27/30 |
| Age (mean ± SD), years | 45.7±13.54 | 51.19±30.26 |
| Disease onset (mean ± SD), years | 32.55±14.35 | 34.15±13.48 |
| Disease duration (mean ± SD), years | 13.59±12.67 | 13.85±12.34 |
| HLA-B51 positivity. n (%) | 17 (62.96) | 40 (70.17) |
| Oral/genital aphtosis | 23 (85.18) | 39 (68.42) |
| Skin manifestations | 10 (37.03) | 12 (21.05) |
| Uveitis | 11 (40.74) | 20 (35.08) |
| SNC involvement | 18 (66.66) | 26 (45.61) |
| Vascular involvement | 2 (7.40) | 4 (07.01) |
| Gastrointestinal manifestations | 4 (14.81) | 4 (07.01) |
| Musculoskeletal involvement | 20 (74.07) | 27 (47.36) |

understanding of the physiopathology processes underlying BD activity and damage as well as to provide useful tools for prognostic purposes and a personalized treatment approach.

**Disclosure of Interest:** None declared

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## FRI0037 CHONDROITIN SULPHATE INHIBITION OF NF-κB ACTIVITY: ATTENTUATION OF HYALURONAN FRAGMENT INDUCED INFLAMMATORY RESPONSE IN MACROPHAGES BY CHONDROITIN SULPHATE IS MEDIATED BY REDUCTION IN NF-κB ACTIVITY

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**Background:** NF-κB activation serves as a master regulatory switch for an inflammatory response in macrophages. Chondroitin sulphate (CS), a natural glycosaminoglycan of the cartilage extracellular matrix, has been shown to have clinical benefit in osteoarthritis (OA) producing anti-inflammatory and positive effects on the joint (1). We have previously shown that hyaluronan (HA) fragments induce an inflammatory response, in the form of IL-1β release, in macrophages that have been primed with the Toll-Like Receptor 4 (TLR4) agonist, lipopolysaccharide (LPS) and that CS can attenuate this response. We further demonstrated that this attenuation by CS occurred upstream of the inflammasome (2).

**Objectives:** Determine if this inhibition is acting at the level of NF-κB activation.

**Methods:** The THP1-Lucia NF-κB reporter monocyte cell line (InvivoGen) was grown as recommended. $10^5$ cells/well were plated along with varying concentrations of CS (0, 10–200 μg/ml) and either 1 μg/ml LPS or $10^7$ heat killed listeria monocytogenes (HKLM). In a 2nd experiment, cells were set up similarly but with the addition of 10 μg/ml ultralow molecular weight (ULMW) HA. In a 3rd experiment cells were set up as above with ULMW HA but substituting a caspase-1 inhibitor (EMD Millipore,10 μM) for CS. After 24 hours, media were tested for the NF-κB activity using QUANTI-Luc reagent (Invivogen) and for cell viability using PrestoBlue reagent (Invitrogen).

After normalizing for cell viability, all results were expressed as fold change from the media only control. One-way ANOVA with Dunnett's post-hoc test and inhibition dose response curves were performed.

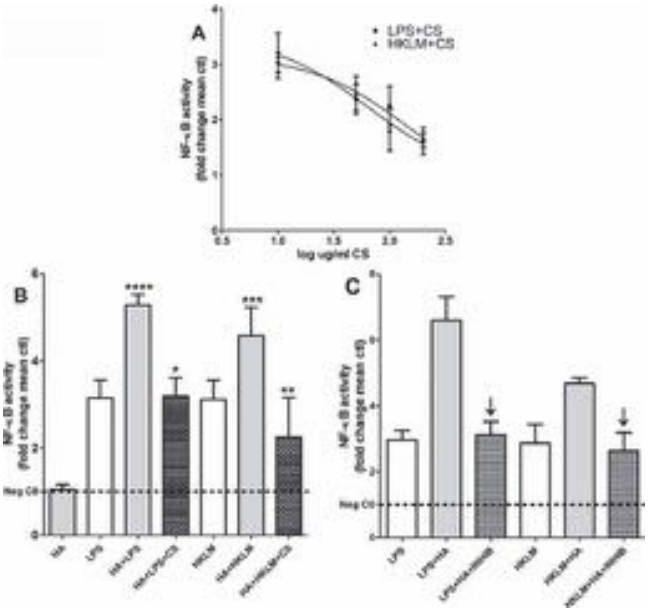



Figure 1

**Results:** NF-κB activity increased significantly ($p<0.0001$) in THP1-Lucia NF-κB reporter monocytes treated with either TLR4 or TLR2 agonists (i.e. 1 μg/ml of LPS or $10^7$ HKLM bacteria). CS (50–200 μg/ml) produced a dose dependent (p=0.02 to p=0.0005) reduction in NF-κB activity in LPS treated cells. In HKLM treated cells, CS (100–200 μg/ml) also produced a similar dose dependent (p=0.004 to p=0.01) reduction in NF-κB activity. Dose response curves indicated a 50% inhibition concentration (IC50) of 146 μg/ml CS for LPS (●) stimulated cells and 64 μg/ml for HKLM (▲) stimulated cells (Fig. 1A). HA fragments alone produced no increase in NF-κB activity but were found to have an additive effect through either the TLR4 or TLR2 pathway (i.e. LPS or HKLM). The combination of TLR activation and HA produced greater NF-κB activity than either LPS or HKLM alone ($p<0.0001$**** and p=0.0017***, Fig. 1A). CS (200 μg/ml) was still an effective inhibitor under these conditions (p=0.045* and p=0.02**, Fig. 1B). Inhibiting caspase-1 activity, and thus blocking IL-1β production, completely blocked the additive effect of HA fragments (↓, Fig. 1C). Caspase inhibition had no effect on LPS or HKLM alone.

**Conclusions:** The inflammatory response induced by HA fragments in the presence of TLR2 or TLR4 activation can be attenuated by CS at physiologically achievable concentrations via inhibition of NF-κB activation. HA's synergistic effect on NF-κB is due to positive feedback through inflammasome mediated active IL-1β production. These data provide a plausible explanation for the clinical effects of CS in OA.

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## FRI0038 ANTI-HINGE ANTIBODIES RECOGNIZE IGG SUBCLASS- AND PROTEASE-RESTRICTED HINGE NEO-EPITOPES

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**Background:** Anti-hinge antibodies (AHAs), autoantibodies that target neo-epitopes exposed in the hinge of IgG molecules after cleavage by proteases, can be found in healthy individuals but more frequently and at higher levels in rheumatoid arthritis (RA) patients. Recently, our group reported that AHAs in RA patients specifically target pepsin-cleaved hinge of IgG4.

**Objectives:** Determine the presence of AHAs and their specificity for protease- and IgG subclass-restricted neo-epitopes in healthy donors (HDs) and patients with RA or systemic lupus erythematosus (SLE).

**Methods:** Presence of AHA-reactivity and specificity of AHAs for protease- and IgG subclass-restricted neo-epitopes was determined with newly developed enzyme-linked immunosorbent assays (ELISAs) that measure AHA-reactivity against the hinge of F(ab')2-fragments generated by cleaving the four IgG subclasses with pepsin or IdeS, an IgG-degrading enzyme of Streptococcus pyogenes (Figure 1). Inhibition experiments were performed to investigate cross-reactivity and results were confirmed using a novel Surface Plasmon Resonance imaging (SPRi) array.

**Results:** Reactivity against at least one of eight F(ab')2-targets was found in 68% (51/75) of HDs, 65% (47/72) of SLE patients, and 83% (59/73) of RA patients. Individual AHA responses targeted protease-restricted neo-epitopes. Reactivity against IdeS-generated F(ab')2-targets was found more frequently in

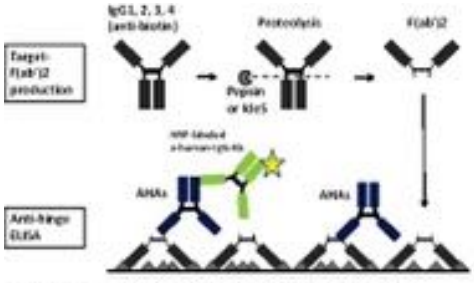



Figure 1: Set-up of newly developed anti-hinge ELISAs

F(ab')2s specific for biotin were produced by cleaving recombinant anti-biotin IgG1-, IgG2-, IgG3- and IgG4 molecules with the proteases pepsin or IdeS. The anti-biotin F(ab')2s were then used to opsonize ELISA plates coated with biotinylated human serum albumin (HSA, grey triangles). AHAs binding to the exposed hinge of the F(ab')2s were detected with horseradish peroxidase (HRP)-labeled anti-human-IgG detection antibodies.

all three groups, but reactivity against pepsin-generated F(ab')2-targets better discriminated between RA patients and HDs or SLE patients, with significantly higher levels of AHAs against pepsin-cleaved IgG1 and IgG3 in RA compared to SLE and HDs respectively. The most discriminatory AHA-reactivity in RA was against pepsin-cleaved IgG4, with at least 5x more positive sera compared to HDs and SLE and significantly higher levels ($P<0.0001$). Cross-reactivity for different IgG subclasses was only observed for subclasses having homologous F(ab')2 C-termini (IgG1, IgG3, IgG4).

**Conclusions:** Anti-hinge antibodies specifically recognize IgG subclass- and protease-restricted hinge neo-epitopes, possibly generated under (chronic) inflammatory conditions. The protease-restricted specificity of AHAs suggests that different AHA responses have developed under distinct inflammatory or infectious conditions and may be markers of -and participants in such conditions. In the proteolytic environment of the inflamed joint AHAs may contribute to immune complex formation, promoting further tissue destruction and inflammation.

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## FRI0039 SYNOVIAL MACROPHAGES PROMOTE TGF-BETA SIGNALING BUT PROTECT AGAINST INFLUX OF S100A8/S100A9-PRODUCING CELLS FOLLOWING INTRA-ARTICULAR INJECTIONS OF OXIDIZED LOW-DENSITY LIPOPROTEINS

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**Background:** In previous studies we found that synovial macrophages regulate joint pathology during experimental osteoarthritis (OA) and, more recently, we found that high systemic levels of low-density lipoproteins (LDL) aggravate joint pathology during experimental OA with synovitis. LDL in inflamed synovium is oxidized and taken-up by macrophages, leading to an activated macrophage phenotype.

**Objectives:** In this study, we investigate whether injection of oxidized LDL directly into a murine knee joint induces joint pathology and elucidate the role of synovial macrophages in that process.

**Methods:** Synovium was obtained from end-stage OA patients and stained for apolipoprotein B (APOB). Murine knee joints were injected five consecutive days with oxLDL, LDL, or an equal volume of vehicle (PBS). This procedure was repeated in mice depleted of synovial macrophages by intra-articular injection of clodronate liposomes seven days prior to the consecutive injections. Joint pathology was investigated by immunohistochemistry and flow cytometry (FCM) analysis, and RNA expression and protein production by synovium were determined using RT-PCR and luminex, respectively. Aggrecanase activity was measured using NITEGE-staining and active TGF-β was measured using a functional CAGA-luciferase assay. Data are depicted as mean ± standard deviation.

**Results:** Synovial macrophages and fibroblasts of end-stage OA patients showed extensive accumulation of APOB, the main protein present in LDL and oxLDL. Multiple injections of oxLDL in murine knee joints significantly increased TGF-β activity in synovial wash-outs by 28% [from 16562 ± 2326 relative light units (RLU) to 21151 ± 3823 RLU; $P<0.05$], but did not induce catabolic or inflammatory processes. In contrast, repeated injections of oxLDL in macrophage-depleted knee joints led to a 3.1 fold increase of synovial thickening, compared with injection of PBS ($P<0.01$), while LDL injections did not alter synovial thickening. Protein and RNA levels of chemokines CCL2 and CCL3 were significantly upregulated in macrophage-depleted joints after oxLDL injections (6.7 fold and 4.6 fold, respectively; $P<0.01$). Furthermore, FCM-analysis revealed increased presence of monocytes (from 1422 ± 1105 to 3029 ± 1644 cells) and neutrophils (from 4014 ± 3511 to 12708 ± 7829 cells) in the synovium of macrophage-depleted joints after injection of oxLDL ($P<0.05$), which was confirmed by immunohistochemical staining. Also protein levels of S100A8/A9, markers for inflammation, were significantly increased in synovial wash-outs of oxLDL-injected joints compared with LDL (fold increase 5.6; $P<0.05$) or PBS (fold increase 8.3; $P<0.01$) injection, as was NITEGE expression (fold increase 1.92; $P<0.05$). Interestingly, no raise in active TGF-β was measured in these macrophage-depleted joints.

**Conclusions:** Synovial macrophages promote anabolic processes after intra-articular oxLDL injections. In absence of synovial macrophages, however, oxLDL induces production of pro-inflammatory mediators and aggrecanase activity, in combination with increased influx of monocytes and neutrophils.

**Disclosure of Interest:** None declared

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## FRI0040 PROTEIN BIOMARKERS IMPROVES THE PREDICTION OF CLINICAL RESPONSE TO METHOTREXATE STEP-UP STRATEGY IN EARLY RA PATIENTS

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**Background:** International guidelines for treatment-to-target in rheumatoid arthritis (RA) recommend methotrexate (MTX) as first line therapy because of its favorable benefit/risk ratio and long-term safety. However, about 50% of patients fail to achieve remission and require other treatment. Identification and application of predictors of inadequate response to MTX may improve clinical outcome by enabling timely step-up treatment in those who need it.

**Objectives:** To evaluate the added predictive value of protein biomarkers compared to use of clinical variables alone, to identify early RA patients failing a MTX step-up strategy, including hydroxychloroquine (HCQ).

**Methods:** In the treat-to-target U-ACT-EARLY trial, 108 DMARD-naïve RA patients initiated MTX step-up therapy (10 mg to 30 mg or maximum tolerable dose) until remission (DAS28 $<2.6$ with SJC $\leq 4$) was achieved. If no remission after 20 weeks, HCQ was added, which after 12 weeks was replaced by tocilizumab (TCZ) if remission still was not achieved. Clinical assessments at baseline were analyzed and missing values were imputed using multiple imputations (n=20). Additionally, serum was collected before treatment and analyzed for 85 inflammatory proteins using Luminex® xMAP technology. Predictors for failing the MTX step-up strategy (MTX+HCQ) were selected using univariate preselection ($p\leq 0.15$) followed by multivariate backward selection ($p\leq 0.10$). A model including only clinical predictors was developed and subsequently, a second model in which protein biomarkers was added. The Area Under the Receiver Operator Curve (AUC-ROC), Net Reclassification Index (NRI, quantifies the improvement in prediction between two models) and Likelihood-ratio (LLR) test were used to assess both models.

**Results:** Within 1 year, 56 (52%) of the 108 patients failed the strategy for various reasons: adverse events (n=4), added TCZ according to treatment protocol (n=42), withdrawal from study because of inefficacy (n=10). Multiple logistic regression identified baseline DAS28, current smoking and alcohol consumption as clinical predictors (*model 1*, AUC-ROC 0.75, 95%>CI 0.66–0.84) and in addition MCP1, IL6, IL33, sCD14 and PD1 (*model 2*, AUC-ROC 0.87, 95%>CI 0.80–0.94) as significant protein biomarkers (Table 1). The LLR test showed a better fit of *model 2* (59.83, $p<0.001$). When using a risk of non-response >80% as cut off, *model 1* correctly predicted 24/51 patients not failing the strategy and *model 2* predicted 15 (29% improvement) extra patients not failing the strategy (Table 2). In those failing the strategy, 50/56 patients were correctly predicted by *model 1* and 4 (-7%) patients less was correctly predicted by *model 2*.

Table 1: Factors predicting the need of other treatment within the first year after starting a MTX step-up strategy.

| | OR (95% CI) | P value |
|---|---|---|
| MODEL1 | | |
| DAS28 | 2.1 (1.4 – 3.2) | 0.001 |
| Current smoking, yes | 3.0 (1.1 – 8.0) | 0.027 |
| Alcohol consumption, yes | 0.4 (0.1 – 0.9) | 0.021 |
| MODEL2 | | |
| DAS28 | 1.6 (1.0 – 2.7) | 0.067 |
| Current smoking, yes | 3.9 (1.1 – 13) | 0.033 |
| Alcohol consumption, yes | 0.2 (0.1 – 0.6) | 0.005 |
| MCP1 | 1.0 (1.0 – 1.0) | 0.013 |
| IL6* | 1.9 (1.1 – 3.1) | 0.017 |
| IL33* | 2.2 (1.2 – 3.7) | 0.010 |
| sCD14* | 9.3 (0.8 – 106) | 0.073 |
| PD1* | 0.5 (0.2 – 1.01) | 0.051 |

OR: odds ratio, CI: confidence interval, DAS28: disease activity score in 28 joints, MCP: monocyte chemoattractant protein, IL: interleukin, sCD: soluble cluster of differentiation, PD: programmed death-ligand, * log transformed data.

Table 2: Classification of MODEL1 and MODEL2 of patients failing the MTX step-up strategy versus those not failing the strategy.

| | | MODEL2 NF | MODEL2 F | trial result |
|---|---|---|---|---|
| MODEL1 | NF | 23 | 1 | not failing n=51 |
| | F | 16 | 11 | |
| | NF | 3 | 3 | failing n=56 |
| | F | 7 | 43 | |

NF: number of patients classified as not failing the strategy, F: numbers of patients classified as failing the strategy, in grey cells numbers with correct reclassification by model 2 and in framed cells numbers with incorrect reclassification by model 2 when compared to model 1.

**Conclusions:** Adding protein biomarkers to clinical predictors increases the predictive accuracy of identifying patients at baseline who will need other treatment after initiating a MTX step-up strategy. These findings could contribute too more personalized treatment in early RA patients to optimize long-term outcomes.

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FRI0041 **THE JAK INHIBITOR (TOFACITINIB) INHIBITS TNF-INDUCED GLIOSTATIN/THYMIDINE PHOSPHORYLASE EXPRESSION IN HUMAN FIBROBLAST-LIKE SYNOVIOCYTES**

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**Background:** The JAK/STAT signaling pathways mediate the effects of many cytokines and growth factors related rheumatoid arthritis (RA). Tofacitinib is a novel oral JAK inhibitor and it has demonstrated high efficacy in RA, even in non-responder to anti-TNF treatment. Gliostatin/thymidine phosphorylase (GLS/TP) is known to have angiogenic and arthritogenic activities. GLS/TP was expressed in inflamed synovial tissues of patients with RA. In cultured fibroblast-like synoviocytes (FLSs), GLS/TP expression was found to be up-regulated by inflammatory cytokines, such as IL-1β, TNFα. GLS acted as a cytokine in FLSs, augmenting its own synthesis, and also induced the extracellular secretion of matrix metalloproteinase (MMP)-1, and MMP-3. Therefore the suppression of GLS production might be an effective therapy in RA. Tofacitinib inhibits the function of T cells, however the mechanism of the action of tofacitinib had not been determined in fibroblast- like synoviocytes.
**Objectives:** The purpose of this study was to investigate the effect of tofacitinib on GLS production in FLSs derived from patients with RA (RAFLSs).
**Methods:** RAFLSs were cultured and stimulated by tumor necrosis factor (TNF)-α with or without treatment of tofacitinib. The expression levels of GLS were determined using reverse transcription-polymerase chain reaction (RT-PCR), enzyme immunoassay and immunocytochemistry.
**Results:** In cultured RAFLSs, GLS mRNA and protein levels were significantly induced by stimulation with TNFα alone and these GLS/TP inductions were significantly suppressed by treatment of tofacitinib in a dose-dependent manner.
**Conclusions:** Our data demonstrated that JAK/STAT activation play a pivotal role in TNF mediated GLS up-regulation in RAFLSs. Suppression of GLS production in inflamed synovia has been suggested as one of the anti-inflammatory effects of tofacitinib.
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## Rheumatoid arthritis - etiology, pathogenesis and animal models

FRI0042 **ALTERED PROFILES OF HISTONE LYSINE METHYLATION AFFECT MMP GENE TRANSCRIPTION IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS**

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that causes progressive joint destruction. A line of evidence suggests that synovial fibroblasts (SFs) play an important role in the pathogenesis of RA. RASFs produce matrix metalloproteinases (MMPs) that degrade articular cartilage. Although interleukin-6 (IL-6) is an inflammatory cytokine and is proved to be involved in the pathogenesis of RA, it is unknown whether IL-6 affects MMPs gene transcription in RASFs. Furthermore, recent advances have revealed that epigenetic mechanisms, including histone modifications, are considered to be important regulators in gene transcription. We hypothesized that epigenetic dysregulation might induce RASF activation.
**Objectives:** The aim of this study is to examine whether IL-6 regulates MMPs expression in RASFs and whether histone modifications are associated with the MMPs gene activation in RASFs.
**Methods:** We compared MMPs gene expression by quantitative RT-PCR and histone methylation in the MMP promoters by chromatin immunoprecipitation (ChIP) assay after stimulation with IL-6 and/or soluble IL-6 receptor α (sIL-6Rα) in RASFs and control, osteoarthritis (OA) SFs. Chromatin structures in the MMP promoters were evaluated with micrococcal nuclease (MNase) assay in RASFs and OASFs. We investigated the change in the MMPs gene expression after silencing of WDR5 that is required for generating H3K4me3, an active histone marker. IL-6 signal induces Signal Transducer and Activator of Transcription 3 (STAT3) activation. To elucidate the mechanisms of IL-6-induced MMPs gene activation in RASFs, we investigated cell surface expression of the IL-6 receptor (gp130 and membrane-bound IL-6Rα) by flow cytometry, phospho-STAT3 (p-STAT3) expression by immunoblotting, and binding of STAT3 to the MMPs 1, 3, 9, and 13 promoters after IL-6 stimulation by ChIP assay in RASFs and OASFs.
**Results:** MMPs 1, 3, 9 and 13 genes were actively transcribed in RASFs. The histone methylation profiles (H3K4me3 and H3K27me3) and the result of MNase assay indicated that chromatin structures were open in the MMPs 1, 3, 9 and 13 promoters in RASFs. The depletion of WDR5 reduced the levels of H3K4me3 as well as the MMPs 1, 3, 9 and 13 gene expression. Interestingly, IL-6 and sIL-6Rα significantly increased the expression of MMPs 1, 3 and 13, but not MMP-9, in RASFs. Although the expression levels of gp130 as well as membrane-bound IL-6Rα were comparable and STAT3 was similarly phosphorylated after IL-6 stimulation in RASFs and OASFs, STAT3 bound to the MMPs 1, 3 and 13 promoters, but not the MMP-9 promoter, after stimulation with IL-6 and sIL-6Rα only in RASFs. It was suggested that binding of STAT3 to the promoters resulted in MMPs 1, 3 and 13 gene activation after IL-6 stimulation in RASFs.
**Conclusions:** Our data indicate that altered profiles of histone methylation and binding of STAT3 to the promoters regulate constitutive and IL-6-induced MMPs gene activation in RASFs and possibly arthritogenic properties of RASFs.
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FRI0043 **SYNOVIAL MAST CELLS CORRELATE WITH LOCAL AND SYSTEMIC INFLAMMATION AND ARE FUNCTIONALLY ASSOCIATED WITH ECTOPIC LYMPHOID STRUCTURES IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

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**Background:** Mast cells (MCs) are immune cells present in the synovial membrane, and many evidences suggest that they contribute to the inflammatory response in Rheumatoid Arthritis (RA). However, their exact role in the pathogenesis of RA is still controversial. In particular, their presence in synovia and their association with the various histological patterns (pathothypes) described in RA have never been analysed systematically.
**Objectives:** To evaluate the presence of MCs in the synovial membrane of early RA patients and their correlation with synovial inflammation and cellular infiltration.
**Methods:** Sections of paraffin embedded synovial tissue obtained by ultrasound-guided synovial biopsy from DMARD-naïve patients with early (<12 months) RA (n=90) were stained with H&E and underwent semi-quantitative (SQ) scoring (0–9) to determine the degree of synovitis. Sequentially cut sections were stained by IHC for CD117+ MCs and immune cells (CD20+ B cells, CD3+ T cells, CD68+ macrophages and CD138+ plasma cells). Upon SQ scoring (0–4), sections were stratified into synovial pathotypes according to the degree of immune cell infiltration: (i) Lymphoid- grade 2/3 B cell aggregates, CD20≥2 and/or CD138>2 ii) Myeloid- CD68 SL≥2, CD20≤1 and/or CD3≥1, CD138≤2 and iii) Fibroid- CD68 SL<2 and CD3, CD20, CD138<1). Additionally, cellular interactions were assessed by double IF in tonsils and in RA synovia (n=6). Finally, naïve B cells isolated from tonsils were co-cultured with MCs.
**Results:** MCs were positively correlated with synovial inflammation ($r_S$=0.657) and infiltrating T cells ($r_S$=0.629), B cells ($r_S$=0.666), macrophages (lining: $r_S$=0.502; sub-lining $r_S$=0.454) and plasma cells ($r_S$=0.623), p<0.0001. In particular, synovial MCs were significantly higher in patients with a lymphoid pathotype (mean MC density in lymphoid 41.06/mm$^2$ Vs fibroid/myeloid 11.66/mm$^2$, p<0.0001). Similarly, when patients were stratified according to MC number, the proportion of lymphoid pathotype was significantly higher in patients with high vs intermediate vs low MC count (83.9% vs 44.8% vs 10.3%, respectively, p<0.0001). Double immunofluorescence showed MCs bordering the germinal centres in secondary lymphoid organs and in close contact with B and T cell aggregates in synovia. Finally, MCs supported naïve B cells survival, proliferation, and differentiation in vitro, as demonstrated by the increased AID expression and the induction of IgG class switching upon co-culture of B cells with MCs.
**Conclusions:** Our study demonstrates that MCs strongly associate with the lymphoid synovial pathotype in early RA patients. Their ability to support B cell survival, activation and differentiation in vitro suggests that they may contribute to functional activation of lymphoid aggregates in vivo. Additional studies are

warranted to establish the role of MC interaction with B cells and assess their usefulness as biomarker for patient stratification in RA.
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## FRI0044 SMOKING INDUCES IRREVERSIBLE DEREGULATION OF MICRORNA EXPRESSION IN RHEUMATOID ARTHRITIS

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**Background:** MicroRNA (miR) represent a part of epigenetic contol of autoimmunity and gain increasing attention in the pathogenesis of RA. Genome-wide and candidate miR surveys indicated deregulation of selected miRs in RA blood and synovial tissue. Smoking belongs to enviromental factors with the ability to reprogram epigenetic control. It is also the most studied risk factor in RA being tightly connected to the production of autoantibodies, high levels of oncoprotein survivin, and resistance to antirheumatic therapy (1,2).
**Objectives:** The aim of this study was to determine effect of smoking on the expression of miRs in leukocytes of RA patients.
**Methods:** Leukocytes of the peripheral blood of 46 female RA patients (age 21–69 years, disease duration 1–22 y) were used as a source of miR. Information about smoking status was collected via a questionnaire and identified current smokers (CS, n=12), former smokers (FS, n=21) and never smokers (NS, n=13). We used the Toray 3D-Gene microRNAs assay-based approach to compare the levels of 2598 miRs between the RA patients with different smoking status. For the comparison between the groups we used only miRs with abundant (raw values >100) expression in leukocytes. Smoking and RA-associated miRs were retrived from the available comprehensive reviews (3,4).
**Results:** The number of detectable miR was highest in the PBMC samples of NS. Former and current smoking was associated with a step-wise decreased global miR expression being most severe in CS. We identified 267 miRs, which had an abundant expression in NS. The expression of 93 of these miRs was significantly affected by smoking being 1.75-times lower in FS and CS (p=0.0002). Analyses of miRs, which had previously been reported sensitive to smoking showed that FS+CS had lower expression of the miRs belonging to the let-7 family compared to NS (2.43 times, p=0.034). Additionally, FS had low expression of the miR-17/92 cluster, where miR-17 family was affected most, reduced 2.05 times (p=0.066), followed by miR-19 and 18 families (1.74 times) and miR-92 family (1.56 times). FS had also 2.1 times lower expression of the miR-16 family. The analysis of miRs described in relation to RA showed that 20 of 30 RA-related miRs were abundantly expressed in the studied samples. The expression of miR-16–5p, miR-126–3p, miR-142–3p, miR-150–5p, miR-22–3p and miR-221–3p showed more then 1.75 times difference between FS and NS.
**Conclusions:** Smoking is associated with a global reduction in miR expression in RA patients, where the members of let-7; miR-17/92 and miR-16 families with key roles in regulation of cell cycle progress, tissue development and immune responses clusers are most affected.
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## FRI0045 THERAPEUTIC BLOCKADE OF INTERLEUKIN-6 TRANS-SIGNALLING RESTORES VASCULAR FUNCTION IN MURINE COLLAGEN INDUCED ARTHRITIS

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**Background:** Mortality is increased in rheumatoid arthritis (RA), mainly due to cardiovascular disease (CVD). While molecular mechanisms underlining this observation are unknown, systemic elevations in inflammatory cytokines, eg interleukin (IL)-6 frequently correlate with increased cardiovascular risk. IL-6 plays roles in both immune homeostasis and driving chronic disease progression. Control of these processes is regulated by two modes of IL-6 signalling; classical IL-6 signalling and IL-6 trans-signalling. Cellular responses controlled by IL-6 trans-signalling are mediated via soluble IL-6 receptor (sIL-6R) and is widely considered to promote pro-inflammatory outcomes. Importantly, a genetic polymorphism within IL6R enhances circulating sIL-6R level and is associated with CVD incidence in the general population. Biological drugs against IL-6 or IL-6R block both classical and trans-signalling. However it is advocated that selective inhibition of IL-6 trans-signalling may reduce clinical complications associated with a more global intervention strategy. Murine collagen induced arthritis (mCIA) is associated with vascular dysfunction, with reduced aortic constriction to 5-HT. Here, we found systemic alterations in vascular tone, as a response to mCIA, was attributable to IL-6 trans-signalling.
**Objectives:** Investigations assessed whether inhibition of IL-6 trans-signalling using the selective antagonist sgp130Fc affected aortic constriction as an index of vascular dysfunction in mCIA.
**Methods:** Arthritis was induced in 8 week old male DBA/1 mice by type-II collagen, as previously described[1]. Animals were administered IV sgp130Fc (2.5mg/kg) or PBS weekly from day 21. Arthritis severity was monitored daily from day 21–30. Vasoconstriction of aortic rings in response to 5-HT was monitored as an index of vascular function using isometric tension myography. Results are expressed as mean ± SEM (n=10).
**Results:** When compared with PBS controls (Arthritis Index:4.3±1.1), disease severity was significantly ($P<0.05$) reduced in sgp130Fc (1.5±0.6) treated mice (Fig1A). PBS control mice with mCIA had reduced vasoconstriction (developed tension 8.5±0.6mN for non-immunised mice, 5.8±0.8mN for mCIA mice; $P<0.05$). Significantly, improvement of disease activity observed for sgp130Fc treated animals was associated with normalisation of vascular function (developed tension 8.1±0.6mN).

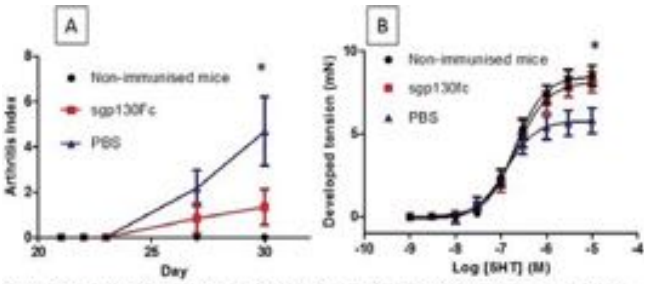


Figure 1 (A) Significant difference in Arthritis Index over time in mice administered sgp130Fc compared with PBS. (B) Vasoconstriction concentration-response curves to 5-HT in aortic rings. N=10

**Conclusions:** Consistent with previous reports[1], sgp130Fc reduced arthritis in mCIA. Sgp130Fc also restored vascular function. Selective IL-6 trans-signaling blockade by sgp130Fc is a promising therapeutic strategy for both RA and its associated CVD. Further work is needed to elucidate the role of IL-6 trans-signaling in pathogenesis of vascular dysfunction in mCIA and RA.
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## FRI0046 TCZ ATTENUATES ATHEROTHROMBOSIS THROUGH THE SPECIFIC INHIBITION OF NETOSIS AND MONOCYTE-MEDIATED PROINFLAMMATORY ACTIVITY

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**Background:** Inhibition of the interleukin IL6 receptor pathway by tocilizumab (TCZ) is an effective treatment for rheumatoid arthritis (RA). TCZ reduces atherosclerosis markers and improves endothelial function. In peripheral blood, TCZ increases the percentage of natural killer and regulatory T cells and decreases the number of inflammatory Th1/Th17 lymphocytes. Monocytes activation and neutrophil extracellular traps (NETs) are key players in the development of cardiovascular disease; however, the specific effect of TCZ on these cells has not been described yet.
**Objectives:** To analyze the molecular changes (focused on monocyte and neutrophil abnormalities) underlying the beneficial effect of TCZ on atherosclerosis and endothelial dysfunction in rheumatoid arthritis.
**Methods:** Fifteen RA patients received 162 mg/week subcutaneous TCZ as combined therapy. Endothelial function was measured through post occlusive hyperemia using Laser-Doppler. To analyze the specificity of TCZ, blood samples

from 5 RA patients with high disease activity no taking TCZ was used to perform in vitro studies. Isolated monocytes and neutrophils were treated in vitro with IL6 and blocking FCRII plus TCZ for 18 and 6 hours, respectively. Oxidative stress markers in leukocytes were analyzed by flow cytometry. NETosis was measured through Sytox staining of DNA fibers. Myeloperoxidase (MPO) and neutrophil elastase (NE) were analyzed in neutrophils by flow cytometry. mRNA expression of peptidyl arginine deiminase (PAD4) was measured by RT-PCR. Percentage of low density granulocytes (LDGs) was analyzed through flow cytometry. mRNA expression of genes involved in monocyte activation, prothrombotic state, lipid uptake and insulin resistance was analyzed in monocytes through RT-PCR. Activation of intracellular pathways was analyzed in monocytes using pathscan intracellular signaling array. Expression of miRNAs was evaluated in plasma.

**Results:** After 6 months of treatment, TCZ reduced clinical parameters of inflammation, autoimmunity and joint damage. Endothelial function was significantly restored. TCZ decreased peroxide and peroxinitrite levels in RA leukocytes, most significantly in monocytes and neutrophils. Percentage of LDGs was also reduced after treatment. TCZ in vivo treatment reduced the expression of MPO, NE and PAD4 in RA neutrophils. The generation of in vitro induced NETs was also inhibited by TCZ. The expression of inflammatory and prothrombotic molecules, genes involved in lipid uptake and cellular activation and insulin signaling and the activation of various intracellular pathways were modulated in monocytes after in vivo TCZ treatment. All these results were recapitulated after in vitro TCZ treatment of RA monocytes and neutrophils. Plasma levels of miRNA-223, miRNA-146 and miRNA-23, previously reported to be modified by anti-TNFalpha drugs, were also upregulated after TCZ treatment.

**Conclusions:** TCZ improves endothelial dysfunction and atherothrombosis through the restoration of the oxidative status, inhibition of the monocyte prothrombotic and inflammatory profile and the generation of NETosis

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## FRI0047 HISTAMINE AND HISTAMINE H4 RECEPTOR PROMOTES OSTEOCLASTOGENESIS IN RHEUMATOID ARTHRITIS

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**Background:** The biological function of histamine is mediated through four types of histamine H1∼H4 receptors. Histamine H4 receptor (H4R) has immune-modulatory and chemotaxic effects and various immune cells express H4R.

**Objectives:** This study aimed to determine the osteoclastogenic role of H4R in rheumatoid arthritis (RA).

**Methods:** The expression of H4R in RA synovial fluid mononuclear cells (SFMCs), synovial fibroblasts and peripheral blood mononuclear cells (PBMCs) using real-time polymerase chain reaction (PCR). After RA SFMCs and PBMCs were treated with histamine, Th17 cytokines, such as IL-17, IL-21 and IL-22, and H4R antagonist (JNJ7777120), the gene expression and protein production of H4R and RANKL were determined by real-time PCR and ELISA. Osteoclastogenesis was assessed by counting tartrate-resistant acid phosphatase–positive multinucleated cells in peripheral blood CD14+ monocytes cultured with histamine, Th17 cytokines and JNJ7777120.

**Results:** The synovial fluid and serum concentration of histamine was higher in RA, compared with osteoarthritis and healthy controls, respectively. The expression of H4R was increased in RA PBMCs compared with healthy controls. Histamine, IL-17, IL-21 and IL-22 stimulated the expression of H4R and RANKL in PBMCs and JNJ7777120 reduced the histamine and Th17 cytokine-induced RANKL expression. Histamine and Th17 cytokines also induced the osteoclast differentiation from peripheral blood monocytes and JNJ7777120 decreased the osteoclastogenesis.

**Conclusions:** H4R mediates RANKL expression and osteoclast differentiation induced by histamine and Th17 cytokines. The blockage of H4R could be a new therapeutic modality for prevention of bone destruction in RA.

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**Disclosure of Interest:** None declared

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## FRI0048 CONCENTRATIONS OF ANTIBODIES AGAINST PORPHYROMONAS GINGIVALIS ARE INCREASED BEFORE THE ONSET OF SYMPTOMS OF RHEUMATOID ARTHRITIS

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**Background:** Citrullination by the periodontal pathogen *Porphyromonas gingivalis* has been hypothesized to play a role in RA aetiology, by contributing to the production of anti-citrullinated protein antibodies (ACPA). We have previously shown that the ACPA response precedes RA by several years, and we have recently demonstrated elevated anti-*P. gingivalis* antibody levels in patients with RA compared with controls (1–3).

**Objectives:** The aim of the present study was to investigate the link between *P.gingivalis* and RA further, by analysing whether anti-*P. gingivalis* antibodies predate RA diagnosis and ACPA production.

**Methods:** A case-control study was performed within the Medical Biobank and the Maternity cohort of Northern Sweden including 251 individuals who had donated 422 blood samples predating the onset of symptoms of RA, and 198 population-based controls from the same cohorts. The median (IQR) predating time until onset of symptoms was 5.2 (6.2) years. For 192 individuals diagnosed with RA, blood samples were available from the time of diagnosis. Samples were analysed using in-house ELISAs for presence of antibodies to the virulence factor arginine gingipainB (RgpB) purified from *P. gingivalis*, and to a citrullinated peptide (CPP3) derived from the *P. gingivalis* peptidylarginine deiminase enzyme *P.*PAD.

**Results:** The concentration of anti-RgpB IgG levels was significantly increased in pre-symptomatic individuals (mean±SEM; 152.7±14.8 AU/ml) and in RA patients (114.4±16.9 AU/ml), compared with controls (82.2±12.1 AU/ml, $p<0.001$ for both). Antibodies against CPP3 were detected in 5% of the pre-symptomatic individuals and in 8% of the RA-patients, with elevated levels in both pre-symptomatic individuals (4.33±0.59 AU/ml) and RA-patients (9.29±1.81 AU/ml) compared with controls (2.36±0.58 AU/ml, $p<0.001$ for both). The anti-CPP3 antibody response followed the ACPA response, with increasing antibody concentrations over time, whilst the anti-RgpB IgG response was elevated and stable in pre-symptomatic individuals during the pre-dating time and showed a trend towards lower levels after RA diagnosis.

**Conclusions:** Anti-*P. gingivalis* antibody concentrations were significantly increased in RA compared with controls and these antibodies were detected years before the onset of symptoms of RA, supporting an aetiological role for *P. gingivalis* in the development of RA.

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## FRI0049 PRECLINICAL CHARACTERIZATION OF GS-9876, A NOVEL, ORAL SYK INHIBITOR THAT SHOWS EFFICACY IN MULTIPLE ESTABLISHED RAT MODELS OF COLLAGEN-INDUCED ARTHRITIS

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**Background:** Spleen Tyrosine Kinase (SYK) mediates signaling in a range of hematopoietic cells involved in the initiation and progression of RA including B cells, monocytes, macrophages, dendritic cells, and osteoclasts. There is strong preclinical validation for SYK as a therapeutic target for RA based on cellular data and animal models of disease. We have identified GS-9876 as a potent and selective SYK inhibitor with pharmaceutical properties compatible with once daily oral dosing in human.

**Objectives:** To characterize the cellular activity of GS-9876 on pathologically relevant pathways in RA, and establish target inhibition requireements for efficacy in rat models of arthritis.

**Methods:** The potency and selectivity of GS-9876 were characterized in biochemical and cellular assays. Effects in B cells were measured by inhibition of BCR-mediated protein phosphorylation, CD69 and CD86 expression, and in macrophages by inhibition of immune-complex (IC)-stimulated cytokine release. Cellular selectivity was demonstrated by comparing the inhibition of B cell proliferation versus T cell proliferation. GS-9876 potency in human blood was evaluated by inhibition of phosphorylated SYK (pSYK), CD63 expression on basophils, and CD69 expression on B cells. The in vivo efficacy of GS-9876 was tested in rat models of collagen-induced arthritis (CIA).

**Results:** GS-9876 is a potent SYK inhibitor ($IC_{50}$=9.5±4.3 nM) and is highly selective against a panel of 456 other kinases. GS-9876 inhibited anti-IgM stimulated phosphorylation of AKT, BLNK, BTK, ERK, MEK, and PKCδ in human B cells with $EC_{50}$ values of 24–51 nM. Functionally, GS-9876 inhibited anti-IgM mediated CD69 and CD86 expression on B-cells ($EC_{50}$=112±10 nM and 164±15 nM, respectively) and anti-IgM /anti-CD40 co-stimulated B cell proliferation ($EC_{50}$=108±55 nM). In human macrophages, GS-9876 inhibited IC-stimulated TNFα and IL-1β release ($EC_{50}$=121±77 nM and 9±17 nM, respectively). Anti-CD3/anti-CD28 stimulated T cell proliferation was weakly inhibited ($EC_{50}$=1291±398 nM), with selectivity >10-fold versus the inhibition of B cell proliferation. In human blood, GS-9876 blocked SYK phosphorylation, CD69 expression on B cells, and CD63 expression in basophils. GS-9876 demonstrated a dose-dependent improvement in clinical

score and histopathology parameters with once-daily dosing in short and long term rat CIA models. Significant efficacy could be achieved with GS-9876 doses that produced trough pSYK inhibition of <50%.
**Conclusions:** GS-9876 is a novel SYK inhibitor that potently inhibits multiple cellular events implicated in RA pathogenesis and displays excellent in vivo efficacy in rat CIA models after once-daily dosing. GS-9876 has markedly improved selectivity over competitor SYK programs. Our data support the development of GS-9876 in inflammatory diseases, with potential for an improved safety profile.
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## FRI0050 DIFFERENTIAL EXPRESSION OF OPG/RANKL/TRAIL SYSTEM IN RHEUMATOID ARTHRITIS

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**Background:** Osteoprotegerin (OPG)/ receptor activator of nuclear factor-κB ligand (RANKL)/ tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) system is involved in the pathophysiology of rheumatoid arthritis (RA) [1–2]. Moreover, this system has been related to cardiovascular (CV) disease and, therefore, these molecules have been proposed as potential biomarkers of CV disease [3–4].
**Objectives:** To evaluate for the first time the differential expression of OPG/RANKL/TRAIL system in RA patients, with and without ischemic heart disease (IHD), and healthy controls, in order to confirm the role of this system in the pathogenesis of RA, the clinical and demographic characteristics of RA patients, and CV disease, assessed by IHD.
**Methods:** *OPG*, *RANKL* and *TRAIL* messenger RNA (mRNA) expression was quantified by quantitative real-time PCR in peripheral blood from 26 RA patients (12 with and 14 without IHD) and 10 healthy controls. Correlation coefficients were also assessed between *OPG*, *RANKL* and *TRAIL* expression levels in RA patients and their clinical and demographic characteristics, as well as the influence of *OPG* expression on its ligands.
**Results:** While *OPG* and *OPG/TRAIL* ratio expression was significantly increased in RA patients compared to controls (fold change=1.79, p=0.01 and 2.07, p=0.03, respectively), *RANKL/OPG* ratio was significantly decreased (fold change=0.50, p=0.02). Additionally, *OPG* mRNA levels were associated with *OPG/TRAIL* ratio (r=0.75, p=0.0002) and inversely related to *RANKL/OPG* ratio (r=-0.70, p=0.0008) in RA. No significant differences were found between patients and controls in *RANKL* and *TRAIL* expression. Interestingly, *TRAIL* mRNA expression was significantly higher in RA patients with compared to those without IHD (fold change=1.46, p=0.03). Moreover, biologic disease-modifying antirheumatic drugs (DMARDs) significantly decreased *RANKL* expression in RA patients (r=-0.54, p=0.02).
**Conclusions:** Our study supports a key role for *OPG* in RA disease and *TRAIL* in IHD in RA patients. Furthermore, it highlights the important modulation of *RANKL* in RA patients treated with biologic DMARDs.
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## FRI0051 IN VIVO IMAGING TO CHARACTERISE THE SPECIFICITY, FUNCTION AND BEHAVIOR OF THE CD4+ T CELLS INITIATING ARTICULAR INFLAMMATION

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**Background:** It is widely accepted that $CD4^+$ T cells are important contributors to the pathogenesis of Rheumatoid Arthritis (RA). The presence of activated T cells in the inflamed synovium, GWAS defined associations with HLA-DR4, ptpn22, ctla4 and cd28, together with the clinical success of CTLA-4-Ig, all implicate a significant contribution (1). Yet it remains unclear when and where $CD4^+$ T cells mediate this pathogenic effect and whether the specificity of the cells is important.
**Objectives:** Characterise the specificity and function of the $CD4^+$ T cells mediating the initiation of experimental arthritis. To relate this to an analysis of the migratory behaviour of $CD4^+$ T cells in the inflamed articular environment thereby defining interactions with antigen presenting cells (APCs) that may control their activation in the joint.
**Methods:** Antigen-induced arthritis using ovalbumin (OVA) as the inciting challenge was used to model articular inflammation (2). Th1 OVA specific fluorescent (DsRed) OT-II TcR transgenic T cells were adoptively transferred and expanded *in vivo* by challenge with OVA/CFA. This allowed analysis and in tracking of antigen-specific T cells as they were recruited to the joint following periarticular injection of heat aggregated OVA (HAO). Flow cytometry allowed phentoyping of cells recruited to the inflamed articular environment. The T cell receptor (TcR) diversity of infiltrating endogenous T cells was assessed by PCR of Vβ genes. Dynamic interactions of responding DSRed T cells with joint residing YFP dendritic cells (DCs) were visualized using intravital multiphoton microscopy.
**Results:** Low numbers of the inciting OVA specific $CD4^+$ T cells could be found in the joint tissue. However, a large influx of endogenous $CD4^+$ T cells of unknown antigen specificity was also detected. This recruited articular T cell population expressed surface activation markers, exhibited a narrower range of T cell receptor Vβ usage and upon *ex vivo* restimulation produced TNFα and IFNγ. Intravital imaging of the inflamed joint revealed that a sub-population of this infiltrate demonstrated slower motility speeds and longer periods of contact with articular DCs, while others rapidly migrated throughout the tissue.
**Conclusions:** We define for the first time the *in vivo* kinetics of early T cell induction of articular inflammation. Numbers of the inciting antigen-specific population recruited to the joint tissue is small, but is associated with a subsequent influx of a large endogenous population of $CD4^+$ T cells of unknown antigen specificity that acquired the ability to secrete pro-inflammatory cytokines. The narrower usage of TcR Vβ genes by the $CD4^+$ T cells in the inflamed joint suggests some degree of antigen-specificity in recruitment while intravital imaging reveals that some of this infiltrate exhibits behaviour consistent with recognition of cognate peptide-MHCII.
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## FRI0052 TARGETING TRISTETRAPROLIN TO TREAT INFLAMMATORY ARTHRITIS

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**Background:** Aberrant activation of MAPK p38 signalling contributes to pathogenesis of RA[1]. MAPK p38 promotes expression of inflammatory mediators via phosphorylation of the mRNA destabilising protein Tristetraprolin (TTP) at two serine residues. These phosphorylations a) protect TTP protein from destruction by the proteasome, and b) inactivate it, resulting in stabilisation of target mRNAs such as TNF[2,3]. Dephosphorylation and activation of TTP is mediated by the phosphatase PP2A. Disruption of the murine TTP gene (*Zfp36*) causes a severe, pervasive inflammatory syndrome, including erosive arthritis. The phenotype is largely due to increased stability of TNF mRNA and overexpression of TNF protein[4]. TTP protein is reported to be strongly expressed in the RA synovium[5]. However, the cells expressing TTP were not identified, and the relationship with inflammation was not explored.
**Objectives:** To test the hypothesis that synovial inflammation requires phosphorylation and inactivation of TTP, and that, conversely, synovial inflammation may be inhibited by promoting the dephosphorylation and activation of TTP.
**Methods:** The expression of TTP and its relationship with p38 activation in normal and RA synovial tissue were examined by confocal microscopy. A knock-in

mouse strain (*Zfp36aa/aa*) was generated, in which sites of p38-dependent phosphorylation were subsituted by non-phosphorylatable alanine residues[3]. Experimental arthritis was induced by K/BxN serum transfer. *In vitro* and *in vivo* experiments were performed to test anti-inflammatory effects of a compound that activates the phosphatase PP2A.

**Results:** TTP expression was significantly higher in RA than non-inflamed synovium, detected in macrophages, vascular endothelial cells and some synovial fibroblasts, and co-localised with MAPK p38 activation. The *Zfp36aa/aa* mouse, in which TTP is non-phosphorylatable and constitutively active, were resistant to induction of experimental arthritis. Protection against arthritis was dependent on constitutive TTP function in both haematopoietic and non-haematopoietic compartments. *In vitro*, a PP2A activating compound impaired the expression of TNF in a manner dependent on the modulation of TTP function. *In vivo*, it reduced inflammation and prevented bone erosion in the K/BxN serum transfer model of RA.

**Conclusions:** The phosphorylation state of TTP is a critical determinant of inflammatory responses, and a tractable target for novel anti-inflammmatory treatments.

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## FRI0053 AMELIORATION OF EXPERIMENTAL ARTHRITIS BY DISSOCIATING THE BINDING OF P53 FAMILY MEMBERS WITH INHIBITORY APOPTOSIS STIMULATING PROTEIN OF P53 TO INDUCE APOPTOSIS IN SYNOVIAL FIBROBLAST

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**Background:** In rheumatoid arthritis (RA), apoptosis-resistant synovial fibroblasts (SFs) constitute the major cell component of pannus tissues [1]. 37 amino acid (37AA), a hybrid small peptide corresponding to p53 residues, inhibits the binding of p53 family members with inhibitory apoptosis stimulating protein of p53 (iASPP), thus activating the downstream apoptosis signaling pathway in tumor cells [2].

**Objectives:** We hypothesized that iASPP is involved in the RA pathogenesis, and examined whether dissociating the binding of p53 family members with this molecule can ameliorate experimental arthritis.

**Methods:** Synovial tissues and SFs from RA and osteoarthritis patients were subjected to immunohistochemical (IHC) and immunofluorescent staining, respectively, for expression of iASPP and p73, a p53 family member molecule. Synovial tissues from male Sprague-Dawley rats immunized with type II collagen, were analyzed by IHC staining and real-time RT-PCR for expression of iASPP and p73. SFs transfected with adenoviral vectors encoding 37AA (Ad37AA), were subjected to TUNEL assay for apoptotic status and real-time RT-PCR for expression of p53 upregulated modulator of apoptosis (PUMA), a downstream apoptosis signaling molecule. The association of iASPP with p73 in Ad37AA-transfected SFs was identified by immunoprecipitation with anti-iASPP, followed by immunoblot with anti-p73. Therapeutic effects of intra-articular (i.a.) injection with Ad37AA on arthritis rats were evaluated by articular index and histological score. IHC staining was performed to analyze synovial expression of cadherin-11 (a specific SF marker), PUMA and IL-6, and apoptotic cells were detected by the TUNEL assay.

**Results:** There were increased levels of iASPP with co-localized p73 expression in synovial lining layers and purified SFs from RA patients and arthritis rats. Enhanced cell apoptosis and increased PUMA expression were identified in Ad37AA-transfected SFs with lower iASPP-associated p73 levels. Articular indexes and histologic scores were reduced in Ad37AA-injected joints with decreased SF densities, increased apoptotic cells, higher PUMA expression and lower IL-6 levels.

**Conclusions:** Our results demonstrate amelioration of experimental arthritis by dissociating the i.a. binding of p53 family members with iASPP to induce apoptosis in SFs, implicating this molecule as a potential therapeutic target in RA patients.

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## FRI0054 MICROPARTICLES FROM RHEUMATOID ARTHRITIS PATIENTS INDUCE APOPTOSIS AND AUTOPHAGY IN CULTURED ENDOTHELIAL CELLS

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**Background:** Microparticles (MPs) are small membrane vesicles released by many cell types under physiological conditions or pathological situations. Increased levels of MPs have been reported in patients with autoimmune diseases, such as Rheumatoid Arthritis (RA) (1) which is characterized by an accelerated atherosclerosis. TNF is the main cytokine involved in the pathogenesis of RA and many studies agree on the pro-atherogenic role of TNF in RA patients (2). Furthermore, MPs could have a role in endothelial dysfunction, contributing to atherosclerosis in RA patients. Many studies have also shown that an imbalance of the mechanisms of apoptosis and autophagy seems to be involved in endothelial dysfunction.

**Objectives:** The aim of this study was to analyze total and platelet (PMPs)-, endothelial (EMPs)-, leucocyte (LMPs)-derived MPs in RA patients. Moreover, in vitro studies were performed to estimate the effects of serum RA-MPs on vascular endothelium, before and after three months of treatment with TNF inhibitors (TNFi), with special focus on apoptosis and autophagy pathways.

**Methods:** Twenty RA patients and ten sex and age matched Healthy Controls (HC) were enrolled in this study. Experiments were performed using flow cytometry and western blot techniques according to consensus guidelines. MPs were expressed as MPs/microl; autophagy and apoptosis were expressed as LC3II/beta-actin ratio and percentage of annexin V double positive cells respectively.

**Results:** At baseline the total number of MPs was significantly increased in RA patients compared with HC (p=0.002). Only the EMPs subset was increased in RA patients compared with HC (p=0.017). After three months of treatment with TNFi, either the total number of MPs and the EMPs were significantly decreased compared with baseline (p=0.003 and 0.04 respectively). In vitro studies showed that at baseline serum RA-MPs significantly increased, in a dose-dependent manner, both apoptosis and autophagy levels in the human umbilical vein cell line EA.hy926 (p=0.005 and p=0.02, respectively versus untreated cells). After three months of treatment this effect was not more evident ($p>0.05$, versus untreated cells for both parameters). Furthermore, co-treating EA.hy926 cells with RA-MPs and 3-methyl-adenine (3-MA), a pharmacological inhibitor of autophagy, induced a significant increase of apoptosis (p=0.007 versus MPs-treated cells without 3-MA).

**Conclusions:** Our data demonstrate that the total number as well as the EMPs are significantly increased in RA patients and their levels significantly decreased after TNFi. Moreover, MPs are able to modulate apoptosis and autophagy in EA.hy926 cells. After three months of treatment with TNFi, MPs decrease their harmful effects. The results with 3-MA suggest a protective role of autophagy on apoptosis induction by RA-MPs on endothelial cells. Therefore, these results confirm the potential contribution of MPs to endothelial dysfunction.

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## FRI0055 SP1 INHIBITOR MODULATES THE AUTOCRINE ACTION OF GLIOSTATIN/THYMIDINE PHOSPHORYLASE (GLS/TYMP) IN RHEUMATOID FIBROBLAST-LIKE SYNOVIOCYTES

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**Background:** Gliostatin/thymidine phosphorylase (GLS/TYMP) is known to have angiogenic and arthritogenic activities, and aberrant GLS production has been observed in the synovial membranes of rheumatoid arthritis (RA) patients. GLS induces its own expression in cultured fibroblast-like synoviocytes from RA patients (RA-FLSs). The promoters of GLS gene contain binding sites for the DNA binding protein Sp1. Previously, we have reported that the Sp1 transcription factor is essential for the expression of GLS in RA-FLSs and that the Sp1 inhibitor, mithramycin, inhibits the TNF-$\alpha$-induced expression of GLS in cultured RA-FLSs.

**Objectives:** In this study we examined the inhibitory effect of the Sp1 inhibitor

mithramycin on the autocrine activity of GLS expression induced by GLS in cultured RA-FLSs.
**Methods:** Samples of synovial tissue were obtained from 11 patients with RA who were undergoing total knee or elbow arthroplasty or arthroscopic synovectomy. RA-FLSs were cultured with GLS, with or without mithramycin. The expression levels of GLS were determined using reverse transcription-polymerase chain reactions (RT-PCR) and enzyme immunoassay.
**Results:** We investigated GLS mRNA and protein expressions in RA-FLSs treated with or without mithramycin, followed by incubation with GLS. Measuring GLS mRNA and protein levels showed significant induction by GLS alone compared with the control with no GLS. Pre-incubation with mithramycin significantly suppressed this induction.
**Conclusions:** The Sp1 inhibitor, mithramycin, down-regulated the increased expression of GLS in RA-FLSs treated with GLS. Because GLS plays a pathological role in RA, blocking GLS stimulation using mithramycin may suggest novel approaches to anti-rheumatic therapy.
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## FRI0056 ALTERED MICRORNA EXPRESSION PATTERN IN SYNOVIAL AND BLOOD NEUTROPHILS IN RHEUMATOID ARTHRITIS REVEALS THE PATHOGENIC PROFILE OF THESE CELLS

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**Background:** MicroRNAs (miRNA) have recently emerged as a new class of modulators of gene expression. Several studies have shown a deregulation of miRNAs in peripheral blood mononuclear cells or T lymphocytes, in synovial tissue and fibroblasts that might contribute to inflammation, degradation of extracellular matrix and invasive behavior of the resident cells in rheumatoid arthritis (RA). Neutrophils are key cells participating in the joint destruction.
**Objectives:** To investigate the miRNA expression profile in synovial and blood neutrophils in RA and its role in the pathogenesis of this disorder.
**Methods:** Neutrophils were isolated from peripheral blood of 20 healthy donors and 20 RA patients. Synovial neutrophils were isolated from paired synovial fluid of 10 RA patients. nCounter microRNA Assay was used to detect simultaneously 800 human microRNAs in each sample.100 ng of RNA from peripheral blood and synovial neutrophils were prepared by ligating a specific DNA tag (miR-tag) onto the 30 end of each mature microRNA according to the manufacturer's instructions. Altered miRNAs were analyzed for potential mRNA targets using Ingenuity pathways analysis (IPA) software. miRNA expression levels were validated through RT-PCR. Several mRNA targets of these miRNAs were analyzed by RT-PCR. Healthy neutrophils were treated in vitro with anti-CCPs isolated from RA patients. mRNA expression of DICER, Ago1, Ago2, exportin was evaluated through RT-PCR. DICER protein expression was analyzed by western blot.
**Results:** Among 800 miRNAs analyzed, 121 were detected in neutrophils from peripheral blood or synovial fluid. Using a 2 fold change cut off, 97 miRNAs were altered in peripheral blood neutrophils from RA patients compared to healthy donors. Most of them were downregulated (94 downregulated and 3 upregulated). Accordingly, RA neutrophils showed a downregulation of the proteins participating in miRNA biogenesis, including DICER, Ago1, Ago2, exportin 5. In addition, treatment of healthy neutrophils with IgGs anti-CCPs isolated from RA patients decreased the expression of these proteins, thus pointing at these autoantibodies as main modulators of microRNA neutrophil expression. Functional IPA analysis showed that altered miRNAs regulated cellular functions such as development, growth, proliferation and movement and were mainly involved in immunological disease. Among the miRNAs found deregulated blood, 34 miRNAs were found even more significantly reduced in synovial neutrophils compared to paired blood neutrophils from RA patients. These miRNAs were mainly involved in inflammatory response, suggesting the abnormal activation of this cell subtype in the joint.
**Conclusions:** 1) RA neutrophils exhibit a defect in the miRNAs processing, showed by a decrease in most of the detected miRNAs and the concomitant downregulation of proteins involved in their biogenesis. This defect seems to be modulated, at least partially, by anti-CCPs antibodies. 2) miRNA downregulation is even more pronounced in synovial resident neutrophils, which may contribute to the high inflammatory profile of these cells in the joint.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2548

## FRI0057 HUMAN MESENCHYMAL STEM CELL CIRCULATION AFTER SURGICAL BONE MANIPULATION BUT ABSENCE OF MSC PERIPHERAL BLOOD CIRCULATION IN RHEUMATOID ARTHRITIS AND HEALTH

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**Background:** Despite the realisation that rheumatoid arthritis (RA) is an autoimmune disease there is still considerable interest in the idea that widespread dissemination of synovial fibroblasts with "transformed" characteristics may play a role in polyarticular joint destruction. An animal model indicated that fibroblast-like synoviocytes (FLS) implanted in one location next played a role in cartilage destruction at remote sites with the circulation the most likely conduit[(1)]. In man FLS are thought to be derived from multipotential mesenchymal stromal stem cells (MSCs) and whilst circulating MSCs have been reported in animal models, this is more contentious in man.
**Objectives:** To use simultaneous superficial and deep venous blood in cases undergoing orthopaedic skeletal manipulation of long bones (lower extremity) prior to definitive stabilisation to explore the basis for potential MSC circulation in skeletal injury, health and RA.
**Methods:** Deep (femoral) and matched anticubital vein blood was collected from 36 patients undergoing lower limb orthopaedic procedures. Peripheral blood was also taken from 11 early RA cases (EULAR/ACR criteria) and 12 healthy controls. CFU-F assays were performed on all samples. Cytometric phenotyping and molecular characterisation of genes related to osteo-, chondro- and adipogenesis were undertaken. To exclude the possibility that CFU-Fs obtained from peripheral vein were merely syringe-trapped fibroblasts, control skin fibroblasts were also used in the molecular analysis.
**Results:** 17/36 femoral vein samples contained CFU-Fs but only 6/59 peripheral vein samples (p=0.0002). Only orthopaedic cases showed peripheral blood MSC circulation which often, but not exclusively, were associated with concomitant presence in the femoral vein. In the 17 femoral vein samples with CFU-Fs their mean frequency was 0.00001% of MNCs. The frequency was higher when sampling post manipulation compared to before/during ($9.7x10^{-8}$ compared to $3.1x10^{-8}$ in femoral vein, $4.0x10^{-8}$ compared to $1.2x10^{9}$ in the periphery). We confirmed the MSC nature of the CFU-Fs by expansion and phenotype: CD105/CD73/CD90 positivity and CD19/CD31/CD33/CD34/CD45/CD61 negativity. Their molecular profiles were typical of MSCs with 39/80 genes (including *ALPL, COL1A1, POU5F1, NGFR, SPARC, SOX9*) showing similarity across multiple MSC tissue controls (iliac crest and femoral marrow-, cortical bone-, periosteum- and adipose-derived MSCs) and neither had profiles that suggested they represented fibroblasts from dermis.
**Conclusions:** There is no evidence that MSCs circulate in early RA. Although MSCs are present in deep veins their presence appears to be, at least in part, linked to skeletal manipulation. Their numbers are so low that a biological role seems unlikely. Biophysical micro-damage to the trabecular vascular architecture, permitting circulation, is a likely explanation. These findings challenge the idea that circulating MSCs or their progeny play a role in early RA or other autoimmune diseases and also challenges the idea that intravenous injection of MSCs with "homing" to sites of injury is a valid strategy since physiological MSC circulation does not occur naturally to a significant degree.
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[1] Nat Med. 2009;15(12):1414
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3468

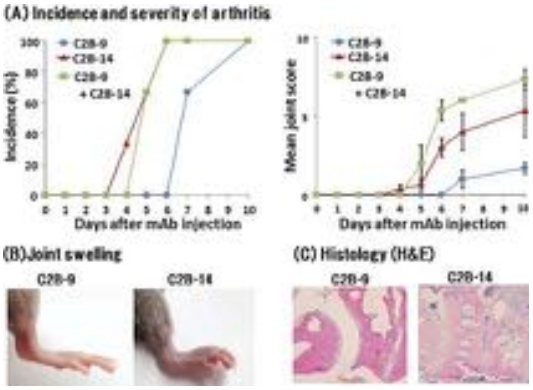
## FRI0058 PRODUCTION OF AN ANTI-TYPE II COLLAGEN IGG2B MONOCLONAL ANTIBODY CAPABLE OF INDUCING DESTRUCTIVE POLYARTHRITIS IN MICE

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**Background:** A mouse model of destructive antibody-mediated polyarthritis (AMPA) induced by a combination of four or five different monoclonal antibodies (mAbs) specific for type II collagen (CII) was previously established. However, it has not been well defined whether an anti-CII mAb is able to induce AMPA.
**Objectives:** The present study aimed to produce an anti-CII mAb that induced destructive AMPA in mice.
**Methods:** To establish anti-CII mAb-producing hybridomas, DBA mice were repeatedly sensitized with chicken CII plus CFA and then CII-sensitized spleen cells were fused with myeloma cells before cloning fused-cells producing mAbs

against mouse CII. To induce arthritis, DBA mice were i.p. injected with various doses of each produced anti-CII mAb (day 0), followed by i.p. administration of LPS on day 3. To evaluate the severity of the arthritis, lesions of the four paws were each graded from 0 to 3 according to the increasing extent of erythema and edema of the periarticular tissue. Histological analysis of inflamed joints and measurement of C3 in serum were also performed.

**Results:** A number of hybidomas producing different isotypes of anti-CII mAbs including IgG1, IgG2a, IgG2b, IgG3, and IgM were established. I.p. injection of various doses of each anti-CII mAb into DBA mice revealed that only two mAbs (C2B-9 and C2B-14) induced arthritis by the injection without a combination of the mAbs. The incidence of AMPA was 100% in the 5 mice injected with either C2B-9 or C2B-14. However, C2B- 9 induced only mild arthritis while C2B-14 induced moderate joint inflammation, although injection of both C2B-9 and C2B-14 induced severe arthritis. The isotype of C2B-9 and C2B-14 was IgG2b. Histologically, marked hyperplasia of the synovium as well as destruction of cartilage and bone was observed in mice injected with C2B-14 but not C2B-9. Significant decreases in C3 in serum were also observed in C2B-14- but not in C2B-9 -injected animals.




**Conclusions:** We successfully produced an anti-CII IgG2b mAb, C2B-14, that induced destructive AMPA. The destructive AMPA by C2B-14 was associated with low levels of C3 in serum, suggesting a role of complement activation in C2B-14-induced AMPA.

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## FRI0059 COMPLEMENT-MEDIATED NEUTROPHIL LYSIS - A MECHANISM PROMOTING HYPERCITRULLINATION IN RHEUMATOID ARTHRITIS?

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**Background:** Protein citrullination, the post-translational conversion of arginine to citrulline, is thought to participate in the development of anti-citrullinated protein antibodies (ACPA) in patients with rheumatoid arthritis (RA). Recently, synovial fluid cells from RA patients were found to have citrullination of several intracellular proteins, a process named hypercitrullination. This unique form of citrullination did not occur in other types of cell death such as apoptosis or NETosis, but was proposed to be induced only through pore-forming membranolytic pathways, including complement-mediated cell lysis through the membrane attack complex.

**Objectives:** To explore the *naturally occurring* humoral mechanisms required for induction of complement-mediated neutrophil lysis in the RA joint.

**Methods:** Neutrophils (PMNs) isolated from synovial fluid (SF) (n=4) or peripheral blood (PB) (n=25) of ACPA-positive RA patients as well as PB of healthy controls (HC) (n=12) were analyzed for anti-PMN binding IgG, C3bi and C5b-9 complement deposition, as well as PMN viability using Annexin V and propidium iodide staining by flow cytometry analysis. In addition, PMNs isolated from HC were incubated with 4 matched RA serum and SF samples as well as 7 additional unmatched RA SF samples, or normal human serum (NHS); complement deposition, complement regulatory protein CD46 expression, and PMN viability were then measured. Finally, the kinetics by which HC PMNs underwent cell death upon stimulation with complement-fixing antibodies (Abs) and NHS were analyzed using the IncuCyte ZOOM® live cell imaging system.

**Results:** In the periphery, RA PMNs had highly increased mean fluorescence intensity (MFI) ratio for C3bi cell-surface deposition as compared to HC (p=0.0183), but no differences were seen for C5b-9 deposition. However, in SF, RA PMNs had elevated MFI ratio for both C5b-9 deposition (p=0.0121) as well as anti-PMN binding IgG deposition (p=0.0011) as compared to PB PMNs from HC, or paired PB PMNs from RA patients (p=0.0177, p=0.0113, respectively). Consistent with the selective increase in complement C5b-9 deposition in SF, we observed a decrease in the expression of CD46 in SF, but not PB PMNs of RA patients (p=0.0270), suggesting a potential mechanism through which SF PMNs are sensitized to complement-mediated lysis. Further, PMNs isolated from SF were, to a higher extent than PB PMNs, undergoing secondary necrosis, supporting the notion of complement-mediated lysis of SF PMNs *in vivo*. Finally, adding RA SF, but not RA serum, to HC PMNs induced markedly elevated C3bi and C5b-9 deposition, reduction in CD46 levels and PMN cell death, clearly demonstrating the PMN cytotoxic properties of RA SF in 10/11 samples, as well as suggesting an important role of complement activation in this process. IgG- and complement-mediated lysis of PMNs was also verified *in vitro* by live cell imaging.

**Conclusions:** RA SF PMNs demonstrate increased complement deposition associated with PMN cell death both *in vivo* and *in vitro*. Elucidating the cause of complement deposition and the role of CD46 in promoting PMN lysis may help to uncover a mechanism for hypercitrullination, ACPA formation and RA disease propagation.

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**Disclosure of Interest:** None declared

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## FRI0060 EXTRACELLULAR MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) IS ESSENTIAL FOR HYPOXIA-INDUCED ANGIOGENESIS IN A HIF-1-AND HIF-2-INDEPENDENT MANNER

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**Background:** Angiogenesis is a hallmark of the pathogenesis of rheumatoid arthritis (RA) but also of other inflammatory processes, tissue regeneration and progressing tumors. In RA, the neovascular network is dysfunctional and fails to restore tissue oxygen homeostasis, so that the inflamed joint remains markedly hypoxic. The hypoxia-induced multifunctional and pro-inflammatory protein macrophage migration inhibitory factor (MIF) participates in the regulation of hypoxia-induced angiogenesis. At cellular level, hypoxia is detected by a mechanism that regulates the amount of the oxygen-sensitive $\alpha$-subunits of the transcription factors, hypoxia-inducible factor (HIF)-1 and -2, which activate a gene program associated with angiogenesis and glycolysis.

**Objectives:** Here, we focus on the role of MIF and its mechanism of action in the process of hypoxia-induced angiogenesis and in the regulation of HIFs.

**Methods:** Therefore, we developed a specific knockdown of MIF and its receptor CD74 in Human Microvascular Endothelial Cell (HMEC) using lentiviral-based shRNA technology allowing us to analyse the role of MIF in hypoxia-induced angiogenesis. We investigated the adaption of these cells towards pathophysiologic hypoxic conditions (1% $O_2$) analysing protein-levels of HIF-1$\alpha$ and HIF-2$\alpha$, HIF-target gene expression, angiogenesis and VEGFA release. To further identify the underlying mechanisms angiogenesis assay was performed with HMECs treated with anti-CD74-IgG, rhMIF and 4-IPP, a small molecule inhibitor of MIF.

**Results:** Lentiviral-mediated reduction of MIF in HMEC led to significantly decreased angiogenesis ($p<0.01$) which could be restored by adding extracellular rhMIF. Interestingly, reduction of MIF did not influence hypoxia-induced (i) protein-levels of HIF-1$\alpha$ and HIF-2$\alpha$, respectively, and (ii) HIF-target gene expression of *PGK1*, *GAPDH* and *VEGFA* but (iii) induced secretion of pro-angiogenic VEGFA and IL8. Moreover, addition of 4-IPP also decreased angiogenic response of non-transduced HMECs but enhanced the hypoxia-induced HIF-target gene expression of *PGK1* and *VEGFA*. Inhibiting MIF-signalling by the addition of extracellular anti-CD74-IgG also reduced angiogenic potential of HMEC ($p<0.001$), which was not restorable by the addition of extracellular rhMIF. Furthermore, lentiviral-mediated reduction of CD74 in HMEC also decreased angiogenesis ($p<0.01$) without influencing HIF-target gene expression of *PGK1*, *GAPDH* and *VEGFA*.

**Conclusions:** Our findings reveal an essential regulatory function of MIF upon the angiogenic potential of HMECs which is independent of the hypoxia-induced HIF-mediated adaptation process activating a gene program associated with angiogenesis and glycolysis. These findings open new possibilities for therapeutic approaches in RA and other inflammatory disorders by targeting specific MIF mediated signalling events.

**Disclosure of Interest:** None declared

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FRI0061 **INVOLVEMENT OF REGULATORY T CELLS AND MICRORNAS IN REGULATION OF COLLAGEN-INDUCED ARTHRITIS IN MICE TREATED WITH IL-2/ANTI-IL-2 IMMUNE COMPLEXES**

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**Background:** Interleukin-2 (IL-2) induces regulatory T cells (Tregs) and reduces disease activity such as graft-versus-host disease and systemic lupus erythematosus. IL-2/anti-IL-2 monoclonal antibody immune complex (IL-2IC) increases the half-life of IL-2 in vivo and strongly induces Tregs. We previously demonstrated that administration of IL-2IC suppressed collagen-induced arthritis (CIA) in mice (EULAR 2015).
**Objectives:** To clarify complex regulatory network of IL-2IC in autoimmune arthritis we examined the effects of IL-2IC on Th1, Th17, Treg inductions and microRNAs (miRNAs) expressions which regulate T cell inductions.
**Methods:** Male DBA/1 mice were immunized by injection of 200μg of Type II collagen emulsified with an equal volume of Complete Freud Adjuvant intradermally at the base of the tail of mice (first immunization). Second immunization was given 21 days after first immunization. IL-2ICs were prepared by mixing 5μg of anti-IL-2 antibody (clone JES6–1D) with 1μg of mouse IL-2 for 15 minutes. The mice were injected with either PBS as a control or IL-2IC (5μg /mouse) intraperitoneally for 3 days. Mouse paws were scored for arthritis using a macroscopic scoring system ranging from 0 to 4 (0, no swelling or redness; 1, swelling/redness of paw or one joint; 2, two joints involved; 3, more than two joints involved; and 4, severe arthritis of the entire paw and joints). The arthritic score for each mouse is the sum of the scores of all four paws. Peripheral blood cells were stained with anti-CD25 (PC61), anti–CD4 (RM4–5), anti-Foxp3 (FJK-16s) and CD4+CD25+Foxp3+ Tregs were analyzed by flow cytometry. Th1 and Th17 cells infiltrating in the synovium were examine by immunohistochemistry stained with anti-IFN-g and IL-17 mAb. MiRNAs expressions in the serum from CIA mice were analyzed using panel real-time PCR analysis (miRCURY LNATM microRNA PCR). Statistical analysis was performed by paired t test.
**Results:** To define the effect of IL-2IC on established CIA, IL-2IC was administered for 3 days from day 21 to day 23 after the first immunization (day 0 to day 2 after the second immunization) of CIA. To define the effect of IL-2IC on early stages of disease induction we administered IL-2IC from day 0 to day 2 after first immunization. We observed a significant decrease in both the incidence and severity of arthritis in these CIA mice. Injection of IL-2IC effectively elicited more than 2-fold expansion of CD4+CD25+Foxp3+ Tregs in peripheral blood cells than control mice. Th1 and Th17 cells infiltrations in the synovium were significantly inhibited by IL-2IC treatment. We identified 24 differentially expressed miRNAs (fold change >2.0) and 72 differentially expressed miRNAs (fold change <0.5) comparing untreated mice. Of note, we observed miR-17–5p and miR-19b-3p which inhibits iTreg induction was significantly augmented in CIA mice but decreased in CIA mice treated with IL-2IC. In addition, miR-326–3p which induces Th17 was significantly augmented in CIA mice but decreased in CIA mice treated with IL-2IC.
**Conclusions:** These observations indicate that IL-2IC might play a complex regulatory role in autoimmune arthritis by regulating Th1, Th17, Tregs and miRNAs which regulate these T cell inductions.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3086

## Rheumatoid arthritis - prognosis, predictors and outcome

FRI0062 **OBESITY IS ASSOCIATED WITH WORSE CLINICAL OUTCOMES YET LIMITED RADIOGRAPHIC PROGRESSION IN EARLY RHEUMATOID ARTHRITIS**

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**Background:** In RA, being overweight or obese has previously been shown to be associated with worse clinical outcomes (1, 2), yet also less radiographic damage (2, 3).
**Objectives:** To confirm if body mass index (BMI) is associated with worse clinical disease activity or inversely associated with radiographic outcomes in early RA.
**Methods:** BMI, categorized as normal (<25, n=141), overweight (25–29.9, n=74), and obese (≥30, n=43), was available in 258 patients who were enrolled in the Swedish pharmacotherapy (SWEFOT) trial. After initial methotrexate for 3 months, non-responders were randomized to triple therapy or anti-TNF therapy, while responders continued on methotrexate. Disease activity (DAS28), functional impairment (HAQ), VAS-pain, and radiographic damage (Sharp van der Heijde score, SHS) were evaluated regularly. Here, results are shown at 24 months of follow-up.
**Results:** Treatment allocation and baseline outcome measures did not differ across the BMI categories. In a dose-response manner, higher BMI at baseline was associated with worse clinical outcomes over 24 months (DAS28, HAQ, and VAS-pain) (Table). Patients with normal (58%) or overweight (50%) BMI had a proportionally greater chance of attaining 24-month clinical remission (DAS28<2.6) than obese patients (23.1%) (OR 3.2 [95% CI 1.6–6.3], p<0.001; OR 2.2 [95% CI 1.2–4.1], p=0.007, respectively). Among absolute radiographic scores, no significant differences were observed, yet radiographic progression (ΔSHS≥1, baseline-24 months) was halted more frequently (56.3%) among obese patients than normal/overweight patients combined (37.6%) (OR 1.9 [95% CI 1.0–3.6], p=0.049) (obese vs. normal (40%), OR 1.7 [95% CI 0.9–3.1], p=0.101; obese vs. overweight (32.7%), OR 1.8 [95% CI 1.1–3.2], p=0.032).

Table 1. Outcome measures after 24 months of disease-modifying antirheumatic agents

| Outcomes [Medians (IQR)] | Normal (n=141) | Overweight (n=74) | Obese (n=43) | P value[a] |
|---|---|---|---|---|
| DAS28 | 2.4 (1.7, 3.4)* | 2.6 (2.2, 3.8)† | 3.2 (2.8, 4.8)†* | p<0.001 |
| HAQ | 0.3 (0.0, 0.8)* | 0.5 (0.0, 1.0)† | 0.8 (0.4, 1.3)†* | p<0.001 |
| VAS-pain | 18.5 (6.0, 35.0)* | 25.0 (8.0, 47.0)† | 39.0 (22.0, 61.0)†* | p<0.001 |
| ESR | 10.0 (6.0, 18.0)* | 13.5 (8.0, 23.0) | 18.0 (11.0, 26.0)* | p=0.008 |
| SHS | 7.0 (2.0, 16.3) | 6.5 (2.0, 14.0) | 5.0 (0.8, 13.0) | p=0.519 |

[a]Kruskal-Wallis test (individual comparisons: Mann-Whitney U test; post-hoc comparisons: Dunn-Bonferroni (DB) correction). †Overweight vs. Obese: DAS28, p=0.012 (DB, p=0.020; adjusted, p=0.060); HAQ, p=0.030 (DB, p=0.021; adjusted. p=0.062); VAS Pain, p=0.025 (DB, p=0.023, adjusted: p=0.069). *Normal vs. Obese: Mann-Whitney or DB + adjustment, p<0.001 (erythrocyte sedimentation rate (ESR): p=0.003 (DB, p=0.003, adjusted: p=0.009)).

**Conclusions:** Obesity at diagnosis was found to be a strong predictor of worse long-term clinical outcomes in early RA – including disease activity, functional impairment, and pain; thus confirming previous findings. Nonetheless – as has also been previously shown – obesity was associated with a better chance of halting radiographic progression.
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**Disclosure of Interest:** A. Levitsky: None declared, S. Saevarsdottir: None declared, K. Brismar: None declared, K. Hambardzumyan: None declared, C. Lourdudoss: None declared, R. van Vollenhoven Grant/research support from: AbbVie, BMS, GSK, Pfizer, Roche, and UCB, Consultant for: AbbVie, Biotest, BMS, Crescendo, GSK, Janssen, Lilly, Merck, Pfizer, Roche, UCB, and Vertex
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FRI0063 **PREDICTORS OF FLARE IN A COHORT OF RA IN REMISSION AFTER 12 MONTHS OF FOLLOW-UP**

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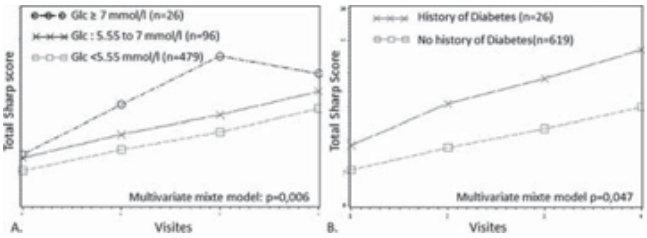
**Background:** Definitive biomarkers have not been identified to predict flares in patients with RA in clinical remission.
**Objectives:** To determine clinical, serological and ultrasonografic variables predicting disease relapse at 12 months of follow-up in a cohort of RA patients in clinical remission.
**Methods:** We included consecutively RA patients in clinical remission defined as DAS28-ESR <2.6 for >6months evaluated by two independent rheumatologist from our Arthritis Clinic. Complete clinical and biological assessment, determination of serum levels of angiogenic and proinflamatory cytokines, and ultrasound scans of both hands were performed at baseline and after 12 months of follow-up. Risk factors odds ratio (OR) related with 12 months flare were adjusted with multivariate logistic models.
**Results:** Sixty patients with RA in remission were included; 78.3% were female. Median age was 53 years (range: 31–74), weight was 67 kg (47–108). Disease and remission mean duration were 111.9 ± 86.4 and 37 months, respectively. 71% of patients were RF positive and 81% were ACPA positive. Patients taking low-dose prednisone, csDMARDs and bDMARDs were 16 (26%), 47 (78%) and 28 (46.7%), respectively. At baseline, 66% had power-doppler (PD) signal and 48% also had synovial hyperplasia grade ≥2, so fulfilling the criteria previously defined of ultrasound defined active sinovitis (UdAS). Twenty-six (43%) patients had disease flare during the follow-up.
In the univariate analysis, disease flares were more frequent in patients with PD signal (p=0.056) or UdAS (p=0.117), and significantly less frequent in patients with mild-moderate intake of alcohol. However, in the multivariate analysis, only higher ESR levels (OR: 1.1, 95%CI: 1–1.1), higher weight (OR: 3.1, 95%CI: 1.4–7) and low-dose prednisone treatment (OR: 1.8, 95%CI: 1.2–2.8) were independent risk factors at baseline for disease flares. This model has a sensitivity of 76.9% (95%CI: 56.4–91), a specificity of 76.5% (95%CI: 58.8–89.3), a predictive positive value of 71.40% (95%CI: 52.4–88.4), a predictive negative value of 81.3% (95%CI: 62.7–91.7) and a good predictive power (ROC: 0.849, IC 95%: 74.4–95.4%). We did not find differences between angiogenic or proinflammatory cytokine serum levels and not differences in RAMRIS between patients relapsing or maintaining the remission at baseline.

**Conclusions:** This prospective study suggests that higher ESR levels, higher weight and low-dose prednisone treatment are relevant independent risk factors for development of disease flares in patients with RA in clinical remission. However, imaging data (Ultrasound or MRI) or angiogenic/cytokine serum levels were no predictors of flare in this study.
**Disclosure of Interest:** None declared
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## FRI0064 HYPERGLYCEMIA IS A PEJORATIVE PROGNOSTIC FACTOR OF CLINICAL OUTCOME AND RADIOGRAPHIC PROGRESSION IN EARLY RHEUMATOID ARTHRITIS: RESULTS OF THE ESPOIR COHORT

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**Background:** Diabetes was found to be increased in patients with rheumatoid arthritis (RA).
**Objectives:** The objective of this study was to evaluate the impact of hyperglycemia and diabetes on clinical activity and radiographic progression within the first 3 years in patients with early RA.
**Methods:** Patients of the ESPOIR cohort with early RA meeting the ACR/EULAR 2010 criteria and with data available for fasting blood sugar at baseline were analyzed. Glycemic status was analyzed with 2 different definitions: i) history of type I or II diabetes; ii) baseline blood sugar splitted into 3 categories: normal (<5.55 mol/l), pre-diabetes (between 5.55 and 7 mmol/l) and diabetes (≥7 mmol/l). DAS28 and total Sharp score evolution during the first 3 years were compared between groups using multivariate mixed models. The multivariate models included the following variables: body mass index, age, gender, presence of rheumatoid factor and/or ACPA, glucorcorticoids. For DAS28 model, CRP was added in the model and for total Sharp score model, DAS28 and total Sharp were included.
**Results:** 26 patients were known to be diabetic and 619 patients were non-diabetic. At baseline, 479 patients had normal blood sugar; 96 had pre-diabetic levels and 26 had diabetic levels. These three groups initially differed on age, body mass index, presence of rheumatoid factor, and score DAS28 Sharp erosion. In multivariate analysis, DAS28 during the first three years were significantly higher in patients with hyperglycemia (p<0.0001) and in patients with history of diabetes (p=0.05). Similarly, the structural progression was greater in patients with hyperglycemia inclusion with a dose-dependent effect (Figure 1A; p=0.006) and in patients with history of diabetes (Figure 1B; p=0.047).




**Conclusions:** In early RA, blood sugar level is an independent predictor of disease activity and structural progression at 3 years, with a dose-dependent effect. Beyond cardiovascular complications, the measurement of blood sugar in patients with early RA may also help to assess more precisely the prognosis of the disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3749

## FRI0065 PRESENCE, GRADE AND LOCATION OF POWER DOPPLER PREDICT PROGRESSION OF RADIOGRAPHIC DAMAGE IN TNFα BLOCKER INDUCED CLINICAL REMISSION IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Functional outcome of patients with rheumatoid arthritis (RA) depends from control of disease activity and arrest of radiographic damage. Clinical remission can be achieved in the majority of RA patients by combinations of steroids, DMARDs and TNFα blockers. Recent imaging studies identified residual subclinical inflammation in many patients in treatment with DMARDs: active synovitis was demonstrated by magnetic resonance imaging (MRI) and ultrasound (US). Power Doppler (PD) positivity correlated best with radiographic progression (1). On the other hand, TNFα blockers are much more efficacious in blocking radiographic damage by direct inhibition of osteoclasts, but it is not known if PD positivity predicts on-going damage also in RA patients in remission by TNFα blockers.
**Objectives:** To determine the usefulness of PD study to predict structural damage in patients considered in clinical remission by TNFα blocker therapy.
**Methods:** A prospective observational study was performed on 121 consecutive RA patients in therapy with TNFα blockers and in DAS28 remission since 6 months. At baseline US examination was performed in all patients on the metacarpophalangeal, proximal interphalangeal, wrist and metatarsophalangeal joints. Active synovitis was identified by PD positivity. Semi-quantitative PD scoring 0–3 and number of positive joints were registered. The location of PD was scored as follows: capsular and within synovia without bone contact (location 1) or with bone contact and penetrating bone cortex (location 2). At baseline and after one year X-rays of hands and feet were executed. Radiographic progression was expressed as difference in total Sharp Score modified by van der Heijde (ΔTSS) >0. Risk ratios for presence, grade and location of PD relative to radiological progression were calculated.
**Results:** Among the 121 patients, 62 (51,3%) showed no PD signal at the time of remission, whereas 59 (48,7%) had PD signal: in 57,6% of cases grade was 1, in 23,7% grade 2 and in 18,6% grade 3. 38 patients showed PD positivity in one joint, 21 in more joints. Among all PD positive joints 92,4% were at the level of the hands. 74,6% of PD signals were in contact with articular bone surface (location 2). All patients without PD signal did not show radiographic progression. 28,8% of patients showing PD positivity (corresponding to 14% of all patients in clinical remission) underwent radiographic progression. Radiographic progression occurred in 20,6% of patients with PD grade 1, 42,8% with grade 2 and 36,3% with grade 3. Whereas only 6,6% of patients with PD in location 1 progressed, 36,3% of patients with PD in location 2 showed deterioration of radiographic damage. Despite presence of PD, higher PD grades (2 and 3) and PD with contact to bone surface (location 2) determined a significantly increased risk for radiographic progression; PD in location 1 resulted protective.
**Conclusions:** PD demonstrated to be very useful in evaluating patients considered in remission. Absence of PD signal guarantees arrest of radiological progression, whereas patients with PD signal are at risk for progression despite TNFα blockers. This risk increases with higher PD grades and with PD in contact or penetrating bone profile.
**References:**
[1] Brown AK. Arthritis Rheum 2006,54:3761–73
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3323

## FRI0066 THE 28-JOINT DISEASE ACTIVITY SCORE (DAS28) USING C-REACTIVE PROTEIN YIELDS LOWER THRESHOLDS COMPARED TO CONVENTIONAL DAS28 WITH ERYTHROCYTE SEDIMENTATION RATE IN EARLY RHEUMATOID ARTHRITIS

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**Background:** The interchangeability of Disease Activity Score 28 joints (DAS28) calculated using the erythrocyte sedimentation rate (ESR) versus C-reactive protein (CRP) has been questioned (1).
**Objectives:** To compare the 28-Joint Disease Activity Score (DAS28) calculated using C-reactive protein (CRP) with that using erythrocyte sedimentation rate (DAS28-ESR) in a multi-centre, usual care, early rheumatoid arthritis (ERA) cohort.
**Methods:** The present study analyzed baseline and 12-month follow up data from the Canadian Early Arthritis Cohort. The study sample included patients with RA with symptom duration less than 12 months and complete data on DAS28-ESR and DAS28-CRP at both time points. The linear association between continuous DAS28-ESR and DAS28-CRP scores was estimated using Pearson's correlation coefficient and differences across the range of DAS28 scores were examined with Bland-Altman Plots. Receiver operating characteristic (ROC) analysis was used to identify optimal thresholds for disease activity for DAS28-CRP scores that would best correspond with established DAS28-ESR thresholds in the total sample as well as in stratified samples by age and sex. Agreement between newly calculated DAS28-CRP and established DAS28-ESR thresholds was examined (kappa statistic).
**Results:** The study sample included 995 ERA patients. Sample baseline mean (SD) age was 53.7 (14.5) with 5.8 (2.9) months of symptom duration and 738 (74%) were female. Though continuous DAS28-CRP and DAS28-ESR scores were highly correlated ($r$=0.92, p<0.0001), Bland-Altman plots showed that DAS28-ESR scores were higher than DAS28-CRP scores across the spectrum of disease activity, with larger positive discrepancies at lower values. Positive discrepancies between DASCRP and DASESR were higher for women and patients over 60 years old. Optimal thresholds identified for the DAS28-CRP were 2.4 for remission, 2.9 for low disease activity, and 4.6 for high disease

activity. Overall, there was moderate to good agreement between newly calculated DAS28-CRP and DAS28-ESR thresholds (k=0.6).
**Conclusions:** Results from this large observational study of "real-world" ERA patients showed that DAS28-CRP and DAS28-ESR scores were strongly correlated but that DAS28-CRP scores were consistently lower than DAS28-ESR scores. Differences between DAS28-CRP and DAS28-ESR were greater at lower ranges of the DAS28 and were most pronounced in women and older patients. This suggests that substituting one continuous score for the other is likely reasonable for research purposes in data analysis and that interpreting the DAS28-CRP using established DAS28-ESR thresholds may be acceptable for higher levels of disease activity, but not for lower levels, particularly not for remission.
**References:**
[1] Siemons L, Vonkeman HE, ten Klooster PM, van Riel PL, van de Laar MA. Interchangeability of 28-joint disease activity scores using the erythrocyte sedimentation rate or the C-reactive protein as inflammatory marker. Clin Rheumatol. 2014 Jun;33(6):783–9.
**Disclosure of Interest:** B. Kuriya: None declared, O. Schieir: None declared, D. Lin: None declared, J. Pope: None declared, G. Boire: None declared, B. Haraoui: None declared, C. Thorne: None declared, D. Tin: None declared, C. Hitchon: None declared, E. Keystone: None declared, V. Bykerk Grant/research support from: The CATCH study was designed and implemented by the investigators. The authors have received unrestricted grants from: Amgen Canada Inc and Pfizer Canada Inc - Founding sponsor since 2007, Hoffmann-La Roche Ltd, UCB Canada Inc, Bristol-Myers Squibb Canada, AbbVie Corporation and Janssen Inc since 2011, Medexus Inc since 2014 and Eli Lilly Canada Inc since 2015.
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## FRI0067 CHANGES IN MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) SCORE CORRELATE WITH CHANGES IN ESTABLISHED DISEASE ACTIVITY MEASUREMENTS IN PATIENTS WITH EARLY RA FROM THE OPERA STUDY

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**Background:** No single biomarker has yet been able to predict disease course in patients with rheumatoid arthritis (RA). However combinations of biomarkers and changes therein early during treatment may be predictive of later treatment response.
**Objectives:** Investigate correlations between early changes (Δ) in the validated multi-biomarker disease activity (MBDA) score and Δ in disease activity measurements – Disease Activity Score (DAS28-CRP), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI) and C-reactive protein (CRP) – in early RA patients (the OPERA cohort).
**Methods:** In the randomized double-blinded OPERA trial, 180 treatment-naive patients were randomized to an adalimumab (ADA) group (oral methotrexate (MTX) in combination with ADA) or a placebo group (oral MTX and placebo-ADA). Intra-articular glucocorticoids were also injected into swollen joints (1). DAS28-CRP, CDAI, SDAI, and CRP were measured at baseline (BL) and at 3, 6 and 12 months. MBDA score, calculated based on serum concentrations of CRP, interleukin-6, chitinase-3-like protein 1, vascular endothelial growth factor A, matrix metalloproteinase 1 and 3, vascular cell adhesion molecule 1, epidermal growth factor, tumor necrosis factor receptor type I, serum amyloid A, leptin and resistin, with a range of 1–100, was determined retrospectively at the same time points on banked serum samples (2).
Correlations between ΔMBDA scores and Δ disease activity measurements were analyzed by Spearman's correlation coefficient.
**Results:** Patients had a median age of 55.2 (range: 18.7–86) years, disease duration of 84 (range: 42–214) days; 66% were female; 72% and 65% were RF and anti-CCP positive, respectively. At BL, median DAS28-CRP was 5.6 (3.3–8.6) and median MBDA score was 59 (12–90). MBDA scores were low (<30) in 8 (4%) patients, moderate (30–44) in 25 (14%) and high (>44) in 147 (82%) patients. There were no statistically significant correlations between BL MBDA score and

Table 1: Spearman correlations between change in MBDA score at 3 months and change in disease activity measures at 6 and 12 months

| | Δ0-6 months | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | DAS28-CRP | | CDAI | | SDAI | | CRP | |
| | Placebo | ADA | Placebo | ADA | Placebo | ADA | Placebo | ADA |
| ΔMBDA score$_{0-3m}$ | Rho= 0.334 (p=0.002) | Rho=0.394 (p=0.001) | Rho=0.322 (p=0.003) | Rho=0.258 (p=0.022) | Rho=0.356 (p=0.001) | Rho=0.309 (p=0.006) | Rho=0.423 (p=0.001) | Rho=0.354 (p=0.001) |
| | Δ0-12 months | | | | | | | |
| | DAS28-CRP | | CDAI | | SDAI | | CRP | |
| | Placebo | ADA | Placebo | ADA | Placebo | ADA | Placebo | ADA |
| ΔMBDA score$_{0-3m}$ | Rho=0.301 (p=0.005) | Rho=0.428 (p=0.001) | Rho=0.322 (p=0.004) | Rho=0.254 (p=0.022) | Rho=0.395 (p=0.001) | Rho=0.306 (p=0.005) | Rho=0.390 (p=0.001) | Rho=0.429 (p=0.001) |

Δ: change; 0-3 m: 0-3 months; ADA: adalimumab; DAS28-CRP: Disease Activity Score (0-9.4); CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; serum C-reactive protein (mg/L) measured in a clinical laboratory; MBDA: multi-biomarker disease activity; Rho: Spearman correlation coefficient; p: p-values.

other disease activity measurements at 3 or 6 months in the placebo or ADA groups.
Median ΔMBDA scores from BL to 3 months (ΔMBDA score$_{0-3m}$) and to 6 months (ΔMBDA score$_{0-6m}$) were -16.5 and -20, respectively. Median ΔDAS28-CRP from BL to 6 months (ΔDAS28-CRP$_{0-6m}$) and to 12 months (ΔDAS28-CRP$_{0-12m}$) were -2.9 and -3.2, respectively. ΔMBDA score$_{0-3m}$ and ΔDAS28-CRP$_{0-6m}$ were significantly correlated in the placebo and ADA groups, as were ΔMBDA score$_{0-6m}$ and ΔDAS28-CRP$_{0-12m}$. ΔMBDA score$_{0-3m}$ also significantly correlated with ΔDAS28-CRP, ΔCDAI, ΔSDAI and ΔCRP from BL to 6 months and from BL to 12 months (Table 1).
**Conclusions:** In patients with early RA from the OPERA cohort, ΔMBDA score from BL to 3 or 6 months were correlated with longer-term ΔDAS28-CRP, ΔCDAI, ΔSDAI and ΔCRP. Correlations were generally similar between treatment groups.
**References:**
[1] Hørslev-Petersen K, et al., Ann Rheum Dis 2014; 73:654–661
[2] Hirata et al. Current Biomarker Findings 2015, 5:69–78
**Disclosure of Interest:** C. H. Brahe: None declared, M. Østergaard Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, T.Jensen, J. Johansen: None declared, N. Defranoux: None declared, C.-C. Hwang: None declared, R. Bolce: None declared, E. Sasso: None declared, K. Hørslev-Petersen: None declared, K. Steengaard-Pedersen Grant/research support from: Meda, Abbvie, Roche, Speakers bureau: UCB, Pfizer, P. Junker: None declared, T. Ellingsen: None declared, P. Ahlquist: None declared, H. Lindegaard Grant/research support from: Boehringer Ingelheim, A. Linauskas: None declared, A. Schlemmer Grant/research support from: Abbvie, Roche, MSD, M. Dam: None declared, I. Hansen: None declared, T. Lottenburger: None declared, C. Ammitzbøll: None declared, A. Jørgensen: None declared, S. Krintel: None declared, J. Raun: None declared, M. Hetland: None declared
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## FRI0068 CONTRIBUTIONS OF SOCIAL DETERMINANTS OF HEALTH ON REMISSION IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Treatment responses vary among rheumatoid arthritis (RA) patients. There is limited evidence on the contribution of social determinants of health (SDH) to treatment responses and disease outcomes in RA.
**Objectives:** This study aimed to determine the contribution of social determinants of health (SDH) to remission in RA.
**Methods:** Data were collected from the Ontario Best-practices Research Initiative (OBRI) Rheumatoid Arthritis Registry, a clinical registry of early and established adult RA patients followed in routine care. Treatment response at 6 and 12 months was assessed by the 2011 ACR/EULAR Simple Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) remission criteria. The SDH assessed include patient demographics, socioeconomic status, health behaviors, living condition, marital status, and depression. Variables with a $p<0.2$ in univariate analyses were included for multivariable regression. The association between SDH and remission was evaluated by logistic regression, controlling for baseline clinical RA confounders such as RA duration and baseline RA medications, presence of X-ray erosion, antibody status, extra articular features, baseline disease activities, and functional disability. All statistical analyses were performed in SAS9.4.
**Results:** Among 2209 patients with baseline CDAI, 1832 and 1583 reached the 6- and 12-month follow-up, respectively. Among 1778 patients with baseline SDAI, 1505 and 1286 reached the 6- and 12-month follow-up. At 6 months, 14.8% and 15.5% of the patients achieved CDAI and SDAI remission. At 12 months, 18.9% and 19.8% of the patients achieved CDAI and SDAI remission.
After adjusting for clinical confounders, higher neighborhood income was associated with 6-month CDAI remission (OR 1.04 per $10,000; 95%CI 1.00–1.07), while having private insurance was associated with 6-month SDAI remission (OR 0.63 95%CI 0.40–0.99 for non-insurer). At 12 months, smoking and not living alone were both associated with CDAI and SDAI remission (CDAI: OR 0.65 95%CI 0.44–0.96 for non-smoker, OR 3.02 95%CI 1.27–7.15 for not living alone; SDAI: OR 0.62 95%CI 0.40–0.96 for non-smoker, OR 2.87 95%CI 1.11–7.40 for not living alone). Living in a rural community was also associated with SDAI remission at 12 months (OR 1.79 95%CI 1.12–2.86).
**Conclusions:** Socioeconomic factors appear to have an effect on remission at 6 months. Health behavior and living environment appear to be associated with remission at 12 months. Different SDH may affect treatment response and disease outcome at different time points and this study highlights the complexity in studying SDH.
**Acknowledgement:** Dr. Bombardier holds a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology. Dr. Bombardier holds a Canada Research Chair in Knowledge Transfer forMusculoskeletal Care and a Pfizer Research Chair in Rheumatology

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## FRI0069 DISCORDANT CLASSES OF INFLAMMATION AND PAIN IN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS: RESULTS FROM THE EARLY RHEUMATOID ARTHRITIS NETWORK AND THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER

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**Background:** Rheumatoid arthritis (RA) disease activity is measured using DAS28 – consisting of patient-reported, clinician-observed and laboratory measures. A higher proportion of DAS28 attributed to patient-reported measures (1), fatigue, anxiety and depression might reflect augmented central pain processing.
**Objectives:** We hypothesised that subgroups of people with RA showed different contributions from inflammation and central pain mechanisms, and had different clinical needs.
**Methods:** Data were analysed from (1) The Early RA Network (ERAN) inception cohort (n=828); and British Society for Rheumatology Biologics Register (BSRBR) cohorts (2) commencing anti-TNF (n=9905) or (3) using non-biologic (control) DMARDs (n=2581). Subgroups were defined by latent class analysis (LCA) using erythrocyte sedimentation rate (ESR), swollen joint count (SJC), tender joint count (TJC), visual analogue scale-general health (VAS), and SF36 Bodily Pain, Vitality and Mental Health. Scores were standardised to permit graphical comparison. Latent classes were named with reference to disease activity and discordance/concordance of patient-reported variables with externally-measured variables. Prognosis was examined using MANOVA.
**Results:** Five, 4 and 4 latent classes were found respectively in ERAN, BSRBR anti-TNF and control cohorts. The latent classes displayed either concordance across different measures; discordantly higher patient-reported measures despite less markedly elevated ESR/SJC; or discordantly lower patient-reported measures despite elevated ESR/SJC. Latent classes with discordantly higher patient-reported measures represented 12%, 32% and 22% of the ERAN, BSRBR anti-TNF and BSRBR control cohorts respectively. The 5 latent classes found in the ERAN cohort are shown in figure 1. The proportion of people assigned with >80% probability into latent classes were 76% in ERAN, 58% in the anti-TNF and 72% in the control cohort. The latent classes showing discordantly higher patient-reported variables contained more females, and showed worse function.
In those latent classes with higher scores at baseline, the DAS28, HAQ and SF36 bodily pain scores improved over the first 12 months of follow up ($p<0.001$ for all comparisons), such that scores differed between latent classes less at follow up than at baseline. Patients in the concordant latent classes with low patient-reported measures, low SJC and ESR at baseline did not further improve after 1 year in ERAN or BSRBR-Control cohorts, and displayed clinically important worsening of Bodily Pain scores in the BSRBR anti-TNF cohort (mean at baseline: 46, at 1 year: 41; $p<0.001$).

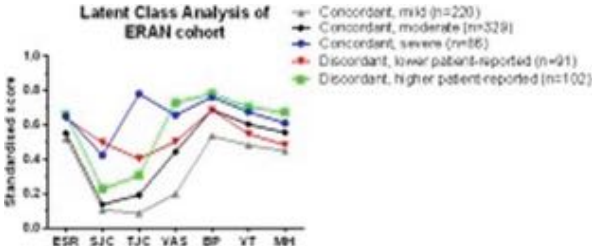


Figure 1. Latent classes showing the mean levels of each variable.

**Conclusions:** Discordant latent classes can be identified in people with RA. There might be a sizeable discordant subgroup with active RA (12 to 32%), and also a group of people with mild disease being considered for anti-TNF treatment, for whom pain management strategies might add benefit to DMARD therapy.
**References:**
[1] McWilliams et al Arthritis Care and Research 2012;64(10):1505–13
**Acknowledgement:** Funded by Pfizer iCRP grant
**Disclosure of Interest:** D. Mcwilliams Grant/research support from: Pfizer Ltd, E. Ferguson: None declared, A. Young: None declared, P. Kiely: None declared, D. Walsh Grant/research support from: Pfizer Ltd, Consultant for: Novartis
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## FRI0070 TRAJECTORIES OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS AFTER ABATACEPT INITIATION AND THEIR ASSOCIATION WITH CLINICAL CHARACTERISTICS

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**Background:** While the effect of disease modifying antirheumatic drugs (DMARDs) in rheumatoid arthritis (RA) is generally presented using population means, the response to DMARDs is heterogeneous. As anti-rheumatic therapy aims to become more personalized, identifying common treatment response trajectories to DMARDs is becoming more important and has major implications for clinical practice.
**Objectives:** To identify different types of trajectories in RA disease activity (DAS28) following the initiation of abatacept (ABA), a T cell costimulation inhibitor, and to examine the determinants of responders' type.
**Methods:** In this pooled analysis of nine RA registries (ARTIS, ATTRA, RHEUMADATA, DANBIO, GISEA, NOR-DMARD, ORA, SCQM, Reuma.pt), inclusion criteria were: diagnosis of RA, initiation of ABA treatment, and at least two assessments of DAS28. Patients were followed until end of ABA treatment. We used growth mixture models to identify groups of patients with similar courses of treatment response and derive empirically based trajectory subgroups. We then examined the association of these groups with socio-demographic-, disease-, and treatment-related predictors.
**Results:** 3898 patients were on ABA (mean DAS28 assessments: 5.2). Trajectory analysis identified three types of treatment response trajectories (Figure). The largest group (3576 patients, 91.7%) can be considered as "classic responders" (CR), with a mean DAS28 at baseline of 3.9 and a progressive improvement over time. The second group (219 patients, 5.6%) can be described as "rapid responders" (RR), with high DAS28 values at baseline (mean 6.4), and a marked improvement in the first two years. The third group (103 patients, 2.6%) seemed composed of "non-responders" (NR) with low DAS28 values at baseline (mean 3.8), a deterioration during the first 2 years, followed by improvement, generally related to a change in therapy.
The three groups were similar in age, sex, BMI, disease duration, and comorbidities (ie. cardiovascular, infectious, metabolic disease, smoking and cancer). However, "classic responders" group had better function at baseline (mean HAQ score: CR: 1.1; RR: 1.7; NR: 1.3, $p<0.001$), and less previous biologics failures (median [Interquartile range] previous bDMARDs: CR: 1 [1; 2]; RR: 2 [1; 3]; NR: 2 [1; 3.5], $p<0.001$).
There were more ABA discontinuation in the "non-responder" group (CR: 55.4%, RR: 61.6%, NR: 77.6%, $p<0.001$). Finally, the proportion of patients with low disease activity (DAS28<3.2) at 6 months were higher among classic responders (CR: 20.5%, RR: 3.7%, NR: 1.9%, $p=0.04$).

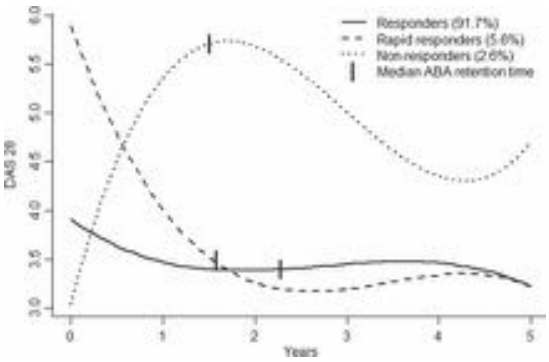


Figure 1

**Conclusions:** There are different types of responders to Abatacept treatment. However, the available baseline information did not allow determination of which trajectory the patient will follow after ABA initiation.
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MSD, Pfizer, Abbott, UCB, Roche, C. Turesson Consultant for: Abbvie, BMS, Janssen, MSD, Pfizer, Roche, UCB, X. Mariette: None declared, D. Choquette: None declared, A. Finckh Consultant for: Abbvie, BMS, MSD, Pfizer, Roche
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## FRI0071 PREDICTORS FOR THE DEVELOPMENT OF ANTI-CITRULLINATED PROTEIN ANTIBODIES IN INDIVIDUALS GENETICALLY AT RISK FOR RHEUMATOID ARTHRITIS

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**Background:** In genetically susceptible individuals, environmental factors induce a pathological activation of the immune system that may eventually lead to systemic autoimmunity and subsequent clinical manifestations. Different risk factors may be relevant for the development of this systemic autoimmunity, representing one of the phases preceding the onset of rheumatoid arthritis (RA) (1).
**Objectives:** To identify predictors for the development of systemic autoimmunity associated with RA in individuals genetically at increased risk.
**Methods:** This is an ongoing prospective cohort study of individuals at increased risk of developing RA, namely first degree relatives of patients with autoimmune diseases (FDRs). Individuals without clinical evidence of RA were enrolled and followed-up yearly. We included all individuals with available anti-citrullinated protein antibodies (ACPA) status (anti-CCP 2, 3.0, or 3.1). We used logistic regression to analyze univariable and multivariable associations between ACPA positivity and putative risk factors or symptoms, including the Connective Tissue Disease Screening Questionnaire (CSQ), 3 or more positive responses represented possible RA (2).
**Results:** A total of 1064 of FDRs were analyzed, of which 57 (5%) were ACPA-positive. FDRs had a median age of 45 (interquartile range (IQR): 34–56) years, 76% were female, 25% had at least one self-reported episode of joint swelling, however on examination only 12% had ≥1 swollen joint (Table 1). In univariable analyses, ACPA-positivity was associated with older age, female sex, tender joints (self reported, ≥1 on examination and mean count), mean swollen joint count, CSQ score and self-reported symptoms associated with possible RA by CSQ. Other variables such as tobacco smoking, alcohol consumption, obesity or tooth loss were not significantly associated with ACPA status. In women, ACPA-positivity was significantly associated with age (OR: 1.1, 95%CI: 1.0–1.1), but not in men (OR: 1.0, 95%CI: 0.9–1.1). In the multivariable adjusted analysis, older age and self-reported symptoms associated with possible RA by CSQ remained independently associated with ACPA positivity. Female sex and tobacco smoking ever had a strong but not significant association.

Table. Characteristics of analyzed FDRs

| Predictors | ACPA negative (n=1007) | ACPA positive (n=57) | Univariable OR (95% CI)[a] | Multivariable OR (95% CI)[b] |
|---|---|---|---|---|
| Age, median (IQR) | 45 (33-55) | 54 (46-60) | 1.0(1.0-1.1)[c] | - |
| Age groups, n(%) | | | | |
| <34 | 262 (26) | 6 (11) | 1 | 1 |
| 34-46 | 258 (26) | 6 (11) | 1.0 (0.3-3.2) | 0.9 (0.2-3.9) |
| 46-56 | 246 (24) | 21 (36) | 3.7 (1.6-8.4)[c] | 3.2 (1.2-8.0)[c] |
| ≥56 | 242 (24) | 24 (42) | 4.3 (1.7-10.8)[c] | 3.4 (1.3-8.5)[c] |
| Sex (female), n(%) | 759 (75) | 50 (88) | 2.3 (1.0-6.2)[c] | 2.1 (0.9-4.9) |
| Smoking ever, n(%) | 491 (49) | 34 (60) | 1.6 (0.9-2.7) | 1.5 (0.9-2.7) |
| Obesity, n(%) | 64 (6) | 3 (5) | 0.6 (0.2-1.9) | - |
| Lost teeth (≥ 10), n (%) | 34 (3) | 4 (7) | 2.1 (0.7-6.3) | - |
| Poor oral health, n(%)[d] | 439 (44) | 27 (47) | 1.1 (0.7-2.0) | - |
| Tender joint self- reported, n(%) | 601 (60) | 45 (79) | 2.6 (1.3-4.8)[c] | - |
| Tender joint≥1 examination, n(%) | 332 (33) | 21 (37) | 1.9 (1.1-3.4)[c] | 1.3 (0.7-2.4) |
| Tender joint count, mean (SD) | 0.9 (3.2) | 2.2 (5.7) | 1.1 (1.0-1.1)[c] | - |
| Swollen joint self reported, n(%) | 201 (20) | 16 (28) | 1.2 (0.6-2.1) | - |
| Swollen joint≥1 examination, n(%) | 121 (12) | 11(19) | 1.8 (0.8-3.5) | - |
| Swollen joint count, mean (SD) | 0.5 (2.8) | 1.8 (5.5) | 1.1 (1.0-1.1)[c] | - |
| CSQ score (number of positive responses), mean (SD) | 0.5 (0.9) | 0.9 (1.3) | 1.3 (1.1-1.7)[c] | - |
| Self reported symptoms related to possible RA by CSQ, n(%) | 99 (9) | 10 (18) | 3.4 (1.6-7.1)[c] | 2.4 (1.1-5.2)[c] |
| SE (2 copies), n(%) | 77 (8) | 3 (5) | 0.7 (0.2-2.2) | 0.6 (0.2-2.0) |

(a) Univariable logistic regression analysis
(b) Multivariable logistic regression analysis
(c) P<0.05
(d) Presence of gingivitis or toothbleeding or mobile teeth or lost bone
(e) FDRs, first degree relatives; CSQ, Connective Tissue Disease Screening Questionnaire; SE, shared epitope.

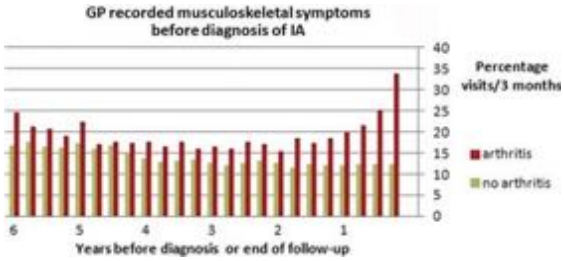
**Conclusions:** In individuals at high risk for RA, the development of ACPAs was associated with older age and self-reported symptoms related with possible RA. We found a trend for an association between female sex and tobacco smoking with ACPA positivity, which did however not reach statistical significance. These findings suggest similar risk factors for the development of ACPAs and for classifiable RA, suggesting that the development of ACPAs is a valid proxy for RA development.
**References:**
[1] Gerlag DM et al. Ann Rheum Dis. 2012; 71(5): 638–41.
[2] Karlson EW, et al. Ann Epidemiol 1995;5:297–302.

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## FRI0072 EARLY DETECTION OF INFLAMMATORY ARTHRITIS: THE ROLE OF MUSCULOSKELETAL SYMPTOMS, INFECTIONS AND RHEUMATOID ARTHRITIS-RELATED COMORBIDITIES IN PRIMARY CARE

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**Background:** Rheumatoid arthritis is characterized by clinically apparent inflammatory arthritis (IA). A preclinical phase has been recognized in which symptoms arise and ambulatory care utilization increases. However, information on location and timing of symptoms before IA diagnosis is still largely lacking.
**Objectives:** The present study was undertaken to identify pathogenetic clues to the development of IA and to assist early identification of future IA patients with a focus on musculoskeletal symptoms, infections and chronic comorbidities.
**Methods:** We conducted a nested case-control study using data from electronic medical records of general practitioners, participating in NIVEL Primary Care Database, to evaluate timing and numbers of visits for symptoms linked to above mentioned groups before a diagnosis of IA. Cases were adults who received a newly diagnosis of IA between 2012 and 2014, in total 2772. Retrospective follow-up had a median of 3.4 years (range 1–9). Controls were matched 1:2 on age, gender, general practice and retrospective duration of follow-up. We studied a total of 192 different symptoms or (chronic) diseases using the International Classification of Primary Care (ICPC-1) coding system. The frequency of primary care visits between the IA patients and controls were compared using logistic regression in different time periods before date of diagnosis. To investigate which of the individual symptoms or diseases were seen often, chisquare tests (chi2) were performed to evaluate the difference in frequency of these symptoms in the IA-patients compared to the controls.
**Results:** The consultation rate for musculoskeletal symptoms was increased in IA patients within the last 1.5 years before diagnosis with odds ratios (ORs) of 1.8 (confidence interval; CI: 1.6–2.1, p-value<0.05), 1.4 (CI 1.2–1.6, p<0,05) and 1.3 (CI 1.1–1.5, p<0.05), respectively, at 6, 12 and 18 months before diagnosis. For infections, the consultation rate was significantly higher 6 and 18 months prior to diagnosis (OR=1.2; both CI: 1.1–1.4, p-value<0.05). Finally, for IA-related disease and other chronic diseases a significant difference was observed only 3 months before diagnosis with ORs of 1.2 (CI 1.02–1.3, p<0.05) and 1.3 (CI 1.1–1.5, p<0.05) respectively. All ORs are corrected for age and gender. Important contributors to the above mentioned significance levels were presence of shoulder complaints (16.1% in the IA-patients versus 9.6% in the controls; chi2 73.9, p<0.001), hand/finger complaints syndrome (12.2% versus 5.6%; chi2 112.5, p<0.001), carpal tunnel syndrome (5% versus 2.5%; chi2 37.1, p<0.001) and foot/toe complaints (15.2% versus 9.2%; chi2 67.0, p<0.001). Numbers of individual infections were too small to find any statistical differences between the groups.




**Conclusions:** We found significantly increased consultation rates in general practice for musculoskeletal symptoms and infectious diseases prior to the diagnosis of IA. This diverging trend started 4–6 years before diagnosis, but becomes statistically significant around 1.5 years preceding diagnosis. IA-related comorbidities and chronic diseases also show this trend, however this did not reach significance until nearly at the IA date. Possibly, these symptoms can be used to develop methods for earlier detection of IA in general practice.
**Disclosure of Interest:** None declared
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## FRI0073 FIRST REPORT OF SYMPTOMS USING THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

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**Background:** Persons at risk of rheumatoid arthritis (RA) may experience a variety of symptoms[1,2]. However, information on location, timing, severity and predictive value of these symptoms is largely lacking. The Symptoms in Persons At Risk of Rheumatoid Arthritis (SPARRA) questionnaire has been developed with support of EULAR to provide more insight into these symptoms.
**Objectives:** Report the symptoms and symptom complexes using the SPARRA questionnaire in an international group of arthralgia patients at risk of developing RA.
**Methods:** The SPARRA questionnaire contains questions on presence, severity, impact and location of 13 symptoms derived from a qualitative study in seropositive arthralgia patients[1]. The items are: joint pain or swelling, joint stiffness, burning and tingling sensations, numbness, changes in skin colour, muscle cramps, weakness, fatigue, emotional distress, concentration difficulties and sleep problems. Answers are given on an ordinal scale. If present, number of days with a symptom per month (0, 1–5, 6–15, 16–30 days), severity (none, mild, moderate and severe) and influence (no, small, moderate or high impact) were recorded. Secondly, we recorded the location of joint pain. Finally, patients were asked to describe the pattern of symptom development over time. Patients were included in the Netherlands (N=68), United Kingdom (N=16), Sweden (N=15), Austria (N=11) and Switzerland (N=21). Validation of the questionnaire is ongoing.
**Results:** Of 131 arthralgia patients included, 85 were positive for anti-citrullinated protein antibodies (ACPA), 29 were positive for rheumatoid factor only, and 17 were seronegative with clinically suspect arthralgia. Most symptoms were present in a high percentage of patients, with pain as the most often experienced symptom and change of skin color rarely reported. When a symptom was present, it was usually experienced as moderate to severe, and with moderate impact by half of the patients (Table 1). The mean presence of symptoms was similar in the ACPA positive and negative groups, however, ACPA positive patients more often had severe symptoms (mean 61% versus 54%, NS) with higher impact (48% versus 41%, NS). Joint pain was most frequently located in the fingers. The most frequently reported pattern of symptoms was "coming and going, but always present" (32%).

Table 1. First results from the SPARRA questionnaire (N=131)

| Items | Duration At least 1 day in the past month | Severity If present, moderate to severe | Influence If present, moderate or high impact |
|---|---|---|---|
| Joint pain | 79% | 66% | 54% |
| Joint swelling | 35% | 52% | 50% |
| Joint stiffness | 69% | 68% | 44% |
| Burning sensations | 29% | 63% | 60% |
| Tingling sensations | 39% | 56% | 39% |
| Numbness | 27% | 49% | 44% |
| Change in skin colour | 15% | 40% | 25% |
| Muscle cramps | 41% | 41% | 21% |
| Weakness or loss of strength | 62% | 67% | 54% |
| Fatigue | 72% | 76% | 65% |
| Emotional distress | 52% | 54% | 43% |
| Concentration difficulties | 37% | 56% | 48% |
| Sleep problems | 54% | 70% | 52% |

**Conclusions:** The first results of the SPARRA questionnaire show multiple symptoms to be present in a high percentage of persons at risk for RA. These are often experienced as severe, with a high impact.
**References:**
[1] Stack, Rheumatology 2014;
[2] van Tuyl, Musculoskel Care 2015
**Disclosure of Interest:** None declared
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## FRI0074 THE PATIENT GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: IDENTIFICATION OF UNDERLYING LATENT FACTORS USING PRINCIPAL COMPONENTS ANALYSIS

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**Background:** The patient global assessment of disease activity is a crucial component of validated disease activity scores, response criteria, and the ACR/EULAR definition of remission in rheumatoid arthritis (RA). Recent work has shown that the patient global reflects persistent undifferentiated symptoms of pain, fatigue, and functional disability, occasionally despite seeming attainment of low inflammatory disease activity. The absence of a conceptual framework for evaluating patients in this scenario is a critical barrier to improving patient-centered outcomes.
**Objectives:** To identify underlying latent factors driving the patient global assessment of disease activity using a quantitative, multivariable data reduction approach.
**Methods:** This was a prospective cross-sectional study of 70 patients with RA fulfilling the ACR/EULAR 2010 classification criteria. Data were collected from the most recent rheumatology visit, including the patient and provider global assessments of disease activity (0–100 mm), tender and swollen joint counts, and current RA drug therapies. The patient sample was stratified to include 50 "discordant" patients (i.e., patient global assessments of disease activity were $\geq$25 mm higher than the provider global assessments) and 20 "concordant" patients. Co-morbid anxiety, depression, osteoarthritis, and fibromyalgia by provider diagnosis were abstracted from the complete electronic medical records. Participants completed several validated patient-reported outcome measures (PROMs), including measures of pain and pain interference, fibromyalgia, physical function, ability to participate, anxiety, depression, and fatigue. Data were evaluated using exploratory principal component analysis (PCA) as a data reduction method to determine the latent constructs in the data. Linear regression models were then used to determine the variability in patient global assessment explained by the PCA scores.
**Results:** The 70 patients had a mean age of 61 years, mean RA duration of 8.0 years, and 73% were female. The mean Clinical Disease Activity Index was 12.9. The mean (SD) for the patient global assessment of disease activity was 44.6 (22.7) and for the provider global assessment was 20.1 (17.7). PCA yielded 8 factor scores that represented domains of pain, fatigue, anxiety, depression, advanced age and degenerative arthritis, physical disability, fibromyalgia, and unknown. Linear regression analysis showed that pain explained the greatest variability in the patient global assessment of any of the factor scores (adjusted R-squared value: 0.06). The factor scores for pain, depression and anxiety, inability to participate, fibromyalgia, and advanced age were all significantly associated with the patient global assessment and altogether explained 33% of the variability in the patient global assessment.
**Conclusions:** Pain, depression and anxiety symptoms, inability to participate, fibromyalgia, and advanced age are key drivers of the patient global assessment. Future studies are warranted to develop a standardized approach to management of these factors toward the realization of patient-centered treat-to-target strategies for RA.
**Disclosure of Interest:** None declared
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## FRI0075 EFFECTS OF DMARDS ON CITRULLINATED PEPTIDE AUTOANTIBODY LEVELS IN RA PATIENTS- A LONGITUDINAL ANALYSIS

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**Background:** Anti-citrullinated cyclic peptide 2 (CCP2) antibodiy levels are considered to be highly stable during disease-modifying anti-rheumatic drug (DMARD) therapy of rheumatoid arthritis (RA). However, no studies have actually analyzed sequential anti-CCP2 antibody levels during various DMARD therapies in a controll manner
**Objectives:** To study whether stable treatment with DMARDs affects anti-CCP2 antibody levels in patients with rheumatoid arthritis.
**Methods:** In this longitudinal observational study 100 RA patients were followed for anti-CCP2 IgG antibody (U/L) and total IgG level (mg/dL) every 6 months for a total period of 2.5 years. All patients received stable DMARD treatment during this period. Five groups comprising each 20 patients were analysed: (1) methotrexate (MTX) alone, (2) tumor necrosis factor inhibitors (TNFi), (3) tocilizumab (TCZ), (4) rituximab (RTX) and (5) abatacept (ABA).
**Results:** Baseline demographic and disease-specific characteristics were comparable between the 5 groups. Anti-CCP2 antibody levels did not show significant changes in patients treated with MTX (mean±SEM: -24.1±8.1%), TNFi (-14.0±11.1%) or TCZ (-24.3±11.3%) between baseline and the 2,5 years follow up. In contrast, anti-CCP2 antibody levels significantly decreased during treatment with RTX (-75.6±4.4%) and ABA (-82.5±3.7%). With respect to total IgG levels, no significant changes were observed with MTX (-24.1±8.1%), TNFi (-14.0±11.1%) or TCZ (-24.3±11.3%) over 2,5 years. In contrast, anti-CCP2 antibody levels significantly decreased during treatment with RTX (-75.6±4.4%) and ABA (-82.5±3.7%). Date for individual patients are summarized in Figure 1.
**Conclusions:** DMARDs targeting the adaptive immune response such as ABA and RTX significantly lowered anti-CCP2 IgG levels, while cytokine inhibitors and methotrexate had no significant effects on anti-CCP2 IgG levels. RTX is the only DMARD, which also lowers total IgG level. Lowering anti-CCP2 IgG levels is a step towards sero-conversion and immunological remission of disease.

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## FRI0076 LOW DISEASE ACTIVITY OR DAS-REMISSION AS TREATMENT TARGET IN EARLY RHEUMATOID ARTHRITIS PATIENTS

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**Background:** It is unknown what the optimum treatment target for early rheumatoid arthritis (RA) patients is.
**Objectives:** To assess which treatment target, low disease activity or disease activity score (DAS)-remission is more effective in early RA patients.
**Methods:** The BeSt study included early (≤2 years symptom duration) active (≥6 of 66 swollen joints, ≥6 of 68 tender joints, and either erythrocyte sedimentation rate ≥28 mm/hour or a visual analogue scale global health score ≥20mm) RA (1987 criteria) patients to compare 4 treatment strategies, targeted at DAS≤2.4. In arm 3 treatment started with a combination of methotrexate (MTX), sulfasalazine and a tapered high dose of prednisone. In the IMPROVED study, early arthritis patients started with MTX and a tapered high dose of prednisone, with subsequent treatment options aiming at DAS-remission (<1.6). We compared clinical outcomes during 5 years in 133 BeSt patients randomized to arm 3 with 175 IMPROVED patients who fulfilled the inclusion criteria of the BeSt study. Predictive factors for DAS<1.6 at year 1 and drug-free remission (DFR) at year 5 were assessed by logistic regression analysis.
**Results:** At baseline IMPROVED patients had a significantly lower mean±SD DAS compared to BeSt patients (4.1±0.7 vs 4.4±0.9, p=0.012) and a shorter median (IQR) symptom duration (17 (8–28) vs 23 (15–53) weeks, p<0.001) (figure). At 3 months in the BeSt study, DAS decreased by 2 to 2.4±1.0, functional ability improved from 1.4±0.7 to 0.6±0.6, 56% of patients achieved DAS≤2.4 and 20% were in DAS-remission. At 4 months in IMPROVED patients, DAS decreased >2 to 1.8±1.0, functional ability improved from 1.5±0.6 to 0.5±0.6, 72% of patients achieved DAS≤2.4 and 53% were in DAS-remission. At year 1, DAS was decreased by 2.5 in IMPROVED and 2.4 in BeSt compared to baseline, to 1.6±1.0 and 2.0±0.9, p=0.004, and more IMPROVED patients than BeSt patients had achieved DAS<1.6 (51% vs 30%, p<0.001). Similar percentages in both studies achieved DAS≤2.4 (73% in IMPROVED vs 67% in BeSt, p=0.333). By protocol, BeSt patients could not achieve DFR at year 1. DFR was achieved in 15% of IMPROVED patients. At year 5, DAS was decreased by 2.7 in IMPROVED and 2.6 in BeSt compared to baseline, to 1.5±0.8 and 1.7±0.8, respectively (p=0.014). DAS≤2.4 was achieved in 61% of IMPROVED patients and in 61% of BeSt patients (p=0.092), DAS<1.6 was achieved in 43% vs 32%, p=0.003, and DFR was achieved in 18% vs 8%, p=0.003.
Predictive factors for DAS<1.6 at year 1 were type of treatment study (OR for IMPROVED (95% CI) 2.16 (1.27–3.68)), male gender (2.31 (1.34–3.98)) and baseline tender joint count (0.94 (0.90–0.99)). IMPROVED study (3.33 (1.44–7.66)) and absence of RF (rheumatoid factor) and ACPA (anti-citrullinated protein antibodies) 4.24 (1.71–10.51) were predictive factors for DFR at year 5.
**Conclusions:** Although the treatment target was less often achieved for DAS<1.6 compared to DAS≤2.4, irrespective of baseline disease activity, patients with early active RA had better outcomes after DAS<1.6 than DAS≤2.4 targeted therapy. Male gender, low baseline tender joint count and absence of RF and ACPA were also associated with more favourable treatment outcomes.
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Figure: Clinical characteristics at baseline and follow up in BeSt and IMPROVED patients

| Baseline | BeSt n=133 | IMPROVED n=175 | p-value |
|---|---|---|---|
| Age (years), mean ± SD | 55 ± 14 | 53 ± 15 | 0.408 |
| Female, n (%) | 88 (66) | 126 (72) | 0.271 |
| Symptom duration (weeks), median (IQR) | 23 (15-53) | 17 (8-28) | <0.001 |
| DAS, mean ± SD | 4.4 ± 0.9 | 4.1 ± 0.7 | 0.012 |
| Tender joint count, median (IQR) | 13 (9-19) | 10 (8-14) | <0.001 |
| Swollen joint count, median (IQR) | 14 (10-18) | 11 (8-17) | 0.023 |
| ESR mm/h, median (IQR) | 35 (17-46) | 32 (17-52) | 0.765 |
| VAS general health, median (IQR) | 50 (34-68) | 57 (45-75) | 0.009 |
| HAQ, mean ± SD | 1.4 ± 0.7 | 1.5 ± 0.6 | 0.114 |
| RF-ACPA-, n (%) | 34 (26) | 44 (25) | 0.933 |
| RF+ ACPA-, n (%) | 22 (17) | 25 (14) | |
| RF-ACPA+, n (%) | 10 (8) | 15 (9) | |
| RF+ ACPA+, n (%) | 58 (44) | 80 (46) | |
| **3 month** | | | |
| DAS, mean ± SD | 2.4 ± 1.0 | - | |
| Δ DAS, mean ± SD | 2.0 ± 1.1 | - | |
| HAQ, mean ± SD | 0.6 ± 0.6 | - | |
| DAS>2.4, n (%) | 56 (42) | - | |
| DAS≥1.6 - ≤2.4, n (%) | 48 (36) | - | |
| DAS-remission, n (%) | 27 (20) | - | |
| **4 month** | | | |
| DAS, mean ± SD | - | 1.8 ± 1.0 | |
| Δ DAS, mean ± SD | - | 2.4 ± 1.1 | |
| HAQ, mean ± SD | - | 0.5 ± 0.6 | |
| DAS>2.4, n (%) | - | 46 (26) | |
| DAS≥1.6 - ≤2.4, n (%) | - | 34 (19) | |
| DAS-remission, n (%) | - | 92 (53) | |
| **1 year** | | | |
| DAS, mean ± SD | 2.0 ± 0.9 | 1.6 ± 1.0 | 0.004 |
| Δ DAS, mean ± SD | 2.4 ± 1.1 | 2.5 ± 1.1 | 0.445 |
| HAQ, mean ± SD | 0.5 ± 0.5 | 0.6 ± 0.6 | 0.148 |
| DAS>2.4, n (%) | 33 (25) | 36 (21) | 0.333 |
| DAS≥1.6 - ≤2.4, n (%) | 49 (37) | 38 (22) | 0.002 |
| DAS-remission, n (%) | 40 (30) | 89 (51) | <0.001 |
| Drug-free remission, n (%) | - | 27 (15) | |
| **5 year** | | | |
| DAS, mean ± SD | 1.7 ± 0.8 | 1.5 ± 0.8 | 0.014 |
| Δ DAS, mean ± SD | 2.6 ± 1.1 | 2.7 ± 1.0 | 0.849 |
| HAQ, mean ± SD | 0.6 ± 0.6 | 0.6 ± 0.6 | 0.738 |
| DAS>2.4, n (%) | 21 (16) | 15 (9) | 0.092 |
| DAS≥1.6 - ≤2.4, n (%) | 38 (29) | 31 (18) | 0.056 |
| DAS-remission, n (%) | 43 (32) | 76 (43) | 0.003 |
| Drug-free remission, n (%) | 10 (8) | 31 (18) | 0.003 |

DAS: disease activity score, ESR: erythrocyte sedimentation rate, VAS: visual analogue scale, HAQ: health assessment questionnaire, RF: rheumatoid factor, ACPA: anti-citrullinated protein antibodies, SD: standard deviation, IQR: interquartile range. Δ DAS was calculated by extracting the baseline DAS.

## FRI0077 ADHERENCE TO DISEASE ACTIVITY SCORE STEERED TREATMENT PROTOCOLS IN EARLY ARTHRITIS PATIENTS

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**Background:** Adherence to treatment-to-target in early arthritis patients may be target dependent.
**Objectives:** To compare physicians' adherence to treatment protocols targeted at Disease Activity Score (DAS)≤2.4 or <1.6.
**Methods:** The BeSt study compared 4 treatment strategies in 508 early rheumatoid arthritis (RA, 1987 criteria) patients, 3-monthly targeted at DAS≤2.4. Seven years later in roughly the same clinic, the IMPROVED study started with induction therapy in 479 early RA (2010 criteria) and 122 undifferentiated arthritis (UA) patients, followed by 2 treatment arms 4-monthly targeted at DAS remission (<1.6). DAS were measured by trained nurses. Physicians adjusted treatment according to the DAS. We evaluated physicians' adherence to the protocols and assessed associated opinions and conditions during 4 years by Generalized Linear Mixed Models.
**Results:** Protocol adherence (PA) over 4 years was higher in BeSt than in IMPROVED (mean over time 88% and 73%, respectively). PA decreased over time in both studies from 100% to 77% (BeSt) and to 61% (IMPROVED). Protocol violations (PV) were against treatment intensification/restart 47% in BeSt vs 67% in IMPROVED and against treatment tapering/discontinuation (42% vs 33%). If physicians did not intensify/restart, measured DAS was median 0.7 (IQR0.3;1.3) above ≤2.4 (BeSt) and 0.5 (IQR 0.2;0.8) above <1.6 (IMPROVED). If they did not taper/stop, measured DAS was 0.7 (-1.2;-0.3) lower than ≤2.4 (BeSt) and 0.6 (-0.9;-0.3) lower than <1.6 (IMPROVED). In BeSt the odds ratio (OR) for PV were higher if physicians were not satisfied with the current treatment effect 1.4 (95% CI 1.0;1.9), however in IMPROVED this was associated with less PV 0.6 (0.5;0.7) (figure). Disagreement with DAS was reported slightly more often in IMPROVED than in BeSt (mean over time 18% vs 13%). In both studies the odds for PV were

Figure: Generalized Linear Mixed Models analysis with protocol violation as outcome variable

| | BeSt n=508 | | IMPROVED n=410 | |
|---|---|---|---|---|
| **Opinion** | **OR (95% CI)** | **p-value** | **OR (95% CI)** | **p-value** |
| Not satisfied with current treatment effect | 1.4 (1.0;1.9) | 0.028 | 0.6 (0.5;0.7) | <0.001 |
| Disagreement with how DAS represents disease activity | 2.5 (2.0;3.0) | <0.001 | 4.4 (3.6;5.3) | <0.001 |
| Not satisfied with the next treatment step | 2.8 (2.3;3.4) | <0.001 | 3.5 (2.8;4.4) | <0.001 |
| **Conditions** | | | | |
| Swollen Joint Count ≤1 and Tender Joint Count ≥1 | 1.0 (0.8;1.2) | 0.898 | 3.0 (2.6;3.4) | <0.001 |
| Swollen Joint Count ≤1 and ESR ≥28 | 1.0 (0.8;1.4) | 0.787 | 1.7 (1.3;2.1) | <0.001 |
| Swollen Joint Count ≤1 and VAS patient ≥20mm | 1.1 (0.9;1.3) | 0.340 | 2.1 (1.8;2.3) | <0.001 |
| VAS patient ≥20mm higher than VAS physician | 1.4 (1.2;1.7) | <0.001 | 2.2 (1.8;2.6) | <0.001 |
| VAS physician ≥20mm higher than VAS patient | 1.4 (1.0;1.9) | 0.065 | 0.8 (0.5;1.1) | 0.191 |

DAS: disease activity score; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; OR: odds ratio; CI: confidence interval

higher if physicians disagreed with the DAS or with the next treatment step and if the visual analogue scale general health of the patient (VASpt) was ≥20 mm higher than that of the physician (VASph). In IMPROVED PV was also higher if the swollen joint count (SJC) was ≤1 but tender joint count (TJC)≥2 (3.0 (2.6;3.4)) or erythrocyte sedimentation rate (ESR) ≥28 (1.7 (1.3;2.1)), or VASpt ≥20 (2.1 (1.8;2.3)).

**Conclusions:** Adherence to DAS steered treatment protocols was high, but PV increased over 4 years. This increase was more distinct in a DAS<1.6 steered protocol, where PV were more likely if the physician disagreed with the measured DAS. This was more often against required treatment intensification than against required tapering, whereas with a target DAS≤2.4 this was balanced. Also, in a DAS<1.6 steered protocol PV occurred more often in case of potential discrepancies between detected joint swelling, pain and ESR. In a DAS≤2.4 steered protocol there were more PV if physicians were not satisfied with the current treatment effect, however in a DAS<1.6 steered protocol this was associated with less PV. These results may indicate that adherence to DAS steered protocols appears to depend at least in part on the height of the target, and in addition on how physicians feel the DAS reflects RA activity.

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## FRI0078 SYMPTOM RECOGNITION AND ITS EFFECT ON HELP-SEEKING IN RHEUMATOID ARTHRITIS, BOWEL CANCER AND ANGINA: A MIXED METHODS APPROACH

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**Background:** Rheumatoid arthritis (RA) requires treatment in its earliest stages in order to reduce the likelihood of permanent joint damage and disability. However, this therapeutic window is often missed as a result of delayed help-seeking by patients. In order to understand symptom recognition by members of the general public in the context of RA, we conducted two studies which compared symptom recognition and its effect on help-seeking for RA symptoms with symptom recognition in the context of angina and bowel cancer.

**Objectives:** To investigate the role of symptom recognition in the decision to seek appropriate and timely medical attention for RA and other illnesses.

**Methods:** We conducted a qualitative interview study with 31 individuals and a postal survey of 1088 members of the general public. Both studies used vignettes developed specifically for this study describing the symptoms of RA, bowel cancer and angina. In the case of RA one vignette described joint pain and stiffness in hands and wrists; one had joint swelling as an additional feature and we included a variation with symptoms in feet and ankles instead of hands and wrists. For each vignette, participants made causal attributions and rated the seriousness of the symptoms and the urgency with which they would seek medical attention.

**Results:** Participants were less likely to recognise the symptoms of RA than those of other conditions. This effect was more pronounced when the symptoms did not include joint swelling. In contrast, the symptoms of bowel cancer and angina were more readily recognised and were considered to be more serious than those of RA. Survey respondents rated bowel cancer and angina symptoms to be significantly more serious than any of the given combinations of RA symptoms ($Z$ values of 16.3 to 25.3, all $p<0.001$). They would also seek help faster for the symptoms of bowel cancer or angina compared to symptoms described in any of the RA vignettes (Z values of 14.7 to 34.2, all $p<0.001$). Correct causal attribution of symptoms further had more effect on the perceived urgency of help-seeking for angina and bowel cancer than it had for any of the RA vignettes.

**Conclusions:** Accurate symptom attribution and the perception that symptoms are indicative of a serious underlying condition are both important drivers for rapid help seeking. In the case of angina and bowel cancer, recent public health campaigns have promoted not only symptom recognition and seriousness, but have also emphasised the consequences of not seeking timely help. Our results suggest that these consequences should also be addressed in any public health campaign for RA.

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## FRI0079 THE EFFECTIVENESS OF INITIAL TIGHT DISEASE CONTROL AND PAIN CONTROL FOR ACHIEVING LONG STANDING COMPREHENSIVE DISEASE REMISSION (CDR) IN RHEUMATOID ARTHRITIS TREATMENT

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**Background:** In recent years, comprehensive disease control (CDC) or comprehensive disease remission (CDR) is being new target of rheumatoid arthritis (RA) treatment. CDR is defined that all of three indices, 28-joint disease activity score (DAS28) less than 2.3 with C-reactive protein (CPR), yearly progress of Sharp/van der Heijde score (dSHS) within 0.5, and Health Assessment Questionnaire Disability Index (HAQ-DI) less than 0.5, are evaluated as remission. Several reports have commented that it is important to control disease activity tightly, in order to achieve CDR. However, how tight is enough to achieve is still unclear.

**Objectives:** This study is designed to clarify comparable level of DAS28 in order to achieve long-lasting CDR.

**Methods:** 421 RA patients who have been treated consecutively for more than three years, were recruited for this study. Treatment term was divided by one year's period. Patients average DAS28, dSHS, and HAQ-DI were calculated and evaluated as remission when each of indices matched as remission, while all of the three matched remission, CDR was evaluated as achieved. Probability for remission of each of the three and CDR from one year's period to the next is calculated. Probability for remission of the four indices from first year to the year after fourth was also evaluated. Sensitivity and specificity were also evaluated in the same manner.

Average DAS28 in the first year period was divided according to level for 0.1 on scale, and sensitivity and specificity of CDR in the year after fourth was evaluated for each level. Patient's average pain score measured with visual analogue scale (PS-VAS) was also calculated according to treatment year period. PS-VAS was divided by 10mm, and sensitivity and specificity of CDR in the year after fourth was evaluated for each level.

**Results:** Probability ratio for each indices were approximately 75% for DAS28, 75% for dSHS which had not changed as years passes, while 75% to 70% as years passes as gradually decreased for HAQ-DI, and 55% to 48% for CDR.

Sensitivity and specificity demonstrated more than 90% for both probabilities in every treatment year term.

CDR achievement ratio demonstrated that sensitivity gradually decreased as DAS28 increased, while specificity increased as increased. Same tendency demonstrated for PS-VAS. When DAS28 was 1.1, sensitivity demonstrated 10%, and specificity demonstrated 50%. When DAS28 was within 1.6, sensitivity kept more than 70%, however when DAS28 was 1.8, sensitivity and specificity had crossed at approximately 63% (Figure1). When PS-VAS was within 10mm, sensitivity demonstrated 80%, and specificity demonstrated 50%. When PS-VAS raised 20mm, sensitivity and specificity had crossed at approximately 58%.

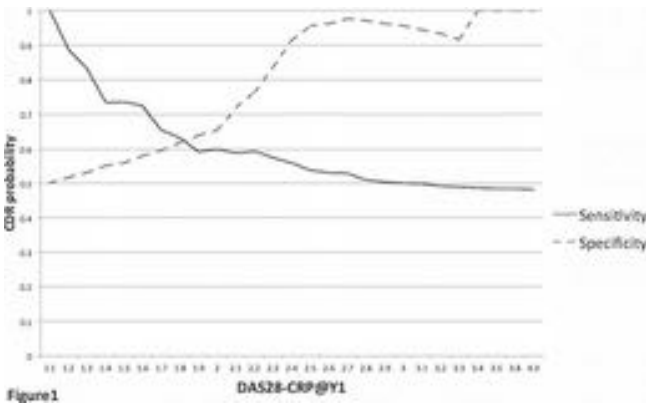



Figure1

**Conclusions:** These results suggest that initial tight disease activity control is most important in order to achieve long lasting CDR. DAS28 is controlled within 1.6 in the first year, CDR is guaranteed more than 70%. PS-VAS can perform as supplemental parameter, whereas PS-VAS is kept within 10mm, probability of CDR is maintained 80%.

**Disclosure of Interest:** None declared

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## FRI0080 EFFECTS OF IL-6 RECEPTOR INHIBITION THERAPY ON THE SERUM LEVELS OF IL-33 AND IL-6 IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Several pro-inflammatory cytokines such as TNF-α, IL-1, IL-6, IL-8 and IL-15 are known to be critical in synovial inflammatory process in RA and successful results have been obtained in RA treatment with targeting pro-inflammatory cytokines including TNF-α, IL-1 and IL-6.
**Objectives:** This study sought to investigate the role of IL-33 and IL-6 in RA patients receiving IL-6 receptor inhibition therapy.
**Methods:** We analyzed the association of the IL-33 and IL-6 level with disease activity and serologic features in 83 patients with RA. We also measured the serum level of IL-33 and IL-6 before and after the administration of tocilizumab for 24 weeks in 40 patients.
**Results:** Serum IL-33 level showed significant correlation with RF (rho =0.660, $p<0.001$) but did not correlate with DAS28, ESR, hsCRP or RA duration. IL-6 level was significantly correlated with hsCRP (rho =0.482, $p<0.001$) but not correlate with DAS28, ESR, RF or RA duration. There was no correlation between serum IL-6 and IL-33 levels.
Serum IL-33 level significantly decreased after 24 weeks of IL-6 receptor inhibition in patients with RA ($p<0.001$). When comparing subgroups according to ACR20 response, serum IL-33 levels were significantly decreased after 24 weeks of IL-6 receptor inhibition therapy in ACR20 responders ($p<0.001$) but not in the non-responders (p=0.084). Baseline IL-33 levels were not significantly different between the two subgroups (p=0.765).
Serum IL-6 levels were not significantly changed after 24 weeks of IL-6 receptor inhibition therapy (median 7.1 to 8.9 pg/mL, p=0.503). Changes of IL-6 levels were insignificant both in ACR20 responders and non-responders after 24 weeks of IL-6 receptor inhibition therapy. Baseline IL-6 levels were not different between ACR20 responders and non-responders.
**Conclusions:** The use of IL-6 receptor inhibitor decreased the serum level of IL-33 and this effect seems to be led by the responder group. IL-33 could be a useful indicator to monitor the response in IL-6 receptor inhibition therapy.
**Disclosure of Interest:** None declared
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## FRI0081 COMPARISON OF DISEASE BURDEN IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), RA WITH SECONDARY OSTEOARTHRITIS (OA), AND OA IN ROUTINE CARE

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**Background:** Recent data indicate that the disease burden experienced by patients with osteoarthritis (OA) is similar to or greater than in rheumatoid arthritis (RA)[1]. Many patients with RA may have secondary OA, which may affect disease burden and clinical management.
**Objectives:** To compare disease burden in patients with RA, RA with 2° OA, and OA, according to scores on a multi-dimensional health assessment questionnaire (MDHAQ) and physician RheuMetric checklist
**Methods:** At one academic rheumatology center, all patients with all diagnoses complete an MDHAQ. The MDHAQ includes 0–10 scores for physical function (FN), pain (PN), and patient global estimate (PATGL), compiled into a 0–30 composite routine assessment of patient index data (RAPID3), and a 0–48 RA disease activity index (RADAI) self-reported joint count. In addition, physicians complete a RheuMetric checklist, which includes four 0–10 visual analog scales (VAS) for overall physician global (DOCGL), inflammation or reversible findings (DOCINF), damage or irreversible findings (DOCDAM), and patient distress unexplained by DOCINF or DOCDAM (e.g. fibromyalgia, depression) (DOCSTR). Patients were classified as RA, RA with 2° OA, and OA, according to medical record diagnoses. Measures were compared in the 3 groups by MANOVA, adjusted for age.
**Results:** 669 patients seen in routine care between September 2014 and June 2015 were studied, including 248 with RA, 47 with 2° OA (16% of all RA), and 374 with OA. Patients with OA were significantly older, but no differences were seen in formal education or gender. MDHAQ scores indicated substantial disease burden in all 3 diagnosis groups, although least in RA patients with no 2° OA, intermediate in RA patients with 2° OA, and greatest in patients with primary OA, e.g., RAPID3 was 11.0±7.7, 12.3±6.7, and 15.1±6.3 in the 3 groups, respectively (Table) ($p<0.001$ adjusted for age). Among RheuMetric checklist scores, DOCGL did not differ significantly in the 3 groups; DOCDAM was higher than DOCINF in all 3 groups, but differed by 0.7 /10 units in RA vs 1.6 units in RA with secondary OA and 3.2 units in patients with primary OA (Table).

| | RA N=248 | RA with secondary OA N=47 | OA N=374 | P |
|---|---|---|---|---|
| Demographic measures | | | | |
| Age, mean, years | 56.8 | 62.4 | 66.3 | <0.001 |
| Education level, mean, years | 13.7 | 14.1 | 13.5 | 0.48 |
| Female, % | 85.8% | 80.6% | 88.1% | 0.20 |
| MDHAQ: Mean patient self-report scores | | | | |
| MDHAQ-Function | 2.4 | 2.8 | 2.8 | 0.12 |
| MDHAQ-Pain | 4.7 | 5.0 | 6.3 | <0.001 |
| MDHAQ-PATGL | 4.2 | 4.5 | 5.6 | <0.001 |
| RAPID3 (0–30) | 11.0 | 12.3 | 15.1 | <0.001 |
| RADAI (0–48) | 10.7 | 10.5 | 12.1 | 0.32 |
| RheuMetric: Mean physician estimates | | | | |
| DOCGL | 3.7 | 3.9 | 4.0 | 0.28 |
| DOCDAM | 2.9 | 3.4 | 4.1 | <0.001 |
| DOCINF | 2.2 | 1.8 | 0.9 | <0.001 |
| DOCSTR | 1.1 | 0.5 | 1.6 | 0.03 |

**Conclusions:** Patients with OA appear to have a greater disease burden than those with RA; the disease burden is intermediate in RA patients who have 2° OA. The low DOCINF relative DOCDAM in RA patients may help explain why RA remission rates are well below 100% even though inflammation appears to be effectively controlled. Patient MDHAQ and physician RheuMetric are useful and feasible to assess and monitor rheumatic diseases in busy clinical settings
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## FRI0082 SUBCLINICAL MRI INFLAMMATION DOES NOT PREDICT RELAPSE RISK IN RHEUMATOID ARTHRITIS PATIENTS TAPERING DMARDS

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**Background:** Tapering and stopping DMARD treatment attracts growing interest due to the steady increase in rheumatoid arthritis (RA) patients achieving sustained disease remission. Since only a subset of RA patients in remission can successfully taper or stop these drugs, reliable predictors, which can help to identify patients with high risk for relapse, need to be detected. In the randomized controlled RETRO study[1] we recently showed that a serum marker (MBDA) indicating residual inflammation was able to predict the relapse risk in the context of DMARD tapering[2].
**Objectives:** To test whether presence of residual inflammation in the magnetic resonance imaging (MRI) is associated with a higher relapse risk in RA patients tapering or stopping DMARD treatment.
**Methods:** Baseline MRI scans were available from 55 patients of the randomized controlled RETRO study. All patients had RA (ACR/EULAR 2010 criteria) in sustained remission (DAS28 <2,6 for at least 6 months) with stable DMARD treatment for at least 6 months. Patients either continued on their DMARD regimen (Arm1), tapered it by 50% (Arm 2) or stopped it after a 6 month tapering phase (Arm3). Follow-up period was 12 months. MRI scans were scored for synovitis, osteitis and tenosynovitis according to RAMRIS and Haavardsholm scores[3,4].
**Results:** MRI synovitis was found in 58%, MRI osteitis in 26% and MRI tenosynovitis in 24% of the patients. Prevalence of baseline MRI changes did not differ between patients experiencing relapse of RA or remaining in remission (62% in both groups, p=0,981). Also, baseline MRI scores were not different between patients relapsing or not relapsing: Median (IQR) total RAMRIS scores in the relapse group were 9 (3,5–48) and in the non-relapse group 8 (2,75–14,5) (p=0,27), median synovitis scores were 3 (0–7) and 1 (0–6) (p=0,65), median osteitis scores 0 (0–0,25) and 0 (0–3,5) (p=0,48) and tenosynovitis scores 0 (0–0,25) and 0 (0–0,5) (p=0,82) respectively. Furthermore, MRI synovitis, osteitis and tenosynovitis scores were not different between ACPA+ than ACPA- individuals (p=0,80, 0,82, and 0,95, respectively).
**Conclusions:** Subclinical MRI changes are frequent in RA patients in sustained remission but do not predict the risk of disease relapse during DMARD tapering.
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## FRI0083 FACTORS ASSOCIATED WITH THE NEED FOR BIOLOGICAL THERAPIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder that leads to an irreversible destruction of diarthrodial joints. Early diagnosis and treatment with disease-modifying antirheumatic drugs (DMARDs) are considered essential in order to achieve an optimal suppression of disease activity and prevent structural and functional deterioration. Biological therapy (BT) is the second-line treatment in case of inadequate response to DMARDs. BT has excellent safety and efficacy profiles. However, its economic burden is high.
**Objectives:** The goal of our study was to identify clinical, epidemiological and analytical characteristics, as well as the delay of diagnosis, DMARD treatment, and inflammatory activity, associated with the need to initiate BT in RA patients.
**Methods:** This is a single-center case-control study. We included patients who were diagnosed with RA from January 1, 2000, fulfilling the 2010 ACR/EULAR criteria. The main outcome (dependent variable) was the need for a first biological drug. The independent variables were time to diagnosis, time to treatment with the first DMARD, time to clinical remission, time to low activity, age, gender, number of swollen joints (NSJ) and tender joints (NTJ) at the time of diagnosis, positivity of RF and ACPA, CRP, ESR, radiologic erosions, smoking, body mass index, education level, and job status. The study was approved by the research ethical committee of our center. Descriptive statistics was used to present the results; chi-square test, Student t test, and Mann-Whitney U test were used to define statistical significance in the univariate analysis; and logistic regression for multivariate analysis. A *P*-value $<0.05$ was predefined as statistical significance. Statistical analyses were performed by using the SPSS v14.0.
**Results:** One hundred and thirty-nine patients were included (mean age 53 years; 82% women; 83% white; 82% RF+; 74% ACPA+). Sixty-one patients (44%) had received BT. The univariate analysis demonstrated significant association between the need for BT and NTJ ($p<0,001$), NSJ (p=0,004), ESR (p=0,026), time to low disease activity ($p<0,001$) and time to remission ($p<0,001$). The multivariate logistic regression indicated that the NTJ at diagnosis, the time to low activity and the time to remission were independently associated with the need for BT during follow-up.
**Conclusions:** In RA patients, the number of tender joints at the time of diagnosis and the time to low disease activity and clinical remission are associated with the need for BT during the course of the disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3016

## FRI0084 CLINICAL, ULTRASONOGRAPHIC AND IMMUNOLOGIC BIOMARKERS OF RAMRIS PROGRESSION IN RA PATIENTS IN CLINICAL REMISSION: A PROSPECTIVE STUDY OF 12 MONTHS OF FOLLOW-UP

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**Background:** A high proportion of patients with rheumatoid arthritis (RA) in clinical remission (CR) present subclinical synovitis when evaluated by sonography. Most prospective studies on baseline biomarkers of radiographic progression in this patients not include immunological biomarkers that could be of interest to better identify the residual inflammatory activity.
**Objectives:** To determine clinical, serological and ultrasonografic variables predicting progression of structural damage as evaluated by MRI at 12 months (mo.) of follow-up in a cohort of RA patients in CR.
**Methods:** We included 42 RA patients in CR defined as DAS28-ESR$<2.6$ for $>6$ mo. Complete clinical and biological assessment, ultrasonography of two hands and MRI of dominant hand were performed at baseline and after 12 mo. We analyzed risk factors related with RAMRIS progression with multivariate lineal models.
**Results:** 42 patients were included (76.7% female). Mean age was 53.5 years, body mass index (BMI) 26.7 kg/m$^2$. Disease and remission median duration were 94 and 37 mo. respectively. 73.8% RF[+] patients and 85.7% ACPA [+]. RAMRIS 10.3 and erosion (RAMRIS) 18.8. At baseline, 66.7% had power-doppler (PD) signal and 45.2% also had synovial hyperplasia grade $\geq 2$, so fulfilling the criteria of previously defined ultrasound defined active synovitis (UdAS)[1]. The risk factors more related with RAMRIS progression at 12 mo. were baseline RAMRIS, BMI, disease duration, low-dose prednisone treatment, absence of csDMARDs treatment and presence of UdAS. Synovitis as defined by only PD positive signal was no associated to erosions.
We excluded the baseline RAMRIS in the multivariate model because it was the strongest predictor factor. We observed that higher serum levels of calprotectin and ENA78 at baseline were significant predictors. Absence of csDMARD treatment, disease duration and the presence of UdAS also remained as independent predictive factors (Table 1).

Table 1. Risk factors and prognostic biomarkers associated with a higher score at one year RAMRIS

| Risk factor | Unadjusted | | Adjusted | |
|---|---|---|---|---|
| | β (95% CI) | p-value | β (95% CI) | p-value |
| Baseline calprotectin levels | r=0.195 | 0.216 | 4.6 (1.2–8) | 0.009 |
| Baseline log2(ENA78) levels | r=0.342 | 0.027 | 5.7 (0.4–11.1) | 0.037 |
| Longer disease evolution | 0.08 (0.003–0.15) | 0.043 | 0.07 (0.01–0.13) | 0.027 |
| No treatment with DMARDs | 19.9 (2.6–37.2) | 0.026 | 18.6 (3.8–33.3) | 0.015 |
| UdAS | 16.7 (3.1–30.3) | 0.017 | 17.1 (6.1–28.2) | 0.003 |
| Predictive value of the model | Model indexes | | | |
| R, R2 (R2 adjusted) | 70%, 49%, (41.9%) | | | |
| Overall significance of the model | <0.0001 | | | |

**Conclusions:** This prospective study confirms a high prevalence of UdAS in patients with RA in CR, which is an independent risk factor to develop structural damage progression at 12 months of follow-up. Baseline RAMRIS, BMI, disease duration, absence of csDMARDs therapy, UdAS, and baseline levels of calprotectin and ENA78, were independent predictors of RAMRIS progression.
**References:**
[1] Ramírez J, et al. Patients with rheumatoid arthritis in clinical remission and ultrasound-defined active synovitis exhibit higher disease activity and increased serum levels of angiogenic biomarkers. Arthritis Res Ther. 2014;16(1):R5
**Disclosure of Interest:** None declared
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## FRI0085 FOREFOOT DISEASE ACTIVITY HAS THE IMPACT ON BOOLEAN REMISSION IN JAPANESE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Treat-to-target (T2T) is recommended and a widely accepted management strategy for rheumatoid arthritis (RA), which aims for remission or low disease activity. Disease activity is valuated by some composite measures which includes patient's and physician's global assessment, finding of joints and C reactive protein (CRP) etc. Patient's global assessment (PGA) is often the limiting factor for achieving remission. It remains unclear what is the factor contributing to elevation of PGA when finding of 28 joints and CRP implement the Boolean remission criteria.
**Objectives:** To detect the factor contributing to elevation of PGA among Japanese RA patients whose scores on the tender joint count, swollen joint count and CRP (in mg/dl) are all 1 or less.
**Methods:** We performed an analysis of data from 15032 RA patients registered in the large database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan) of 2014 (1). Patients whose scores of the tender joint count, swollen joint count and CRP (in mg/dl) were all 1 or less were included. Patients whose PGA was 1 or less and patients whose PGA was more than 1 were compared with a probabilistic approach employing logistic regression to investigate factor contributing to elevation of PGA among Japanese RA patients whose scores on the tender joint count, swollen joint count and CRP are all 1 or less.
**Results:** Seven thousand and two hundred and twenty-four patients were included; 5754 were women (79.7%) with a median age 65 years, a median disease duration 9 years, 826 (11.4%) had swelling or tenderness of forefoot joints which are not included in 28 joints (forefoot disease activity), 2313 (32.0%) were prescribed glucocorticoid, methotrexate 4993 (69.1%), biologic DMARDs 1986 (27.5%). In two groups; PGA $\leq 1$ 3584 (49.6%) and PGA $>1$ 3640 (50.4%), the median modified health assessment questionnaire (mHAQ) was 0 (interquartile range: 0–0) and 0.13 (0–0.63), hospital anxiety and depression scale (HADS)-anxiety (A) was 2 (1–4) and 4 (2–7), HADS-depression (D) was 4 (2–6) and 5 (3–8), forefoot disease activity was 226 (6.3%) and 600 (16.5%), respectively. We

performed the logistic regression analysis with age, Steinbrocker's stage, mHAQ, HADS-A, HADS-D and forefoot disease activity. Thereafter all variables were found factors of associating to elevation of PGA (Table).

| Variable | OR (95% CI) | VIF |
|---|---|---|
| age, per decade | 1.08 (1.02, 1.13) | 1.05 |
| mHAQ | 3.62 (2.94, 4.49) | 1.21 |
| Steinbrocker's stage | 1.20 (1.13, 1.28) | 1.12 |
| HADS-A | 1.07 (1.04, 1.09) | 1.37 |
| HADS-D | 1.04 (1.02, 1.07) | 1.36 |
| forefoot disease activity | 2.56 (2.05, 3.20) | 1.01 |

**Table. Logistic regression analysis model for PGA elevation**
CI: confidence interval; HADS-A: hospital anxiety and depression scale-anxiety; HADS-D: hospital anxiety and depression scale-depression; mHAQ: modified health assessment questionnaire; OR: odds ratio; PGA: patient's global assessment; VIF: variance inflation factor

**Conclusions:** Forefoot disease activity, mHAQ, HADS-A and HADS-D contribute to elevation of PGA in patients who implement the Boolean remission criteria except PGA in Japanese rheumatoid arthritis patients. We should care about the foot joints in addition to functional disability and psychological distress for implementation of T2T strategy.

**References:**

[1] Matsui T, Kuga Y, Kaneko A, et al. Disease Activity Score 28 (DAS28) using C-reactive protein underestimates disease activity and overestimates EULAR response criteria compared with DAS28 using erythrocyte sedimentation rate in a large observational cohort of rheumatoid arthritis patients in Japan. Ann Rheum Dis 2007;66(9):1221–6.

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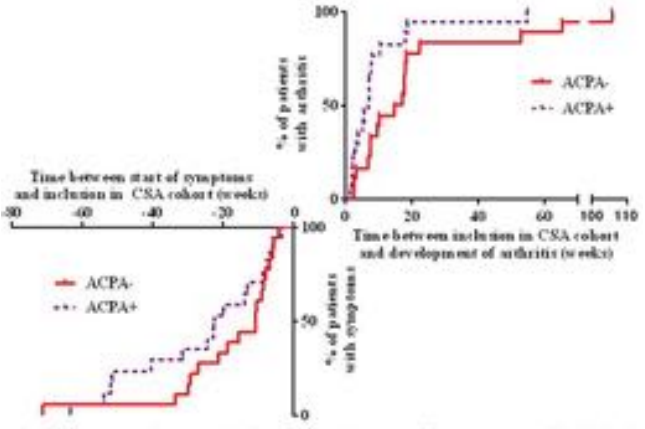
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## FRI0086 BEFORE CLINICALLY DETECTABLE ARTHRITIS DEVELOPS, ACPA-POSITIVE AND ACPA-NEGATIVE ARTHRALGIA PATIENTS HAVE DIFFERENT SYMPTOMS

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**Objectives:** Anti-citrullinated protein antibody (ACPA)-positive and ACPA-negative rheumatoid arthritis (RA) have different genetic risk factors and underlying biological mechanisms. Therefore, we hypothesized that patients' characteristics in the symptomatic phase before clinical arthritis has emerged are also different. We investigated this by studying the arthralgia phase of ACPA-positive and ACPA-negative patients.

**Figure 1: Duration of symptomatic disease phase before arthritis development split up in (1) the time between start of symptoms and inclusion in the CSA cohort and (2) the time between inclusion and development of clinically detectable arthritis**




The left bottom graph presents the time between the onset of first symptoms and inclusion in the CSA cohort (p=0.32). The right upper graph presents the time between inclusion in the CSA cohort and conversion to arthritis (p= 0.04). In the left lower graph the curve increases when symptoms start. In the right upper graph every step up indicates a patient developing arthritis.
Inclusion in CSA cohort generally coincided with first presentation at the outpatient clinic.

**Methods:** Patients included in a clinically suspect arthralgia (CSA)-cohort were followed for 2 years or until arthritis development. At inclusion, information on initial symptoms and current symptoms was obtained, physical examination and MRI performed and blood samples taken. A comparison was made between ACPA-positive and ACPA-negative CSA-patients that later developed arthritis.

**Results:** 35 patients (17-ACPA-positive, 18 ACPA-negative) included between April 2012 and May 2015 developed arthritis. 88% of ACPA-negative patients experienced morning stiffness as an initial symptom, compared to 40% of ACPA-positive patients (p=0.01). ACPA-positive patients more often had symptoms in both upper and lower extremities than ACPA-negative patients (35% versus 6%, p=0.03). Important reasons for rheumatologists to identify CSA was morning stiffness in ACPA-negative patients (38% versus 7%, p=0.04) and inflammatory-type arthralgia in ACPA-positive patients (67% versus 19%, p=0.01). ACPA-positive patients had a longer symptom duration at first presentation (median of 22.4 weeks versus 10.6 weeks, Figure 1) but converted to arthritis quicker (median 6.9 versus 15.9 weeks after inclusion, p=0.04, Figure 1). A combination of variables clustered ACPA-positive and ACPA-negative patients in PLS-analysis.

**Conclusions:** In the phase preceding clinical arthritis, ACPA-negative and ACPA-positive arthralgia patients have different characteristics. This contributes to the notion that ACPA-positive and ACPA-negative RA are different disease subsets.

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## FRI0087 PREDICTORS FOR ATTAINING REMISSION AT TWO CONSECUTIVE VISITS IN NEWLY DIAGNOSED EARLY RA PATIENTS

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**Background:** Early and intensive treatment with DMARDs are essential for remission induction in newly diagnosed RA patients. However, demographic, psychosocial and disease related factors may play a role as well.

**Objectives:** To investigate which demographic, psychosocial and disease related factors are associated with attaining remission at two consecutive visits in early RA patients treated in a treat-to-target manner

**Methods:** We used 12 months follow-up data from patients participating in the tREACH trial[1,2] in which induction therapy strategies were compared:

**Table 1 Predictors for attaining remission**

| | Remission within 6 months (logistic regression) | | | | Time to remission (12 months), (Cox regression) | | | |
|---|---|---|---|---|---|---|---|---|
| | Univariate | | Multivariate* | | Univariate | | Multivariate* | |
| | OR | P | OR | P | HR | P | HR | P |
| **Demographics** | | | | | | | | |
| Age | 0.988 | 0.207 | | | 0.990 | 0.122 | 0.979 | 0.010 |
| Sex (female) | 0.322 | <0.001 | 0.281 | <0.001 | 0.502 | <0.001 | 0.481 | 0.001 |
| Dutch ethnicity | 2.232 | 0.087 | | | 1.174 | 0.544 | | |
| Paid work | 1.437 | 0.211 | | | 1.238 | 0.254 | | |
| | | | | | | | | |
| **Disease** | | | | | | | | |
| MTX monotherapy | 0.594 | 0.080 | | | 0.785 | 0.206 | | |
| DAS (baseline) | 0.380 | <0.001 | 0.455 | 0.001 | 0.705 | 0.001 | | |
| HAQ (baseline) | 0.286 | <0.001 | | | 0.591 | <0.001 | | |
| SvH (baseline) | 0.970 | 0.500 | | | 0.962 | 0.310 | | |
| RF positive | 1.751 | 0.140 | | | 1.207 | 0.422 | | |
| ACPA positive | 0.790 | 0.473 | | | 0.761 | 0.190 | | |
| Duration of complaints | 0.999 | 0.345 | | | 0.999 | 0.497 | | |
| Physical functioning (SF36 PCS) | 1.115 | <0.001 | | | 1.054 | <0.001 | | |
| | | | | | | | | |
| **Psychosocial** | | | | | | | | |
| Mental functioning (SF36 MCS) | 1.047 | 0.036 | | | 1.025 | 0.080 | | |
| Internal locus of control (MHLC) | 1.083 | 0.030 | | | 1.043 | 0.086 | | |
| External locus of control (MHLC) | 1.017 | 0.557 | | | 0.992 | 0.694 | | |
| Chance locus of control (MHLC) | 1.022 | 0.455 | | | 1.006 | 0.769 | | |
| Anxiety (HADS) | 0.866 | 0.001 | | | 0.930 | 0.008 | | |
| Depression (HADS) | 0.827 | <0.001 | | | 0.895 | 0.001 | 0.987 | 0.003 |
| Fatigue (VAS) | 0.971 | <0.001 | 0.979 | 0.004 | 0.987 | 0.001 | | |
| Coping with pain (CQRS) | 0.895 | 0.001 | | | 0.962 | 0.050 | | |

* Backward selection, variables with p<0.20 in univariate analysis were entered

(A) combination high dose conventional therapy ((MTX + sulfasalazine + hydroxychloroquine or (B) MTX. Both groups had glucocorticoid (GCs) bridging. Disease activity (DAS) was assessed every 3 months. Remission was defined as DAS<1.6 at 2 consecutive visits (3 months). Univariate and multivariate logistic and Cox regression analyses were performed including demographic, disease related and psychosocial factors evaluated at baseline as predictors for attaining remission during 12 months of follow-up.

**Results:** 281 patients (68% female; mean DAS 3.4, median HAQ 1.00) were included. During 1 year of follow-up, 129 of 281 (46%) patients (group A: 90 (49%), group B: 39 (40%)) attained remission at 2 consecutive visits. 76/281 (27)% achieved remission within 6 months. Univariate analyses revealed that female sex was associated with a lower chance of attaining remission (demographic factors). Similar relations were observed for higher DAS, HAQ and worse physical functioning (disease factors) and higher levels of anxiety, depression, fatigue and passive coping with pain and lower levels of mental functioning and internal locus of control (psychosocial factors). In multivariate analyses, female sex, treatment and higher levels of fatigue were associated with a lower chance to attain remission within 6 months, whereas older age, female sex and higher levels of depression were associated with increased time to remission within 12 months.

**Conclusions:** In the tREACH trial, 46% of early RA patients attained remission within 1 year of follow-up. Female sex, higher baseline DAS, HAQ, and several psychosocial factors were predictors for attaining remission, but in the final models age, sex, baseline DAS, fatigue and depression remained. Results suggest that high levels of fatigue and depressive symptoms may prevent patients from attaining remission despite treatment according to a tight control and treat-to-target strategy.

**References:**

[1] Claessen et al. BMC Musculoskelet Disord 2009:71.
[2] De Jong et al. Ann Rheum Dis. 2013 Jan;72.

**Disclosure of Interest:** None declared

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## FRI0088 COMPARISON OF RHEUMATOID FACTOR, ANTI-CITRULLINATED PROTEIN ANTIBODIES, ANTI-CARBAMYLATED PROTEIN ANTIBODY, ANTI-PEPTIDYL ARGININE DEIMINASE TYPE-3 ANTIBODIES AND CALPROTECTIN IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS

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**Background:** A significant proportion of patients with Rheumatoid Arthritis (RA) are negative for rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). There is a unmet need for new biomarkers to better define the severity and prognosis of RA.

**Objectives:** To study the sensitivity and specificity of numerous auto-antibodies and calprotectin in RA patients compared with patients with spondyloarthritis (SpA) and to investigate the relationship between these biomarkes and measures of disease activity and severity.

**Methods:** Data was obtained from the "Swiss Clinical Quality Management" (SCQM) registry which recruits adults with RA, psoriatic arthritis (PsA) and axial spondylarthritis (axSpA). All patients with a Biobank sample were tested for RF (IgM and IgA, QUANTA Flash (QF), Inova), ACPA (anti-CCP2 (Eurodiagnostica) and anti-CCP3 (IgG QF and QUANTA Lite (QL) and IgA QF, Inova), anti-carbamylated proteins (anti-CarP, carbamylated fetal calf serum, prototype ELISA, Inova), anti-peptidyl arginine deiminase type-3 antibodies (anti-PAD3-E.Coli QF and anti-PAD3-insect QF, Inova) and serum calprotectin (QL prototype ELISA, Inova). The control group consisted of patients with PsA (CASPAR criteria positive) and axSpA (ASAS criteria positive). In univariable analyses we tested for associations between the biomarkers and the 28-joint disease activity score (DAS28) and the presence of erosive disease at inclusion. Multivariable analyses were corrected for age, sex, disease duration and anti-CCP2 positivity.

**Results:** A total of 1471 patients were included, 969 with RA and 502 in the SpA control group (317 with axSpA and 185 with PsA). Statistical measures of the biomarkers for the diagnosis of RA are shown in Table 1. In univariable analyses, RA patients positive for anti-PAD3-E.Coli, anti-PAD3-insect or calprotectin were significantly more likely to have a moderate to high DAS28 (DAS28>3.2) than patients with negative values (68.2% vs. 54.8%, p=0.001, 67.7% vs. 56.0%, p=0.027 and 70.4% vs. 56.2%, p=0.020 respectively). RA patients positive for anti-CarP, anti-PAD3-E.Coli or anti-PAD3-insect were significantly more likely to demonstrate joint erosions compared with patients with negative values (66.3% vs. 57.7%, p=0.037, 68.5% vs. 57.7%, p=0.015 and 71.6% vs. 58.3%, p=0.020 respectively). In multivariable analyses, the odd ratios (and 95% confidence intervals) for the association of anti-PAD3-E.Coli, anti-PAD3-insect or calprotectin with a moderate to high DAS28 were 1.65 (1.15, 2.39), 1.64 (1.02, 2.64) and 1.90 (1.08, 3.35) respectively, and for the association of anti-CarP, anti-PAD3-E.Coli or anti-PAD3-insect with joint erosions were 1.32 (0.90, 1.93), 1.43 (0.95, 2.15) and 1.82 (1.05, 3.15) respectively.

**Table 1**: Frequencies of the different biomarkers in patients with RA, PsA and axSpA, and the sensitivities, specificities, PPV and NPV for a diagnosis of RA as defined by the treating rheumatologist.

| Biomarker | Cut-off (units) | % of samples positive | | | | Sens (%) | Spec (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|---|---|---|---|---|
| | | Overall N=1471 | RA N=969 | PsA N=185 | axSpA N=317 | | | | |
| Anti-CCP2 | 25 U/ml | 55.0 | 77.2 | 11.4 | 12.3 | 70.9 | 88.0 | 92.0 | 61.0 |
| Anti- CCP3 IgG QL | 20 U/ml | 41.1 | 61.8 | 0.5 | 1.6 | 61.7 | 98.9 | 99.0 | 57.2 |
| Anti-CCP3 IgG QF | 20 U/ml | 40.8 | 61.3 | 1.1 | 1.3 | 61.3 | 98.8 | 99.0 | 56.9 |
| Anti-CCP3 IgA QF | 20 U/ml | 18.1 | 26.8 | 1.6 | 1.3 | 26.7 | 98.6 | 97.4 | 41.1 |
| RF IgM QF | 10344 RLU | 48.6 | 67.1 | 14.1 | 12.3 | 67.2 | 87.1 | 90.9 | 57.9 |
| RF IgA QF | 7425 RLU | 27.8 | 40.9 | 10.8 | 3.5 | 40.9 | 97.4 | 96.8 | 46.0 |
| Anti-CarP QL | 20 U/ml | 18.6 | 22.3 | 11.9 | 11.0 | 22.3 | 88.6 | 79.1 | 37.1 |
| Anti-PAD3 (E.coli) QF | 20000 RLU | 15.6 | 18.5 | 9.7 | 10.4 | 18.5 | 89.8 | 77.8 | 36.3 |
| Anti- PAD3 (insect) QF | 8300 RLU | 7.2 | 10.2 | 1.6 | 1.3 | 10.2 | 98.6 | 93.4 | 36.3 |
| Calprotectin QL | 473 mg/kg | 5.8 | 7.3 | 1.6 | 3.5 | 7.3 | 97.2 | 83.5 | 35.2 |

QL = Quanta Lite, QF= Quanta Flash, Sens=sensitivity, Spec=specificity, PPV=positive predictive value, NPV=negative predictive value, RLU=relative light unit

**Conclusions:** Although anti-PAD3 and calprotectin are only present in a minority of RA patients, they are significantly associated with more active disease and anti-PAD3-insect is significantly associated with the presence of joint erosions, independently of ACPA (anti-CCP2).

**Disclosure of Interest:** None declared

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## FRI0089 C4M – A BLOOD-BASED BIOMARKER – IS AN OBJECTIVE MARKER OF DISEASE ACTIVITY AND RADIOGRAPHIC STATUS: REPLICATION AND VALIDATION OR PREVIOUS FINDINGS IN THE OSKIRA RHEUMATOID ARTHRITIS STUDIES

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**Background:** Rheumatoid arthritis (RA) is an inflammatory joint disease affecting multiples tissues including the soft connective tissue surrounding the joints as well as the cardiovascular system. C4M is a biomarker of type IV collagen degradation, which is solely released from the basement membrane of, for example, the vasculature system. C4M was tested in the phase III clinical trial LITHE and was found to be a biomarker of disease activity and radiographic burden.

**Objectives:** The aim of this study was to replicate and validate previous findings of C4M by measuring patient samples from the OSKIRA phase III clinical trials.

**Methods:** OSKIRA 1, 2 and 3 (NCT01197521; NCT01197534; NCT01197755) (n=543) were all phase 3, randomized, double-blind, placebo-controlled studies of fostamatinib on a MTX background including RA patients with moderate to severe disease. Only baseline serum samples from the placebo arms were assessed. Patient population differed between the studies in that patients had inadequate response to: MTX (OSKIRA 1), DMARDs (OSKIRA 2) and single anti-TNF-$\alpha$ treatment (OSKIRA 3). Disease activity was assessed by disease activity score 28 (DAS28), swollen joint count 28 (SJC28), tender joint count 28 (TJC28) and health assessment questionnaire (HAQ). Radiographic Status was evaluated by joint space narrowing (JSN), erosion score (ERN) and mTSS. Serum C4M was measured in fasting serum by solid-phase competitive ELISA. Spearman rank correlations were applied to investigate the association between C4M and clinical parameters. Independent t-tests were applied for intergroup comparisons. Data that did not meet the criteria of normal distribution were log transformed prior to t-tests.

**Results:** Demographics were comparable for the three OSKIRA studies and the placebo groups of each were therefore pooled together. Baseline levels of C4M were significantly correlated with the disease activity parameters DAS28 (r=0.377, p=0.0001), HAQ (r=0.206, p<0.0001), TJC28 (r=0.117, p=0.0068) and SJC28 (r=0.166, p=0.0001) and radiographic scores: ERN (r=0.135, p=0.003), mTSS (0.151, p=0.001) and JSN (r=0.152, p=0.001). There were no significant correlations between C4M and sex, age or BMI. There were no significant differences in C4M2 measurements in escapers versus non escapers or at baseline compared to the concentrations measured at week 24.

**Conclusions:** The OSKIRA studies support previous findings of the LITHE study. C4M is highly associated with disease activity as well as radiographic progression level in patients with RA. Basement membrane remodelling, measured by C4M, appears to be highly important to the pathogenesis of RA. Further studies may reveal if alterations in basement membrane are linked to vascular dysfunction in patients with RA.

**Disclosure of Interest:** None declared

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## FRI0090 BMI AND TENDER JOINTS ARE PREDICTORS OF NOT REACHING SUSTAINED REMISSION IN PATIENTS PARTICIPATING IN AN AGGRESSIVE TREAT-TO-TARGET STUDY

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**Background:** Modern rheumatoid arthritis (RA) care is based on early DMARD initiation, tight control and treat-to-target strategies aiming for abrogation of inflammation to optimize long term outcomes. However, even in the most aggressive treatment studies a substantial proportion of patients do not reach sustained remission.
**Objectives:** We aimed to identify predictors of not reaching sustained DAS remission in early RA patients followed by a treat-to-target algorithm with pre-specified DMARD adjustments.
**Methods:** RA patients who fulfilled the ACR/EULAR 2010 classification criteria, with <2 years from first swollen joint and who were DMARD naïve with indication for DMARD treatment were included in the ARCTIC trial between 2010 and 2013. Patients were followed by a structured tight control algorithm aiming for a target of DAS<1.6 and no swollen joints, and in half the patients the treatment target also included no joints with ultrasound power-Doppler signal. For patients with established risk factors for joint destruction (ACPA or RF positive with radiographic erosions or MRI bone marrow edema at baseline) treatment could be escalated more rapidly to biologic therapy. Data collection included 44 SJC, Ritchie articular index (RAI), laboratory tests, patient reported outcomes, ultrasound examination and radiographs. Multivariate logistic regression was used to assess the associations between baseline variables and not being in sustained DAS remission at 16 to 24 months. A univariate p-value of <0.25 was used for variable selection, and a p-value of <0.05 to keep the variable in the model. Patient reported physical function and physician global were not included in the model building because of collinearity.
**Results:** A total of 221 patients were included, with mean [SD] age 51.1 [13.7] years, disease duration 7.2 [5.4] months, DAS 3.5 [1.2]. 63% were female, 72% RF- and 82% ACPA positive, and 16% escalated treatment more rapidly to biologic therapy. 103 (47%) did not reach sustained DAS remission between 16 and 24 months. Tender joints assessed by RAI (OR 1.11 per unit, p<0.001) and BMI (OR 1.07 per unit, p=0.046) were independent predictors for not reaching sustained DAS remission.

Table 1. Baseline predictors for not being in sustained DAS remission between 16 and 24 months. Variables included in multivariate model building shown, with the final model highlighted. The model was adjusted for age and gender

| Baseline variables variables | Not in sustained DAS remission between 16 and 24 months (N=103/221) | | | |
|---|---|---|---|---|
| | Univariate Analysis | | Multivariate Analysis | |
| | OR [CI] | P-value | OR [CI] | P-value |
| Tender joints (RAI) | 1.11 [1.06, 1.17] | <0.001 | 1.11 [1.06, 1.16] | <0.001 |
| BMI | 1.06 [1.00, 1.13] | 0.05 | 1.07 [1.00, 1.14] | 0.046 |
| Patient global | 1.02 [1.00, 1.03] | 0.005 | | |
| RF pos (IgM+IgA) | 1.78 [0.98, 3.25] | 0.06 | | |
| Female gender | 1.51 [0.87, 2.62] | 0.15 | | |
| ESR | 1.01 [0.99, 1.02] | 0.24 | | |

**Conclusions:** In early RA patients treated by an aggressive treat-to-target strategy, tender joints assessed by Ritchie articular index and BMI at time of diagnosis were independent predictors for not reaching sustained DAS remission. Our results are supported by previous studies indicating that overweight decreases the chance of achieving treatment success in early RA (1).
**References:**
[1] Sandberg ME et al. ARD 2014;73(11):2029–33.
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## FRI0091 THE RELATIONSHIP OF ULTRASONOGRAPHIC SIGNS OF INFLAMMATION AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) – is a chronic inflammatory disease, which by natural course of the disease results in erosive polyarthritis, i.e. destruction and dysfunction of joints.
**Objectives:** To investigate the relationship between ultrasonographic (US) evidence of "active" inflammation and radiographic progression in patients with RA and assess the potential of ultrasonographic imaging in evaluation of prognosis of patients with RA.
**Methods:** The study included 83 patients with early RA (median age 54 [45;61] years. All patients were administered methotrexate (MTX) and/or biologic therapy in accordance with the treat-to-target concept (REMARCA study). Clinical and laboratory parameters were analyzed at baseline, in 12,24,36 and 48 weeks after initiation of therapy. Treatment efficacy was assessed using EULAR criteria and indices of activity. Ultrasound with gray scale (GS) and power Doppler (PD) were performed at baseline, 12,24,36 and 48 weeks after initiation of therapy. The wrist, MCP2, MCP3, PIP2, PIP3, MTP2 and MTP5 joints of the clinically dominant side were examined by US according to the European League Against Rheumatism (EULAR) guidelines. ESAOTE MyLabTwice and GE Logiq 9 US machines with 13–18 MHz-transducer were used. Plain X-rays were taken before treatment and at week 48 of therapy. Modified Sharp van der Heijde (SHS) scale was used to quantify the radiographic findings. Structural damage progression was evaluated based on changes in the SHS (ΔSHS) between baseline and 1 year.
**Results:** At 48th weeks 56% patients had remission according to DAS28. The proportions of PD(+) and PD(–) patients were 47% and 53%, respectively. There was a correlation between ΔSHS by 48th week of treatment and PD at the 36 and 48th weeks (r=0,31 *p*=0,005;r=0,3 *p*=0,003 respectively) and GS at the 36th week (r=0,31 p=0,006). In patients, who had PD(+) synovitis at 48th week ΔSHS was significantly higher (r=0,01) as compared to patients without synovitis. Thus, in the group of PD(+) patients baseline radiological changes were more pronounced, than in patients without synovitis, but differences weren't statistically significant. The difference between the two groups of patients, based on the degree of radiological progression by 48th week of therapy, was significant for DAS28 at the 36th week: the DAS28 was higher in the group with radiological progression (r=0,004), while all other used clinical activity indices did not show any difference between the two groups. TJS and SJS were higher at the 12th week of therapy (r=0,04 and r=0,02, respectively), and CRP level at the 24th week was also higher in PD(+) group (r=0,03). PD synovitis score was higher at the 36 and 48th weeks (r=0,04 and r=0,000, respectively), and difference by GS synovitis score was established between the groups at the 36th week (r=0,02). Linear regression model revealed that GS synovitis score at week 24 correlated with ΔSHS during the first year of the therapy (OR=0,15, 95%CI: 0,023–0,207; *p*=0,015). The similar trend, though not significant, was noticed with PD synovitis score after 24 weeks of therapy (OR=0,104, 95%CI:-0,043–0,251; r=0,16).
**Conclusions:** Thus, the analysis of annual structural damage progression confirmed that US (PD and GS synovitis) have prognostic value to predict future radiographic damage.
**Disclosure of Interest:** None declared
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## FRI0092 INFLUENCE OF TEMPERATURE AND HUMIDITY ON DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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**Objectives:** To evaluate whether meteorological parameters influence disease activity in patients with rheumatoid arthritis (RA).
**Methods:** We assessed correlations between individual meteorological variables and clinical measures of disease activity: clinical disease activity index (CDAI), self-reported pain (by visual analogue scale), tender- and swollen 28 joint counts (TJC and SJC). Assessments documented in our RA database as well as the average temperature and relative humidity, obtained from the Central Institute for Meteorology and Geodynamics, were matched on a daily basis for a period of 10 years between 2005 and 2015, and analyzed using generalized estimating equations (longitudinal data analysis).
**Results:** A total of 1437 patients with RA (average disease duration at first visit: 4.88±8.63 years; 77% female, mean CDAI 17.8±11.7, mean time in study: 75 month, mean number of visits during study period: 19) were analyzed. Higher temperature and lower humidity were significantly associated with lower CDAI (p=0.0002, and p=0.0332, respectively). Regarding pain, the effects of temperature showed an interaction with humidity: while lower temperatures were associated with higher pain levels at the low and middle tertile of relative humidity, they corresponded to a lower pain level at the high tertile of relative humidity. Temperature showed a significantly negative correlation with TJC (p<0.0001), while relative humidity showed a significantly positive correlation with SJC (p=0.0321). Similar to pain, there was again an interaction of temperature and humidity in the SJC analysis.
**Conclusions:** In this largest association study of meteorological parameters with RA specific outcomes both temperature and relative humidity were shown to have significant effects on disease activity. Individual measures of disease activity and pain correlated either with temperature or humidity, while the composite CDAI measure correlated with both meteorological variables. These aspects may have to be taken into account in longitudinal analyses of disease activity of RA.
**Disclosure of Interest:** None declared
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FRI0093 **IMMUNOGENICITY OF TNF INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS OR POLYARTICULAR PSORIATIC ARTHRITIS IN CLINICAL REMISSION OR LOW DISEASE ACTIVITY: A ONE-YEAR MULTICENTRE PROSPECTIVE STUDY (THE INMUNOREMAR STUDY)**

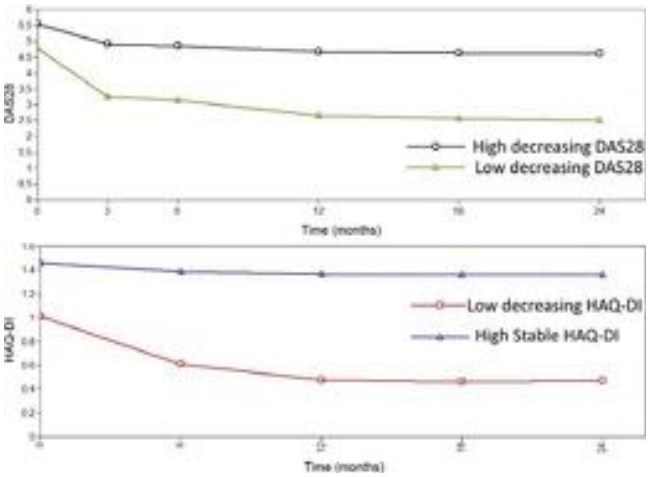
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**Objectives:** To determine drug trough serum levels and anti-drug antibodies (Ab) in rheumatoid arthritis (RA) or polyarticular psoriatic arthritis (PsA) patients in clinical remission (CR) or low disease activity (LDA) receiving TNF inhibitors [adalimumab (ADA), etanercept (ETN) and infliximab (IFX)], to correlate trough serum levels and Ab with disease flare after a 1-year follow-up, and to determine predictive factors of disease flare.
**Methods:** Prospective, multicentre study of RA and PsA patients attended in 3 hospital outpatient clinics (Catalonia, Spain) treated with ADA, ETN or IFX for ≥3 months in CR or LDA measured by DAS28-ESR at ≥2 consecutive visits. Ab and trough serum levels (ELISA Kit Promonitor®, Progenika SA, Spain) were determined at 0, 4, 8 and 12 months. Disease flare was defined as DAS28>3.2 and a delta DAS28 >0.6 during the 1 year follow-up compared with visit 0. Variables collected: demographic data; disease activity, diagnosis; disease duration; biologic drug; reduced dose, and concomitant csDMARD therapy. Differences between patients with and without disease flare were studied by univariate analysis. Multivariate Cox regression analysis was used to establish associations between baseline variables and disease flares.
**Results:** 187 patients (RA 103 [57%], PsA 81 [43%]), 66% female, mean age 57±12 years, were included. 138 (74%) patients were in CR, 49 (26%) with LDA, 69 ADA, 83 ETN, and 35 IFX. Mean treatment duration was 60±41 months. 34% and 58% of RA and PsA patients were on reduced doses of TNFi, and 75% and 44% on concomitant csDMARD, respectively. Thirty-two patients (17.1%: 9 ADA, 13 ETN, 10 INF) had a disease flare during follow-up: 15 at month 4, 12 at month 8 and 5 at month 12. Ab (2ADA, 2IFX) were detected in 12.5% of these patients. Patients with disease flares had lower mean baseline trough serum TNFi levels (2.36±0.45 μ/ml vs. 3.92±0.29 μ/ml p<0.01), although the difference was significant only for ADA (2.2±1.4 μ/ml vs. 6.6±4.1 μ/ml p=0.02), higher baseline DAS28 (2.42 vs. 2.04 p<0.001), and CDAI (5.80 vs. 4.15 p=0.001) and a lower frequency of remission (53% vs. 78% =0.003). During flares, trough serum levels of the three TNFi decreased, although the different was significant compared with baselines only in ETN (0.9±1.2 μ/ml vs. 2.3±1.26 μ/ml p=0.02). Cox multivariate analysis showed associations between disease flares and serum levels of TNFi (hazard ratio (HR) =0.84), glucocorticoids use (HR=2.11), and higher DAS28 (HR=2.19) and CDAI (HR=1.14) levels. Other baseline variables were not associated with disease flares.
**Conclusions:** Over a one-year follow up disease flares were observed in 17% of RA and PsA patients treated with TNFi for a prolonged period who achieved clinical remission/low disease activity. Anti-drug antibodies explained only 12.5% of disease flares. Low drug trough serum levels and high disease activity levels at baseline were associated with disease flares.
**References:**
[1] Sanmarti et al. Ann Rheum Dis. 2015 Aug;74(8):e42.
**Disclosure of Interest:** R. Sanmarti Grant/research support from: This Study was supported by an Investigator Initiated Research (IIR) from Pfizer (WS2392358), J. Inciarte-Mundo: None declared, P. Estrada-Alarcón: None declared, M. García-Manrique: None declared, J. Narvaez Grant/research support from: This Study was supported by an Investigator Initiated Research (IIR) from Pfizer (WS2392358), A. Gómez-Centeno Grant/research support from: This Study was supported by an Investigator Initiated Research (IIR) from Pfizer (WS2392358), J. Rodríguez-Moreno Grant/research support from: This Study was supported by an Investigator Initiated Research (IIR) from Pfizer (WS2392358), M. Pascal: None declared, J. Yagüe: None declared
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FRI0094 **DISABILITY IN EARLY RHEUMATOID ARTHRITIS MAY PERSIST DESPITE IMPROVEMENT IN DISEASE ACTIVITY: EVIDENCE FROM YORKSHIRE EARLY ARTHRITIS REGISTER**

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**Background:** Disability adversely affects the wellbeing of individuals with rheumatoid arthritis (RA) and contributes to direct and indirect health care costs (1). However, owing to substantial advances in drug treatment for RA, management often focuses on suppression of inflammation. In the United Kingdom, treatment with biological agents is guided by disease activity score from counts of 28 joints (DAS28) (2) and EULAR guidance recommends treatment goals of low disease activity or remission (3). Although these targets are of undoubted importance, the relationship between the treatment target (inflammation or disease activity) and disability is not well described.
**Objectives:** 1. Describe the relationship between disease activity and disability over 2 years in early RA
2. Identify predictors of adverse outcome.
**Methods:** Cases with rheumatologist-confirmed early RA were recruited to Yorkshire Early Arthritis Register (YEAR). Data from 1415 patients were applied to separate latent growth curve models of change in DAS28 and disability index of Health Assessment Questionnaire (HAQ-DI) over 2 years. A parallel process growth curve model described how HAQ-DI varied with DAS28. Dual trajectory analysis (4) was used to describe distinct dual trajectories of change in both variables. Predictors of likely dual trajectory group membership were identified using multinomial logistic regression.
**Results:** Two trajectories of DAS28 (high decreasing DAS28 and low decreasing DAS28) and HAQ-DI (high stable HAQ-DI and low decreasing HAQ-DI) were identified, shown in Figure 1. Four distinct dual trajectory groups were: group 1, high decreasing DAS28 and high stable HAQ-DI (23% of cohort); group 2, high decreasing DAS28 and low decreasing HAQ-DI (1%); group 3, low decreasing DAS28 and high stable HAQ-DI (26%); group 4, low decreasing DAS28 and low decreasing HAQ-DI (50%). Predictors of group 1 membership (compared to group 4) were similar to known predictors of poor outcome in RA: female gender, social deprivation and greater baseline fatigue. Predictors of group 3 membership were the same as group 1, but also included older age and greater overall contribution of tender joint count and visual analogue score to baseline DAS28.




**Conclusions:** Persistence of disability despite improvement in disease activity was more likely in older patients and those with greater subjective components of baseline DAS28. This suggests that current therapies, which target inflammation, may not be sufficient to reduce disability in early RA. Future work should examine the impact of comorbidity and pain on function in early RA.
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**Disclosure of Interest:** None declared
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FRI0095 **DIVERSITY OF THE PERIPHERAL IMMUNOLOGICAL PHENOTYPE AFTER BIOLOGIC DMARD THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** In the pathogenesis of rheumatoid arthritis (RA), T cells can differentiate into functionally distinct subsets, leading to the persistent inflammation and immune abnormality associated with the interactive activation between B cells, monocytes and dendritic cells. However, little is known about pathological immune cell subsets targeted by biologic DMARDs (bDMARD) therapy.
**Objectives:** The aim of this study was to assess the relationship between the phenotype of peripheral immune cells with clinical manifestations and responsiveness to bDMARD therapy in patients with RA.
**Methods:** Peripheral blood mononuclear cells were obtained from 108 patients with bio-naïve RA and 26 healthy controls (HC). The study included 46 patients

treated with TNF inhibitors such infliximab, etanercept and adalimumab, 40 patients treated with abatacept, and 22 patients treated with tocilizumab. The blood samples were taken at baseline and week 24 after treatment. The peripheral immune cell subset was defined based on comprehensive 8-color flow cytometric analysis for human immune system termed "the Human Immunology Project" by NIH and FOCIS, and the correlation with clinical characteristics and responsiveness to bDMARD therapies were evaluated.

**Results:** The frequency of $CD3^+CD4^+CD45RA^-CCR7^-$ effector memory, $CD3^+CD4^+CD45RA^+CCR7^-$ effector T helper cells and $CD4^+CXCR5^+ICOS^+$ T follicular helper (Tfh) cells was higher in patients with active RA than that in HC. The frequency of $CD3^+CD8^+CD45RA^-CCR7^+$ central memory cytotoxic T cells or $CD3^+CD4^+CXCR3^-CCR6^+$ Th17 cells was correlated with RF titers and that of $CD19^+CD20^-CD27^+CD38^+$ plasmablast was correlated with disease activity scores such as DAS28-ESR and SDAI. The proportion of Tfh cells and $CD19^+CD20^+CD27^-IgD^-$ effector B cells made statistical clusters with that of plasmablast. All of bDMARDs markedly improved the disease activity scores after 24 week treatment. TNF inhibitors decreased $CD3^+CD4^+CD45RA^+CCR7^+$ naïve T cells but increased effector memory T cells and Th17 cells, and tocilizumab increased $CD4^+CCR4^+CD25^+CD127^{low}$ T regulatory (Treg) cells and decreased effector B cells. However, abatacept characteristically decreased the proportions of T helper cell subsets which consisted of Tfh, Th17, and Treg cells and consequently the proportion of naïve T cells increased.

**Conclusions:** These results indicated that the abnormal T cell differentiation correlated with autoantibody production while plasmablast did with disease activity of RA. In addition, the molecular targeted therapies may alter contradictory changes of T helper cell subsets, i.e. abatacept decreases activated Tfh, Th17 and Treg cells whereas TNF inhibitor increases Th17 cells and tocilizumab increases Treg cells. The peripheral immunophenotyping might be useful in evaluating the pathogenesis and in determining the therapeutic target of each patient.

**Disclosure of Interest:** S. Nakayamada: None declared, S. Kubo: None declared, M. Yoshikawa: None declared, Y. Miyazaki: None declared, N. Yunoue: None declared, S. Iwata: None declared, K. Nakano: None declared, K. Saito: None declared, Y. Tanaka Grant/research support from: SantenMitsubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-Kirin, Abbvie, Bristol-Myers, Consultant for: Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD,

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## FRI0096 PREDICTIVE VALUE OF THE MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) SCORE FOR FLARE AND SUSTAINED REMISSION IN THE HONOR STUDY

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**Objectives:** To determine the predictive value of the multi-biomarker disease activity (MBDA) (Vectra® DA) score for flare and sustained clinical remission after discontinuation of adalimumab (ADA) in patients with rheumatoid arthritis (RA) from the HONOR study [1,2].

**Methods:** This retrospective sub-analysis was conducted on 42 RA patients from the HONOR study. Patients receiving ADA and methotrexate (MTX) who maintained DAS28-ESR remission ($<2.6$) for $\geq 24$ weeks and who subsequently agreed to discontinue ADA were enrolled. Clinical disease activity, functional status, and joint damage were recorded at ADA discontinuation (baseline), and after 24 and 52 weeks. MBDA scores (remission, $\leq 25$; low, 26–29; moderate, 30–44; high, $>44$) were determined from serum samples collected at baseline. The ability to predict flare (DAS28-ESR $\geq 3.2$) or sustained clinical remission (SC-REM) (absence of flare with DAS28-ESR $<2.6$ at all visits) by MBDA score and patient characteristics were determined.

**Results:** At ADA discontinuation, all patients had DAS28-ESR $<2.6$ with 81% female, 69% RF+, 81% ACPA+ and 30-month mean disease duration. The median MBDA score was 24.5 [quartile; 14.3, 30.8] with 22 (52.4%) patients in remission, and 6 (14.3%) low, 9 (21.4%) moderate and 5 (11.9%) high MBDA score. At 52 weeks, flare and SC-REM were observed in 12/42 (28.6%) and 19/42 (45.2%) patients, respectively. Rate of flare and percentage of SC-REM by MBDA category (remission/low/moderate/high) were 13.6%/50.0%/33.3% and 60.0% (p=0.033) and 63.6%/33.3%/33.3% and 0% (p=0.0066), respectively (P-value by two-sided Cochran-Armitage trend test). Univariate regression analyses identified MBDA score, DAS28-ESR and disease duration as predictors of flare at 52 weeks ($p \leq 0.05$).

**Conclusions:** These findings suggest that the MBDA score could predict flare and SC-REM in RA patients in stable clinical remission, undergoing ADA withdrawal while maintaining MTX treatment.

**References:**

[1] Hirata S, et al, Arthritis Res Ther. 2013;15:R135

[2] Tanaka Y, et al, Ann Rheum Dis. 2015;74:389–395

**Disclosure of Interest:** S. Hirata Speakers bureau: AbbVie, Eisai, Bristol Meyers Squibb, S. Tang Employee of: Crescendo Bioscience Inc., C. Hwang Employee of: Crescendo Bioscience Inc., I. Miyagawa: None declared, S. Kubo: None declared, K. Nakano: None declared, S. Nakayamada: None declared, K. Saito: None declared, N. Defranoux Employee of: Crescendo Bioscience Inc., Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Chugai, MSD, Astellas, Novartis, Speakers bureau: Abbvie, Chugai, Astellas, Takeda, Santen, Mitsubishi-Tanabe, Pfizer, Janssen, Eisai, Daiichi-Sankyo, UCB, GlaxoSmithKline, Bristol-Myers

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## FRI0097 BASELINE SERUM 14-3-3 ETA INDEPENDENTLY PREDICTS CLINICALLY IMPORTANT IMPROVEMENTS IN HAQ-DI IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB

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**Background:** Serum 14–3-3η is a mechanistic marker that is involved in the pathogenesis of RA and is a direct and potent up-regulator of IL-6.[1] We previously reported that baseline 14–3-3η levels were significantly lower in a cohort of 49 established RA patients who achieved better clinical outcomes when treated with Tocilizumab.[2] Recently there has been increased interest in assessing therapy response using alternative measures to DAS that are independent of CRP, including patient reported outcomes such as HAQ-DI.

**Objectives:** The aim of this study was to evaluate whether baseline measurement of 14–3-3η was associated with and independently predicted clinical response, in a cohort of 106 RA patients treated with tocilizumab.

**Methods:** Serum 14–3-3η levels were measured in a cohort of 106 Japanese patients prior to the initiation of tocilizumab therapy (BL). 14–3-3η positivity was defined by the diagnostic cut-off of $\geq 0.19$ ng/ml, and 2 and 4 times that, at 0.40 and 0.80 ng/ml, respectively. Patients were sub-grouped according to changes in HAQ-DI based on the minimal clinically important difference (MCID) of $\geq 0.22$, $\geq 0.31$, and $\geq 0.49$. Group differences were assessed by Mann-Whitney U-test. ROC curve analysis was performed to identify the optimal 14–3-3η cut-point for a $\Delta$HAQ-DI $\geq 0.49$. Uni- and multi-variable analysis controlling for baseline HAQ-DI was used to assess 14–3-3η's independence of other clinical/serological variables at informing patient reported outcomes.

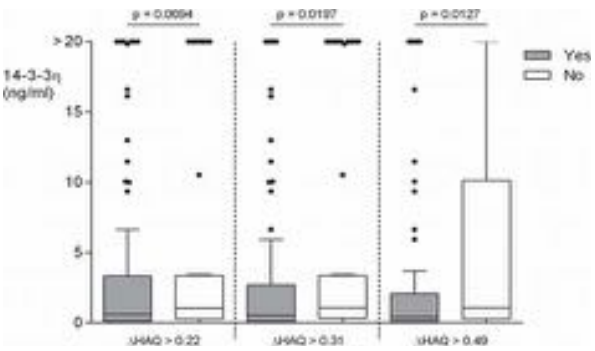
**Results:** At baseline, 75 (71%) of the 106 patients were 14–3-3η positive. At year 1, 70 (66%), 58 (55%) and 52 (40%) of the 106 patients achieved changes in HAQ-DI of $\geq 0.22$, $\geq 0.31$, and $\geq 0.49$, respectively. Baseline HAQ-DI values were significantly higher in those patients that achieved a $\Delta$ HAQ-DI $\geq 0.22$ when compared with those that did not; p=0.009. The HAQ-DI values were also significantly higher at the two other HAQ-DI cut-points ($\geq 0.31$, and $\geq 0.49$), $p<0.0001$.

As shown in the Figure, serum 14–3-3η levels were significantly lower in patients that achieved HAQ-DI MCID of $>0.31$ and $>0.49$.

In patients who achieved a DHAQ-DI $\geq 0.49$, ROC analysis returned the best cut-off of $\leq 0.18$ ng/ml yielding a specificity of 83.3% (95%CI: 70.7–92.1) and sensitivity of 42.3% (95%CI: 28.7–56.8), LR =2.5. By univariate analysis, all three 14–3-3η cut-points were significantly associated with better clinical outcomes.

| | 14–3–3η positivity cut-off | | | | | |
|---|---|---|---|---|---|---|
| | ≤0.19 ng/ml | | ≤0.40 ng/ml | | ≤0.80 ng/ml | |
| | LR | p-value | LR | p-value | LR | p-value |
| ΔHAQ >0.22 | 6.75 | 0.0098 | 2.36 | 0.0950 | 0.94 | 0.2222 |
| ΔHAQ >0.31 | 9.57 | 0.0021 | 6.18 | 0.0114 | 3.56 | 0.0456 |
| ΔHAQ >0.49 | 8.61 | 0.0034 | 6.61 | 0.0090 | 3.88 | 0.0382 |

Multi-variable modeling controlling for BL HAQ-DI indicated that lower levels of 14–3-3η, age and disease duration, but not CRP, were independent predictors of achieving the HAQ-DI MCID outcomes.




**Conclusions:** Lower serum 14–3-3η levels prior to the initiation of therapy are associated with and independently predict better patient reported outcomes in patients treated with tocilizumab. The predictive capacity of 14–3-3η at informing

therapy response to anti-IL-6 therapy should be investigated across all anti-IL-6 compounds.

**References:**
[1] Arthritis Rheum. 2014; 66 (Suppl 11):1975.
[2] Arthritis Res Ther. 2015; 17:280.

**Disclosure of Interest:** S. Hirata Speakers bureau: AbbVie, Eisai, Bristol Meyers Squibb, K. Hanami: None declared, A. Marotta Employee of: Augurex Life Sciences Corp., (Co-inventor of 14–3-3η), Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Chugai, MSD, Astellas, Novartis, Speakers bureau: Abbvie, Chugai, Astellas, Takeda, Santen, Mitsubishi-Tanabe, Pfizer, Janssen, Eisai, Daiichi-Sankyo, UCB, GlaxoSmithKline, Bristol-Myers

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## FRI0098 A CERTAIN PORTION OF ACTIVE ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS WITH SIGNIFICANT JOINT DESTRUCTION ARE MISCLASSIFIED AS BEING IN BOOLEAN REMISSION: A CROSS-SECTIONAL STUDY USING ULTRASOUND SONOGRAPHY

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**Background:** The goal of the treatment of rheumatoid arthritis (RA) is remission, however the remission induction for established RA (eRA) patients with long disease duration and significant radiographic damage is difficult. One of the reasons for this is that Patient Global Assessment score (PtGA) continues to be high even after the synovitis resolves through appropriate treatment, because of disability or pain from the structural damage. Although such high PtGA of eRA patients is thought to be acceptable, there is little evidence which supports this concept.

**Objectives:** To evaluate whether high PtGA of eRA patients is acceptable by assessing synovitis using ultrasound sonography (US).

**Methods:** Three hundred and thirty two RA patients were recruited with informed consent. Bilateral 2–5 MCP, wrist, ankle, and 2–5MTP joints were scanned by using the Aplio500 (TOSHIBA) with a 12 MHz transducer. Power Doppler (PD) images were obtained by Superb Micro-vascular Imaging (SMI). Gray scale (GS) and PD images were scored using a 0–3 semi-quantitative scale. Clinical information was obtained from the Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) database, which is based on the assessment by physicians who were blind to the US results. We defined "Semi-Boolean remission (SBR)" as the condition which is composed of 3 elements of Boolean remission (BR) criteria, excluding PtGA. All the patients were classified into 1–4 Steinbrocker stages according to their joint X-rays.

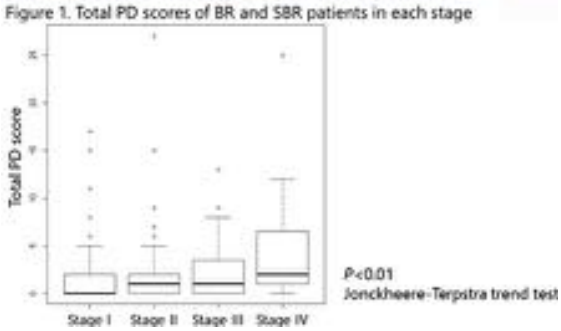
**Results:** The number of patients who fulfilled BR or SBR criteria were 99 and 122, respectively. As shown in table 1, age, disease duration, total GS score, and total PD score were virtually the same between the two groups. PtGA become higher in accordance with the stages ($P<0.01$, Jonckheere-Terpstra trend test. Mean values of PtGA of stage I, II, III, and IV were 13.6±15.6, 19.6±21.0, 26.6±26.1, and 28.0±22.0, respectively). PtGA and total PD score showed no correlation in BR+SBR patients, or in each of the stages (Spearman's rho=0.14, 0.16, 0.04, 0.03, or 0.07, respectively). The median values of total GS scores of each stage were, 10.0 (8.0–15.0), 12.0 (9.0–16.0), 11.0 (8.0–15.0), and 12.0 (7.5–17.0). There is no significant difference between stages. On the other hand, the median values of total PD scores of each stage were 0.0 (0.0–2.0), 1.0 (0.0–2.0), 1.0 (0.0–3.5), and 2.0 (1.0–6.5), respectively (figure 1). There was significant accordance between total PD score and stages ($P<0.01$, Jonckheere-Terpstra trend test).

Table 1. Comparison between Boolean remission (BR) and Semi-Boolean remission (SBR) groups

| Total N=221 | BR N=99 | SBR N=122 | P |
|---|---|---|---|
| Age, mean±SD years | 62.9±12.1 | 62.3±14.4 | 0.87* |
| Women, % | 80.8 | 77.0 | 0.50¶ |
| Disease duration, mean±SD years | 10.7±10.7 | 11.1±10.5 | 0.59* |
| Steinbrocker stage (I/II/III/IV) | 39/30/14/16 | 32/38/21/31 | 0.02*¶ |
| PtGA, mean±SD mm | 4.1±2.9 | 34.0±20.3 | <0.01*¶ |
| Total GS score, median (IQR) | 11.0 (8.0-15.0) | 11.5(8.0-16.0) | 0.35* |
| Total PD score, median (IQR) | 1.0 (0.0-2.0) | 1.0 (0.0-4.0) | 0.08* |

IQR: Interquartile range, *P<0.05, *Mann–Whitney U test, ¶Chi-Square test, ¶Cochran-Armitage trend test

Figure 1. Total PD scores of BR and SBR patients in each stage




**Conclusions:** PtGA did not always reflect the activity of synovitis. This was not limited to eRA but also to RA without radiographic damage. However, we must be careful as higher total PD scores were seen in eRA patients even though they were thought of as being in BR or SBR. This result means that a certain portion of active eRA patients are misclassified as being in remission. Before accepting the high PtGA, we should use US for correct evaluation of eRA.

**Disclosure of Interest:** None declared

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## FRI0099 INDICATIONS OF REVERSIBILITY OF CENTRAL SENSITIZATION ACCORDING TO THE PAINDETECT QUESTIONNAIRE IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM THE PROSPECTIVE FRAME-COHORT STUDY

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**Background:** Pain in rheumatoid arthritis (RA) is typically regarded as related to on-going synovial inflammation in peripheral joints. However, in a subgroup of patients evidence indicates that pain can become an entity of its own caused by central sensitization (CS), elicited by but in time not directly related to ongoing inflammation. The painDETECT questionnaire (PDQ) was developed to differentiate neuropathic pain from unclear and non-neuropathic pain. In several studies it has been used to indicate CS owing to similarities in somatosensory profiles. Magnetic resonance imaging (MRI) can be used as an objective inflammation marker, quantified by the RA MRI Score (RAMRIS).

**Objectives:** To evaluate the prognostic value of a PDQ score >18 on DAS28 response in RA patients taking a possible interaction with inflammation defined by RAMRIS synovitis scores into account.

**Methods:** RA patients were included when they were to: 1) initiate a disease modifying antirheumatic drug (DMARD) or 2) initiate or switch a biological agent. At baseline and after 4 month of follow up patients went through an examination program incl. standard demographics, clinical examination, hand MRI, patient reported outcomes (incl. PDQ), and blood samples. Least-Squares Mean change (95% CI) was calculated using ANCOVA adjusting for the value at baseline. Multivariable regressions with DAS28 or RAMRIS synovitis change as outcome were performed to determine the prognostic variables. The model included PDQ-category, RAMRIS synovitis score and their interaction. Possible confounders were: gender, disease duration, baseline DAS28, and initiation group. PDQ score was interpreted as: >18 indication of CS, 13–18 unclear pain mechanism, <13 nociceptive pain. Pain classification consistency was explored.

**Results:** 102 patients were included, 75 had an MRI scan performed. Mean changes stratified by PDQ-group are presented in the table showing the greatest changes in the CS-group (>18). Only baseline DAS28 was a significant predictor of DAS28 change ($P<0.001$) with a β-estimate (95%CI) of -0.65 (-88;-0.41). Baseline DAS28 and RAMRIS synovitis were significant predictors of RAMRIS synovitis change (P=0.01, P=0.02) with β-estimates of -0.67 (-1.17;-0.17) and -0.19 (-0.35;-0.03). Among the 12 patients with indication of CS (>18) at baseline all had changed classification-group at follow-up (8 to nociceptive pain and 4 to unclear).

Table: Mean change stratified by PDQ-group adjusted for baseline value

| | PDQ-score <13 (n = 66) | PDQ score 13-18 (n=23) | PDQ score > 18 (n = 12) | p-value |
|---|---|---|---|---|
| Classification consistency N (%)* | 64 (97) | 19 (83) | 0 (0) | <0.001† |
| Δ 28 SJC | -2.71 | -2.27 | -2.48 | 0.71 |
| Δ 28 TJC | -4.63 | -4.36 | -5.57 | 0.28 |
| Δ CRP, mg / mL | -6.93 | -2.81 | -6.28 | 0.04a |
| Δ DAS28 | -1.47 | -0.8 | -1.62 | 0.03b |
| Δ Tender point count | -2.70 | -1.56 | -3.83 | 0.35 |
| Δ VAS-fatigue | -18.31 | -8.19 | -22.20 | 0.09 |
| Δ VAS-pain | -23.27 | -12.99 | -26.86 | 0.07 |
| Δ VAS-global health | -26.20 | -13.49 | -31.72 | 0.01b |
| Δ HAQ-DI | -0.34 | -0.15 | -0.74 | <0.001c |
| Δ RAMRIS H synovitis | -1.68 ¹ | -1.75² | -2.46 ³ | 0.72 |
| Δ RAMRIS H oedema | -2.14 ¹ | -0.62² | -3.43 ³ | 0.58 |

* No change of PDQ classification group from baseline to follow up. † Chi square. 1: N=51. 2: N=18. 3: N=6. a; no difference between PDQ-score <13 and >18, and 13-18 and >18. b; no difference between PDQ score <13 and PDQ score >18. c; no difference between PDQ score <13 and 13-18.

**Conclusions:** In this pragmatically sampled population of RA patients, pain classification by PDQ at treatment initiation had no prognostic value with regard to change in DAS28 or RAMRIS synovitis. In contrast, all patients classified with indication of CS by PDQ at baseline changed classification group and were even to gain most from treatment start in net changes. This might indicate that in RA, CS reflects normal neuroplasticity that is reversible with reduction of inflammation.

**References:**

[1] Koroschetz J, et al. Fibromyalgia and neuropathic pain-differences and similarities. A comparison of 3057 patients with diabetic painful neuropathy and fibromyalgia. BMC Neurol 2011;11:55

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.3141

## FRI0100 APOLIPOPROTEIN A1 IS PROTECTIVE FOR JOINT DAMAGE PROGRESSION IN ACPA-POSITIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Lipoproteins are considered to excess pleiotropic functions in inflammation and autoimmunity. Apolipoprotein (apo) A1 has been reported to associate with arthritis development and hypercholesterolemia with radiographic progression in patients with rheumatoid arthritis (RA). Although a higher risk for more destructive RA in the presence of anti-citrullinated protein antibodies (ACPA) is recognized, responses driving the joint damage and protective mechanisms that could inhibit the pathological process are not defined.

**Objectives:** We hypothesized that radiological joint damage progression would be influenced by lipoproteins. We aimed firstly to explore association between lipoproteins and radiographic damage, and secondly, to investigate if this association was different in ACPA+ and ACPA- patients.

**Methods:** In all, 114 patients with early RA were included, 68% women, 71% ACPA+, mean age 50.6 (11.2) years. Apolipoproteins and oxidized low-density lipoprotein (oxLDL) were assessed in baseline serum and at 3, 12, 24 and 60 month after RA diagnosis. Radiographs of hands and feet were taken at inclusion, 12, 24 and 60 months and scored by the Sharp-van der Heijde (SHS) method. There were no differences between ACPA+ and ACPA- patients by age, sex, initial treatment, baseline DAS28, levels of lipoproteins and SHS, but ACPA+ patients had a longer symptom duration at inclusion, mean 6.8 (3.1) months vs. 4.8 (3.3), p=0.002. Normal regression was performed with adjustments for age, sex and initial treatments. Constant effects were tested in the final analyses as interaction with time was not significant. Significant associations were assessed within ACPA stratum.

**Results:** Higher apoA1 at inclusion was associated with lower SHS over 5 years, β=-0.204 (-0.400; -0.008), p=0.042. When stratified by ACPA status, this association was shown in ACPA+ patients, β=-0.237 (-0.456; -0.017), p=0.035, after additional adjustment for baseline disease duration, β=-0.207 (-0.421; 0.012), p=0.064. In ACPA- patients, association between baseline apoA1 and SHS overtime were not found, p=0.99. There was a trend for association between apoB/apoA1 at baseline and SHS over follow-up, β=0.351 (-0.055; 0.758), p=0.090.

Higher levels of apoA1 over 5 years were associated with lower SHS progression (ΔSHS = SHS 5 years – SHS inclusion), β=-0.004 (-0.006; -0.002), p<0.001. This association was confirmed in ACPA+ patients, β=-0.004 (-0.006; -0.001), p=0.002, but not in ACPA-, p=0.39. The result in ACPA+ stratum was unchanged after adjustment for disease duration, β=-0.004 (-0.006; -0.001), p=0.002. Further, a positive relationship was observed between apoB/apoA1 over 5 years and ΔSHS, β=0.002 (0.001; 0.003), p=0.006, also valid for ACPA+ patients, β=0.002 (0.001; 0.003), p=0.021, but not ACPA- patients, p=0.79. The finding in ACPA+ stratum was stable after adjustment for disease duration, β=0.002 (0.001; 0.003), p=0.016.

There were no significant associations between apoB and oxLDL and radiographic outcome, p>0.05.

**Conclusions:** We observed associations between apolipoproteins and radiographic outcome in patients with early RA. Apolipoprotein A1 showed a protective effect for radiographic joint damage in ACPA positive patients. Further exploring role of apolipoproteins may contribute to the understanding of immune-specific pathways.

**Disclosure of Interest:** None declared

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## FRI0101 ASSESSMENT OF LARGE JOINT DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY USING FDG-PET/CT AND ARASHI SCORING METHOD

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**Background:** Larsen method has been widely used to assess large joint destruction in patients with rheumatoid arthritis (RA). In that method, various changes might be included within one grade. 18F-fluorodeoxyglucose positron emission tomography combined with computed tomography (FDG-PET/CT) can visualize the disease activity in large joints affected by RA.

**Objectives:** The associations between destruction of the large joint and FDG-PET/CT findings were investigated using a new radiographic evaluation method "ARASHI Scoring system"[1].

**Methods:** A total of 260 large joints (shoulder, elbow, hip, knee and ankle) in 26 RA patients (six males and 20 females; mean age of 66.9 years) were assessed in this study. FDG-PET/CT was performed at baseline and six months after the initiation of biological therapy. The extent of FDG uptake in large joints was analyzed using the maximum standardized uptake value (SUVmax). Radiographs of the 10 large joints per patient obtained at baseline and after three years were evaluated according to the ARASHI change score. A multiple regression analysis was performed to determine the factors most significantly contributing to the progression of large joint destruction within three years.

**Results:** Eighteen joints had previously been treated with joint replacement surgery at baseline and nine joints were treated with joint replacement surgery in three years. They were excluded from this study, so we evaluated 233 large joints. The ARASHI status score (score at baseline), SUVmax at baseline, DAS28-ESR and ΔSUV (SUVmax at baseline – SUVmax at six months) were significantly associated with high level changes of ARASHI change score. A multiple regression analysis revealed ΔSUV was found to be the most associated factor with joint destruction at three years (p<0.05).

**Conclusions:** We investigated large joint destruction in RA patients using FDG-PET/CT and ARASHI scoring method. This study suggested the importance to decrease SUV value in RA patients with high level of SUVmax at baseline for the prevention of large joint destruction.

**References:**

[1] Kaneko A, Matsushita I, Kanbe K, Arai K, Kuga Y, Abe A, Matsumoto T, Nakagawa N, Nishida K. Development and validation of a new radiographic scoring system to evaluate bone and cartilage destruction and healing of large joints with rheumatoid arthritis: ARASHI (Assessment of rheumatoid arthritis by scoring of large joint destruction and healing in radiographic imaging) study. Mod Rheumatol. 2013 Nov;23(6):1053–62.

**Disclosure of Interest:** None declared

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## FRI0102 CHARACTERISTICS OF FUNCTIONAL IMPAIRMENT IN PATIENTS WITH LONG-STANDING RHEUMATOID ARTHRITIS BASED ON RANGE OF MOTION OF JOINTS: MULTICENTER PROSPECTIVE COHORT STUDY FOR EVALUATION OF JOINT SURGERY ON PHYSICAL FUNCTION

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**Background:** Even now, in clinical practice, most of RA patients have long-standing disease and structural damage in their joints. Reconstructive joint surgery should be needed for further improvements of physical function for long-standing RA patients. It is very important to understand how much range of motion (ROM) should be needed to gain better physical function in each case.

**Objectives:** The purpose of this study is to explore the characteristics of functional impairment in RA patients who were needed joint surgery based on ROM of joints using multicenter prospective cohort.

**Methods:** We conducted this prospective study from 2012 to2015 (Study registration: UMIN000012649) We collected data on age, sex, disease duration, drug therapies, disease activity, and physical functional including HAQ-DI. Joint range of motion including shoulder, elbow, wrist, hip knee ankle was also measured. ROM in each joint by disability in HAQ-DI categories was compared by ANOVA with adjustment of age and sex. Association between ROM of each joint and no disability of daily activity in each 8 HAQ-DI categories was determined using ROC curve and logistic regression analysis.

**Results:** 460 patients who have data of ROM of any joints in registry were analyzed. Mean values for age, disease duration, DAS28-CRP and sex were 64.6 years, 16.9 years, 3.17, and 86.3% female, respectively. Median values for CRP was 0.2 mg/dl. We could find significant association between ROM and disability in HAQ-DI category based on area under the ROC curve. ROM of each joints had different impact on disability of each category (ie, ROC curve for category Arising, Fig. 1). The cut-off values of ROM of each joints for daily activity in each HAQ-DI category was shown in Table 1 using ROC curves (Table 1). Multivariate analysis

adjusting disease activity, age, and sex, showed which joint had significant impact on disability of each category (Table 2).

Table 1: Cut off value of ROM of each joint for no disability in daily activity based on HAQ-DI

| | HAQ-DI category | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Dressing | Arising | Eating | Walking | Hygiene | Reach | Grip | Activity |
| shoulder abduction | 134.5 | 142.8 | 131.3 | 141.0 | 141.0 | 133.5 | 131.3 | 131.3 |
| elbow flex-extension | 120.5 | 125.5 | 118.8 | 126.5 | 126.5 | 113.8 | 120.5 | 120.5 |
| wrist supination-pronation | 153.3 | | 150.8 | | 153.3 | 156.0 | 144.5 | 144.5 |
| wrist flexion-extension | 78.8 | 69.5 | 76.3 | | 78.8 | 86.3 | 89.0 | |
| knee flexion-extension | 133.8 | 133.8 | | 133.8 | 131.3 | 123.8 | 123.8 | 123.8 |
| hip flexion-extension | 126.3 | 131.3 | 131.3 | 126.3 | 126.3 | 113.8 | 131.3 | 131.3 |
| ankle flexion-extension | 53.8 | 61.3 | 56.3 | 58.8 | 56.3 | 56.3 | 53.8 | 53.8 |

Cut off values were determined using ROC curve, when it showed significant association of the ROM to disability in each category.

Fig.1: Association of ROM of each joint in Arising

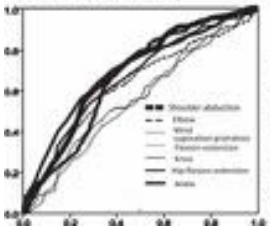


Table 2: Association of ROM of each joint to disability in daily activity based on HAQ-DI category

| | HAQ-DI category | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Dressing OR | Arising OR | Eating OR | Walking OR | Hygiene OR | Reach OR | Grip OR | Activity OR |
| shoulder abduction | .98 | .99 | .91 | .99 | .97 | .97 | .98 | .97 |
| wrist flexion-extension | | .89 | .94 | | .89 | .99 | .99 | 1.00 |
| knee flexion-extension | | .96 | 1.01 | .96 | | | | |
| hip flexion-extension | | .98 | .91 | .96 | | .97 | | .97 |
| ankle flexion-extension | | | | .97 | | | | |

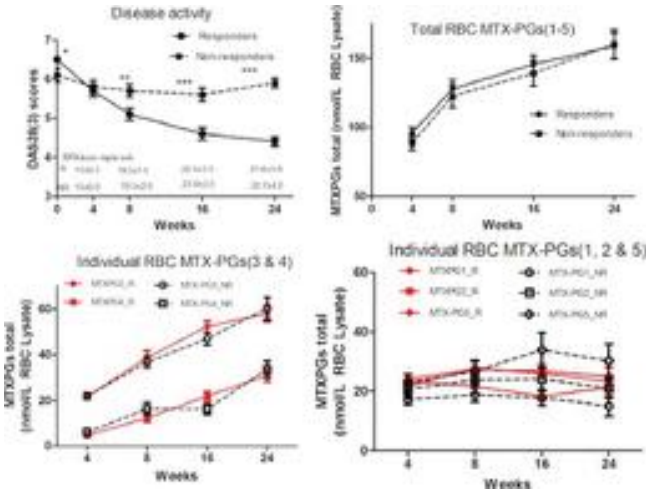
Only significant independent factors [OR /increase 1 degree of ROM] were shown.

**Conclusions:** ROMs of the joints were significantly associated with functional impairment. The information should be important for assessment of disability in patients with long-standing RA. The cut-off of ROM as shown in this study could be target of surgical procedure. It will be validated by further analysis of longitudinal data of this study.
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**Disclosure of Interest:** None declared
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## FRI0103 ERYTHROCYTE METHOTREXATE POLYGLUTAMATE LEVELS DO NOT DETERMINE EFFICACY AND TOLERABILITY OF METHOTREXATE IN RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX), a mono-glutamate, by addition of 2–6 more glutamate moieties, is converted to methotrexate polyglutamates (MTX PGs) intracellularly. These are the active compounds mediating folate pathway inhibition and increase in adenosine. Erythrocyte polyglutamate levels (RBC MTX PGs) are surrogate markers for levels inside lymphocytes and hepatocytes.Variability in RBC MTX PGs formed intracellularly (despite similar MTX dose) may be one of the factors determining variability in efficacy of MTX. Previously, contrasting results have been found on their association with efficacy and few prospective studies exist.
**Objectives:** To assay levels of erythrocyte methotrexate polyglutamate (1–5) levels in patients with rheumatoid arthritis and assess their relationship to efficacy and adverse effects.
**Methods:** Prospective study that included patients of RA (fulfilling 1987 ACR), aged 18–65 years with active disease (DAS28–3v>3.2) and not on methotrexate. Oral MTX was started at 15 mg/week and increased to 25 mg/week at 8 weeks. Disease activity measured using DAS28 (3 variables), and at 24 weeks patients classified into responders (EULAR good or moderate response) or non-responders. MTX-PG levels (PGs 1–5) assayed in deproteinised packed RBCs by HPLC using reverse phase (C18 column) and post-column derivitization using UV photo-oxidation followed by fluorescent detection (ex 274; em 470 nm).
**Results:** Included 117 patients, with mean (±SD) age of 42.7±11.9 years, disease duration 2.0±1.7 years, 71.8% RF+ and 85.7% CCP+. At 24 weeks, there were 57 responders and 33 non-responders with no significant difference in mean (±SD) MTX dose (21.7±3.9, 22.7± 4.1mg/week, p=ns), age, disease duration, but with lower BMI (21.7±3.9, 24±4.5 kg/m$^2$, p=0.02) and higher baseline DAS28(3) (6.5±0.7, 6.1±0.9, p=0.02). There was an early and sustained gap between the curves of DAS28(3) between responders and non-responders (Figure, left upper quadrant). Methotrexate PG levels increased till 24 weeks (mainly PG3 and PG4), with reasonable correlation between dose and MTX PG levels (r=0.38, p<0.05). There was no significant difference in the mean methotrexate polyglutamate levels (sum of pgs 1–5) nor individual PGs between responders and non-responders at any of the visits (4, 8, 16 and 24 weeks) ((Figure, right upper quadrant and lower panel). Symptomatic adverse effects occurred in 34 patients (57 episodes)




– most commonly nausea. There was no significant difference in MTX-PG levels between patients with and without symptomatic adverse effects. Mild transaminitis occurred in 43 patients (at atleast one visit) and mild thrombocytopenia in 16 patients; with no difference in methotrexate polyglutamate levels.
**Conclusions:** Our study suggests that MTX-PG levels is not a determinant for response to MTX or their adverse effects. This is different from a previous prospective study, we think the differnce lies in MTX dose and clear classification as reponder and non-responders in our study.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2342

## FRI0104 LONG-TERM FOLLOWUP OF BIOLOGIC AGENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Biologic agents have altered treatment strategy and improved outcome in rheumatoid arthritis (RA). More than 10 years have passed since the emergence of the first biologic agent, and the switch to alternative agent for insufficient efficacy and intolerance is not infrequent. However, the continuation rate of biologic agents and reasons for discontinuation in a long-term are unclear.
**Objectives:** To evaluate followup data for more than10 years of biologic agents in patients with RA.
**Methods:** Patient who started biologic agents including infliximab, etanercept, adalimumab, tocilizumab and abatacept for RA between 2003 and 2013 were enrolled in the study. The continuation rate was calculated by Kaplan-Myere analysis, and reasons for discontinuation were retrospectively investigated. Factors contributory to the continuation rate were identified. The analyses were performed in all patients, and subsequently in patients on individual biological agents.
**Results:** A total of 1500 biologic agents were introduced in 1036 patients with RA for the 11 years. At the initiation of biologic agents, the mean age was 57.2 years old, the rate of female 82.5%, disease duration 103 months, rheumatoid factor positivity 78.8% DAS28 4.90, and health assessment questionnaire 1.09. Methotrexate (MTX) was used in combination with biologic agents in 81.1%. Overall continuation rate was 68.7% at year 3, 58.8% at year 5, and 27.6% at year 10. Reasons for discontinuation were insufficient efficacy in 64.3% and adverse effect in 45.7%. Baseline characteristics to predict the continuation of biologic agents were the concomitant use of MTX (OR=1.61, P=0.03), lower baseline values for 28 joints (DAS28, OR=1.14, P=0.02) and shorter disease duration (OR=1.01, P=0.03). In bio-naïve patients, continuation rate was 69.3% at year 3, 59.4% at year 5, and 28.5% at year 10). In terms of individual biologic agents, high continuation rate was ascribed to lower disease activity for infliximab (OR=1.32, P=0.001), the concomitant use of MTX for etanercept (OR=1.22, P=0.03) and adalimumab (OR=1.53, P=0.04), shorter disease duration for abatacept (OR=1.00, P=0.05). No specific factor for tocilizumab continuation was found.
**Conclusions:** In the initiation of biologic agents, patients using concomitant MTX with shorter disease duration in lower disease activity were inclined to continue the biologic agents. Factors for good continuation rate were different among biologic agents. The present study can contribute optimal usage of biologic agents in the treatment of RA.
**Disclosure of Interest:** Y. Kaneko Speakers bureau: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Pfizer, Janssen, Santen, Kyowa Hakko Kirin and UCB, H. Kondo: None declared, M. Ohta: None declared, T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Sanofi–Aventis K.K., Santen Pharmaceutical Co., Ltd., Teijin Pharma Ltd., abbvie GK, Asahikasei

Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd. Janssen Pharmaceutical K.K., Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Abbvie GK., Speakers bureau: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Abbvie GK, Asahikasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd. Janssen Pharmaceutical K.K., Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K.

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### FRI0105 LOW THORACIC BONE MINERAL DENSITY AND GLUCOCORTICOID ARE RISK FACTORS FOR CLINICAL FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS: FIVE-YEAR FINDINGS OF THE TOMORROW STUDY

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**Background:** Patients with rheumatoid arthritis (RA) who have muscle weakness and stiff or painful joints might be at increased risk of falls and fracture.
**Objectives:** The present study aimed to prospectively determine the incidence of clinical fractures and associated risk factors in patients with RA who participated in the TOMORROW study (UMIN000003876) that started in 2010.
**Methods:** We evaluated anthropometric parameters, bone mineral density (BMD), disease activity, RA medication, and the incidence of clinical fractures over a five-year period in 202 patients with RA (mean age, 58.6 y; medication with biological agents, 54.9%) and 202 age- and sex-matched healthy volunteers (controls; mean age, 57.4 y). We compared the incidence of clinical fractures between patients and controls between 2010 and 2015 and analyzed associated risk factors in the patients using multivariate regression analysis.
**Results:** The incidence of clinical fractures did not significantly differ between patients with RA (0.042/person-years; py) and controls (0.034/py) within the five-year period (p=0.35). Fractures sites also did not significantly differ between the two groups. Multivariate logistic regression analysis adjusted for fracture risk factors including age, sex, smoking, and body mass index revealed that low BMD at the thoracic vertebrae (<0.7 g/cm$^2$) was significantly associated with the incidence of clinical fractures (odds ratio [OR], 2.95) in all participants group (Table 1). Although medication with glucocorticoid (GC) at entry was also a significant risk factor for fractures (OR, 2.58), RA morbidity was not (Table 1). Among patients with RA, low BMD at the thoracic vertebrae (<0.7 g/cm$^2$) was the most prominent risk factor for fractures (OR, 4.44; Table 1). Additionally, medication with GC at entry (OR, 2.58) was a significant risk factor for fractures in the patients. A mean GC dose of ≥2 mg/day during the five-year period increased risk for fractures in the patients (OR, 3.48; Table 1).

Table 1. Multivariate logistic regression analysis of risk factors for fractures

| | | Odds ratio | 95% CI | *p* |
|---|---|---|---|---|
| All participants | History of fractures | 1.68 | 0.97–2.89 | 0.064 |
| N=404 | Morbidity of RA | 1.22 | 0.71–2.11 | 0.478 |
| | GC use | 2.58 | 1.22–5.44 | 0.013 |
| | Bisphosphonate medication | 3.37 | 1.51–7.54 | 0.003 |
| | Low BMD at thoracic vertebrae (<0.7 g/cm$^2$) | 2.95 | 1.59–5.48 | 0.001 |
| RA patients | History of fractures | 1.99 | 0.95–4.16 | 0.069 |
| N=202 | GC medication | 2.58 | 1.22–5.44 | 0.013 |
| | Average GC dose ≥2 mg/day/5 y | 3.48 | 1.19–10.21 | 0.023 |
| | Bisphosphonate medication | 3.37 | 1.51–7.54 | 0.003 |
| | Low BMD at thoracic vertebrae (<0.7 g/cm$^2$) | 4.44 | 1.69–11.64 | 0.002 |

CI, confidence interval; RA, rheumatoid arthritis; GC, glucocorticoid; BMD, bone mineral density.

**Conclusions:** The incidence of clinical fractures did not significantly differ between patients with RA and controls during a period of five years. Low BMD at the thoracic vertebrae and low GC doses are apparently significantly associated with an increased frequency of fractures among patients with RA.
**Disclosure of Interest:** None declared
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## Rheumatoid arthritis - comorbidity and clinical aspects

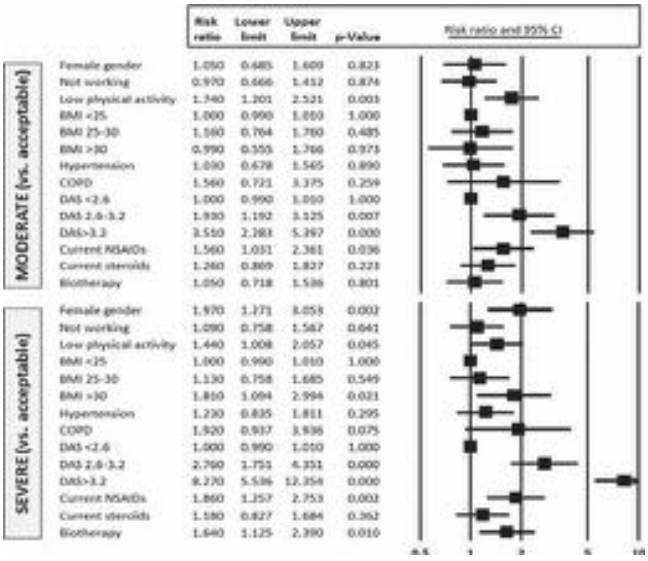
### FRI0106 THE ASSOCIATION OF FATIGUE, COMORBIDITIES AND ANTI RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS: RESULTS FROM THE COMEDRA STUDY

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**Background:** The mechanisms of fatigue in rheumatoid arthritis (RA) are still unclear and the effect of antirheumatic drugs on fatigue not fully established.
**Objectives:** To analyse in a large cohort of RA the factors associated with fatigue focusing on social aspects, comorbidities and treatment intake.
**Methods:** Cross sectional analyses were performed on RA patients from the French cohort study of comorbidities COMEDRA (1). Fatigue was assessed as a quantitative variable (RAID3 0–10 numeric scale) or by class (acceptable <3; moderate 3–4; severe ≥5 out of 10). Relationship with demographic, social, disease characteristics, treatments, comorbidities, physical activity, quality of life was investigated in univariate analyses (Table) and multivariate polynomial regression (Figure).
**Results:** 962 patients were analysed (age 57.7 ± 11.1 years, disease duration 11.1 years [6.2–19.1], mean DAS28 3.1 ± 1.3), 763 (79%) were female. The mean fatigue score was 3.8± 2.7. Severe fatigue was more frequent in women, in patients not working, with less physical activity and more obesity. Fatigue was correlated with disease duration (p=0.05), all disease activity index (p<0.001), pain (p<0.001), mHAQ (p<0.001), sleep (p<0.001) and emotional well-being (p<0.001). Among comorbidities, hypertension, chronic obstructive pulmonary disease (COPD), fracture history and RA-related surgery were associated with fatigue. Fatigue was more severe in patients with current NSAID, steroid, biologic treatments. Methotrexate use and the type of biologic did not impact fatigue score.

| | RAID3 (0–10) Beta [95% CI] | RAID3 by class, RR [95% CI] Moderate vs acceptable<br>Severe vs acceptable |
|---|---|---|
| Female gender (n=763) | 1.03 [0.6; 1.45]*** | 1.16 [0.78; 1.70]<br>2.07 [1.43; 3.01]*** |
| Low educational level (n=680) | 0.38 [0.01; 0.76]* | 0.95 [0.66; 1.36]<br>1.33 [0.94; 1.80] |
| Not working (n=628) | 0.38 [0.02; 0.74]* | 1.10 [0.78; 1.56]<br>1.43 [1.05; 1.94]* |
| Low physical activity (n=353) | 0.69 [0.33; 1.05]*** | 1.80 [1.26; 2.55]***<br>1.71 [1.25; 2.34]*** |
| BMI | | |
| 25–30 (n=276) | 0.16 [–0.24; 0.55] | 1.20 [0.83; 1.75]<br>1.13 [0.81; 1.59] |
| ≥30 (n=155) | 1.20 [0.72; 1.68]*** | 1.32 [0.78; 2.23]<br>2.39 [1.56; 3.67]*** |
| DAS28 | | |
| 2.6–3.2 | 1.30 [0.86; 1.74]*** | 2.20 [1.39; 3.48]***<br>3.13 [2.04; 4.81]*** |
| >3.2 | 2.50 [2.15; 2.84]*** | 3.89 [2.58; 5.87]***<br>9.35 [6.41; 13.64]*** |
| Hypertension (n=281) | 0.67 [0.29; 1.05]*** | 1.19 [0.82; 1.75]<br>1.75 [1.26; 2.42]*** |
| COPD (n=63) | 0.72 [0.02; 1.41]* | 1.53 [0.73; 3.20]<br>2.10 [1.12; 3.93]* |
| Fracture history (n=296) | 0.44 [0.06; 0.81]* | 1.42 [0.99; 2.04]<br>1.38 [0.99; 1.90] |
| RA-related surgery (n=287) | 0.40 [0.02; 0.78]* | 0.99 [0.68; 1.45]<br>1.27 [0.92; 1.75] |
| Current NSAIDs (n=249) | 0.75 [0.36; 1.14]*** | 1.70 [1.14; 2.52]**<br>1.96 [1.39; 2.77]*** |
| Current steroids (n=364) | 0.75 [0.40; 1.1]*** | 1.49 [1.05; 2.11]**<br>1.72 [1.27; 2.33]*** |
| Biotherapy alone or in combination (n=672) | 0.46 [0.07; 0.84]* | 0.96 [0.67; 1.38]<br>1.45 [1.04; 2.01]** |

***p<0.001; **p<0.01; *p<0.05.




**Conclusions:** Beyond the expected association of fatigue with disease activity, female gender, pain, sleep and emotional well-being, comorbidities and less physical activity could contribute to the frequent fatigue noted in RA. Fatigue was

associated with steroids, NSAIDs, biotherapies but not with methotrexate and did not depend of the type of biotherapy.

**References:**
[1] Dougados M et al. Ann Rheum Dis. 2015;74(9):1725–33

**Disclosure of Interest:** None declared

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## FRI0107 NO INCREASED RISK OF HIGH GRADE CERVICAL DYSPLASIA IN WOMEN WITH RHEUMATOID ARTHRITIS

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**Background:** There is concern that women with rheumatoid arthritis (RA) are at increased risk of high-grade cervical dysplasia (HGCD) detected via cervical smear. There is also controversy regarding the effect of chronic disease/disability on routine cancer screening attendance in this population.
**Objectives:** To (1) compare uptake of cervical screening for women with RA in the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA) with the general population and (2) compare frequency of HGCD between RA and the general population and between patients with RA ever versus never exposed to biologics.
**Methods:** The BSRBR-RA, a prospective cohort study, was linked to the NHS Cervical Screening Programme England (CSPE). Data from 2004–2014 was analysed in line with CSPE methods who publish coverage analysis annually; coverage is defined as the number of women who have been adequately screened at the defined age-dependent review period out of the total number of women eligible for screening in this period. Annual coverage was calculated for the eligible BSRBR-RA population and compared to national statistics. Within the BSRBR-RA, coverage was also compared between those patients with mild/moderate disability (mean Health Assessment Questionnaire (HAQ) scores $<2$) and high disability (HAQ $\geq 2$).
Rates of HGCD (moderate dyskariosis or greater) and low grade cervical dysplasia (LGCD, borderline or mild dyskariosis) were compared to rates of negative smears using risk difference calculations between the BSRBR-RA and national statistics, and between the biologic naïve (standard DMARD therapy) and biologic exposed cohorts within the BSRBR-RA.
**Results:** Of 13565 linked records, 12939 women had RA of which 12785 had cervical screening data, 2132 (17%) on nbDMARD therapy and 10653 (83%) with biologic exposure. Between 2004–2014 mean five-year coverage was higher in the BSRBR-RA population at 82.5% (95% CI 81.9, 83.1) compared to 79.0% (95% CI 78.5, 79.6) nationally. This mostly reflects significantly higher age appropriate coverage in the 25–49 year group for the BSRBR-RA population: 77.2% (95% CI 75.9, 78.6) compared to 71.4% (95% CI 70.2, 72.6) nationally. Coverage was higher among women with HAQ $<2$ (n=6631) compared to those with HAQ $\geq 2$ (n=5163): 85.4% (95% CI 84.7, 86.1) and 78.1% (95% CI 77.3, 78.8) respectively. The risk of HGCD was lower in the BSRBR (0.9%) compared to the general population (1.3%) with a risk difference of -0.004 (95% CI -0.005, -0.002). The risk of LGCD was higher in the BSRBR (7.5%) compared to the general population (5.4%) with a risk difference of 0.021 (95% CI 0.017, 0.025). There was no significant risk difference for HGCD between the biologic and nbDMARD cohorts at 0.009 (95% CI -0.003, 0.021).
**Conclusions:** Women in the BSRBR-RA in England have higher rates of cervical screening attendance than the general population, although high HAQ scores had a negative effect on screening attendance. Those aged 25–49 years had markedly higher attendance; this may reflect familiarity with accessing healthcare. Cytology analysis suggests lower risk for HGCD in the RA group but higher risk for LGCD; this may reflect increased screening attendance. Women receiving biologic therapy were not at an increased risk of HGCD compared to those receiving standard DMARD therapy.

**Disclosure of Interest:** None declared

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## FRI0108 RHEUMATOID ARTHRITIS IS ASSOCIATED WITH INCREASED RATE OF MALIGNANCY: A CROSS-SECTIONAL ANALYSIS OF 69755 PATIENTS

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**Background:** Rheumatoid Arthritis (RA) is a common autoimmune disease, which carries a wide variety of comorbidities. The risk of developing malignancy amongst RA patients is of increased both due to the constant inflammatory activity (1) and disease therapies.
**Objectives:** To evaluate the association between RA and malignancies.
**Methods:** In this cross-sectional population based study, data were collected from Israel's largest HMO database, comprising over 4 million patients. Study sample included all RA patients (n=11,782) and sex and age matched controls (n=57,973), total of 69755 patients. Medical records were scanned for anthropometric measurements and diagnosis of malignancy. Logistic regression was used to adjust for age, gender, BMI and socioeconomic status.
**Results:** The total malignancy rate was higher among RA patients comparing to controls (21.4% vs. 11.2%, respectively; $p<0.001$). In multivariate analysis, Hodgkin's and non-Hodgkin's lymphoma, multiple myeloma, sarcomas and malignancies of thyroid and cervix were found to be independently associated with RA. Following multivariate analysis lung carcinoma were not found to be independently associated with RA.

| | Malignancy of: | | | | | | |
|---|---|---|---|---|---|---|---|
| | Non Hodgkin Lymphoma | Hodgkins Lymphoma | Lung | Thyroid | Cervix | Sarcoma | Multiple Myeloma |
| Age (Per year) | 1.04 (1.03, 1.04) | 1.01 (1.00, 1.03) | 1.06 (1.05, 1.07) | 1.02 (1.01, 1.03) | 1.01 (1.00, 1.02) | 1.04 (1.02, 1.05) | 1.05 (1.04, 1.07) |
| Male | 1.37 (1.16, 1.57) | 1.17 (0.76, 1.58) | 1.04 (0.73, 1.34) | 0.33 (-0.03, 0.69) | | 1.04 (0.65, 1.43) | 1.49 (1.09, 1.89) |
| SES - Medium vs. Low | 1.34 (1.13, 1.56) | 1.18 (0.78, 1.57) | 0.88 (0.56, 1.20) | 1.39 (1.14, 1.63) | 1.09 (0.67, 1.52) | 0.89 (0.52, 1.25) | 1.12 (0.70, 1.54) |
| SES - High vs. Low | 1.36 (1.12, 1.61) | 0.88 (0.38, 1.39) | 1.01 (0.65, 1.37) | 1.61 (1.34, 1.89) | 1.15 (0.65, 1.65) | 0.91 (0.48, 1.35) | 1.16 (0.68, 1.64) |
| Smoking | 1.28 (1.09, 1.48) | 1.11 (0.73, 1.50) | 3.99 (3.70, 4.29) | 1.07 (0.84, 1.30) | 1.59 (1.22, 1.96) | 0.89 (0.51, 1.26) | 0.86 (0.44, 1.27) |
| BMI (Per 1 kg/m2) | 1 (0.98, 1.01) | 0.99 (0.95, 1.02) | 0.94 (0.92, 0.97) | 1.01 (1.00, 1.01) | 1 (0.97, 1.03) | 1 (0.97, 1.03) | 1 (0.97, 1.03) |
| **RA** | **1.64** (1.43, 1.84) | **1.94** (1.56, 2.32) | **1.29** (0.96, 1.62) | **1.3** (1.06, 1.55) | **1.66** (1.24, 2.08) | **1.59** (1.23, 1.96) | **1.73** (1.33, 2.13) |

**Conclusions:** RA is independently associated with both hematological and solid malignancies. Appropriate measures for screening for malignancies amongst this patient population should be assessed and implemented.

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**Disclosure of Interest:** None declared

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## FRI0109 INFLUENCE OF AROMATASE INHIBITORS THERAPY ON THE OCCURRENCE OF RHEUMATOID ARTHRITIS IN WOMEN WITH BREAST CANCER. RESULTS FROM A LARGE POPULATION BASED STUDY OF THE ITALIAN SOCIETY FOR RHEUMATOLOGY

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**Background:** Though aromatase inhibitors (AIs) and tamoxifen are an essential part of estrogen receptor-positive breast cancer therapy, many patients discontinue the treatment for musculoskeletal symptoms [1]. Whether the musculoskeletal symptoms can be attributed to an underlying rheumatologic disease remain unknown. Sporadic case reports have described the onset of rheumatoid arthritis (RA) in patients who started therapy with tamoxifen or AIs [2].
**Objectives:** The purpose of this study was to evaluate the risk of developing rheumatoid arthritis (RA) in the population of patients with breast cancer treated with AIs.
**Methods:** Data were collected from the administrative health-care database of Lombardy Region, Italy, from 2004 to 2013. This study follows a nested case-cohort design, including women with diagnosis of breast cancer (ICD9-CM codes 174) starting treatment tamoxifen, anastrozole, exemestane or letrozole. Level of neoplasia was defined according to relevant ICD9-CM codes as localized, node-positive, metastatic, unspecified. The risk of RA related to the prescription of the different drugs was estimated by survival models for competing risks and the results are presented as hazard ratios (HRs) and 95% confidence interval (95% CI), adjusted for age and disease duration. Interaction with age and time varying effects were also explored.
**Results:** Out of a total of 10493 women with breast cancer with a median (IQR) age of 66 (57–74), 7533 (71.8%) started an active treatment with adjuvant endocrine therapy. In this subgroup of patients a total of 113 new cases of RA developed during the 26105.9 person-year of 10186 exposure periods, including time varying exposures in the same patient. Using tamoxifen as reference

category, AIs therapy was associated with an increased risk of RA [adjusted HR 1.62 (95%1.03–2.56)], in particular due to anastrozole, even after adjusting for age and level of neoplasia (Table). Interaction with age was not statistically significant, and no time varying effects were observed.

| | Crude HR | Adjusted HR (95% CI)* | Adjusted HR (95% CI)*§ |
|---|---|---|---|
| Tamoxifen | reference | reference | reference |
| Anastrozole | 1.77 (1.10–2.85) | 1.73 (1.06–2.81) | 1.75 (1.07–2.86) |
| Letrozole | 1.51 (0.89–2.56) | 1.49 (0.87–2.56) | 1.47 (0.86–2.51) |
| Exemestane | 1.78 (0.76–4.17) | 1.75 (0.74–4.16) | 1.47 (0.63–3.43) |

*Adjusted for age at surgery, level of neoplasia; §Competitive risk survival model.

**Conclusions:** In a large population-based sample of women with breast cancer, the exposure to AI therapy compared with tamoxifen is associated with a significantly increased risk of developing RA, which is not influenced by the cancer severity and the relationship of age with indication to specific drugs. In patients with breast cancer treated with AIs and presenting arthralgia referral to rheumatologist is useful to exclude the onset of rheumatoid arthritis.

**References:**

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[2] Bertolini E, et al. Jt Bone Spine Rev Rhum 2011;78:62–4.

**Disclosure of Interest:** None declared

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## FRI0110 ASSESSMENT OF IMMUNOGENICITY OF LIVE ZOSTER VACCINATION IN RHEUMATOID ARTHRITIS PATIENTS ON BACKGROUND METHOTREXATE BEFORE AND AFTER INITIATING TOFACITINIB OR PLACEBO

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of RA. Clinical guidelines recommend live zoster vaccine (LZV) to prevent shingles in RA, but this has not been studied in RA patients (pts) and the effect of tofacitinib on humoral or cell-mediated responses to LZV is unknown.

**Objectives:** To evaluate the effect of tofacitinib upon the immune response (IR) and safety of LZV.

**Methods:** Pts were aged ≥50 years with active RA (≥4 tender/painful joints and ≥4 swollen joints) despite methotrexate (MTX) ≥4 months (15–25 mg/wk before screening) (study NCT02147587). Pts with prior history of zoster vaccination were excluded, as were those receiving any vaccine in the 6 wks prior to randomisation. After screening, eligible pts on background MTX received LZV and then either tofacitinib 5 mg BID or placebo (PBO) starting 2–3 wks post-vaccination. Both humoral (varicella-zoster virus [VZV]-specific IgG via gpELISA) and cell-mediated responses (VZV-specific T cell enumeration via ELISPOT) before vaccination (baseline [BL], day of vaccination), and then at 2, 6 and 14 wks post-vaccination were measured. Primary endpoint: geometric mean fold rise (GMFR) in VZV-specific IgG titre at 6 wks post-vaccination. Secondary endpoint: proportion of pts achieving a ≥1.5 fold rise in VZV-specific IgG titre 6 wks post-vaccination. Exploratory endpoint: GMFR in VZV-specific T cells (spot-forming cells/$10^6$ peripheral blood mononuclear cells) by ELISPOT between BL and 6 wks post-vaccination. Pts were followed for 12 wks after randomisation for safety.

**Results:** 112 pts were randomised to PBO (n=57) and tofacitinib (n=55). Most PBO (93%) and tofacitinib (98%) pts were evaluable for IR endpoints. Pts were similar with regard to sex, age, baseline disease activity and baseline VZV immune measures (i.e. IgG, ELISPOT). The GMFR in VZV-specific IgG titre at 6 wks was 2.11 for tofacitinib and 1.74 for PBO. GMFRs in tofacitinib and PBO pts were comparable with GMFRs in healthy people ≥50 years as indicated in the LZV labels. The proportion of pts with a 1.5 fold rise in IgG titre at 6 wks post-vaccination rise trended higher for tofacitinib (57.4%) vs PBO (43.4%). The VZV-specific T cell GMFR at 6 wks increased similarly for tofacitinib (1.50) and PBO (1.29). SAEs occurred in 0 and 3 (5.5%) of PBO and tofacitinib arms respectively. One pt had cutaneous dissemination with vaccine-strain VZV (Oka strain virus) 2 days after starting tofacitinib (16 days post-vaccination). This pt was found to lack pre-existing immunity to VZV, consistent with vaccine-induced disease. The event resolved after tofacitinib discontinuation and antiviral therapy.

**Conclusions:** Pts starting tofacitinib had similar VZV-specific humoral and cell-mediated IRs to LZV as compared to PBO-treated pts. Vaccination appeared safe in pts subsequently treated with tofacitinib; however, one patient who lacked pre-existing VZV immunity developed vaccine-induced disease.

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## FRI0111 DENTAL ASSOCIATION OR INCIDENTAL FINDING? A META-ANALYSIS AND SYSTEMATIC REVIEW OF THE RELATIONSHIP BETWEEN RHEUMATOID ARTHRITIS AND PERIODONTITIS

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**Background:** Rheumatoid arthritis (RA) and periodontitis are both chronic inflammatory diseases sharing potential mechanisms including histopathology and demography. An association between these conditions has been demonstrated previously but published studies have not been subjected to meta-analysis with respect to large populations worldwide to fully unravel associations across distinct ethnicities.

**Objectives:** The aim of this analysis was to interogate the relationship between rheumatoid arthritis and periodontitis in the context of the earliest to the most recent literature.

**Methods:** The published databases MEDLINE, EMBASE and PsycINFO were searched using search terms related to RA and periodontitis. Articles were selected if they included data on the number of people with RA diagnosed with periodontitis (or periodontal disease parameters) compared to a control comparison group. Review articles, case reports, animal model studies, non-English language and articles with unavailable abstracts were excluded. Data was extracted, critically appraised using the Downs and Black appraisal tool and a fixed-effect Mantel-Haenszel meta-analysis was performed.

**Results:** A total of 21 papers met the eligibility criteria and provided data for the meta-analysis; 17 studies (including a total of 153,492 participants) comparing RA to healthy controls and 4 (including a total of 1378 participants) comparing RA to osteoarthritis (OA) were evaluated. Studies included patients populations from diverse geographical locations including Taiwan, Japan, India, Holland and the United States. There was a significantly increased risk of periodontitis in people with RA compared to healthy controls (RR: 1.13; 95% CI: 1.04, 1.23; p=0.006; N: 153,277) with a significantly raised mean probing depth, risk of bleeding on probing (BOP) and absolute value of clinical attachment loss in those with rheumatoid arthritis (Figure 1). When comparing RA and OA, there was no significant difference in the prevalence of periodontitis, however the risk of BOP was greater in OA than RA.




Figure 1. Forest-plot representing risk ratio of periodontitis between people with RA and healthy control comparisons.

**Conclusions:** The very strong association between RA and periodontitis is supported by the results of our systematic review and meta-analysis of studies comparing RA to healthy controls Our data show that the association of RA and periodontitis is a significant observation seen worldwide across a range of ethnicities, suggesting common shared mechanisms in both conditions. Future work is required to unravel the basic molecular pathways underlying RA and periodontitis.

**Disclosure of Interest:** None declared

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## FRI0112 PERIODONTITIS AND RHEUMATOID ARTHIRTIS: CHARACTERISTICS OF CHRONIC PERIODONTITIS AND ITS ASSOCIATION WITH RHEUMATOID ARTHRITIS

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**Background:** Recent clinical-epidemiological data suggest that periodontitis (P) shows higher prevalence in patients with rheumatoid arthritis (RA). However, the strength of association is limited, with odds ratios (OR) ranging from 1,82–8,05. Meanwhile, prevalence of P in adult Spanish population[1] varies from 16–30%,with smaller prevalence of severe P (5–11%). Nevertheless, there is no evidence of the P prevalence in RA patients in Spanish population.
**Objectives:** 1.To describe the prevalence of P and its association with RA in patients located in our reference area. 2.To explain the characteristics of P in RA patients.
**Methods:** Observational, descriptive, cross-sectional, case-control study of RA patients ≥18 years old (ACR/EULAR 2010) in a hospital Rheumatology Service, and a control group with a non-inflammatory joint disease, who had at least 4 teeth, had not received dental prophylaxis or antibiotic intake 6 months before study. Socio-demographic and anthropometric variables with smoking status, Graffar scale, stress level, annual dental prophylaxis, and co-morbidities such as osteoporosis (OP),diabetes mellitus (DM),dyslipidemia (DS),ischemic cardiovascular disease (ICD). Periodontal Variables: plaque index (PI), bleeding on probing (BoP), probing pocket depth (PPD), recession (REC), clinical attachment level (CAL). Dental team: 2 periodontists/2 general dentists with inter-observer variability <30%. Full mouth CAL, PPD and periapical x-rays were taken. CAL was classified according to the European Workshop in 2005 (Tonetti), into level 0 (absence), N1T (mild), N2T (severe). Statistical Analysis: t-student, Kruskal Wallis, Chi-square. Statistical program: Stata 13.1.
**Results:** 344 patients:187 RA (147 F/40 M) and 157 control (101F/56M). Both groups were comparable in age 54,9 (17,9), BMI 27,8 (4,6), stress level, DM and ICD. Differences in gender (>n° of males in controls), socioeconomic status (lower level in RA), >n° of current and former smokers RA (19,25%vs 8,92%/ 24,6%vs 11,46%),OP (23,45% RA vs 7,8%), DS (hipertrygliceridemia 11,23% RA vs 4,46%). There were182/187 (97, 33%) RA patients with P vs 104/157 (66,24%) patients with P in controls; N1T 52,41% RA vs 54,14%; N2T 44,92% RA vs 12,1% controls p<0,001, OR 18,55 (CI 95% 7,188–47,872),which is maintained after adjusting by confounding variables: OR 16,248 ± 9,295 (CI95% 5,295–49,858).Moreover, there was a poor periodontal status in RA patients with a dramatic increase in all periodontal parameters: PI, PPD, n° and percentage of PPD ≥5mm and BoP (p<0,001) compared with control group.
**Conclusions:** 1.Our study shows a strong association between RA and P with an adjusted OR 16,25 2.RA patients presented an increased prevalence of severe P compared to controls with statistical significance, and estimated prevalence in Spanish population. 3. RA patients showed a more severe periodontitis than control patients.4. there were no differences in the prevalence of mild periodontitis between both groups.
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**Disclosure of Interest:** None declared
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## FRI0113 POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING A BIOLOGICAL AGENT – A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Objectives:** To evaluate through a systematic review of the literature the association between the use of biological disease-modifying antirheumatic drugs (bDMARDs) and surgical site infection or wound healing delay after orthopedic surgery in patients with rheumatoid arthritis (RA).
**Methods:** A systematic review was performed of articles indexed in the Cochrane Library, PubMed, and Web of Science from 1992 to 2012. The search aimed to identify studies describing surgical site infection (SSI) or wound healing delay in patients with RA treated with or without bDMARDs. Articles fulfilling the predefined inclusion criteria were reviewed systematically and their quality appraised.
**Results:** There was no Cochrane review on this subject. We found 75 articles through specific searches of PubMed and Web of Science, and hand searching. After inclusion and exclusion by full-text review, 10 articles were found for SSI, and five articles for delayed wound healing. The use of bDMARDs appeared to increase the rate of SSI slightly, especially in large joint-replacement surgery. Delayed wound healing was not increased by the use of bDMARDs. However, the definitions of SSI and delayed wound healing varied between the reviewed articles. Most of the articles focused on tumor necrosis factor-a inhibitors.
**Conclusions:** bDMARDs slightly increase the relative risk of SSI but not that of delayed wound healing after orthopedic surgery and should be used with appropriate caution.
**Disclosure of Interest:** None declared
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## FRI0114 DEVELOPMENT OF THE PATIENT MOTIVATION QUESTIONNAIRE: CONCEPTUALIZING AND MEASURING MOTIVATION IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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**Background:** Motivation is literally the desire to do things, and patient motivation was reported to play an important role in determining the outcome of therapy. Measuring patients' motivation reflects their proactivity, engagement and activation to self-manage their disease which is of value both at the individual level (e.g. tailoring management and interventions) and at the educational program evaluation (e.g. monitor efficacy in enhancing activation).
**Objectives:** to develop a questionnaire for evaluating the patient's "motivation" and assess the psychometric properties of that measure in patients with chronic inflammatory arthritis.
**Methods:** the conceptualization stage identified that inflammatory arthritic patients who are likely to have better health outcomes are those who: (1) Understand the nature of their disease, 2. Are involved in treatment and diagnostic choices through a shared decision process; 3. Are aware of the patient's health-engagement role; 4. Able to self-manage symptoms/problems; 5. Able to collaborate with providers; 6. Can find solutions; 7. Able to maintain functioning and reduce health declines; 8. Can engage in activities; 9. Able to administer medications; 10. Able to find resources and select providers based on performance or quality.
Using Rasch analysis and 76 questions item pool; content analysis and semi structured group discussion, the questionnaire was developed including: 10-items scale (0–10 on VAS scale). Construct validity was assessed by correlating the score of the questionnaire to parameters of disease activity (DAS-28, ASDAS and DAPSA scores), functional disability, quality of life, patient self-helplessness measure [1] as well as the patients' compliance to therapy [2]. Reliability and comprehensibility and sensitivity to change were also assessed.
**Results:** The questionnaire was assessed in 432 RA, 415 Psoriatic arthritis patients, and 232 Ankylosing spondylitis patients. Dimensionality analysis revealed a 1-factor solution, explaining 98% of the total variance. It showed acceptable validity as it correlated significantly with disease activity measures: DAS-28: r = -0.85; ASDAS: r = -0.86, DAPSA: r= -0.89. It also correlated significantly with Functional disability score: r= -0.91, and QoL: r= -0.90 as well as patient self-helplessness r= -0.88. The questionnaire was reliable (Cronbach's alpha 0.958) and had no misfitting items. In addition, it was comprehensible (9.4) and sensitive to change (p<0.01). The patient motivation score showed significant (p<0.01) variation with the medication compliance.
**Conclusions:** The Patient Motivation Measure is a patient-reported tool that is valid, reliable, comprehensible and unidimensional scale that reflects the patients': (1) awareness of their role in their disease management, (2) confidence and knowledge necessary to take action, (3) actual ability of taking action to maintain and improve one's health, and (4) staying the course even under stress, (5) ability to find reliable resources. The measure has good psychometric properties indicating that it can be used at the individual patient level to tailor management and monitor changes.
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**Acknowledgement:** Omar El Miedany: Data Entry and Analysis
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## FRI0115 THE INFLUENCE OF HANDEDNESS TO THE LATERALITY OF CLINICAL AND RADIOLOGICAL ARTICULAR INVOLVEMENT IN RHEUMATOID ARTHRITIS

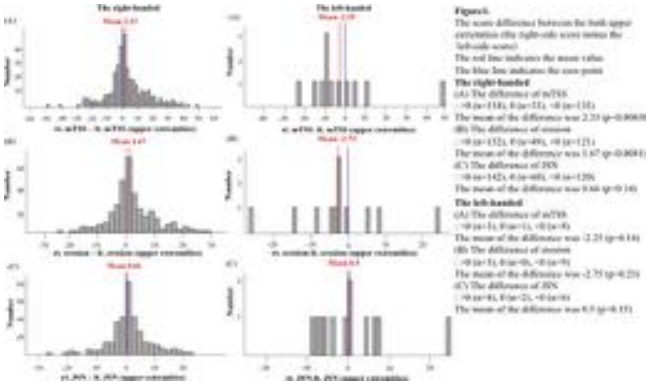
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**Background:** Mechanical stress would play an important role on inflammation of rheumatoid arthritis (RA). Some studies reported that the dominant hand joints were more affected than the non-dominant ones, but many of them led to the conclusion by evaluating only the right-handed subjects.[1–3]Therefore, it is still inconclusive whether right or dominant hand gets more damaged in RA.
**Objectives:** To clarify the relationship of handedness with clinical and radiological joint involvement in RA.
**Methods:** We enrolled a total of 334 patients from the KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort.[4] Clinical and radiological joint involvement were compared between the right and left sides, using the tender

joint count (TJC) and swollen joint count (SJC) of the 28 joints evaluated for the Disease Activity Score-28, and erosion and joint space narrowing (JSN) of X-rays scored by the modified Total Sharp Score (mTSS). The right-handed and the left-handed groups were separately evaluated.

**Results:** The right-handed were 96% (n=322) and the left-handed were 4% (n=12). Clinical and radiological involvement of upper extremities tended to be worse in dominant hands than in non-dominant ones. (The mean of the score difference (the right-side score minus the left-side score); mTSS 2.33 (p=0.00030), erosion 1.67 (p=0.0081), JSN 0.66 (p=0.14), SJC 0.32 (p=0.00080) and TJC 0.26 (p=0.00010) in the right-handed. mTSS -2.25 (p=0.14), erosion -2.75 (p=0.23), JSN 0.5 (p=0.15), SJC -0.05 (p=0.95) and TJC -0.03 (p=0.72) in the left-handed). There was a statistical significance in the number of affected joints between the right and left upper extremities in the right-handed group. Although this tendency was also seen in the left-handed group, it was not statistically significant likely due to the smaller sample size.

On the contrary, non-dominant foot showed more damage than dominant foot in the right-handed subjects (The mean of the score difference (the right-side score minus the left-side score); mTSS-1.11 (p=0.57), erosion -0.89 (p=0.37), JSN -0.22 (p=0.63)



**Conclusions:** Handedness influences the laterality of clinical and radiological joint involvement in RA. Laterality of damage in foot may be different from that in hand. This might be because the right-handed usually pivot with the left foot.[5]

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## FRI0116 HABITUAL PHYSICAL ACTIVITY IN PEOPLE WITH RHEUMATOID ARTHRITIS WITHIN THE FIRST FIVE YEARS OF DIAGNOSIS

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**Background:** Physical activity (PA) plays an important role in the management of RA in improving function, reducing risk of CVD and promoting a sense of well-being.

**Objectives:** To identify habitual PA profiles, including time spent sedentary, and self-efficacy to perform exercise. To investigate the association between PA and demographic variables, functional status, quality of life and self-efficacy.

**Methods:** Data were obtained from 76 people within the first five years of RA diagnosis and who were attending Rheumatology clinics in Glasgow, UK. Demographic data (age, sex, level of education, and employment) were recorded. Anthropometric data (Waist to hip ratio (WHR) and body mass index (BMI)) were assessed. PA profiles; the number of steps per day (step count) and time spent sedentary (sitting or lying down) were recorded for seven days using an ActivPAL activity monitor. Quality of life was measured with the Rheumatoid Arthritis Quality of Life questionnaire (RAQoL); functional status was assessed with a six minute walk test (6MWT), Health Assessment Questionnaire (HAQ) and hand grip strength (using a dynamometer). Self-efficacy was evaluated using the Self-efficacy to Regulate Exercise Scale. The data were analysed using Pearson's correlations, t test and ANOVA as appropriate. A multiple linear regression model was developed to investigate the baseline variables that contributed significantly to PA. Statistical significance was accepted at $p<0.05$.

**Results:** Of the 76 participants, 63 were women, mean age was 56 (± 15) years, 42.1% were in employment, WHR was 0.84 (± 0.09) and BMI was 27.4 (± 5.6) kg/m$^2$. The mean 6MWT was 351 (±122.7) m and hand grip strength was 21.6 (±11.3) kg, the RAQoL score was 11.7 (±8.7) and HAQ score was 1.1 (±0.84). Self-efficacy was 40.3% (± 25%). Step count was 7236 (± 2142) steps/day, and time spent sedentary was 18 (± 1.7) hrs. There were weak but statistically significant relationships between step count and: sedentary time (r =-0.238, P=0.039), HAQ (r =-0.318, P=0.005), 6MWT (r=0.265, P=0.021) and self-efficacy, (r=0.284, P=0.013). A multiple linear regression model showed significant association between step count and sedentary time (P=0.033), HAQ (P=0.002) and WHR (P=0.045). There was a significant weak association between sedentary time and self-efficacy (r=-0.262, P=0.022). No other variables showed significant correlations with step count or sedentary time.

**Conclusions:** PA, as determined by steps count is about 30% lower than 10.000 steps/day recommended for health benefits. A higher step count was associated with reduced sedentary time, lower physical disability and WHR. Other variables not included in this analysis, such as pain, and fatigue may also be associated. Participants were within the first five years of being diagnosed with RA however, it is important to maintain/improve levels of PA as the disease progresses to improve the cardiovascular health and functioning of the individual.

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## FRI0117 THE PREVALENCE OF DIABETES MELLITUS AMONG RHEUMATOID ARTHRITIS PATIENTS IS MORE THAN TWICE THE PREVALENCE IN THE DANISH POPULATION

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**Background:** Rheumatoid arthritis (RA) is a systemic, autoimmune disease that mainly affects the joints.[1] Furthermore, patients with RA may suffer from different concurrent comorbidities. These comorbidities should be considered when treating RA patients, as they are closely related to treatment response and long-term prognosis.[2] Earlier studies were in favor of increased prevalence of diabetes mellitus (DM) among RA patients; however the association of RA disease characteristic and DM has not previously been evaluated.[3] Considering the prevalence of DM in Denmark (5.7%), patients with RA are at higher risk of DM, possibly due to autoimmunity and RA treatment e.g. steroids.

**Objectives:** To determine the association between clinical characteristics of RA and DM as well as estimate the prevalence of DM among RA patients.

**Methods:** A cross sectional study of the prevalence and association of DM and RA was conducted on all RA patients who had been diagnosed with RA since 1st of January 2010 at the department of Rheumatology. For each patient, data on demographics (age, sex, year of diagnosis), serology test results including rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (anti-ccp) and antinuclear antibody (ANA) as well as disease activity score in 28 joints (DAS28) at the time of diagnosis and after 4 months (±1–2 months) of treatment were collected in December 2015. To identify patients with concurrent diagnosis of DM, we consequently evaluated all patients' previous medical history, medications and laboratory tests. Chi-square test and t-test were used to compare different variables in patients with/without diabetes.

**Results:** 439 patients were included in this study. Of all included patients 60.14% were female and the mean of age and disease duration were 64.64±15.03 and 2.59±1.66 years respectively. Prevalence of DM was 57/439 (13%). Of 57 patients, 9 patients had hemoglobin A1C $\geq$48 mmol/mol without receiving antidiabetic medication and 9 patients had been prescribed prednisolone with an average of 6.4±2.4 mg daily. The results of our study revealed that longer RA disease duration is associated with higher prevalence of DM, since patients who were diagnosed before 2012 had higher prevalence of DM in comparison with patients who were diagnosed within 2012 and later (P=0.05). We did not find any association between presence of DM and gender, RF, anti-ccp, ANA as well as $\Delta$DAS28.

**Conclusions:** DM is more prevalent among patients with RA compared to general population (13% versus 5.7%). Routine measurement of hemoglobin A1C, at diagnosis and on a yearly basis, in patients with RA should be taken into consideration leading to earlier diagnose of DM and better overall prognosis.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3157

## FRI0118 CAROTID ULTRASONOGRAPHY AND ANKLE-BRACHIAL INDEX IN THE CARDIOVASCULAR RISK ASSESSMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) associates with higher mortality rates than general population, mostly due to cardiovascular (CV) disease [1]. Guidelines recommend CV risk assessment in all RA patients. The European League against Rheumatism (EULAR) has proposed a modified version of SCORE risk estimation system (mSCORE) [2]. Few studies assessed the impact of an increased carotid intima media thickness (cIMT), carotid plaques, and ankle-brachial index (ABI) on the CV risk assessment in patients with RA.
**Objectives:** To assess whether the value of carotid ultrasonography and ABI in the stratification of CV risk in RA.
**Methods:** All RA patients who consecutively attended the outpatient rheumatology clinic of our hospital were enrolled. Exclusion criteria: diabetes mellitus, history of cardio and cerebrovascular events and age>75 years old.
**Results:** The study population was represented by 78 patients, 61 women (78.2%), median age 60 years old and disease duration 6.0 years. The SCORE (median) and EULAR mSCORE were 1.25 and 1.5.

Table 1. ABI and carotid ultrasound findings according to CV risk stratification

| SCORE CV risk (n) | mSCORE | Abnormal ABI | cIMT >0.90 mm | Carotid plaques | cIMT >0.90 mm and/or carotid plaques |
|---|---|---|---|---|---|
| Low (23) | 23 | 2/23 (17.4) | 0/23 (0.0%) | 0/23 (0.0%) | 0/23 (0.0%) |
| Moderate (48 | 47 | 2/47 (4.3%) | 3/47 (6.4%) | 15/47 (31.9%) | 15/47 (31.9%) |
| High (7) | 8 | 0/8 (0.0%) | 1/8 (12.5%) | 4/8 (50.0%) | 4/8 (50.0%) |
| Total (78) | 78 | 4/78 (5.1%) | 4/78 (5.1%) | 19/78 (24.4%) | 19/78 (24.4%) |

All patients with an abnormal ABI had a normal cIMT. 27/78 (34.6%) patients had High CV risk defined as a)mSCORE ≥5% or b)mSCORE<5% plus cIMT>0.90 mm and/or plaques or an abnormal ABI. A SCORE>5% had a Sensitivity of 29.6% (8/27), an Abnormal ABI 14.8% (4/27), a cIMT>0.90mm plus carotid plaques 70.4% (19/27), a mSCORE<5% plus Abnormal ABI 14.8% (4/27), a mSCORE<5% plus cIMT>0.90mm and/or carotid plaques 55.6% (15/27) and an Abnormal ABI plus cIMT>0.90mm and/or carotid plaques 85.2% (23/27).
**Conclusions:** SCORE showed a low sensitivity to identify high risk RA patients, and mSCORE did not improve it. Carotid ultrasonography assessment showed a higher sensitivity than mSCORE and ABI to detect high CV risk. Despite its low sensitivity, an abnormal ABI identify high risk patients not discriminated by using mSCORE nor cIMT. Carotid ultrasound seems to be more sensitive than ABI, SCORE and mSCORE to identify high CV risk in patients with RA.
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**Disclosure of Interest:** None declared
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## FRI0119 THE ASSOCIATION BETWEEN QTC INTERVAL AND MYOCARDIAL ABNORMALITIES IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT CARDIAC SYMPTOMS, BY ASSESSED USING CARDIAC MAGNETIC RESONANCE IMAGING

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**Background:** Individuals with rheumatoid arthritis (RA) have a twofold higher risk of developing sudden death than age and gender matched controls without RA. The underlying mechanisms have not yet been clarified.
**Objectives:** The aim of this study was to prospectively investigate the association of myocardial involvement assessed by a cardiac magnetic resonance imaging (CMR) and the QTc interval in RA without cardiac symptoms.
**Methods:** RA patients and control subjects with no history and/or clinical findings of systemic and pulmonary hypertension, coronary artery disease, valvular heart disease, atrial fibrillation, diabetes mellitus, and dyslipidemia were enrolled and underwent CMR. RA patients received conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs). Late gadolinium enhancement (LGE) was obtained for the assessment of myocardial fibrosis. Using a black-blood T2-weighted image (T2-WI), myocardial inflammation could be assessed. The QTc intervals were manually measured on a 12-lead electrocardiogram, according to standard criteria. The QTc interval of 440 ms was considered to be prolonged in this study. We compared the patients and controls in terms of prevalence of CMR abnormalities and the QTc interval, and explored possible associations between CMR abnormalities and the QTc interval.
**Results:** Sixty-seven patients (mean age, 54.2 ± 1.7 years; 89% female) and 30 controls (mean age 53.6 ± 2.5 years; 87% female) were enrolled. Thirty-one RA patients received csDMARDs [25, methotrexate (MTX) (9.7±2.1 mg); 7, other drugs)] and 36 RA patients received bDMARDs [(15, infliximab; 15, tocilizumab; 6, abatacept, plus MTX respectively. (9.6±1.4 mg)]. The control group showed no myocardial abnormalities. Twenty seven RA patients (40%) demonstrated myocardial abnormalities. T2-WI was seen in seven RA patients (10%). LGE-positive was found in 20 RA patients (30%), six of whom also demonstrated T2-WI. All RA patients and control patients displayed a normal QTc interval. However, there was significant difference in the QTc interval between the control and LGE-positive (p=0.013). Also LGE-positive was significant higher in the QTc interval than LGE -negative. LGE-positive was associated with the QTc interval. The use of bDMARDs was significantly associated with LGE-negative findings (p=0.001) and the QTc interval. (p=0.001). High titer of anticitrullinated protein antibodies was associated with the QTc interval (p=0.04). Receiver operating characteristic analysis showed the QTc interval reliably detected myocardial abnormalities (area under the curve 0.898; 95% confidence interval, 0.830–0.900). Considering patients with RA and a normal QTc interval and using a cutoff of 420 ms, sensitivity and specificity were 91% and 70% in the detection of myocardial abnormalities.
**Conclusions:** Subclinical myocardial inflammation and fibrosis are common in active RA patients without cardiac manifestation. Abnormal CMR findings were associated with a QTc interval. Even if the QTc interval is normal, we should keep in mind the possibility of subclinical myocardial involvement in RA.
**Disclosure of Interest:** None declared
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## FRI0120 THE INCIDENCE OF HERPES ZOSTER (HZ) IN A POPULATION OF PATIENTS WITH INFLAMMATORY ARTHRITIS: A 12-YEAR ANALYSIS FROM THE RHUMADATA CLINICAL DATABASE AND REGISTRY

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**Background:** Herpes Zoster (HZ) is caused by the reactivation of the varicella zoster virus. It is more prevalent in older populations. Post-herpetic neuralgia, defined as pain lasting longer than 90 days post-eruption, is the most common serious complication of HZ. Immunosuppression from any cause including immunosuppressive treatments increases the risk by a minimum of ten times. Vaccination against HZ in patients with auto-immune diseases appears to be safe and effective[1].
**Objectives:** To describe the 12-year incidence of HZ in a population of patient with either rheumatoid arthritis (RA), ankylosing spondylitis (AS) or psoriatic arthritis (PsA) with and without any biologic treatment.
**Methods:** All treatment episodes of patients with RA, AS, or PsA recruited in the RHUMADATA database from January 1, 1998, to October 1, 2015, were included in the analysis. All episode of HZ as reported by the patient to the healthcare provider were tabulated. Two cohorts were created. Patients with AS and PsA were pooled, and RA patients were analysed separately. Demographics included age, gender and disease duration. Data on exposure biologic agents, nbDMARDs, and to recent corticosteroid use (90 days before HZ or censoring) were also extracted. The incidence rates of HZ were estimated in biologic exposed and naïve patients from both cohorts. Univariate and multivariate Cox models were used to assess the relationship between age, biologic, nbDMARD and recent corticosteroid use, and the development of HZ.
**Results:** RA patients (n=3431) were mostly women (77%) while AS/PsA patients (n=1,727) were mostly men (55%). RA patients were older than AS/PsA patients (53.3 years (SD=12.6) vs. 45.4 years (SD=12.1)) and also had longer disease duration (5.5 years (SD=8.5) vs. 4.8 years (SD=25.1)).
Thirty-six and 119 HZ episodes were observed in the AS/PsA and RA cohorts respectively. Among AS/PsA patients, the incidence rate of HZ per 100 patient-years was 0.80 (95% CI=0.53–1.16) among patients taking biologics and 0.29 (0.12–0.56) for biologic naïve patients (p-value=0.0071). The incidence rate of HZ among biologics treated RA patients was 1.08 (0.83–1.37) per 100 patient-years

and 0.55 (0.41–0.72) among biologic naïve patients (p-value=0.0002). Overall, RA patients and AS/PsA patients had similar HZ incidence rates (0.62 (0.52–0.73) vs 0.53 (0.37–0.71), p-value=0.3460). The hazard ratios for "biologic use" among RA and AS/PsA patients were estimated at 1.866 (1.275–2.733) and 3.467 (1.529–7.859) respectively, after adjusting for age at treatment initiation, concurrent use of nbDMARDs and recent corticosteroid use.

**Conclusions:** Biologic agents doubled the risk of HZ episodes in RA and AS/PsA patients. Significant predictors of HZ episodes among RA patients included age and use of biologics. Among AS/PsA patients, use of biologics and recent use of corticosteroids were significantly associated with the development of HZ. HZ immunization should be considered in patients before initiating biologic agents.

**References:**

[1] Background paper on herpes zoster vaccines- SAGE working group accessed from the WHO website on: 07DEC2015.

**Disclosure of Interest:** None declared

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## FRI0121 PROSPECTIVE ASSESSMENT OF CARDIOVASCULAR RISK FACTORS IN RELATION TO DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic, inflammatory joint disease, characterized by accelerated atherosclerosis and increased cardiovascular (CV) morbidity, with cardiovascular disease (CVD) as the leading cause of death. Chronic systemic inflammation responsible for the joint damage, along with traditional CV risk factors, are synergistically involved in the development of progressive atherosclerosis. Carotid intima-media thickness (cIMT) has been approved as a surrogate marker of early atherosclerosis.

**Objectives:** The goal of the study was to assess prospectively traditional CV risk factors and cIMT in patients with established RA; to evaluate relationship between cIMT and RA activity, estimated by clinical examination and ultrasonography of joints.

**Methods:** The study group consisted of 40 consecutive RA patients, 33 (82,5%) female and 7 male (17,5%), with the mean (SD) age 52.3 (9.8) (range 24–68) and disease duration 18.6 (9.6) years (range 6.5–45). The assessment of cIMT was performed twice, at an interval of 6 years [the initial in 2008 (visit 1, V1) and consecutive in 2014 (visit 2, V2)] and was determined by high-resolution B-mode ultrasonography. The activity of RA was estimated by clinical examination at V1 and V2 [with disease activity score in 28 joints (DAS28)] and ultrasonography of joints at V2 (synovial hypertrophy in 24 small joints). At V1 and V2 body mass index (BMI), lipid profile and atherogenic index (AI) were assessed. During the 6 years between V1 and V2, 35 (87,5%) patients were treated with biological disease modifying antirheumatic drugs (DMARDs); nothing by synthetic DMARDs were used in 5 (12,5%) patients. At V2, high disease activity was observed in 7 (17,5%) patients; low RA activity or remission in 23 (57,5%).

**Results:** The mean (SD) cIMT value was significantly greater at V2 than V1 assessment [0.86 (0.45) vs 0.75 (0.13) mm, p=0.02]. The number of RA patients with advanced atherosclerosis (presence of plaques) increased from 6 (15%) at V1 to 9 (22,5%) at V2 (NS). The number of patients without atherosclerosis (cIMT $<$0.6 mm) decreased from 4 (10%) at V1 to 3 (7,5%) at V2. There were positive correlations between cIMT value and the age of patients at V1 and V2 ($p<0.001$). The value of cIMT at V2 correlated negatively with HDL-cholesterol at V1 (p=0.02) and positively with AI at V1 (p=0.01), as well as DAS28 at V1 (p=0.02). There was no correlation between cIMT value and parameters of RA activity at V2 (DAS28, synovial hypertrophy in ultrasonography). A positive correlation was found between DAS28 value and number of joints with synovial hypertrophy assessed in ultrasonography. Lipid profiles and AI value did not differ significantly between V1 and V2. The value of BMI increased significantly between V1 and V2 [24.7 (3.1) vs 25.8 (3.5) kg/m$^2$, p=0.002].

**Conclusions:** During the six-years course of established RA, progression of atherosclerosis was observed, estimated by significantly greater mean cIMT value, as well as increased number of patients with atherosclerotic plaques. In patients with long-standing RA, treated intensively with DMARDs, progressing atherosclerosis seems not to be correlated with the current RA joint activity. The atherosclerotic burden seems to be dependent on the age, previous disease activity and unfavorable lipid profiles associated with high grade inflammation.

**Disclosure of Interest:** None declared

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## FRI0122 EULAR 2015 RECOMMENDATIONS FOR CARDIOVASCULAR RISK COULD RADICALLY CHANGE PATIENTS CARE IN CHRONIC INFLAMMATORY RHEUMATISMS

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**Background:** Patients with chronic inflammatory rheumatic disease have a greater risk of cardiovascular (CV) diseases. European recommendations of cardiology propose to classify patients with asymptomatic atheromatous plaques as high CV risk patients. New EULAR recommendations about CV risk management propose the use of supra-aortic vessel ultrasound for atheromatous plaques detection and total CV risk estimation. Moreover, EULAR-2015 recommendations suggest multiplying by a 1.5 factor the global CV risk for all patients with Rheumatoid Arthritis (RA) unlike 2010 recommendations.

**Objectives:** The objective of our study was to evaluate the impact of these new recommendations on CV management, especially on indication of statin use, in patients with RA in daily practice, in comparison to EULAR-2010 recommendations.

**Methods:** Total CV risk estimation included physical examination, glucidic and lipidic blood tests, supra-aortic and abdominal vessels ultrasound, echocardiography and global risk SCORE calculation. Heart-SCORE was multiplied according to EULAR-2010 (mSCORE2010) or EULAR-2015 (mSCORE2015) recommendations. For EULAR-2015 recommendations, patients with ultrasound carotid plaques were classified at high CV risk. LDL targets and immediate need of statin use were defined according to European cardiology recommendations with need of statin when LDL $>$0.7 g/L for patients at very high CV risk and $>$1 g/L for those at high risk. In moderate and low risk patients, statins are not immediately recommended.

**Results:** 157 RA patients underwent the screening with a mean disease duration of 13 (6–19) ± 9 years and mean age of 61 ± 11 years. 56/76 (73.7%) of patients classified as moderate risk with Heart-SCORE and 3/12 (25%) of patients with low risk had asymptomatic carotid plaques. Application of the EULAR 2010 recommendations should lead to immediate statin prescription in 42 patients (28%) whereas applications of the EULAR 2015 recommendations should lead to statin prescription in 92 (61%) patients.

**Conclusions:** In our experience, the use of carotid ultrasound to estimate total CV risk and thus to define LDL targets led to prescribe statins in 61% of patients with RA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2967

## FRI0123 CLINICAL CORRELATES, OUTCOMES AND PREDICTORS OF INFLAMMATORY OCULAR DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS

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**Background:** Inflammatory ocular disease (IOD) has traditionally been regarded as a severe extra-articular manifestation (ExRA) of rheumatoid arthritis (RA) with high mortality.

**Objectives:** This study aims to evaluate IOD, namely scleritis (SC), episcleritis (EP), peripheral ulcerative keratitis (PUK) and uveitis (UV), identified in a large single-institution cohort of patients with RA to determine clinical correlates, outcomes and risk factors.

**Methods:** A retrospective review was performed to assemble a cohort of patients with IOD among patients with RA evaluated between Jan. 1, 1996-Dec. 31, 2013. All cases met the 1987 ACR criteria for RA. Cases were compared to age- and sex-matched comparators with RA without IOD to identify risk factors. Chi-square and rank sum tests were used to compare characteristics between groups. Kaplan-Meier methods were used to analyze outcomes.

**Results:** A total of 92 patients (69% female; mean age 62 y) were identified with IOD (33 SC, 23 EP, 21 PUK, 14 UV). Median follow-up was 4.1 years (IQR 1.5–9.4 y). Patients with EP were younger than those with UV (p=0.032). More than 80% of SC, EP and PUK patients were seropositive compared to only 62% of UV (p=0.048). Severe extra-articular (ExRA) manifestations (Malmö criteria) before IOD were more common in SC and EP than in UV and PUK, but the latter had a higher prevalence of Sjögren's syndrome (20%). Only 8% of UV had rheumatoid nodules as compared to 35% and 36% of PUK and SC. PUK and SC were more symptomatic compared to EP. EP and UV were primarily treated with topical therapy while SC and PUK often required systemic glucocorticoids, cyclophosphamide, additional DMARDs or biologic therapy.

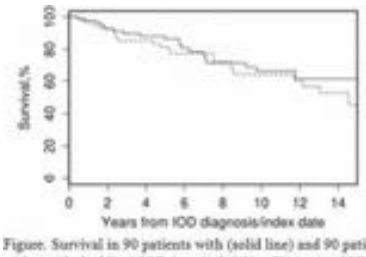



Figure. Survival in 90 patients with (solid line) and 90 patients without (dashed line) IOD (survival 64% ± 7% in non-IOD vs 66% ± 7% in IOD at 10 years after IOD diagnosis/index date; hazard ratio: 0.84; 95% CI: 0.48 – 1.50, p=0.56).

Time to resolution for first episode of IOD was significantly different between various IOD (p=0.015) and in particular longer in SC than in EP (p=0.010). More than 58% of patients with PUK, SC or UV showed a vision loss of at least 2 Snellen lines, as compared to only 11% of EP (p=0.045).
Ninety IOD patients were compared to 90 age, sex and disease duration matched RA subjects without IOD (median disease duration 10.2 y vs. 9.9 y, p=0.612; median follow up 5.7 y (IQR 1.9–10.2) for IOD patients and 4.4 y (IQR 2.0–9.0) for comparators). Cases had a higher prevalence of severe ExRA (18% vs 4%, p=0.004) and dry eye syndrome (42% vs 26%, p=0.024). Ten year survival was 66% for IOD vs 64% for non-IOD subjects (HR 0.84: 95% CI: 0.48–1.50, p=0.56) (figure). No differences were found between IOD after correcting for age. The incidence of new ExRA in 5-year follow up was higher among cases (29% vs 11%, p=0.002).
**Conclusions:** The clinical presentation and treatments differ among the different forms of IODs in RA. Severe ExRA and dry eye syndrome increase the risk for IOD. IOD further predispose patients to develop more ExRA, increasing disease burden. In contrast to older literature, survival among IOD patients is now at least as good as in those without IOD, perhaps due to modern RA treatment strategies or secular disease trends.
**Disclosure of Interest:** None declared
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## FRI0124 NONTUBERCULOUS MYCOBACTERIAL INFECTION IN RHEUMATOID ARTHRITIS PATIENTS: A SINGLE-CENTER EXPERIENCE IN SOUTH KOREA

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**Background:** The incidence of nontuberculous mycobacteria (NTM) infection has been increasing worldwide in both general population and in immunocompromised patients, including rheumatoid arthritis (RA) patients. However, most of previous studies focused on clinical features of NTM infection during treatment with anti-tumor necrosis factor (TNF) or were conducted in western countries, where NTM infection is more common than tuberculosis (TB) infection.
**Objectives:** The aims of our study were to identify the incidence and clinical characteristics of NTM infection in RA patients who live in the TB endemic area.
**Methods:** We performed a retrospective analysis of cases with NTM infection in the RA registry at a tertiary referral center from January 1995 to December 2013. The clinical features of the NTM cases were compared to those of 52 patients with TB infection.
**Results:** Among 1,397 patients with RA, NTM infection was newly developed in 26 (1.86%) patients and the incidence of NTM infection was 164.8 per 100,000 patient-years. The mycobacterium avium complex was the most frequent isolate (76.9%). None of the NTM infections had extrapulmonary involvement, which was rather common in TB infection (26.9%) (Table). Patients with NTM infection were older, received higher cumulative doses of corticosteroid, had higher rates of history of TB infection, and had higher incidence of concomitant interstitial lung disease (ILD) than cases with TB infection.

Table 1. Clinical and laboratory characteristics of the study patients with NTM infection and TB

| Characteristic | NTM (n=26) | TB (n=52) | *p* value |
|---|---|---|---|
| Sex, female (%) | 18 (69.2) | 34 (65.4) | 0.803 |
| Age at diagnosis of RA , years | 54.7±10.3 | 50.2±13.7 | 0.108 |
| Age at infection, years[a] | 63.2±7.7 | 57.5±12.0 | 0.014 |
| Duration of RA , years | 8.5±4.9 | 7.2±7.2 | 0.803 |
| Ever-smoker (%) | 9 (34.6) | 13 (25) | 0.374 |
| History of TB (%)[a] | 10 (38.5) | 6 (11.5) | 0.008 |
| Concomitant ILD (%)[a] | 11 (42.3) | 5 (9.6) | 0.001 |
| Extrapulmonary infection (%)[a] | 0 (0) | 14 (26.9) | 0.003 |
| Antirheumatic drugs at infection | | | |
| Biologics (%) | 6 (23.1) | 5 (9.6) | 0.165 |
| PD (%) | 20 (76.9) | 40 (76.9) | 1.000 |
| MTX (%) | 21 (80.8) | 32 (61.5) | 0.123 |
| Leflunomide (%) | 4 (15.4) | 4 (7.7) | 0.430 |
| Others (%) | 10 (38.5) | 22 (42.3) | 0.810 |
| Dosage of PD at infection (mg/day)[b] | 3.6±2.7 | 3.1±4.4 | 0.682 |
| Cumulative dose of PD at infection (g)[a,b] | 4.5±3.3 | 2.9±3.1 | 0.042 |
| ACPA, U/mL | 697.9±1311.4 | 415.47±1097.4 | 0.340 |
| RF, IU/mL | 199.3±142.7 | 187.19±143.3 | 0.780 |

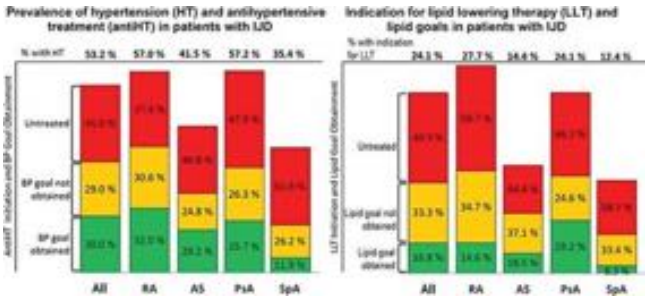
NTM: nontuberculous mycobacteria; TB: tuberculosis; BMI: body mass index; ILD: interstitial lung disease; PD: prednisolone; [a]$p<0.05$; [b]equivalent dose with prednisolone.

**Conclusions:** In South Korea, NTM infection is not rare in RA patients. Physicians should be cautious about NTM infection in patients with history of TB infection or concomitant ILD, even in endemic areas of TB.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3199

## FRI0125 EXPLORING THE INADEQUATE CARDIOVASCULAR DISEASE PREVENTION IN INFLAMMATORY JOINT DISEASES: RESULTS FROM THE NOCAR PROJECT

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**Background:** Antihypertensives (antiHT) and lipid lowering therapies (LLT) prevent cardiovascular disease (CVD) effectively. It has been reported that patients with rheumatoid arthritis (RA) receive suboptimal CVD-prevention, possibly contributing to their increased CVD risk. Whether other inflammatory joint diseases (IJD), such as ankylosing spondylitis (AS), psoriatic arthritis (PsA) and other spondyloarthropathies (SpA), also receive inadequate CVD management remains unknown.
**Objectives:** In a large IJD cohort we aimed to evaluate 1) Rate of indications for antiHT and/or LLT, 2) rate of antiHT and/or LLT initiation, and 3) blood pressure (BP) and low-density lipoprotein cholesterol (LDL) goal attainment in patients treated with antiHT or LLT, respectively.
**Methods:** The present IJD cohort is derived from the Norwegian COllaboration on Cardiovascular disease in patients with Rheumatic joint diseases (NOCAR). In NOCAR, CVD risk factors are collected in daily rheumatology practice. Need for antiHT was defined as systolic BP (sBP) $\geq$140mmHg, diastolic BP (dBP) $\geq$90 mmHg or self-reported hypertension (HT). sBP/dBP levels $<$140/90 mmHg were recognized as BP goal attainment. The 10-year risk of a fatal CVD event was estimated by the Systematic COronary Risk Evaluation (SCORE). According to guidelines, patients with diabetes, hyperlipidemia (total cholesterol $>$8 mmol/L, LDL $>$6 mmol/L) or SCORE $\geq$5% are at high CVD risk and should receive LLT (LDL target $<$2.6 mmol/L); whereas established CVD or SCORE $\geq$10% imply a very high CVD risk (LDL target $<$1.8 mmol/L). Rates were calculated for the whole cohort, and compared across IJD entities using logistic regression, age and sex adjusted.
**Results:** Fifty-eight% of the 2647 patients (RA: n=1696, AS: n=445, PsA: n=376, SpA: n=130) were females and the median (inter-quartile range [IQR]) age and disease duration was 57.4 years (46.8–66.8) and 8.0 years (3.8–15.9), respectively. In total, 53.2% had indication for antiHT, and this was significantly higher in RA (57.0%) and PsA (57.2%). Among patients for whom antiHT was indicated, 59.0% received treatment (comparable across IJD entities) and half of the patients on antiHT had obtained BP goal. There was indication for LLT in 24.1%, which was comparable across the IJD entities except for AS (14.4%) ($p<0.0001$). In the group with indication for LLT, 55.6% had high CVD risk which was most frequently seen in PsA (p=0.02), whereas 43.7% had very high CVD risk, which was more common in AS patients (p=0.02). Half of the patients with indication for LLT received this therapy, and treatment rates were higher for patients with very high CVD risk compared to those with high CVD risk ($p<0.001$). In total, 16.8% had achieved LDL treatment targets; LDL goal attainment was particularly high in PsA patients ($p<0.01$), and higher in patients with high CVD risk than in those with very high CVD risk ($p<0.001$).




**Conclusions:** CVD-preventive medication is often indicated, but infrequently initiated in IJD patients. Moreover, when antiHT and LLT are started, quite few patients obtain treatment goals. There is a need for improving CVD risk assessment, initiation of proper CVD-prevention and careful monitoring of target achievements to successfully reduce the excess CVD risk in IJD patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3546

## FRI0126 WHO IS AT GREATER RISK FOR MYOCARDIAL INFARCTION IN RHEUMATOID ARTHRITIS?

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**Background:** Patients with rheumatoid arthritis (RA) have increased mortality and morbidity due to premature cardiovascular disease (CVD). Some factors involved in the development of RA-associated CVD have not yet been fully delineated.
**Objectives:** The aim of the study was to verify whether female gender, the reproductive period, smoking history, atherosclerotic lesions in brachiocephalic

vessels, carotid intima-media thickness (IMT), traditional CV risk factors, as well as RA disease activity and disease duration influence excess CVD and cerebrovascular disease in patients with RA.
**Methods:** A case-control study was performed within the prospective cohort of 94 RA patients (female: 84%; age: 20–82). Cases were 26 patients who developed their first myocardial infarction (MI) after the diagnosis of RA. Controls and cases had comparable disease duration. Traditional (BMI, smoking history, diabetes mellitus), pulmonary arterial hypertension (PAH) and disease-specific risk factors for MI were assessed. Atherogenic Index of Plasma (AIP; log TG/HDL-C) calculated. Carotid artery hemodynamic parameters, IMT and plaques were assessed using high resolution B-mode and Doppler-mode ultrasound in order to detect blood flow velocities, maximal IMT and size of atherosclerotic plaques, respectively. RA activity and severity were determined by DAS28, CDAI, SDAI scores, ultrasonography of synovitis and HAQ questionnaires. Statistical analysis was performed by using IBM SPSS 21.0
**Results:** Patients with MI were mostly females (96%), with a median age of 61 (54–69) years. The mean disease duration was 3.5 (1–9) years. About 34% of cases were smokers. The risk of MI in RA women was 3.91 (OR). In female patients, who smoked it was 1.36. Patients with MI were not significantly older compared to control RA patients (p=0.316). Interestingly, 88% of RA cases with MI and 100% of non-MI conrtols (p=0.005). High RA disease activity (DAS28 above 4,17) was observed in 46% of patients with MI. Seropositivity was found in 92%, while erosions in small joints in 58% of cases. Joint replacement surgery was necessary in 13% of MI cases. Strokedeveloped in 13% of cases and 10% of controls. PAH was detected in 75%, of patients with MI. No statistically significant difference in IMT between MI cases and controls could be found (p=0.217). Furthermore, atherosclerotic lesions were not more pronounced in RA patients with versus without MI (p=0.874).
Altogether 91,7% patients with MI had atherosclerotic plaques in brachiocephalic vessels resulting in $<$50% luminal stenosis, while 8,3% of patients had plaques causing $>$50% lumen obstruction. IMT exerted significant correlation with age ($p<0,001$), plaques in brachiocephalic vessels (p=0.045), PAH (p=0.001), joint erosions ($p<0.05$) and symptom onset in RA ($p<0.05$). PAH also correlated with brachiocephalic vessel plaques (p=0.01). Bivariate logistic regression revealed that in females with late onset menarche ($>$16 years) and early menopause ($<$45 years) had lower, while patients with late onset menopause had greater risk for developing MI
**Conclusions:** In our case-control study, brachiocephalic plaques, PAH, the onset of menarche and menopause may be associated with the development of MI in RA patients. These preliminary observations indicate the existence of less evident risk factors, which should be further characterized in future studies
**References:**
[1] no references
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**Disclosure of Interest:** None declared
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## FRI0127 ANGIOGENIC PLACENTAL FACTORS DURING PREGNANCY IN RHEUMATOID ARTHRITIS

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**Background:** Reduced birth weight in infants born to women with rheumatoid arthritis (RA) is often related to active maternal disease during pregnancy.
**Objectives:** We hypothesized that RA might have an influence on placental function and investigated whether pro-angiogenic and anti-angiogenic placental proteins such as placental growths factors (PLGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) were differently regulated in patients with RA compared to healthy controls.
**Methods:** Sera of 27 pregnancies in RA patients and of 10 aged-matched healthy women were analyzed for PLGF and sFLT-1 by ELISA once at each trimester (gestational week 10–12, 20–22 and 30–32). Disease activity of all RA patients was measured by DAS28-CRP and CRP. Neonatal birth weights and birth weight percentiles were correlated with PLGF- and sFLT-1- levels.
**Results:** Of the 37 pregnancies there was no case of preeclampsia, neither in the group of RA patients nor in the group of healthy controls. Median birth weight of the newborns from RA patients was 2890 g (range 1250–4000). Among all pregnancies of RA patients, the levels of PLGF and sFLT-1 were similar in active and inactive disease. At the third trimester of pregnancy, RA patients showed lower levels of the pro-angiogenic placental protein PLGF than healthy controls (P=0.021). By contrast, levels of the anti-angiogenic protein sFLT-1 did not differ between RA patients and healthy women. The sFLT-1/PLGF ratio was lower in healthy women than in RA patients (P=0.021). Moreover the sFLT-1/PLGF ratio showed a negative correlation with the birth weight percentile.
**Conclusions:** RA patients showed reduced levels of the pro-angiogenic placental protein PLGF which might reflect a dysfunction of the placenta with an effect on birth weight in this disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3520

## FRI0128 EFFICACY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE IN SLE PATIENTS (PRELIMINARY RESULTS)

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**Background:** Comorbid infections (CI) appear to have detrimental effect on the course and the prognosis of systemic lupus erythematosus (SLE) as current rheumatology practice indicates. These CIs become not only the predictors of lethal outcome, but also number two among known causes of death after the activity of the disease as the cause number one. Pneumonia remains the leading clinical entity among infectious diseases in SLE pts, thus immunization of SLE pts with pneumococcal vaccine is an essential issue in clinical practice.
**Objectives:** To study the relevance of 23-valent pneumococcal vaccine for immunization of SLE pts, receiving immunosuppressive therapy.
**Methods:** The study included 24 SLE patients, 22 females, 2 males aged 19 - 62 years. Low disease activity was documented in 18 patients, moderate – in 3 patients, and drug-induced remission – in 3. 23 patients were getting glucocorticoids (GCs) (4 pts - metipred - 24 mg/day.), 19 pts – plaquenil 200–400 mg/day, 13 pts – cytostatic (CS) drugs, including 8 – mycophenolate mofetil 1–2 g/day, 3 – methotrexate 10–15 mg/week, 1- mycophenolic acid 1080 mg/day, 1-azathioprine 50 mg. Eight patients were on biologic diseases modifying anti rheumatic drugs (bDMARDs), including 5 – on rituximab at 500–1000 mg per course of treatment, 3 – on belimumab at doses of 720, 480 and 400 mg per infusion. One or two episodes of lower respiratory tract infections occurred in 4 pts during the year prior to vaccination. One dose (0,5 ml) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously without discontinuation of GCs and CSs, or 1 months before initiation of bDMARDs /6 mo after the last injection of bDMARDs. The duration of FUP was 1–10 months.
**Results:** Vaccine tolerability was good in 10 (41,7%) patients, local injection site reactions of varying intensity without accompanying fever were registered in 13 (54,2%) patients, lasting 2 to 7 days; they completely resolved spontaneously without additional treatment. One patient (4,2%) developed hyperergic reaction in the form of Arthus phenomenon (hyperemia, induration and swelling of the injection site up to 10 cm in diameter, pain and subfebrile fever). These symptoms subsided within 7 days with 3 days intake of antihistaminic drug and local use of GCs. These reactions were typical and assessed as having casual relationship with vaccination. In one patient with SLE and interstitial lung disease, manifesting as recurrent bronchitis and pneumonia, non-severe bilateral bronchopneumonia was documented 9 months post-vaccination, which resolved after 7 days of antibiotic therapy in the out-patient setting. One patient developed post- stress non-severe SLE exacerbation 5,5 months after vaccination, requiring GC dose escalation from 4 to 8 mg/day. Casual relationship of this exacerbation with vaccination was very unlikely.
**Conclusions:** Thus preliminary results are indicative of good 23-valent pneumococcal vaccine tolerability in SLE patients. Further studies are required for comprehensive assessment of vaccine efficacy and safety in this group of patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2947

## FRI0129 ASSOCIATION BETWEEN HEARING LOSS AND CAROTID SUBCLINICAL ATHEROSCLEROSIS IN FEMALE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The incidence of hearing loss (HL) has been on the rise in patients with rheumatoid arthritis (RA). However, limited information exists regarding the pathogenic mechanisms of HL in RA patients[1,2].
**Objectives:** This study sought to evaluate the prevalence and characteristics of HL in RA patients compared with a control group and to identify factors associated with the degree of HL in RA patients.
**Methods:** We enrolled 64 RA patients and 70 healthy controls in a prospective manner. Each subject was tested with pure tone audiometry including high frequencies ranging from 0.5 to 16 kHz. For each set of tests, mean values for air conduction at each frequency and tympanometric values were calculated to exclude middle ear disease. In the RA group, auto-antibodies, erythrocyte sedimentation rate, high-sensitivity C-reactive protein, and RA disease activity were measured, and carotid ultrasonography was performed for the detection of indicators of subclinical atherosclerosis, including arterial stiffness index beta ($\beta$-index) and carotid intima-media thickness (cIMT).
**Results:** The prevalence of HL was higher in the RA group than the control group (37.1% vs. 65.6%, p=0.001). The hearing threshold value difference between groups was significant at frequencies of 0.5, 1, 2, 4, and 8 kHz ($p<0.05$). Age showed the strongest correlation to HL at all frequencies in RA patients ($p<0.01$). cIMT was also strongly related to HL at all frequencies, whereas $\beta$-index was related to HL only at high frequencies (8, 12, and 16 kHz), acting as an early marker of HL (both $p<0.05$).

**Conclusions:** HL was more prevalent in the RA group than the control group. cIMT and β-index were strongly correlated with HL in the RA group, which implies that subclinical atherosclerosis may play an important role in HL in RA patients.

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## FRI0130 EFFICACY OF A COMPREHENSIVE CARDIOVASCULAR RISK REDUCTION PATIENT EDUCATION PROGRAMME IN PATIENTS WITH EARLY INFLAMMATORY ARTHRITIS FOLLOWING A TREAT TO TARGET THERAPEUTIC REGIME

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**Background:** Evidence suggests cardiovascular disease (CVD) risk in patients (pt, pts) with Inflammatory arthritis (IA), Rheumatoid arthritis (RA) is equivalent to that of type II diabetes mellitus[1]. The accepted guidance is lifestyle factor modifications should be addressed in IA[2], but little is known of the impact of CVD risk reduction pt education programmes delivered to pts with IA within a Rheumatology service setting.
**Objectives:** To describe the utility of a comprehensive CVD risk reduction pt education programme in pts with newly diagnosed IA following a treat to target standard therapeutic regime.
**Methods:** 387 pts with IA (RA and Undifferentiated Inflammatory Arthritis: UIA) were assessed at baseline (BL) for CV risk factors (RFs) (see Table 1) Pts were; RA; pts (1987 or 2010 ACR criteria) (n=237) and UIA; pts not meeting ACR RA criteria (n=150). A standardized co-morbidity pt education programme, which included CVD risk reduction, was delivered throughout the first 12 months (M). The impact on modifiable CVD RFs was assessed at 12M.
**Results:** 108 RA, 34 UIA pts had complete datasets (see Table 1). Of those smoked at BL, 15% reported being ex-smokers at 12M and the number smoked had decreased in 44%. 10% who reported being ex-smokers at BL altered their status to never having smoked by 12M and their reported number previously smoked reduced by 43% at 12M. Alcohol use reduced in 39% and increased in 24% (overall decrease, p=0.033). At BL, 56% of pts reported doing no moderate exercise at all; at 12M around a third of the pts had either increased or decreased the amount of exercise (no overall change). Disease activity generally decreased ($p<0.001$) and mobility increased (p=0.004).

Table 1. Changes in cardiovascular disease risk factors at 12 months

| Risk factors | N | Baseline | Change at 12 months | % of patients whose 12 months value was | | | P value |
|---|---|---|---|---|---|---|---|
| | | | | Improved | Unchanged | Worse | |
| BMI | 117 | 26.7 (23.9, 30.1) | 0.2 (–0.6, 1.0) | 44% | 1% | 55% | 0.145 |
| Smoking | | | | | | | |
| Never | 62 | 46% | – | – | 95% | 5% | 0.725 |
| Ex-smoker | 41 | 30% | – | 10% | 83% | 7% | |
| Current | 33 | 24% | – | 15% | 85% | – | |
| Number smoked/day | | | | | | | |
| Ex-smokers | 35 | 15 (7, 20) | 0 (–5, 0) | 43% | 34% | 23% | 0.810 |
| Current smokers | 32 | 15 (6, 20) | 0 (–5, 3) | 44% | 22% | 34% | 0.262 |
| Alcohol, units/week | 123 | 2 (0, 12) | 0 (–2, 0) | 39% | 37% | 24% | 0.033 |
| Moderate exercise, mins/week | 114 | 7 (0, 120) | 0 (–60, 30) | 34% | 30% | 36% | 0.861 |
| DAS28-CRP (3)[a] | 126 | 3.6 (2.5, 4.9) | –1.0 (–2.5, 0.0) | 74% | 4% | 22% | <0.001 |
| Mobility (EQ5D) | | | | | | | |
| No problems | 209 | 50% | – | – | 84% | 16% | 0.004 |
| Some problems | 206 | 50% | – | 30% | 70% | – | |

Figures are median (interquartile range) or number (%). BMI: Body Mass Index, DAS28: Disease Activity Score 28 Joints, CRP: C-Reactive Protein, EQ5D: European Quality of Life-5 Dimensions, a DAS28-CRP 3 variables.

**Conclusions:** A significant reduction in alcohol units and improvement in smoking habits were seen. However, despite significant improvements in IA disease activity and mobility, there was no improvement in exercise from the low level reported at BL. The need to address modifiable CVD RFs in IA is widely accepted by Rheumatologists but effecting lifestyle change is challenging. Behavioural change in exercise is complex, particularly in chronic disease. Further studies are required to optimise the approach in IA.

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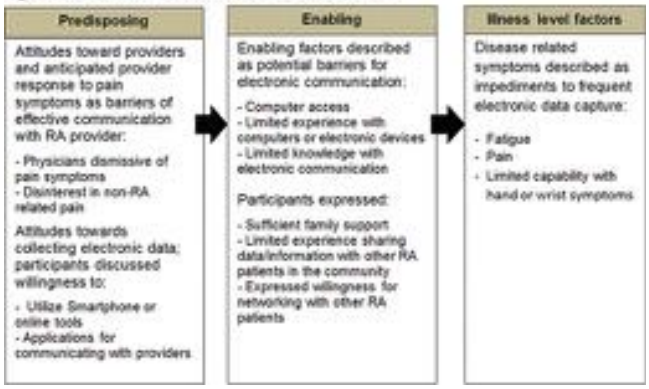
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3270

## FRI0131 ATTITUDES AND BARRIERS OF USING ELECTRONIC DATA COLLECTION TO TRACK DISEASE ACTIVITY OUTSIDE OF CLINICAL SETTINGS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Effective use of patient reported outcomes (PROs) is important for ensuring high quality care in rheumatoid arthritis (RA). The current standard of care is to measure PROs at the point of care. However, more frequent measures may provide a more accurate representation of disease activity. How best to encourage patients to report PROs outside of the clinical setting is not known.
**Objectives:** Initiate a qualitative assessment of RA patients' preferences for engagement in PRO collection and electronic health communication outside of clinical settings.
**Methods:** RA patients were recruited from one academic medical center to participate in a series of focus groups from December 2014-April 2015. Session topics were modeled using the Andersen and Newman Individual Determinants of Health Service Utilization Framework, emphasizing predisposing, enabling, and illness-level factors that may influence patient willingness to share data on Smartphones and the web as well as uptake and utilization of RA clinical and support services related to electronic data collection such as assistance with computer for electronic data entry. Ninety minute sessions were audio-recorded, transcribed, independently coded, and analyzed for themes in combination with post-session survey responses.
**Results:** A total of 31 patients participated in 7 groups. Median age was 51 years, 94% Female, 52% Black, 11% Hispanic, 37% Caucasian. In post-session surveys, 58.1% of respondents were "very" or "extremely" comfortable sharing arthritis information with persons outside their healthcare team, 54.8% were very/extremely likely to use electronic or online tools to share RA information, and 64.5% reported that their RA was "high" or "essential/highest" health priority.
Preliminary qualitative data from the first two focus groups showed several predisposing beliefs, enabling factors and illness level factors (Figure). RA patients expressed willingness to logging RA disease activity data for sharing with healthcare providers and other patient generated data via Smartphone. However, few participants had experience sharing RA information or seeking support for RA outside of their family/partner, such as another RA patient or group support, to assist with understanding RA, use a computer or explain knowledge of PRO evaluation. These patients expressed willingness to participate with other RA patients in these areas to expand their knowledge.

Figure: Individual determinants of health service utilization




**Conclusions:** Incorporating these aspects and even the experience of sharing RA data information guided by another trained RA patient (peer-coach), as a facilitator for PRO collection, will help overcome some of the barriers to RA data collection expressed by patients. These aspects can improve the patient willingness to collect RA disease activity data and PRO that can lead to improvement in the clinical care of these patients.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2751

## FRI0132 LIPID MANAGEMENT AMONG INDIVIDUALS WITH INFLAMMATORY ARTHRITIS IN THE NATIONAL REASONS FOR GEOGRAPHIC AND RACIAL DIFFERENCES IN STROKE COHORT

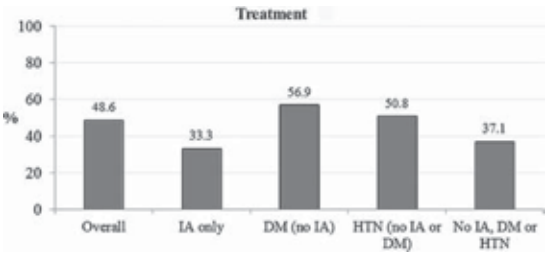
I. Navarro-Millan[1], C. Gamboa[2], J.R. Curtis[1], M.M. Safford[3]. *[1]Rheumatology; [2]Preventive Medicine, University of Alabama at Birmingham, Birmingham; [3]Internal Medicine, Cornell Medical Center, New York, United States*

**Background:** Cardiovascular (CVD) risk factor management may be suboptimal in people with inflammatory arthritis (IA) (rheumatoid arthritis [RA], psoriatic arthritis [PsA], ankylosing spondylitis [AS]).

**Objectives:** We compared hyperlipidemia treatment of participants with and without IA, controlling for individual-level factors that influence health services utilization.
**Methods:** The REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort includes 30,239 community dwelling black and white adults from the 48 contiguous US states recruited between 2003–7 and assessed with a telephone survey and in-home visit that included a blood draw and pill bottle review.[1] IA was identified through medications specific to autoimmune disease. Individuals with IA (without diabetes or hypertension) were compared to those with diabetes (but no IA), hypertension (but no diabetes or IA), or IA, diabetes, or hypertension. Logistic regression models examined odds of treatment among those with hyperlipidemia after accounting for predisposing, enabling, and need factors guided by Andersen and Aday's model.[2]
**Results:** IA participants were younger and predominately women, with lower Framingham risk scores, and lower functional status (Table 1). Proportionately fewer IA patients were treated than others (Figure 1). The fully adjusted odds of treatment for those with IA were 27% lower but not significantly different from those without IA, hypertension, or diabetes. Participants with diabetes and HTN were 2-times more likely to be managed for hyperlipidemia than those without IA, diabetes, or hypertension.

Table 1. Characteristics of REGARDS participants with hyperlipidemia at the time of enrollment

| Demographic | IA only (no DM or HTN) n=39 | DM (no IA) n=5,423 | HTN (no IA or DM) n=7,534 | No IA, DM or HTN n=5,288 |
|---|---|---|---|---|
| Women, n (%) | 23 (59.0) | 2896 (53.4) | 4063 (53.9) | 2312 (43.7) |
| Mean age, years ±SD | 63.3±9.4 | 65.7±8.7 | 66.7±9.1 | 64.3±9.2 |
| Aware of high cholesterol, n (%) | 23 (59.0) | 3829 (71.1) | 5355 (71.6) | 3235 (61.9) |
| Perfect medication adherence, n (%) | 28 (71.8) | 3539 (67.9) | 5009 (69.3) | 3175 (70.6) |
| Current smoking, n (%) | 10 (25.6) | 736 (13.6) | 1083 (14.4) | 900 (17.0) |
| Low HDL, n (%) | 11 (28.2) | 2662 (49.1) | 2879 (38.2) | 1837 (34.7) |
| Mean LDL, mg/dL ±SD | 122.6±35.2 | 108.4±35.9 | 120.9±36.9 | 132.7±37.7 |
| Median Pysical Component Summary Score [25th, 75th%] | 42.3 [33.2, 52.1] | 44.3 [33.2, 52.0] | 48.8 [39.2, 53.8] | 52.6 [46.2, 55.7] |
| Median Framingham Risk Score [25th, 75th%] | 5.0 [2.0, 12.0] | 10.0 [4.0, 16.0] | 11.0 [5.0, 17.0] | 8.0 [3.0, 12.0] |

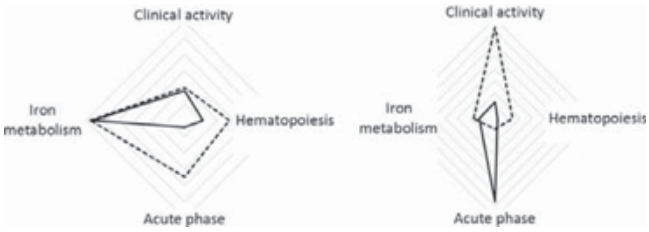



**Conclusions:** In this study, hyperlipidemic participants with IA were less likely to be treated for hyperlipidemia than participants with diabetes or hypertension - diseases well known to increase CVD risk – even after accounting for levels of CVD risk. This study was limited by power. If confirmed in larger samples, these results reflect a potential gap in the management of hyperlipidemia for IA patients.
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**Acknowledgement:** A full list of participating REGARDS investigators and institutions can be found at http://www.regardsstudy.org.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2403

## FRI0133 UNDERSTANDING ANEMIA IN RHEUMATOID ARTHRITIS: THE ASSOCIATION OF HEMOGLOBIN AND HEPCIDIN LEVELS WITH CLINICAL DISEASE ACTIVITY AND ACUTE PHASE RESPONSE

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**Background:** Hepcidin is an important link between inflammation and anemia in patients with rheumatoid arthritis (RA); hemoglobin itself is considered a negative acute phase measure in chronic inflammatory conditions like RA. However, the longitudinal association of hepcidin and hemoglobin with RA disease activity and acute phase remains to be explored.
**Objectives:** We aimed to explore these associations in patients with RA.
**Methods:** We consecutively included RA outpatients in a routine academic setting. Each patient was evaluated at baseline and 12 weeks thereafter using the clinical disease activity index (CDAI) and extensive peripheral blood tests, including serology, acute phase response (erythrocyte sedimentation rate, ESR; C reactive protein, CRP; and fibrinogen) and measures of iron metabolism (ferritin; transferrin; transferrin saturation, TS; hepcidin; and peripheral erythroid burst forming units, BFU-E). We analyzed baseline and week 12 values cross-sectionally in all patients; and change scores from baseline to week 12 in a subset of active patients with CDAI≥10 and a new DMARD initiation at baseline. We performed principal component analysis (PCA) to identify themes for all included variables. The strength of association of hepcidin and hemoglobin with the identified themes from the PCA was then analyzed.
**Results:** Eighty-eight patients (68 females, 77%) were included (mean±SD age: 58±12 years; disease duration: 9.3±9.6 years). PCA identified four themes for all included parameters: clinical activity, acute phase, iron metabolism and hematopoiesis. At baseline and week 12 (steady state), both hepcidin and hemoglobin levels were ascribable primarily to the theme "iron metabolism". Hemoglobin was also ascribable to "clinical activity" – to a similar extent as other acute phase parameters; but even more to the theme "acute phase". Conversely, 12-week changes in hepcidin levels were ascribable to "changes in acute phase", while changes in hemoglobin levels were ascribable to "changes in clinical activity" (Figure). In multivariable analysis CDAI changes were negatively, and BFU-E changes were positively, associated with hemoglobin changes ($R^2$=0.615, $p<0.05$ for both); hepcidin changes were not associated with hemoglobin changes.
Figure: Loadings of hepcidin (solid lines) and hemoglobin (dotted lines) to the themes identified by principal component analysis, for baseline values (left), and for changes between baseline and week 12 (right)




**Conclusions:** In patients with RA, changes in hepcidin levels reflect changes in acute phase response, but not changes in clinical disease activity; changes in hemoglobin levels occur in conjunction with changes in clinical disease activity, but not with changes of the acute phase response. The association of clinical disease activity with hemoglobin seems to be stronger than its association with other acute phase parameters.
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[1] Song SN et al. Arthritis Res Ther. 2013;15:R141.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3296

## FRI0134 INTERLEUKIN-6 BLOCKADE RAISES LDL VIA REDUCED CATABOLISM RATHER THAN VIA INCREASED SYNTHESIS – A CYTOKINE-SPECIFIC MECHANISM FOR CHOLESTEROL CHANGES IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is associated with significant alteration in circulating lipids, in particular reduced serum total cholesterol and low-density lipoprotein cholesterol (LDL-c) levels. Various RA modulatory therapeutics can increase serum LDL-c; mechanisms underlying this phenomenon are poorly understood but may be mediated via cytokine signalling, particularly JAK dependent pathways. Herein we have explored the effects of IL-6 receptor blockade upon cholesterol metabolism in a clinical experimental study using tocilizumab.
**Objectives:** We sought to define the metabolic pathways (i.e. synthesis versus clearance) whereby specific inhibition of IL-6R signalling in patients with active RA modulates circulating LDL levels.
**Methods:** We performed kinetic studies of LDL metabolism in 12 patients with severe, active RA (DAS28 ≥5.1) eligible for biologic DMARD therapy – one patient withdrew from the study and did not contribute evaluable data. A stable isotope of d3-leucine was administered and incorporated into newly-synthesised apoB; the formation and catabolic rates of apoB-containing lipoproteins were then assessed using an established multi-compartmental model. Kinetic studies were performed at baseline and after at least three consecutive infusions of IV tocilizumab 8mg/kg every 4 weeks. Changes in kinetic parameters (fractional catabolic and synthesis rates, FCR and FSR, respectively), serum lipids and measures of disease activity from baseline were assessed using student's t-test or Wilcoxon matched-pairs

test as dictated by normality of data. Correlations between parameters were assessed by Pearson's or Spearman's coefficient as appropriate.
**Results:** In 11 evaluable patients who completed the study, profound reductions were observed after treatment in mean CRP (19 vs 0.75 mg/l, p=0.015) and ESR (38 vs 3mm/hr, p=0.004), with significant changes in CDAI (29.9 v 8.0, p<0.001). Elevations were seen in total cholesterol (4.9 vs 5.7mmol/l, p=0.003), HDL-cholesterol (1.2 vs 1.6mmol/l, p=0.006) and LDL-cholesterol (2.9 vs 3.5mmol/l, p=0.014).
The FCR of LDL fell significantly following IL-6 blockade (median 0.53 vs 0.27 pools/day, p=0.006, with median change of -30% from baseline). No significant change was observed in the FSR of LDL (median 0.45 vs 0.72 mg/kg/day, p=0.41). FCR correlated inversely with LDL-c at baseline (r=-0.77, p=0.007) and after treatment (r=-0.66, p=0.031). At baseline, FCR also associated with CRP (r=0.74, p=0.012), but not CDAI (r=0.04, p=0.91).
**Conclusions:** IL-6 blockade increases serum LDL-c primarily by reducing the fractional catabolic rate of LDL from a state of hypercatabolism to levels seen previously in healthy cohorts. Of note, FCR of LDL is most closely associated with the acute phase response rather than with RA disease activity as quantified by CDAI. Normalisation of this acute phase-driven increased catabolism largely explains the LDL-c elevations observed following tocilizumab therapy. Our study for the first time clearly defines IL-6 as the key driver of the increased catabolism of LDL which results in low serum LDL-c levels in RA.
**Disclosure of Interest:** None declared
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## FRI0135 INCREASED INTRINSIC BRAIN CONNECTIVITY BETWEEN AFFECTIVE PAIN PROCESSING REGIONS AND BILATERAL SENSORIMOTOR CORTEX IN RA PATIENTS COMPARED TO HEALTHY CONTROLS

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**Background:** Rheumatoid arthritis (RA) is commonly accompanied by pain that is discordant with the degree of peripheral pathology. Very little is known about the cerebral processes involved in pain processing in RA.
**Objectives:** To investigate resting state brain connectivity associated with prolonged pain in RA.
**Methods:** 24 RA subjects and 19 matched controls were compared with regard to both behavioral measures of pain perception and resting-resting state fMRI data acquired subsequently to fMRI sessions involving pain stimuli. The resting-state fMRI brain connectivity was investigated using 159 seed regions located in cardinal pain processing brain regions. Additional principal component based multivariate pattern analysis of the whole brain connectivity pattern was carried out in a data driven analysis to localize group differences in functional connectivity.
**Results:** When RA patients were compared to controls, we observed significantly lower pain resilience for pressure on the affected finger joints (i.e. P50-joint) and an overall heightened level of perceived global pain in RA patients.
Relative to controls, RA patients displayed increased brain connectivity predominately for the supplementary motor areas, mid-cingulate cortex and the primary sensorimotor cortex. Additionally, we observed an increase in brain connectivity between the insula and prefrontal cortex as well as between anterior cingulate cortex and occipital areas for RA patients. None of the group differences in brain connectivity were significantly correlated with behavioral parameters.
**Conclusions:** Our study provides experimental evidence of increased connectivity between frontal midline regions that are implicated in affective pain processing and bilateral sensorimotor regions in RA patients.
**Disclosure of Interest:** None declared
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## FRI0136 RISK FOR LUNG CANCER IN RA AND DIFFERENT RA PHENOTYPES: RESULTS FROM A POPULATION-BASED CASE-CONTROL STUDY

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**Background:** It has been shown that patients with Rheumatoid Arthritis (RA) are at increased risk for certain malignancies, among them lung cancer.
**Objectives:** To investigate the association between lung cancer and different RA phenotypes based on rheumatoid factor (RF) and anti-citrullinated peptide antibody (ACPA) status.
**Methods:** We used the population-based case-control study EIRA (Epidemiological Investigation of Risk factors for Rheumatoid Arthritis). Patients with RA and controls (matched for age, sex, calendar period and area of residence) were included during 1996–2013. The data were linked to the Swedish nationwide cancer register. Cox regression was used to calculate RR. Due to the significant correlation between smoking and RA as well as presence of RF and ACPA, stratified analyses based on smoking status were performed, in order to account for effect modification.
**Results:** A total of 3547 RA patients and 5586 controls were included in the study. The mean age (SD) was 52 (13) years and the percentage of female was 72%. Significantly more RA patients than controls were diagnosed with lung cancer after RA diagnosis (58 vs. 26 per 100,000 patient-years, respectively, p=0.002). RA itself gave twice an increased risk for developing lung cancer when adjusted for age and sex (RR=1.9, 95% CI=1.2–3.2, p=0.01), but the statistical significance disappeared when smoking was included in the model. However, after stratification according to smoking status, RA was significantly associated to lung cancer development in never or ex-smokers (RR=2.4, 95% CI=1.0–6.2, p=0.05) but not in current smokers (RR=1.2, 95% CI=0.6–2.3, p=0.6). In RA patients, higher age, smoking, RF positivity, RF and/or ACPA positivity and double seropositivity were significant risk factors for lung cancer (table 1). In a stratified analysis RF positivity was significantly associated to lung cancer in non-smokers (table 2).

Table 1. Cox regression analysis (adjusted for age and sex) with lung cancer after RA diagnosis as the dependent variable and several potential risk factors as independent variables

| Variable | RR (95% CI) | P-value |
|---|---|---|
| Sex (female vs. Male) | 0.6 (0.3–1.2) | 0.64 |
| Age | 1.1 (1.1–1.2) | <0.0001 |
| Smoking (current vs. Never/ex) | 3.2 (1.6–6.6) | 0.002 |
| Smoking (ever vs. Never) | 3.6 (1.1–12.0) | 0.03 |
| Silica | 2.2 (0.7–6.9) | 0.18 |
| RF (pos vs. Neg) | 4.6 (1.6–13.0) | 0.004 |
| ACPA (pos vs. Neg) | 1.9 (0.9–4.0) | 0.11 |
| ACPA and/or RF pos vs. neg | 7.0 (1.7–28.9) | 0.008 |
| Double pos (RF and ACPA) vs. Double neg. | 6.8 (1.6–28.8) | 0.01 |

Table 2. Risk for development of lung cancer for different RA phenotypes

| Variable | Non-Smokers (never or ex-smokers) | | Smokers (current) | |
|---|---|---|---|---|
| | No. of patients (seropositive with lung ca/total with lung ca) | RR (95% CI) | No. of patients (seropositive with lung ca/total with lung ca) | RR (95% CI) |
| RF (pos vs neg) | 11/12 | 7.4 (1.0–57.4) | 17/20 | 2.4 (0.7–8.2) |
| ACPA (pos vs neg) | 9/12 | 2.3 (0.6–8.7) | 14/20 | 1.2 (0.4–3.1) |
| ACPA and/or RF pos vs double neg | 11/12 | 5.5 (0.7–42.5) | 19/20 | 5.8 (0.8–43.2) |
| Double pos (RF and ACPA) vs double neg | 9/10 | 6.1 (0.8–47.9) | 12/13 | 4.8 (0.6–36.5) |

**Conclusions:** In this study RA, especially RF positive RA, was associated to the development of lung cancer in never or ex-smokers. Although not statistically significant, patients who developed lung cancer were more often positive for RF and/or ACPA irrespective of smoking status.
**Disclosure of Interest:** None declared
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## FRI0137 ASSOCIATION BETWEEN NUMBER AND TYPE OF DIFFERENT ACPA FINE SPECIFICITIES AND PARENCHYMAL LUNG CHANGES IN HIGH RESOLUTION COMPUTED TOMOGRAPHY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Anti-CCP2 antibodies are associated with parenchymal lung changes in early RA.
**Objectives:** To examine the association between ACPA fine specificities and parenchymal lung changes in early RA.
**Methods:** Patients with newly diagnosed RA, glucocorticoids and DMARDs-naive, were included. High-resolution computed tomography (HRCT) was performed to assess parenchymal lung changes (ground glass changes, nodules, infiltrates or fibrosis). ImmunoCAP was used to detect RF IgA, RF IgM, anti-CCP2 IgA, anti-CCP2 IgG and ISAC microarray system was used to detect antibodies against 10 citrullinated (Cit) peptidic antigens: CCP-1 (Filaggrin), CEP-1 (α-enolase), Vim 2–17, Vim 60–75 (Vimentin), Fib β 36–52, Fib α 573, Fib α 591, Fib α 36–50, Fib β 60–74, Fib α 621–635 (Fibrinogen). Logistic regression was performed to examine associations between lung changes and autoantibodies, adjusted for age and sex. Due to risk for effect modification of smoking and co-linearity between smoking and Cit peptides, we stratified the cohort according to ever vs. never smokers.
**Results:** A total of 106 patients were included. The mean (SD) age was 57 (14) years. 69% were females; 73% were ever smokers; 70% were RF positive and 69% were positive for anti-CCP2. Parenchymal lung changes were found in 58

patients (54.7%). Higher age [≥65 vs <65, OR (95% CI) =2.5 (1.1–5.9)], pos RF IgA [OR (95% CI) =2.7 (1.2–5.9)], pos CCP2 IgG [OR (95% CI) =2.3 (1.0–5.4)], ever smoking [OR (95% CI) =2.6 (1.1–6.2)] and pack-years above 24 [OR (95% CI) =6.9 (2.0–23.5)], were significant predictors of parenchymal lung changes. Some ACPA fine specificities were associated to parenchymal lung changes in ever smokers (table 1). Having five or more ACPA specificities at the time of diagnosis increased the risk of having lung changes in ever smokers by 6.6 times (table 1).

Table 1. Association between ACPA fine specificities and parenchymal lung changes according to smoking status

| | Non-smokers [N=29] | | Ever smokers [N=77] | |
|---|---|---|---|---|
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| Cit Fibrinogen peptides | 2.3 (0.4–13.1) | 0.35 | 3.0 (1.0–8.8) | 0.05 |
| Fib β 36–52 cit | 1.1 (0.2–5.9) | 0.87 | 2.7 (0.9–7.6) | 0.07 |
| Fib α 573 cit | 2.3 (0.4–13.0) | 0.35 | 3.9 (1.3–12.5) | 0.02 |
| Cit Vimentin peptides | 3.5 (0.5–24.9) | 0.22 | 2.9 (1.0–8.5) | 0.06 |
| Vim 2–17 cit | 1.2 (0.2–6.5) | 0.80 | 2.9 (1.0–8.6) | 0.05 |
| Vim 60–75 cit | 4.9 (0.7–32.7) | 0.10 | 2.2 (0.8–6.3) | 0.15 |
| CEP-1 (α-enolase) | 0.4 (0.06–2.4) | 0.30 | 2.0 (0.7–6.0) | 0.20 |
| N. ACPAs 0 (ref) | | | | |
| 1–4 | 2.6 (1.9–35.9) | 0.47 | 5.2 (1.3–21.2) | 0.02 |
| >4 | 3.6 (0.3–44.7) | 0.32 | 6.6 (1.6–27.3) | 0.009 |

**Conclusions:** RF IgA, anti-CCP2 IgG, antibodies to Cit Fib and Cit Vim peptides were strongly associated to parenchymal lung changes in ever smokers with early RA. The more ACPA fine specificities, the higher the risk of parenchymal lung changes.
**Disclosure of Interest:** None declared
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## FRI0138 S100A12 AND CALPROTECTIN IN SERUM AND THE AORTA OF PATIENTS WITH CARDIOVASCULAR DISEASE AND INFLAMMATORY RHEUMATIC DISEASE: A BIOPSY STUDY

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**Background:** Increased serum calprotectin (s-calprotectin) and S100A12 (s-S100A12) levels are associated with inflammatory rheumatic disease (IRD), and might be involved in the pathogenesis of cardiovascular disease (CVD).
**Objectives:** To compare s-calprotectin and s-S100A12 levels in CVD patients with and without IRD, to IRD patients without CVD, and to healthy controls (HC). Furthermore, to search for relationships between s-calprotectin levels and calprotectin expression in the aortic adventitia.
**Methods:** We examined s-calprotectin and s-S100A12 in patients from the Feiring Heart Biopsy Study: 69 IRD (CVD-IRD group) and 53 non-IRD (CVD group) patients undergoing coronary artery bypass grafting (CABG), 32 IRD patients without any clinical or laboratory sign of CVD (IRD group) and 30 HC. Using immunohistochemistry, we scrutinized biopsies taken during CABG from the aortic adventitia in 19 CVD-IRD and 20 CVD patients for the presence and extent of inflammatory cell infiltrates (ICIs) and calprotectin expression.
**Results:** We found no significant differences in levels of s-S100A12 between the four groups (p=0.56). There was not a significant difference in the calprotectin levels between the CVD-IRD and the IRD (1.30 vs 1.73 mg/l; p=0.16) groups. The groups with CVD (CVD and CVD-IRD) had significantly higher s-calprotectin level than the HC group (1.47 vs. 0.30 mg/l; p<0.0001), and a statistically non-significant trend towards a higher s-S100A12 level (44.12 vs 25.36 mg/l; p=0.13). The groups with IRD (IRD and CVD-IRD) had a significantly higher s-calprotectin level than the CVD (without IRD) group (1.42 vs. 0.25 mg/l; p<0.0001) and the HC group (1.42 vs. 0.29 mg/l; p<0.0001). CVD was not independently related to s-calprotectin (p=0.36) neither in the total population nor in the RA subgroup. Calprotectin expression in the aortic adventitia was significantly related to the presence of inflammatory cell infiltrates (ICI; p=0.05), but not to s-calprotectin levels (p=0.95).

Table 1. S-calprotectin and S100A12 values for the four groups in the study: CVD-IRD, CVD, IRD, and HC

| | CVD-IRD (n=69) | CVD (n=53) | IRD (n=32) | HC (n=30) | p† |
|---|---|---|---|---|---|
| s-calprotectin, mg/l | 1.30±1.5 | 0.25±0.17 | 1.73±1.42 | 0.30±0.15 | <0.001 |
| s-S100A12, μg/l | 20 (19.75) | 16 (27.5) | 17 (32.33) | 16.0 (20.85) | 0.56 |

s-calprotectinis reported as the mean ± SD whereas S100A12 is reported as the median (IQR). Numbers may not add up to the expected total due to missing data for some variables. †P values for continuous dependent variables are from analysis of variance (ANOVA).

**Conclusions:** s-Calprotectin is independently related to IRD, but not to CVD (neither in the general population nor in RA). Thus, in theory, the previously observed association between s-calprotectin and CVD might be caused by the underlying inflammatory process, e.g. IRD, not by a causal role of calprotectin in the CVD pathogenesis.
**Disclosure of Interest:** None declared
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## FRI0139 RISK OF TYPE 2 DIABETES MELLITUS DEVELOPMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is associated with insulin resistance (IR), a precursor to type 2 diabetes mellitus (DM). However, IR indexes are uncomfortable to examine the DM risk in clinical practice. International Diabetes Federation recommends the use of patient questionnaires to quickly identify people who may be at a higher risk of DM development.
**Objectives:** To determine the 10-years risk of DM development in patients with RA by questionnaire Finnish Type 2 Diabetes Risk Assessment Form (FINDRISK).
**Methods:** The study included 234 RA patients without DM (202 women, 32 men, 56 [42; 64] years old). The median disease duration was 7 [2,14] years, DAS28 was 4,73 [3,5;5,5]. The majority of pts were seropositive for IgM RF (75%) and anti-CCP (80%). RA pts were treated with glucocorticoids (43%), methotrexate (52%) or other disease-modifying antirheumatic drugs (19%), and biological agents (26%). The control group consisted of 100 subjects without inflammatory arthritis or DM, matched by age and sex with RA patients. Eight factors for FINDRISK questionnaire (increasing age, overweight, abdominal obesity, family history of diabetes, physical inactivity, eating habits, high blood pressure, history of hyperglycemia) were taken into account to calculate the total test score (TS). The risk of DM development within following 10 years is regarded as low (1%) or slightly elevated (4%) with TS ≤11 points, as moderate (17%) with TS =12–14 points, as high (33%) or very high (50%) with TS ≥15 points. Fasting glucose level was investigated in 230 RA pts after the interview.
**Results:** The risk of DM development was low or slightly elevated in 133 (56,8%) RA pts, moderate in 51 (21,8%) pts, and high or very high in 50 (21,4%) pts. Hyperglycemia (≥6,1mmol/l) was observed in 5/131 (3,8%) pts with low or slightly elevated DM risk, 5/50 (10,0%) pts with moderate risk, and 10/49 (20,4%) pts with high or very high risk (p<0,01 for low vs high risk group). The median TS of RA pts (10 [5;14] points) was not differ from these of control subjects (11 [7;15] points). DM risk factors profile were similar in two groups, excluded more higher prevalence of unhealthy diet (51% vs 37%, p=0,02) and trend to more frequently physical inactivity (73% vs 62%, p=0,053) in RA. There were correlations between TS and fasting glucose level (r=0,38, p<0,01), HAQ (r=0,13, p=0,04), but no DAS28. Currently glucocorticoids use did not effect on TS in RA. Men had increased TS and number of risk factors compared with women with RA (13 [9;16] vs 10 [5;14] points and 5 [4;6] vs 4 [2;5] factors, p<0,01 for all cases). The number of risk factors was correlated with CRP (r=0,14, p=0,05), ESR (r=0,14, p=0,05), DAS28 (r=0,16, p=0,02) in women, but no men with rheumatic disease.
**Conclusions:** Risk of DM development in RA pts caused by traditional risk factors as the same as in general population and partly by the presence of inflammation. Clarification of RA-specific phenomena in DM pathogenesis requires further research. FINDRISK is simple, inexpensive and effective way to identify RA pts who should be carefully observed with lifestyle change to lower their DM risk, and who need additional examination to determine if they have DM without symptoms.
**Disclosure of Interest:** None declared
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## FRI0140 IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE FOR PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 1-YEAR FOLLOW UP

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**Background:** Comorbid infections have significant impact on morbidity and mortality, especially in autoimmune diseases. Prevention of infection is an integral part of supervision of these patients.
**Objectives:** To investigate immunogenicity and safety of 23-valent polysaccharide pneumococcal vaccine in patients with rheumatoid arthritis (RA) treated with diseases modifying anti rheumatic drugs (DMARDs) and biologic diseases modifying anti rheumatic drugs (bDMARDs).
**Methods:** Out of 110 subjects (81 females (73,6%), 29 males (26,4%) aged 23–76 years) included into the study, 79 were RA patients and 31 were controls (GK) with a history of ≥2 episodes of lower respiratory tract infections (bronchitis, pneumonia). 52 patients with RA were on methotrexate (MTX), 14 were on leflunomid (LEF), 13 were on tumor necrosis factor alpha (iTNF-α) inhibitors+MTX. One dose (0,5 ml) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously without discontinuation of MTX/LEF or 28–30 days prior to initiation of iTNF-α. Totally four study visits were preplanned: initial vaccination visit and 3 control visits in 1, 3 and 12 months after vaccination. Routine evaluation during each visit included physical exams and laboratory tests. Levels of antibodies to pneumococcal capsular polysaccharide were measured

using VaccZymeTM PCP IgG 2 kit (The Binding Site Group Ltd, Birmingham, UK). Post-immunization response coefficient was calculated for each participant as the ratio of AB levels during visits II, III, and IV to baseline AB level at Visit I.
**Results:** Not a single case of clinically or radiographically confirmed pneumonia was documented during the follow up period. Dynamics of post-immunization response coefficient in RA patients on different therapeutic modalities and in the controls are presented in the Table. Pronounced positive immune reaction after administration of the vaccine under investigation was documented in RA patients during different therapies, i.e., significant post-immunization response coefficient increase. There were 61% responders among RA patients and 70% responders among the controls. Good tolerability of the vaccine was documented in 65% of cases, satisfactory (injection site pain, swelling and hyperemia of the skin up to 2 cm in diameter and subfebrile fever) in 35% of cases. As these reactions had no casual relationship with current RA therapy, and fully resolved within 24 hours without additional treatment, no RA therapy modification was required. Univariate analysis of total 21 variables showed that negative results at Visit II (in one month after vaccination, OR 5,47, 95% CI 1,3–22,9) and Visit III (in three months after vaccination, OR 4,49 95% CI 1,6 -12,7) may cause negative response to vaccination in RA patients after 12 months follow up. Pronounced DAS28 positive dynamics in RA patients (4,32 and 3,31 at Visit I and Visit IV, respectively, $p<0{,}001$) indicates the absence of any negative impact of vaccination on disease activity).

Table. Post-immunization response coefficient dynamics in RA and control subjects during 1 year follow up.

| Treatment groups | Post-immunization response coefficient dynamics, M±σ. | | |
|---|---|---|---|
| | Visit II (1 month) | Visit III (3 Month) | Visit IV (12 month) |
| MTX (n=52) | 2,4 ±1,2 | 3,4±3,56 | 2,7±2,02 |
| Lef (n=10) | 5,01±4,7 | 6,9±2,1 | 4,3±1,8 |
| iTNF-α+MTX (n=10) | 2,6±0,3 | 3,5±1,7 | 3,14±2,86 |
| GK (n=30) | 2,15±0,25 | 3,49±2,27 | 2,2±1,78 |

**Conclusions:** Thus, all given prove the sufficient immunogenicity and safety of 23-valent pneumococcal vaccine in RA patients, getting different therapeutic regimens.
**Disclosure of Interest:** None declared
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## FRI0141 BONE MINERAL DENSITY OF WHOLE BODY CAN PREDICT FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS: FINDINGS FROM THE TOMORROW STUDY

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**Background:** Rheumatoid arthritis (RA) is an independent risk factor for osteoporosis. Patients with RA have a higher risk of fractures than healthy individuals[1]. We previously reported that bone mineral density (BMD) is lower in patients with RA than in healthy individuals[2]. Whether or not BMD and fracture correlate in patients with RA has remained unclear.
**Objectives:** We aimed to determine whether whole body BMD could predict fracture during five years of follow in patients with RA.
**Methods:** This prospective cohort study analyzed data collected over a period of five years from the TOMORROW study (TOtal Management Of Risk factors in Rheumatoid arthritis patients to lOWer morbidity and mortality clinical trial (registration number, UMIN000003876)), which is a 10-year prospective study of 208 age and sex matched patients with RA and 213 volunteers (controls). The BMD, lean body mass, and fat ratio (%) were measured using whole body dual-energy X-ray absorptiometry (DXA). Patients and volunteers who had received metal implants were excluded. We measured BMD, lean mass, and fat ratio (%) at baseline between groups with and without fractures, to identify a cut-off for increased risk of fracture using ROC curve analysis.
**Results:** Fracture rates did not significantly differ between RA patients and controls (14.9% vs. 10.4%; p=0.231) over the five-year period. The DXA data derived from a total of 358 participants (158 patients and 200 controls) identified 39 individuals with and 319 without fracture. The BMD was significantly lower in the group with fracture, than that without (0.914 vs. 0.995 g/cm$^2$, respectively: p=0.001 and the tendency was the same in the patients with RA (0.873 vs. 0.977 g/cm$^2$, respectively; p=0.002). Lean mass and fat percentage did not significantly differ between the groups with and without fracture. At a BMD cut-off of 0.869 g/cm$^2$, the area under the curve was 0.734, sensitivity was 72.2% and specificity was 65.7% (p=0.01) in patients with RA (Figure 1 and Table 1). The odds ratio of fracture among the patients with RA over a period of five years was 5.3 when the BMD was <0.869 g/cm$^2$.

Table 1. AUC of parameters

| | AUC | 95% CI | P |
|---|---|---|---|
| Bone mineral density | 0.734 | 0.628–0.839 | 0.01 |
| Lean mass | 0.531 | 0.431–0.632 | 0.583 |
| Fat percentage | 0.606 | 0.493–0.720 | 0.063 |

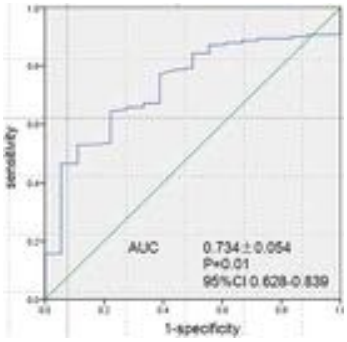


Figure 1

**Conclusions:** The baseline BMD was significantly lower in the group with, than without fracture. However, lean mass and fat percentage did not significantly differ between them. Baseline total BMD was more useful than lean mass and the fat percentage to predict fracture within five years among patients with RA.
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**Disclosure of Interest:** None declared
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## FRI0142 HIGH PREVALENCE OF DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS - DATA FROM THE LARGE CROSS-SECTIONAL VADERA II STUDY

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**Background:** Depression is a frequent if not the most frequent comorbidity in patients with rheumatoid arthritis (RA) [1].
**Objectives:** To investigate the prevalence of depressive symptoms in RA patients in a standardized manner in the clinical setting using two previously validated questionnaires and to test for clinical characteristics associated with depressive symptomatology.
**Methods:** To assess depressive symptoms the validated 9 item version of the patient health questionnaire (PHQ-9) and the Beck-Depression Inventory II (BDI-II) were used. In addition, demographic background, RA disease activity according to DAS28, RA disease symptoms according to the RAID questionnaire, comorbidities and anti-rheumatic as well as anti-depressive treatment were recorded. Cut-off values for depressive symptomatology were PHQ-9≥5 or BDI-II≥14 (ie mild depressive symptoms or worse). Numbers for frequency of depressive symptomatology were derived by frequency analysis while factors independently associated to depressive symptomatology were investigated by odds ratios and 95% confidence intervals using multiple logistic regression analyses. IRB approval was obtained and all patients completed an informed-consent form prior to participation.
**Results:** In 1004 RA-patients (75.1% female, mean age: 61.0±12.9 years, mean disease duration: 12.2±9.9 years, DAS28(ESR): 2.5±1.2) the prevalence of depressive symptoms was 55.4% according to predefined cut-offs (more restrictive cut-offs indicating moderate depressive symptoms at least, i.e. PHQ-9 ≥10 or BDI-II ≥20 still classified 22.8% of our patients as being depressed). Characteristics independently associated with depressive symptomatology were: age >60 years (OR=0.62 (95%CI: 0.46, 0.83)), DAS28(ESR) ≥3.2 (OR=1.52

(95%CI: 1.03, 2.27)), RAID score >5 (OR=8.28 (95%CI: 5.36, 12.80)) and presence of chronic pain (OR=2.55 (95%CI: 1.42, 4.57)). Only 11.7% of patients classified as having depressive symptoms received anti-depressive drug therapy.
**Conclusions:** More than half of RA patients showed symptoms of depression, which were associated with age, RA disease activity, a high impact of RA symptoms on the life of patients and the presence of chronic pain. However, only a small number of RA patients were receiving appropriate anti-depressive therapy. These findings strongly suggest the need for better assessment of depression in routine rheumatologic care.
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**Disclosure of Interest:** M. Englbrecht Grant/research support from: Research grant for VADERA: Chugai Pharma Europe Ltd. and Roche Pharma AG, R. Alten Grant/research support from: Roche, Chugai, Speakers bureau: Roche, Chugai, M. Aringer Consultant for: Roche, Chugai, Speakers bureau: Roche, Chugai, C. Baerwald: None declared, H. Burkhardt Grant/research support from: Roche, Chugai, Consultant for: Roche, Chugai, N. Eby Consultant for: Fees from Roche Pharma AG for statistical analysis and manuscript preparation during the conduct of the study, J.-P. Flacke Employee of: Roche Pharma AG, G. Fliedner Consultant for: Roche, Chugai, Paid instructor for: Roche, Chugai, B. Gauger Employee of: Roche Pharma AG, U. Henkemeier: None declared, M. Hofmann Employee of: Chugai Pharma Europe Ltd., S. Kleinert Speakers bureau: Abbvie, Chugai, Pfizer, Roche, UCB, Medac, C. Kneitz Grant/research support from: Pfizer, Consultant for: AbbVie, Janssen, Pfizer, Berlin Chemie, Chugai, Roche, Speakers bureau: AbbVie, Janssen, Pfizer, Berlin Chemie, Chugai,Celgenge, Novartis, Roche, MSD, UCB, K. Krüger Employee of: Chugai Pharma Europe Ltd., R. Lüthje: None declared, C. Pohl: None declared, G. Schett Grant/research support from: Research grant for VADERA: Chugai Pharma Europe Ltd. and Roche Pharma AG, M. Schmalzing Consultant for: Chugai, Novartis, Roche, Speakers bureau: AbbVie, Actelion, BMS, Chugai, Genzyme, Janssen-Cilag, Novartis, Pfizer, Roche, UCB, A.-K. Tausche: None declared, H. P. Tony Grant/research support from: Roche Pharma AG, Consultant for: Abbvie, BMS, Chugai, Janssen, Lilly, Novartis, Roche, UCB, Speakers bureau: Abbvie, BMS, Chugai, Janssen, Lilly, Novartis, Roche, UCB, J. Wendler Consultant for: Roche, Chugai, Speakers bureau: Roche, Chugai
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## FRI0143 RISK FACTORS FOR MALIGNANCY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON THE IORRA COHORT DURING A 14-YEAR OBSERVATION PERIOD

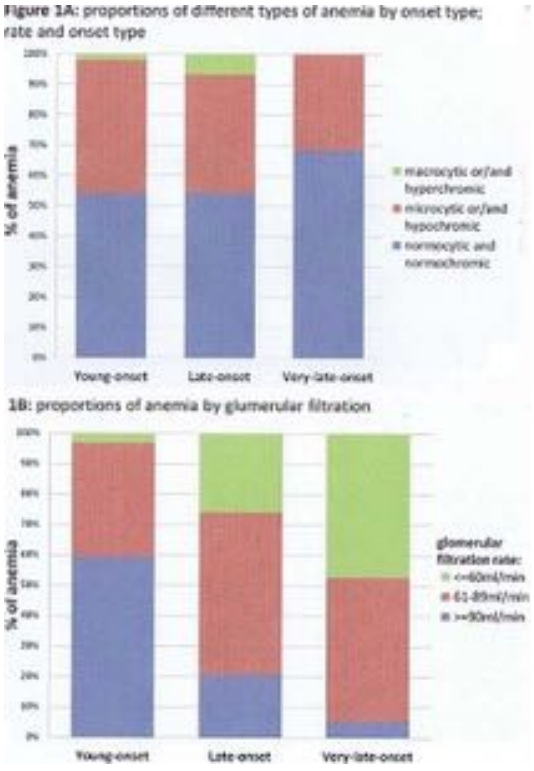
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**Background:** As treatments for rheumatoid arthritis (RA) such as methotrexate (MTX) and biological agents have made dramatic progress in this decade, it is desirable to improve patient quality of life and prognosis, including management of various comorbidities. Malignancy is an important comorbidity in patients with RA[1,2]. No significant difference in the overall incidence of malignancies in Japanese patients with RA (standardized incidence ratio [SIR] 0.96, 95% confidence interval [CI] 0.90–1.03) was noted compared with the general Japanese population[3]. However, a markedly significant increase in the incidence of malignant lymphoma was observed (SIR 5.10, 95% CI 4.21–6.13), and the incidence of lung cancer in males was also increased significantly[3]. In contrast, the incidence of gastric cancer and colorectal cancer was decreased significantly[3]. It is important to investigate the risk factors for malignancies to examine the prognosis of patients with RA.
**Objectives:** To investigate the risk factors for overall and site-specific malignancies in a large observational cohort of Japanese patients with RA over a long-term period.
**Methods:** Among Japanese patients with RA enrolled in the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort from April 2000 to September 2013, all malignancies were extracted from patients' self-reporting and confirmed by medical records. Patients who dropped out of the IORRA cohort were asked about comorbidities, including malignancies, by follow-up mail. With regard to overall malignancies and malignancies at frequently involved sites (lung cancer, malignant lymphoma, breast cancer, gastric cancer and colorectal cancer), risk factors were analysed with time-dependent Cox regression adjusted by age, gender, smoking history and BMI.
**Results:** Among 11,106 Japanese patients with RA representing 122,706 person-years, a total of 830 overall malignancies, including 114 lung cancers, 114 malignant lymphomas, 105 breast cancers, 95 gastric cancers and 90 colorectal cancers, were confirmed. RA disease duration was a significant risk factor for lung cancer (hazard ratio [HR] 0.95, $P$ =0.001) and malignant lymphoma (HR 0.95, $P$ =0.004). RF positivity was a significant risk factor for lung cancer (HR 2.26, $P$ =0.018). DAS28 score was a significant risk factor for overall malignancies (HR 1.10, $P$ =0.008), lung cancer (HR 1.25, $P$ =0.012) and malignant lymphoma (HR 1.22, $P$ =0.049). Neither MTX nor biological agent use was a significant risk factor for overall malignancies or malignancies at specific sites.
**Conclusions:** Higher disease activity was a risk factor for overall malignancies, lung cancer and malignant lymphoma in Japanese patients with RA. However, treatment with MTX and biological agents was not a risk factor for malignancy. These results suggest that tight control of RA disease activity would protect against the occurrence of malignancies in patients with RA.
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**Disclosure of Interest:** N. Sugimoto: None declared, E. Tanaka Speakers bureau: ET has received speaker fees or consulting fees from Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Santen Pharmaceutical., E. Inoue: None declared, Y. Shimizu: None declared, K. Shidara: None declared, A. Nakajima: None declared, A. Taniguchi: None declared, S. Momohara Speakers bureau: SM has received speaker fees from Abbott, AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi Tanabe, Pfizer, Takeda, and Teijin., H. Yamanaka Speakers bureau: HY has received speaker fees from Abbott, AbbVie, Asahikasei, Astellas, AstraZeneca, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, GlaxoSmithKline, Janssen, Mitsubishi Tanabe, MSD, Nippon Kayaku, Pfizer, Santen, Taishotoyama, Takeda, and Teijin.
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## FRI0144 ANEMIA IS A MORE COMMON SYMPTOM IN LATE-ONSET RA COMPARED TO YOUNG-ONSET RA AND IS STRONGER RELATED TO IMPAIRED KIDNEY FUNCTION

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**Background:** Rheumatoid arthritis is an inflammatory musculoskeletal disease, which presents mainly by joint swelling and pain, but also with a variety of other symptoms. Anemia has already been detected as additional marker for disease activity but there is no evidence about the differences between young- (YO) and late-onset (LO) (onset of disease after 60 years of age) RA patients.
**Objectives:** To investigate differences in the prevalence of anemia between YO-RA and LO-RA over the course of the disease and find factors that can be linked to anemia.
**Methods:** We selected an inception cohort of RA patients that was treated with DMARDs for at least a year from a prospective longitudinal database and used data of the first 20 blood draws of these patients, which were performed over up to 7 years of disease course. We used longitudinal, logistic regression and chi-square analyses to determine different aspects of anemia. We evaluated the risk for developing anemia, as well as factors associated with different types of anemia based on the mean corpuscular volume, the mean haemoglobin, kidney function, and disease activity.



**Results:** 326 RA patients were included in this study, 126 patients were late-onset RA (mean±SD: age: 69.4±6.6 years, 71% female, glomerular filtration rate (GFR) 72.5±15.6ml/min, haemoglobin (HB) 13.1±1.3g/dl, 47% rheumatoid factor (RF) positive and 42% anti-citrullinated antibodies (ACPA) positive) and 200 patients young-onset RA (mean±SD: age: 47.4±9.6 years, 75% female, glomerular filtration rate (GFR) 86.6±16.5ml/min, haemoglobin (HB) 13.3±1.4g/dl, 55.5% RF positive and 50% ACPA positive). At baseline there was no significant difference in composite measures of disease activity, however LO-RA showed significant higher acute phase reactants and swollen joints and lower GFR than YO-RA. Over the observation period there was a significant higher prevalence of anemia in LO than in YO (23.4% vs. 17.6%), this relates to an odds ratio (OR) of 1.4 (CI: 1.2–1.7, $p<0.001$). When using the time point of the lowest haemoglobin level, there was even a higher OR of 1.67 (1.09–2.54) for LO to have anemia. 45% of YO have at least one incident episode of anemia over the follow-up period, whereas this is the case in 54% of LO (p=0.03). This difference increased when looking at the very late-onset patients (age at onset >75years, n=20) to 70%. Anemia was present during 24.2±31.5% versus 17.6±27.6% of the observed time period. Haemoglobin levels were also significantly lower in patents with later onset of RA ($p<0.001$).
Normocytic normochromic anemia tended to be more prevalent in very-late-onset RA. (see figure 1A). Among patients with anemia impaired kidney function (GFR<60ml/min) was observed in 26% of LO patients and 47% of very-late-onset patients, which was significantly higher compared to 3% in YO (p=0.015; figure 1B).
**Conclusions:** RA patients with late-onset disease show a greater risk of anemia. Anemia in late-onset RA patients is more strongly associated with decreased kidney function, and anemic episodes are longer and more severe.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2410

## FRI0145 MANAGEMENT OF GOUT IN PRIMARY CARE: WHAT ARE THE FACTORS ASSOCIATED WITH ADHERENCE? RESULTS FROM THE ADAGIO COHORT

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**Background:** According to EULAR recommendations, long term management of gout encompasses pharmacological and non pharmacological treatments. Patient education and adherence to medication and lifestyle advices are key factors of management [1].
**Objectives:** An observational and cross-sectional study was conducted by general practitioners (GP). The main objective was to determine factors associated with adherence to treatment of gout. Secondary objectives were to analyse adherence to lifestyle recommendations and achievement of therapeutic goal for uricaemia, and also to describe the perception of the disease and treatments.
**Methods:** Adult patients with gout, taking a urate lowering therapy for more than 3 months, were included by 630 GP. Data were collected during a unique visit. Adherence to treatment was assessed through a 5-item self-questionnaire [2,3]. Factors associated with adherence were analysed using a multivariate logistic regression. Adherence to lifestyle recommendations were assessed via questions on alcohol, beer and soda intake. Patients also completed the Brief Illness Perception Questionnaire (B-IPQ) [4] and the Beliefs about Medicines Questionnaire (BMQ) [5].
**Results:** 1441 patients with gout (85% male, age: 64.4 ± 11.4 years) were retained in the analysis. Main symptoms were pain and swelling (85%), podagra (60%) and erythema (49%). Mean serum uric acid level was 63.4 ± 16.4 mg/L (42% were below the therapeutic goal of 60 mg/L); 85% of patients were overweighted (including 38% obese); 70% had hypertension; 62% had dyslipidemia; 24% had type 2 diabetes; they took 4.9 ± 3.5 tablets daily in average. Overall, 80% of patients were assessed as adherent to medicines and 32% to lifestyle recommendations. Main factors associated with a good adherence to medicines were: being more than 70 years (OR=1.9; CI95%: [1.2–2.9]), having an uricaemia below the therapeutic goal (OR=1.8; CI95%: [1.3–2.5]), regularly checking uricaemia (OR=1.5; CI95%: [1.0–2.1]), and taking few tablets daily (OR/unit=0.9; CI95%: [0.9–1.0]). Besides, good adherence to medicines was associated with a better perception of the disease and treatments (lower impact on quality of life, better control of gout) and a better relationship with health care professionals.
**Conclusions:** The ADAGIO study indicates that a good adherence to the pharmacological treatment of gout is associated with regular uricaemia controls and achievement of the recommended therapeutic goal, i.e. maintaining serum uric acid below 60 mg/L [1]. The data suggests that patients under multiple medications would benefit from special attention to help improving gout management.
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**Disclosure of Interest:** R.-M. FLIPO Grant/research support from: Menarini, L. Martinez Grant/research support from: Menarini, P. Maigret Employee of: Menarini, G. Reach Grant/research support from: Menarini
**DOI:** 10.1136/annrheumdis-2016-eular.3178

## FRI0146 INCIDENCE RATE AND THE RISK OF HERPES ZOSTER IN PATIENTS WITH RHEUMATOID ARTHRITIS USING JAPANESE HEALTH INSURANCE DATABASE

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**Background:** A high risk of herpes zoster (HZ) in patients with rheumatoid arthritis (RA) has been reported[1]. The risk of HZ in Asian patients, especially Japanese, on tofacitinib was higher than that of Western countries [2]. It is essential for rheumatologists to diagnose and manage HZ early not only to prevent post-herpetic neuralgia but also hamper developing cutaneous dissemination and visceral end organ involvement. However, there are no reports investigating the incidence rate (IR) and risk of HZ in RA patients using large population-based data in Asia.
**Objectives:** To compare the IR of HZ between RA cases and non-RA cases, and estimate the risk of HZ during three years using Japanese health insurance database.
**Methods:** This retrospective longitudinal population-based study was conducted using claims data provided by the Japan Medical Data Center Co., Ltd. We defined individuals as RA cases if they met all of the following: 1) had at least 6 months of continuous enrollment in the health insurance database; 2) had at least one RA diagnostic code (ICD10 codes; M05, M060, M062, M063, M068, and M069); 3) had at least one prescription of disease-modifying antirheumatic drugs (DMARDs) between January 2005 and December 2013; and 4) were 18 years old or older (RA group, n=6,712). Among individuals who met above criteria 1), but did not meet 2) to 4), we selected age- (±5 years), gender-, calendar year of the observation start, and observation length-matched non-RA cases at 1:5 ratio (RA cases: non-RA cases) (non-RA group, n=33,560). The start of the observation in the RA group was defined by the month of the first prescription of DMARDs with RA diagnostic code after the first 6 months of the enrollment in the health insurance database. Observation stopped either 3 years after the start of the observation, or on the month individuals withdrew from the health insurance or on December 2014, whichever came first. Patients who had the ICD 10 codes for HZ (B02) and were prescribed antivirus drugs for HZ at least one time during observation term were deemed as developing HZ. We compared the IR of HZ between the two groups and investigated the association between RA and HZ using conditional logistic regression analysis.
**Results:** The median age was 52, and 75.6% were female in the both groups. Biological DMARDs were prescribed in 13.9% of RA cases, methotrexate in 58.3%, synthetic DMARDs other than methotrexate in 46.9%, and oral corticosteroids in 35.0% at baseline. The IR of HZ in the RA group [14.1/1,000 person-years (PY)] was significantly higher than that of the non-RA group (8.3/1,000 PY). The odds ratio [95% confidence interval] of RA for HZ was 1.5 [1.2–1.8] after adjusting for past history of HZ, pulmonary and renal comorbidities at baseline, and use of oral corticosteroids at baseline.
**Conclusions:** This study revealed that patients with RA had significantly higher risk of HZ than non-RA individuals using health insurance database for the first time in Asia.
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**Acknowledgement:** This work was supported by the research grant from the Ministry of Health, Labour, and Welfare, Japan.
**Disclosure of Interest:** R. Sakai Grant/research support from: Abbvie Japan Co. Ltd., Astellas Pharma Inc., Bristol Meyears Squibb, Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Mitsubishi Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., and UCB Japan, S. Kasai: None declared, F. Hirano: None declared, M. Kihara: None declared, W. Yokoyama: None declared, M. Tsutsumino Grant/research support from: Abbvie Japan Co. Ltd., Astellas Pharma Inc., Bristol Meyears Squibb, Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Mitsubishi Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., and UCB Japan, K. Nagasaka Grant/research support from: Abbvie Japan Co. Ltd., Astellas Pharma Inc., Bristol Meyears Squibb, Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Mitsubishi Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., and UCB Japan, R. Koike: None declared, H. Yamanaka Grant/research support from: Chugai Pharmaceutical Co. Ltd., Astellas Pharma Inc., Bristol-Meyers Squibb, AbbVie Japan Co. Ltd., Daiichi-Sankyo, Mitsubishi-Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., UCB Japan, Consultant for: Chugai Pharmaceutical Co. Ltd., Astellas, Bristol-Meyers Squibb, AbbVie Japan Co. Ltd., Daiichi-Sankyo, Mitsubishi-Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., UCB Japan, N. Miyasaka: None declared, M. Harigai Grant/research support from: Abbvie Japan Co. Ltd., Astellas Pharma Inc., Bristol Meyears Squibb, Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Mitsubishi Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., UCB Japan, Pfizer Japan Inc., Sanofi-Aventis KK., Santen Pharmaceutical Co., Ltd and Sekisui Medical Co., Ltd
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## FRI0147 SERUM RANKL LEVEL AND FRACTURE RISK USING FRAX TOOL IN POST-MENOPAUSAL RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Osteoporosis and related fragility fractures are one of the most common complications seen in patients with rheumatoid arthritis (RA). Increased osteoclast activity contributes to local and systemic abnormalities of bone remodelling, including bone erosions and focal and systemic osteoporosis. Receptor Activator of Nuclear Factor Kappa Beta Ligand (RANKL) is essential for osteoclast formation, function, and survival, and it is a key mediator of increased osteoclast activity in RA. As fracture prevention is the major target in prevention and diagnosis of osteoporosis, we are evaluating fracture risk in RA patients using the fracture risk assessment (FRAX) tool developed by the WHO. Moreover, we are searching for a potential association between serum RANKL and fracture risk aiming at identifying patients at high risk of fractures.
**Objectives:** To assess the level of serum RANKL in post-menopausal rheumatoid arthritis patients and its correlation with fracture risk using Fracture Risk Assessment Tool (FRAX).
**Methods:** We recruited 116 individuals (78 postmenopausal RA patients and 38 age-matched post-menopausal control subjects). All patients and controls were not receiving osteoporosis treatment. We measured serum RANKL, C reactive protein (CRP) and Rheumatoid Factor (RF). Disease activity score (DAS)-28 was used to assess RA activity. We measured bone mineral density (BMD) at lumbar spine (L1- L4), right femur neck and right forearm radius with dual-energy X-ray absorptiometry. We have calculated the absolute 10-year major osteoporotic fracture and hip fracture risks with FRAX tool.
**Results:** Mean age was 54.83± 6.6 years in RA patients versus 55.05± 6.2 years in controls. Mean body mass index (BMI) of the patients was 30± 5.6. Mean disease duration was 10.53± 6.6 years. Mean DAS was 3.94± 1.3, mean CRP level was 8± 5.2 mg/L and 76.9% of patients were on steroids. Two of the patients were smokers and no one was taking alcohol. One of the patients reported history of fragility fracture at the forearm but no one reported parent hip fracture. Serum RANKL was significantly higher in RA patients versus controls (971.0pmol/L vs. 177.85 pmol/L, P value $<0.0001$). Mean BMD of RA patients at lumbar spine was 0.990± 0.2 g/cm$^2$, at femur neck was 0.870±0.19 g/cm$^2$ and at forearm was 0.568± 0.14 g/cm$^2$. Prevalence of osteoporosis in RA patients at lumbar spine was 34.6%, at femur neck was 23.1% and at forearm was 42.3%. Risk of major osteoporotic fracture in RA patients was 8.62% and the risk of hip fracture was 3.3%. There was a highly significant positive correlation between serum RANKL and the risk of major osteoporotic fracture (r =0.736, P value$<0.0001$). There was a highly significant positive correlation between serum RANKL and the risk of hip fracture (r =0. 859, P value $<0.0001$). Serum RANKL was negatively correlated with femur neck BMD (r= -0.529, P value $<0.001$) and negatively correlated with forearm BMD (r= -0.289, P value $<0.01$). No significant correlation was found between serum RANKL and BMD at lumbar spine, RF, CRP level or DAS-28.
**Conclusions:** In post-menopausal RA patients, increased serum RANKL level is associated with an increased risk of major osteoporotic and hip fractures. Therefore, serum RANKL could be a marker to identify post-menopausal RA patients at high risk of fractures.
**Disclosure of Interest:** None declared
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## FRI0148 DETERMINATION OF THE LIPID PROFILE IN ACTIVE DISEASE LEADS TO INCORRECT CARDIOVASCULAR RISK PREDICTION IN EARLY RA PATIENTS

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**Background:** Rheumatoid arthritis (RA) is associated with increased cardiovascular morbidity and mortality. This cardiovascular risk is mainly determined by the lipid profile, which may change during the course of the disease (1). For a proper cardiovascular risk assessment stable lipid values should be used and in cardiovascular risk prediction models mostly lipid ratios are applied.
As the increased cardiovascular risk is already present at the time of diagnosis, it is important to initiate cardiovascular risk management as early as possible in the disease (2). However, first it is necessary to know if measurement of the lipid profile is adequate (i.e. stable lipid values) early in the disease.
**Objectives:** The aim of this study was to 1) investigate the change in lipid profile during the first 4 weeks of RA treatment 2) analyse the association between the alteration in the lipid profile and the change in ESR.
**Methods:** In 66 consecutive DMARD-naive early RA patients lipid profile and disease activity were measured. This was repeated after four weeks of treatment with methotrexate (3 weeks 10 mg, 4th week 17.5 mg) and prednisolone (30 mg tapered to 10 mg). Lipid profile assessment comprised TC, HDL-C, LDL-C, triglycerides and apolipoprotein A and B (Apo A and Apo B). Disease activity was assessed by the disease activity score of 44 joints (DAS44), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Patients on statins were excluded. The change in lipid profile (week 4 minus week 0) versus change in ESR was analysed in 2 patient groups: a group with high (median -31.0 mm/hour) and a group with low (median -3.0 mm/hour) improvement in ESR.
**Results:** Three patients on statins were excluded, analyses were thus performed on 63 early RA patients. All components of the lipid profile increased significantly during treatment, except for Apo B. In addition, ratios of lipid values, particularly the TC/HDL cholesterol ratio improved significantly (table 1). The group with high ESR versus the group with low ESR improvement had a significantly higher increase in TC, HDL-C, LDL-C and Apo A levels. The spearman rho test showed a correlation between delta ESR and delta TC, HDL, LDL and Apo A of r=0.456, r=0.313, r=0.507 and r=0.281, respectively (all p$<0.05$).

Table 1

| | Baseline samples | Week 4 samples | P-value |
|---|---|---|---|
| Total cholesterol, mmol/l (mean, SD) | 4.9 (1.1) | 5.6 (1.3) | 0.000 |
| Triglycerides, mmol/l (mean, SD) | 1.3 (0.6) | 1.4 (0.8) | 0.023 |
| HDL, mmol/l (mean, SD) | 1.3 (0.4) | 1.9 (0.6) | 0.000 |
| LDL, mmol/l (mean, SD) | 3.1 (0.9) | 3.3 (1.1) | 0.020 |
| Apo A, g/l (mean, SD) | 1.4 (0.3) | 1.8 (0.3) | 0.000 |
| Apo B, g/l (median, IQR) | 0.9 (0.8–1.1) | 0.9 (0.8–1.1) | 0.740 |
| TC/HDL ratio (mean, SD) | 4.0 (1.4) | 3.2 (1.1) | 0.000 |
| Apo B/ Apo A ratio (mean, SD) | 0.7 (0.2) | 0.6 (0.2) | 0.007 |

**Conclusions:** Lipid levels increased significantly after four weeks of methotrexate and prednisolone treatment after RA diagnosis and this change is associated with the improvement in ESR. In both groups ratios of lipid values improved substantially.
Hence, cardiovascular risk management in early arthritis should be postponed until low disease activity has been obtained, as assessment during active disease leads to an inappropriately high cardiovascular risk estimation.
**References:**
[1] Nat Rev Rheumatol 2013 Sep;9(9):513–23.
[2] Arthritis Res Ther 2010;12(4):R158.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3382

## FRI0149 ATTRIBUTES OF MAXIMUM RELEVANCE IN THE CHOICE OF A BIOLOGICAL DMARD IN THE FIRST LINE TREATMENT OF RHEUMATOID ARTHRITIS. ACORDAR 2015 PROJECT

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**Background:** According to clinical guidelines, treatment with a DMARD should be initiated as soon as possible, and any patient who does not improve with at least one relevant synthetic DMARD is a candidate for a biological one. However, up to one third of the patients treated with a biological DMARD do not accomplish the therapeutic objective.
**Objectives:** To identify and assess the attributes of the biological DMARDs which determine the most suitable treatment of patients with RA.
**Methods:** We performed a systematic search with the following MeSH terms: rheumatoid arthritis, biologic, DMARD, characteristic, efficacy, safety, side effects, pharmacology, route–administration, adherence y cost. More than 500 publications were reviewed, from which we selected 77 attributes: 7 about general aspects, 5 about pharmacological aspects, 18 about efficacy, 31 about safety, 6 administration aspects and 10 related with cost. Between May and September 2015, 12 meetings were held, followed by a Delphi process of 2 rounds in which the degree of importance was awarded to each attribute on a Likert scale from 1 (minimum) to 9 (maximum). The consistency and concordance of the agreement were determined and they were circulated, obtaining the percentage supported for each one of them.
**Results:** 83 Spanish rheumatologists participated, reaching a high degree of agreement with the attributes, 75 with a high importance (97.4%) and none of low importance. Fifteen attributes were ratified by all the participants:
– Product with approved indication in RA as first-line biological.
– Product recommended in the guidelines as first-line biological.
– Product that shows efficacy following the failure of another biological.
– Treatment accompanied by a reduction in articular damage progression.
– Treatment that reduces comorbidities associated with RA.
– Treatment characterised by a sustained long-term response.
– Safe product (globally).
– Proven long-term safety.

– Treatment with a low incidence of serious infections.
– Product that does not increase the incidence of solid malignancies.
– Product that does not increase the incidence of haematological neoplasms.
– Safe product in patients with cardiovascular pathology.
– Safe product in patients with interstitial pulmonary disease.
– Product that has demonstrated a reduction in mortality.
– Product that presents a scant incidence of serious adverse events.

**Conclusions:** There was a high degree of agreement with the selected attributes, none of which were regarded as being of low importance; 15 of them received the full support of the work group. These attributes would help to define the ideal profile of the biological DMARD following the failure of a synthetic or previous biological DMARD.

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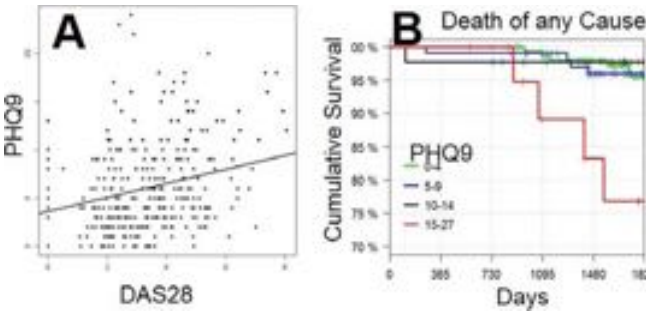
## FRI0150 DEPRESSION, INFLAMMATION AND MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Patients with rheumatoid arthritis (RA) have a high prevalence of depressive symptoms and an increased mortality.
**Objectives:** The current prospective follow-up study investigates prevalence of depression, its association with inflammation and mortality in RA patients.
**Methods:** 764 consecutive patients attending the rheumatology outpatient department of the University Hospital Würzburg underwent a comprehensive cardiovascular (CV) risk assessment. Inflammation in RA patients was characterized by DAS28 and CRP. Quality of life and depressive symptoms were investigated by SF-36 and PHQ-9 (range 0–27 score points), respectively. A PHQ score $\geq$15 points is considered indicative for severe depressive symptoms.
**Results:** 352 subjects suffered from rheumatoid arthritis (RA: 79.5% female, 64.9% RF positive, mean age 54.3 (SD 14.3)), Severe or moderate depressive symptoms were prevalent in 6.6%, respectively 14.4% of RA patients. DAS28, but not CRP, was significantly associated with the prevalence of depressive symptoms (r=0.26 (p<0.001), figure A, table 1).

| PHQ9 | DAS28 | | | |
|---|---|---|---|---|
| | Mean | SD | Median | IQR |
| 0–4 | 2.99 | 1.35 | 2.8 | 2.05–3.87 |
| 5–9 | 3.45 | 1.53 | 3.56 | 2.41–4.5 |
| 10–14 | 3.81 | 2.07 | 4.1 | 2.44–4.93 |
| 15–27 | 4.31 | 1.7 | 4.2 | 2.85–4.86 |

Patients with severe depressive symptoms (PHQ 9 $\geq$15) had an increased a HR of 6.42 (95% CI, 2.04 – 20.2, p=0.004) for mortality compared to patients with a PHQ $\leq$14 (figure B).




**Conclusions:** DAS28 in RA patients was associated with severity of depressive symptoms. Severely depressed patients had an increased mortality.

**Disclosure of Interest:** None declared
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## FRI0151 THE ASSOCIATION BETWEEN AGE AND INFLAMMATORY FINDINGS ON HAND AND FOOT MRI IN EARLY ARTHRITIS, RHEUMATOID ARTHRITIS AND SYMPTOM-FREE CONTROLS

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**Background:** A recent MRI study performed in symptom-free persons from the general population showed that MRI-detected inflammation is present in the general population and that the prevalence increases with age.[1] The relation between age and the severity of MRI-detected inflammation is unexplored in early arthritis patients. Therefore this study explored the association between age and MRI-detected inflammation in early arthritis and early rheumatoid arthritis (RA). Furthermore, the localization of inflammatory findings in RA-patients presenting at young and old age were compared.
**Methods:** Unilateral, contrast-enhanced 1.5T MRI of the metacarpophalangeal, wrist and metatarsophalangeal joints was performed at baseline in 589 patients of the Leiden Early Arthritis Clinic (EAC); of these 230 patients fulfilled the 2010-criteria for RA at presentation. MRIs were scored according to RAMRIS. The sum of the bone marrow edema, synovitis and tenosynovitis scores yielded the total MRI-inflammation score. The association with age in early arthritis patients and RA patients was compared to the association previously observed in 193 symptom-free controls.[1] Linear regression analyses were performed on log-transformed MRI-inflammation scores. The localization of the inflammation was studied in different age groups (<40, 40–60, >60 years).
**Results:** Patients with early arthritis and RA-patients had more severe MRI-inflammation than symptom-free controls, they had respectively 2.6 (95%CI 2.3–3.0 p<0.001) and 3.7 (95%CI 3.2–4.3 p<0.001) times more inflammation. A higher age was associated with more MRI-detected inflammation in both early arthritis and RA-patients (in both groups: 1.03 fold increase in inflammation per year, p<0.001). These effect sizes were similar to the association observed in symptom-free controls (1.03 fold increase in inflammation per year, p<0.001). The interaction term between age and group (symptom-free controls and (rheumatoid) arthritis) was non-significant, demonstrating that the effect of age was similar in (rheumatoid) arthritis and symptom-free controls. The localization of MRI-inflammation was similar in RA-patients of the different age groups, indicating no different preferential locations in different age groups.
**Conclusions:** Older patients have more MRI-detected inflammation. Although early arthritis and RA patients have more severe inflammation than symptom-free controls, the effect of age is similar in early arthritis, RA and symptom-free controls. Thus, the effect of age is not disease specific. This study indicates that age should be considered when interpreting MRI-results.

**References:**

[1] Mangnus L, van Steenbergen HW, Reijnierse M, van der Helm-van Mil AHM. OP0218 Prevalence of MRI-Detected Inflammation in Symptom-Free Persons from the General Population and the Generation of Age-Dependent Ramris-Based Reference Values. Ann Rheum Dis. 2015;74(Suppl 2):153–153. doi:10.1136/annrheumdis-2015-eular.4414.

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## FRI0152 RELATIONSHIP BETWEEN BIOLOGICAL DMARDS TREATMENT AND COMPLICATIONS AFTER SURGICAL TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Biological DMARDs (bDMARDs) have changed prognosis of rheumatoid arthritis (RA) dramatically and it is possible to reduce RA synovitis and to inhibit progression of joint destruction using bDMARDs. However, surgical treatment such as arthroplasty is still the important procedure in especially long-standing established RA patients. Information about safety and specific adverse events in surgical treatment under bDMARD treatment is lacking.
**Objectives:** This retrospective study investigated difference of complications between surgical treatment under bDMARDs treatment and that under conventional synthetic DMARDs (csDMARDs) treatment in RA patients.
**Methods:** 122 surgical operations for RA patients except operation to treat infectious conditions in our institute from 2010 to 2015 were included. 45 operations were performed under bDMARDs treatment (BG) and 77 operations were performed under csDMARDs treatment (nonBG). Patients' characteristics, usage of dDMARDs, surgical site infection (SSI) and delayed wound healing (DWH) were compared between two groups. Time courses of hemoglobin (Hb), total protein, DAS28-CRP, SDAI and mHAQ after surgical operations were also compared between two groups.
**Results:** Mean age in BG was significantly younger than that in nonBG (60.1 years old vs. 66.9 years old). MTX usage in BG was significantry higher than that in nonBG (82.2% vs. 64.9%). 48 total knee arthroplasties, 14 total hip arthroplasties, 17 operation in hand and wrist, 29 operations in foot and ankle and 14 others were included. Used bDMARDs were etanercept in 24 cases, infliximab in 7 cases, abatacept in 6 case, adalimumab in 4 cases, tocilizumab in

3 cases and golimumab in 2 cases. Mean duration between stopping bDMARDs and surgical operation was 20.5 days. There was no significant difference in occurrences of SSI cases between two groups (BG: 0.0%, nonBG: 1.3%). There was no significant difference in occurrences of DWH between two groups (BG: 4.4%, nonBG: 11.7%). SDAI and mHAQ at 1–2 months after operation in nonBG were better than that in BG. mHAQ and recovery of Hb in nonBG were also better than that in BG. A SSI occurred in operation of ankle (1/29, 3.4%). DWH were frequently observed in foot and ankle operations (6 cases, 20.7%) and hand and wrist operations (3 cases, 17.6%) (Fig1).

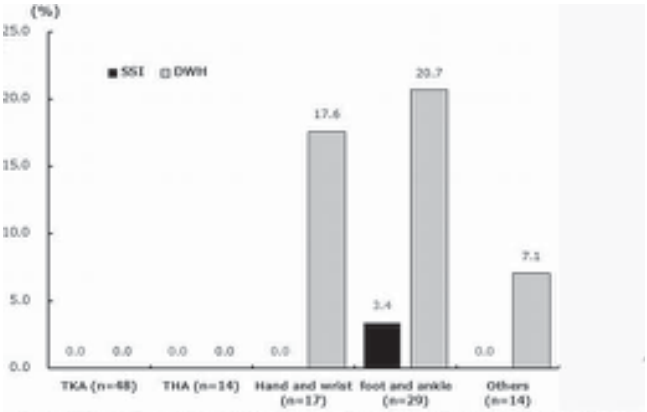



Fig 1. Rates of Complications after Surgical Operation in Respect to Surgical Regions

SSI: Surgical Site Infection, DWH: Delayed Wound Healing, TKA: Total Knee Arthroplasty, THA: Total Hip Arthroplasty

**Conclusions:** There were no significant differences in SSI and DWH between BG and nonBG. mHAQ and Hb recovery after surgical operations in BG were slightly inferior to that in nonBG. This may be due to RA flare after operation in BG or differences of characteristics of patients. It was suggested that surgical region influences the occurrences of SSI and DWH and more complications were observed in foot and ankle operations.
**Disclosure of Interest:** None declared
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### FRI0153 RELATIONSHIP BETWEEN SERUM OXYTOCIN LEVELS AND DISEASE ACTIVITY, DEPRESSIVE STATE, ADL, AND QOL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Oxytocin, which is also called a happy hormone, has been reported to be related to various conditions including depressive state. However, the positioning of oxytocin in rheumatoid arthritis (RA) remains unclear.
**Objectives:** The objective of this study was to investigate the relationship between serum oxytocin levels and disease activity, depressive state, activity of daily life (ADL), and quality of life (QOL) in RA.
**Methods:** The study included 20 patients with RA who received treatment with a biological agent. We measured the following items before and at 6 months after the start of treatment. The baseline characteristics included the age, sex, prednisolone dose, methotrexate dose, duration of disease, anti-cyclic citrullinated peptide antibody (anti-CCP antibody), rheumatoid factor (RF), serum matrix metalloproteinase-3 (MMP-3), erythrocyte sedimentation rate, and C-reactive protein (CRP). The disease activity of rheumatoid arthritis was assessed using the Simplified Disease Activity Index (SDAI), depressive state using Hamilton Depression Rating Scale (HAM-D), ADL using the Health Assessment Questionnaire (HAQ), and QOL using the 36-Item Short Form Health Survey (SF-36). Serum oxytocin levels were determined by enzyme-linked immunosorbent assay (ELISA). The correlation between each item and the serum oxytocin levels were examined.
**Results:** The serum oxytocin levels before the start of treatment were correlated with RF (r=–0.529), HAQ (r=0.446), HAM-D (r=0.508), and among the 8 categories of the SF-36, physical function (r=–0.676), role function (physical) (r=–0.801), pain (r=–0.506), general health perception (r=–0.787), role function (emotional) (r=–0.844), and mental health (MH) (r=–0.516). On the other hand, the serum oxytocin levels did not correlate with the SDAI (r=–0.078). The serum oxytocin levels after the start of treatment were correlated with the age (r=–0.549), SDAI (r=–0.539), HAQ (r=0.813), HAM-D (r=0.584), and all of the SF-36 categories except for MH (r=0.038) ($r>0.4$). Other items did not correlate to the serum oxytocin levels.
**Conclusions:** The serum oxytocin levels before the start of treatment were correlated with depressive state, ADL, and QOL but not with disease activity. Those after the start of treatment were correlated with the SDAI, depressive state, ADL, and QOL.
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## Rheumatoid arthritis - anti-TNF therapy

### FRI0154 ARE THERE NEGATIVE EFFECTS ON DISEASE ACTIVITY AND FUNCTION ASSOCIATED WITH FAILED ANTI-TNF DOSE REDUCTION STRATEGIES FOR RA PATIENTS?

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**Background:** We have previously described a strategy for Tumour Necrosis Factor inhibitor (TNFi) dose reduction (TDR) for patients with rheumatoid arthritis (RA) that selects patients with “deep remission” using combined clinical and ultrasound (US)[1].
**Objectives:** The aim of this study was to assess the consequences of this TDR strategy [1] on the HAQ, DAS28-CRP and Area Under the Curve of CRP ($AUC_{CRP}$) after follow-up (mean 28 months).
**Methods:** A longitudinal observational study was performed. Patients with RA (ACR-EULAR 2010), on TNFi for >1 year, not taking oral corticosteroids, DAS28 ≤2.6 for >6 months and absent power Doppler synovitis on US underwent TDR by one third. Patients failing TDR (clinically/on US) were re-escalated to full dose. Patients were divided into 3 groups: Non-reducers (group A), sustained dose reducers (group B) and failed dose reducers (group C). We investigated the initial (TNFi start date) and the last HAQ, DAS28 and $AUC_{CRP}$, as well as before and after TDR.
**Results:** 152 patients with RA receiving TNFi were included. Between Oct 2011 & May 2015, 67 (44%) underwent TDR. 3 patients were lost to follow-up. Dose reducers have been followed-up for a mean 30.5 months after TDR. A total of 29 (45%) failed the TDR after a mean (SD) of 9.5 (7.9) months. By a mean (SD) of 22.4 (11.6) months following dose re-escalation, 27 (93%) continued to receive their TNFi, while 2 (7%) had switched to a different biologic.
Baseline characteristics of all groups were similar. However, we found that the initial HAQ score on starting TNFi was significantly higher for group A compared to groups B and C (mean 1.59 versus 0.95 and 1.28, respectively, $p<0.05$) and was higher for group C compared to group B ($p=0.05$).
When compared before and after reduction, both groups B and C showed a similar pattern of functional capacity and $AUC_{CRP}$. Nevertheless, group B had lower last DAS28 ($p<0.05$). While analysing the most recent DAS28 of group C following dose re-escalation, 32% had achieved DAS28 remission, 20% developed lower (LDA), 44% moderate (MDA) and 4% severe disease activity (SDA).
Finally, we assessed the changes over time of DAS28 and HAQ scores. Group B had a higher DAS28 reduction then groups A and C (mean 3.6 vs. 2.43 and 2.75, respectively) ($p<0.05$), who both had similar changes. Nonetheless, HAQ score changed similarly between all patients.
**Conclusions:** RA patients who fail dose reduction appear to have a higher DAS28 than those who were successful despite reintroduction of a standard dose of TNFi. However, in the majority of cases the level of DAS28 was <3.2 (LDA or better). Failed dose reduction did not appear to cause loss of functional capacity (HAQ) or a greater cumulative exposure to inflammation ($AUC_{CRP}$) compared to successful reduction. The functional capacity (HAQ) at TNFi initiation appears to predict the likelihood of successful dose reduction.
**References:**
[1] Marks JL et al. Does combined clinical and ultrasound assessment allow selection of individuals with rheumatoid arthritis for sustained reduction of anti-tumor necrosis factor therapy? Arthritis Care Res. 2015 May;67(6):746–53.
**Disclosure of Interest:** L. Serhal: None declared, C. Holroyd: None declared, J. Zarroug: None declared, R. Armstrong: None declared, B. Davidson: None declared, N. Harvey: None declared, E. Dennison: None declared, C. Cooper: None declared, C. Edwards Grant/research support from: Abbvie, MSD, Samsung, Novartis, Lilly, Sandoz, Celltrion, Celgene, Pfizer, BMS, Roche, Consultant for: Consultant, Speakers bureau: Speaker events
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### FRI0155 FIFTY PERCENT OF PATIENTS WHO TAPERED TNF-BLOCKERS WHILE IN STABLE REMISSION ARE ABLE TO MAINTAIN A TAPERED REGIMEN AT 3 YEAR: LONG TERM FOLLOW-UP EXTENSION OF THE STRASS TRIAL

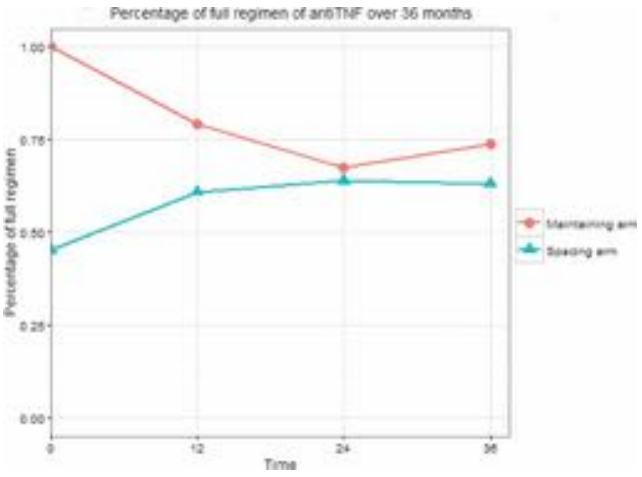
J. Sigaux, F. Bailly, L. Gossec, T. Alfaiate, F. Gandjbakhch, V. Foltz, J. Morel, E. Dernis, P. Gaudin, O. Brocq, J.-M. Berthelot, J.-C. Balblanc, X. Mariette, F. Tubach, B. Fautrel. *STRASS investigator group, Paris, France*

**Background:** Step-down strategy of spacing anti-tumor necrosis factor (TNF)

agents in patients with rheumatoid arthritis (RA) in remission are feasible in the context of randomized clinical trials (RCTs). However, we lack information on the long-term sustainability of a DAS driven step down strategy in clinical practice.
**Objectives:** This long-term extension study of a tapering RCT (STRASS trial (1)) aimed to assess the rate of patients who maintained the tapered regimen of etanercept (ETA) or adalimumab (ADA) in the in S-arm (progressive injection spacing) and M-arm (full regimen) and to evaluate the rate of treatment switch for inefficacy during the 3 years following the trial.
**Methods:** This observational 36 months follow-up considered all patients who completed the STRASS RCT (1). During the follow-up, the physicians were completely free of therapeutic decision making. Physicians were contacted between April and October 2015 and the data on the 36-month period after the end of trial retrospectively collected. The co-primary outcomes were the rate of patients who were taking their initial biologic at tapered regimen and the switch rate for loss of efficacy or safety. Percentage of full regimen anti-TNF intake was calculated over the 3 first years after trial end in both arms, using data from 12-monthly follow-up time points.
**Results:** 96 patients (70.1% of patients completing the RCT) had follow-up data available up to 3 years. At the end of the STRASS RCT (Table), 72 (75%) were in LDA or remission: 47 (48.9%) were taking ETA, 35 (36.5%), ADA, 2 (2.1%) another biologic and 12 (12.5%) no biologic because of remission. In addition, amongst patients still on their initial TNF blockers, 59/80 (74%) were treated at full regimen, 21/80 (26%) at tapered regimen. 3 years later, 65/96 (67.7%) were still on their initial anti-TNF: 73.1% vs 61.4% respectively in M and S-arm, p=0.23), either at full regimen 36/96 (38%), tapered regimen 29/96 (30%, 32% vs 29%, p=0.75), or completely stopped (11.5%: 5.8% vs 18.2%, p=0.06). 28 patients (29.2%, 25% vs 34.1%, p=0.33) had switched for another biologic. The mean percentage of full regimen of antiTNF over 3 years was 70.1±30.4%: respectively 74.3±28.2% vs 64.6±32.9% (p=0.19). DAS28-VS was not different between M and S-arm (2.42 vs 2.01 (p=0.23)).

Table 1. Disease activity and treatment strategy

| | | Initial M-arm (n=52) | Initial S-arm (n=44) |
|---|---|---|---|
| RCT end | LDA or remission, n (%) | 42 (80.8) | 30 (68.2) |
| | Treatment spaced or no biologic, n (%) | 0 (0) | 33 (75.0) |
| At 3 years | LDA or remission, n (%) | 31 (72.1) | 27 (73.0) |
| | Full dose of initial antiTNF, n (%) | 23 (44) | 13 (30) |
| | Spacing initial antiTNF without stop, n (%) | 15 (29) | 14 (32) |
| | No biologic, n (%) | 3 (6) | 8 (18) |
| | Switch rate over 3 years due to relapse, n (%) | 12 (32) | 10 (20) |




**Conclusions:** Maintenance of anti-TNF was high (68% at 3 years) in this cohort of patients with established RA treated according to the treat-to-target paradigm, with no difference between the 2 initial RCT arms. More than 1/3 of patients were received tapered anti-TNF regimen.
**References:**
[1] Fautrel B, ARD 2016;75(1):59–67
**Disclosure of Interest:** None declared
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## FRI0156 EFFECTIVENESS OF TUMOR NECROSIS FACTOR-INHIBITORS IN THE TREATMENT OF RHEUMATOID ARTHRITIS: A COMPARISON BETWEEN RANDOMIZED CONTROLLED TRIALS AND ROUTINE CLINICAL PRACTICE

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**Background:** Efficacy of Tumor Necrosis Factor (TNF)-inhibitors in treatment of rheumatoid arthritis (RA) measured in randomized controlled trials (RCTs) may not be fully generalizable to routine care owing to the stringent inclusion criteria [1].
**Objectives:** The objective of this study was to observe the effectiveness of TNF-inhibitors in Finland and to assess the real-world patients' potential eligibility for the RCTs.
**Methods:** RA patients starting a TNF-inhibitor as their first, second or third biologic treatment between 2004 and 2014 were identified from the National Register for Biologic Treatment in Finland (ROB-FIN), which is an observational cohort study. Effectiveness was measured using the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) response criteria and as the proportion of patients reaching Disease Activity Score 28 (DAS28) remission. Logistic regression was employed to identify any predictors of achieving EULAR response. The patients' baseline characteristics were compared against the inclusion criteria of 28 RCTs identified from two systematic reviews [2,3]. Treatment responses measured in the RCTs were compared to those achieved by routine care patients either eligible or not eligible for the same RCTs.
**Results:** Of the 4067 TNF-inhibitor treatment periods, 2259 periods from 1899 patients with valid baseline visit were included in this study. The included patients were predominantly female (73%) with a median age of 55. Adalimumab, etanercept infliximab, golimumab and certolizumab pegol accounted for 41%, 40%, 9.7%, 5.1% and 4.6% of the medication periods, respectively.
Moderate and good EULAR responses at 6 months were achieved by 69% and 40% of the users of the first biologic drug, respectively. ACR20, ACR50 and ACR70 responses were reached by 47%, 25% and 13%, respectively. DAS28 remission was reached by 45%. Concomitant use of methotrexate (MTX) was associated with higher odds of achieving at least moderate EULAR response (odds ratio 1.8, 95% confidence interval 1.1– 3.0) as compared to TNF-inhibitor monotherapy. Golimumab and certolizumab pegol were possibly more effective than infliximab, depending on whether the discontinuers were included in the analysis or not.
Only 3.8% to 50% of the patients would have been eligible for the included RCTs. The eligible patients had generally better ACR50 responses as compared to the non-eligible ones.
**Conclusions:** Different TNF-inhibitors were mostly equipotent in routine clinical practice, but the use of MTX co-therapy had a major influence on treatment response. The efficacy of TNF-inhibitors measured in RCTs cannot be directly generalized into Finnish routine healthcare.
**References:**
[1] Zink A et al. Arthritis Rheum 2006;54:3399–407.
[2] Nam JL et al. Ann Rheum Dis 2010;69:976–86.
[3] Nam JL et al. Ann Rheum Dis 2014;73:516–28.
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## FRI0157 A BASELINE PREDICTION MODEL FOR RESPONSE TO CERTOLIZUMAB-PEGOL: ROLE OF SYNOVIAL HISTOPATHOLOGY

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**Background:** Rheumatoid Arthritis (RA) is a severe joint disease characterized by chronic inflammation of synovial tissue. The inflammatory infiltrate within the rheumatoid synovium may be differently arranged, defining three distinct histopathotypes: myeloid (prevalent macrophage infiltration), lymphoid (B/T lymphocyte aggregates), and fibroid (fibroblastic infiltration with paucity of immune cells)[1]. Despite enabling a remarkable improvement of the disease's outcome, biologics are not effective in around 30–40% of treated patients. To date, no reliable pre-therapy predictors of response have been identified. The histological characterization of synovitis may represent a valuable tool in predicting response to biologics prior to treatment.
**Objectives:** To evaluate the role of synovial pathology in predicting clinical response to certolizumab-pegol combined with DMARD.

**Methods:** 32 RA patients fulfilling UK NICE criteria for starting TNF-inhibitors were enrolled at Barts Health Trust. Patients underwent a baseline US-guided biopsy prior to commencing certolizumab-pegol and a second biopsy after 12 weeks of treatment. Synovial immune infiltrate was assessed through immunohistochemical staining for CD3/CD20/CD68/CD138 and quantified using a semi-quantitative scoring system (0–4); accordingly, patients were classified as lymphoid (B cells aggregates grade $\geq$2), myeloid (sub-lining macrophages $>$2, +/– grade 1 aggregates) and fibroid (sub-lining macrophages $\leq$2). Therapeutic response was evaluated at 3 months according to EULAR criteria. Logistic regression model was performed to identify factors associated with good EULAR response at 3 months; the factors included clinical and biochemical parameters (ESR, CRP) as well as histopathology. The model selection was implemented using forward processes by AIC with 5-fold cross-validation (error=0.25).
**Results:** Out of 32 baseline biopsies, 53% were classified as lymphoid, 19% myeloid and 28% fibroid. Decrease in the number of sub-lining CD68-positive macrophages significantly correlated with clinical response ($p<0.05$). Baseline demographic and clinical parameters were comparable between the three histological groups; the CRP level was significantly higher in the myeloid compared to fibroid. The histological pathotype adjusted for baseline VAS pain and patient global health score, ESR, HAQ score and concomitant steroid treatment, was identified as a significant predictor of good response to certolizumab-pegol by forward selection (AUC 0.97, CI 0.92–1). The chance of achieving a good EULAR response to certolizumab-pegol was 91% lower in patients classified as a fibroid pathotype at baseline compared to myeloid/lymphoid pathotypes (OR 0.09, CI 0, 1.75).
**Conclusions:** Our study shows that patients with a fibroid pathotype at baseline are less likely to respond to Certolizumab-pegol. Moreover, we identified a novel prediction model of response based on clinical parameters and synovial histopathological classification. Histological assessment of synovial tissue may be of critical importance for developing personalised treatment for RA.
**References:**
[1] Pitzalis C et al, New learnings on the pathophysiology of RA from synovial biopsies. Curr Opin Rheumatol. 2013
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4218

## FRI0158 CLINICAL EVALUATION USEFULNESS OF STANDARDIZED PROTOCOL STRATEGIES OF DOSE REDUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION TREATED WITH BIOLOGIC THERAPIES. THE OPTIBIO STUDY

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**Objectives:** The OPTIBIO study is a clinical trial whose primary endpoint is to evaluate the proportion of patients that after one year are maintained in clinical remission with a dose reduction treatment regimen of biological therapy in patients with Rheumatoid Arthritis, and to evaluate if the proportion of patients in remission with new regimen dose of treatment is not inferior to patients in remission with standard dose regimen. In our present work, we describe the preliminary results obtained so far.
**Methods:** Open, randomized and controlled study of patients in clinical remission (DAS 28 $<$2.6 or SDAI $<$5 or ACR/EULAR 2011 criteria) at least 6 months followed in Third level Hospital Rheumatology Department. Patients treated with TNF inhibitors therapies (Etanercept, Infliximab, Adalimumab, Certolizumab, Golimumab), Tocilizumab and Abatacept.
Patients are assigned to two groups randomly. Intervention group: according to a standardized protocol of dose reduction of biological therapies. Control group: according to standard dose regimen. Flare is considered when DAS28$>$2.6 or SDAI$>$5 or ACR/EULAR criteria are not fulfilled. Patients are following during after a minimum period of one year and maximum period of 3 years. The frequency of visits is every 12 weeks.
**Results:** 58 patients have been included from 14 April 2014 to 11 January 2016. Forty-eight women (82,76%) and 10 men (17,24%) with an average age of 59,34 ± 11,28 years. Twenty-nine in standard regimen dose and 29 patients in dose reduction regimen. None of the patients had tender or swollen joints at the beginning. At baseline, ESR and CRP values were 16,84 mm/1hour y 0,22 mg/dl respectively. DAS 28-ESR value was 1,84 ± 0.72 and DAS28-CRP was 1.34 ± 0.26. Rheumatoid Factor is positive in 79.31%. Forty-one patients have erosive disease. Seventeen patients have presented a flare: 24,13% in control group and 34,48% in intervention group without statistical signification (p=0.5640). The characteristics of the patients are described in table 1. Statistic differences were not found.
**Conclusions:** Preliminary results show that dose reduction of biological therapies with a standardized protocol it does not seem to increase reactivation risk of disease activity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4839

**Table 1**

| | PACIENTS (WHICH STILL REMAIN IN CLINICAL REMISSION (41 PATIENTS)) | PACIENTS WHICH PRESENT A FLARE (17 PATIENTS)) | PACIENTS (WHICH PRESENT A FLARE (17 PATIENTS)) | | PACIENTS (WHICH STILL REMAIN IN CLINICAL REMISSION (41 PATIENTS)) | |
|---|---|---|---|---|---|---|
| | | | CONTROL GROUP (7 PATIENTS) | INTERVENTION GROUP (10 PATIENTS) | CONTROL GROUP (23 PATIENTS) | INTERVENTION GROUP (18 PATIENTS) |
| AVERAGE AGE | 60,22 ± 10,56 years | 57,23 ± 12,05 years | 55,57± 15,65 years | 55,40 ±15,22 years | 57,96 ± 11,55 years | 63,53 ± 8,66 years |
| SEX | 36[ 5,] | 12[ 5,] | 5[ 2,] | 7[ 3,] | 36[ 2,] | 18[ 4,] |
| AVERAGE TIME FROM RHEUMATOID ARTHRITIS DATE OF DIAGNOSIS TO BASELINE DATE | 172,10 months | 159,18 months | 156,43 months | 195,50 months | 167,91 months | 159,56 months |
| AVERAGE TIME FROM BASELINE DATE TO FLARE DATE | ——— | 52,41 months | 12,43 months | 11,80 months | ——— | ——— |
| DAS 28-ESR BASELINE | 1,96 ± 0,57 | 1,78 ± 0,64 | 1,86 ± 0,50 | 1,72 ± 0,62 | 1,92 ± 0,73 | 1,91 ± 0,63 |
| DAS 28-CRP BASELINE | 1,31 ± 0,25 | 1,43± 0,28 | 1,52 ± 0,39 | 1,37 ± 0,15 | 1,32 ± 0,21 | 1,29 ± 0,19 |
| POSITIVE RHEUMATOID FACTOR | 33 (80,36%) | 11 (64,70%) | 7 (100%) | 4 (40%) | 13 (77,27%) | 18 (94,73%) |
| EROSIVE DISEASE | 28 (68,29%) | 13 (76,47%) | 6 (85,71%) | 7 (70%) | 12 (54,54%) | 10 (62,31%) |

## FRI0159 PERSISTENCE WITH BIOLOGIC MONOTHERAPY IN COMPARISON WITH COMBINATION THERAPY WITH DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS; RESULTS FROM AN ONTARIO RHEUMATOID ARTHRITIS COHORT

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**Background:** Clinical evidence suggests concomitant treatment with a biologic Disease-Modifying Antirheumatic Drug (bDMARD) and a conventional synthetic DMARD (csDMARD), especially with methotrexate (MTX), has greater efficacy than treatment with a bDMARD as monotheapy in patients with rheumatoid arthritis (RA). However, not all patients are able to tolerate a csDMARD.
**Objectives:** Our objective was to compare the persistence of a bDMARD used as monotherapy, versus combination therapy in patients with active RA.
**Methods:** Physician data were collected from the Ontario Best Practices Research Initiative Rheumatoid Arthritis Registry (OBRI-RA), a clinical registry of RA patients followed in routine care. Inclusion criteria comprised of patients over age 18 years, active RA (defined as $\geq$1 swollen joint) and started on their 1st bDMARD within 30 days before registry enrolment, or started after enrolment. Combination therapy was defined as treatment with a bDMARD plus at least one csDMARD, while monotherapy was defined as treatment with only a bDMARD.
The primary outcome was persistence with 1st bDMARD therapy, which was defined as the length of time the patients continued to receive their first bDMARD therapy. Persistence of treatment was examined using Kaplan-Meier survival analysis. Patients were censored at date of 1st bDMARD stop, switch to another bDMARD or at date of last follow-up, whichever came first.
**Results:** Among 2591 RA patients, 701 patients started their 1st bDMARD within 30 days before cohort enrolment or after enrolment with the mean (standard deviation) of follow-up 1.9 (1.6) person-years. A total of 598 (85.3%) patients were on combination therapy, and 103 (14.7%) patients were on monotherapy. At baseline, there was a similar mean age, proportion of females between the two groups. A TNF$\alpha$ inhibitor was the biologic used in 22.6% and 14.5% of the monotherapy and combination group respectively.
The mean time to failure of 1st bDMARD was 4.3 years (95%CI: 3.7–4.9) and 4.6 years (95%CI: 4.3–4.8) in the monotherapy and combination group respectively. At 12 months follow-up, 74% (95%CI: 64–81) in the monotherapy group and 81% (95%CI: 77 -84) in the combination group remained on their first bDMARD (table 1).

**Table 1: Survival function (95% CI) for patients stopping their initial bDMARD therapy by year of follow-up for the monotherapy versus combination group in patients with active rheumatoid arthritis**

| Time (year) | Whole cohort N=701 | Monotherapy N=103 | Combination therapy N=598 |
|---|---|---|---|
| 1 | 0.80 (0.76-0.83) | 0.74 (0.64-0.81) | 0.81 (0.77-0.84) |
| 2 | 0.72 (0.69-0.76) | 0.67 (0.56-0.76) | 0.73 (0.69-0.77) |
| 3 | 0.69 (0.65-0.73) | 0.67 (0.56-0.76) | 0.70 (0.65-0.74) |
| 4 | 0.65 (0.61-0.70) | 0.64 (0.52-0.74) | 0.66 (0.60-0.70) |
| 5 | 0.60 (0.53-0.65) | 0.55 (0.38-0.69) | 0.61 (0.54-0.67) |

**Conclusions:** Our study demonstrates that a higher proportion of patients on monotherapy failed therapy at 12 months, and the mean time to treatment failure was shorter with monotherapy, but these results were not statistically significant. Although combination therapy is recommended, these real-world results suggest that patients who are unable/unwilling to continue on a csDMARD, bDMARD monotherapy can still provide an efficacious option.

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## FRI0160 ANTI-TNF THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS DOES NOT ATTENUATE CUTANEOUS TNF ACTIVITY FOLLOWING A TUBERCULIN SKIN TEST

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**Background:** Anti-TNF therapy has revolutionised treatment of rheumatoid arthritis (RA). This success is partly tempered by the substantially increased risk of granulomatous infectious diseases, particularly tuberculosis (TB). However the mechanisms underlying the effectiveness of the treatment are poorly understood. We used the tuberculin skin test (TST) as an in vivo challenge model to investigate whether TNF activity is attenuated by anti-TNF therapy in a prototypic cell mediated immune response.
**Methods:** 50 stable RA patients (treated with Adalimumab, Etanercept or Methotrexate) and healthy volunteers with immunological memory to TB antigens were identified using an interferon-gamma ELISpot of peripheral blood. TST or saline (controls) was injected into the forearm of study participants and 3mm punch skin biopsies were taken from the injection site after 72 hours. Samples were collected for RNA analysis and histology. Genome wide transcriptional profiling was performed to compare gene expression changes in response to the TST challenge between treatment groups. As a surrogate marker for TNF activity the expression of TNF-regulated genes was quantified using a modular approach.
**Results:** Clinical TST responses were significantly diminished in RA patients compared to healthy controls. Anti-TNF therapy did not have a further significant effect on skin induration compared to those treated with methotrexate. However clinical TST skin induration did not correlate with peripheral blood response to TB antigens, as interferon-gamma responses to TB antigens in peripheral blood were not attenuated by rheumatoid disease or treatment. Genome wide transcriptional profiling showed that TNF was induced following the TST, and this was not attenuated by anti-TNF therapy, compared to RA patients treated with methotrexate or healthy controls. Furthermore, downstream activity of this induced TNF was preserved in patients on anti-TNF therapy.
**Conclusions:** Attenuated clinical TST responses have been previously shown in RA patients with active disease. Our results expand these findings to patients with stable disease, where the clinical TST responses were also diminished. Intriguingly, based on the transcriptional response to a TST challenge, we did not observe any reduction in TNF activity in patients on anti-TNF therapy. We conclude that anti-TNF therapy is unable to block a surge in TNF activity following an acute challenge. Therefore we infer that anti-TNF therapy is more likely to have biological effects on basal levels of TNF activity in steady state and rather than blocking TNF activity at the site of acute inflammation.
**Disclosure of Interest:** None declared
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## FRI0161 SUSTAINED EFFICACY AND COMPARABLE SAFETY AND IMMUNOGENICITY AFTER TRANSITION TO SB5 (AN ADALIMUMAB BIOSIMILAR) VS CONTINUATION OF THE ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULT OF PHASE III STUDY

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**Background:** SB5 is a biologic agent developed as a biosimilar of the adalimumab reference product (ADL). The 24-week results of Phase III study results have been reported[1].
**Objectives:** To evaluate the efficacy, safety, and immunogenicity in patients with RA who transitioned from ADL to SB5 vs. patients who maintained ADL and patients who continued to receive SB5 during the transition period after Week 24 up to Week 52.
**Methods:** Patients with RA were randomised in a 1:1 ratio to receive either SB5 or ADL 40 mg every other week (EOW) via subcutaneous injection. At Week 24, patients receiving ADL were re-randomised in a 1:1 ratio to either be transitioned to SB5 or continue on ADL EOW up to Week 50. Patients receiving SB5 continued to receive SB5 but they also followed the randomisation procedure to maintain blinding. Efficacy, safety, and immunogenicity were assessed up to Week 52.
**Results:** At Week 24, 254 patients from SB5 continued to receive SB5 (SB5/SB5), 125 patients from ADL were transitioned to SB5 (ADL/SB5), and the 129 patients from ADL continued to receive ADL (ADL/ADL). The ACR responses at Week 52 in per-protocol set were comparable between SB5/SB5, ADL/SB5, and ADL/ADL (76.9% vs 81.1% vs 71.2% for ACR20, respectively). Other efficacy endpoints were also comparable across the treatment groups. The change of modified total Sharp score was comparable with mean change of 0.17 in SB5/SB5 vs 0.25 in ADL/SB5 vs 0.50 in ADL/ADL. The safety profile during the transition period was comparable. Two patients newly reported injection site reactions only in ADL/ADL. The incidence of anti-drug antibody was 15.7% in SB5/SB5, 16.8% in ADL/SB5, and 18.3% in ADL/ADL during the transition period.

Table 1. Safety profile of the study population during the transition period (from Week 24 to Week 52)

| Number of patients with | SB5/SB5 (N=254) | | ADL/SB5 (N=125) | | ADL/ADL (N=127) | |
|---|---|---|---|---|---|---|
| | n | (%) | n | (%) | n | (%) |
| At least 1 TEAE | 82 | (32.3) | 47 | (37.6) | 42 | (33.1) |
| At least 1 SAE | 6 | (2.4) | 4 | (3.2) | 4 | (3.1) |
| Serious infections | 0 | (0.0) | 2 | (1.6) | 0 | (0.0) |
| Active tuberculosis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Injection site reactions[a] | 0 | (0.0) | 0 | (0.0) | 2 | (1.6) |
| Malignancy[b] | 1 | (0.4) | 1 | (0.8) | 1 | (0.8) |
| Death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |

SAE: serious adverse event; TEAE: treatment-emergent adverse event. [a]Defined as high level group terms of administration site reactions. [b]Small cell lung cancer, Glioblastoma multiforme, and Seminoma were reported in SB5/SB5, ADL/SB5 and ADL/ADL, respectively.

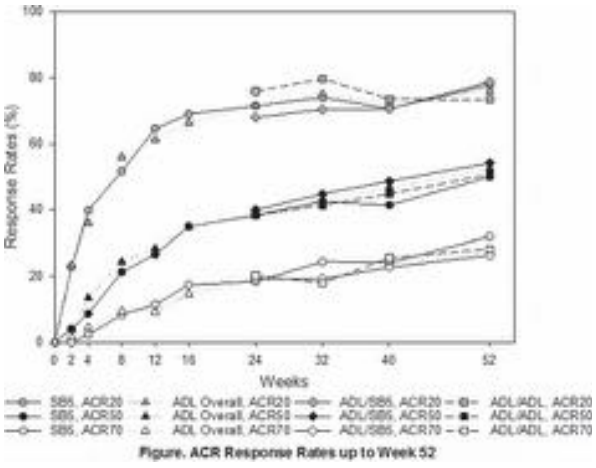


Figure. ACR Response Rates up to Week 52

**Conclusions:** During the transition period after Week 24 up to Week 52, the efficacy, safety, and immunogenicity profiles were comparable between SB5/SB5, ADL/SB5, and ADL/ADL. There were no treatment emergent issues or clinically relevant immunogenicity precipitated by switching.
**References:**
[1] Weinblatt ME et al. Arthritis Rheumatol. 2015; 67 (suppl 10), 8L
**Disclosure of Interest:** M. Weinblatt Consultant for: AbbVie, Samsung Bioepis, Amgen, A. Baranauskaite Grant/research support from: AbbVie, Samsung Bioepis, J. Niebrzydowski Grant/research support from: Samsung Bioepis, E. Dokoupilova Grant/research support from: Samsung Bioepis, A. Zielinska Grant/research support from: Samsung Bioepis, K. Sitek-Ziolkowska Grant/research support from: Samsung Bioepis, J. Jaworski Grant/research support from: Samsung Bioepis, A. Racewicz Grant/research support from: Samsung Bioepis, M. Pileckyte Grant/research support from: Samsung Bioepis, K. Jedrychowicz-Rosiak Grant/research support from: Samsung Bioepis, V. Zhdan Grant/research support from: Samsung Bioepis, S. Y. Cheong Employee of: Samsung Bioepis, J. Ghil Employee of: Samsung Bioepis
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## FRI0162 COMPARABLE SAFETY AND IMMUNOGENICITY AND SUSTAINED EFFICACY AFTER TRANSITION TO SB2 (AN INFLIXIMAB BIOSIMILAR) VS ONGOING INFLIXIMAB REFERENCE PRODUCT IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF PHASE III TRANSITION STUDY

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**Background:** SB2 is developed as a biosimilar of the infliximab reference product (INF). The 30-week and 54-week results of Phase III study have been reported[1,2].
**Objectives:** To evaluate the safety, immunogenicity, and efficacy in patients with RA who transitioned from INF to SB2 vs maintained INF and who continued to receive SB2 after Week 54 up to Week 78.
**Methods:** This study is a randomised, double-blind phase III transition study. Patients with moderate to severe RA were randomised in a 1:1 ratio to receive either SB2 or INF at Weeks 0, 2, 6, and then every 8 weeks thereafter until week 46. At Week 54, patients previously receiving INF were re-randomised in a 1:1 ratio to either receive SB2 (INF/SB2) or continue INF (INF/INF) up to week 70; patients receiving SB2 continued to receive SB2 (SB2/SB2) up to Week 70. Safety, immunogenicity and efficacy were assessed up to week 78.
**Results:** At Week 54, 94 patients from INF were transitioned to SB2 (INF/SB2), 101 patients from INF continued to receive INF (INF/INF), and 201 patients from SB2 continued to receive SB2 (SB2/SB2). The safety profile during the transition period was comparable between INF/SB2, INF/INF, and SB2/SB2. The incidence of adverse events during the transition period was 36.2% in INF/SB2, 35.6% in INF/INF, and 40.3% in SB2/SB2. The incidence of infusion related reaction during the transition period was 3.2%, 2.0%, and 3.5%, respectively. Among the patients with overall negative anti-drug antibodies (ADA) results up to Week 54, ADAs were newly developed in 14.6% (6/41) in INF/SB2, 14.9% (7/47) in INF/INF, and 14.1% (11/78) in SB2/SB2. The efficacy was sustained and comparable between the treatment groups.

Table 1. Safety Profile During the Transition Period (From Week 54 to Week 78)

| Number of patients with | INF/SB2 (N=94) | | INF/INF (N=101) | | SB2/SB2 (N=201) | |
|---|---|---|---|---|---|---|
| | n | (%) | n | (%) | n | (%) |
| At least 1 treatment-emergent adverse event | 34 | (36.2) | 36 | (35.6) | 81 | (40.3) |
| At least 1 serious adverse event | 6 | (6.4) | 3 | (3.0) | 7 | (3.5) |
| Serious infections | 2 | (2.1) | 1 | (1.0) | 1 | (0.5) |
| Active tuberculosis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Infusion-related reaction | 3 | (3.2) | 2 | (2.0) | 7 | (3.5) |
| Malignancy | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Overall ADA positive | 43 | (45.7) | 51 | (50.5) | 104 | (53.6)[a] |
| Newly ADA positive[b] | 6 | | 7 | | 11 | |

[a]Percentage is based on 194 patients with available ADA results. [b]Newly developed ADA in patients with negative overall ADA up to Week 54.

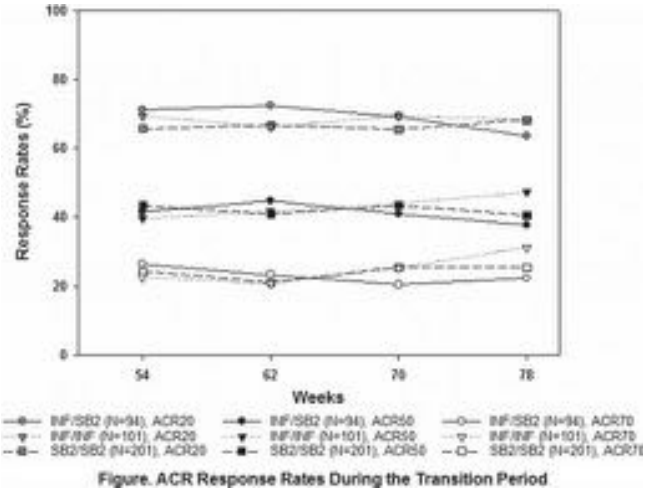



Figure. ACR Response Rates During the Transition Period

**Conclusions:** The safety, immunogenicity, and efficacy profiles remained comparable between the INF/SB2, INF/INF, and SB2/SB2 up to Week 78, revealing that there were no treatment emergent issues or clinically relevant immunogenicity after switching from INF to SB2.

**References:**

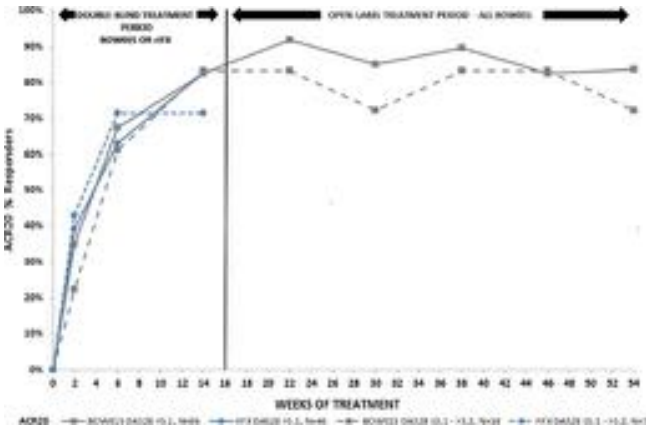
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## FRI0163 EFFICACY OF THE BIOSIMILAR BOW015, COMPARED TO ORIGINATOR INFLIXIMAB, INITIATED AT MODERATE AND SEVERE DISEASE ACTIVITY THRESHOLDS IN RHEUMATOID ARTHRITIS

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**Background:** In 2010 the British Society of Rheumatology guidelines[1] adjusted the recommended threshold for biologic therapy in rheumatoid arthritis (RA) to a DAS28 score of >3.2, from a DAS28 score of >5.1. However, adoption of this recommendation for the use of TNF-inhibitors such as infliximab in RA patients with moderate disease activity despite methotrexate may be limited, especially in regions that wish to minimise biologic usage due to cost.
**Objectives:** To examine the effectiveness of Remicade (rIFX) in RA patient subgroups with severe or moderate disease activity, and to compare the efficacy of this treatment to BOW015, an infliximab biosimilar.
**Methods:** Sub-groups of RA patients on a stable dose of methotrexate which included a EULAR diagnostic criteria ≥6 and a CRP≥10 mg/L were identified from within the cohort of a randomised double-blind, group comparison of BOW015 compared to rIFX (2:1) treated with 3 mg/kg IV at Week 0, 2, 6, 14, 22, 30, 38, and 46. Subject responses to treatment (ACR20, 50 and 70) were followed up until the end of the blinded phase (Week 16) and also following the switch to a BOW015 in an open-label phase (until Week 54). Severe and moderate patient sub-groups were determined by DAS28 (>5.1, ≤5.1 - >3.2) and CRP (≤10, >10 - ≤20, and >20mg/L) status at Week 0 pre-treatment. Analysis of the difference in the proportions of subjects achieving ACR20, 50 and 70 between subgroups and within treatments were performed by Fisher's exact test and 95% confidence intervals by exact method for the difference in proportions.
**Results:** 189 subjects entered the study, 127 were dosed with BOW015 and 62 with rIFX. At the end of the double-blind period, patients were transitioned to open label BOW015 (104 continued BOW015 and 53 switched to BOW015). ACR20 responses by both high and low-activity DAS28 subgroups were comparable (Figure 1). There was no significant difference in proportions of ACR20 response to BOW015 or rIFX during the double-blind period and in the open-label period for those continuing on BOW015. Comparisons of ACR20 response by CRP sub-group were not significantly different during the double-blind or open-label period between CRP categories for each treatment or previous treatment.



**Conclusions:** The proportion of ACR20 responders to BOW0I5 is comparable across subgroups of RA with severe or moderate disease activity, as assessed by DAS28 and CRP. The increased financial burden of widening access of biologics to patients with moderate disease activity could be offset by use of less expensive biosimilars.

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**Acknowledgement:** This research was sponsored by EPIRUS Biopharmaceuticals Inc.

**Disclosure of Interest:** P. Taylor Consultant for: Epirus Biopharmaceuticals Inc. and Merck, M. Wyand Shareholder of: Epirus Biopharmaceuticals Inc., Employee of: Epirus Biopharmaceuticals Inc., A. Knight Consultant for: Epirus Biopharmaceuticals Inc., C. Costantino Employee of: Epirus Biopharmaceuticals Inc., C. Lassen Shareholder of: Epirus Biopharmaceuticals Inc., Employee of: Epirus Biopharmaceuticals Inc.

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## FRI0164 T CELLS EXPANSION IN RHEUMATOID AND PSORIATIC ARTHRITIS PATIENTS UNDER ANTI-TNF-ALPHA AGENTS

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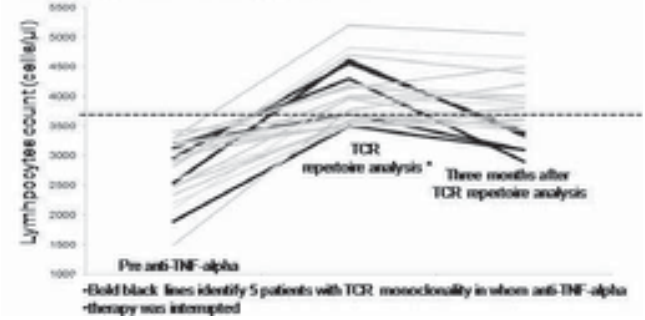
**Background:** An increased risk for lymphoproliferative disorders, specially Hodgkin's and non- Hodgkin's lymphoma has been reported in Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) patients.Several factors such as the genetic background, the persistent stimulation of T and B cells by unknown antigens and immunosuppressive therapies can be involved in increasing the risk of malignancies in these patients. A role for anti- TNF-α therapy is still controversial

**Objectives:** To analyse the induction of lymphocytosis in RA and PsA patients under anti-TNF-α therapy and explore its possible malignant evolution

**Methods:** RA and PsA patients under anti-TNF-alpha therapy that presented a de novo lymphocytosis (circulating lymphocytes >3400 cells/μl for at least 3 months) were evaluated for lymphocyte subpopulations: total T cells (CD3+), T helper (CD3+CD4+CD45+), T suppressor (CD3+CD8+CD45+), natural killer (CD16+CD56+CD45+) and B cells (CD19+CD45+). Molecular analysis of the T Cell Receptor (TCR) was also performed as follow: total DNA was extracted from PB using Qiagen DNA Kit Extraction; molecular evaluation of TCRγ gene rearrangements was performed using a multiplex PCR with fluorescent labelled oligonucleotides; PCR reactions for TCRγ gene were carried out using "TCRγ rearrangements molecular analysis kit" and amplifications products analyzed on a 3130 Genetic Analyzer. The lengths of the Vγ1–8/Jγ1·3/2·3 and Vγ1–8/Jγ1·1/2·1 PCR products were 145–230 base pairs (bp) and 230–255bp, respectively. Samples were scored as monoclonal if one unequivocal peak in the expected range was observed

**Results:** 25/208 patients (12%) (15 RA and 10 PsA) showed a de novo appearance of a mild persistent lymphocytosis (from 2800 to 4000 mean cells/ul; p<0.001). 11 patients were treated with Etn, 7 with Ada, 4 with Ifx and 3 patients with GoI. The analysis of PBL subsets revealed that B and NK cells were not the cause for the lymphocytosis because the distribution of these populations was at the lowest limit of the normal range (9.6% and 10% respectively). In contrast, we observed a mild increase in the mean percentage of CD3+CD4+ cells (51%). TCRγ gene rearrangement showed a polyclonal distribution in 11 patients (44%), oligoclonal in 9 patients (36%), whereas in 5 patients (20%) we observed the predominance of a monoclonal peak. Lymphnodes ultrasonography did not reveal any sign of malignant proliferation. Despite of this result in the absence of clear guidelines we decided to interrupt the biological therapy in these 5 patients to reduce the risk of developing malignancy. Three months after biological suspension a significant decrease in the total lymphocyte count was observed (mean value from 4134 to 3168cells/μl; P<0.008), whereas TCRγ repertoire maintained its monoclonality

**Figure 1**
Total lymphocyte count (cells/μl) in 25 patients with lymphocytosis before anti-TNF-alpha therapy, at the moment of TCR repertoire analysis and three months after. Dashed line indicates the upper limit of normal lymphocyte count




**Conclusions:** We observed in both RA and PsA a de novo appearance of lymphocytosis in a relevant percentage of patients within which five showed the emergence of a single TCR clone. Strict follow-up of the RA and PsA disease activity and of TCR diversity evolution will allow the early detection of lymphoma or the re-establishment of TCR diversity thus permitting the application of a more targeted therapy

**Disclosure of Interest:** None declared

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## FRI0165 EFFECTIVENESS AND SAFETY OF BIOSIMILAR INFLIXIMAB (CT-P13) IN A REAL-LIFE SETTING IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

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**Background:** Over the past decade, the introduction of biologics has significantly changed the management of rheumatoid arthritis (RA) and ankylosing spondylitis (AS). However, the high cost of biologics imposes limits on their use, particularly in developing countries. The development and commercialization of biosimilars can help address unmet medical needs by improving access to well-established therapeutic interventions while improving healthcare affordability. Biosimilar infliximab (CT-P13) was the first monoclonal antibody biosimilar approved in the EU.

**Objectives:** To demonstrate the safety and effectiveness of CT-P13 when administered in a real-life setting in adults with active RA or AS.

**Methods:** This multicenter, non-interventional, observational study was conducted in Romania, Czech Republic, Poland, Bulgaria and Latvia in patients with active RA with an inadequate response to methotrexate (MTX) or other DMARDs, or active AS with inadequate response to NSAIDs. Patients received CT-P13 at baseline (visit 1), weeks 2 (visit 2), 6 (visit 3), and between weeks 12 and 14 (visit 4: month 3). Dosages were established according to CT-P13 SPC. Safety was assessed by early dropouts and adverse events (AEs). Effectiveness was assessed at baseline and visit 4 (month 3) using the Disease Activity Score (DAS28) for RA patients and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for AS patients.

**Results:** By January 1st 2016, 122 subjects (49% male, mean [SD] age 48.2 [14.6] years) have been enrolled in the study, with a median follow-up of 165 days. At visit 4 (month 3), mean (SD) CT-P13 doses were 246 (52) mg/3.3 (0.6) mg/kg for RA, and 372 (82) mg/5.1 (0.5) mg/kg for AS. A total of 20 AEs were recorded: 4 definitely related, 3 possibly related, and 13 unrelated to CT-P13 treatment. Among these AEs, 2 were serious (a spontaneous pneumothorax, unrelated to CT-P13, and a dyspnea due to allergic infusion reaction, definitely related to CT-P13; both resolved without sequelae) and a total of 4 dropouts were reported due to AEs (3 definitely-related allergic infusion reactions and 1 possibly related). Currently, 59 patients (RA: 26; AS: 33) have baseline and follow-up primary effectiveness measurements at month 3. Patients who terminated the study prematurely were excluded from effectiveness analyses. After 3 months of CT-P13 treatment, patients showed significant improvements in disease activity relative to baseline in terms of DAS28 (baseline: mean [SD]=6.7 [1.1], month 3: mean [SD]=2.7 [1.4]; t=8.1, df=25, p<0.0001, Cohen's d=2.5) and BASDAI (baseline: mean [SD]=6.5 [1.7], month 3: mean [SD]=2.8 [2.1]; t=10.5, df=32, p<0.0001, Cohen's d=2.0). Patients with RA (baseline: mean [SD]=23 [16.3], month 3: mean [SD]=9.3 [19.8]; t=2.5, df=25, p=0.02, Cohen's d=0.9) or AS (baseline: mean [SD]=26.7 [26.3], month 3: mean [SD]=5.5 [8.6]; t=5, df=38, p<0.0001, Cohen's d=1.2) also showed a significant decrease in C-reactive protein (CRP) levels after 3 months of treatment.

**Conclusions:** Biosimilar infliximab (CT-P13) is safe and effective in a real-life setting in patients with RA or AS.

**Disclosure of Interest:** None declared

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## FRI0166 PERSISTENCE OF BIOLOGIC THERAPY FOR PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: DATA FROM THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES

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**Background:** Data on the efficacy and safety of biological therapies for Rheumatoid Arthritis (RA) that come from Patient Registries present the results of clinical practice all over the world. In terms of efficacy, treatment persistence

in RA is largely related to reaching the therapeutic target, i.e. remission or low disease activity.
**Objectives:** To measure drug persistence with tumor necrosis factor alpha (TNF) antagonists and anti CD20 monoclonal antibody, among RA patients in Romania, as well as identify/determine additional factors that could influence it.
**Methods:** Population-based cohort study carried out with RA patients in Romania. Data was gathered from the Romanian Registry of Rheumatic Diseases. The study cohort included RA patients who initiated the first course of a TNF antagonist or anti CD20 monoclonal antibody, anytime between 2004 and 2015. Persistence was measured as the time period during which the drug had been administered to a patient. Drug discontinuation was defined as drug treatment being interrupted due to adverse events, primary or secondary non-responder, or switching to another molecule. The influence of any other factors on persistence used T test and persistence was estimated using survival analysis.
**Results:** The study cohort included 4,395 RA patients, mean age 59.55 yrs, 85.3% women, mean RA duration 14.37 yrs, treated with etanercept (29.7%), adalimumab (23.5%), infliximab (original 7.1%, biosimilars 0.7%), rituximab (38.9%); 23.1% used steroids (19.8% with <7.5mg dayli); mean current DAS28 score 3.08 (±1.20) and mean SDAI 3.62 ((±7.39). The persistence estimated in weeks (95% confidence interval) with infliximab was 330.8 (303.8–357.8), with rituximab it was 301.0 (262.2–339.8), with etanercept it was 240.6 (232.7–248.4) and with adalimumab it was 200.4 (191.0–209.9). There was a poor positive correlation between general persistence and RA duration (r=0.2, $p<0.001$) and a negative association with DAS28 (r= - 0.3, $p<0.001$). The use of methotrexate resulted in longer persistence (170.5±139.8) compared to other csDMARDs (152.0±120.2), $p<0.001$. Using steroids in dosages less than 7.5mg/day resulted in a significantly longer persistence compared to larger doses (131.2±121.3 vs 100.1±110.7), $p<0.005$. Patients being in remission or LDA maintained the biologics significantly longer than those with MDA or HAD (190.9±139.0 vs 121.1±107.8), $p<0.001$. All other factors that were analysed (age, sex, residency, education, work status, disease characteristics) had no significant effect on drug persistence. Adverse events, primary non-responders, and secondary non-responders were comparable among these molecules.
**Conclusions:** Longer persistence was observed with infliximab, followed by rituximab, etanercept, and adalimumab in RA patients in Romania, for more than 10 years of biologics use. Reaching the state of remission or LDA, as well as low steroids regimens and long-standing disease seem to positively correlate with drug persistence.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4426

## FRI0167 LOW LEVELS OF INFLIXIMAB AT EARLY STAGES PREDICT THE LOSS OF DRUG LEVELS AND THE CLINICAL RESPONSE AT ONE YEAR OF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The anti-TNF monoclonal antibody Infliximab (Ifx), has proven effective in treating rheumatoid arthritis (RA), although in 40% of cases may fail, mainly due to immunogenicity. A good clinical response is usually associated with high serum drug levels; however, it is not clear why some patients have a faster drug clearance since the beginning of the therapy. Formation of immunocomplexes between antibodies to Ifx (ATI) and Ifx can increase drug clearance, leading to treatment failure.
**Objectives:** To analyze whether serum Infliximab trough levels (ITL) at the induction phase were related to Ifx disappearance and clinical outcomes at week (w) 54. The early development of immunogenicity as a related factor with low ITL was also investigated.
**Methods:** In this observational retrospective study ITL were measured from 66 RA patients from the prospective biological cohort of La Paz Hospital. Serum samples were taken at w2, w6, w14 and w22. Serum-dependent receiver operating characteristics (ROC) curves were used to establish the ITL value that better predicts the absence of Ifx at w54. ATI were measured by bridging ELISA and by an acid-dissociation method without drug interference IDK (Immundiagnostik®, Germany). Patients were grouped as ITLpos if they had detectable Ifx at w54 and ITLneg otherwise.
**Results:** ITLneg patients (n=25) had significantly lower levels at all time points than ITLpos (n=41). Based on ROC values ITL at w6 (4.44 μg/ml) had the best predictive value for disappearence of Ifx at w54 with a 70% sensitivity (95%CI 45.7–88.1), 95% specificity (95%CI 83.1–99.4) and positive likehood ratio of 14. Most patients in low disease activity or remission at w54 had at w6 ITL upper the predictive cut-off [20/44 (45%) upper cut-off vs 3/20 (15%) under cut-off p=0.02] and most EULAR responder at w54 had ITL upper the predictive cut-off at w6 [33/43 (77%) vs 10/21 (48%); p=0.08]. Treatment survival of patients with ITL upper 6w cut-off was longer: 5 years (1.6–5.0) vs 1.7 years (0.2–0.6); p=0.012.
In the multiple logistic regression analysis, after adjusting for confounders (age, sex, body mass index, baseline DAS28, PCR, TNF and IL6) with ITL at w2 and at w6, the absence of Ifx levels at w54 was significantly associated with ITL under the cut-off at w2 (OR: 15.85; 95%IC 2.95–85.03; p=0.01), at w6 (OR: 86.64; 95%IC 6.58–1139.99; p=0.001) and no MTX use (OR: 12.26; 95%IC 1.83–82.22; p=0.001 for w2; OR: 6.9; 95%IC 1.04–45.84; p=0.04 for w6)
Most patients with ITL under the cut-off at w6 were positive for ATI along the first year [15/20 (75%) under cut-off vs 5/44 (11%) upper cut-off, $p<0.0001$]. Most ATI were detected earlier by the IDK than with bridging.
**Conclusions:** Low ITL at early stages (w2 and w6) are associated with the Ifx absence, the early drop-out of the treatment and the clinical outcome at w54, being the presence of ATI the main reason for the low early circulating drug levels. We also conclude that the cut-off value at w6 (4.44 μg/ml) provides the clinicians with a useful prognostic tool of treatment efficacy.
**Acknowledgement:** This work is partially funded by a non restricted grant from Pzifer and from Leti laboratories.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3515

## FRI0168 EFFECT OF METHOTREXATE IN THE PRESENCE OF DRUG AND THE APPEARANCE OF ANTIBODIES AGAINST TNF INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Several factors influence pharmacokinetics of TNFinhibitors (TNFi). One relevant factor is the formation of anti drug- antibodies (ADA) associated with low drug levels and a worse clinical response. Recent publications in rheumatoid arthritis (RA) [1,2] have demonstrated a beneficial effect of concomitant use of anti-TNF drugs and methotrexate (MTX), with a dose-dependent effect.
**Objectives:** To analyze the MTX influence on the presence of drug and appearance of ADA in a cohort of RA patients treated with Infliximab (Ifx), Adalimumab (Ada) or Etanercept (Etn) with a long follow-up (3 years).
**Methods:** This is a retrospective study that analyzed patients with RA treated with Ifx (112 patients), Ada (71 patients) and Etn (110 patients), in a prospective observational biological cohort from the University Hospital La Paz, Madrid, Spain. Patients were grouped according to the use of MTX: no MTX, low dose (≤12.5 mg/week), intermediate dose (12.5–20 mg/week) and high dose (≥20 mg/week). Levels of drug and ADA were measured by capture and bridging ELISA respectively at baseline, 0.5, 1, 2 and 3 years. All samples were obtained just before drug administration. Statistical analysis was performed using GraphPad Prism 5.0 software.
**Results:** Out of 293 RA patients with a TNFi treatment; 184 (71 with Ifx, 40 with Ada and 73 with Etn) were included. In this cohort, 111 (61%) were on MTX and 72 (39%) were on monotherapy. Most patients with high dose of MTX had levels of drug over 3 years of treatment (93% with MTX ≥20 mg/week vs 77% without MTX; p=0.01) being significant since 0.5 years (≥60% with MTX 20 mg/week vs 39% without MTX; p=0.02)
To analyze the ADA development, patients treated with Ifx and Ada were grouped and we observed a trend to a higher percentage of ADA in the group which did not receive MTX (n=37) compared to those who received high-dose MTX (n=27) although not statistically significant (32% vs 19%, p=0.21). Analysing by separate drugs MTX significantly reduced the immunogenicity of Ada, (53% in patients with MTX vs 15% in monotherapy; p=0.02).
When we study the lack of circulating drug (Ifx, Ada and Etn) as an indicator of immunogenicity, patients who did not receive MTX (n=56) had higher absence of drug than patients with high-dose MTX (n=61) (34% vs 10%, respectively; $p<0.01$). This effect was significant since 0.5 years of treatment (16% MTX ≥20 mg/week vs 3% without MTX; p=0.017)
**Conclusions:** In our cohort of RA patients the concomitant use of MTX has a positive effect in the persistence of TNFi levels together with a decrease of immunogenicity. Furthermore, the MTX has a dose-dependent effect being greater at high dose of MTX.
**References:**
[1] Krickaert C et al.ARD 2012; 71:11.
[2] Vogelzang E H et al.ARD 2015; 74:2
**Acknowledgement:** This work is partially funded by a non restricted grant from Pfizer
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5809

## FRI0169 INFLUENCE OF BODY MASS INDEX (BMI) ON SERUM LEVELS OF INFLIXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** Loss of response of TNFα inhibitors (TNFi) over time resulting in discontinuing of this therapy is a major issue in RA, but underlying reasons for this remains unknown. A few studies suggest the influence of BMI on serum levels of subcutaneous TNFi. However, there is no available data on the possible influence

of BMI on infliximab (IFX) serum levels, which is intravenously administred and adjusteing the dose according to patient weight.
**Objectives:** To determine the possible influence of BMI on serum IFX levels in patients with RA.
**Methods:** Retrospective observational study incluiding 72 patients with RA treated with infliximab, at 3 mg/kg dose in a standard regimen, in our department between 2000 and 2015. Serum IFX levels were determined by ELISA in 3 visits: i)2 weeks, ii)six months and iii)one year after treatment onset. BMI (kg/m$^2$) was classified in four categories: underweight ($<$18,5), normal ($\geq$18,5- $<$25), overweight ($\geq$25-$<$30) and obesity ($\geq$30). Descriptive analysis was used to compare drug levels between these four groups at each visit. To analyse the relationship between BMI and IFX drug levels, generalized estimation equation models adjusted for age, gender and concomitant treatment were employed.
**Results:** Characteristics of patients included in the study when initiating IFX therapy were: 88% female, median (range) age 52 (21–82) years, 71% RF+, 79% ACPA+, disease duration 10,4 (1,0–39,0) years, 79% with concomitant methotrexate and 57% with other DMARDs. Median (range) BMI was 25,5 (16,7–40,2) kg/m$^2$. According to BMI, patients with underweight, normal, overweight and obesity were 2 (2,7%), 35 (48,6%), 23 (31,9%) and 12 (16,7%), respectively. Median (range) IFX serum levels, in ng/ml, for each of the four BMI categories,and for each of the visits, are presented in Table 1.

| | At 2 weeks | At 6 months | At 1 year |
|---|---|---|---|
| Underweight | 34.977 (20.992–48.962) | 7.500 (0–15.000) | NA |
| Normal | 24.576 (2.944–150.000) | 776 (0–12.800) | 2.012 (0–14.336) |
| Overweight | 26.213 (768–50.000) | 661 (0–3.456) | 486 (0–9.416) |
| Obesity | 22.033 (9.891–34.816) | 315 (0–5.344) | 1.088 (0–3.904) |

In the longitudinal analysis, an inverse statistically significant relationship between BMI and drug serum levels was observed: $\beta$: -441,7; 95%CI (-829,7 to -53,8). This relationship remained despite of adjusting the model for potential confounders: $\beta$: -457,3; 95%CI (-858,8 to -55,8).
**Conclusions:** BMI influences serum IFX levels in patients with RA treated with infliximab. Higher BMI values are associated with lower serum drug levels.
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## FRI0170 TREATMENT WITH BIOLOGICAL AND NON-BIOLOGICAL DMARDS IS A MODIFIER CONDITION OF PERIODONTAL DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Periodontitis and rheumatoid arthritis (RA) are two chronic destructive inflammatory diseases with significant worldwide prevalence. Periodontal disease and RA are characterized by the destruction of articular and periodontal tissue, and they share several biological and pathological features.
**Objectives:** Evaluate the effects of conventional drug treatment and anti-TNF therapy in patients with RA on periodontal condition and subgingival microbiota, establishing the association of markers of periodontal infection with indexes of rheumatic activity.
**Methods:** A cross-sectional study was conducted in two groups of RA patients with more than two years of diagnosis. The first group used conventional therapy, and the second group used anti-TNF treatment. An association analysis was performed to observe the relationship between clinical and microbiological markers of periodontal infection, and RA activity. A comparative analysis was performed to assess clinical and microbiological periodontal markers and RA activity.
The data were released to STATA v11. Frequencies of nominal variables and means and standard deviations for continuous variables were calculated for sociodemographic, periodontal and rheumatological data. Associations between periodontal status and rheumatological variables by Chi square/Fisher's exact test and Mann-Whitney U tests. The results were considered statistically significant at p$\leq$0.05. The ethics committee of institution approved the study.
**Results:** An overall high frequency of periodontal disease 91%, in most cases from moderate to severe, was observed in all subjects. The frequency of periodontal disease was 93.22% in the anti-TNF-alpha group and 88.7% in the conventional treatment group. The percentage of sites with clinical attachment loss $\geq$4 mm was significantly associated with the group receiving methotrexate and leflunomide p=0.05. Steroid therapy was associated with the presence of teeth p=0.027. Significant associations were observed with the use of more than one DMARD and the presence of P. gingivalis p=0.004. *T. denticola* was found in the anti-TNF-$\alpha$ therapy group compared to the conventional therapy group p=0.001.
**Conclusions:** Different pharmacological treatments for RA affect the clinical condition and sub-gingival microbiota. Patients treated with more than one DMARD promote the increase subgingival microbiota. Therefore, a more strict periodontal monitoring is necessary in these RA patients
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## FRI0171 EVALUATING TREATMENT EFFICACY IN RHEUMATOID ARTHRITIS: INTERRELATION DISEASE ACTIVITY – FUNCTIONAL STATUS – UTILITY

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**Background:** Rheumatoid Arthritis (RA) treatment targets remission or low disease activity. Patient Registries offer real-world data about effectiveness on long term. Comparing different tools for assessing effectiveness (disease activity, functional status and utility) could provide a more comprehensive approach on the term "achieve and maintain" the therapeutic goal, as a measure of efficacy.
**Objectives:** To evaluate interrelations of disease activity – functional status – utility in a group of RA patients, treated with tumor necrosis factor alpha (TNF) antagonists and anti CD20 molecule, as well as any factor that could influence it.
**Methods:** Cross-sectional study carried out over a cohort of RA patients in Romania. Data was gathered from the Romanian Registry of Rheumatic Diseases and included only RA patients treated with biologics, for who were available all three variables under study: EQ5D (for utility), HAQ score (for functional status), and DAS28 and SDAI (for disease activity). The interrelations of the efficacy parameters were analyzed using correlation tests, T test, ANOVA.
**Results:** The study cohort included 777 RA patients, mean age 58.72 (±12.37) yrs, 84.4% women, mean RA duration 14.08 (±8.33) yrs, 77.1% retired, treated with etanercept (30.6%), adalimumab (22.7%), infliximab (original 6.3%, biosimilars 0.7%), rituximab (26.3%) with a mean treatment duration 174.90 (±143.40) weeks; 27.3% used steroids (20.2% with $<$7.5mg daily); mean current DAS28 score = 3.66 (±1.52), mean delta DAS28 = 0.13 (±1.28), mean SDAI = 14.27 (±13.79), mean HAQ score = 1.14 (±0.64), mean EQ5D = 0.61±0.31. There was a strong positive correlation between HAQ score and DAS28, as well as SDAI: r=0.5 (p$<$0.001) and a negative association between HAQ and EQ5D: r= -0.6 (p$<$0.001). Utility score showed a strong negative association with DAS28 and with SDAI: r= -0.7 (p$<$0.001), whereas disease activity dynamics (delta DAS28 for the last 6 months) had a poor negative association with EQ5D: r= -0.2 (p$<$0.01), but not with HAQ. Patient global assessment (PGA) on disease activity had a significant association both with HAQ (r=0.6, p$<$0.001) and EQ5D (r= -0.6, p$<$0.01). Analyzing distribution of EQ5D and HAQ in DAS28 categories, there was a significant difference between categories (p$<$0.001); for EQ5D-DAS28: $<$2.6 = 0.81 (±0.19), 2.6–3.2 = 0.68 (±0.17), 3.2–5.1 = 0.63 (±0.18), $>$5.1 = 0.16 (±.38); for HAQ-DAS28: $<$2.6 = 0.73 (±0.57), 2.6–3.2 = 0.98 (±0.5), 3.2–5.1 = 1.25 (±0.52), $>$5.1 = 1.76 (±0.56). Steroids use belongs to more active disease; doses $>$7.5 mg/day represent a cutoff for patients with severe disease activity [HDA]. Disease duration had not any influence on EQ5D, HAQ or DAS28, as well as all other factors (age, sex, residency, education, work status).
**Conclusions:** Disease activity influences the patient well-being and functionality. Considering the dynamics of disease activity over time and the fluctuating values of utility and HAQ score within DAS28 categories, analyzing treatment efficacy from a combined perspective may be helpful in evaluating the time trends on achieving and maintaining the therapeutic goals.
**Disclosure of Interest:** None declared
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## FRI0172 PRIMARY AND SECONDARY NON-RESPONSE IN RA PATIENTS TREATED WITH AN ANTI-TNF: AN ANALYSIS FROM A PROSPECTIVE, OBSERVATIONAL REGISTRY

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**Background:** Despite the well documented effectiveness of anti-TNF treatment in rheumatoid arthritis (RA), some patients can be refractory to treatment (primary [1ry] failure) or may lose responsiveness (secondary [2ry] failure). In such cases, switching to another anti-TNF or a different biologic class can often restore therapeutic response.

**Objectives:** The aim of this analysis was to assess the rate of non-response among RA patients treated with anti-TNFs in Canadian routine clinical practice.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, ankylosing spondylitis, or psoriatic arthritis with infliximab (IFX) or golimumab (GLM). RA patients treated with IFX since 2002 or with GLM since 2010 who had at least one post-baseline assessment were eligible. Patients with available information on DAS28 or EULAR response in at least one post-baseline visit were included in the respective analyses.
**Results:** 1,127 patients (75.6% female) were included with mean (SD) age of 56.1 (13.4) years and disease duration of 8.4 (8.9) years at baseline. The majority were biologic naïve (93.2%), treated with IFX (76.0%), and received a concomitant DMARD (86.2%) at baseline. Mean (SD) disease parameters at baseline were: CDAI: 33.9 (17.6); HAQ: 1.6 (0.7); SJC: 9.8 (6.8); TJC: 11.5 (8.0).
After a mean (SD) follow-up of 35.5 (36.8) mos, 764 (67.8%) patients were discontinued overall and 226 (20.1%) due to effectiveness reasons (lack of response: n=67; loss of response: n=83; disease progression: n=76). Among the patients discontinued due to effectiveness reasons, the majority were discontinued after 12 months (54.4%) and had achieved prior good EULAR response (66.2%). Among patients discontinued due to lack of response, 17.7% and 45.5% had previously achieved DAS28 low disease activity (LDA) and good EULAR response, respectively; whereas, among patients discontinued due to loss of response, 46.9% and 76.8% had a previously documented achievement of the two targets, respectively.
**Conclusions:** The results of this analysis have shown a low rate of failure during treatment with IFX and GLM. Non achievement of DAS28 LDA was a good predictor of lack of response and more predictive than good EULAR response; non-achievement of good EULAR response, on the other hand, was a better predictor of loss of response. Overall, significant variation exists depending on each investigator's definition of 1ry and 2ry failure, which highlights the importance of establishing standardized definitions of these terms.
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## FRI0173 ROLE OF METHOTREXATE AS COMBINATION THERAPY WITH ADALIMUMAB AND ETANERCEPT IN RHEUMATOID ARTHRITIS: RETROSPECTIVE ANALYSIS FROM A LOCAL REGISTRY

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**Background:** The role of methotrexate (MTX) in association with TNF inhibitors (TNFi) for the treatment of rheumatoid arthritis (RA) is well defined, although the optimal MTX dose is still unclear.
Recently the CONCERTO randomized controlled trial demonstrated efficacy and safety of ascending MTX doses in combination with adalimumab (ADA) for the treatment of MTX-naïve RA [1], but observational data from real-life registries are still lacking.
**Objectives:** The aim of our study is to retrospectively evaluate the effect of different MTX regimen as combination therapy with 1st line ADA and etanercept (ETN) on 6- and 12-month clinical response and safety profile in RA patients.
**Methods:** We selected all RA patients treated with ADA or ETN as 1st line biotherapy in our Rheumatology Department from January 2000 to October 2015. The analysis was performed only on subjects with at least 1-year follow-up and the study population was stratified according to concomitant MTX regimen in 3 subgroups: TNFi as monotherapy (group 1), TNFi in association with low MTX dose ($\leq$10 mg/week, group 2), and TNFi combined with high MTX dose ($\geq$12.5 mg/week, group 3). Six- and 12-month clinical response was evaluated as mean change from baseline of disease activity score 28 (DAS28) and as DAS28 remission/low disease activity (LDA) rates, comparing the 3 subgroups by Kruskal-Wallis and Dunn tests.
**Results:** The study population included 322 RA patients (265 [82.3%] female, mean age [± standard deviation] 55.4 [±12.8] years, disease duration 11.4 [±9.4] years, positive rheumatoid factor 248 [77%], mean baseline DAS28 5.39 [±1.18]) treated with ADA (n=166) or ETN (n=156). According to concomitant MTX regimen, 108 patients were assigned to subgroup 1, 110 to subgroup 2, and 104 to subgroup 3. No significant differences were found in baseline characteristics among the 3 subgroups. The mean change from baseline of DAS28 was significantly higher in subgroup 3 compared with subgroup 1 and 2 at both 6 (2.14, 1.2, and 1.44, respectively; $p<0.0001$) and 12 months (2.33, 1.26, and 1.46, respectively; $p<0.0001$). Similarly, in the subgroup 3 we found a significantly higher proportion of patients achieving 1-year remission (44.1, 23.1, and 24.1%, respectively; $p<0.0001$) or LDA (57.3, 31.7, and 36.1%, respectively; $p<0.0001$). Treatment withdrawals due to adverse events were significantly more frequent in both subgroup 1 and 2 compared with subgroup 3 (19.3, 16.5, and 9.2%, respectively; p=0.02).
**Conclusions:** Our retrospective analysis demonstrated that in a real life setting the 6- and 12-month clinical response of ADA and ETN was significantly improved by combination strategy only when MTX has been used at high doses ($\geq$12.5 mg/week). Interestingly, increasing MTX dose was also associated with a more favorable safety profile.
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## FRI0174 TWO-YEAR RETENTION RATE OF SUBCUTANEOUS ANTI-TUMOR NECROSIS FACTOR AGENTS FOR RHEUMATOID ARTHRITIS: A RETROSPECTIVE ANALYSIS OF THE LORHEN REGISTRY

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**Background:** To date four subcoutaneus TNF inhibitors (TNFis) have been licensed for the treatment of rheumatoid arthritis (RA). Although data from real-life registries have largely confirmed the favourable long term retention rates of adalimumab (ADA) and etanercept (ETN), data on golimumab (GOL) and certolizumab pegol (CZP) drug survival are still lacking.
**Objectives:** The aim of the study is to evaluate the 2-year retention rate of TNFis used as 1st or 2nd line biotherapy in RA patients in a multicentric observational cohort (the LORHEN registry).
**Methods:** Data of all RA patients treated with a TNFi were retrospectively extracted from the LORHEN registry, including a cohort of more than 3000 RA subjects who received at least one biologic agent since 1999. The analysis was limited to patients who received ADA, ETN, CZP, or GOL as first- or second-line biotherapy in the period when all the considered TNFis were available in Italy (from January 2010 to November 2015). The 2-year retention rate was calculated by Kaplan-Meier method and the comparative risk for discontinuation among individual TNFi was compared by a stratified log-rank test. Sub-analyses according to first or second line treatment have been performed.
**Results:** The study population included 677 RA patients (79.7% female, mean age [±SD] 54.3 [±13.5] years, mean disease duration 8.9 [±8.8] years, mean baseline disease activity score 28 4.9 [±1.3]), treated with a first (n=444) or a second line (n=233) TNFi. In the biologic naïve group, 141 patients received ADA, 88 CZP, 130 ETN, and 85 GOL, whereas in the switcher group 68 patients have been treated with ADA, 38 with CZP, 76 with ETN, and 51 with GOL. The overall 2-year retention rate was 58.5% (63.3 and 49.4% in first- and second-line group, respectively; $p<0.001$). The 2-year drug survival of individual TNFi was 46% for ADA, 66% for CZP, 56% for ETN, and 53% for GOL (p=0.006 for CZP vs ADA, p=n.s. for other comparisons). Sub-analyses according to line of TNFi treatment demonstrated 2-year retention rate of ADA, ETN, CZP, and GOL to be 57.4, 66.9, 73.9, and 56.5%, respectively (p=0.048 for CZP vs ADA, p=n.s for other comparisons) in biologic naïve patients and 38.2, 46.1, 60.5, and 60.8%, respectively (p=0.017 for GOL vs ADA, p=n.s for other comparisons) in switchers.
**Conclusions:** In the real-life scenario of the Lorhen registry, overall 2-year retention rate of TNFis was about 60% with a significantly higher persistence in biologic naïve patients compared with switchers. In the comparison among individual TNFis, no significant differences were found with the exception of a lower drug survival of ADA compared with CZP in biologic naïve subjects and with GOL in switchers.
**Disclosure of Interest:** None declared
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## FRI0175 TWO-YEAR RETENTION RATE OF GOLIMUMAB FOR RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS: A RETROSPECTIVE ANALYSIS OF THE ITALIAN LORHEN REGISTRY

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**Background:** Golimumab (GLM), a subcutaneous TNF inhibitor, has been licensed for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Data from real-life registries on long term retention rates of GLM in these diseases are scarce.

**Objectives:** To assess the 2-year retention rate of GLM in RA, PsA and AS patients from a multicentre observational cohort (the LORHEN registry).
**Methods:** We performed a retrospective analysis of data from all patients with RA, PsA and AS included in the LORHEN registry who started GLM from October 2010 to September 2015. Only patients with at least one reported visit of follow-up were included. The 2-year retention rate was calculated by Kaplan-Meier method for each disease. The risk of discontinuation between patients who received GLM as first- or second-line biotherapy was compared by a stratified log-rank test.
**Results:** Overall 410 subjects were included in the analysis: 180 patients with RA, 110 with PsA and 120 with AS.
RA patients had a mean (Standard Deviation, SD) age of 54,6 (13,6) years and a mean (SD) disease duration of 9,5 (9,3) years; most of them were female (81,6%). Among them, 79 patients stopped the treatment with GLM due to inefficacy or adverse events before 24 months of treatment; the overall 2-year retention rate was 48%. GLM was given as first and second line treatment in 85 and 51 patients, with a 2-year retention rate of 49% and 53%, respectively; the comparison between first and second line treatment groups did not show any significant difference in mean survival time (p=0.724).
Among PsA patients, 50% were male, with a mean (SD) age of 47,9 (12,8) years and a mean (SD) disease duration of 7,9 (6,7) years. Among them, 42 patients stopped the treatment with GLM due to inefficacy or adverse events before 24 months of treatment; the overall 2-year retention rate was 48%. GLM was given as first and second line treatment in 47 and 30 patients, with a 2-year retention rate of 66% and 54%, respectively; the comparison between first and second line treatment groups did not show any significant difference (p=0.333).
SA patients had a mean (Standard Deviation, SD) age of 45,2 (12,2) years and a mean (SD) disease duration of 9,7 (10) years; 56,7% of patients were male. Among them, 33 patients stopped the treatment with GLM due to inefficacy or adverse events before 24 months of treatment; the overall 2-year retention rate was 65%. GLM was given as first and second line treatment in 51 and 42 patients, and the 2-year retention rate was of 57% and 76%, respectively; the comparison between first and second line treatment groups did not show any significant difference (p=0.127).
**Conclusions:** GLM showed a similar 2-year retention rate in first and second line treatment of patients with RA, PsA and SA in real-world data from the LORHEN registry. The 2-year retention rate was higher in SA patients than in RA and PsA patients.
**Disclosure of Interest:** None declared
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## FRI0176 SAFETY OF ANTI-TNF ALFA AGENTS DURING PREGANCY AND BREASTFEEDING: LONGTERM FOLLOW UP OF EXPOSED CHILDREN IN A CASE-SERIES OF MOTHERS WITH CHRONIC ARTHRITIDES

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**Background:** Anti-TNFalfa agents are used to control disease activity in patients with Chronic Arthritides (Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis), often during the wash-out period of teratogenic DMARDs and are usually discontinued at positive pregnancy index. However, the presence of a moderate to severe maternal disease activity during pregnancy or puerperium may require the use of the drugs also in the 2nd-3rd trimester and/or in the postpartum period. Few data are available in literature regarding their use in pregnancy and only anecdotal during lactation.
**Objectives:** To compare the health and developmental conditions of children exposed in utero and/or with breastfeeding to anti-TNFalfa agents with non-exposed children born to women with the same disease.
**Methods:** Data on birth, lactation, weaning, growth parameters, developmental milestones, vaccinations and disease conditions were collected submitting an ad-hoc created questionnaire to women affected by chronic arthritides treated with an anti-TNF alfa agent during one or more trimesters of gestation and/or during breastfeeding (cases). Data have been compared to those obtained from mothers affected from the same disease but not exposed to anti-TNF alfa therapy (controls)
**Results:** The table reports the characteristics of 34 cases (15 male, 19 female) (26 exposed to Etanercept, 5 to Adalimumab, 2 to Golimumab and 1 to Certolizumab) and 34 controls (19 M, 15 F). Twenty-six children were exposed during the first trimester (discontinuation of anti-TNFalfa agent at positive pregnancy index), while 8 during the 2nd-3rd trimester (discontinuation at 34th-37th week, mean exposure of 81 days). Both cases and controls underwent vaccinations without any severe complications. Vaccinations were protective; only one child with periconception exposure to etanercept developed chicken-pox despite vaccination. Seven children were breastfed during maternal anti-TNFalfa therapy (5 etanercept, 2 adalimumab): no differences in growth parameters, developmental milestones, vaccinations and diseases in the first year of life were highlighted in comparison to those not exposed to the drugs with lactation.
**Conclusions:** No differences in birth parameters, congenital malformations, and developmental steps in the first 24 months of life have been found between cases and controls. Growth parameters were within the curves of the general population. Cases received more vaccinations than controls. This may be due to the feeling by either parents or paediatricians that these children exposed to immunosuppressive agents could be more susceptible to infectious diseases. No relevant infectious diseases nor post-vaccine complications have been noted in the 6 children exposed to anti- TNFalfa during the 2nd-3rd trimester of gestation nor in the 5 exposed during lactation. Globally, the long-term follow-up of children supports the safety of use of anti-TNFalfa agents, either preconceptionally or during the 2nd-3rd trimester of pregnancy. Data on use during breastfeeding are still anecdotal but can be helpful for counseling the patients who are strongly motivated to breastfeed.

| | Children exposed to anti- TNF alfa (CASES) n=34 | Children not exposed to anti- TNF alfa (CONTROLS) n=34 |
|---|---|---|
| Gestational week at birth | 38 (37-39) | 39 (38-40) |
| Birth weight (g) | 3370 (2988-3495)[*,**] | 3552 (3037-3684)[*] |
| Birth lenght (cm) | 50 (48-51) | 50 (49-52) |
| Apgar index 1 min | 9 (9-9) | 9 (9-10) |
| Apgar index 5 min | 10 (9-10) | 10 (9-10) |
| Congenital malformations at birth | 1 female with Patent Foramen Ovale, pervius duct of Botallo, pulmonary hypertension; 1 female with Pierre Robin sequence + severe myopia; 1 male with cryptorchidism; 1 female with reversible metatarsal varus condition[#] | 1 male with Ventricular Septal Defect, Patent Foramen Ovale, lumbar enterothecal fusion; 1 male with cardiac murmur due to 3 mild Ventricular Septal Defects; 1 male with right testicular hydrocele |
| Perinatal complications | 1 female with emithoracical left angioma + jaundice | 1 male with jaundice; 1 male with spontaneous[#]; 1 male with neonatal cyanosis with spontaneous resolution |
| Maternal breastfeeding (number of children) | 22 (64.7%) | 25 (73.5%) |
| Age at breastfeeding discontinuation (months) | 4 (3-10) | 5 (3-8) |
| Weight: 6 months (g) 12 months (g) 24 months (g) | 7350 (7075-7800) 9350 (9175-10450) 11250 (10825-13000) | 7990 (7275-8335) 9750 (9180-10920) 12740 (11575-13515) |
| Length: 6 months (cm) 12 months (cm) 24 months (cm) | 66 (65-67) 75 (73.5-76.2) 83 (81.5-89) | 68 (65.6-69.4) 76.5 (75-78) 89 (85.6-90) |
| Age at seated position (months) | 6 (6-7) | 6 (6-7) |
| Age at walking (months) | 12 (11-13) | 12 (11-14) |
| Age at speaking (months) | 13 (13-20) | 17.5 (12-24) |

[*]1 female Small for Gestional Age; [**]1 male with macrosomia; [#]1 male with IntraUterineGrowthRestriction; [#]newborn exposed to methotrexate in the periconception period.
The values of weight, lenght, head circumference at birth and at 6, 12, 24 months are comprised within the normal Italy's population growth range.
Data reported in the table as median value, (interquartile range).

**Disclosure of Interest:** None declared
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## FRI0177 TIME TO ACHIEVE REMISSION PREDICTS LONG TERM SURVIVAL OF LOW-DOSE ETANERCEPT: AN OBSERVATIONAL STUDY

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**Objectives:** To investigate survival of low-dose etanercept (ETN) (25 mg weekly) and possible predictors.
**Methods:** We collected retrospectively data of RA patients starting ETN between April 2001 and September 2014 who achieved and maintained low-dose ETN for at least 12 months. Patients were evaluated every 3 months. Patients who achieved and maintained remission (DAS28 <2.6) for at least 6 months started low dose ETN. If remission was lost *in two consecutive visits* the patient returned to full dose. We recorded the time to achieve remission (TTR), the time in which ETN dose was reduced since remission (TRL) and the time in which patients returned to full dose or were switched to other biologics. Variables collected are reported in Table I. Survival was analysed with Cox-regression.
**Results:** Among 532 patients, 276 were excluded because of missing data or because they were lost from follow-up leaving 256 patients eligible. After 11.28±4.05 years, 151/256 (59.0%) maintained half dose (Table 1). TTR, and TRL were associated to low-dose failure (Table 1) and correlated with each other (TTR and TRL R 0.45, p<0.001). We run two separate analyses for TTR and TRL, covariates were positive rheumatoid factor or anti-citrullinated peptides and mean prednisone dose. TTR was a significant predictor of low-dose failure (OR 1.50 per year increase, 95% C.I. 1.34–1.68, p<0.001) while TRL was not (Table 2).
**Conclusions:** A shorter TTR is a predictor of long-term survival of low-dose ETN.
**Disclosure of Interest:** None declared

**Abstract FRI0177** – Table 1. Survival of half-dose etanercept: univariate and Cox regression analysis

| | All patients | Univariate Analysis | | | Cox Regression Analysis | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Low-dose success | Low-dose failure | p value | | Model I Time to remission | | Model I Time between remission and low-dose | |
| Number | 256 | 151 | 105 | | | | | | |
| Patients who stopped etanercept t, n (%) | 55 (21.5%) | – | 55 (52.4%) | – | | – | | – | |
| Patients who returned to full dose etanercept, n (%) | 50/(19.5%) | – | 50 (47.6%) | – | | – | | – | |
| Age, median (IQR), years | 59.00 (49.00; 67.00) | 60.00 (50.00; 68.00) | 58.00 (47.00; 66.50) | 0.266 | | – | | – | |
| Females, n (%) | 217 (84.8%) | 126 (83.4%) | 91 (86.7%) | 0.301 | | – | | – | |
| Positive rheumatoid factor or anti-citrullinated peptides, n (%) | 164 (64.6%) | 101 (67.3%) | 63 (60.6%) | 0.165 | | 0.92 (0.62; 1.37) | 0.692 | 0.75 (0.50; 1.11) | 0.151 |
| Disease duration, median (IQR), years | 15.00 (9.25; 21.00) | 14.00 (9.00; 21.00) | 15.00 (10.00; 22.00) | 0.510 | | – | | – | |
| Etanercept treatment duration, median (IQR), years | 8.00 (5.00; 10.00) | 8.00 (5.00; 10.00) | 7.00 (5.00; 10.00) | 0.177 | | – | | – | |
| Low-dose etanercept treatment duration, median (IQR), years | 4.00 (1.27; 8.00) | 7.00 (4.00; 9.00) | 1.75 (0.58; 3.00) | <0.001 | | – | | – | |
| Mean prednisone daily dose, median (IQR), mg | 2.50 (0.00; 5.00) | 2.50 (0.00; 5.00) | 5.00 (2.50; 5.00) | 0.011 | per milligram increase | 1.10 (1.01; 1.19) | 0.025 | 1.11 (1.02; 1.21) | 0.020 |
| Combination with methotrexate or leflunomide, n (%) | 129 (50.4%) | 78 (51.7%) | 51 (48.6%) | 0.360 | | – | | – | |
| Baseline DAS28, median (IQR) | 5.17 (4.50; 5.53) | 5.20 (4.48; 5.47) | 5.08 (4.68; 5.65) | 0.646 | | – | | – | |
| Baseline C-reactive protein, median (IQR), mg/L | 12.00 (6.00; 25.00) | 12.00 (6.00; 22.00) | 12.65 (5.00; 31.50) | 0.491 | | – | | – | |
| Time to remission, median (IQR), months | 0.25 (0.08; 1.56) | 0.25 (0.08; 0.83) | 1.17 (0.08; 2.88) | <0.001 | per year increase | 1.50 (1.34; 1.68) | <0.001 | – | – |
| Time between remission and low-dose, median (IQR), months | 6.00 (6.00; 13.00) | 6.00 (6.00; 9.00) | 6.00 (6.00; 18.00) | 0.004 | per year increase | – | – | 1.33 (1.11; 1.60) | 0.002 |

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## FRI0178 ANTI-ETANERCEPT ANTIBODIES AND ETANERCEPT LEVES LEVELS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH LOW AND FULL-DOSE ETANERCEPT IN DAS28 REMISSION

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**Objectives:** To investigate etanercept (ETN) serum levels and anti-etanercept antibodies (AEA) and evaluate whether ETN levels are associated with SDAI remission in rheumatoid arthritis patients in DAS28 remission treated with full-dose (25 mg twice weekly) and low-dose (25 mg once weekly) ETN.

**Methods:** We selected 70 patients in stable (≥12 months) full-dose (35) or low-dose (35) ETN, in remission (DAS28<2.6 for ≥12 months) and with a treatment duration ≥5 years. AEA and basal ETN levels were tested by ELISA. A cut-off >142AU/ml was adopted for defining positive AEA. A concentration of ETN ≥3.1μg/mL was considered as a high ETN level [1]. Multivariate regression analysis was used to investigate whether high ETN levels were associated with SDAI remission.

**Results:** One blood sample in the low-dose group resulted inadequate. AEA were present in 1 patient in low-dose (1/34, 2.9% low-dose ETN vs 0/35, 0% full-dose ETN, p=0.507). Full-dose and a lower weight were associated with high ETN levels: 15/35, 42.9% vs 3/34, 8.8% p=0.001 and 55.0 kg (57.0;80.0) and 65.0 (51.0;69.8), p=0.014 for high and low ETN levels respectively. Lower ETN levels, low-dose and a longer low-dose duration were associated with SDAI remission but were not confirmed with multivariate regression (Table 1).

**Conclusions:** AEA are almost absent in patients in stable remission, patient with full-dose ETN and lower weight have higher ETN levels. ETN levels are not predictive of SDAI remission.

**References:**

[1] Daïen CI, Daïen V, Parussini E, et al. Etanercept concentration in patients with rheumatoid arthritis and its potential influence on treatment decisions: a pilot study. J Rheumatol 2012.39(8):1533–8.

**Disclosure of Interest:** None declared

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## FRI0179 ANTI-TNF THERAPY IS ASSOCIATED WITH AN IMPAIRED FUNCTION OF NK CELLS AND A DEFECTIVE IMMUNOSURVEILLANCE AGAINST B-CELL LYMPHOMAS

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**Background:** Rheumatoid arthritis (RA) is associated with an increased risk of lymphoma linked to activity of the disease. Immunosuppressive drugs have been suspected to induce an additional risk. Since, NK cells have been recently shown to participate to anti–lymphoma immunosurveillance, we aimed to assess if anti-TNF might impact their anti-lymphoma activity.

**Methods:** NK cells have been assessed ex vivo in patients with RA treated with methotrexate (MTX) with (n=19) or without (n=20) anti-TNF. Phenotype has been studied by flow cytometry and function (degranulation and IFNg production) has been assessed after NKp30-cross linking. Then, we have studied the consequences of in vitro exposure of NK to anti-TNF, to TNF-R inhibitors or to controls during 6 days: phenotype has been studied and then cytotoxicity against 2 B non-Hodgkin lymphoma cell lines [Farage (EBV+) and SU-DHL4 (EBV-)] was assessed. Results are shown as median [interquartile range (IGR)]. The Mann Whitney test was used to compare independent samples.

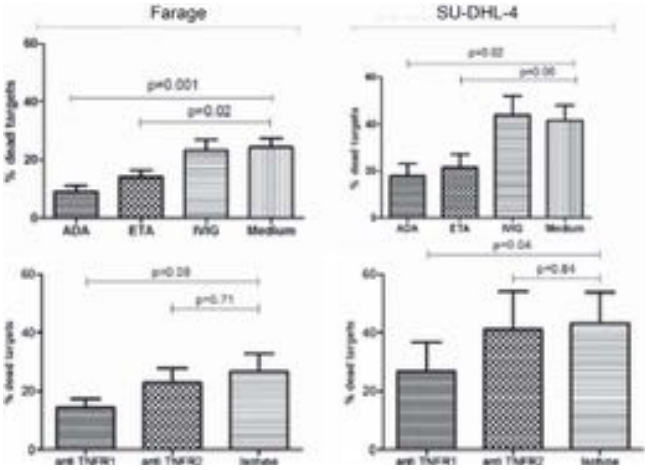
**Results:** Firstly, in patients, we found that the proportion of activated NK cells, assessed by the expression of CD69, was significantly decreased in patients treated with anti-TNF + MTX compared to patients treated with MTX alone (8.9% [2.9–40.7] vs 48.4% [27.4–58.3], p=0.005). Moreover, we found that NK cells exhibited an impaired function in patients treated with anti-TNF compared to patients treated with MTX alone as assessed by the percentage of degranulation (20.9% [18.5–32.9] vs 31.3% [21.5–49.1], p=0.04) and the loss of capacity of IFN-γ secretion ((17.4% [8.9–25.9] vs to 29.7% [22.5–43.1], p=0.007). Secondly, we have confirmed that in vitro exposure to anti-TNF negatively impact NK cells activation and function leading to an impaired anti-lymphoma activity (figure 1A). In all these experiments, no difference was observed between etanercept and monoclonal anti-TNF. Last, we have demonstrated that negative impact of anti-TNF on NK cells may be the consequence of inhibition of TNF-R1 signaling (figure 1B).

**Conclusions:** Even if meta-analysis of randomized controlled trials and of

**Abstract FRI0178** – Table 1. Predictors of SDAI Remission

| | All Patients | Univariate Analysis | | | Multivariate Regression Analysis | | |
|---|---|---|---|---|---|---|---|
| | | No SDAI remission | SDAI remission | p value | | OR (95% CI) | p value |
| Number | 69 | 49 | 20 | | | | |
| Females† | 58 (84.1%) | 41 (83.7%) | 17 (85.0%) | 0.602 | | | |
| Age (years)* | 61.80 (52.54; 69.68) | 66.46 (58.62; 72.84) | 59.27 (47.54; 68.61) | 0.070 | per year increase | 1.01 (0.92; 1.11) | 0.782 |
| Weight (kg)* | 63.00 (55.00; 77.50) | 63.50 (59.00; 79.75) | 56.00 (53.00; 74.50) | 0.574 | | | |
| Positive rheumatoid factor or anti-citrullinated peptides† | 46 (66.67%) | 35 (71.43%) | 11 (55.00%) | 0.151 | | 0.59 (0.09; 3.92) | 0.586 |
| Disease duration (years)* | 17.08 (13.48; 25.27) | 17.47 (13.23; 22.71) | 16.51 (11.61; 31.38) | 0.963 | | | |
| ETN treatment duration (years)* | 9.50 (6.92; 11.05) | 8.70 (6.46; 11.02) | 9.68 (7.79; 11.42) | 0.667 | | | |
| Low-dose ETN duration (years)* | 6.74 (5.73; 8.70) | 6.35 (4.75; 8.48) | 8.14 (6.74; 9.05) | 0.031 | per year increase | 1.31 (0.89; 1.94) | 0.168 |
| Full-dose Etanercept | 35 (50.7%) | 29 (59.2%) | 6 (30.0%) | 0.026 | | 0.408 (1.06; 1.57) | 0.191 |
| Basal ETN serum levels (μg/mL)* | 2.22 (1.27; 3.36) | 1.32 (0.66; 2.47) | 1.48 (1.26; 1.98) | 0.781 | | | |
| Positive anti-ETN antibodies† | 1 (1.4%) | 1 (2.0%) | 0 (0%) | 0.710 | | | |
| High ETN level (≥3.1 μg/mL)† | 1.65 (1.00; 2.89) | 2.34 (1.24; 3.54) | 1.59 (1.28; 2.24) | 0.426 | | | |
| Concomitant MYX use† | 17 (%) | 13 (24.5%) | 4 (25.0%) | 0.603 | | | |
| Prednisone daily dose* | 2.50 (0.00; 5.00) | 2.50 (0.00; 3.63) | 0.50 (0.00; 2.50) | 0.338 | | | |
| HAQ* | 1.00 (0.60; 1.25) | 1.00 (0.75; 1.43) | 0.41 (0.24; 0.78) | <0.001 | per unit increase | 0.04 (0.00; 1.04) | 0.053 |
| DAS28* | 2.11 (1.36; 2.35) | 2.23 (2.02; 2.47) | 1.10 (0.87; 1.15) | <0.001 | | | |

*Median (interquartile range); †number (percentage).




registries have not demonstrated to date an increased risk of lymphoma with anti-TNF, cautious must be pursued concerning this possible side effect in patients with long-term exposure. Moreover, negative impact of anti-TNF on NK cells may participate to infectious adverse events.

**Disclosure of Interest:** None declared

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## FRI0180 NO PREDICTION OF RELAPSE BY TNF BLOCKER CONCENTRATIONS OR DETECTION OF ANTIBODIES AGAINST ANTI-TNF: DATA FROM STRASS STUDY

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**Background:** The goal of rheumatoid arthritis (RA) strategy is to reach remission or at least a low disease activity. When this gaol is reached, no clear guideline exist to manage therapy. Recently, STRASS (*Spacing TNF-blocker injections in RA Study*) provided evidence of step-down therapeutic strategy with adalimumab or etanercept (1).

**Objectives:** We investigated if drug dosages and their antidrug antibodies (ADAb) could predict relapse during the 18 months of STRASS study.

**Methods:** We assessed 131 serum among the 137 included in STRASS study (60 and 71 for adalimumab and etanercept, respectively). Serum were collected at the time of randomisation. Adalimumab and etanercept blood concentrations and theirs ADAb were assessed by ELISA (Theradiag, Marne-La-Vallee, France). For this study, relapse was defined as DAS28>2.6 with DAS28 increase >0.6 since the previous study visit.

**Results:** Characteristics of the 131 patients similar to 137 from the initial STRASS study (data not shown). The median age was 54.5 [48.3–61.8] years. One hundred and two (77%) were female. The median disease duration was 6.5 [4.5–12.4] years. The median DAS28, ESR, and CRP were 2.0 [1.5–2.3], 10 [6–17], and 3 [2–4]mg/mL, respectively. Methotrexate was the main DMARDs used (n=91; 70%). No baseline characteristics were associated with relapse during tapering or not. In patients treated with etanercept, etanercept level was similar in case of relapse or not. Similarly, adalimumab level was comparable in case of relapse or not. However, in patients treated with adalimumab, ADABs was significantly higher in case of relapse compared to no relapse (0.94±0.27 ng/ml *vs.* 0.27±0.76 ng/ml; P=0.03, respectively). However, this difference was not clinically pertinent.

**Conclusions:** No difference was observed in adalimumab or etanercept blood level to predict relapse in RA patients with low disease activity. However, a slight increased of ADAb for adalimumab was observed. Its signification needs further investigation.

**References:**

[1] Fautrel B, Pham T, Alfaiate T, et al. Step-down strategy of spacing TNF-blocker injections for established rheumatoid arthritis in remission: results of the multicentre non-inferiority randomised open-label controlled trial (STRASS: Spacing of TNF-blocker injections in Rheumatoid ArthritiS Study). Annals of the Rheumatic Diseases 2016; 75: 59–67.

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**Disclosure of Interest:** None declared

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## FRI0181 CHANGING USE OF METHOTREXATE (MTX) AND BIOLOGICS IN THE TREATMENT OF RHEUMATOID ARTHRITIS (RA) IN THE UNITED STATES (US): RESULTS OF A COMPREHENSIVE PHARMACEUTICAL CLAIMS ANALYSIS

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**Background:** European and US guidelines recommend MTX as part of initial treatment for patients with RA.[1,2] Biologic agents are recommended for patients with poor prognostic indicators and those who fail to achieve treatment goals after 3–6 months of conventional therapy.[1,2] Currently, it is not clear how closely these recommendations are being followed in the US.

**Objectives:** To assess patterns of treatment for patients who initiated DMARD treatment in the US in either 2009 or 2012 and were followed for at least 2 years.

**Methods:** The analysis used Symphony Health Solutions' anonymized patient-level claims data which captures ~274 million US patients. Analysis included RA patients identified by ICD-9 codes 714.0 and 714.30 who initiated treatment with either oral MTX or a biologic therapy in 2009 or in 2012 and were followed for 2 years. Information obtained included: demographic characteristics, initial treatments, switches from oral to subcutaneous (SC) MTX and/or biologics (with or without concomitant MTX), timing of treatment changes, and oral MTX or SC MTX dosing at the times of switches/additions or end of follow-up.

**Results:** The study included 48,910 patients who initiated treatment in 2009 and 107,636 who started treatment in 2012 (Table). For the RA patients who started treatment in 2009, 27.1% initiated therapy with a biologic and 72.9% started on oral MTX. The respective values for patients initiating therapy in 2012 were 35.6% and 64.4%. Over the first 2 years of follow-up, 35.2% of patients who started MTX in 2009 and 21.6% of those started on MTX in 2012 switched to a biologic or had one added to MTX. A small percentage of patients in each cohort switched from oral to SC MTX. The median duration of oral MTX treatment prior to switching to or adding a biologic was 60 days for patients who initiated treatment in 2009 and 177 days for those who initiated MTX in 2012.

**Conclusions:** In the US, a large percentage of RA patients receive a biologic without a prior trial of MTX and this approach to treatment increased from 2009 to 2012. While there is a trend toward underuse of MTX as initial treatment from 2009 to 2012, a higher percentage of patients who started MTX in 2012 remained on this treatment for at least 2 years vs those started in 2009. This suggests many clinicians may not be following best practice with regard to the use of SC MTX.

**References:**

[1] Smolen JS, Landewe R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 2014;73:492–509.

[2] Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016;68:1–26.

**Acknowledgement:** Study sponsored by Medac Pharma, Inc.

**Disclosure of Interest:** J. O'Dell: None declared, S. Cohen Grant/research support from: Abbvie, Amgen, Astellas, Medac, Pfizer, UCB, C. Thorne Grant/research support from: Abbive, Amgen, Celgene, CaREBiodam, Lilly, Novartis, Pfizer, Sanofi, UCB, Consultant for: Abbvie, Centocor, Genzyme, Hospira, Medexus, Pfizer, Paid instructor for: Abbvie, Centocor, Genzyme, Hospira, Medexus/Medac, Pfizer, T. Mikuls Grant/research support from: Roche/Genentech, Consultant for: Pfizer

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**Abstract FRI0181** – Table 1

| | Start on Biologic (%) | Start on Oral MTX (%) | Oral MTX for Duration of Follow-up (%)* | Switch to or Add Biologic to Oral MTX (%)* | Switch from Oral to SC MTX (%)* |
|---|---|---|---|---|---|
| 2009 (N=48,910) | 13,270 (27.1%) | 35,640 (72.9%) | 21,850 (61.3%) | 12,554 (35.2%) | 1,236 (3.5%) |
| MTX dose at 90 days** | – | – | – | 15.3 | 16.1 |
| 2012 (N=107,636) | 38,309 (35.6%) | 69,327 (64.4%) | 50,338 (72.6%) | 15,013 (21.6%) | 3,976 (7.8%) |
| MTX dose at 90 days** | – | – | – | 15.9 | 16.7 |

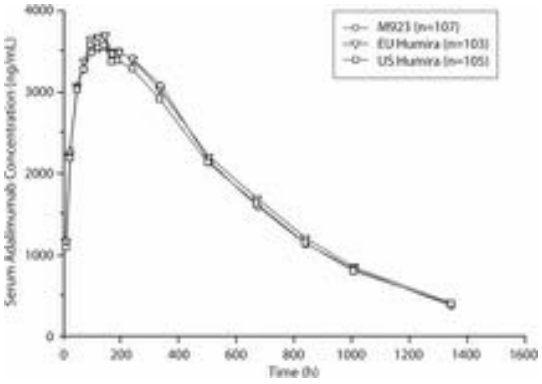
*Percent started on oral MTX, **mg/week.

## FRI0182 A SINGLE DOSE STUDY COMPARING PHARMACOKINETICS, SAFETY, AND IMMUNOGENICITY OF M923 (A PROPOSED BIOSIMILAR TO ADALIMUMAB), US-SOURCED ADALIMUMAB, AND EU-SOURCED ADALIMUMAB IN HEALTHY SUBJECTS

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**Background:** M923 is being developed as a biosimilar to the reference product HUMIRA® (adalimumab). An extensive panel of tests were used to characterize the physicochemical, functional, and in vivo attributes to support the initiation of clinical testing.

**Objectives:** The primary objective of this study was to evaluate pharmacokinetic (PK) equivalence between M923 and US-sourced adalimumab, between M923 and EU-sourced adalimumab, and between US- and EU-sourced adalimumab. Safety and immunogenicity were also assessed.
**Methods:** This was a randomized, double-blind, 3-arm, parallel group, single-dose study. A total of 324 healthy volunteers were randomized 1:1:1 to receive a single 40 mg dose of M923, US-sourced adalimumab, or EU-sourced adalimumab by subcutaneous injection on Day 1. Subjects were then followed for a total of 71 days; serum concentration of adalimumab, anti-drug antibodies (ADAs), and adverse events (AEs) were recorded. The primary PK endpoints were: $C_{max}$, $AUC_{0\text{-}inf}$, and $AUC_{0–336}$. PK bioequivalence was achieved if 90% confidence intervals for the geometric least squares (LS) mean ratios for all comparisons were within the confidence bounds (CI) of 80.00 to 125.00%.
**Results:** Bioequivalence was observed for all primary PK endpoints. Specifically, for the comparison of M923 with US-sourced adalimumab, the geometric LS mean ratios (90% CI) were $C_{max}$ =102.58 (97.31–108.14); $AUC_{0\text{-}inf}$=104.20 (96.47–112.54); and $AUC_{0–336}$=102.94 (97.88–108.27). Similarly, for the comparison of M923 with EU-sourced adalimumab, the geometric LS mean ratios (90% CI) were $C_{max}$ =99.39 (94.25–104.81); $AUC_{0\text{-}inf}$=100.90 (93.48–108.90); and $AUC_{0–336}$=100.51 (95.55–105.73). Lastly, for the comparison of US-sourced with EU-sourced adalimumab, the geometric LS mean ratio (90% CI) were $C_{max}$=103.21 (97.85–108.86); $AUC_{0\text{-}inf}$=103.27 (95.50–111.67); and $AUC_{0–336}$=102.42 (97.30–105.81). Similar concentration-time profiles were observed across groups (graph). The incidence, type, and severity of AEs were comparable across groups. The incidence, titer, and time to emergence of ADAs at any time during the study were similar across groups (proportion of subjects with confirmed positive titers: M923 =78.0%; US-sourced adalimumab =80.6%; EU-sourced adalimumab =78.5%).




**Conclusions:** Bioequivalence was observed for all treatment comparisons (M923/US-sourced adalimumab; M923/EU-sourced adalimumab; EU-sourced adalimumab/US-sourced adalimumab). In addition, the safety and tolerability profile of M923 was demonstrated to be comparable to what has been established in previous studies of EU-sourced adalimumab and US-sourced adalimumab.
**Disclosure of Interest:** J. Hillson Shareholder of: Momenta, Employee of: Momenta, T. Mant Consultant for: Momenta/Baxalta, T. Ganguly Shareholder of: Momenta, Employee of: Momenta, M. Rosano Shareholder of: Momenta, Employee of: Momenta, C. Huntenburg Shareholder of: Momenta, Employee of: Momenta, M. Alai-Safar Shareholder of: Baxalta, Employee of: Baxalta, S. Darne Shareholder of: Baxalta, Employee of: Baxalta, D. Palmer Shareholder of: Baxalta, Employee of: Baxalta, B. Pavlova Shareholder of: Baxalta, Employee of: Baxalta, J. Doralt Shareholder of: Baxalta, Employee of: Baxalta, R. Reeve Consultant for: Momenta/Baxalta, N. Goel Consultant for: Momenta/Baxalta, D. Weilert Consultant for: Momenta/Baxalta, P. Rhyne Consultant for: Momenta/Baxalta, J. Caminis Shareholder of: Baxalta, Employee of: Baxalta, J. Roach Shareholder of: Momenta, Employee of: Momenta
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## FRI0183 PREGNANCY OUTCOMES IN WOMEN EXPOSED TO INFLIXIMAB (INNOVATOR)

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**Background:** Rheumatologic, dermatologic and inflammatory bowel disorders (IBD) can affect women of childbearing potential. Infliximab ([IFX], Innovator) is approved for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC) and psoriasis (PsO).
**Objectives:** To characterize pregnancy outcomes in patients treated with IFX (Innovator), data obtained from maternal exposure to IFX (Innovator) are presented.
**Methods:** Dataset includes individual patient cases within the company safety database through 23 August 2015. Cases originated from various sources, including spontaneous reporting, clinical studies, and registries. Cases include prospectively reported (ie, pregnancy outcome not known when first reported) maternal exposures to IFX (Innovator) during pregnancy or within 2 months prior to conception with a known pregnancy outcome in RA, PsA, AS, CD, UC, or PsO pts. Birth outcome was stratified by grouped indication.
**Results:**

Table 1. Summary of pregnancy reports with known outcomes in patients treated with IFX (Innovator) for RA, PsA, AS, CD, UC and PsO

| Pregnancy outcome | All IFX (Innovator)-exposed pregnancies n, (%) | T1 IFX (Innovator)-exposed pregnancies n, (%) |
|---|---|---|
| Total no of reports with known outcome | 1362 | 695 |
| Live birth | 1115 (81.9) | 592 (85.2) |
| Congenital anomalies | 25 (2.2) | 11 (1.9) |
| Preterm birth | 85 (7.6) | 40 (6.8) |
| Abortion | | |
| Spontaneous | 147 (10.8) | 68 (9.8) |
| Elective/Induced | 72 (5.3) | 23 (3.3) |
| Scheduled | 12 (<1) | 4 (<1) |
| Unspecified | 1 (<1) | 0 |
| Ectopic pregnancy | 9 (<1) | 3 (<1) |
| Still birth | 2 (<1) | 1 (<1) |
| C-section | 3 (<1) | 3 (<1) |
| Molar pregnancy | 1 (<1) | 1 (<1) |

**Conclusions:** Pregnancy outcomes among pregnancies with T1 IFX (Innovator)-exposure did not differ from the pregnancy outcomes among all prospectively reported pregnancies exposed to IFX (Innovator). Higher percentages of CA were reported among rheumatological indications in comparison to IBD and PsO. The combined rate of CA among pregnancies with IFX (Innovator) exposure was comparable to US general population (3%)[1]. Potential confounders will be further characterized. Limitations of this analysis include lack of a direct comparison group and missing data in the reports.
**References:**
[1] Birth Defects. Centers for Disease Control and Prevention. http://www.cdc.gov/ncbddd/birthdefects/data.html. Accessed 14JAN16
**Disclosure of Interest:** J. Slater Employee of: Janssen Scientific Affairs, LLC, J. Phillips Employee of: Janssen Scientific Affairs, LLC, C.-Y. Guo Employee of: Janssen Scientific Affairs, LLC, M. Clark Employee of: Janssen Scientific Affairs, LLC, A. Geldhof Employee of: Janssen Biologics Europe, N. Gearhart Employee of: Janssen Scientific Affairs, LLC, R. Nissinen Employee of: Janssen Biologics Europe
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## FRI0184 INCREASING TREATMENT TIME ON INFLIXIMAB IS PREDICTIVE OF INCREMENTALLY BETTER LONG-TERM RETENTION IN STABLE INFLIXIMAB RHEUMATOLOGY PATIENTS IN CANADA

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**Background:** A high percentage of patients treated with TNF antagonists discontinue therapy mainly due to lack of efficacy or side effects. Recent studies of stable infliximab (IFX) patients switched to biosimilar infliximab (INB) seem to suggest similar safety and efficacy outcomes as IFX[1,2]. However, these studies often have small sample sizes, short follow-up periods and, where reported, high discontinuation rates post-switch.
**Objectives:** To demonstrate long-term retention patterns of stable Canadian rheumatic disease (RD) patients treated with originator IFX.
**Methods:** We conducted a population cohort study using IMS health™|Brogan's longitudinal Canadian patient claims database, the largest such database in Canada. The analysis captured a robust sample of thousands of claims from private insurers across Canada, and public claims from Ontario and Quebec. The retention analysis included RD patients with: a) an initial IFX claim during the selection period of Jan 2008-May 2015; b) absence of IFX claims in the 12 months prior to the initial claim; c) ≥1 claim for any drug other than IFX drug during that 12-month period; and d) ≥1 claim in the 4 months following the end of the longitudinal patient tracking period. Retention was measured at 12-month intervals and analyzed accordingly. Unadjusted odds ratios were then calculated based on retention data and 10 pairwise comparisons were calculated at the 95% confidence interval.
**Results:** The analysis captured 3,131 IFX RD patients in the selection period of which 1,822 had ≥2 years of claims history and had been on IFX for ≥1year. The table below demonstrates that the patient's probability of being retained on IFX

| # Years on Originator IFX | # Patients | # Retained 12 months later (%) | OR (vs. 1 year on on Originator IFX) | CI (95%) | *P* value |
|---|---|---|---|---|---|
| 1 | 1,822 | 1,338 (73.4%) | | | |
| 2 | 1,102 | 898 (81.5%) | *1.5923* | *1.3245–1.9143* | *<0.0001* |
| 3 | 721 | 610 (84.6%) | *1.9879* | *1.5836–2.4955* | *<0.0001* |
| 4 | 465 | 396 (85.2%) | *2.0760* | *1.5753–2.7359* | *<0.0001* |
| 5 | 248 | 204 (82.3%) | *1.6771* | *1.1914–2.3609* | *0.0030* |

in the subsequent 12 months increases concurrently with elapsed time on IFX. Specifically for patients on IFX for 2, 3, 4 and 5 years, retention in subsequent 12 month periods was significantly higher than for patients retained for 1 year ($P<0.005$).

**Conclusions:** Real world patients treated with IFX have excellent long term treatment retention. Incrementally longer time on IFX appears to be predictive of better future retention. This becomes statistically significant for patients who are retained on therapy for ≥2 years. Stability on IFX is a factor to consider when deciding whether to switch stable patients to another biologic (including biosimilars) for non-medical reasons. Studies in which stable patients receiving IFX are switched to INB for non-medical reasons have claimed similar safety and efficacy outcomes as IFX, albeit with much higher INB discontinuation rates[1,2]. Safety and efficacy outcomes need to consider an intention to treat population that includes patients who discontinue INB after switching and retention results need to be further investigated with larger sample sizes and longer follow-up periods to better understand what drives post-switch discontinuation from INB.

**References:**

[1] J Crohns Colitis.2015Dec30 Advanced Access.
[2] Expert Opin Biol Ther.2015Dec;15(12):1677–83

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## FRI0185 ARE THERE DIFFERENCES IN BASELINE CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS ACCORDING TO THE PRESENCE OF COMORBIDITIES?

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**Background:** Rheumatoid arthritis (RA) is often associated with comorbidities that may affect the therapeutic choice or a different management in clinical practice. It is unclear whether patients with comorbidities have a different profile from those without

**Objectives:** To analyze differences in the baseline characteristics of RA patients treated with tumor necrosis factor inhibitors (TNFi) according to the presence or not of concomitant comorbidities

**Methods:** All patients from the BIOBADASER 2.0 register with a diagnosis of RA treated with TNFi from January 2008 to December 2014 were selected and divided into 2 groups according to the presence or not of comorbidities. Comorbidity was defined as ≥1 of the following at initiation of TNFi: ischemic heart disease; malignancy; diabetes; chronic pulmonary obstructive disease; smoking; hypercholesterolemia; hypertension; heart failure; renal failure; osteoporosis; Epstein Barr, hepatitis B or C virus infection; and others. Variables analyzed were: age; gender; disease duration; disease activity at initiation of biological therapy measured by the DAS-28 score; number of previous biological agents (0, 1, ≥2); concomitant glucocorticoids or synthetic DMARD; and biological duration. Differences between groups were analyzed

**Results:** From January 2008 to December 2014, 640 RA treated with TNFi were included in the BIOBADASER 2.0 register. Baseline characteristics are shown in Table 1. Patients with associated comorbidities were significantly older, less frequently female, had received a higher number of previous biologics, and had a higher baseline DAS-28 compared with patients without comorbidities

Table 1

| Variable | Total (n=640) | With baseline comorbidity (n=322) | Without baseline comorbidity (n=318) | p-value |
|---|---|---|---|---|
| Age at initiation of first biologic agent (years), mean (SD) | 54.7 (13.7) | 60.1 (11.8) | 49.1 (13.3) | <0.001 |
| Women, n (%) | 497 (77.7) | 237 (73.6) | 260 (81.8) | 0.013 |
| Disease duration (years), mean (SD) | 7.3 (8.0) | 7.6 (8.1) | 7.0 (7.9) | 0.330 |
| Number of previous biologic agents | | | | |
| 0 | 578 (90.3) | 290 (90.1) | 288 (90.6) | 0.706 |
| 1 | 50 (7.8) | 22 (6.8) | 28 (8.8) | 0.381 |
| ≥2 | 12 (1.9) | 10 (3.1) | 2 (0.6) | 0.049 |
| Baseline DAS28, mean (SD) | 4.68 (1.62) | 4.98 (1.43) | 4.48 (1.75) | <0.001 |
| Concomitant sDMARD (%) | | | | |
| 0 | 130 (20.3) | 65 (20.2) | 65 (20.4) | 0.891 |
| 1 | 411 (65.9) | 205 (63.7) | 206 (64.8) | |
| ≥2 | 99 (15.5) | 52 (16.1) | 47 (14.8) | |
| Concomitant corticosteroids (%) | 378 (59.1) | 202 (62.7) | 176 (55.3) | 0.057 |
| Duration of TNFi (months)* | 13.9 (13.5) | 13.3 (13.1) | 14.5 (13.9) | 0.446 |

*From TNFi initiation to switch to other biologic.

**Conclusions:** RA patients treated with TNFi with baseline comorbidities are significantly older, have a higher baseline DAS 28 and had received more previous biologics, suggesting a RA population with higher activity than those without comorbidities. Whether this higher baseline activity favors the development of comorbidities, or whether comorbidities limited therapy in these patients, requires analysis.

**Disclosure of Interest:** None declared

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## FRI0186 RETENTION OF FIRST-LINE ANTI-TNF TREATMENTS AND IN CASES OF FAILURE RETENTION RATES OF ANTI-TNF DRUG OR A NON-TNF-TARGETED BIOLOGIC IN A MONOCENTRIC COHORT OF 200 RHEUMATOID ARTHRITIS PATIENTS

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**Background:** While several registries have already evaluated the retention of first-line anti-TNF therapy in RA, divergent conclusions have at times been reported. Following treatment failure with a first-line anti-TNF agent, a non-TNF-targeted biologic is recommended rather than a second anti-TNF drug.

**Objectives:** This study sought to compare the retention rate (RR) of a first-line anti-TNF treatment in routine care and in patients with inadequate or insufficient response the RR of either a second-line anti-TNF drug or a non-TNF-targeted biologic, in a monocenter cohort from Auvergne.

**Methods:** All RA patients treated with anti-TNF between 2008 and 2015 were enrolled.

**Results:** In total, 200 RA patients were analyzed, including 37 men and 163 women (81.5%). The mean age was 55.1 ± 13.1 years and disease duration was 8 years [3–15]. 89 (70.1%) patients had RF and 75 (72.8%) anti-CCP antibodies; 96 cases were erosive (69.6%). DAS-ESR was 4.87 ± 1.30. The first-line anti-TNF drugs were etanercept (ETA) (61%), adalimumab (ADA) (24%) or infliximab (IFM) (15%), either as monotherapy (14.6%) or associated with a DMARD (85.4%) (MTX: 64.5%). 131 patients had corticosteroids (mean dose: 7.5 mg/day). At 6 months, 73.8% were EULAR responders (27.8%: moderate; 46%: good). The overall median retention time (RT) was 55.1 months (ADA: 73.9 [19.3 -136.2], ETA 59.3 [17.1 –NA], IFM: 31.1 [7.1 -65.1] months). The RR of the first anti-TNF drug 2 years after initiation was 67.4% for ETA, 67.8% for ADA, and 55% for IFM. The hazard ratios (HR) for treatment cessation did not significantly differ between ETA and monoclonal antibodies. Inefficiencies were observed for 78 patients (70%), including 26 primary inefficiencies (33%) and 30% treatment discontinuations due to side-effects. Reasons for discontinuation did not significantly differ between the anti-TNF groups. IFM exhibited lower safety. Predictors of treatment discontinuation were older age, high activity disease, CRP, and rheumatoid nodules. In contrast, association with a DMARD significantly improved the median RT (17.5 *vs.* 60 months, 76 *vs* 29 months for MTX) for all anti-TNF drugs. Following treatment failure with the first anti-TNF therapy, a second anti-TNF was administered in 61 patients, while 44 were switched to a non-TNF-targeted biologic (22: rituximab; 8: abatacept; 10: tocilizumab; 4: anakinra). A second treatment failure was more common when using a second anti-TNF agent than with non-TNF-targeted biologics (77.1% *vs.* 9.1%, $p<0.001$). Loss of efficacy was the principal reason for discontinuing second anti-TNF drugs (46.8%). The median RT was 12 months [5–25] for second anti-TNF drugs and 10 months [6.5–14.5] for non-TNF-targeted agents. Treatment cessation did significantly differ between anti-TNF drugs and non-TNF-targeted agents (HR: 5.37 [51.92 -15.02]).

**Conclusions:** Our results showed near-identical retention levels recorded for anti-TNF, lower safety for infliximab, improvement of retention when anti-TNF were associated with a DMARD and better efficacy achieved with a non-TNF-targeted biologic following the failure of a first-line anti-TNF treatment.

**Disclosure of Interest:** None declared

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## FRI0187 A RANDOMIZED CROSSOVER COMPARISON OF INJECTION SITE PAIN WITH 40 MG/0.8 ML AND 40 MG/0.4 ML FORMULATIONS OF ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** A new 40 mg/0.4 mL formulation of adalimumab was developed that has fewer excipients, a smaller volume, and a delivery presentation with a smaller gauge needle than the current 40 mg/0.8 mL formulation.

**Objectives:** Evaluate injection site–related pain, safety, and tolerability of the new and current formulations of adalimumab in patients with rheumatoid arthritis (RA).

**Methods:** In 2 identically designed, phase 2, randomized, single-blind, 2-period

crossover studies, adults with RA (biologic-naive or current users of 40 mg/0.8 mL adalimumab with an average injection site–related pain rating ≥3 cm on a visual analog scale [VAS; 0–10 cm]) were randomized to receive 40 mg/0.8 mL or 40 mg/0.4 mL adalimumab at visit 1; after 1–2 weeks (depending on patient medication schedule), patients received the other formulation at visit 2. A pain VAS (McGill Pain Questionnaire [MPQ-SF]) and the Draize scale were evaluated immediately after injection and 15 minutes postinjection; the primary endpoint was immediate pain after injection.

**Results:** Sixty-four and 61 patients were randomized in Studies 1 and 2, respectively. Both studies found significantly lower immediate pain after injection for the 40 mg/0.4 mL versus the 40 mg/0.8 mL formulation (Table). The mean difference on the VAS for the pooled data (–2.48 cm) was statistically significant ($P<0.001$) and clinically relevant; the median percent reduction was –84%. Most other endpoints in both studies favored the 40 mg/0.4 mL formulation (Table), and its tolerability and safety profiles were consistent with 40 mg/0.8 mL adalimumab (data not shown).

Table. Pain Parameters After Injection

| Assessment, mean (SD) | Immediately After Injection | | | | 15 Minutes After Injection | | | |
|---|---|---|---|---|---|---|---|---|
| | 40 mg/0.8 mL Formulation | 40 mg/0.4 mL Formulation | Within-Patient Difference* (95% CI) | P Value† | 40 mg/0.8 mL Formulation | 40 mg/0.4 mL Formulation | Within-Patient Difference* (95% CI) | P Value† |
| Study 1 | N=61‡ | N=61‡ | | | N=61§ | N=61§ | | |
| Pain of injection | 3.3 (2.11) | 1.4 (2.00) | −1.79 (−2.33 to −1.24) | <0.001 | 1.8 (2.12) | 0.9 (1.64) | −0.89 (−1.41 to −0.37) | 0.001 |
| Present pain intensity | 1.3 (0.79) | 0.7 (0.84) | −0.6 (−0.84 to −0.35) | <0.001 | 0.3 (0.54) | 0.2 (0.48) | −0.05 (−0.17 to 0.07) | 0.564 |
| MPQ-SF pain experience total score | 4.4 (5.09) | 2.4 (3.33) | −2.03 (−3.13 to −0.94) | 0.009 | 0.9 (2.32) | 0.7 (2.64) | −0.16 (−0.91 to 0.61) | 0.678 |
| Study 2 | N=63‖ | N=63‖ | | | N=63‖ | N=63‖ | | |
| Pain of injection | 4.2 (2.72) | 0.9 (1.44) | −3.25 (−4.03 to −2.48) | <0.001 | 1.0 (1.41) | 0.4 (1.09) | −0.62 (−1.04 to −0.17) | 0.009 |
| Present pain intensity | 1.9 (1.12) | 0.5 (0.69) | −1.35 (−1.64 to −1.06) | <0.001 | 0.7 (0.84) | 0.2 (0.53) | −0.42 (−0.62 to −0.22) | <0.001 |
| MPQ-SF pain experience total score | 6.9 (7.36) | 1.1 (1.61) | −5.84 (−7.63 to −4.05) | <0.001 | 1.6 (2.69) | 0.5 (1.03) | −1.17 (−1.81 to −0.52) | 0.001 |

ANOVA, analysis of variance; MPQ-SF, short-form McGill Pain Questionnaire.
*Within-patient difference for 40 mg/0.4 mL adalimumab − 40 mg/0.8 mL adalimumab from the crossover ANOVA model with period, sequence, and treatment as fixed effects, and subject as a random effect.
†For differences between treatment groups from ANOVA with period, sequence, and treatment as fixed effects, and subject as a random effect.
‡2 patients discontinued from the study, 1 before receipt of study drug and 1 after the first dose of study drug (pharyngitis).
§1 patient discontinued from the study before receipt of study drug.

**Conclusions:** A 40 mg/0.4 mL adalimumab formulation was well tolerated and associated with less injection site–related pain than the 40 mg/0.8 mL adalimumab formulation.

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## FRI0188 SAFETY, TOLERABILITY, AND PHARMACODYNAMICS OF ABT-122, A DUAL TNF- AND IL-17–TARGETED DUAL VARIABLE DOMAIN (DVD)-IG™ IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** TNF and IL-17 independently contribute to the pathophysiology of RA, synergistically inducing inflammatory mediators and joint destruction. Selective dual neutralization of TNF and IL-17 confers superior protection vs inhibition of either alone in mouse RA models. ABT-122 is a novel dual variable domain immunoglobulin (DVD-Ig™) targeting both human TNF and IL-17A and hypothesized to provide greater clinical responses in RA patients (pts).

**Objectives:** Investigate safety, tolerability, and exploratory pharmacodynamics of multiple doses of ABT-122 in pts with stable RA

**Methods:** Two phase 1, placebo (PBO)-controlled, multiple-dose studies randomized 43 pts with stable RA receiving stable methotrexate (7.5–25 mg/wk). Pts received subcutaneous PBO, ABT-122 1 mg/kg every other wk (4 doses), or ABT-122 0.5, 1.5, or 3 mg/kg weekly (8 doses), and were evaluated through 45 d after last dose. Serum for inflammation markers and chemokines, based on preclinical studies with dual TNF and IL-17 neutralization, was collected at baseline (BL) through d 92 and analyzed by multiplex assays.

**Results:** No clinically significant safety findings were observed. Rates of treatment-emergent AEs were similar in the ABT-122 and PBO groups, with no evidence of a dose response. There were no AE or serious AE trends, systemic hypersensitivity reactions, or dose-limiting toxicities with ABT-122. Infections were reported, as expected in RA, with no apparent patterns related to etiology, type, or dose with ABT-122 vs PBO, and no pt discontinued the study owing to infection. There were no clinically significant laboratory, vital sign, or ECG abnormalities. CXCL9 and CXCL10 decreased within 3 d of ABT-122 administration (–25% and –30% vs BL, respectively) relative to PBO. Maximal decreases occurred by d 15 (–60% and –45% for CXCL9 and CXCL10, respectively) and persisted through 14 d after last dose. CCL23 decreased following ABT-122, with maximal decreases (–30%) at d 64, and continued through d 92. Consistent with TNF inhibition, soluble E-selectin decreased following ABT-122, persisting through d 92 for the 3 mg/kg group.

**Conclusions:** ABT-122 demonstrated a well-tolerated safety profile in RA pts through 8 wk of dosing up to 3 mg/kg, consistent with the prior first-in-human study in healthy subjects. Because CXCL9, CXCL10, and CCL23 are involved in lymphocyte and myeloid cell recruitment into inflamed tissues, decreases in these chemokines indicate that ABT-122 rapidly modulates potential pathophysiologic pathways in RA pts, with evidence for persistent effects after cessation of dosing. These results suggest that dual neutralization of TNF and IL-17 may provide an opportunity to control inflammation and its clinical manifestations in RA and other immune-mediated inflammatory diseases.

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## FRI0189 THE USE OF INTERFERON GAMMA RELEASE ASSAYS IN SCREENING FOR LATENT TB PRIOR TO BIOLOGICS IN PATIENTS WITH RHEUMATIC DISORDERS; VALIDATION OF NICE GUIDANCE

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**Background:** Patients with rheumatic disorders treated with TNF-α inhibitors have a 3–4 fold increased risk of developing TB. Our local population (Slough, UK) has a very high TB incidence with a rate of 58.5 per 100,000 population in 2012, approximately four times the national average. Latent TB in our population, many of whom are on immunomodulatory treatment, is thus likely to be several-fold higher. NICE guidance recommends that immunocompromised patients should be screened for latent TB using either an Interferon Gamma Release Assay (IGRA) alone or in combination with a tuberculin skin test.

Two currently available IGRAs are the TB-ELISPOT and QuantiFERON-TB Gold In Tube (QFT) test. The NICE guidelines do not distinguish between these two assays. Whilst they have enhanced our ability to diagnose latent TB their use in immunosuppressed patients has not been widely evaluated. Furthermore, there is limited evidence to support the superiority of either of the two assays.

**Objectives:** We aim to:

- Study the effectiveness and outcomes of our current TB screening programme prior to biologic therapy in our high risk immunosuppressed patients
- Compare two currently used IGRAs (ELISPOT and QFT) in this population of patients.

**Methods:** Retrospective data was obtained from our patient database. 246 consecutive patients (39% male and 61% female; age range 29 – 86 years; 78.5% Caucasian, 19.5% Asian and 2% other) were identified with inflammatory rheumatic disorders who had undergone clinical screening, a chest radiograph and an IGRA (either one or both of TB ELISPOT or QFT) prior to use of a biologic agent between 2008 and 2015.

**Results:** 16/246 (6.5%) patients had a positive IGRA. Of these 15 received chemoprophylaxis for latent TB. 12 (75%) of these patients were Caucasian and the remainder were Asian. 230/246 (93.5%) patients were IGRA negative. 190 patients were receiving immunosuppressant therapy at the time of screening and 245 patients screened were subsequently treated with TNF inhibitors. In this 7-year period there have been no cases of TB reactivation reported to date.

Of the patients screened with both IGRAs, the majority of patients tested negative for both (158/171, 92.4%). 13/171 (7.6%) patients had a positive result. Of these 6 tested positive for both ELISPOT and QFT, 4 had a positive ELISPOT only, and the remaining 3 had a positive QFT test only. The concordance of the two assays used was thus 95.9% (164/171 patients).

**Conclusions:**

- The absence of TB reactivation in our high risk immunosuppressed population receiving biologic therapy indicates the effectiveness of our current screening strategy.
- The current study demonstrates good concordance between the ELISPOT and QFT assays, suggesting that the use of either test on its own is sufficient for screening for latent TB in this population. This data supports current NICE guidance on diagnosing latent TB in the immunocompromised population.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4272

## FRI0190 INDUCTION-MAINTENANCE IN EARLY RA: A META-ANALYSIS OF TRIALS USING MTX PLUS TNF-INHIBITOR AS INDUCTION THERAPY

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**Background:** The goal of rheumatoid arthritis (RA) treatment is remission or, when not achievable, low-disease-activity (LDA). Initial combined therapy with MTX + TNF-inhibitor (TNFi) achieves these goals more often than MTX alone, but at a high cost. Some trials have therefore used the combined treatment for a limited time only ("induction-maintenance").
**Objectives:** It has remained unclear if the benefits from the induction phase are sustained during maintenance, and individual trials may not have been sufficiently powered to resolve this issue. Therefore, we performed a meta-analysis of trials using the initial combination of MTX+ TNFi in DMARD-naïve early RA-patients.
**Methods:** A systematic literature search was performed for induction-maintenance randomized controlled trials where initial combination therapy was compared with MTX-monotherapy in patients with clinically active early RA. Our primary outcome was the proportion of patients who achieved LDA (DAS28<3.2) and/or remission (DAS28<2.6), at 12–76 weeks of follow-up comparing patients who started with MTX+TNFi to those who started with MTX alone. A random effects model was used to pool the risk ratio (RR) for LDA and clinical remission.
**Results:** The literature search identified 1269 studies that matched the predefined search terms. We identified six published randomized trials, four of them where MTX+ADA was given as initial therapy and where ADA was withdrawn in a subset of patients after LDA/remission had been achieved. For two of these trials (Guépard and Hit-Hard) original data were re-examined, for the other two (Optima and Opera) only published data were available. Two of the additional identified trials (T20 and BeST) used MTX+Infliximab as initial combination-therapy. For BeST, only LDA could be assessed. As expected, the RR of achieving LDA or clinical remission with combination therapy was significantly greater than with MTX monotherapy; 1.70 (95%CI 1.21–2.38) and 1.67 (95%CI 1.42–1.95), respectively. The pooled RRs for achieving LDA and clinical remission at follow-up after discontinuation of TNFi were 1.41 (95%CI 1.05–1.89) and 1.34 (95%CI 0.95–1.89), respectively, with significant heterogeneity between trials (Figure 1).

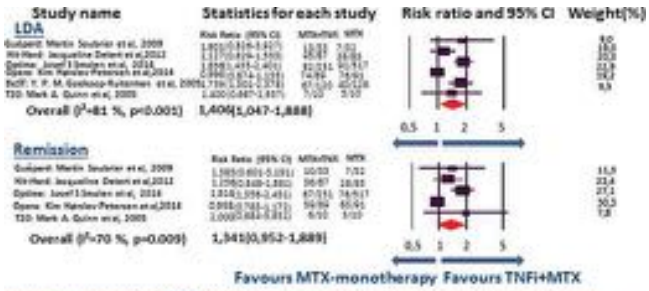



Figure 1A) Forest plot of the risk ratio of attaining LDA using combination therapy versus monotherapy at follow up. 1B) Forest plot of the risk ratio of attaining remission using combination therapy versus monotherapy at follow up. The $I^2$ and p-values for heterogeneity are shown. (Remission= disease activity score (DAS)28<2.6; LDA=low-disease activity(DAS28<3.2)

**Conclusions:** This meta-analysis supports the hypothesis that in early RA, initial therapy with MTX+TNFi is associated with a higher chance of retaining LDA and/or remission even after discontinuation of TNFi.
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**Disclosure of Interest:** S. Emamikia: None declared, E. Arkema: None declared, J. Detert: None declared, K. Chatzidionysiou: None declared, M. Dougados Consultant for: Maxime Dougados has participated at symposia and advisory boards organized by ABBVIE, PFIZER, UCB, MERCK, SANOFI, NOVARTIS, ROCHE, BMS, G. Burmester Grant/research support from: Abbott, R. van Vollenhoven Grant/research support from: AbbVie, Amgen, BMS, GSK, Pfizer, Roche, UCB, Consultant for: AbbVie, Biotest, BMS, Crescendo, GSK, Janssen, Lilly, Merck, Pfizer, Roche, UCB, Vertex
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## FRI0191 BIOSIMILAR CANDIDATE ABP 501: ADDITIONAL EFFICACY ANALYSES FROM THE PHASE 3 STUDY

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**Background:** ABP 501 is being developed as a biosimilar candidate to adalimumab, a fully human recombinant monoclonal antibody. Evidence from analytical and pharmacokinetic comparisons indicates that ABP 501 is highly similar to adalimumab. Results of efficacy and safety from a phase 3 study comparing ABP 501 with adalimumab in subjects with rheumatoid arthritis (RA) have been previously presented.[1,2]
**Objectives:** To report descriptive results from additional efficacy analysis based on clinical disease activity index (CDAI) and simplified disease activity index (SDAI) composite indices as well as results for the ACR individual components. These analyses provide information on alternate methods for disease management.
**Methods:** This was a randomized, double-blind, active-controlled study in adult subjects with moderate to severe RA who had an inadequate response to methotrexate. Subjects were randomized in a 1:1 ratio (ABP 501: n=264; adalimumab: n=262) to receive either ABP 501 or adalimumab 40 mg subcutaneously every 2 weeks. Details of the study design have been previously reported.[1] For these analyses descriptive summaries of CDAI, SDAI and individual American College of Rheumatology response criteria (ACR) components were generated.
**Results:** Baseline characteristics were well balanced between groups. At week 24, the mean (SD) CDAI improvement from baseline was 25.94 (12.62) for ABP 501 and 25.06 (12.02) for adalimumab. At week 24, the mean (SD) SDAI improvement from baseline was 26.57 (12.97) for ABP 501 and 25.64 (12.31) for adalimumab. Results for CDAI, SDAI and individual ACR components at baseline and week 24 are shown in the Table. The overall safety and immunogenicity profile of ABP 501 was comparable to that of adalimumab and has been previously reported.[1,2]

Table 1. Results [mean (SD)] for individual ACR components at week 24

| Parameter | ABP 501 | | Adalimumab | |
|---|---|---|---|---|
| | Baseline | Week 24 | Baseline | Week 24 |
| CDAI | 39.1 (12.08) | 13.3 (11.67) | 38.7 (11.87) | 13.5 (11.20) |
| SDAI | 40.5 (12.54) | 14.0 (11.95) | 40.1 (12.28) | 14.3 (11.55) |
| ACR Component | | | | |
| Swollen Joint Count | 14.7 (9.05) | 4.0 (7.55) | 14.1 (7.98) | 3.7 (5.38) |
| Tender Joint Count | 24.3 (14.35) | 7.7 (9.99) | 23.9 (13.49) | 8.0 (10.67) |
| Subject's Global Health Assessment | 6.5 (1.92) | 3.4 (2.25) | 6.6 (1.86) | 3.4 (2.10) |
| Investigator's Global Health Assessment | 6.8 (1.29) | 2.4 (1.80) | 6.7 (1.59) | 2.5 (1.73) |
| Subject Assessment of Disease-related Pain | 58.3 (21.82) | 25.6 (23.25) | 60.6 (22.37) | 27.3 (23.50) |
| C-reactive Protein (mg/L) | 13.88 (20.69) | 7.30 (9.57) | 14.68 (19.38) | 7.48 (10.97) |
| Health Assessment Questionaire – Disability Index (HAQ-DI) Total Score | 1.48 (0.62) | 0.97 (0.69) | 1.50 (0.65) | 0.95 (0.68) |

**Conclusions:** These additional analyses confirm that the of efficacy ABP 501 is comparable to adalimumab in multiple clinical characterisitics providing further evidence that ABP 501 is similar to adalimumab.
**References:**
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[2] Matsumoto et al. Presented at: American College of Rheumatology Annual Meeting; November 2015; San Francisco, CA. Abstract 2757.
**Acknowledgement:** Monica Ramchandani, PhD for medical writing.
**Disclosure of Interest:** S. Cohen Consultant for: Amgen, N. Zhang Shareholder of: Amgen, Employee of: Amgen, P. Kaur Shareholder of: Amgen, Employee of: Amgen
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## FRI0192 CLINICAL IMPORTANCE OF ANTI-DRUG AND SERUM DRUG LEVEL TESTING IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ETANERCEPT

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**Background:** In the past two decades TNF inhibitors have proved especially effective in the treatment of chronic inflammatory diseases such as rheumatoid arthritis. However, despite a high responder rate there is a substantial number of patients showing a primary therapy failure or loss of efficacy after initial response. The presence of anti-drug antibodies and serum drug levels are considered as variables that influence therapy outcome.
**Objectives:** It was the aim of the study to analyse the clinical relevance of anti-drug antibodies and drug levels in the course of a long term treatment of rheumatoid arthritis (RA) patients with etanercept (ETN).
**Methods:** In this retrospective analysis, 508 serum samples from 104 RA patients (86 female/18 male, mean age 51.1±11.5 years (mean±SD), mean disease duration 10.8±8.3 years) were obtained after 6, 12, 24, 36, and 48 months

of treatment with ETN, and selected for determination of anti-ETN antibodies and drug levels. If available, serum samples obtained at least 2 weeks after discontinuation of ETN treatment (due to side effects, non-response, remission or surgery) were used for analysis to exclude any interference of high drug levels with the anti-drug antibody assay. For the determination of anti-ETN and ETN levels, Promonitor® - assays (Proteomika, Spain) were used according to the manufacturer's instructions.

**Results:** Mean baseline disease activity (DAS28) of 5.77±1.19 decreased to 3.69±1.35, 3.43±1.27, 3.39±1.27 and 3.16±1.19 after 6, 12, 24, and 48 months of ETN treatment. No anti-ETN antibodies were found at any time point, neither in the course of treatment nor in samples from 72 of these patients obtained at least two weeks after discontinuation of ETN treatment (mean 51±3.9 months, range 18–120 months).

Mean ETN serum levels for all patients were 3.58±0.17μg/ml, 4.33±0.24μg/ml, 4.22±0.29μg/ml, 4.21±0.27, and 4.66±0.42μg/ml after 6, 12, 24, 36, and 48 months, respectively.

In the course of treatment ETN levels remained stable in most patients, mean levels (calculated from up to 5 single values) between individual patients ranged between 0.9 and 9.91μg/ml. ETN serum levels were not associated with patient related variables such as age, disease duration, rheumatoid factor, ACPA reactivity, creatinine or estimated glomerular filtration rate. There was a slight trend that a higher body weight is associated with lower ETN levels without reaching statistical significance.

In the lower quartile of patients with mean ETN level ≤2.5μg/ml, the DAS28 decreased from 5.52±1.34 to 3.73±0.96 (-1.79, 3.81±1.62 (-1.71), and 3.54±1.54 (-1.98) after 6, 24, and 48 months. A stronger DAS28 improvement was found in the upper quartile >5.07μg/ml from 6.01±1.19 to 3.68±1.57 (-2.33), 3.19±1.14 (-2.82), and 3.08±0.88 (-2,93), respectively.

**Conclusions:** Our study confirms the lack of anti-drug antibodies in a large cohort of RA patients in the course of a long-term treatment with ETN.

ETN drug levels are characterized by a wide inter-individual variability with limited prognostic value for therapy outcome. Our findings do not explain the treatment failure in some patients indicating that other factors/mechanisms determine the lack or loss of efficacy.

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## FRI0193 ETANERCEPT DOSE REDUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS – A PILOT STUDY IN SOUTH WALES

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**Background:** In the era of biologics,increasing numbers of patients achieve full remission.Although biological agents play an important role in reducing morbidity associated with long-term disease of rheumatoid arthritis (RA),they also present risks associated with side effects,increased risk of infection and a significant cost to the Healthcare Provider. There is an increasing body of evidence supporting dose reduction in RA patients[1] and, recently, European League Against Rheumatism (EULAR) updated their recommendations for the management of RA suggesting biologic dose reduction in stable patients[2].

**Objectives:** The aim of this study was to investigate the effect of Etanercept dose reduction on our symptom-stable RA patients. We wished to examine whether patients were receptive to the idea,what their preferred delivery timescales/dose would be and the outcome to the individual.

**Methods:** Suitable RA patients (on Etanercept for >1 year with 2 consecutive Disease Activity Score (DAS)<2.6 over at least 12 months and no steroid therapy in the preceding 6 months) were identified by clinicians and reviewed by a Clinical Nurse Specialist (CNS) for suitability. No limits were set for DMARD use. Informed consent was obtained; patients were offered 4 choices of reduced dose and could withdraw and return to standard dose at any time. A DAS score was performed at baseline and at each follow up visit planned at 3, 6 and 9 months before consultant review at 12 months. Patients also received a telephone consultation by our CNS 6 weeks after starting dose reduction.

**Results:** 50 patients met inclusion criteria and were invited to participate. Three patients (6%) declined due to concerns regarding potential flare. The most popular regime was 50mg fortnightly (n=24), followed by 50mg every 10 days (n=11), then 25mg weekly (n=10), and 50mg four weekly (n=2). In total, 9 (19%) patients discontinued dose reduction – 1 patient at 6 weeks and, by 3 months, a further 8 reported loss of symptom control. Of these 9 patients, 5 were on biologic monotherapy while 4 were taking concomitant DMARDs. On withdrawal, 7 resumed the full Etanercept dose while 2 elected to switch to the 10 day regime. All patients who reported loss of efficacy were in the 50 mg fortnightly group, demonstrating a 38% failure rate for this group.

**Conclusions:** Our pilot study suggests that biologic dose-reduction is mutually beneficial for patients and healthcare providers. Patients are open to the concept of dose-reduction, and were reassured by easy access and frequent review by our CNS. Nurse-led monitoring offers patients a longer and more cost effective assessment, and frees resources for consultant-led commitments. Outcomes from six- and twelve-month follow-up are awaited and larger studies are needed to determine the optimal regime for dose reduction.

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**Disclosure of Interest:** None declared

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## FRI0194 DRUG SURVIVAL ON TNF INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN FINLAND

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**Background:** Previous studies have found that 26 to 34% of Rheumatoid Arthritis (RA) patients using Tumor Necrosis Factor (TNF)-inhibitors discontinue their treatment within one year [1,2]. Infliximab has been associated with poorer drug survival as compared to adalimumab and etanercept.

**Objectives:** The aim of this study was to assess the drug survival on TNF-inhibitors including golimumab and certolizumab pegol among patients with RA and the effect of co-medication on drug survival.

**Methods:** Patients were identified from the National Register for Biologic Treatment in Finland (ROB-FIN), which is a longitudinal cohort study established in 1999 to monitor the effectiveness and safety of Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) in rheumatic diseases. Inclusion was limited to TNF-inhibitor treatments started as the patients' first, second or third biologic treatment between 2004 and 2014. Missing baseline data was imputed by multiple imputation. Follow-up data was available until the end of 2015; however follow-up of individual treatment periods was truncated at 36 months. A Cox proportional hazards model with age as well as conventional synthetic DMARD (csDMARD) and glucocorticoid use as time-dependent confounders was carried out to compare the survival of individual TNF-inhibitors and to study the effect of co-medication. The results were reported as adjusted Hazard Ratios (HRs) with 95% Confidence Intervals (CI).

**Results:** Of the 4,067 TNF-inhibitor treatment periods identified from ROB-FIN, 3,345 periods from 2,641 patients met the inclusion criteria, accumulating a total of 5,620 patient years. Median baseline age and DAS28 score were 55 and 3.8, respectively while 74% of the included patients were women. Etanercept, adalimumab, infliximab, golimumab and certolizumab Pegol were used by 1320 (39%), 1306 (39%), 333 (10%), 195 (5.8%) and 191 (5.7%) patients, respectively. Infliximab (34%) and golimumab (20%) were associated with the highest and the lowest percentages of patients discontinuing their treatment within one year, respectively while the overall percentage was 23%. Infliximab (HR 2.2, 95% CI 1.6–3.1) and certolizumab pegol (HR 1.8, 95% CI 1.3–2.6) had lower drug survival when compared to golimumab. Similar although statistically non-significant trend was seen with adalimumab (HR 1.3, 95% CI 0.99–1.8) and etanercept (HR 1.4, 95% CI 0.99–1.8) as well. Concomitant use of methotrexate (MTX) with or without any additional csDMARDs was associated with improved drug survival (HR 0.78, 95% CI 0.66–0.92) in comparison with TNF-inhibitor monotherapy.

**Conclusions:** We found that golimumab was better in terms of drug survival than infliximab or certolizumab pegol and at least as good adalimumab and etanercept. Concomitant use of MTX improves drug survival on TNF-inhibitors.

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**Acknowledgement:** This study was sponsored by MSD. In addition, ROB-FIN has received financial support from the following pharmaceutical companies: Abbvie, Pfizer and Roche.

**Disclosure of Interest:** None declared

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## FRI0195 SWITCHING FROM ANTI-TNF TO NON ANTI-TNF THERAPY YIELD BETTER SURVIVAL IN RHEUMATOID ARTHRITIS (RA): RESULTS FROM BRAZILIAN REGISTER OF BIOLOGICAL AGENTS IN RHEUMATIC DISEASES – BIOBADABRASIL

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**Background:** There are few studies evaluating switching strategies of biological therapy in RA[1]. Survival studies are indirect evidence of treatment efficacy and safety besides being an useful tool to evaluate switching options in the real life[2].
**Objectives:** To compare the survival of different strategies of switching to a second biological therapy.
**Methods:** Data from a population-based cohort including 1,109 RA patients biological therapy were analyzed at baseline (beginning of the first biologic therapy) up to 7 years (2009–2015). Sex, age, disease duration, DAS-28 and concomitant treatments at baseline were recorded. Kaplan-Meier estimates, Chi-square, Kruskal-Wallis and Wilcoxon-Mann-Whitney tests, Cox regression analysis were applied when appropriate. Results expressed in mean±SD, % (n). Small sample precluded golimumab (GOL) and certolizumab (CER) from the survival analysis.
**Results:** 85% of the patients were women; mean age=50.10±11.81yrs; 86,56% rheumatoid factor positive. At baseline, mean DAS28=5.36±1.35; 77% receiving methotrexate, 78% prednisone, and 40% leflunomide. Regarding biological therapy, 32.1% (356) started with infliximab (INF), 33.36% (370) with adalimumab (ADA), 23.26% (258) with etanercept (ETA), 4.33% (48) with rituximab (RTX), 3.15% (35) with tocilizumab (TOC), 1.26% (14) with abatacept (ABA), 1.70% (19) with GOL and 0.81% (09) with CER. 32.28% (358) switched to second biological therapy. Of those, 65.92% (236) switched from anti-TNF to anti-TNF (INF=33, ETA=105, ADA=83) vs 27.93% (100) from anti-TNF to non anti-TNF (RTX=38, TOC=32, ABA=30), 6.13% from non anti TNF to anti-TNF (n=15) or to non anti-TNF (n=7). Discontinuation of first anti-TNF therapy was due to inefficacy (57%, n=134), adverse effects (31%, n=73) or other (12%, n=29). Better switching strategy was from anti-TNF to non-anti-TNF: 50.72±3.00 (95%CI 44.84,56.60) vs 44.67± 2.46,(95%CI 39.85,49.49)months; p=0.010. Patients that switched to TOC were using less corticosteroid, had higher DAS28 at baseline, and yield better survival (55.80±4.74 95%CI 46.51,65.09 months, p=0.029) as second biological therapy compared to ETA (50.06±3.61 95%CI 42.99–57.14), RIT (47.75±4.93 95%CI 38.10,57.40), ABA (44.89±5.94 95%CI 33.25,56.53), ADA (39.45±3.89 95%CI 31.83,47.08), and INF (34.43±4.65 95%CI 25.31,43.55).

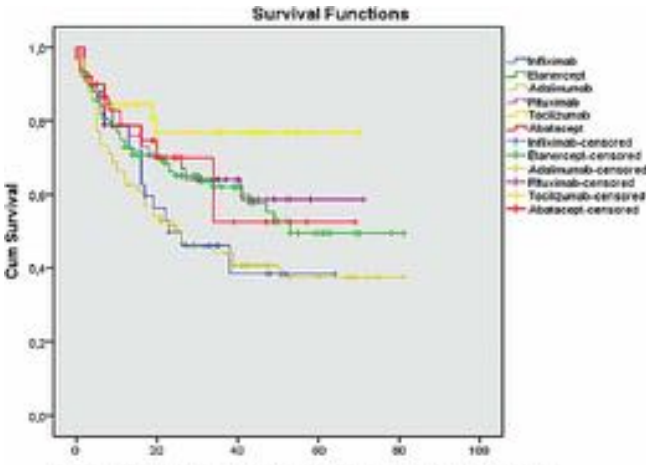


Figure 1. Survival of second biological therapy from baseline.

**Conclusions:** Switching from anti-TNF to non anti-TNF therapy seems to be a better option in the treatment of RA patients. Tocilizumab showed a better survival as second biological therapy, especially in severe disease.
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**Disclosure of Interest:** None declared
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## FRI0196 REAL-WORLD IMPACT OF TAIWAN HEALTH POLICY ON DOSE TAPERING AND WITHDRAWING BIOLOGICS IN RHEUMATOID ARTHRITIS PATIENTS: A RETROSPECTIVE CHART REVIEW STUDY

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**Background:** The OuTcomes Associated with taPering biologics among patiEnts with Rheumatoid arthritis (TAPER) study is a multicenter retrospective chart review to assess real-world implication of the Taiwan National Health Insurance Administration policy on tapering and withdrawing biologics in stable rheumatoid arthritis (RA) patients.
**Objectives:** To assess the clinical and health resource utilization (HRU) outcomes associated with dose tapering and withdrawing of biologics among stable RA patients.
**Methods:** Medical chart data were collected from RA patients tapering adalimumab (ADA) or etanercept (ETN) who had been on the treatment for ≥2 years prior to tapering. RA disease flares and HRU were assessed for the 6-month pre-tapering period, and for the 6-month short-term and up to 18-month longer-term post-tapering periods. A flare was defined *a priori* as any of the following: 1) an increase in DAS28 ≥1.2; 2) an increase in the number of swollen/tender joints; or 3) use of injectable steroids during outpatient or emergency room (ER) visits.
**Results:** Data were collected from medical charts of 261 patients (ADA=106, 40.6%; ETN=155, 59.4%). The majority were female (76.2%), with a mean age of 57.2±13.0 years, and an average RA duration of 10.1±5.6 years. Hypertension (31.4%), osteoporosis (19.2%), other autoimmune diseases (16.9%), and dyslipidemia (14.2%) were the most common comorbidities. More than half of the patients had a longer-term follow-up between one year and18 months (58.6%: ADA=62, 40.5%; ETN=91, 59.5%). The majority of ADA patients were tapered to 40mg every three weeks (63.6%) or 40mg every four weeks (30.8%); most ETN patients were tapered to 25mg every 5 days (49.4%) or once a week (30.5%). Greater proportions of patients had an RA flare post-tapering (pre-tapering: 20.7%; post-tapering short-term: 44.1%; post-tapering longer-term: 73.9%). When compared to the pre-tapering period, the mean RA flare events per patient per year increased substantially post-tapering (pre-tapering: 0.5; post-tapering short-term: 1.2; post-tapering longer-term: 1.6, all $p<0.001$). Patients had increased office visits during the short-term (pre: 1.2 vs. post: 1.4 per patient per month, $p<0.001$).
**Conclusions:** Tapering biologic agents among stable RA patients may lead to an increase in RA flare and an increase in outpatient visits.
**Disclosure of Interest:** C. Chang: None declared, K. Chen: None declared, Y. Chen: None declared, T. Cheng: None declared, P. Hsu: None declared, N. Lai: None declared, J. Lan: None declared, C. Lee: None declared, S. Lee: None declared, H. Lin: None declared, G. Tsay: None declared, J. Yen: None declared, C. Tsai Shareholder of: AbbVie, Employee of: AbbVie, Y. Bao Shareholder of: AbbVie, Employee of: AbbVie, M. Skup Shareholder of: AbbVie, Employee of: AbbVie, M. Yang Employee of: Analysis Group, E. Wu Employee of: Analysis Group, V. Garg Shareholder of: AbbVie, Employee of: AbbVie
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## FRI0197 TIME LAG OF IMPROVEMENT IN SYNOVIAL HYPERTROPHY COMPARED TO RAPID RESPONSE IN POWER DOPPLER SYNOVIAL VASCULARITY IN POST-ADALIMUMAB RHEUMATOID ARTHRITIS

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**Background:** In previous studies, the patients achieved greater disease control by adalimumab at 24 weeks, this response was maintained over the next 24 weeks[1], however, we could not found the characteristic in image to confirm the clinical presentations.
**Objectives:** This study aimed to validate the use of power Doppler ultrasonography (PDUS) for evaluating synovial vascularity and synovial hypertrophy for synovitis in patients with rheumatoid arthritis (RA) treated with adalimumab.
**Methods:** The synovial disease activity and vascularity of RA on both wrists (radio-carpal joint) were assessed using GS and PDUS to derive the composite US scores based on abnormal counts and severity. The relationship between each measure was determined.
**Results:** The 71 patients who received adalimumab therapy had significantly decreased DAS28, ESR, and CRP. After one month, PD score decreased and then remained low for 12 months. Synovial hypertrophy did not change until 3–6 months after, when it started to improve ($p$=0.017). By multivariate analysis, sex,

age, BMI, and DAS28 did not lead to any difference between synovial hypertrophy and PDUS changes ($p$=0.498).
**Conclusions:** Composite US markers of synovial hypertrophy correlate significantly to the DAS28 score and ESR/CRP in adult RA. The time needed for synovial hypertrophy to decrease may be up to 3–6 months after adalimumab therapy. Using ultrasound Doppler measurements predict success of treatment with anti-TNF-alpha has been a trend in monitoring biological therapy in patients with RA
**References:**
[1] Keystone EC, et al. Arthritis and rheumatism. May 2004;50(5):1400–1411.
**Disclosure of Interest:** None declared
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## Rheumatoid arthritis - other biologic treatment

### FRI0198 WHICH SERONEGATIVE RA PATIENTS RESPOND TO RITUXIMAB?

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**Background:** RF-CCP- RA patients have inferior response to rituximab (RTX) but a subset respond as well as seropositive RA. RF-CCP- RA may have alternative markers of B cell dysfunction such as ANA or hypergammaglobulinaemia.
**Objectives:** To identify clinical predictors of response to rituximab in RF-CCP-RA as a means to select patients suitable for RTX.
**Methods:** Data from 7 clinical trials were pooled. Binary logistic regression models were used to test whether baseline factors affected odds of ACR20 at 24 weeks in patients negative for RF and CCP patients, controlling for trial. Non-response was imputed for patients who withdrew or were retreated prior to 24 weeks. Interaction terms were added to identify potential treatment effect modifiers ($p<0.2$ criterion).
**Results:** 396 patients had data available (mean age 52.3, 82% female, mean baseline DAS28CRP 5.5) of whom 155 (39%) achieved ACR20 at 24 weeks. Odds ratios are presented in Table 1. In addition to expected markers of therapy response, we found a relationship between higher IgG and increased odds of response with an interaction with rituximab dose. Overall, 2x1000mg was more effective than placebo, and the level of IgG did not influence the odds of response. In contrast, 2x500mg was increasingly effective compared to placebo with increasing IgG titre. Data on ANA status were more limited. We tested a model including ANA in a set of 301 patients. There was a trend to greater response in ANA positive patients (OR 1.49, CI 0.87 – 2.58). Controlling for ANA the interaction with IgG remained for rituximab 500mg (OR 1.1, CI 0.96 – 1.34)

Table 1. Odds of ACR20 response at 24 weeks according to variables at baseline, adjusted for all variables and data source (trial)

| Variable | Odds ratio (95% CI), *P* value | |
|---|---|---|
| | Main effects model | Interaction model |
| RTX dose 2x500mg | 1.4 (0.6, 2.9), p=0.442 | 1.3 (0.6, 2.8), p=0.507 |
| 2x1000mg | 2.5 (1.3, 5.0), p=0.009 | 2.4 (1.2, 4.8), p=0.010 |
| Number of previous DMARDs | 1.0 (0.8, 1.3), p=0.822 | 1.0 (0.8, 1.3), p=0.840 |
| Number of previous bDMARDs | 0.6 (0.4, 1.0), p=0.043 | 0.6 (0.4, 1.0), p=0.040 |
| Age, per 10 years | 1.23 (1.01, 1.50), p=0.036 | 1.23 (1.01, 1.50), p=0.038 |
| Female | 1.1 (0.6, 1.9), p=0.858 | 1.0 (0.6, 1.9), p=0.902 |
| BMI, per unit | 1.0 (0.9, 1.0), p=0.005 | 1.0 (0.9, 1.0), p=0.005 |
| Disease duration, per 5 years | 1.1 (0.9, 1.3), p=0.441 | 1.1 (0.9, 1.3), p=0.390 |
| Oral steroid use at baseline | 1.3 (0.8, 2.1), p=0.229 | 1.4 (0.8, 2.2), p=0.202 |
| DAS28CRP, per unit | 1.2 (0.9, 1.6), p=0.305 | 1.2 (0.9, 1.6), p=0.275 |
| HAQ, per unit | 0.8 (0.5, 1.2), p=0.343 | 0.8 (0.5, 1.2), p=0.295 |
| IGA, per g/L | 1.2 (1.0, 1.5), p=0.093 | 1.2 (1.0, 1.5), p=0.099 |
| IGG, per g/L | 1.1 (1.0, 1.1), p=0.021 | 1.0 (0.9, 1.2), p=0.867 |
| IGM, per g/L | 1.0 (0.7, 1.4), p=0.966 | 1.0 (0.7, 1.4), p=0.959 |
| IGG x RTX500 | | 1.1 (1.0, 1.3), p=0.140 |
| IGG x RTX1000 | | 1.0 (0.9, 1.2), p=0.614 |

**Conclusions:** The lower dose RTX appeared less effective in this group of patients overall. A subset of RF-CCP- patients with alternative markers of B cell mediated inflammation have more scope to respond to RTX. However, this effect is less relevant when the licensed dose is used. The efficacy of RTX in RF-CCP-ANA+ arthritis patients supports its efficacy in connective tissue diseases.
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### FRI0199 RITUXIMAB IN COMBINATION WITH LEFLUNOMIDE: RESULTS FROM A MULTICENTER RANDOMIZED PLACEBO CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL IN ACTIVE RHEUMATOID ARTHRITIS (AMARA-STUDY)

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**Background:** Use of biologicals such as Rituximab (RTX) in Rheumatoid Arthritis (RA) is effective and often only licensed in combination with Methotrexate (MTX). In cases of contraindications to or intolerances, other cDMARDs are frequently used in routine care without data from RCTs.
**Objectives:** To demonstrate safety and efficacy of RTX in combination with Leflunomide (LEF) in a multicenter randomized placebo (PLA) controlled clinical trial in Germany.
**Methods:** A total of 189 patients with active RA (DAS28 >3.2 and at least 3 SJC and 3 TJC) despite stable LEF treatment were screened for a 52-weeks double-blind placebo controlled multicenter RCT. Patients were randomized to receive either two times 1000mg RTX i.v. or PLA, followed by a second course of RTX of either two times 500 or 1000 mg at week 24. The primary endpoint of the study was superiority of RTX in ACR20 and 50 responses vs. PLA during 24-weeks treatment period. Adult patients who had inadequate response to more than one antiTNF or failed more than three cDMARDs were excluded. Disease activity as well as patient reported outcomes were measured at each visit. For safety evaluation, frequency and severity of adverse events were documented.
**Results:** Of 189 screened patients 148 were randomized. The mean age was 56 years; the mean body weight 76 kg and 74% were female. The disease activity (DAS28) at baseline was 5.57 for RTX and 5.54 in the PLA group. All baseline-characteristics were well balanced between the treatment arms. RTX demonstrated significant superiority compared to PLA at week 16 in both, ACR 20 and ACR 50 response. ACR 20 response was significant superior for RTX treatment at weeks 12, 16 and 24 in both analyses, per protocol and modified intention to treat (see table). DAS28 levels in the RTX treatment-group decreased to 3.69 at week 24 (PLA 4.51) and to 3.01 at week 52. A total of 372 adverse events (AE) were observed during the one-year study period, only 14 were classified as severe (10 in RTX and 4 in PLA). 43 serious adverse events were reported, 28 of them in the RTX treatment group during the placebo controlled period.

Table 1

| | *Week 12* | | Week 16 | | Week 24 | |
|---|---|---|---|---|---|---|
| | RTX+LEF | PLA+LEF | RTX+LEF | PLA+LEF | RTX+LEF | PLA+LEF |
| ACR 20 (mITT) | 53.8* | 25.5 | 51.6* | 23.4 | 46.2* | 27.6 |
| ACR 50 (mITT) | 24.7* | 12.8 | 31.2* | 14.9 | 27.0 | 14.9 |
| ACR 20 (PPS) | 56.1* | 26.67 | 56.1* | 24.44 | 48.78* | 28.89 |
| ACR 50 (PPS) | 25.6 | 13.3 | 32.9* | 15.6 | 29.3 | 15.6 |

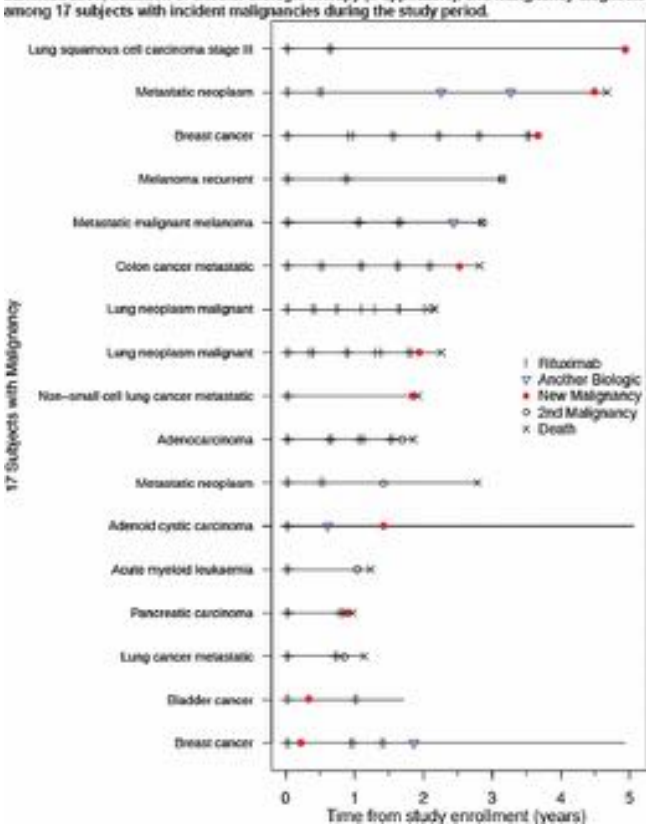
**Conclusions:** Here we report for the first time data of a RCT of combination of RTX with LEF. The treatment with RTX in combination with LEF demonstrated significant efficacy compared to the PLA for ACR20 response and for ACR50 response as well as reduction in DAS28. The highest level of response was seen at week 16. The combination of RTX and LEF demonstrated a reasonable safety profile.
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## FRI0200 INCIDENT MALIGNANCIES FOLLOWING INITIATION OF RITUXIMAB FOR RHEUMATOID ARTHRITIS: ANALYSIS FROM THE SUNSTONE REGISTRY

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**Background:** Rheumatoid arthritis (RA) is associated with an increased incidence of malignancy compared to the general population. The long term safety of biologic therapies continues to be defined. Clinical trials of rituximab in the treatment of RA report an incident malignancy rate of 0.74 per 100 person years.[1]
**Objectives:** To describe the frequency and characteristics of incident malignancies in a real-world, observational cohort of rheumatoid arthritis (RA) patients initiating rituximab in the United States.
**Methods:** The Prospective Study of the Safety of Rituximab in Patients With Rheumatoid Arthritis After an Inadequate Response to Previous Anti-TNF Therapy (SUNSTONE) recruited patients from January 2007 to October 2008 from 173 private and academic practices across 38 states within the United States and Puerto Rico, with more than 350 rheumatologists contributing data. Included subjects were age 18 or greater with a diagnosis of RA and inadequate response to anti-tumor necrosis factor-$\alpha$ therapy (TNF-IR). Enrollment occurred at the time of treatment initiation with rituximab. Subjects were followed for 5 years or until death or loss to follow-up. Targeted safety events including malignancies were reported at follow up visits occurring at least every 6 months. Nonmelanoma skin cancers and non-malignant events were excluded. Standardized incidence rate (SIR) was calculated using the US National Cancer Institute Surveillance Epidemiology and End Results (SEER) reference population and matched for age and sex.
**Results:** 989 subjects were followed for a mean of 3.9 years and contributed 3844 person-years in total. There were 17 incident malignancies yielding an event rate of 0.44 per 100 person years (95% C.I. 0.27–0.71) and age- and sex-adjusted standardized incidence ratio (SIR) of 0.36 (95% C.I. 0.21–0.57). Malignancy diagnosis occurred a median of 22 months after rituximab initiation (range 2.6–59.3) and following a median of 2 treatment cycles (range 1–6). Lung cancer was the most common malignancy reported (n=5) followed by melanoma (n=2). Subjects diagnosed with malignancy were older (67.7 vs. 57.1 years, $P<0.001$) and more likely to report current or prior tobacco use (94% vs. 57%, P=0.002) than those not diagnosed with malignancy.

Schematic illustration of the temporal relationship between study enrollment, rituximab administration, initiation of another biologic therapy (if applicable), and malignancy diagnosis among 17 subjects with incident malignancies during the study period.




**Conclusions:** At five years' follow up, the observed rate of incident malignancies in this real-world cohort of RA patients treated with rituximab is not increased compared to the background population or clinical trials.

**References:**
[1] Van vollenhoven RF, et al. J Rheumatol. 2015;42(10):1761–6.
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## FRI0201 RITUXIMAB TREATED NON RESPONDER RHEUMATOID ARTHRITIS PATIENTS ARE GENERATING A NEW AUTOANTIBODY REPERTOIRE

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**Background:** Rituximab (RTX) has shown clinical efficacy but up to 40% of RTX treated rheumatoid arthritis (RA) patients are poor responders (ref:1) and the commonly used RA biomarkers (*RF/ACPA*) are poor predictors for therapy response. Others reported associations between BAFF/BLyS levels, Fcg RIII and IL-6 genotype, interferon type I signatures and Epstein-Barr virus genome in bone marrow and clinical outcome (ref:2).
**Objectives:** Analysis of the autoantibody repertoire from RA patients under RTX treatment on human genome protein macroarrays and it's correlation to clinical DAS28 response.
**Methods:** Screening of RA sera was conducted on 37.830 unique human expression clones with sera taken before and 24 weeks after treatment. The autoantibody response of different immunoglobulin classes IgD, IgA, and IgG was recorded and bioinformatically evaluated. Response was determined according to DAS28 criteria. DAS 28 scores in the responder group before treatment was from 5.4 – 7.8 and in the non-responder group 5,6 – 6,8. We analyzed 26 RA patient sera (9 responder, 7 non-responder and 10 patients with blinded response classification) investigated the data of found autoantigens *in silico* and by hierarchical clustering.
**Results:** In the cohort of 26 patients 1292 different autoantigens (IgD,IgA,IgG) were detected. Using protein array we investigated clusters of autoantigen responses that disappeared or developed during RTX treatment of RA patients. Post treatment developing responses against new autoantigens can be correlated to mRNA tissue expression data and were interestingly found organ-specifically expressed. RA autoantigenic patterns before and 6 month after RTX treatment were patient-specific and no relevant autoantigenic cluster was found that was shared between patients or associated with response. However, RTX reduced the repertoire of autoantibodies after 24 weeks of treatment in the tested RA patient cohort on average by 60%. RA patients which do not respond are generating on average 63% new autoantibodies. In good responders to RTX only 5,5% (±3%) new autoantibodies can be detected. The IgA and IgG autoantibody repertoire in the serum after 24 weeks of RTX treatment is reduced (IgA: 41%, IgG: 31%) in good responders whereas it is increased (IgA: 1,3%, IgG: 24%) in non responders to RTX.
**Conclusions:** RA patients present highly individual autoantibody profiles before and after RTX treatment, which do not reveal antigen-specific patterns for outcome prediction. However, after 6 month of RTX treatment the autoantibody repertoire in all good responding RA patients is reduced and non responders to RTX change their autoantibody repertoire directed against new but patient specific antigens. The fast rebuilding of functional B cells might be a underlying mechanistic difference between responders and non-responders to rituximab.

**References:**
[1] Ann Rheum Dis. 2005 Feb;64(2):246–52.
[2] Arthritis Res Ther. 2012 Apr 27;14(2):R95
**Disclosure of Interest:** None declared
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## FRI0202 SAFE AND EFFECTIVE TOCILIZUMAB THERAPY IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The single-arm non-interventional study ICHIBAN was set up to evaluate the effectiveness and safety of intravenously administered Tocilizumab (TCZ IV) in patients (pts) with moderate to severe rheumatoid arthritis (RA) in Germany. Clinical data were collected during routine medical consultations including concomitant therapies, co-morbidities, therapeutic responses and adverse events.

**Objectives:** This interim analysis assessed the effectiveness and safety of long-term TCZ IV treatment with respect to patients' age.

**Methods:** Since February 2010 ~250 German rheumatology study centres collected these prospective data. Pts were observed for a maximum period of 2 years (104 weeks). The present interim analysis included pts with complete baseline (BL) data before 03rd December 2015 (group total; n=2999). 902 pts have completed the maximal 104 week observation period (group W104). Subgroups according to age have been defined as <50 years, 50–65 years, >65 years.

**Results:** At BL the age distribution showed the following proportions: <50 years 28.9%, 50–65 years 48.6%, and >65 years 22.5%. The mean TCZ IV treatment duration was 1.7, 1.8, and 1.7 years, respectively, for the three age groups.

In comparison to younger pts, the elderly (>65 years) showed longer disease duration, higher inflammatory parameters, higher disease activity, and higher co-morbidity rates at BL. Nevertheless, TCZ IV showed comparable effectiveness in all age groups. At last visit, DAS28-BSG remission (<2.6) was reached by 55.2%, 51.6%, and 48.8% of pts aged <50, 50–65, and >65 years, respectively. The mean reduction from BL in DAS28-BSG was 2.6, 2.7, and 2.8, respectively.

Regarding co-medication, the mean glucocorticosteroid (GC) dose was reduced from 7.1 (BL) to 4.6 mg/d (last visit) and was similar in all subgroups. About 12% of pts stopped GC therapy completely, again similar in all subgroups. At baseline, the rate of TCZ monotherapy (without concomitant sDMARD) was highest in the elderly (53.2%) while combination therapy is more common in younger pts (47.1%). The rate of sDMARD discontinuation while receiving TCZ is comparable in all subgroups (11.5%, 12.1%, 12.3%).

| | W104 | < 50 years | 50 – 65 years | > 65 years*** |
|---|---|---|---|---|
| N | 902 | 261 | 436 | 203 |
| Adverse events (AEs) | | | | |
| • No. of patients with AEs, % (n) | 49.6 (447) | 47.9 (125) | 48.9 (214) | 53.2 (108) |
| • Rate of AEs per 100 patient years | 80.1 | 82.9 | 75.5 | 86.3 |
| Serious adverse events (SAEs) | | | | |
| • No. of patients with SAEs, % (n) | 17.7 (160) | 13.8 (36) | 18.3 (80) | 21.7 (44) |
| • Rate of SAEs per 100 patient years | 19.4 | 14.1 | 19.5 | 25.9 |
| Fatal cases | 1 | 0 | 0 | 1 |
| Infections (AEs) * | | | | |
| • No. of patients with infections, % (n) | 22.1 (199) | 24.1 (63) | 20.8 (91) | 22.2 (45) |
| • Rate of infections per 100 patient years | 21.8 | 27.2 | 19.8 | 19.2 |
| Infections (SAEs) * | | | | |
| • No. of patients with infections, % (n) | 4.1 (37) | 4.2 (11) | 3.4 (15) | 5.4 (11) |
| • Rate of infections per 100 patient years | 2.9 | 2.9 | 2.9 | 3.1 |
| Gastrointestinal perforation (AEs) | | | | |
| • No. of patients with gastrointestinal perforation, % (n) | 0.2 (2)# | 0.4 (1)# | 0.2 (1)# | 0.0 (0) |
| • Rate of gastrointestinal perforations per 100 patient years | 0.1 | 0.2 | 0.1 | 0.0 |
| Gastrointestinal perforation (SAEs) | | | | |
| • No. of patients with gastrointestinal perforation, % (n) | 0.2 (2)# | 0.4 (1)# | 0.2 (1)# | 0.0 (0) |
| • Rate of gastrointestinal perforations per 100 patient years | 0.1 | 0.2 | 0.1 | 0.0 |
| Discontinuation of TCZ due to AEs ** | | | | |
| • No. of patients with discontinuations due to AEs, % (n) | 5.0 (45) | 5.0 (13) | 4.8 (21) | 5.4 (11) |
| • Rate of discontinuations due to AEs per 100 patient years | 2.9 | 2.9 | 2.7 | 3.1 |

**Table 1**

* Infections: All AEs/SAEs with a MedDRA Preferred Term indicating an infection

** In case of discontinuation of TCZ due to an AE, the last AE reported under TCZ administration was used

*** 5 Patients of this subgroup were older than 80 years. No serious infection, no gastrointestinal perforation nor a TCZ discontinuation due to an AE was observed within those 5 patients

# For both patients no history of gastrointestinal disease was documented

Despite slightly higher incidence rates of adverse events (AE) and serious adverse events (SAE) for the elderly, the rates of infections, serious infections and TCZ discontinuation rates due to an AE did not increase with age (Table 1). Gastrointestinal perforation was rarely observed.

**Conclusions:** TCZ IV treatment resulted in improvement of disease activity and reduction in concomitant GC dosing were observed. Despite higher disease burden at baseline, elderly RA patients (>65 years) benefited to the same extent as younger patients, without increased risk of infections. Considering natural age related risks, the low infection and gastrointestinal perforation rates of elderly patients seem to be attributable to the steroid sparing effect of TCZ therapy. Safety concerns should be no reason to argue against anti-IL-6 therapy in elderly patients.

**Disclosure of Interest:** C. Specker Consultant for: Roche, Chugai, Speakers bureau: Roche, Chugai, J. Kaufmann: None declared, H. Kellner: None declared, P. Kästner: None declared, C. Volberg: None declared, V. Braunewell: None declared, A. Aringer Consultant for: Roche, Chugai, Speakers bureau: Roche, Chugai, M. Sieburg: None declared, L. Meier: None declared, M. Hofmann Employee of: Chugai Pharma Europe Ltd., J.-P. Flacke Employee of: Roche Pharma AG, H.-P. Tony Grant/research support from: Roche Pharma AG, Consultant for: Abbvie, BMS, Chugai, Janssen, Lilly, Novartis, Roche, UCB, Speakers bureau: Abbvie, BMS, Chugai, Janssen, Lilly, Novartis, Roche, UCB, G. Fliedner Consultant for: Chugai Pharma Europe Ltd., Paid instructor for: Chugai Pharma Europe Ltd.

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## FRI0203 SUSTAINED DRUG FREE REMISSION IN EARLY RA PATIENTS TREATED TO TARGET WITH TOCILIZUMAB, METHOTREXATE OR THEIR COMBINATION

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**Background:** The U-ACT EARLY study is a 2-year, randomized placebo-controlled, double blind study in which disease modifying antirheumatic disease (DMARD)-naive early RA patients were randomized to initiate tocilizumab (TCZ, n=103), methotrexate (MTX, n=108)) or their combination (n=106), and treated according to a step-up strategy. The primary endpoint, sustained remission (SR, defined as DAS28 <2.6 and <4 swollen joints for >24 weeks), was achieved by significantly more patients in the TCZ+MTX (86%) and TCZ (84%) groups, compared to MTX (44%). Here we report a post hoc analysis of sustained drug free remission (sDFR).

**Objectives:** To compare the number of patients achieving sDFR between the three treatment strategies.

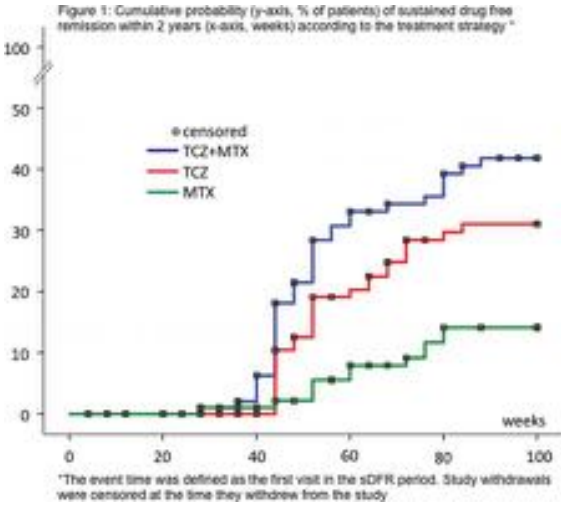
**Methods:** We analyzed data of all 317 patients included in the study. TCZ was given intravenously (8 mg/kg 4 weekly) and MTX was increased over 3 months from 10 to 30 mg/week (or maximum tolerated dose) until remission. If remission was not reached after 20 weeks, hydroxychloroquine was added. Twelve weeks thereafter, if the target was not achieved, the placebo was substituted by TCZ/MTX. If SR was achieved, medication was tapered stepwise and stopped provided remission persisted. Differences in prevalence, time-to, and duration of sDFR (drug-free for >3 months with remission) were analyzed. To identify predictive factors for achieving sDFR, baseline data were analyzed using a backward selection procedure ($p \leq 0.10$).

**Results:** Table 1 shows baseline characteristics. The proportion of patients achieving sDFR was significantly higher in the TCZ+MTX (35%, $p<0.01$) and TCZ (27% $p<0.01$) strategy, compared to MTX (11%, Fig. 1). In patients achieving it, the median time (IQR) to achieve sDFR was shorter in the TCZ+MTX (48 (44–56) weeks; p=0.09) and TCZ strategy (52 (44–67) weeks; p=0.18) when compared to MTX (60 (52–76) weeks). The median duration (IQR) of sDFR within the study period was 44 (16–56), 32 (20–48) and 28 (20–44) weeks (p=0.15) in the TCZ+MTX, TCZ and MTX group, respectively. Baseline HAQ (OR 0.2 (95% CI: 0.1–0.4), any (RF and/or anti-CCP) seropositivity (OR 0.5 (95% CI: 0.2–0.8) and initiation with TCZ+MTX (OR 3.9 (95% CI: 1.9–8.3) or TCZ (OR 3.4 (95% CI: 1.5–7.3) were significant predictors for achieving sDFR. The Area Under the Curve (AUC-ROC) of the multivariable model was 0.73 (95% CI: 0.67–0.80), indicating fair discriminative ability. In our sample, a classifier with

Table 1. Characteristics of the 317 patients with early rheumatoid arthritis

| | |
|---|---|
| Mean (SD) age, years | 53 (13) |
| Female gender, n (%) | 212 (67) |
| Mean (SD) BMI, kg/m$^2$ | 26 (4) |
| Current smoker, n (%) | 90 (28) |
| Median (IQR) alcohol consumption, unit per week | 1 (0–6) |
| Median (IQR) symptom duration, days | 26 (16–43) |
| Any seropositivity*, n (%) | 251 (79) |
| Mean (SD) DAS28 | 5.2 (1.1) |
| Median (IQR) CDAI | 25 (19–34) |
| Median (IQR) VAS pain | 60 (40–70) |
| Median (IQR) HAQ | 1.1 (0.6–1.6) |

*RF and/or anti-CCP positive.




84% sensitivity and 53% specificity correctly predicted achievement of sDFR in 66% of patients.
**Conclusions:** Early RA patients initiating tight-control TCZ treatment achieve sDFR more often and earlier, compared to MTX. Predictors of sDFR include TCZ treatment itself, as well as baseline HAQ and being seronegative.
**Disclosure of Interest:** X. Teitsma: None declared, J. Jacobs: None declared, P. Welsing: None declared, T. Woodworth Employee of: Roche, A. Pethö-Schramm Employee of: Roche, M. Borm Employee of: Roche, C. Bernasconi Employee of: Roche, F. Lafeber: None declared, J. Bijlsma Grant/research support from: received research grants (to his department) from AbbVie, BMS, Crescendo, MSD, Mundipharma, Pfizer, Roche, Sun, UCB./, Consultant for: received consultancy fees from AbbVie, BMS, Crescendo, MSD, Mundipharma, Pfizer, Roche, Sun, UCB.
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## FRI0204 EFFECT OF TOCILIZUMAB TREATMENT ON QTC INTERVAL IN PATIENTS WITH RHEUMATOID ARTHRITIS WITHOUT CARDIAC SYMPTOMS

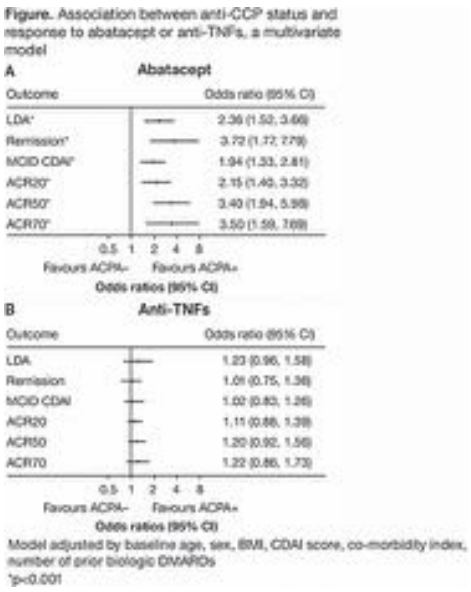
I. Yokoe, H. Kobayashi, A. Nishiwaki, K. Sugiyama, Y. Nagasawa, H. Karasawa, M. Iwata, T. Nozaki, N. Ikumi, H. Inomata, H. Shiraiwa, N. Kitamura, M. Takei.
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**Background:** Individuals with rheumatoid arthritis (RA) are at a 2-fold increased risk of sudden death compared with age- and gender-matched controls without RA. Although mechanisms underlying the increased risk are yet unclear, evidence indicates effects of systemic inflammation on ventricular repolarization. Accordingly, corrected QT (QTc) interval prolongation is more frequent in patients with RA than in those without RA. A previous pilot study reported that tocilizumab (TCZ) normalizes the QTc interval by dampening systemic inflammation.
**Objectives:** Our study prospectively evaluates TCZ treatment effects on the QTc interval of patients with RA without cardiac symptoms and explores the association between this QTc interval and RA disease activity and severity measures.
**Methods:** This prospective interventional study was conducted between March 2012 and August 2015 at the Itabashi Chuo Medical center. Patients who fulfilled the American College of Rheumatology (ACR) RA classification criteria or the 2010 ACR/ European League against Rheumatism RA criteria were included. Exclusion criteria included diabetes, history of cardiovascular events, hypertension (systolic blood pressure (BP) >140 mm Hg and/or diastolic BP >90 mm Hg), dyslipidemia (LDL cholesterol levels >140 mg/dL, HDL cholesterol level <40 mg/dL, or triglyceride level >150 mg/dL), cardiomyopathy, renal disease, and current atrial fibrillation. Age- and gender-matched healthy controls without any cardiac symptoms were selected. Patients with active RA with inadequate clinical response to methotrexate (MTX) were administered tocilizumab (TCZ 8 mg/kg IV every 4 weeks or 162 mg SC biweekly). Electrocardiography and clinical and biological monitoring were performed at baseline and 24 weeks after TCZ treatment in patients with RA.
**Results:** Ninety patients with RA (mean age: 56.4±10.4 yers; 85% female) and 40 age and gender matched healthy controls (mean age 55.6±3.4 years; 86% female) were included, of which 20% and 13% of RA patients received antihypertensive and antihyperlipidemia therapy, respectively. No significant differences were observed in mean Framingham 10 scores between healthy controls and patients with RA at baseline. The 24-week Simplified Disease Activity Index scores were significantly lower than those at baseline. Using previously established cutoffs (440 ms), we identified 8 (10%) patients with abnormal QTc interval prolongation. However, QTc intervals at baseline were higher in patients with RA than in controls (mean SD 420.3 ± 35.8 msec, mean SD 411 ± 31.2 msec; p=0.04). The QTc interval decreased by 20.9 msec from baseline to 24 weeks (p=0.001) following TCZ treatment. QTc interval prolongation at baseline was significantly correlated with the anticyclic citrullinated peptide antibody (ACPA) at baseline (p=0.003). ACPA at baseline (p=0.001) was associated with %change in QTc interval. Furthermore, no significant associations between QTc interval and RA activity were observed.
**Conclusions:** Tocilizmab treatment in patients with RA decreases QTc interval. Furthermore, anti-arrhythmic potential of TCZ treatment may have beneficial effects in patients with RA. Our results provide further evidence regarding the close association between ACPA degree and QTc intervals.
**Disclosure of Interest:** None declared
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## FRI0205 RELATIONSHIP BETWEEN ANTI-CITRULLINATED PROTEIN ANTIBODY STATUS AND RESPONSE TO ABATACEPT OR ANTI-TUMOUR NECROSIS FACTOR THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A US NATIONAL OBSERVATIONAL STUDY

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**Background:** Anti-citrullinated protein antibodies (ACPA) are associated with more severe, erosive rheumatoid arthritis (RA), but the extent to which ACPA status predicts response to therapy is not known.[1,2]
**Objectives:** To evaluate in a real-world, observational RA cohort whether baseline ACPA status is associated with response to biologics among patients with RA.
**Methods:** Using the Corrona RA registry, we identified patients with RA who initiated abatacept (ABA) or a tumour necrosis factor-alpha inhibitor (TNFi) between June 2002 and January 2015, had a follow-up visit 6 months (±3 months) after initiation and anti-cyclic citrullinated peptide (anti-CCP [a surrogate of ACPA]) measured at or prior to initiation. Anti-CCP positivity was defined as anti-CCP ≥20 U/mL. The primary outcome was mean change from baseline in Clinical Disease Activity Index (CDAI) at 6 months. Secondary outcomes at 6 months included: 1) achievement of low disease activity (LDA; CDAI ≤10) among those with moderate or high disease activity who initiated treatment; 2) achievement of remission (CDAI ≤2.8) in those with low, moderate or high disease activity who initiated treatment; 3) Minimally Important Clinical Difference (MCID) in CDAI; and 4) modified ACR20/50/70. Unadjusted and adjusted linear and logistic analyses were performed based on anti-CCP status (positive [+] vs negative [–]).
**Results:** 566 patients initiated ABA: 204 (36.0%) were anti-CCP– and 362 (64.0%) anti-CCP+. There were no differences by CCP status for age (mean 57–58 years), disease duration (median 7 years) or prior biologic use (0, 1 or ≥2 prior); however, median baseline CDAI was greater in anti-CCP– vs anti-CCP+ patients (21 vs 19, p=0.035). 1715 patients initiated a TNFi: 602 (35.1%) were anti-CCP– and 1113 (64.9%) anti-CCP+. There were no differences by CCP status for age (mean 55–56 years), prior biologic use or median baseline CDAI; however, median disease duration was greater in anti-CCP+ vs anti-CCP– patients (4 vs 3 years, p=0.021). In adjusted analyses, anti-CCP+ ABA initiators had a mean (SE) change in CDAI of –8.5 (0.6) vs –4.1 (0.8) for anti-CCP– (p<0.001); in TNFi initiators, this was –7.4 (0.3) vs –6.4 (0.4) (p=0.071). In the multivariate model for secondary outcomes, the magnitude of response was greater in anti-CCP+



vs anti-CCP– ABA initiators. Outcomes did not differ by anti-CCP status in TNFi initiators (Figure).

**Conclusions:** In a clinical practice setting, anti-CCP positivity was associated with a differential treatment response to abatacept, but not TNFis. These real-world data suggest that anti-CCP+ patients with RA show incremental improvements in response while receiving abatacept therapy compared with anti-CCP– patients.

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[1] Lv Q, et al. PLoS One 2014;9:e89442.
[2] Sokolove J, et al. Ann Rheum Dis 2015; doi:10.1136/annrheumdis-2015-207942.

**Disclosure of Interest:** L. R. Harrold Grant/research support from: Pfizer, H. J. Litman Employee of: Corrona, S. E. Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Kelly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, W. Hua Employee of: Corrona, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, L. Rosenblatt Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Rebello Employee of: Corrona, J. Kremer Shareholder of: Corrona, Grant/research support from: AbbVie, Bristol-Myers Squibb, Genentech, Lilly, Novartis, Pfizer, Employee of: Corrona, Speakers bureau: Genentech (non-branded talks only)

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## FRI0206 SERO-POSITIVITY FOR RHEUMATOID FACTOR IS AN INDEPENDENT PREDICTOR FOR ACHIEVEMENT OF GOOD EULAR RESPONSE AT 24 WEEKS IN ACPA POSITIVE RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT: RESULTS FROM JAPANESE MULTICENTER REGISTRY

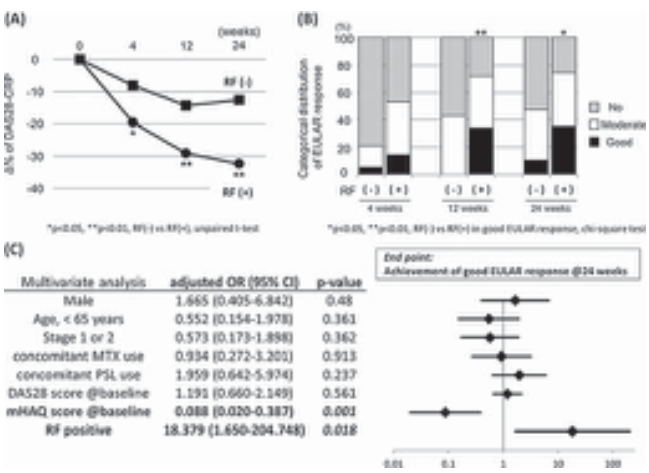
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**Background:** Abatacept is a new class of biologic agent for the treatment of rheumatoid arthritis (RA) that inhibits T cell activation by binding to CD80/86. Although some clinicians feel that the rapidity of treatment response of abatacept is slower than that of tumor necrosis factor (TNF)-inhibitors, some patients can respond to abatacept treatment quite rapidly. Recently, some reports have been published regarding the positive association between sero-positivity for anti-citrullinated protein antibody (ACPA) and clinical efficacy of abatacept in RA patients (1).

**Objectives:** The aim of this study was to demonstrate the effect of double-seropositivity for ACPA and rheumatoid factor (RF) on the rapidity of treatment response of abatacept using data from a Japanese multicenter registry system for RA patients treated with biologic agents.

**Methods:** Participants were selected from the consecutive 508 RA patients treated with abatacept who were registered in the Tsurumai Biologics Communication Registry (TBCR). We excluded the patients with previous biologic agent treatment history since it has been already reported as an independent factor affecting the clinical efficacy of abatacept (2). A total of 146 biologics-naïve and ACPA positive patients with baseline data of RF were included in this study. We compared the proportion of patients that achieved good EULAR response at 24 weeks between the RF negative and RF positive (>20 U/ml) group within the ACPA positive patients. We defined the ACPA positive as >13.5 U/ml of anti-CCP antibody (3 times cutoff value) to ensure that the positivity was reasonably sure.

**Results:** In the ACPA positive patients, the percent decreasing of DAS28-CRP scores in the RF positive group were significantly greater than those in the RF negative group at all time points (Figure A, e.g. -32.3 vs -12.6% at 24 weeks, $p<0.01$). The proportion of patients that achieved the good EULAR response was significantly higher in the RA positive group at 12 and 24 weeks (Figure B). Multivariate logistic regression analysis (adjusted with gender, age, Steinbrocker's stage, concomitant MTX and oral steroid usage, and DAS28-CRP score at baseline) revealed that the RF positivity, along with the modified HAQ score at baseline, was the independent predictor for the achievement of good EULAR response at 24 weeks (Figure C).




**Conclusions:** We clearly demonstrated that the positive association of the double-seropositivity for ACPA and RF with the rapid and good clinical response for abatacept in the biologics-naïve RA patients. This new clinical evidence regarding the effect of double-seropositivity is the valuable real-world data for the prediction of clinical efficacy of abatacept in daily clinical practice.

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**Disclosure of Interest:** N. Takahashi Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, Takeda Pharma, Bristol-Myers Squibb, T. Kojima Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, Takeda Pharma, Bristol-Myers Squibb, K. Funahashi Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, Takeda Pharma, Bristol-Myers Squibb, N. Ishiguro Grant/research support from: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, Takeda Pharma, Bristol-Myers Squibb, Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, Takeda Pharma, Bristol-Myers Squibb

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## FRI0207 REAL-WORLD COMPARATIVE RISKS OF HERPES VIRUS INFECTIONS IN TOFACITINIB AND BIOLOGIC-TREATED RHEUMATOID ARTHRITIS PATIENTS

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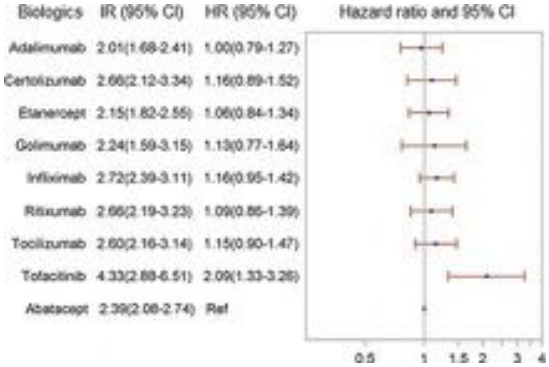
**Background:** While placebo-controlled clinical trials have suggested an increased rate of herpes zoster (shingles) with tofacitinib, the real-world risks of herpes zoster and herpes simplex associated with tofacitinib compared to other biologics for rheumatoid arthritis are largely unknown.

**Objectives:** To evaluate the risks of herpes zoster (HZ) and herpes simplex virus infection (HSV) associated with tofacitinib compared to biologic agents among patients with rheumatoid arthritis (RA).

**Methods:** Using health plan data, we identified RA patients without a history of HZ or HSV who initiated tofacitinib or biologics from 2010–2013. Among this cohort, new cases of HZ or HSV were found and incidence rates calculatedby drug. We used Cox proportional hazards models evaluated the adjusted association between tofacitinib and either HZ, and a composite outcome of HZ or HSV.

**Results:** A total of N=1,746 patients initiating tofacitinib were compared with initiations of other biologics including anti-TNF (n=38,871), abatacept (n=11,434), rituximab (n=4,785), and tocilizumab (n=6,266). Tofacitinib patients were somewhat younger (mean age 57 years) versus those on other biologics, and somewhat less likely to use concomitant MTX (39% vs. 44–56%, depending on drug).

Crude incidence of HZ associated with tofacitinib was 4.33/100py and after multivariable adjustment, was significantly elevated (hazard ratio, HR=2.09, 95% CI 1.33–3.26) compared to abatacept (referent). Rates and adjusted HRs for all other RA biologics were comparable to each other and abatacept. Older age, female sex, prednisone >7.5mg/day, prior outpatient infection, and greater number of hospitalizations were also associated with increased HZ risk Incidence rates for the combined outcome were greatest for tofacitinib (9.33/100py) and also significantly elevated after adjustment (HR=1.65, 95%CI 1.21–2.23).




**Conclusions:** Zoster infections were relatively common among RA patients. The

risk for zoster associated with tofacitinib was approximately double that observed in patients using biologics.

**Acknowledgement:** This project had no external funding

**Disclosure of Interest:** J. Curtis Grant/research support from: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, AbbVie, Consultant for: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, AbbVie, F. Xie: None declared, H. Yun Grant/research support from: Amgen, S. Bernatsky Grant/research support from: Supported by the Drug Safety and Effectiveness Network, Canadian Institutes of Health Research, K. Winthrop Grant/research support from: Unrelated work with Pfizer, UCB, Genentech, AbbVie, Lilly, BMS, Consultant for: unrelated work with Pfizer, UCB, Genentech, AbbVie, Lilly, BMS

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## FRI0208 ABATACEPT THERAPY COMBINED WITH TACROLIMUS FOR RHEUMATOID ARTHRITIS PATIENTS SHOWS SUPERIOR EFFICACY THAN ABATACEPT THERAPY WITHOUT TACROLIMUS

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**Background:** Abatacept (ABT) and tacrolimus (TAC) are similar at the point that both drugs block the T cell activation. ABT blocks co-stimulatory signaling from CD80/86 on the surface of antigen-presenting cell. TAC blocks the calcineurin activity in T cells. The each effectiveness of ABT and TAC respectively for the treatment of rheumatoid arthritis (RA) is apparent, however, the efficacy and safety at concomitant use of ABT and TAC was not unclear and there are few reports [1,2].

**Objectives:** The objective of this study is comparison between ABT therapy for RA patients with and without TAC.

**Methods:** Forty eight RA patients were included in this observational retrospective study, who were undertaken intravenous ABT therapy at Osaka Rosai Hospital after February 2011 and could be observed over 52 weeks. Patient background, efficacy, and safety were examined.

**Results:** Mean age was 67.4 years, disease duration was 10.8 years. Concomitant use of methotrexate was 58%, of prednisolone was 56% and prior biologics use was 48%. Concomitant use of TAC was 31%. Mean tacrolimus dose was 2.0g (1.0–3.0). The retension rate of ABT at 52 weeks was 80.8%. DAS28CRP was decreased significantly at 4 weeks (-16.5% from baseline, $p<0.001$), and gradually decreased until 24 weeks (-37.3%, $p<0.001$) and maintained until 52weeks (-39.3%, $p<0.001$) by Wilcoxon signed rank test. Patient background between ABT + TAC group (n=15) vs ABT group (n=33) were not significantly different (age, sex, disease duration, stage, class, concomitant use of prednisolone, MTX, prior biologics, baseline DAS28CRP, positivity of RF, ACPA) by chi-square test and Mann-Whitney U test. DAS28CRP of ABT + TAC group decreased significantly greater than ABT group at 16 weeks (-42.9% vs -30.3%, p=0.048), maintained until 52 weeks (-50.1% vs -34.5%, p=0.017) by Mann-Whitney U test. Adverse event between ABT + TAC and ABT group was not different. Predictive factor that achieve the low disease activity at 52weeks were Steinbrocker class1/2 (p=0.047), concomitant use of TAC (p=0.043) and DAS<3.3 at 12 weeks (p=0.005) by multivariate logistic regression analysis.

**Conclusions:** ABT therapy concomitant with TAC has the possibility to show higher effectiveness for RA patients than ABT therapy without TAC.

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[2] Takahashi N. Rheumatol Int 35: 1707–16, 2015

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2073

## FRI0209 MORAB-022, AN ANTI-GRANULOCYTE MACROPHAGE-COLONY STIMULATING FACTOR (GM-CSF) MONOCLONAL ANTIBODY (MAB): RESULTS OF THE FIRST STUDY IN PATIENTS WITH MILD-TO-MODERATE RHEUMATOID ARTHRITIS (RA)

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**Background:** GM-CSF plays a central role in the inflammatory immune response cascade. GM-CSF is expressed at higher levels in the synovial fluid of patients with RA. Therefore, neutralization of GM-CSF activity by specific mAbs could be beneficial in treating RA (Cornish, et al., 2009). MORAb-022 is an investigational monoclonal antibody with high affinity for GM-CSF.

**Objectives:** This Phase 1 study (NCT01357759) evaluated the safety and tolerability, pharmacokinetics/pharmacodynamics and preliminary evidence of activity of MORAb-022 in healthy subjects (HS) as well as in patients (Pts) with mild-to-moderate active RA.

**Methods:** This was a double-blind, placebo-controlled, randomised, dose-escalating study in HS as well as in Pts with mild-to-moderate RA (according to ACR 2010 criteria) receiving stable MTX doses for ≥12 weeks prior to randomisation. HS received a single intravenous (IV) infusion of MORAb-022 0.0085, 0.042, 0.12, or 0.36 mg/kg or placebo and Pts received 0.36, 0.7, 1, 3, or 10 mg/kg or placebo on Day 1 with 85 days' follow-up. Clinical efficacy was an exploratory endpoint measured by DAS28 (CRP), ACR20 and ACRn.

**Results:** 26 HS and 25 RA patients were enrolled (HS:77% male, mean age 41.1 years; Pts:56% females, mean age 55.4 years). Mean DAS28 (CRP) at baseline: placebo=4.1; MORAb-022, 0.36=3.6; MORAb-022, 0.7=4.5; MORAb-022, 1=3.8; MORAb-022, 3=3.8; MORAb-022, 10=4.8. MORAb-022 was generally well-tolerated. 14 treatment-emergent adverse events were observed in 25 Pts (56%). There was no evidence of immunogenicity. The mean $C_{max}$ and $AUC_{0\text{-}inf}$ for MORAb-022 increased approximately dose proportionally in both HS and Pts. The median half-life for MORAb-022 ranged from 9 to 13 days in both HS and Pts. All of the MORAb-022 dose cohorts demonstrated decreases in median DAS28 (CRP), however only the 10 mg/kg cohort showed a median decrease of more than 1.2 units by Day 2 (see Table). For Pts who received placebo, there was no discernable change in median DAS28 (CRP) results. 3/6 Pts who received placebo achieved an ACR20 response at any time as compared to 3/4 Pts in each of the 0.7 mg/kg, 3 mg/kg, and 10 mg/kg cohorts. 10 mg/kg dose cohort Pts demonstrated improvement in ACRn at Day 2, which was maintained through Day 29. The best mean (SD) ACRn for these Pts was 54.96 (40.52).

Table 1. DAS28 (CRP)

| Visit | Placebo | 0.36 | 0.7 | 1 | 3 | 10 |
|---|---|---|---|---|---|---|
| Baseline, n | 6 | 3 | 4 | 4 | 4 | 4 |
| Mean (SD) | 4.13 (0.4) | 3.76 (0.3) | 4.66 (0.9) | 3.94 (1.5) | 3.72 (1.3) | 4.62 ( 0.7) |
| Change from baseline | | | | | | |
| Day 2, n | 6 | 3 | 4 | 4 | 4 | 4 |
| Mean (SD) | 0.02 (0.7) | 0.49 (0.4) | –0.56 (0.60) | 0.07 (1.2) | –0.25 (1.2) | –1.34 (1.6) |
| Day 8, n | 6 | 3 | 4 | 4 | 4 | 4 |
| Mean (SD) | –0.28 (1.0) | –0.65 (0.7) | –0.29 (0.6) | –0.71 (0.6) | –0.52 (0.9) | –1.29 (1.0) |
| Day 15, n | 6 | 3 | 4 | 4 | 4 | 4 |
| Mean (SD) | –0.28 (1.3) | –0.48 (0.4) | –0.45 (0.6) | –0.78 (0.4) | –0.19 (1.1) | –1.02 (0.7) |
| Day 29, n | 6 | 3 | 4 | 4 | 4 | 3 |
| Mean (SD) | –0.56 (1.2) | –0.55 (0.5) | –0.46 (0.6) | –0.34 (0.8) | –0.04 (0.9) | –1.40 (1.6) |

**Conclusions:** MORAb-022 was generally well-tolerated in HS as well as in active RA Pts. Preliminary evidence of activity was observed but further evaluation is needed due to the small sample size in this study. PK was linear with a t1/2 =9–13 days.

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## FRI0210 CD16+ NK CELLS ARE PERSISTENTLY INCREASED AFTER RITUXIMAB THERAPY IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The clinical response of rituximab (RTX) is related to the degree of B cell depletion, although flow cytometry analysis of peripheral blood leukocytes after RTX therapy has shown some effects on other cell types in addition to B lymphocytes. Currently, however, data on NK cells changes after RTX are lacking.

**Objectives:** The primary objective was to investigate the changes in lymphocyte sub-populations in real-life rheumatoid arthritis (RA) patients treated with RTX, with particular attention to NK cells and their subpopulations. The secondary objective was to analyze the correlations between lymphocyte changes and the therapeutic response of RA patients treated with RTX.

**Methods:** In 33 RA patients diagnosed according the 1987 ACR criteria peripheral blood B and T lymphocytes and NK cells subtypes were counted by flow cytometry before and 3, 6 and 12 months after RTX administration. Patients received a 1,000-mg infusion of RTX preceded by a 100-mg methylprednisolone intravenous pulse, at baseline and at week 2. Twenty-two patients (67%) were treated with another course of RTX after 6 months from baseline. Clinical assessment was performed with the disease activity score in 28 joints (DAS28) with C-reactive protein (CRP) and the EULAR response criteria at each visit. Natural killer (NK) cells were counted using APC-CY7-conjugated anti-CD16 and PE-conjugated antiCD56.

**Results:** RTX significantly increased $CD56^+3^-$ and $CD56^{dim}CD16^+$ NK cells at 3 months (27% [interquartile range, IQR =46] and 33% [50] respectively, $p\leq0.001$). The punctual increase persisted both at month 6 and month 12 only for $CD56^{dim}CD16^+$ NK cells (24% [88], p=0.011 and 41% [80], p=0.002, respectively). The 22 patients who were treated with a second course of RTX showed an increase respect month 6 values in $CD56^{dim}CD16^+$ cell counts, at month 12 (nonretreatment vs retreatment: - 18% [21] vs 24% [41]; p=0.002). $CD56^{dim}CD16^+$ absolute counts were correlated with DAS28 values at baseline ($\rho$=0.355, p=0.043), month 3 ($\rho$=0.353, p=0.044) and month 6 ($\rho$=0.526, p=0.002), and were higher in nonresponders than in responders (n.s.). The $CD56^{bri}16^-$ NK cells were unaffected from RTX. No significant changes in $CD3^+$, $CD4^+$ and $CD8^+$ cells were observed during the whole study period.

**Conclusions:** In RA patients, RTX treatment is associated with a persistent increase in $CD56^{dim}CD16^{+}$ NK cells, although a trend to restoration to baseline values is seen after 12 months. A second course could mantain the initial increase. Therefore, homeostasis of $CD16^{+}$ cells is somehow influenced by anti-CD20 therapy. A correlation between $CD16^{+}$ NK cell changes and disease activity after RTX is probable, although the association with clinical response remains to be proved.
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## FRI0211 TAPERING MTX VERSUS STEADY-STATE MTX IN COMBINATION WITH TOCILIZUMAB FOR TREATMENT OF RHEUMATOID ARTHRITIS (ACT-TAPER): A RANDOMISED, DOUBLE-BLIND, CONTROLLED PHASE 4 TRIAL

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**Background:** For most DMARD-IR patients (pts) with severe active RA, therapy with a biologic and methotrexate (MTX) is effective. However, nearly 1/3 discontinue or are non-compliant with MTX because of toxicity or preference[1–4]. Previous data showed tocilizumab (TCZ) was effective as monotherapy in MTX-intolerant pts or pts for whom MTX was ineffective or inappropriate[4,5]. In addition, the ACT-RAY study suggested tapering MTX may result in maintained efficacy and an improved safety profile.
**Objectives:** To explore if TCZ + tapering MTX has comparable efficacy and safety vs TCZ + stable MTX in pts with inadequate response to MTX [EudraCT 2011–005260–20].
**Methods:** ACT-TAPER was a randomised, placebo-controlled non-inferiority study investigating efficacy and safety of tapering MTX vs stable MTX in DMARD-IR pts with severe active RA (DAS28 $>$5.1) who had initiated TCZ + MTX at study start. At Week (Wk) 0, DMARDs except MTX were discontinued; pts started open-label TCZ (8 mg/kg IV 4 weekly) and open-label MTX. At Wk 24, pts achieving good/moderate EULAR response were randomised to Group A (double-blind MTX taper) or Group B (double-blind MTX maintenance). Both continued open-label TCZ. Pts achieving adequate improvement stayed in treatment groups to Week 72. Primary analysis: proportion of pts maintaining good/moderate EULAR from wks 24–60 in TCZ + MTX taper vs TCZ + stable MTX. Secondary analyses included safety outcome measures.
**Results:** The study stopped early due to low recruitment; 427 pts entered the initial open-label phase (IP) of the study and 272 pts were randomised (36% withdrew or were not eligible to be randomised; protocol required 494 pts to be randomised), 136 in each arm. Of the IP population, 64.4% achieved good/moderate EULAR at Wk 24, with 45.0% achieving DAS28 $\leq$3.2, 33.5% remission (DAS28 $<$2.6) and 64.2% with DAS28 change $\geq$1.2. After Wk 24 randomisation, the proportion of pts maintaining good/moderate EULAR to Week 60 was greater for MTX taper vs stable MTX (76.5% vs 65.4%). This allowed the pre-determined criteria for non-inferiority to be fulfilled despite the reduced recruitment. The proportion of pts achieving a change $\geq$1.2 DAS28 at Wk 60 did not differ significantly between groups; mean (SD) change from Wk 24–60 was -0.179 (1.1702) Group A and -0.233 (1.5156) Group B. The proportion of pts with DAS28 $\leq$3.2 at Wks 60 and 72 did not differ significantly between groups (59.6% and 61.0% for Group A; 62.5% and 60.3% for Group B). The proportion of pts in remission at Wks 60 and 72 did not differ significantly between treatments. Safety analysis revealed no unexpected TCZ safety signals.
**Conclusions:** Tapering MTX in RA pts using TCZ was non-inferior to continuing stable MTX in maintaining a good/moderate EULAR response. No significant change in DAS28 was observed between groups. There were no unexpected safety signals; TCZ and MTX therapy was generally well tolerated in both groups.
**References:**
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[5] Jones Ann Rheum Dis 2013;72(suppl):457
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## FRI0212 COMPARISON STUDY OF TESTS AVAILABLE TO MONITOR TOCILIZUMAB THERAPY IN RHEUMATIC PATIENTS

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**Background:** The options for treatment of rheumatic diseases is constantly growing. Tocilizumab (TCZ) is an anti-interleukin 6 receptor monoclonal antibody indicated for the treatment of severe active and progressive rheumatoid arthritis (RA) and active systemic juvenile idiopathic arthritis (sJIA). Monitoring of drug levels (DL) and anti-drug antibodies (ADA) in clinical practice is highly advisable in order to establish normal therapeutic ranges, complement clinical assessment and optimise patient treatment. As a consequence several tests and technologies have been developed. However, a common objection that limits implementation of biological drug monitoring in medical practice is the claim that the magnitude of measurements varies among assays and that assay standardisation is lacking.
**Objectives:** The purpose of this study was to evaluate the correlation and agreement between different commercially available tests to measure TCZ and antibodies to TCZ (ATT) in patients with rheumatic diseases.
**Methods:** Trough levels of TCZ and ATT were analyzed in a retrospective cohort of 26 rheumatic patients (42 serum samples, 88% RA and 12% sJIA) under maintenance therapy with TCZ for up to two years. Samples were assayed using Promonitor-TCZ and Promonitor-ANTI-TCZ ELISA kits (PR, Progenika, Spain), LISA-TRACKER Duo Tocilizumab ELISA kit (LT, Theradiag, France), and by Sanquin Blood Supply testing service (SQ, Amsterdam, The Netherlands) that uses ELISA and RIA technologies to measure TCZ and ATT levels, respectively. One-way analysis of variance (ANOVA) and Spearman's test was used to study correlation between the DL tests; the difference (bias) in values obtained with DL assays was also assessed with Bland-Altman analysis. Percentage of positive and negative agreement was used to study the association between the ADA assays.
**Results:** TCZ trough level in patients are much higher than other biological treatments like anti-TNF infliximab and adalimumab. ANOVA analysis showed that the differences in the median values among the three DL assays are not statistically different (median 4.4 vs 4.7 vs 5.4 $\mu$g/mL, IQR 0 – 8.7 $\mu$g/mL vs 0 – 7.8 $\mu$g/mL vs 0 – 9.4 $\mu$g/mL for Promonitor-TCZ, LISA-TRACKER and Sanquin ELISA tests, respectively, $p$=0.693). Spearman's coefficient showed a very high correlation between the each pair of assays ($r$=0.951, 0.935 and 0.944 for PR vs LT, PR vs SQ and LT vs SQ, respectively, p$<$0.0001). Bland-Altman analysis shows an excellent association between each pair of DL assays with no significant difference in bias (-0.3, -0.5 and -0.2 $\mu$g/mL for PR vs LT, PR vs SQ and LT vs SQ, p$>$0.05). Antibodies to TCZ were not detected with any of the assays in the patient cohort confirming the low immunogenicity of TCZ.
**Conclusions:** Despite different reagents, assay formats and technologies, all tests studied here provide exactly the same results and measure the same magnitude of TCZ in rheumatic patients. Assays can be safely exchanged in a clinical setting even in the absence of a gold standard test, and should lead to similar drug therapeutic ranges and actions.
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## FRI0213 IDENTIFICATION OF SYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION DURING THERAPY WITH TOCILIZUMAB

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**Background:** The aim of therapy rheumatoid arthritis (RA) is the achievement of remission of the disease and slowing destruction of the joints. Tocilizumab (TCZ), anti-interleukin-6 receptor monoclonal antibody was used in treatment of active RA. TCZ has a rapid positive effect on the clinical manifestations and laboratory disoders, slowing destruction of joints in RA.
**Objectives:** To assess the effect of TCZ on synovitis on MRI of bilateral wrist and metacarpophalangeal joints in accordance with the OMERACT RA MRI scoring system (RAMRIS).
**Methods:** 43 adult patients with active RA were enrolled in the open label, phase IV trial to confirm the effectiveness and safety TCZ. Average age (median, interquartile range) 50,5 (43,0–55,0) years, duration of RA 56,5 (23,0–81,0) months, RF (+) 81%, ACCP (+) 77%. Patient had to be naive to biologics and have moderate to severe active RA (based on the 1987 ACR criteria). Patients remained on stable doses of disease-modifying antirheumatic drugs and received TCZ 8 mg/kg every 4 weeks for 24 weeks (total 6 infusions). Disease remission was assessed according to the criteria of EULAR and EULAR/ACR 2011. MRI performed at 0 and 24 weeks of observation.
**Results:** Before therapy indices DAS28 (6,4; 5,9–7,0), CDAI (41,5; 32,0–53,0) and SDAI (45,0; 36,2–57,0) corresponded to high activity of RA. The value of DAS28 to 24 weeks of treatment was 2,1; 1,3–2,8, p$<$0.05. Indicators SDAI and CDAI up to 24th week match the low activity of RA (4,4; 2,0–8,8 and 3,6; 1,4–7,6, respectively). Remission was achieved by 24 weeks of treatment on indices:

DAS28<2.6 for 30 patients (71%), CDAI<2.8 to 14 (33%), SDAI<3.3 to 13 (31%) and according to the criteria of ACR/EULAR 2011 (Boolean) – 10 (24%). MRI of the bilateral wrist and metacarpophalangeal joints was performed for patients who achieved remission according to the DAS28 criteria (n=27) and Boolean (n=10). Synovitis was detected in 81.5% and 80%, osteitis in 11.1% and 10% of patients, respectively.
**Conclusions:** Despite the pronounced clinical effect of TCZ in patients with RA and remission according to the criteria of DAS28 and ACR/EULAR, synovitis was detected in most patients. MRI examination allows to observe the patients during the therapy to achieve complete remission of the disease.
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## FRI0214 SIX-YEAR RETENTION RATE OF ABATACEPT IN RHEUMATOID ARTHRITIS: A MULTICENTRIC RETROSPECTIVE ANALYSIS

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**Background:** Abatacept (ABT) short-term efficacy and safety profile in the treatment of rheumatoid arthritis (RA) is well established and supported by randomised controlled trials. However, data on ABT long-term effects are still lacking and reported drug survival analyses are often limited to no more than 2-year follow-up.
**Objectives:** The aim of the study is to evaluate in a real-life scenario the overall 6-year retention rate of ABT in the treatment of RA and to compare its survival rate as first or second line biotherapy.
**Methods:** Data were retrospectively extracted from six local registries including all RA patients treated with ABT between January 2008 and April 2015. The analysis was limited to patients treated with ABT as first or second line biologic agent. The 6-year retention rate was calculated by Kaplan-Meier method and the comparative risk for discontinuation between the two lines of treatment was compared by a stratified log-rank test.
**Results:** 236 RA patients (78.5% female, mean age [± standard deviation, SD] 57.6 [±12.7] years, mean disease duration 14.3 [±13.4] years, positive rheumatoid factor 82.2%, positive anti-citrullinated peptide antibodies 71.1%, mean DAS28 5.19 [±1.2]) were retrospectively enrolled. 83 patients were treated with ABT as first-line biotherapy, whereas 153 were second-line users. The overall retention rate was 63.7% at 3 years and 61.8% at 6 years. The 6-year retention rate was significantly higher in the first-line compared with the second-line therapy group (68% and 61.8%, respectively; p=0.04). Overall, ABT was discontinued in 69 (29.2%) patients. Twenty-one (8.9%) patients (4 first-line and 17 second-line users, p=0.15) withdrew ABT because of adverse events, whereas 41 (17.4%) patients (10 first-line and 31 second-line users, p=0.1508) stopped the therapy because of primary or secondary inefficacy. Seven (2.7%) patients discontinued ABT because of other reasons (i.e. lost at follow-up, pregnancy and remission) and were excluded from the retention analysis.
**Conclusions:** In our multicentric experience the 6-year retention rate of both first and second line ABT was about 60%. Used as first line ABT showed a significantly higher survival on treatment compared with the second line. Moreover, ABT demonstrated an overall favourable safety profile, with a very low occurrence of adverse events leading to discontinuation.
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## FRI0215 SUBCUTANEOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS – INTERIM ANALYSIS OF A LARGE PHASE IV INTERNATIONAL UMBRELLA STUDY, "TOZURA"

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**Background:** Tocilizumab (TCZ), administered as intravenous (TCZ-IV) and subcutaneous (TCZ-SC) formulations, has been approved for treatment of patients (pts) with rheumatoid arthritis (RA) both as mono- and combination therapy.
**Objectives:** To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as monotherapy and in combination with conventional synthetic DMARDs (csDMARDs) over 24 weeks in adult pts with moderate to severe RA.
**Methods:** TOZURA is a multinational, open-label, single-arm umbrella study comprising 7 single-country and 4 regional multicountry protocols. It aimed to enroll ≈ 1,850 pts who were biological DMARD inadequate responders (IR; 8/11 protocols) and/or csDMARD-IR (11/11 protocols). Pts received TCZ-SC 162 mg qw for 24 weeks, administered at the investigator's discretion as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (CCS), ≤10 mg/day prednisone or equivalent, were allowed. Efficacy and safety were evaluated at weeks 1, 2, 4 and every 4 weeks thereafter.
**Results:** In this interim analysis, 1246 pts were included by end of 2014; 283 pts received monotherapy, 963 combination; 25% of pts were biologic DAMRD-IR (monotherapy: 36%, combination: 22%). Background characteristics: 80.5% female, mean age 54.5 years, mean RA disease duration 7.7 years and 81.4% seropositive – similar between treatment groups. Baseline oral CCS use was less frequent in the mono- group (42.8%) than in the combination group (51.2%); however, their mean dose was similar (6.673 vs 6.505 mg/day, respectively). Pts continuation of TCZ at week 24 based on Kaplan-Meier estimates (95% CI) were 0.784 (0.732, 0.828) for mono- and 0.855 (0.831, 0.875) for combination therapy. All pts had significant reductions in mean 28-joint Disease Activity (DAS28) scores by week 24 (mean decrease: monotherapy 3.41 and combination 3.44; $P$ <0.0001 for both) with no significant difference between groups ($P$ =0.788). Results were similar for the Clinical Disease Activity Index (CDAI), which does not include acute phase reactants (mean change by week 24: 24.03 and 23.28, $P$ <0.0001 for both groups: between groups $P$ =0.629). The proportion of pts who achieved DAS28 or CDAI-based remission and low disease activity and ACR20/50/70/90 responses was similar between the treatment groups (Figs 1A, 1B). Of the 231 pts (18.5%) who withdrew, 92 (7.4%) did so for safety reasons (29 [10.2%] monotherapy, 63 [6.5%] combination). Serious AEs (SAEs) occurred in 78 pts (6.3%; 11.5/100 PY) and rates of AEs and SAEs were similar between groups (Table 1). Serious infections and infestations occurred in 18 pts (1.4%; 2.2/100 PY), with similar rates between groups. Five deaths occurred, 1 in the monotherapy group (coronary artery disease) and 4 in the combination group (intestinal ischemia, myocardial infarction, pneumonia, septic shock).

**Figure 1: DAS28 and CDAI Disease Activity, and ACR Responses**

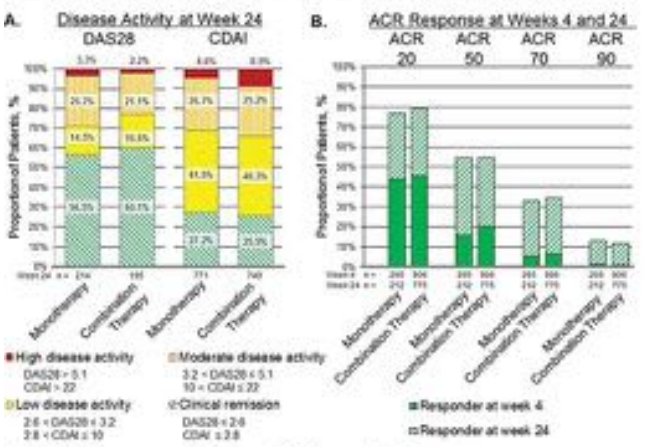



**Table 1: Summary of Relevant Adverse Events**

| | | Total Population (N = 1246; 892.4 PY) | Monotherapy (n = 283; 200.4 PY) | Combination Therapy (n = 963; 692.0 PY) |
|---|---|---|---|---|
| Adverse Events | Total patients with ≥ 1 AE, n (%) | 1058 (84.9%) | 228 (80.6%) | 830 (86.2%) |
| | Rate of AEs (per 100 PY) | 507.5 | 517.4 | 504.6 |
| Serious Adverse Events | Total patients with ≥ 1 SAE, n (%) | 78 (6.3%) | 23 (8.1%) | 55 (5.7%) |
| | Rate of SAEs (per 100 PY) | 11.5 | 16.0 | 10.2 |
| Serious Infections and infestations | Total patients with ≥ 1 SAE, n (%) | 18 (1.4%) | 6 (2.1%) | 12 (1.2%) |
| | Rate of SAEs (per 100 PY) | 2.2 | 3.0 | 2.0 |
| Withdrawals ≥ 1 reason, n (%) | Total patients with ≥ 1 reason, n (%) | 231 (18.5%) | 68 (24.0%) | 163 (16.9%) |
| Withdrawals due to safety reasons* | Patients, n (%) | 92 (7.4%) | 29 (10.2%) | 63 (6.5%) |
| Deaths | Number of deaths, n (%) | 5 (0.4%) | 1 (0.4%) | 4 (0.4%) |
| | Rate of deaths (per 100 PY) | 0.56 | 0.50 | 0.58 |

AE: adverse event; PY: patient-year; SAE: serious adverse event
*Includes AEs, deaths, withdrawals and abnormal laboratory findings. † Coronary artery disease. ‡Intestinal ischemia, myocardial infarction, pneumonia, septic shock.

**Conclusions:** TCZ-SC demonstrated convincing and comparable efficacy in mono- and combination therapy in pts with RA as previously observed with TCZ-IV. The safety profile of TCZ-SC is consistent with the known safety profile of TCZ as monotherapy and in combination with csDMARDs.
**Disclosure of Interest:** E. Choy Grant/research support from: F. Hoffmann-La Roche and Chugai Pharmaceutical, Consultant for: F. Hoffmann-La Roche and Chugai Pharmaceutical, Speakers bureau: F. Hoffmann-La Roche and Chugai Pharmaceutical, R. Caporali Consultant for: Abbvie, Bristol-Myers Squibb, F. Hoffmann-La Roche, UCB and MSD Pharmaceuticals, R. Xavier Consultant for: F. Hoffmann-La Roche, Pfizer, Janssen Pharmaceutica, Abbvie, Eli Lilly and Com-

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## FRI0216 LONG-TERM SAFETY AND EFFICACY OF MAVRILIMUMAB, A FULLY HUMAN GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR RECEPTOR-ALPHA MONOCLONAL ANTIBODY, IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Mavrilimumab, a fully human monoclonal antibody, which targets granulocyte-macrophage colony-stimulating factor receptor-α, has demonstrated efficacy and an acceptable safety profile in prior 12- and 24-week studies.[1,2]
**Objectives:** This analysis evaluated all long-term (LT) safety and efficacy, through 74 weeks of treatment, of mavrilimumab.
**Methods:** This open-label extension (OLE) study (NCT01712399) enrolled adult rheumatoid arthritis (RA) patients (pts) who had completed the EARTH EXPLORER 1[2] and 2 (NCT01715896) Phase IIb studies or were rescued as inadequate responders (from Week 12). Pts received subcutaneous mavrilimumab 100 mg every other week (eow), consistent with data from the Phase IIa study[1]. The primary objective was to assess the LT risk:benefit ratio of mavrilimumab via evaluation of i) Treatment emergent adverse events (TEAEs), TE serious AEs (TESAEs), and independently adjudicated pulmonary function tests (PFTs) ii) Exploratory LT efficacy endpoints (DAS28–CRP/ACR responses). AEs with onset date after start of mavrilimumab are presented. Change from baseline (BL) in modified Total Sharp Score (mTSS) was used to explore radiographic progression in EARTH EXPLORER 1 pts.
**Results:** At the 74 week (includes original study) cutoff, 391 pts had been enrolled in the OLE study. Of these, 329 (84.1%) continued on treatment, 62 (15.9%) discontinued (due to withdrawal of consent, 9 [2.3%]; adverse event, 7 [1.8%]; non study-related site closure, 20 [5.1%]; other, 24 [6.1%]; lost-to-follow-up, 1 [0.3%]; death [sudden cardiac arrest, preferred term cardiopulmonary failure], 1 [0.3%]), and 239 (61.1%) were assessed for efficacy at Week 74. Between the Phase IIb and OLE studies, 440 pts received mavrilimumab, with a safety exposure of 603 pt years (yr) and median duration of 1.6 yr. Most common TEAEs (n [/100 pt yr]) were nasopharyngitis (51 [8.45]), bronchitis (36 [5.97]) and hypertension (32 [5.30]); the serious infection rate was 1.82/100 pt yr. Pulmonary events/defined PFT changes occurred in a few pts and were generally transient with no signal identified (Table). Mavrilimumab demonstrated sustained efficacy (DAS28–CRP/ACR responses) (Table). After 74 weeks of treatment, 68% of pts showed no radiographic progression (<0.5 change in mTSS vs. BL) (Table).
**Conclusions:** Mavrilimumab continues to demonstrate a sustained efficacy and safety profile in pts with active RA, over the 74 week treatment duration reported. Although mavrilimumab 100 mg eow is suboptimal compared with 150 mg eow in DMARD-IR pts,[2] efficacy results are comparable with those of previous studies.[1,2]



**References:**
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Joint senior authors: D. Close and M. Weinblatt
**Disclosure of Interest:** G. Burmester Consultant for: MedImmune, I. McInnes Grant/research support from: Research award to University of Glasgow, Consultant for: MedImmune, AstraZeneca, J. Kremer Shareholder of: Corrona, Grant/research support from: Abbvie, Amgen, Genentech, Lilly, Pfizer, Consultant for: Abbvie, Amgen, BMS, Genentech, Lilly, Pfizer, Employee of: Corrona, P. Miranda Grant/research support from: Clinical trials Amgen, Medimmune, Janssen, Pfizer, Celltrion, Abbott, Sanofi, Actelion, Merck & Co, Boehringer, BMS, Consultant for: Pfizer for Etanecept (fee less than USD5000), J. Vencovský Consultant for: Pfizer, Servier, Samsumg, Eli lilley, BMS, Novartis, A. Godwood Shareholder of: AstraZeneca, Employee of: MedImmune, M. Albulescu Employee of: MedImmune, D. Close, Employee of: MedImmune, M. Weinblatt, Grant/research support from: BMS, UCB, Crescendo Bioscience, Consultant for: MedImmune, AstraZeneca, Amgen, Abbvie, BMS, Crescendo Bioscience, Lilly, Pfizer, UCB, Roche
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## FRI0217 ANAPHYLACTIC-TYPE REACTIONS ASSOCIATED WITH ABATACEPT AND OTHER BIOLOGIC AGENTS: REVIEW OF SAFETY REPORTS FROM FAERS

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**Background:** The US Food and Drug Administration AE reporting system (FAERS) contains information for all marketed and investigational drugs in the US and provides sufficient safety data for disproportionality analysis for specific events associated with the use of drugs.
**Objectives:** To perform the disproportionality analysis of anaphylactic reactions among users of abatacept (ABA) and other biologics for the treatment of RA, utilizing data from FAERS.
**Methods:** The disproportionality of anaphylactic-type reactions associated with ABA and other biologics was analysed using cumulative safety data retrieved from the FAERS database up to 22 June 2015. The preferred terms in the Standardized Medical Dictionary for Regulatory Activities Queries (SMQ) for anaphylactic reactions (narrow terms) were used for the database search and included anaphylactic reaction, anaphylactic shock, anaphylactic transfusion reaction, anaphylactoid reaction, anaphylactoid shock, circulatory collapse, Kounis syndrome, shock and type I hypersensitivity. Biologics searched for included ABA, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab. Penicillin was included as positive control due to its known association with anaphylactic-type reactions.[1] The disproportionality report is defined as a ratio of observed to expected frequencies of reports mentioning both the targeted drug (Y) and targeted AE (X). The observed frequency is calculated as the number of reports for event X with drug Y, and the expected frequency is the number of drug–event combinations of interest that would be expected if the event of interest (X) is reported independently of the drug of interest (Y). The disproportionality measure (i.e. observed/expected) referred to by empirical Bayesian geometric mean and the corresponding 90% CI (EB05, EB95) were calculated. The threshold of EB05 ≥2 for any drug–event pair identifies drug–event combinations that are reported at least twice as often as all other drug–event combinations.
**Results:** Among the evaluated drugs, the EB05 scores for anaphylactic reaction, anaphylactic shock and anaphylactoid reaction were the highest with penicillin use, as expected (Table). The EB05 scores for all drug–event pairs for ABA were

| Generic name | SMQ Anaphylactic Reaction (Narrow) | n | EBGM | EB05 | EB95 |
|---|---|---|---|---|---|
| Abatacept | Anaphylactic reaction | 53 | 1.45 | 1.16 | 1.81 |
| Abatacept | Anaphylactic shock | 11 | 0.59 | 0.36 | 0.92 |
| Abatacept | Anaphylactoid reaction | 5 | 1.12 | 0.56 | 2.04 |
| Abatacept | Circulatory collapse | 6 | 0.49 | 0.26 | 0.85 |
| Abatacept | Shock | 11 | 0.68 | 0.42 | 1.06 |
| Abatacept | Type I hypersensitivity | 1 | 0.86 | 0.27 | 2.17 |
| Infliximab | Anaphylactic reaction | 598 | 2.16 | **2.02** | 2.31 |
| Infliximab | Anaphylactoid reaction | 145 | 2.75 | **2.40** | 3.15 |
| Penicillin | Anaphylactic reaction | 54 | 3.96 | **3.16** | 4.91 |
| Penicillin | Anaphylactic shock | 42 | 4.86 | **3.76** | 6.20 |
| Penicillin | Anaphylactoid reaction | 169 | 3.68 | **3.24** | 4.16 |
| Tocilizumab | Anaphylactic reaction | 71 | 2.91 | **2.39** | 3.52 |

EBGM=empirical Bayesian geometric mean; SMQ=Standardized Medical Dictionary for Regulatory Activities Queries

<2. The EB05 scores for drug–event pairs for other biologics were <2 except anaphylactic reaction and anaphylactoid reaction for infliximab, and anaphylactic reaction for tocilizumab.
**Conclusions:** Overall, there were few signals of disproportionality for anaphylactic-type reactions with the use of abatacept and other biologics for RA, with the exceptions of anaphylactic reaction and anaphylactoid reaction for infliximab and anaphylactic reaction for tocilizumab. This observation is consistent with the results reported from clinical studies that were documented in the prescribing information for abatacept and other respective drugs for RA.[2–4]
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## FRI0218 SAFETY OF NON ANTI-TNF BIOLOGIC AGENTS IN RHEUMATIC PATIENTS WITH PAST HEPATITIS B VIRUS INFECTION. A SINGLE-CENTER REAL-LIFE STUDY

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**Background:** The safety of newer non anti-TNF biologic agents [abatacept (ABA), tocilizumab (TCZ) and rituximab (RTX)] in patients with autoimmune rheumatic diseases and past HBV infection [defined as HBsAg(–), anti-HBc(+), anti-HBs(±)] has not been firmly established.
**Objectives:** To assess the safety [reactivation of hepatitis B virus (HBV)] of non anti-TNF biologic agents in patients with serologic evidence of past HBV infection in real-life clinical settings.
**Methods:** Retrospective chart review of patients followed in the Department of Rheumatology of the University Hospital of Crete. Patients who received ABA, TCZ or RTX during the period 2005–2015 and were HBsAg(–), anti-HBc(+), anti-HBs(±) at baseline were identified and reviewed for cases of HBV reactivation (defined as increased ALT accompanied by an increase of serum HBV DNA levels by >1 $\log_{10}$ compared with baseline or a switch in HBV DNA detection from negative to positive). Changes in anti-HBs titers during biologic therapy in patients who were anti-HBs(+) at baseline were also documented.
**Results:** 83 different cases of non anti-TNF biologic therapy (34 ABA, 26 RTX and 23 TCZ) from 58 patients (56 RA - 2 ANCA-associated vasculitis) were identified. 64 cases (77.1%) were anti-HBc(+) anti-HBs(+) and 19 (22.9%) were anti-HBc(+) anti-HBs(–). Mean (SD) age at disease diagnosis and at non anti-TNF initiation was 53.6 (13.1) and 63.4 (9.2) years, respectively. All cases with RA had received prior anti-TNF agents [mean (SD) number of anti-TNF agents 1.1 (0.8)]. During treatment with non anti-TNF, concomitant synthetic disease modifying drugs or glucocorticoids were received by 91.5% and 46.3% of cases, respectively. Only 7 cases (8.4%) received antiviral prophylaxis concomitant with non anti-TNF treatment (4 with lamivudine - 3 with entecavir). After a mean (SD) of 41.9 (24.6) months of follow-up and a mean (SD) of 18.0 (15.9) therapy cycles, one anti-HBc(+) anti-HBs(–) case experienced HBV reactivation 12 months after treatment with abatacept and was treated with tenofovir with good outcome. Of anti-HBs(+) patients at baseline, titers of anti-HBs antibodies did not show statistically significant delay from baseline to most recent follow-up (456.9 mIU/ml vs. 390.7 mIU/ml, respectively, p=0.08) (Figure 1).

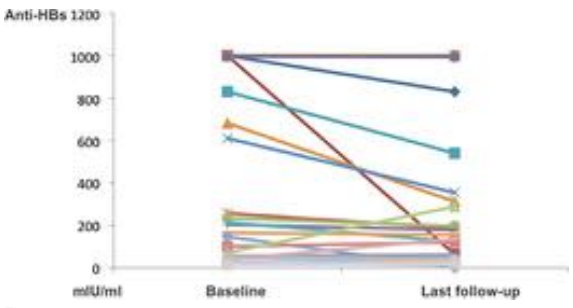


Figure 1

**Conclusions:** One case of HBV reactivation underlines the need for diligent monitoring in patients with serologic evidence of past HBV infection receiving non anti-TNF biologic agents. More data are needed to determine the need for universal prophylactic antiviral therapy in this subset of patients.
**Disclosure of Interest:** None declared
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## FRI0219 RISK FACTORS OF SEVERE INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB IN THE FRENCH REGISTRY REGATE (REGISTRY –ROACTEMRA)

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**Background:** Observational studies have already reported the risk of severe infections in rheumatoid arthritis (RA) treated with tocilizumab but in limited samples.
**Objectives:** The aim of this study was to investigate the predictive risk factors of severe infections in the largest European registry of patients treated with tocilizumab for RA.
**Methods:** 1491 RA patients included in the French REGistry –RoAcTEmra (REGATE) were analysed to calculate incidence rate of severe infections and to identify independent factors associated with severe infections.
Kaplan -Meier method was used to assess probability of remaining severe infection-free. Cox models were performed to identify independent factors associated with severe infections. Variables showing bivariate association with the dependent variable with a *P* value less than 0.15 were entered into the multivariate model. Multiple imputation was used to compensate missing data in some variables. A *P* value <0.05 was considered statistically significant.
**Results:** Exposure was 2,606 person-years (mean age±SD, 56.6±13.6). 125 serious infections occurred in 122 patients (4.7/100 patient-years). Most frequent infections were lung and respiratory tract and skin/soft tissue in 35 (28%) and 32 (26%) cases respectively. Three deaths were related to one septic chock secondary to pyelonephritis, one pneumocystosis, and one *Haemophilus influenzae* infection. Favourable outcome was observed in most cases. Four opportunistic infections were reported: 1 Pneumocystosis, 1 tuberculosis, 1 *Haemophilus influenzae* infection and 1 infection related to *Klebsiella pneumoniae*. A pathogen was identified in 41 cases. TCZ was definitively stopped for 35 patients. The incidence of serious infection was stable over the first 3 years of follow-up in the registry. Bivariate analysis identified initial ACPA positivity as the only factor associated with a lower risk of severe infection (HR 0.55 CI95% 0.35–0.86). Factors significantly associated with a risk of severe infections were DAS28-CRP, DAS28-ESR, and number of polymorphonuclear neutrophils (PMN) at baseline. Initial PMN above 4.5 G/L (HR 1.62 CI95% 1.06–2.5, p=0.02) and negative ACPA (HR 0.63 CI95% 0.41–0.95, p=0.03) remains significantly associated with severe infections in multivariate analysis after imputation for missing data.
**Conclusions:** The rate of severe infections in current practice is similar to that reported in clinical trials. High PMN above 4.5 G/L at baseline and negative ACPA are predictive factors of serious infection requiring in this case a tighter surveillance.
**Acknowledgement:** The French registry REGATE was supported by an unrestricted grant of Roche Chugaï. We thank Isabelle Pane for assistance with database management.
**Disclosure of Interest:** J. Morel Consultant for: ROCHE CHUGAI, NORDIC PHARMA, A. Constantin Consultant for: ROCHE CHUGAI, Speakers bureau: NORDIC PHARMA, E. Dernis: None declared, S. Rist Speakers bureau: ROCHE CHUGAI, R. M. Flipo Consultant for: ROCHE CHUGAI, NORDIC PHARMA, Speakers bureau: ROCHE CHUGAI, NORDIC PHARMA, T. Schaeverbeke Consultant for: ROCHE CHUGAI, NORDIC PHARMA, Speakers bureau: ROCHE CHUGAI, NORDIC PHARMA, O. Vittecoq Speakers bureau: ROCHE CHUGAI, M. Soubrier: None declared, A. Saraux Grant/research support from: ROCHE CHUGAI, Consultant for: ROCHE CHUGAI, Speakers bureau: ROCHE CHUGAI, B. Combe Consultant for: ROCHE CHUGAI, Speakers bureau: ROCHE CHUGAI, M. Dougados Consultant for: ROCHE CHUGAI, Speakers bureau: ROCHE CHUGAI, A. Pinta Employee of: ROCHE CHUGAI, G. Baron: None declared, J.-E. Gottenberg: None declared, X. Mariette: None declared, P. Ravaud: None declared, J. Sibilia Consultant for: ROCHE CHUGAI, Speakers bureau: ROCHE CHUGAI
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## FRI0220 PRESCRIPTION OF TOCILIZUMAB ALONE OR IN COMBINATION WITH DMARDS IN RHEUMATOID ARTHRITIS PATIENTS IN A REAL LIFE SETTING: THE ACT-SOLO STUDY 12 MONTHS RESULTS

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**Background:** Although the use of a biologic as monotherapy is not the standard in Rheumatoid Arthritis (RA), it concerns around a third of the patients. The objectives of the Act Solo study was to evaluate tocilizumab (TCZ) alone (Mono) or in combination (Combo) at 12 months in real life.
**Methods:** Prospective, multicenter, longitudinal, non-interventional 12-month study in RA pts requiring TCZ according to their physician. Besides drug retention rate, efficacy and safety, the effect of Mono when compared to Combo was evaluated using a propensity score. Efficacy population was pts fulfilling inclusion and non-inclusion criteria and with ≥1 TCZ infusion. Safety population was all pts with ≥1 TCZ infusion.
**Results:** 608 pts were recruited of whom 603 were analysed for safety and 577 (Total) for other endpoints. At baseline: mean age 57±13 years, 454 (79%) females, at least 1 co-morbidity: 409 (71%), mean RA duration 11±9 years, RF or ACPA positive: 478 (86%), erosive disease: 435 (77%), mean DAS28 5.2±1.3. Past RA treatments included DMARDs + biologics in 75%, only DMARDs in 24%. MTX was previously prescribed in 95% of pts and in 71% within the last 2 years. TCZ Mono was initiated in 228 (40%) pts and TCZ Combo in 349 (60%) pts of whom 80% received MTX (mean 16±5mg/w). Steroids (GCs) were used in 386 (67%) pts (mean 10±7mg/d). 337 pts completed M12 visit. 194 pts withdrew for: AE 53 pts, inefficacy 88, patients wish 12, lost to follow-up 23, other 18. At M12, drug retention rate was 69% in Total, 67% in Mono, 71% in Combo (Fig.). Mean number of TCZ infusions was 9.4±4.1; mean time between infusions was 31.8 ±12.6 days. 29% of the pts experienced at least 1 discontinuation, 25% and 33% in Mono and Combo groups respectively. DMARD was added in 20 Mono and definitely stopped in 25 Combo pts. 170 (50%) pts remained on GCs, 66 (51%) in Mono group and 104 (50%) in Combo group. At M12, mean DAS28 in Total, Mono and Combo were 2.4±1.3, 2.4±1.3 and 2.3±1.2 respectively. DAS28 remission was 35% in Total, 35% and 36% in Mono and Combo respectively (p=0.83). Using the propensity score, no effect of Mono was observed on drug retention HR=1.194 [0.852,1.673], p=0.30; DAS remission OR=1.111 [0.773,1.597], p=0.57; or GCs use OR=0.880 [0.558,1.387], p=0.58 at M12.
No new safety signal was reported. 325 (54%) patients had at least one AE, 74 (12%) had at least one serious AE with no differences between Mono and Combo.

Fig. : TCZ Drug retention rate at 12 months




**Conclusions:** The Act Solo study confirms, in real life, the clinical results of RCTs showing a comparable efficacy of TCZ as monotherapy when compared to combotherapy. No new safety signal occurred.
**Disclosure of Interest:** J. Tebib: None declared, I. Idier Employee of: Chugai Pharma France, M. Coudert: None declared, J.-F. Maillefert: None declared, R.-M. Flipo Consultant for: Roche SAS and Chugai Pharma France
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## FRI0221 OCCURRENCE OF SERIOUS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS AND DENOSUMAB OBSERVED IN A CLINICAL SETTING

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**Background:** Studies combining immunosuppressive biologics have shown an increased risk of infections.
**Objectives:** Examine the occurrence of serious and opportunistic infections in RA patients treated concurrently with DMAb and an immunosuppressive biologic, and those treated with only an immunosuppressive biologic.
**Methods:** We reviewed RA patients from two rheumatology practices in Ontario (Canada) between 01July2010 and 31July2014. Eligible patients were ≥18 years of age with RA, registered in the practice ≥3 months before and after the index date, and received ≥1 injection/infusion or filled a prescription for an immunosuppressive biologic therapy for RA. Patients with HIV or AIDS, or who were receiving cancer treatment or immunosuppressive therapies for conditions other than RA or living in a nursing home were excluded. The incidence of serious infections was counted for two different groups: 1) those who had used DMAb and an immunosuppressive biologic concurrently and 2) those who had used an immunosuppressive biologic alone. Serious infection was defined as resulting in hospitalization or an emergency room (ER) visit with associated use of IV antibiotics and a primary diagnosis of infection. The observational period was from the index date to 31July2014 or loss to follow-up, whichever came first. For the concurrent group, index date was defined as their first DMAb injection. A frequency-matching technique utilizing the index date of the concurrent group was used to select the index date of the biologic-alone group.
**Results:** 308 patients met the eligibility criteria; patient characteristics (± 6 months of index event) are shown below. Three events of serious infection occurred in three patients in the concurrent group (all three were cases of pneumonia); four events of serious infection occurred in four patients in the biologic-alone group (three cases of pneumonia, one upper respiratory tract infection, all resulting in hospitalization). One event of opportunistic infection (*mycobacterium avium* complex and pleural infection) occurred in the biologic-alone group. All patients recovered, with no instances of death.

Patient characteristics

| | Concurrent (N=102) | Biologic-alone (N=206) |
|---|---|---|
| Women, n (%) | 90 (88) | 158 (77) |
| Age, years | 66.4 (10.8) | 57.4 (11.6) |
| Average follow-up time, years | 2.4 (1.2) | 2.5 (1.3) |
| History of fracture, n (%) | 8 (8) | 4 (3) |
| T-score ≤–2.5 at the spine or hip, n (%) | 45 (47) | 23 (13) |
| Chronic kidney disease, n (%) | 1 (1) | 4 (2) |
| Chronic obstructive pulmonary disease, n (%) | 4 (4) | 16 (8) |
| Cardiovascular disease, n (%) | 7 (7) | 19 (9) |
| Diabetes, n (%) | 8 (8) | 25 (12) |
| Liver disease, n (%) | 1 (1) | 1 (0.5) |
| Prednisone use, % (n) | 21 (21) | 15 (7) |
| C-reactive protein, mg/L | 4.6 (6.8) | 4.5 (8.0) |
| Erythrocyte sedimentation rate, mm/h | 19.0 (17.0) | 17.2 (15.2) |

Data are means (SD) unless otherwise noted.

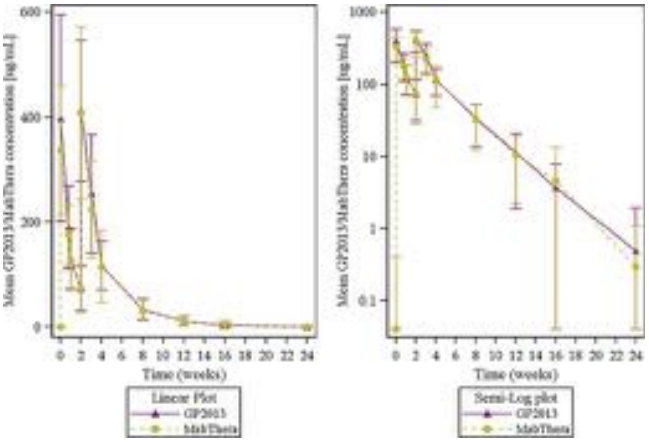
**Conclusions:** RA patients may require treatment for bone loss due to intrinsic disease, steroid use, and advancing age. This study demonstrates a low occurrence of serious infections in biologically-treated RA patients, including patients with concurrent DMAb use.
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## FRI0222 PHARMACOKINETICS, PHARMACODYNAMICS, SAFETY AND EFFICACY OF PROPOSED RITUXIMAB BIOSIMILAR (GP2013) VS. EU-APPROVED RITUXIMAB (RTX) IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL (GP13-201) OVER 52 WEEKS

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**Background:** GP2013 has been developed as a proposed biosimilar to originator rituximab (RTX), by Sandoz, a Novartis Company. The stepwise development program is comprised of structural and functional characterization with highly sensitive analytical methods followed by nonclinical testing and clinical studies.
**Objectives:** The primary objective of the study was to demonstrate PK bioequivalence of GP2013 and EU-approved rituximab (RTX) in patients with RA, defined as equivalence of AUC(0–inf) up to week 24. Secondary endpoints included other PK and PD parameters and evaluation of safety and efficacy.

**Methods:** In this prospective, randomized, double blind study patients with active RA refractory or intolerant to standard DMARDs and TNF inhibitor(s) were randomized to GP2013 or RTX. Read-out of the primary analysis was performed at week 24. Efficacy and PD data were collected to week 52, while safety follow-up ended 24 weeks after the last infusion of study medication. For anti-drug antibody (ADA) assessment a validated in-house ELISA method for binding ADAs was applied.
**Results:** Of the 325 patients screened, 173 were randomized to either GP2013 or RTX. There were no relevant differences in baseline characteristics between the treatment arms. A similar number of patients received a second treatment course after week 24: 58 (67.4%) patients in the GP2013 and 56 (64.4%) patients in the RTX arm.
The study met its primary objective by demonstrating PK bioequivalence based on AUC0-inf. The ratio of the geometric means (GP2013/RTX) was 1.064, and the 90% confidence interval (CI) was maintained within the standard bioequivalence limits [0.8 to 1.25] (Figure 1).
For maximum serum concentration (Cmax) after the first infusion, the upper limit of the 90% CI of the ratio of the geometric means (1.262) was slightly above the upper bound of the bioequivalence limit (1.25) whereas for Cmax after the second infusion, the CI was fully within the 90% CI. This outcome was attributed to a higher variability in infusion rates and durations during the first infusion. The study met all other secondary PK endpoints.
Equivalence of GP2013 and RTX was also demonstrated in terms of peripheral B cell depletion. The ratio of the geometric means (GP2013/RTX) was 1.019 and the 95% CI was within the equivalence limits [0.8 to 1.25]. Non-inferiority to reference RTX was demonstrated for disease activity score DAS28(CRP) change from baseline at week 24. The LS mean difference between the groups was 0.07 and the 95% confidence interval was below the non-inferiority margin of 0.6. The number of adverse events, serious adverse events and potential infusion related reactions were similar between the treatment arms. Nine (11.0%) patients in the GP2013 vs. 18 (21.4%) patients in the RTX group developed anti-drug antibodies (ADAs).




**Conclusions:** The proposed biosimilar GP2013 met the primary endpoint demonstrating bioequivalence to originator EU-approved RTX. No clinically meaningful differences were found between GP2013 and the reference RTX in PD and safety, as well as efficacy and immunogenicity at week 24.
**Disclosure of Interest:** J. Smolen Grant/research support from: Abbvie, Janssen, Lilly, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, M. Scheinberg: None declared, H.-P. Tony Consultant for: AbbVie, BMS, Chugai, Janssen, Lilly, MSD, Novartis, Roche, UCB, Speakers bureau: AbbVie, Chugai, Jenssen, Lilly, Roche, P. Zhu Employee of: Sandoz, a Novartis company, T. Shisha Employee of: Sandoz, a Novartis company
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## FRI0223 THE BEST SELECTION OF SECOND BIOLOGICS FOR PATIENTS WITH RHEUMATOID ARTHRITIS IN DAILY CLINICAL PRACTICE

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**Background:** Since the approval of infliximab (IFX) in 2003, 8 biologics have been approved for rheumatoid arthritis (RA) in Japan. However, little is known regarding what to do when patients have an inadequate response to first biologics in daily clinical practice.
**Objectives:** This study aimed to evaluate the effectiveness of biologics as 2nd-line use in RA patients in daily clinical practice from our university cohort (FIRST registry).
**Methods:** We retrospectively examined 2553 patients who were treated with biologics in our institute between July 2003 and December 2015. We compared the effectiveness of TNF-inhibitors (TNFi), TCZ, ABA as 2nd-line use and efficacy of switching from 1st TNFi to 2nd TNFi, TCZ or ABA based on retention rates and change in disease activity such as CDAI at 1 year, ΔCDAI (0–52W), ΔDAS28-ESR (LOCF). Propensity score (PS) were generated using multinomial logistic regression and the study groups were matched regarding baseline variables including age, disease duration, disease activity, concomitant use of MTX and PSL. In addition, in order to find out the characteristic of 2nd biologics, we conducted comparison between the upper (1yCDAI-H; low response) and lower (1yCDAI-L; good response) quartiles in CDAI at 1 y after switching.
**Results:** In terms of switching of biologics, better treatment outcome of ΔCDAI was observed in order of TCZ (n=141) >2nd TNFi (n=186) >ABT (n=91) but was comparable after the adjustment by PS. Comparison between the upper (1yCDAI-H) and lower (1yCDAI-L) quartiles in CDAI at 1 y after switching revealed that disease activity might improve despite of a high disease activity at switching in the case of TCZ as shown in Figure. In addition, high CRP and MMP-3 at switching were higher in the 1y CDAI-L group only in the case of switching to TCZ.

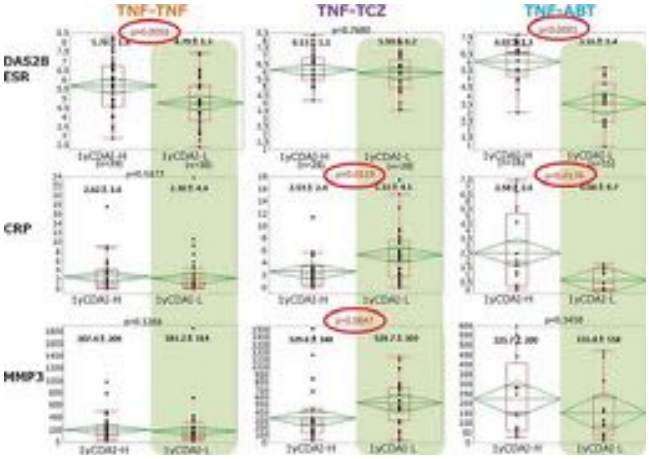



Figure 1. Comparison of DAS28, CRP and MMP3 at initiation of 2nd biologics between the upper (1yCDAI-H) and lower (1yCDAI-L) quartiles in CDAI at 1 y after switching.

**Conclusions:** After adjustment using PS-score, RA patients with prior anti-TNF exposures had similar outcomes if they switched to a new TNFi as compared with initiation of TCZ or ABA. Also our results imply us that TCZ might bring about good outcome despite of disease activity at switching. Furthermore, higher CRP or MMP-3, suggesting inadequate suppression of IL-6 by first biologics, might predict better outcome of TCZ.
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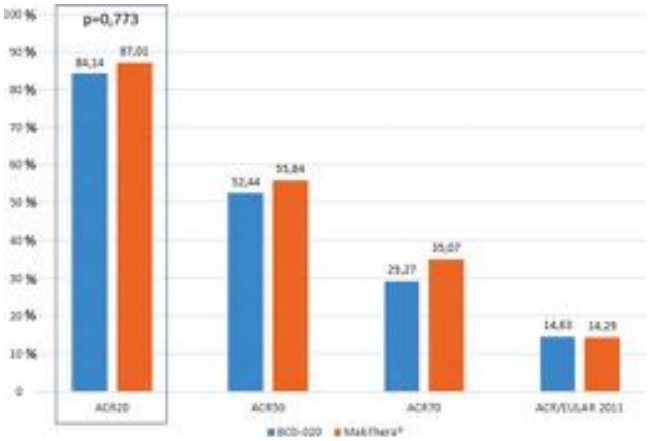
## FRI0224 COMPARISON OF EFFICACY AND SAFETY OF RITUXIMAB BIOSIMILAR, BCD-020, AND INNOVATOR RITUXIMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS REFRACTORY TO TNFA INHIBITORS

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**Background:** BCD-020 is the first Russian rituximab (RTX) biosimilar which was approved for medical use in lymphoma patients in Russia and some CIS countries. Previous preclinical and clinical studies showed that BCD-020 is highly similar to innovator RTX. Since there are several differences in mechanism of action of RTX in NHL and RA it is recommended to conduct separate clinical studies in oncology and autoimmune indications to prove similar efficacy and safety of biosimilar and original medicine.
**Objectives:** The primary objective was to evaluate the efficacy and safety of BCD-020 used in combination with MTX in patients with RA with inadequate response or intolerance to other DMARDs including 1 or more TNF inhibitor. The secondary objectives included direct comparison of safety, efficacy, pharmacokinetics, pharmacodynamics and immunogenicity of RTX biosimilar and innovator RTX.
**Methods:** This international multicenter randomized double-blind phase 3 clinical study was conducted in patients with active RA despite DMARD therapy, which included 1 or more TNF inhibitor. After completion of screening all eligible patients were stratified by age (<40 years/40 years), ACCPA positive/ACCPA negative,

presence/absence of the need for oral steroids. Then patients were randomized in 1:1 ratio into 2 arms: patients from the main arm received BCD-020 1000 mg as an IV infusion on day 1 and day15, patients from the reference arm received innovator RTX by the same regimen. In this work results of the first 6-months period of observation are presented.

**Results:** A total of 160 patients were enrolled; 159 patients had data eligible for efficacy analysis. ACR20 at Week 24 was reported in 84.14% patients in BCD-020 arm and 87.01% in reference arm. The 95% CI for the difference in proportion of ACR20 between groups was [-13.95; 8.74%], where the limits of 95% CI lie within the pre-specified equivalence margin. Both drugs caused deep and sustained depletion of B-cells from peripheral blood without any toxicity to other cell populations. Favorable safety profiles were demonstrated in both groups without any significant differences: AEs have been reported in 59.34% patients from BCD-020 arm and 54.12% patients from reference arm. Treatment discontinuation caused by AE/SAE was reported only for 3 (3.30%) patients in BCD-020 arm and 4 (3.53%) patients in the reference arm (p=1.00). SAEs occurred only in the reference group (2.35%). Binding antibodies were revealed in 3 patients from BCD-020 arm and in 7 patients from reference arm (p=0.209). There were 2 events of neutralizing antibodies against RTX, both in the reference arm (p=0.232).




**Conclusions:** Equivalent efficacy of BCD-020 compared to innovator RTX in patients with active RA has been confirmed. Further clinical evaluation of BCD-020 is planned to confirm long-term efficacy and safety.

**References:**

[1] interim study report.

**Disclosure of Interest:** A. Eremeeva Employee of: CJSC BIOCAD, E. Chernyaeva Employee of: CJSC BIOCAD, R. Ivanov Employee of: CJSC BIOCAD, E. Nasonov: None declared, L. Knyazeva: None declared

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## FRI0225 SHORT COURSE OF TOCILIZUMAB INCREASES RISK OF HEPATITIS B VIRUS (HBV) REACTIVATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A REAL-WORLD, PROSPECTIVE COHORT STUDY

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**Background:** Our previous study showed approximately 11% of Chinese RA patients combined with chronic Hepatitis B virus (HBV) infection and 32% with resolved HBV infection. HBV reactivation may occur as an adverse event of biologic DMARDs and TNFIs or abatacept have been categoried as moderate risk of HBV reactivation, rituximab as high risk [1]. However, tocilizumab (TCZ) is still unclassified due to few data. TCZ has been approved for RA patients in combination with csDMARDs by CFDA in November 2013 and most of Chinese RA patients can only afford short course of TCZ for self-paid and expensive price.

**Objectives:** To investigate the impact of short course of TCZ on HBV reactivation in RA patients.

**Methods:** RA patients with moderate or high disease activity were recruited. Three consecutive doses of intravenous TCZ were given combined with csDMARDs. RA disease activity, liver function and HBV infection status were evaluated at baseline, week 4, week 8 and week 12 during TCZ based therapy.

**Results:** Fifty-seven RA patients were recruited and 51 were qualified for statistics (Figure 1). They were divided into chronic HBV infection group (n=7, 13.7%), resolved HBV infection group (n=33, 64.7%) and non-HBV infection group (n=11, 21.6%). Three patients (6%) developed HBV reactivation after 1–3 doses of TCZ and all of them had chronic HBV infection without antiviral prophylaxis. All reactivation patients were asymptomatic along with normal aminotransferases and resolution of virological response after therapeutic antiviral therapy. None of patients with resolved HBV infection suffered from HBV reactivation. Aminotransferases elevated in 24% (12/51) of RA patients with 4% (2/51) exceeding 2-fold of ULN and returned to normal 4 weeks after adding hepatinica. Anti-HBs titer was positive (≥10 IU/L) in 82% (27/33) of patients with resolved HBV infection and reduced significantly after first dose of TCZ compared to baseline [426 (59–978) IU/L vs. 446 (78–000) IU/L, $P<0.05$], which was below protective level (<10 IU/L) in 19% (5/27) of patients and unable to recover in 7% (2/27) up to week 28–36. All patients were kept follow-up after 12 weeks. No additional HBV reactivation occurred during 4–80 weeks on extended period.

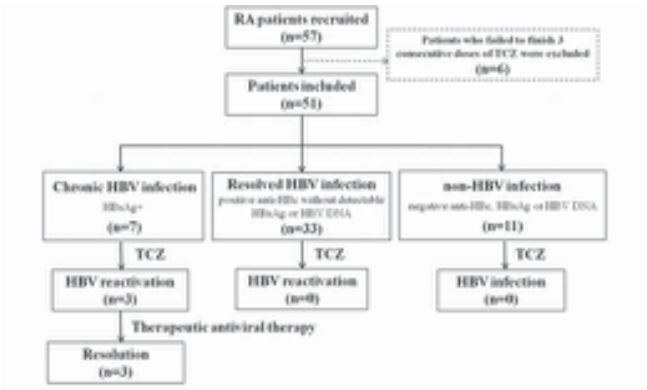



**Figure 1 Flow diagram illustrating cohort selection and the development of hepatitis B virus (HBV) reactivation/infection during 12 weeks of tocilizumab (TCZ) based therapy.**
**RA: rheumatoid arthritis; HBsAg: surface antigen of HBV; anti-HBc: antibody to core antigen of HBV.**

**Conclusions:** This real-world, prospective cohort study suggests that short course of TCZ has moderate risk of HBV reactivation in RA patients and high risk in RA patients with chronic HBV infection especially without antiviral prophylaxis, which indicate the importance of HBV screening and antiviral prophylaxis for patients with chronic HBV infection before starting TCZ therapy.

**References:**

[1] Reddy KR, Beavers KL, Hammond SP, et al. American Gastroenterological Association Institute guideline on the prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. Gastroenterology, 2015,148:215–219.

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**Disclosure of Interest:** None declared

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## FRI0226 TOCILIZUMAB IS SIMILARLY EFFECTIVE IN RA PATIENTS WITH NO OR UP TO TWO PRIOR BDMARD FAILURES: RESULTS FROM THE GERMAN PROSPECTIVE COHORT STUDY RABBIT

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**Background:** In Germany, Tocilizumab (TCZ) is used for the treatment of rheumatoid arthritis both in biologic-naïve patients and those with previous failures of biologic (b)DMARDs.

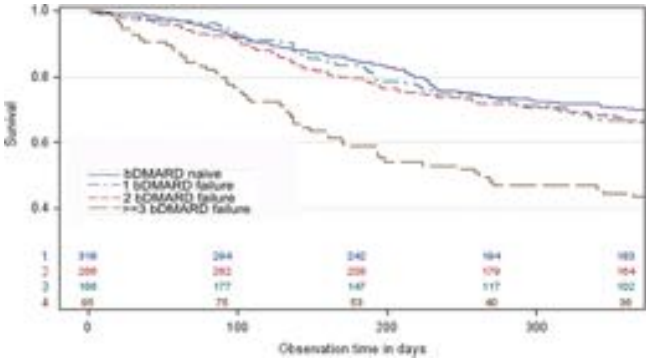
**Objectives:** To investigate effectiveness and retention rates of TCZ in patients with multiple bDMARD failures.

**Methods:** We included 885 RA patients enrolled with the start of TCZ treatment between 2009 and 2015 in the German biologics register RABBIT (Rheumatoid arthritis: Observation of biologic therapy). Patients were stratified according to the number of bDMARD failures prior to the initiation of TCZ: biologic naive (n=318), 1 bDMARD failure (n=286), 2 bDMARD failures (n=186), ≥3 bDMARD failures (n=95).

We used Kaplan-Meier survival methods to examine the retention rates within 12 months after the initiation. Discontinuation was defined as stopping TCZ therapy. Effectiveness regarding the control of disease activity (mean DAS28-ESR) over 3, 6 and 12 months was examined with linear mixed models.

**Results:** Compared to biologic naive patients those with prior bDMARD failures at start of TCZ were younger but had significantly longer disease duration (bio-naive: 8, 1 bDMARD failure: 11.6, 2 failures: 13.3 and ≥3 failures: 15.3 years; p<0.01). The DAS28 at baseline and loss of physical function were significantly higher in patients with ≥3 bDMARD failures. In the latter group patients with more than 2 comorbidities were also more frequent (21% (bio-naive), 31% (1), 24% (2), 38% (≥3 failures)). No differences were found regarding concomitant use of glucocorticoids and csDMARDs. All patients with ≥3 bDMARD failures had been exposed to TNF-inhibitors (TNFi), 60% had also been exposed to other bDMARD

classes. In contrast, only 5.9% (12.9%) of patients with 1 (2) bDMARD failures had been exposed to non-TNFi.
During follow-up in RABBIT, patients with ≤2 bDMARD failures reached low disease activity (DAS28) on average while those with ≥3 bDMARD failures remained in moderate disease activity. Treatment continuation on TCZ therapy was similar in biologic naive patients and in those with ≤2 bDMARD failures. Patients with ≥3 bDMARD failures had significantly lower continuation rates (Figure). Adverse events (AEs) were the most frequent reason for discontinuation in all strata; in patients with ≥3 bDMARD failures the withdrawal of TCZ due to AEs occurred in 52% of patients.




**Conclusions:** TCZ was similarly effective in biologic naive patients and in patients with up to 2 prior TNFi failures. The majority of those patients achieved low disease activity (DAS28<3.2). However, in patients with ≥3 bDMARD failures disease activity remained on a higher level and treatment continuity was significantly lower. It seems that despite all progress in the treatment of RA during the last decades a small patient group remains in which the disease is difficult to be controlled despite effective treatment.
**Disclosure:** Supported by a joint, unconditional grant from AbbVie, Celltrion, Hospira, Bristol-Myers Squibb, MSD Sharp&Dohme, Pfizer, Roche, and UCB.
**Disclosure of Interest:** None declared
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## FRI0227 FIVE-YEAR SAFETY AND EFFICACY OF SUBCUTANEOUS ABATACEPT IN PATIENTS WITH MODERATE TO SEVERELY ACTIVE RA AND AN INADEQUATE RESPONSE TO MTX: LONG-TERM EXTENSION OF THE PHASE III, DOUBLE-BLIND, RANDOMIZED ACQUIRE STUDY

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**Background:** The ACQUIRE study demonstrated non-inferiority of the SC to the IV formulation.[1]
**Objectives:** To assess the 5-yr safety and efficacy of SC ABA 125 mg/wk plus background MTX in the LT extension (LTE).
**Methods:** The 6-month, double-blind (DB) period was followed by an open-label LTE in which patients (pts) received SC ABA 125 mg/wk. Dose adjustments to MTX, corticosteroids and NSAIDs were permitted. Safety, efficacy and immunogenicity assessments were performed at 12-wk intervals. Safety and efficacy analyses included all pts who entered the LTE and received ≥1 dose of ABA.
**Results:** 1373/1385 pts who completed the DB period entered the LTE, 427 (31.1%) had discontinued by end of Yr 5 (due to AE: 100 [7.3%]; lack of efficacy: 89 [6.5%]; withdrawal of consent: 81 [5.9%]). In the LTE, 1240 pts (90.3%) had an AE (Table), most (79.8%) were mild/moderate; most frequent non-serious AEs were infections. Overall, 353 pts (25.7%) had an SAE. The incidence rate/100 pt-yrs (95% CI) for SAEs decreased from 9.02 (6.31, 12.90) in the DB period to 7.73 (6.96, 8.58) during the LTE (332.6 and 4566.2 pt-yrs of exposure, respectively). Efficacy in the LTE was consistent with the DB phase and was maintained to 5 yrs in pts who remained on study: at Day 1821, 356/421 (84.6%), 277/423 (65.5%) and 191/425 (44.9%) had an ACR20, 50 or 70 response, respectively. ABA trough concentrations were stable over the LTE. Immunogenicity was low over 5 yrs (4.6/100 pt-yrs); there was no association between immunogenicity and ABA efficacy, safety or PK.

| Adverse event | Adverse events in 5-yr LTE (n=1373) n (%) of pts |
|---|---|
| All AEs | 1240 (90.3) |
| AE related to study drug | 632 (46.0) |
| AE leading to discontinuation | 97 (7.1) |
| SAEs | 353 (25.7) |
| Death | 41 (3.0) |
| AEs of special interest | |
| Infections | 962 (70.1) |
| Serious infections | 85 (6.2) |
| Opportunistic infections* | 4 (0.3) |
| Systemic injection reactions | 161 (11.7) |
| Autoimmune disorders† | 67 (4.9) |
| Malignancies‡ | 56 (4.1) |
| Local injection-site reactions | 33 (2.4) |

*Peritoneal tuberculosis, fungal oesophagitis, fungal eye infection, fungal sinusitis (n=1 each); †Including psoriasis (n=13), chronic gastritis (n=11), Sjögren's syndrome (n=10), vasculitis (n=6); ‡Including basal cell carcinoma (CA) (n=15); breast cancer, squamous cell CA, squamous cell CA of skin (n=4 each); thyroid neoplasm (n=3); cervical CA Stage 0, invasive ductal breast CA, non-small cell lung cancer, prostate cancer (n=2 each).

**Conclusions:** During this 5-yr LTE of the ACQUIRE study, the safety and efficacy of SC abatacept were consistent with that seen in the initial DB phase, with no new safety signals.
**References:**
[1] Genovese M, et al. Arthritis Rheum 2011;63:2854–64.
**Disclosure of Interest:** M. C. Genovese Grant/research support from: Bristol-Myers Squibb, C. Pacheco Tena Grant/research support from: UCB, Speakers bureau: Bristol-Myers Squibb, Roche, AbbVie, UCB, Janssen, A. Covarrubias: None declared, G. Leon: None declared, E. Mysler Grant/research support from: Bristol-Myers Squibb, Roche, Speakers bureau: Bristol-Myers Squibb, Roche, M. Keiserman Grant/research support from: AbbVie, Actelion, Anthera, Biogen, Bristol-Myers Squibb, Celltrion, Eli Lilly, HGS, Janssen, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Janssen, R. Valente Grant/research support from: Novartis, Bristol-Myers Squibb, Pfizer, Takeda, Sanofi, Lilly, Boehringer Ingelheim, AbbVie, AstraZeneca, Sandoz, P. Nash: None declared, J. A. Simon-Campos: None declared, J. Box: None declared, C. W. Legerton III Grant/research support from: AbbVie, Ablynx, Acerta, Amgen, AstraZeneca, Celgene, GSK, Janssen, Eli Lilly, Bristol-Myers Squibb, Pfizer, Novarits, Sandoz, UCB, Daiichi Sankyo, ChemoCentryx, Boehringer Ingelheim, Speakers bureau: Celgene, Amgen, E. Nasonov: None declared, P. Durez Speakers bureau: Bristol-Myers Squibb, Samsung, Pfizer, UCB, Mundipharma, Hospira, Lilly, A. Elegbe Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, R. Wong Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, X. Li Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, R. Alten Grant/research support from: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb
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## FRI0228 SARILUMAB DOSE REDUCTION TO MANAGE LABORATORY ABNORMALITIES IN AN OPEN-LABEL EXTENSION STUDY IN RA PATIENTS

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**Background:** The investigational agent sarilumab is a human monoclonal antibody directed against the interleukin 6 (IL-6) receptor. In the phase 3 MOBILITY (NCT01061736) and TARGET (NCT01709578) studies, sarilumab (150 or 200 mg subcutaneously every 2 weeks [q2w] + conventional synthetic disease-modifying antirheumatic drugs [csDMARDs]) demonstrated efficacy in adults with active, moderate-to-severe rheumatoid arthritis (RA).[1] Among the most common treatment-emergent adverse events in both studies were infections, neutropenia, injection site reactions, and increased transaminases. Laboratory changes were consistent with IL-6 signaling blockade.
**Objectives:** This analysis examined laboratory changes and treatment continuation after sarilumab dose reduction in EXTEND (NCT01146652), an open-label, follow-up study that evaluated long-term safety and efficacy of sarilumab with or without concomitant csDMARDs.
**Methods:** Adults with RA who previously participated in sarilumab studies were eligible. Patients who entered into EXTEND before dose selection for the phase 3 studies received sarilumab 150 mg every week. After dose selection for the phase 3 studies, patients were switched to or initiated on sarilumab 200 mg q2w. Per protocol, investigators could have reduced the dose of sarilumab to 150 mg q2w for absolute neutrophil count (ANC) ≥0.5 to 1.0 Giga/L, platelet count ≥50 to 100

Giga/L, or alanine aminotransferase (ALT) ≥3 to 5× upper limit of normal. Dose reductions to avoid laboratory changes were also performed at the investigator's discretion. Efficacy data from EXTEND were analyzed before and 24 weeks after dose reduction for patients entering from the MOBILITY (n=158) and TARGET (n=42) studies.

**Results:** As of the April 2015 interim analysis, dose reduction from sarilumab 200 to 150 mg q2w had occurred in 15% of patients. The most common reasons for dose reduction were decreases in ANC (9.5%) and elevations in ALT (3.3%) (Table). Infection was the most common non-laboratory reason for dose reduction (0.4%). At the time of analysis, 80.1% of patients who dose reduced were continuing treatment, with a mean treatment duration of 1.5 years after dose reduction. Improvements in ANC and ALT were observed over the 6 months after dose reduction. Efficacy of sarilumab was maintained in patients from MOBILITY and TARGET after dose reduction in EXTEND as assessed by ACR20 responses (83.3% and 77.4%, respectively) and HAQ-DI scores (-0.68 and -0.73, respectively).

Table. Reasons for Dose Reduction

| | Patients on 200 mg q2w (N=1843) n (%) |
|---|---|
| Patients who dose reduced from 200 mg q2w to 150 mg q2w | 276 (15%) |
| Decrease in ANC | 175 (9.5%) |
| ANC <1.0 Giga/L and ≥0.5 Giga/L | 92 (5.0%) |
| Precautionary measure to avoid ANC <1.0 Giga/L | 83 (4.5%) |
| Increase in ALT level | 61 (3.3%) |
| ALT increase >3 × ULN and ≤5 × ULN | 54 (2.9%) |
| Precautionary measure to avoid ALT increase >3 × ULN | 7 (0.4%) |
| Decrease in platelet count | 19 (1.0%) |
| Platelet count ≥50 Giga/L and <100 Giga/L | 8 (0.4%) |
| Precautionary measure to avoid platelet count <100 Giga/L | 11 (0.6%) |
| Other AE | 16 (0.9%) |
| Other reason | 5 (0.3%) |

AE, adverse event; ALT, alanine aminotransferase; ANC, absolute neutrophil count; q2w, every 2 weeks; ULN, upper limit of normal.

**Conclusions:** In patients whose sarilumab dose was decreased from 200 mg q2w to 150 mg q2w, there was an improvement in laboratory abnormalities and continuation of treatment for the majority of patients. Improvements in signs and symptoms of RA and physical function were maintained after dose reduction.

**References:**

[1] Genovese et al. Arthritis Rheumatol. 2015;67:1424–1437.

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## FRI0229 RISK OF HOSPITALIZED INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING ABATACEPT AND OTHER BIOLOGICS: ANALYSIS OF A UNITED STATES CLAIMS DATABASE

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**Background:** Some studies have shown an increased risk of serious infection in patients with RA on biologic therapy.[1,2] Abatacept, the first selective co-stimulation modulator for the treatment of RA, has a mechanism of action that is fundamentally different from that of other biologic agents.

**Objectives:** The purpose of this cohort study was to compare the risk of hospitalized infection between patients initiating abatacept and patients initiating other biologic treatments.

**Methods:** Adult patients diagnosed with RA in the MarketScan® Commercial and Supplemental Medicare database, who initiated treatment with abatacept or another biologic treatment between 1 July 2006 and 30 September 2014, were eligible for inclusion in the analysis. Patients were required to have at least 180 days of continuous health plan enrolment prior to, and ≥1 day following, initiation of the qualifying RA treatment. Patients were presumed to have initiated a treatment if there was no claim for that drug in the 180 days prior to the index date. Hence, patients initiating abatacept or another biologic may have been initiating a biologic for the first time or switching from one biologic to another. Hospitalized infections were identified by International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes indicating an infection in conjunction with a hospital stay. Patients were followed up from the date of initiation of abatacept or another biologic treatment until the event of interest, end of the initiated treatment (last treatment date plus days' supply, where the last treatment date was defined as no subsequent treatment within 90 days from last treatment date plus days' supply), end of enrolment in the database or end of data collection, whichever occurred first. Patients who were hospitalized for an infection in the 6 months prior to the date of initiation were excluded. Crude incidence rates were calculated for each cohort and a Cox regression analysis was conducted to compare patients, matched by propensity score, in the two groups.

**Results:** A total of 18,474 patients with RA initiating abatacept and 53,591 initiating another biologic were identified and eligible to be included in the analysis. There were 546 incident events among abatacept initiators and 1,716 events among other biologic initiators, resulting in crude incidence rates of 35 (95% CI: 32, 38) and 36 (34, 37) per 1000 person-years, respectively. A total of 17,517 patients initiating abatacept and 32,277 patients initiating another biologic were included in the matched analysis. After adjusting for prior biologic treatment, the hazard ratio comparing hospitalized infections in the abatacept cohort and the other biologic cohort was 0.97 (0.82, 1.14).

**Conclusions:** In this study, the risk of hospitalized infection was not significantly different in patients who initiated abatacept compared with patients who initiated other biologics.

**References:**

[1] Curtis JR, et al. Arthritis Rheum 2007;56:1125–33.
[2] Schneeweiss S, et al. Arthritis Rheum 2007;56:1754–64.

**Disclosure of Interest:** N. Baker Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Boers Consultant for: Bristol-Myers Squibb, M. Hochberg Consultant for: Bristol-Myers Squibb, H. Kawabata Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, N. Ray: None declared, T. Simon Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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## FRI0230 ASSESSMENT OF SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF A NOVEL ANTI-CD40 MONOCLONAL ANTIBODY, CFZ533, IN HEALTHY VOLUNTEERS AND IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Aberrant CD40-CD154 pathway signaling has been linked to pathology in autoimmune disease. Blocking the CD40-CD154 pathway prevents T cell-dependent antibody responses, germinal center formation and prolongs renal allograft survival in non-human primates. CFZ533 is a novel, fully human, non-agonistic Fc-silent, anti-CD40 monoclonal antibody being developed for treatment of autoimmune diseases and prevention of rejection in solid-organ transplantation.

**Objectives:** To assess the safety, pharmacokinetics (PK) and pharmacodynamics activity (PD) of CFZ533 in humans.

**Methods:** A double-blind, placebo controlled, ascending, single-dose study was conducted in 48 healthy volunteers (HV) receiving 0.03, 0.1, 0.3, 1.0, 3.0 mg/kg i.v., 3.0 mg/kg s.c. CFZ533 or matching placebo (3:1) as well as in 12 rheumatoid arthritis (RA) patients receiving 10.0 mg/kg i.v. CFZ533 or placebo (1:1). HVs were immunized with a single intramuscular dose of a T-cell dependent neo-antigen, Keyhole Limpet Hemocyanin (KLH) with alum adjuvant on Day 3 and again between Day 29–85 depending on predicted loss of CD40 receptor occupancy (RO) as a function of CFZ533 dose. Blood samples for PK, CD40 RO and anti-KLH IgG and IgM profiling were collected at multiple time points during the study. Anti-KLH antibodies were assessed using a validated human ELISA system with an LOQ of 0.7 (IgG) and 2.1 (IgM) μg/mL. RA patients were evaluated for safety, PK and RO.

**Results:** All doses of CFZ533 and KLH were safe and well tolerated. CFZ533 PK concentrations were quantifiable at all dose levels tested. Complete (≥90%) peripheral CD40 RO by 3 mg/kg i.v. CFZ533 in HVs was maintained for 28 days. During this period of full RO, full suppression of the primary humoral response to KLH was evident in all treated subjects (KLH administered 2 days after CFZ533 dosing). After complete CFZ533 washout in 3 mg/kg cohort, all subjects mounted a robust anti-KLH response following a re-challenge on Day 85. Full RO in RA patients who received 10 mg/kg i.v. CFZ533 was maintained for at least 6 weeks and up to 10 weeks.

**Conclusions:** The favorable safety and tolerability profile of CFZ533 coupled with a predictable concentration-CD40 receptor occupancy relationship and suppression of a primary T cell-dependent antibody response supports future clinical trials of CFZ533 in select autoimmune diseases and transplantation.

**Disclosure of Interest:** A. Slade Employee of: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, P. Koo Employee of: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, Y. He Employee of: Novartis Pharmaceuticals Corporation, Cambridge, MA, USA, P. Espie Employee of: Novartis Pharmaceuticals Corporation, Basel, Switzerland, A. Auger-Sarrazin Employee of: Novartis Pharmaceuticals Corporation, Basel, Switzerland, J. Rush Employee of: Novartis Pharmaceuticals Corporation, Basel, Switzerland, P. Gergely Employee of: Novartis Pharmaceuticals Corporation, Basel, Switzerland
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## FRI0231 TREATMENT WITH BI 655064 (ANTAGONISTIC ANTI-CD40 ANTIBODY) MODULATES BIOMARKERS ASSOCIATED WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** Co-stimulation through the CD40- CD40L axis has been implicated in the pathogenesis of RA including T cell mediated responses, B cell driven autoantibodies, adhesion molecule expression, synovial hyperplasia, and pannus formation, in addition to the secretion of proinflammatory cytokines and MMPs. Circulating CD40L levels are elevated in RA patients versus healthy controls. BI 655064 is a humanized antagonistic anti-CD40 monoclonal antibody which blocks the CD40/ CD40L interaction in in vitro CD40L induced B cell and APC activation assays with IC50 of $<$1nM.
**Objectives:** To characterize the effect of BI 655064 on cellular and protein biomarkers in RA patients with prior inadequate response to a stable dose MTX $\geq$15 mg over a 12 wk period of treatment.
**Methods:** In this double-blinded, randomized trial RA patients were treated with either 120 mg BI 655064 or placebo q1w for 12 wks as add-on to MTX. Inclusion criteria were $\geq$6 swollen and $\geq$6 tender joints, CRP $>$8 mg/L or ESR$>$28 mm/1h. The primary efficacy endpoint was ACR20 response at wk 12.Select biomarkers were assessed in whole blood and serum pre and post treatment with BI 655064.
**Results:** Treatment with BI 655064 resulted in minimal changes in median %CD19+ B cell population but larger median decreases in select %CD95+ activated B cell subsets, specifically class switched (CD19+IgD-CD27+CD95+), pre-switched (CD19+IgD+CD27+CD95+) and double negative (CD19+IgD-CD27-CD95+) cells and decreases in autoantibodies (IgG-RF and IgA-RF), total IgG and IgM levels in RA patients vs placebo at 12 wks. Median decreases in IL-6 levels (important for B cell and monocyte differentiation) and select bone resorption biomarkers (MMP-3 and RANKL) were also observed in the BI 655064 treated patients vs placebo through 12 wks. Baseline levels of IgG RF, IgM RF, TNFa and COMP correlated with improvement in swollen joint counts at 12 wks and IgA RF levels correlated with improvement in DAS-28 CRP scores at 12 wks in patients treated with BI 655064.

Table 1. Median % or change from baseline to 12 wks in select biomarkers by treatment group

| | | N | BI 655064 | Placebo | p-value* |
|---|---|---|---|---|---|
| Change in | % CD19+CD27+IgD+CD95+ | 28/15 | –16.8 | –8.0 | 0.0831 |
| Change in | % CD19+CD27+IgD-CD95+ | 28/15 | –15.3 | +2.3 | 0.0765 |
| Change in | % CD19+CD27-IgD-CD95+ | 28/15 | –14.6 | +4.0 | 0.0097 |
| % change in | IgG ACPA | 35/19 | –19 | –11.9 | 0.2771 |
| % change in | IgG RF | 35/17 | –22.7 | +14.3 | 0.0018 |
| % change in | IgA RF | 35/17 | –13.9 | 0 | 0.0050 |
| % change in | Total IgG | 34/18 | –8.6 | –0.6 | 0.0082 |
| % change in | Total IgM | 34/18 | –12.3 | –0.3 | 0.0002 |
| % change in | CD40L | 34/17 | –47.2 | –59.6 | 0.9920 |
| % change in | IL-6 | 34/18 | –17.3 | +18.7 | 0.1001 |
| % change in | MMP-3 | 34/18 | –7.8 | +2.3 | 0.1574 |
| % change in | RANKL | 35/19 | –29.4 | 0 | 0.0041 |

*Wilcoxon 2-sample test.

**Conclusions:** These results demonstrate that treatment of RA patients with BI 655064 decreases activated B cell subsets, inhibits the production of pathogenic autoantibodies, and reduces the level of circulaiting inflammatory and bone resorption biomarkers at 12 wks. Baseline levels of select biomarkers significantly correlated with clinical response to treatment with BI 655064 at 12 wks.
**Disclosure of Interest:** S. Visvanathan Employee of: Boehringer Ingelheim, M. Ramanujam Employee of: Boehringer Ingelheim, C. Schoelch Employee of: Boehringer Ingelheim, R. Vinisko Employee of: Boehringer Ingelheim, U. Mueller-Ladner Consultant for: Boehringer Ingelheim, S. Padula Employee of: Boehringer Ingelheim, J. Fine Employee of: Boehringer Ingelheim, J. Steffgen Employee of: Boehringer Ingelheim
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## FRI0232 FACTORS INFLUENCING THE CHOICE OF FIRST AND SECOND LINE BIOLOGIC THERAPY FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: REAL LIFE DATA FROM THE ITALIAN LORHEN REGISTRY

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**Background:** The therapeutic armamentarium for the treatment of rheumatoid arthritis (RA) has been significantly implemented with the use of biologic-disease modifying anti-rheumatic drugs (bDMARDs). TNF inhibitors (TNFi), abatacept (ABA) or tocilizumab (TCZ) are all approved as first-line biologic agents. International Recommendations (1) do not provide a preference on the mechanism of action (MoA) to be chosen first or after the failure of bDMARD therapy.
**Objectives:** To analyse the factors influencing the choice of the first-line bDMARD or the switching strategy in RA, focusing on the prescription of ABA or TCZ compared to TNFi.
**Methods:** Patients were selected from the Lombardy Rheumatology Network (LORHEN) Registry. The analysis was limited to patients enrolled after 2008, when all three different MoA were available. The study population was divided into "first-line" and "second-line" bDMARD.
**Results:** A total of 1910 patients were included. First line n=1264, second line n=646 patients. Both age at diagnosis and at bDMARD initiation were significantly lower in patients treated with first-line TNFi compared to ABA and TCZ ($p<0.0001$). A positive screening for latent tuberculosis was more represented in the group treated with first-line ABA compared to TCZ or TNFi (p=0.002). Combination therapy with methotrexate (MTX) was significantly lower in the TCZ group (50.77% of patients), compared to both ABA (86.70%) and TNFi (64.28%); p=0.02. The presence of dyslipidemia (p=0.018), hypertension (p=0.002) or concomitant pulmonary disease ($p<0.0001$) was significantly associated with the choice of ABA first-line. The presence of other comorbidities in general and of $\geq$2 comorbidities influenced the choice of the bDMARD towards ABA (p=0.01). When switching to a second line of treatment, patients with higher DAS28 were more frequently treated with TCZ compared to TNFi (p=0.005) or ABA (p=0.038). The presence of peripheral neuropathy also influenced the choice towards ABA Vs TNFi (p=0.005). TCZ, followed by ABA showed the lowest interruption rate compared to TNFi (p=0.002 and p=0.003, respectively). Multinomial logistic regression demonstrated that a second-line treatment, higher age, dyslipidemia, pulmonary disease, other comorbidities, and extra-articular RA manifestations such as vasculitis were all associated with the choice of ABA compared to TNFi. The choice of TCZ was associated with a second line of treatment, higher age and more severe disease activity.
**Conclusions:** According to International Guidelines, the selection of the first and second-line bDMARD is left to the clinician's preference. However, real-life data suggest that higher age and comorbidities influence the choice towards ABA and TCZ compared to TNFi. After failing a first-line TNFi, a strategy of swapping to a different MoA is more common.
**References:**
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## FRI0233 REAL-WORLD TREATMENT PERSISTENCE AND CLINICAL OUTCOMES OF TNFI CYCLING VS SWITCHING TO NEW MECHANISM-OF-ACTION DMARDS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN THE UNITED STATES

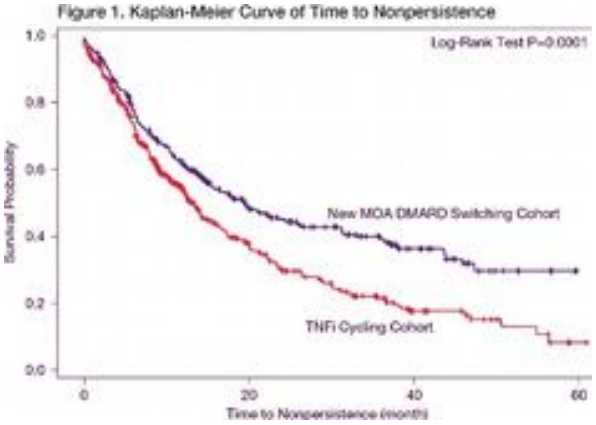
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**Background:** Recent studies suggested that in rheumatoid arthritis (RA) patients discontinuing their prior tumor necrosis factor inhibitor (TNFi), treatment persistence was greater in those switching to a disease-modifying antirheumatic drug (DMARD) with a new mechanism-of-action (MOA) than in those cycling to a second TNFi.
**Objectives:** To evaluate in RA patients real-world treatment persistence and clinical outcomes associated with TNFi cycling vs switching to a new MOA DMARD.
**Methods:** This retrospective analysis of RA patients used the US clinical JointMan® database, an evidence-based rheumatology software application that

rheumatologists use to systematically document patient-level data in routine clinical practice. Adult RA patients were included if they had a physician prescription record of a TNFi from April 1, 2010 through March 31, 2015 *and* a subsequent DMARD that was a different TNFi (TNFi cycling cohort) or new MOA DMARD (new MOA DMARD switching cohort). Patients were indexed on the date of the subsequent TNFi or new MOA DMARD from a prior TNFi during the pre-index period. Treatment persistence was assessed, defined as neither discontinuing nor switching the drug post-index before the end of the observational period. Change in Clinical Disease Activity Index (CDAI) at 1 year post-index and its correlation with treatment persistence were evaluated. Kaplan-Meier survival analysis measured time to nonpersistence. Cox proportional hazards regression and ordinary least-squares regression were used to identify independent factors predicting time to nonpersistence and 1-year CDAI change, respectively.

**Results:** Included were 613 patients (mean age 56.5 years; 78.5% women; 82.9% white; baseline CDAI 22.7). After discontinuing a prior TNFi, 54.2% (n=332) of patients cycled to another TNFi and 45.8% (n=281) switched to a new MOA DMARD. During follow-up, 36.7% (n=225) of patients were persistent with their index drug, 34.1% (n=209) switched from their index drug to another drug, and 29.2% (n=179) discontinued their index drug. Compared with TNFi cyclers, new MOA DMARD switchers were more likely to be persistent at 1 year (45.2% vs 29.5%; $P<0.0001$) and to persist for a longer period of time (Figure 1). After adjusting for covariates, TNFi cyclers were more likely to be nonpersistent than new MOA DMARD switchers (adjusted hazard ratio 1.511; $P<0.001$). Reduction in CDAI at 1 year was lower in TNFi cyclers than in new MOA DMARD switchers (–4.73 vs –7.64; $P=0.027$); however, this effect was not statistically significant when baseline CDAI was controlled for in the regression model (–5.83 vs –6.39; $P=0.607$). Overall, treatment persistence was associated with a significantly higher reduction in CDAI (–8.69 vs –3.16; $P<0.001$).

Figure 1. Kaplan-Meier Curve of Time to Nonpersistence




**Conclusions:** This real-world study suggests that after discontinuing their prior TNFi, RA patients who switched to a new MOA DMARD demonstrated better treatment persistence than those cycling to another TNFi. Persistence with RA treatment was associated with better clinical outcome.

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## FRI0234 PREDICTIVE FACTORS OF DISCONTINUATION OF THERAPY WITH ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Biomarkers who facilitate clinicians in decision making regarding the drugs that could be more effective for their patients with rheumatoid arthritis (RA) are needed.

**Objectives:** To look for predictors of abatacept (ABA) therapy discontinuation in patients with RA.

**Methods:** Seventy-one consecutive patients with RA who received treatment with intravenous ABA from 2008 to 2014 were enrolled. Demographical, clinical and laboratory parameters were evaluated, including peripheral blood T- and B-cell populations, rheumatoid factor and anti-cyclic citrullinated peptide (autoantibodies ACPA) isotypes, and serum free light chains. To evaluate the predictors of therapy discontinuation by logistic multivariable analysis, both variables associated with $p<0.05$ in univariable analysis, and variables previously reported by literature as potential confounders were considered. Receiver-operating characteristic (ROC) analysis was used to verify the applicability of predictive biomarkers. The Kaplan-Meier method and the log-rank test were applied to compare the probability of discontinuing therapy in the different groups.

**Results:** Comparing patients who discontinued ABA (n:28) with those still in therapy (n:41) we observed: a higher proportion of smokers (51.9% vs 25.6%; p=0.03); a lower proportion of terminally-differentiated effector-memory cells (TDEM) among total CD8+ T-lymphocytes at baseline (22.0% (7.8–39.2) vs 38.7% (20.7–55.9); p=0.002). The proportion of patients with positivity for ACPA was lower among patients who discontinued ABA, but not significantly (76% vs 89.5%; p=0.13). Logistic multivariate analysis showed that only the proportion of CD8+TDEM T-cells was an independent predictive factor of therapy discontinuation (OR (95% IC)=6.2 (1.2 to 30.8); p=0.026). ROC analysis showed a significant performance of this biomarker for prediction of therapy discontinuation (using a cut-off of 30.6%: AUC: 0.760+0.07; p=0.002). Patients with a low proportion of CD8+TDEM at baseline had a higher probability of discontinuing the treatment during time (log-rank test: $p<0.01$).

**Conclusions:** A high number of circulating TDEM T-cells might be a marker of a stronger activation of costimulatory signals in the history of RA patients. It might be speculated that these patients may be particularly responsive to costimulation blockade by ABA. T-cell characterization for identification of TDEM CD8+ T-cells might be a useful test to predict discontinuation of ABA therapy.

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**Disclosure of Interest:** None declared

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## FRI0235 INCIDENCE OF PARADOXICAL REACTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS DURING TOCILIZUMAB THERAPY: DATA FROM THE FRENCH REGISTRY REGATE

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**Background:** Tocilizumab is a humanized monoclonal antibody specific to the alpha subunit of the receptor of interleukin-6 (IL-6) indicated in the management of some rheumatic diseases. The monitoring of patients under biotherapy has led to the discovery of particular side effects called paradoxical effects, that is to say, conditions that are supposed to be treated with the biotherapy itself [1–2]. To our knowledge, there is no clinical trial or "real life" data assessing the occurrence of paradoxical effects under tocilizumab therapy from a large cohort.

**Objectives:** To assess the frequency of paradoxical effects encountered in everyday practice under tocilizumab therapy, using the REGATE (Registry-RoActemra) registry [3]. The secondary objectives are to determine the type of paradoxical effect and the consequences of these effects.

**Methods:** The REGATE registry is an independent prospective registry, promoted by the French Society of Rheumatology, consisting of patients with rheumatoid arthritis treated by tocilizumab. For every paradoxical reaction, the data was validated by the clinician in charge of the patient. The paradoxical effect was noted if the induced pathology appeared after exposure to at least one tocilizumab infusion, and if tocilizumab was likely to treat the condition in question [4]. If patients had one of these conditions de novo while under tocilizumab therapy for another condition, we considered it as a paradoxical effect. The aggravation of a preexisting condition was also considered as a paradoxical effect [1].

**Results:** Among the 1499 patients included with at least one follow-up visit (3429 patient-years), a paradoxical reaction occurred in 14 patients (0.93% of patients; 4.08/1000 patient-years). These were 10 de novo pathologies (3 vasculitis, 3 uveitis, 2 psoriasis, 1 lupus, 1 ulcerative colitis) and 4 exacerbations

of pre-existing conditions (2 psoriasis, 1 vasculitis, 1 lupus). The average time between the initiation of tocilizumab and the appearance of the first manifestation of the paradoxical effect was 14.85 (±12.79) months. Permanent discontinuation of tocilizumab was chosen for 5 patients (35%), a transitional stop for 3 patients, a dosage adjustment for 1 patient. One paradoxical effect (psoriasis) recurred with continued tocilizumab.

**Conclusions:** Paradoxical reactions under tocilizumab are not frequent (less than 1%) but require an adaptation of treatment in over 50% of cases.

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**Disclosure of Interest:** None declared

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## FRI0236 SAFETY, PHARMACOKINETICS AND EFFICACY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN A FIRST-IN-PATIENT PHASE 1/2 STUDY IN RHEUMATOID ARTHRITIS

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**Background:** Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. Accumulating evidence is telling that FKN-CX3CR1 axis plays a pivotal role in leukocyte/lymphocyte accumulation in inflamed tissues in RA[1]. We developed E6011, a novel humanized anti-FKN monoclonal antibody.

**Objectives:** To evaluate safety, pharmacokinetics and efficacy of E6011 in a Phase 1/2, open-label, multiple ascending dose study in RA patients for the first time (NCT02196558).

**Methods:** Active RA patients with inadequate response to MTX or TNF inhibitors were received 7 consecutive doses (subcutaneous: SC) of E6011 at week 0, 1, 2 and thereafter every 2 weeks up to week 10. A hundred and 200 mg of E6011 were chosen for the study as putatively appropriate doses for patients by the PK/PD modeling previously obtained in the Ph1 healthy volunteer study of E6011.

**Results:** Twelve subjects were enrolled in the cohort of 100 mg and subsequently 15 subjects were enrolled in the 200 mg cohort, in total, 27 subjects received repeated subcutaneous administrations of E6011. As a result, repeated dose of E6011 was found safe and well tolerated. The incidence of AE, treatment-related AE and SAE was 59.3%, 29.6% and 7.4%, respectively. There were no severe AE or deaths, and no significant differences were observed in the incidence or severity of AE between the 100 mg and 200 mg cohorts. After starting multiple SC injection of E6011, serum E6011 concentration reached steady-state at week 2, and its level was maintained up to week 12. Mean trough E6011 concentrations from week 2 through week 12 were 11.6 – 15.7 ug/mL and 29.2 – 38.8 ug/mL after dosing of 100 and 200 mg, respectively. Clinical outcome was also available in the study in which response rates of ACR20, 50 and 70 at week 12 were 75.0%, 33.3%, 8.3% and 80.0%, 26.7%, 20.0% in the cohort of 100 and 200 mg, respectively. At week 12, 33.3% of subjects achieved DAS28-CRP remission in both cohorts, 16.7% and 20.0% for SDAI remission and 8.3% and 26.7% for Boolean remission were observed in the 100 and 200 mg cohorts, respectively.

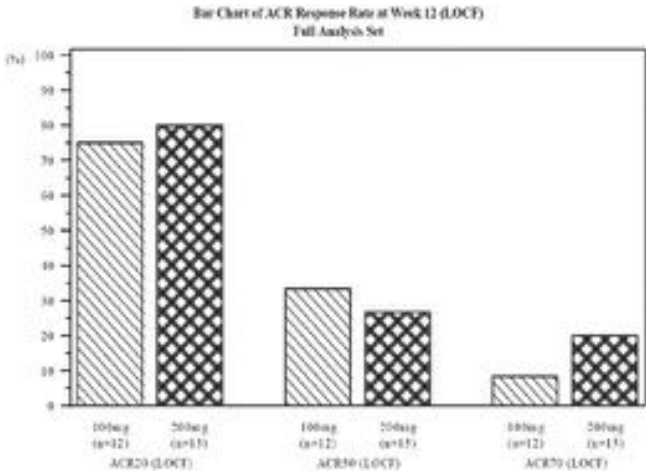



Figure 1

**Conclusions:** E6011 was safe and well tolerated, and demonstrated a promising efficacy in active RA patients with MTX or TNFi-IR. While further clinical studies are required, the results obtained indicate that a novel biological DMARD targeting FKN/CX3CR1 interaction will be clinically beneficial for active RA patients.

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**Disclosure of Interest:** Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-Kirin, AbbVie, Bristol-Myers, Speakers bureau: AbbVie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, Santen, T. Takeuchi Grant/research support from: Astellas, Bristol-Myers, Chugai, Daiichi-Sankyo, Eisai, AYUMI, Takeda, Teijin, AbbVie, Asahikasei, Taisho-Toyama, Consultant for: Astra Zeneca, Eli Lilly, Novartis, Mitsubishi-Tanabe, AsahiKasei, AbbVie, Daiichi-Sankyo, Bristol-Myers, Nipponkayaku, Janssen, Merck Serono, Takeda, Astellas, Speakers bureau: AbbVie, Bristol-Myers, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Pfizer, Takeda, Astellas, Daiichi-Sankyo, Celtrion, Nipponkayaku, H. Umehara: None declared, T. Nanki Grant/research support from: Chugai, Eisai, Takeda, Teijin, Eli Lilly, Bristol-Myers, AbbVie, Mitsubishi-Tanabe, Ono, Daiichi-Sankyo, Shionogi, Asahikasei, Nippon Boehringer Ingelheim, Ajinomoto, Consultant for: UCB, Eisai, Chugai, Speakers bureau: Mitsubishi-Tanabe, Chugai, Eisai, Takeda, Astellas, Janssen, Eli Lilly, Ono, AbbVie, Bristol-Myers, Daiichi-Sankyo, Santen, H. Akama Shareholder of: EISAI, Employee of: EISAI, N. Yasuda Shareholder of: EISAI, Employee of: EISAI, F. Tago Employee of: EISAI, M. Kawakubo Shareholder of: EISAI, Employee of: EISAI, S. Hojo Employee of: EISAI, T. Kawano Employee of: KAN Research Institute, T. Imai Employee of: KAN Research Institute

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## FRI0237 TOCILIZUMAB IMPACT ON KINETICS OF TREATMENT TARGET PARAMETERS IN SYSEMIC NEPHROTIC TYPE AA-AMYLOIDOSIS, SECONDARY TO RA

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**Background:** Systemic AA-amyloidosis is a severe complication of RA occurring due to upregulated production of serum amyloid A (SAA), induced predominantly by IL-6.

**Objectives:** To assess Tocilizumab (humanized monoclonal antibody to IL-6 receptors) impact on kinetics of treatment target parameters in sysemic nephrotic type AA-amyloidosis, secondary to RA.

**Methods:** DAS28, SAA levels, CRP, ESR, 24-hour proteinuria, glomerular filtration (GFR), and gistomorphologic examination of biopsy samples were monitored in all participants to the study in addition to the standard clinical and lab parameters. Statistical processing covered the number of participating subjects, arithmetic mean (AM), standard deviation from AM (δ). Difefferces were considered statistically significant with $p$ values $<0,05$. Student's $t$-test was used. Data was processed with Statistica 7.0 for Windows ("StatSoft Inc.") software.

**Results:** The study included 10 pts (mean age 52±9,1 y.) with systemic AA amiloidosis and morphologically verified nephrotic syndrome (biosy samples of duodenal mucous), secondary to RA, meeting ACR 1987 criteria (average disease duration - 17,1±8,9 y). All poor responders to DMARDs, NSAIDs and GCs at a stable dose for at minimum 6 preceding mo (peroral $<10$ mg/day prednisolone or its equivalent) were administered Tocilizumab i/v by drop infusions each 4 weeks at 8 mg/kg during total 12 mo.

After 12 mo of therapy significant decrease was documented for mean SAA (from 46,7±28,1 mg/mL to 14,7±24,3 mg/mL; $p$=0,03), DAS28 score (from 5,5±1,4 to 3,3±1,15; $p$=0,003), 24-hour proteinuria (from 0,8±0,7 g/day to 0,08±0,6 g/day; $p$=0,04). At the same time no desiarable changes occurred in ESR (from 32,1±19,5 mm/hour to 17±26,5 mm/hour; $p$=0,1), GFR (from 62,2±42,9 mL/min to 54,2±31,9 mL/min; $p$=0,3). Although, second control biopsy& histomorphology did not reveal amiloid depositions in duodenal mucous in 2 pts.

**Conclusions:** 12-mo Tocilizumab therapy resulted in target decrease of RA activity, accompanied by simultaneous decrease in SAA and 24-hour proteinuria (although not all pts achieved the desired target levels), and complete disappearance of amiloid depositions in duodenal mucous in 2 pts.

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**Disclosure of Interest:** None declared

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## Scleroderma, myositis and related syndromes

### FRI0238 INCREASED SERUM FREE LIGHT CHAINS OF IMMUNOGLOBULINS IN SYSTEMIC SCLEROSIS PATIENTS: CORRELATION WITH LUNG INVOLVEMENT AND INFLAMMATORY MILIEU

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**Background:** Humoral immunity and B cells are thought to play an important role in the pathophysiology of the systemic sclerosis (SSc). The production of free light chains (FLC) of immunoglobulins is abnormally high in different pathological autoimmune conditions and reflects B cell activation. Furthermore FLCs demonstrated different biological activities including their capability to modulate the immune system, proteolytic activity, complement cascade activation, as well as FLC binding to antigens and chemotactic factors.
**Objectives:** To determine the FLC levels in patients with SSc and in healthy controls and to study their possible association with organ involvement and disease characteristics.
**Methods:** Sixty-five SSc patients (90.0% females; mean age 50.8±17.0 years; 27 (41.5%) with diffuse skin involvement-dcSSc) and 20 age and sex matched healthy controls (HC) were studied. Clinical and immunological inflammatory characteristics were assessed for all the SSc patients. FLC levels were quantified by nephelometry (Freelite TM Human Kappa and Lambda Free Kits, The Binding Site, UK). IL6 and BAFF levels were measured in SSc patients by ELISA.
**Results:** The mean serum FLC-κ level (SSc: 20.4±7.5 ng/ml *vs* HC 9.4±4.3 ng/ml, $p<0.001$) and FLC ratio (SSc: 1.6±0.6 *vs* HC 0.8±0.2, $p<0.001$) were significantly higher in patients with SSc compared to healthy controls, while the serum FLC-$_{\lambda}$ levels were comparable (SSc: 13.6±4.8 ng/ml *vs* HC 11.9±6.2 ng/ml, p=ns).
The levels of FLC were comparable in patients with diffuse skin disease and limited skin involvement, while FLC-κ levels were increased in patients with restrctive lung (FVC<79%) disease (SSc: 26.4±7.4 ng/ml) when compared to patients with FVC>79% (HC 19.6±7.3 ng/ml, p=0.009).
In SSc patients the levels of serum FLC-κ level directly correlate with the IL-6 levels (R=0.6, $p<0.001$), while no correlation was found with skin involvement and autoantibodies distribution.
**Conclusions:** Free light chains of immunoglobulins (sFLC) levels are elevated in systemic sclerosis. High levels of sFLC are associated with the fibrotic lung involvement and with an higher degree of inflammation, supporting the role of B cell activation in the pathophysiology of SSc.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5735

### FRI0239 COMPLEMENTARY VALUE OF ELF TEST AND NT-PROBNP IN REFLECTING FIBROSIS AND VASCULOPATHY IN SYSTEMIC SCLEROSIS

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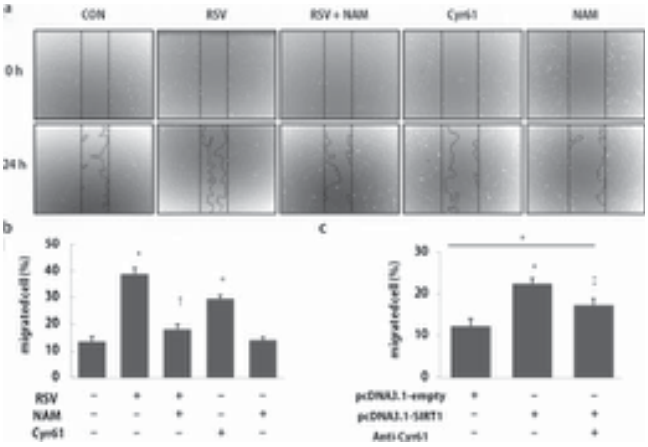
**Background:** The ELF test and its components (PIIINP, TIMP-1 and HA) have been shown to correlate with skin, lung and overall fibrosis and not with any vascular manifestation of Systemic Sclerosis (SSc)[1]. On the contrary, NT-proBNP has been suggested to be useful for stratification of SSc patients, especially to identify those at risk of pulmonary hypertension[2].
**Objectives:** Aims of this study were: a) to validate ELF score and its single analytes on an independent cohort of scleroderma patients; b) to evaluate whether NT-proBNP could provide additional value to the development of an SSc-specific algorithm.
**Methods:** 250 sera from SSc patients from a single UK centre were analysed employing a high-throughput in vitro diagnostic of a routine NHS pathology lab to measure ELF score, its analytes and NT-proBNP levels. All patients fulfilled 2013 ACR/EULAR classification criteria for SSc. Clinical, laboratory and instrumental data were collected at time of sampling. Statistical analysis was performed using SPSS. $P<0.05$ was considered statistically significant.
**Results:** Multivariate analysis of ELF score (including the variables found statistically significant in univariate analysis) identified age, mRSS and DLCO% as independently associated with ELF score ($p<0.0001$ for all), confirming results previously published on an independent Italian cohort. As previously shown, ELF score and single analytes were not associated with heart and vascular manifestations of the disease. On the contrary NT-proBNP significantly correlated with heart severity ($p<0.0001$) and peripheral vasculopathy (p=0.005). Its levels were higher in patients with current digital ulcers (p=0.001), digital pitting scars (p=0.01), telangiectasias (p=0.01), systemic arterial hypertension (p=0.004), pulmonary artery hypertension (PAH) (p=0.01), diastolic dysfuction (p=0.002), reduced ejection fraction (p=0.0002), arrhythmias ($p<0.0001$) and dyspnoea (p=0.003) compared to those without the manifestation. Multivariate analysis identified presence of arrhythmias ($p<0.0001$), age ($p<0.0001$), PAH ($p<0.001$) and DLCO% (p=0.006) as independently associated with NT-proBNP. All the biomarkers significantly correlated with total Medsger's severity scale and EScSGactivity index ($p<0.0001$).
**Conclusions:** Our findings validate the value of ELF score in a second independent cohort of 250 SSc sera and suggest that NT-proBNP has a complementary value correlating with other aspects of the disease such as PAH and heart severity. Longitudinal multicentres studies are warranted to determine the sensitivity to change and the predictive value of these biomarkers in SSc patients and to build up a new combined scleroderma specific algorithm including markers of fibrosis and vasculopathy.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2250

## Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

### FRI0240 SIRT-1 REGULATES TGF-β INDUCED DERMAL FIBROBLAST MIGRATION VIA MODULATION OF CYR61 EXPRESSION

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**Background:** SIRT1 is a NAD-dependent protein deacetylase that participate in cellular regulation. The increased migration of fibroblast is important phenotype in fibroblast activation. The role of SIRT1 in cell migration remains controversial whether SIRT1 act as a activator or suppressor for cell migration.
**Objectives:** The aim of this study was to establish the role of SIRT1 in human dermal fibroblast migration and explore a target of SIRT1 for dermal fibroblast migration.
**Methods:** Levels of SIRT1 expression were analysed in human dermal fibroblast by RT-PCR and western blotting before and after stimulation with tumour gowth factor-β (TGF-β) and resveratol. Human dermal fibroblasts were transfected with active SIRT1 expression vectors or with siRNA targeting SIRT1 or were treated with nicotinamide. Cyr61 expression analysis was performed by western blotting to study the role of SIRT1 on cell migration. The wound healing assay was performed due to analyze migration of human dermal fibroblasts.
**Results:** SIRT1 and Cyr61 was expressed in human dermal fibroblasts and the stimulation of TGF-β further induced expression levels of SIRT1 and Cyr61 (figure a). Treatment of resveratol, SIRT1 agonist or overexpression of SIRT1 also promoted expression of SIRT1 and Cyr61 in human dermal fibroblasts, whereas inhibition of SIRT1 activity by nicotinamide or knock down of SIRT1 down-regulated Cyr61 basal level as well as TGF-β or resveratol-induced Cyr61expression. Blocking of ERK signaling by PD98509 reduced TGF-β or resveratol-induced Cyr61 expression. Resveratol increased migration and nicotinamide attenuated resveratol-induced migration of human dermal fibroblasts. Furthermore, SIRT1 overexpression promoted cell migration whereas blocking Cyr61 attenuated SIRT1-stimulated migration of human dermal fibroblasts (figure b and c).




**Conclusions:** We suggested a role of SIRT1 in human dermal fibroblast migration.

SIRT1 increased cell migration by stimulated Cyr61 expression for their target through the ERK signaling. SIRT1-induced Cyr61 production is very important for human dermal fibroblasts migration.

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**Disclosure of Interest:** None declared
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## FRI0241 HMGB1 INDUCES REACTIVE OXYGEN SPECIES (ROS)-DEPENDENT ACTIVATION OF THE ER STRESS PATHWAY IN C2C12 MYOTUBES

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**Background:** The term myositis describes a heterogeneous spectrum of autoimmune diseases, which cause symmetrical proximal muscle weakness and atrophy, and resulting dysfunction. Infiltration of immune cells into muscle has long been regarded as the primary pathological event in myositis. However, the magnitude of inflammatory cell loads often correlates poorly with the levels of detected muscle weakness, so myositis patients often remain weak in the absence of inflammation; while in a murine myositis model muscle weakness may actually precede inflammatory cell infiltrations. Thus, non-immune cell mediated mechanisms, such as those related to ER stress pathway activation, likely play an important role in weakness and atrophy induction, [1]. High-mobility group box protein 1 (HMGB1) is a chromatin protein which is localised outside of the nucleus in myositis, and induces muscle dysfunction and fatigue, via TLR4 signalling, [2, 3]. Given the likely importance of ER stress pathology activation in myositis, and knowledge that HMGB1 can alter ER stress mechanisms and thus induce reactive oxygen species generation (ROS) in non-muscle systems; we wondered whether HMGB1 could induce ROS generation in muscle, and so contribute to ER stress pathway activation, [4].
**Objectives:** To determine whether antioxidant compounds can ameliorate *in vitro* HMGB1-induced activation of the ER stress pathway in skeletal muscle.
**Methods:** C2C12 myotubes were treated with rHMGB1 (10ng/ml) without and with (10nM) of the broad-spectrum antioxidant N-acetyl-L-cysteine (NAC) or (5uM) of the mitochondrial-targeted antioxidant SS-31, for a period of 24 hours. Cells were then harvested, RNA-isolated using TRIzol extraction, and cDNA synthesised. Changes in gene expression associated with ER stress pathway activation, mitochondrial function/dynamics and antioxidant defence mechanisms were examined using qPCR.
**Results:** HMGB1 exposure significantly unregulated the gene expression of the ER stress pathway components ATF4, ATF6 and IRE1. Treatment of cells with HMGB1 in the presence of NAC significantly inhibited this expected upregulation of expression of ATF4, ATF6 and IRE1 genes. Treatment with SS-31, a specific scavenger of mitochondria-derived ROS, similarly inhibited upregulation of expression of these genes, but where inhibition was clearly greater than that due to NAC exposure.
**Conclusions:** In myositis, ER stress has been widely implicated in the pathogenesis of non-immune cell mediated weakness and atrophy induction. Our *in vitro* findings here suggest that HMGB1 plays a role in ER stress pathway activation, and that both broad spectrum and targeted antioxidant interventions can ameliorate this effect. Thus, the development of therapies to selectively inhibit HMGB1 upregulation of ROS, and/or to selectively block pathogenic ROS effects, may represent worthwhile therapeutic avenues to explore to address issues of myositis-induced weakness and atrophy.

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## FRI0242 ROLE OF MITOCHONDRIA- AND NADPH OXIDASE-DERIVED ROS IN FIBROBLASTS ISOLATED FROM PATIENTS AFFECTED BY SYSTEMIC SCLEROSIS

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**Background:** Oxidative stress plays an important role in the development of fibrosis under various pathological conditions. Fibroblasts isolated from patients with Systemic Sclerosis (SSc) overproduce reactive oxygen species (ROS), overexpress type I collagen and α-smooth muscle actin (α-SMA) and show DNA damage and activation of checkpoint kinase ATM (1, 2). NADPH oxidase (NOX) is an important source of ROS, and its overactivity or overexpression are often associated with chronic diseases, characterized by tissue damage and fibrosis. Recently, we have demonstrated that NOX2 and NOX4 are critical components of NADPH oxidase complex in SSc fibroblasts and ROS generated by NOX play a primary role in the pathological activation of dermal fibroblasts (3). Since a recent study reported that NOX4 localizes to membranes and mitochondria and contributes to the generation of mitochondrial ROS (4), we wondered whether mitochondria also play a role in ROS production in SSc fibroblasts.
**Objectives:** The aim of this study was to investigate the contribution of mitochondrial ROS to oxidative stress in SSc.
**Methods:** ROS production was analysed by confocal microscopy using dihydroethidium (DHE, to assess all intracellular superoxide), or MitoSOX™ Red (to detect mitochondria superoxide), or using a microplate reader following Amplex® Red kit protocol (to measure $H_2O_2$). Mitochondria were purified using a mitochondria isolation kit. For protein expression, mitochondrial and cytosolic fractions were subjected to western blot with specific antibodies.
**Results:** SSc fibroblasts incubated with the mitochondria-targeted antioxidant MitoQ showed a reduced MitoSOX™ Red staining, and a partially decreased DHE fluorescence, suggesting that mitochondria contribute to the redox state in SSc fibroblasts. Mitochondria purified from SSc fibroblasts generated significantly higher levels of ROS compared to controls. Incubation of normal cells with PDGF, a profibrotic cytokine able to activate a SSc-like phenotype, led to a significant increase of total and mitochondrial ROS levels compared to unstimulated cells. Mitochondrial and cytosolic fractions from SSc and activated normal fibroblasts were also analyzed to evaluate different protein expression patterns.
**Conclusions:** In this study we demonstrated that mitochondria contribute to the abnormal redox state of SSc fibroblasts and activated normal cells. Further studies may clarify whether mitochondrial ROS are generated by a mitochondrial NOX isoform or are the result of the interplay between mitochondria and NOX enzymes located outside the organelles.

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## FRI0243 IS THE BMP ANTAGONIST GREMLIN-1 A TARGET IN SYSTEMIC SCLEROSIS?

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**Background:** Gremlin-1 is BMP antagonist that mediates its effects through negative regulation of BMP signalling. BMP signalling is important in development and has been found to be deregulated in various rheumatic diseases. It also has BMP-independant effects that are poorley described. Systemic sclerosis is an autoimmune disease that results in fibrosis of the skin and internal organs. We have previously found elevated levels of gremlin-1 in systemic sclerosis skin biopsies compared to controls. Gremlin-1 genetically reduced mice are protected from kidney fibrosis. It is suggested that fibrosis may be associated with reactivation of development programs.
**Objectives:** The aim of this work was to measure the levels of gremlin-1 and to determine its effects on dermal fibroblasts.
**Methods:** Skin biopsies were taken from systemic sclerosis patients and analysed by PCR for gremlin-1 and 18S as the housekeeing gene. Bleomycin was injected into mice and skin fibrosis developed, control mice received saline. Biopsies were taken and fixed and processed. Laser capture was used to dissect the tissue using a guided laser. Dissected tissue was processed for RNA and qPCR was performed for gremlin-1 and collagen-1. C-Myc tagged human Gremlin-1 was cloned into a vector and empty vector was transfected into human fibroblasts and HEKs. After transfection collagen and alpha-Smooth muscle actin was measured.
**Results:** Elevated levels of gremlin-1 was found in systemic sclerosis skin biopsies. We also found elevated levels of gremlin-1 in skin sections from an animal model of fibrosis, the bleomycin model. Laser capture microdissection found that this was in the dermal proportion of skin and not in the epithelial section. Overexpression of gremlin-1 in a vector system in dermal fibroblasts showed elevated levels of collagen, but not alpha-smooth muscle actin.
**Conclusions:** Gremlin-1 is dsyregulated in systemic sclerosis and in the bleomycin model of fibrosis. Overexpressing gremlin-1 induced higher levels of collagen. Targeting gremlin-1 may represent a novel target in systemic sclerosis.

**Disclosure of Interest:** None declared
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## FRI0244 LYSYL OXIDASE AS A BIOMARKER IN SYSTEMIC SCLEROSIS– A MULTICENTER STUDY

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**Background:** Fibrosis and vasculopathy are the major concerns in systemic sclerosis (SSc), the pathogenesis of which is not clear. Lysyl oxidase (LOX) is an extracellular copper enzyme that cross-links collagen and elastin, thus stabilizing collagen fibrils [1]. In a preliminary study, LOX was found to be overexpressed in SSc patients and was suggested to be related to diffuse disease [2]. We evaluated skin and lung biopsies from 11 SSc patients and were able to show LOX located in the epidermis in the skin and in the endothelium of blood vessels within the dermis and in lung tissue. It is not clear whether the source of elevated LOX levels in SSc is damaged vascular endothelium or fibrotic tissues.
**Objectives:** To evaluate LOX serum level of patients with SSc compared to patients with very early diagnosis of SSc (VEDOSS), patients with primary Raynaud's phenomena (PRP) and healthy controls in order to validate the elevated levels in SSc and to delineate its source.
**Methods:** We prospectively evaluated patients for demographics, clinical manifestations and laboratory results including blood count, chemistry, urine examination, autoantibodies and serum LOX concentration determined by ELISA. We further evaluated lung function tests, echocardiography, lung high resolution CT scans, as needed, and determined lung involvement, modified Rodnan skin score (mRSS), Medsger disease severity scale and Valentini activity index [3].
**Results:** 86 SSC patients (76 women and 10 men) at a mean age of 49±12.4 were evaluated and compared with 110 patients with VEDOSS, 86 patients with PRP, and 80 age and gender matched healthy controls. Of the SSc patients, 42 had diffuse disease- 23 of them with lung fibrosis, and 44 had limited disease. LOX concentration in SSc was higher than VEDOSS, PRP and healthy controls, 12.8±7.5 ng/ml vs. 9.7±7.4 ng/ml vs. 8.1±5.4 vs. 8.9±5.1 ng/ml, respectively ($p<0.0001$). LOX level correlated with Medsger disease severity scale, correlation coefficients 0.24 ($p=0.025$) and inversely correlated with DLCO in patients with diffuse disease, correlation coefficients -0.35 ($p=0.03$). Age, duration of disease, mRSS, activity score, capillaroscopy pattern and pulmonary hypertension, did not correlate with LOX concentration.
**Conclusions:** LOX level was found to be high in the serum of patients with SSc correlating with disease severity and inversely correlated with lung diffusion, suggesting a vascular source of LOX excretion in SSc. LOX was not elevated in patients with VEDOSS or PRP. Our study confirms our former observation of elevated LOX level in SSc and suggests LOX to be a possible biomarker of disease severity and vasculopathy in SSC.
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## FRI0245 SCCA-IGM IS UP-REGULATED IN SCLERODERMA PATIENTS WITH REDUCED DLCO: A NEW BIOMARKER OF PULMONARY INVOLVEMENT?

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**Background:** Systemic sclerosis (SSc) is a connective tissue disease characterized by diffuse fibrosis of skin and internal organs. The pulmonary involvement represents the first cause of death in these patients (1). The reduction of DLCO is the first functional alteration observed in interstitial lung disease (ILD). The detection of sera biomarkers predictive of ILD is still discussed in SSc.
Squamous Cell Carcinoma Antigen (SCCA) is a serin protease inhibitor typically expressed by dysplastic and neoplastic cells of epithelial origin, and in pulmonary tissue of patients with idiopathic ILD (2). SCCA is detectable in serum as free protein and as circulating immune complex coupled to IgM.
**Objectives:** The aim of this study was to evaluate the serum levels of free SCCA and SCCA-IgM in a group of scleroderma patients and to investigate the correlation with different SSc subsets.
**Methods:** Forty patients, 31 women and 9 men affected by SSc (according to ACR/EULAR 2013 criteria), with mean age of 55±2 years and mean disease duration of 14±8 years were recruited. Seventeen patients had the diffuse cutaneous form of SSc and 23 the limited one. ANA were positive in all subjects with specificity for ACA in 16 cases, anti-Scl70 in 14, anti-RNA polymerasis III in 3, without specific pattern in 7. We considered the avascular score (detected at nailfold capillaroscopy), the Rodnan skin score, the pulmonary function tests, the coronary flow reserve (CFR), EUSTAR score and the systolic pressure in pulmonary artery (PAPs) as clinical parameters.
SCCA-IgM (AU/ml) and free SCCA (ng/ml) serum levels were measured in all patients using a validated ELISA assay. SCCA-IgM positivity was considered for values >200 AU/ml, according to our laboratory.
**Results:** SCCA-IgM serum levels were found increased in 14 SSc patients (35%). We didn't find significant differences in patients with diffuse and limited cutaneous form of disease, and not even statistically significant correlations with skin score, avascular score, CFR and PAPS.
SCCA-IgM and free SCCA levels were found significantly increased in patients with reduced DLCO (<75%) at pulmonary functions test in comparison to those without ($p<0.05$). At multivariate analysis SCCA-IgM positivity (OR: 6.25; CI: 1.26–31.02) and EUSTAR score >3 (OR: 7.75; CI: 1.28–46.3) were independently associated with diagnosis of ILD.
**Conclusions:** Serum levels of SCCA-IgM and free SCCA were increased in a group of patients with SSc. Patients with reduced DLCO, the first functional alteration observed in ILD, showed a significant increase of SCCA-IgM. Futhermore this biomarker is independently associated with the diagnosis of ILD, suggesting a possible role of this molecule in the first phases of the pathogenesis of pulmonary involvement in systemic sclerosis.
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## FRI0246 DYSREGULATION OF CCN PROTEINS IN SYSTEMIC SCLEROSIS PATIENTS WITH PIGMENTARY DISORDERS

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**Background:** Pathogenesis of Systemic Sclerosis (SSc) is complex and includes impaired communication between endothelial cells, epithelial cells and fibroblasts, leading to connective tissue fibrosis such as dermal fibrosis. About half of the patients present pigmentation patches. It is already known that CCN2 (CTGF) is increased in SSc and that polymorphism of its promoter is associated with the disease. More recently, it was shown that CCN2 is increased in the epidermis of SSc patients. CCN2 is part of a family of 6 members, including CCN3 (NOV), which often antagonizes CCN2. We have previously observed that CCN3 is modulated in non-segmental vitiligo, a hypopigmentary skin disorder, and that fibroblasts can regulate skin pigmentation. In SSc, CCN2 upregulation is sustained by an autocrine activating loop of endothelin 1 (ET-1). ET-1 is a well known pigmentary factor and its secretion by endothelial cells has recently been demonstrated as inducer of skin pigmentation.
**Objectives:** We hypothesize that in patients with pigmentary disorders, secretion of CCN by dermal cells is dysregulated (isoforms, levels). Thus, we plan to study the expression profile of CCNs, among other factors implicated both in fibrosis and pigmentation (ET-1, PPARγ, HIF1α) in SSc patients presenting or not skin pigmentary disorders.
**Methods:** Skin biopsies were obtained from 10 SSc patients, both in abnormally pigmented zones (hypo and/or hyperpigmented) and in non-lesional skin areas. Two patients with morphea were also included. Normal skin from healthy donors was used as control. Biopsies were used to culture fibroblasts, endothelial cells and keratinocytes and to perform histological and immunohistochemical analysis. We performed proteomic analysis, and immunocytochemistry regarding CCN2 and CCN3 on skin cells.
**Results:** Clinical examination of patients with SSc revealed two patterns of pigmentary troubles. Some patients have hypo and/or hyperpigmentary patches in non sun-exposed areas, whereas other patients have only hyperpigmentation in exposed areas which looks like photoaging. In most patients, it seems that pigmentary troubles appeared during the early development of the disease. Our preliminary datas revealed that level of expression of CCN3 observed by

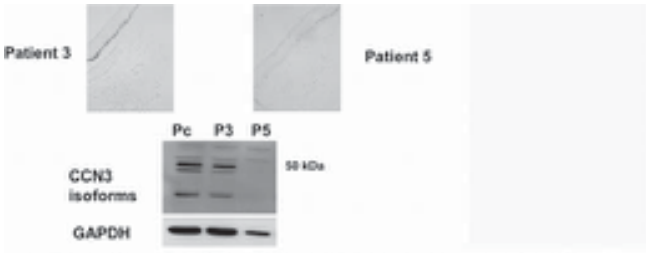



Figure 1: Top, Observation of degree of pigmentation (Fontana Masson staining) in lesional skin of two SSc patients : Patient 3 with hyperpigmented skin and Patient 5 without pigmentary disorder. Bottom, Study of CCN3 expression in lesional fibroblasts by Western Blot assay : marked decrease in CCN3 expression for Patient 5, as compared to fibroblasts from control donor (Pc).

immunohistochemistry or in fibroblasts protein extracts differed in lesional and non-lesional areas. Moreover, SSc patients presented various CCN3 isoforms according to pigmentary status. CCN2 examination also revealed variation of its expression as compared to healthy controls. Interestingly, these abnormalities could also be found in apparently non-lesional skin areas from SSc patients, which suggests that CCN2 and 3 expression is altered at early stages of the disease.

**Conclusions:** Differential level of expression and presence of various isoforms of CCNs have to be confirmed in fibroblasts and endothelial cells according to the pigmentary status of the fibrotic areas. This will allow us to verify our hypothesis of two different types of SSc, depending on time of apparition and localization of pigmentary patches. This could help to detect the disease early, which is essential for therapeutic issues. Moreover, if spatio-temporal variations of CCN are confirmed, it could open a specific therapeutic window for the use of CCNs modulators.

**Disclosure of Interest:** None declared

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## FRI0247 THE INVOLVEMENT OF THE LONG NONCODING H19X IN TGFβ SIGNALING AND ITS PROFIBROTIC EFFECTS IN SYSTEMIC SCLEROSIS AND OTHER FIBROTIC DISEASES

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**Background:** Long noncoding RNAs (lncRNAs) are an emerging class of noncoding transcripts involved in the regulation of gene expression in health and disease. We have recently identified a novel lncRNA, H19X, which is strictly regulated by TGFβ in a dose and time dependent manner.

**Objectives:** To detail the differential expression of H19X in SSc and other fibrotic diseases and to characterize its function in fibrotic diseases.

**Methods:** Skin and lung biopsies from patients with SSc, idiopathic lung fibrosis (IPF), and healthy controls (HC) were obtained from cohorts at four different expert centers. Expression of H19X was analyzed by RNA Sequencing Ilumina HiSeq2000 and real-time PCR respectively. H19X was silenced in skin fibroblasts using locked nucleic acid antisense oligonucleotides (LNA GapmeRs), followed by qPCR analyses, immunofluorescence staining, SIRCOL assay, contraction assay and Western blot. In situ hybridization of H19X on SSc dermal fibroblast was performed using Stellaris FISH probes.

**Results:** H19X expression was consistently upregulated across all four cohorts (SSc n=34, HC n=26). Notably, the upregulation was also consistent across different subsets of patients. H19X showed a similar expression profile in clinically non-involved skin compared to established fibrotic skin. Moreover, expression of H19X was also significantly increased in SSc interstitial lung disease patients versus HC (n=11 each, $p<0.05$). A significant H19X overexpression was also detected in IPF samples indicating a broader role of H19X in fibrotic diseases (n=11 each, $p<0.05$). The knockdown of H19X by GapmeRs in skin fibroblasts led to a strong downregulation of collagen 1, fibronectin and αSMA mRNAs (n=5, $p<0.05$). Furthermore, H19X knockdown followed by SIRCOL assay and Western blot analysis confirmed the importance of this lncRNA in the regulation of extracellular matrix components such as collagens and fibronectin. Additionally, silencing of H19X significantly impaired αSMA fiber formation, stress fiber formation and cell contractility showing an important role of H19X in the development of the myofibroblast phenotype. Because the H19X gene hosts the sequence for two microRNAs, miR-424 and miR-503, it could exert its function acting as reservoir for these microRNAs. However, the effects of miR-503 and miR-424 loss and gain of function experiments on fibrosis measures were minimal compared to the effects after H19X silencing indicating that H19X employs another main molecular mechanism. Indeed, in situ hybridization showed that TGFβ-induced expression of H19X is localized to a defined spot in the nucleus indicating that H19X could influence gene expression by directly interacting with the chromatin.

**Conclusions:** H19X is a novel lncRNA which is a key factor in mediating the pro-fibrotic effects of TGFβ in systemic sclerosis and other fibrotic diseases.

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# Scleroderma, myositis and related syndromes

## FRI0248 PREDICTORS OF DISABILITY IN SYSTEMIC SCLEROSIS: A STUDY FROM THE DESSCIPHER PROJECT

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**Background:** Systemic sclerosis (SSc) can greatly impact the patients' quality of life due to the multisystem manifestations. The health assessment questionnaire (HAQ) is one of the most commonly used measures of disability in musculoskeletal disorders and was extended to form the scleroderma HAQ (SHAQ), a more disease-specific disability scale that incorporates the HAQ and the 5 SHAQ-visual analogue scales (VAS) into one score.

**Objectives:** This study aims to identify predictors of disability in SSc by means of the SHAQ.

**Methods:** Patients from the DeSScipher cohort were included in the analysis if they had at least one complete SHAQ recorded, fulfilled either the 1980 ACR or the 2013 ACR/EULAR criteria for SSc and were above 18 years of age.

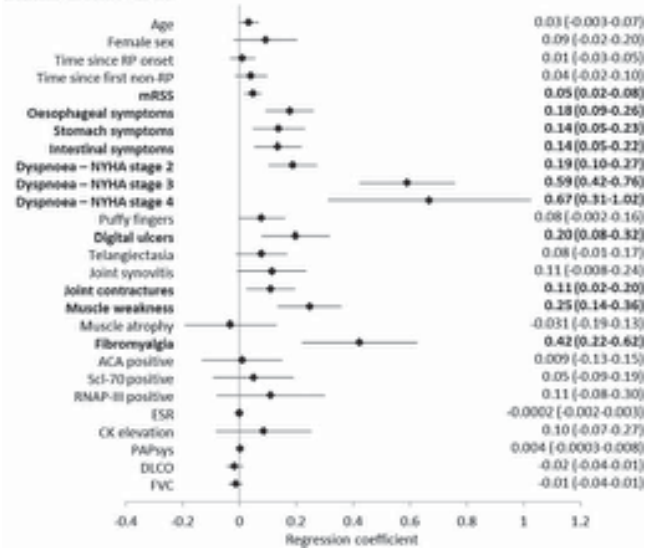
Multiple linear regression analysis was used to assess the combined effect of factors possibly associated with disability. Variables included in the model were defined *a priori.*

**Results:** 813 patients had one complete SHAQ recorded between June 2013 and January 2016 (34.1% of all patients followed in the DeSScipher cohort). Of these, 12% fulfilled only the 2013 ACR/EULAR criteria, 2% fulfilled only the 1980 ACR criteria and 86% fulfilled both, the median age was 58 years (IQR 49–67) and 15% were male. 26% of the patients were in the diffuse SSc subset, 56% in the limited and 18% had SSc sine sclerosis.

The patients had a median SHAQ score of 0.79 (IQR 0.28–1.31) and a median HAQ score of 0.88 (IQR 0.25–1.5). The medians of the five VASs included in the SHAQ were (in order of the VAS magnitude): overall disease severity (30, IQR 10–51), Raynaud's phenomenon (21, IQR 3–50), pulmonary symptoms (10, IQR 1–40), gastrointestinal symptoms (6, IQR 1–31) and digital ulcers (2, IQR 1–30). 60% of the patients were in the lowest SHAQ category (score of 0 to 1) which is regarded as "mild to moderate difficulty", 34% in the category regarded as "moderate to severe disability" (score of 1 to 2) and 6% in the category regarded as "severe to very severe disability" (score of 2 to 3).

In multiple linear regression, the main factors associated with high SHAQ scores were dyspnoea (NYHA-stage 4 (β=0.67), 3 (β=0.59) and 2 (β=0.18; all

**Figure:** Multivariable regression coefficients with 95% confidence intervals for the composite SHAQ score (range 0 to 3).
RP, Raynaud's phenomenon; mRSS, modified Rodnan skin score; NYHA, New York Heart Association; DPS, digital pitting scars; DU, digital ulcers; ACA, anti-centromere autoantibodies; Scl-70, anti-topoisomerase-I autoantibodies; RNAP-III, anti-RNA-polymerase-III autoantibodies; ESR, erythrocyte sedimentation rate; CK, creatinine kinase; PAPsys, systolic pulmonary artery pressure as estimated by echocardiography; DLCO, single breath diffusing capacity for carbon monoxide; FVC, forced vital capacity.
Age, time since RP onset and first non-RP, increase per 10 year; mRSS, increase per 5 points; dyspnoea, vs NYHA stage 1; ESR, increase per mm/hr; PAPsys, increase per mmHg; DLCO and FVC, increase per 10% of predicted; all others, yes/no.



*vs.* stage 1), fibromyalgia (β=0.42), muscle weakness (β=0.25), current digital ulcers (β=0.20) and gastrointestinal symptoms (oesophageal symptoms, β=0.18; stomach symptoms, β=0.14; intestinal symptoms, β=0.14; figure).
**Conclusions:** Patients perceive dyspnoea, pain, digital ulcers, muscle weakness and gastrointestinal symptoms as the main factors driving their level of disability.
**Acknowledgement:** The DeSScipher project was funded by the European Community's Framework Programme 7 (FP7-HEALTH-2012.2.4.4–2-Observational trials in rare diseases) under grant agreement N° 305495.
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**Disclosure of Interest:** None declared
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## FRI0249 RISK FACTORS FOR DEVELOPMENT OF PULMONARY ARTERIAL HYPERTENSION IN AUSTRALIAN SCLERODERMA PATIENTS

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**Background:** Pulmonary arterial hypertension (PAH) is the leading cause of mortality in patients with scleroderma (SSc).
**Objectives:** To determine the incidence, prevalence and risk factors for PAH development in a large Australian SSc cohort.
**Methods:** PAH was diagnosed on right heart catheterization (mPAP >25 and PAWP <15 mmHg at rest). Patients with PH secondary to interstitial lung disease (ILD; defined as abnormal HRCT scan and FVC<60%) were excluded. Summary statistics, chi-square tests, univariate and multivariable logistic regression along with post-estimation diagnostics were used to determine the associations of different combinations of risk factors with PAH.
**Results:** Among 1579 SSc patients, 8.4% (132 patients) were diagnosed with PAH over a mean (±SD) follow-up of 3.2 (±2.5) years. The incidence of PAH in this cohort was 0.7% per annum. Of these, 68.9% had limited disease subtype (lcSSc). In multivariable regression analysis, the presence of anti-centromere antibody (ACA) (OR 1.6, 95%CI 1.1–2.5, p=0.03), oesphageal stricture (OR 2.0, 95%CI 1.2–3.3, p=0.006), calcinosis (OR 1.9, 95%CI 1.2–2.9, p=0.003), sicca symptoms (OR 1.6, 95%CI 1.1–2.5, p=0.03), mild ILD (OR 2.3, 95%CI 1.5–3.7, p<0.001) and digital ulcers (OR 1.6, 95%CI 1.0–2.4, p=0.03) were predictive of PAH. This model had an area under the curve of 0.7 and concordance of 91.8%. Risk factors for PAH were were analyzed by disease subtype and are presented in Table 1 and 2.

Table 1. Multivariable analysis of predictors of PAH in lcSSc

| Predictors of PAH | OR (95% CI) | *p* |
|---|---|---|
| Calcinosis | 2.24 (1.4–3.7) | 0.001 |
| Sicca | 2.63 (1.5–4.6) | 0.001 |
| ILD | 2.31 (1.4–3.8) | 0.001 |
| Digital Ulcers | 1.85 (1.2–3.7) | 0.01 |

Abbreviations: ILD, Interstitial lung disease; PAH, pulmonary arterial hypertension.

Table 2. Multivariable analysis of predictors of PAH in dcSSc

| Predictors of PAH | OR (95% CI) | *p* |
|---|---|---|
| Oesphageal stricture | 4.42 (1.9–10.5) | 0.001 |
| ILD | 2.83 (1.2–6.8) | 0.02 |
| ACA | 5.16 (1.8–14.8) | 0.002 |

Abbreviations: ILD, Interstitial lung disease; PAH, pulmonary arterial hypertension; ACA, anticentromere antibody.

**Conclusions:** The incidence and prevalence of PAH in this cohort are 0.7% per annum and 8.4%, respectively. The clinical-serologic risk factors for PAH differ based on disease subtype. In both subtypes, mild ILD is associated with PAH, suggesting the possibility of a common pathogenic mechanisms underlying both of these disease manifestations. This model identifies a subset of patients at an appreciably higher risk of developing PAH, who should be screened and would in future, benefit from preventative therapies.
**Acknowledgement:** This work was supported by Scleroderma Australia, Arthritis Australia, Actelion Australia, Bayer, CSL Biotherapies, GlaxoSmithKline Australia, Pfizer and BMS. Dr Morrisroe is a recipient of an NHMRC and RACP Shields Fellowship. Dr Nikpour holds a University of Melbourne Faculty of Medicine Dentistry and Health Science David Bickart Clinician Researcher Fellowship and is a recipient of an NHMRC Fellowship (APP1071735).
**Disclosure of Interest:** None declared
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## FRI0250 SELF REPORTED GASTROINTESTINAL TRACT SYMPTOMS IN SYSTEMIC SCLEROSIS: EXPERIENCE FROM A LARGE CONSECUTIVE COHORT

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**Background:** Gastrointestinal tract (GIT) involvement in systemic sclerosis (SSc) is common, occurring in 50–90% of the patients (1). However, there is limited knowledge of self reported GIT symptoms affecting patients in daily life.
**Objectives:** To describe frequency and severity of self reported gastrointestinal symptoms in a large SSc cohort and evaluate possible correlations between special clinical characteristics and GIT-symptoms.
**Methods:** Patients from the The Norwegian Systemic Connective Tissue Disease and Vasculitis Registry (NOSVAR) who fulfilled the 2013 ACR/EULAR SSc criteria were included (N=245)). The patients completed the UCLA SCTC GIT 2.0 questionnaire which comprises seven clinical symptoms; Reflux, distention/bloating, diarrhea, fecal soilage, social functioning, emotional well-being and constipation. All variables are scored from better to worse in health related quality of life (HRQL) with a mean total score of 2.8. In addition we used the visual analogue scale on intestinal problems (VAS-GIT) of the Scleroderma Health Assessment Questionnaire (SHAQ) with a maximum score of 3. Disease duration was defined as time from diagnosis to the completion of the questionnaires. Possible correlations were tested by Spearman's correlation coefficient.
**Results:** Patient characteristics and frequencies of the different GIT symptoms are presented in Table 1. Distention bloating, reflux and diarrhea were the most frequent symptoms reported (80%, 69% and 61%, respectively. The least reported symptom was fecal soilage (16%) (Figure 1). Mean (SD) total GIT score was 0.42 (0.41), indicating mild symptoms. The seven subscales ranged from mean (SD) 0.22 (0.55) for fecal soilage to mean (SD) 0.95 (0.50) for distention/bloating. Mean (SD) VAS-GIT score was 0.33 (0.37) and correlated strongly with the mean total UCLA-GIT score (0.667, p<0.001). Female sex and disease duration correlated weakly with mean total UCLA-GIT score (r=-.234, r=199, respectively), as did positive anticentromere-antibody (r=.229).No correlation was found between mean total UCLA-GIT score and subset of SSc, interstitial lung disease, pulmonary hypertension, digital ulcers, Rodnan skin score or Raynaud.

Table 1

| Clinical characteristics | |
|---|---|
| Female sex, n (%) | 210 (86) |
| Age, yrs, mean (SD) | 53 (14) |
| Diffuse, n (%) | 57 (24) |
| Limited, n (%) | 178 (73) |
| Sine, n (%) | 10 (4) |
| Disease duration, yrs, median (25th, 75th centile) | 5.8 (2.1, 10.7) |
| Anti-SCL70 antibody, n (%) | 32/208 (15) |
| Anticentromere antibody, n (%) | 133/223 (60) |

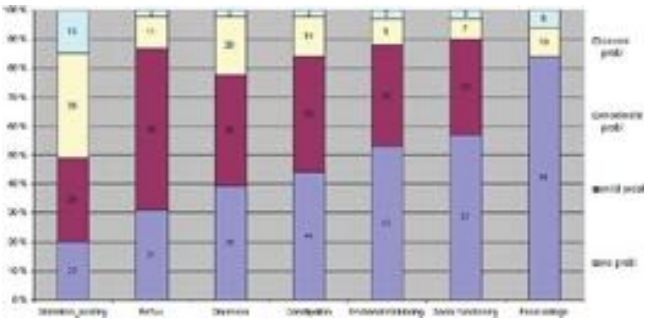


Figure 1

**Conclusions:** This study describes a high frequency of self-reported gastrointestinal symptoms in systemic sclerosis patients classified as mild to moderate symtoms. Positive anticentromere-antibody, disease duration and female sex had a minor impact on mean total UCLA-GIT score. The correlation between mean total UCLA-GIT score and the VAS-GIT score of the SHAQ was highly significant indicating a good conformity between the tests.
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**Disclosure of Interest:** None declared
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## FRI0251 ANTI-MDA5 AUTO-ANTIBODY: EXPANDING THE CLINICAL SPECTRUM IN PATIENTS WITH DERMATOMYOSITIS IN NORTH AMERICA

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**Background:** Clinically amyopathic dermatomyositis (CADM) is a subset of dermatomyositis (DM) presenting with the characteristic DM rash (es) without objective proximal muscle weakness. Asian studies report that anti-MDA5 autoantibody (autoAb) in CADM is associated with a unique clinical phenotype, which has not been well established in US.
**Objectives:** The goals of our study were to determine the clinical features associated with anti-MDA5 autoAb in CADM as compared to classic DM in US.
**Methods:** CADM patients were selected consecutively from the patients enrolled in the University of Pittsburgh Myositis Database from January 1985 to July 2013 (n=450). CADM was defined a typical DM rash without objective muscle weakness for at least 6 months after rash onset and no or minimal abnormalities of serum muscle enzymes [<3 x ULN], electromyography or muscle biopsy. The classic DM was defined as per probable and definite criteria of Bohan and Peter. DM patients were selected similarly and 1:1 matched (gender and age ±5 years) to CADM patients. The clinical features were assessed using our prospective myositis database, along with electronic medical record review when necessary.
**Results:** We identified 61 CADM patients and 61 matching DM controls. Demographics were similar in both groups. Anti-MDA5 frequency was similar in two cohorts (13.1% [8/61] vs. 13.1% [8/61]). Anti-MDA5 positivity was associated with a higher likelihood of abnormal capillary microscopy, vasculitic rash and digital tip ulceration (18.7% vs. 2.8%) and a lower frequency of Raynaud's as compared to anti-MDA5 negativity. The frequency of DM rashes (Gottron sign or papule, heliotrope, mechanics hands, etc were similar in both groups. However, puffy finger frequency was higher in the anti-MDA5+ patients as compared to anti-MDA5- patients (20% vs. 4.7%). Anti-MDA5 positivity was significantly associated with ILD (p=0.043), RPILD (p<0.001), and poor survival (p=0.007). Multivariate analysis suggested that anti-MDA5 positivity was predictive of survival even after controlling for diagnosis, age at diagnosis, gender, ethnicity, smoking, and ILD (p=0.001). ILD frequency was similar in CADM and DM (31.1% vs. 26.2%) as was RPILD (8.2% vs. 5%). CADM patients were more likely to have puffy fingers (9.8% vs. 4.9%) but less likely to have mechanic's hands (3.2% 9.8%) and heliotrope rash (36.1 vs. 19.7%) than DM patients. Rest of the clinical features were similar for both CADM and DM cohorts.

Table 1

| Clinical features | MDA5+ (N=16) | MDA-5– (N=106) | P value | CADM (N=61) | Classic DM (N=61) | P value |
|---|---|---|---|---|---|---|
| ILD | 50% | 25.5% | 0.04 | 31% | 26% | 0.46 |
| RPILD | 44% | 1% | <0.001 | 8% | 5% | 0.55 |
| Raynaud's | 12.5% | 26.4% | 0.35 | 22.9% | 26.2% | 0.67 |
| Vasculitic rash | 18.7% | 1.8% | 0.01 | 3.2% | 4.9% | 1 |
| Abnormal capillary microscopy | 43.7% | 26.4% | 0.15 | 29.5% | 27.8% | 0.8 |
| Digital tip ulceration | 18.7% | 2.8% | 0.02 | 4.9% | 4.9% | 1 |
| Heliotrope rash | 18.7% | 29.2% | 0.55 | 36% | 19.6% | 0.04 |
| Dysphagia | 31.2% | 10.3% | 0.03 | 24.5% | 1.6% | <0.001 |

**Conclusions:** Anti-MDA-5 autoAb is seen in similar frequency in CADM and DM patients in US. Anti-MDA-5 autoAb is associated with a unique clinical phenotype consisting of ILD, RPILD, abnormal nailfold capillary, vasculitic rash, and digital tip ulceration in U.S. patients. CADM patients were similar to DM apart from obvious disease defining features of muscle weakness and muscle enzyme. In addition there was more puffy fingers, less mechanics hands and heliotrope rash in CADM.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1049

## FRI0252 EFFICACY OF MYCOPHENOLATE MOFETIL (MMF) VERSUS ORAL CYCLOPHOSPHAMIDE (CYC) ON SKIN THICKNESS IN THE SCLERODERMA LUNG STUDY II

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**Background:** Mycophenolate mofetil (MMF) has been shown to improve skin thickness, as assessed by the modified Rodnan skin score (mRSS), in patients with diffuse cutaneous SSc (dcSSc) in retrospective analyses of different cohorts (1). In addition, oral cyclophosphamide (CYC) had a favorable impact on mRSS in SLS-I (2).
**Objectives:** Our objectives were to: 1. Assess the impact of MMF and CYC on the mRSS in a randomized controlled trial of MMF vs. oral CYC in patients with symptomatic scleroderma-related interstitial lung disease (SLS II) over 24 months, and 2. Compare the improvement in mRSS in the SLS I vs. SLS II cohorts at 6 and 12 months.
**Methods:** 142 patients with SSc-ILD were randomized in the SLS II. Patients received MMF (≤3 g daily) for two years or oral CYC (≤2 mg per kilogram of body weight) for one year followed by placebo twice daily for an additional year. In addition, we compared the change in mRSS in the dcSSc subset in the SLS-II vs. SLS-I oral CYC (≤2 mg per kilogram of body weight) and matching placebo prescribed for 1 year.
**Results:** The baseline (mean± SD) disease duration was 2.6±1.8 years and mRSS was 14.0±10.6 for CYC and 15.3±10.4 for MMF groups in the SLS II; 58.5% were classified as dcSSc and 42.5% were classified as limited cutaneous SSc (lcSSc). Both treatments were associated with improvement in mRSS over the period of 24 months but there was no statistically significant between 2 groups at any time points in the dcSSc and lcSSc subsets (p>0.05 for all comparisons). The mean improvement in the CYC group was 1.4 vs. 2.0 in the MMF group in the lcSSc subset and 8.0 vs. 6.3 in the dcSSc subset at 24 months.
For our second objective, there was no statistical difference in the baseline mRSS scores in the dcSSc in SLS-I (mean disease duration=3.1 years) and SLS-II (mean disease duration=2.5 years) trials (Table). In addition, the change in mRSS at 6- and 12-month period was similar in the SLS-II pooled (MMF+ CYC) and SLS-I CYC groups (Table; p>0.05). In contrast, SLS-II pooled and SLS-I CYC groups showed statistically significant improvement at 12-month period vs. SLS-1 placebo group (p<0.05).

Table 1. Mean change in mRSS in the dcSSc subset in the SLS-1 and SLS-2

| | SLS-2 pooled group | | SLS-1 CYC group | | SLS-2 pooled and SLS-1 CYC groups | | SLS-1 Placebo group | |
|---|---|---|---|---|---|---|---|---|
| | N | | N | | N | | N | |
| Baseline | 83 | 20.8 | 49 | 21.6 | 132 | 21.1 | 46 | 20.4 |
| 6 month | 69 | –2.4† | 45 | –2.7† | 114 | –2.6† | 43 | –2.6† |
| 12 month | 66 | –5.5† | 43 | –5.3† | 109 | –5.4*† | 37 | –1.7* |

†P<0.05 for for mRSS at follow up vs. baseline within each group. *P<0.05 for SLS-II pooled and SLS-I CYC groups compared to SLS-1 Placebo group.

**Conclusions:** In the SLS II, 2 years of daily MMF and 1-year of CYC were associated with clinically important improvements in mRSS in the dcSSc over 24 months. The change in mRSS in the SLS-II paralleled that in the SLS-I CYC group and was significantly superior to the SLS-I placebo group. These data support the use of MMF or CYC for management of skin fibrosis in early dcSSc.
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**Disclosure of Interest:** None declared
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## FRI0253 A 18 MONTH OBSERVATION IN PATIENTS WITH PROGRESSIVE SYSTEMIC SCLEROSIS TREATED WITH AN INTENSIFIED B-LYMPHOCYTE DEPLETION -CLINICAL AND IMMUNOLOGICAL RESPONSE

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**Background:** B cells (BC) play a critical role in progressive systemic sclerosis (SS). BC depletion therapy is an attractive option.
**Objectives:** to evaluate the efficacy of an intensified B cell depletion therapy in patients with progressive SS
**Methods:** Eighteen patients with SS [2 males, mean age 58.33 yrs (46–82)] with severe multiorgan involvement including skin [16], lung, with pulmonary fibrosis (17 patients) and pulmonary hypertension (5), esophagous [9], with polyarthralgias [2] have been prospectively treated with an intensified B cell depletion therapy (IBCDT) protocol due to their resistance or intolerance to previous therapy (4 cases) or as a front line treatment in 14 patients with unsatisfactory therapeutic compliance. IBCDT included: Rituximab (RTX) 375mg/sm on days 1, 8, 15, 22, and 2 more doses after 1 and 2months, associated with 2 IV administrations of 10mg/kg of cyclophosphamide and 3 methylprednisolone pulses (15mg/kg) followed by oral prednisone (0.8mg/kg/day, rapidly tapered to 5mg/day by the end of the 3rd month after RTX). No further immunosuppressive maintenance therapy has been given.
**Results:** Patients had been followed-up for a mean of 21,67 ± ds 11,05 (06–43) months. Significant decreases (p<0.05) were found in Rodnan skin score (baseline: 12.28; end of follow-up: 11.67), visual activity score (baseline mean value: 6.8 mm; end of follow-up: 4.2. A significant increase (p<0.05) FVC (baseline: 92.35; end of follow-up: 95.44), FEV (baseline: 86.5; end of follow-up: 90.43), DLCO (baseline: 57.15; end of follow-up: 66.75), and NTpro BNP (baseline: 345.19; end of follow-up: 62.29). PAP values did not change during the observation (baseline: 29.77mmHg; end of follow-up: 26.57). During the follow-up, pulmonary fibrosis, as established on a radiological level, was found to be ameliorated in 2 out of the 14 evaluable patients, worsened in 3, and unchanged in 9.
**Conclusions:** A promising role of RTX in an intensified protocol of induction therapy can be envisaged in patients for whom avoiding prolonged immuno-

suppressive therapy particularly appealing. Our data confirm the opportunity to consider the regimens of BL depletion in the treatment of the most severe or refractory forms of SS.

**Disclosure of Interest:** None declared

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## FRI0254 THE EFFECT OF CYCLOPHOSPHAMIDE ON LUNG FUNCTION IN DIFFERENT STAGES OF INTERSTITIAL LUNG DISEASE ASSOCIATED TO SYSTEMIC SCLEROSIS

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**Background:** The primary cause of death in patients with systemic sclerosis (SSc) is interstitial lung disease (ILD). Several retrospective studies have shown some effect of cyclophosphamide (CYC) on ILD. In one randomized controlled trial a small but significant effect on pulmonary function was shown after oral CYC (Taskin,2006). Hoyles (2006) showed a trend towards improvement of forced vital capacity after monthly CYC infusions. In our centre, intravenous CYC pulses are the first choice of therapy in SSc-ILD.

**Objectives:** To analyze 1) the effects of iv CYC pulses (750mg/m$^2$) on pulmonary function in SSc-ILD in our cohort, and 2) whether this effect is dependent on the extent of ILD.

**Methods:** Patients with SSc-ILD receiving CYC pulses between 2003 to 2015 were classified by the Goh criteria (2008) in either limited or extensive ILD, using HRCT at baseline judged by two raters. Pulmonary function tests were performed at 0, 6 and 12 months. Missing outcome data due to drop-out, but not death, were replaced by last observation carried forward.

**Results:** 79 patients were included, 42 with limited ILD, 37 with extensive ILD. There were no differences in age, gender, SSc subtype classification, disease duration or autoantibody status between the two groups. Baseline FVC (median 80% vs. 91%) and DLCO (39% vs. 50%) were lower in extensive ILD ($p<0.05$). After 12 months, FVC (p=0.08)), and DLCO (p=0.62) did not worsen compared to baseline values. There were no differences in the degree of change in FVC and DLCO between limited and extensive ILD. Forty-eight patients completed 12 cycles of CYC. Per protocol analyses showed not significant differences between limited and extended ILD.

Table 1. Changes in pulmonary function test after 1 year

| | Limited ILD (n=42) | | | Extensive ILD (n=37) | | | Difference with 95%>CI | P-value† |
|---|---|---|---|---|---|---|---|---|
| | Baseline | 1 year | Δ* | Baseline | 1 year | Δ* | | |
| FVC | 91 (78–104) | 94 (82–109) | 2.9±13 | 80 (66–92) | 82 (63–95) | 2.0±9 | 0.9 (–4.7–6.4) | 0.76 |
| DLCO | 51 (39–60) | 47 (41–60) | –1.4±11 | 39 (31–51) | 41 (32–52) | 1.3±6 | –2.6 (–7.6–2.4) | 0.29 |
| *Last observation carried forward* | | | | | | | | |
| FVC | 88 (75–102) | 93 (81–108) | 2.4±13 | 80 (66–92) | 82 (65–93) | 0.8±9 | 1.6 (–3.8–7.0) | 0.56 |
| DLCO | 51 (39–60) | 48 (41–59) | –1.5±11 | 39 (31–51) | 39 (29–50) | 0.04±6 | –1.6 (–6.1–3.0) | 0.50 |
| *Per protocol analysis* | | | | | | | | |
| FVC | 83 (74–100) | 90 (80–106) | 2.3±13 | 83 (68–92) | 83 (66–98) | 3.0±9 | –0.7 (–7.5–6.1) | 0.83 |
| DLCO | 50 (40–60) | 48 (41–60) | 0.7±11 | 41 (32–55) | 40 (31–57) | 2.3±7 | –1.6 (–7.6–4.4) | 0.59 |

Values are the median of %> predicted (p25–75); *mean ± SD; Δ: difference between baseline and 1 year; CI: confidence interval. †Significance of the degree of change in the limited ILD group versus the extensive ILD group at 1 year; FVC: forced vital capacity; DLCO: diffusing capacity of the lung for carbon monoxide.

**Conclusions:** 1. CYC pulse therapy does not worsen pulmonary function in SSc-related ILD after 1 year. 2. The extent of ILD does not influence the effect of CYC.

**Disclosure of Interest:** None declared

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## FRI0255 COMBINATION THERAPY WITH RITUXIMAB AND MYCOPHENOLATE MOFETIL IN SYSTEMIC SCLEROSIS. SAFETY AND EFFICACY FROM 12 MONTHS

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**Background:** Systemic Sclerosis (SSc) is a chronic systemic disease characterized by immune abnormalities, microangiopathy and progressive fibrosis of skin and internal organs. Only few therapeutic options have shown a proved disease-modifying effect for skin thickening and SSc-associated interstitial lung disease. Rituximab (RTX) and Mycophenolate Mofetil (MMF) have separately proven some evidence of efficacy and safety in clinical trials or case series

**Objectives:** Assess efficacy and safety of a combination therapy, with RTX and MMF in a cohort of SSc patients with pulmonary and cutaneous involvement rapidly progressive or resistant to conventional therapy.

**Methods:** Eligible patients were treated with RTX in two different regimens (1000 mg fortnightly x 2 or 375 mg/m$^2$/week for 4 consecutive weeks) at baseline and after 6 months, associated with MMF 2000 mg/day. They received anti-infective prophylaxis with Valacyclovir 1000 mg and Cotrimoxazole 160/800 mg alternate days. Patients with previous malignancy or HBV, HCV or TB infection or connective overlap were excluded. Patients underwent clinical and laboratory evaluation every 3 months. Skin involvement was assessed by using the modified Rodnan Skin Score (mRSS) performed by the same physician at baseline and after 3, 6 and 12 months. Chest high-resolution computed tomography (HRCT) and pulmonary function tests (PFTs) and single-breath diffusing capacity were performed at baseline, after 6 and 12 months. The assessment of the extension of pulmonary fibrosis (PF) was analysed with the semiquantitative Warrick score and with the OsiriX quantitative computerized analysis. Data were analysed by Friedman test (GraphPadPrism V5).

**Results:** 18 SSc patients were enrolled (M/F: 8/10, median age 51y, median disease 1 y, diffuse SSc 9, limited SSc 9). Three patients withdrew from the study: one was lost to follow-up, one had a minor infusion reaction which led to RTX discontinuation and one died for different causes. The analysis includes all 15 of 18 patients who completed 12 months of follow-up. The mRSS showed a statistically significant improvement (p**=0,0036), more remarkable in patients with diffuse cutaneous SSc. Concerning PFTs there was a statistically significant increase of FVC (p**=0,0093), $FEV_1$ (p**=0,0061), with stable values of DLCO (p=0,3375). The HRCT scan showed an improvement statistically significant evaluated with analysis by OsiriX (p*=0,0331), while the Warrick score showed a not significant trend toward improvement. No serious adverse events were observed during the follow-up. In two patients the MMF dose was reduced for mild neutropenia.

**Conclusions:** Despite preliminary and limited to a small number of patients, our results suggest that combination therapy with RTX and MMF is well tolerated, safe, and potentially effective for cutaneous and pulmonary involvement in SSc patients.

**Disclosure of Interest:** None declared

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## FRI0256 SIGNIFICANCE OF COGNITIVE IMPAIRMENT IN SYSTEMIC SCLEROSIS

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**Background:** There is an increased appreciation of the burden of cognitive impairment in people with autoimmune diseases (1). Recent studies have demonstrated that patients with systemic sclerosis (SSc) have a specific pattern of cognitive impairment: the dysexecutive syndrome (2).

**Objectives:** We evaluated the prevalence of cognitive impairment in SSc and assessed the association with the disease features and impact on daily living

**Methods:** Consecutive SSc from EUSTAR center 096 were examined. Montreal Cognitive Assessment (MoCA) was used to assess cognitive dysfunction and scores ≤26 were considered abnormal (3). SSc patients were assessed according tu MEDS evaluation sheets to determine organ involvement, autoantibody profile, disease activity (Valentine Activity Index) and disease severity (Medsger Severity Index). sHAQ (Scleroderma Health Assessment Questionnaire) has also been completed. Data were compared by difference tests according to the types of variables: t-test, Mann-Whitney or chi-square. To evaluate correlations between variables Pearson or Spearman correlations were used.

**Results:** A total of 70 SSc patients [36 (51.42%) limited SSc (lSSc) and 34 (48.57%) with diffuse SSc (dSSc), 60 female; mean age 54.5 (±11.62) years; mean disease duration 66 (±429.6) months] were included in the study. 47.14% of the patients had active disease, the mean Rodnan score was 7 (±4.17), the mean Medsger score was 5.5 (±2.89), 24.28% of the patients had lung involvement and 20% had pulmonary arterial hypertension. The mean HAQ was 1 (±0.59). Cognitive impairment was identified in 65.71% SSc patients; the mean MOCA score was 26 (±2.83).

Cognitive impairment of SSc patients was related to older age (r=-0.378, p=0.001), rural provenience (r=-0.351,p=0.003), severity of the disease evaluated by the Medsger score (r=–0.262,p=0.029) and poor quality of life evaluated by sHAQ (r=-0.323,p=0.003).Correlations were also identified with musculoarticular involvement (r=-0.330,p=0.006), advanced capillaroscopy patttern (r=-0.331, p=0.006). The diiffuse SSc patients were more likely to have cognitive dysfunction (likehood ratio 0.012) as were those with SCL70 positive (0.0.18). No relationship was identified between cognitive impairment and lung, heart or renal involvement, the presence of digital ulcers, the use of corticosteoids or immunosuppression.

**Conclusions:** An increased prevalence of cognitive impairment was observed in SSc and associated with age, rural provenience, more severe disease, muscle involvement and poor quality of life. Further studies are needed to be compared with healthy controls and to assess the role of microvascular damage or that of other confounders.

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**Disclosure of Interest:** None declared
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## FRI0257 AUGMENTED CONCENTRATIONS OF CX3CL1 ARE ASSOCIATED WITH PROGRESSIV INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a complex, immune-mediated disorder that carries high risk for progressive interstitial lung disease (ILD). CX3CL1 (Fractalkine) is expressed in lungs; and has the ability to act as an adhesion molecule as well as a potent chemoattractant of mononuclear cells via its interaction with CX3CR1. Here, we hypothesized that the CX3CL1/CX3CR1 axis could play an important role in the immune pathogenesis of SSc associated ILD.
**Objectives:** (i) To explore CX3CL1 concentrations in lung homogenates from patients with SSc-ILD at the time of lung transplant (LT) compared to donor lung homogenates with no lung disease. (ii) To test whether CX3CL1 concentrations in serum differ between SSc patients and healthy controls. (iii) To assess associations between serum CX3CL1 and the development of SSc-ILD.
**Methods:** Lung tissue was collected at LT from SSc (n=12) and donor lungs (n=12) at the UCLA. Concentrations of CX3CL1 in lung homogenates were determined by Luminex technology. Cellular sources of CX3CL1were assessed by immunohistochemistry (IHC). Sera from the prospective Oslo University Hospital SSc cohort (n=240) and healthy controls (n=100) were analysed for CX3CL1 concentration by ELISA. Paired pulmonary function tests (PFTs) and HRCT images were obtained at baseline and follow-up. Non-parametric statistical analysis was performed via Kruskal-Wallis testing. Categorical data were analyzed by Chi-squared testing. Predictive values were analyzed by multivariate linear regression and cox regression.
**Results:** Concentrations of CX3CL1 in lung homogenates and serum were increased in SSc compared to healthy controls (Table 1). IHC demonstrated a CX3CL1 co-localization with reactive type II pneumocytes, airway epithelial cells, epithelial cells involved in bronchiolization, and infiltrating mononuclear cells. Serum CX3CL1 was significantly associated with anti-Topoisomerase I antibody and extensive ILD (Table 1). Linear regression analyses showed associations between CX3CL1 and extent of lung fibrosis at follow up (Regression coefficient (B): 0.86, SE 0.41, p=0.038) when adjusting for age and gender. Cox regression analysis showed predictive associations of CX3CL1 to extensive ILD (HR 1.43, 95% CI 1.02–1.26, p=0.017) and to ΔDLCO% decline >7.5% (HR 1.13, 95% CI 1.02–1.25, p=0.023). However, following further adjustment, including PFT parameters and autoantibodies, CX3CL1 was no longer significant.

Table 1: CX3CL1 concentrations in the SSc study cohorts and corresponding controls. Also shown are CX3CL1 in SSc subsets stratified by demographics and clinical characteristics.

| | OUH cohort (serum) | | | UCLA cohort (lung) | | |
|---|---|---|---|---|---|---|
| | No (%) | CX3CL1 ng/ml (SD) | p-value | No | CX3CL1 ng/ml (SD) | p-value |
| Total SSc cohort | 240 | 1.79 (2.25) | 0.010 | 12 | 0.892 (0.839) | 0.026 |
| Controls | 100 | 1.16 (1.36) | | 12 | 0.253 (0.271) | |
| SSc subsets | | | | | | |
| Male | 44 (13) | 1.80 (1.86) | 0.959 | 7 | 0.924 (0.961) | 0.845 |
| dcSSc | 69 (20) | 1.93 (2.86) | 0.533 | 3 | 0.946 (0.774) | 0.964 |
| Deceased | 56 (16) | 1.89 (2.43) | 0.689 | 5 | 0.736 (0.646) | 0.434 |
| ATA | 36 (11) | 3.09 (4.07) | 0.030 | 3 | 1.335 (1.440) | 0.654 |
| PH | 45 (13) | 1.94 (2.43) | 0.612 | 8 | 1.176 (0.901) | 0.217 |
| Extensive lung disease* | 27 (8) | 2.80 (4.09) | 0.023 | | n.a. | |

OUH: Oslo University Hospital; UCLA: University of California Los Angeles; No: number; SD: standard deviation; SSc: systemic sclerosis; FVC: Forced vital capacity; DLCO: diffusing lung capacity for carbon monoxide; dcSSc: diffuse cutaneous systemic sclerosis; ATA: anti-topoisomerase I antibody; *defined as total lung fibrosis ≥20% and FVC <70%

**Conclusions:** We have demonstrated an association between elevated protein levels of CX3CL1 in SSc-ILD and have shown that within the lungs, CX3CL1 are predominately co-localized with epithelia and infiltrating mononuclear cells. Augmented concentrations in the serum of SSc patients may be predictive of ILD.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4406

## FRI0258 VALIDATION OF BIOELECTRICAL IMPEDANCE ANALYSIS FOR THE ASSESSMENT OF BODY COMPOSITION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Malnutrition is a frequently reported complication in patients with systemic sclerosis (SSc) [1]. Especially low fat free mass (FFM) has been identified a prognostic factor for morbidity and mortality. Different methods are available to assess body composition. Bioelectrical impedance analysis (BIA) is a bedside method that has not yet been validated in this patient group.
**Objectives:** To validate BIA against whole body dual-energy x-ray absorptiometry (DXA), for the assessment of body composition in patients with SSc.
**Methods:** Body composition was assessed in 72 patients with whole body DXA (Hologic, Discovery A) and BIA (Bodystat Quadscan 400). The Geneva equation [2] was used to estimate FFM. The agreement between BIA and whole body DXA was assessed with Bland-Altman analysis and intraclass correlation coefficients (ICCs). The occurrence of malnutrition was assessed and defined as fat free mass index (FFMI) $\leq$14.5 kg/m$^2$ for women or $\leq$16.6 kg/m$^2$ for men [3].
**Results:** No difference was found between BIA and whole body DXA for the assessment of FFM as predicted by the Geneva equation (mean difference 0.02 ± 2.4 kg). ICC was 0.97 (95% CI: 0.95–0.98). The 95% limits of agreement, as assessed by Bland-Altman analysis were -4.6 kg and 4.6 kg. Despite normal BMIs (24.6 ± 4.3 kg/m$^2$), malnutrition was found in 14 (19.4%) patients with SSc.

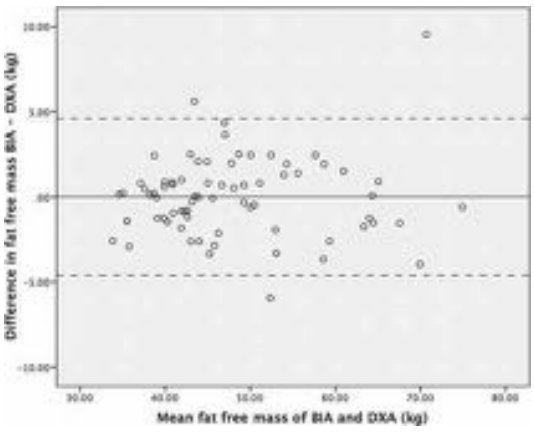



Figure 1. Bland-Altman plot comparing fat free mass measured by whole body DXA and fat free mass measured by BIA using the Geneva equation. The solid line represents the mean and the dotted lines represent the limits of agreement.

**Conclusions:** This study shows acceptable validity of BIA in determining FFM in patients with SSc on a group level, while on an individual level, FFM may vary by 4.6 kg. This study also demonstrated a high prevalence (19.4%) of malnutrition in patients with SSc, underlining the necessity of assessing body composition in this patient group.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2513

## FRI0259 A RETROSPECTIVE STUDY: PREDICTIVE FACTORS FOR INSUFFICIENT IMPROVEMENT OF MUSCLE WEAKNESS AFTER TREATMENT AMONG PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS

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**Background:** The severity of muscle involvement and the response to immunosuppressive drugs are highly variable among patients with polymyositis (PM) and dermatomyositis (DM). Although previous studies reported that some clinical and laboratory features were associated with a poorer prognosis, the results were not consistent through those studies. A decade ago, we reported that the height of the baseline serum creatine kinase (CK) elevation predict the course of disease among patients treated with glucocorticoids (GCs) alone. However, other groups reported conflicting results. In addition, we later changed our basic treatment strategy to combination therapy with another immunosuppressive agent to improve response and reduce the need for GCs.
**Objectives:** We aimed to identify predictive factors for insufficient improvement of muscle weakness after treatment among patients with PM/DM, focusing more recent patients than those included in our previous report.

**Methods:** Patients were included in this retrospective study when they met all these criteria: 1) fulfill the Bohan and Peter classification criteria for PM/DM; 2) were administered to our university hospital for the treatment of muscle manifestations of PM/DM from 2008 through 2015. In addition, these patients were excluded from the study: those with clinically amyopathic DM and those complicated with other overlapping systemic autoimmune diseases or cancer. Manual muscle testing (MMT) was assessed using traditional 5 point MMT scales (i.e. the Medical Research Council Scale.) The Total MMT score included 2 axial and 8 proximal muscle groups, with a maximum potential value of 50. The Total MMT score less than 48 at 6 to 8 weeks after initiation of GC treatment was defined as insufficient improvement of muscle weakness. Clinical and laboratory parameters were statistically compared between patients with sufficient and insufficient improvement of muscle weakness. Odds ratios (ORs) for insufficient improvement of muscle weakness were assessed by multiple logistic regression analysis.
**Results:** Ultimately, 45 patients, comprising 30 PM and 15 DM patients were included in the present study. Among these, 22 were positive for anti-aminoacyl-tRNA synthetase (anti-ARS) antibodies, the mean age was 55 years, and the mean CK level before treatment was 2,544 U/l. GCs (≥0.5 mg/kg/day) were administered in all the patients and another immunosuppressant were concomitantly used in 39 patients. By univariate analyses, age and CK levels before treatment were significantly higher in patients with insufficient improvement of muscle weakness than those with sufficient improvement ($p<0.05$). The cut off values were determined by receiver operating characteristic curve analyses as ≥65 years for age and ≥1,900 U/l for CK level. The patients with ≥65 years old, CK ≥1,900 U/l, or negative anti-ARS antibodies were more frequent in patients with insufficient improvement. By multivariate analyses, ORs (95% confidence interval) for ≥65 years old, CK ≥1,900 U/l, and negative anti-ARS antibodies were 16 (2 to 342), 22 (3 to 526), and 9 (1.3 to 104), respectively.
**Conclusions:** The present study suggested that ≥65 years old, CK ≥1,900 U/l before treatment, and negative anti-ARS antibodies were predictive factors for insufficient improvement of muscle weakness in patients with PM/DM.
**Disclosure of Interest:** None declared
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## FRI0260 QUANTITATIVE CT INDEXES IN ILD-SSC PATIENTS WITH DIFFERENT AUTOANTIBODIES

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**Background:** Quantitative Computed Tomography (QCT) is an innovative method to assess the severity of interstitial lung disease (ILD) related to systemic sclerosis (SSc). QCT is correlated to semi-quantitative radiological scores (SQs) and functional outcomes (e.g. FVC, DLco, oxygen desaturation after exercise) in SSc patients. However, the autoimmune profile can deeply influence the respiratory system's involvement.
**Objectives:** The main aim of this study is to verify the correlation between SQs, FVC, DLco and QCT in SSc patients clustered according to their autoimmunity.
**Methods:** Three hundred three (303) SSc patients were enrolled and underwent functional and radiological assessment. Chest CTs of each patient were evaluated with both SQs and Horos (a software up to perform voxel-wise analysis) in order to obtain QCT indexes.
**Results:** Patients were divided in three groups (94 with ACA, 93 with antiScl70, 116 with other autoantibodies). QCT indexes taken into account were kurtosis (Kurt), skewness (Skew), Standard Deviation (SDev), Mean Lung Attenuation (MLA) and fibrosis ratio (FR). Except for the last one, all QCT indexes were assessed both in the parenchymal (pQCT) and in the whole lung (tQCT). The statistically significant ($p<0,05$) correlation coefficients between SQs, FVC and DLco vs QCT are listed in Table 1.
In ACA patients there are not correlations between DLco and QCT indexes.
**Conclusions:** Our results confirm that the majority of QCT indexes are correlated to SQS and functional outcomes. The strongest correlation coefficients were in the antiScl70 subgroup while the weakest ones were in ACA patients. This relevant difference, possibly due to the different prevalence of ILD and type of lung involvement in these two subgroups, should be taken into account when applying the QCT assessment to SSc patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3021

## FRI0261 OBSERVATIONAL STUDY OF OUTCOME IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS TREATED WITH IMMUNOSUPPRESSIVE THERAPIES (ESOS STUDY)

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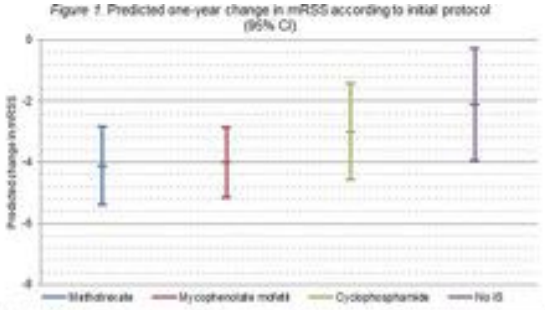
**Background:** Early diffuse cutaneous systemic sclerosis (dcSSc) has high morbidity and mortality, and there is currently no cure.
**Objectives:** The main objective of ESOS (European Scleroderma Observational Study) was to compare the effectiveness of currently used immunosuppressant treatments.
**Methods:** ESOS was a prospective observational cohort study, capturing entry and outcome data in a standard way. Four recommended treatment protocols were decided by the steering committee: methotrexate (MTX), mycophenolate mofetil (MMF), cyclophosphamide, and "no immunosuppressant". Patients were assessed at baseline, and then 3-monthly for 24 months or (for those entering the study subsequent to September 2013) at least 12 months. The primary outcome measure was the change in modified Rodnan skin score (mRSS – 17 sites) between 0 (baseline) and 12 months. Secondary endpoints largely reflected routine clinical practice and are not reported here. Effects of treatment on the skin score were assessed using linear regression with baseline treatments as predictors. Confounding by indication at baseline was accounted for using inverse probability of treatment (IPT) weights, while censoring weights adjust for bias due to patient attrition. Survival in each protocol was estimated using Kaplan-Meier curves and survival differences were tested based on the results of an IPT-weighted Cox regression model.
**Results:** Target recruitment was achieved, with 326 patients from 50 centres (median age 52.3 years, 72% female, median disease duration 11.1 months). Because this was not a randomized study, the number of patients starting on each treatment protocol differed: 65 MTX, 117 MMF, 87 cyclophosphamide, and 57 no immunosuppressant treatment. 273 patients (84%) completed 12 months follow-up and 179 (55%) 24 months follow-up. Median mRSS at baseline was 21.0 units. After 12 and 24 months, 153 (56%) and 139 (78%) of remaining patients had an improved skin score with respect to baseline. The mean change in mRSS after 12 and 24 months was -2.9 and -6.8 units. Predicted decreases in mRSS in each of the protocols are summarized in Figure 1. In both weighted and unadjusted models, the differences between the treatment groups are non-significant (p=0.27 and p=0.16).
At 24 months, Kaplan-Meier predicted survival rates (adjusted for confounding) are 94% (MTX), 90% (MMF), 91% (cyclophosphamide) and 87% (no immunosuppressant). However, differences are non-significant (p=0.42).
**Conclusions:** 1. All groups showed improvement in MRSS which was not

**Abstract FRI0260** – Table 1

| | All vs SQs | ACA positive pts vs SQs | antiScl70 positive pts vs SQs | Other auto-antibodies vs SQs | All vs FVC | ACA positive pts vs FVC | antiScl70 positive pts vs FVC | Other auto-antibodies vs FVC | All vs DLco | antiScl70 positive pts vs DLco | Other auto-antibodies vs DLco |
|---|---|---|---|---|---|---|---|---|---|---|---|
| pKurt | –0.528** | –0.227 | –0.596** | –0.543** | 0.512** | 0.417** | 0.378* | 0.487** | 0.365** | 0.429** | 0.315 |
| tKurt | –0.427** | – | –0.494** | –0.443** | 0.440** | 0.356* | 0.519** | 0.250 | 0.315** | 0.405** | 0.252 |
| pSkew | –0.500** | –0.217 | –0.543** | –0.540** | 0.484** | 0.424** | 0.349* | 0.442** | 0.365** | 0.462** | 0.295 |
| tSkew | –0.561** | –0.212 | –0.590** | –0.575** | 0.513** | 0.413** | 0.458** | 0.416** | 0.377** | 0.446** | 0.338 |
| pSdev | 0.497** | 0.192 | –0.585** | 0.603** | –0.391** | –0.239 | –0.240 | –0.427** | –0.306** | –0.349* | –0.242 |
| tSdev | 0.132 | – | 0.345* | 0.303** | –0.197 | –0.273 | – | – | – | –0.222 | – |
| pMLA | 0.459** | 0.188 | 0.386* | 0.479** | –0.515** | –0.479** | –0.414** | –0.454** | –0.395** | –0.366* | –0.350 |
| tMLA | 0.460** | 0.195 | 0.405* | 0.470** | –0.502** | –0.458** | –0.437** | –0.421** | –0.403** | –0.379* | –0.351 |
| FR | – | – | 0.226 | 0.307 | – | – | – | – | – | – | – |

**p<0,0001, *p<0,001.

*Figure 1.* Predicted one-year change in mRSS according to initial protocol (95% CI)




| Model specification | p | Methotrexate | Mycophenolate mofetil | Cyclophosphamide | No immunosuppressant |
|---|---|---|---|---|---|
| Adjusting for confounding (weighted model), n=326 | 0.27 | -4.1 (-5.4, -2.8) | -4 (-5.1, -2.9) | -3 (-4.6, -1.4) | -2.1 (-3.9, -0.3) |
| No adjusting, n=326 | 0.16 | -4.8 (-6.1, -3.5) | -3.8 (-4.9, -2.7) | -3.4 (-4.9, -1.9) | -2.5 (-4, -1) |

Significance p: Fisher's test for equality of mRSS change rates between protocols
No IS: No immunosuppressant

significantly different between groups although there was a trend in favour of methotrexate and MMF.
2. Survival was similar between groups although the no immunosuppressant group had lower survival (but it is important to stress that this was not a true "control" group).
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2261

## FRI0262 PERIPHERAL BLOOD PERFUSION IS LOWER IN PRIMARY RAYNAUD'S PHENOMENON PATIENTS THAN IN THOSE WITH SYSTEMIC SCLEROSIS SHOWING THE "EARLY" PATTERN OF NAILFOLD MICROANGIOPATHY

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**Background:** Peripheral blood perfusion is reduced in patients with both primary (PRP) or secondary Raynaud's phenomenon (SRP) (1–2).
**Objectives:** To investigate blood perfusion (BP) in different skin areas of hands in patients with PRP, SRP to systemic sclerosis (SSc), and healthy subjects (CNT).
**Methods:** 70 SSc patients (ACR/EULAR criteria) (3) (mean age 63±12 years, mean disease duration 6±5 years), 31 PRP patients (LeRoy criteria) (4) (mean age 48±18 years, mean Raynaud duration 3±2 years) and 68 CNT (mean age 59±19 years) were enrolled during winter time, after informed consent. BP was assessed by Laser speckle contrast analysis (LASCA) at the level of fingertips, periungual areas, dorsal and palmar aspect of 3rd finger bilaterally, dorsum and palm of both hands, and the average BP calculated as perfusion units (PU) (1). Nailfold videocapillaroscopy (NVC) was also performed to distinguish between PRP and SRP, and to detect the proper pattern of nailfold microangiopathy ("early", "active" or "late") in SSc patients (5). Patients were not taking vasodilator drug since at least two weeks.
**Results:** Both PRP and SSc patients showed a statistically significant lower BP than CNT at the level of fingertips (median 86, 88, 186 PU, respectively, $p<0.0001$), periungual (median 75, 76, 142 PU, respectively, $p<0.0001$), palmar aspect of 3rd finger (median 71, 81, 134 PU, respectively, $p<0.0001$), and palm areas (median 61, 78, 112 PU, respectively, $p<0.0001$). On the contrary, the three groups displayed similar BP values at the level of other areas of hands. Of interest, PRP patients showed lower BP values than SSc patients in all areas of hand, even if BP was found statistically different only at the level of both palmar aspects of 3rd finger ($p=0.04$) and palm of hands ($p=0.008$). The gradients of BP fingertip-phalanx-palm and periungual-phalanx-dorsum were significantly lower in PRP than in SSc patients ($p<0.0001$), as well as significantly higher in CNT when compared with both PRP and SSc patients ($p<0.0001$). A statistically significant progressive decrease of BP was observed in SSc patients with progressive pattern of nailfold microangiopathy ("early", "active", and "late") at the level of fingertips, periungual, palmar aspect of 3rd fingers and palm areas ($p<0.05$). Moreover, BP was significantly lower in PRP than in SSc patients with the "early" pattern of microangiopathy in all areas ($p<0.04$), with the exception of dorsal phalanx and hand dorsum.
**Conclusions:** By considering a small cohort of patients, BP of hand was found lower in PRP than in SSc patients with the "early" NVC pattern of microangiopathy. Also the gradients of perfusion between distal and proximal areas of hand were significantly lower in PRP than in SSc patients. The clinical value of this new early finding is matter of further analysis.
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**Disclosure of Interest:** None declared
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## FRI0263 NODULAR REGENERATIVE HYPERPLASIA OF THE LIVER – A RARE VASCULAR COMPLICATION OF SSC

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**Background:** Nodular regenerative hyperplasia (NRH) is a rare liver disease causing non-cirrhotic intrahepatic portal hypertension (1). The knowledge of NRH is based mainly upon case reports. Although patients with NRH may remain asymptomatic, at least 50% develop life-threatening complications. Among the autoimmune diseases, SSc has been hypothesized to be associated with NRH. In SSc, microvascular injury is considered one of the earliest pathologic events, followed by inflammation and fibrosis. Similar mechanisms are supposed to be operative in NRH. Therefore, it might be hypothesized that NRH represents a yet unidentified vascular complication of SSc.
**Objectives:** To investigate the prevalence and clinical phenotype of NRH in SSc.
**Methods:** Published cases of SSc-NRH were identified by systematic literature review. Next, we screened the Zurich SSc cohort. In accordance with international guidelines, the diagnosis of NRH had to be established by liver biopsy showing a characteristic diffuse micronodular transformation without fibrous septa (2). SSc characteristics were derived from the EUSTAR database. Information on NRH was extracted from the patients' charts. The study was approved by the local institutional review board. For the statistical analysis, SPSS version 20 was used. Continues variables are presented as mean±SD or median+range. Categorical variables are given as absolute numbers and percentage.
**Results:** The Pubmed search review retrieved 9 cases of SSc-NRH. In the Zurich cohort, 5 out of 278 patients with established SSc were diagnosed with NRH resulting in a prevalence of 1.8%. The main characteristics of all 14 patients are provided in Fig.1. The majority of patients was female (69.2%) with an average age of 44.5±12.3 years at diagnosis of SSc. Mean disease duration of SSc was 8.2±7 years when NRH was diagnosed. NRH occurred in both diffuse and limited cutaneous SSc. ACR/EULAR criteria were fulfilled by all patients. Of note, in the majority of patients, vascular features of SSc were present at the time point of the diagnosis of NRH including digital ulcers (ever 100%, active 71.4%), an active pattern on nailfold capillaroscopy (100%), and pulmonary hypertension (50%). The most prevalent auto-antibodies were anti-centromere (40%) and anti-U1nRNP (33%), whereas no patient was positive for anti-Scl70 or anti-RNA-Polymerase III. In the majority of patients, an elevation of AP and GGT (75%, 60%) was observed, whereas transaminases were not

| Patients' characteristics (n=14) | |
|---|---|
| Age at time point of diagnosis of SSc (years) (n=12/14) | 44.5 ± 12.3 |
| Disease duration of SSc at time point of diagnosis of NRH (years) (n=13/14) | 8.2 ± 7 |
| Female gender | 9/13 (69.2%) |
| MRSS (n/51) at time point of diagnosis of NRH (n=4/14) | 10 ± 7 |
| **Skin involvement** | |
| Diffuse cutaneous SSc | 5/10 (50%) |
| Limited cutaneous SSc | 4/10 (40%) |
| None | 1/10 (1%) |
| **Peripheral vasculopathy** | |
| Raynaud's phenomenon | 14/14 /100%) |
| Digital ulcers ever | 7/7 (100%) |
| Active digital ulcers | 5/7 (71.4%) |
| **Nailfold capillaroscopy** | |
| Early | 0/5 (0%) |
| Active | 5/5 (100%) |
| Late | 0/5 (0%) |
| **Laboratory parameters** | |
| ANA | 9/11 (81.8%) |
| Anti-Centromere | 4/10 (40%) |
| Anti-Scl-70 | 0/7 (0%) |
| Anti-RNA-Polymerase III | 0/5 (0%) |
| Anti-U1nRNP | 2/6 (33.3%) |
| GOT elevated (n=8) | 2/10 (20%) |
| GPT elevated (n=6) | 3/9 (33.3%) |
| GGT elevated (n=9) | 6/10 (60%) |
| AP elevated (n=9) | 9/12 (75%) |
| Bilirubin elevated (n=7) | 0/10 (0%) |
| **Organ involvement** (most relevant findings) | |
| Lung | |
| Dyspnoea present | 8/8 (100%) |
| Pulmonary hypertension (on echocardiography) | 3/6 (50%) |
| Lung fibrosis (defined as FVC <60% or FVC <70% + presence of lung fibrosis on HRCT) | 5/8 (62.5%) |
| Gastrointestinal tract | |
| Esophageal symptoms | 9/9 (100%) |
| Intestinal symptoms | 4/6 (66.7%) |
| Stomach symptoms | 3/6 (50%) |
| Melaena | 4/6 (66.7%) |
| Haematemesis | 4/8 (50%) |
| **Ultrasound of the liver** | |
| Liver size normal | 6/8 (75%) |
| Surface smooth | 3/4 (75%) |
| Parenchyma homogeneous | 3/4 (75%) |
| Focal lesions | 0/5 (0%) |
| Portal vein flow normal | 4/5 (80%) |
| Ascites | 3/5 (60%) |
| Splenomegaly | 6/8 (75%) |
| **Fibroscan** | |
| Increased stiffness | 3/4 (75%) |
| **Complications** | |
| Portal hypertension (increased pressure) | 6/7 (86.7%) |
| Gastric varices (by gastroscopy) | 2/6 (33.3%) |
| Esophageal varices (by gastroscopy) | 7/10 (70%) |
| Variceal hemorrhage (by gastroscopy) | 4/9 (44.4%) |

increased. Melaena and hematemesis occurred in 66.7%, resp. 50% of patients. Ultrasound detected ascites (60%) and splenomegaly (75%), but no pathologic liver morphology, although an increased stiffness was diagnosed by fibroscan (75%). Portal hypertension was diagnosed in 85.7% with oesophageal varices (70%) and variceal haemorrhage (44.4%) as main complications.

**Conclusions:** NRH might represent a rare, yet clinically important, potentially life-threatening complication in SSc patients, especially in those with prominent vascular features and positivity for anti-centromere. Elevated levels of AP and GGT, ascites and splenomegaly by ultrasound and increased stiffness by fibroscan might alert to the presence of NRH. If suspected, the diagnosis should be confirmed by liver biopsy.

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## FRI0264 PREVALENCE, RISK FACTORS AND ASSESSMENT OF DEPRESSIVE SYMPTOMS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** The development of depressive symptoms is very common among patients with Systemic Sclerosis (SSc).[1]

**Objectives:** Evaluation of the prevalence of depressive symptoms among German SSc patients at our centre, identification of possible risk factors and analysis of the current standard of care in clinical settings.

**Methods:** 94 of 134 patients (82 women (87.2%), age 58.3 ± 13.6 years, BMI 24.5 ± 5.4 kg/m$^2$) in our study met the inclusion criteria of matching the ACR/EULAR 2013 classification criteria, being at least 18 years old, able to consent and having completed the Major Depression Inventory (MDI), Short Form 36 (SF-36®), Scleroderma Health Assessment Questionnaire (SHAQ), Brief Fatigue Inventory (BFI) and Physical Activity Questionnaire (IPAQ). The prevalence of depressive symptoms was evaluated using the MDI. The identifying potential of patient questionnaires for the risk of an SSc patient to suffer from depressive symptoms was evaluated using the SF-36® for quality of life, the SHAQ for disability, the BFI for fatigue and the IPAQ for activity. Discharge letters of the time when the patients were included were analyzed regarding the assessment and treatment of depressive symptoms and mental health. Clinical and para clinical parameters were measured according to standardized procedures. The data were analyzed with IBM SPSS® Statistics by using Chi-Square/Fisher-, Mann-Whitney-U-test, correlation and regression analysis.

**Results:** The prevalence of depressive symptoms according to the MDI score ≥20 was 22.3%. In the analysis of risk factors between two subgroups (MDI Score <20 and MDI Score ≥20), underweight (BMI <18.5 kg/m$^2$) turned out to be a significant risk factor (p=0.002) (Image 1). Also, there was a significant correlation between general health (SHAQ) (r=0.508, p=0.01), quality of life (SF 36®) (r= -0.769, p=0.01), fatigue (BFI) (r=0.721, p=0.01) and physical activity (IPAQ MET/min) (r= -0.331, p=0.01) with the level of the MDI score. The analysis of the current standard of care showed that the majority of the patients 84 (89.4%) were not assessed for depressive symptoms or mental health, including 19 with an MDI score ≥20. Mood disorders were diagnosed in 5 (5.3%) patients, 13 (13.8%) were treated with antidepressants and in 6 (6.4%) cases psychological intervention was carried out or suggested.

| Variable | MDI < 20 | MDI ≥ 20 | p |
|---|---|---|---|
| n | 73 | 21 | |
| Woman, n (%) | 61 (83.6) | 21 (100.0) | **0.047** |
| Age in years, mean ± SD | 58.1 ± 13.5 | 58.9 ± 14.4 | n.s |
| Disease duration in years, mean ± SD | 7.8 ± 5.6 | 6.8 ± 6.8 | n.s |
| Body-Mass-Index, mean ± SD | 24.5 ± 4.3 | 24.7 ± 8.5 | n.s |
| Underweight, n (%) | 1 (1.4) | 5 (23.8) | **0.002** |
| MDI score, mean ±SD | 9.5 ± 5.2 | 28.7 ± 6.0 | |
| SHAQ score, mean ± SD | 0.85 ± 0.59 | 1.4 ± 0.67 | **0.003** |
| SF-36 score, mean ± SD | 59.9 ± 14.4 | 36.2 ± 13.3 | **0.000** |
| SF Mental Health total score, mean ± SD | 67.8 ± 15.7 | 38.7 ± 10.6 | **0.000** |
| IPAQ MET/min, mean ± SD | 3114 ± 2327 | 1760 ± 1954 | **0.048** |
| BFI score, mean ± SD | 3.4 ± 1.8 | 6.0 ± 1.7 | **0.000** |

**Table 1** Analysis of risk factors between two subgroups (MDI < 20; MDI ≥ 20)

**Conclusions:** There is a high prevalence of depressive symptoms, which should be kept in mind when treating patients with SSc. Special attention should be paid to weight loss and fatigue, results in the SF-36®, SHAQ and IPAQ. The mental health should be assessed during consultations on a regular basis. The questionnaires applied in this study could be used as indicators for the risk of an SSc patient to suffer from depressive symptoms with the BFI and SF-36 being the most sensitive ones.

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## FRI0265 SELEXIPAG IN RAYNAUD'S PHENOMENON SECONDARY TO SYSTEMIC SCLEROSIS: A RANDOMISED, PLACEBO-CONTROLLED, PHASE II STUDY

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**Background:** Raynaud's phenomenon (RP) occurs in >95% of patients (pts) with systemic sclerosis (SSc) and contributes to digital ischaemia that may lead to digital ulcers (DUs) and gangrene.[1,2] Empirical treatment of SSc-associated RP includes oral vasodilators, particularly calcium channel blockers and intermittent intravenous prostacyclin analogues.[3,4] However, there is a need to identify oral therapies that are more efficacious than those currently available.

**Objectives:** To determine the activity of selexipag, an oral, selective, prostacyclin receptor agonist, on RP attack frequency in pts with SSc.

**Methods:** The study comprised a placebo single-blind run-in phase of 2–4-weeks followed by an 8-week double-blind treatment phase. Pts (≥18 years) with definite SSc and ≥7 RP attacks on ≥5 days in the week before randomisation were assigned 1:1 to selexipag or placebo. Study drug was titrated to an individual highest tolerated dose (200–1600 μg BID). The primary efficacy endpoint was the number of RP attacks per week in the maintenance phase (5 weeks) as determined from the pt's daily entries in the eDiary, and was analysed using a negative binomial model adjusted for the baseline number of RP attacks. Other outcomes included Raynaud Condition Score (RCS),[5] RP attack duration, new DU frequency, and treatment-emergent adverse events (AEs).

**Results:** Baseline (BL) characteristics were comparable between the groups (selexipag n=36, placebo n=38). No significant difference in effect was demonstrated for selexipag vs placebo (observed average number of RP attacks per week during the maintenance phase: 18.0 [vs 22.4 at BL, selexipag, n=27], 14.2 [vs 21.5 at BL, placebo, n=32]), adjusted mean treatment difference 3.43 in favour of placebo. During the maintenance phase, 63.0% (selexipag) and 81.3% (placebo) of pts had an improvement in the average number of RP attacks per week vs BL. No significant treatment effect was observed on RCS, RP attack duration and new DU frequency. At least one AE occurred in 100% (selexipag) and 86.8% (placebo) of pts; ≥1 prostacyclin-associated AE occurred in 91.7% (selexipag) and 55.3% (placebo) of pts. AEs were mostly reported as mild (16.7% selexipag pts, 34.2% placebo pts) or moderate (61.1% selexipag pts, 44.7% placebo pts) in intensity.

**Conclusions:** The primary efficacy endpoint was not met (no reduction in number of RP attacks per week for selexipag vs placebo). The robust study design may nevertheless provide a template for future studies in RP. The marked reduction in attack frequency on placebo may underlie failure to show additional potential benefit with selexipag, which should be considered when designing future studies in RP. The safety profile of selexipag was similar to previous studies,[6] with no new safety signals identified.

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## FRI0266 LONG-TERM EFFICACY AND TOLERABILITY OF MYCOPHENOLATE MOFETIL THERAPY IN DIFFUSE SCLERODERMA SKIN DISEASE

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**Background:** Skin involvement in diffuse systemic sclerosis (dSSc) is progressive and can be extremely debilitating, however, treatment options remain limited. Although many disease modifying agents have been examined in dSSc, only cyclophosphamide has randomised controlled data suggesting efficacy in the treatment of skin thickening.[1] Several observational studies suggest benefit in skin disease with mycophenolate mofetil (MMF) therapy;[2] which, given its more favourable side effect profile, would be a preferable alternative to cyclophosphamide.
**Objectives:** To assess the long-term efficacy and tolerability of MMF in patients with dSSc in the Australian Scleroderma Cohort Study.
**Methods:** The Australian Scleroderma Cohort Study is a longitudinal study of disease outcomes in patients with SSc. Patients with dSSc and baseline modified Rodnan skin score (mRSS) $\geq$12 who were treated for a minimum twelve months with MMF for the primary indication of skin disease were included, and their prospectively collected data were retrieved. The proportion with clinically significant improvement in skin scores (defined as reduction in mRSS$\geq$4 from baseline) and stable disease (change in mRSS $<$4) were compared to those with clinical deterioration (increase in mRSS$\geq$4) as well as adverse effects resultant of therapy.
**Results:** 74 participants were identified and of these, 44 met inclusion criteria. The mean age of participants was 53±12 years and 36 (82%) were female. The mean duration of disease at MMF commencement was 4.9±4.3 years, with 23 participants (52%) commencing MMF within 2.5 years. The mean duration of therapy was 2.7±1.7 years. The mean mRSS at baseline was 25.3 with a reduction of 3.7 (p-value $<$0.01) after one year of therapy and a mean total reduction in mRSS of 8.0 (p-value $<$0.01). Response to treatment was not affected by disease duration at onset of MMF therapy as expected. Over the first year of therapy, 24 participants (48%) demonstrated clinically significant improvement in skin scores, increasing to 92% clinically improved after four years of therapy. MMF was well tolerated, with two participants (5%) ceasing the drug due to adverse effects.
**Conclusions:** MMF was associated with improved skin scores and was well tolerated in the treatment of dSSc. Given the natural history of dSSc where skin involvement can spontaneously improve, placebo-controlled studies are required to confirm whether improvement can be attributed to MMF therapy.
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## FRI0267 MYCOPHENOLATE MOFETIL VERSUS ORAL CYCLOPHOSPHAMIDE IN SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE: SCLERODERMA LUNG STUDY II

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**Background:** Progressive Interstitial lung disease (ILD) occurs in $\sim$ 40% of scleroderma (SSc) patients and is the leading cause of death. Oral CYC for 1 year in SSc-ILD led to modest but significant improvements in lung function and dyspnea vs. placebo (Tashkin, NEJM, 2006) but the benefits were lost over the ensuing year and drug therapy was not extended due to the known toxicity profile of CYC. (Tashkin AJRCCM 2007). Preliminary data from uncontrolled clinical studies suggest that MMF may be an effective and safer immunosuppressive therapy than CYC for SSc-ILD.
**Objectives:** A randomized controlled trial was performed to determine the efficacy, safety and tolerability of mycophenolate mofetil (MMF) administered for two years compared with CYC administered for one year followed by matching placebo for SSc-ILD.
**Methods:** 142 patients with pulmonary function and high-resolution computed tomography (HRCT) defined SSc-ILD were randomized at 14 centers to receive MMF or CYC. The primary endpoint, change in forced vital capacity (FVC%$>$predicted) over 24 months, was assessed using a joint longitudinal model (Elashoff, Statist Med 2006).
**Results:** 126 patients (63 MMF; 63 CYC) had $\geq$3 months of outcome data and were included in the primary analysis. A greater number of patients on CYC than on MMF prematurely withdrew from (32 vs 20) and failed treatment (2 vs 0), and the time to stopping treatment was significantly shorter in the CYC arm (p=0.019). At 24-months, the adjusted FVC%$>$predicted had improved by 2.17 in the MMF arm (95% CI, 0.53–3.84; p$<$0.01) and 2.86 in the CYC arm (95% confidence interval 1.19–4.58; p$<$0.001) with no significant between-treatment difference (p=0.24). Significant within- (but not between-) treatment improvements in skin score, dyspnea and whole-lung HRCT scores were also observed. Leukopenia and thrombocytopenia occurred more often with CYC (p$<$0.05). Sixteen deaths occurred (11 CYC; 5 MMF) with most due to underlying disease.
**Conclusions:** In this first RCT comparing MMF with CYC in SSc-ILD, both agents appeared to have comparable efficacy but MMF was better tolerated with significantly fewer premature withdrawals from treatment and fewer adverse events. These findings support the increasingly common clinical practice of prescribing MMF for this disease.
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## FRI0268 SAFETY AND EFFICACY OF SUBCUTANEOUS TOCILIZUMAB IN EARLY SYSTEMIC SCLEROSIS: RESULTS FROM THE OPEN-LABEL PERIOD OF THE FASSCINATE TRIAL

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**Background:** Systemic sclerosis (SSc) is a debilitating disease with few treatment options. Interleukin-6 (IL-6) appears to play a role in SSc pathogenesis.[1,2] Data from the 48-week, double-blind (DB), placebo (PBO)-controlled period of the faSScinate trial were previously presented,[3] and open-label (OL) data are presented herein.
**Objectives:** To assess safety and efficacy of tocilizumab (TCZ) in SSc patients during 48 weeks of OL TCZ treatment.
**Methods:** Patients $\geq$18 y with active SSc ($\leq$5-year duration, modified Rodnan skin score [mRSS] 15–40, and elevated acute-phase reactants) received OL TCZ 162 mg SC weekly from week 48 to week 96. Change from baseline in mRSS, patient-reported outcomes (PROs), and FVC at week 96 were exploratory measures. Observed means used all available data.
**Results:** In total, 27/43 (63%) TCZ and 24/44 (55%) PBO patients completed week 96. Baseline (BL) characteristics were similar at BL and at entry into the OL period. Patients who switched from PBO→OL TCZ showed improvement in observed mean change from BL in mRSS at week 96 (–9.4) relative to the end of the 48-week DB period (–3.1). In patients initially randomized to TCZ (TCZ→OL TCZ), mean change in mRSS was –5.6 at week 48 and –9.1 at week 96. In the OL period, improvements in PROs were noted at week 96 vs week 48 in the PBO→OL TCZ group (mean [SD] change from BL at week 96 vs week 48 in HAQ-DI: –0.3 [0.4] vs 0.2 [0.4]; Patient Global VAS: –23.8 [36.0] vs –4.0 [24.0]; FACIT-Fatigue:11.3 [12.8] vs 1.4 [7.6]). In patients who completed the study, none experienced a $>$10% decline in % predicted FVC during the OL period on TCZ therapy. Rates (95% CI) of serious adverse events/100 patient-years (PY) in the DB period were 76.1 (50.6, 110.0) in PBO patients and 66.7 (42.3, 100.1) in TCZ patients and were 36.0 (18.0, 64.4) in PBO→OL TCZ patients and 16.5 (5.4, 38.5) in TCZ→OL TCZ patients in the OL period. Rates (95% CI)/100PY of serious infections in the DB period were 10.9 (3.0, 27.9) in PBO patients and 34.8 (18.0, 60.8) in TCZ patients. In the OL period they were 19.6 (7.2, 42.7) in PBO→OL TCZ patients and 0.0 (0.0, 12.2) in TCZ→OL TCZ patients. No deaths occurred in the OL period (deaths in DB period: 3 TCZ, 1 PBO).
**Conclusions:** Although OL data have to be interpreted with caution, efficacy and safety in PBO-treated patients who switched to OL TCZ were generally similar to those observed in patients randomized to TCZ in the DB period. Results over 96 weeks of TCZ treatment suggest maintenance of the clinical response for mRSS in SSc patients. Serious infection rates increased in PBO patients after they switched to OL TCZ. Long-term safety was consistent with the natural history of SSc and the safety profile of TCZ.

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**Disclosure of Interest:** D. Khanna Grant/research support from: NIH/NIAMS, NIH/ NIAID, Bayer, BMS, Consultant for: Bayer, BMS, Genetech/Roche, GSK, Genkyotex, Sanofi-Aventis, Actelion, Gilead, C. Denton Grant/research support from: GSK, Actelion, CSL Behring, Consultant for: GSK, Bayer, Actelion, Roche, Merck-Serono, MedImmune, A. Jahreis Shareholder of: Roche, Employee of: Genentech, J. van Laar Grant/research support from: MSD, Consultant for: MSD, Roche, Pfizer, BMS, Eli Lilly, L. Burke Employee of: Roche Products Ltd., H. Spotswood Shareholder of: Roche, Employee of: Roche Products Ltd., C. Lin Shareholder of: Amgen, Roche/Genentech, Employee of: Genentech, J. Pope Grant/research support from: Roche, Bayer, BMS, Consultant for: Roche, Actelion, Bayer, BMS, Y. Allanore Grant/research support from: Bristol-Myers Squibb, Roche/Genentech, Inventiva, Pfizer, Sanofi, and Servier, Consultant for: Actelion, Bayer, Roche/Genentech, Inventiva, Medac, Pfizer, Sanofi, Servier, and UCB, U. Müller-Ladner Consultant for: Roche, Chugai Pharma, Speakers bureau: Roche, Chugai Pharma, J. Siegel Shareholder of: Roche, Employee of: Genentech, D. Furst Grant/research support from: AbbVie, Actelion, Amgen, BMS, Gilead, GSK, NIH, Novartis, Pfizer, Roche/Genentech, UCB, Consultant for: AbbVie, Actelion, Amgen, BMS, Cytori, Janssen, Gilead, GSK, NIH, Novartis, Pfizer, Roche/Genentech, UCB
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## FRI0269 DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC) REFERRAL AND DIAGNOSIS: RESULTS OF A SURVEY OF HEALTHCARE PROVIDERS

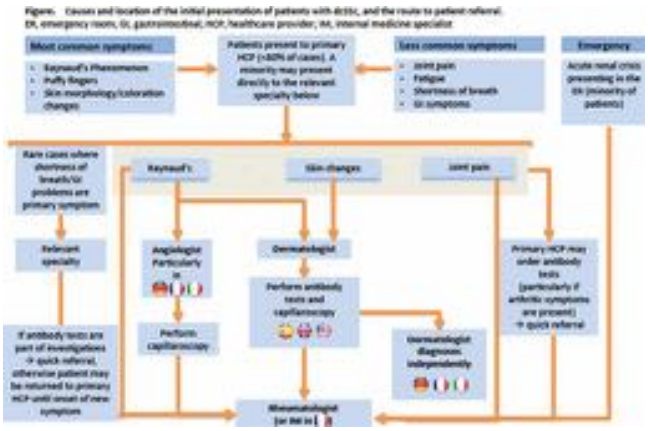
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**Background:** Diffuse cutaneous systemic sclerosis (dcSSc) is a severe subset of SSc, a chronic rare autoimmune connective tissue disease associated with high morbidity and mortality, and reduced quality of life. There are few treatments approved for dcSSc. Using semi-structured discussions, our objective was to gain better insight into clinical practice regarding referral and diagnosis of patients with dcSSc in different geographic regions.
**Methods:** Physicians participated in 60- or 30-minute interviews, following a discussion outline, to determine how dcSSc patient care is structured in the USA and EU. Physicians were asked to identify key steps in the patient pathway, typical patient presentation, and the diagnostic, treatment, and follow-up processes used, and those responsible for their implementation.
**Results:** Physicians in six countries (France, Germany, Italy, Spain, UK, and USA) were interviewed; 84 60-minute interviews with rheumatologists (or internal medicine specialists in France), and 40 30-minute interviews with dermatologists were conducted. Patient care was coordinated mostly by rheumatologists (except in France, where internal medicine specialists can be responsible), or to a lesser degree by dermatologists (in Germany, France, Italy) (Figure). Specialist centers are not well defined, and do not exist in all countries; therefore, most patients continued their treatment in the hospital where first diagnosed. Patients were slow to present to primary healthcare providers (HCPs), with presentation taking on average 6 months to 1 year, as they considered very early dcSSc symptoms to be trivial. Once referred to a rheumatologist, clinical evaluation and antibody testing led to quick diagnosis; however, dcSSc awareness among primary HCPs is variable, and delayed referral to a rheumatologist is common. Use of the 2013 ACR/EULAR updated classification of SSc, and the modified Rodnan skin score (mRSS) were limited to specialist centers and clinical trials, rather than daily practice, although physicians follow a similar diagnostic process. Where mRSS was measured (n=46 in this survey, predominantly by rheumatologists), patients had an mRSS of 10–22 at diagnosis, and >50% of diagnosed patients had an mRSS of ≥15. Physicians were vigilant for signs of organ involvement, but the priority given to skin changes differed according to specialty.
**Conclusions:** Improved patient and primary HCP awareness of dcSSc could lead to earlier referral to a rheumatologist or dermatologist and the avoidance of delayed diagnosis. Specialized centers need better definition in most countries. Use of the mRSS at diagnosis and follow-up may help to monitor disease progression.
**Disclosure of Interest:** D. Khanna Grant/research support from: NIH/NIAMS, NIH/ NIAID, Bayer, BMS, Consultant for: Bayer, BMS, Genetech/Roche, GSK, Genkyotex, Sanofi-Aventis, Actelion, Gilead, Employee of: University of Michigan, Y. Allanore Grant/research support from: Bristol-Myers Squibb, Roche/Genentech, Inventiva, Pfizer, Sanofi, Servier, Consultant for: Actelion, Bayer, Roche/Genentech, Inventiva, Medac, Pfizer, Sanofi, Servier, UCB, C. Denton Grant/research support from: Actelion, GSK, Novartis, CSL Behring, Consultant for: Bayer, Roche, GSK, Actelion, Inventiva, CSL Behring, Takeda, Merck-Serono, Medimmune, Biogen, M. Matucci-Cerinic Consultant for: Actelion, GSK, Pfizer, BMS, J. Pope Grant/research support from: Actelion, Bayer, Consultant for: Actelion, Bayer, B. Hinzmann Shareholder of: Bayer Pharma AG, Employee of: Bayer Pharma AG, S. Briody: None declared, J. de Oliveira Pena Employee of: Bayer HealthCare Pharmaceuticals Inc., O. Distler Grant/research support from: Actelion, Pfizer, Sanofi-Aventis, Bayer, Consultant for: Ergonex, United BioSource, Biovitrium, Novartis, Biogen Idec, Inventiva
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## FRI0270 PATIENT PERCEPTION OF DISEASE BURDEN IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC)

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**Background:** DcSSc is associated with high morbidity and mortality, and reduced quality of life. Patient priorities are rarely discussed, with physicians focusing on organ involvement. Using discursive approaches and ethnography, we evaluated the impact of dcSSc on patients' daily lives, and examined how disease burden shapes patient outlook.
**Methods:** Patients were recruited via healthcare professionals (HCPs) or patient associations. In France, Italy, the UK and USA, patients filmed short (~15-minute) daily video diaries about their lives over 7 days. On Days 1 and 7, patients participated in a moderator-led discussion of their experiences, and an observation session. In Germany and Spain, patients participated in 60-minute telephone interviews. Video footage and transcribed discussions were reviewed, and the data were categorized and assessed for themes, patterns, and indicators of emotion, ambivalence, and conflict.
**Results:** Twenty-three patients (mean age 54 years; 83% women) participated. Of these, 17 made video diaries, and 6 took part in telephone interviews. The majority of video diaries and interviews took place in patients' homes; on average 5.25 hours of video footage were collected per patient.





Results show that time to diagnosis was often delayed, as patients trivialized symptoms and HCPs attributed symptoms to other causes. Patients had a poor understanding of their diagnosis, and rarely received patient information. DcSSc patients had a high treatment burden; on average this patient sample received 10 tablets of prescribed drugs daily. Importantly, while patients were aware of the seriousness of organ involvement, they reported that skin changes, pain, and fatigue had a dominant effect on daily life, impairing their ability to perform routine tasks. Skin tightening in the lower limbs and feet lead to deformity and loss of mobility, while Raynaud's phenomenon, calcinosis, and digital ulcers caused significant pain and loss of function. Changes in appearance lead to embarrassment, social withdrawal, and depression. Patients experienced dcSSc as a series of losses, including independence and self-esteem, and the unpredictability of the disease made acceptance of the condition difficult (Figure 1). Moreover, patients tended to have small support networks and support services were not offered as part of standard care.

**Conclusions:** Patients with dcSSc had high treatment and emotional burdens, with skin complications, pain, and fatigue profoundly affecting their lives. Patients placed the greatest emphasis on these issues rather than the possibility of organ involvement. There is an unmet need for patient information at the time of diagnosis, and for emotional support services throughout their journey with dcSSc. Directing patients to websites such as SSc patient organizations may be helpful.

**Disclosure of Interest:** D. Khanna Grant/research support from: NIH/NIAMS, NIH/ NIAID, Bayer, BMS, Consultant for: Bayer, BMS, Genetech/Roche, GSK, Genkyotex, Sanofi-Aventis, Actelion, Gilead, Employee of: University of Michigan, Y. Allanore Grant/research support from: Bristol-Myers Squibb, Roche/Genentech, Inventiva, Pfizer, Sanofi, Servier, Consultant for: Actelion, Bayer, Roche/Genentech, Inventiva, Medac, Pfizer, Sanofi, Servier, UCB, C. Denton Grant/research support from: Actelion, GSK, Novartis, CSL Behring, Consultant for: Bayer, Roche, GSK, Actelion, Inventiva, CSL Behring, Takeda, Merck-Serono, Medimmune, Biogen, M. Matucci-Cerinic Consultant for: Actelion, GSK, Pfizer, BMS, J. Pope Grant/research support from: Actelion, Bayer, Consultant for: Actelion, Bayer, B. Hinzmann Shareholder of: Bayer Pharma AG, Employee of: Bayer Pharma AG, S. Briody: None declared, J. de Oliveira Pena Employee of: Bayer HealthCare Pharmaceuticals Inc., O. Distler Grant/research support from: Actelion, Pfizer, Sanofi-Aventis, Bayer, Consultant for: Ergonex, United BioSource, Biovitrium, Novartis, Biogen Idec, Inventiva

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## FRI0271 PERFORMANCE OF MODIFIED RODNAN SKIN SCORE IN EARLY DIFFUSE CUTANEOUS SCLERODERMA–ANALYSIS FROM 4 COHORTS

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**Background:** The modified Rodnan skin score (mRSS) is used as a primary outcome measure in clinical trials of dcSSc. EUSTAR analysis has proposed that a lower mRSS and earlier disease duration are associated with progressive disease, as defined by worsening mRSS [1].

**Objectives:** 1. To find an optimal cut off for worsening mRSS in 4 cohorts of dcSSc, and 2. To assess if presence of anti-RNA polymerase III [RNAP] vs. anticentromere /or anti-SCL-70 is associated with different mRSS cut off for worsening disease.

**Methods:** We used 4 cohorts with early dcSSc (defined as $\leq$60 months from 1st non-RP sign or symptom) – 2 US cohorts [Combined Response Index in Systemic Sclerosis [CRISS] and Prospective Registry in Early Systemic Sclerosis [PRESS]], the UK Royal Free Hospital [RFH] cohort, and the Australian Scleroderma Interest Group [ASIG] cohort. Inclusion criteria included dcSSc diagnosed by a scleroderma physician, mRSS data at 2 time points (12±3 months apart), and availability of disease duration (defined as 1st non Raynaud phenomenon sign or symptom). Worsening of skin fibrosis was defined as increase in mRSS $>$5 points and $\geq$25% from baseline to 2nd visit.

To identify the optimal cut point of baseline MRSS that yields the highest sensitivity for worsening disease, we developed the ROC curves. For worsening of mRSS, we fitted logistic regression model with worsening as outcome variable and a binary variable of baseline mRSS cut point as predictor. We also explore the differences between the proportion of patients with worsening of mRSS among the patients with presence of RNAP vs. anticentromere /or anti-SCL-70 and tested using proportion z-test.

**Results:** There were 235 patients with early dcSSc included in the analysis. Mean (SD) disease duration was 26.61 (14.67) months, median=23.67 months. We evaluated 3 cut points for disease duration based on inclusion criterion from recent clinical trials: $\leq$24, 36, and 60 months. For all disease durations, approximately 10.5% of patients had mRSS worsening at 1-year period. A mRSS cut off of 26 had the highest probability of worsening (Table). mRSS of $\leq$26 was able to enrich worsening mRSS from 10.5% to 15.0% for different cut points but excluded 33–35% of patients with early dcSSc. 64 patients (27.23%) had RNAP and 48 (20.43%) had anti-centromere and anti-SCL-70 and there was no difference in cut off for worsening of mRSS at 1-year.

**Conclusions:** In this preliminary analysis, a mRSS$\leq$26 was the optimal cut point for worsening disease in 4 cohorts with dcSSc. This threshold gained an additional 5% of patients who worsened but excluded 33–35% of patients with early dcSSc.

**References:**
[1] Maurer B Ann Rheum Dis 2015

**Disclosure of Interest:** None declared

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## FRI0272 EVALUATION OF BLEOMYCIN INDUCED RAYNAUD'S PHENOMENON AND SYSTEMIC SCLEROSIS VASCULOPATHY IN GERM CELL TUMOUR PATIENTS

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**Background:** Bleomycin forms part of the chemotherapy regimen ("BEP") for germ cell testicular cancer (1). The drug is known to cause Raynaud's phenomenon (RP) in up to 25% of men who receive the BEP regime (2). RP is also a feature of systemic sclerosis (SSc), a connective tissue disease that is studied in a mouse model using bleomycin as the agent to induce pulmonary fibrosis (3,4). There have been isolated cases where patients, treated for lymphoma with bleomycin containing regimens, have developed SSc (5,6) thus evaluation of RP and SSc is warranted in testicular cancer patients.

**Objectives:** In men with germ cell testicular cancer who have received BEP in Leeds: 1) Evaluate the prevalence, nature, and onset of RP. 2) Compare the characteristics of those that developed RP with those that did not. 3) Determine whether those reporting RP have microvascular features of SSc.

**Methods:** A patient questionnaire completed retrospectively by men receiving follow up post BEP treatment was used to collect data on the prevalence, nature, and onset of RP. A subset of patients reporting RP then underwent capillaroscopy and thermography.

**Results:** 24 eligible men completed the questionnaire. RP was prevalent in 13 of the men (54% CI 0.34–0.74), usually bilaterally (92%) and accompanied by sensory disturbance (92%). Onset was most commonly reported to be following chemotherapy completion (77%). There was no association between RP and marital status, smoking status, tumour type or total bleomycin dose (p values $>$0.05). No evidence was found to suggest SSc in the patients who underwent capillaroscopy and thermography. Hallmark capillary changes indicative of SSc were absent at the nailbed. The mean (SD) recovery of the fingers back to baseline temperature was 93.8 (14.57)% at ten minutes post cold challenge and the mean (SD) re-warming rate of the fingers was 0.925 (0.17) ℃/minute.

**Conclusions:** The prevalence of RP in this patient group was higher than expected. The absence of SSc vasculopathy was reassuring, however not all of the men reporting RP underwent Rheumatology assessment. The retrospective nature and small sample size of this study are key limitations but our findings justify further prospective evaluation of the prevalence and the basis for bleomycin-associated RP.

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[4] Matucci-Cerinic M, Kahaleh B, Wigley F M. Evidence That Systemic Sclerosis Is a Vascular Disease. Arthritis & Rheumatism 2013; 65(8): 1953–1962.
[5] Passiu G, Cauli A, Atzeni F, et al. Bleomycin-induced Scleroderma: Report of a Case with a Chronic Course Rather Than the Typical Acute/Subacute Self-Limiting Form. Clinical Rheumatology 1999; 18: 422–424.
[6] Kin K H, Yoon T J, Oh C W, Ko G H, Kim T H. A Case of Bleomyin-induced Scleroderma. Journal of Korean Medical Science 1996; 11(5): 454–456.

**Abstract FRI0271** – Table 1

| | N | Disease duration $\leq$24 months | N | Disease duration $\leq$36 months | N | Disease duration $\leq$60 months |
|---|---|---|---|---|---|---|
| All subjects without mRSS cut point | 123 | 13 (10.57%) | 179 | 19 (10.61%) | 235 | 25 (10.64%) |
| Proportion who worsen with mRSS $\leq$26 (worsen/total cohort with mRSS $\leq$26) | 79 | 15.19% | 119 | 15.13% | 155 | 15.48% |
| Probability of worsening for mRSS $\leq$26 (worsen with mRSS$\leq$26/all patients who worsened) | 13 | 92.31% | 19 | 94.74% | 25 | 96.0% |
| Probability of improvement with mRSS $\leq$26 (improved*/total cohort with mRSS $\leq$26) | 29 | 38.66% | 46 | 38.66% | 60 | 38.71% |

*Defined as mRSS improvement of $>$5 units and $\geq$25%.

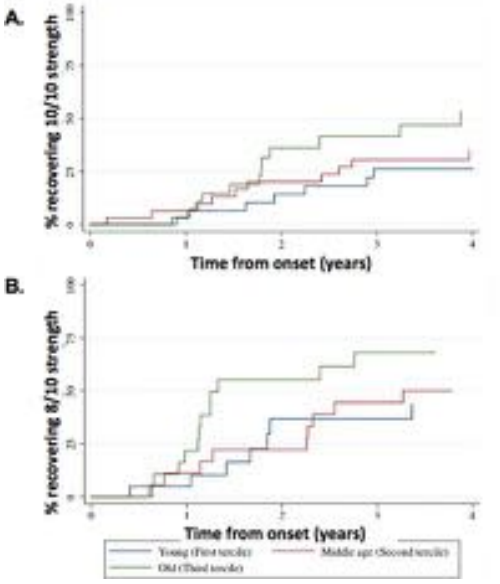
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1826

## FRI0273 SLOW RECOVERY OF MUSCLE STRENGTH IN YOUNG ANTI-HMG-COA REDUCTASE POSITIVE MYOPATHY PATIENTS

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**Background:** Anti-HMG-CoA reductase (HMGCR) myopathy is characterized by proximal muscle weakness, necrosis of muscle fibers on biopsy, elevated serum creatine kinase (CK) levels, and anti-HMGCR autoantibodies[1]. Although statins are associated with anti-HMGCR myopathy in patients over 50 years old, some patients have no history of statin exposure. In a previous longitudinal analysis including 17 patients with anti-HMGCR myopathy followed over a mean of 26 months, we found that only statin-exposed subjects had improvements in strength and CK with treatment during the observed time period[2].
**Objectives:** Here, we studied factors influencing disease progression in an expanded cohort of anti-HMGCR patients treated with immunosuppressive therapy.
**Methods:** A retrospective cohort study was conducted with all anti-HMGCR positive patients enrolled in the Johns Hopkins Myositis Cohort between May 2002 and June 2015. Anti-HMGCR antibodies were screened for by ELISA and verified by immunoprecipitating in vitro-transcribed and translated HMGCR protein. Anti-HMGCR levels, CK levels, and proximal muscle strength (on a 0–10 scale) were assessed. A multilevel linear regression model was used to identify clinical factors that influence recovery of strength over time.
**Results:** We identified 104 anti-HMGCR positive patients, 77 (74%) of whom were exposed to statins. The clinical characteristics for each of three age groups divided into tertiles (<51, 51–61 and >61 years old) were similar except statin exposure, which was 97% for the older group compared to 37% for the younger group of patients. There was no statistical significant difference of the CK, anti-HMGCR antibody titers and muscle strength between the different groups.
We analyzed factors that might influence recovery of muscle strength in 81 patients with more than one visit (mean follow-up time of 2.7 years; SD 2.6, 0–12 years). Older age at onset and greater weakness at first clinic visit were associated with faster recovery times in univariate and multivariate analyses, whereas statin exposure had no statistically significant effect.
We identified a subgroup of young, African American, statin naive women who were refractory to treatment, compared to older patients of both races.

Kaplan-Meier survival estimates show that a higher proportion of older patients recover 10/10 muscle strength (Figure 1A) and at least 8/10 muscle strength (Figure 1B) after 4 years of treatment:

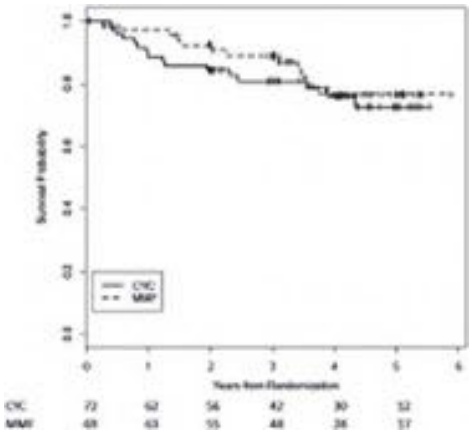



**Conclusions:** The current study suggests that older age, rather than statin exposure, predicts faster recovery after initiating immunosuppressive treatment for anti-HMGCR myopathy. Four years after disease onset, ~50% of patients older than 61, but only ~25% less than age 51, had recovered full strength. We also found that a subset of young, African American women were refractory to treatment. Some of these had progressive weakness despite aggressive immunosuppressive therapy.
**References:**
[1] Mammen A, et al., Arthritis and Rheumatology, 2011
[2] Werner J, et al., Arthritis and Rheumatology, 2012
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1106

## FRI0274 PREDICTORS OF SURVIVAL IN PATIENTS WITH SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE ENROLLED IN THE SCLERODERMA LUNG STUDY II

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**Background:** The results of the first randomized controlled trial comparing cyclophosphamide (CYC) and mycophenolate (MMF) for systemic sclerosis-related interstitial lung disease (SSc-ILD) demonstrated that MMF had improved safety and tolerability profiles compared with CYC over 2 years (Tashkin ACR Abstract 2015); however, the comparative long-term effects of these agents are unknown.
**Objectives:** To compare survival of patients randomized to MMF versus CYC in Scleroderma Lung Study (SLS) II and to determine which baseline factors predict survival.
**Methods:** All SSc-ILD patients in SLS II (Comparing 2 years of MMF versus 1 year of CYC followed by 1 year of placebo) were eligible for inclusion. During the 2-year trial, mortality outcomes were collected by the individual study sites and sent to the SLS II morbidity and mortality committee for adjudication. Following the trial, deaths were ascertained from reports by the next of kin or the coordinator/principal investigator at the study site, as well as reports from online obituaries and the National Death Index. Kaplan Meier curves were generated and the log-rank test was used to compare survival rates. Cox proportional hazards modeling was used to determine which baseline demographic and disease features, as well as which molecular markers predict survival.
**Results:** Of the 142 patients in SLS II, contact was established (or mortality was confirmed) with 88%. The median follow up was 3.3 years from randomization. 16 deaths occurred during the 2-year trial (5 MMF; 11 CYC), and an additional 11 deaths occurred after the trial (6 MMF; 5 CYC). One patient underwent lung transplantation (CYC). The majority of deaths were deemed to be due to respiratory failure (44%), followed by congestive heart failure (7%) and lung cancer (7%). Patients assigned to MMF had a trend for improved survival at 1- (HR 3.8; $P$=0.09), 2- (HR 2.1; $P$=0.1), and 3-years (HR 1.9; $P$=0.1) post-randomization. However, by 3.5 years, there was no difference in survival between treatment arms (Figure 1). In univariate analysis, male gender (HR 2.2; $P$=0.04), age (HR 1.1; $P$<0.001), disease duration (HR 0.7; $P$=0.02), and baseline DLCO (HR 0.9; $P$=0.02), were associated with increased risk of death. Of the molecular markers, higher baseline level of the chemokine CCL18 was associated with increased mortality (HR=1.003; $P$=0.05). In the multivariate analysis, the best 1-variable model for predicting survival was age (HR 1.1; $P$<0.001). The best 2-variable model for predicting survival was age (HR 1.1; $P$<0.001) and disease duration (HR 0.7; $P$=0.02), and the best 3-variable model for predicting survival was age (HR 1.1; $P$<0.001), disease duration <3 years from the onset of the first non-Raynaud's symptom (HR 4.6; $P$=0.008), and baseline FVC (HR 0.9; $P$=0.004).

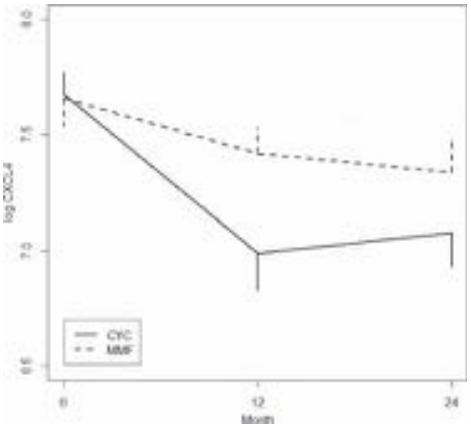



**Conclusions:** Treatment with MMF for SSc-ILD appears to be associated with improved survival during the first 3 years following treatment initiation; however, beyond this time frame, there is no clear MMF survival advantage. Of the factors associated with SSc-ILD survival in prior observational cohorts, increased age, shorter disease duration, and lower baseline FVC were the most important predictors of mortality in SLS II participants.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2999

FRI0275 **CHANGE IN CXCL4 LEVELS MAY PREDICT TREATMENT RESPONSE IN SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE (SSC-ILD)**

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**Background:** Baseline circulatory levels of the chemokine CXCL4 have been associated with both extent and progression of SSc-ILD[1]. No studies have examined whether changes in CXCL4 levels may predict progression of SSc-ILD.
**Objectives:** To determine whether CXCL4 levels change in response to treatment for SSc-ILD and to explore whether these changes predict future progression of SSc-ILD.
**Methods:** All SSc-ILD patients enrolled in the Scleroderma Lung Study (SLS) II (Comparing 2 years of mycophenolate [MMF] versus 1 year of cyclophosphamide [CYC] followed by 1 year of placebo) were included. CXCL4 levels were measured at baseline, 12 and 24 months using validated, commercially available ELISA kits (Human CXCL4/PF4 Quantikine Kit - R&D Systems). CXCL4 levels were log-transformed. Spearman's correlations were performed to examine the relationship between the change in CXCL4 levels from baseline to 12 months and the change in the FVC from baseline to 18, 21, and 24 months. A mixed effects model was created to determine whether the change in CXCL4 from baseline to 12 months predicted the course of the FVC from 12 to 24 months, while controlling for treatment arm and baseline ILD severity. A T-test was used to compare the change in CXCL4 from baseline to 12 months between patients who experienced a clinically meaningful improvement in FVC at 24 months (defined as a $\geq$5% increase in FVC from baseline) and those who did not.
**Results:** Of the 142 patients in SLS II, 136 had CXCL4 levels measurements performed. The mean FVC% predicted for this cohort was 66.5 and the mean disease duration was 2.5 years. CXCL4 levels decreased significantly in both treatment arms at 12 months (Mean difference: CYC -0.71 [1.4], $P<0.001$; MMF -0.32 [0.86], $P=0.006$) and at 24 months (Mean difference: CYC -0.53 [1.3], $P<0.001$; MMF -0.43 [1.1], $P=0.01$). There was no significant difference in the change in CXCL4 levels between treatment groups at 12 ($P=0.12$) or 24 months ($P=0.38$) (Figure 1). There was a trend for a significant relationship between the change in CXCL4 level at 12 months and the change in the FVC from baseline to 18 months (r= -0.2; $p=0.06$), 21 months (r= -0.21; $p=0.06$), and 24 months (r=-0.18; $p=0.08$). In the mixed effects model, the change in CXCL4 level at 12 months significantly predicted the course of the FVC from 12 to 24 months (Estimate -1.2; Std Err 0.6; $p=0.04$). Patients with a $\geq$5% increase in FVC at 24 months had a greater decrease in CXCL4 levels compared with patients with a $<$5% increase in FVC at 24 months (-0.83 [1.46] vs. -0.24 [0.94]; $P=0.03$).




**Conclusions:** Treatment with immunosuppression led to significant decreases in CXCL4 levels in patients with SSc-ILD. Patients who experienced the greatest decrease in CXCL4 from baseline to 12 months had improved course of FVC from 12 to 24 months, suggesting that short-term change in CXCL4 may be a potential biomarker for predicting long-term treatment response in SSc-ILD.
**References:**
[1] van Bon, et al. NEJM 2014;370:433–43.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3799

FRI0276 **PERIPHERAL STRUCTURAL EVALUATION (RADIOGRAPHIC) AND AXIAL (SCAN) IN A POPULATION OF 77 PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Objectives:** The objective of this study was to describe for the first time the prevalence and characteristics of radiographic lesions of the hands and calcifications of the spine visible on CT scans (thoracic, thoracic-abdominal pelvic (TAP), and lumbar), in a population of patients with systemic sclerosis (SSc) (n=77) treated at the Nancy University Hospital (CHU) and to determine the relationships of these with the clinical and biological expression of the disease and its prognosis.
**Methods:** This was a single centre, retrospective, descriptive and analytical study involving 77 patients treated in the CHU for limited cutaneous SSc (lcSSc) or diffuse cutaneous SSc (dcSSc) complying with the ACR/EULAR 2013 classification criteria and having had an X-ray examination of the hands and a thoracic, TAP or lumbar CT scan within the same year. The X-ray evaluation of the hands was performed as described by Erre G.L et al. The morphological and topographical evaluation of the calcifications was performed on 3 spinal segments: discovertebral, intracanal and posterior. The prognostic factors were interstitial pulmonary lesions on the CT scan, pulmonary arterial hypertension (PAH) and death.
**Results:** Of the 77 patients of mean age 56.9 years (88.3% females), 55 (71%) suffered from lcSSc and 22 (29%) from dcSSc. There were statistically significantly more patients with interstitial disease on the CT scan and restrictive syndrome in the dcSSc group than in the lcSSc group. Study of the radiographic lesions revealed the following prevalences: calcinosis 26%, acro-osteolysis 20.8%, periarticular calcifications 28.6%, erosions 24.7%, narrowing 42.9%, subluxations 19.9% and flexion 27.3% of cases. Calcinosis, acro-osteolysis and periarticular calcifications were related to the duration of progression of the disease and to the onset of digital ulcers (DU) ($p=0.002$; $p<0.001$ and $p=0.014$). On the CT scan, the presence of calcifications was observed in the anterior segment in 62 patients (80.5%), in the canal segment in 21 patients (27.3%) (9 of which were foraminal) and in the posterior segment in 27 patients (35.1%). There was a relationship between the presence of axial calcifications and the existence of peripheral periarticular calcifications ($p=0.012$). From a prognostic viewpoint, the presence of calcinosis was associated with PAH ($p=0.02$), the existence of calcifications in the posterior segment ($p=0.029$) and foraminal calcifications ($p=0.041$) were associated with interstitial lung disease (ILD). The presence of foraminal calcifications was the only factor related to death ($p=0.001$).



**Conclusions:** This study shows for the first time, a link between peripheral periarticular calcifications and spinal calcifications detected on the CT scan. These results suggest that spinal calcifications could provide an indicator of severity and predict mortality in patients suffering from SSc.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1517

FRI0277 **SIX-MINUTE WALK TEST IN SYSTEMIC SCLEROSIS PATIENTS WITHOUT INTERSTITIAL LUNG DISEASE AND PULMONARY ARTERIAL HYPERTENSION**

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**Background:** Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) are the leading causes of death in Systemic Sclerosis (SSc). Although the six-minute walk test (6MWT) is used for evaluating ILD and PAH in clinical practice, no data are available on six-minute walk distance (6MWD) in SSc without ILD and PAH.
**Objectives:** This study wants to evaluate the 6MWT at baseline and 6-month follow-up in a cohort of unselected SSc patients without ILD and PAH.
**Methods:** Prospectively collected data of the 6MWTs at baseline and 6-month

follow-up of 300 consecutive SSc patients, included in the Ghent University Hospital Systemic Sclerosis Cohort between May 2006 and April 2015 were analysed.
**Results:** 98% (286/292) of the SSc patients performed a 6MWT at baseline or 6-month visit, after exclusion of 8 of the 300 SSc patients due to logistic problems. Two patients were unable to perform a 6MWT due to leg amputation and 4 due to immobility. 76% of the patients were female with a mean age of 51±14 years. Six patients had PAH, five had ILD and four were not evaluated with HRCT.
Eventually 271 SSc patients without ILD and PAH performed a 6MWT at baseline or 6-month visit and 193 at both moments. The mean 6MWD of those 271 SSc patients was 460±108m. Patients in the diffuse cutaneous (DcSSc) subgroup (422±118m) walked less than in the limited (LSSc) subgroup (476±109m, p=0.02) and tended to walk less than in the limited cutaneous (LcSSc) subgroup (463±101m, p=0.06). In 193 SSc patients without ILD and PAH who walked at both moments, there was no significant difference between the 6MWDs (mean difference 2.11m 95%CI [-6.75m; 10.98m], p=0.64).

Table 1. 6MWD during the first 6MWT and the evolution of the 6MWD from baseline to 6-month visit in different subgroups of SSc patients without ILD and PAH

| | N | First 6MWD mean ± SD | P | N | 6MWD T0 mean ± SD | 6MWD T6 mean ± SD | r | Mean Diff (95% CI) | P |
|---|---|---|---|---|---|---|---|---|---|
| SSc | 271 | 460±108 | *0.02 | 193 | 466±100 | 468±95 | 0.80 | 2 (–7; 11) | 0.64 |
| LSSc | 70 | 476±109*#† | #0.67 | 53 | 471±115 | 466±104 | 0.83 | –5 (–23; 13) | 0.58 |
| LcSSc | 156 | 463±101*#‡ | †0.02 | 109 | 474±87 | 477±80 | 0.72 | 3 (–8; 15) | 0.57 |
| DcSSc | 45 | 422±118*†‡ | ‡0.06 | 31 | 432±111 | 441±121 | 0.87 | 10 (–12; 32) | 0.38 |

N: number of patients, T0: baseline visit, T6: 6-month visit, 6MWD and mean difference expressed in meter, r: Pearson's correlation coefficient, Diff: difference.

**Conclusions:** In SSc, execution of the 6MWT is feasible, as 98% of the SSc patients were able to perform a test. The baseline mean 6MWD of 271 SSc patients without ILD and PAH is 460±108m and is clinically stable over a 6 months period. The DcSSc subgroup walks less than the LSSc subgroup and the LcSSc subgroup.
**Disclosure of Interest:** None declared
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## FRI0278 MACROVASCULAR DYSFUNCTION OF UPPER AND LOWER LIMBS CORRELATES WITH DIGITAL ULCERATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a chronic connective tissue disorder of unknown etiology characterized by tissue fibrosis and vascular damage [1]. Digital ulcerations (DUs) are common manifestations of vascular involvement [2]. Althoughthe vascular dysfunction of SSc has been considered mainly to affect microvasculature [3], there is recent evidence showing that SSc is associated with the prevalence of large vessel disease [4]. However, only a few studies investigated the relationship between macrovascular disease and its role in the clinical manifestations of SSc such as ulcers.
**Objectives:** To assess the relationship between the Macrovascular dysfunction of upper and lower limbs with digital ulceratioins (DUs) in patients with systemic sclerosis and identification of the other possible factors that correlate with DUs.
**Methods:** Ninety patients with SSc (45 cases with DUs and 45 cases without DUs) enrolled in this study. Patients with other rheumatologic diseases and diabetics patients were excluded from the study. Data which were collected from the patients, included, age, past medical history of cardiovascular disease and dyslipidemia, SSc disease duration, type of SSc (lcSSc or dcSSc), Raynaud's phenomenon (RP), RP duration and digital ulcerations (DUs), Body weight (BW), Height, Waist circumference (WC), Body mass index (BMI), Blood pressure (BP), serum levels of SCL-70 antibody and Anti β2 microglobulin antibody. Then Doppler sonographies were performed. The outcome variables were the peak systolic velocity (PSV) and resistance index (RI) of ulnar, radial, popliteal, dorsalis pedis and tibia artery.
**Results:** The SSc patients with DUs have significantly lower PSV and higher RI in the ulnar (PSV:52.1±7.9 vs 55.7±4.1, p=0.006 and RI: 0.58±0.15 vs 0.52±0.06, p=0.003), dorsalis pedis (PSV: 33.9±1.9 vs 34.5±0.4, p=0.027 and RI: 0.54±0.11 vs 0.50±0.04, p=0.045) and tibial artery (PSV: 32.6±3.1 vs 34.4±0.9, p<0.001 and RI: 0.62±0.16 vs 0.51±0.07, p<0.001) in comparison to SSc patients without DUs. PSV and RI of ulnar artery were significantly correlated with age (p=0.012 and p=0.019), disease duration (p=0.001and p=0.001) and Raynaud's phenomenon (RP) duration (p=0.048 and p=0.028). PSV and RI of tibial artery had significant correlation with age (p=0.038 and p=0.009), systolic blood pressure (p=0.022 and p=0.037) and diastolic blood pressure (p=0.015 and p=0.010).
**Conclusions:** We concluded that digital ulceration in patients with SSc might be frequently related to the macrovascular dysfunction in below the elbow and knee.
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**Disclosure of Interest:** None declared
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## FRI0279 CURRENT IMMUNOSUPPRESSIVE DRUGS ARE NOT ENOUGH TO TREAT THE PULMONARY INVOLVEMENT OF CONNECTIVE TISSUE DISEASES

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**Background:** Interstitial lung diseases (ILDs) may occur secondary to connective tissue diseases (CTDs) and increase morbidity and mortality due to ventilation impairment.
**Objectives:** To reveal clinical, laboratory and imaging features of CTD -ILDs and to analyze treatment approaches.
**Methods:** One hundred thirty two consecutive patients were included in this cohort. Demographic characteristics, laboratory and HRCT results and treatment results were analyzed. More than 10% increase of pulmonary function tests were categorized as improvement, >10% decrease were categorized as deterioration and ±10% changes were categorized as stable disease.
**Results:** There were 111 ILD patients (86.5% CTD-ILD) with follow-up time for more than 6 months. Median follow up time was 48 (Min-Max:6–260) months and mean age was 54.5±11.9 years. HRCT scan was repeated in median 3 (1–10) times per patients, with median 12.5 month intervals. The most frequent HRCT findings were ground-glass opacities, interlobular septal thickening and honeycomb patterns. 89.6% of CTD-ILD patients recieved corticosteroids and 44.8% recieved hydroxylchloroquine sulphate. Azathioprine and cyclophosphamide were the most common used immunosupresive drugs. Eighty four patients recieved at least one immunosuppressive agent. There were only 2 patients treated with four different immunosuppressive drugs. After treatment, mean pulmonary function tests did not significanty differ from baseline (p>0.05) (Table). 35% of the patients improved *forced vital capacity*(FVC >%10 increase) by treatment whereas 31% had decreased and 34% were stable.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Female (n, %) | 90 (81.1) | | | | | | | |
| Age (y) (Mean±SD) | 54.5 ± 11.9 | | | | | | | |
| Follow-up time (Mo) (Median, Min-Max) | 48 (6-260) | | | | | | | |
| The total number of HRCT (n) | 404 | | | | | | | |
| HRCT per patient (Median, Min-Max) | 3 (1-10) | | | | | | | |
| The median duration of HRCT imaging (mo) | 12.5 (3-66) | | | | | | | |
| Corticosteroids | 86 (89.6 %) | | | | | | | |
| Antimalarials | 43 (44.8 %) | | | | | | | |
| Immunosuppressive | First (n=84) | | Second (n=44) | | Third (n=13) | | Fourth (n=2) | |
| | n | (%) | n | (%) | n | (%) | n | (%) |
| Azathioprine | 32 | 38.1 | 17 | 38.6 | 6 | 41.2 | - | - |
| Cyclophosphamide | 31 | 36.9 | 7 | 15.9 | - | - | - | - |
| Methotrexate | 16 | 19.0 | 10 | 22.7 | 3 | 23.0 | - | - |
| Mycophenolate mofetil | 1 | 1.2 | 7 | 15.9 | 3 | 23.0 | 2 | 100 |
| Etanercept | 1 | 1.2 | 3 | 6.8 | 1 | 7.7 | - | - |
| Leflunamide | 3 | 3.6 | - | - | - | - | - | - |
| Baseline FVC- The last FVC | (74.9±18.5)- (76.6±20.4) 1.81 [95%-CI (-1.63- 5.25)] p:0.298 | | | | | | | |
| Baseline $FEV_1$- The last $FEV_1$ | (78.7±18.9) – (79.5±20.2) 0.86 [95%-CI (-2.05- 3.76)] p:0.559 | | | | | | | |
| Baseline DLCO- The last DLCO | (66.7±23.0) –(64.4±22.7) -2.36 [95%-CI (-11.31- 6.57)] p: 0.585 | | | | | | | |
| | Number of patients | | | | | | | |
| | Improvement | | Stable | | Worsening | | | |
| FVC | 32 (35 %) | | 31 (34 %) | | 28 (31 %) | | | |
| $FEV_1$ | 26 (28.5 %) | | 39 (43 %) | | 26 (28.5 %) | | | |

**Conclusions:** It is not detected to have significant improvement by current immunosuppressive drugs in patients with CTD-ILDs. There is need more effective novel drugs to treat for CTD-ILD.
**Disclosure of Interest:** None declared
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FRI0280 **USEFULNESS OF THE EUSTAR PRELIMINARY CRITERIA FOR VERY EARLY SYSTEMIC SCLEROSIS AND LE ROY CRITERIA FOR EARLY-SYSTEMIC SCLEROSIS IN IDENTIFYING PATIENTS AT RISK OF DEVELOPMENT OF SYSTEMIC SCLEROSIS**

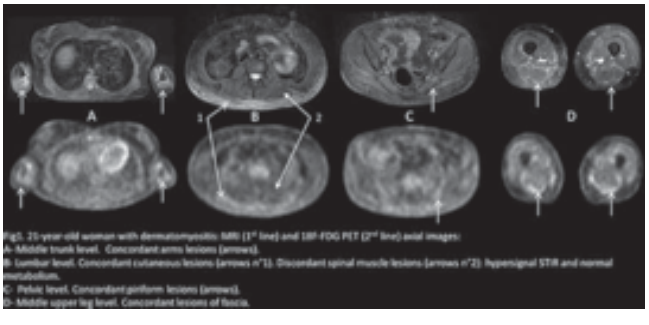
F.M. Ortiz Sanjuan, J. Ivorra Cortés, L. González Puig, I. Chalmeta Verdejo, E. Grau Garcia, C. Feced Olmos, E. Labrador Sánchez, K. Arévalo Ruales, R. Negueroles Albuixech, J. Fragio Gil, I. Martínez Cordellat, J. Valero Sanz, C. Alcañiz Escandell, C. Nájera Herranz, G. Poveda Marín, J. Román Ivorra. *Rheumatology Department, HUP la Fe, Valencia, Spain*

**Background:** Previously, Early Systemic Sclerosis (Early-SSc) patients were defined as patients with Raynaud phenomenon (RP) and either a scleroderma marker autoantibody or typical capillaroscopy abnormalities or both.
Since 2013 the definition of Early-SSc has been updated: Patients should not meet the new 2013 ACR/EULAR criteria for the classification of Systemic Sclerosis (SSc). EUSTAR group also proposed preliminary criteria for the very early diagnosis of SSc which have not yet been validated.
**Objectives:** Our aim was to revise the usefulness of Le Roy criteria and Very Early EUSTAR criteria in identifying patients at risk of development of SSc.
**Methods:** Retrospective study of a wide and unselected series of patients with Early-SSc and SSc from a single university hospital from June 2012 to August 2015. We excluded patients who fulfilled 2013 ACR/EULAR criteria at first visit. Patients were classified as Early-SSc following Le Roy criteria and classified as SSc according to the 2013 ACR/EULAR criteria during follow-up. We reviewed EUSTAR criteria in both groups.
**Results:** We included a total of 56 patients with a mean age of 55±15 years (94.6% women; 5.4% men). At first visit, 15 (26.8%) of our patients fulfilled 2013 ACR/EULAR criteria and were excluded of the final analysis. 37 (66.1%) of our patients fulfilled Le Roy criteria at first visit. The remaining 4 patients (7.1%) did not meet any of these criteria in the first visit. During the follow-up of this group of 41 patients, 37 (90.2%) presented RP and 9 (22%) presented puffy fingers. Antinuclear antibodies (ANA) were present in 34 (82.9%) of the patients, Anti-centromere antibodies in 24 (58.5%) patients and 29 (70.7%) patients presented pathologic capillaroscopic exam.
After a mean follow-up period of 26.1±16.6 months, 20 (48.8%) patients fulfilled 2013 ACR/EULAR criteria. The remaining 21 patients remaining classified as Early-SSc following Le Roy criteria. Of the following EUSTAR criteria, only significant positivity of ANA was observed more frequently in patients that fulfilled 2013 ACR/EULAR criteria: ANA (100%vs63.6%;p=0.005), anti-centromere antibodies (65%vs50%;p=0.41), raynaud phenomenon (95%vs85.7%;p=0.31), abnormal capillaroscopic exam (65%vs76.2%;p=0.8), presence of puffy fingers (25%vs19%;p=0.65).
**Conclusions:** In our study, over the half of the patients initially classified as Early-SSc progressed to SSc during follow-up. EUSTAR preliminary criteria were more frequent in patients who during follow-up fulfilled 2013 ACR/EULAR criteria for SSc, although only the positivity of ANA was statistically significant. Further studies are needed to better characterize the patients with Early-SSc and Very Early-SSc.
**Disclosure of Interest:** None declared
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FRI0281 **MRI VERSUS 18F-FDG PET IN INFLAMMATORY MYOPATHIES AND FASCIITIS**

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**Background:** Idiopathic inflammatory myopathies (IIM) and eosinophilic fasciitis (EF) are defined as idiopathic inflammation of muscle or fascia. In patients clinically suspected of having those entities, Magnetic Resonance Imaging (MRI) is performed to assess muscle involvement, and 18F- Fluorodeoxyglucose Positron Emission Tomography (PET) to exclude a paraneoplastic origin of the symptoms.
**Objectives:** In this study, we aimed to compare the relative performance of MRI and PET in the detection of muscle and/or fascia inflammation.
**Methods:** This retrospective board – approved study included 18 patients suspected of MII (12) or EF (6) in which both MRI and an $^{18}$F-FDG PET were available and performed within a interval ≤3 months, and in which no therapeutic changes occurred between the two exams. The mean interval between MR and PET was 7 days [range -62 (PET performed between MRI) to +91].
For each subject, muscular involvement was independently evaluated on MRI and PET in up to 17 possible predefined muscular groups, subdivided on 3 categories: upper limbs, lower limbs and trunk. A total of 220 corresponding muscular groups were analyzed. A group was considered abnormal on MR when a high signal was seen on fat saturated T2w images (either in muscle or fascia) and, on PET, when high uptake was present. The Kappa statistics between the two imaging modalities were calculated.




**Results:** MRI detected significantly more lesions than $^{18}$F-FDG PET in the 3 categories (upper limbs, lower limbs and trunk) ($p<0.001$). The overall agreement between MRI and $^{18}$F-FDG PET was 0.67 (95% confidence interval 0.57 to 0.77); it was 0.81 (CI 95 0.70–0.93), 0.50 (CI 95 0.31–0.68) and 0.65 (CI 95 0.34–0.97) for upper limbs, lower limbs and trunk, respectively.
**Conclusions:** MRI seems more accurate to detect inflammatory changes of muscle or fascia than 18FDG PET when myositis or fasciitis is clinically suspected.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1520

FRI0282 **POST-TREATMENT SHORT-TERM CHANGES IN NEEDLE ELECTROMYOGRAPHY AMONG PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS AND THEIR CLINICAL USEFULNESS: A RETROSPECTIVE STUDY**

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**Background:** There is no established single outcome measure of muscle manifestations in polymyositis (PM) and dermatomyositis (DM) although there are partially validated preliminary definitions of improvement by the International Myositis Assessment & Clinical Studies Group (IMACS). They are core set measures including Manual Muscle Testing (MMT), muscle-associated enzymes such as creatine kinase (CK), and so on. Needle electromyography (EMG) is useful in the diagnosis of PM/DM. However, the degree and time course of changes in its findings after treatment and their associations with other measures remain elusive.
**Objectives:** We aimed to study post-treatment short-term changes in needle EMG among patients with PM/DM and their clinical usefulness.
**Methods:** Patients were included in the present study when they met all these criteria: 1) fulfill the Bohan and Peter classification criteria for PM/DM; 2) were administered to our university hospital for the treatment of muscle manifestations of PM/DM from 2008 through 2015; 3) received needle EMG before and after treatment. Needle EMG was performed by a single experienced electromyographer/neurologist in all the patients. The data of findings of needle EMG, MMT, serum CK levels, and other demographic and clinical information were retrospectively collected. The following findings of needle EMG were transformed into semiquantified relative frequencies on 0–7 point scale: fibrillation potential (Fib), positive sharp wave (Pos), low-amplitude motor unit potential (MUP) (Low), short-duration MUP (Short). MMT was assessed in 10 muscles on 0–5 point scale and their sum scores with maximum of 50 were used. Treatment was determined by physician preference in each individual.
**Results:** Ultimately, 24 patients were included in the present study, and 17 and 10 patients received needle EMG at 4 and 8 weeks after treatment, respectively: 3 patients received at both 4 and 8 weeks after treatment. Fib was detected in 23 patients, and Pos, Low, and Short were detected in all the patients before treatment. Fib, Pos, Low, and Short improved in 59%, 65%, 29%, and 24% of the patients at 4 weeks, and in 90%, 90%, 100%, and 90% of the patients at 8 weeks, respectively. When assessed by Wilcoxon signed-rank tests, Fib and Pos significantly improved at 4 weeks, and all of the needle EMG findings improved at 8 weeks ($p<0.05$ in each comparison). Although MMT scores and CK levels also significantly improved, their improvement did not significantly agree with the improvement of needle EMG findings except for Fib and Pos and CK levels at 8 weeks.
**Conclusions:** The present study showed that electrical activity in muscle recorded at rest (Fib and Pos) and during voluntary movement (Low and Short) significantly improved at as early as 4 and 8 weeks after treatment, respectively. It is also suggested that needle EMG findings can serve as different outcome measure from MMT and CK in PM/DM.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1092

FRI0283 **ARE PATIENTS WITH EXTENDED INTERSTITIAL LUNG DISEASE BETTER TARGET FOR THE TREATMENT IN SSC?**

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**Background:** Systemic sclerosis (SSc) is characterized by systemic excessive fibrosis, and interstitial lung disease (ILD) is an important organ involvement strongly associated with morbidity and mortality[1)]. Recent report showed that

extent of ILD could predict prognosis of patients with SSc-ILD, and 70% as %FVC or 20% involvement determined by HRCT were reported as thresholds for the differentiation of patients into limited (LD) or extended (ED) ILD[2]. On that note, adequate target for the introduction of the treatment is still unclear.
**Objectives:** To elucidate the better target for the treatment of patients with SSc-ILD.
**Methods:** This was a single-center study. Patient with SSc-ILD treated with cyclophosphamide during 2008 to 2015 in our hospital were consecutively involved. SSc patients were fulfilled 1980 American College of Rheumatology (ACR) classification criteria[3] or 2013 ACR/EULAR classification criteria[4]. Patients were stratified into 2 groups, extensive or limited lung disease, based on the disease extent over 20% or less using CT scan[2], respectively. Baseline data of pulmonary function tests and other clinical parameters were retrospectively collected from medical records, and response at 6 months after the treatment was evaluated by the change of data of pulmonary function tests before and after the treatment. Each parameter was compared between ED and LD groups.
**Results:** Sixteen patients with SSc-ILD who were treated with cyclophosphamide were involved. Mean age was 57.3±15.1 years and ratio of female patients and diffuse cutaneous SSc were 81%, 50%, respectively. Autoantibody profiles were 2 with anticentromere antibodies (13%), 8 with anti-topoisomerase I antibodies (50%), 1 with anti-U1 ribonucleoprotein antibody (6%) and 5 with antinuclear antibody positive without SSc-specific antibodies (31%). Disease duration at diagnosis of ILD was 26.4±31.9 months. Based on the criteria, 9 (56%) were stratified as ED and 7 (44%) as LD. At baseline, %FVC was higher (86.1±14.2 vs 67.2±16.8%, $p<0.05$) and disease duration was shorter in LD (12.6±24.8 vs 37.2±33.8 months, $p<0.05$) but other clinical parameters including age, sex, smoking, autoantibody profiles, mean cumulative dose of prednisolone or cyclophosphamide and serum KL-6 levels were comparable between 2 groups. Response to treatment was better in patients with LD compared to ED; improvement of %FVC (6.80±5.59 vs 0.04±3.92%, $p<0.05$), favorable outcome of %DLCO but not significant (3.37±12.77 vs 0.70±6.18%).
**Conclusions:** SSc patients with LD, who had earlier and milder disease, showed better short-term response to treatment compared to those with ED. These results suggest that earlier intervention could lead to better prognosis in patients with SSc.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3825

## FRI0284 ANTI-SRP-ASSOCIATED AUTOIMMUNE MYOPATHY: YOUNGER AGE AT ONSET IS ASSOCIATED WITH MORE SEVERE DISEASE AND WORSE OUTCOME

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**Background:** Anti-SRP autoantibodies are associated with an immune-mediated necrotizing myopathy. Although some anti-SRP-positive patients respond well to therapy, others continue to have active disease and persistent weakness despite treatment[1,2].
**Objectives:** Here, we studied a large cohort of anti-SRP-positive patients to identify factors associated with disease severity and clinical improvement.
**Methods:** All anti-SRP positive patients in the Johns Hopkins Myositis Cohort from 2002 to 2015 were included in the study. Longitudinal information regarding proximal muscle strength, creatine kinase levels, and immunosuppressive therapy were recorded at each visit. Univariate and multivariate analyses using multilevel regression models were used to assess prognostic factors influencing the recovery of strength over time.
**Results:** Thirty-seven anti-SRP-positive patients (78% female) were included. Older age at onset was associated with greater strength at the first visit (p=0.02) and at all subsequent visits (p=0.002) independent of sex, race, disease duration and immunosuppressive treatment. Younger patients had worse outcomes, with less strength at the last visit (p=0.003) independent of disease duration, sex, and race. Although we could not definitively study response to treatment in this longitudinal cohort, rituximab appeared to be effective in 13 of 17 patients who received it (76%, 95%CI: 53% 90%). Younger patients often required continuous and intensive therapy with multiple immunosuppressive drugs to sustain full strength even two years after the onset of the disease.
**Conclusions:** In anti-SRP-associated myositis, a younger age at disease onset is associated with more severe weakness and worse outcomes. Rituximab may be an effective treatment in both young and old patients.
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## FRI0285 SENSITIVITY TO CHANGE OF NAILFOLD VIDEOCAPILLAROSCOPY AND RELATIONSHIP WITH DISEASE PROGRESSION

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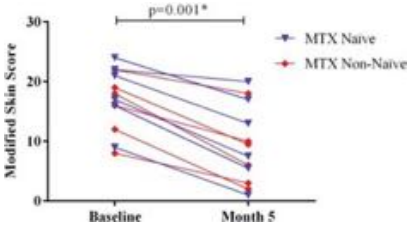
**Background:** Nailfold videocapillaroscopy (NVC) is a simple, non-invasive and inexpensive imaging technique that allows a detailed assessment of skin microcirculation. Although NVC has face and content validity for the detection of microvascular damages related to systemic sclerosis (SSc), its sensitivity to change has not been assessed in detail.
**Objectives:** Our aim was to determine in a prospective cohort the merit of NVC to detect meaningful changes over time and whether these changes are associated with disease progression.
**Methods:** A prospective cohort of 140 SSc patients was recruited over a 12-month period and was followed up on an annual basis for 3 years. NVC was performed at inclusion and repeated once a year by four investigators (ET, GL, CH and AV) according to a standardized procedure. NVC pictures were analysed by one investigator (JA) and classified as early, active and late patterns. Organ progression was defined according to validated definitions. The worsening of the Medsger severity scale (from category 1–2 to category 3–4) was considered as a marker of disease progression.
**Results:** 140 SSc patients were included (111 women, 56±11 year-old, disease duration of 9±8 years). A change of NVC pattern was observed in 29 SSc patients (21%) during the follow-up period.At least 3 annual NVC evaluations were available for each patient.
A progression from a normal or early NVC pattern to an active NVC pattern was detected in 15 patients (10%). Patients who progressed to the active NVC pattern were significantly less at risk to develop ischemic digital ulcers (DU) during follow-up (hazard ratio, HR: 0.78, 95% Confidence Interval, CI 0.17–0.95). A progression to a late NVC pattern was observed in 14 patients (10%). Progression to a late NVC pattern was associated with the occurrence of new ischemic DU (HR: 4.51, 95% CI 1.68–12.14), lung vascular progression (HR: 5.12 95% CI 1.23–21.27), progression of skin fibrosis (HR: 3.70, 95% CI 1.14–11.94) and the worsening of Medsger disease severity scale (HR: 4.47, 95% CI 1.63–12.26).
**Conclusions:** Change of the NVC pattern was observed in 21% of patient with SSc during a follow-up of 3 years. NVC has the ability to detect meaningful changes over time associated with markers of disease progression. Our results support the use of NVC for the routine follow-up of SSc patients in order to improve their risk stratification. NVC might be used in the future to select high-risk patients and change to a late NVC pattern might be regarded as potential surrogate marker for disease severity.
**Disclosure of Interest:** None declared
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## FRI0286 HIGH-DOSE INTRAVENOUS PULSE METHOTREXATE IN PATIENTS WITH EOSINOPHILIC FASCIITIS: AN OPEN PROSPECTIVE STUDY

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**Background:** Eosinophilic Fasciitis is a rare scleroderma-like connective tissue disorder. No treatment has shown to be effective in randomized trials. The treatment most often reported is combination of moderate to high-dose glucocorticoids (1–1,5mg/kg/day) with weekly methotrexate (MTX), up to 25mg, but often with disappointing results.[1,2]
**Objectives:** To examine the effect and safety of monthly intravenous (IV) high dose MTX in patients wtih eosinophilic fasciits.
**Methods:** Patients with biopsy proven eosinophilic fasciits and progression of skin involvement, who were either treatment naïve or not responsive to glucocorticoids and MTX were included in this open prospective study. Treatment consisted of IV pulse MTX 4 mg/kg/month for 6 doses in 5 consecutive months. Twenty-four hours after the administration of MTX, 5mg folinic acid was orally taken every six hours, to a maximum of 25 mg/day. Patients were evaluated monthly, prior to every infusion. Primary outcome measure was the absolute improvement at month 5 compared to baseline of the modified skin score (mSS), according to Zachariae.[3] Secondary outcome measures were durometer scores, Range of Motion (RoM) and Visual Analogue Scale (VAS) scores for disease activity by physician and patient and Short-Form-36.

**Results:** Between 2006 and 2009, 12 patients were included and the median monthly MTX dose was 288mg (range 252–336). The median mSS improved from 17.5 [range 8.0–24.0] at baseline to 8.5 [range 1.0–20.0] at 5 months (p=0.001) (Fig 1). Compared to baseline, secondary outcome measures improved significantly, except for durometer scores and the range of motion of the elbows. There was no significant difference in skin improvement between the treatment naïve and non-naïve patients (p=0.968). After the last dose of IV MTX, EF flared in six patients after a median of 2 months (range 2–5). A second cycle with IV MTX (3 pulses) was administered to these 6 patients, with a favourable response in all patients. One patient was withdrawn due to increased liver enzymes (2 – times upper limit of normal) after 5 administrations, which normalized after MTX withdrawal. Gastro-intestinal symptoms were present in the majority of the patients (n=9), but manageable with anti-emetics.




**Conclusions:** High dose IV MTX could be an effective and safe treatment option in patients with eosinophilic fasciitis.

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## FRI0287 THE USE OF A DORSAL APPROACH FOR THE INJECTION OF BOTULINUM TOXIN A IN THE TREATMENT OF RAYNAUDS PHENOMENON SECONDARY TO SCLERODERMA

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**Background:** Raynaud's phenomenon (RP) is common in scleroderma patients and causes pain, paraesthesia, ulceration, and gangrene. Botulinum toxin A (Btx-A), injected via a palmar approach, has been shown to be effective in the treatment of severe RP. However, hand weakness is a common complication, with rates as high as 27% and can last for up to 6 months (1–5).
**Objectives:** This study aimed to determine the effect of Btx-A injected via a dorsal approach, on hand function and improvement in symptoms, in patients with RP secondary to Scleroderma.
**Methods:** Twenty one patients diagnosed with RP secondary to scleroderma were included. All patients met the criteria for systemic sclerosis of the American College of Rheumatology.
They were treated with 10 units of Btx-A, injected into the hand via a dorsal approach. Each patient had a baseline hand assessment and thermographic image (FLIR E60bx). Hand assessment included pinch and power grip strength measurements (Jammar plus digital pinch gauge and dynameter), range of movement of each joint in the hands using a goniometer, Kapandji thumb opposition test and a pain score using the 0–10 visual analogue scale. Patients were asked to report any symptoms of pain, colour change, cold intolerance and complete a Disabilities of the Arm, Shoulder and Hand (DASH) score. Post injection, the hand assessment and thermography was performed at 15 minutes and at 6 weeks in a temperature controlled room at 23.7±2°C.
Patients were followed up for 6 weeks and filled out a daily Raynaud's attack diary.
**Results:** 89% of patient reported an overall improvement in symptoms. There was a reduction in the overall number and severity of Raynaud's attacks. There was a significant improvement in both the DASH score value (P=0.008) and Kapandji score value (p=0.007). Pain score decreased by 1 point on average, from 4.9 to 3.9.
No patients reported hand weakness as a complication. One patient reported pain at the site of injection for 3 days and 1 patient reported itching for the first 2 days. The effect on range of movement and blood flow was variable.
**Conclusions:** Btx-A injected via a dorsal approach improves symptoms reduces number of attacks in patients with RP secondary to scleroderma. This approach has lower rates of Btx-A related complications compared to the palmar approach.

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## FRI0288 IS IMMUNOSUPPRESSION EFFICIENT IN DIGITAL ULCER PREVENTION? A EUSTAR CENTER EXPERIENCE

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**Background:** Digital ulcers are frequent in patients with systemic sclerosis and have a high morbidity. No previous studies have evaluated the efficacy of immunosuppression on digital ulcers risk. Current treatment guidelines do not include the use of immunosuppressants as routine treatment for digital ulcers.
**Objectives:** To asses the efficacy of imunosuppresive therapy on the digital ulcer prevention in patients with systemic sclerosis
**Methods:** Prospective study on EUSTAR cohort 096 during september 2005-september 2015. Patients with systemic sclerosis (SSc) without previous digital ulcers at their first presentation in the clinic were selected. Immunosupression was started based on current recommandations according to specific organ involvement. Patients were evaluated every 6 month according to MEDS evaluation sheets and a special evaluation form for digital ulcer (number, type of ulcer, date of onset).
**Results:** 116 systemic sclerosis (SSc) patients were evaluated, but only those without previous ulcers at their first presentation in the clinic were selected – 60 patients; 12 of them were lost to follow-up.
There were 40 females, 8 males, 23 diffuse and 25 limited SSc. 26 out of the 48 patients received immunosupressants. The mean (±SD) interval of follow up was 72.67 (±60.75) months. No significant statistical difference was identified between patients with immunosuppression and those without regarding the age, the disease duration, the visceral involvement and the follow-up period. 69.23% received Methotrexate, 3,84% received Mycophenolate and 26.92% received monthly pulses of Cyclophosphamide. The use of immunosupresants was related to diffuse subset (R=0.631,p=0.001), antiSCL70 positivity (R=0.624, p=0.001) and lung involvement (R=0.331, p=0.034). There was no difference of the immunosuppressants efficacy regarding the new digital ulcers onset. The incidence of digital ulcers was 15.38% in patients receiving immunosuppression and 68.18% in patients without immunosuppression (p=0.001). The mean (±SD) number of ulcers in the follow-up period was 0.85 (±1.4) in immunosuppresed patients and 6.18 (±4.79) in the other group, p=0.001. The onset of new digital ulcers was also correlated with advanced age (R=0.392, p=0.032) and longer follow-up interval (R=0.036, p=0.049). The mean (±SD) interval from first visit of the patient until the appearence of the first digital ulcer was 7.3 (±5.43) month in patients with immunosuppression and 30 (±11.78) months in patients without immunosuppression.
**Conclusions:** Immunosupression might decrease the risk and the number of digital ulcers of patients with SSc, but they do not seem to extend the interval until their first appearance. More prospective, multicentric studies on larger cohorts with longer follow-up interval are needed in order to aasses the efficacy of immunosuppression on digital ulcers onset, number, rate and time to healing.

**Disclosure of Interest:** None declared
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## FRI0289 MULTICENTER REGISTRY ON INFLAMMATORY MYOPATHIES IN MADRID (REMICAM): MORTALITY ANALYSIS

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**Background:** Classically the prognosis of idiopathic inflammatory myopathies (IIM) has improved in recent decades, but can still be poor in certain subgroups or in the presence of some clinical factors.
**Objectives:** To analyze survival, causes of death and poor prognosis factors in a cohort of patients diagnosed with IIM.

**Methods:** A multicenter retrospective study from REMICAM[1] myositis study group was performed. All patients were diagnosed with IIM according to Bohan and Peter[2] criteria and were classified into 5 different clinical subgroups: primary dermatomyositis (DM), primary polymyositis (PM), juvenile dermatomyositis (JuvM), cancer associated myositis (CAM) and overlap myositis (OM).
**Results:** 478 IIM cases were included. 74% of the cases were women, with an age at diagnosis of 43.7±22.6 ys. and a mean follow-up of 9.7±8.3 ys. During the follow-up period there were a total of 114 deaths (24%), the main causes were infections (24%), cancer (24%), and cardiovascular events (22%). Factors associated with poor prognosis were CAM (HR 15.4) and OM subgroups (HR 4.55), older age at diagnosis (HR 1.05), shorter time of disease (HR 1.30), serious infections (HR 4.57), cancer (HR 3.07), systemic symptoms (HR 1.64), heart (HR 2.52) and haematological manifestations (HR 1.53), ESR/CRP elevation at baseline (HR 3.05) and chronic renal failure (HR 2.41). The clinical characteristics that showed a protective effect were arthralgia (HR 0.68), typical skin lesions (HR 0.62), drug use (HR 0.53) and female sex (HR 0.5). In multivariate analysis the independent variables associated with mortality were CAM (HR 8.83) and OM (HR 5.17) subgroups, severe infections (HR 3.42), older age at diagnosis (HR 1.03), shorter course of the disease (HR 1.34), thrombocytopenia (HR 2.93) and elevated ESR/CRP (HR 2.47).
**Conclusions:** In our REMICAM registry on inflammatory myopathies 24% of patients died, mainly due to infections, cancer and cardiovascular events. The independent predictors of mortality were belonging to the subgroups of paraneoplastic myopathies or overlap syndrome, the presence of severe infections, thrombocytopenia, elevated ESR/CRP at baseline, shorter course of the disease and older age at onset.
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**Disclosure of Interest:** L. Nuño Grant/research support from: SORCOM-MSD grant for myositis study, M. J. García: None declared, B. Joven: None declared, V. Maldonado: None declared, I. Llorente: None declared, C. Barbadillo: None declared, P. García de la Peña: None declared, L. Ruiz: None declared, H. Moruno: None declared, T. Cobo: None declared, R. Almodovar: None declared, L. Lojo: None declared, F. J. López Longo: None declared
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## FRI0290 IDENTIFICATION OF AT RISK PATIENTS FOR CARDIAC MRI DETERMINED SUB-CLINICAL SSC-CARDIOMYOPATHY (CM)

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**Background:** SSc-CM carries a poor prognosis once clinically evident. No clear management algorithm to guide screening & investigation for SSc-CM exists.
**Objectives:** To describe cardiac MR (CMR) abnormalities in SSc pts free of CM/CVD & their association with disease (dis.) phenotype to identify the "at risk" pt.
**Methods:** We compared 35 pts with ACR/EULAR criteria SSc & no diabetes/clinical CVD who received SSc/cardiovascular (CV) profile & pulse wave velocity (PWV) assessment & 3T delayed enhancement-CMR reported by CMR-cardiologists to 30 healthy controls (HC). Univariate analysis variables (var.): CV traditional risk factors (TRF), waist/hip ratio (WHR), dis. duration, prev. digital ulceration (DU), known ILD, palpitations hx, dis. subtype, ACA, Scl70, MRSS, NFC, prev. use of cyclophosphamide, SHAQ, FVC, PASP & PWV.
**Results:** Mean (SD) age (yrs) SSc pts 55 (13), 74% female; HC 50 (15), 63% female. Median (IQR) yrs from 1st non-RP symptom 9.5 (2.3, 19.6); 43% dcSSc, 31% ACA+ve, 34% Scl70+ve, 43% known ILD, 37% DU, 0% pulmonary hypertension, 29% prev. use of cyclophosphamide. CMR markers of fibrosis were increased in SSc: ECV (31% SSc vs 25% HC, p<0.001 after adj. for age/sex/TRFs); late gadolinium enhancement (LGE) in 9 SSc vs 1 HC. In SSc, diastolic dysfunction was evident (reduced torsion p0.038), there was a trend for reduced LV mass & RVEF was unexpectedly increased (p=0.028) vs HC. Higher ECV in SSc was associated (ass.) with DU (r0.397 p0.22), decreasing WHR (r-0.510 p0.004) & decreasing TC/HDL (r-0.376 p0.037); none significantly ass. in multi-variable analysis with age/sex. LGE was significantly ass. with ILD (78% vs 33%, p0.047), absence of ACA (0% vs 42%, p0.032), reduced sysBP (mean diff. (95%CI) -14 (27, -1)mmHg p0.034) & lower BMI (mean diff. (95%CI) -4.13 (-8.24, -0.02), p0.049). Other SSc LGE observations: male gender (56% vs 17% LGE-ve), 56% (vs 38% LGE-ve) dcSSc, 56% (vs 29%) Scl70+ve & shorter dis. duration (median (IQR) 7.4 (1.2, 15.8) vs 10.9 (2.5, 19.7) yrs).

Table 1. CMR measures in SSc & HC

| Variable | SSc pts (n=35) | HC (n=30) | Mean difference (95% CI), p adj. for age/sex/ever smoked/sys. BP |
|---|---|---|---|
| LVEF, % | 61.5 (4.6) | 61.8 (4.6) | –0.51 (–2.78, 1.75), 0.652 |
| LVEDV/BSA, ml/m$^2$ | 79.5 (15.1) | 79.8 (10.8) | –0.63 (–7.30, 6.03), 0.850 |
| LVESV/BSA, ml/m$^2$ | 30.9 (8.0) | 30.6 (6.2) | 0.22 (–3.16, 3.60), 0.896 |
| LVmass/BSA, g/m$^2$ | 44.5 (11.1) | 49.2 (7.7) | –4.27 (–9.18, 0.64), 0.087 |
| LVmass/EDV, g/ml | 0.56 (0.10) | 0.62 (0.10) | –0.053 (–0.108, 0.001), 0.054 |
| RVEF, % | 57.2 (12.0) | 53.7 (6.2) | **5.55 (0.61, 10.49), 0.028** |
| RVEDV/BSA, ml/m$^2$ | 85.4 (18.0) | 92.4 (16.5) | –6.53 (–15.21, 2.15), 0.137 |
| RVESV/BSA, ml/m$^2$ | 38.8 (12.5) | 43.1 (10.7) | –4.08 (–9.73, 1.57), 0.154 |
| Torsion, ° | 12.98 (4.06) | 14.95 (4.46) | **–2.41 (–4.68, –0.14). 0.038** |
| ECV, % | 30.6 (3.8) | 25.1 (2.8) | **5.0 (3.2, 6.8), <0.001** |
| LGE +ve | 9 (25.0)* (n=33) | 1 (3)* | 8.71 (0.74, 102.17), 0.085** |
| Distensibility, $10^{-3}$mmHg$^{-1}$ | 3.78 (2.25) | 4.70 (1.95) | –0.61 (–1.48, 0.26), 0.163 |

Values = mean (SD). *n (%), **OR (95% CI) p.

**Conclusions:** This study reports CMR detected sub-clinical SSc-CM with detailed SSc phenotype, associating with poor prognostic factors. These data indicate an at risk group for further evaluation that would justify more intensive monitoring for SSc-CM & its complications. The association of ECV with lower lipids/WHR, & LGE with lower BMI/sysBP is new & we postulate may reflect cachexia/medication use in severe disease.
**Disclosure of Interest:** None declared
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## FRI0291 CLINICAL SPECTRUM TIME COURSE IN NON ANTI JO-1 POSITIVE ANTISYNTHETASE SYNDROME

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**Background:** The clinical phenotype of the antisynthetase syndrome (AS) has been related with the underlying autoantibody specificity. The typical disease triad (arthritis, myositis, and interstitial lung disease -ILD) is common in anti Jo-1 + AS, whereas isolated ILD is associated with anti PL-7 and PL-12 Ab. The majority of anti Jo-1 + patients without all triad findings at the onset (incomplete ASSD) will develop lacking features during the followup
**Objectives:** To assess the triad clinical spectrum time course in non anti Jo-1 + AS
**Methods:** The study cohort included patients + for anti-EJ, OJ, PL-7, or PL-12 Ab with at least 1 triad finding. Clinical features were retrospectively collected and analyzed
**Results:** we included 65 non anti Jo-1 + AS (7 anti EJ, 4 anti OJ, 30 anti PL-12, 24 anti PL-7; 49 females, 16 males). In median, age at disease onset was 53 years (IQR 42–64), diagnostic delay 9 months (IQR 3–23.5), followup 60 months (IQR 20.5–113). Patients' characteristics are reported in Table 1. During the followup, 22/61 patients with incomplete AS developed new triad findings, in median 12 months (IQR 6–27) after disease onset. The frequency of incomplete AS developing new triad findings and the length of followup were significantly reduced in non anti Jo-1 + patients with respect to our corresponding anti Jo-1 + cohort (respectively: 22/61 vs 138/220, p<0.001; median 60 months, IQR 18.5–113 vs median 75 months, IQR 39–134; p=0.002)

Table 1

| | Characteristics | | p† |
|---|---|---|---|
| | At disease onset | At last follow-up | |
| Arthritis (% of total) | 23 (37) | 31 (48) | 0.016 |
| Myositis (% of total) | 26 (40) | 34 (52) | 0.008 |
| Interstitial lung disease (ILD) (% of total) | 38 (58) | 54 (83) | 0.001 |
| Isolated arthritis (% of total) | 10 (15.5) | 2 (3) | 0.008 |
| Isolated ILD (% of total) | 21 (32.5) | 17 (26) | 0.125 |
| Isolated myositis (% of total) | 15 (23) | 8 (12) | 0.016 |
| Arthritis and myositis (% of total) | 2 (3) | 1 (2) | 1.000 |
| Arthritis and ILD (% of total) | 8 (12) | 12 (18) | 0.219 |
| Myositis and ILD (% of total) | 5 (8) | 9 (14) | 0.219 |
| Arthritis, myositis and ILD (% of total) | 4 (6) | 16 (25) | 0.001 |
| Fever/patients assessed* (%) | 16/59 (27) | 18/59 (30.5) | 0.500 |
| Mechanic's hands/patients assessed* (%) | 14/63 (22) | 17/63 (27) | 0.250 |
| Raynaud's phenomenon/patients assessed* (%) | 23/58 (43) | 26/58 (45) | 0.250 |

†McNemar test; *only patients with the complete timing of features.

**Conclusions:** In non anti Jo-1 + patients the ex novo occurrence of classic triad

finding is common, but less frequent than in anti Jo-1 + patients. The different length of followup may explain at least partly this difference

**References:**
[1] Cavagna L, et al. Medicine (Baltimore) 2015;94:e1144

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## FRI0292 RISK FACTORS FOR RECURRENCE OF POLYMYOSITIS/DERMATOMYOSITIS ASSOCIATED INTERSTITIAL LUNG DISEASE

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**Background:** Polymyositis (PM)/dermatomyositis (DM) are characterized by a systemic inflammation of a proximal skeletal muscles and/or a skin. Interstitial lung disease (ILD) is a common but life-threatening complication with PM/DM and often recurs despite intensive induction therapy. However, risk factors for the ILD flare are not determined.
**Objectives:** To identify risk factors of the recurrence of PM/DM-ILD.
**Methods:** Consecutive patients with PM/DM-ILD treated in our institution from 2002 to 2015 were enrolled in the study. The patients were divided into two groups according to the presence or absence of recurrence of ILD after the improvement by induction therapy; the recurrence group and the non-recurrence group. The patients were observed until the recurrence or the last visit to our clinic. The patients' characteristics and treatment between the two groups were compared.
**Results:** A total of forty four patients with PM/DM-ILD underwent induction therapy. After excluding 1 deceased patient (induction failure) and 1 lost to follow-up, forty five PM/DM-ILD cases who had been treated with predonisolone (PSL) and/or immunosuppressive agents as induction therapy were included in the analysis. Recurrence occurred in 17 cases (37.8%). The mean duration from the time of induction therapy to the recurrence was 124 (42.5–241.0) weeks. The following period was 338.5 (166.3–777.5) weeks in the non-recurrence group. At the time of induction therapy, no difference was found between the recurrence group and the non-recurrence group in the mean age (47.6±14.3 vs 47.8±11.9 years, P=0.95), the male ratio (23.5% vs 30.8%, P=0.54), and the proportion of DM (64.7% vs 78.6%, P=0.31), respectively. The levels of C-reactive protein, lactate dehydrogenase and KL-6 were also not different. The percentage of vital capacity (%VC) in the recurrence group was lower than that of the non- recurrence group (59.6% vs 78.3%, P=0.004). The induction therapy regimen was not different between the 2 groups; glucocorticoid pulse, 17.6% vs 21.4% (P=0.84), the initial PSL dose, 0.87 mg/kg vs 0.89 mg/kg (P=0.17), the concomitant use of immunosuppressive agents including cyclophosphamide and/or calcineurine inhibitor with PSL, 47.1% vs 50.0% (P=0.85), in the recurrence and the non-recurrence group, respectively. The PSL dose was 8.3 mg at the recurrence in the recurrence group, and 7.9 mg at the last observation in the non-recurrence group (P=0.40). Immunosuppressive agent was more frequently used as maintenance therapy in the non-recurrence group than the recurrence group (89.3% vs 64.7%, P=0.047).
**Conclusions:** PM/DM-ILD patients with low %VC at the induction therapy are inclined to recur. The concomitant use of immunosuppressive agent as maintenance after induction is important to prevent the recurrence of PM/DM-ILD. The study can improve the management of the PM/DM-ILD.

**Disclosure of Interest:** None declared
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## FRI0293 SCREENING FOR MALIGNANCIES IN SYSTEMIC SCLEROSIS PATIENTS POSITIVE FOR ANTI-RNA POLYMERASE III ANTIBODIES: A DELPHI EXERCISE AMONG EUSTAR EXPERTS

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**Background:** A temporal relationship between the onset of systemic sclerosis (SSc) and malignancies has been described in patients with anti-RNA polymerase III antibodies (anti-RNAP). Our analysis of the EUSTAR cohort (1) provided further information, highlighting the relationship of anti-RNAP with malignancies synchronous (±2 years) to the onset of SSc (OR 3.85, 95%CI 1.3–10.9). In particular, an increased rate of synchronous breast cancer was found (OR 20.2, 95%CI 1.4–355). These results suggest the possible need of a cancer screening program for these patients.
**Objectives:** To draw up a possible list of recommendations to guide the clinicians in every-day practice to screen anti-RNAP+ SSc patients for cancer.
**Methods:** A web-based Delphi approach was used to address the questions concerning possible screening for malignancies in anti-RNAP+ SSc patients. Prior to the first stage of Delphi exercise, the number of anti- RNAP+ patients needed to screen to find one synchronous malignancy was calculated using the results of the EUSTAR cohort. All EUSTAR centres were contacted: information on the analysis of the EUSTAR cohort was presented and centres were asked to participate to the exercise, voting on the opportunity of a screening for malignancies in anti-RNAP+ patients and its modality. In the second stage, questions that remained unsolved at the first step, and new suggestions from experts were re-proposed. Finally, possible recommendations were draft, and participants were asked to vote on them in stage 3 of the Delphi exercise. The level of agreement with each statement was voted using a 10-point visual analogue scale (10: fully agree).
**Results:** The number needed to screen to detect one synchronous malignancy in anti-RNAP+ patients in the EUSTAR cohort was 15; the number needed to screen to detect synchronous breast cancer was 22 (or 17, considering only female patients). Eighty-two experts from EUSTAR centers participated to the third stage of the Delphi exercise voting on possible recommendations on screening for synchronous cancer in anti-RNAP+ SSc patients: the results are shown in Table 1.

**Table 1. Levels of agreement among 82 EUSTAR experts**

Degree of agreement with the some statements about a screening for synchronous cancer in SSc anti-RNA Polymerase III positive patients (1-10; 10: fully agree)

| Statement | Mean | SD |
|---|---|---|
| A screening for synchronous malignancies is recommended | 8.73 | 1.70 |
| A screening for synchronous breast cancer in female patients is recommended with the execution of mammography (or US/MRI when needed) | 9.02 | 1.35 |
| Screening for other malignancies should be guided by clinical suspicion and patient age. Non invasive tests (e.g. fecal occult blood, gynecological evaluation, prostatic specific antigen) may be considered in all patients | 8.63 | 1.48 |
| Serum tumoral markers are NOT useful for screening in every patients | 8.59 | 2.18 |
| A period of 2-5 years of tight surveillance for cancer is recommended | 8.26 | 2.01 |
| If the screening tests for cancer performed at the diagnosis of scleroderma are negative, tests for breast cancers should be repeated (e.g. annually); other tests should be repeated in case of clinical suspicion | 7.90 | 2.14 |
| PET/CT may be considered when aspecific systemic signs suggest the possible presence of neoplasms | 8.00 | 2.02 |
| Further tight surveillance for cancer is not recommended after a period of 2-5 years | 7.10 | 2.27 |
| Prospective studies are needed to clarify how long should the tight surveillance lasts and which exams are most indicated for a screening of cancer in these patients | 9.56 | 1.04 |

**Conclusions:** Most EUSTAR experts who participated to the Delphi exercise would recommend screening for synchronous malignancies at the moment of diagnosis in anti-RNAP+ SSc patients. In particular, screening for synchronous breast cancer in female patients, and for other malignancies, guided by clinical suspicion and patient age, would be recommended. Non-invasive tests may be considered in all patients. Although most experts agreed on the proposed statements, some degree of discordance was found on the use of PET/CT and the program of follow-up in subsequent years: in particular on how long should the tight surveillance lasts, and which exams are most indicated to be repeated. The experts agreed that prospective studies are needed to clarify these issues.

**References:**
[1] M.G. Lazzaroni et al. Anti-RNA Polymerase III Antibodies in Patients with Systemic Sclerosis: A Eustar Multicenter Collaborative Study. Ann Rheum Dis 2015;74:Suppl 2 88 doi:10.1136/annrheumdis-2015-eular.1728

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## FRI0294 THE PROGNOSIS INTERVALS FOR PTS WITH SSC-ILD USING DISCRIMINANT ANALYSIS

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**Background:** Pulmonary alterations are the major cause of mortality in SSc. The most pts develop some degree of lung injury over the course of the disease.
**Objectives:** to assess predictors of poor prognosis in a single center cohort of SSc pts with interstitial lung disease (ILD) and to build a predictive model of prognosis disease SSc-ILD.
**Methods:** 77 pts with SSc-ILD were involved in a longitudinal study over a five-year period. We used discriminant analysis and our selection involved missing value. So discriminant analysis was held at 58 pts (4 were men). The mean age was 47±13 years. Pts. were divided into 3 subgroups based on HRCT changes estimated at the entry of the study and at last visit. The mean time between two evaluations was 57±10 months. The 1st group included 13pts with improvement (n=13), 2nd –pts without any changes (n=30) and 3rd – pts with deterioration negative dynamics (n=15). ROC analysis was used for determination of prognostic intervals.
**Results:** We got the discrimination function that included: ground glass opacities (GGO) (1 – the absents of GGO; 2 – the presents of GGO); index EScSG (the digital value); FVC (FVC $\geq$75 = 0, FVC $<$75 = 1); the maximum daily dose of glucocorticoids (the digital value, mg); Gamma globulins (the digital value, %); cyclophosphamide (CYC) (the absence of CYC =0, the treatment of CYC =1); DLco (DLco $<$52% =0, DLco $\geq$52 =1). We assessed all parameters at the entry in the study except DLco evaluated after one year of follow up. Based on this analysis the equation was developed.
The equation of prognosis is 3.14 GGO + 0,70 index EScSG – 1,326 FVC - 0,1 the maximum daily dose of glucocorticoids + 0,136 Gamma globulins + 1.066 CYC – 1.075 DLCO $\leq$ 5,8.
Value of equation of prognosis to 5.8 corresponds to stabilization or good prognosis and value after 5.8 corresponds to poor prognosis. The equation of prognosis had 86% sensitivity and 56% specificity. The cut-off point 4.7 was

represented 65% sensitivity and 67% specificity. The prognosis intervals were following: value of equetion to 4.7 corresponds to good prognosis; value from 4.8 to 5.8 corresponds to stabilization and vaule after 5.8 corresponds to poor prognosis.
The mean value of discrimination function for each group is shown in table.

| Groups | N | The mean value |
|---|---|---|
| Group 1 | 13 | 3,6±1.3* |
| Group 2 | 30 | 4,7±1.4** |
| Group 3 | 15 | 6,7±2.5* ** |

* **p<0.001.

**Conclusions:** using discrimination analysis we got the prognosis intervals for the pts with SSc. It can give an opportunity to determine the prognosis of SSc-ILD.
**Disclosure of Interest:** None declared
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## FRI0295 DLCO /VA: A POSSIBLE PREDICTOR OF PULMONARY VASCULAR DISEASE IN SYSTEMIC SCLEROSIS

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**Background:** Pulmonary function tests (PFTs) are used for screening of pulmonary involvement in systemic sclerosis (SS). Decreased DLCO is the earliest and most sensitive alteration detected. It has been seen that there are some SS patients with reduced values of DLCO (<80%) who have no demonstrable ILD by HRCT or pulmonary arterial hypertension (PAH) criteria by screening methods (pulmonary artery pressure (PAP) and tricuspid regurgitation (TR), by echocardiography). DLCO divided by the alveolar volume (DLCO/VA) is usually normal or moderately low in the ILD; its drop suggests an alveolar-capillary membrane dysfunction, thus might suggest the presence of a possible pulmonary vascular disease (no-PAH) related to SS, like in other locations, or could be a predictor of PAH presence
**Objectives:** To describe and compare the clinical, immunological, echocardiographic and spirometric data of two patients groups with SS and decreased DLCO; differentiating those with unknown causes for the DLCO and DLCO/VA decrease, suggestive of alveolar-capillary membrane disease, from those with ILD, PAH or other pulmonary disease associated which could justify this finding
**Methods:** Retrospective review of a hospital cohort of 115 SS patients. All patients with DLCO <80% were included. We defined: "Cases", patients with DLCO/VA decreased without known causes for DLCO decrease, and "controls", patients with a known cause of decreased DLCO: PAH (PAP>36mmHg by echocardiogram), ILD by HRCT, two groups were compared FVC <80%, FEV <80% or other known lung disease
**Results:** 75 patients with SS and DLCO <80%, 20 cases and 55 controls, were compared. We found statistically significant differences in the pattern disease, with a greater proportion of cases with limited SS (LSS) and anticentromere Ab positive whereas predominance of diffuse SS (DSS) and antiScl70 positive in controls. Esophageal involvement was higher in controls and tricuspid regurgitation (TR) higher in cases (p<0.005). "Cases" had mean values: DLCO: 65.60%, DLCO/VA: 62.65%, PAP: 26.29mmHg, right atrial diameter: 12.10cm$^2$ and max. tricuspid speed: 2.23m/s. There were no differences in sex, evolution time, the presence of digital ulcers, telangiectasia, Raynaud's phenomenon, ischemic heart disease, smoking, or in the capillaroscopic pattern.

| | Cases (%) | Controls (%) | p |
|---|---|---|---|
| DSS | 1 (5) | 33 (60) | 0.000 |
| LSS | 18 (90) | 21 (38.2) | |
| Raynaud's fenomenon | 20 (100) | 54 (98.2) | 1.00 |
| Digital ulcers | 7 (35) | 30 (54.5) | 0.298 |
| Telangiectasia | 13 (65) | 36 (65.5) | 0.971 |
| Esophageal afection | 9 (45) | 41 (74.5) | 0.016 |
| Tricuspid regurgitation | 17 (85) | 28 (53.8) | 0.014 |
| Ischemical disease | 1 (5) | 2 (3.7) | 1.000 |
| Smoking | 3 (15) | 3 (5.5) | 0.333 |
| Anticentromere | 19 (95.0) | 22 (40.0) | 0.000 |
| AntiScl70 | 0 (0) | 15 (27.3) | 0.008 |

**Conclusions:** There are a group of patients with SS, LSS and anticentromere Ab positive predominantly, without respiratory symptoms and decreased DLCO/VA with no justifiable cause. The decrease in DLCO/VA suggest the existence of an alveolar-capillary membrane dysfunction.These patients often present TR without PAH by echocardiographic criteria, so there might be some alteration of the lungs microvasculature suggesting a "pre-PAH" pattern.We should consider a subgroup of patients who would be candidates, in clinical practice, to the application of the DETECT algorithm, cardiorespiratory response to exercise testing and/or cardiac hemodynamic study, despite the absence of symptoms and PAH criteria by ultrasound
**Disclosure of Interest:** None declared
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## FRI0296 THE OPTIMAL MODIFIED RODNAN SKIN SCORE TO PREDICT SKIN PROGRESSION OVER ONE YEAR DIFFERS BETWEEN AUTOANTIBODY SUBSETS

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**Background:** There are muliple potential therapeutic a gents under development for sstemic sclerosis (SSc). Given that SSc is uncommon, there is interest in cohort enrichment to maximize the potential of identifying a drug effect, One area of interest is a modified Rodnan skin score (mRSS) cut-off as an inclusion criterion in early diffuse SSc trials. Autoantibody profiles of SSc patients vary by geographical region. Given that the mRSS differs between autoantibody groups and that many trials are multinational, it is important to understand the differences in mRSS patterns between autoantibodies to choose optimal mRSS cut-off points that facilitates enrichment for patients likely to develop skin progression.
**Objectives:** We sought to determine the baseline mRSS to maximally predict progressive skin involvement over one year in US patients with early diffuse SSc, and assess if this differed by autoantibody.
**Methods:** We examined a US single-center cohort of prospectively followed early diffuse SSc patients seen for an initial visit between 1980 and 2014. To reflect modern early diffuse SSc clinical trial design, early was defined as <3 years of symptoms and diffuse SSc as proximal skin thickening. Eligible patients had ≥2 mRSS within one year of the first SSc center visit, for a minimum of 3 mRSS over one year. The outcome of interest was mRSS progression at any time over that year, defined as an increase of 5 points or more and a 25% increase in the mRSS from baseline. Autoantibodies were confirmed by immunodiffusion for Scl-70, immunofluorescence for anti-centromere and immunoprecipitation for RNA polymerase III (RNAP) and all other SSc-associated antibodies. Descriptive statistics using Receiver Operating Curve (ROC) analysis were used with mRSS progression as the state variable to determine cut-off points for mRSS.
**Results:** Among 317 eligible patients the mean age was 50.8±13.5 years, 74% were female and 92% Caucasian. The median disease duration was 0.90 years (IQR 0.63, 1.46). The mean baseline mRSS was 23±11. 25% (n=79) were scl-70 positive, 56% n=178) RNAP positive, 54 (17%) other SSc-associated antibody and 2% (n=6) missing. The median baseline mRSS (IQR) for RNAP was 24 (17,33), compared to 18 (13,25) for Scl-70 and 20 (13,28) for other antibodies (p=0.0004). In total, 163 patients (51%) developed progressive skin disease over one year. 59% of RNAP positive patients progressed, versus 48% of Scl-70 and 33% of other antibody positive patients (p=0.004). The mean time to peak mRSS was 0.51±0.23 years overall. The baseline mRSS below which there was the maximal likelihood of predicting progressive skin disease, with the greatest area under the curve (AUC) in Scl-70 positive patients was ≤24 (AUC 0.72; 95%CI 0.64, 0.80). This contrasted with RNAP patients, for which the maximal AUC occurred at ≤29 (AUC 0.74;95% CI 0.67, 0.80). Patients with other autoantibodies had a much lower baseline mRSS of ≤17 for optimal prediction (AUC 0.67; 95%CI 0.53, 0.80).
**Conclusions:** The mRSS cut-off that predicted skin progression over one year was different between RNAP, Scl-70 and other SSc antibodies. his supports the concept that cohort enrichment in clinical trials may be enhanced by modifying the mRSS cut-off point for the major autoantibody groups. A lower cut-off point will exclude some US patients who are likely to progress.
**Disclosure of Interest:** R. Domsic Consultant for: Biogen-Idec, M. Lucas: None declared, V. Steen: None declared, R. Lafyatis Grant/research support from: Regeneron, Consultant for: Regeneron, T. Medsger: None declared
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## FRI0297 A QUANTITATIVE VIDEOCAPILLAROSCOPIC STUDY ABOUT THE MAIN CATEGORIES OF THE "SCLERODERMA PATTERN" AND THEIR CORRELATION WITH THE CLINICAL FEATURES OF SYSTEMIC SCLEROSIS (SSC)

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**Background:** Many studies have been carried out in systemic sclerosis (SSc) in order to correlate the microvascular damage with the clinical features and/or organ involvement, most of them through qualitative assessment of the morphological abnormalities forming the so-called "scleroderma pattern" (SP). Quantitative studies about the SP are currently scarce, rarely addressing the relationship with the disease characteristics.
**Objectives:** To evaluate in a series of SSc patients the association between the types and extent of the SP with the clinical features and the disease severity.
**Methods:** Fifty-four patients (47 women and 7 men, mean age 59.5 years, median disease duration 13.0 years) consecutively enrolled, underwent nailfold videocapillaroscopy. For each patient, a total of 32 images were collected (4 images for the II, III, IV, V finger of both hands). All images were classified according to the following patterns: normal, non-specific, SP (with no reduction of the capillary density and with avascular areas). The patterns were correlated with such features as sex, age, disease duration, Raynaud's phenomenon and/or digital ulcers (DU). Moreover, skin, muscle, gastrointestinal, pulmonary, heart and renal involvement were considered. Statistical analysis was performed using MedCalc version 12.0 (MedCalc Software, Mariakerke, Belgium).

**Results:** A total of 1728 images were analyzed and patients were divided into 4 subsets, on the basis of the extent of the SP. In subset 1 (6 patients, 11.2%) the extent was less than 25%, in subset 2 (5 patients, 9.2%) the extent was between 25–50%, in subset 3 (16 patients, 29.6%) between 50–75%, in subset 4 (27 patients, 50%) was more than 75%. Subsets 1 and 2 showed no significant relationship with any of the variables considered. Patients of subset 3 had a significant correlation with the presence of DU (p=0.007). The subset 4 showed a significant correlation with disease severity (p=0.03), history of DU (p=0.04) and the presence of DU ($p \leq 0.0001$). SP without reduction of the capillary density was correlated with the presence of lung fibrosis (p=0.04). The SP with avascular areas showed a significant relationship with disease severity (p=0.001), lung fibrosis (p=0.01), gastrointestinal involvement (p=0.01), skin involvement (p=0.03), history of DU (p=0.04), and DU (p=0.001). No association was found between patterns and disease duration.
**Conclusions:** The correlation observed between the presence of DU and/or history of DU both with the extent of the SP and the avascular areas represent a relevant data, confirming the hypothesis of a strong relationship between the fingertip blood perfusion and the integrity of the nailfold microvasculature. Unexpectedly, lung fibrosis showed a significant association both with the SP without reduction in capillary density and with the avascular areas. This fact leads us to consider the possibility of the multifactorial nature of pulmonary involvement, not only determined by a reduced number of capillaries. The lack of correlation between type and extent of the scleroderma pattern with the disease duration supports the concept that the severity of microangiopathy is not a characteristic of the late stages of the SSc.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3673

## FRI0298 TREATMENT PATTERNS AMONG ADULT SYSTEMIC SCLEROSIS PATIENTS IN A US HEALTHCARE CLAIMS POPULATION

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**Background:** In the United States, systemic sclerosis (SSc) develops in adults at an annual estimated incidence rate of 20 cases per million, and the estimated prevalence is 240 cases per million.[1] Published research on the epidemiology of SSc and common treatments for US SSc patient cohorts is limited. In general, SSc patients are treated based on their specific organ involvement; patients with diffuse skin involvement or severe organ involvement, or both, are treated with systemic immunosuppressive therapy.
**Objectives:** To understand the treatment patterns for and the real-world use of immunosuppressive drugs in adults with SSc using data from a large US healthcare claims database.
**Methods:** The analysis is a retrospective cohort study of patients with SSc diagnosed from 2006 to 2012 using data from Truven Health MarketScan® Research Databases, a medical insurance claims database of insured active employees and their dependents, early retirees, Medicare-eligible retirees, and Medicaid recipients. An SSc diagnosis was determined by $\geq$1 inpatient claim for an SSc diagnosis (*ICD-9* 710.1) or $\geq$2 outpatient claims for an SSc diagnosis. During the study time period, patients were allowed enrollment gaps of $\leq$30 days but had to have enrollment data 6 months before and 12 months after the SSc diagnosis.
**Results:** The prevalence of SSc in the MarketScan database from 2006 to 2013 ranged from 204 to 247 cases per million adults who were actively enrolled in health insurance plans. There were 6872 patients $\geq$18 years of age diagnosed with and treated for SSc during the study time period. Eighty-six percent of the treated SSc population were female, and the average age of the cohort was 54 years. The most common medication claims among patients in the first year after an SSc diagnosis were for antibiotics (54%), opioids (44%), corticosteroids (40%), and proton pump inhibitors (PPIs) (31%). Approximately 30% of SSc patients initiated $\geq$1 of the following disease-modifying antirheumatic drugs (DMARDs), alone or in combination, in the first year after the SSc index, with a median time to initiation of 70 days: methotrexate (21%), mycophenolate mofetil (17%), biologics (3%), cyclophosphamide (2%), or other DMARDs (62% of which included azathioprine, chloroquine, cyclosporine, hydroxychloroquine, penicillamine, quinacrine, and sulfasalazine). Among patients who filled a DMARD prescription in the first year, 15% switched to a second type of DMARD. Of the 70% of patients who did not fill a prescription for DMARD in the first year after the SSc index, 63% filled prescriptions for antibiotics, 56% opioids, 33% corticosteroids, 26% PPIs, 20% NSAIDs, 10% ACE inhibitors, 10% calcium antagonists, 5% prokinetics, 1% ERA, and $<$1% prostacyclin.
**Conclusions:** These data show that the prevalence of SSc among adults in a US healthcare claims population is consistent with the estimated US prevalence. Most SSc patients do not initiate DMARD treatment in the first year after diagnosis, and most SSc patients have received antibiotics, opioids, and systemic corticosteroids.
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**Disclosure of Interest:** S. Gale Shareholder of: Roche, Employee of: Roche, N. Mathew: None declared, C. Lin: None declared, A. Jahreis: None declared, K. Sarsour Shareholder of: Roche, Employee of: Roche
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## FRI0299 PULMONARY ARTERIAL HYPERTENSION IN IDIOPATHIC INFLAMMATORY MYOPATHIES: DATA FROM THE FRENCH PULMONARY HYPERTENSION REGISTRY AND REVIEW OF THE LITERATURE

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**Background:** Occurrence of pulmonary arterial hypertension (PAH) in idiopathic inflammatory myopathies (IIM) without extensive interstitial lung disease (ILD) has been rarely described.
**Objectives:** This study aimed to report all cases with association of PAH and IIM in the French Pulmonary Hypertension (PH) Registry, to identify IIM features associated with PAH, and to describe treatment modalities of these patients.
**Methods:** All cases of IIM-PAH were retrieved from the French PH Registry, which gathers PAH patients prospectively enrolled by 21 referral centers across France. Patients were excluded if they had an extensive ILD or overlap syndrome. Characteristics of IIM-PAH patients were compared to a control group of IIM patients without PH.
**Results:** Among the 5223 PAH patients in the Registry, 34 had a diagnosis of IIM. Among them, 3 IIM-PAH patients had no sign of extensive ILD or overlap syndrome, and were included in this study. In these patients, dermatomyositis (DM) was the only identified IIM. Two of them had a myopathic DM, confirmed by electromyography and biopsy. The last patient had an amyopathic DM, associated with anti-Ku antibodies. Pre-capillary PH was hemodynamically proven in all patients. PAH always developed after IIM onset, was severe in all cases, and led to a marked functional impairment.
By pooling our cases with 6 previously reported patients, and comparing them to a control cohort of 35 IIM patients without PH, we identify several IIM characteristics possibly associated with PAH occurrence, including DM subtype (78% vs. 46%, $p$=0.02), skin involvement ($p$=0.04), anti-SSA antibodies ($p$=0.05) and peripheral microangiopathy ($p$=0.06).
Overall, IIM-PAH patients were managed by corticosteroids and/or immunosuppressants, either alone or combined with PAH therapy. Patients that did not receive PAH therapy did not seem to respond to IIM treatment alone.
**Conclusions:** Our study reports for the first time the rare but possible association of PAH and IIM in a large prospective PH Registry. In that setting, PAH seems associated with DM, skin involvement, peripheral microangiopathy and anti-SSA positivity. The best therapeutic strategy for IIM-PAH remains to be defined.
**Disclosure of Interest:** None declared
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## FRI0300 CORRELATIONS OF Δ HIGH-RESOLUTION COMPUTED TOMOGRAPHY (HRCT) SCORE WITH Δ CLINICAL VARIABLES IN EARLY SYSTEMIC SCLEROSIS (SSC) PATIENTS

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**Background:** The high-resolution computed tomography (HRCT) score showed correlation with % predicted Forced Vital Capacity (%pFVC) in our previous study[1]. However, the correlations of the delta (Δ) HRCT scores with Δ %pFVC and Δ clinical variables have not been reported.
**Objectives:** To evaluate the correlation of the Δ HRCT scores with Δ %pFVC, Δ

Modified Rodnan Skin Score (MRSS) and Δ ESR in patients with early SSc.
**Methods:** We used an inception cohort of early SSc patients seen at the Rheumatology clinic, Chiang Mai University, between January 2010 and June 2014. All patients underwent HRCT at study entry and every 12 months thereafter. The extent of ground glass (GG), lung fibrosis (Fib), bronchiectasis (B) and honeycombing (HC) was scored and then were aggregated to produce a total (t) HRCT score[1]. Thirty-one SSc patients who underwent pulmonary function test within 12 weeks of their corresponding HRCT were identified. The Δ HRCT score (the difference between the last visit and the baseline HRCT score) along with their corresponding clinical variables were used for analysis. Data abstracted include the HRCT scores: total (t)-GG, t-Fib, t-B, t-HC and t-HRCT; %pFVC; MRSS; and ESR.
**Results:** Mean±SD age and disease duration (from non-Raynaud's phenomenon to undergo first HRCT) were 52.2 ± 8.8 years and 11.7 ± 7.1 months, respectively. Seventeen (54.8%) patients were female and 20 (64.5%) were classified as diffuse cutaneous SSc. Mean±SD interval between the two HRCT tests was 16.0 ± 7.2 months. The mean±SD baseline t-GG, t-Fib, t-B, t-HC and t-HRCT scores were 3.2± 3.3, 4.0±3.5, 2.4±3.3, 0.7 ±2.2 and 10.3±10.3, respectively. The mean ±SD baseline %pFVC, MRSS and ESR were 69.0±15.9, 15.4±9.9 and 34.0±25.3, respectively. The mean ±SD absolute Δ HRCT scores were: t-GG, -0.5±2.1 (range -6.0 to 3.0); t-Fib, 0.3±1.9 (range -7.0 to 5.0); t-B, 0.5±1.2 (range -2.0 to 4.0); t-HC, 0.3±0.8 (range 0 to 3.0); t-HRCT, 0.7±3.8 (range-9.0 to 10.0). The mean ±SD absolute Δ clinical variables were: % of predicted FVC, 4.8 ±12.8 (range -33 to 26); MRSS, 4.9± 6.5 (range -17.0 to 8.0); ESR, -5.8 ±22.3 (range -60 to 58). Spearman rank correlations coefficient between the mean absolute ΔHRCT scores and the other variables were (N=31):

| | Δt-GG | Δt-Fib | Δt-B | Δt-HC | Δt-HRCT |
|---|---|---|---|---|---|
| Δ%pFVC | −0.09 | −0.16 | 0.05 | −0.15 | −0.05 |
| ΔMRSS | 0.05 | −0.08 | 0.01 | −0.02 | −0.01 |
| ΔESR | −0.02 | −0.09 | −0.29 | −0.44* | −0.33 |

*p<0.05.

**Conclusions:** In this study, the HRCT scores were fairly stable over the first two years of patients with early SSc; while %pFVC, MRSS and ESR showed relatively more change over the times. We found significantly negative correlation between Δ t-HC and Δ ESR. However, no significant correlations of Δ HRCT scores with Δ %pFVC and Δ MRSS were observed. Further longer study duration with larger study population is needed to confirm our findings.
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## FRI0301 PROGNOSIS OF THE IDIOPATHIC INFLAMMATORY MYOPATHIES ASSOCIATED WITH INTERSTITIAL LUNG DISEASE: PRELIMINARY ANALYSIS OF THE REGISTRY REMICAM

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**Background:** Some studies suggest that clinical subgroups of idiopathic inflammatory myopathies (IIM) and several myositis-specific antibodies (MSAs) could influence the prognosis of IIM with interstitial lung disease (ILD).
**Objectives:** To investigate the prognosis value of different clinical subgroups and of MSAs in a cohort of patients with IIM -associated ILD.
**Methods:** We analyzed patients with IIM-associated ILD included in the multicenter registry REMICAM (1980–2014). We compared prognosis between a) subgroups of IIM: dermatomyositis (DM) vs. polymiosytis (PM) (primary, juvenile, cancer-associated myositis or overlap myositis); and b) absence (–) or presence (+) of anti-Jo1 vs. anti-RO vs. anti-Jo1 and anti-RO. In this preliminary analysis, outcomes were mortality and change between final and initial visit in FVC and DLCO.
**Results:** 478 patients were included in the registry, of which 143 had ILD, 66% PM and 34% DM. The distribution by MSAs was: 56% anti-Jo1-/RO-, 20% anti-Jo1+, 9% anti-RO+ and 15% anti-Jo1+/RO+. There were 52 deaths; the main causes were 32.6% cardiovascular events and 22.4% infections without difference between subgroups of IIM. The probability of survival was 50% to 18.8 years and the mortality rate was 37.7/1000 patient-ys. We did not find differences when we compared survival between subgroups of IIM or we compared by MSAs. FVC seemed to improve more in DM than in PM patients (1.2±5.2vs. 0.5±4.7;p=0.059), but there were no significant changes in DLCO of DM patients or in FVC and DLCO according to MSAs.
**Conclusions:** We did not find prognostic differences in the causes of mortality, mortality rate between subgroups of IIM, or in mortality rate according to MSAs in patients with ILD. In DM patients there was a trend towards a greater improvement of FVC than in PM patients.
**Disclosure of Interest:** None declared
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## FRI0302 SCREENING FOR PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS USING THE DETECT PROTOCOL IN SECONDARY CARE

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**Background:** Pulmonary arterial hypertension (PAH) may occur in 20% of patients with systemic sclerosis (SS) which has a poor prognosis with survival approaching 50% at 2 years following diagnosis [(1)]. Early diagnosis of PAH may enable prompt pharmacological intervention, retard disease progression and improve long term outcomes[(2)]. It is recognised that proactive screening for SS-PAH with lung function testing and echocardiography (ECHO) is superior to investigations after PAH symptoms are established. In the UK, screening is based on the ESC/ESR guidelines, which includes annual ECHO and lung function testing. Although not widely utilised, screening with the DETECT protocol[(3)], an evidence based 2 step algorithm which includes serum urate, N-terminal pro-brain natriuretic peptide (BNP) and lung function testing may assist with earlier identification of patients with SS-PAH.
**Objectives:** To evaluate the utility of the DETECT protocol in identifying SS associated PAH in a secondary care connective tissue disease service.
**Methods:** A retrospective review of 74 patients with Systemic Sclerosis (Limited, Diffuse and Mixed CTD) attending a secondary care connective tissue disease clinic in Northwest London. All patients were analysed for general demographics, autoantibody profiles and parameters required for a DETECT 1 and DETECT 2 score within a 12 month period. Each score was correlated with diagnosis of PAH made at the regional PAH centre.
**Results:** 90% (68) of patients were female, mean age 56 years (range 27–85). Limited Systemic Sclerosis (LSSc) accounted for 53% of patients (Diffuse 24%, Mixed CTD 23%) and 43% (32) of all patients were anti-centromere positive (RNP- 24%, Scl-70 20%, PM-Scl 9%). DETECT 1&2 parameters were available for 26–100% of variables (Table 1). A full set of parameters to calculate DETECT 1 was achievable in 32/74 (43%) patients. 21/32 patients had a detect score >300 recommending ECHO with LSSc accounting for a majority of this group (LSSc 14, Diffuse 4, Mixed CTD 3). DETECT 2 parameters were complete in 15/21 patients. 7 of these patients had a score >35 recommending right heart catheterisation (RHC). 1 patient had RHC and a diagnosis of PAH was made in 3 patients (3/32) consistent with respective DETECT scores. Conversely, 7 patients with a DETECT 1 score<300 had echocardiography, against protocol recommendations.

Table 1. DETECT scores and parameters

| DETECT Score Variable (N=74) | N | % |
|---|---|---|
| FVC:TLCO | 49 | 66% |
| BNP | 46 | 62% |
| Serum Urate | 34 | 46% |
| ECG | 31 | 42% |
| Anti-centromere | 74 | 100% |
| Telangectasia | 74 | 100% |
| ECHO | 50 | 68% |
| TRV | 43 | 58% |
| RAA | 19 | 26% |
| PAP | 28 | 38% |
| | | |
| DETECT 1 | 32 | 43% |
| ECHO recommended (DETECT 1>300) | 21/32 | |
| ECHO performed | 19/21 | |
| PAP > 25 mmHg | 19/21 | |
| | | |
| DETECT 2 | 15 | |
| Referral & RHC recommended (DETECT 2 >35) | 7/15 | |
| Referred to Tertiary service | 5/15 | |
| RHC performed | 1/15 | |
| PAH diagnosed | 3/15 | |
| PAP > 25 mmHg | 7/15 | |

**Conclusions:** This small study indicates that the DETECT screening protocol for SS-PAH may be effective in secondary care connective tissue disease services enabling earlier diagnosis and a more prudent approach to using ECHO and rationalising tertiary service referrals. Limitations of this screening tool include the timely collection of clinical parameters required for calculation of DETECT scores, as was evident in our attrition rate.
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FRI0303 **AUTOIMMUNE DISEASES ASSOCIATED WITH ANTI-KU ANTIBODIES: A RETROSPECTIVE CASE SERIES**

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**Background:** The anti-Ku antibodies are directed against a DNA-binding nuclear protein complex composed of 2 polypeptides of 86 and 70 kDa in a 1:1 ratio. These autoantibodies were originally described in 1981 by Mimori et al. in patients with systemic sclerosis (SSc)-polymyositis (PM) overlap syndromes, but further studies have associated anti-Ku antibodies with a wide variety of autoimmune diseases (AD) including systemic lupus erythematosus, Sjögren's syndrome, SSc, mixed connective tissue disease (MCTD) and idiopathic lung fibrosis (ILF).
**Objectives:** To describe the clinical and immunological features of patients with positive anti-Ku antibodies treated in a Spanish tertiary center.
**Methods:** We performed a retrospective study of anti-Ku-positive patients seen in our center during the period 2007–2015. Positivity for anti-Ku was detected through line immunoassay and confirmed by indirect immunofluorescence. Demographic, clinical, therapeutic and outcome data were obtained through review of their medical records.
**Results:** During the study period 14 anti-Ku-positive patients were found, 10 of them women (71.4%), mostly Caucasian (85.7%) with a mean age of 53.2 years (range: 14–79). Three patients had ES-PM overlap syndrome, 3 dermatomyositis (1 paraneoplastic), 2 unspecified myositis, 1 diffuse cutaneous SSc, 1 limited cutaneous SSc, 1 SSc sine scleroderma, 1 MCTD, 1 ILF and 1 IgM mesangial glomerulonephritis. The most frequent clinical manifestations were: arthralgia 50%, Raynaud 42.8%, muscular weakness 42.8%, hand edema 42.8%, sclerodactyly 35.7%, dyspnea 35.7%, myalgia 28.5% and Gottron papules 28.5%. Interstitial lung disease (ILD) was detected in 6 cases (42.8%), 3 with radiological pattern of usual interstitial pneumonia, 2 nonspecific interstitial pneumonia and 1 without a characteristic pattern. The acute phase reactants were elevated in 5 cases and muscle enzymes in 9 (creatine kinase mean value 1096 IU/L, range: 309–2256), 3 showed lymphopenia and 4 polyclonal hypergammaglobulinemia. Myositis (demonstrated by electromyography and muscle biopsy) was present in 4 cases (29.5%). Antinuclear antibodies were positive in 12 cases (85.7%), anti-Ro/SSA antibodies in 3 (21.4%) and anti-centromere, anti-RNP, anti-DNA, anti-PM/Scl75 and anti-MDA5 in 1 case each (7.1%). After a mean follow-up of 35.2 months 4 patients with ILD developed impairment of respiratory function tests despite treatment with corticosteroids and immunosuppressants, but not worsening of myositis or mortality.
**Conclusions:** The features of anti-Ku-positive patients in our series are comparable to those reported in other series published. These antibodies are not specific markers of any AD but are more common in overlap syndromes, so that should be considered in these disorders, especially when myositis is present. ILD frequency was relatively high and the outcome was unfavorable in most cases. Anti-Ku antibodies have been associated with severe and corticoresistant ILD but not with a significant risk of malignancy.
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FRI0304 **THE CHANGE OF THE FREQUENCY OF RIGHT HEART CATHETERIZATION FOR THE DIAGNOSIS OF PULMONARY HYPERTENSION AMONG PATIENTS WITH CONNECTIVE TISSUE DISEASES IN A HOSPITAL IN OSAKA, JAPAN – COMPARISON OF THE FIRST 5 YEARS AND THE LATTER 5 YEARS**

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**Background:** Pulmonary hypertension (PH) is defined as an increase in mean pulmonary arterial pressure (PAPm) greater than or equal to 25 mmHg at rest as assessed by right heart catheterization (RHC), but RHC is not routinely performed for the diagnosis of PH in a "real world" setting in Japan.
**Objectives:** The aim of this study is to assess the change of frequency of RHC for the diagnosis of PH among patients with connective tissue diseases in our hospital, and to know if the decision to prescribe pulmonary hypertension drugs is affected by whether we perform RHC.
**Methods:** Clinical records of admitted patients describe both the main diseases which were constantly followed by physicians and the actual diseases which were the reasons for admission. We analyzed the clinical records retrospectively of who was admitted to the wards of our rheumatology section for 10 years from Aug 1, 2005 to July 31, 2015. These 10 years were divided into two periods: the first half is from Aug 1, 2005 to July 31, 2010 (period A) and the latter half is from Aug 1, 2010 to July 31, 2015 (period B). We checked echocardiography, RHC and prescription for PH drugs. PH drugs include prostacyclin pathway agonists, endothelin receptor antagonists, and nitric oxide-cGMP enhancers.
**Results:** We reviewed clinical records of 5,428 patients for ten years and we found 57 patients with the diagnosis of PH either in the section of main diseases or actual diseases. We used the label "tentative pulmonary hypertension (tentative PH)" for patients who showed peak tricuspid regurgitation gradient in thoracic echocardiography of more than or equal to 30 mmHg. Among the tentative PH patients, those whose PAPm were confirmed by RHC were labeled "true pulmonary hypertension (true PH)". Forty patients among the 57 selected patients were categorized as having tentative PH and their original diseases were 20 with systemic sclerosis, 4 with Sjögren's syndrome, 3 with mixed connective tissue disease, and 2 with systemic lupus erythematosus, and so on. Among these 40 patients, 25 belonged to period A and 15 belonged to period B. RHC was performed for 9 patients (36.0%) in period A and true PH was diagnosed in 5 of those 9 patients (55.6%). Also RHC was performed for 12 patients (80.0%) in period B and 7 patients were found to have true PH (58.3%). In period A, 60% of true PH patients (3/5) and 60% of tentative PH patients (12/20) took PH drugs, and in period B, 71.4% of true PH patients (5/7) and 37.5% of tentative PH patients (3/8) took PH drugs.
**Conclusions:** The frequency of RHC increased from 36% in the first half period to 80% in the latter half period in our hospital. In addition, the use of PH drugs did not depend on the confirmation of PH by RHC, particularly in the first half period. In Japan rheumatologists, including doctors at our hospital have a tendency to prescribe PH drugs without RHC data, but recently this tendency is changing. This tendency to not always perform RHC may be partly explained by the content of the guidelines from the Ministry of Health, Welfare and Labor in Japan.
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## SLE, Sjögren's and APS - clinical aspects (other than treatment)

FRI0305 **FACTORS DETERMINING HYDROXYCHLOROQUINE SERUM LEVELS IN A COHORT OF CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Objectives:** To study the factors determining the hydroxychloroquine (HCQ) serum concentration in a cohort of Chinese patients with systemic lupus erythematosus (SLE).
**Methods:** Consecutive patients who fulfilled $\geq$4 of the 1997 ACR criteria for SLE and had received HCQ for 6 months or more were recruited from our lupus clinic and hospital admissions in a 9-month period starting from November 2011. Patients were prescribed HCQ at fixed daily dosages of 400 mg, 300 mg, 200mg or less than 200mg (eg. 200mg 3 or 5 times per week) at the discretion of their attending doctors according to disease activity, organ manifestations and risk factors for HCQ toxicities. Blood was assayed for the serum levels of HCQ by an in-house technique using the tandem mass spectrometry (SPE-MS/MS). Factors affecting HCQ serum concentrations were studied by univariate and multivariate linear regression analyses. Covariates being tested in the regression models included age, sex, body mass index (BMI), prescribed dosage of HCQ, SLE disease activity score (SLEDAI), ever smoking, estimated glomerular filtration rate (eGFR) and concomitant prednisolone.
**Results:** 276 SLE patients were studied (94% women; mean age 41.0±13.8 years; SLE duration 8.7±6.6 years). HCQ was primarily used for the treatment of mucocutaneous or musculoskeletal manifestations, or both, in 73%, 78% and 93% of the patients, respectively. Patients were stratified into 3 groups according to the HCQ levels: (1) Total non-compliance ($<$10 ng/ml); (2) Sub-therapeutic (10–500 ng/ml); and (3) Therapeutic ($\geq$500 ng/ml). The proportion of patients with HCQ levels of $<$10, 10–500, $\geq$500 ng/ml was 11%, 77% and 12%, respectively. Patients with total non-compliance to HCQ were more likely to be in clinical and serological remission when compared to the remaining patients (42% vs 24%; p=0.04). However, no difference in the clinical manifestations could be observed between patients with total non-compliance and other patients. After excluding patients with total non-compliance to HCQ therapy, the mean and median HCQ serum concentration of the remaining 245 patients was 300±87ng/ml and 276ng/ml (interquartile range 167–401), respectively. Univariate linear regression revealed that the prescribed HCQ dosage (beta 0.47; $p<0.001$) and the SLEDAI score at the time of recruitment (beta 0.16; p=0.02) were the significant factors associated with the HCQ serum concentrations. Multivariate linear regression with all the factors being considered in the model showed that the prescribed HCQ dosage (beta 0.50; $p<0.001$) and eGFR (beta -0.14; p=0.02) were independent factors

associated with HCQ serum levels. Age, sex, BMI, smoking, SLEDAI score and concomitant prednisolone were not significantly associated with the HCQ serum concentrations.
**Conclusions:** Non-compliance and sub-therapeutic HCQ serum levels were frequent in our cohort of SLE patients, which was related to the low prescribed dosage for maintenance treatment in those with clinical and serological remission. Patients with lower eGFR or receiving higher doses of HCQ were more likely to achieve higher HCQ serum concentrations. Thus, HCQ level monitoring and dosage adjustment may be helpful in SLE patients with impaired renal function to reduce the risk of toxicities.
**Disclosure of Interest:** None declared
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## FRI0306 SERUM ANTI-MÜLLERIAN HORMONE LEVELS IN SLE PATIENTS: INFLUENCE OF DISEASE SEVERITY AND THERAPY ON THE OVARIAN RESERVE

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**Background:** Systemic lupus erythematosus (SLE) predominantly affects women of reproductive age and may negatively affect their fertility due to severe organ involvement and the prolonged immunosuppressive therapy used. The Anti-Müllerian Hormone (AMH) is secreted from granulosa ovary cells and serum levels of Anti-Müllerian Hormone are used as a measure of ovarian reserve, reflecting the number of primary follicles. Systemic lupus erythematosus (SLE) predominantly affects women of reproductive age and may negatively affect their fertility due to severe organ involvement and the prolonged immunosuppressive therapy used. The Anti-Müllerian Hormone (AMH) is secreted from granulosa ovary cells and serum levels of Anti-Müllerian Hormone are used as a measure of ovarian reserve, reflecting the number of primary follicles.
**Objectives:** To compare serum levels of AMH in a cohort of patients with SLE and healthy controls and to assess whether the presence of the disease, the treatments used and/or other clinical parameters may affect the ovarian reserve.
**Methods:** Eighty-six consecutive female patients with SLE of childbearing age, aged between 18 and 42 years and with regular menses and 44 healthy controls age-matched were evaluated. Anti-Müllerian Hormone levels were measured in peripheral blood samples (kit AMH Gen II ELISA, Beckman Coulter). Clinical and demographic characteristics, disease duration, pattern of organ involvement and previous and current therapies were collected at the time of sampling. Fourteen patients (16.3%) had been treated with cyclophosphamide (CTX, cumulative dose 8.3 ± 5.4 g), and of the remaining, 39 (45.3%) with other DMARDs (methotrexate-MTX, azathioprine, mycophenolate mofetil, cyclosporine) and 33 (38.4%) with anti-malarials only.
**Results:** Patients with SLE had a mean age of 30.4±6.3 years, a disease duration of 7.7±5.1 years and 25 patients (33.3%) had a severe organ involvement (mainly renal and neurological, 14 were treated with cyclophosphamide, 11 with other DMARDs). Serum levels of AMH were comparable between patients and controls (4.2±3.3 vs 5.0±3.1 ng/ml, respectively, p=0.2). Considering patients on the basis of organ involvement, patients with major organ involvement had AMH levels (3.6±2.8 ng/ml) significantly lower than control subjects (p=0.03); no difference was found between patients with minor organ involvement (AMH 4.4±3.4 ng/ml) and control subjects (p=0.4). Considering the treatments used, patients with major organ involvement treated with cyclophosphamide showed serum AMH levels lower than controls (2.9±3.3 ng/ml, p=0.04). Moreover, patients previously exposed both to CTX and MTX, showed the lower AMH levels with respect to other groups (1.1±1.9 ng/ml, p=0.01). There were no associations between the use of other DMARDs than cyclophosphamide and lower AMH levels in SLE patients compared to controls.
**Conclusions:** In the whole cohort of SLE patients, the ovarian reserve was overall comparable to that of healthy controls, whereas a reduction of the ovarian reserve was associated with the use of cyclophosphamide and the severity of the disease.
**Disclosure of Interest:** None declared
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## FRI0307 CHANGES IN URINARY BIOMARKER LEVELS CAN PREDICT TREATMENT RESPONSES IN LUPUS NEPHRITIS

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**Background:** The relapsing and remitting nature of lupus nephritis (LN) poses a challenge to clinicians who must balance the risk of long term kidney damage with the side effects of treatment. Management of this condition would be greatly aided by the identification of biomarkers that accurately reflect and predict treatment responses. We previously identified and validated a panel of urinary biomarkers that are specifically elevated in SLE patients with active LN as compared to active patients without LN or LN patients in remission.
**Objectives:** To determine whether changes in the levels of these urinary biomarkers predict treatment responses.
**Methods:** 21 SLE patients with biopsy-proven LN were followed longitudinally for a minimum of 2 years after treatment. Levels of 15 urinary biomarkers including Clusterin, Cystatin C, NGAL, PF4, vWF,sVCAM-1, GM-CSF, GRO, IL-15, IL-6, MCP-1, Adiponectin, PAI-1, MMP-7, and TIMP-1, were measured by Luminex. Patients were classified as having a complete response (n=12), partial response (n=4), or treatment (Tx) failure (n=5) at 2 years following initiation of treatment, based upon previously established criteria. Urinary biomarker levels were considered abnormal if they were >2 SD above the mean for 24 healthy controls. Data were analyzed using non-parametric statistics.
**Results:** At 3–6 months following treatment, the changes in biomarker levels from the first visit were not significantly different between complete responders and partial responders or Tx failures. However, at 1 year (11–16 months) following treatment, 5 urinary biomarkers, sVCAM-1, Adiponectin, IL-15, vWF, and MCP-1, demonstrated significantly different changes from baseline in complete responders as compared to Tx failures, with the majority of responders demonstrating improvement and the majority of Tx failures demonstrating worsening. As urinary biomarker levels not corrected for urinary osmolality correlated best with clinical outcomes, subsequent analyses were done with the uncorrected values. Normalization of urinary Adiponectin by 11–16 months was the best predictor of a complete response, with 11 of 12 patients who normalized being complete responders and 1 a partial responder. Similar but slightly less discriminative results were obtained for the other 4 urinary biomarkers. Conversely, the presence of an abnormal urinary vWF at 11–16 months was the strongest predictor of an adverse outcome with 4 of 6 patients with abnormal levels being Tx failures. Notably, all patients that were Tx failures that had normal levels of urinary biomarkers at 11–16 months subsequently developed abnormal levels, whereas patients who were complete responders eventually normalized the majority of these 5 biomarkers. Partial responders demonstrated normalization with delayed kinetics.
**Conclusions:** Measurement of urinary biomarkers can provide valuable insight into treatment responses in lupus nephritis.
**Disclosure of Interest:** None declared
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## FRI0308 SURFACE TETHERIN IS A NOVEL CELL-SPECIFIC BIOMARKER FOR INTERFERON RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Type I interferons (IFN-I) have diverse effects on immune cell populations in SLE, Measuring IFN-I response using PBMCs or whole blood interferon-stimulated gene (ISG) expression does not completely explain clinical features of SLE and IFN blocking therapy. Furthermore, the proportions of cell populations in blood altered with disease activity. Bone marrow stromal antigen 2/Tetherin (BST2), is a cell surface protein eminent in viral immunology as interferon-induced viral restricting molecule expressed on most circulating leucocytes.
**Objectives:** To develop a cell-specific IFN-I assay
**Methods:** PBMCs were collected from 133 SLE patients and 19 healthy controls. Disease activity was measured using BILAG-2004. PBMCs were analysed by flow cytometry for cell surface BST2 protein on each immune cell subset. Cells were FACS-sorted into naïve and memory B-cells, plasmablasts, CD3+ T-cells, NK-cells and monocytes in 12 SLE patients and 16 healthy controls. Expression of *BST2,* as well as 32 other ISGs, were measured using qPCR and a 33-gene IFN score calculated.
**Results:** Analysis of sorted cells confirmed that surface BST2 is a valid cell-specific IFN assay. *BST2* expression correlated with BST2 surface protein within each immune subset: naïve B-cells (r=0.63, p=0.009); memory B-cells (r=0.78, p<0.001); plasmablasts (r=0.58, p=0.018); NK cells (0.63, p=0.008); T-cells (r=0.61, p=0.012); monocytes (r=0.47, p=0.064).
We next used surface BST2 to compare IFN activity of each subset with clinical features in 133 patients. A strong correlation between the PBMC 33-gene IFN score and surface BST2 was found for each cell subset (all p<0.001) confirming validity of BST2 as a biomarker.
BST2 was significantly higher in SLE than HC on naïve and memory B-cells (p=0.004, p=0.003), plasmablasts (p=0.047), T cells (p=0.043), but not different on monocytes (p=0.406).
Association of total BILAG score with BST2 on naïve and memory B-cells (Tau-a =0.23 and 0.22 respectively) was substantive and approximately twice as strong as monocytes and T-cells (Tau-a =0.12 and 0.14). A similar pattern was seen for anti-dsDNA titre, with no association with monocyte BST-2 (Tau-a =0.07) but a substantive association for memory B cell BST-2 (Tau-a =0.18).
**Conclusions:** IFN-I response differs in cell subsets. This can be measured in a fast, cost-effective, convenient assay using flow cytometric analysis of surface BST2. Our results show that IFN activity measured on B cells is more clinically relevant than on other cell populations.
**Disclosure of Interest:** None declared
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## FRI0309 TYPE I INTERFERON ACTIVITY IS ASSOCIATED WITH MUCOCUTANEOUS BUT NOT MUSCULOSKELETAL DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** SLE is clinically and immunologically heterogeneous. Type I interferons (IFN-I) are pathogenic but expression of IFN-I stimulated genes varies. Many existing reports on clinical phenotype and IFN-I were limited by using categorical measures of IFN-I and disease activity scores that were not organ-specific. IFN-I targeted therapies are in development.
**Objectives:** To define the clinical phenotype of IFN-I mediated SLE.
**Methods:** 108 SLE patients and 20 age and sex matched healthy controls were studied. Activity was measured using BILAG-2004. PBMCs were collected for gene expression analysis using TaqMan. Relative expression of 7 interferon stimulated genes was ln-transformed, normalized to healthy control and summed to derive a 7-gene IFN-I score.
**Results:** The most common activity was mucocutaneous and musculoskeletal, which were analysed in detail (Table 1). The relationship between activity and IFN-I score differed between these domains. Overall, IFN-I scores were higher in active mucocutaneous disease. Scores were more variable for BILAG B: this was explained by subtype of BILAG B disease. IFN-I score was increased in subacute and discoid forms (25.3 (16.8–32.9), n=7) compared to acute forms (18.4 (4.9–31), n=15). Score was also higher in patients with anti-Ro60. In contrast, there was no relationship between musculoskeletal disease activity and IFN-I score.
Numbers of patients with renal, haematological and neuropsychiatric activity were limited but there was a trend to higher IFN-I scores with disease activity.

| BILAG domain score (n) | IFN score median (IQR) | P value vs. D+E | P value vs. E |
|---|---|---|---|
| Mucocutaneous | | | |
| A (6) | 27.2 (26.3–31.5) | 0.027 | 0.005 |
| B (22) | 20.5 (9.1–32) | 0.255 | 0.181 |
| C (18) | 30.7 (11.7–38.2) | 0.025 | 0.042 |
| D (46) | 19.3 (3.7–28.1) | NA | 0.469 |
| E (16) | 14 (4.2–22.6) | NA | NA |
| D+E (62) | 17.6 (3.7–27.6) | NA | NA |
| Musculoskeletal | | | |
| A (6) | 24.9 (5–31) | 0.846 | 0.662 |
| B (15) | 19.8 (6.5–28.4) | 0.652 | 0.925 |
| C (37) | 17.2 (3.5–30.7) | 0.445 | 0.965 |
| D (42) | 24.2 (6.2–31.8) | NA | 0.746 |
| E (8) | 19.4 (10.8–26.3) | NA | NA |
| D+E (50) | 23.5 (6.2–31.4) | NA | NA |

**Conclusions:** We identify a relationship between clinical presentation of SLE and IFN-I. High IFN-I activity is linked to anti-Ro60 and non-acute forms of skin disease. We previously reported a worse response to rituximab in this subgroup, whilst response in musculoskeletal disease was consistently good. Measurement of B cell and interferon biomarkers may therefore be important in the selection of the most appropriate targeted therapy for SLE.
**Disclosure of Interest:** None declared
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## FRI0310 SERUM INSULIN-LIKE GROWTH FACTOR-BINDING PROTEIN 2 (IGFBP2) AS A BIOMARKER OF CLINICAL AND HISTOPATHOLOGICAL TREATMENT RESPONSE IN LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) is a severe manifestation of Systemic Lupus Erythematosus (SLE). Renal biopsy is the gold standard for evaluation of renal activity and damage in LN. Evaluation of new biomarkers for non-invasive assessment of renal pathology is warranted. Insulin-like growth factor-binding protein 2 (IGFBP2) has been found to be a robust diagnostic and prognostic biomarker in malignancies. In animal models, IGFBP2 expression was increased in anti-glomerular basement membrane (anti-GBM) glomerulonephritis and MRL/lpr lupus mice.
**Objectives:** We aimed to investigate the role of IGFBP2 in LN.
**Methods:** Serum levels of IGFBP2 were assessed by ELISA (R&D Systems) in 64 patients with biopsy-proven active LN (52 proliferative, 12 membranous), before and after completion of induction treatment. Post-treatment renal biopsies were performed after a median time of 7.7 months. Clinical responders (CR) were defined by $\geq$50% reduced proteinuria, normal or $\geq$25% improved estimated glomerular filtration rate (eGFR), and inactive urinary sediment. Histopathological responders (HR) were defined by $\geq$50% improvement of renal Activity Index (AI) in post-treatment biopsies. Long-term renal outcome after a median time of 11.3 years (range: 3.3–18.8) was determined by the last eGFR.
**Results:** Serum IGFBP2 levels decreased following induction therapy ($p<0.001$). Serum IGFBP2 levels decreased in both CR ($p<0.001$) and HR ($p<0.001$), but remained unchanged in clinical non-responders (CNR; p=0.44) and histopathological non-responders (HNR; p=0.16). Post-treatment, but not baseline, IGFBP2 levels were higher in CNR compared to CR (p=0.004). Serum IGFBP2 levels correlated with proteinuria, both at baseline (r=0.34, p=0.006) and post-treatment (r=0.48, $p<0.001$). Post-treatment, but not baseline, IGFBP2 levels correlated with Activity Index (r=0.31, p=0.015) and Chronicity Index (CI) scores (r=0.35, p=0.006) in post-treatment renal biopsies, as well as with post-treatment SLE disease activity index 2000 (SLEDAI-2K) scores (r=0.32, p=0.009). Baseline IGFBP2 levels were associated with decreases in eGFR following treatment (p=0.028); no other association was found between baseline IGFBP2 and changes in proteinuria (p=0.14), SLEDAI-2K (p=0.97), AI scores (p=0.54) or CI scores (p=0.07). Following induction treatment, patients showed improvements in eGFR ($p<0.001$). No correlation was found between IGFBP2 and eGFR at either baseline or post-treatment, and there was no association between baseline (p=0.48) or post-treatment (p=0.91) serum IGFBP2 levels and changes in eGFR during long-term follow-up.
**Conclusions:** The decreases in serum IGFBP2 levels following induction therapy in responding, but not in non-responding, patients suggest serum IGFBP2 as a marker of disease activity and response to treatment in LN. Interestingly, baseline IGFBP2 levels were associated with renal function deterioration following treatment, despite an overall improvement in eGFR. Post-treatment, but not baseline, levels mirrored both global SLE activity and histopathological findings, which together with the observed correlation with proteinuria levels suggests IGFBP2 as a marker of activity in patients with history of LN and no or low-grade proteinuria.
**Disclosure of Interest:** None declared
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## FRI0311 NEUROPSYCHIATRIC LUPUS: COMBINING ADVANCED MORPHOMETRIC METHODS, DIFFUSION TENSOR IMAGING AND CONVENTIONAL MRI LEADS TO THE PATHWAYS OF BRAIN ABNORMALITIES. CORRELATION WITH CLINICAL AND LABORATORY DATA

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**Objectives:** To combine conventional and advanced magnetic resonance imaging (MRI) to describe brain abnormalities in neuropsychiatric (NP) systemic lupus erythematosus (SLE), and to correlate them with clinical data.
**Methods:** Prospective study including patients presenting central primary NPSLE, non-NPSLE and healthy controls (HC) undergoing brain MRI at 3T in 2014–2015. Conventional MRI data using visual scales for atrophy and white matter (WM) lesions, brain volumetry (voxel-based morphometry and Freesurfer), and diffusion-tensor imaging (DTI) were analyzed. Group differences were correlated with clinical, laboratory and treatment data.
**Results:** Twenty-eight females with NPSLE, 22 non-NPSLE and 20 HC, mean age around 40 years, were recruited. Conventional MRI showed brain atrophy in NPSLE (p=0.005). Total cortical volume was reduced in NPSLE compared to HC (p=0,042). Non-NPSLE had a reduction of left temporal gray-matter (GM) volume compared to HC (p=0.028). NPSLE had a decrease of left frontal WM volume compared with HC (p=0.002). Corpus callosum was reduced in NPSLE compared to HC (p=0.033) and non-NPSLE (p=0.043). DTI showed increased diffusivity (mean, axial and radial: MD, AD, RD) in bilateral temporal WM ($p<0,010$) and reduced fractional anisotropy (FA) in right frontal WM (p=0.018) in NPSLE versus HC.
SLEDAI score was correlated with atrophy (p=0.046); negatively with left temporal cortex volume (p=0.029) and with FA in WM hippocampal regions (p=0.002 left, p=0.048 right). SLICC score was correlated with diffusivity in bilateral temporal WM (MD:p=0.033; AD:p=0.039; RD:p=0.016) and right frontal WM (p=0.005); and negatively with FA in left WM hippocampal regions ($p<0.001$). SLE duration was correlated with diffusivity in temporal WM (MD:p=0.007; AD:p=0.007 and RD:p=0.007); and negatively with FA in right frontal and left temporo-occipital WM ($p<0.0005$ and p=0.014) and with right frontal cortex volume (p=0.028). Low C4 and CH50 were inversely correlated with left temporal cortex volume (p=0.003 and 0.002).
Antimalarials were negatively correlated with atrophy on conventional MRI (p=0.004), total GM volume (p=0.021) and subcortical GM volume (p=0.020); specifically with right and left frontal cortex (p=0.029 and 0.015) and right and left thalamus (p=0.009 and 0.047). Antimalarials were correlated with lower diffusivity in multiple WM clusters (right and left temporal: decreased MD, p=0.006 and

0.004; AD, p=0.007 bilaterally; RD, p=0.005 bilaterally; and right frontal: decreased RD, p=0.010).
**Conclusions:** Atrophy and DTI changes indicating microstructural damage in frontal and temporal white and gray matter are the most important radiological findings in NPSLE. Assessing them should become the milestone of monitoring this disease. This changes correlates with the severity, activity and duration of the disease. Antimalarial treatment could produce some protective effect on the brain in SLE patients.
**Disclosure of Interest:** None declared
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## FRI0312 PREDICTORS OF INCIDENT EPISODES OF PROTEINURIA AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Lupus nephritis remains one of the most devastating SLE complications, occurring in over 50% of the patients. It is important to identify clinical conditions that precede nephritis for the purposes of patient care and to identify preventive strategies. Most previous studies of predictors of incident nephritis in SLE are cross-sectional or do not incorporate time-varying predictors.
**Objectives:** We leveraged a large clinical cohort which evaluated patients quarterly to identify fixed and time-varying predictors of lupus nephritis.
**Methods:** Since 2006, the urine protein/creatinine ratio was measured quarterly in patients in our SLE cohort. This analysis was based on cohort follow-up after 2006 in patients who did not have a history of diabetes and who did not have a prior episode of sustained elevated proteinuria, nor a history of nephritis, renal insufficiency, or failure. Among these patients, we defined an incident case of proteinuria as two or more measures of urine protein/creatinine (or 24-hour protein measure) greater than 0.5 in two visits separated by more than 30 days and less than 180 days, among patients with no prior episodes of proteinuria. We estimated rates of incident proteinuria in subgroups of patients defined by time-invariant and time-varying predictors.
**Results:** Among 895 patients included in the analysis, 840 (94%) were female, and 518 (58%) were Caucasian, 304 (34%) African-American, with mean age of 42 at the start of follow-up. We observed 58 incident cases of proteinura over a span of 4669 person-years of cohort follow-up. The overall rate of incident proteinuria was 12.4 per 1000 person-years. The Table shows the association between select predictors and the rate incident proteinuria. The rate was significantly lower among those of older age, and significantly higher among those who were not Caucasian. Among those with a history of low C3, the rate was 8 times higher, and highest among those with a recent measure of low C3. The rate among those prescribed hydroxychloroquine was similar to those not prescribed hydroxychloroquine. Among those taking medicine for hypertension, the rate among those prescribed ACE inhibitor or ARB was similar to the rate among those prescribed other treatments.

Table 1: Rates of incident proteinuria by patient characteristics.

| Subgroup | Observed Number of new cases of proteinuria | Person-years of follow-up | Rate of events per 1000 py's | Rate Ratios | P-value |
|---|---|---|---|---|---|
| Everyone | 58 | 4669 | 12.4 | | |
| Age | | | | | |
| 18-39 | 39 | 1515 | 25.7 | 1.0 (Ref) | |
| 40-49 | 11 | 1171 | 9.4 | 0.4 (0.2, 0.7) | 0.0031 |
| 50-59 | 5 | 1183 | 4.2 | 0.2 (0.1, 0.4) | 0.0001 |
| 60+ | 2 | 780 | 2.5 | 0.1 (0.0, 0.4) | 0.0013 |
| Sex | | | | | |
| Female | 54 | 4376 | 12.3 | 1.0 (Ref) | |
| Male | 4 | 293 | 13.7 | 1.1 (0.4, 3.1) | 0.84 |
| Ethnicity | | | | | |
| Caucasian American | 20 | 2803 | 7.1 | 1.0 (Ref) | |
| African American | 30 | 1548 | 19.4 | 2.7 (1.5, 4.8) | 0.0005 |
| Other | 8 | 319 | 25.1 | 3.5 (1.6, 8.0) | 0.0026 |
| Ever Low C3 | | | | | |
| No | 7 | 2463 | 2.8 | 1.0 (Ref) | |
| Yes | 51 | 2205 | 23.1 | 8.2 (3.7, 18.0) | <0.0001 |
| Recent Low C3 | | | | | |
| No | 26 | 3893 | 6.7 | 1.0 (Ref) | |
| Yes | 32 | 559 | 57.2 | 8.6 (5.1, 14.4) | <0.0001 |
| Ever anti-dsDNA | | | | | |
| No | 9 | 1928 | 4.7 | 1.0 (Ref) | |
| Yes | 49 | 2740 | 17.9 | 3.8 (1.9,7.8) | 0.0002 |
| Recent anti-dsDNA | | | | | |
| No | 17 | 3636 | 4.7 | 1.0 (Ref) | |
| Yes | 41 | 810 | 50.6 | 10.9 (6.2, 19.1) | <0.0001 |
| Currently on Plaquenil? | | | | | |
| No | 11 | 699 | 15.7 | 1.0 (Ref) | |
| Yes | 46 | 3783 | 12.2 | 0.8(0.4, 1.5) | 0.44 |
| Currently on ACE/ARB | | | | | |
| No | 10 | 628 | 15.9 | 1.0 (Ref) | |
| Yes | 24 | 1592 | 15.1 | 0.9 (0.5, 2.0) | 0.89 |

**Conclusions:** Older SLE patients who have not previously had renal involvement are at low risk for developing proteinuria. The highest rates of incident proteinuria were among those with recent low complement. There was not strong evidence that hydroxychloroquine or ACE inhibitor's reduced the risk of proteinuria.

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## FRI0313 EVALUATION OF THROMBOTIC RISK IN PATIENTS WITH POSITIVE ANTIPHOSPHOLIPID ANTIBODIES WITHOUT CLINICAL CRITERIA OF THE DISEASE

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**Background:** The prevalence of thrombosis in antiphospholipid syndrome (APS) and the factors vary depending on the population studied. Although aPL have a strong relationship with thrombosis and pregnancy morbidity, the value of each type of aPL as a marker to develop APS it is not fully clarified.
**Objectives:** To analyze the incidence of thrombosis in patients with positive aPL that do not meet clinical criteria for disease. To identify potential risk factors for thrombosis. To analyze the possible protective role of primary thromboprophylaxis.
**Methods:** Retrospective study of patients with positive aPL on at least 2 times, separated by a minimum of 12 weeks in medium or high titers without fulfilling clinical criteria for APS. The patients were selected from the database of the Department of Immunology of a tertiary hospital (1999- 2004). The presence of vascular event was confirmed through imaging tests. Cases of ischemic optic neuropathy (ION) were diagnosed by clinical and electrophysiological testing.
**Results:** After a mean follow-up of 146±60.3 months, of the 138 patients included in the study, 13 (9.4%) developed thrombosis. The mean time to thrombotic episode was 81.4±41.7 months. Several classic cardiovascular risk factors (CVRF) such as tobacco (61.5% in thrombosis group vs 23.2% in the group without thrombosis;p=0.003), hypertension (53.8% vs 15.3%;p=0.001) and dyslipidemia (DLP) (38.5% vs 5.6%;p=0.001) were more frequent in patients with thrombosis. These 3 classic CVRF were independent risk factors for thrombosis in the univariate analysis, with an OR of 6.5 (95%CI 2.0–21.3) for hypertension, 5.3 (95%CI 1.6–17.5) for tobacco and 10.5 (95%CI 2.7–40.8) for DLP. Regarding the different antibodies, only the lupus anticoagulant (LA) (p=0.062) and anticardiolipin antibodies (aCL) IgM (p=0.14) tended to be more frequent in patients with thrombosis. Positivity to the 3 types of antibodies (AL, aCL, AB2GPI) was associated with increased risk of thrombosis (OR 7 [95%CI 1.9–28.5]; p=0.004). Multivariate analysis showed as independent risk factors for thrombosis: smoking (OR 8.3 [95%CI 1.3–52.5]; p=0.024), hypertension (OR 15.9 [95%CI 1.8–138.7]; p=0.012), DLP (OR 16.9 [95%CI 1.4–108.3]; p=0.027) and IgM aCL (OR 18.7 [95%CI 12–277.7]; p=0.033). Of the 13 thrombotic events, 10 were arterial: 4 acute myocardial infarctions, 2 thrombosis of central retinal artery, 2 OIN 1 transient ischemic attack and 1 stroke. Three thrombosis occurred in venous territory as deep venous thrombosis of lower extremities, with secondary pulmonary thromboembolism in 2 patients. Regarding treatment, 102 patients received prophylaxis with ASA 100 mg, showing a tendency towards protection (OR 0.774 [95%CI 0.2–2.7]; p=0.686).
**Conclusions:** The incidence of thrombosis in patients with positive aPL that do not meet clinical criteria for the disease is about 10%. The tobacco, DLP, hypertension and IgM aCL are independent risk factors. Autoantibodies load increases the risk of thrombosis. The protective role of aspirin in this population seems limited and may raise primary thromboprophylaxis with oral anticoagulation in patients considered as high risk.
**Disclosure of Interest:** None declared
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## FRI0314 ANTIPHOSPHOLIPID SYNDROME ALLIANCE FOR CLINICAL TRIALS AND INTERNATIONAL NETWORKING (APS ACTION) CLINICAL DATABASE AND REPOSITORY ANALYSIS: THE IMPACT OF SYSTEMIC LUPUS ERYTHEMATOSUS ON THE CLINICAL PHENOTYPE OF ANTIPHOSPHOLIPID ANTIBODY-POSITIVE PATIENTS

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**Background:** APS ACTION International Clinical Database and Repository ("Registry") was created to study the natural course of persistently antiphospholipid antibodies (aPL)-positive patients with or without autoimmune disorders over 10 years. The main autoimmune disease associated with aPL is Systemic Lupus Erythematosus (SLE); limited data exist on the impact of SLE on the clinical phenotype of persistently aPL-positive patients.
**Objectives:** Our objective was to compare the prevalence of clinical and laboratory characteristics of aPL-positive patients with or without SLE.
**Methods:** A secure web-based data capture system is used to store patient demographics, pertinent aPL history, and aPL profile. The inclusion criteria include aPL positivity according to the Updated Sapporo Classification Criteria. Only patients fulfilling the ACR SLE Classification Criteria and those with no other autoimmune diseases were included in this cross sectional analysis to study the

impact of SLE on aPL-positive patients. Baseline clinical characteristics were compared using $\chi^2$ or t-tests accordingly.
**Results:** As of June 2015, 573 aPL-positive patients recruited from 24 centers; 130 (22.7%) were excluded due to other or overlapping autoimmune diseases, SLE-like disease (fulfilling 3/11 ACR SLE Classification Criteria), or missing data. The mean ages (± SD) of individuals with persistently positive aPL but without other autoimmune diseases ("aPL only") (female: 218, 73%), and of those with SLE ("aPL with SLE") (female: 110, 77%) were 44±13 and 49±77, respectively. The majority of patients were Caucasians in both groups (62% and 65%, respectively), followed by Latin Americans (19.3% and 10.5%). Table shows the distribution of the clinical and laboratory characteristics (historically and/or at registry entry). The frequency of criteria and non-criteria APS manifestations was not different between two groups except persistent thrombocytopenia and autoimmune hemolytic anemia, which were more common in the "aPL with SLE" group (14% vs 28% and 2% vs 12%, respectively; both $p \leq 0.001$). Nephrotic syndrome, chronic or end-stage renal disease, and hypocomplementemia were also more common in the "apL with SLE" group.

| Variables, n (%) | aPL Only (n=300) | | aPL with SLE (n=143) | | P value |
|---|---|---|---|---|---|
| **Clinical Manifestations** | 222 | 74.0% | 99 | 69.2% | 0.31 |
| Number of Events | | | | | 0.39 |
| Arterial Thrombosis | 108 | 36.0% | 44 | 30.8% | 0.45 |
| Venous Thrombosis | 135 | 45.0% | 65 | 45.5% | 0.41 |
| Small Vessel Thrombosis | 17 | 5.7% | 9 | 6.3% | 0.53 |
| Catastrophic APS | 2 | 0.7% | 1 | 0.7% | 0.57 |
| > 3 Early Fetal Loss | 14 | 4.7% | 3 | 2.1% | 0.35 |
| Late Fetal Loss | 55 | 18.3% | 25 | 17.5% | 0.48 |
| Preeclampsia/Eclampsia | 31 | 10.3% | 11 | 7.7% | 0.51 |
| **Cardiovascular Risk Factors** | | | | | |
| Hypertension | 78 | 26.0% | 50 | 35.0% | 0.06 |
| Diabetes | 17 | 5.7% | 5 | 3.5% | 0.46 |
| Hyperlipidemia | 73 | 24.3% | 29 | 20.3% | 0.40 |
| Obesity | 73 | 24.3% | 49 | 34.3% | 0.03 |
| Smoking | 30 | 10.0% | 23 | 16.1% | 0.16 |
| **Other Thrombosis Risk Factors** | | | | | |
| Nephrotic Syndrome | 0 | 0% | 3 | 2.1% | 0.03 |
| Chronic/End-Stage Renal Disease | 6 | 2.0% | 8 | 5.6% | 0.04 |
| Active Malignancy | 2 | 0.7% | 0 | 0% | 0.33 |
| Hyperhomocysteinemia | 153 | 51% | 52 | 36.4% | 0.007 |
| Atrial Fibrillation | 6 | 2.0% | 2 | 1.4% | 0.66 |
| **Laboratory Parameters** | | | | | |
| Low C3 | 15/66 | 22.7% | 48/83 | 57.8% | <0.001 |
| Low C4 | 10/66 | 15.2% | 50/82 | 61.0% | <0.001 |
| Antiphospholipid Antibodies | | | | | |
| Lupus Anticoagulant | 234 | 78.0% | 107 | 74.8% | 0.47 |
| Anticardiolipin Antibodies | 208 | 69.3% | 101 | 70.6% | 0.83 |
| Anti-β2-GPI Antibodies | 150 | 50.0% | 56 | 39.2% | 0.03 |
| Double Positivity | 86 | 28.7% | 55 | 38.5% | 0.01 |
| Triple Positivity | 104 | 34.7% | 37 | 25.9% | 0.44 |

[1]<100,000/mm³ twice at least 12 weeks apart; [11]neuropsychological test proven

**Conclusions:** Concomitant SLE diagnosis in persistently aPL-positive patients is associated with an increased risk of thrombocytopenia, hemolytic anemia, nephrotic syndrome, chronic or end-stage renal disease, and hypocomplementemia; however the risk of other non-criteria manifestations, thrombosis, and pregnancy morbidity remains the same.
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**Disclosure of Interest:** None declared
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## FRI0315 A PROSPECTIVE STUDY TO ASSESS RESPONSIVENESS OF CLINICAL AND ULTRASOUND OUTCOME MEASURES FOR MUSCULOSKELETAL SLE

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**Background:** Musculoskeletal manifestations affect up to 95% of SLE patients. Assessment can be problematic as not all patients have swelling. There is a clinical need to better select SLE patients with musculoskeletal symptoms who may respond to therapy and assess their response. We previously analysed 100 patients with MSK symptoms and showed that ultrasound (US) detects synovitis in patients with no clinical swelling.
**Objectives:** To assess the responsiveness of clinical assessment tools and US in musculoskeletal SLE.
**Methods:** 107 patients fulfilling ACR/SLICC criteria for SLE with musculoskeletal involvement were analysed in a cross-sectional study. 16 of these with current inflammatory symptoms entered a pilot study of US before and after intramuscular injection of depomedrone 120mg. These 16 patients were followed up and assessed clinically using BILAG, SLEDAI, patient VAS, physician VAS, tender joint count, swollen joint count) and US of hand (joints and tendon sheath) at 0, 2 and 4 weeks.
**Results:** Of 107 patients only 35 (32.7%) had swelling clinically at baseline but 53 (49.5%) had US synovitis. Response in US and clinical parameters for the 16 longitudinal patients is shown in Table1.

Table 1

| | Week 0 | Week 2 | P* | Week 4 | P |
|---|---|---|---|---|---|
| BILAG-MSK n (%) | | | | | |
| A | 6/16 (37.5) | 3/16 (18.7) | | 1/16 (0.06) | |
| B | 6/16 (37.5) | 3/16 (18.7 | | 2/16 (12.5) | |
| C | 4/16 (25) | 5/16 (31.2) | | 6/16 (37.5) | |
| D | 0/16 (0) | 5/16 (31.2) | | 6/16 (37.5) | |
| BILAG improved, n (%) | N/A | 10/16 (62.5) | | 13/16 (81) | |
| SLEDAI MSK Criterion = 4 points, n (%) | 14/16 (87.5) | 10 /16 (62.5) | | 9 /16 (56) | |
| SLEDAI improved, n (%) | | 4/14 (28.5) | | 5/14 (36) | |
| TJC (0–28), median (IQR) | 8 (4.3–12.3) | 4 (1.0 –13.5) | 0.228 | 4 (1–14.8) | 0.197 |
| SJC (0–28), median (IQR) | 3 (0.3–5) | 0 (0–1) | 0.059 | 0 (0–0) | 0.003 |
| Symptomatic joints, median (IQR) | 15 (5.8–21.5) | 2 (0–13) | 0.047 | 3.5 (1–14.8) | 0.066 |
| Patient VAS (0–100), median (IQR) | 55 (30–78.5) | 30 (8.8–40) | 0.016 | 35 (10–48.8) | 0.059 |
| Physician VAS (0–100), median (IQR) | 31 (13–65.5) | 23 (5–50) | 0.001 | 21 (3.8–43.5) | 0.001 |
| US- total PD, median (IQR) | 8.5 (4.8–34.8) | 1 (0–6.3) | 0.002 | 1 (0–1) | 0.001 |
| US-total GS, median (IQR) | 24 (17–46) | 12.5 (5.3–23.8) | 0.002 | 10.5 (7–13.8) | 0.001 |
| No. joints with synovitis, median (IQR) | 8 (5–19.3) | 3 (0.8–7.5) | 0.004 | 2 (1–4) | 0.001 |

P values compare 2 and 4 weeks with baseline. Value under 0.05 considered as trend, values under 0.025 considered significant.

**Conclusions:** Although swollen joint count was responsive to change with therapy, US was more sensitive in detecting active joints disease at baseline and showed greater and more significant change with therapy. The responsiveness of swollen joints likely explains the responsiveness in BILAG musculoskeletal system index and physician VAS. However, tender and symptomatic joint counts, as well as SLEDAI, were poorly responsive to therapy. Overall, US is the tool most responsive to change for monitoring musculoskeletal disease activity in SLE.
**Disclosure of Interest:** None declared
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## FRI0316 ASSESSING ATTRIBUTION OF NEUROPSYCHIATRIC EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS. PERFORMANCE OF A NEW ALGORITHM IN AN INTERNATIONAL MULTICENTER COHORT

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**Background:** In a recent study of a large cohort of systemic lupus erythematosus (SLE) patients, we evaluated a new algorithm to determine the attribution of neuropsychiatric (NP) events to SLE or other causes [1].
**Objectives:** In the present study, we tested the performance of the algorithm in a new international multicenter cohort of patients, all of whom had one or more NP events as per the 1999 ACR case definitions.
**Methods:** A similar methodology to that used in the first study, was adopted. A dedicated electronic chart was created, including the core set of items for classification. Four factors were considered for each NP event (i) the time of onset of the NP event; (ii) the presence of concurrent or confounding non-SLE factors (i.e. "associations" suggested in the glossary for the 1999 ACR case definition); (iii) the type of NP event (major vs minor or common according to what has been proposed by Ainiala *et al.* [2]; (iv) the presence of "favouring factors" (i.e. supporting attribution). Patients from each center satisfied classification criteria for SLE and had one or more NP events. To maintain blinding, thus avoiding circular thinking, all events were evaluated by two independent assessors from each center, each assigned different tasks: the first assessor provided an attribution diagnosis (related/uncertain/not related to SLE) on the basis of their clinical judgement utilizing all of the information available in the patient record; the second assessor applied the attribution algorithm using the same available information and provided an attribution score. The performance of the attribution score was compared to the attribution determined by clinical judgement, which was taken as the "gold standard". Receiver Operating Curve (ROC) analysis was used to determine the area under the curve (AUC) and the calculation of sensitivity, specificity, positive and negative predictive values [PPV and NPV (CI 95%)] using dichotomous outcomes (related *vs* uncertain/not related to SLE).
**Results:** There were 243 SLE patients (23 M, 220 F; mean (SD) age 47 (12.7) years with 336 NP events. Using a pre-defined attribution score cut-off $\geq 7$ (derived by our previous national validation study of NP events related vs uncertain/not related to SLE) the AUC was 0.89 for NP events attributed to SLE with sensitivity of 88.5% (95% CI 77.7, 87.5), specificity of 74.6% (95% CI 67.9, 80.53), a PPV of 81.8% (95% CI 75.8, 86.8) and a NPV of 83.4% (95% CI 75.9, 89.3).
**Conclusions:** The attribution algorithm for evaluating NP events in SLE patients compared favourably to the judgement of experienced clinicians for the majority of NP events. It is a valid tool and provides a standardized approach to determining the attribution of NP events in future studies of NPSLE.

**References:**
[1] A. Bortoluzzi et al. Rheumatology 2015;54:891–898.
[2] H. Ainiala et al. Neurology 2001;57:496–500.
**Disclosure of Interest:** None declared
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## FRI0317 CIRCULATING LEVELS OF IC3B & C3 PREDICTS SLE DISEASE ACTIVITY: THE CASTLE (COMPLEMENT ACTIVATION SIGNATURES IN SYSTEMIC LUPUS ERYTHEMATOSUS) STUDY

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**Background:** A major unmet need in SLE is identifying a biomarker that consistently tracks with disease activity. One approach is measuring complement activation by evaluating consumption of serum C3 and C4. However, since they are acute phase reactants (1), interpretation of these levels is challenging as serum levels may not decrease until late in a disease flare (2). iC3b is a proteolytically derived molecule of C3b, and increases with complement activation. iC3b/C3 ratio measures complement consumption relative to production, which may provide for a more accurate assessment of complement activation.
**Objectives:** We hypothesize that blood iC3b and iC3b/C3 levels will provide a more specific and reliable marker of complement activation and disease activity in SLE.
**Methods:** 137 adult SLE patients were enrolled in this prospective observational study. The number of patient visits varied from 1 to 7 times during the study period, encompassing 376 visits. C3 and C4 were measured by nephelometry; iC3b using an investigational lateral flow assay test (Kypha, Inc, St. Louis, MO). SLE disease activity was measured using the SLEDAI 2K Responder Index-50 (S2K RI-50) instrument. Patients with active disease are considered to have a S2K RI-50 score $>4$. Clinically meaningful improvement is defined as a decrease in S2K RI-50 score $\geq 4$ from prior visit, while clinically meaningful worsening is defined as an increase in S2K RI-50 score $\geq 4$ from prior visit. Multilevel regression models were performed to examine associations with disease activity. Ordinal logistic regression models with the generalized estimating equation modeling (GEE) were used to examine associations for clinically meaningful changes since the outcome variable is ordinal (i.e. clinical deterioration, stability, and improvement). Odds ratios and 95% confidence intervals for iC3b, C3, C4, ESR, CRP, dsDNA values, prednisone usage, and race were estimated using Proc GLIMMIX and Proc GENMOD (SAS v9.4).
**Results:** Blood levels of iC3b, C3, iC3b/C3 ratio, C4, dsDNA, ESR, and prednisone use each correlated with SLE disease activity. Multilevel multiple logistic regression analysis revealed only iC3b/C3 ratio, dsDNA levels, and prednisone use were significant predictors of disease activity (Table 1). To determine whether iC3b/C3 ratio can predict clinically meaningful changes in SLE disease activity, we evaluated the interpatient association between clinical deterioration, stability, and improvement and iC3b/C3 ratios. Multiple ordinal logistic regression with GEE showed that iC3b/C3 ratio, dsDNA levels, and prednisone use significantly predicted both clinically meaningful improvement and deterioration in disease activity.

**Table 1. Univariate and multivariate logistical regression analysis of variables predictive of active SLE.**

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| Predictor Variable | Odds Ratio | Lower 95% CI | Upper 95% CI | Predictor Variable | Odds Ratio | Lower 95% CI | Upper 95% CI |
| iC3b (Δ1 µg/mL) | 1.27 | 1.08 | 1.47 | iC3b/C3 ratio (Δ0.01 units) | 1.28 | 1.11 | 1.47 |
| iC3b/C3 ratio (Δ0.01 units) | 1.34 | 1.18 | 1.52 | dsDNA Ab (Δ10 IU/mL) | 1.04 | 1.01 | 1.06 |
| C3 (Δ10 mg/mL) | 0.82 | 0.72 | 0.93 | Prednisone (Yes vs No) | 3.44 | 1.73 | 6.84 |
| C4 (Δ10 mg/mL) | 0.57 | 0.36 | 0.85 | | | | |
| dsDNA Ab (Δ10 IU/mL) | 1.05 | 1.02 | 1.07 | | | | |
| ESR (Δ10 mm/hr) | 1.18 | 1.01 | 1.37 | | | | |
| CRP (Δ10 mg/L) | 1.27 | 0.95 | 1.70 | | | | |
| Prednisone (Yes vs No) | 4.03 | 1.87 | 8.68 | | | | |
| Race (White vs AA) | 0.96 | 0.40 | 2.31 | | | | |

**Conclusions:** In this prospective study, blood iC3b/C3 ratios were predictive of active SLE disease. Furthermore, iC3b/C3 ratio was predictive of clinical meaningful changes in disease activity. These data warrant further investigation of iC3b/C3 ratio as a potential biomarker for disease activity in SLE.
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[1] Gabay & Kushner, N Engl J Med. 1999;340(6):448–454.
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## FRI0318 SERUM ADIPOCYTE FATTY ACID-BINDING PROTEIN LEVEL IS ELEVATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) BUT NOT ASSOCIATED WITH BIOPHYSICAL MARKERS OF CARDIOVASCULAR DISEASE

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**Background:** Adipocyte fatty acid-binding protein (aFABP) is an intracellular lipid-binding protein expressed in adipocytes and macrophages, particularly in inflammatory conditions. Recently, high circulating serum aFABP levels have been shown to predict the development of carotid atherosclerosis, metabolic syndrome and ischaemic stroke. As an inflammatory disease, circulating aFABP level is expected to be raised in patients with SLE. However, a recent study failed to demonstrate higher aFABP levels in SLE patients than in healthy controls (HC), likely due to the lack of power of study and an optimally matched HC group.
**Objectives:** We aimed to address if serum aFABP level is indeed higher in SLE patients by comparing a larger number of SLE patients with HC stringently matched for age, sex and BMI. In addition, potential associations between serum aFABP levels and clinical and disease-related factors, as well as biophysical markers of cardiovascular (CVS) disease were explored in SLE patients.
**Methods:** Patients with SLE and HC matched for age, gender and BMI were recruited. Subjects with a history of hypertension, diabetes mellitus, renal impairment, CVS and cerebrovascular diseases, and those who were on statins were excluded. Clinical parameters including daily prednisolone dose, SLEDAI, SLICC/ACR DI, and serum C3, C4, anti-dsDNA, total cholesterol (TC) and HDL-c levels were obtained. Serum aFABP levels were determined by commercially available ELISA kit. Endothelial function, arterial stiffness and carotid atherosclerosis were assessed by brachial artery flow-mediated dilation (FMD), pulse-wave velocity (PWV) and carotid intima-media thickness (cIMT) respectively using the Prosound Alpha-10 ultrasound system. Relationships between serum aFABP levels and disease-related factors, FMD, PWV and cIMT were explored by bivariate correlations.
**Results:** Seventy one SLE patients and 71 matched HC (6 men in each group) were studied. The mean±SD age (year), BMI and atherogenic index (TC/HDL-c) of SLE patients and HC were 39.21±13.4 and 40.37±12.9, 22.06±4.3 and 22.86±4.2 and 3.09±1.6 and 3.22±1.4 ($p=0.611$) respectively. In SLE patients, the mean±SD daily prednisolone dose, SLEDAI and SLICC were 13.43±14.4mg, 6.52±5.4 and 0.17±0.4 respectively. SLE patients had significantly lower FMD than HC (3.82±2.9% vs 4.76±3.0%, $p=0.027$). PWV and cIMT did not differ between both groups ($p=0.739$ and $p=0.762$ respectively). Serum aFABP was significantly higher in SLE patients than that in HC (14.82±3.3ng/ml vs. 13.69±4.6ng/ml, $p<0.001$). However, no association between serum aFABP levels and serum C3, C4 and anti-dsDNA levels, SLEDAI, SLICC, atherogenic index, daily prednisolone dose, FMD, PWV and cIMT was found in the SLE group. In HC, no association was noted between serum aFABP levels and BMI, FMD, PWV, cIMT and atherogenic index.
**Conclusions:** While we confirmed that SLE patients had significantly higher aFABP levels and lower FMD than age-, sex-, and BMI-matched HC, no association between aFABP and various biophysical markers of CVS disease was found. Prospective studies addressing the CVS impact of aFABP by evaluating adjusted mean aFABP levels over time and CVS events in SLE patients are warranted.
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## FRI0319 THE RISK OF PULMONARY EMBOLISM AND DEEP VENOUS THROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS IN THE UNITED KINGDOM: A POPULATION-BASED STUDY

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**Background:** Many studies have found that patients with SLE have a substantially increased risk of cardiovascular complications. However, the magnitude of the risk for venous thromboembolism (VTE) has not been well quantified in this patient group, particularly within the general population context.
**Objectives:** Our objective was to determine magnitude and temporal trend of the risk of venous thromboembolism (VTE), pulmonary embolism (PE), and deep vein thrombosis (DVT) in individuals with incident systemic lupus erythematosus (SLE) in the general population.
**Methods:** Using the Health Information Network (THIN) database, a population database that includes 11.1 million patients, 6.2% of the population of the United Kingdom, we conducted a cohort study of all patients with incident SLE and up to 10 age-, sex-, and entry time-matched individuals from the general population. SLE patients were identified by read codes for systemic involvement of lupus,

excluding cutaneous-only disease. We compared incidence rates of PE, DVT, and VTE between the two groups and within the SLE group according to SLE disease duration. We calculated hazard ratios (HRs), adjusting for confounders.
**Results:** Among 1494 individuals with SLE (87.1% female, mean age 50 years), there were 13 cases of DVT and 14 of PE. Among the 10,473 individuals without SLE, there were 38 cases of DVT and 33 of PE. The incidence rates of PE, DVT, and VTE were 1.6, 1.4, and 2.9 per 1000 person-years in the SLE group, whereas the corresponding rates were 0.5, 0.6, and 1.1 per 1000 person-years among individuals without SLE. Compared with non-SLE individuals, the multivariable HRs among SLE patients were 3.17 (95% CI, 1.65–6.10), 3.42 (95% CI, 1.72–6.81), and 3.14 (95% CI, 1.94, 5.07) for PE, DVT and VTE, respectively. The age-, sex-, BMI-, and entry time-matched incidence ratios for PE, DVT, and VTE were highest during the first year after SLE diagnosis 14.30 (95% CI, 4.02–50.82), 8.70 (95% CI, 1.74–43.40), and 10.82 (95% CI, 3.91–29.90), respectively. HRs remained similar after adjusting for covariates including BMI, smoking, relevant comorbidities, and use of pertinent medications.

Table 1. Age and sex adjusted risk for PE, DVT, or both (VTE) in SLE according to follow-up period

| Time after diagnosis | PE IRR (95% CI) | DVT IRR (95% CI) | VTE IRR (95% CI) |
|---|---|---|---|
| 1 year | 11.24 (3.47–36.97) | 11.48 (2.56–51.59) | 10.44 (4.02–27.12) |
| 3 years | 6.03 (2.97–12.25) | 4.65 (1.93–11.17) | 5.21 (2.97–9.11) |
| 5 years | 3.74 (1.92–7.28) | 3.48 (1.62–7.46) | 2.56 (2.12–5.93) |
| Total follow-up | 2.40 (1.33–4.33) | 3.31 (1.84–5.94) | 2.76 (1.82–4.21) |

IRR = age-, sex-, and BMI and entry time-matched Incidence Rate Ratio.

**Conclusions:** These findings provide population-based evidence that patients with SLE are at a considerably increased risk of VTE, especially within the first year after SLE diagnosis. Increased vigilance for this potentially fatal outcome and its modifiable risk factors appears warranted in this patient population, particularly early after disease onset.
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## FRI0320 DISEASE SEVERITY IN PATIENTS WITH DISCOID LUPUS ERYTHEMATOSUS FROM A REAL-WORLD SETTING

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**Background:** Real-world data on the severity of discoid lupus erythematosus (DLE) are scarce, limiting our understanding of the clinical course of this chronic disease that disproportionately affects minorities.
**Objectives:** To assess the clinical burden and unmet need by disease severity in DLE patients.
**Methods:** Data were drawn from a 2013 multinational survey of clinical practice that included 101 dermatologists across the US and EU (France, Germany, Italy, Spain & UK). Dermatologists completed the patient record (PRFs) for their next five consulting patients with cutaneous lupus erythematosus. The present analyses were a subset of patients with DLE, categorized by dermatologists into two groups based on their severity at the current visit: 1) mild, and 2) moderate/severe. The two groups were compared in bivariate analyses, using Mann-Whitney-U tests and Fisher's exact tests.
**Results:** Final analyses included 315 DLE patients; 72% were female; mean age at diagnosis=39.7 years; mean disease duration=4.4 years. At diagnosis, 74% of DLE patients had moderate-to-severe DLE, and 10% had joints affected; at the current visit, the corresponding proportions were 27% and 11%. Among DLE patients currently presenting as moderate-to-severe, achieving remission was less common (14% vs. 60% among mild DLE patients; $p \leq 0.0001$). Patients moderate-to-severe during the present visit were more likely to be currently flaring (18% vs. 4%; $p \leq 0.0001$) or have flared in the last 12 months (37% vs. 16%; p=0.0001). Finally, dermatologist satisfaction with the level of control from treatment was also significantly lower amongst currently moderate/severe DLE patients (39% satisfied vs. 91% mild; $p \leq 0.0001$), with dermatologists reporting that better control can be achieved in over a quarter of moderate/severe DLE patients (27% vs. 3% mild; $p \leq 0.0001$).
**Conclusions:** Across regions and despite an average of 4 years since diagnosis, a sizeable proportion of DLE patients (nearly one-third) in clinical care were moderate-to-severe at their current visit, indicating persistence, relapse or worsening. Results suggest an unmet need for better disease control. This study contributes to the scant literature on DLE by informing our understanding of the disease in real-world settings of clinical care, and may help development of appropriate new interventions amongst those not currently controlled under standard therapies.
**Acknowledgement:** These analyses were supported by Biogen.
**Disclosure of Interest:** B. Hoskin Employee of: Adelphi Real World, S. Lobosco Employee of: Adelphi Real World, D. Bell Employee of: Adelphi Real World, A. Kao Employee of: Employee at Biogen at the time of the research, S. Hall Shareholder of: Biogen, Employee of: Biogen, S.-Y. Chen Shareholder of: Biogen, Employee of: Biogen
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## FRI0321 ASSOCIATION BETWEEN DISEASE SEVERITY AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH DISCOID LUPUS ERYTHEMATOSUS IN REAL-WORLD CLINICAL PRACTICE

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**Background:** Cutaneous diseases are often associated with high humanistic burden. Current understanding of the patient perspective among those with discoid lupus erythematous (DLE), a chronic disease disproportionately affecting minorities, is particularly lacking. We undertook this analysis to gain insight into the patient perspective on the impact of DLE, and how impact might vary across severity levels.
**Objectives:** To assess the patient's self-reported burden associated with disease severity and perceived unmet need amongst moderate-to-severe vs. mild DLE patients from a real-world setting.
**Methods:** Data were drawn from a multinational survey of 101 dermatologists across the US and EU (France, Germany, Italy, Spain & UK) conducted in 2013. Dermatologists completed patient record forms (PRFs) for their next five prospectively consulting patients with cutaneous lupus erythematosus and patients provided data via self-completion forms (PSCs). Patient-reported outcomes (PROs) collected in the PSC included the EuroQol 5D (EQ5D), visual analog scores, work and activity impairment indices, and the functional assessment of chronic illness therapy scale (FACIT-Fatigue). For the current visit, patients were categorized by dermatologists into moderate/severe vs. mild groups. PRO measures by severity status were compared in bivariate analyses, using Mann-Whitney-U tests and Fisher's exact tests.
**Results:** A total of 180 DLE patients in the EU and US provided PSC data and were included in the analyses (mean age 39.5, disease duration 3.9 years, majority female [69%])
At the current visit, 25% of DLE patients were categorized as having moderate-to-severe disease. These patients self-reported a significantly and clinically lower EQ5D score compared to mild patients (0.86 vs. 0.94; p=0.0004), whilst also reporting a lower visual analog score (66.0 vs. 76.8; p=0.0005) indicating worse health-related quality of life. The reported impact of fatigue was also significantly greater amongst moderate-to-severe patients (FACIT-Fatigue score 36.0 vs. 43.4 among mild; p=0.0004). Moreover, moderate-to-severe DLE patients reported a greater degree of overall work impairment (30.0% vs. 18.0%; p=0.0612) and activity impairment (30.0% vs. 17.9%; p=0.0178). Finally, self-reported satisfaction with disease control was also significantly lower amongst these moderate-to-severe DLE patients (55% satisfied vs. 84%; $p < 0.0001$).
**Conclusions:** As reported by patients from a multinational sample in clinical care and compared to having a mild disease, having moderate-to-severe DLE was associated with a negative impact on quality of life, the ability to work and the ability to participate in activities, and satisfaction with disease control. Our research using PROs in a real-world setting, rather than in a clinical trial, adds to our limited understanding of the humanistic impact of DLE.
**Acknowledgement:** These analyses were supported by Biogen.
**Disclosure of Interest:** B. Hoskin: None declared, S. Lobosco Employee of: Adelphi Real World, D. Bell Employee of: Adelphi Real World, A. Kao Employee of: Employee at Biogen at the time of the research, S. Hall Shareholder of: Biogen, Employee of: Biogen, S.-Y. Chen Shareholder of: Biogen, Employee of: Biogen
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## FRI0322 DIAGNOSTIC UTILITY OF THE MINIMALLY INVASIVE BIOPSY OF THE MINOR SALIVARY GLAND

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**Background:** Sjögren's syndrome (SS) is a disease with a wide spectrum of clinical manifestations which can make diagnosis difficult. Due to difficult diagnosis the Americo-European classification criteria (AECC) are used. The positivity of antibodies or histology are essential to comply with these criteria, forcing in certain situations, especially in cases with negative immunology, to carry out a lip biopsy.
**Objectives:** To evaluate the diagnostic utility of the minimally invasive biopsy of the minor salivary gland.
**Methods:** Transversal study of 159 biopsies of the minor salivary gland. *Inclusion Criteria:* patients with dry syndrome. *Biopsy Technique:* vertical incision ($\leq$5 mm) of the internal surface of the lower lip whithout suturing. *Variables studied:* 1) Clinical: age, sex, presence and duration of the symptoms. 2) Diagnostic: The necessary examinations were performed to fulfill the AECC: Schirmer, salivary scintigraphy, ANA, RF, Ab-SSA and Ab-SSB. 3) Histological: a) degree of atrophy: absent, mild, moderate and severe; b) Chisholm-Mason scale (I-IV) considering as positive biopsy grade III or IV; c) degree of lymphocyte infiltration: absent, mild, moderate, severe; d) histological patterns: normal, nonspecific chronic sialadenitis (NSCS), sclerosing chronic sialadenitis (SCS), focal lymphocytic sialadenitis (FLS)
**Results:** The characteristics of the sample group were; age 59.9 ±12.43 years,

91% women, 88% xerostomia, 89% xerophthalmia for a period of 49±37 months, 45% positive salivary scintigraphy, 54% positive Schirmer, 54% AAN, RF 22%, Ab-Ro and Ab-La of 28% and 6.2% respectively. Appropriate material was obtained for histological study in 92.5%, being more frequent in older patients (60 ± 53 vs 12.2 ± 12.8; $p<0.05$). Analyzing the data after the biopsy, 16% (n=22) of patients met diagnostic criteria. Depending on the number of previous classificatory criteria 22% and 26% of patients met 3 and 4 criteria, respectively, were diagnosed of SS. Glandular atrophy was observed in 65% (n=95) with the following distribution: mild 38%, moderate 23%, severe 4%. The histological degree of atrophy was related to patient age ($r=0.38$; $p<0.0001$). Chisholm-Mason scale classified biopsies as normal (n=22; 15%), grade I (n=73; 50%), grade II (n=15; 10%), grade III (n=22; 15%) and grade IV (n=15; 10%), being biopsies positive in 25%. The most frequent histopathological pattern was NSCS (n=83; 57%), followed by FLS (n=37; 25%), normal (n=22; 15%) and SCS (n=5; 3%). Lymphocytic sialadenitis was observed in 85% (n=125; 47% mild, moderate 18%, severe 20%) but only 25% (n=37) presented the focal lymphocytic infiltration characteristic of SS. The positive biopsy was related to the positivity of Ab-Ro (40% vs. 22%; $p<0.0352$), Ab -La (10% vs 1%, $p<0.0002$), RF (35% vs. 18%; $p<0.03$) and ANA (70% vs 46%;. $p<0.01$) There was no difference between age and the different histological patterns, but SCS was more likely in patients with more advanced age

**Conclusions:** The minimally invasive biopsy of the minor salivary gland, could be currently considered essential for the diagnosis of SS, especially in patients who meet $\geq$3 criteria.

**Disclosure of Interest:** None declared

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## FRI0323 A "COMPOSITE-INDEX" APPROACH FOR DEFINING SALIVARY GLAND INFLAMMATION, DYSFUNCTION AND ITS IMPACT ON PATIENT-REPORTED OUTCOMES: A ROLE FOR SALIVARY GLAND ULTRASONOGRAPHY?

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**Objectives:** To investigate the role of salivary gland ultrasonography (SGUS) in a composite index for the assessment of glandular involvement in primary Sjögren's syndrome (pSS), exploring whether SGUS may correlate with minor salivary gland focus score (MSG-FS), unstimulated salivary flow (USFR), patients' glandular symptoms, laboratory abnormalities, and physician global assessment (PhGA).

**Methods:** Consecutive patients with pSS (AECG criteria) were included in this cross-sectional study and systematically evaluated. SGUS was carried out by the same radiologist recording: size, parenchymal echogenicity and inhomogeneity, number of hypo/anechoic area, presence of lymph nodes and calcifications. A modified version of the De Vita score was adopted. All patients underwent sialometry and completed the ESSPRI, the VAS for xerostomia and the oral health impact profile (OHIP). The same physician assessed the ESSDAI and provided a PhGA score based on patients symptoms and laboratory abnormalities to quantify salivary gland activity according to a four grade scale (inactive, mild, moderate and severe glandular activity).

**Results:** We included 156 (152F:4 M) patients with pSS; out of them, 37 (23.7%) presented a small glandular swelling and 6 (3.8%) a major glandular swelling as defined according to the ESSDAI. MSG-FS was available for 125/156 (80%) patients. The median (IQR) USFR was 1,9 (0.2,3) ml/15'. Abnormal findings at SGUS examination were detected in 85/156 (55.5%) pSS patients. Forty-four (28.2%) pSS patients presented abnormal sonographic findings in both parotid and submandibular glands, whereas isolated pathological findings in either parotid glands or in submandibular glands were found in 22 (14.1%) and 19 (12.2%) patients, respectively. Age or disease duration did not influence the SGUS result. Higher SGUS scores were significantly more common in patients with glandular swelling with a direct correlation between the "glandular" domain of the ESSDAI and the SGUS score ($r=0.390$, $p=0.000$). A good correlation was also observed between PhGA and the SGUS score ($r=0.566$, $p=0.000$). A positive correlation was found between MSGB-FS and the total SGUS score ($r=0.431$, $p=0.000$) as well as between MSGB-FS and the single SGUS scores assigned to both parotid glands ($r=0.366$, $p=0.001$) and submandibular glands ($r=0.431$, $p=0.000$). The USFR and the SGUS score were inversely correlated ($r=-0.309$, $p=0.001$). VAS Dryness, ESSPRI and the OHIP index did not differ between normal or abnormal SGUS and were not correlated to the scores assigned to the ESSDAI "glandular" domain, to the MSGB-FS and to the USFR impairment. Finally, we confirmed that higher SGUS scores were significantly more common in patients with a higher total ESSDAI, lower C3/C4 levels, leukopenia, hypergammaglobulinemia, antiRo/SSA, antiLa/SSB, Rheumatoid Factor positivity and cryoglobulins ($p<0.01$).

**Conclusions:** This results highlight that to capture SS glandular activity a "composite index" would be the best choice. SGUS findings, significantly correlated with histopathology, salivary gland dysfunction, and both the ESSDAI "glandular" domain and the PhGA thus appearing as a complementary, promising tool for an integrate assessment of pSS salivary gland involvement in clinical practice and in clinical trials.

**Disclosure of Interest:** None declared

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## FRI0324 WORK PRODUCTIVITY IN PRIMARY SJÖGREN'S SYNDROME: A CROSS-SECTIONAL MULTICENTER STUDY

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**Background:** Sjögren's syndrome (pSS) is generally considered a benign disease; however, given the high frequency of fatigue, articular and musculoskeletal pain and/or peripheral neurological disorders among pSS patients, the disease represents a potentially disabling disorder negatively affecting patient quality of life and work productivity. However, only limited information is available regarding the work ability of pSS patients.

**Objectives:** To assess work participation in a multicenter cohort of patients with pSS, and to explore whether work productivity differed across groups of patients when stratified according to disease activity and damage.

**Methods:** Consecutive pSS patients (AECG 2002) were recruited in 5 referral centers. Data collection included clinical examination, patient reported outcome measures (i.e. EULAR SS Patient Reported Index (ESSPRI), oral health impact profile questionnaire (OHIP), ocular surface disease index questionnaire (OSDI), Work Productivity and Activity Impairment Questionnaire (WPAI)) and laboratory assessment. The EULAR SS Disease Activity Index (ESSDAI) and the Sjögren's syndrome disease damage index (SSDDI) were used to assess disease activity and damage. We used data from WPAI and additional information on work participation to assess absenteeism (work time missed), presenteeism (impairment while at work) and overall work productivity loss (absenteeism plus presenteeism) due to pSS. We then compared work participation across patient groups stratified according to disease manifestations by Mann-Whitney U-test or chi-square test as appropriate.

**Results:** A total of 223 patients were included with median (IQR) age 62.5 (53, 69.5) years, median follow-up 5 (3, 11) years, 98% female gender and 56.2% anti-Ro/SSA positivity. Seventy-two patients (32.2%) reported current employment. Patients not reporting employment were retired (29.5%), or unemployed for other reasons (42.9%). On average, employed pSS patients reported a 9% (20%) mean (SD) absenteeism rate, a 35% (23%) mean (SD) presenteeism rate and a 38% (26%) mean (SD) overall work impairment rate due to health. In the entire cohort the mean (SD) activity impairment (AI) was 47,5% (27%). Primary SS patients with more aggressive disease manifestations, requiring steroids and immunosuppressive drugs, presented the highest rates of absenteeism and disability as assessed by AI. Additional determinants of AI were presence of arthritis ($p=0.02$) and fibromyalgia ($p=0.005$). Similarly, patients presenting arthritis reported significantly higher rates of absenteeism ($p=0.04$). Moreover, higher rates of presenteeism ($p=0.02$) and work productivity loss ($p=0.01$) were detected in patients showing a SSDDI$\geq$1. Finally, positive correlations were found between the ESSPRI, the VAS score for pain and fatigue, and the absenteeism rates, presenteeism rates, work productivity loss and AI, respectively ($p<0.01$).

**Conclusions:** Employment rates were particularly low among pSS patients. Determinants of work disability were fatigue, articular involvement and comorbidities, including fibromyalgia.

**Disclosure of Interest:** None declared

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## FRI0325 CLINICAL AND SEROLOGICAL FEATURES ACCORDING TO AGE AT DIAGNOSIS OF PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjögren's syndrome (pSS) is a chronic systemic autoimmune disease that usually affects middle age women. It is characterized mainly by the involvement of the exocrine glands; However, patients with pSS presents a broad spectrum of systemic involvement and serologic characteristics.

**Objectives:** The aim of this study is to analyze clinical and serological differences in different age at diagnosis groups in a pSS Spanish cohort.

**Methods:** This is a multicenter transversal study of pSS patients whose fulfilled European-American consensus criteria from thirty-three Rheumatology Units. The patients were randomized into the following age groups: $<$35 years, 35–50 years, 50–65 years and$>$65 years. Epidemiological, clinical and serological data were collected. All patients signed an informed consent, and the study was approved by the local ethics committees. Qualitative data were compared using the Chi-square tests. Quantitative variables were analyzed with a Kruskal-Wallis test. A value of $p<0.05$ was considered as significant.

**Results:** Four hundred and thirty-seven patients were included. The median age of the cohort was 58 years. Ninety-five percent of them were women.There were no statistically significant differences in the men and women percentage.The disease symptoms were initiated more frequently in 35–50 years group (38.5%).There

were no statistically significant differences in the time to disease progression in the four age at diagnosis groups. No statistically significant differences were found in sicca syndrome among age groups. Ocular and oral symptoms were present in 95% of patients. The glandular involvement (46.7%), central nervous system (14.13%) and Raynaud's phenomenon (29.3%) showed significantly more often in patients under 35 years. Genital involvement (54.5%) and asthenia (72.4%) showed significantly more often in the group of 35–50 years. The gastrointestinal involvement (20%) occurred significantly more frequently in the group of 50–65 years. Splenomegaly and cardiac involvement were less frequent manifestations in all four groups of patients (<4%). Rheumatoid factor (RF) positive was significantly higher in those under 35 years (77.1%). The anti-anti-SSA and SSB antibodies tended to be more frequently positive in groups <35 years (96.7% and 79.3% respectively) and>65 years (100% and 75% respectively). There were no significant differences in the ANA, anti-DNA, anti-Sm, anti-RNP, cryoglobulins and antiphospholipid antibodies values between groups.
**Conclusions:** Patients under 65 years old have an increased degree of systemic involvement. There are no differences in the presence of sicca syndrome. The FR is significantly more common in patients younger than 35-year-old, while the anti-Ro and anti-La antibodies tend to be it in more extreme age groups.
**Disclosure of Interest:** None declared
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## FRI0326 PERIPHERAL LYMPHADENOPATHY IN PRIMARY SJÖGREN'S SYNDROME: FREQUENCY, PATTERN OF DISTRIBUTION AND CLINICAL SIGNIFICANCE - A SINGLE CENTER EXPERIENCE

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**Objectives:** To analyze frequency and clinical determinants of SLN-US prescription in clinical practice; to explore patterns of nodal size/location and their clinical significance in Sjögren's syndrome (pSS)
**Methods:** In this retrospective, single center study we included patients with a diagnosis of pSS, regularly followed at our University Hospital in the time frame 2010–2015. Demographic, clinical and serological data were recalled from clinical charts. Patients with lymphadenopathy secondary to infections, malignancy, NHLs were excluded from the study. Variables analyzed included: clinical determinants of SLN-US, number of US evaluation/time, frequency, size and nodal locations of the SLN (axillary, inguinal, cervical, supraclavicular, other).
**Results:** We enrolled in this study 229 (224 F: 5M) patients with pSS (AECG 2002), mean age at diagnosis (DS) 49 yrs (14) and mean follow-up 5.6 yrs (6.6). All the patients included in the study underwent a SLN-US at least once in the time frame 2010–2015. Peripheral lymphoadenopathy was documented in 136/229 (59.4%) patients. The most common site for peripheral lymphadenopathy was the cervical region with the most affected LN groups at this level being the lateral – cervical lymph groups (55.5%). Inguinal LN were involved in the 11.4% of the cases and axillary LN in the 10.9%. In 29 (12.7%) patients, pSS affected simultaneously the LN groups located in several segments. On average, pSS patients underwent an US of SLN every 18 (12) months (mean (SD)) with a negative correlation between the frequency of SLN-US and the duration of follow-up (r=-0.742 p=0.000). Patients underwent a SLN-US either to characterize peripheral LN, palpable at physical examination, or as a routine screening test during the assessment of the disease activity in asymptomatic patients. On the basis of the SLN-US results we distinguished different patient groups: a) 26 patients with palpable LN and pathological SLN-US, b) 110 patients without palpable LN and subcentimer lymphadenopathy at SLN-US and c) 93 patients without palpable LN and normal SLN-US. Patients included in group a) were significantly younger at the diagnosis (p=0.003), more frequently male (p=0.001), had a significantly higher disease activity (p=0.001) and presented more often salivary gland swelling (p=0.007), low C3 levels (p=0.008), hypergammaglobulinemia (p=0.006), anti-Ro/SSA (p=0.000), anti-La/SSB (0.02), Rheumatoid Factor positivity (p=0.003) and cryoglobulins (p=0.02). No significant differences were detected when patients included in the group b) and c) were compared one to each other. No specific association was observed between LN location and disease related clinical and serological manifestations. However, patients with pathological LN located in several segments presented a significantly higher disease activity and a more complex serological profile (p<0.01).
**Conclusions:** Peripheral lymphadenopathy is quite common in pSS patients. However, only patients with palpable lymphadenopathy at clinical examinations or LN located simultaneously in several segments presented a distinguished more severe phenotype. Subcentimer lymphadenopathy tends to remain stable over the time and does not seem to represent a poor prognosis factor in pSS patients.
**Disclosure of Interest:** None declared
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## FRI0327 SERUM ANTI-PHOSPHOLIPID ANTIBODY PREVALENCE AND CARDIOVASCULAR SIGNIFICANCE IN THE GENERAL POPULATION OF THE CAMELIA STUDY

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**Background:** The serum anti-phospholipid antibody (aPLs) prevalence in the general population and the association with cardiovascular disease and risk factors remain unclear.
**Objectives:** To test serum samples from a population study for aPLs and determine the presence of cardiovascular and metabolic comorbidities in a Northern Italian city.
**Methods:** We performed a cross-sectional study on 1712 adult subjects (median age 47 year-old, interquartile range 37–61, 49.8% women), randomly enrolled in 2010 from the voting lists of a 32.000-population city in the Lombardia region. All subjects completed a questionnaire for medical history and ongoing/past medications and underwent physical examination and abdomen and carotid ultrasound. Anti-cardiolipin (aCL), anti-beta2 glycoprotein I (aGPI), anti-phosphatidylserine-prothrombin (aSP) IgG, IgM, and IgA antibodies were tested in all subjects by ELISA.
**Results:** At least one aPL was positive in 258 (15.1%), at high titer in 56 (3.3%) subjects; 35 (2%) were positive for two or more aPL, 15 (0.9%) at high titer. Serum aCL were positive in 26 (1.5%) subjects, at high titer in 17 (1%), without additional aPL in 2; IgG in 15 (0.9%; at high titer in 11), IgM in 18 (1.1%, at high titer in 10), IgA at high titer in 4 (0.2%). Serum aGPI were positive in 73 (4.3%) subjects, at high titer in 48 (2.8%), without additional aPL in 4; IgG in 20 (1.2%; at high titer in 3), IgM in 28 (1.6%, at high titer in 6), IgA in 35 (2%, at high titer in 12). Serum aSP were positive in 201 (11.7%) subjects, at high titer in 29 (1.7%), without additional aPL in 167; IgG in 157 (9.2%, at high titer in 19), IgM in 65 (3.8%, at high titer in 12). Women represented 53.1% of aPL positive subjects, with higher incidence for aGPI, especially IgA, and aSP. Among aPL positive subjects, there were 10 cases of acute myocardial infarction, 7 strokes, 17 peripheral arteriopathy and 22 increased intimal-medial-thickness. Positivity for aPL was associated with older age, particularly for aGPI and aSP, while high-titer aCL IgG and aSP IgG were associated with tobacco smoking. Hypertension and hypercholesterolemia were significantly associated to aGPI IgG and IgM positivity, respectively. Hyperhomocystinemia was significantly associated with high titer multiple aPLs. Hyperuricemia was associated with aSP IgG positivity. Subjects with positive aPL had significantly higher frequency of thyroid disease (p=0.02 for high titer), peripheral arteriopathy (crude odds ratio –OR- 2; 95% confidence interval –CI- 1.2–3.6; isolated aCL crude OR 25.1; 95% CI 1.6–405.4), myocardial infarction (isolated aCL crude OR 28.5; 95%CI 1.8–460.5). Importantly, adjusted ORs for cardiovascular risk factors were not statistically significant.
**Conclusions:** We confirm that serum aPL are common in the general population, particularly at older age and possibly in association with smoking. Serum aPL is associated with common cardiovascular risk factors and specific events, however this latter effect needs to be clarified in the follow-up study to determine the real impact of aPL on the risk of cardiovascular events.
**Disclosure of Interest:** None declared
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## FRI0328 A COMPLETE REMISSION LASTING AT LEAST ONE YEAR INFLUENCES THE OUTCOME IN PATIENTS AFFECTED BY SLE: RESULTS FROM A LARGE MONOCENTRIC COHORT

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**Background:** The achievement of complete remission is one of the most important goal in the management of patients with Systemic Lupus Erythematosus (SLE). Even though a definition of remission has been proposed (complete absence of any clinical and serological sign or symptom of activity) and the concomitant acceptable treatment (including antimalarial drugs only) has been identified, however the minimum lapse of time is still controversial. This issue is of primary importance in a disease characterized by a relapsing-remitting course. Several cut-off have been suggested, ranging from 1 to 5 years.
**Objectives:** The primary end-point of the present study was to analyze the frequency of complete remission lasting at least 1 year in a large monocentric SLE cohort. Furthermore, we aimed at evaluating its association with different clinical and serological parameters and its impact on the chronic damage accrual.
**Methods:** Data on Caucasian SLE patients, diagnosed according to the ACR Classification Criteria for SLE, were collected. We included in the present analysis SLE patients evaluated at least twice per year during the last 5 years. The frequency of complete remission, defined as an SLE Disease Activity Index 2000 (SLEDAI-2k) =0, was assessed in glucocorticoid-free and immunosuppressant-free patients. Antimalarial drugs were the only SLE-related acceptable treatment.
**Results:** Our database includes 658 SLE patients evaluated at least once. From these patients non-Caucasian were excluded, resulting in 622 patients. Among

these, 179 (M/F 13/166, mean age 46.3±12.7 years, mean disease duration 173.9±101.9 months) fulfilled the above-reported selection criteria. During the 5-year follow-up, 27 patients (15.1%) experienced a complete remission lasting for at least 1 year, with a mean duration of 37.5±15.8 months. Notably, six patients experienced a prolonged complete remission lasting 5 years (4.6%). There were no significant differences in terms of demographic characteristics between patients achieving and those not achieving remission. Patients in remission showed a significantly lower frequency of renal involvement (29.0 vs 18.4, P=0.04) and low C3 and C4 (14.8% vs 36.8%, P=0.0005; 14.8% vs 33.5%, P=0.0002, respectively). There were no other differences in terms of clinical and laboratory features. The frequency and the severity of chronic damage, evaluated by SLICC Damage Index (SDI), resulted significantly lower in patients achieving remission (11.1% vs 51.9%, P<0.000001; 0.48±0.8 vs 0.8±1.2, P=0.03, respectively). The length of the remission status did not influence the chronic damage. At the multivariate analysis, no independent factors were associated with remission; conversely, low C3 resulted a risk factor for absence of remission (OR=0.15, 95% CI 0.03–0.06).

**Conclusions:** In the present SLE cohort, a complete remission lasting at least 1 year has been identified in 15% of patients. The remission status, regardless of its duration, is associated with a lower chronic damage, in terms of frequency and severity. These results suggest that the achievement of a state of remission lasting at least one year may represent a favorable prognostic factor in patients with SLE.

**Disclosure of Interest:** None declared

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## FRI0329 BONE EROSIVE DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS IS ASSOCIATED WITH LOCAL HYPERVASCULARIZATION INDEPENDENTLY FROM ACPA POSITIVITY

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**Background:** Joint involvement is one of the most frequent manifestations in patients affected by Systemic Lupus Erythematosus (SLE). It is characterized by a wide heterogeneity ranging from arthralgia to a severe erosive disease. The presence of local hypervascularization, evaluated by power Doppler (pD), is a well-established risk factor for the development of erosive damage in patients affected by Rheumatoid Arthritis (RA), together with the positivity for anti-citrullinated peptide antibodies (ACPA). To date, these data are not confirmed in SLE patients.

**Objectives:** The aim of the present study was to estimate whether pD-evaluated local hypervascularization and the presence of ACPA represent risk factors for the development of erosive damage, assessed by ultrasonography, in SLE patients.

**Methods:** One hundred two SLE patients with joint involvement were enrolled (M/F 1/101; mean age 44.5±11.6 years; mean disease duration 144.6±103.2 months). The ACPA presence was evaluated in 64 patients (ELISA, Euroimmun Italia, Italy). Ultrasonographic assessment of metacarpophalangeal (MCP), proximal interphalangeal (PIP) and metatarsophalangeal (MTP) was performed in all patients. The presence of pD and erosive damage were recorded by a dichotomic (present/absent) and a semiquantitative (0–3) score. A total score was obtained by the sum of modifications observed in every single joint.

**Results:** Hypervascularization in at least one joint was identified in 25/102 (24.5%) patients (median score 4, range 1–23). This feature was more frequent at level of II and III MCP (12.7% and 8.8% respectively). Erosive damage was detected in 19 patients (18.7%). The presence of pD signal was significantly associated with the presence of erosive damage. Indeed, 13 pD-positive patients showed erosions (13/25, 52.1%) in at least one joint, compared with 6/77 (8.4%) pD-negative patients (median 1, range 0–9 *vs* median 0, range 0–7, P<0.0001). 21.8% of patients tested ACPA positive. However, there was no association between erosive damage and ACPA positivity. The erosive damage was reported in 21.4% of ACPA-positive patients and in 22.0% of ACPA-negative (P=NS).

**Conclusions:** In the present study, we described for the first time the association between the presence of local hypervascularization, identified by pD ultrasonography, and erosive damage in a cohort of SLE patients with joint involvement. These results, similarly to RA, suggest the role of pD signal as a negative prognostic factor for erosive bone damage. This could help in the choice of a more aggressive therapeutic strategy. Conversely, the presence of ACPA does not seem to be associated with erosive damage, suggesting the presence of an alternative pathogenetic mechanism underlying the erosive damage in SLE patients.

**Disclosure of Interest:** None declared

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## FRI0330 PREDICTIVITY OF OCULAR SURFACE PARAMETERS AND TEAR PROTEIN EXPRESSION IN THE DIAGNOSIS OF SJÖGREN SYNDROME VERSUS DRY EYE

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**Background:** Several studies report alterations of protein expression profiles of inflammatory cytokines in the tears of patients with dry eye syndrome. Futhermore several non cytokine proteins such as lysozyme, lactoferrin, lipocalin, etc were found to be altereted too (1). The minimal invasiveness of the methods of sample collection using glass microcapillary tubes makes tear fluid very interesting option for proteomic studies, although analysis may be challenging because of the small volume of tear fluid (>5nl) that can be collected (2).

**Objectives:** to discriminate the difference between ocular surface parameters and protein expression in tears of patients with dry eye syndrome and patients affected by Sjögren syndrome.

**Methods:** 80 patients (female 77) with sicca syndrome arrived in a period included from September 2010 to May 2015, in our Rheumatologic Unit were evaluated. Break Up time (BUT), Schirmer and Jones test, fluorescin and green lisamin coloration, citologic analysis of conjuctive for scraping/impression was done in each patients to evaluate the ocular surface parameters. 5 nl of tear fluid, was collected on external angle by using a glass microcapillary tube. The tear fluid sample was then analysed by Agilent 2100 Bioanalyzer system to detect non cytokine protein patterns. Scintigrafic parameters for salivary gland impairment, ANA, ENA, rheumatoid factor and albumin was researched too. The sensibility, the specificity and the predictive value (PV+ and PV -) was calculated for each protein evaluated. Statistic analysis was performed by using SPSS 20.0 IBM, Mann-Whitney test for indipendent samply and ROC curve.

**Results:** 25/80 patients was affected by Sjögren syndrome according to Vitali Criteria of 2002. Demografic and laboratoristic data of both groups were calculated. Significant reduction of BUT, fluorescin and green lisamin coloration value were observed in patients with Sjögren syndrome versus patients with dry eye. Significant reduction of lipocalin and lysozyme concentration were evaluated in patients affected by Sjogren syndrome versus the dry eye group. Lipocalin and fluorescin coloration risult having a high predictive value to discreminate patiens affected by Sjogren syndrome from patient with dry eye.

**Conclusions:** Protein pattern alterations in tears represent a high potential to generate biomarkers for disease state determination and provide sources for new diagnostic procedures and treatment response. In this study the observed reduction of lipocalin concentration and fluorescin coloration value was determinant to distinguish patients affected by Sjögren syndrome from patients with dry eye.

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## FRI0331 PREVALENCE OF COMORBIDITIES IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS: A COMPARATIVE, REGISTRY-BASED STUDY WITH EMPHASIS IN CARDIOVASCULAR DISEASE

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**Background:** Reliable data regarding the prevalence of specific medical comorbidities among patients with PrimarySjögren's Syndrome (pSS) remain sparse and there are not comparative studies among patients with pSS and patients with Systemic Lupus Erythematosus (SLE).

**Objectives:** To compare the prevalence of the main comorbidities of two large cohorts of patients with pSS and SLE, with focus in cardiovascular (CV) diseases.

**Methods:** Cross-sectional multicenter study comparing cumulative prevalence of the most relevant comorbidities, with identical definition in both cohorts. Patients on follow-up from SJOGRENSER (Spanish Register of pSS) and RELESSER (Spanish Register of SLE), fulfilling AECG-2002 and ACR-97 classification criteria, were included. Binomial logistic regression analysis was carried out to explore

potential differences, adjusting for age, sex and disease duration with further specific adjustments for each variable, including CV risk factors and treatments, when it was considered convenient.
**Results:** 437 pSS (95.2% female) and 2,960 SLE (89.5% female) patients were included. Mean age: 58.6 (p55-p75: 50.0–69.9) and 46.4years (22.4–41.6) respectively ($p<0.001$). Disease duration 10,4 (6.0–16.7) and 13.3 years (8.80–20.04) respectively ($p<0.001$).
Patients with pSS were hospitalized by the disease activity lesser than SLE: 17% vs 53%, $p<0.001$; OR 0.18 (95%CI:0.14–0.24). Moreover, the use of GC or IS were less prevalent in pSS [GC: 49.4% in pSS vs 88.2% in SLE; OR:0.13 (0.10–0.16); azathioprine: 10.1% vs 32.4%; OR: 0.24 (0.17–0.33); mycophenolate: 3.9% vs 16.2%; OR:0.21 (0.13–0.35); cyclophosphamide: 3.0% vs 22.6%; OR: 0.11 (0.06–0.18)].
The following comorbidities were less prevalent in pSS: Smoking [25.3% vs 48.2%, $p<0.001$, OR:0.50 (95%CI:0.40–0.64)], hypertension [25.3%vs 27.3%, $p<0.001$, OR: 0.44 (0.33–0.58)] and life-threatening CV events [(6.8% vs 8.5%, OR:0.53 (0.32–0.87)]. Severe infections were also more frequent in SLE [17.7% vs 10.1%, $p<0.001$, OR: 0.52 (0.37–0.72)], but this difference lost statistical significance when adjusted for glucocorticoid (GC) and immunosupressors (IS) use. Conversely, fibromyalgia and lymphoma were more frequent in pSS [14.6 vs 5.2%, $p<0.001$, OR: 2.70 (1.93–3.80)] and [1.6 vs 0.3%, $p=0.002$; OR: 5.71 (1.83–17.79)] respectively.
**Conclusions:** pSS patients have consistently less serious comorbidity burden compared with SLE patients, namely less CV diseases and less infections. In contrast, the risk of lymphoma exceeds that seen in SLE patients. The higher prevalence of CV events in SLE does not seem to be explained only by traditional CV risk factors, suggesting that SLE derived factors could be involved.
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## FRI0332 FACTORS AFFECTING THE ATTITUDES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS REGARDING POTENTIAL CLINICAL TRIAL PARTICIPATION

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disorder affecting skin, joints, kidneys, brain, and other organs[1]. Recruiting participants for SLE clinical trials may be challenging for several reasons including patients' concerns that medications may exacerbate their condition or cause side effects[2].
**Objectives:** To address challenges of recruiting patients with SLE into clinical trials, we conducted a survey study to: (1) explore patients' satisfaction with their current treatment; (2) assess participants' motivations to switch to a new treatment; and (3) identify the characteristics of patient who indicated a willingness to participate in a clinical trial.
**Methods:** 259 members of an online patient network aged 18–77 (mean age = 47; 96% female, 78% white) with SLE completed an online survey about their experience and attitudes. The data was collected within 7 days. We used the Chi-square test to analyze the distribution of categorical variables; two sample t-tests to compare group means and Pearson r correlation to identify the association between continuous variables.
**Results:** 60% of SLE patients report being at least "somewhat satisfied" with their current treatment; 74% name worsening symptoms as an important factor for changing medications. Those patients (36%) who said they were motivated to change to a new treatment reported a slightly more severe daily impact of SLE (mean = 3.6 on a scale 1: not at all – 5 very much) than patients who did not see new treatment availability as a reason to change their current medication (SLE impact mean = 3.3; $t(258)=2.49$; $p<0.01$). 29% say knowing that a trial drug has never been tested before will increase the likelihood of their participation in the trial. The correlation analyses revealed slight, but statistically significant association between this favorable view of novel drug trials and higher number of treatments, frequency of healthcare utilization, and lupus daily impact (r ranged 0.13–0.22, $p<0.03$). The disease-related factors positively associated with likelihood of clinical trial participation are SLE daily impact ($r=0.26$, $p<0.03$), headaches ($\chi^2=14.06$, $p<0.01$), and pain ($\chi^2=8.8$, $p<0.05$); the treatment-related factors are burden of treatment, frequency of flares, frequency of healthcare utilization, number of medications (r ranged 0.14–0.18, $p<0.03$), and use of pain medications ($\chi^2=12.6$, $p<0.05$).
**Conclusions:** Investigators and clinical trial coordinators may achieve a higher recruitment and retention rate by targeting: 1) patients whose SLE symptoms are under poor control and who therefore frequently utilize the healthcare system rather than patients with low disease activity or stable disease; and 2) those patients who are experiencing more pain and headaches and more frequently using pain medications.
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## FRI0333 HEMOGLOBIN, COMPLEMENT 3 AND CAROTID IMT ARE ASSOCIATED WITH LOW FREE PROTEIN S IN SLE

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**Background:** Protein S plays a role as a cofactor not only in coagulation pathway, but also in the removal of apoptotic remnants. Free protein S was investigated whether it could represent as a disease related marker in systemic lupus erythematosus (SLE), which has a defect in clearance of apoptotic debris[1,2]. In SLE, cardiovascular diseases including myocardial infarction and stroke develop more frequently and earlier than healthy population. It has become important to find underline mechanisms about the advanced atherosclerosis in SLE[3].
**Objectives:** We measured free protein S and carotid atherosclerosis using Doppler sonography among SLE patients, and analyzed their associations with clinical features including disease activity markers.
**Methods:** Total of 110 female patients with SLE were recruited and serum free protein S level was evaluated by enzyme-linked immunosorbent assay. The carotid artery intima media thickness (cIMT) and plague were measured by Doppler ultrasound and the clinical characteristics were collected.
**Results:** Mean level of free protein S was 67.4±19.7%, and 21 patients had low level of free protein S, defined as less than 50%. Hemoglobin and lymphocyte count were significantly lower (11.4±1.4 vs 12.5±1.4, $p$=0.002 and 1, 221±609 vs 1,720±1,097, $p$=0.047), and erythrocyte sedimentation rate (ESR) was significantly higher (30.1±20.6 vs 20.8 ± 17.8, $p$=0.033), complement 3 (C3) and complement4 (C4) were significantly lower (80.8±27.6 vs 103.4±25.8, $p$=0.001 and 15.6±10.4 vs 21.5±7.6, $p$=0.005) in SLE patients with low free proteins S level compared to those not. Carotid IMT levels were different (3.78±0.69 vs 4.13±0.87, $p$=0.051) while plaque index was not different between two groups. On univariate logistic analysis, hemoglobin (OR 0.6, $p$=0.003), lymphocyte (OR 1.0, $p$=0.03), ESR (OR 1.03, $p$=0.041), C3 (OR 0.96, $p$=0.001), and C4 (OR 0.91, $p$=0.007) were related with free protein S. With adjustments, hemoglobin (OR 0.57, $p$=0.023), C3 (OR 0.94, $p$=0.017) and cIMT (OR 0.51, $p$=0.046) were associated with low free protein S.
**Conclusions:** Hemoglobin, complement 3 and cIMT were independently associated with low free protein S in SLE patients. Moreover, cIMT showed negative influence to low free protein S. From this clinical data, endothelial thickness might contribute free protein S rise in SLE patients.
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## FRI0334 ALTERED CUTANEOUS MICROVASCULAR FUNCTION IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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**Background:** Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by thrombotic events and/or pregnancy morbidity in the persistent presence of antiphospholipid antibodies (aPL). The mechanisms by which aPLs cause thrombosis have not been completely elucidated. Recent studies suggest that thrombosis may be linked to diminished production of nitric oxide (NO) in endothelial cells. Endothelium-derived NO normally exerts anti-thrombotic and vasodilator effects. Diminished NO production in APS patients may therefore result not only in thrombosis but also blunted vasodilator responses. Whether patients with APS display blunted NO-stimulated vasodilation has not been directly determined.
**Objectives:** We determined endothelium-dependent and endothelium-independent vasodilator response in cutaneous microvasculature of APS patients and healthy controls.
**Methods:** Patients with primary or secondary APS (all positive for at least two different aPL) and healthy controls were enrolled between May 2014 and May 2015. Participants were asked to avoid coffee, tea or energy drinks on the day the measurements were performed. During the 2-hour measurement protocol electrocardiogram, arterial blood pressure and laser Doppler flux of cutaneous

microvessels were monitored. Iontophoresis of acetylcholine, which stimulates NO production in endothelial cells, was used to assess endothelium-dependent vasodilation. Iontophoresis of sodium nitroprusside, a direct NO donor, was used to assess endothelium-independent vasodilation. Finally, local warming (42°C) of skin on the left forearm skin was used to assess heat-stimulated vasodilator response. Data were analyzed using independent samples t-test or repeated measures ANOVA followed by Dunnett's test.
**Results:** Thirty four APS patients and 34 healthy age and sex-matched controls completed the study (24 female and 10 male in each group, age range 22–74). Participants were divided into three age groups, 22–38 years (12 female per group), 39–49 (5 female, 6 male per group) and ≥50 (7 female, 4 male per group). Acetylcholine iontophoresis, sodium nitroprusside iontophoresis or local heating stimulated vasodilation in all participants. Endothelium-dependent vasodilator response to acetylcholine was blunted in APS patients aged ≥50 ($P<0.050$ vs. healthy controls), but remained unaltered in younger participants. Conversely, vasodilator response to local heating was blunted in APS patients from the 22–38 age group ($P<0.050$ vs. healthy controls). Endothelium-independent vasodilation stimulated by NO donor sodium nitroprusside was similar in all groups.
**Conclusions:** Here we show that endothelium-dependent vasodilator response in cutaneous microvasculature is diminished in older APS patients, while changes in vasodilator response to local heating affect mainly younger APS female patients. Our results indicate that cutaneous microvasculature in APS is functionally altered. This study supports diminished endothelial NO production in patients with APS.
**Disclosure of Interest:** None declared
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## FRI0335 AN EVALUATION OF CLINICAL OUTCOME MEASURES FOR MUSCULOSKELETAL LUPUS USING ULTRASOUND AS A GOLD STANDARD

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**Background:** Musculoskeletal symptoms in SLE patients are common, but difficult to assess clinically. Ultrasound (US) is an objective measure of synovitis.
**Objectives:** To test clinical tools currently used for musculoskeletal lupus against US as a gold standard.
**Methods:** A multicentre cross-sectional study recruited 107 patients in Leeds and Southampton fulfilling ACR/SLICC criteria for SLE, all had history of musculoskeletal symptoms and 79% had pain at the time of evaluation. Patients with positive CCP or RF were excluded. Patients were clinically assessed using BILAG, SLEDAI, tender joint count (TJC), swollen joint count (SJC), physician and patient VAS (both 0–100, for MSK symptoms). US hand was used to examine joints and tendon sheaths.
**Results:** There was disagreement between US and clinical joint swelling in 26% of patients. In the 40% with clinical joint swelling, US confirmed this in 83%. 20% of all patients had US synovitis that was not detected clinically. Overall, objective synovitis was found in 40% of patients using clinical swelling and 53% using US. US was correlated with SJC (R=0.389, P≤0.001), MSK-BILAG numeric score (R=0.503, P≤0.001), and physician VAS (R=0.5, P≤0.001), but not with TJC, SLEDAI, or patient VAS. We then looked for clinical appearance of patients with US-proven synovitis: see table 1. We identified significant associations in the whole cohort. In multivariate analysis only physician-VAS was significant (p=0.018). However, in 50 patients with no joint swelling, 15 had US synovitis, but no clinical variable could identify this.

Table 1

| | US+ve, median (IQR) | US–ve, median (IQR) | p |
|---|---|---|---|
| MSK- BILAG | 2 (2) | 3 (1) | <0.001 |
| SLEDAI | 4 (6) | 2 (4) | 0.006 |
| Physician VAS | 41 (50) | 8 (20) | <0.001 |
| Patient VAS | 55 (33) | 45 (70) | 0.085 |
| ESR | 21 (45) | 12.5 (24) | 0.086 |
| TJC | 6.5 (10) | 3 (9) | 0.034 |
| SJC | 1.5 (4) | 0 (0) | <0.001 |

**Conclusions:** Swollen Joint Count, Physician VAS, and MSK-BILAG all correlate with true synovitis as defined by US. However, these variables are all based on the clinical detection of joint swelling and 50% of this cohort did not have joint swelling. In the latter group, no clinical variable was helpful in identifying the 30% of patients with US-proven synovitis. US should be used to evaluate MSK-SLE patients who do not have clinical synovitis.
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## FRI0336 HYPOCOMPLEMENTEMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS; ESTABLISHING THE IMPORTANCE OF LOW C3 AND C4 IN A LONGITUDINAL COHORT

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**Background:** Despite inclusion in systemic lupus erythematosus (SLE) disease activity indices and classification criteria, the relationship between hypocomplementemia, disease manifestations and cumulative organ damage has not been systematically investigated. It is also unknown whether there is a particular disease phenotype associated with chronic, unresolving hypocomplementemia.
**Objectives:** To evaluate SLE patients with a history of hypocomplementemia, to establish the relationship between clinical manifestations and organ damage. To compare low C3 to low C4 and establish relative importance for manifestations and damage parameters. To assess SLE patients with persistent hypocomplementemia to ascertain whether these patients have unique clinical characteristics.
**Methods:** As part of a lupus cohort, C3 and C4 were measured quarterly. Using univariate and multivariate methods, those with and without a history of low C3, low C4 and both were compared and an odds ratio calculated and compared using generalized linear hypothesis testing. We then considered those who had persistent hypocomplementemia (i.e. complement never normalized, on a minimum of 3 evaluations) and compared them to patients with a similar number of assessments.
**Results:** 2399 patients were included in the analysis; 47% had a history of low C4 and low C3 in 55%. Persistently low C3 was found in 83 (4.0%) and C4 in 65 (3.2%). A history of low C3 associated strongly with nephritis and with renal damage parameters. Low C4, in isolation, associated only with false positive RPR and the presence of arthritis. With unresolving hypocomplementemia (Table 1), strong associations were demonstrated between low C3, low C4 and both in combination and hematologic, serologic and antiphospholipid-related parameters. No associations were found for cutaneous disease. Persistently low C3 associated with nephritis.

Table 1

| Manifestation | | Persistent low C3 OR | P value | Persistent low C4 OR | P value | Persistent low C3+C4 OR | P value |
|---|---|---|---|---|---|---|---|
| Arthritis | | 1.48 | 0.2266 | 0.87 | 0.6787 | 1.59 | 0.3639 |
| Serositis | Pleurisy | 1.15 | 0.6116 | 1.22 | 0.5334 | 0.94 | 0.8786 |
| | Pericarditis | 1.76 | 0.0647 | 1.52 | 0.2597 | 0.45 | 0.2837 |
| Renal | | 3.40 | 0.0030 | 0.53 | 0.5407 | 1.89 | 0.3978 |
| Neurologic | Seizures | 1.14 | 0.7664 | 0.80 | 0.7089 | 0.44 | 0.4224 |
| | ACS | 1.21 | 0.8014 | 0.86 | 0.8834 | 1.49 | 0.6992 |
| Hematologic | Hemolytic anemia | 1.68 | 0.2536 | 4.56 | 0.0001 | 0.62 | 0.6453 |
| | Leukopenia | 3.78 | <0.0001 | 2.35 | 0.0079 | 2.58 | 0.0240 |
| | Lymphopenia | 1.99 | 0.0114 | 2.78 | 0.0019 | 1.11 | 0.8009 |
| | Thrombocytopenia | 2.44 | 0.0032 | 2.44 | 0.0122 | 1.64 | 0.3375 |
| Immunologic | Anti-dsDNA | 10.71 | <0.0001 | 2.93 | 0.0021 | 8.48 | 0.0006 |
| | Anti Sm | 6.8 | <0.0001 | 3.31 | 0.0013 | 2.98 | 0.0252 |
| Anti-phospholipid | Anti-cardiolipin | 1.49 | 0.1467 | 2.39 | 0.0089 | 1.44 | 0.4020 |
| | Anti-B2 GP | 4.48 | 0.0001 | 2.42 | 0.1264 | 2.59 | 0.1462 |
| | FP RPR | 2.83 | 0.0041 | 2.87 | 0.0119 | 3.65 | 0.0300 |
| | LAC | 1.98 | 0.0159 | 2.1 | 0.0255 | 1.38 | 0.4858 |

**Conclusions:** A history of, and chronically low C3 associates uniquely with renal disease whilst a history of low C4, associated only with arthritis and a false positive RPR.
Persistent hypocomplementemia associated strongly with other hematological and serological abnormalities. While a history of low C4 was not strongly associated with other disease activity parameters, chronically low C4 appears to be a more important marker.
**Disclosure of Interest:** None declared
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## FRI0337 ANTI-C1Q AUTOANTIBODIES, C1Q CIRCULATING IMMUNE COMPLEXES AND COMPLEMENT LEVELS IN PATIENTS WITH NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Experimental SLE-models show that complement activation may be a key part of lupus cerebritis and lupus-thrombosis. It is also known that complement factors contribute to the pathology of inflammatory central nervous system (CNS) and neurodegenerative diseases
**Objectives:** To analyse serum levels of anti-C1q, C1q circulating immune complexes (CIC), complement activation and complement components in systemic lupus erythematosus (SLE) patients during the first CNS neuropsychiatric (NP) event and to define the possible association between these results and clinical and laboratory characteristics
**Methods:** Patients suspected of having NP involvement due to SLE were recruited in the Leiden NPSLE-clinic. All SLE patients were classified according to the ACR 1982 revised criteria for the classification of SLE. The clinical disease activity was measured by the SLE Disease Activity Index 2000 (SLEDAI-2K) and NP diagnoses were classified according to the 1999 ACR case definitions for NPSLE.

We measured in serum of all patients anti-C1q and C1q CIC levels using ELISA, the activation capacity of complement (CH50 and AP50) using functional assays and different complement components (C1q, C3, C4) using laser nephelometry. Two-hundred healthy controls (HC) were also included for comparison

**Results:** A total of 280 patients were included. In 92 patients the symptoms were attributed to SLE. NPSLE patients consisted of 63 patients with focal NPSLE and 34 patients with diffuse NPSLE. Anti-C1q antibodies were significantly higher and CH50, AP50 and C3 were significantly lower in NPSLE patients compared to SLE and HC. This association was specially marked for diffuse NPSLE (SLE: 20.8 versus 8.7; HC: 20,8 versus 7,04; both comparisons $P<0.05$). No differences in antibody titters were found for C1q CIC when SLE and NPSLE patients where compared. Low C4 was significantly associated with focal NPSLE after using potential predictors, but we lost this association when antiphospholipid antibodies (aPL) were excluded from the model. Low C3, AP50 and CH50 were independently associated with diffuse NPSLE ($P<0.001$). When SLEDAI-2K was included in the model we did not find any association. When individual NPSLE syndromes were analysed, psychosis and cognitive dysfunction showed significantly lower values of AP50 and CH50 ($P<0.001$ for psychosis and $P<0.05$ or cognitive dysfunction). Furthermore, patients with lupus psychosis showed higher prevalence of low C1q (OR=5, 95% CI 1.5–15.8, $P<0.05$), low C3 (OR=28.6, 95% CI 3.5–230.4, $P<0.001$) and low C4 (OR=3.8, 95% CI 1.1–13.3, $P<0.05$) and cognitive dysfunction showed a higher prevalence of low C1q (OR=5, 95% CI 1.5–15.8, $P<0.05$), low C3 (OR=4.4, 95% CI 1.8–10.5, $P<0.001$) and low C4 (OR=3.6, 95% CI 1.5–8.6, $P<0.05$) when compared with SLE. No significant associations were seen with other individual NPSLE syndromes

**Conclusions:** No association was found between anti-C1q, C1q CIC and NPSLE. The associations between diffuse NPSLE and low C3/AP50 and focal NPSLE and low C4 may be explained by disease activity and the presence of aPL respectively. The role of complement activation and complement components in lupus psychosis and cognitive dysfunction merits further research

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**Disclosure of Interest:** None declared

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## FRI0338 EVALUATION OF THE SENSITIVITY AND SPECIFICITY OF THE SJÖ® DIAGNOSTIC TEST

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**Background:** An early and accurate diagnosis of Sjögren's Syndrome is an important factor in limiting complications of the disease. Achieving this diagnosis has historically proved challenging, requiring a number of diagnostic tests including serology [1]. The utility of the traditional serological markers (SSA/Ro, SSB/La, Antinuclear Antibody, Rheumatoid Factor) have several limitations, including a combined sensitivity and specificity of approximately 40–60%, lack of detectability in approximately 20–30% of cases, lack of detectability early in the disease process, and lack of target-organ specificity [1,2].

Sjö™ is an advanced diagnostic panel for the early detection of Sjögren's Syndrome. It includes the traditional biomarkers as well as three novel, proprietary biomarkers (SP-1, CA6, PSP) that provide high sensitivity and specificity for Sjögren's Syndrome, are target-organ specific and appear early in the disease process [3,4].

**Objectives:** To Evaluate the sensitivity and specificity of the advance Sjö panel in comparison to the traditional serological markers.

**Methods:** Antibodies to the traditional markers (SSA [Ro], SSB [La], antinuclear antibody [ANA], and rheumatoid factor [RF]) and the novel biomarkers (salivary protein-1 [SP1], carbonic anhydrase-6 [CA6] and parotid secretory protein [PSP]) in patient sera samples were detected using the Sjö panel. To assess sensitivity, sera samples from 267 confirmed SS patients across 3 clinical studies were analyzed with Sjö. To assess specificity, sera samples from 125 age- and sex-matched controls, as well as 64 pediatric controls, were analyzed with Sjö.

**Results:** Overall, the cumulative sensitivity of the complete Sjö panel was 91.4% (244/267); sensitivity of SSA/SSB alone was 74.9% (200/267), while sensitivity for the novel biomarkers alone was 49.8% (133/267). The cumulative specificity for the complete Sjö panel was 79.8% (151/189), and the cumulative specificity for the novel biomarkers was 83.5% (158/189).

**Conclusions:** An early and accurate diagnosis of SS is an important factor in limiting complications of the disease. The Sjö panel incorporates traditional and novel markers and increases the sensitivity in the diagnosis of SS by over 25% without compromising specificity. Patients who may have SS would benefit from screening with the Sjö panel to facilitate early diagnosis and contribute to better management of dry eye symptoms and other systemic manifestations.

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## FRI0339 ADHERENCE TO VACCINATION AND OSTEOPOROSIS PREVENTION IN A FRENCH SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

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**Background:** Systemic lupus erythematosus (SLE) is a chronic inflammatory disease in which improvements in treatments have led to new challenges in patient care. Longer survival and patients aging come with long-term complications that the rheumatologists should work to recognize and prevent effectively. In fact, osteoporosis and infections bear a great importance in disease-related morbidity, mortality and care-related costs of SLE patients.

**Objectives:** Evaluate adherence to influenza and pneumococcal vaccination as well as to osteoporosis prevention in regard of the 2003 french recommendations, in a SLE patient cohort. Describe the factors associated with osteoporosis as well as with adherence to adequate vaccinal prevention.

**Methods:** We included all SLE patients (fulfilling the American College of Rheumatology criteria), seen from May 2014 to November 2014, in Rheumatology or Internal medicine department from Bordeaux teaching hospital, France. Using 2 questionnaires and medical records, informations concerning patients, disease-related characteristics and adherence to preventions were collected. Statistical analyze was made with appropriate tests regarding the type of data and a p-value $<0,05$ was considered of statistical significance.

**Results:** One hundred and nine patients were included. There was 100 women (92%), mean disease duration was 9,9 years. Renal and neurologic involvement were present in 20 and 9% of patients respectively. At the time of the study 76% were receiving hydroxychloroquine, 57% corticoids with 34% of them on a dose $\geq$7,5mg prednisone/day and 57% had received an immunosuppressant.

Twenty-one (19%) patients had an indication for anti-osteoporotic treatment. These patients were older (mean 54 versus 42 years, $p<8.10^{-4}$), had a longer use of corticosteroid (103.7 versus 62,5 months, $p<0.01$) and a greater use of immunosuppressant (81% versus 51%, $p<0.01$). Lombar and femoral head T-score were negatively correlated with SLICC-ACR damage index after excluding fractures from the score (b = -0,35 and -0,27; $p<0,006$ and $p<0,03$ respectively). Only 12/21 (57%) patients received the indicated anti-osteoporotic treatment, mainly by lack of prescription by the attending physician.

Only 11 patients (10%) received both influenza and pneumococcal vaccines, 35% received influenza vaccination at least once and 18% received pneumococcal vaccination. Reasons for non-vaccination were: lack of recommendation by general practitioner or rheumatologist (51%), fear of side effects (29%), contraindication with lupus (14%), inefficiency (2%). Predictive factors for an appropriate vaccination for both vaccines were: higher SLICC-ACR damage index ($p<0,03$) and past or current treatment with rituximab ($p<0,02$). Longer disease duration was associated with a better vaccination against influenza ($p<0,02$), and contact with elderly for pneumococcal vaccine ($p<0,04$).

**Conclusions:** Osteoporosis treatment and infection prevention with influenza and pneumococcal vaccination remains low among SLE patients. Rheumatologists need to better implement these aspects in the global care of their SLE patients.

**Disclosure of Interest:** None declared

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## FRI0340 BREASTFEEDING IN SYSTEMIC LUPUS ERITHEMATOSUS

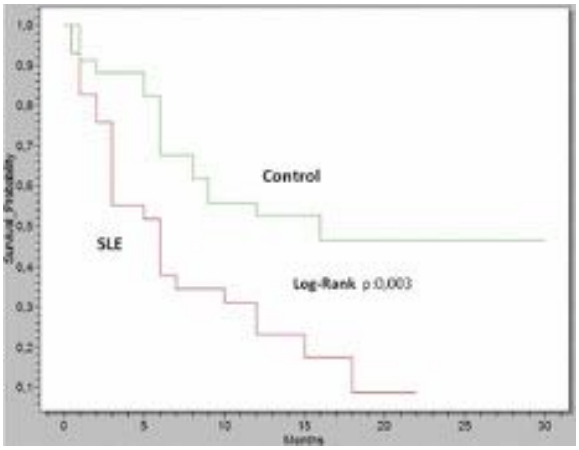
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**Background:** Breastfeeding is the optimal source of nourishment for newborns and infants during their first year of life.Both short and long benefits accrue to mothers who breastfeed (1,2). The clinical condition of patients with systemic lupus erythematosus (SLE) may have an impact on breastfeeding onset and duration.

**Objectives:** Assess breastfeeding in patients with SLE.

**Methods:** Retrospective case-control study. Patients who had got pregnant after being diagnosed with SLE (4 or more SLICC ACR/EULAR criteria) and whose pregnancies had been followed up in the hospital were interviewed. The control group consisted of patients approached in the waiting-room of the paediatrics service. The data collected included epidemiological information, main features of their pregnancies and newborns, breastfeeding duration, and reasons for

weaning. This study was approved by the Bioethics Committee of the Ramos Mejia Hospital, and both patients and controls signed the informed consent form.
**Results:** Thirty-six pregnancies in 31 patients with SLE and the same number of controls were studied. The following features were similar in both groups: current age, age at the time of delivery, level of education, average number of children, number of patients that breastfed for the first time, and preterm birth rates.
Patients with SLE had planned their pregnancies ahead less frequently than controls (16.7% vs 44.4%, p 0.02), they had experienced a greater number of complications during the pregnancies (33.6% vs 5.6%; p 0.007), and their newborns showed a higher trend to minor complications (25% vs 11.1%; p 0.2).
Twenty-five percent of the patients with SLE presented some kind of complication during puerperium, mainly related to disease activity, versus none in the controls (p 0.001). Also, a higher number of patients with SLE did not even initiate breastfeeding (19.4% vs 5.6% in the controls; p 0.07). Breastfeeding average duration in patients with SLE was 6 months (SD 6 months) versus 12 months (SD 8 months) in the controls (Log Rank p: 0.003).
Fifty-two percent of the controls mentioned that there had been no reason for weaning and considered that they had nursed their children a suitable amount of time. Conversely, patients with SLE frequently set weaning in motion on the grounds that they had been placed on medication (42%). However, when the medication was analysed, in 6 of 11 cases (55%), it consisted of low doses of corticoids or Hydroxychloroquine.




**Conclusions:** In this retrospective case-control study it was observed that patients with SLE show a lower trend to initiate breastfeeding, and they sustain it for less time than controls (6 months vs 12 months respectively). Although the most common reason for weaning is the administration of medication, breastfeeding duration could be optimised by improving the level of information provided to patients.
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**Disclosure of Interest:** None declared
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## FRI0341 DO PATIENTS WITH SLE AT ONSET DIFFER FROM MIMICKERS? A COMPARISON OF CLINICAL AND SEROLOGICAL MANIFESTATIONS IN A MULTICENTER COHORT TO INFORM THE DEVELOPMENT OF NEW CLASSIFICATION CRITERIA FOR SLE

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**Background:** Current SLE classification criteria may not classify patients with early SLE well. SLE mimickers can have an initial presentation similar to SLE and need to be distinguished from early SLE patients by classification criteria.
**Objectives:** To describe the clinical and serological presenting manifestations of SLE at disease onset and those of SLE mimickers.
**Methods:** We collected clinical and laboratory data on patients newly presenting with potential SLE (symptoms <12 months) within the past 3 years at centers in Europe (2), North America (3), South America (1) and Asia (1). Patients were diagnosed as SLE or mimicking conditions by clinical experts. We compared the presenting manifestations in SLE vs. mimickers. We examined combinations of autoantibodies, clinical and laboratory manifestations for their association with SLE vs. SLE mimickers in multivariable analyses.
**Results:** Of 616 patients, 389 were diagnosed with SLE (89% female) and 227 were given other diagnoses (97% female). A smaller proportion of SLE patients than patients with mimicking conditions were White (55% vs. 90%). Mimickers included UCTD, Sjögren's syndrome, rheumatoid arthritis, scleroderma, and fibromyalgia. Clinical and autoantibodes presenting manifestations in new onset SLE and mimickers are represented in table 1. In univariable analyses, the following autoantibodies profiles were associated with SLE vs. mimickers: Profile 1 (ANA, anti-Sm, anti-Ro and anti-RNP; OR 3.49, 95% confidence interval [CI] 2.29–5.31) and Profile 2 (ANA, anti-cardiolipin IgG/IgM, Beta2 and lupus anticoagulant; OR 2.82, 95% CI 1.75–4.55). In multivariable analyses, the following autoantibodies profiles were associated with SLE vs. mimickers: Profile 1 (OR 3.02, 95% CI 1.90–4.80) and Profile 2 (OR 3.11, 95% CI 1.80–5.36). Adding hypocomplementemia to Profile 1 and 2 showed a high association with SLE [OR 3.40, 95%CI 2.21–5.22 and OR 2.41, 95%CI 1.53–3.80] respectively.

Table 1

| | SLE (N=389) | Mimickers (N=227) | P-value |
|---|---|---|---|
| Fever | 134 (34.5%) | 31 (13.7%) | <0.001 |
| Fatigue | 110 (28.3%) | 84 (37.0%) | 0.024 |
| Malar rash | 193 (49.6%) | 14 (6.2%) | <0.001 |
| Oral ulcers | 84 (21.6%) | 12 (5.3%) | <0.001 |
| Alopecia | 119 (30.6%) | 27 (11.9%) | <0.001 |
| Inflammatory arthritis | 224 (57.6%) | 60 (26.4%) | <0.001 |
| Pleuritis | 87 (22.4%) | 6 (2.6%) | <0.001 |
| Kidney | 51 (13.1%) | 0 | <0.001 |
| Seizures | 11 (2.8%) | 0 | 0.009 |
| Dry eyes | 15 (3.9%) | 63 (27.8%) | <0.001 |
| Raynaud's | 86 (22.1%) | 110 (48.5%) | <0.001 |
| ANA | 387 (99.5) | 216 (95.1%) | <0.001 |
| anti-dsDNA | 251 (71.7%) | 14 (6.9%) | <0.001 |
| Anti-Sm | 90 (30.2%) | 5 (2.6%) | <0.001 |
| Anti-Ro | 98 (33.2%) | 53 (25.6%) | 0.067 |
| Anti-RNP | 85 (28.5%) | 12 (5.9%) | <0.001 |
| Low complement | 243 (73.4%) | 104 (48.4%) | <0.001 |
| Leucopenia | 61 (74.4%) | 315 (61.9%) | 0.029 |

**Conclusions:** We identified clinical manifestations and autoantibodies more commonly associated with SLE than with mimickers at initial presentation. Autoantibody profiles particularly including ANA and especially in the presence of hypocomplementemia, showed associations with SLE.
**Acknowledgement:** New SLE classification criteria for clinical research are being developed, sponsored by EULAR and ACR.
**Disclosure of Interest:** None declared
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## FRI0342 VULVAR HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL CHANGES IN PATIENTS WITH PRIMARY SJÖGREN SYNDROME

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**Background:** Primary Sjogren Syndrome (pSS) is an autoimmune disease mostly affecting women, characterized by a lymphocyte-mediated infiltration and destruction of several exocrine glands, which causes mucosal dryness. Genital involvement is frequent and characterized by vulvar and vaginal dryness, dyspareunia and pruritus, that significantly impairs sexual function. However, despite the high frequency of genital involvement, few data were published about the histopathology of external genitalia in pSS. The studies performed until now show that vaginal and vulvar dryness are due to the presence of a vulvar inflammatory infiltrate and to the atrophy of minor and major vestibular glands, whose secretions are important for the sexual function.
**Objectives:** To evaluate the presence and the characteristics of histopathological and immunohistochemical changes in vulvar tissues in women with pSS.
**Methods:** Women with pSS (21 patients) underwent vulvar biopsies that have been evaluated for histopathological and immunohistochemical changes and finally compared with those obtained from 26 patients with lichen sclerosus.
**Results:** An inflammatory infiltrate (composed predominantly by T lymphocytes (CD3+), sparse CD20+ B cells and mean CD4:CD8 T-cell ratio of 1.5) was evidenced in all 21 biopsies and classified in mild (10), moderate (11) and severe (0). No correlation was shown between vulvar inflammatory infiltrate score and salivary Chisholm e Mason score.
No differences were found neither in gynecological symptoms neither in clinical and demographical characteristics between patients with mild and those with moderate vulvar inflammatory score.
A higher prevalence of moderate inflammatory infiltrate was observed in biopsies from women with lichen sclerosus than in pSS.
**Conclusions:** Women with pSS show high prevalence of vulvar inflammation that could explicate the high frequency of gynaecological symptoms, but the severity don't correlate with the grade of histological changes.

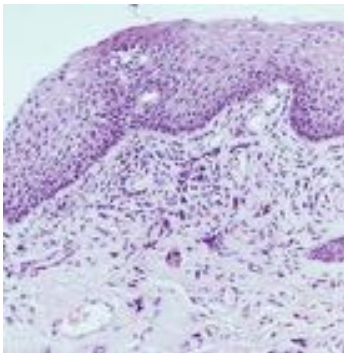


Figure 1

The gynaecological evaluation is mandatory in pSS to assess genital involvement and, eventually, to address a therapy targeted to genital symptoms.

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**Disclosure of Interest:** None declared
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## FRI0343 SLEEP DISORDERS IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) WITH PROLONGED INACTIVE DISEASE

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**Background:** Sleep disturbances are frequently observed in systemic lupus erythematosus (SLE) patients, but the relationship with disease activity has not been unequivocally established.
**Objectives:** To assess the prevalence of and factors associated with sleep disorders in a cohort of SLE patients with persistent complete (no clinical activity, no serological activity and no treatment other than antimalarials) or clinical remission (only serological activity; stable immunosuppressive therapy with or without corticosteroids allowed) (1).
**Methods:** Consecutive adult SLE patients attending the outpatient clinic of the Second University of Naples were enrolled in a cross-sectional study. A complete clinical and laboratory assessment was carried out. Moreover, the Pittsburgh Sleep Quality Index (PSQI), Health Assessment Questionnaire – Disability Index (HAQ-DI), Short-Form 36 (SF-36), VAS pain, VAS fatigue, VAS global health, were administered.
**Results:** Ninety SLE patients (86 females) with a mean±SD age of 43±18 and a median disease duration of 17 years (range 2–38) were enrolled in the study. A poor sleep quality (i.e. PSQI score>5) was observed in 38 (42.2%) patients, with no difference between patients in complete remission (13/30) and those in clinical remission with or without GCs (25/51; p=0.651). PSQI score was found to be significantly correlated with physical component score of SF-36 (rho -0.467, 95% CI -0.632 to -0.262; p<0.0001), mental component score of SF-36 (rho -0.501, 95% CI -0.657 to -0.303; p<0.0001), HAQ-DI (rho 0.497, 95% CI 0.303 to 0.651; p<0.0001), VAS pain (rho 0.480, 95% CI 0.283 to 0.639; p<0.0001), VAS fatigue (rho 0.491, 95% CI 0.296 to 0.697; p<0.0001). No correlation was found between the physician assessment of disease activity and sleep disturbance (rho 0.113, 95% CI -0.114 to 0.128; p=0.329).
**Conclusions:** Sleep disorders are frequent in SLE patients with persistent complete or clinical remission. An impaired mental and physical quality of life, disability, fatigue and pain represent the main features associated with a low quality of sleep.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4581

## FRI0344 EXTRA-GLANDULAR MANIFESTATIONS OF PRIMARY SJÖGREN SYNDROME EXCLUDED FROM DISEASE ACTIVITY INDEXES

M. Fernandez Castro[1], J.L. Andreu[2], C. Sanchez-Piedra[3], A. Olive[4], J. Rosas[5], V. Martinez Taboada[6] on behalf of members of the Sjogren-SER study group (EAS-SER). *[1]H. Infanta Sofía; [2]H. Puerta de Hierro; [3]Unidad de Investigacion de la SER, Madrid; [4]H. Germans Trias i Pujol, Barcelona; [5]H. Marina Baixa, Alicante; [6]H. Marqués de Valdecilla, Santander, Spain*

**Background:** Primary Sjögren syndrome (pSS) is a systemic autoimmune disease characterized by lymphocyte infiltration of the exocrine glands. Nevertheless, it can affect any organ and develop extra-glandular manifestations that even can precede the typical glandular manifestations and delay the diagnosis.
**Objectives:** The aim of our study was to evaluate the extra-glandular manifestations not included in disease activity indexes (Sjogren's Syndrome Disease Activity Index and EULAR Sjogren's Syndrome Disease Activity Index).
**Methods:** We conducted a multicenter descriptive transversal study of pSS patients fulfilling European/American criteria, from 33 Spanish rheumatology departments. Patients were selected by randomization. Every patient was interviewed for data collection and signed an informed consent. Data were also collected by reviewing medical records. Local ethics committees approved the study. Variables were analysed by descriptive statistical methods, using means, medians and rates. Chi-square was used to establish the statistical associations. A p<0.05 was considered significant.
**Results:** Four hundred and thirty-seven patients were included. Ninety-five percent of them were women. The median age of the cohort was 58 years. Nineteen percent of the patients referred involvement of the trachea or upper airway. Twenty-one percent of the patients developed Raynaud phenomenon. Twelve (2.7%) patients suffered cardiac impairment (6 pericarditis and 6 cardiac conduction disorders). Thirteen percent of the patients referred digestive involvement, being chronic atrophic gastritis the most frequent condition (21 patients), followed by esophageal motility alteration (12 patients), followed by lymphocytic colitis (3 patients). Seven percent of the patients developed hepatic involvement: primary biliary cirrhosis and autoimmune hepatitis were the most frequent (15 and 14 patients, respectively), followed by autoimmune cholangitis in 3 patients; 55 patients (13%) had anti-LKM antibodies, 15 patients anti-mitochondrial antibodies, and 5 patients anti-smooth muscle antibodies. Seven patients had pancreatic involvement. Seventy-eight patients (18%) had thyroid involvement: anti-thyroid peroxidase (anti-TPO) hypothyroidism was the most frequent (41 patients), followed by subclinical hypothyroidism in 23 patients, negative anti-TPO hypothyroidism in 12 patients, anti-TPO+ hyperthyroidism in one patient and anti-TPO- hyperthyroidism in one patient. Thyroid involvement was significantly more frequently in patients with anti-Ro+. Raynaud phenomenon was significantly more frequent in patients with anti-La antibodies. Digestive involvement was significantly more frequent in patients with low C3. Pancreatic involvement was significantly more frequent in patients with low C3 and C4. Hepatic and trachea involvement were significantly more frequent in patients with hypergammaglobulinemia.
**Conclusions:** Twenty percent of the patients with primary Sjögren syndrome developed extra-glandular manifestations not included in disease activity indexes. Serological characteristics may be helpful in identifying this subgroup of patients.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3865

## FRI0345 NEUROLOGICAL MANIFESTATIONS OF PRIMARY SJÖGREN SYNDROME

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**Background:** Primary Sjögren syndrome (pSS) is a chronic systemic autoimmune disease with a relevant impact in patients' quality of life. Neurological manifestations of pSS could have an important impact on morbidity and mortality.
**Objectives:** The aim of our study was to evaluate central and peripheral neurological manifestations of a pSS cohort of patients assisted in Spanish Reumathology Departments.
**Methods:** This is a multicentre descriptive transversal study of pSS patients from thirty-three rheumatology departments. Patients fulfilling European/American consensus criteria were included after randomisation. By reviewing clinical records and interviewing the patients, we collected epidemiological, clinical, serologic, therapeutic, and disease activity indexes data. Informed consent was obtained and local ethics committees approved the study. Variables were analysed by descriptive statistical methods, using means, medians, and rates. Chi-square was used to establish the statistical associations, being considered a p<0.05 as significant.
**Results:** Four hundred and thirty-seven patients were included. Ninety five percent of them were women. The median age of the cohort was 58 years. Thirty-four (7.8%) patients developed central nervous system (CNS) involvement. Interestingly, 15 patients developed CNS manifestations before the diagnosis of pSS. Fourteen patients referred headache, 11 patients some psychiatric disorder, 6 patients cerebral ischemic attack, 5 patients cognitive impairment, 5 patients

multiple sclerosis, 3 patients cranial nerve involvement of central origin, 3 patients cerebral vasculitis, 2 patients optic neuritis, a patient aseptic meningitis and a patient myelopathy. ESSDAI index was significantly higher in patients with CNS involvement. Systemic treatments (glucocorticoids, bolus of glucocorticoids, azathioprine, methotrexate and cyclophosphamide) and biological treatments (anti-TNF, abatacept and tocilizumab) were used significantly more frequently in patients with CNS impairment. Thirty-nine (8.9%) patients developed peripheral nervous system (PNS) involvement, 14 of them, before the diagnosis of pSS. Thirteen patients had mixed polyneuropathy, 2 patients motor polyneuropathy, 8 patients sensitive polyneuropathy, 3 patients small fiber neuropathy, a patient developed mononeuritis multiplex and 8 patients focal mononeuropathy. Three patients had trigeminal sensory neuropathy, a patient III cranial neuropathy and 3 patients VII cranial neuropathy. SSDAI and ESSDAI indexes were significantly higher in patients with PNS involvement. Systemic therapies (glucocorticoids, bolus of glucocorticoids, methotrexate, mycophenolate mofetil and cyclophosphamide), biological treatments (rituximab) and intravenous immunoglobulins were used significantly more frequently in patients with PNS impairment.

**Conclusions:** More than 7% of pSS patients with pSS of our cohort developed nervous system manifestations. The CNS and PNS involvement led to a significantly higher disease activity, scored by formal activity indexes. The use of systemic and biological treatment was significantly higher in patients with nervous system involvement.

**Disclosure of Interest:** None declared

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## FRI0346 EVALUATING DIFFERENCES IN THE ENROLLED POPULATIONS OF RANDOMIZED CLINICAL TRIALS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Most randomized controlled trials (RCTs) in systemic lupus erythematosus (SLE) specify specific populations of interest for eligibility, but still vary in the populations included. These differences include the level of baseline disease activity, the relative contribution of clinical vs laboratory disease manifestations, baseline corticosteroid dosage, the presence and number of specific immunosuppressant therapy, antimalarials and racial/ethnic mix. Data have been presented previously highlighting regional differences in SLE populations potentially influencing treatment responses.[1]

**Objectives:** Evaluate the demographics and baseline disease characteristics of randomized SLE patients across three different clinical trials conducted through our organization.

**Methods:** We evaluated combined screening demographic and disease-specific data from three recently conducted SLE studies post hoc. Eligibility criteria were targeted at the enrollment of patients with moderate to severe active SLE (SELENA-SLEDAI $\geq$8 for two studies of approximately 700 and 850 patients each, and SLEDAI-2K $\geq$6 for the third study of approx. 300 patients). Two studies were globally recruited, one was regional. Patients with varying degrees of severely active lupus nephritis or neuropsychiatric SLE were excluded. Differences between each combination of two study populations were evaluated via a two-tailed t-test for disease duration, corticosteroid use, immunosuppressant use, C3/C4 and anti-dsDNA status.

**Results:** Of the 1857 randomized patients, 39.3% were white and 93.4% were female. Details regarding treatment medications (corticosteroids, immunosuppressant use and antimalarials), SLEDAI scores (total and clinical); anti-dsDNA, ANA, and C3 and C4 status are presented in the table for the overall population. Mycophenolate (20.0%) was the most common immunosuppressant used, followed by azathioprine (15.8%) and then methotrexate (9.5%). Differences were determined to exist between each study population at the $p<0.001$ level for the percentage of subjects on corticosteroids, on immunosuppressants (except for a nonsignificant difference in the proportions using concomitant immunosuppressants between the two global studies); with hypocomplementemia, with elevated anti-dsDNA titers or with both.

| Screening Characteristics of All Randomized SLE Subjects | Results (N=1857) |
|---|---|
| Age, years, mean (SD) | 36.1 (11.7) |
| Disease duration, years, mean (SD) | 6.2 (6.2) |
| Positive ANA (≥1:80 titer or equivalent), % | 97.3 |
| Elevated anti-dsDNA ≥30 IU/mL, % | 70.8 |
| Hypocomplementemia (low C3 and/or C4), % | 55.5 |
| Elevated anti-dsDNA and hypocomplementemia, % | 47.4 |
| Corticosteroids, % | 90.3 |
| Corticosteroids ≥10 mg prednisone equivalent, % | 57.9 |
| Corticosteroid dose, mg, mean (SD) in subjects using corticosteroids (prednisone equivalent) | 14.19 (9.34) |
| Antimalarials, % | 70.0 |
| Immunosuppressants, % | 54.3 |
| Corticosteroids and immunosuppressants, % | 50.8 |
| Corticosteroids, antimalarials and immunosuppressants, % | 33.0 |
| No corticosteroids, antimalarials or immunosuppressants, % | 1.2 |
| SLEDAI score ≥8, % | 95.2 |
| Clinical SLEDAI score ≥6, % | 84.7 |
| SLEDAI ≥8 and Clinical SLEDAI score ≥6, % | 83.6 |
| Proteinuria >1g/day, % | 18.2 |

ANA=antinuclear antibody; anti-dsDNA=double-stranded deoxyribonucleic acid antibody; SD=standard deviation; SLE=Systemic Lupus Erythematosus; SLEDAI=Systemic Lupus Erythematosus Disease Activity Index.

**Conclusions:** SLE patients enrolled in RCTs, despite having similar levels of disease required by SLEDAI scores, had differences in critical baseline laboratory characteristics as well as in standard of care medications. These differences may have been impacted by regional differences, e.g., treatment standards of care as well as culturally driven behaviors, and study size; and may impact evaluation of the treatment response. Further differences in regional levels of disease activity are being evaluated as a next step. Understanding such differences may influence the design of SLE trials moving forward.

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**Disclosure of Interest:** N. Goel Employee of: Quintiles Inc., B. Barrett Employee of: Quintiles Inc., A. Duncan Employee of: Quintiles Inc., M.-B. Gallagher Employee of: Quintiles Inc., M. Mackey Employee of: Quintiles Inc.

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## FRI0347 PHENOTYPIC CHANGES OF LYMPHOCYTES IN PATIENTS WITH SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH AN INTENSIFIED B-CELL DEPLETION THERAPY WITH RITUXIMAB

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**Background:** B cells (BC) play a critical role in systemic lupus erythematosus (SLE). BC depletion therapy still remains an attractive option, despite the disappointing results of randomized controlled trials. However, the effects of rituximab treatment on T –cells including regulatory T cells (Treg) in SLE have not been fully determined.

**Objectives:** We prospectively investigated the differentiation and phenotypic changes of peripheral B cells and T regulatory lymphocytes (Treg) in patients with SLE after an intensified B-Cell depletion therapy with Rituximab

**Methods:** Ten patients with sever SLE [2males, mean age 41.6 yrs (25–57)] with severe multiorgan involvement have been prospectively treated with IBCDT protocol due to their resistance or intolerance to previous therapy. Protocol: Rituximab (RTX) 375 mg/sm on days 1, 8, 15, 22, and 2 more doses after 1 and 2 months, associated with 2 IV administrations of 10 mg/kg of cyclophosphamide and 3 methylprednisolone pulses (15 mg/kg) followed by oral prednisone (0.8 mg/kg/day, rapidly tapered to 5mg/day by the end of the 3rd month after RTX). No further immunosuppressive maintenance therapy has been given. Circulating B cells and Treg in the peripheral blood were investigated by flow-cytometry at baseline, month 1, month 2, and every other month thereafter up to 1 year. Whole blood samples obtained in the morning, in EDTA, were stained with monoclonal antibodies against CD45, CD3, CD4 CD19, CD20, CD25 and FOXP3. Response was evaluated by assessing the changes in clinical signs and symptoms, laboratory parameters and SLEDAI score.

**Results:** All patients had complete peripheral blood-B cell depletion after IBCDT and the CD20+ B cells were not detectable in the circulation by the 12th month (detection limit of $0.005 \times 10^9$/l). Upon detection of B cell depletion, we observed in 12 months a 4-fold increase in the circulating Treg (CD4+CD25+FOXP3+) (2% at baseline, 3% after 1 month, 4,5% at 6 month, 8% at 12 months). All patients achieved clinical remission after IBCTD and no flare were observed during the one-year follow-up. IBCDT resulted in a decrease of median global SLEDAI from 14.6 [11–23] to 4 [1–5] at 12 months ($p<0.01$)

**Conclusions:** Our results suggest a phenotypic change of peripheral T lymphocytes as a result of B cells depletion obtained with IBCTD. Treg considered being essential in the maintenance of peripheral self-tolerance, progressively increased after B cell depletion. Such immunological re-assessment was observed in association with clinical remission in the absence of further disease flare.

**Disclosure of Interest:** None declared

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## FRI0348 FEASIBILITY AND VALIDITY OF PATIENT REPORTED OUTCOME MEASUREMENT INFORMATION SYSTEM (PROMIS) IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Accurate measurement of patient reported outcomes (PROs) is important in systemic lupus erythematosus (SLE), a heterogeneous disease in which similar symptoms can have disparate impact across patients. PROMIS

offers dynamic computer adaptive tests (CATs) to precisely and efficiently measure PROs in a variety of relevant domains.
**Objectives:** The aims of this study were to: 1) assess the feasibility of administering PROMIS CATS serially to SLE outpatients 2) correlate PROMIS CATs with legacy PRO measures, SLE disease activity and organ damage 3) assess retest reliability of PROMIS CATs.
**Methods:** Adults meeting American College of Rheumatology SLE classification criteria were recruited from a SLE Center of Excellence. Subjects completed the Short Form-36 (SF-36), LupusQoL-US, and selected PROMIS CATs. SLE disease activity, flare, and damage were evaluated with the SELENA-SLEDAI and SLICC-ACR damage index. PROMIS domains were compared with disease activity, damage, and similar domains in legacy instruments using Spearman correlations. Retest reliability was evaluated among subjects reporting stable SLE activity at two assessments one week apart using intraclass correlation coefficients (ICC).
**Results:** Of 198 patients approached, 163 (82%) completed at least one assessment, 130 (80%) completing it remotely. 138 (85%) completed a retest. Most PROMIS domains showed moderate to strong correlations with similar domains in both legacy instruments (Figure 1). However, correlations between PROMIS and the physician global assessment, SELENA-SLEDAI, and SLICC-ACR damage index were generally weak and statistically insignificant. PROMIS CAT retest ICCs ranged from 0.74 to 0.89.

Figure 1. Spearman's Correlations of PROMIS CATs with Legacy Instruments, Disease Activity, & Damage

| PROMIS CAT | Legacy Instrument Domain | | Physician Global Assessment | SELENA-SLEDAI | SLICC-ACR DI |
|---|---|---|---|---|---|
| Physical Function | SF-36/Physical Function | 0.85 | 0.32 | 0.18 | 0.32 |
| | SF-36/Role Physical | 0.69 | | | |
| | SF-36/PCS | 0.62 | | | |
| | Lupus QoL-US/ Physical Health | 0.85 | | | |
| Mobility | SF-36/Physical Function | 0.87 | 0.38 | 0.20 | 0.34 |
| | SF-36/Role Physical | 0.59 | | | |
| | SF-36/PCS | 0.60 | | | |
| | Lupus QoL-US/ Physical Health | 0.83 | | | |
| Pain Behavior | SF-36/Bodily Pain | 0.78 | 0.31 | 0.19 | 0.26 |
| | Lupus QoL-US/Pain | -0.83 | | | |
| Pain Interference | SF-36/Bodily Pain | 0.72 | 0.40 | 0.27 | 0.26 |
| | Lupus QoL-US/Pain | -0.79 | | | |
| Fatigue | SF-36/Vitality | 0.07 | 0.27 | 0.20 | 0.11 |
| | Lupus QoL-US/Fatigue | 0.75 | | | |
| Anger | SF-36/Mental Health | -0.18 | 0.26 | 0.19 | 0.12 |
| | SF-36/Role Emotional | -0.51 | | | |
| | SF-36/MCS | -0.56 | | | |
| | Lupus QoL-US/ Emotional | -0.70 | | | |
| Anxiety | SF-36/Mental Health | -0.30 | 0.21 | 0.15 | 0.18 |
| | SF-36/Role Emotional | -0.49 | | | |
| | SF-36/MCS | -0.58 | | | |
| | Lupus QoL-US/ Emotional | -0.73 | | | |
| Depression | SF-36/Mental Health | -0.28 | 0.20 | 0.13 | 0.16 |
| | SF-36/Role Emotional | -0.53 | | | |
| | SF-36/MCS | -0.64 | | | |
| | Lupus QoL-US/ Emotional | -0.75 | | | |
| Ability to Participate in Social Roles | SF-36/Social Function | 0.05 | 0.34 | 0.22 | 0.17 |
| Satisfaction with Social Roles | SF-36/Social Function | 0.01 | 0.20 | 0.15 | 0.14 |

Bold correlations indicate p < 0.0001.

**Conclusions:** To our knowledge, these data are the first to show that PROMIS CATs can be successfully administered to a diverse cohort of SLE patients at the point of care or remotely, and are valid and reliable for many SLE relevant domains. Importantly, PROMIS scores did not correlate well with physician-derived measures. This disconnect between objective signs and symptoms and the subjective patient disease experience underscores the crucial need to integrate PROs into clinical care to ensure optimal disease management.
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## FRI0349 A SURVIVAL ANALYSIS OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease with unknown aetiology and involves mainly salivary and lacrimal glands. It is an autoimmune disease with a broad range of systemic manifestations. Mortality rate might reduce in pSS patients with treated new medications. There is no information on survival of pSS patients in our country.
**Objectives:** This study was conducted to determine clinical features and survival in pSS patients
**Methods:** All pSS patients who diagnosed betwen 2004–2014 years were included in this study. The clinical and laboratory features and mortality rates were reevaluated
**Results:** There were 718 patients with suspected pSS at 10 years. 372 patients were classified as pSS according to 2012 American Collage of Rheumatology Classification Criteria for Sjögren's Syndrome. Women/men ratio was 11/1. The mean age at the time of diagnosis was 50.3±11.81 years. 14 patients (3.8%) were diagnosed different malignancy and 18 patients died (4.8%). The rate of 10-year survival was 95.6% (%96.6 for women, %86.6 for men, p:0.004). 10-year survival rate was % 98.7 in patients without pulmonary involvement, but 79.2% in patients with pulmonary involvement. Multivariate Cox analysis showed that pulmonary involvement (OR:12.8, %95 CI: 4.52–44.8, $p<0.001$) and male gender (OR:1.7%95, CI: 1.17–4.53, p=0.004) were independent mortality risk factors
**Conclusions:** Our data revealed that cumulative survival was 95.6% at 10 years in pSS patients. Pulmonary involvement represented the main cause of death. pSS patients with pulmoner involvement have greater risk of death.
**Disclosure of Interest:** None declared
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## FRI0350 THE IFN BIOMARKER SIGLEC1 INDICATES EXTRAGLANDULAR MANIFESTATION IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** Over the last decades evidence of an activated type I interferon (IFN) system in the pathogenesis of different autoimmune diseases such as Sjögren's Syndrome (pSS) (1,2) has emerged to an extent, that anti-IFN therapies are tested in clinical trials.(3) On the other hand, IFN biomarkers are missing in clinical practice, although those biomarkers might be useful to guide clinical decision making or as pharmacodynamic marker.(4)
**Objectives:** To investigate the IFN biomarkers Sialic acid-binding Ig-like lectin 1 (SIGLEC1) and IFN$\gamma$-inducible protein-10 (IP-10) in patients with pSS.
**Methods:** 23 patients with pSS were included. Disease activity was obtained by EULAR Sjögren's syndrome disease activity index (ESSDAI). SIGLEC1 expression on monocytes was analyzed by flow cytometry. IP-10 was determined by Bioplex human Cytokine 27-plex kit. The correlation analysis was performed by Spearman rank test (SRT) and MannWhitney U (MWU) test was used to delineate differences between glandular and extraglandular manifestations.
**Results:** Increased SIGLEC1 expression was found in 60% of our cohort. In a subsequent analysis, SIGLEC1 was up-regulated in all patients with extraglandular manifestation, with an observed significant difference in SIGLEC1 expression (p=0.02, MWU) between glandular and extraglandular manifestation. SIGLEC1 expression correlated with the disease activity (p=0.002, r=0.6, SRT). Elevated levels of IP-10 levels were found in patients with pSS but did not show a difference between glandular and extraglandular manifestation nor did it correlate with the disease activity.
**Conclusions:** SIGLEC1 is up-regulated in pSS patients with a known higher mortality and morbidity (5,6), which therefore may be of value for a risk stratification, differential therapeutic approaches and guiding clinical decision making in pSS.
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## FRI0351 INFLUENCES OF HYDROXYCHLOROQUINE USE ON THE RISK OF CANCERS IN PATIENTS WITH SJÖGREN'S SYNDROME: PROPENSITY SCORE MATCHED LANDMARK ANALYSIS

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**Background:** Hydroxychloroquine is a disease-modifying anti-rheumatic drug for patients with Sjögren's syndrome who have an increased risk of malignancies, particularly lymphoma. Inhibition of systemic inflammation and autophagy by hydroxychloroquine has been linked to antineoplastic effects but there is a lack of evidence on the effect of hydroxychloroquine on the risk of cancers in patients with Sjögren's syndrome.
**Objectives:** This study aimed to explore the effect of hydroxychloroquine on the risk of cancers in patients with Sjögren's syndrome.
**Methods:** We compared cancer incidence in incident patients with Sjögren's syndrome who received hydroxychloroquine for at least 6 months within one year or three years to those did not using the Taiwan National Health Insurance Research Database. Landmark analysis was used to account for immortal time bias and propensity score matching was used to control for potential effects of known confounders.
**Results:** Of 4,262 Sjögren's syndrome patients was identified between 2000 to 2005, we included 4,175 patients who were alive and did not have cancer at one year from initial diagnosis of Sjögren's syndrome. The propensity score matched 1,141 patients who exposed to 6 months of hydroxychloroquine prescription on the date 1 year from the initial diagnosis and 1,141 patients who was not exposed to hydroxychloroquine. The median follow year was 6 years from one-year landmark. There were 71 hydroxychloroquine users and 56 non-hydroxychloroquine users had cancer during the follow-up. The hazard ratio for cancer was 1.31 (95% confidence interval [CI], 0.92–1.86) in the one year landmark analysis. We further conducted three-year landmark analysis and 6-month hydroxychloroquine exposure was associated with a hazard ratio of 1.33 (95% CI, 0.98–1.81) in the three-year landmark analysis between hydroxychloroquine users and non-hydroxychloroquine users, was 1.31 (0.92–1.86) in the one landmark analysis. There was no difference in overall survival based on Kaplan-Meier estimates between hydroxychloroquine user and non-users in both the one-year (log-rank test p=0.15) and three-year landmark analysis (log-rank test p=0.09).
**Conclusions:** This propensity score matched landmark analysis in a population of incident patients with Sjögren's syndrome in Taiwan found a neutral effect of 6-month hydroxychloroquine treatment early in the clinical course on the risk of cancer, but whether a higher dose or an longer exposure to hydroxychloroquine could influence the risk of cancer remains to be determined.
**Disclosure of Interest:** None declared
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## FRI0352 SMALL FIBRE NEUROPATHY AND GANGLIONOPATHY IN PRIMARY SJOGREN'S SYNDROME (PSS)

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**Background:** Neuropathy occurs in 5–15% of cases with Sjogren's syndrome. Small fibre neuropathy and ganglionopathy are said to be the commonest types of neuropathy in pSS[1]. Small fibre neuropathy is under-recognised since physical examination is often normal and nerve conduction studies show no abnormalities. The increased use of skin biopsy has improved our diagnostic sensitivity.
**Objectives:** To estimate the frequency of small fibre neuropathy and ganglionopathy in pSS patients with neuropathic symptoms using skin biopsy, and to describe the clinical characteristics of these patients.
**Methods:** We identified 25 patients with pSS who were investigated for symptoms of small fibre neuropathy and/or ganglionopathy between January 2010 and December 2015. Patients were assessed by neurological examination, nerve conduction studies, skin biopsy and imaging where appropriate.
**Results:** 13/25 patients had conclusive evidence of small fibre neuropathy (n=12) or ganglionopathy (n=1) on skin biopsy. A further 2/25 patients had borderline skin biopsies suggestive of small fibre neuropathy. 12/13 patients with clear evidence of small fibre neuropathy/ganglionopathy were female. Median age at time of neuropathy diagnosis was 60 years (range 42 – 84, interquartile range 56 – 63). 2 presented initially to a neurologist, and the remainder to a rheumatologist. At least one autoantibody was detected in 11/13. Autoantibody frequencies were ANA 62%, RF 31%, anti-Ro 46%, and anti-La 23%. 7/13 patients met the American-European Consensus Group (AECG) criteria for the diagnosis of definite pSS. 4 of the 6 who did not meet the AECG criteria had a positive ANA or RF. Of these four, 2 had a salivary gland ultrasound (US) characteristic of pSS, and 1 was anti-Ro antibody positive. Both patients with borderline skin biopsies had anti-Ro antibodies and one also had antibodies to La. Median time from diagnosis of pSS to diagnosis of small fibre neuropathy or ganglionopathy was 16 months. In a quarter of patients, the diagnosis of neuropathy was made within 6 months of the diagnosis of pSS. Nerve conduction studies (NCS) did not show a neuropathy in 8/13. In the remaining 5 patients, NCS showed sensory axonal neuropathy in 4 patients, one of whom had diabetes mellitus, and ganglionopathy in 1. In the 2 patients with borderline skin biopsies, NCS suggested a mild sensory axonal neuropathy in one and a mild sensorimotor abnormality in the other.
**Conclusions:** Small fibre neuropathy is an under-recognised complication of pSS in clinical practice. In over half of our pSS patients who presented with neuropathic symptoms, a diagnosis of small fibre neuropathy or ganglionopathy was confirmed. Rheumatologists should consider the possibility of small fibre neuropathy in pSS, and not be falsely reassured by normal clinical examination or nerve conduction studies. 2 patients presented initially to a neurologist. Neurologists should consider Sjogren's syndrome in patients presenting with small fibre neuropathy.
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**Disclosure of Interest:** None declared
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## FRI0353 A LONGITUDINAL ANALYSIS OF CHANGE IN LUPUS DISEASE ACTIVITY PATTERN IN HOPKINS LUPUS COHORT USING A MULTISTATE MARKOV MODEL APPROACH

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**Background:** Systemic Lupus Erythematosus (SLE) is a multi-systemic inflammatory disease with extreme variability of its activity over time. We have described three main patterns: long quiescence (LQ), chronic activity (CA) and relapsing-remitting (RR). Patients may move through a series of these activity states over time. To capture these complex fluctuations, we used a Multistate Markov model to evaluate SLE disease activity patterns over time in a longitudinal lupus cohort.
**Objectives:** To describe burden of disease activity patterns over time among patients with SLE. To estimate the probability of transition between disease activity patterns and survival at 1, 2 and 5 years after SLE diagnosis. To identify predictors of change in disease activity patterns.
**Methods:** SLE patients were followed up quarterly in Hopkins Lupus Cohort for 1–28 years. Medication, disease activity (by Physician Global Assessment (PGA) and SLE Disease Activity Index (SLEDAI)), C3, C4, anti-dsDNA, antiphospholipid antibodies and urine protein/creatinine ratio were recorded at each visit.
For each patient, visits were divided into 1-year blocks. Any 1-year block with only one visit or patients followed for only 1 year were excluded. SLE disease activity patterns were defined using PGA and SLEDAI. LQ: SLEDAI/PGA=0 for all visits within 1-year blocks; RR: periods of disease activity (SLEDAI/PGA>0) interspersed with periods of disease inactivity (SLEDAI/PGA=0) within 1-year block; CA: SLEDAI/PGA>0 for all visits within 1-year block. Multistate Markov models were used to provide estimates of relative transition rates and identify predictors of change in disease activity patterns.
**Results:** 1735 SLE patients were included in this analysis. 92.3% were females, mean ± SD age 32.8±13.1 years at diagnosis. 52.9% were Caucasian and 40.3% African American, the remainders were mostly Asian. 127 patients died during follow up.
Likelihood of deterioration (LQ to RR; RR to CA; LQ to CA) was greater than improvement (RR to LQ; CA to RR; CA to LQ). At year 1, 63.6% remained in LQ, while at year 2 and year 5, 58.2% and 84.1% had deteriorated from LQ pattern to either RR or CA pattern. From the RR pattern, the estimated probability for deterioration (to CA pattern) was higher than improvement (to LQ pattern), regardless of years since SLE diagnosis.
Multivariate analysis (see table 1) identified that race/ethnicity (African American), low C3, low C4, ESR >20, taking prednisone, plaquenil or anti-hypertension drug were predictors for deterioration. Plaquenil improved survival.

Table 1. Hazard ratio and 95% confidence interval of predictors of transitions

| | RR → CA | RR → LQ | RR → Death |
|---|---|---|---|
| African American vs. Caucasian | 1.81 (1.59,2.06)* | 0.72 (0.58,0.89) | 1.57 (0.93,2.64) |
| Urine protein creatine ratio | 1.11 (0.96,1.28) | 0.48 (0.34,0.68)* | 1.79 (1.11,2.89) |
| Low C3 | 1.75 (1.51,2.03)* | 0.38 (0.24,0.59)* | 1.46 (0.82,2.59) |
| Low C4 | 1.56 (1.32,1.83)* | 0.2 (0.1,0.4)* | 1.69 (0.88,3.26) |
| ESR.c | 1.28 (1.13,1.45)* | 0.68 (0.56,0.81)* | 2.4 (1.34,4.29) |
| Prednisone | 1.06 (0.94,1.19) | 0.65 (0.54,0.78)* | 3.83 (1.99,7.38)* |
| Plaquenil | 1.28 (1.12,1.45)* | 0.98 (0.81,1.18) | 0.37 (0.23,0.59)* |
| Anti hypertension drug | 1.08 (0.96,1.21) | 1.1 (0.92,1.31) | 2.99 (1.7,5.26)* |

*P value <0.0006, accounting for multiple comparison.

**Conclusions:** 1 year after SLE diagnosis, more than half of patient with LQ deteriorated. Patients in RR were more likely to deteriorate than improve. Plaquenil showed great promise in improving survival.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4493

## Vasculitis

### FRI0354 CARDIOPULMONARY INVOLVEMENT IN TAKAYASU ARTERITIS

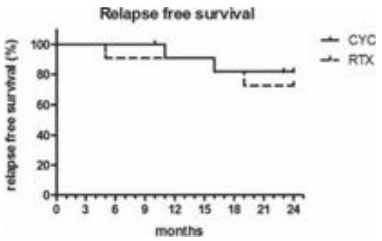
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**Background:** Takayasu arteritis (TAK) is an inflammatory large-vessel vasculitis of unknown etiology affecting the proximal aorta and its primary branches. Heart disease is a major cause of death in patients with TAK but studies evaluating coronary/pulmonary artery involvement and myocardial dysfunction in this population have been limited.
**Objectives:** To evaluate cardiopulmonary (CP) involvement in patients with TAK and assess the impact on disease outcomes.
**Methods:** A retrospective cohort of patients with newly diagnosed TAK from 1984 to 2009 was assembled. All patients included met 1990 American College of Rheumatology classification criteria for TAK. Demographics, baseline disease characteristics, relapse events, surgeries and mortality were abstracted from direct medical record review. Angiograms (invasive and non-invasive), echocardiograms, nuclear medicine scans, and electrocardiograms (ECG) were reviewed for evidence of CP involvement. For the purpose of this study, CP abnormalities were defined as coronary or pulmonary artery vasculitis, left ventricular (LV) dysfunction, left atrial (LA) enlargement, moderate-severe valvular disease, pulmonary arterial hypertension (PAH), regional wall hypokinesis/akinesis, LV hypertrophy or persistent ECG axis deviation. Cox models with time-dependent covariates were used to assess the association between CP involvement and outcomes.
**Results:** A total of 117 patients with TAK were identified. The mean (±SD) age at diagnosis was 31.8 (±10.5) years. Fifty-four (46%) patients had at least one objective CP abnormality observed during the course of follow-up. No difference in age, sex, inflammatory markers or Hata classification were seen between those with and those without CP involvement. Baseline characteristics and symptoms were similar, except shortness of breath, which was more frequently observed at TAK diagnosis in patients with CP involvement compared to those without (54% vs 33%, respectively; p=0.035). PAH was identified in 8, pulmonary arteritis in 9, coronary arteritis in 3, aortic valve insufficiency in 10 (6 moderate, 4 severe), LV systolic heart failure in 5, LV enlargement in 19, and LA atrial enlargement in 21 patients.
Seventy-nine patients had at least 1 year of follow-up [median (IQR): 5.5 (2.9–10.1) years]. Of these 79 patients, 46 had at least one vascular or valvular surgery during the follow-up period. Composite CP involvement was not associated with risk of first surgery [Hazard ratio (95% CI): 1.40 (0.75–2.59); p=0.29]. However, PAH on echocardiogram was significantly associated with risk of first surgery [HR (95% CI): 14.2 (2.1–96.9); p=0.007]. During follow-up 6 patients died. CP involvement was not significantly associated with mortality [HR (95% CI): 1.81 (0.30–10.98); p=0.52].
**Conclusions:** Cardiopulmonary abnormalities in TAK are common. In this population, the presence of PAH predicted a 14-fold increased risk for vascular or valvular surgery. In this cohort, the presence of CP involvement did not increase mortality.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5156

### FRI0355 COMPARISON OF RITUXIMAB WITH CYCLOPHOSPHAMIDE AS INDUCTION THERAPY IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (CHURG-STRAUSS SYNDROME): A 24 MONTHS FOLLOW-UP ANALYSIS

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**Background:** Eosinophilic granulomatosis with polyangiitis (EGPA) forms part of the ANCA associated vasculitides (AAV) and is associated with eosinophilia and asthma. To date no consensus exists on induction and maintenance therapy and refractory patients still represent a considerable therapeutic challenge. We recently reported on the efficacy of rituximab (RTX) as induction therapy in EGPA. So far there are no data on RTX in comparison with cyclophosphamide (CYC) in this disease.
**Objectives:** To investigate the potential of RTX compared with CYC in EGPA as induction therapy and during long-term follow-up.
**Methods:** Retrospective analysis in a single-center cohort of 46 EGPA patients. Remission and disease activity were determined by BVAS. Laboratory follow-up included C-reactive protein, eosinophils, IgE, IgG, IgA, IgM, ANCA, and peripheral $CD19^+$ B-cell count.
**Results:** Eleven patients treated with RTX for relapsing or refractory disease were compared with twelve age- and sex-matched patients treated with CYC for remission induction. Median disease duration was longer in RTX patients (49 months, IQR 7–66 vs. 8.5 months, IQR 0–7; p=0.0025). Prior to induction therapy there was no significant difference in median BVAS (14 vs. 12.5) and in FFS (1 vs. 0.75). Median eosinophil percentages were increased in both RTX (18.4%) and CYC (6.75%) treatment groups (n.s.). 73% of the RTX-treated patients were ANCA-positive compared to only 23% of the CYC-treated patients. Median prednisolone dose per day at induction was significantly higher in CYC-treated patients (35 mg/day, IQR 26–138) than in RTX-treated patients (17.5 mg/day, IQR 10–30). After 3 months all patients in both treatment groups were in partial or complete remission. For maintenance therapy all but two patients per group received standard immunosuppressive treatment with a predominance of azathioprine (AZA) (n=7 per group). Median cumulative prednisolone doses during the first treatment year including high doses for remission induction were 3.6 g in RTX- and 3.8 g in CYC-treated patients (p=0.725). Within an observation period of 24 months after remission induction 3 patients in the RTX group and 2 patients in the CYC group had major relapses (n.s.). In two of the 3 relapsing patients after RTX treatment peripheral B-cell counts were evaluated showing a beginning repopulation of the peripheral B-cell compartment. Serum concentrations of IgG, IgA, and IgM remained stable in both treatment groups during follow-up.




**Conclusions:** RTX was effective in remission induction in EGPA patients. Remarkably this was the fact even in patients refractory to prior CYC treatment and in ANCA negative patients. During follow up the number of major relapses was comparable in both treatment groups. Prior to relapse the peripheral B cell compartment showed beginning repopulation in RTX-treated patients.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4209

### FRI0356 PRIMARY CENTRAL NERVOUS SYSTEM VASCULITIS ASSOCIATED WITH LYMPHOMAS

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**Background:** Vasculitis as a complication of lymphoproliferative diseases is relatively uncommon. Some cases of primary central nervous system vasculitis (PCNSV) have been described in association with lymphoma, particularly Hodgkin's lymphoma (HL).
**Objectives:** The aim of this study is to report the presenting clinical, laboratory, and imaging features of patients with PCNSV associated with lymphoma and compare them with the characteristics of patients with PCNSV without lymphoma.
**Methods:** We reviewed all patients diagnosed with vasculitis and lymphoma seen at the Mayo Clinic, Rochester, MN over the 32 year period of 1982–2014. 10 patients had PCNSV in association with lymphoma. We also used our updated cohort of 158 consecutive patients with PCNSV without lymphoma who were examined at Mayo Clinic over a 29-year period from 1983 to 2011. The diagnosis of PCNSV was based on brain/spinal cord biopsy or cerebral angiography, or both. Clinical data were collected.
**Results:** 10/168 (5.9%) patients had PCNSV associated with lymphoma: 6 with HL and 4 with non-HL. PCNSV diagnosis was established by cerebral biopsy in 8 patients, and by cerebral arteriogram in 2. Two patients had spinal cord involvement. A granulomatous inflammatory histologic pattern was found in all 8 patients, accompanied by vascular deposits of β-amyloid peptide in 2. In 7 patients (5HL and 2NHL) neurologic symptoms preceded lymphoma diagnosis and subsequent medical workup revealed lymphoma.The 10 patients with lymphoma were compared with the 158 patients with PCNSV without lymphoma. The patients with lymphoma were more frequently males (80% vs 44%, p=0.04). No significant differences in the clinical manifestations at presentation and CSF findings were observed in the two groups, although cognitive dysfunction was more frequent in patients with lymphoma (80% vs 53%), while visual field deficit and intracranial hemorrhage less frequent (0% vs 19%, and 0% vs 10%, respectively). Systemic manifestations were infrequent in both groups (10% vs 9.5%). More patients with lymphoma showed meningeal gadolinium enhancing lesions at MRI (50% vs 19%, p=0.03). The frequencies of PCNSV relapse (20% vs 28.4%) and patients not requiring therapy at last follow-up (30% vs 25.5%) were similar in both groups. Patients with lymphoma had a higher frequency of poor outcome (modified Rankin disability score $\geq$4) at last followup (60% vs 21.5%, p=0.01). Considering all 168 patients, univariate Cox proportional hazards modeling showed an increased mortality rate in those with increasing age [hazard

ratio (HR) 1.3], lymphoma (HR 3.9), cerebral infarction on MRI (HR 3.4), and angiographic large vessel involvement (HR 3.9), while mortality rate was lower in those with gadolinium–enhanced lesions on MRI (HR 0.3).
**Conclusions:** PCNSV is associated with a diagnosis of lymphoma in 5.9% of PCNSV cases. Neurological manifestations of PCNSV may precede the diagnosis of lymphoma. Clinical characteristics of those with lymphoma were similar to those without lymphoma, however they had a more severe cerebral vasculitis with increased neurological disability and mortality.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5583

## FRI0357 INCIDENCE AND PREDICTORS OF THORACIC AORTIC DAMAGE IN BIOPSY-PROVEN GIANT CELL ARTERITIS: A SINGLE-INSTITUTION COHORT STUDY

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**Background:** Patients with giant cell arteritis (GCA) are at an increased risk for aortic structural damage; however, the timing and predisposing characteristics for development of aortic aneurysm is poorly understood.
**Objectives:** The aim of this study was to evaluate the incidence and predictors of thoracic aortic aneurysm in a large single-institution cohort of patients with biopsy-proven GCA.
**Methods:** A retrospective review was performed to identify all patients with biopsy-proven GCA from 1998 through 2013. Demographic, clinical, laboratory, radiographic, and treatment data at baseline and subsequent followup visits were collected. Kaplan-Meier methods were used to estimate cumulative incidence and Cox models were used to examine potential predictors of development of aneurysm/dilatation of the thoracic aorta.
**Results:** The cohort included 286 patients with biopsy-proven GCA (213 females and 73 males, mean [±SD] age 75 [±7.6] years) with a mean (±SD) follow up of 6 (±3.9) years.
130 patients had 280 imaging studies (41% magnetic resonance angiography [MRA], 55% computed tomographic angiography [CTA] and 4% conventional angiography). The median time from diagnosis to first imaging study was 0.2 [interquartile range (IQR) 0.0, 2.7] years. Of the 130 patients, 48% underwent follow up imaging studies.
At the first imaging study, 14 (11%) patients had evidence of aneurysm or dilatation of the thoracic aorta and 28 (22%) patients had thoracic aorta thickening. Excluding prevalent cases, the cumulative incidence (±SE) for aneurysm/dilatation of the thoracic aorta during followup was 0% at both 1-yr and 2-yrs but increased to 9% (±0.4) at 5-years. Among all patients with GCA evaluated with vascular imaging, thoracic aortic aneurysm/dilatation was detected in 11% (±3) at 1-yr, 11% (±3) at 2-yrs, and 15% (±3) at 5-yrs.
Patient baseline demographics, cardiovascular risk, clinical presentation, laboratory values, and initial treatment were assessed to predict incidence of thoracic aortic damage. Baseline thickening of the thoracic aorta was not a risk factor for subsequent aneurysm/dilatation (p=0.99). Neither the presence of relapse (p=0.99) nor the number of relapses (p=0.65) were associated with development of thoracic aortic damage [HR (95% CI): 0.88 (0.50, 1.54); p=0.65]. Furthermore, there was no difference in initial prednisone dose between patients who did and did not develop aortic damage. The sole predictor for development of thoracic aortic aneurysm/dilatation was a history of smoking [HR (95% CI) 28.1: (1.59, 495.71); p=0.023].
**Conclusions:** In our cohort, thoracic aortic aneurysm/dilatation was seen in 11% of patients at baseline evaluation and increased to 15% at 5-yrs after diagnosis. Former smokers were at a 28-fold increased risk for developing thoracic aortic damage. Surveillance for aortic damage should be pursued in all patients with GCA, particularly those with a smoking history. Prospective investigations into screening methods and optimal frequency are warranted.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2463

## FRI0358 SHORT TERM PROGNOSIS OF A PROSPECTIVELY FOLLOWED COHORT OF UNSELECTED ADULT IGA VASCULITIS CASES – A SINGLE RHEUMATOLOGY CENTRE EXPERIENCE

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**Background:** The acute phase of adult IgA vasculitis (IgAV) is well characterized. Data of even short-term prognosis of adult IgAV is scarce, mostly retrospective and usually limited to patients with significant renal disease.
**Objectives:** Our aim was to examine the short-term prognosis in a cohort of unselected adult IgAV cases.
**Methods:** We analysed medical records of newly diagnosed, histologically proven cases of IgAV at our department of rheumatology between 1 January 2010 and 30 June 2015, that were followed until 31 December 2015.
**Results:** We identified 139 IgAV cases during the observation period. The clinical characteristics at presentation and the initial treatment are shown in Table 1. During the acute phase of the disease 3/139 patients died (2 due to active vasculitis, 1 due to generalized CMV infection and heart failure). Twenty patients were lost to follow-up. The clinical characteristics of the remaining 116 patients who were followed for a median 8.9 (IQR 5.5 – 22.7) months at follow-up are shown in Table 2. During the follow-up new malignancy was diagnosed in 6/116 (5.2%) patients and 8/116 (6.9%) patients died. All deaths were due to causes unrelated to IgAV.

Table 1. Clinical characteristics at presentation and initial treatment of IgAV

| | |
|---|---|
| Male, % | 57.6 |
| Median age (IQR), years | 65.4 (41.3–77.4) |
| Purpura, # (%) | 139 (100) |
| necrotic, # (%) | 61 (43.9) |
| generalized, # (%) | 63 (45.3) |
| Joint involvement, # (%) | 62 (44.6) |
| GI tract involvement, # (%) | 49 (35.3) |
| severe GI, # (%) | 13 (9.4) |
| Renal involvement, # (%) | 69 (49.6) |
| severe, # (%) | 19 (13.7) |
| Median BVAS-3 (IQR) | 10 (5–16) |
| Malignancy, # (%) | 3 (2.2%) |

Legend: # – number of patients; IQR – interquartile range; GI – gastrointestinal tract; severe GI tract involvement- - bloody diarrhoea or ileus or surgical intervention; severe renal involvement – acute renal failure or nephrotic syndrome; BVAS-3 – Birmingham vasculitis activity score; Malignancy – concurrently diagnosed malignancy.

Table 2. Clinical characteristics at last follow-up visit

| | Patients, n (%) |
|---|---|
| Relapse | 17 (14.7) |
| once; twice; three times | 14 (12.1); 2 (1.7); 1 (0.9) |
| skin limited | 15 (12.9) |
| skin + renal; skin + GI | 1 (0.9);1 (0.9) |
| Urinary abnormalities | 42 (36.2) |
| microhematuria | 33 (28.4) |
| proteinuria – $<$1g/day; $\geq$1g/day | 10 (8.6); 5 (4.3) |
| Renal function worsening | 10 (8.6) |
| Treatment, # (%) | 107 (77.0) |
| local GC, # (%) | 9 (6.5) |
| systemic GC, # (%) | 98 (70.5) |
| cyclophosphamide, # (%) | 11 (7.9) |
| IVIG, # (%) | 4 (2.9) |

Legend: GC – glucocorticoids; IVIG – intravenous immunoglobulin.

**Conclusions:** Contrary to the experience in children, IgAV in adults does not seem to be a benign disease even in the short-term. Admittedly, it is impossible to conclude whether this is due to the nature of the adult IgAV or because adults have more comorbidities than children.
**Disclosure of Interest:** None declared
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## FRI0359 ASSESSMENT OF THE FREQUENCY OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH TAKAYASU'S ARTERITIS

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**Background:** Accelerated atherosclerosis associated with chronic inflammation is one of the major complications of systemic inflammatory diseases. Takayasu arteritis (TAK) is a rare, systemic large-vessel vasculitis predominantly affecting the aorta and its major branches. The prevalence of atherosclerotic risk factors and cardiovascular (CV) disease in patients with TAK has not been well defined.
**Objectives:** The purpose of this study was to assess the frequency of CV risk factors and the incidence of CV events (CVE) in patients with TAK.
**Methods:** Patients fullfilling the American College of Rheumatology criteria for TAK from Mayo Clinic, Rochester, USA and Marmara University, Istanbul, Turkey were included in this retrospective cohort study. Data on cardiovascular risk factors at the time of TAK diagnosis and incident CVE during follow-up were abstracted from the medical records. Patients with TAK were compared to age, sex and calendar year–matched controls from the same geographic region without TAK. The 2008 Framingham 10-year general cardiovascular risk score (FRS) was used for the evaluation of CV risk at the time of TAK incidence/index date. For patients without lipid profiles, the office-based FRS, which does not require lipid values, was computed according to previously published algorithms.
**Results:** A total of 175 patients with TAK and 175 non-TAK controls were included in the study (115 from Mayo Clinic, 60 from Marmara University for each group). Among patients age $\geq$30 years at index date (107 TAK,109 non-TAK), complete data to calculate FRS were available in 93 (87%) TAK and 91 (83%) non-TAK subjects. Hypertension diagnosis and lipid lowering treatment were significantly more frequent in the TAK group compared to non-TAK). Prior to the incidence/index date, the occurrence of CVE was significantly higher in the TAK group The overall Framingham 10-year CV risk score was significantly higher in the TAK group compared to non-TAK at incidence/index date (Table 1).)After

excluding patients with prevalent CVE, 18 TAK and 3 non-TAK patients developed CVE during a mean follow-up of 7.4 years in TAK and 7.9 years in non-TAK groups. The cumulative incidence of CVE was 16.4% at 10 years in TAK group vs. 6.0% in non-TAK group and the risk of CVE was increased among patients with TAK (hazard ratio: 4.52; 95% CI: 1.29, 15.78 adjusted for age, sex and country).

**Table 1:** Baseline characteristics of TAK and non-TAK cohorts in index dates.

| | TAK (n=175) | Non-TAK (n=175) | P value |
|---|---|---|---|
| Age (Years)* | 34.1±32.7 | 34.9±32.9 | 0.70 |
| Sex (female/male) | 157 / 18 | 160 / 15 | 0.58 |
| Hypertension, n (%) | 69 (40%) | 22 (13%) | **<0.001** |
| Diabetes mellitus, n (%) | 12 (7%) | 8 (5%) | 0.35 |
| Lipid profile (mg/dl)* | | | |
| Total cholesterol, mg/dL | 200±50 (n=113) | 190±37 (n=60) | 0.23 |
| Low density lipoprotein, mg/dL | 119±42 (n=101) | 108±35 (n=51) | 0.12 |
| High density lipoprotein, mg/dL | 52±17 (n=103) | 54±15 (n=53) | 0.50 |
| Triglycerides, mg/dL | 137±90 (n=108) | 126±90 (n=60) | 0.13 |
| Lipid lowering treatment, n (%) | 22 (13%) | 7 (4%) | **0.004** |
| Chronic kidney disease (physician diagnosis), n (%) | 3 (2%) | 4 (2%) | 0.71 |
| BMI (kg/m$^2$)* | 26±6.7 | 26± 6.4 | 0.94 |
| Obesity (BMI >30 kg/m$^2$), n, (%) | 52 (22%) | 37 (25%) | 0.78 |
| Smoking status, ever, n, (%) | 80 (47%) | 70 (41%) | 0.36 |
| Framingham risk score, %† | 3.6 (2.2-10) | 2 (1.2-5) | **0.001** |
| Any prior atherosclerotic vascular event | 37 (21%) | 6 (3%) | **<0.001** |

*Mean ±SD †Median (Interquartile range); BMI, body mass index; n = number; SD = standard deviation; TAK = Takayasu arteritis; bolded p-values statistically significant at <0.05

**Conclusions:** CV risk factors are more common in patients with TAK, and the Framingham 10-year cardiovascular risk score is higher in patients with TAK at the time diagnosis compared to non-TAK subjects of similar age and sex. The cumulative incidence of CVE was also significantly higher during follow-up in the TAK group. Patients with TAK should undergo careful assessment of CV risk factors, and an aggressive risk modification approach is warranted.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2194

## FRI0360 AORTITIS DIAGNOSIS BY PET. A REPORT OF 33 PET FROM A UNIVERSITY HOSPITAL IN A 3 YEAR PERIOD

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**Background:** Early diagnosis and treatment of aortitis are important to prevent possible serious complications such us aneurysm, aneurismal ruptured or aortic dissection. Aortitis may present with non-specific symptoms. Positron emission tomography (PET) is useful in diagnosing aortitis. However, PET is an expensive technique.
**Objectives:** Our aim was to evaluate those PET performed by suspected aortitis in order to find some predictive factors for positive PET for aortitis.
**Methods:** Study of PET performed by suspected aortitis in a University Hospital (from January 2013 to December 2015). The main epidemiological, clinical and laboratory data of these patients were extracted from clinical records according to a specifically designed protocol, reviewed for confirmation of the diagnosis, and stored in a computerized file. To minimize entry error all data were double checked.
A comparative study was made between positive and negative PET to identify red flags of an underlaying aortitis.
Quantitative variable results were expressed as mean±standard deviation (SD) or median [IQR] and were analyzed by Mann-Whitney U test. Qualitative variable results were expressed as percentages and frequency and were analyzed by Fisher's exact test. Statistic analysis was performed with the SAS System for Windows V 9.2.
**Results:** In last 3 year period 33 PET were requested to confirm aortitis (5 of them in 2013, 7 in 2014 and 21 in 2015). We had 3 positive results of 5 (60%) in 2013, 3 of 7 (42.85%) in 2014 and 7 of 21 (33.33%) in 2015. The mean age of the 33 (22 female/11 male) patients was 70.30±14.16 years (range, 31–89).
The underlying diseases associated to these patients were: giant cell arteritis (GCA) (n=12), polymyalgia rheumatic (PmR) (n=8), connective tissue diseases (Sjögren syndrome, dermatomyositis, undifferentiated connective pathology) (n=5), seronegative polyarthritis (n=3), relapsing polychondritis (n=2), idiophatic (n=2), hiper-IgG syndrome (n=1).
Comparative study between positive and negative PET is summarized in TABLE. Inflammatory back pain and irradiated lower limb pain conditions were more common among patients with positive PET. They were the unique variables with statistically significant difference. The rest of both epidemiologic, clinical, laboratory or the possible influence of treatment with steroids and/or immunosuppressants at the time of conducting PET did not differ between groups.
**Conclusions:** In this estudy we observed an increasing in demand for PET for suspected aortitis every year and more cases were diagnosed in recent years. However, positive test percentage progressively decreased. The presence of inflammatory back pain and pain radiating to the lower extremities may have clinical relevance to suspect aortitis and a positive PET result. Prospective studies are needed with larger numbers of patients to establish a predictive model for aortitis.

**TABLE. Comparative study between Positive and negative PET**

| | Positive PET n= 10 | Negative PET n= 20 | p |
|---|---|---|---|
| Mean age ±SD | 72.2±12.36 | 71.6±15.2 | 0.89 |
| Age ≥ 75 years, n (%) | 9 (69.2%) | 14 (70%) | 0.99 |
| Sex (M/F) | 3/10 | 8/12 | 0.46 |
| Underlying disease | | | |
| - GCA, n (%) | 7 (53.8%) | 5 (25.0%) | 0.14 |
| - PmR, n (%) | 2 (15.4%) | 6 (30.0%) | 0.43 |
| - Connective tissue disease, n (%) | 1 (7.7%) | 4 (20.0%) | 0.63 |
| - Others, n (%) | 3 (23.1) | 5 (25.0%) | 0.99 |
| - Period between the diagnosis of the underlying disease and PET >6 months, n (%) | 6 (46.2%) | 14 (70.0%) | 0.31 |
| Clinical features when PET requested(†) | | | |
| - Constitutional syndrome, n (%) | 5 (38.5%) | 3 (15.0%) | 0.21 |
| - Fever, n (%) | 1 (7.7%) | 4 (20.0%) | 0.99 |
| - Inflammatory low back pain, n (%) | 4 (30.8%) | 0 (0.0%) | 0.02* |
| - Irradiated lower limb pain, n (%) | 4 (30.8%) | 0 (0.0%) | 0.02* |
| - Atypical PmR, n (%) | 1 (7.7%) | 0 (0.0%) | 0.39 |
| - Headache, n (%) | 3 (23.1%) | 3 (15.0%) | 0.66 |
| - Visual symptoms, n (%) | 1 (7.7%) | 2 (10.0%) | 0.99 |
| - PmR syndrome, n (%) | 1 (7.7%) | 8 (40.0%) | 0.06 |
| Laboratory test at the PET request | | | |
| - Anaemia, n (%) | 5 (38.5%) | 14 (70.0%) | 0.15 |
| - ESR, mean±SD | 62.9±33.8 | 61.8±35.3 | 0.93 |
| - ESR ≥ 30 mm 1ª hour, n (%) | 9 (69.2%) | 13 (65.0%) | 0.68 |
| - CRP, median [IQR] | 3.43 [2.27-5.43] | 2.53 [0.71-5.45] | 0.33 |
| - CRPe (mg/dl, n (%) | 9 (69.2%) | 8 (40.0%) | 0.10 |
| Treatment when PET was performed | | | |
| - Patients receiving corticosteroids, n (%) | 9 (69.2%) | 14 (73.7%) | 0.99 |
| - Patients receiving >10 mg/day prednisone, n (%) | 4 (30.8%) | 8 (42.1%) | 0.72 |
| - Prednisone dose (mg/day), median [IQR] | 7.5 [5-40] | 25 [10-45] | 0.26 |
| - Patients receiving immunosuppressants, n (%) | 4 (30.8%) | 7 (35.0%) | 0.99 |

*p<0.05.
Abbreviations: GCA: giant cell arteritis // PmR: polymyalgia rheumatic.

**Conclusions:** To assess whether the extension of inflammatory infiltrates and/or the degree of intimal hyperplasia in temporal artery biopsies (TAB) from GCA patients correlate with CTA detection of aortitis at the time of diagnosis.

**Disclosure of Interest:** None declared
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## FRI0361 THE EXTENSION OF INFLAMMATORY INFILTRATES OR INTIMAL HYPERPLASIA IN TEMPORAL ARTERIES DO NOT SIGNIFICANTLY PREDICT CTA-DETECTION OF AORTIC THICKENING IN NEWLY-DIAGNOSED PATIENTS WITH BIOPSY-PROVEN GIANT-CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is a granulomatous vasculitis preferentially targeting the carotid and vertebral artery branches. Aortic involvement is common and may lead to severe complications such as aortic dilatation/aneurysm or dissection[1]. While small necropsy studies detected histopathologically-proven aortic inflammation in more than 90% of patients, aortic wall thickening suggesting aortitis is detected in 65% of patients using CTA at diagnosis [2]. We hypothesized that histological features underlying arterial wall thickening (transmural inflammatory infiltrate or intimal hyperplasia) observed in temporal artery biopsies might predict CTA-detection of aortic wall involvement.
**Objectives:** To assess whether the extension of inflammatory infiltrates and/or the degree of intimal hyperplasia in temporal artery biopsies (TAB) from GCA patients correlate with CTA detection of aortitis at the time of diagnosis.
**Methods:** TABs from biopsy-proven GCA included in an ongoing prospective study for detection of large vessel vasculitis (LVV) at diagnosis[1] were scored for the extent of inflammatory infiltrates or intimal hyperplasia as described[3]. Aortitis was defined by CTA as concentric thickening of the aortic wall $\geq$2mm. TABs were categorized according to the extent of inflammatory infiltrates (inflammation limited to adventitia vs transmural inflammation) and the degree of intimal hyperplasia. The latter was considered mild/moderate or severe depending on the ratio between the maximal thickness of the intima layer and the distance between the center of the lumen and the internal elastic lamina ($<$75%vs$>$75%). Fisher exact test was used for statistical analysis.
**Results:** Between November 2006 and June 2013, 51 patients diagnosed with biopsy-proven GCA were included in a CTA-based screening protocol for LVV. Overall, aortitis was detected by CTA in 34 (66.7%) of cases. Inflammation limited to the adventitia was observed in 10 (19.6%) of cases and transmural inflammation in 41 (80.4%). Mild/moderate intimal hyperplasia was observed in 17 (33.3%) biopsies and severe intimal hyperplasia in 34 (66.7%). CTA-detected aortitis was observed in 27 (79.4%) of patients with transmural inflammation compared with 7 (70%) of patients with inflammation limited to the adventitia (p=1.00). Aortitis was seen in 23 (67.6%) of patients with severe intimal hyperplasia compared to 11 (64.7%)of patients with mild/moderate neointima formation (p=1.00).
**Conclusions:** Although the limited size of this cohort prevents definitive conclusions, the extension of inflammatory infiltrates or intimal hyperplasia in temporal

arteries do not significantly predict CTA-detection of aortic thickening in GCA. Variability in the distribution of lesions along the vascular tree may account for these findings. Supported by Marato TV3 2014/201507.

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**Disclosure of Interest:** None declared

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## FRI0362 PRONOSTIC FACTORS OF SURVIVAL IN ANCA-ASSOCIATED VASCULITIS (AAV). CHANGES IN THE NEW CENTURY

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**Background:** AAV are still related to a high morbidity and mortality in spite of new available therapies. To recognize factors associated with a worse prognosis is essential to tailor the treatment

**Objectives:** To identify survival prognostic factors in a large cohort of patients with AAV from Spain and analyze changes in the new century

**Methods:** multicenter retrospective-longitudinal study that included patients diagnosed with AAV between Jan95 and Nov14 in 20 Hospitals from Spain (REVAS Study). Statistical analysis was done using SPSS vs21

**Results:** 455 patients were included: 188 (41.3%) GPA, 167 (36.7%) MPA, 100 (22%) EGPA. Mean age at diagnosis was 55.7±17.2 y. ANCA were positive in 86.8% of cases:35.8% C-ANCA and 51% P-ANCA. Median time to diagnosis was 4 weeks (IQR 10). Median follow-up was 80 months (IQR 105). Renal, lung, neurological and cardiac involvement were present in 56.7, 54.7%, 34.5% and 12.7% of cases,respectively. Pulmonary-renal syndrome was observed in 17%, ENT in 44.8% and eye involvement in 13.4%. Mean BVAS at diagnosis was 17.7±7.7. All patients received oral glucocorticoids; 342 (75%) cyclophosphamide (50.3% oral), and 6.6% biological therapy. Dialysis was required in 16.4% of cases and plasma exchange in 7%. During follow-up, 22.2% of patients suffered leucopenia, 39% bacterial infections, 12.7% opportunistic infections and 5.3% neoplasms. One hundred thirty (28.6%) patients died: 74 (44.3%) with PAM, 42 (22.3%) with GPA and 14 (14%) with EGPA ($p<0.001$). Median time to death was 57.5 months (IQR 105): significantly higher for EGPA (94m vs 69m for GPA and 50m for PAM;LogRank=0.01). Comparing diagnostic century, the percentage of deaths was higher in the XXth than in XXIth (48% vs 21%, $p<0.001$). No differences were found in clinical manifestations, but yes in treatment and rate of infections: in the actual century more plasma exchange is used (9% vs 2.2%, p=0.008), more biological therapy (9% vs 0.7%, $p<0.001$), less oral CF (29% vs 57.8%, $p<0.001$) and more CF IV pulses (52% vs 35.6%, p=0.001). Multifactorial Cox regression analysis showed that prognostic factors associated with survival were age>65y (HR 4.6), cardiac (HR 3.9) and renal involvement (HR 2.0). ENT involvement was a protector factor (HR 0.4). Bacterial infections during follow-up were also independent predictor of poor prognosis (HR 2.0)

**Conclusions:** survival rate in AAV has significantly improved in the new century probably due to new treatment strategies, including less CF and biological therapy. Poor prognostic factors are age>65y, cardiac and renal involvement at diagnosis,and bacterial infections, while ENT involvement is protective.

**Disclosure of Interest:** None declared

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## FRI0363 TRIGGERS OF BEHÇET'S DISEASE-RELATED ORAL ULCER RECURRENCES

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**Background:** Recurrent oral ulcers (ROU) are an almost constant feature of Behçet's disease (BD) but its pathophysiology is not well understood. It is widely admitted that certain foods or other external factors play a role in BD-related ROU. Thus, the proportion of patients with BD able to identify a specific triggering factor of their ROU and the nature of these factors remain unknown.

**Objectives:** To study the role of dietary and non-dietary factors as triggers of BD-related ROU.

**Methods:** A 23-item self-report questionnaire was given to consecutive in- and outpatients with BD who attended 7 French hospital departments for internal medicine over a 12-month period. Patients were enrolled if they consented to participate in the study and if they had a history of ROU that had not become definitively extinct to ensure patients' ability to provide accurate information. The questionnaire consisted of 13 items collecting general information, e.g., demographic characteristics, dietary habits, age at onset and severity of ROU. Six additional open-ended, dichotomous ("Yes" or "No") or scaled questions ("Yes, I am sure", "Yes, that's possible", "No, that's highly unlikely", or "I don't know") collected information on potential triggering factors of ROU. In particular, the questionnaire evaluated the influences of 6 general triggering situations (i.e., fatigue/stress, dental care, tooth brushing, menstruation, infection, and food/drinks), 24 selected food and drink items, 8 physicochemical properties of food (i.e., salty, sweet, bitter, acid, astringent, hard, hot, cold), and the effect of fast eating. The results were described as percentages of positive responses; for scaled questions, the combined responses of "Yes, I am sure" or "Yes, that's possible" were considered positive.

**Results:** Of the 100 questionnaires distributed, 87 were returned and 80 could be used for the analyses. Among those 80 patients (mean age: 41 years, men: 63%), 96% fulfilled the International criteria for BD, 75% had non-French origins and 81% consumed European-style food. The mean time since ROU onset was 19 years and the ROU was judged by 53% as "very discomforting" or "discomforting" over the previous 12 months. Among the 6 general situations suggested, 91% recognized at least 1 of them as "surely" or "possibly" related to their ROU: fatigue/stress (75%) and food/drinks (70%) were the most frequently cited triggering factors. Among the 24 food/drinks items suggested, the most frequently reported items were: walnuts (49%), pineapple (43%), peanuts (33%), Emmental cheese (30%), lemon (25%), almonds (24%), and other cheeses (21%). Acidity was the most frequently reported physicochemical food characteristic triggering ROU (58%).

**Conclusions:** Fatigue/stress and food are frequently recognized triggering factors of BD-related ROU. This implies the need to take into account such external factors in the management of ROU. The fact that most food items identified as common triggers of ROU are histamine-rich or histamine-releasing could suggest a role of histamine in the pathophysiology of BD-related ROU. Hormonal and traumatic components seemed to be of lesser importance in ROU.

**Disclosure of Interest:** None declared

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## FRI0364 DOES AN ELEVATED SERUM IMMUNOGLOBULIN A LEVEL PREDICT THE COURSE OF ADULT IGA VASCULITIS?

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**Objectives:** Our objective was to evaluate the impact of serum IgA level on the clinical presentation and severity of adult IgA vasculitis (IgAV).

**Methods:** We prospectively collected data on newly diagnosed histologically proven adult IgAV cases between January 2013 and December 2015 at our at our secondary/tertiary rheumatology centre. Patients were stratified according to the serum level of IgA into two groups (elevated IgA (>4.10 g/l) vs. normal IgA (0.7–4.10 g/l)).

**Results:** During the 36 month observation period, 92 new adult IgAV cases (54% male) were identified. The median age was 65.8 (interquartile range (IQR) 48.7–77.3, range 19–88) years and the median disease duration (IQR, range) 7 (6–21, 2–120) days. The serum level of IgA was elevated in 39 (42.4%) cases.

Table 1. Clinical characteristics

| | Normal serum IgA level (N=53) | Elevated serum IgA level (N=39) | P value |
|---|---|---|---|
| M : F ratio | 1.1 | 1.2 | 0.83 |
| Age (years; median (IQR)) | 60.7 (41.3–76.9) | 72.4 (51.6–78.0) | 0.13 |
| Disease duration (days; median (IQR)) | 8 (6–21) | 7 (5–19) | 0.50 |
| Prior infection (%) | 39.6 | 20.5 | *0.07* |
| History of cancer (%) | 9.4 | 15.4 | 0.52 |
| General symptoms (%) | 20.8 | 10.3 | 0.26 |
| Generalized purpura (%) | 49.1 | 46.2 | 0.84 |
| Skin necroses (%) | 41.5 | 43.6 | 1.0 |
| Isolated skin involvement (%) | 26.4 | 25.6 | 1.0 |
| Joint involvement (%) | 47.2 | 30.8 | 0.14 |
| Arthritis (%) | 18.9 | 10.3 | 0.38 |
| GI tract involvement (%) | 39.6 | 25.6 | 0.19 |
| Severe GI tract involvement (%) | 11.3 | 2.6 | 0.23 |
| Renal involvement (%) | 28.3 | 43.6 | 0.18 |
| Severe renal involvement (%) | 11.3 | 23.1 | 0.16 |
| BVAS (median (IQR)) | 8 (3–14) | 6 (2–16) | 0.57 |
| IgAV relapses (%) | 14.3 | 16.7 | 1.0 |
| Persistent urinary abnormalities (%) | 53.6 | 57.1 | 1.0 |
| Newly diagnosed cancer (%) | 0 | 12% | *0.06* |

Legend: M – Male; F – Female; Severe GI tract involvement – bloody diarrhea or ileus or surgical intervention; Severe renal involvement – acute renal failure or nephrotic syndrome; BVAS – Birmingham Vasculitis Activity Score.

The characteristics of IgAV groups with increased and with normal serum IgA level at presentation and at follow-up are presented in Table 1. Follow-up data were available for 59 (24 had elevated IgA) patients, with a median (IQR) follow-up of 7.2 (5.0–14.5) months.

**Conclusions:** Elevated IgA serum level does not seem to have any significant impact on the disease manifestations and severity of adult IgAV. However, there was a trend toward less frequent antecedent infections and more frequent malignancy development in the group with high serum IgA.

**Disclosure of Interest:** None declared

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## FRI0365 LIMITED EVIDENCE OF ACTIVE VARICELLA ZOSTER VIRUS (VZV) INFECTION IN A COHORT OF ACUTE GIANT CELL ARTERITIS (GCA) PATIENTS

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**Background:** Recent studies have identified a high prevalence of VZV antigen in temporal artery biopsy specimens from patients with GCA. The clinical implication of this finding is uncertain. Some researchers have proposed that reactivation of VZV infection may have a role in inducing arteritis and have promoted antiviral therapy as adjunctive therapy to corticosteroids in cases of biopsy negative and positive GCA. While not currently recommended in GCA, antiviral therapy is used in the clinically distinct condition of VZV vasculopathy which is associated with angiographic abnormalities in the anterior and middle cerebral arteries.

**Objectives:** We aimed to assess if there was clinical, serological or imaging evidence of active VZV in patients with acute GCA. Positive findings may have supported a role for antiviral therapy.

**Methods:** We prospectively assessed the clinical, serological and angiographic profile of all 13 patients referred for assessment of acute GCA to our tertiary referral rheumatology service from June to December 2015 to identify evidence of active VZV infection.

**Results:** 10 patients with an average age of 77 years (range 66 to 87 years) were ultimately diagnosed with GCA. Nine met the American College of Rheumatology 1990 criteria for the classification of GCA, three had positive and one had an equivocal biopsy. Eight were female. All ten had visual disturbance and three had evidence of acute ischaemic optic neuropathy on fundoscopy.

One patient had an episode of cutaneous herpes zoster affecting the right sixth thoracic dermatome two months after onset of GCA headache. This was treated with a five day course of valaciclovir and resolved three weeks before referral to our service. GCA symptoms progressed despite valaciclovir. Seven patients recalled an episode of primary VZV infection in childhood but no other patients had a history of herpes zoster.

VZV serology was performed in all ten patients within 24 days of referral. Time from GCA symptom onset to serology ranged from 15 days to five months. All patients had positive VZV IgG indicating past exposure to the virus. Nine had negative IgM serology. IgM was equivocally elevated in the patient with recent herpes zoster.

Six patients underwent magnetic resonance imaging or computer tomographic cererbral angiography and there was no evidence of VZV vasculopathy of the anterior or middle cerebral arteries.

Patients were treated with pulse intravenous methylprednisolone 500 mg to 1000 mg for three days plus an antiplatelet agent with subsequent oral prednisone. We did not add antiviral therapy. All demonstrated rapid clinical improvement with normalization of inflammatory markers and no progression of visual loss.

**Conclusions:** We did not find clinical, serological or imaging evidence of active VZV infection contributing to acute GCA to support routine adjunctive antiviral therapy.

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**Disclosure of Interest:** None declared

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## FRI0366 COCAINE-LEVAMISOLE INDUCED VASCULITIS: A SERIES OF 11 CASES

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**Background:** Levamisole, an antihelmintic and immunomodulatory agent currently used as a cocaine adulterant; is related with levamisole-induced vasculopathy (LIVEN), characterized by necrosis of ears, retiform purpura, cytopenias and positive anti-neutrophilic cytoplasmic antibody (ANCA)[1].

**Objectives:** To describe the clinical features and laboratory findings of 11 patients with LIVEN.

**Methods:** We describe 11 consecutive patients with LIVEN, evaluated at 3 Colombian hospitals from December 2010 to May 2015.

**Results:** Hispanic patients with a median age of 35 years (IR 31–39), 82% were male, had a history of more than 2 years of cocaine abuse, and 1 year of symptoms (IR 10–24). All had necrosis of ears, 91% retiform purpura (limbs, buttocks, face and abdomen), 45% fever, 27% genital necrosis and 9% digital necrosis (image). Skin biopsy (n=9) reported thrombotic vasculopathy (78%), pseudo-vasculitis (33%), and leukocytoclastic vasculitis (33%). Fifty five percent of patients had arthralgia/arthritis, 55% glomerulonephritis, 18% pulmonary disease, serositis or lymphadenopathy, 9% hepatosplenomegaly; 64% chronic disease anemia, 27% leucopenia, 73% lymphopenia, 9% neutropenia, 100% raised acute phase reactants. ANCA were positive in 91%, with perinuclear pattern (IIF) and anti-MPO positive (ELISA) or double positivity (anti-MPO and anti-PR3). Forty five percent exhibit ANA (homogeneous pattern), 29% anti-dsDNA and anti-Ro, 55% hypocomplementemia, 73% lupus anticoagulant, 20% anticardiolipin antibodies and cryoglobulins. Most patients received prednisolone (median dose 50 mg/d, IR 35–60). Lesions resolved in all patients with treatment and cocaine suspension; relapses were associated with resuming consumption.



**Conclusions:** LIVEN cases had increased due to the use of levamisole-adulterated cocaine[1]. Besides the typical skin lesions, there are hematological, renal, joint and lung manifestations. Main laboratory findings are high ESR and CRP levels, positive ANCA and lupus anticoagulant, although other autoantibodies could be present (aCL, ANA and anti-dsDNA). The differential diagnosis includes systemic vasculitis, systemic lupus erythematosus and antiphospholipid syndrome. The characteristic skin lesions, the relationship with the consumption and the improvement at suspension are diagnostic clues. In this series the clinical and laboratory features were similar to those described in the literature but we found higher renal involvement[2]. LIVEN should be considered in patients with retiform purpura, ear involvement and multiple autoantibodies posivity.

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**Disclosure of Interest:** None declared

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## FRI0367 PET/MRI FUSION DEMONSTRATES HAMSTRING PERI TENDONITIS IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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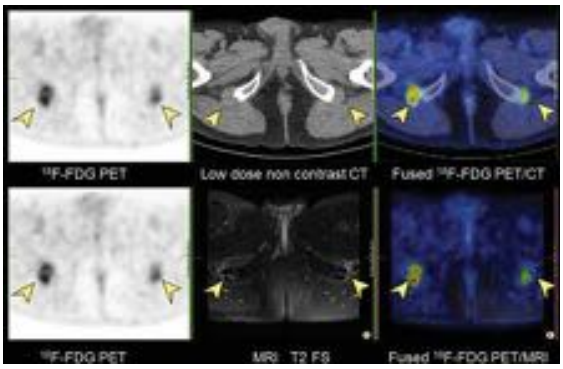
**Background:** Positron emission tomography/computed tomography (PET/CT) possesses the unique potential to document whole body inflammation in polymyalgia rheumatica (PMR), however the precise anatomical structures involved have not been well characterised.

**Objectives:** To characterise the pattern of $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) uptake on whole body PET/CT in patients with newly diagnosed PMR, and to precisely identify anatomic correlates of $^{18}$F-FDG uptake with magnetic resonance imaging (MRI).

**Methods:** Patients with newly diagnosed PMR according to the 2012 EULAR/ACR classification criteria (1) were prospectively recruited. Participants with symptoms suggestive of giant cell arteritis were excluded. A whole body $^{18}$F-FDG PET/CT scan was performed at baseline in all untreated patients. Qualitative and semi-quantitative (standardised uptake value maximum [$SUV_{max}$]) scoring of $^{18}$F-FDG

uptake was undertaken, with statistical analyses completed using Stata 13.0 (Statcorp, College Station, TX, USA). MRI of the pelvis, knee and hand/wrist was then performed in three patients with representative $^{18}$F-FDG PET/CT findings using a 1.5 Tesla magnet. Medview fusion software was utilised to anatomically correlate sites of $^{18}$F-FDG uptake.

**Results:** Nineteen patients were recruited. Mean age was 67.52±6.36 years and there was a slight male predominance (63.16%). On whole body PET/CT, adjacent to the ischial tuberosities was the most common site of abnormal $^{18}$F-FDG uptake (18/19 patients [94.74%]) and showed the highest mean $SUV_{max}$ value (3.95 ± 1.81). Eleven patients (11/18 [61.11%]) were found to have knee involvement, with intense $^{18}$F-FDG uptake in posteromedial knee structures in ten participants. $^{18}$F-FDG uptake was similarly appreciated at the hand/wrist in twelve patients (63.16%). At the hand/wrist, a volar distribution was typical. MRI of the pelvis demonstrated bilateral and symmetric high T2 signal surrounding the proximal hamstring tendon origins of semimembranosus and the conjoint tendon of semitendinosus and biceps femoris. At the knee, peri tendinous oedema surrounding the distal insertion of semimembranosus was similarly visualised. Hand/wrist MRI revealed synovial thickening and enhancement in the flexor compartment, in keeping with tenosynovitis. PET/MRI fusion at the pelvis and knee confirmed semimembranosus peri tendonitis as the anatomical correlate of $^{18}$F-FDG uptake adjacent to the ischial tuberosities and of posteromedial knee structures on whole body PET/CT.




**Conclusions:** PET/MRI fusion demonstrates that hamstring peri tendonitis is a distinctive manifestation of PMR. This further characterise the imaging phenotype of PMR and highlights a predilection for tendon involvement in this condition.

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**Disclosure of Interest:** None declared

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## FRI0368 THE USE OF ULTRASOUND IN THE DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH GIANT CELL ARTERITIS: EXPERIENCE OF A SINGLE CENTRE

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**Background:** Giant cell arteritis (GCA), the most common primary vasculitis, can cause irreversible blindness in 20–30% of untreated cases, but glucocorticoid therapy leads to significant toxicity in >80% of patients. Ultrasound has proven to be effective in diagnosing giant cell arteritis (GCA) and has the potential to monitor disease activity.

**Objectives:** We reviewed data on all patients referred to a single university hospital between August 2014 and December 2015 who were seen in a "fast-track" service established to diagnose and evaluate suspected GCA or a suspected flare.

**Methods:** All patients underwent rapid evaluation by a combination of standard clinical assessment and ultrasound of the temporal and axillary arteries. The ultrasound scan was considered positive when we identified the presence of a dark halo around the temporal artery wall or a homogeneous hypoechoic wall thickness >1.5 mm in the axillary arteries. We performed a retrospective analysis and comparison of the ultrasound findings with the clinical features, temporal artery biopsy (TAB) results and decision to treat patients with suspected or established GCA.

**Results:** We performed 206 scans in 169 patients (71% females, mean [SD] age 72 ± 11 years). In 123 cases, patients were referred for suspected GCA: 63% were already receiving high-doses of steroids (mean of 12 ± 10 days); 78% had headache; 60% high inflammatory markers; 33% abnormal vascular examination (e.g. diminished/absent pulse or bruits); 31% scalp tenderness; 28% jaw claudication; 26% polymyalgia rheumatica and 26% visual symptoms. In 39 cases the scan was positive: 9 also had a TAB (4 positive) and all were treated as GCA. In 77 cases the scan was negative: 27 also had a TAB (1 positive) and 9 were treated as GCA. In 7 cases the scan was inconclusive requiring further investigations (e.g. TAB). Patients with a positive scan had a mean CRP of 17.6 ± 30.1 g/dl and a mean ESR of 41.3 ± 43.3 mm/hour; patients with a negative scan had a mean CRP of 13.8 ± 17.9 g/dl and a mean ESR of 16.3 ± 17.6 mm/hour (p=0.979 and p=0.048, respectively). We scanned 83 patients with an established diagnosis of GCA to assess for flare or monitor disease activity: 29 had a positive scan (21 increased medication; 8 were follow-ups with improvement from baseline) and 54 had a negative scan (4 increased medication; 50 allowed a safer taper or withdrawal of glucocorticoids). Patients with a positive scan had a mean CRP of 8.0 ± 10.1 g/dl and a mean ESR of 15.6 ± 17.3 mm/hour; patients with a negative scan had a mean CRP of 9.6 ± 16.9 g/dl and a mean ESR of 20.5 ± 19.3 mm/hour (p=0.970 and p=0.190, respectively).

**Conclusions:** The combination of rapid clinical evaluation and ultrasound were key elements in diagnosis and monitoring of GCA, allowing more flexible use of glucocorticoid dose regimens and reducing the number of TABs required. The only patient with a negative scan but a positive TAB had already received 20 days of glucocorticoids, suggesting that delay in investigation after starting therapy could affect the results of the scan.

**References:**

[1] Luqmani RA, et al. The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis. Arthritis Rheumatol 2015; 67 (suppl 10)

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## FRI0369 PATTERN OF CLINICAL PRESENTATION AND DISEASE SEVERITY IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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**Background:** Polymyalgia rheumatica (PMR) is an inflammatory disorder of the elderly characterized by girdle pain and stiffness, constitutional symptoms and elevation of inflammatory indexes. In its classical form, the shoulder girdle is affected, associated or not with pelvic and spinal pain. The latter two locations can occasionally precede shoulder involvement. It is not known if the pattern of clinical presentation is related to disease severity at onset.

**Objectives:** In this study, disease severity of PMR has been correlated with clinical characteristics at presentation.

**Methods:** 394 patients (251 women, median age 73 yrs, range 47–92 yrs) with PMR diagnosed according to Bird's criteria, visited between 1990 and 2014 by the same clinician were studied. Clinical features recorded at disease presentation included initial involvement of: i) the shoulder girdle; ii) the pelvic girdle; iii) the column; iv) two or more of the previous locations; v) presence of giant cell arteritis (GCA); vi) acute onset, defined as completion of full symptoms and signs in ≤72h; or vii) peripheral arthritis. Disease severity of PMR was evaluated by considering: i) weight loss; ii) fever; iii) morning stiffness (MS); iv) ESR; v) CRP; and vi) initial dose of prednisone.

**Results:** Acute onset and classical involvement of the shoulder girdle were not associated with our indicators of PMR severity. By contrast, onset in the pelvic girdle (p=0.002), simultaneous onset in multiple locations (p=0.006), peripheral arthritis (p=0.045) and GCA (p=0.0004) were associated with a higher initial dose of prednisone; multiple locations onset correlated also with MS (p=0.044).

**Conclusions:** The presentation with multiple locations, including column and pelvic girdle, peripheral arthritis, and GCA resulted in a more severe onset at least in the perception of the clinician who used a higher initial dose of prednisone. Clinicians should consider the pattern of disease presentation when evaluating the burden of PMR.

**Disclosure of Interest:** None declared

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## FRI0370 TWO SUBSETS OF GIANT CELL ARTERITIS CHARACTERIZED BY THE ABSENCE OR PRESENCE OF SPONDYLOARTHRITIS OR ITS ASSOCIATED DISEASES

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**Background:** Whilst large vessel vasculitis (LVV) predominantly occurs in isolation, associations with other infectious and non-infectious diseases have been reported. Limited data describing associations with various autoimmune diseases, including spondyloarthritis exists. The aim of this study was to characterize the association of LVV and spondyloarthritis or its associated diseases (SpAD).

**Methods:** A single centre, retrospective study of patients ≥50yrs with first presentation LVV between 01.06.2008–01.06.2015 was performed. Patients were categorized according to SpA or associated disease, other autoimmune disease or controls. Clinical, laboratory and imaging findings were compared. Kaplan-Meyer survival analysis, with relapse taken as the primary end-point, was performed.
**Results:** LVV was confirmed in 62 pts, of who 16/62 (26%) had SpA or associated disease. In these patients, LVV presented earlier (59.2 SpAD vs. 68.1 AI and 70.3yrs Controls; p=0.01) and occurred predominantly in spring compared to autumn and winter in non-SpA patients, was associated with more centralised pattern of distribution (p=0.05) and was more likely to exhibit a refractory course (p=0.05). Overall relapse rates were similar across groups. Smoking-status influenced age of onset in all groups, being associated with earlier onset.
**Conclusions:** A clear association between LVV and SpAD exists. LVV associated with SpAD has a particular phenotype characterised by earlier onset, thorax-limited disease and increased risk of a refractory course. Given on-going LVV treatment trials further genetic and pathophysiological characterization appears warranted, to evaluate potential variation in treatment response and optimize future care.
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**Disclosure of Interest:** None declared
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## FRI0371 THE CLINICAL SPECTRUM OF MEDIUM-SIZED VESSEL VASCULITIS

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**Background:** Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis of medium sized visceral vessels. The 2012 Chapel Hill Consensus Conference Nomenclature of vasculitides defined vasculitis affecting any size of vessel in a single organ without systemic manifestations as single organ vasculitis (SOV). However, cutaneous arteritis (CA) and Gastrointestinal (GI) vasculitis are forms of SOV having indistinguishable histopathological findings from PAN.
**Objectives:** In this study, we aimed to evaluate and compare the demographics, clinical characteristics, treatment, and outcomes of patients with systemic PAN, CA and GI vasculitis.
**Methods:** We assembled retrospective cohorts of patients with PAN, CA and GI vasculitis between 1980 and 2014. The demographics, clinical characteristics, treatment and outcomes of patients were abstracted from medical records. Birmingham Vasculitis Activity Score (BVAS), prognostic Five Factor Score (FFS) and vasculitis damage index (VDI) were calculated.
**Results:** The study included 48 patients with PAN, 41 patients with CA, and 19 patients with GI vasculitis. Only 1 patient presenting as CA evolved to systemic PAN during the disease course. Most cases of PAN were idiopathic, while only 7 patients had hepatitis B and 2 patients had hepatitis C positivity. Constitutional and musculoskeletal manifestations were the most common clinical manifestations in the PAN group and were less frequent in CA and GI vasculitis. At diagnosis, 94% of patients with PAN, 93% of patients with CA and 67% of patients with GI vasculitis were treated with glucocorticoids. Additional immune-suppressive agents were used in 67% of PAN, 37% of GI vasculitis and 32% of CA. Twenty-seven patients with PAN, 18 patients with CA and 9 patients with GI vasculitis had mean follow-up of about 6 years. The five year cumulative relapse rate was 45.2% in CA, and only 9.6% in PAN. VDI was comparable in PAN and GI vasculitis, but was lower in CA. While no deaths were observed in the CA group, survival at 10-years was 66% in the PAN and 61% in GI vasculitis group.
**Conclusions:** CA and GI vasculitis appear to be distinct diseases rather than a limited expression of systemic PAN. Progression of CA to systemic PAN is very rare. Relapse risk is very low during follow-up in PAN. Patients with CA have a higher relapse rate compared to those with systemic PAN, possibly due to lower use of immunosuppressive therapy in the former group.
**Disclosure of Interest:** None declared
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## FRI0372 RITUXIMAB FOR ANCA ASSOCIATED VASCULITIS REFRACTORY TO CONVENTIONAL TREATMENT: A RETROSPECTIVE STUDY ON 25 PATIENTS

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**Background:** The efficacy of rituximab (RTX) in ANCA associated vasculitis (AAV) has been shown in controlled trials. Observational data reflecting its real life use in AAV is limited.
**Objectives:** Here we present our experience with RTX therapy in AAV patients refractory to conventional treatment.
**Methods:** We retrospectively reviewed the records of 25 AAV patients (11 men, 14 women; mean age 42.8±14.2 SD years; mean disease duration 45.5 ± 47.5 SD months) treated with RTX between 2011 and 2015 due to inadequate response or relapse under conventional treatment modalities. Among these 25 patiens the main types of involvement at baseline were renal involvement in 14 patients, pulmonary involvement in 16, upper respiratory system in 10, ocular in 2, peripheral nervous system in 2, CNS in 1, skin in 1 patient and ear in 2 patients. We assessed treatment response with disease activity using BVAS scores, decrease in corticosteroid dose, improvement in renal functions and other organ manifestations.
**Results:** RTX was given for a median of 2 courses (range 1–5, courses given at fixed intervals in 21 patients) during a mean follow-up of 17.4±13.9 SD months. The reasons for RTX treatment were active renal disease in 11 patients, pulmonary involvement in 9, upper respiratory system involvement in 4, and CNS involvement in 1 patient. In addition to RTX, corticosteroids were used in 13 patients, azathioprine + corticosteroids in 7 patients, methotrexate + corticosteriods in 2 patients, solo azathioprine in 2 patients and RTX was given solo in 1 patient. At final assessment 22 patients were under follow-up, 1 was lost to follow-up after 7 months and 2 had died, due to renal failure in one and respiratory failure in the other patient. 17/25 (68%) patients were in remission (BVAS score 0) at the final assessment. 3/25 patients (12%) had experienced relapses during follow-up. The mean BVAS score during the final assessment was 1.6 ± 4.1. Mean corticosteroid dose was reduced from 42±21.9 mg/day to 15.5±21.0 mg/day ($p<0.001$).The last evaluation of patients with renal involvement showed stable disease in 6 improvement in 6 and worsening in 2 patients. Mean creatinine level had slightly improved from 2.1 ± 1.2 mg/day to 1.9 ± 1.4 mg/day (p=0.36). Proteinuria had decreased from 1686±1466 mg/day to 1010±1100 mg/day (p=0.02). RTX treatment was terminated in 2 patients because of infusion reaction. Four patients were hospitalized while being on RTX. The first had pneumonia and responded to antibiotics. The second patient with diffuse lung involvement had died. The third died due to renal failure and the last patient developed end stage renal disease.
**Conclusions:** Our retrospective study showed that RTX is an effective treatment modality that enables corticosteroids tapering and remission in majority of AAV patients refractory to conventional treatment modalities. It was generally well tolerated with few serious adverse events.
**Disclosure of Interest:** None declared
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## FRI0373 THE CLINICAL AND DEMOGRAPHIC FEATURES OF RELAPSING POLYCHONDRITIS: A NATIONWIDE STUDY

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**Background:** Relapsing polychondritis (RP) is a rare systemic and inflammatory disease.
**Objectives:** to assess clinical features, management and prognosis in RP.
**Methods:** Retrospective medical records were collected from 16 centers for 37 patients with RP diagnosed by Michet criteria. Data included patients' demographics, clinical features, laboratory findings and outcome.
**Results:** A total of 37 patients, (Male/female=19/18) with a mean disease onset of 45.7±11.8 years and median follow up period is 20 (1–360) months were enrolled. The most common initial complaints and organs involved were showed in table 1. Mean lead time to diagnose was 28.6±54.3 (0–228) months. Four patients had a known history of cartilage injury before the RP diagnosis (Three goiter operation and 1 resuscitation due to a drowning). Twelve of the patients (32.4%) had also various autoimmune or hematologic diseases. After the diagnosis, moderate or high dose prednisone (n=37, 100%), plus methotrexate (n=15, 40.5%) or azathioprine (AZA) (n=11, 29.7%) or hydroxychloroquine (HQ) (n=3, 8.1%) or cyclophosphamide (CYP) (n=2, 5.4%), or (AZA+ HQ n=3, 8.1%) treatments were initiated. In the case of resistant disease, CYP (n=6, %16.2), tocilizumab (n=2, 5.4%), etanercept (n=1, 2.7%), infliximab (n=1, 2.7%) and bevacizumab (n=1, 2.7%) treatments were given. Due to tracheal stenosis surgery applied to 2 patients, one patient died due to respiratory collapse, 21 patients on remission without any complications, 13 (35.1%) patients had developed tracheal stenosis

Table 1. Clinical features at diagnosis

| Complaints | n (%) | Organ involvement | n (%) |
|---|---|---|---|
| Pain and redness in the auricular area | 32 (86.4) | Auricular chondritis | 32 (86.4) |
| Constitutional symptoms | 30 (81.8) | Arthritis | 22 (59.4) |
| Arthralgia | 28 (75.7) | Eye | 19 (51.3) |
| Swollen joints | 22 (59.4) | Skin lesions | 14 (37.8) |
| Myalgia | 21 (56.8) | Nasal chondritis | 11 (29.7) |
| Red eye and pain | 20 (54.1) | Major airway | 10 (27) |
| Erythema and pain in the nose | 16 (43.2) | Costochondritis | 9 (24.3) |
| Dyspnea | 13 (35.1) | Hearing loss | 7 (18.9) |

(n=5, 13.5%), major airway cartilage loss (n=5, 13.5%), auricular collapse (n=2, 5.4%), nasal collapse (n=3, 8.1%), subglottic stenosis (n=2, 5.4%), hearing loss (n=5, 13.5%), vision loss (n=1, 2.7%) and deforming arthritis (n=1, 2.7%). In the univariate analysis, only major airway involvement had a relationship with complication development. (OR 12, 95% CI 1.97–72.8, p=0.007)

**Conclusions:** RP is a rare disease which diagnosis is commonly delayed and lead to cartilage loss. RP developed after trauma in 4 patients, possibly trauma can be blamed as an etiologic factor. Awareness and early diagnosis results with better prognosis

**Disclosure of Interest:** None declared

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## FRI0374 THE DIAGNOSTIC VALUE OF ALPHA-1-ANTITRYPSIN PHENOTYPE IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS (WEGENER'S GRANULOMATOSIS)

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**Background:** Deficiency of alpha-1 protease inhibitor, or alpha-1-antitrypsin (A1AT), predisposes to chronic lung diseases and some extra-pulmonary pathology. Besides classical implications, such as pulmonary emphysema and other associated lung diseases, A1AD is also known to be associated with granulomatosis with polyangiitis (GPA, or Wegener's).

**Objectives:** The aim of our study was to evaluate the frequency of mutated A1AT forms and its clinical significance among GPA patients.

**Methods:** We analysed 38 samples of sera, collected from GPA patients. Detailed clinical data, including Birmingham Vasculitis Activity Score (BVAS), incidence of lung involvement, anti-(Pr3) antibodies concentrations and other laboratory data were collected. We also studied control group of 46 healthy donors. All collected samples underwent A1AT phenotyping by isoelectrofocusing (IEF) and turbidimetric A1AT measurement.

**Results:** Mutated A1AT variants were revealed in 18.4% (7/38) cases and included following phenotypes: 1ZZ, 4MZ and 2MF. The mean A1AT concentration in samples with pathological genetic A1AT forms was significantly lower (P=0,0038), than in normal A1AT phenotype. According to reference values, only 2 of 7 pathological samples demonstrated decreased A1AT concentration. Comparing BVAS activity, we found that patients with mutated A1AT phenotype had significantly higher vasculitis activity, as well as anti-PR3 antibodies concentration. When analysis of nonspecific systemic inflammation markers was performed, the significant difference ($P<0.05$) was found only between means of erythrocyte sedimentation rate (ESR)

**Conclusions:** Laboratory testing to find pathological A1AT forms are not usually ordered for patients with systemic vasculitides. During medical examination of GPA patients the possibility of A1AT deficiency should be considered and may be verificated by IEF.

**Disclosure of Interest:** None declared

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## FRI0375 CLINICAL IMPROVEMENT ACCORDING TO PATIENT REPORTED OUTCOMES IN PATIENTS WITH POLYMYALGIA RHEUMATICA: A LONGITUDINAL ANALYSIS FROM ROUTINE CARE

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**Background:** Several outcomes and clinical response measures have been used in patients with polymyalgia rheumatica (PMR), but there is no consensus about the optimal endpoint for evaluating response to treatment. A PMR activity score has been proposed which includes three patient reported outcomes (PROs)[1]. RAPID3 is an index found on a multidimensional health assessment questionnaire (MDHAQ) only including PROs, which is effective to document improvement not only in RA but also in other rheumatic diseases[2]

**Objectives:** To prospectively evaluate the performance of RAPID3 and other PROs included on the MDHAQ to document improvement in clinical status over time in patients with PMR.

**Methods:** This study was conducted at an academic rheumatology center at which all patients complete a MDHAQ, which includes 0–10 scores for physical function (FN), pain (PN), and patient global estimate (PATGL), compiled into a 0–30 RAPID3. The MDHAQ also scores fatigue, morning stiffness, self-reported joint counts and demographic data. Data collection included MDHAQ, acute-phase reactants, and prednisone dose. PMR patients with complete data seen between 2010 and 2014 were included. A baseline visit and the most recent visit were compared using paired t-test and McNemar's test. Spearman correlation analysis for non-normally distributed variables was performed between RAPID3 and ESR and CRP.

**Results:** 34 PMR patients seen in routine care were included: 59% were females, 71% Caucasian, and mean age was 71.6 years. The mean duration from a baseline visit to most recent visit was 15.5 months. At initial presentation, RAPID3 was 12.2, FN 2.2, pain 5.3, and PATGL 4.7, fatigue 3.9, and morning stiffness 63.1 minutes; 64.7% of the patients had painful hips, 79.4% had painful shoulders, 73.5% had abnormal ESR, and 70.6% had abnormal CRP. Significant improvement was seen between baseline and last visit in mean level of RAPID3 and all other MDHAQ measures, except fatigue ($p<0.05$), as well as ESR and CRP (Table). The mean dose of prednisone was decreased from 12.2 mg at first visit to 4.3 mg at most recent visit. The RAPID3 was significantly correlated with ESR (rho=0.52), and with CRP (rho=0.50).

Table 1

| | PMR patients (n=34) | | | Mean change | % Improvement |
|---|---|---|---|---|---|
| | Baseline | Most recent visit | P value | | |
| MDHAQ: patient self-reported measures | | | | | |
| RAPID3, mean (SD) | 12.2 (7.0) | 8.5 (7.2) | 0.02 | 3.7 | 30.7% |
| MDHAQ – Function, mean (SD) | 2.2 (2.1) | 1.5 (1.7) | 0.03 | 0.6 | 27.2% |
| MDHAQ – Pain, mean (SD) | 5.3 (2.9) | 3.4 (3.4) | 0.002 | 1.9 | 35.8% |
| MDHAQ – PATGL, mean (SD) | 4.7 (2.9) | 3.1 (3.1) | 0.01 | 1.6 | 34.0% |
| RADAI – painful hip, n (%) | 22 (64.7%) | 12 (35.3%) | 0.02 | 29.4 | 45.4% |
| RADAI – painful shoulder, n (%) | 27 (79.4%) | 17 (50%) | 0.005 | 10 | 37.0% |
| MDHAQ – Fatigue, mean (SD) | 3.9 (3.6) | 3.5 (3.3) | 0.54 | 0.4 | 10.5% |
| Morning stiffness duration, minutes, mean (SD) | 63.1 (97.7) | 19.1 (34.1) | 0.05 | 43.9 | 69.5% |
| Laboratory measures | | | | | |
| Abnormal ESR, n (%) | 25 (73.5%) | 14 (41.1%) | 0.002 | 32 | 43.5% |
| Abnormal CRP, n (%) | 24 (70.6%) | 13 (38.2%) | 0.01 | 32 | 45.3% |
| Medication | | | | | |
| Prednisone dosage, mg, mean (SD) | 12.2 (6.8) | 4.3 (3.5) | <0.001 | 7.9 | 64.7% |

**Conclusions:** In patients with PMR, improvement was seen according to PROs included on a self-reported MDHAQ questionnaire in a similar range to ESR and CRP, documenting effective response to prednisone.

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**Disclosure of Interest:** None declared

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## FRI0376 COMPARISON OF CLINICAL CHARACTERISTICS OF PATIENTS WITH TAKAYASU'S ARTERITIS BY AGE AND GENDER

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**Background:** Takayasu's arteritis (TA) is a rare and heterogeneous disease that can be difficult to diagnose.

**Objectives:** In this study we distinguish clinical characteristics in the different groups with TA and aimed to improve the diagnosis ability of this disease in different people.

**Methods:** We retrospectively analyzed the clinical manifestations and laboratory and angiographic findings of 53 TA patients divided into groups by age and by gender.

**Results:** Ratio of incidence in males and females was 1:4; mean age at onset was (35 ± 11) years in males and (28 ± 11) years in females. In 17% of patients, at onset was over the age of 40. The most common symptom at onset was chest pain and reduced glomerular filtration rate (GFR) in males [7 (63.6%) *vs.* 12 (28.6%), *P*=0.031; 8 (72.7%) *vs.* 14 (33.3%), *P*=0.034], especially in young males [age≤40 years, 5 (62.5%) *vs.* 8 (22.2%), *P*=0.024; 7 (87.5%) *vs.* 12 (33.3%), *P*=0.006]. Significantly more male patients, especially males over the age of 40, had multi-vessel involvement [10 (90.9%) *vs.* 24 (57.1%), *P*=0.038; 2 (66.7%) *vs.* 0, *P*=0.033]. Significantly more young males had aortic insufficiency [5 (62.5%) *vs.* 8 (22.2%), *P*=0.024]. Pulselessness [2 (66.7%) *vs.* 0, *P*=0.03] and radial artery weakening [2 (66.7%) *vs.* 0, *P*=0.03] were found in more males over 40 years of age at onset. There were no differences in laboratory data between males and females. Chest pain [13 (29.5%) *vs.* 6 (66.7%), *P*=0.031] and fever [0 *vs.* 1 (11.1%), *P*=0.027]occurred significantly more often in patients over the age of 40., and patients over 40 years of age at onset had significantly less renal artery [1 (11.1%) *vs.* 21 (47.7%), *P*=0.042], abdominal aortic [0 *vs.* 16 (38.1%), *P*=0.030], and multi-vessel involvement [2 (22.2%) *vs.* 32 (72.7%), *P*=0.004]. Patients over 40 years of age were rarer in type V [1 (11.1%) *vs.* 22 (50%), *P*=0.032)] while more common in type IIa [3 (33/3%) *vs.* 4 (9.1%), *P*=0.050] than young ones. Multivariate analysis showed that thoracic aortic involvement was an independent risk factor for developing hypertension (OR =3.918, 95% confidence interval [CI] 1.616–1566.185, *P* =0.026), and ascending aortic involvement was an independent risk factor for both aortic insufficiency (OR =3.674, 95% CI 2.734–567.621, *P* =0.007) and aneurysm formation (OR =7.255, 95% CI 7.255 ~ 1,628,614; *P* =0.044).

**Conclusions:** Patients with disease at onset after age 40 are more likely to present with chest pain and fever and only rarely have renal artery, abdominal aortic or multi-vessel involvement. Males are likely to present with multi-vessel involvement and reduced GFR, and these differences are more prominent in young males, who are more likely to develop aortic insufficiency. Aortic stenosis was an independent risk factor for hypertension, while ascending aortic involvement was an independent risk factor for aortic valvular insufficiency and aneurysm formation. Aortic valve lesion and ascending aorta involvement may play reciprocal role to aggravates destructions of each other and induce chest pain.

**Disclosure of Interest:** None declared

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## FRI0377 CLASSIFICATION CRITERIA FOR GIANT CELL ARTERITIS: DATA FROM GIACTA INFORMING THE NEED FOR REVISION

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**Background:** Classification criteria are often used to standardize the enrollment of patients (pts) in clinical studies. American College of Rheumatology (ACR) classification criteria for giant cell arteritis (GCA)[1] are >25 years old. Advances in diagnosis and clinical understanding of GCA make their relevance to current studies questionable.
**Objectives:** To compare inclusion criteria for the GiACTA (tocilizumab for GCA) study[2] with 1990 ACR GCA classification criteria.
**Methods:** Pts were enrolled into GiACTA according to study inclusion criteria and were evaluated as to whether they met the 1990 ACR classification criteria (Table). Data are from a live database.
**Results:** Of the 251 pts enrolled into GiACTA, 198 (79%) pts met the 1990 ACR classification criteria. The 53 pts who did not fulfill ACR criteria were eligible for GiACTA based on cross-sectional imaging studies and/or polymyalgia rheumatica (PMR) symptoms. In total, 156 (62%) pts had positive temporal artery biopsies (TAB); of these, 24 also had positive imaging findings. The remaining 95 (38%) pts had no TAB or negative TAB; diagnosis of GCA was confirmed by positive findings from large-vessel imaging studies. Positron emission tomography (PET), often coupled with computed tomography (CT), was important in diagnosis. Positive PET/CT findings contributed to GCA diagnosis in 97 (39%) GiACTA pts. CT angiography and magnetic resonance angiography contributed to diagnosis in 14 (6%) and 8 (3%) pts, respectively. New-onset headache, the only GCA symptom in the ACR criteria, was absent in 33% of GiACTA pts. However, other symptoms that often accompany GCA (PMR, scalp tenderness, jaw claudication, ischemia-related vision loss) were present in 62%, 36%, 34%, and 10% of pts, respectively.

| GiACTA Entry Criteria for the Classification of GCA | ACR Criteria for the Classification of Giant Cell (Temporal) Arteritis[a] |
|---|---|
| Age ≥50 y | Age at disease onset ≥50 y |
| History of ESR ≥50 mm/h (or CRP ≥2.45 mg/dL if ESR unavailable) | Elevated ESR ≥50 mm/h |
| At least one of the following:<br>– Unequivocal cranial symptoms of GCA (new-onset localized headache, scalp or temporal artery tenderness or decreased pulsation, ischemia-related vision loss, or otherwise unexplained mouth or jaw pain on mastication)<br>– Unequivocal symptoms of PMR, defined as shoulder and/or hip girdle pain associated with inflammatory stiffness | New-onset headache |
| | Temporal artery abnormality (tenderness to palpation or decreased pulsation) |
| At least one of the following:<br>– TAB revealing features of GCA<br>– Evidence of large-vessel vasculitis by angiography or cross-sectional imaging study such as MRA, CTA, or PET-CT | Positive TAB |

CRP, C-reactive protein; CTA, computed tomography angiography; ESR, erythrocyte sedimentation rate; MRA, magnetic resonance angiography. [a]The presence of ≥3 criteria classifies a patient as having GCA.

**Conclusions:** The 1990 ACR classification criteria for GCA require updating. Cross-sectional imaging, particularly PET/CT, now plays a major role in establishing the diagnosis of GCA. Symptoms in addition to headache merit consideration as part of revised classification criteria.
**References:**
[1] Arthritis Rheum 1990;33:1122.
[2] Int J Rheumatol 2013;2013:912562. doi: 10.1155/2013/912562.
**Disclosure of Interest:** K. Tuckwell Shareholder of: Roche, Employee of: Roche Products Ltd., N. Collinson Shareholder of: Roche, Employee of: Roche Products Ltd., M. Klearman Shareholder of: Roche, Employee of: Genentech, S. Dimonaco Employee of: Roche Products Ltd., J. Stone Grant/research support from: Roche, Genentech, Consultant for: Roche, Genentech
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## FRI0378 NATIONAL AUDIT OF VASCULITIS INPATIENT COMORBIDITIES AND MORTALITY FROM 2005-14

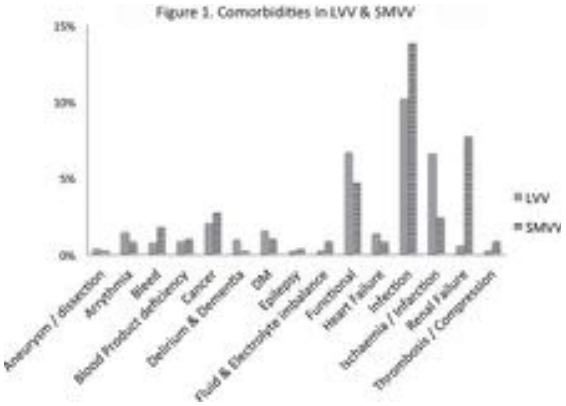
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**Background:** Incidence of inpatient (inpt) events, comorbidities and age of death for Irish vasculitis patients is currently unknown
**Objectives:** Establish mortalitity & comorbidities in Irish vasculitis inpts
**Methods:** The HIPE system was evaluated from 57 Irish hospitals between 2005–2014 for vasculitis inpt episodes (not individual patients) based on ICD10. Age, length of stay (LOS), gender and admitting indication and mortality were recorded. Results are shown as totals, % & median (IQR). The Mann–Whitney U test and $\chi^2$ were employed
**Results:** 5,841 vasculitis inpt records were reviewed with median annual admissions of 601 (601–622). 2,229 inpt admissions had large vessel vasculitis (LVV – Takayasu's & GCA) whose median age was 75yrs (66–81), LOS 6 days (3–13) and 68% were female. 3612 inpt admissions had small & medium vessel vasculitis (SMVV –GPA, eGPA, MPA, PAN, Behcet's, Goodpastures, Necrotizing & Juvenile Vasculitis) with a median age 58yrs (42–70), LOS 6 days (2–13) and 48% were female. MPA, eGPA and GPA admissions were more common for men whereas GCA, Takayasu's and Behcets admissions were more common for women (*table 1)*. 58% LVV inpts & 50% SMVV inpts were admitted for systemic inflammation ($p<0.001$). Infection was the next most common cause for admission (14% SMVV & 10% LVV, $p<0.001$). Ischaemic events were the 3rd most common reason for admission in LVV (7% v 3%, $p<0.001$) whereas renal failure was for SMVV (8% v 1%, $p<0.001$). Symptoms without a diagnosis were the 4th most common reason for admission (7% LVV & 5% SMVV, p=0.002). *Figure 1.* Admission for cancer occurred in mean 2.5% and all other diagnoses accounted for <2% each. A greater percentage of SMVV inpts died than LVV inpts (4.1% v 2.7%, p=0.006) and they died younger (71yr (61–79) v 82 (76–86), $p<0.001$). Infection accounted for 28% of all deaths without difference between LVV and SMVV (p=0.5). More SMVV inpts died due to disease activity than LVV inpts (19% v 6%; p=0.03) and from renal failure (12% v 1%, p=0.05). More LVV inpts died from vascular infarction than SMVV (19% LVV v 6% SMVV; $p<0.001$). Male GPA inpts died younger than female (69yrs (62–78) v 79yrs (68–82); p=0.02).

Table 1. Admission and mortality data of specific vasculitides

| | n | Age | Male | % Died | Age at death |
|---|---|---|---|---|---|
| Behcets disease | 437 | 36 (29–48) | 36%* | 2% | 63 (42–72) |
| Eosinophilic granulomatosis polyangiitis | 257 | 59 (51–65) | 57%* | 2% | 70 (59–78) |
| Giant cell arteritis | 2187 | 75 (67–81) | 33%* | 3% | 82 (76–86) |
| Goodpasture's syndrome | 432 | 60 (45–73) | 53% | 7% | 70 (60–78) |
| Granulomatosis polyangiitis (GPA) | 1806 | 60 (48–70) | 55%* | 4%* | 72 (63–80) |
| Juvenile polyarteritis | 29 | 10 (8–12) | 3%* | 0% | – |
| Microscopic polyarteritis | 125 | 66 (59–76) | 64%* | 2% | 72 (66–77) |
| Necrotising vasculopathy | 236 | 64 (49–73) | 53% | 7% | 71 55–80) |
| Polyarteritis nodosa | 220 | 51 (39–69) | 52% | 7% | 71 (56–80) |
| Takayasu's arteritis | 112 | 38 (23–54) | 8%* | 0% | – |

Values are whole numbers, percentage and medians (IQR). *Indicates significant gender difference.




**Conclusions:** Around 600 vasculitis admissions occurred each year across the 57 hospitals directing the need for a concentrated number of centres of excellence to facilitate expert care, research and education. Small vessel vasculitis admissions were more common for men and large vessel and Behcet's for women. Despite advances in therapy systemic autoimmune disease and infection prevailed as causes for admission and death in vasculitis inpts, with greater mortality in SMVV from disease activity and renal failure and from vascular infarction in LVV. There is a need for improved diagnostic tests.
**Disclosure of Interest:** None declared
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## FRI0379 SURVIVAL ANALYSIS IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

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**Background:** The mortality of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis is generally greater than for other types of vasculitis. The long-term survival of patients (pts) with ANCA-associated vasculitis in Ukraine is uncertain.

**Objectives:** To determine predictors of survival of pts with ANCA-associated vasculitis.
**Methods:** Outcome data was collected for 49 pts who had been diagnosed with ANCA-associated vasculitis (27 pts with granulomatosis with polyangiitis (GPA), 10 pts with microscopic polyangiitis (MPA) and 12 pts with eosinophilic granulomatosis with polyangiitis) according to the ACR 1990 criteria or the CHCC diagnostic criteria in the two city hospitals in Kyiv between 1972 and 2013. There were 15 males and 34 women aged from 20 to 77 years (median age 48.5±13.8). The duration of disease at time of diagnosis was from 1 to 156 months (mean 22.5±34.3 months). All pts received glucocorticoids, 37 - cytotoxic drugs and 3 – rituximab according to local treatment protocols. Survival was evaluated as a function of the main demographics, clinical and laboratory parameters and Birmingham Vasculitis Activity Score (BVAS) assessed at diagnosis. Statistical analyses used the Kaplan-Meier method and the multivariate Cox proportional hazards regression model.
**Results:** The median duration of follow-up was 62 months and 6 deaths (12.2%) were recorded (4 pts with MPA and 2 pts with GPA). The predominant causes of deaths were renal failure and disease activity. Cumulative survival rates at 1, 3, 5 and 10 years was 91.8, 87.6, 87.6 and 76.7%, respectively. Comparison survival of pts with ANCA-associated vasculitis according to age at onset of the disease and sex revealed that gender and age cumulative survival function didn't differ significantly. According to univariate analysis, a poor prognostic value was attributed to serum creatinine more than 176 umol/l (p=0.0001) and hemorrhagic alveolitis (p=0.01). Other factors (including ear, nose and throat, joints, skin, heart and nervous system involvement, increased ESR, leukocytosis, anemia, ANCA positivity, etc) didn't have influence on the survival curves. Survival curves of groups of pts with different disease activity determined by BVAS were not significantly different (p=0.88). Multivariate analysis showed that presence of increased creatinine levels more than 176 umol/l (HR=3.04, p=0.0001) and hemorrhagic alveolitis (HR=1.94, p=0.02) were independent predictors of poor outcome in pts with GPA and MPA.
**Conclusions:** Cumulative survival of pts with ANCA-associated vasculitis at 1, 3, 5 and 10 years of observation is 92, 88, 88 and 77%, respectively. The increased creatinine levels more than 176 umol/l and presence of hemorrhagic alveolitis are independent predictors of poor survival of pts with GPA and MPA. Vasculitis activity detected by BVAS and other clinical and laboratory parameters no effect on mortality.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1942

## FRI0380 IL-6 RECEPTOR POLYMORPHISM IN POLYMYALGIA RHEUMATICA; RELATIONSHIP BETWEEN ASP358ALA (T/G) POLYMORPHISM OF THE INTERLEUKIN 6 RECEPTOR (IL6R) GENE AND SUSCEPTIBILITY AND SEVERITY OF THE DISEASE

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**Background:** In previous study, we found in Polymyalgia rheumatica (PMR) patients a significant correlation between the number of relapses and serum soluble interleukin-6 receptors (sIL-6R) concentrations at baseline and after 1, 3, and 12 months of therapy (1). The Asp358Ala (T/G) polymorphism of the interleukin 6 receptor (IL6R) was related with high levels of ser1um sIL-6R.
**Objectives:** The Aim of our study was to evaluate the relationship between Asp358Ala (T/G) polymorphism of IL6R gene and susceptibility and severity of the PMR
**Methods:** We studied 104 patients with pure PMR and 94 healthy controls. Serum levels of s-IL6R were evaluated using highly sensitive, commercial sandwich enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN) according to the manufacturer's instructions. The IL6R Asp358Ala polymorphism (rs8192284) were molecularly genotyped
**Results:** The distribution of allele and genotype frequencies did not differ significantly between PMR patients and healthy controls. Carriers of the Asp358Ala T allele (TT+GT) in PMR patients was 58.7% and in Healthy controls was 60.6% (p=0.78).
Homozygosity for the T allele in PMR patients was 16.3% and in healthy control was 12.8% (p=0.48). However the patients and controls with this polymorphism presented higher level of serum s-IL6R. Finally, PMR patients with relapses/recurrences showed more frequently homozygosity for the T allele, but the difference with patients without relapses/recurrences was not statistically significant (p=0.07).
**Conclusions:** Asp358Ala (T/G) polymorphism of the IL6R was related with high serum levels of s-IL6R; however, no correlation existed between this polymorphism and PMR susceptibily. Moreover, a bordeline correlation existed between TT homozygosity and relapses/recurrences in these patients.
**References:**
[1] Pulsatelli L, Boiardi L, Pignotti E et al. Serum interleukin-6 receptor in polymyalgia rheumatica: a potential marker of relapse/recurrence risk. Arthritis Rheum. 2008;59:1147–54.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4232

## FRI0381 PATTERN OF CLINICAL PRESENTATION AND OUTCOME OF POLYMYALGIA RHEUMATICA

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**Background:** Polymyalgia rheumatica (PMR) is an inflammatory disorder of the elderly characterized by girdle pain and stiffness, constitutional symptoms and elevation of inflammatory indexes. Glucocorticoid (GC) treatment is effective but often prolonged, with associated side effects. Data on risk factors of poor prognosis are scanty: in particular it is not known if the pattern of clinical presentation can influence PMR outcome.
**Objectives:** To test the hypothesis that clinical presentation of PMR can predict its outcome.
**Methods:** 394 patients (251 women, median age 73 yrs, range 47–92 yrs) with PMR diagnosed according to Bird's criteria, visited between 1990 and 2014 by the same clinician were studied. Median follow up was 13.8 months (range 1–250 months). Clinical features recorded at disease presentation included involvement of: i) the shoulder girdle; ii) the pelvic girdle; iii) the column; vi) two or more of the previous locations; v) with giant cell arteritis (GCA); or vi) with acute onset, defined as completion of full symptoms and signs in $\leq$72h. PMR outcome was evaluated by considering: i) duration of follow-up; ii) appearance of peripheral arthritis; iii) appearance of GCA; iv) number of exacerbations/ relapses; v) cumulative dosage of GC; vi) use of methotrexate (MTX); and vii) death.
**Results:** At multivariate analysis, acute onset predicted a longer follow-up duration (p=0.007) and death (p=0.037); involvement of the spine predicted longer follow up duration (p=0.001) and use of MTX (p=0.018); presentation at the pelvic girdle predicted a high number of exacerbations/relapses (p=0.034) and association therapy with MTX (p=0.009); onset in multiple locations predicted a high number of exacerbations/relapses (p=0.03); presentation with GCA predicted a higher cumulative dosage of GC (p=0.0001) and use of MTX (p=0.027).
**Conclusions:** Apart from the obvious association between concomitant GCA and negative prognosis of PMR, other clinical characteristics at disease onset influence outcome. In particular, the initial presentation with multiple locations, including spine and pelvic girdle, resulted in longer follow-up, more relapses, and need of MTX treatment, whereas the classic one with only shoulder girdle involvement was associated with a milder disease. An acute onset was also a negative prognostic factor. Clinicians should consider the pattern of disease presentation when evaluating the burden of PMR.
**Disclosure of Interest:** None declared
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## FRI0382 LARGE VESSEL VASCULITIS AND PERIVASCULAR DISORDERS UNDERGOING IMMUNOSUPPRESSIVE THERAPY: THE USE OF PERFUSION-CT FOR RESPONSE MONITORING

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**Background:** Inflammatory disorders of the large vessel walls (aortitis-A) or such arising around large vessels (periaortitis-P) are rare and generally difficult to diagnose. Acute phase inflammatory markers are used for monitoring these entities, but they knowingly fail in up to 20% of cases, in particular in patients with periaortitis. Moreover, these follow-up markers rapidly turn normal after onset of some novel therapeutic agents like biologicals (e.g. anti-IL6)[1]. Therefore, functional imaging techniques have advanced to the methods of choice in A/PA diagnosis, and even therapy monitoring [2].
**Objectives:** To evaluate the role of perfusion-based CT for monitoring inflammatory activity in patients with aortitis and chronic periaortitis (A/PA) undergoing immunosuppressive therapy (IST).
**Methods:** A retrospective database search at our institution between January 2010 and March 2015 identified 17 patients (8 female; median age 68.5 years) with A/PA that underwent combined anatomical and functional CT, including CT perfusion-based monitoring for assessment of disease activity. Institutional review board approval was obtained for data analysis. All patients were symptomatic at the time of 1st CT-imaging. Patients first underwent segmental volume perfusion-CT (VPCT) for assessment of the degree of vascularization of A/PA as a surrogate marker for inflammatory activity. Blood flow (BF) and blood volume (BV) were determined. The thickness of the increased perivascular connective tissue formation was measured. Perfusion data was correlated with C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).
**Results:** In all patients, perfusion parameters dropped at FU under IST, this reduction was significant for BF and BV ($p<0.05$). 15 patients had elevated ESR and CRP at the time of the 1st perfusion-CT; 2 patients had normal values. In aortitis patients, CRP dropped from 3.86±5.31 to 0.9±1.37 and in periaortitis patients from 1.78±2.25 to 0.79 ±1.55, whereas ESR dropped from 45.71±37.59 to 8.57 ±3.1 and 36.78±34.67 to 17.22±21.82, in aortitis and in periaortitis, respectively. Correlation between serologic data and perfusion parameters was very good. Clinical symptoms were resolved in 12 patients at FU. At follow-up, the mean thickness of aortic or perivascular tissue formation decreased by 41.7±25.63% (range, 0–87.5%). The response was more vigorous in PA-patients (47.7±27.0%; range: 9–87.5%) than in A-patients (35.4±23.88%;

range: 0–62.5%). The difference between baseline and follow-up imaging was significant for both disease entities ($p<0.001$).

**Conclusions:** The course of perfusion-CT parameters in A/PA undergoing IST correlated well with that of serological markers with respect to disease activity assessment. In cases with bland serological data, perfusion-CT was the sole reliable monitoring parameter.

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[1] Loricera J, Blanco R, Castaneda S, et al. Tocilizumab in refractory aortitis: study on 16 patients and literature review. Clinical and experimental rheumatology 2014; 32:S79–89

[2] Bier G, Henes J, Eulenbruch C, Xenitidis T, Nikolaou K, Horger M. Perfusion-based assessment of disease activity in untreated and treated patients with aortitis and chronic periaortitis: correlation with CT morphological, clinical and serological data. The British journal of radiology 2015; 88:20150526

**Disclosure of Interest:** None declared

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## FRI0383 PREDICTORS OF FRAGILITY FRACTURES IN PATIENTS WITH POLYMYALGIA RHEUMATICA ON STEROIDS: AN OBSERVATIONAL STUDY

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**Background:** Fragility fractures are a consequence of poor bone health, this is especially seen in patients on corticosteroids. Polymyalgia rheumatica (PMR) is usually treated with corticosteroids for a median of two years (1). The predictors of fragility fractures in this cohort have not been explored in a large observational cohort. Furthermore it is unknown which other risk factors for Osteoporosis contribute to the risk of fractures in this cohort The FRAX™ tool uses the BMD in the femoral neck as a predictor for fracture, the ability of the lumbar spine bone mineral density (BMD) to increase prediction of fragility fracture has not been explored.

**Objectives:** To explore the further predictors of fragility fractures in patients with PMR on corticosteroids and to explore the added predictive value of lumbar spine BMD.

**Methods:** Patients referred for BMD estimation using a dual X-ray absorptiometry (DEXA) machine to a scanner in the North West of England between 2004 and 2014 were included in the study. Patients with a history of PMR on steroids were extracted. Initially those that sustained a fracture were compared to those that had not sustained a fracture using the chi squared test for categorical variables and Students T test for continuous variables. The predictors of fracture in that cohort were explored using a logistic model, initially in a univariate manner, and subsequently in a stepwise logistic model. Predictors included age at scan in years, gender, smoking, excess alcohol consumption, the presence of rheumatoid arthritis, body mass index (BMI) and family history of fragility fracture in addition to BMD in the lumbar spine and femoral neck.

**Results:** 703 patients were included in the analysis, 525 (74.7%) were female. Mean age was 70.4 years (SD 8.9 years). 154 (21.9%) had sustained a fracture. Comparing the patients who had and who had not sustained a fracture showed that they were more likely to be female 138/525 (26%) vs 16/178 (9%) ($p<0.001$), older 72.5 years (SD9.0) vs 70.0 (SD8.8) p=0.002 and have a lower BMD in the lumbar spine and the femoral neck. The results of the logistic models unadjusted and adjusted for age are shown in table 1 below with significant values denoted with an asterisk (*)

Table 1

| Variable | Unadjusted OR (95%CI) | Adjusted OR (95%CI) |
|---|---|---|
| Age at scan in decades | 1.39 (1.131.71)* | – |
| Female gender | 3.61 (2.08,6.25)* | 3.90 (2.24,6.80)* |
| Smoking | 1.07 (0.74,1.55) | 1.09 (0.75,1.59) |
| Alcohol excess | 0.40 (0.14,1.16) | 0.44 (0.15,1.28) |
| Rheumatoid arthritis | 0.37 (0.08,1.59) | 0.38 (0.09,1.65) |
| Body mass index (kg/m$^2$) | 1.00 (0.97,1.03) | 1.01 (0.98,1.05) |
| Family history of fracture | 1.32 (0.67,2.62) | 1.57 (0.78,3.15) |
| L1-L4 BMD | 0.07 (0.03,0.19)* | 0.08 (0.03,0.21)* |
| Femoral neck BMD | 0.03 (0.01,0.11)* | 0.04 (0.01,0.15)* |

In the multivariate model aside from age, female gender (OR 2.010 95%CI 1.11,3.99) and femoral neck but not lumbar spine BMD remained in the model (OR 0.07 95%CI 0.01,0.59), surprisingly family history of fracture (OR 2.21 95%CI 1.01,4.84) and a higher BMI (OR 1.06 95%CI 1.01,1.10) also were significant predictors.

**Conclusions:** In this cohort of patients the females, older patients and low BMD in the femoral neck were all associated with fractures, which is not unexpected, however added risks were identified which are not necessarily clinically obvious. BMD in the lumbar spine did not add to the predictive value of sustaining a fracture. Further prospective work is needed to validate these findings.

**References:**

[1] doi:10.1093/rheumatology/kep303b

**Disclosure of Interest:** None declared

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## FRI0384 HEALTHCARE UTILIZATION AND DIRECT MEDICAL COSTS OF GIANT CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is the most common systemic vasculitis in patients aged ≥50 years. Few studies have evaluated the economic impact of this condition and have been limited to inpatient-only data sources. Although the majority of healthcare for patients with GCA is provided as an outpatient, utilization and costs from this healthcare sector is largely unknown.

**Objectives:** To determine the health care utilization and direct medical cost of GCA in a population-based cohort.

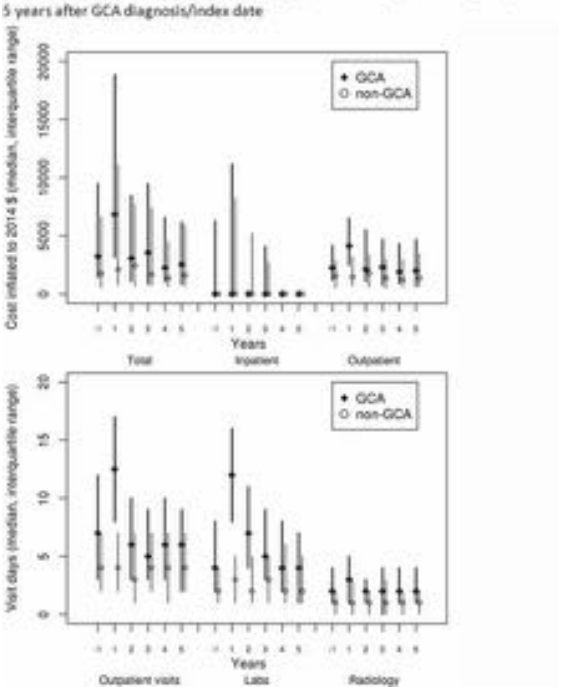
**Methods:** This study utilized a retrospective, population-based cohort of patients diagnosed with GCA, as defined by 1990 ACR criteria, in 1982–2009 and a reference cohort of patients without GCA matched on age, sex, and calendar year from the same population. Standardized cost data (inflation-adjusted to 2014 dollars) for 1987–2014 and outpatient utilization data for 1995–2014 were obtained from the Mayo Clinic Cost Data Warehouse and analyzed from one year before and up to five years after the GCA diagnosis/index date. Utilization and costs were compared between GCA and non-GCA cohorts using signed rank two-tailed paired analyses.

**Results:** The GCA cohort consisted of 147 patients (118 female, 29 male) with a mean (±SD) age of 77.2 (±8.2). The non-GCA cohort comprised 147 patients with a mean (±SD) age of 76.9 (±8.5) years.

During the year preceding diagnosis, excess healthcare cost related to GCA was only significantly increased in the month immediately preceding GCA diagnosis [mean (±SD) excess cost $1127 (±5154)]. Following diagnosis, significant annual excess outpatient cost was observed for patients with GCA in each of the first four years [mean excess cost (±SD): 0–1 yrs $1307 (±15581), $p<0.001$; 1–2yrs $908 (±5917), p=0.009; 2–3 yrs $1324 (±4648), p=0.007; 3–4 yrs $609 (±4596), p=0.04] but was similar between GCA and non-GCA subjects in the 5th year. There were no significant differences in inpatient costs between GCA and non-GCA subjects.

Patients with GCA had higher utilization of laboratory visit days annually for each of the first 3 years following diagnosis, as well as increased outpatient physician visits and combined radiology for years 0–1, 1–2, and 3–4 years (figure). Ophthalmologic procedures/surgery were increased for years 0–1, 1–2, and 4–5. Emergency medicine visits, musculoskeletal and cardiovascular procedures/surgery were similar between GCA and non-GCA groups throughout the study period.

Figure. Costs (upper panel) and utilization of health care resources (lower panel) in patients with GCA and non-GCA subjects by year of followup from one year prior to 5 years after GCA diagnosis/index date




**Conclusions:** Direct medical costs were increased in the month preceding and outpatient costs were increased in the first 4 years following GCA diagnosis and then return to levels similar to non-GCA subjects. A higher utilization of outpatient physician, laboratory and radiology visits, as well as ophthalmologic procedures among these patients accounts for the observed increased cost of care.

**Disclosure of Interest:** None declared

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## FRI0385 CLINICAL CHARACTERISTC OF VALVULAR INVOLVEMENT IN TAKAYASU'S ARTERITIS

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**Background:** Takayasu's arteritis (TKA) is a chronic large-vessel vasculitis that predominantly affects aorta and its major branches. Cardiac lesion in TKA could reach up to 8.6%, involving valve, myocardium and coronary artery or secondary to hypertension or pulmonary hypertension due to TKA [1]. The valvular involvement is one of the causes for the unfavorable prognosis of TKA [2]. Limited data about TKA with valvular involvement in Chinese patients have been reported yet.
**Objectives:** To investigate the clinical features of valvular lesions in TKA.
**Methods:** We retrospectively analyzed 22 medical records of TKA with valvular lesions from a total of 116 TKA admitted patients in Anzhen Hospital, Capital Medical University from January 2012 to January 2015.
**Results:** The spectrum of valvular involvements were aortic regurgitation (11,50%,), mitral regurgitation (1,4.5%), aortic stenosis (1,4.5%), mitral stenosis (1,4.5%) and multiple valvular disease (7,36.5%). 64.7% of the aortic regurgitation patients had aortic root dilation. Heart failure was the commonest manifestation (63.6%). Patients with aortic regurgitation were more likely to be positive for elevated erythrocyte sedimentation rate than those without aortic regurgitation (i58.8% vs. 0, P=0.04). Glucocorticoid and/or immunosuppression were administered on 11 (50%) patients. One (4.5%) patient received Tocilizumab injection. Surgeries were performed on 12 (54.5%) patients with cardiac architecture changing reversibly within one week after operation ($P<0.05$, Table 1). Three patients had aortic valve detachment or perivalvular leakage 6–36 months after primary valvular surgery. Three patients died during 10–46 month follow-up, with none of whom taking any anti-inflammatory treatments.

Table 1. Comparison of echocardiogram before and after cardiac operation in 12 Takayasu's arteritis patients with valvular lesion (x ± SD)

| | Pre-operation | Post-operation | P value |
|---|---|---|---|
| Aortic root (mm) | 41.64±8.79 | 26.50±5.84 | 0.004 |
| Ascending aorta (mm) | 44.17±7.89 | 28.33±5.05 | 0.017 |
| Interventricular septum (mm) | 9.88±1.28 | 10.58±1.57 | 0.102 |
| Main pulmonary artery (mm) | 25.09±2.39 | 24.18±3.97 | 0.356 |
| Left atrium (mm) | 47.08±14.98 | 35.17±10.18 | 0.014 |
| Left ventricular end-diastolic diameter (mm) | 58.50±5.92 | 48.50±10.03 | 0.001 |
| Left ventricular end-systolic diameter (mm) | 41.75±7.85 | 36.00±11.01 | 0.006 |
| Posterior wall of left ventricle (mm) | 9.40±1.46 | 10.41±1.62 | 0.096 |
| Posterior wall motion of left ventricle (mm) | 9.87±1.92 | 8.97±2.70 | 0.296 |
| Right ventricular (mm) | 19.91±3.83 | 18.55±3.50 | 0.236 |
| Ourflow tract of right ventricular (mm) | 26.80±5.27 | 21.80±4.49 | 0.004 |
| Ejection fraction (%) | 53.42±9.88 | 53.75±12.13 | 0.841 |

**Conclusions:** Aortic regurgitation is the prominent valvular lesion in TKA, mainly secondary to aortic root dilation. Operation could cut off the myocardium reconstruction promptly. The early surgical complication is rare, while perivalvular leakage may occur during longstanding follow-up. Poor inflammatory control might lead to adverse prognosis.
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**Disclosure of Interest:** None declared
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## FRI0386 IMMUNOGENICITY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN PATIENTS WITH VASCULITIS RECEIVING STANDARD OF CARE THERAPY AND CONTROLS

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**Objectives:** To study the effect of standard of care therapy on antibody (Ab) response and functionality of Abs following pneumococcal vaccination using 13-valent conjugate vaccine (PCV13) in patients with systemic vasculitis compared to healthy controls.
**Methods:** In total 49 patients with vasculitis (granulomatosis with polyangiitis=21, Churg-Strauss vasculitis=8, giant cell vasculitis=13; Takayasu=4 and other vasculitis=3) and 49 controls were immunized with a single dose (0.5 ml) PCV13 intramuscularly. Vasculitis patients were treated with azathioprine (n=11), cyclophosphamide +prednisolone (n=6), MTX (n=9), prednisolone without DMARD (n=16), rituximab+DMARDs (3); anti-TNF (n=2), mycophenolate mofetil (n=1) and no active treatment (n=1). Only patients with unchanged dose of DMARDs for at least 4 weeks before vaccination were eligible for the study. Blood samples were taken immediately before and 4–6 weeks after vaccination. Standard ELISA was used to determine pre- and post-PCV13 serotype-specific Ab concentrations for serotypes 6B and 23F. The measurement of functional Abs against one of serotypes (23F) was performed using opsonophagocytic (OPA) assay. Proportions of individuals with postvaccination Ab concentrations $\geq$1.0 μg/mL (i.e. putative protective levels) for both serotypes were determined, and groups were compared using Chi2 test. Proportion of individuals with positive Ab response (i.e. $\geq$2-fold increase from pre-PCV13 concentrations) for both serotypes was calculated. Geometric mean Ab concentrations (GMCs) were calculated. Pre- and post-PCV13 Ab levels were compared using paired T-test. Controls were younger (mean age 50.6 years vs 61.5 years) at vaccination and a larger proportion were women (63% vs 51%). Mean disease duration in vasculitis patients was 5.2 years.
**Results:** Pre- to post-PCV13 Ab concentrations increased significantly for 6B and 23F in both patient and control groups ($p<0.001$). Compared to controls, patients with vasculitis had lower pre- and postvaccination Ab levels for serotype 23F (p=0.012 and p=0.033, respectively) and numerically but not statistically significant lower pre- and post-PCV13 levels for 6B (Table). OPA shows significant increase after vaccination in both patients and controls ($p<0.001$) although this was numerically more pronounced in controls. Patients receiving any DMARD had significantly lower proportion of subjects reaching protective Ab concentrations ($\geq$1.0 μg/mL) for both serotypes (p=0.04) compared to controls. In addition, patients on DMARDs had lower proportion of responders for both serotypes which was most pronounced for azathioprine and rituximab+DMARD. Prednisolone without DMARD was not associated with impaired Ab responses.

| | Patients with vasculitis | Controls |
|---|---|---|
| Pre PCV13 GMC Pn6B (95% CI) | 0.5 (0.3–0.9) | 0.8 (0.5–1.3) |
| Post PCV13 GMC Pn6B (95% CI) | **1.7 (0.9–2.9)** | 3.**1 (1.9–5.0)** |
| Pre PCV13 GMC Pn23F (95% CI) | 0.3 (0.2–0.4) | 0.6 (0.4–1.0) |
| Post PCV13 GMC Pn23F (95% CI) | **1.8 (1.2–2.8)** | **3.3 (2.0–5.5)** |

**Conclusions:** PCV13 was immunogenic in patients with established vasculitis. Functionality of serotype specific antibodies was confirmed in both patients and controls although the opsonophagocytotic activity was more pronounced in controls. Treatment with DMARDs, mostly azathioprine or rituximab combined with DMARD but not systemic prednisolone lead to impaired antibody response.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2764

## FRI0387 PERIPHERAL NEUROPATHY IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA). INCAT DISABILITY SCORE TO EVALUATE DAMAGE AND TO PREDICT LONG TERM OUTCOME IN 50 PATIENTS

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**Background:** Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare necrotizing vasculitis characterized by bronchial asthma, hypereosinophilia and extrapulmonary granulomatous inflammation. One of the most frequently involved organ is the peripheral nervous system (PNS), followed by the lung and the skin. PNS involvement is usually characterized by mononeuritis multiplex or symmetrical peripheral neuropathy. Administration of corticosteroids and immunosuppressive agents typically achieves remission and results in good survival rates. However, patients may suffer from chronic residual functional deficits caused by neuropathy even after remission has been achieved. Although such deficits may disrupt the day-to-day functioning and quality of life, studies to target the residual neuropathy are still poor.
**Objectives:** VDI can't precisely indentify the severity of peripheral neurologic damage, so we propose the INCAT (Inflammatory Neuropathy Cause and Treatment) disability score, to evaluate long term outcome and damage in this patients.
**Methods:** We selected retrospectively patients affected by EGPA, satisfying ACR criteria, followed up by Rheumatology and Clinical Immunology Units, from 2005 through 2015. Basic demographic, duration of disease, clinical and serological features, treatments of each patient were routinely monitored at baseline, six, twelve months and last visit. Disease activity, relapses, damage and neurological involvement were also evaluated with Birmingham Vasculitis Activity Score (BVAS v3), Vasculitis Damage Index (VDI) and INCAT disability score. The INCAT score ranges from 0 (no signs of disability) to 10 (most severe disability). Statistical analyses were done using Mann Whitney test, Spearman correlation and Fisher's exact test.
**Results:** 50 patients were included, middle aged (49.9±13.8 years), mainly women (31:19). Twentyfive patients (50%) presented with peripheral neurological involvement; this patients were older (56.3±13.4 yrs, p=0.0009) and mostly ANCA positive (48%, p=0.015). Patients who presented with an INCAT score $\geq$3, compared to those with a lower score, at baseline (52%, 13/25), had also at the end of follow up (6.3±3.8 yrs) a higher INCAT score (2.7±1.2, $p<0.0001$), higher VDI (2.70±1.48, p=0.0046) and mostly relapses with a peripheral neurological flare (46%, 6/13). These patients were also treated more frequently with cyclophosphamide (76.9%, p=0.034). In all patients INCAT score was also significantly correlated to VDI (p=0.0046), but not to BVAS.
**Conclusions:** INCAT disability score measures daily activities limitation and it's used frequently as a primary end point in inflammatory polyneuropathy clinical trials. It's easy to administer and can be completed quickly, imposing a minimal burden on the administrator and the responder. It appears to be a valid tool, able

to evaluate peripheral neurological damage, treatment response and to predict long term outcome. Further studies in a larger patients cohorts are needed.

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**Disclosure of Interest:** None declared

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## FRI0388 USSEFULNES OF BVAS AND FFS AT DIAGNOSIS TO PREDICT SURVIVAL IN ANCA ASSOCIATED VASCULITIS (AAV)

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**Background:** The Birmingham Vasculitis Activity Score (BVAS), and the Five Factor Score (FFS) at the time of diagnosis have been shown useful to asses prognosis in AAV (1,2), but few studies have been done comparing these tools to predict survival

**Objectives:** To compare the usefulness of BVAS vs 3, 1996 FFS and 2009 FFS at the time of diagnosis, to predict survival in a large cohort of patients with AAV from Spain

**Methods:** multicenter retrospective-longitudinal study that included patients diagnosed with AAV between Jan1995 and Nov13 in 20 Hospitals from Spain (REVAS Study). Patient survival was assessed by life-table analysis using the Kaplan-Meier method. Statistical analysis was done using SPSS vs21

**Results:** 455 patients were included: 188 (41.3%) GPA, 167 (36.7%) MPA and 100 (22%) EGPA; 50.8% were men. Mean age at diagnosis was 55.7±17.2 y. ANCA were positive in 86.8% of cases: 35.8% C-ANCA and 51% P-ANCA. Median time to diagnosis was 4 weeks (IQR 10). Median follow-up time was 80 months (IQR 105) for global population. Renal involvement was present in 61.5% of cases, lung involvement in 54.7%, pulmonary-renal syndrome in 16.9%, neurological involvement in 34.5%, and cardiac involvement in 12.7%. ENT was observed in 44.8% of cases and eye involvement in 18.9%. Mean BVAS at diagnosis was 17.7±7.7; 1996FFS was $\leq$1 in 390 (85.8%) patients, and 2009FFS was $\leq$2 in 361 (79.4%). All patients received oral corticoids, 342 (75.1%) cyclophosphamide (49.7% IV and 50.3% oral), and 6.6% biological therapy. Dialysis was required in 16.4% of cases. During the follow-up, 39.1% of patients suffered bacterial infections, 9.2% sepsis,12.7% opportunistic infections and 5.3% neoplasms. One hundred thirty (28.6%) died:74 (44.3%) with PAM, 42 (22.3%) with GPA and 14 (14%) with EGPA ($p<0.001$). Univariate analysis showed that BVAS, 1996FFS and 2009FFS at diagnosis were significantly related to death ($p<0.001$). A multifactorial Cox regression analysis including the three activity scores confirmed that all of them were statistically related to survival rate but the stronger predictor of poor prognosis was the 2009FFS with a HR 2.7. This result was confirmed by curve ROC: 2009FFS showed the greater area under the curve (75%), in front of 1996FFS (66%) and BVAS (62%)

**Conclusions:** BVAS and FFS at diagnosis are signifivantly related to survival in AAV, but the stronger predictor of survival is the 2009 FFS.

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**DOI:** 10.1136/annrheumdis-2016-eular.2427

## FRI0389 AN INCREASE IN TREG- AND TH2-ASSOCIATED SERUM CHEMOKINES, MDC (CCL22) AND TARC (CCL17) DURING TOCILIZUMAB MONOTHERAPY IN PATIENTS WITH MICROSCOPIC POLYANGIITIS

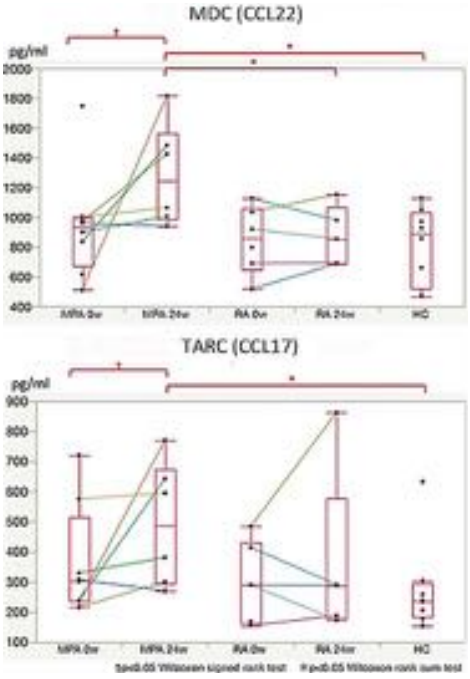
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**Background:** We have recently reported a case series that tocilizumab (TCZ) monotherapy without corticosteroids (CSs) may be an alternative treatment strategy in patients with microscopic polyangiitis (MPA). We found that four of six patients (66.7%) could be maintained drug-free after TCZ cessation for 6–15 months [1]; however, the mechanism remains unclear.

**Objectives:** To elucidate the TCZ efficacy mechanism in patients with MPA, we examined multiple serum levels of cytokines and chemokines in patients with MPA at 0 (baseline), 4, and 24 weeks after initiating TCZ monotherapy and compared the outcomes with those of healthy controls (HC) and patients with rheumatoid arthritis (RA).

**Methods:** The patients employed in this study were newly diagnosed with MPA (n=8; 71.0 ± 7.4 years) according to the Watts' classification algorithm, RA (n=6; 54.5 ± 13.0 years) according to the 2010 RA classification criteria, and HC (n=8, 65.1 ± 9.5 years). All MPA and RA patients received 8 mg/kg of intravenous TCZ monthly for 1 year without any CS or disease-modifying antirheumatic drugs, except for six out of eight patients with MPA who fortnightly received TCZ for the first 2 months, and then monthly for the next 10 months [1]. Multiple cyto- and chemokines in the serum of patients at 0, 4 and 24 weeks of the treatment of TCZ were analyzed by micro-spot-based multiplex assays using electrochemiluminescence. Complete remission (CR) was defined as the Birmingham Vasculitis Activity Score (BVAS) of 0 at two consecutive visits made at least a month apart, and partial response (PR) was defined as a 50% reduction of BVAS from the baseline.

**Results:** CR/PR was achieved in six out of eight patients with MPA at 6 months (75%, LOCF). MPA at baseline showed elevated levels of various cyto- and chemokines compared with HC, such as IL-10, IL-12/IL-23p40, IL-15, IL-16, IL-17A, IL-1$\alpha$, IL-4, IL-5, IL-6, IL-7, TNF$\alpha$, VEGF-A, IL-8 (CXCL8), IP-10 (CXCL10), MCP-1 (CCL2), MIP-1$\alpha$ (CCL3), MIP-1$\beta$ (CCL4), MCP-4 (CCL13), and eotaxin-3 (CCL26) ($p<0.05$). Conversely, RA at baseline showed elevated levels of cyto- and chemokines compared with HC, such as IL-6, IL-7, IL-16, TNF$\alpha$, VEGF-A, MIP-1$\beta$, eotaxin-3 ($p<0.05$). Moreover, serum levels of MDC (CCL22), TARC (CCL17), GM-CSF, IL-12p70 were not significantly different among these groups. Most of enhanced levels of serum cyto- and chemokines in MPA significantly decreased during the 24 weeks with TCZ monotherapy except IL-12/IL-23p40, IL-4, IL-13, and IL-1$\beta$, whereas only VEGF-A level was significantly decreased in RA under TCZ treatment. Interestingly, only the levels of MDC and TARC in MPA, the Th2 and Treg related chemokines, significantly increased after TCZ monotherapy, but not in RA (baseline vs 24 weeks: $p<0.05$) (Figure 1), even though other Th2 related cyto- and chemokines significantly decreased or remained unchanged.




**Conclusions:** Our study suggest that TCZ monotherapy provides a new insight into the treatment strategy for MPA and TCZ may suppress the disease activities of

MPA by increasing chemokines, such as MDC and TARC while other inflammatory cyto- and chemokines decreased.

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## FRI0390 USE OF MUSCLE BIOPSIES FOR THE DIAGNOSIS OF SYSTEMIC VASCULITIS IN A RHEUMATOLOGY SERVICE

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**Background:** Systemic vasculitis (SV) comprises a group of diseases characterized by inflammation of vessels in various organs. Histopathological confirmation is required for the diagnosis. The biopsy of an involved organ is invasive and carries the risk of complications. By contrast, gastrocnemius muscle biopsy is simple and minimally invasive technique that may be performed by a rheumatologist.

**Objectives:** To evaluate the diagnostic use of muscle biopsies for the diagnosis of SV.

**Methods:** Retrospective study 1984 - 2015. Center: tertiary academic hospital, referral area 850.000 inhabitants. We analyzed the database of all muscular biopsies performed at our hospital. We selected patients undergoing a muscular biopsy for possible diagnosis of SV and we analyzed the clinical, laboratory, neurophysiological and pathologic data. Biopsies were classified as positive (presence of necrotizing vasculitis or non necrotizing vasculitis seen by optical microscopy) or negative for vasculitis. Muscular biopsy was performed in all cases at the medial gastrocnemius muscle ("open" and unilateral) by a rheumatologist. The diagnosis of SV was based on clinical, serological and histological data.

**Results:** A total of 619 muscular biopsies were performed, 55 were indicated with suspicion of SV, 52.7% female, 47.3% male, median age 64.4 years (DS 15.22); 47 (85.4%) were positive (sensitivity of 85%) and 8 (14.6%) were negative. The positive biopsy group showed more electromiographic alterations (p=0.01) than negative group. Furthermore, the positive biopsy group showed more frequently systemic manifestations such as: weight loss, myalgia, paresthesias, purpura and testicular pain but these differences were not statistically significant. No complications were encountered in the procedure.

| Features | Biopsy-positive | Biopsy-negative | p-value |
|---|---|---|---|
| ANCA positive/negative | 20 (54.1%)/17 (45.9%) (n=37) | 4 (50%)/4 (50%) | 0,8 |
| Serum VSG (mm), mean (sd) | 58.2 (35.6%) | 64.7 (36.3%) | 0.6 |
| Hemoglobine (g/dL), mean (sd) | 11.2 (1.4%) | 10,25 (1.3%) | 0.8 |
| Weight loss (≥2 kg) | 13 (27.7%) | 2 (25%) | 0,8 |
| Fever | 20 (42.5%) | 5 (62.5%) | 0.3 |
| Myalgia/arthralgia | 18 (38.3%)/12 (25,5%) | 3 (37,5/ 2 (25%) | 0.9 |
| Paresthesias | 20 (42.6%) | 2 (25%) | 0,3 |
| Purpura | 7 (14.9%) | 1 (12.5%) | 0.8 |
| Testicular pain | 3 (6.4%) | 0 | 0.4 |
| Legs ulcers | 5 (10.6%) | 2 (25%) | 0,3 |
| Abdominal/calf pain | 3 (6.4%)/12 (25.5%) | 1 (12.5%)/ 3 (37.5%) | 0,5 |
| Patologic EMG | 36 (76.6%) | 2 (25%) | 0.01 |

**Conclusions:** Our results suggest that muscle biopsy is a simple, clinically useful, safe and minimally invasive procedure for the diagnosis of SV with high sensitivity. No significant differences were observed in clinical or analytical features between patients with positive or negative biopsy, except in electromyography patients with positive biopsy had more a frequent pathological pattern.

**Disclosure of Interest:** None declared

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## FRI0391 ANKLE BRACHIAL INDEX, PULSE WAVE VELOCITY AND ECHOCARDIOGRAPHIC STUDY IN 81 PATIENTS WITH BEHÇET'S DISEASE

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**Background:** Behçet's disease (BD) is a multisystemic vasculitis of unknown etiology. Cardiovascular (CV) involvement has been reported in 1–6% of BD patients. In case of CV involvement, prognosis is poor. The incidence of the CV involvement in Korean patients with BD is not clearly documented.

**Objectives:** The aim of this study is to evaluate the CV findings in Korean patients with BD and to prevent or lower mortality and morbidity through early diagnosis and early treatment.

**Methods:** We performed Ankle Brachial Index (ABI), Pulse wave velocity (PWV) and Echocardiographic screening in 81 patients with BD who fulfilled the International Study Group criteria. PWV was calculated as the brachial-ankle path length divided by the brachial-ankle transit time (baPWV). We compared the result between two groups of patients with BD. Two groups are patients who have been treated with immunosuppressant agent and without immunosuppressant agent. The patients of former group are patients who have been suffered from severe complication or refractory disease.

**Results:** Fifty-nine (72.8%) patients were female. Mean age was 50.6 ± 2.5 years old. Mean age at diagnosis was 40.5 ± 2.3 years old and disease duration was 10.2 ± 1.5 years. Mean ABI was 1.10 ± 0.03. There was no significant difference between with and without immunosuppressant agent treated group. (1.11 ± 0.03 vs. 1.09 ± 0.03, P=0.167). The number of patients with abnormal ABI was 7 (17.5%) vs. 6 (14.6%), P=0.781. Mean PWV (m/sec) was 14.0 ± 0.67. There was no significant difference between two groups (13.8 ± 1.09 vs. 14.2 ± 0.83, P=0.144). But the immunosuppressant treated group had more patients with elevated levels of PWV (>12.0 m/sec) compared to non-immunosuppressant treated group [n =34 (82.9%) vs. n=25 (62.5%), P=0.024]. Echocardiography was done. Left ventricular ejection fraction (%) (64.9 ± 1.5 vs. 63.7 ± 1.7, P=0.254), Left ventricular mass index ($g/m^2$) (74.9 ± 5.0 vs 74.1 ± 5.7, P=0.970), E/E' ratio (8.35 ± 0.9 vs 9.17 ± 1.0, P=0.228), Tricuspid regurgitating velocity (TRV) max (m/sec) (2.35 ± 0.09 vs 2.39 ± 0.11, P=0.572) were similar in both groups. We detected 39 minimal mitral, aortic and tricuspid valve insufficiencies. One patient showed suspiciously resting pulmonary hypertension (TRVmax – 3.3m/sec). In two patients, dilatation of ascending aorta was showed. There was aortic arch mass in one patient.

**Conclusions:** The CV involvement in BD can be a cause of death. In this screening study, asymptomatic patients showed many CV manifestations. And in 59 (72.8%) patients, PWV was elevated. Arterial stiffness can be a surrogate marker of CV disease. Larger study about CV manifestations in BD must be planned. And during treatment of patients with BD, CV screening study needs to be considered.

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**Disclosure of Interest:** None declared

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## FRI0392 ULTRASONOGRAPHIC SCORING REVEALED THAT THE RATIO OF EXTRA-SYNOVIAL INFLAMMATION TO SYNOVIAL INFLAMMATION IN THE SHOULDER IS HIGHER IN PMR PATIENTS THAN THAT IN ELDERLY-ONSET RA PATIENTS WITH PMR-LIKE ONSET

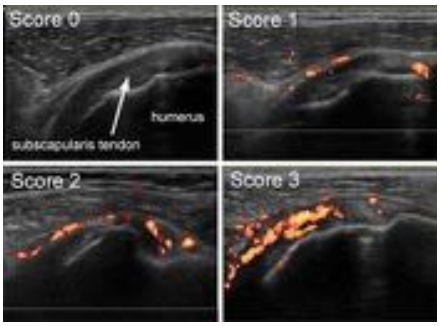
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**Background:** We previously reported that shoulder synovitis in polymyalgia rheumatica (PMR) is milder than that in elderly-onset rheumatoid arthritis (EORA) patients with PMR-like onset (polymyalgic-EORA) by using semi-quantitative ultrasound (US) scoring of the synovial components in the shoulder in spite of the higher serum CRP (1).

**Objectives:** We aimed to evaluate the contribution of the extra-synovial inflammation in PMR patients by power Doppler (PD) US.

**Methods:** We analyzed US records of 14 untreated PMR patients and 14 untreated polymyalgic-EORA patients using a semi-quantitative four-point scale (0 = absent, 1 = mild, 2 = moderate or 3 = severe). For the comprehensive evaluation of shoulder synovitis, the severity of the biceps tenosynovitis, subacromial/subdeltoid bursitis and glenohumeral joint synovitis were subjectively scored on a gray scale and by PD on a 4-point scale (0–3). The sum of six scores (0–18) for one shoulder was defined as shoulder synovitis score (SSS). For the evaluation of extra-synovial inflammation in the shoulder, the hyperemia adjacent to the anterior

aspect of the subscapularis tendon (SubST) was analyzed in the horizontal long axis view. The severity of PD-signals on SubST was subjectively scored on a 4-point scale (0–3) as exemplified in the figure, and the score was defined as the extra-synovial hyperemia score (ESHS).
**Results:** The ESHS/SSS ratio was significantly higher in PMR shoulders than in polymyalgic-EORA shoulders (0.447 ±0.251 vs 0.303 ±0.277, p=0.0138). The bilateral ESHS/bilateral SSS ratio was significantly higher in PMR patients than in polymyalgic-EORA patients (0.475 ±0.269 vs 0.236 ±0.182, p=0.00776).




**Conclusions:** Semi-quantitative US scoring of the synovial and the extra-synovial components in the shoulder revealed the larger involvement of the extra-synovial soft tissue inflammation in PMR patients than in EORA patients with PMR-like onset.
**References:**
[1] Arthritis Rheumatol. 2015; 67 (suppl 10)
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2602

FRI0393 **CUT-OFF VALUES FOR INTIMA-MEDIA THICKNESS OF TEMPORAL, FACIAL AND AXILLARY ARTERIES IN GIANT CELL ARTERITIS**

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**Background:** Ultrasound (US) is increasingly used in the diagnosis of giant cell arteritis (GCA). US findings mainly rely on morphology ("halo-sign" and "compression sign"). Increasing resolution of modern US probes allows exact intima-media thickness (IMT) measurement of normal and vasculitic temporal arteries. No data have yet been published on IMT of temporal, facial and axillary arteries in GCA patients compared to healthy controls.
**Objectives:** To evaluate the mean IMT thickness of arteries commonly involved in GCA in GCA patients and controls, and to determine if cut-off values can define pathology.
**Methods:** Fourty newly diagnosed GCA patients of a fast-track GCA clinic and 40 age- and sex-matched controls were included between October 2014 and December 2015. The diagnosis of GCA was established by two very experienced rheumatologists (WAS or AJ) on the basis of clinical presentation, laboratory tests and US results. The diagnosis was confirmed after 6 months in patients who were included until July 2015. IMT measurement was performed at or within 24 hours after the first visit. The common superficial temporal arteries with their frontal and parietal branches and the facial arteries were bilaterally examined with a 10–22 MHz probe (Esaote MyLab Twice). A 6–18 MHz probe was used for both axillary arteries. In total, IMT measurement was performed at 800 sites. The mean IMT values of the different arteries were compared between controls and patients with active vasculitis of the corresponding artery by means of a Mann-Whitney test. ROC analysis was performed to determine the best cut-off value, balancing sensitivity and specificity, to discriminate between a normal and a vasculitic artery.
**Results:** Both groups of 40 participants, each, included 27 females. The mean age was 72 years (SD 9).
Of the 40 GCA patients, 22 (55%) had indurated temporal arteries on clinical examination, 16 (40%) had symptoms of polymyalgia rheumatica. The mean duration of symptoms was 15 weeks (SD 19). Five patients (13%) had visual impairment (anterior ischaemic optic neuropathy, 3; amaurosis fugax, 1; diplopia, 1). Twenty-eight patients (70%) described headache; and 17 (43%) had jaw claudication. The mean ESR was 82 mm/h (SD ± 28); and the mean CRP was 107 mg/dL (SD 79). In 26 patients (65%) the axillary arteries were involved of whom 9 had no involvement of temporal arteries.
Table 1 shows IMT of affected arteries in GCA patients compared to controls and cut-off values for distinguishing normal from inflamed arteries.
Maximum IMT of controls and minimum IMT of vasculitic segments in GCA was 0.34 mm/0.42 mm for the common superficial temporal arteries, 0.32 mm/0.34 mm for the frontal branch, 0.31 mm/0.24 mm for the parietal branch, 0.42 mm/0.31 mm for the facial artery and 0.86 mm/1.0 mm in the axillary arteries, i.e. no overlap occurred in the common superficial temporal arteries, the frontal branch and the facial arteries.

*Table 1: Measurements and cut-off values for each artery*

| Artery | N | IMT in mm | Cut-off in mm | Sensitivity | Specificity | Correctly classified |
|---|---|---|---|---|---|---|
| Common superficial temporal artery | 40 | C: r. 0.23 (SD 0.03) l. 0.23 (SD 0.04) | r. 0.42 l. 0.45 | 100 % 100 % | 100 % 100 % | 100 % 100 % |
| | 28 | P: r. 0.66 (SD 0.18) l. 0.65 (SD 0.19) | | | | |
| Frontal branch | 40 | C: r. 0.19 (SD 0.03) l. 0.19 (SD 0.04) | r. 0.35 l. 0.34 | 100 % 100 % | 100 % 100 % | 100 % 100 % |
| | 26 | P: r. 0.53 (SD 0.19) l. 0.55 (SD 0.18) | | | | |
| Parietal branch | 40 | C: r. 0.19 (SD 0.03) l. 0.20 (SD 0.03) | r. 0.32 l. 0.29 | 100 % 94.4 % | 100 % 100 % | 100 % 98.3 % |
| | 25 | P: r. 0.51 (SD 0.18) l. 0.48 (SD 0.16) | | | | |
| Facial artery | 40 | C: r. 0.24 (SD 0.05) l. 0.23 (SD 0.05) | r. 0.37 l. 0.40 | 92.3 % 81.8 % | 100 % 97.5 % | 98.1 % 94.1 % |
| | 15 | P: r. 0.55 (SD 0.19) l. 0.51 (SD 0.19) | | | | |
| Axillary artery | 40 | C: r. 0.59 (SD 0.10) l. 0.59 (SD 0.10) | r. 1.1 l. 1.0 | 100 % 100 % | 100 % 100 % | 100 % 100 % |
| | 26 | P: r. 1.80 (SD 0.41) l. 1.62 (SD 0.39) | | | | |

IMT, intima-media thickness; C, controls; P, GCA patients; r, right side; l, left side

**Conclusions:** IMT measurement of temporal, facial and axillary arteries can correctly distinguish vasculitic from normal arteries in suspected GCA in addition to morphological parameters. Data for wall diameters are needed for future longitudinal trials to monitor GCA treatment.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2760

## Spondyloarthritis - clinical aspects (other than treatment)

FRI0394 **ASSESSMENT OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH SPONDYLOARTHRITIS AND THEIR ASSOCIATION WITH DISEASE FEATURES AND ITS ACTIVITY. A COMPARISON BETWEEN TWO POPULATION GROUPS FROM ASAS-COMOSPA**

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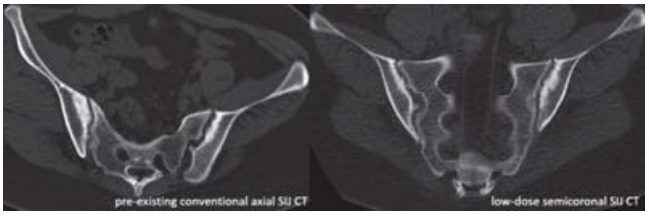
**Background:** Data from epidemiologic studies suggest that patients with Spondyloarthritis (SpA) have an increased risk of developing cardiovascular disease[1] (CVD). In healthy people this risk is different depending on the country, ambient factors and lifestyle. However, in SpA patients these differences have not been studied yet, so it is unknown whether they are attributable to the socio-demographic factors or to the disease itself and its activity.
**Objectives:** To assess the prevalence of cardiovascular risk factors in SpA patients by making a comparison between two population groups which have socio-demographic differences, and to recognize the items which define the variability of the Framingham risk score.
**Methods:** An observational, cross-sectional and multicenter study which included 1982 patients with SpA selected from the ASAS-COMOSPA register and belonging to two groups of countries: Northern Europe (UK, Germany, Belgium and Netherland) and Mediterranean Basin countries (Spain, France, Italy, Morocco, Turkey and Egypt).
Univariate logistic regressions, stratified by sex and disease duration (with a cut-off of 10 years) were performed to contrast the two groups of countries and the cardiovascular risk factors (smoking, BMI, dyslipidemia, diabetes, renal deficiency, family history, ischemic heart disease and stroke).
A multiple linear regression was performed in order to determine the variability in Framingham risk score attributable to different items (socio-demographics, disease related factors and disease activity).
**Results:** There were 1336 (67.40%) patients from Mediterranean basin countries and 646 (32.60) from Northern Europe; 797 (40.21%) were women and 1185 (59.78%) were men.
Men and women from Northern Europe have a higher frequency in smoking (OR 1.85 and OR 1.37 respectively). However, for both sex, HTA (OR 0.48 and OR 0.45) and ischemic heart disease (OR 0.25 and OR 0.29) is less frequent than in those from Mediterranean countries.
It is less frequent obesity (OR 0.70 and OR 0.50), HTA (OR 0.49 and OR 0.59) and ischemic heart disease (OR 0.21 and OR 0.47) in patients from Northern Europe countries, both in a disease duration of $<10$ and $\geq 10$ years respectively,

than in patients from Southern countries. In patients with a disease duration of <10 years, it is also less usual dyslipidemia (OR 0.66) and renal deficiency (OR 0.24).
In the overall population, 70.5% of Framingham risk score was explained by sex, age, disease duration, belonging to Northern countries, current smoking, number of tender joints, physician's global assessment (all of them $p<0.001$) and erythrocyte sedimentation rate (being the latter one a confounding factor, p=0.091).
**Conclusions:** Northern Europe patients with SpA have a lower cardiovascular risk than those from Mediterranean basin countries, both women and men. However these differences can't be only attributable to socio-demographic characteristics, because disease related factors and disease activity are contributory causes in the appearance of cardiovascular risk.
**References:**
[1] Bremander A, et al. Population-based estimates of common comorbidities and cardiovascular disease in ankylosing spondylitis. Arthritis Care Res (Hoboken) 2011;63:550–6.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3292

## FRI0395 LOW-DOSE SEMI-CORONAL CT OF THE SACROILIAC JOINTS IN THE EARLY DIAGNOSIS OF ANKYLOSING SPONDYLITIS

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**Background:** Imaging modalities are essential for the diagnosis of ankylosing spondylitis (AS). Radiographic sacroiliitis is the requirement of 1984 modified New York (mNY) criteria for AS but with the disadvantage of low sensitivity. MRI has the advantage of detecting active inflammatory lesions but was criticized for low specificity. Computerized tomography (CT) has higher diagnostic accuracy than radiography in detecting structural changes, but its application has been limited for high radiation dose. The reduction of radiation dose can be achieved by decreasing the tube current[1] and previous study has demonstrated that effective dose (ED) of semi-coronal sacroiliac joint (SIJ) CT is at least six times lower in female or nearly four times lower in male than that of axial SIJ CT[2].
**Objectives:** To evaluate the value of low-dose semi-coronal SIJ CT in the early diagnosis of AS.
**Methods:** Thirty-three patients diagnosed by mNY criteria who had pre-existing axial SIJ CT in past two years with visible structural damage were enrolled. These patients underwent low-dose semi-coronal SIJ CT examination which was obtained at 3-mm slices, 140 kV and 120 mAs, with the gantry tilted 20–25° cranially. The ED of the low-dose semi-coronal CT and the pre-existing conventional axial CT were compared. Image qualities of the low-dose semi-coronal CT were blind-graded separately by 2 rheumatologists into poor, fair, good or excellent. And the correlation between image quality and body mass index (BMI) was analyzed. The CT scans were read in a blinded manner by 2 rheumatologists who had been trained by radiologists. CT scans of the two groups were graded respectively by mNY criteria, the criteria established by Lee[3] and the Innsbruck criteria[4]. The kappa coefficient was used to assess the consistency of grading between the two groups.
**Results:** Thirty-three patients received low-dose semi-coronal CT examination with an average ED of 3.37 mSv, which meant a 49% reduction in radiation compared to the pre-existing CT. The quality of images of male patients with BMI<25 kg/m$^2$ and all female patients were good or excellent. Image qualities were assessed as poor or fair in 58% (7/12) male patients whose BMI>25 kg/m$^2$. There was a significant negative correlation between image quality and BMI (r=-0.784,*P*=0.000). The grading of low-dose semi-coronal CT showed no differences as compared with the pre-existing CT by mNY criteria (see below). For the other two classification criteria, the consistency of grading between the two groups were satisfactory (kappa=0.897 by Lee criteria; kappa=0.814 by Innsbruck criteria; $P>0.05$).




**Conclusions:** The radiation dose of low-dose semi-coronal SIJ CT was reduced significantly compared with the conventional axial SIJ CT with acceptable diagnostic efficacy.
**References:**
[1] Gurung J, et al. Multislice CT of the pelvis: dose reduction with regard to image quality using 16-row CT. Eur Radiol. 2005;15:1898–905.
[2] Jurik AG, et al. Effective radiation dose from semicoronal CT of the sacroiliac joints in comparison with axial CT and conventional radiography. Eur Radiol. 2002;12:2820–5.
[3] Lee YH, et al. Value of multidetector computed tomography for the radiologic grading of sacroiliitis in ankylosing spondylitis. Rheumatol Int. 2013;33:1005–11.
[4] Klauser A, et al. Workshop report: clinical diagnosis and imaging of sacroiliitis, Innsbruck, Austria, October 9, 2003. J Rheumatol. 2004;31:2041–7.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4683

## FRI0396 WHICH IS THE MOST RELIABLE IMAGING METHOD FOR DETECTION OF STRUCTURAL CHANGES IN THE SACROILIAC JOINTS OF PATIENTS WITH ANKYLOSING SPONDYLITIS? A CROSS-SECTIONAL STUDY COMPARING MRI, CT AND CONVENTIONAL RADIOGRAPHS

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**Background:** Magnetic resonance imaging (MRI) is the gold standard for detection of inflammation and fat metaplasia in the sacroiliac joints (SIJ) and the spine of patients with axial spondyloarthritis (axSpA). Structural changes (erosions, sclerosis and ankylosis) assessed by conventional radiographs (CR) or computed tomography (CT) are characteristic for ankylosing spondylitis (AS). Direct comparisons of these imaging techniques have not been performed to date.
**Objectives:** Compare the reliability of CR and MRI as compared to CT for detection of structural changes in SIJs of AS patients.
**Methods:** Complete sets of MRI, CT and CR of SIJs of 69 AS patients and 49 age- and gender-matched controls in whom CTs had been performed for other reasons than back pain were analyzed. Two readers evaluated the images independently and blinded to diagnosis and clinical characteristics in random order. Assessment of lesions was performed based on SIJ-quadrants (SQ). Only definite erosions, sclerosis and ankylosis were recorded, and only SQ changes for which readers agreed on were used for analysis.
**Results:** The mean age of AS patients was 44.6 years, 72.5% were male, 85.5% were HLA-B27 positive, the mean time since diagnosis was 4.8±5.8 years (range 1 14 years), the mean BASDAI was 4.9±1.8 and the mean CRP was 1.9±2.3mg/dl. In total, 552 SQ (276 pairs) were analyzed. *Erosions* were found in 131 (23.7%) SQ by CR, 141 (25.5%) by CT and in 167 (30.3%) SQ on T1-MRI. Agreement for erosions was seen for 64 SQ assessed by CR/CT, 100 SQ by CT/MRI and 70 SQ by CR/MRI, with 48.9% of SQ detected by CR also seen on CT and 45.4% detected on CT also seen by CR. The corresponding numbers for CT/MRI were 70.9% and 59.9% and for CR/MRI 53.5% and 41.9%, respectively. Disagreement for erosions was found in 144 (26.1%), 108 (19.6%) and 158 (28.6%) SQ, respectively. *Sclerosis* was seen in 86 SQ on CR (15.6%), 91 SQ on CT (16.5%) and 63 on T1-MRI (11.4%). Agreement was found in 31 SQ on CR/CT, 22 SQ on CT/MRI and 45 SQ on CR/MRI, with 36.0% SQ detected on CR also seen on CT and 34.1% detected on CT also seen by CR. The corresponding numbers for CT/MRI were 24.2% and 34.9% and for CR/MRI 52.3% and 71.4%. Disagreement for sclerosis was found in 95 (17.2%), 72 (13.0%) and 66 (12.0%) SQ, respectively. *Ankylosis* was seen in 91 SQ pairs on CR (33,3%), 130 SQ pairs on CT (47,1%) and 106 SQ pairs on MRI (38,4%). Agreement was found in 87 SQ pairs on CR/CT, 94 SQ pairs on CR/MRI and 72 SQ pairs on CT/MRI, with 95.6% SQ detected on CR also seen on CT and 66.9% detected on CT also seen by CR. The corresponding numbers for CT/MRI were 72.3% and 88.7% and for CR/MRI 79.1% and 67.9%. Disagreement for ankylosis was seen in 47 (17.0%), 48 (17.4%) and 53 (19.2%) SQ pairs, respectively.In controls, 392 SQ were analyzed. Erosions were found in only 19 (4.8%) SQ and sclerosis in 23 (5.9%) SQ, while no patient showed ankylosis.
**Conclusions:** Erosions and ankylosis are more common than sclerosis in SIJs of AS patients and rarely seen in controls. The agreement between methods was rather limited. Compared to CT, less erosions were detected by MRI and CR when only erosions agreed on were counted. CT and MRI were more reliable than CR for the detection of ankylosis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5954

## FRI0397 THE DIAGNOSTIC VALUE OF THE SYMPTOM OF INFLAMMATORY BACK PAIN IN AXIAL SPONDYLOARTHRITIS IN THE RHEUMATOLOGY SETTING

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**Background:** Inflammatory back pain (IBP) as a symptom has been shown to perform effectively for selecting patients in primary care/orthopaedic settings for referral of chronic back pain patients to the rheumatologist for further diagnostic work-up. IBP is also being used as a diagnostic test of axial spondyloarthritis (axSpA) by rheumatologists, but no validations studies have been performed so far with IBP as a diagnostic tool.
**Objectives:** The aim of the DIVERS study was to evaluate the diagnostic value of the IBP symptom in axSpA in the rheumatology setting.

**Methods:** A total of 405 consecutive patients referred to a rheumatologist because of chronic back pain starting at an age <45 years and suspicion of axSpA were included in this multicentre study. A questionnaire containing all relevant IBP parameters was first answered by the patient, followed by a rheumatologist blinded for presence or absence of other SpA features and for the diagnosis, and finally by the rheumatologist responsible for the diagnosis. A global evaluation of IBP by rheumatologists, and IBP according to the previously published Calin's, Berlin and ASAS criteria as well as single items of IBP were compared regarding their diagnostic performance.
**Results:** The diagnosis of definite axSpA was made in 180 (44.4%) patients (88 with ankylosing spondylitis and 92 with non-radiographic axSpA). The sensitivity, specificity and the positive likelihood ratio of IPB for the axSpA diagnosis was 81%, 44%, and 1.5, respectively, if globally assessed by the blinded rheumatologist, and 90%, 58% and 2.2, respectively, if globally assessed by the diagnosing rheumatologist - table. There was no clear superiority of any of the three criteria sets regarding sensitivity for the axSpA diagnosis with an overall sensitivity of about 80% and specificity between 25% and 45% if symptoms were assessed by a rheumatologist - table. The performance of the criteria sets based on patient's own evaluation of IBP symptoms was generally lower. No single IBP parameter showed superiority regarding sensitivity or specificity in comparison to the criteria sets.

Table. Sensitivity, specificity, a positive and a negative predictive value (PPV and NPV) of inflammatory back pain (IBP) for the diagnosis of axSpA.

| Assessor | IBP according to... | Sensitivity, % (95% CI) | Specificity, % (95% CI) | PPV (95% CI) | NPV (95% CI) | LR+ | LR- |
|---|---|---|---|---|---|---|---|
| Blinded rheumatologist | Global evaluation | 81.3 (75.4-86.3) | 44.0 (37.6-50.5) | 53.9 (48.0-59.8) | 74.2 (66.8-81.7) | 1.5 | 0.4 |
| | Calin's criteria | 79.4 (73.5-85.4) | 24.9 (19.2-30.5) | 45.8 (40.3-51.4) | 60.2 (50.3-70.2) | 1.1 | 0.8 |
| | Berlin Criteria | 81.1 (75.4-86.8) | 32.4 (26.3-38.6) | 49.6 (43.5-54.7) | 68.2 (59.6-77.1) | 1.2 | 0.6 |
| | ASAS criteria | 76.4 (68.1-83.8) | 39.6 (31.2-45.9) | 49.4 (43.7-55.4) | 65.9 (57.9-73.6) | 1.2 | 0.7 |
| Diagnosing rheumatologist | Global evaluation | 90.8 (83.4-94.4) | 58.2 (51.8-64.7) | 65.3 (57.4-69.2) | 87.9 (82.6-93.2) | 2.2 | 0.2 |
| | Calin's criteria | 85.8 (79.8-90.2) | 26.7 (20.9-32.6) | 48.1 (42.6-53.6) | 69.0 (59.2-78.7) | 1.2 | 0.6 |
| | Berlin Criteria | 81.9 (75.5-88.3) | 44.0 (38.4-51.6) | 54.9 (49.0-60.8) | 77.3 (70.3-84.9) | 1.5 | 0.4 |
| | ASAS criteria | 83.3 (78.5-88.3) | 35.6 (29.3-41.8) | 51.8 (45.3-56.7) | 73.4 (65.1-81.7) | 1.3 | 0.5 |
| Patient | Calin's criteria | 75.3 (68.8-81.3) | 39.4 (33.1-25.7) | 46.8 (37.5-48.6) | 58.8 (49.2-61.0) | 0.9 | 1.2 |
| | Berlin Criteria | 86.4 (82.4-91.3) | 18.6 (12.9-23.7) | 46.8 (42.6-51.3) | 69.3 (51.3-74.8) | 1.1 | 0.7 |
| | ASAS criteria | 76.8 (67.3-80.3) | 35.2 (29.1-37.2) | 46.3 (40.5-52.1) | 68.0 (51.1-69.0) | 1.3 | 0.8 |

**Conclusions:** IBP demonstrated high sensitivity but rather modest specificity for the diagnosis of axSpA among patients with chronic back pain referred to a rheumatologist. A resulting moderate diagnostic value of IBP in the rheumatology setting is likely to be counterbalanced by increase in the pre-test probability of axSpA in this patients population.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2892

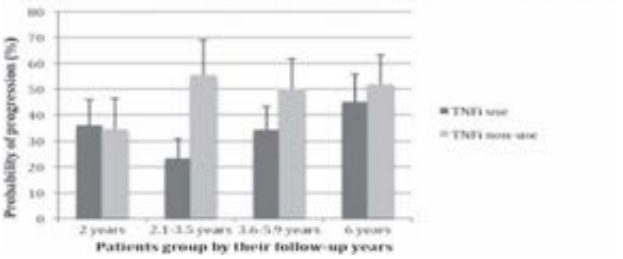
## FRI0398 PHARMACOLOGIC THERAPY AND RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS: A GROWING CONTROVERSY

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**Background:** Pharmacologic therapies in Ankylosing Spondylitis (AS) have informed debatable effects on radiographic progression. Two-year studies using Tumor Necrosis Factor inhibitors (TNFi) showed no benefit, yet longer-term studies reported less radiographic progression. Similarly, NSAID effects have been controversial.
**Objectives:** To determine the relationship between pharmacologic therapies and radiographic progression in AS.
**Methods:** This is a prospective cohort of 505 AS patients meeting the modified New York criteria with at least 2 years of radiographic follow up. Using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), progressors were defined with at least one mSASSS unit increase per year of follow up or patients who rapidly progressed at any time point (2 new syndesmophytes in 2 years). Patients with an mSASSS=72 at baseline (n=17) were excluded. TNFi use was defined at each 6-month study visit and adjusted for baseline use and total duration of use. High NSAID use was defined if the patient was taking NSAIDs at least 50% of the study period. We grouped patients according to their follow-up period (interval between baseline and last visit) and used progressor status (progressor vs. non-progressor) as a dichotomized outcome in univariable and multivariable mixed effects logistic regression models.
**Results:** The progressors made up 35.45% of the cohort (n=179). We found that TNFi use was related to a lower likelihood of radiographic progression and this association appeared to be strongest for patients with 2.1–3.5 years of follow-up (OR=0.25, 95% CI 0.07,0.92; p=0.0376). Although not statistically significant, in patients who were followed up for 3.6 years or longer, the odds of progression for the TNFi user group was 46% lower in the 3.6–5.9 year group (OR=0.54) and 23% lower in the 6+ year group (OR=0.77) than in TNFi non-users. Patients exposed to NSAIDs (≥50% exposure) also had a lower likelihood of radiographic progression (OR=0.47, 95% CI 0.22,0.99); p=0.046) [Table 1]. The probability of progression by years of follow up per TNFi user group is shown in Figure 1.

| Label | Odds Ratio | p-value |
|---|---|---|
| *TNFi* follow-up (FU) year group* | | |
| TNFi user vs. no for patients with FU year 2 | 1.10 (0.34, 3.60) | 0.87 |
| **TNFi user vs. no for patients with FU year 2.1–3.5** | **0.25 (0.07, 0.92)** | **0.04** |
| TNFi user vs. no for patients with FU year 3.6–5.9 | 0.54 (0.17, 1.72) | 0.29 |
| TNFi user vs. no for patients with FU year 6– | 0.77 (0.23, 2.59) | 0.67 |
| **High NSAID user vs. no** | **0.47 (0.22, 0.99)** | **0.04** |
| **Baseline mSASSS** | **1.03 (1.02, 1.05)** | **<0.0001** |
| **Disease duration >10 years** | **1.97 (1.15, 3.39)** | **0.01** |
| **Male gender** | **1.95 (1.06, 3.60)** | **0.03** |
| Education > college | 1.11 (0.58, 2.14) | 0.74 |
| **Current smoking** | **2.52 (1.23, 5.16)** | **0.01** |
| # Comorbidity ≥1 | 1.17 (0.69, 1.97) | 0.56 |
| Baseline BASDAI ≥40 | 1.04 (0.60, 1.81) | 0.88 |
| Baseline BASFI ≥40 | 0.94 (0.49, 1.78) | 0.84 |
| **Baseline CRP (high)** | **1.69 (1.03, 2.78)** | **0.03** |

**Figure 1. Probability of progression in patients exposed to vs. not exposed to TNFi**




**Conclusions:** TNFi use is associated with a lower likelihood of radiographic progression in AS with the most significant effect after longer than 2 years of follow up. Use of NSAIDs was also associated with less radiographic progression.
**Disclosure of Interest:** L. Gensler Consultant for: AbbVie, Amgen, Janssen, Novartis, UCB, J. Reveille: None declared, M. Ward: None declared, M. Brown Grant/research support from: Janssen, Abbvie, UCB, Leo Pharma, Complete Genomics, Consultant for: Abbvie, UCB, Janssen, Pfizer, Speakers bureau: Abbvie, UCB, Pfizer, UCB, M. Rahbar: None declared, M. Lee: None declared, M. Weisman Grant/research support from: UCB, Human Genome Sciences, Sanofi, Eli Lilly and Co, Genentech, Inc., Santarus Inc., EMD Serono, ChemoCentryx, GSK, Immunomedics Inc., Consultant for: Boehringer Ingelheim/Proskauer, Ardea Biosciences, Epirus Biopharmaceuticals, Acerta Pharma
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## FRI0399 BACKFILL IS MORE IMPORTANT THAN EROSION AND FAT DEPOSITION IN DIAGNOSING AXIAL SPONDYLOARTHRITIS AS SEEN ON MRI

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**Background:** The structural lesions in patients with axial spondyloarthritis (SpA) seen on magnetic resonance imaging (MRI) include erosion, fat deposition, backfill and ankylosis. Backfill is the new tissue fills in the excavated bone in the sacroiliac joint (SIJ) which can be seen on T1SE MRI. Recent studies have shown that backfill is a key intermediary step in the development of ankylosis in patients with axial SpA. But data comparing the diagnostic value of backfill and other lesions is rare.
**Objectives:** To record erosion, fat deposition and backfill seen on T1SE MRI and to evaluate whether backfill is more important than other lesions in diagnosing axial SpA.
**Methods:** Three readers investigated erosion, fat deposition and backfill seen on T1SE MRI scans from 423 patients with axial SpA and 224 subjects with non-specific back pain (NSBP) or healthy (classified as control group). The SPARCC SIJ Structural Score (SSS) method was used to assess these three kinds of lesion. The sensitivity, specificity and positive likelihood ratio (LR) of three kinds of lesion for diagnosing axial SpA were calculated.
**Results:** 246 axial SpA patients (58.2%) were recorded with backfill, 343 (81.1%) were recorded with erosion, and 372 (88.0%) were recorded with fat deposition. While in healthy controls, only 4 (1.8%) were seen with backfill, 26 (11.6%) were with erosion, and 43 (19.2%) were with fat deposition. The SSS score of backfill, erosion, and fat deposition were all much higher in axial SpA patients than in control group (backfill: 2.8 ± 1.6 vs. 0.1± 0.7; erosion: 18.4 ± 9.7 vs. 4.5 ± 6.3; fat deposition: 25.8 ±17.2 vs. 16.4 ± 18.1; all p<0.01). The sensitivity and specificity of backfill, erosion, and fat deposition for diagnosing axial SpA were (0.58, 0.98),

(0.81, 0.88), and (0.88, 0.81), respectively. The positive LR of using backfill to diagnose axial SpA was quite high (32.6), while it was moderate for erosion (7.0) and fat deposition (4.6).
**Conclusions:** Backfill is more important than erosion and fat deposition in diagnosing axial spondyloarthritis as seen on MRI.
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## FRI0400 A FIVE YEAR PROSPECTIVE STUDY OF SPINAL RADIOGRAPHIC PROGRESSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** The knowledge about what predicts progress of syndesmophytes that characterize patients with ankylosing spondylitis (AS) is limited. The strongest known predictor for radiographic progression in the spine is existing syndesmophytes at baseline.
**Objectives:** To study the radiographic progression in the spine in AS patients in total and by gender and search for predictors for the changes.
**Methods:** 204 patients with AS, all meeting the New York criteria, from three rheumatology departments in western Sweden were included in a longitudinal study. At baseline and after five years lateral radiographs of the cervical and lumbar spine were obtained and graded according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). All radiographs were assessed by the same experienced radiologist (MG). Predictors were assessed through questionnaires, back mobility tests and blood samples.
**Results:** Of the 204 patients included at baseline, 169 (83%) patients were re-examined at the five year follow-up, 92 (54%) men and 77 (46%) women. At baseline, the median age (IQR) of the 169 patients was 49 (40 to 61.5) years old and the median duration of symptoms (IQR) was 22 (12 to 34) years, no significant difference in age or duration of symptoms between gender. Baseline mean mSASSS was 14.9±20.0 with progression to 16.4±20.8 at follow-up, an increase with 1.5±3.0 units ($p<0.001$). In men, mean baseline mSASSS was 22.0±23.5 and at follow-up 23.8±23.8, an increase of 1.8±2.8 units ($p<0.001$). In women, mean baseline mSASSS was 6.4±9.6 and 7.6±11.7 at follow-up, an increase of 1.2±3.3 ($p=0.002$). The mSASSS score at both baseline and at follow-up differed significantly between gender ($p<0.001$), whereas the progression of mSASSS did not differ significantly ($p=0.2$) between the groups. The presence of syndesmophytes at baseline was 47% in the whole group, 59.0% for men and 32.5% for women (p-value difference gender $<0.001$). In the total group 18.9% had had significant progression ($\geq$4 mSASSS units over five years), 23.9% of the men and 13.0% of the women ($p=0.11$). Such rapid progression of mSASSS was in age-adjusted logistic regression models significantly predicted by baseline syndesmophyte and mean CRP during follow-up in men and baseline BASMI in women (table).
**Conclusions:** The progression rate was 1.5±3.0 mSASSS units over five years and did not differ significantly between men and women, although being much higher in men at baseline in this cohort of AS patients with longstanding disease. Presence of existing syndesmophytes and persistent elevated CRP during follow-up were significant predictors for a change in $\geq$4 mSASSS units over five years in men whereas in women instead high BASMI was a significant predictor.

Table. Univariate logistic regression analyses adjusted for age, with increase of ≥4 mSASSS units during 5 years as dependent variable. Covariates are baseline values, except for CRP and treatment (mean during follow-up).

| | Men (N=92) | Women (N=77) |
|---|---|---|
| **Covariates** | **OR (95% CI)** | **OR (95% CI)** |
| Pack years (per year) | 1.03 (0.99 to 1.08) | 0.76 (0.53 to 1.10) |
| History of anterior uveitis | 1.77 (0.63 to 4.97) | 0.90 (0.22 to 3.63) |
| **BASMI, score (0-10, per unit)** | 1.10 (0.79 to 1.53) | **2.60 (1.27 to 5.32)** |
| **Presence of syndesmophyte** | **7.26 (1.75 to 30.18)** | 3.29 (0.82 to 13.26) |
| **Mean CRP during follow-up >10 mg/L** | **5.23 (1.69 to 16.18)** | 0.86 (0.09 to 8.13) |
| NSAID-index, 0-100 (per unit) | 1.00 (0.99 to 1.01) | 1.00 (0.98 to 1.02) |
| Part of time TNFi during follow-up, 0-1 (per unit) | 1.29 (0.39 to 4.30) | 2.46 (0.40 to 15.20) |
| Part of time bisphosphonate during follow-up, 0-1 (per unit) | 2.96 (0.52 to 16.76) | 4.12 (0.58 to 29.47) |

BASMI, Bath Ankylosing Spondylitis Metrology Index, CRP, C-reactive protein, NSAID, non-steroidal anti-inflammatory drug; TNFi, tumor necrosis factor inhibitor. For dichotomous variables, no was coded 0, yes 1.

**Disclosure of Interest:** None declared
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## FRI0401 SAFETY OF RESUMING TUMOR NECROSIS FACTOR INHIBITORS IN ANKYLOSING SPONDYLITIS PATIENTS CONCOMITANT WITH THE TREATMENT OF ACTIVE TUBERCULOSIS: A RETROSPECTIVE NATIONWIDE REGISTRY OF THE KOREAN SOCIETY OF SPONDYLOARTHRITIS RESEARCH

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**Background:** Patients who develop an active tuberculosis infection (TI) during tumor necrosis factor (TNF) inhibitor treatment typically discontinue TNF inhibitor and receive standard anti-tuberculosis treatment. However, there is currently insufficient information on patient outcomes following resumption of TNF inhibitor treatment during ongoing anti- tuberculosis treatment.
**Objectives:** Our study designed to investigate the safety of resuming TNF inhibitors in ankylosing spondylitis (AS) patients who developed TI as a complication of the use of TNF inhibitors.
**Methods:** Through the nationwide registry of the Korean Society of Spondyloarthritis Research, 3929 AS patients were recruited who were prescribed TNF inhibitors between June 2003 and June 2014 at fourteen referral hospitals. Clinical information about the patients who experienced TI after exposure to TNF inhibitors was analyzed. The clinical features of resumers and non-resumers of TNF inhibitor were compared and the outcome of TI was surveyed individually.
**Results:** Fifty-six AS patients were treated for TI associated with TNF inhibitors. Among them, 23 patients resumed TNF inhibitors and these patients were found to be exposed to TNF inhibitors for a longer period of time and experienced more frequent disease flare up after discontinuation of TNF inhibitors compared with those who did not resume. Fifteen patients resumed TNF inhibitors during anti-tuberculosis treatment (early resumers) and 8 after completion of TI treatment (late resumers). Median time to resuming TNF inhibitor from TI was 3.3 and 9.0 months in the early and late resumers, respectively. TI was treated successfully in all resumers and did not relapse in any of them during follow-up (median 33.8 (IQR; 20.8–66.7) months).

| | Total patients (n = 56) | Resumers (n = 23) | Non-resumers (n = 33) | *P* |
|---|---|---|---|---|
| Age, yr (median, IQR) | 43.0 (32.9-55.8) | 43.3 (32.8 - 47.7) | 39.3 (33.3 – 61.9) | 0.16 |
| Male sex, n (%) | 50 (89.3) | 22 (95.7) | 28 (84.8) | 0.19 |
| Disease duration, yr (median, IQR) | 8.9 (5.9-13.4) | 9.3 (6.1 – 13.4) | 8.5 (5.9 – 13.9) | 0.54 |
| LTBI, n (%) | 15 (26.8) | 6 (26.0) | 9 (27.3) | 0.94 |
| Previous TI history, n (%) | 10 (17.8) | 5 (21.7) | 5 (15.2) | 0.53 |
| Type of TNFi at TI infection | | | | 0.07 |
| Infliximab, n (%) | 23 (41.7) | 13 (56.5) | 10 (30.3) | |
| Adalimumab, n (%) | 21 (37.5) | 8 (34.8) | 13 (39.4) | |
| Etanercept, n (%) | 12 (21.4) | 2 (8.7) | 10 (30.3) | |
| Duration of total TNFi exposure, mon (median, IQR) | 27.8 (11.2-64.0) | 42.8 (19.1-72.0) | 24.1 (7.0-36.7) | 0.03 |
| Increased AS activity after stopping TNFi, n (%) | 36 (64.3) | 21 (91.3) | 15 (45.5) | <0.001 |

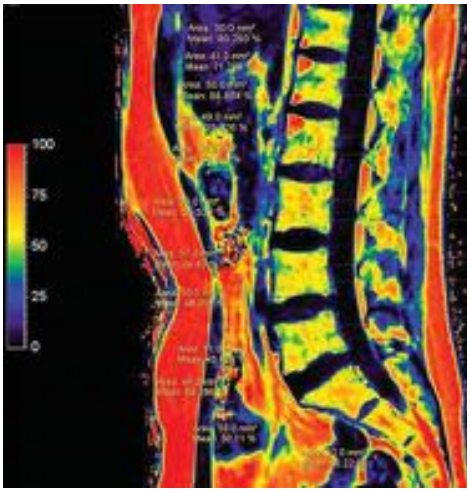
**Conclusions:** TI were treated successful in our AS patients, even when given

concomitantly with TNF inhibitors. We suggest that early resuming TNF inhibitors in AS patients could be safe under effective coverage of the TI.
**Disclosure of Interest:** None declared
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## FRI0402 QUANTIFICATION OF FAT FRACTION OF VERTEBRAL BONE MARROW IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Focal fat deposition is frequently seen on magnetic resonance imaging (MRI) of the spine in patients with ankylosing spondylitis (AS)[1]. Fat metaplasia in bone marrow is known as one of disease progression in AS[2].
**Objectives:** To evaluate clinical characteristics and the correlation between bone marrow fat-signal fraction (FF), Bath AnkylosingSpondylitis Disease Activity Index (BASDAI), Bath AnkylosingSpondylitis Functional Index (BASFI) and modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).
**Methods:** A total of 55 patients with AS who underwent a spine MRI at our institution from March 2015 to December 2015 were retrospectively evaluated. Quantification of vertebral bone marrow was assessed on the FF maps using the three-point Dixon technique[3]. FF was quantified after measuring the signal intensity within the region of interest (ROI) over anterosuperior and anteroinferior corner of bone marrow where there was no contamination from the bony cortex or syndesmophyte. The ROIs were drawn twice in sagittal FF map and average was used. mSASSSs were independently recorded by two musculoskeletal radiologists. Correlation, univariate and multivariate regression analyses were done for identifying significant predictors of FF.
**Results:** Patients had a mean age of 35.6±10.5 years, and 43 were male (78.2%). A significant correlation was found between FF, mSASSS, BASDAI, and BASFI (p=0.005, p=0.021, and p=0.050)in Pearson correlation analysis. Multivariate regression analysis showed that decrease total BASDAI associated with to increase FF (p=0.005). Measurements of mSASSS had excellent intraobserver (mean intraclass correlation coefficient [ICC] = 0.997 [95% confidence interval (CI): 0.994–0.999] and interobserver agreement (mean ICC =0.941–0.995).However, erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) did not correlated with FF.




**Conclusions:** The quantitative assessment of FF using MRI might be another useful novel imaging technique to correlateactivity index of AS.
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**Disclosure of Interest:** None declared
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## FRI0403 EXPLORING THE NATURAL HISTORY OF BONE MARROW OEDEMA LESIONS IN AXIAL SPONDYLOARTHRITIS: WHEN TO REPEAT AN MRI?

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**Background:** MRI determined bone marrow oedema (BMO) lesions in the sacroiliac joints (SIJ) and spine have both diagnostic and prognostic value in axial spondyloarthritis (axSpA). It is unclear how quickly BMO may change on MRI and MRI scans are often normal in early axSpA. There is no clear evidence to guide the role of repeat MRI in the early diagnosis of axSpA.
**Objectives:** To identify:1. If negative MRI scans in patients with clinically suspected axSpA may become positive within a 12-week period. 2. The natural change in BMO MRI lesions over 12-weeks in patients with IBP
**Methods:** 29 patients, <40yrs, fulfilling ASAS Inflammatory Back Pain (IBP)criteria, with normal SIJ x-rays were recruited from 2 sites in the UK. Participants had MRI scans at baseline, 4, 8, and 12 weeks (total 109 scans). The MRI protocol included sagittal T1 and STIR cervico-thoracic and thoraco-lumbar spine and coronal oblique T1 and STIR sequences of the SIJs. NSAIDs were allowed if either continued at stable doses or discontinued throughout the study. Scans were read by consensus by 2 experienced readers unaware of clinical details or date sequence using the Leeds MRI Scoring system. In addition, each scan was scored as either positive or negative according to the ASAS definitions for the SIJ and spine.
**Results:** 28 patients completed the study. Male n=18 (66%), HLA-B27+ve n=21 (75%), mean symptom duration 5 (±2.1) years. Regular NSAIDs were used by n=13 (46%) of patients. Mean baseline BASDAI 4.8 (±0.7) and mean baseline CRP 2.7 mg/dl (±1.7). 10 (36%) met the ASAS clinical criteria for axSpA prior to any imaging. 64% (n=18) of the patients were ASAS (spine and SIJ) negative at baseline and remained so during the entire study. 25% (7) were ASAS SIJ positive, 0.04% (1) were ASAS spine positive and 7% (2) were ASAS (spine and SIJ) positive. A total of 4 (14%) patients changed from ASAS axSpA imaging classification criteria negative to positive (spine (n=3) or SIJ (n=1)) during the study. All of these met ASAS clinical arm classification criteria at baseline.
At any time point, 15 patients had 212 lesions in the spine: 185 vertebral corners (98 inflammatory and 87 fatty), 15 inflammatory endplates (3 patients over all time points) and 12 inflammatory posterior elements (3 patients over all time points).
At baseline, there were 22 inflammatory and 18 fatty corner lesions in the spine. 12 inflammatory corner lesions resolved between any 2 time points. 26 new spinal inflammatory corner lesions appeared at any time point when the baseline MRI was normal.
At baseline, BMO was present in 38 (33%) SIJ quadrants. Between any 2 time points, 16 (14%) BMO quadrant lesions resolved and new BMO lesions appeared in 6 (5%) SIJ quadrants.

Table 1. Change in ASAS status between any 2 time points

| | Spine | SIJ |
|---|---|---|
| Negative ASAS status to positive ASAS status | 3 | 1 |
| Positive ASAS status to negative ASAS status | 1 | 0 |
| Unchanged ASAS status | 77 | 82 |
| Total number of repeat scans | 81 | 83 |

**Conclusions:** These findings do not support the routine use of rescanning in new onset IBP cases suspected of having SpA. In a patient with severe IBP and high BASDAI with an initial negative MRI scan, a repeat scan has a 14% chance of changing the diagnosis which would thus make an otherwise ineligible patient suitable for potentially effective therapy
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4092

## FRI0404 ILLNESS PERCEPTIONS AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND OTHER FORMS OF CHRONIC BACK PAIN IN THE SPACE-COHORT

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**Background:** Knowledge about the impact of illness perceptions on Health-Related Quality of Life (HRQoL) in patients (pts) with axial Spondyloarthritis (axSpA) and other forms of chronic back pain (CBP) is lacking.
**Objectives:** To explore the association between illness perceptions and HRQoL in pts with short symptom duration of axSpA and other forms of CBP at baseline.
**Methods:** The Spondyloarthritis Caught Early (SPACE) study includes pts with CBP (≥3 months, ≤2 years, onset <45 years) recruited from 5 European centres. The Revised Illness Perception Questionnaire (IPQ-R) was completed at baseline. In the illness identity dimension, pts reported if they have experienced

and believed that a certain symptom is CBP related. Other illness perceptions and causal dimensions used 5-point Likert scales (1 strongly disagree, 5 strongly agree). HRQoL was assessed by 36-item Short-Form (SF-36). Scale scores ranged from 0 (worst) to 100 (best). Physical (PCS) and Mental Component Summary (MCS) scores were calculated. Univariable regression models were built for each IPQ-R subscale as independent and PCS or MCS as dependent variable. The models were adjusted for age and gender and stratified in case of effect modification by gender ($p<0.10$).

**Results:** 315 pts were included; 123 fulfilled axSpA ASAS criteria and 192 did not fulfil the criteria. Mean age was 31.3 (SD 8.3) years, mean duration of CBP was 13.2 (SD 7.2) months and 36.5% was male. Mean PCS was 28.0 (SD 16.3) for axSpA pts and 24.9 (SD 14.4) for CBP. As the MCS was only slightly decreased compared to the general population (48.0 (SD 13.3) axSpA and 49.7 (SD 11.5) CBP pts), analyses focused on PCS. Pts reported a mean of 4.3 (axSpA) and 4.8 (CBP) symptoms to be associated with back pain. Most reported symptoms were pain and joint stiffness. All other subscales showed a mean of approximately 3, except psychological attributions, risk factors, immunity and accident (mean approximately 2). All pts attributed their complaints mostly to genetic factors. In both pts groups attribution of multiple symptoms to CBP (Figure 1;-1.8 axSpA, -2.1 CBP) was associated with lower PCS. However more dimensions showed association with PCS in axSpA (8) than CBP pts (6). In male axSpA pts belief in severe consequences (-12.1), more negative emotions towards their complaints (-9.3), and stronger belief of psychological attributions as a cause (-8.8) were associated with lower PCS. Whereas in male CBP pts stronger belief in risk factors (-8.1) and immunity as a cause (-10.0) were associated with lower PCS. More illness coherence was associated with higher PCS in male axSpA (6.2) and all CBP pts (2.8). In women consequences (-6.3, axSpA) and strong emotional representations (-4.0, CBP) were statistically significant. No gender differences were found for risk factors (-6.0) or immunity (-5.7) in axSpA and consequences (-7.9) in CBP pts.

**Figure 1:** Linear regression models of Physical Component Scale (PCS) of Health-Related Quality of Life (HRQoL) and subscales of the Revised Illness Perception Questionnaire (IPQ-R) at baseline adjusted for age and gender (n=315)

| Scale | Range | axSpA | Coefficient (SE) | p-value | CBP | Coefficient (SE) | p-value |
|---|---|---|---|---|---|---|---|
| *Illness identity* | | *(n=119)* | | | *(n=175)* | | |
| Identity | 0-15 | | *-1.8 (0.6)* | *0.003* | | *-2.1 (0.5)* | *<0.001* |
| *Illness perceptions* | | *(n=123)* | | | *(n=190)* | | |
| Consequences | 1-5 | Men | *-12.1 (2.7)* | *<0.001* | | *-7.9 (1.1)* | *<0.001* |
| | | Women | *-6.3 (1.9)* | *0.002* | | | |
| Timeline (acute/chronic) | 1-5 | | -1.6 (2.2) | 0.474 | | -2.3 (1.5) | 0.122 |
| Personal control | 1-5 | | 1.8 (2.3) | 0.448 | | 3.0 (1.6) | 0.074 |
| Treatment control | 1-5 | | 2.9 (3.0) | 0.339 | | 2.9 (2.2) | 0.174 |
| Illness coherence | 1-5 | Men | *6.2 (3.0)* | *0.048* | | *2.8 (1.2)* | *0.019* |
| | | Women | -1.5 (1.6) | 0.379 | | | |
| Timeline (cyclical) | 1-5 | | 1.2 (1.8) | 0.503 | | -0.1 (1.3) | 0.938 |
| Emotional representation | 1-5 | Men | *-9.3 (3.0)* | *0.002* | Men | 0.9 (2.4) | 0.712 |
| | | Women | -1.5 (1.9) | 0.419 | Women | *-4.0 (1.2)* | *0.001* |
| *Causal attributions* | | *(n=123)* | | | *(n=191)* | | |
| Psychological attributions | 1-5 | Men | *-8.8 (3.0)* | *0.004* | | -0.5 (1.4) | 0.717 |
| | | Women | -0.3 (0.2) | 0.874 | | | |
| Risk factors | 1-5 | | *-6.0 (2.6)* | *0.023* | Men | *-8.1 (3.0)* | *0.010* |
| | | | | | Women | 3.1 (2.3) | 0.170 |
| Immunity | 1-5 | | *-5.7 (2.0)* | *0.004* | Men | *-10.0 (2.2)* | *<0.001* |
| | | | | | Women | -2.5 (1.6) | 0.114 |
| Accident | 1-5 | | *-3.8 (1.5)* | *0.016* | | -1.1 (1.0) | 0.279 |
| Chance | 1-5 | | -0.4 (1.4) | 0.776 | | -1.8 (1.0) | 0.069 |

**Conclusions:** Negative illness perceptions are associated with lower PCS of HRQoL in pts with axSpA and other forms of CBP. The impact of negative illness perceptions on PCS was more pronounced in men than in women.

**Disclosure of Interest:** None declared

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## FRI0405 EXTRAARTICULAR MANIFESTATIONS IN PATIENTS WITH SPONDYLOARTHRITIS UNDER BIOLOGIC TREATMENT

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**Background:** The spondyloarthritides are a heterogeneous group of interrelated and overlapping chronic inflammatory arthropathies. The increasingly use of DMARDs and biologic treatments has led to a change in the profile of the spondyloarthritis patients as well as in the extraarticular manifestations.

**Objectives:** Analyze the extraarticular involvement in patients with Spondyloarthritis under biologic therapy.

**Methods:** A retrospective observational study was conducted in all the patients diagnosed of spondyloarthritis under biologic treatment in our Day-Care Hospital. We analyzed socialdemographic, serological (HLA-B27, ASCAS, IgA, urate levels), clinical aspects and extraarticular manifestations such as cardiological, mucocutaneous, pulmonary, ophthalmological and renal involvement. The association between subgroup diseases, risk factors and extraarticular manifestations was performed with linear regression analysis SPSS.

**Results:** 394 patients were analyzed. 58.8% were male with median age 51 years. We included 173 (43.96%) Ankylosing Spondylitis (AS), 71 (18.2%) non radiographic spondyloartritis (axial and peripheral Spa), 25 (6.35%) Spondyloarthritis associated with inflammatory bowel disease (IBD), 102 (25.9%) Psoriatic Arthritis (PsA), 18 (4.57%) juvenile idiopathic arthritis (JIA) and 5 (1.27%) reactive arthritis. All the patients had received at least one Anti TNF drug and 31.2%, more than one. Infliximab (38.1%) was the most employed drug, followed by Etanercept (31.2%). 69.6% were HLA-B27 positive and 10.4% had high IgA levels.

57.6% presented extraarticular manifestations. By subgroups, the extraarticular involvement was up to 48% in AS, 19.7% in Spa and 27.8% in JIA. Excluding the mucocutaneous and digestive symptoms, we found nonarticular activity in 31.4% PsA and 31.1% IBD. (See Table bellow).

12.4% had uveitis. Despite the biologic therapy, 6% had ophthalmological flares, 1/3 of which was under optimization strategy. The mucocutaneous involvement was shaped as psoriasis (nail, plaque, inverse and pustular psoriasis), erythema multiforme and erythema nodosum. Only one patient developed psoriasis during treatment. The most common nephrologic manifestations was hematuria (58.9%). 9.6% presented hyperuricemia which incidence was higher in AS than in PsA (55.3% Vs 34.2%). Only 8% of those patients had renal insufficiency. Finally, we would like to highlight the development of cancer in 11 patients (2.79%). 5 patients presented renal cancer (1.27% being all of them diagnosed of HLA-B27 positive AS with axial involvement.

The risk factors statistically associated with the extraarticular activity found were the positivity of HLA-B27 and the hyperuricemia ($p=0.000$, $p<0.002$). We found no correlation with age, sex and hyperIgA. In the development of uveitis, only the HLA-B27 positive was significantly associated.

| Manifestation | Total population | Subtypes |
|---|---|---|
| Uveitis | 12.4% | Acute Anterior 34.3%<br>Recidivating AA 55.1%<br>Chronic 2.05%<br>Posterior 4.1%<br>Non determinate 24.5% |
| Cutaneous | 28.7% | PsA 88.44%<br>Non PsA 9.8%<br>Rest of the cutaneous involvement 1.8% |
| Hyperuricemia | 9.6% | EA 55.3%<br>Spa 2.6%<br>APs 34.2%<br>EII 7.9% |
| Digestive | 10.4% | EII 73.2%<br>Chronic Diarrhea 26.8% |
| Renal | 9.89% | Hematuria 61.5%<br>Renal insufficiency 23.1%<br>Amiloidosis 5.13%<br>TIN 5.13%<br>Proteinuria 5.13% |
| Aortic insufficiency | 2.5% | |
| Pulmonary | 3.8% | EPID 21.4%<br>HTP 28.6%<br>Bronchiectasis 42.9%<br>Nodules 7.14% |

**Conclusions:** We observed a high prevalence of extraarticular manifestations in our sample of patients with Spondyloarthritis under biologic treatment. Nonetheless, the presence of serious manifestations was still low. The hyperuricemia, cutaneous psoriasis and anterior uveitis were the most frequent extraarticular manifestations. The risk factors associated were HLA-B27 positive and the high levels of urate.

**Disclosure of Interest:** None declared

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## FRI0406 PREVALENCE AND SIGNIFICANCE OF RADIOGRAPHIC SACROILIITIS IN A LARGE INFLAMMATORY BOWEL DISEASE POPULATION

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**Background:** Inflammatory bowel disease (IBD) is associated with a myriad of extra-intestinal manifestations (EIMs). Musculoskeletal EIMs are the most common EIM in IBD. Previous studies of sacroiliitis (SI) in IBD have a broad prevalence range of 2%>45%[1–3]. In these patients, HLA-B27 positivity ranged anywhere from 0–50%[1,2,4].

**Objectives:** To determine the prevalence of radiographic SI in a large IBD population, and identify risk factors associated with the development of SI.

**Methods:** 1,247 consecutive patients from our IBD clinic, 350 with ulcerative colitis (UC), and 897 with Crohn's disease (CD) were investigated as long as they had a pre-existing computed tomography (CT) of the abdomen and pelvis. These CTs were re-interpreted for evidence of SI. Each sacroiliac joint was graded

based on the modified New York Criteria[5]. Each patient was classified as having no disease, suspected disease, or definite disease. Definite SI was defined as bilateral grade 2, or unilateral grade 3 or 4. Suspicious SI was defined as unilateral or bilateral grade 1 or unilateral grade 2. Gender, age, type of IBD, HLA-B27 status (by next generation sequencing), and IBD serologies (ASCA, antiCBir1, anti-OMPc, ANCA) were also analyzed.
**Results:** Prevalence of either definite or suspicious SI was found in 16.1% and 19.4% in CD and UC respectively. The prevalence of definite SI was 8.7% and 8.1% in CD and UC respectively. In patients with SI (definite and suspicious), 57% were male and 43% were female. When looking only at the definite group, there 68% males and 32% females (p=0.002). This is in contrast to the suspicious SI group, where there were 48% males and 52% females. Of significance, 16% of patients in the definite SI group were positive for HLA-B27, while only 6% of the patients in the negative group were positive for HLA-B27 (OR 4.36, p=0.006). In the suspicious group, 8% of patients were positive for HLAB27. Definite SI was associated with: anti-Cbir1 (p=0.002) in CD, and ASCA (p=0.05) in UC.
**Conclusions:** In this study, the largest of its kind, we observed an overall SI prevalence of 17% in our IBD cohort. The prevalence of SI seen on CT was similar between UC and CD. Historically, UC and CD occur evenly between genders. However, when gender and SI in IBD were compared, there were more males in the definite group, while in the suspicious group there was a greater predominance of females. It remains unclear if the suspicious group represents a subtle phenotype of SI that has not yet progressed. Significant associations with clinically relevant subsets of IBD defined by serological markers were observed. The observed HLAB27 positivity is at the lower end of what has previously been reported, and is not as strong as is seen in ankylosing spondylitis without IBD. This further suggests that SI and spondylitis in the IBD population are different pathologic entities, with unique genetic risks, compared with the pure AS population.
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## FRI0407 ELECTROPHYSIOLOGICAL CARDIAC REMODELING IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** The question of the defeat of the cardiovascular system in patients with ankylosing spondylitis (AS) is very actual
**Objectives:** To study early pre-clinical parameters of myocardial electric instability and changing the geometry of the myocardium of the left ventricle (LV) in patients with AS and their relationship to the course of the disease.
**Methods:** 30 patients (22 men and 8 women) aged 21 to 56 years (mean 40,3±10,0 years) with significant AS without clinical manifestations of cardiovascular pathology at the time of inspection, in a disease history and/or according to medical records were observed. The duration of AS symptoms at the time of examination was less than 5 years – 15 patients (50%), from 5–10 years – in 5 (16.6%), more than 10 years – in 10 (33.4%) patients. Disease activity (BASDAI) was low in 6 (20%), moderate – in 9 (30%), high – in 7 (23.3%), very high – in 8 (26.7%) patients, the mean BASDAI 5 06 ± 1,4. Echocardioscopy with determination of left ventricular hypertrophy (LVH) according to recommendations of the ASE and EAE (2005/2006) was used to estimate the heart. geometry. The direction of maximum QRS vector to the left and back, the excess of 2.0 mV on the horizontal plane, and 2.2 mV on the frontal plane were assessed by vectorcardiography
**Results:** According to echocardioscopy in 9 (30%) patients with AS revealed changes in the geometry of the heart were found: concentric remodeling – in 2 (22.2%), eccentric hypertrophy – in 4 (44.5%), concentric hypertrophy – 3 (33.3%) patients. Vectorcardiography showed changes in the QRS loop in 4 (13.3%) patients. Also, a change in direction of the maximum vector during normal QRS loop area was revealed, which is associated with an increase in the size of the left ventricular chambers. Changes of the heart geometry were different depending on the AS activity: moderate activity concentric remodeling occurred in 2 (22.2%) patients, high activity–concentric hypertrophy in 3 (33.3%) patients, very high activity–eccentric hypertrophy in 4 (44.5%) ($p \leq 0.05$). The change in QRS loop was in 1 (3.3%) patient with low activity, and in 2 (6.6%) patients with high and very high disease activity. The concentric remodeling was found in 2 (22.2%) patients, concentric hypertrophy – in 3 (33.3%) patients with disease duration from 5 to 10 years; more than 10 years – eccentric hypertrophy in 4 (44.5%) patients.
**Conclusions:** The high frequency of preclinical changes in the geometry of myocardium in AS was assessed, more frequent in patients with high activity and disease duration less than 10 years. According to echocardioscopy, electrophysiological abnormalities in the myocardium were found in patients with saved geometry
**Disclosure of Interest:** None declared
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## FRI0408 A TWELVE MONTH FOLLOW-UP STUDY OF PATIENTS RECRUITED THROUGH SOCIAL MEDIA WHO FULFILLED ASAS/CALIN CRITERIA FOR INFLAMMATORY BACK PAIN

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**Background:** Epidemiology data on inflammatory back pain (IBP) prevalence within the UK is still lacking. Previous studies from the UK show delay in diagnosis of IBP for up to 8 years. This is partly due to lack of awareness among Public and Primary care practitioners. New criteria have been developed to identify conditions at an early stage with a view to reducing times to referral. Our previous work, using social media, helped identify patients with IBP. New IBP classification criteria were applied to the identified patients in the present analysis.
**Objectives:** To follow up IBP positive patients over a twelve month period to see how their back pain had changed, whether treatment was actively sought and what treatment(s) were provided.
**Methods:** A cross-sectional survey was carried out between December 2013 and May 2014 to identify adults (≥18 years) who had IBP. Recruitment was targeted in a novel way to enlist UK participants using social media (Facebook) and national newspaper (Daily Mail) advertisements. Online questionnaire-based surveys supplemented by telephone response were completed. Those participants who fulfilled either the ASAS or Calin criteria at the initial assessment were offered an information leaflet on IBP. The participants were also asked to complete follow-up questionnaires at 6 and 12 months.
**Results:** A total of 586 participants completed the initial survey; of these, 304 (51.87%) satisfied either the ASAS or Calin criteria for IBP. Many patients at both 6 and 12 months follow-up reported that their back pain was unchanged, with more reporting a decline (37% of responses) than an improvement (31% of responses). Evaluation of changes in quality of life using mean EQ5D scores also suggested a small deterioration.
Of the 91 patients who completed a follow-up questionnaire at 6 months 57 (63%) had seen a GP, 6 (7%) had seen a rheumatologist, 16 (18%) had physiotherapy and 8 (9%) were finally diagnosed with a spondyloarthropathy (eg. Ankylosing Spondylitis). Of the 67 patients who completed a follow-up questionnaire at 12 months 41 (61%) had seen a GP, 5 (7%) had seen a rheumatologist, 13 (19%) had physiotherapy and 9 (13%) were finally diagnosed with a spondyloarthropathy. Only 1 patient (1.5%) at 12 month follow-up (none at 6 month follow-up) had received biologic treatment with anti-TNF.
Of the 91 patients who completed the 6 month follow-up questionnaire only 28 downloaded the IBP information leaflet and no new IBP diagnoses resulted.
**Conclusions:** Patients who were IBP positive (ASAS or Calin) in an online survey, many recruited using social media, deteriorated slightly over a 12 month follow-up period. Providing these IBP positive participants with a link to an information leaflet did not result in any new IBP diagnoses. Although most patients had seen a GP, only 7% had seen a rheumatologist despite fulfilling the IBP criteria. Primary care education on IBP is key in the early diagnosis of Spondyloarthropathy.
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## FRI0409 SUBCLINICAL ATHEROSCLEROSIS IN ANKYLOSING SPONDYLITIS. DOES IT REALLY EXIST AND WHICH ARE THE EFFECTS OF TREATMENTS? A SYSTEMATIC REVIEW

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**Objectives:** Accelerated atherosclerosis and increased cardiovascular morbidity and mortality have been associated with ankylosing spondylitis (AS). Noninvasive angiological methods have been developped to evaluate endothelial and vascular dysfunction which is correlated with future development of atherosclerosis. The objectives were to determinate the presence or not of a subclinical vascular dysfunction in AS and if treatments could have an effect on it. A systematic review was done.
**Methods:** Studies evaluating subclinical atherosclerosis and vascular function in AS were identified using Pubmed, (Ovid, EMBASE). Search terms included

"ankylosing spondylitis" AND (endothelial OR vascular OR intima media thickness (IMT) OR Flow mediated dilatation (FMD) OR pulse wave velocity (PWV) OR atherosclerosis). This identified 353 results after limiting to French and English. The final selection identified 29 articles.

**Results:** Overall, 1529 AS patients were included representing 38 studies: 8 studies about endothelial function, 198 AS patients and 130 healthy control (HC); 20 studies about carotid IMT, 900 AS and 644 HC; 10 studies about arterial rigidity, 431 AS and 285 HC. In cross-sectional studies, 4/6 indicated endothelial dysfunction in AS versus HC, 9/18 indicated increased cIMT and 3/5 increased arterial rigidity. About ED, 3 open label studies noted positive effect of TNFα blockers and spironolactone on FMD and rosuvastatin improved FMD in a placebo controlled study after 24 weeks. TNFα blockers seems not to improve neither cIMT (2 studies) nor arterial rigidity (5 studies). Exercise alone has improved arterial rigidity in 15 patients after 12 weeks.

**Conclusions:** Whereas early and accelerated atherosclerosis is patent in AS, presence of subclinical atherosclerotic lesions is controversial in the literature especially concerning cIMT and arterial stiffness. This is reinforced by the lack of TNF blockers efficacy. Conversely it seems that endothelial dysfunction is present and reversible after treatment with TNF blockers, statin and spironolactone. These results are consistent to treat AS patients with early effective treatment to prevent the risk of CV morbidity and mortality.

**Disclosure of Interest:** None declared

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## FRI0410 ULTRASONIC FOLLOW UP HALF A YEAR ETANERCEPT TREATMENT FOR EARLY SPONDYLOARTHROPATHY INDUCED PERIPHERAL ENTHESITIS

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**Background:** Mardird sonographic enthesis index (MASEI) was one of the most wide used scoring systems for peripheral enthesitis. A report ever observed the efficacy of Sulfasalazine for peripheral enthesitis in Ankylosing Spondylitis. However, no reports followed up biological agents treatment for early axial spondyloarthropathy (SpA) by MASEI method so far.

**Objectives:** Our study is to find out whether MASEI is suitable for accurately reflecting the therapy effect of biological agents like Etanercept for early axial SpA.

**Methods:** Ultrasound was performed by 2 observers blinded to the other examinations and the final diagnosis once per 3-months and it is planned to carry on for a year. All cases were diagnosed as early axial SpA fulfilling 2009 classification criteria but not 1996 New York Criteria with sacroilliac X-ray and MRI.US examination referred to MASEI related regions. The count of swollen joint, the count of tender joints, ESR, CRP, PGA, PhGA, BASDI, BASFI, BASMI, MASES, ASDAS were employed to assess disease activity.

**Results:** 1) 95 early axial SpA subjects were finally enrolled in the program. All of them finished 24-week follow up, and 33 of them finished 48-week follow up until now. Mean age was 25.0±5.9 years old, female-male ratio was 0.48:1, and disease duration was 36.3months. Only 2 were negative HLA-B27.

2) The response for Etanercept was pretty good with the evidence of all the indexes above had prominent progress both in 12 week and 24 week except the count of swollen joint between 0w and 12w (paired Wilcoxon test, sig$<$0.05)

3) The good response for Etanercept was also well reflected by the ultrasonic scores: average sum scores (0w:12w:24w = 26.51:13.57:9.57,), tendon thickness scores (0w:12w:24w = 0.88:0.50:0.58, 12w:24w sig=0.11), structure disturbance scores (0w:12w:24w = 5.94:3.13:2.04), bone erosion scores (0w:12w = 6.49: 6.52:6.42), calcification scores (0w:12w:24w = 6.45:3.09:1.98), bursitis scores (0w:12w:24w = 1.44:0.46:0.30), Power Doppler scores (0w:12w:24w = 5.32:1.87: 1.25). All the scores above were significantly decreased except tendon thickness score between 12week and 24week and bone erosion scores during half a year.

4) There are no correlations between US scores and all the disease activity indexes at baseline, 12 week or 24 week visit point in early axial SpA perhaps due to the peripheral enthesitis might not reflect the axial circumstance.

**Conclusions:** Though the trial was still carried on for the last half a year, our study proved MASEI assessment is a good tool to supervise the effect of Etanercept for peripheral enthesitis in early SpA.

**Disclosure of Interest:** None declared

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## FRI0411 A CROSS SECTIONAL STUDY OF THE CLINICAL AND ULTRASOUND ENTHESEAL INVOLVEMENT IN PATIENTS WITH IBD

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**Background:** Previous studies have reported the high prevalence of occult SpA in IBD patients.

**Objectives:** To investigate the presence of clinical and ultrasound peripheral entheseal abnormalities in a consecutive series of IBD patients.

**Methods:** 61 IBD consecutive patients [26 Crohn's disease (CD) and 35 ulcerative colitis (UC), M/F 32/29, mean age 35.7+12.4 years, mean disease duration 57+93 months] entered the study. Gastroenterological examination consisted of the determination of bowel involvement, extraintestinal manifestations, MAYO and CDAI score. A complete rheumatological examination which included 66 peripheral join count, MASES and Leeds entheseal evaluation, BASDAI, BASFI and evaluation of spine mobility was done at study entry. ESR and CRP were evaluated at study entry. US examination was done using an Esaote MyLabClass, 18–6MHz linear multifrequence transducer both in gary scale and with PD. The following enthesis were separately studied clinical and US by two rheumatologist unaware of the other evaluation: lateral elbow epicondyle, distal quadricipital insertion at the patella, proximal and distal patellar tendon insertions, Achilles tendon an plantar fascia insertion at the calcaneous. Knee and ankle joints were evaluated for synovial hyertrophy, PD signal and fluid. Extensor and flexor tendons of the foot and ankle were evalutaed for the presence of tendon sheat fluid, synovial hypertrophy and PD signal. Quadriceps, patellar, Achille and plantar fascia entheses were scored according to the 0–36 Glasgow Ultrasound Enthesitis Scoring System (GUESS) and power Doppler (PD). Correlations of GUESS and PD with IBD features [duration, type (CD/UC) and activity (disease activity index for CD/Truelove score for UC)] were investigated.

**Results:** 29/61 (47.5%) patients had at leat one entheseal alteration at clinical examination and 56 (91.8%) presented almost one US entheseal abnormality with a mean 3.05±1.7 number of abnormal enthesis /patient. The mean MASEI was 11±9 and the mean GUESS 5.8±3.9 with 56/61 patients with value $>$1. The US evidence of enthesitis was higer in CD with ileo-colon localization as compared to ileo or colon involvement (100% vs 89% and 50%, p=0.03). Patients with disease duration $>$12 months have significantly grater number of cronical (2.48±1.5vs3.7±1.7, p=0.01) and acute enthseal alteration (3.0±1.3vs1.9±1.3,p=0.01) as compared with patients with disease duration $<$12 months.

**Conclusions:** US entheseal abnormalities are present in a high percentage of IBD patients. US enthesopathy is associated with longer disease duration and topographical localization of gut disease.

**Disclosure of Interest:** None declared

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## FRI0412 MANNOSE BINDING LECTIN GENE POLYMORPHISMS IN SPONDYLOARTHROPATHIES

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**Background:** Genetic and environmental factors are known to play a role in the pathogenesis of spondyloarthropathies (SPA). Mannose binding lectin (MBL) which is a member of collectin family proteins, is an important component of innate immunity. Low levels of MBL is associated with susceptibility to infections. Several variants of MBL gene may result in MBL deficiency. MBL gene polymorphisms and MBL deficiency are shown to be related with several autoimmune and inflammatory diseases.

**Objectives:** The relationship between the MBL levels or MBL gene polymorphisms and SPA predisposition has previously been investigated in a few small studies with conflicting results. In this particular study, we aimed to assess the relationship of the MBL genes in the develepoment of SPA in a group of Turkish patients.

**Methods:** Study included 132 patients with SPA (75 female, 57 male, mean age: 43.0±12.4) and 87 healthy subjects (58 women, 29 men, mean age: 40.3±13.4) as control group. Eighty nine of the SPA patients had ankylosing spondylitis (AS) and 43 had non-AS SPA. MBL gene single nucleotide polymorphisms (SNP) in the codons 52, 54 and 57 of exon 1 were studied by sequencing method.

**Results:** G54D G$>$A polymorphism was not different between the patient and the healthy control groups (p=0.291). The frequencies of R52C C$>$T and G57E G$>$A polymorphisms were found to be significantly higher in the SPA patients than those of the healthy controls (p=0.019 and 0.001 respectively). While the non-AS subgroup showed significancy for both R52C C$>$T and G57E G$>$A polymorphisms (p=0.004 and 0.000 respectively), the AS subgroup showed significancy only for G57E G$>$A (p=0.113 and 0.014 respectively). Clinical characteristics of either AS or non-AS SPA patients were not associated with any of the MBL polymorphisms. In a previous study, haplotypes of MBL genetic polymorphisms were found to be associated with AS in Korean patients. Our study is the first one from Turkey indicating the relationship between SPA's and MBL gene polymorphisms.

**Conclusions:** Even though we had rather small sample size, our results showed significantly higher R52C C$>$T and G57E G$>$A polymorphisms in Turkish patients with SPA. Therefore we may suggest that MBL gene polymorphisms could be related with the predisposition of the disease.

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**Disclosure of Interest:** None declared

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## FRI0413 CLINICAL RISK FACTORS FOR THE PRESENCE AND DEVELOPMENT OF VERTEBRAL FRACTURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Vertebral fractures are the hallmark of bone fragility and are frequently present in patients with ankylosing spondylitis (AS). For treating rheumatologists, it is important to know which patients already have vertebral fractures and which patients are at risk to develop new fractures. Limited longitudinal data are available concerning the development of new vertebral fractures in AS.
**Objectives:** To investigate the prevalence and incidence of radiographic vertebral fractures and the association with patient characteristics, clinical assessments, and medication use in a large prospective cohort of patients with ankylosing spondylitis (AS) in daily clinical practice.
**Methods:** Consecutive AS patients from the Groningen Leeuwarden AS (GLAS) cohort with baseline and 2-year lateral radiographs of the thoracic and lumbar spine were included. Radiographs were scored for vertebral fractures by two readers according to the method of Genant *et al*. Vertebral fractures were defined as $\geq$20% reduction in vertebral height. Severity of fractures were divided into mild (20–25% reduction), moderate (25–40% reduction), and severe ($>$40% reduction) fractures. Differences in baseline characteristics were explored between patients with and without radiographic vertebral fractures.
**Results:** Of 292 included AS patients, 70% were male, 82% HLA-B27+, mean age was 43±13 years, median symptom duration 16 (IQR: 8–25) years, and mean BASDAI 5.3±2.2. Radiographic vertebral fractures were present in 59 (20%) patients at baseline. During 2 years of follow-up, 15 (6%) patients developed new vertebral fractures and 7 (2%) showed an increase in severity of existing fractures. Most fractures were mild and located in the mid-thoracic and thoracolumbar region of the spine.
The presence of vertebral fractures was significantly associated with older age, higher BMI, longer smoking duration, larger occiput-to-wall distance, more spinal radiographic damage, and lower hip BMD. Occiput-to-wall distance was identified as an independent risk factor for prevalent vertebral fractures; 44% of the patients with hyperkyphosis (occiput-to-wall distance $\geq$10 cm) had vertebral fractures. The development of new or progressive vertebral fractures was also associated with older age and low BMD. Patients using NSAIDs at baseline showed less prevalent (18% vs. 31%) and incident (5% vs. 17%) vertebral fractures than patients without NSAIDs.
**Conclusions:** In this large AS cohort in daily clinical practice, radiographic vertebral fractures were frequently present, especially in older patients with more advanced disease, low hip BMD, and a less healthy lifestyle. Interestingly, NSAID use was associated with a reduced vertebral fracture risk.
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## FRI0414 ASSOCIATION OF ANTERIOR UVEITIS AND OTHER CLINICAL FINDINGS IN PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** Anterior uveitis (AU) is considered to be one of the most common extra-articular manifestations of spondyloarthritis (SpA), and its prevalence may vary according to the genetic background of the study population. Uveitis can appear both before and after the onset of osteoarticular symptoms. It can lead to serious complications that can compromise the visual function.
**Objectives:** The aim of this study was to compare demographic, clinical and laboratory data among SpA patients with and without AU.
**Methods:** Cross-sectional study including 190 SpA patients that fullfilled the modified New York criteria. The patients were asked to complete a questionnaire assessing their disease type, age at diagnosis, clinical presentation, disease-activity (BASDAI, ASDAS) and functional-indices (BASFI) and BASMI was calculated. The following parameters were taken out of the patients' files: the presence of HLA-B27 antigen, inflammation biological markers (ESR, CRP), and conventional radiographs of spine, hip and sacroiliac joints were evaluated. Ocular involvement passively reported by the patients and confirmed by ophthalmological exams was noted and the group with AU diagnosis (current or past) was compared to those without uveitis. The statistical analysis was performed using SPSS 21.0 software, and $p<0.05$ was taken to indicate statistical significance. To compare the differences between the groups, Mann-Whitney U, $\chi^2$ and Fisher tests were used.
**Results:** 190 patients were included, of which 56.3% were males, with median age of 46.0 (range 21–79) years. 58 (30.5%) patients had AU, which was significantly more frequent in patients with ankylosing spondylitis (84.5% of patients with AU) comparing with the other subtypes of SpA (p=0.01). There were no statistically significant differences in age at diagnosis, time to diagnosis or gender between the two groups. However, median age and disease duration were significantly greater in SpA patients with AU than those without AU (50.5 vs 44.0 years, p=0.015 and 24.0 vs 15.9 years, $p<0.001$ respectively). HLA-B27 was positive in 60,3% of patients with AU, comparing with 43.2% in those without AU ($p<0.005$). Ankylosis of bilateral sacroiliac joints was more frequent in patients with AU (46.6% vs 20.9%, $p<0.001$). The patients with AU had less frequently skin lesions and dactylitis (10.3% vs 30.3%, p=0.02 and 0% vs 7.5%, p=0.024), but there were no differences in the prevalence of peripheral arthritis or enthesitis. BASMI was significantly higher in patients with AU (median 4.9 vs 4.0, p=0.041), but there were no significant differences in disease activity, functional outcomes.
**Conclusions:** This study showed that AU could be more frequently seen in HLA-B27 positive patients with long-standing SpA, especially ankylosing spondylitis, and may be less frequent in patients with skin lesions and dactylitis.
**Disclosure of Interest:** None declared
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## FRI0415 SERUM AMYLOID A PROTEIN IN SPONDYLOARTHRITIS PATIENTS UNDER ANTI-TUMOUR NECROSIS FACTOR-ALPHA: AN USEFUL BIOMARKER?

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**Background:** Inflammation is known to play a major role in rheumatologic disorders. Hence quantitating the degree of inflammation has become essential to tailor the treatment strategy. Traditionally used measures to assess disease activity in spondyloarthritis (SpA) are ESR, CRP, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS). Serum amyloid A (SAA) is an acute-phase reactant predominantly synthesized in the liver by hepatocytes in response to proinflammatory cytokines. Some studies have shown that SAA correlates with disease activity in SpA and suggest it as a valuable indicator of disease activity, however it has not been extensively used in clinical practice.
**Objectives:** To investigate if SAA levels have better correlation with conventional clinical and serological assessments in SpA than CRP and ESR.
**Methods:** Cross-sectional study, including SpA patients under anti-TNF$\alpha$ treatment at a Rheumatology Department of a Portuguese Universitary Hospital. We compared the correlation between SAA, CRP and ESR levels with BASDAI, ASDAS-CRP, ASDAS-ESR, BASFI, BASMI, swollen and tender joints counts (SJC and TJC), MASES, SPARCC, and patient global assessment, physician global assessment, total back pain, nocturnal back pain rated on a visual analogue scale (VAS). The statistical analysis was performed using SPSS 21.0 software, and $p<0.05$ was taken to indicate statistical significance. Correlation was calculated using the Spearman rank correlation (r).
**Results:** 88 patients were included, 61.4% (n=54) were male. The median age was 44,0 years (range 21.0–74.6). Median disease duration was 19.0 years (2-51.6). According to ASDAS criteria, 23 patients (26.1%) had inactive disease, 21.7% moderate disease activity, 40.9% high disease activity and 11.4% very high disease activity.
SAA levels were moderately correlated with CRP levels (r=0.51, $p<0.001$) and had lower correlation with ESR (r=0.36, p=0.001). There was no statistically significant correlation between SAA levels and the following parameters: physician global assessment-VAS, total back pain-VAS, nocturnal back pain-VAS, MASES, SJC and TJC. SAA levels correlated with patient global assessment-VAS (r=0.218, p=0.04) but also did ESR (r=0.277, p=0.01). There was no significant correlation between SAA and BASDAI (r=0.161, p=0.134), however CRP levels and ESR showed little correlation (r=0.232, $p<0.03$ and r=0.366, $p<0.001$).
We found statistically significant correlation between SAA levels and ASDAS-ESR (r=0.298, p=0.005), ASDAS-CRP (r=0.330, p=0.002), SPARCC (r=0.221, p=0.034), BASFI (r=0.327, p=0.002) and BASMI (r=0.262, p=0.014). CRP and ESR also showed significant correlation with BASFI, but it was weaker than that observed with SAA (r=0.285, p=0.007 and 0.310, p=0.004, respectively). ESR and CRP did not correlate with BASMI.
**Conclusions:** This study suggests that SAA can be a valuable indicator not only of disease activity but also of damage and functional impairment, that could be introduced in clinical pratice. However more studies, with larger sample sizes, and prospective ones should be undertaken to better assess this subject.
**Disclosure of Interest:** None declared
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## FRI0416 EVALUATING THE IMPACT OF A LOCAL INFLAMMATORY BACK PAIN AWARENESS CAMPAIGN IN THE UNITED KINGDOM

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**Background:** The average delay to diagnosis in the UK is 8.5 years, even though

the majority of patients consult their GP within one year of symptom onset. The lack of awareness and recognition of IBP (Inflammatory Back Pain) is one of the main reasons for the unacceptable delay in diagnosis[1]. A public awareness campaign to raise awareness of IBP was held in Bath on 13th September 2014

**Objectives:** The aim of the study was to assess referral rates pre and post campaign - number of referrals for IBP, number of newly diagnosed Axial Spondyloarthritis (AxSpa)/ Ankylosing Spondylitis (AS) and mechanical back pain patients who were referred with reference to IBP and for new AxSpa/AS patients - age, length to diagnosis from symptom onset, sex, HLA B27 status and CRP were also assessed.

**Methods:** Referrals to the Royal National Hospital for Rheumatic Diseases (RNHRD), Bath Pre Campaign from January-March 2014 and Post Campaign in Months October-December 2014 were evaluated.

Referral letters were reviewed and categorised as either likely inflammatory referrals or likely non-inflammatory referrals. A referral was considered as inflammatory if it contained key words such as Sacroiliitis, HLA B27 status, mention of Family history of Ankylosing spondylitis/Axial spondyloarthritis, spondyloarthropathy or inflammatory back pain/arthropathy

Based on history and investigations, patients were classified using the ASAS Axial SpA classification criteria as either nr-AxSpa orAS, or if they didn't meet the criteria "Mechanical Back pain". It was assessed whether this was a new or an old diagnosis.

**Results:** There were 91 back pain referrals pre campaign and 96 post campaign. Pre campaign, 40 patients with AxSpa were referred. 8/40 were diagnosed as new AS (20%) and 16 had known AS. 10/40 (25%) were diagnosed as new nrAxSpa. 6 had known nrAxSpA. Of the 18 new AxSpa cohort 14 had "inflammatory" referrals from the referrer. ie. 77% accurate referrals.51 cases of mechanical back pain were diagnosed; 19 of the referrals contained "inflammatory" key words

Post campaign,38 patients with AxSpA were referred. 3/38 were diagnosed with new AS. 11/38 were diagnosed with new nrAxSpa. 12/14 of new AxSpa patients had "inflammatory" referrals.ie 85% accuracy.

58 cases of mechanical back pain were diagnosed; 21 of the referrals had "inflammatory" key words.

| AxSpA patients | Pre campaign | Post campaign |
|---|---|---|
| Males | 9/18 (50%) | 10/14 (71%) |
| Mean age (years) | 40.6 | 41.1 |
| HLAB27 +ve | 6/16 (38%) | 10/12 (83%) |
| Raised CRP | 5/16 (31%) | 4/14 (29%) |
| Mean symptom duration | 8 years | 12.1 years |

**Conclusions:** In a local setting, the campaign did not significantly increase the number of new back pain referrals to rheumatology. Reassuringly, we found that the index of suspicion from referrers for AxSpA to be high in both cohorts.

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## FRI0417 PREVALENCE OF OSTEOPOROSIS IN AN ANKYLOSING SPONDYLITIS COHORT

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**Background:** The Ankylosing Spondylitis Registry of Ireland (ASRI) is a web-based database established in 2013, the objectives of which are to provide descriptive epidemiological data on the ankylosing spondylitis (AS) population in Ireland and to establish a registry for potential future studies of genetics, aetiology and therapeutics. The prevalence of osteoporosis is higher in AS patients than age- and sex-matched controls, with potential for vertebral fractures increased. However, the true prevalence is unknown. There is no data on the prevalence of osteoporosis in an Irish cohort.

**Objectives:** To determine the prevalence of low bone mineral density (BMD) in an Irish AS cohort.

**Methods:** A standardised detailed clinical assessment was performed on each patient. Disease activity was assessed by Bath AS Disease Activity Index (BASDAI), function by the Bath AS Functional Index (BASFI) and Health Assessment Questionnaire (HAQ) and quality of life by AS Quality of Life (ASQoL). Structured interviews provided patient-reported data. Presence or absence of dual-energy x-ray absorptiometry (DXA) testing and result was recorded. Bone mineral density (BMD) was categorised according to the World Health Organisation criteria into normal BMD, osteopenia or osteoporosis. Statistical analysis was performed using SPSS.

**Results:** As of October 2015, 416 patients are enrolled in ASRI: 78.1% males, mean age 47.95 (SD 12.4), mean disease duration 20.9 years (SD 12.2), average delay to diagnosis of 8.8 years (SD 8.3). Mean BASDAI is 3.8 (SD 2.5), BASFI 3.7 (SD 2.7), HAQ 0.53 (SD 0.51) and ASQoL 6.15 (SD 5.5). DXAs have been performed in 24.75% (n=103) of the cohort, of which 39.8% (n=41) have osteopenia and 10.7% (n=11) have osteoporosis. Low BMD is significantly correlated with men and advancing age. There is no association with disease activity or duration. Low BMD is more prevalent in patients treated with one or more biologics compared to those never treated. The self-reported prevalence of osteoporosis is 6.4% (n=27; 19 males).

**Conclusions:** There is an elevated prevalence of low BMD in this cohort, with no association with disease severity. The majority of affected patients were unaware, as demonstrated by the low self-reported prevalence. More research and education is needed.

**Disclosure of Interest:** None declared

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## FRI0418 MALE GENDER BUT NOT HLA-B27 POSITIVITY OR OCCURRENCE OF UVEITIS AS SEVERITY PROGNOSTIC FACTOR IN SARDINIAN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Susceptibility to develop Ankylosing Spondylitis (AS) is strongly influenced by the presence of the HLA-B27 gene, but much less defined are prognostic factors which may predict erosions and new bone formation lesions leading to organic damage and spinal ankylosis. Given the differences in the genetic background among populations, it is conceivable that prognostic factors may also mirror this genetic variability.

**Objectives:** The main aim was to study, in a cohort from the genetic isolate of Sardinia, possible clinical prognostic factors which may predict a more severe spinal damage as assessed by a validated radiological score.

**Methods:** Medical history, clinical and radiological data from 100 consecutive patients with AS were collected in a tertiary referral rheumatology clinic; 73 were male (mean age 44.9±10.5; disease duration 18.3±10.6 years) and 27 females (mean age 44.5±13.0; disease duration 14.9±8.9 years). Radiological cervical and lumbar spinal assessment was performed by means of the mSASSS index, sacro-iliac joints were evaluated according to New York criteria. Rx films were blindly assessed by an expert rheumatologist (GP) and by a radiologist (MM). Results were expressed as mean or median, according to numerical distribution. Statistical analysis was performed by means of GraphPad Prism software according to Mann-Whitney and Spearman's tests.

**Results:** Analysis of data revealed a good inter-observer and intra-observer agreement 0.94 (0.91–0.97) and 0,95 (0,88–0,96), respectively. Radiological spinal and sacroiliac joint severity indexes were positively correlated with patient's age and disease duration ($p<0.0001$). mSASSS was shown to correlate with BASDAI, BASFI and BASMI ($p=0.002$, $p<0.0001$ and $p<0.0001$, respectively) while New York sacroiliac score was found to correlate with BASMI only ($p<0.0001$). Radiological spinal involvement resulted more severe in male vs female patients (mSASSS 8; 3.5–33 vs 4; 1–10, p=0,008), mainly due to a greater involvement of the lumbar tract with similar cervical severity. These objective data are in contrast to clinical metrology and patient reported outcomes which showed similar BASMI and BASFI scores and lower BASDAI (2.5±2.1 vs 3.9±2.3, p=0.02) in male versus female. Interestingly, the occurrence of an extra-articular feature such as acute anterior uveitis (AAU) did not result to be a severity prognostic factor (p=ns). Furthermore, it is noteworthy that no statistical differences were noted comparing HLA-B27 positive patients for radiological severity (mSASS 6.5; 2–19) vs HLA-B27 negative (mSASS 8.5; 2–45 p=ns), as well as for disease activity, functional and metrology indexes (BASDAI 2.8±2.3 vs 3.9±2.3; BASFI 2.7±2.6 vs 3.4±2.9; BASMI 2.3±2.4 vs 3.8±3.1; p=ns). Finally, mSASSS or sacroileiitis indexes were not correlated with anti-TNF treatment.

**Conclusions:** In AS patients from the genetic isolate of Sardinia, male gender but not HLA-B27 positivity or occurrence of AAU is associated with a more severe radiological outcome.

**Disclosure of Interest:** None declared

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## FRI0419 ASSOCIATION BETWEEN OBJECTIVELY ASSESSED PHYSICAL ACTIVITY AND DISEASE PROGRESSION IN A POPULATION BASED SAMPLE OF ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Ankylosing spondylitis (AS) is a chronic, systemic disease that is characterized by inflammation, especially at the spinal column. Chronic inflammation of the spinal and extraspinal joints and enthesis frequently lead to

limitation of spinal and joint mobility. Although AS results in decreased physical and functional capacity, recent studies have suggested that physical activity (PA)/exercise is as crucial as drug treatment in the management of AS [1,2]. However the relationship between PA and AS disease activity remain s uncertain as the studies conducted thus far have used non-objective measures to assess PA.
**Objectives:** The aim of this study was to examine the association between PA at baseline and AS disease progression over 2 years especially in male participants.
**Methods:** 113 participants, initially recruited if they had inflammatory back pain or extra-articular features of AS for 10 years or less, were studied at baseline and 2 years. PA was assessed at the baseline visit only using a pedometer (steps/day) over 10 days. MRI scans of the spine were performed to assess inflammation at baseline and 2 years. Images were scored, using the Spondyloarthritis Research Consortium of Canada method. Disease activity, functional limitations and mobility were assessed at both time points using the Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI) and Bath AS Metrology Index (BASMI) respectively.
**Results:** 113 participants [mean-age (years) 41 (range 17–72); 64% male, BMI 27 (18–54)] were studied at baseline and two years. 62% of the participants had radiographic evidence of AS according to the modified New York criteria. 100 participants showed some evidence of spinal inflammation (mean 9.86 (0–60)). Mean steps/day were 4665 (1666–9711).
Higher number of steps/day at the baseline visit showed an independent negative association with change in spinal MRI inflammation (β (per 1000 steps) = -0.49 (-0.91, -0.07) over 2 years. Further analysis (figure-1) showed a dose response relation between PA and change in spinal inflammation. Participants who had an increase in severity of inflammation had on average least number of steps/day, whereas participants who had a decrease in severity of inflammation had the highest number of steps/day at the baseline visit.
Higher number of steps/day at the baseline visit were negatively associated with change in BASDAI (β (per 1000 steps) = -0.33 (-0.66, -0.04) score over 2 years. However we did not see any significant associations between PA and changes in BASFI and BASMI scores.
We further explored sex interactions for the associations between PA and changes in spinal inflammation and BASDAI scores, and found that higher number of steps/day resulted in a significantly higher decrease in the severity of MRI inflammation and BASDAI scores ($p<0.05$) in the male participants.

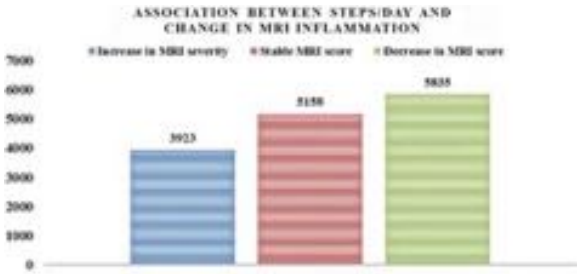


Figure-1 Association between steps/day and change in MRI inflammation

**Conclusions:** Higher PA was associated with a decrease in disease activity both clinically and on imaging.
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## FRI0420 PLASMA CALPROTECTIN IN SPA-PATIENTS, A BIOMARKER FOR PERIPHERAL ARTHRITIS

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**Background:** Spondyloarthritis (Spa) is a rheumatic disease with axial and peripheral inflammatory arthritis. The disease is associated with psoriasis, inflammatory bowel disease and uveitis. Inflammatory biomarkers as Sedimentation rate (SR) and CRP ar not as well correlated with disease activity in Spa as it is in Rheumatoid arthritis. Calprotectin, mainly secreted by neutrophilic granulocytes is elevated in sites of active inflammation Serum or plasma Calprotectin is elevated in rheumatoid arthritis, SLE and in IBD
**Objectives:** To investigate Plasma Calprotectin in Spa patients from Rana, Norway. Is Calprotectin elevated in Spa compared to healthy relatives, and relatives with symptoms of Spa? Is Calprotectin associated to age and gender? Is Calprotectin correlated to body mass index, other markers of inflammation, disease manifestations?
**Methods:** Patients with spondyloarthritis, were recruited from hospital registers, family doctors and by advertisement in local newspaper. Clinical data, Crp and HLAB27 were collected, x-ray and mri of SI-joint was performed if the patient had inflammatory backpain. If they fulfilled the ESSG-critera for Spondylarthritis they were included. The first degree relatives of the included patients were contacted and asked for symptoms of synovitis or inflammatory backpain by questionnaire. Symptomatic relatives were investigated, and included if they fulfilled the ESSG-critera. 387 spondylarthrits patients were included. 273 patients had mri of SI-joints235 patients, 51 symptomatic relatives and 74 healthy relatives were tested for Plasma Calprotectin, by Statistic testing with SPSS Chi square test or Students T-test
**Results:** Calprotectin levels are not significantly different in men and women, in Spa-patients, relatives with symptoms and healthy relatives of Spa patients. In Spa-patients there is no difference in Calprotectin-levels in inflammatory back-pain, radiological sacroiliitis, sacroiliitis on mri, psoriasis, inflammatory bowel disease, acute uveitis, reactive arthritis and HLA B27 positivity. Calprotectin levels are correlated to other inflammatory markers: SR, Crp, Hb and Trc, The best correlation is with Crp. Calprotectin is correlated to swollen joint count but not to BASDAI, BASFI or MHAQ

| Calprotectin | N | Calprotectin (nG/mL), mean | T-test |
|---|---|---|---|
| Healthy relatives/Spa-patients | 74/235 | 460/719 | 0.308 |
| Symptomatic relatives/ Spa-patients | 61/235 | 520/719 | 0.515 |
| Male | 158 | 812 | 0.097 |
| Female | 202 | 501 | |
| Correlations with Calprotectin in spa-patients | 235 | Spearmans rho | Chi-square test |
| Body mass index | | 0.164 | 0.013 |
| Age | | –0.105 | 0.111 |
| Disease duration | | 0.050 | 0.480 |
| SR | | 0.421 | 0.000 |
| Crp | | 0.725 | 0.000 |
| Hb | | –0.249 | 0.000 |
| Trc | | 0.545 | 0.000 |
| Lkc | | 0.050 | 0.457 |
| Tender joint count | | 0.057 | 0.437 |
| Swollen joint count | | 0.250 | 0.002 |
| Basdai | | –0.044 | 0.504 |
| Basfi | | 0.003 | 0.962 |
| MHAQ | | 0.024 | 0.745 |

**Conclusions:** Se-Calprotectin could be a valuable biomarker I Spa, especially in peripheral Spa with polyarthritis
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**Disclosure of Interest:** None declared
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## FRI0421 WHAT IS THE LOCATION OF ENTHESITIS IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS PATIENTS AND HOW DO THEY RESPOND TO ANTI-TNF TREATMENT?

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**Background:** Enthesitis is characterized by inflammation at the insertion of ligaments, tendons, joint capsule, or fascia to bone, and represents a well-known characteristic feature of ankylosing spondylitis (AS) and related spondyloarthropathies.
**Objectives:** To identify the location of enthesitis in ankylosing spondylitis (AS) and psoriatic arthritis (PsA) patients and to determine their response to anti-TNF treatment.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis, AS, or psoriatic arthritis (PsA) with infliximab (IFX) or golimumab (GLM). Eligible people for this analysis included AS and PsA patients treated with IFX who were enrolled since 2005 or with GLM enrolled since 2010 who had available information on enthesitis. The paired sampled t-test was used to compare the enthesitis count at baseline and 12 months.
**Results:** A total of 260 AS patients and 261 PsA patients were enrolled with a mean (SD) age at baseline of 46.1 (13.0) vs. 50.0 (12.0) years, respectively, and disease duration of 6.4 (9.8) vs. 5.2 (6.8) years. Among patients with AS, 28.1%, 21.7%, 22.4% had enthesitis at baseline, 6 months and 12 months, respectively. For PsA these numbers were 32.2%, 19.7%, and 22.6%, respectively. The presence of enthesitis by anatomical site and visit are described in Table 1 with

higher proportions observed for the greater trochanter (GT) in AS patients and the lateral epicondyle humerus (LEH) in PsA patients.

Table 1: Presence of enthesitis by anatomical site

| | AS | | | PsA | | |
|---|---|---|---|---|---|---|
| | Baseline (N=260) | 6 Months (N=203) | 12 Months (N=134) | Baseline (N=261) | 6 Months (N=189) | 12 Months (N=133) |
| LEH, % | 10.8 | 6.9 | 7.5 | 16.1 | 8.5 | 6.8 |
| MEH, % | 8.1 | 5.9 | 4.5 | 12.6 | 7.4 | 6.8 |
| PA, % | 10.8 | 5.4 | 3.0 | 13.0 | 6.4 | 6.8 |
| GT, % | 14.2 | 8.4 | 10.4 | 10.7 | 9.0 | 6.0 |
| IPF, % | 7.7 | 3.4 | 4.5 | 11.9 | 5.3 | 3.8 |
| SI, % | 11.5 | 8.9 | 7.5 | 10.7 | 8.0 | 8.3 |
| QIP, % | 6.9 | 3.9 | 1.5 | 9.6 | 5.9 | 6.0 |
| PATT, % | 6.9 | 4.4 | 1.5 | 13.8 | 5.9 | 8.3 |

LEH: Lateral epicondyle humerus; MEH: Medial epicondyle humerus; PA: Proximal achilles; GT: Greater trochanter; IPF: Insertion plantar fascia; SI: Suprapsinatus insertion; QIP: Quadriceps insertion patella; PATT: Inferior pole patella or tibial tubercle.

Presence of enthesitis in all anatomical sites was significantly associated with higher HAQ among AS and PsA patients. The mean (SD) enthesitis count at baseline and 12 months was 4.4 (3.4) vs. 2.6 (2.3) (P=0.061) among AS patients and 5.0 (3.8) vs. 3.8 (3.0) (P=0.006) in PsA patients, respectively.

**Conclusions:** A considerable proportion of PsA and AS patients had enthesitis at anti-TNF initiation in this Canadian real-world cohort. Overall, presence of enthesitis was associated with significantly higher functional disability. Treatment with IFX or GLM for 12 months was associated with significant reduction in the mean enthesitis count.

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## FRI0422 PERIODONTAL DISEASE IN SPONDYLOARTHRITIS SUBTYPES. IS THERE A DIFFERENCE?

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**Background:** Spondyloarthritis (SpA) are a group of interconnected inflammatory arthritides that include ankylosing spondylitis (AS), reactive arthritis (ReA), and undifferentiated SpA (uSpA). Periodontal disease (PD) is a chronic inflammatory disease that may increase the risk for immune diseases like rheumatoid arthritis and AS.

**Objectives:** To evaluate the periodontal condition and presence of *Porphyromona gingivalis* (*P. gingivalis*) and *P. gingivalis* IgG1 and IgG2 antibodies within three subgroups of SpA (AS, uSpA and ReA) and establish possible associations with disease activity measures.

**Methods:** A cross-section observational study was designed. Seventy-nine subjects were included (AS: 19, ReA: 14 and uSpA: 46). Clinical evaluation of rheumatologic and periodontal condition was performed. *P. gingivalis* presence by polymerase chain reaction (PCR) and *P. gingivalis* IgG1 and IgG2 antibodies as well as erythrocyte sedimentation rate (ESR), high sensitive C reactive protein (hsCRP), rheumatoid factor, cyclic citrullinated peptide antibody (ACPAs), HLA-B27 and disease activity measures were assessed. A descriptive analysis of frequency distributions for clinical, laboratory and demographic data was made. Associations between clinical and microbiological markers of *P. gingivalis* infection, including IgG1 and IgG2 antibodies, and SpA disease activity measures were evaluated. Chi-squared test was performed to determine associations. Comparisons between groups were made with Kruskal Wallis, Mann-Whitney U and Wilcoxon test. The study was approved by local ethics committee.

**Results:** Forty-four (55.7%) patients with SpA presented PD, of which uSpA had a higher frequency (65.2%). Most patients had moderate PD (AS: 26.3%, uSpA: 50.0%, ReA: 21.4%). A high frequency of retired uSpA patients (87.5%) had moderate PD (p=0.044). The clinical attachment level (CAL) ≥4mm (8.1 ± 10.5) and % of CAL ≥4mm (5.7 ±7.7) was more frequent in uSpA patients (p=0.033 and p=0.034 respectively). *P. gingivalis* presence in uSpA patients was associated with the use of sulfasalazine (p=0.017), and in retired patients (p=0.028). In AS patients, positive IgG1 to *P gingivalis* was associated with % periodontal pocket depth ≥4mm (p=0.04) and % sites with sample pocket depth (SPD) ≥4mm (p=0.02). Also in this subtype, positive IgG2 was associated with bacterial plaque index (p=0.03). Positive levels of IgG2 in uSpA were associated with bleeding of probing (BOP) (p=0.03) and the number of compromised periodontal interproximal sites (p=0.05). See Table 1.

**Conclusions:** We found a high frequency of PD in patients with SpA without significant statistical differences between each subtype. The differences in clinical periodontal variables in SpA subtypes probably suggest a better oral hygiene in these patients. *P. gingivalis* IgG antibodies may be a useful tool for the physician to assess periodontal condition in these patients.

Table 1. Spondyloarthritis subtypes and periodontal disease

| | SpA (n = 79) | AS (n = 19) | uSpA (n = 46) | ReA (n = 14) |
|---|---|---|---|---|
| **Periodontal disease** | 44 (55.7) | 7 (36.8) | 30 (65.2) | 7 (50.0) |
| **Severity** | | | | |
| None | 35 (44.3) | 12 (63.2) | 16 (34.8) | 7 (50.0) |
| Mild | 11 (13.9) | 2 (10.5) | 6 (13.0) | 3 (21.4) |
| Moderate | 31 (39.2) | 5 (26.3) | 23 (50.0) | 3 (21.4) |
| Severe | 2 (2.5) | 0 (0.0) | 1 (2.2) | 1 (7.1) |
| **Total sample sites** | 158.0 (± 25.4) | 168.5 (± 17.3) | 157.3 (± 29.5) | 160.0 (± 18.8) |
| % Sites SPD ≥4mm | 2.1 (± 2.5) | 1.5 (± 2.0) | 2.0 (± 2.3) | 3.1 (± 3.6) |
| CAL ≥4mm* | 6.4 (± 9.4) | 2.2 (± 3.1) | **8.1 (± 10.5)*** | 5.5 (± 9.2) |
| % CAL ≥4mm* | 4.4 (± 6.7) | 1.4 (± 2.0) | **5.7 (± 7.7)*** | 3.6 (± 5.9) |
| **Interproximal sites** | 105.3 (± 16.9) | 105.6 (± 11.5) | 104.9 (± 19.6) | 106.6 (± 12.5) |
| Pocket probing depth | 3.2 (± 1.8) | 2.8 (± 2.0) | 3.2 (± 1.8) | 3.8 (± 1.2) |
| % Pocket depth ≥4mm | 3.9 (± 4.8) | 3.0 (± 4.2) | 3.7 (± 4.2) | 5.6 (± 7.1) |
| CAL | 1.8 (± 0.6) | 1.8 (± 0.5) | 1.9 (± 0.5) | 1.8 (± 0.7) |
| % CAL | 40.7 (± 28.5) | 34.5 (± 27.0) | 45.4 (± 28.2) | 31.4 (± 29.9) |
| **Gingival index (%)** | 32.1 (± 22.5) | 23.8 (± 23.3) | 33.7 (± 21.2) | 36.4 (± 25.6) |
| **Plaque index (%)** | 45.2 (± 23.2) | 34.2 (± 21.9) | 45.1 (± 21.3) | 59.0 (± 25.5) |
| **Bleeding on Probing (%)** | 32.9 (± 18.5) | 31.8 (± 18.3) | 32.2 (± 19.1) | 37.0 (± 17.6) |
| **Bacteria** | | | | |
| *Pg* | 24 (30.4%) | 5 (26.3%) | 16 (34.8%) | 3 (21.4%) |

*p=0.01; **p=0.001
SPD: sample pocket depth; CAL: clinical attachment loss. Pg: Porphyromonas gingivalis

**Disclosure of Interest:** None declared

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## FRI0423 FREQUENCY OF DACTYLITIS AND ENTHESITIS IN SPONDYLOARTHRITIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASES:A CASE-CONTROL STUDY

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**Background:** Dactylitis, is observed in approximate 30% of patients spodnyloarthritis (SpA),with the highest frequency in psoriatic arthritis (PsA).SpA features complicate inflammatory bowel diseases (IBD) in at least one third of the cases.The frequency of dactylitis in IBD-SpA has been assessed in a few open studies with conflicting results[1,2].

**Objectives:** *Primary end point:* To compare the frequency of dactylitis in a clinical series of patients with IBD-associated SpA (IBD-SpA) compared with other types of SpA. Secondary end point: to evaluate the frequency of articular and extra-articular manifestations of IBD-associated SpA compared to controls.

**Methods:** 24-month case-control study. *Case patients:* all consecutive patients meeting the ASAS criteria for both axial and peripheral SpA,and with a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) certified by the gastroenterologist. *Controls:* the 2 consecutive patients with other SpA (ASAS criteria) observed after the case patient during the same time interval. Dactylitis diagnosis was accepted if observed at visit or if certified in the past by a rheumatologist working in our center.Patients were followed by the same rheumatologist,and follow-up visits were scheduled at baseline and every 4 months.All clinical and laboratory data were recorded in a computed patients'chart. The date of the last visit constituted the end of the follow-up.

**Results:** *Case patients:*88 IBD-SpA patients, 29 UC and 59 CD, 42 F/46M, mean age 47.66±15.09 ys, 10 (11.3%) B27+.Mean IBD duration was 60.05±54.66 months. *Controls:* 176 SpA patients, 98 PsA, 46 AS, and 32 non-radiographic axial SpA (nrx-AxSpA); 89F/87M, mean age 46.35±24.88 ys. 70 (40.7%) B27+, mean disease duration of 43.21±28.34 months. In IBD-SpA axial involvement was observed in 46 (52%) patients, peripheral in 29 (33%) and mixed in 13 (15%). Peripheral SpA was oligoarticular (≤4 joints involvement) in 26/29 (90%) patients and polyarticular in 3 (10%). Psoriasis (Pso) was associated in 14/88 (16%) of the cases. Dactylitis was recorded in 4 (4.5%) of IBD-SpA patients and in 30 (17.4%) of controls with a significant statistical difference (p=0.018). Dactylitis was recorded in only 2/74 (2.7%) IBD-SpA patients without Pso (p vs controls=0.010).Also enthesitis prevalence was significantly lower in IBD-SpA occurring in 16/88 (18.1%) patients and in 78/176 (44.3%) controls (p=0.004). Enthesitis frequency

was significantly higher in 14 IBD-SpA patients associating Pso (28.5%) compared with the remaining 74 cases (16.2%) (p=0.012). Dactylitis occurred in 2/29 (6.9%) and in 2/59 (3.38%) patients with UC and CD, respectively. Anterior uveitis was recorded in 3 (3.4%) IBD-SpA patients and in 26 (14.7%) controls (p=0.02).

**Conclusions:** Dactylitis and enthesitis were significantly lower in IBD-SpA patients compared to other SpA. As reported[3], Pso was frequent in our cohort of IBD-SpA,and its coexistency significantly increased the frequency of enthesitis and to a lesser extent of dactylitis.Anterior uveitis was significantly less frequent in IBD-SpA compared to controls.

**References:**

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## FRI0424 ACCESSIBILITY TO BIOLOGICAL THERAPY FOR PATIENTS WITH ANKYLOSING SPONDYLITIS IN ROMANIA IS INFLUENCED BY AREA OF RESIDENCE, SOCIO- ECONOMIC AND DEMOGRAPHIC FACTORS

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**Background:** The efficacy of anti TNFblockers in active ankylosing spondylitis (AS) is widely accepted. In Europe, high costs related to biological treatment lead to significant differences regarding the patient's accessibility to treatment depending on the level of economic development of different countries. In Romania, according to the national reimbursement protocol, a patient is eligible for treatment with TNF blockers if the disease is active despite using at least two non-steroidal anti-inflammatory drugs and sulfasalazine (for peripheral arthritis).

**Objectives:** The aim of the study is to assess the accessibility of patients with AS to biological therapy in Romania, depending on their area of residence and socio- economical indicators for each region.

**Methods:** A cross-sectional study was performed in 41 counties and Bucharest. Data were collected from the Romanian Registry of Rheumatic Diseases and the socio- economic indicators from the yearbook of the National Institute for Statistics.

**Results:** Data were gathered for 2013 AS patients treated with biologics. The mean age was 45.46 yrs (±12.07), 78% were male, 71% live in urban residences and the mean disease duration was 11.53 yrs. 74% (n=1498) of patients had access to biologics in their county of residence, while 26% (n=524) of patients had to travel for treatment to another county. Compared to the group treated inside their county of residence, those treated outside, originated from areas with a lower gross domestic product per capita (5701.77 € compared to 8722.44 €; $p<0.001$; t test) and with high deficit of physicians (1.28 physicians/ 1000 inhabitants, compared to 2.63 physicians/ 1000 inhabitants; $p<0.001$; t test). The urban habitat was associated with a higher accessibility to biologics (75.9%) inside their county of residence compared to patients living in rural areas (69.2%) (p=0.002, $\chi^2$ test); so the latter have to travel in order to being cared by a rheumatologist. The patients' age had a great influence on the accessibility to biologics: the patients treated outside of their county of residence were younger than those treated inside (44.1 yrs compared to 45.9 yrs; p=0.003, t test). On a national scale, the majority of AS patients treated outside their county of residence (86%; 449); were treated in Bucharest (the capital city); so the majority of patients treated with biologics in Bucharest are originating from other counties (60%; n=449/751).

**Conclusions:** In Romania, although there is a national protocol for biological therapy in AS, applied in the same way in every region of the country, the accessibility to biologic therapy varies a lot, mostly due to differences in the socio-economic status of each area of residence.

**Disclosure of Interest:** None declared

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## FRI0425 SEROLOGICAL MARKERS AND THEIR CORRELATION WITH DISEASE ACTIVITY INDEXES AND IMAGING IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS (ITALIAN CENTER OF SPACE STUDY)

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**Background:** Recently studies have focused on the role of new markers to diagnose early axial spondyloarthritis (axSpA), to evaluate disease activity (DA) and to predict patients (pts) at higher risk for a worse outcome. Common biomarkers, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are often ineffective in assessing DA.

**Objectives:** To evaluate some biomarkers and their correlation with clinical parameters, DA indexes and imaging in pts with early axSpA.

**Methods:** Sixty pts with low back pain (≥3 months, ≤2 years, onset ≤45 years) attending the SpA-UOC Rheumatology of Padua (SpondyloArthritis-Caught-Early SPACE study), were studied following a protocol including physical examination, questionnaires', lab tests, X-rays and MRI of spine and sacroiliac joints (SIJ)at baseline.An experienced rheumatologist made axSpA diagnosis according to ASAS criteria. The DA and physical functioning were assessed using: Bath Ankylosing Spondylitis Metrology Index (BASMI); Maastricht Ankylosing enthesitis Spondilities Score (MASES); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); Ankylosing Spondylitis disease activity score (ASDAS); Visual Analogue Scale (VAS pain); VAS night pain; VAS disease activity;Bath Ankylosing Spondylitis Patient Global Score (BASG1); BASG2; Health Assessment Questionnaire (HAQ); ESR; serum ultrasensitive CRP (hs-CRP); matrix metalloproteinase (MMP3); interleukin (IL) IL-22, IL-17, IL-23.Positive spine and SIJ MRI images were scored independently by 2 readers using the Spondyloarthritis Research Consortium of Canada (SPARCC) method; the spine and SIJ X-rays images were scored using mSASSS and NY-criteria. After the X-rays and MRI images of all pts were read, they were classified into the following cohorts: pts with signs of radiographic sacroiliitis (r-axSpA), pts without signs of radiographic sacroiliitis but with signs of sacroiliitis on SIJ-MRI (nr-axSpA MRI SIJ+), pts without signs of sacroiliitis on MRI and X-rays (nr-axSpA MRI SIJ-).The Spearman test and Kruskal Wallis test were used to compare all indexes in these cohorts.

**Results:** There was a significant difference between the three cohorts with regard to the prevalence of radiographic sacroiliitis, active sacroiliitis on MRI and the SPARCC SIJ score (Table 1). There were no differences in these groups in IL-17, IL-22, IL-23, MMP-3 and hsCRP. ILs remained below detection value in all cohorts. The correlation of IL-17 and IL-23 with other indexes was not significant. There was instead a correlation between IL-22 and some clinical indexes (BASFI, BASG1, HAQ, VAS pain). The correlation between mSASSS and MMP3 and hsCRP was an interesting finding.

Table 1. Serological and DA indexes and imaging score at baseline in all patients (n=60) and in the following three cohorts (r-axSpA, nr-axSpA MRI SIJ+, nr-axSpA MRI SIJ -)

| Serological and DA indexes and imaging | Cohort 1 r-axSpA, n=20 | Cohort 2 nr-axSpA MRI SIJ+, n=17 | Cohort 3 nr-axSpAMRI SIJ-, n=20 | p § | totale=60 pts |
|---|---|---|---|---|---|
| ESR (mm/h), mean (SD) | 17.57 (14.48) | 18.41 (12.73) | 18.00 (21.83) | ns | 18.27 (18.61) |
| hsCRP (mg/L), mean (SD) | 2.54 (2.79) | 2.56 (2.71) | 2.76 (3.76) | ns | 2.61 (2.92) |
| MMP-3 (ng/L), mean (SD) | 3.04 (1.69) | 3.51 (3.12) | 2.47 (1.66) | ns | 3.01 (2.02) |
| IL-22 (pg/mL), mean (SD) | 6.44 (3.32) | 8.91 (2.43) | 9.88 (8.34) | ns | 12.38 (12.89) |
| IL-17 (pg/mL), mean (SD) | 5 (0.12) | 5 (0.12) | 5 (0.97) | ns | 5 (4.11) |
| IL-23 (pg/mL), mean (SD) | 29.5 (31.2) | 21.87 (5.21) | 10.69 (21.56) | ns | 71.55 (80.56) |
| HLA B27, n(%) | 11 (47.8) | 9 (52.9%) | 3 (13%) | ns | 23 (38.3) |
| BASMI, mean (SD) | 0.74 (1.01) | 1.06 (1.39) | 0.75 (0.97) | ns | 1.83 (1.09) |
| MASES, mean (SD) | 2.87 (2.39) | 4.35 (2.69) | 3.6 (2.57) | ns | 3.51 (2.51) |
| BASFI, mean (SD) | 16.2 (2.96) | 14.74 (5.19) | 15 (3.57) | ns | 18.25 (21.37) |
| HAQ, mean (SD) | 0.32 (0.52) | 0.68 (0.61) | 0.38 (0.39) | ns | 0.58 (0.49) |
| BASG1, mean (SD) | 3.28 (1.99) | 4.24 (2.73) | 3.85 (1.96) | ns | 3.73 (2.01) |
| BASG2, mean (SD) | 4.78 (2.78) | 5.47 (2.79) | 5.05 (1.96) | ns | 5.07(2.82) |
| VAS pain, mean (SD) | 3.70 (3.01) | 4.06 (3.07) | 4.35 (3.27) | ns | 4.08 (3.08) |
| VAS disease activity, mean(SD) | 3.90 (2.98) | 4.94 (3.35) | 4.3 (3.55) | ns | 4.29 (3.31) |
| VAS pain night, mean (SD) | 3.81 (3.68) | 5.71 (3.57) | 5.8 (3.44) | ns | 5.07 (3.49) |
| BASDAI, mean (SD) | 3.63 (2.56) | 5.3 (2.61) | 4.43 (2.77) | ns | 4.05 (2.83) |
| ASDAS, mean (SD) | 2.48 (0.79) | 2.7 (0.86) | 2.30 (0.87) | ns | 2.53(0.81) |
| Sacroiliitis x-ray **, n(%) | 15 (100%) | 0 (0) | 0 (0) | <0.001 | 15 (41.7) |
| Sacroiliitis MRI *, n(%) | 17 (73.9%) | 17 (100%) | 0 (0) | <0.001 | 32 (53.3) |
| mSASSS, mean (SD) | 5.28 (5.21) | 5.53 (4.84) | 3 (3.73) | ns | 5.23 (5.04) |
| score SIJ*, mean (SD) | 1.30 (0.68) | 0 (0) | 0 (0) | ns | 0.5 (0.78) |
| SPARCC spine, mean (SD) | 7.38 (12.35) | 5.18 (15.52) | 1.05 (3.49) | ns | 4.93 (11.44) |
| SPARCC SIJ, mean (SD) | 15.03 (16.37) | 12.35 (9.12) | 0 (0) | <0.001 | 9.43 (13.10) |

ESR, erythrocyte sedimentation rate; hsCRP, high sensitive C-reactive protein; MMP-3 matrix-metallo-proteinase 3; IL, interleukin; mLA-B27, mu man Leukocyte Antigen; BASMI, Bath Ankylosing Score Metrology Index; MASES, Maastricht Ankylosing Spondilitis Enthesitis Score; BASFI: Bath Ankylosing Spondylitis Functional Index; HAQ: Health Assessment Questionnaire; BASG1,Bath Ankylosing Spondylitis Patient Global Score 1; BASG2, Bath Ankylosing Spondylitis Patient Global Score 2,BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS, Visual Analogue Scale; ASDAS, Ankylosing Spondylitis Disease Activity Score; SPARCC, Spondyloarthritis Research Consortium of Canada; mSASSS, modifiedStokeAnkylosingSpondylitis Spine Score, SIJ, sacroiliac joints. * Sacroiliitis MRI according ASAS/EULAR
** Sacroiliitis x-ray according New York criteria §§ Anova (Kruskal Wallis) at baseline: p<0.05

**Conclusions:** ILs, MMP-3 and hsCRP values were not significantly increased in any of the study groups and were not related to radiographic SIJ involvement or to clinical and DA indexes. This finding can probably be explained by the fact that pts had early stage axSpA and by the small sample size. Further studies are needed to analyze the validity and reproducibility of these biomarkers in early axSpA.

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## FRI0426 DO THE VALIDATED TOOLS OF DISEASE AND FUNCTIONAL ACTIVITY IN ANKYLOSING SPONDYLITIS MEASURE FIBROMYALGIA SYMPTOMS?

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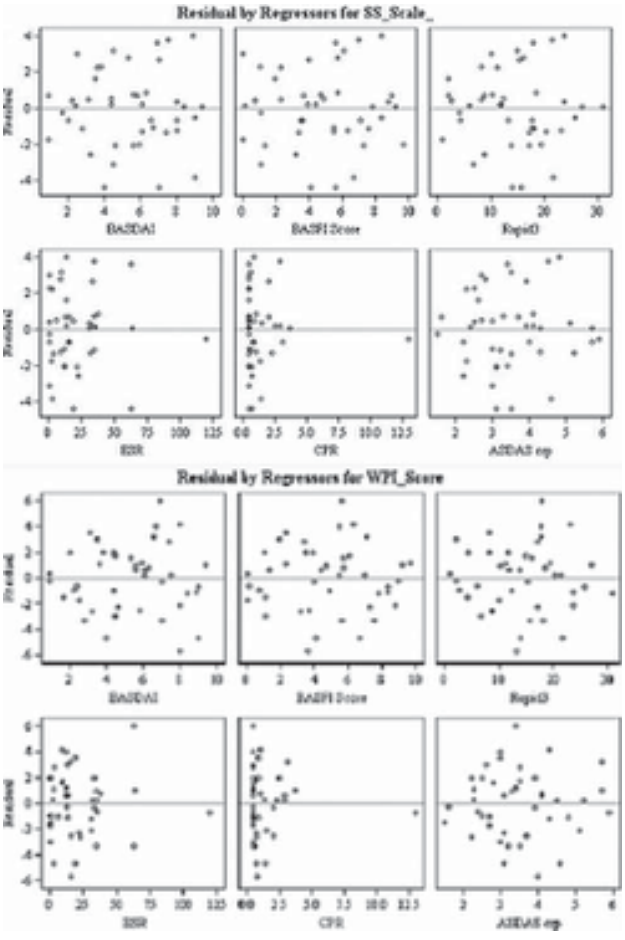
**Background:** Concomitant fibromyalgia syndrome is a common problem in ankylosing spondylitis (AS) and its recognition is important for optimal management of

AS. There is a concern that validated tools of disease activity, function and patient reported outcomes in AS may be measuring fibromyalgia pain and symptoms in patients with concomitant AS and fibromyalgia.

**Objectives:** We studied the relationship between the validated AS measures of disease activity, functional index, and markers of inflammation and ACR fibromyalgia diagnostic criteria.

**Methods:** Study was approved by our IRB. We prospectively recruited 51 subjects ≥18 years of age with AS (meeting modified New York criteria with grade 3 or 4 sacroiliitis and high disease activity (BASDAI ≥3). Demographic and clinical data were collected and stored in Redcap data base. Various validated Questionnaires to assess disease, functional activity and patient reported outcomes in AS were administered to the patients. The frequency of FMS was determined using validated 2010 ACR diagnostic criteria for fibromyalgia [1]. The patient met the fibromyalgia criteria if (i) widespread pain index (WPI) of ≥7 & symptom severity score (SS) ≥5 or WPI 3–6 & SS score ≥9,(ii) symptoms were present at a similar level for at least 3 months and (iii) the pain was not attributed to AS by the clinician. ESR and CRP was measured using routine laboratory methods. Descriptive analysis included continuous variables (the mean ± SD) and the categorical variables percentage. Linear regression analysis was performed to assess the association between BASDAI, BASMI, ASDAS, Rapid 3 and fibromyalgia status

**Results:** There 34 males and 17 females with mean age of 49.8 ± 12.2; 30.6% African-Americans, 63.2% whites and 4.0% Asians, with 47.0% HLA-B27 positive, 29.4% negative and 23% unknown.18/47 (38.3%) have had acute anterior uveitis. 45% of the patients had been on TNF-α inhibitors. Mean BASDAI was 5.23 (±2.5); BASFI 4.7 (± 2.8); PGA 5.1 (±2.4); ASDAS-CRP 3.4 (±1.13); and RAPID 3 score 13.76 (± 7.21), ESR 22.4 mm/hr (±22.0) and CRP 1.3 mg/dl (±1.9).21 AS patients (41.2%) satisfied the diagnostic criteria of fibromyalgia. No statistically significant relationship was found between WPI score (Figure 1) with BASDAI (p=0.56), ASDAS (p=0.19), BASFI (0.50), RAPID 3 (p=0.70), CRP (p=0.25), and ESR (p=0.30). Also, no statistically significant relationship was found between SS score (Figure 1) with BASDAI (p=0.12), ASDAS (p=0.87), BASFI (0.73), RAPID 3 (p=0.75), CRP (p=0.79), and ESR (p=0.90).




**Conclusions:** Despite high frequency of fibromyalgia prevalence in our patients with AS and active disease, the validated tools of disease and functional activity in AS did not measure fibromyalgia pain and symptoms.

**Disclosure of Interest:** None declared

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## FRI0427 THE PREVALENCE OF AXIAL SPONDYLOARTHRITIS IN PATIENTS PRESENTING WITH ACUTE ANTERIOR UVEITIS

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**Background:** Estimates for the prevalence of axial spondyloarthritis (axSpA) in patients presenting with acute anterior uveitis (AAU) range from 11–28%. However, to date no studies have classified patients according to the MRI-based Assessment of Spondyloarthritis International Society (ASAS) criteria.

**Objectives:** To determine the prevalence of axSpA in patients presenting with AAU and identify new "undiagnosed" cases using contemporary MRI-based classification criteria.

**Methods:** Consecutive adult patients presenting to a university teaching hospital between February 2014 and March 2015 with a diagnosis of non-traumatic, non-infective AAU were invited to participate. Patients with a pre-existing diagnosis of axial SpA or another underlying cause of AAU (e.g. sarcoidosis) were not evaluated further. Patients who reported chronic back pain commencing before age 45 were evaluated clinically by an experienced rheumatologist and investigated with laboratory tests and magnetic resonance imaging (MRI). Those patients newly diagnosed with axSpA were classified according to ASAS criteria and the burden of disease recorded.

**Results:** Two hundred and forty-one of 366 patients responded; 57 had a pre-existing diagnosis of axSpA, 77 others fulfilled the study eligibility criteria and 73 (95%) completed the study. Sixteen patients (22%) were diagnosed with axSpA according to the ASAS definition of a positive MRI (12 sacroiliac, 4 spinal). Including those with a previous diagnosis, the minimum prevalence of axSpA in patients presenting with AAU was 19.9%; of these 22% were previously undiagnosed.

The median age of "new" axSpA patients was 54 (IQR 41.5 – 58) and 8 (50%) were female. Nine patients (56%) were HLA-B27 positive; 31.3% had a raised CRP. The median duration of back pain was 20.5 years (IQR 17–30.25), and median number of episodes of AAU prior to the diagnosis of axSpA was 3 (IQR 1–7). The median duration of back pain at the time of first episode of uveitis was 15.5 years (IQR 8.5–20.5).

Amongst the undiagnosed cases, 6.3% of patients had a pre-existing diagnosis of psoriasis, 18.8% inflammatory bowel disease, 12.5% peripheral inflammatory arthritis and 6.3% a family history of axSpA. The mean BASDAI was 3.17 (SD 1.50), spinal pain visual analogue scale 4.31 (SD 2.02), BASMI 1.63 (SD 1.36), BASFI 2.74 (SD 2.20) and BAS-G 4.70 (SD 1.45).

**Conclusions:** This is the first study to use MRI in order to classify patients with AAU and chronic back pain. At least one fifth of patients presenting to secondary care with AAU have an underlying diagnosis of axSpA. There was a significant hidden burden of disease in that 22% of axSpA patients were previously undiagnosed despite having a long duration of symptoms. Patients presenting with AAU should be screened for chronic back pain and referred to a rheumatologist; this represents an opportunity to shorten the diagnostic delay.

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## FRI0428 EPIDEMIOLOGY OF ANKYLOSING SPONDYLITIS IN TAIWAN: A NATIONWIDE POPULATION STUDY

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease and there are few nationwide estimates for prevalence and incidence in Taiwan.

**Objectives:** The aim of this study was to determine trends in the incidence and prevalence of AS between 2005 and 2010 among general population of Taiwan.

**Methods:** The National Health Insurance Research Database was used to identify gout patients and to estimate the prevalence and incidence of AS for each year from 2005 to 2010. To determine the trends in prevalence, incidence and management of AS, we calculated age- and sex-standardised prevalence and incidence of gout in each calendar year from 2005 to 2010 with the population structure in year 2010 as the reference.

**Results:** A total of 54,857 cases with an AS diagnosis alive in December 2010 was identified. Men had a higher prevalence (0.28% versus 0.19%) and incidence (0.51 versus 0.33 per 1,000 person-year) of AS than women. The standardised prevalence of AS had decreased from 0.30% in 2005 to 0.24% in 2010. The incidence of AS is between 0.42 and 0.50 per 1,000 person-years during 2005 and 2010. The incidence of AS in men was low in individuals younger than 19 years of age, peaked rapidly in the ages 20 to 24 years and decreased gradually. The incidence and prevalence of regions in 2010 highest in the town of Tainan (0.6% and 1.79 per 1,000 person-years) and Ilan (1.17% and 1.52 per 1,000 person-years) than other regions.

**Conclusions:** AS is a common rheumatic disease in Taiwan with a similar prevalence to rheumatoid arthritis.

**Disclosure of Interest:** None declared
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## FRI0429 WHAT IS THE LOCATION OF DACTYLITIS IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS PATIENTS AND HOW DO THEY RESPOND TO ANTI-TNF TREATMENT?

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**Background:** Dactylitis is one of the most commonly reported features in spondyloarthritis. It has been hypothesized that dactylitis is a functional enthesitis at the proximal interphalangeal joints, resulting in synovitis, tenosynovitis, bone and soft tissue oedema to the digit, and may simultaneously involve more than one digit.
**Objectives:** Our objective was to identify the location of dactylitis in ankylosing spondylitis (AS) and psoriatic arthritis (PsA) patients and to determine their response to anti-TNF treatment.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriatic arthritis (PsA) with infliximab (IFX) or golimumab (GLM). Eligible people for this analysis included AS and PsA patients treated with IFX who were enrolled since 2005 or with GLM enrolled since 2010 who had available information on dactylitis. The McNemar (paired Chi-square) test was used to compare the presence of dactylitis over time.
**Results:** A total of 260 AS patients and 261 PsA patients were enrolled with a mean (SD) age at baseline of 46.1 (13.0) vs. 50.0 (12.0) years, disease duration of 6.4 (9.8) vs. 5.2 (6.8) years, and proportion of females 40.6% vs. 48.5%, respectively. Among patients with AS, dactylitis was reported in 6.2% and 2.2% of patients at baseline and 6 months, respectively; at 6 months of treatment 73.3% of AS patients with dactylitis at baseline had no dactylitis and 1.6% developed dactylitis (P=0.057). For PsA higher proportions of dactylitis were observed with 30.7%, and 12.7%, respectively; at 6 months of treatment 69.0% of PsA patients with dactylitis at baseline had no dactylitis and 4.6% developed dactylitis (P<0.001). The distribution of dactylitis amongst digits is described in Table 1 with the highest prevalence observed for feet in AS and PsA patients.

Table 1. Distribution of dactylitis amongst digits in AS and PsA

| | AS | | PsA | |
|---|---|---|---|---|
| | Baseline (N=260) | 6 Months (N=207) | Baseline (N=261) | 6 Months (N=189) |
| HD1, % | 1.9 | 0.5 | 4.2 | 2.6 |
| HD2, % | 3.1 | 1.0 | 9.2 | 5.3 |
| HD3, % | 3.1 | 2.4 | 8.0 | 5.3 |
| HD4, % | 1.5 | 1.0 | 8.0 | 2.6 |
| HD5, % | 1.5 | 1.4 | 5.4 | 3.2 |
| FD1, % | 2.7 | 0.5 | 8.0 | 1.1 |
| FD2, % | 3.8 | 0.5 | 12.6 | 3.7 |
| FD3, % | 2.3 | 0.5 | 11.1 | 3.2 |
| FD4, % | 2.3 | 1.0 | 14.9 | 5.3 |
| FD5, % | 1.5 | 0.0 | 10.0 | 1.6 |

HD=hand digit; FD=foot digit.

Presence of dactylitis in hands or feet (any digit) was associated with significantly higher HAQ in AS and PsA (AS: ΔHAQ=1.36 (P≤0.001); PsA: ΔHAQ=0.64 (P≤0.001)).
**Conclusions:** A considerable proportion of PsA patients had dactylitis at anti-TNF initiation in this Canadian real-world cohort. Although a lower proportion of patients had dactylitis among AS patients, the presence of dactylitis was associated with higher functional disability in both AS and PsA patients. Treatment with IFX or GLM for 6 months was associated with significant reduction in the prevalence of dactylitis.
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## FRI0430 GOLIMUMAB IN REFRACTORY UVEITIS RELATED TO SPONDYLOARTHRITIS. MULTICENTER STUDY OF 15 PATIENTS

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**Objectives:** To assess the efficacy of golimumab (GLM) in refractory uveitis associated to spondyloarthritis (SpA).
**Methods:** Multicenter study of SpA-related uveitis refractory to at least one immunosuppressive drug. The main outcome variables were degree of anterior and posterior chamber inflammation, visual acuity, and macular thickness.
**Results:** Fifteen patients (13 men/2 women; 18 affected eyes; mean age 39±6 years) were evaluated. The underlying SpA subtypes were ankylosing spondylitis (n=8), psoriatic arthritis (n=6) and non-radiographic axial SpA (n=1). The ocular involvement patterns were recurrent anterior uveitis in 8 patients and chronic anterior uveitis in 7. Before GLM they have received methotrexate (n=13), sulfasalazine (n=6), pulses of methylprednisolone (n=4), azathioprine (n=3), leflunomide (n=2) and cyclosporine (n=1). Ten of them had also been treated with TNF-α blockers; etanercept (n=7), adalimumab (n=7), infliximab (n=6), and certolizumab (n=1). GLM was given at the standard dose (50 mg/sc/monthly) as monotherapy (n=7) or in combination with conventional immunosuppressive drugs (n=8), mainly methotrexate. Most patients had rapid and progressive improvement of intraocular inflammation parameters. The median number of cells in the anterior chamber at 2 years (0 [0–0]) was significantly reduced compared to baseline findings (1 [0–3]); p=0.04). The mean best corrected visual acuity value also improved (0.84±0.3 at 2 years versus 0.62±0.3 at baseline; p=0.03). Only minor side effects were observed after a mean follow-up of 23±7 months.
**Conclusions:** Our results indicate that GLM may be a useful therapeutic option in refractory SpA-related uveitis.
**Disclosure of Interest:** None declared
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## FRI0431 FATIGUE IS A DETERMINANT OF REDUCED WORK PRODUCTIVITY IN ANKYLOSING SPONDYLITIS: RESULTS FROM A PROSPECTIVE COHORT STUDY

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**Background:** Work disability is a critical issue for patients with ankylosing spondylitis (AS). In the general population, fatigue is a principal determinant of reduced work productivity. This potentially modifiable risk factor has yet to be investigated in AS.
**Objectives:** To investigate the relationship between fatigue and work productivity among AS patients.
**Methods:** Data were obtained from an observational study which followed a large German cohort of AS patients treated with etanercept as part of routine clinical practice between October 2007 and May 2014.
The exposure of interest, fatigue (Bath Ankylosing Spondylitis Disease Activity Index subscale, BASDAI), was collected at baseline (at etanercept commencement) and 6 months. Putative confounders were also evaluated at these time-points: age, gender, pain (visual analogue scale, VAS), depression (EQ5D item), physician's disease activity assessment (VAS) and C-reactive protein (CRP).
The primary outcome, work productivity loss, was measured using subscale 3 of the Work Productivity and Activity Index: Specific Health Problem (WPAI: SHP).
Two stepwise ANCOVA models (adjusted for confounders and baseline work productivity loss) were developed to examine: 1) the association between baseline fatigue and 6 month work productivity loss; 2) the association be-

Table 1. Multivariate analyses examining relationship between fatigue and work productivity loss

| Predictor | p-value | Coefficient Estimate | Standard Error |
|---|---|---|---|
| Model 1: Work Productivity Loss at 6 months | | | |
| BASDAI (fatigue) score at Baseline | 0.0346 | 1.116 | 0.527 |
| Work productivity loss at Baseline | <0.0001 | 0.218 | 0.042 |
| Age (years) at Baseline | <0.0001 | 0.576 | 0.095 |
| Gender (male relative to female) | 0.0208 | –5.021 | 2.165 |
| Pain Score at Baseline | 0.0330 | 1.242 | 0.580 |
| Model 2: Change in Work Productivity Loss from Baseline to 6 months | | | |
| Change in BASDAI (fatigue) score from Baseline | 0.0444 | 0.869 | 0.431 |
| Work productivity loss at Baseline | <0.0001 | –0.601 | 0.032 |
| Age (years) at Baseline | <0.0001 | 0.381 | 0.089 |
| Change in Pain Score from Baseline | <0.0001 | 2.629 | 0.456 |
| Change in Physician's Disease Activity Assessment from Baseline | 0.0006 | 1.696 | 0.494 |

tween change in fatigue and change in work productivity loss (baseline to 6 months).
**Results:** Of the n=1663 study participants included in the analysis population, n=1003 (60%) were in employment at baseline: mean (SD) age 40.7 (10.6) years, 63.3% male, mean (SD) disease duration 7.3 (7.8) years at baseline. At 6 months, 837 contributed to the analyses of which 93% remained on etanercept therapy. Following adjustment of putative confounders, baseline fatigue was significantly associated with work productivity loss at 6 months (p=0.035, see table). Similarly, the change in fatigue levels between baseline and 6 months was independently associated with a change in work productivity loss (p=0.044, see table).
**Conclusions:** In AS patients receiving etanercept therapy, high levels of fatigue are predictive of future work productivity loss. Furthermore, reductions in fatigue are significantly associated with improvements in work productivity. Together, these data support a potential causal role for fatigue in AS related work disability.
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## FRI0432 INCREASE IN IL-31 SERUM LEVEL IN RECENT SPONDYLOARTHRITIS: DATA FROM THE DESIR COHORT

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**Background:** IL-31 is a newly-described cytokine mainly produced by activated Th2 cells. IL-31 acts through IL31-RA and oncostatin heterodimeric receptors that activate STAT3 and STAT5. So far, IL31 has been mainly involved in airway hypersensitivity and atopic dermatitis. More recent data suggest its involvement in psoriasis, inflammatory bowel disease and osteoporosis.
**Objectives:** We aimed to assess IL-31 serum levels in patients with recent onset axial spondyloarthritis (SpA) from DESIR cohort.
**Methods:** The DESIR cohort is a prospective, multicenter French cohort of 708 patients with early inflammatory back pain (IBP) (duration >3 months and <3 years) suggestive of AxSpA (mean age 33.8 years; 53.8% women, 57% fulfilled the ASAS criteria). IL-31 and sCD40L were assessed using the multiplex and high sensitive 17-Plex ELISA (Bio-Plex Pro Human Cytokine 17-Plex Immunoassay, BioRad). Serum levels were assessed at baseline in 3 subgroups of patients: i. patients from the DESIR cohort fulfilling the ASAS criteria (ASAS+ group, n=443); ii. IBP patients from the DESIR cohort not fulfilling the ASAS criteria (ASAS– group, n=265); iii. Healthy controls age and sex-matched to a random sample of the DESIR cohort patients (control group, n=79).
**Results:** IL31 was significantly increased (p<0,001) in the ASAS+ group (median=7.7 pg/ml ± 15.4, mean 12.6 pg/ml) and ASAS– group (6.3 pg/ml ± 16, mean=11.3 pg/ml) compared to the control group (median=0.0±3.1, mean=1.1 pg/ml). IL31 was correlated with sCD40L (r=0.62; p<0.0001), and with DKK-1 (r=0.27; p<0,001). Patients exhibiting a high level of IL31 had a mSASSS score <1 (Yes 7.7 ± 10.7 versus No 13.02 ± 15.07; p=0.005). The multivariate analysis in ASAS+ group showed an association between IL-31 and sCD40L (p<0.0001), mSASSS≥1 (p=0.007), DKK-1 (p=0.002) and low bone density defined by Z-score < -2 (p=0.04). In the multivariate logistic analysis, IL-31 was independently associated with low bone density (p=0.02) in a model also including age (ns), gender (p=0.0008), and CRP (P=0.0003).When assessing patients with osteoporosis (T score <2.5), IL-31 was still independently associated (p=0.025) as well as gender (p=0.005). IL-31 was also independently associated with protection from axial structural damages (OR 0.07 [0.96–0.99];p=0.005) as well as other parameters included in the model: age (p<0.0001), and smoking (p=0.04). The same significant association between IL-31 and protection from structural damage when focussing on ASAS+ patients (p=0.007) or on patients fullfilling the Amor criteria (p=0.009). Only a trend was observed for patients fullfilling the ESSG criteria (p=0.07).

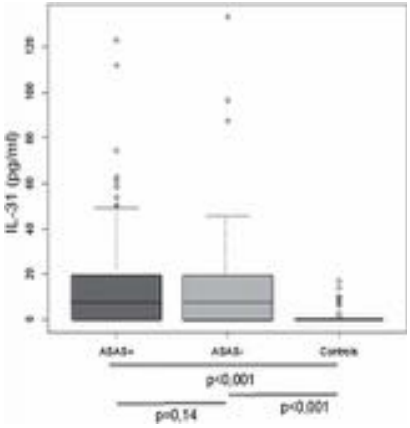


Figure 1. levels of IL31 in ASAS+ group, ASAS– group, Controls groups

**Conclusions:** IL31 serum levels are correlated with sC40L suggesting the role of activated T-cells in IL-31 expression. IL31 is also significantly correlated with the Wnt signaling inhibitory protein DKK-1. Increased levels of IL-31 might protect patients from structural damages but are also associated with low bone density. These preliminary results regarding IL-31 mediated bone effects in DESIR cohort need to be confirmed in more severe forms of the disease.
**Disclosure of Interest:** None declared
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## FRI0433 FACTORS ASSOCIATED WITH ELEVATED ACUTE PHASE REACTANTS IN PATIENTS WITH RECENT INFLAMMATORY BACK PAIN: IMPACT OF C REACTIVE PROTEIN ON THE PHENOTYPE OF PATIENTS. DATA FROM THE PROSPECTIVE MULTICENTER FRENCH COHORT DESIR

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**Objectives:** To determine the prevalence of increased C reactive protein (CRP) in patients with recent inflammatory back pain (IBP) suggestive of spondylarthritis (SpA) and to describe the overall features of these patients.
**Methods:** The DESIR cohort is a prospective multicenter French cohort of 708 patients with early IBP suggestive of SpA. An abnormal acute phase reactants level was determined based on normal upper range of values determined by centralized assessment of CRP. Data on the baseline demographic characteristics, functional status and quality of life, imaging features and HLA B27 status were compared in patients with and without increased CRP. We studied the total population of 708 patients and the subgroup of patients fulfilling ASAS criteria at the inclusion. Significant parameters in univariate analysis were tested in multivariate models.
**Results:** The prevalence of increased CRP (>5mg/L) at inclusion in the DESIR cohort was 233/684 (34.1%). The presence of increased CRP was significantly associated (univariate) with a younger age, previous history of arthritis, a history of dactylitis, clinical synovitis, BMD, radiographic sacroiliitis, a higher baseline modified Score of Ankylosing Spondylitis Spinal Score (mSASSS), MRI inflammatory lesions of spine and sacroiliac joints, scores of disease activity including Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity (ASDAS-CRP), physical function assessed by Bath Ankylosing Spondylitis Functional Index (BASFI), and health status indicators (Ankylosing Spondylitis Quality of Life, Health Assessment questionnaire for Ankylosing Spondylitis and the Physical Component Score from Short Form 36) in both populations. Increased CRP was associated with the absence of HLA-B27 only in the subgroup of patients fulfilling ASAS criteria.
Stepwise multivariate analysis found an association between increased CRP and male gender, younger age, history of arthritis, BMD >25kg.m$^2$, radiographic sacroiliitis, mSASSS, MRI inflammation on sacroiliac joints and ASDAS-CRP (p<0,05).
**Conclusions:** In recent IBP suggestive of SpA, increased CRP is associated with younger age, presence of peripheral articular manifestations, radiologic abnormalities, and both with higher activity and functional disability. Patients with elevated acute phase reactants seem to have a more severe form of the disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5849

## FRI0434 PREVALENCE OF STRUCTURAL CARDIAC DISEASE AND DIASTOLIC DYSFUNCTION IN AXIAL SPONDYLOARTHRITIS: A PROSPECTIVE CASE-CONTROL STUDY

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**Background:** Aortic dilation, aortic insufficiency (AI) and diastolic dysfunction (DD) have been described as complications of Ankylosing Spondylitis (AS), although their prevalence remains uncertain. Newer therapies for Axial Spondyloarthritis (AxSpA) may have further influenced the prevalence of cardiac disease. Prior studies were small and uncontrolled, resulting in controversial recommendations for routine echocardiographic screening of AxSpA patients.
**Objectives:** The objective of our study was to describe the prevalence of structural heart disease (SHD) and DD among a cohort of AxSpA patients matched with a healthy control population.

**Methods:** Prospective transthoracic echocardiograms were performed on 125 AxSpA patients and 56 age-matched controls. Leading edge aortic root (AoR) measurements were made and normalized for body size. Measurements were also taken at the aortic annulus, sino-tubular junction and ascending aorta. DD was graded according to the American Society of Echocardiography guidelines. Chi square tests and Wilcoxan rank sum analyses were used in the univariate analysis. A subgroup analysis was performed in a matched group of 90 AS patients meeting the modified New York criteria and 45 healthy controls.
**Results:** Participants were 68% male with a mean age of 43 ± 12 years. Mean AxSpA disease duration was 18 ± 12 years. mSASSS for the overall AxSpA population was 7.1 ± 14.5 units and was 9.9 ± 16.5 units for the AS population. Mean AoR diameter was 3.29 ± 0.36 cm for cases and 3.24 ± 0.32 cm for controls. There were no differences in linear aortic measurements, AI or DD between groups. The subgroup analysis of AS patients alone did not show differences in any of these outcomes when compared to controls.

Table 1

| Characteristics | AxSpA cases (n=125) | AS cases (n=90) |
|---|---|---|
| Baseline CRP (mg/L), Reference range <6.3 mg/L | 16.2±22.7 | 13.6±14.8 |
| CRP at time of echo (mg/L), Reference range <6.3 mg/L | 5.5±6.5 | 6.12±6.8 |
| Baseline disease activity (ASDAS – CRP) | 2.97±1.3 | 3.09±1.4 |
| Disease activity at time of echo (ASDAS – CRP) | 2.0±0.9 | 1.99±0.9 |
| NSAID therapy | 57% | 46% |
| TNFi therapy | 52% | 56% |

**Conclusions:** AxSpA patients showed no differences in AoR size or AI when compared with healthy controls. While there were differences among individual measurements used to assess diastology, there is no clinically relevant difference in DD between groups. These findings are the first evidence-base to support the recommendations against routine echocardiographic screening in asymptomatic AxSpA patients.
**References:**
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**Disclosure of Interest:** None declared
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## FRI0435 ABOUT HALF OF THE PATIENTS WITH ANKYLOSING SPONDYLITIS ALREADY HAVE RADIOGRAPHIC CHANGES IN T SPINE AT THE POINT OF DIAGNOSIS; CROSS SECTIONAL STUDY, BY WHOLE SPINE CT

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease, which destructs spine. After ivnolvement of sacroiliac joint, inflammation usually spreads from lower L spine to C spine. But it is hard to evaluate radiographic changes in T spine due to air in lung by X-ray.
**Objectives:** We performed this study to find out how many patients have radiographic changes in T spine at first visit and if bone spurs of vertebral bodies are associated with radiographic changes in facet joints in spine.
**Methods:** We enrolled the patients who were diagnosed as AS by modified NY criteria in Kyung Hee university hospital at Gangdong in Seoul, South Korea from Mar 2008 to Dec 2015. After diagnosis, we performed a whole spine CT in each patient according to the routine protocol of our clinic to evaluate the radiographic involvement of spine. Total 1,170 patients were enrolled and analyzed. We examined the presence of bone spurs in vertebral bodies (VB) and radiographic changes of facet joints in L and T spine and costovertebral joints (CVJ).
**Results:** Of the 1,170 enrolled patients. 920 were men (79%) and 85% were HLA B27 positive. Incidences of past history of peripheral arthritis and uveitis were 29.0% and 30.6%, respectively. Mean age was 33.0 ± 10.0 years and mean disease duration was 10.5 ± 9.5 years. 34.1% of patients had at least one bone spur and 26.3% had at least one lesion in facet joints in L spine. In T spine, 47. 2% of patients had already at least one bone spur, 28.2% had at least one lesion in facet joints. 32.8% had already at least one lesion in CVJs. Each radiographic change is associated with one another (p=0.00). These all radiographic changes were significantly more frequently observed in the patients with old age and long disease duration at the point of diagnosis (p=0.00). The lesion of CVJs and facet joints in T spine were observed more frequently in male than female significantly (respectively p=0.02, 0.00). 19.2% of the patients had radiographic changes in T spine without in L spine.
**Conclusions:** At the point of diagnosis, many patients already had radiographic changes in T spine. We suggest if radiographic change of T spine is included in radiographic progression score system such as mSASSS, we can more sensitively detect radiographic progression even in a short interval.
**Disclosure of Interest:** None declared
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## FRI0436 FATIGUE IS ASSOCIATED WITH WORK PRODUCTIVITY IMPAIRMENT IN UK PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA): A CROSS-SECTIONAL OBSERVATIONAL STUDY

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**Background:** Many patients with axSpA experience work disability (WD: not working due to axSpA) which is preceded by impairment whilst working (presenteeism), absenteeism, and overall work productivity loss (WPL). Studies addressing these and health-related factors are few, with only one done in a UK sample.
**Objectives:** To determine key factors associated with absenteeism, presenteeism, WPL, and daily activity impairment (other than employed work) in UK patients with axSpA using standardized measures.
**Methods:** In a cross-sectional, observational study, during visits to the Royal National Hospital for Rheumatic Diseases axSpA clinic, 490 patients completed validated questionnaires for: (1) Work productivity using the Work Productivity and Impairment questionnaire (WPAI) which produces 4 measures: absenteeism, presenteeism, WPL and activity impairment; (2) Health-related disease factors using: BASDAI, BASFI, BASMI, Jenkins Sleep scale, Patient Global Assessment (PGA) for disease activity, back pain at night, back pain at any time, EQ-5D for mobility, self-care ability, usual daily activities, pain/discomfort, anxiety/depression, EQ-VAS for Health State Today, FACIT for fatigue in the last week scale, and the Margolis Pain Diagram. Statistics package STATA V. 13.1 was used for analyses. Univariate and multivariate linear and logistic regression were applied to determine associations between WPAI measures and health-related factors.
**Results:** Of 490 patients, 301 (61%) provided WPAI measurements, 261 (53%) were in employment, 76% were male, 87% HLA-B27+, mean (±SD) years (i) age of first symptoms 21.5 (8.8), (ii) age at diagnosis 30.8 (11.7), (iii)disease duration 21.7 (13.0), and 29% were receiving biologics. Mean scores: BASDAI 3.8 (2.2), BASFI 4.0 (2.7), BASMI 3.8 (2.1), Jenkins 13.0 (2.7), PGA 3.9 (2.6), PGA night pain 3.3 (2.6), PGA pain anytime 3.6 (2.6), FACIT 34 (12), EQ-VAS 63 (22), Margolis pain 8.7 (6.9). Mean WPAI scores for absenteeism were=5.1% (19.2), presenteeism=22% (24.3), WPL=23.2% (25.7), activity impairment=34.8% (27.3).

| WPAI outcome | N | Variable | *OR/Coefficient (95% CI) | P |
|---|---|---|---|---|
| *Absenteeism | 301 | FACIT | –0.68 (0.56, 0.82) | <0.001 |
| | | Smoking – Non | 1 | 0.07 |
| | | Ex | 0.82 (0.24, 2.74) | <0.001 |
| | | Current | 2.86 (1.07, 7.64) | |
| | | Category – Radiographic | 1 | |
| | | Non | 6.07, (1.83, 20.1) | |
| Presenteeism | 301 | FACIT | –3.1 (–4.7, –1.6) | <0.001 |
| | | BASDAI | 3.0 (1.1, 5.0) | 0.002 |
| | | BASFI | 1.6 (0.0, 3.3) | 0.04 |
| | | Duration diagnosis (yrs) | –2.0 (–4.2, 0.3) | 0.08 |
| WPL | 301 | FACIT | –3.9 (–5.5, –2.3) | <0.001 |
| | | BASDAI | 3.0 (1.0, 4.9) | 0.003 |
| | | BASFI | 1.6 (0.1, 3.2) | 0.05 |
| Activity Impairment | 301 | FACIT | –3.9 (–4.7, –3.1) | <0.001 |
| | | Smoking – Non | 0 | 0.02 |
| | | Ex | –4.4 (–7.6, –1.2) | <0.001 |
| | | Current | –0.8 (–4.8, 3.2) | 0.003 |
| | | BASFI | 4.4 (3.6, 5.2) | <0.001 |
| | | EQ-VAS | –1.2 (–2.0, –0.4) | |
| | | PGA disease activity | 1.7 (0.8, 2.5) | |

**Conclusions:** Work productivity and activity impairment are associated with

**Abstract FRI0434** – Table 2

| | AxSpA cases (n=125) | Matched controls (n=56) | 95% CI | p-value | AS cases (n=90) | Matched controls (n=45) | 95% CI | p-value |
|---|---|---|---|---|---|---|---|---|
| AoR diameter >1.96 Z score above predicted mean | 3% | 2% | –0.3, –0.05 | 0.97 | 2% | 2% | –0.37, –0.4 | 1.00 |
| AI (trace and above) | 45% | 54% | – | 0.27 | 49% | 53% | – | 0.88 |
| DD (grade 1 and above) | 22% | 23% | – | 0.9 | 27% | 22% | – | 0.58 |
| Mean E wave velocity, cm/s | 77 | 69.4 | 71.8, 76.9 | 0.01 | 76.5 | 69.6 | 71.1, 77.2 | 0.03 |
| Mean A wave velocity, cm/s | 58.4 | 48 | 52.8, 57.4 | 0.00 | 59.9 | 46.4 | 52.5, 58.0 | 0.00 |
| Mean deceleration time, ms | 195.3 | 212.9 | 194.6, 207.2 | 0.02 | 193.9 | 212.9 | 193.1, 207.7 | 0.03 |
| Mean lateral e' velocity, cm/s | 12.7 | 14.3 | 12.7, 13.8 | 0.02 | 12.6 | 14.5 | 12.6, 13.9 | 0.08 |
| Mean septal e' velocity, cm/s | 9.6 | 9.5 | 9.2, 10 | 0.77 | 9.5 | 9.6 | 9.0, 9.96 | 0.83 |

fatigue, disease activity, and functional ability in UK patients with axSpA. The strong association of fatigue with work disability and activity impairment emphasize the need to measure and better understand the impact of fatigue in axSpA.
**Disclosure of Interest:** None declared
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### FRI0437 WHAT PREDICTS ABSENCE OF SPINAL DAMAGE IN PATIENTS WITH SPONDYLOARTHRITIS AFTER PROLONGED FOLLOW UP?

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**Background:** After 20 years of follow up the majority of patients with axial SpA have developed new bone in the spine although disease may remain isolated in the sacroiliac joints (SIJ) without any new bone in the spine. Assessment of these patients may provide new insights into the factors that influence disease progression. A new hypothesis has proposed that MRI can identify a "progressive phenotype" in early SpA characterized by the appearance of fat metaplasia in the SIJ. Fat metaplasia can occur both in subchondral bone and at the site of erosion after resolution of inflammation, this being termed backfill.
**Objectives:** To determine which clinical and MRI lesions in the SIJ are associated with absence of spinal damage after extensive follow up of patients with AS.
**Methods:** In the FORCAST prospective cohort, AS patients (n=431) attending community and academic practices were assessed for clinical and laboratory outcomes every 6 months, radiography every 2 years, and MRI annually. MR scans of the SIJ were assessed by SPARCC SIJ and SSS methods for inflammation and structural features, respectively, by 2 readers and an adjudicator. Absence of spinal damage was pre-specified as no syndesmophytes or ankylosis on cervical and lumbar spine radiographs after ≥10 years from onset of symptoms and for the entire duration of prospective follow up. Patients with and without spinal damage were matched for age and symptom duration and compared by t-test, Mann-Whitney, and Fisher's exact tests. We used univariate and multivariate conditional logistic regression to determine which demographic, clinical, and imaging variables were associated with absence of spinal damage.
**Results:** Mean (SD) duration of symptoms and prospective follow up was 18.0 (7.0) and 2.3 (0.49) years in cases with no damage (n=42) and 17.5 (8.2) and 2.6 (1.4) years in those with damage (n=81). The group with no damage had fewer males (p=0.004), lower CRP (p=0.02), and lower MRI SIJ scores for fat (p=0.03) and ankylosis (p=0.003) while score for SIJ erosion was significantly higher (p=0.02). Definite SIJ ankylosis (SSS score ≥2 by both readers) was evident in 20.7% of cases in the no damage group versus 53.3% of those with damage (p=0.007). Univariate regression indicated that no damage was associated with female sex (p=0.002), lower ASDAS (p=0.048), and lower SSS values for fat (p=0.032), backfill (p=0.014), and ankylosis (p=0.001). Smoking and B27 were not significant. A multivariate logistic regression model that included gender, ASDAS, and MRI SIJ features indicated that lower values for SSS backfill and ankylosis were independently associated with no damage (OR [95%CI]=0.83 [0.69–0.99] and 0.89 [0.82–0.96], respectively). When all definite MRI features (SSS score ≥2 by both readers) were included in the model, definite SIJ ankylosis was significantly less likely in those who did not develop spinal damage (OR [95%CI]=0.24 [0.08–0.70].
**Conclusions:** The absence of radiographic damage in the spine after prolonged duration of symptoms is associated with the lack of fat metaplasia and ankylosis in the SIJ on MRI. This supports the hypothesis that fat metaplasia identifies a progressive phenotype and that its appearance in the SIJ, together with SIJ ankylosis, may predispose to spinal progression.
**Disclosure of Interest:** None declared
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### FRI0438 DESCRIPTION AND PREVALENCE OF SPONDYLOARTHRITIS IN A LARGE COHORT OF PATIENTS WITH ANTERIOR UVEITIS: THE SENTINEL INTERDISCIPLINARY COLLABORATIVE PROJECT

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**Background:** While the diagnosis of many SpA is usually made in rheumatology units based on other clinical findings as the inflammatory low back pain or arthritis (1,2), it has been described that there could be patients with AU with an undiagnosed SpA (3). Therefore, an early recognition of a possible SpA in patients attending the ophthalmology units with uveitis is vital in order to improve these patient's management
**Objectives:** To describe and analyse the prevalence of spondyloarthritis (SpA) in patients with anterior uveitis (AU).
**Methods:** In a multicentric prospective study, consecutive patients with AU HLA-B27 positive or HLA-B27 negative with more than one episode of AU separated by at least 3 months were selected and evaluated by an ophthalmologist and a rheumatologist following a pre-defined visits schedule. Patients with previous diagnosis of SpA were excluded. Sociodemographic and clinical variables including the diagnosis of SpA according to ASAS criteria and an exhaustive ophtalmological examination were collected. Baseline descriptive, bivariate and concordance analyses were performed.
**Results:** We included 798 patients, most men (59%) with a mean age of 45 years, 60% with AU HLA-B27 positive, 40% with recurrent AU HLA-B27 negative. A total of 50.2% and 17.5% presented axial and peripheral SpA according to ASAS criteria respectively. Patients with AU and HLA-B27 were more frequently diagnosed of axial (69.8% vs 27.3%, p<0.0001) and peripheral SpA (21.9% vs 11.1%, p<0.0001) than patients with recurrent AU with HLA-B27 negative. In general, we did not detect important differences between groups in the ophthalmologic variables.
**Conclusions:** A high rate of patients with clinically significant AU have an undiagnosed SpA, higher if HLA-B27 was positive.
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## Psoriatic arthritis

### FRI0439 EFFECTS OF DIFFERENT ANTI TNF ALPHA TREATMENTS ON LIPID AND CARBOHYDRATE METABOLISM IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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**Background:** TNFa plays a key role in the pathogenesis of both rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Recent data support the hypothesis that TNFa is involved in the regulation of carbohydrate and lipid metabolism and it is well know that patients with RA and PsA present a high prevalence of metabolic syndrome and insulin resistance.
**Objectives:** The aim of this study is to evaluate the effects of three different anti TNFa drugs on lipid profile, insulin resistance and circulating levels of various adipokines in a cohort of patients with RA and PsA and the possible relationship with activity disease
**Methods:** We evaluated 25 consecutive patients fulfilling the 2010 revised American College of Rheumatology criteria for RA and 66 consecutive patients age and sex matched fulfilling the CASPAR criteria for PsA. At time of recruitment all patients were treated with methotrexate (10 – 15 mg/weekly) and low dose of prednisone (up to 7,5 mg/day). PsA and RA patients were randomly assigned to receive adalimumab (ADA), infliximab (IFX) or etanercept (ETN). For each group we evaluated the effect of treatment on body mass index (BMI), lipid profile, atherogenic index, insulin resistance index (HOMA2-IR), insulin sensitivity index (QUICKI), circulating levels of adipokines (resistin, leptin, adiponectin) and Framingham cardiovascular risk score at baseline (T0) and after 3 (T1) and 6 (T2) months and we correlated these data with disease activity (DAS28).
**Results:** At baseline we found that compared to PsA, RA patients presented a significantly higher disease activity (p<0,01), atherogenic index and insulin resistance (p<0,05 and p<0,01 respectively), whereas serum levels of adiponectin were significantly lower (p<0,05). No differences in BMI, insulin sensitivity index, Framingham cardiovascular risk score, serum lipid profile and circulating levels of resistin and leptin were observed between AR and PsA patients.
Both in RA and in PsA patients the activity disease at baseline positively correlated with atherogenic index and circulating levels of leptin and resistin (r=0,62, p<0,01); conversely, a negative correlation was observed at baseline between disease activity and circulating levels of adiponectin (r=-0,58, p<0,01). Both in RA and PsA patients ADA, IFX and ETN induced a significant reduction of atherogenic index (p<0,05 both at T1 and T2), insulin resistance (p<0,05 both at T1 and T2) and serum levels of leptin and resistin (p<0,01 both at T1 and T2); this reduction positively correlated with the reduction of disease activity. On the other hand, circulating levels of adiponectin and insulin sensitivity index significantly increased after treatment with ADA, IFX and ETN (p<0,05 at T1, p<0,01 at T2) and presented an inverse relationship with the disease activity. No differences were found between different anti TNFa treatments in the two group of patients.
**Conclusions:** These preliminary data confirm the hypothesis that treatment with

anti TNFa biologic drugs can positively affect the lipid metabolism, the atherogenic index and the insulin resistance profile in RA and PsA patients.

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## FRI0440 PROGRESSION OF RADIOGRAPHIC AXIAL DAMAGE IN PATIENTS WITH PSORIATIC ARTHRITIS. RELATION WITH CLINICAL AND ANALYTICAL FACTORS

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**Background:** Axial involvement in psoriatic arthritis (PsA) is a controversial issue. Lack of unanimity in the definition has led to a wide range of levels of prevalence. Moreover, although radiographic progression in patients with spondylitis (AS) is widely known, the different radiographic characteristics of both entities advise against establishing a parallelism between the evolution of the different lesions or the clinical factors which may have an influence on them.
**Objectives:** Measure radiographic progression over four years in patients with PsA and axial involvement. Relate radiographic damage with clinical and analytical factors.
**Methods:** Prospective study with patients diagnosed with PsA according to the CASPAR criteria. Axial involvement was defined as the presence of inflammatory back pain along with sacroiliitis and/or syndesmophytes. Patients with less of five years of evolution from the onset were included. The radiographic damage was measured with the PASRI method. The difference between both measurements was four years. The assessment was carried out by two observers. The clinical factors measured were: age, sex, peripheral involvement, smoking, use of NSAIDs (continuous vs on-demand), biological treatment, measures of activity (BASDAI), function (BASFI) and mobility (BASMI). The analytical variables measured were: VSG, PCR, B-CrossLaps, P1NP and HLA-B27. The presence of a dorsal or lumbar fracture was also assessed according to the semiquantitative Gennant method.
**Results:** 45 patients with PsA and axial involvement were included. The average age was 53.5 years (SD: 12.9). 31 patients were men. The kappa coefficient between both raters was 0.70. Radiographic progression was higher in men (3.13 vs 1.14, p=0.04; in the multivariate analysis: p=0.04, OR: 0.61, 95%CI: 0.39–0.98) and in smokers (active and ex-mokers) (3.81 vs 1.14, p=0.04; in the multivariate analysis: p=0.04, OR: 0.61, 95%CI: 0.48–0.93). The presence of vertebral fracture was associated to patients with a higher radiographic progression (4.85 vs 1.82; p=0.001; in the multivariate analysis: p=0.008, OR: 0.59, 95%CI: 0.39–0.87). No differences were found regarding the presence of peripheral manifestations (2.32 vs 3.57, p=0.3), peripheral joints erosions (2.61 vs 3.1, p=0.4), continuous use of NSAIDs (1.67 vs 2.91, p=0.3), biological prescription (2.04 vs 3.72, p=0.3) or HLA-B27 (2.00 vs 2.79, p=0.5). A correlation was observed between radiographic progression and the initial PASRI score (p=0.001) and between progression and a lower P1NP concentration (p=0.02). Twelve patients did not show radiographic progression. These patients showed lower initial PASRI scores (5.35 vs 12.6, p=0,001; in the multivariate analysis: p=0.03; OR: 0.73, 95%CI: 0.55–0.98) and a lower P1NP concentration (38.7 vs 61.1; p=0.006: in the multivariate analysis: p=0.01; OR: 1.05, 95%CI: 1.008–1.096).
**Conclusions:** As in patients with AS, male gender, smoking and the presence of initial damage were associated to a higher radiographic progression. These patients were associated to a higher rate of vertebral fracture and lower levels of P1NP. Radiographic progression was not associated to inflammatory parameters, peripheral manifestations or to the treatment used. 25% of the patients did not show radiographic progression

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## FRI0441 BENEFITS OF DOSE TAPERING STRATEGIES WITHIN THE PSORIATIC ARTHRITIS MULTIDISCIPLINARY UNITS

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**Background:** *Psoriatic Arthritis* (PsA), due to the involvement of both the skin and joints, is one of the rheumatic diseases that can most benefit from multidisciplinary work.The collaboration improved the management of difficult-to-diagnose and/or uncontrolled disease in addition to the early diagnosis and treatment of psoriatic arthritis.Biological therapy is a well-established treatment for PsA. Taking into account the proven long-term efficacy and the cost of these treatments, the *Psoriatic Arthritis* Units (PAU) try to consider new strategies of doses as an alternative to the standard dosage in those suitable patients whom achieved clinical remission.
**Objectives:** We present the demographic, economic, and disease activity data of the 88 patients with PsA who were seen in our PAU in the last year.
**Methods:** Distribution: 71,6% Peripheric 11,4% axial; 17% both. The average age was 49.55 years, with 41 males and 47 females. Comorbidities: dyslipidemia 21,6%, Hypertension 18,2%, Diabetes Mellitus 10,2%, Obesity 6,8%, Smoker 22,7%.
**Results:** 63, 6% were treated with at least one systemic treatment (47,7% methotrexate, 8% salazopyrin, 5,7% combined MTX/SSZ and 2,2% others drug). Only 26,1% were treated with Biological therapy (8%adalimumab;8%etanercept;5,7%certolizumab;2,3% ustekinumab and2,3%infliximab). 30,43% of all patients were under lower-dose treatment according to technical data.We reduced the biological dosage after achieving PGA $\leq$1 (clear or almost clear) and DAS28- ERS $<$2, 6 for at least 12 months. Results: 57% with adalimumab 40mg every 21 days; 28% with etanercept (25 mg /week and 25 mg/10 days) and 14% with ustekinumab without induction dose.We calculated the cost savings in euros of the direct expenditure of the pharmaceutical procedures with the modification of the dosage according to each biological treatment. Adalimumab 4295, 25 euros/year/patient (total: 17,181 euros/year) Etanercept (25 mg /week and 25 mg/10 days) 3.937,96 euros /year- 2.503,8 euros/year; Ustekinumab 2.642,96 euros/year. Subsequently, the total savings amount to 26.265,72 euros /year. These savings translate to at least 3 more patients/year to treat with the same budget.
**Conclusions:** The implementation of dose modification strategies with biological therapies is considered to be an innovative tool that maintains treatment goals using the minimum effective dose for those selected patients. The consequences of an adequate treatment strategy directed to keep long-term clinical response in our patients could be both the reduction of the treatment costs and that of the drug exposure. The Psoriatic Arthritis Units permits this new point of view to control the patients and their treatments.

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## FRI0442 HISTOPATHOLOGY OF TREATMENT-NAÏVE PSORIATIC SYNOVITIS: A COMPARISON WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is an inflammatory joint disease associated with psoriasis. With biologics entering the therapeutic scene, treatment outcome has dramatically improved; nonetheless, pathogenesis of the condiiton is still under investigation. Exploring the biological differences between PsA and RA at tissue level may help in understanding their pathological pathways. Little comparative data is available in early and untreated disease. With the use of a minimally-invasive, ultrasound-guided, needle biopsy technique, synovium from patients with early and untreated disease and small joint involvement may be studied.
**Objectives:** To evaluate clinical, sonographic and histological features of early untreated psoriatic arthritis versus rheumatoid arthritis.
**Methods:** Patients were selected from a large prospective cohort of treatment-naïve patients with inflammatory arthritis of under 12 months' duration. All patients underwent a clinical and sonographic assessment of arthritis activity and an ultrasound-guided synovial biopsy prior to treatment. 32 PsA and 23 gender- and age-matched RA patients were included in this cross-sectional analysis. Synovial inflammatory infiltrate were assessed using immunohistochemical staining for CD3, CD68, CD20 and CD138. Tissue was classified as lymphoid (presence of grade 2/3 CD20+ aggregates); fibroid (CD68 sublining score $\leq$2 on a semi-quantitative scale of 0 to 4); or myeloid (CD68 sublining score $>$2, with or without grade 1 aggregates). Gene-expression analysis of 46 pre-selected genes was performed on 16 PsA and 22 RA patients using Fluidigm technology.
**Results:** Demographic and clinical data at the time of biopsy were comparable between PsA and RA; mean symptom duration was 5.5 for PsA and 4.8 months for RA. Mean tender and swollen joint counts were lower in PsA, nonetheless no significant difference could be found in DAS28. US synovial thickness was similar between the two groups, however a significantly higher Power Doppler score was detected in the biopsied joints of RA patients. Histologically, PsA synovitis score was significantly lower compared to RA; accordingly, PsA synovial tissue showed a lower number of B and T lymphocytes, plasma-cells and sub-lining macrophages. Around 50% of RA synovium demonstrated features of the lymphoid pathotype; in contrast, fibroid (40%) and myeloid (37%) pathotypes were prevalent in PsA (chi-square p$<$0.05). Surprisingly, expression of pro-inflammatory cytokines such as TNFa, IL1b, IL6, IL23, IL17A, IL12A at mRNA level was comparable between RA and PsA.
**Conclusions:** Despite similar clinical features, early treatment-naïve PsA and RA are histologically deeply different; inflammatory infiltrate is lower in PsA compared to RA. However, pro-inflammatory cytokines are similarly expressed, suggesting differential pathways of translation from synovitis to clinical phenotype.

**Disclosure of Interest:** None declared
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## FRI0443 DOES THE CYTOKINE PATTERN, INCLUDING THE IL23 - IL17 IMMUNE AXIS, CHANGE IN PREGNANT WOMEN WITH PSORIATIC ARTHRITIS?

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**Background:** During pregnancy, most patients with psoriatic arthritis (PsA) experience a natural improvement of their symptoms. This might be due to the immunological changes that occur in normal pregnancy to allow tolerance to the semiallogeneic fetus. Pregnancy induces a down-regulation of the adaptative immune system and generates a specific cytokine milieu. The balance between T helpers cells (Th), Th1/Th2/Th17, depends on the cytokine milieu and interleukin (IL) 23 promotes the expansion and survival of Th17 cells. The IL23-IL17 axis is up-regulated in PsA.
**Objectives:** The aim of our study is to investigate changes of the cytokines pattern with focus on the IL23-IL17 immune axis during and after pregnancy in PsA patients compared with non-pregnant PsA patients and healthy controls (HC).
**Methods:** Nineteen PsA patients (10 pregnant, 9 non-pregnant) and 19 HC (11 pregnant and 8 non-pregnant) were prospectively studied. Clinical assessment and blood sampling was done in pregnant women before, during and after pregnancy and once in the non-pregnant group. Sera were analyzed for levels of C reactive protein (CRP) and high sensitive CRP (hsCRP) by enzyme linked immunoassay. The following cytokines and regulatory molecules were measured by magnetic bead-based multiplex immunoassay: the activation marker soluble CD40 ligand (sCD40L), the Th1 cytokines tumor necrosis factor α (TNFα) and Interleukin (IL)-1β, the Th2 cytokines IL-4, IL-10, IL-31, IL-33, IL-25 and the Th 23/17 pathway cytokines IL-6, IL-17A, IL-17F, IL-21, IL-22, IL23.
**Results:** In the non-pregnant groups we observed that patients with PsA had higher levels of hsCRP, sCD40L, TNFα, IL-1β, IL-33, Il-6 and IL-22 than HC.
Though pregnant PsA patients had inactive or mild disease activity with normal CRP levels, the hsCRP levels were higher than those of pregnant HC.
In the HC group, pregnant women at the third trimester showed higher levels of IL-10, Il-33 and TNFα than at the postpartum time point. Moreover, healthy women at the third trimester had higher levels of IL-1β, IL-33 and IL-22 than age-matched non-pregnant women.
At the third trimester of pregnancy, patients with PsA displayed higher levels of hsCRP, sCD40L, TNFα and IL-6 than HC. Interestingly, pregnant PsA patients did not show any differences in the cytokine pattern compared to non-pregnant PsA patients.
Most differences appeared when comparing PsA and HC at the postpartum time point. Postpartal patients with PsA showed higher levels of sCD40L, TNFα, IL-1β,IL-10, IL-33, IL-31, IL-6 and IL-22 compared to HC
**Conclusions:** Pregnancy induces no predominance of circulating Th2 cytokines but rather a coexistence of Th1, Th2 and Th17 cytokines. Patients with PsA present a more pronounced inflammatory profile consisting of elevated hsCRP levels, Th1 and Th17 cytokines during pregnancy and postpartum. Thus, inactive disease in pregnant PsA patients was associated with persisting immunological activity including the IL-23 /Th17 immune axis.
**Disclosure of Interest:** None declared
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## FRI0444 EARLY DETECTION OF PSORIATIC ARTHRITIS: A MULTI-OMIC APPROACH TO DEVELOPING A NEW BLOOD TEST

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**Background:** Psoriatic Arthritis (PsA) is a form of seronegative inflammatory arthritis (IA) frequently associated with psoriasis. Similar to other forms of IA, it is a complex heterogeneous disease. While PsA can be characterised by distinct clinical manifestations, at early onset, it often resembles other disease types - especially rheumatoid arthritis (RA). During the treatment and management of the disease important clinical decisions are made and these have a significant impact on patient outcomes. Making an accurate and early diagnosis is particularly important to ensuring that individual patients receive effective and safe medication. Thus, it is widely acknowledged by physicians and patients alike that a new test is needed to facilitate the early and specific diagnosis of PsA [1].
**Objectives:** To (i) identify candidate biomarkers with the potential to segregate patients with PsA from those with RA (ii) explore the value of combining different omic discovery platforms.
**Methods:** Serum samples were obtained from a cohort of 64 patients (32 PsA and 32 RA) defined as early onset (<12 months) and DMARD naïve. Individual baseline samples were analysed using microRNA (miRNA) (n=63), Luminex xMAP (n=62), an aptamer based platform called SOMAscan (n=36) and label free LC-MS/MS (n=64), platforms. Data was imported into Perseus (version 1.5.0.8) for statistical analysis ($p \leq 0.05$). Additionally, data was analysed using a random forest model in R software (version 3.1.0).
**Results:** In this study, by combining 4 different omic technologies it was possible to quantify 376, 48, 1129, 387 analytes by miRNA, Luminex, SOMAscan and LC-MS/MS analysis, respectively. Statistical analysis revealed that a total of 287 analytes were differentially expressed across the two conditions ($p \leq 0.05$). Furthermore, random forest analysis revealed the most discriminatory biomarkers from the miRNA, Luminex and SOMAscan analysis. Figure 1 A-C illustrates the receiver operating characteristic (ROC) curves generated from these analyses. The application of the random forest model to the LC-MS/MS data is part of ongoing work.

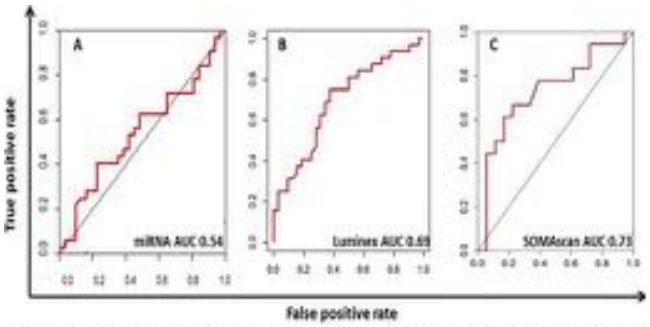



Figure 1. Random forest (RF) Receiver Operating Characteristic (ROC) curves PsA Vs RA. RF analysis of (A) the miRNA data revealed patients could be segregated with an AUC of 0.55. (B) the Luminex data revealed patients could be segregated with an AUC of 0.69 and (C) the SOMAscan data revealed patients could be segregated with an AUC of 0.73

**Conclusions:** By combining the most discriminatory analytes from each type of analysis into a single algorithm, a biomarker signature with increased predictive potency should be identified. Thus, these molecules represent candidates for inclusion into blood based mulit-analyte test that could be used in the diagnosis of PsA.
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## FRI0445 TILDRAKIZUMAB TREATMENT IMPROVED MEASURES OF PSORIATIC ARTHRITIS IN ADULTS WITH CHRONIC PLAQUE PSORIASIS

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis. Recent evidence with biologic medications that target IL-17 and IL-12/23 (i.e., secukinumab and ustekinumab) have demonstrated efficacy in the treatment of PsA leading to their inclusion in the 2015 EULAR recommendations for the management of psoriatic arthritis [(1)]. Tildrakizumab is an investigational high-affinity, humanized, IgG1/κ, anti-IL-23p19 monoclonal antibody.
**Objectives:** This analysis was done to evaluate the effect of tildrakizumab on PsA endpoints in a small population of patients with PsA participating in a Phase 2 chronic plaque psoriasis study.
**Methods:** A randomized, double-blind study (NCT01225731) was conducted in 355 adults with moderate to severe plaque psoriasis. Patients were randomized to receive tildrakizumab 5 mg, 25 mg, 100 mg, 200 mg or placebo subcutaneously at Weeks 0 and 4, then every 12 weeks for 52 weeks. The primary efficacy endpoint was the proportion of patients achieving a PASI 75 at Week 16. Patients with PsA (defined by subject history) were examined. PsA endpoints included: mean change in Psoriatic Arthritis Screening and Evaluation (PASE), Health Assessment Questionnaire (HAQ), pain assessed with Visual Analog Scale (VAS), and high-sensitivity C-Reactive Protein (hsCRP), measured from baseline through Week 16.
**Results:** 339 patients completed 16 weeks of treatment, PASI 75 responses were 33.3%, 64.4%, 66.3%, 74.4% and 4.4%, in the 5 mg, 25 mg, 100 mg, 200 mg tildrakizumab and placebo groups, respectively ($p \leq 0.001$) [(2)]. Overall, 65 patients (18%) had PsA (5 mg n=8, 25 mg n=15, 100 mg n=17, 200 mg n=17, placebo

n=26). Mean changes from baseline are listed below. Results show numerically greater improvements for all doses of tildrakizumab vs. placebo for PASE, and pain parameters. Additionally, tildrakizumab 25 mg and 200 mg demonstrated numerically greater improvement vs. placebo for HAQ (Table). In the overall study population, mean (SD) changes from baseline at Week 16 in observed hsCRP (mg/L) was -0.8 (5.7), -2.3 (6.1), -2.7 (9.2), -3.0 (13.4), and -1.3 (3.6) for the 5 mg, 25 mg, 100 mg, 200 mg, and placebo groups, respectively; hsCRP results for PsA patients only are shown (Table).

**Table: Mean Changes from Baseline in PsA Parameters***

| | 5 mg (n=6) | 25 mg (n=12) | 100 mg (n=14) | 200 mg (n=13) | Placebo (n=10) |
|---|---|---|---|---|---|
| PASE | 2.2 (-10.3, 14.7) | -7.9 (-17.1, 1.3) | -6.1 (-14.7, 2.5) | -6.1 (-16.1, 4.0) | -0.3 (-10.9, 10.4) |
| HAQ | 0.0 ( -0.3, 0.3) | -0.3 ( -0.5, -0.1) | 0.0 ( -0.2, 0.2) | -0.2 ( -0.4, 0.0) | 0.1 ( -0.1, 0.3) |
| VAS Pain | -13.8 (-38.9, 11.3) | -17.2 (-34.7, 0.3) | -12.3 (-28.7, 4.0) | -16.9 (-33.9, 0.1) | 10.2 ( -8.9, 29.2) |
| hsCRP | -1.9 (2.3) | -3.1 (5.5) | -2.4 (4.3) | -6.0 (21.7) | -1.6 (1.9) |

*Mean changes (95% CI) for PASE, HAQ, and VAS Pain are based on constrained longitudinal data analysis; mean changes (SD) for hsCRP are based on observed data

**Conclusions:** Numerical improvements in measures of PsA were observed with tildrakizumab in a small sample of patients with chronic plaque psoriasis who had concomitant PsA. Tildrakizumab 25 mg, 100 mg, and 200 mg were associated with numerically lower hsCRP levels compared with 5 mg and placebo. Further research is needed to better evaluate tildrakizumab in the treatment of PsA.

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**Disclosure of Interest:** R. Langley Consultant for: AbbVie, Celgene, Centocor, Janssen-Cilag, LEO Pharma, Merck & Co., Inc., Novartis and Pfizer, D. Thaçi Consultant for: Abbott (AbbVie), Almiral, Amgen, Astellas, Biogen Idec, Boehringer Ingelheim, Celgene, Dignity, Forward Pharma, Galderma, GlaxoSmithKline, Isotechnika, Janssen-Cilag, LEO Pharma, Lilly, Maruho, Medac, Medimmune, MSD, Merck Serono, Novartis, Regeneron, Sandoz, Sanofi-Aventis, Takeda and Pfizer., K. Reich Consultant for: AbbVie, Amgen, Biogen Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Lilly, Medac, Merck, Novartis, Pfizer, Vertex and Takeda., K. Papp Consultant for: Abbott (AbbVie), Amgen, Biogen Idec, Boehringer Ingelheim, Celgene, Centocor, Foreward Pharma, Galderma, Genentech, Incyte, Isotechnika, Janssen, Kyowa Kirin, LEO Pharma, Lilly, Medimmune, Merck Sharp Dome, Merck Serono, Novartis, Regeneron, Stiefel, Takeda, Pfizer and USB., A. Mehta Employee of: Merck & Co., Inc., Q. Li Employee of: Merck & Co., Inc., C. La Rosa Employee of: Merck & Co., Inc.

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## FRI0446 TREATMENT WITH TILDRAKIZUMAB, AN ANTI-IL-23P19 MONOCLONAL ANTIBODY, IMPROVES HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH CHRONIC PLAQUE PSORIASIS

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**Background:** Tildrakizumab is a high-affinity, humanized, IgG1/κ, anti-IL-23p19 monoclonal antibody that has demonstrated efficacy in the treatment of chronic plaque psoriasis, a disorder associated with significant quality-of-life impairment.
**Objectives:** This analysis evaluated Dermatology Life Quality Index (DLQI) questionnaire responses to assess how clinical improvements with tildrakizumab affect specific areas of daily life in psoriasis patients.
**Methods:** This randomized, controlled study (NCT01225731) included 355 patients with moderate-to-severe chronic plaque psoriasis who were randomized to receive placebo, tildrakizumab 5 mg, 25 mg, 100 mg, or 200 mg for 16 weeks in Part 1 of the study. The primary endpoint was the proportion of patients achieving a 75% reduction in the Psoriasis Area and Severity Index (PASI 75). Patients completed the Dermatology Life Quality Index (DLQI) questionnaire to assess the effect of treatment on health-related quality of life. Responses to individual DLQI questions were scored in terms of the level of impairment due to psoriasis: 3 (Very Much) to 0 (Not Relevant or Not at All). Individual questions were grouped and assessed in following categories: Symptoms/Feelings (total score of 6); Daily Activities (total score of 6); Leisure (total score of 6); Work/School (total score of 3); Personal Relationships (total score of 6); Treatment (total score of 3)[(1)]. A change of at least 4 points in the overall score is considered a clinically important change[(2)].
**Results:** There were 339 patients who completed 16 weeks of treatment. PASI 75 responses at Week 16 were 33.3%, 64.4%, 66.3%, 74.4% and 4.4%, in the 5 mg, 25 mg, 100 mg, 200 mg tildrakizumab and placebo groups, respectively ($p \leq 0.001$ vs. placebo); mean changes (95% CI) from baseline in DLQI were associated with PASI 75 responses and are presented in the Table [(3)]. All tildrakizumab doses were associated with a clinically important change (>4 points)[(2)]. Mean changes from baseline to Week 16 in individual DLQI categories are presented (Table). Tildrakizumab 25 mg, 100 mg, and 200 mg doses were associated with the largest improvements in individual categories, particularly in Symptoms/Feelings and Daily Activities.

**Table:** Mean Change from Baseline in DLQI at Week 16

| | 5 mg (N=39) | 25 mg (n=86) | 100 mg (n=88) | 200 mg (n=84) | Placebo (n=41) |
|---|---|---|---|---|---|
| **Mean Change (SD) in Categories*** | | | | | |
| Symptoms/Feelings (total score of 6): | -1.5 (1.5) | -2.9 (1.8) | -2.4 (1.6) | -2.6 (1.9) | 0 (1.7) |
| Daily Activities (total score of 6): | -1.0 (1.4) | -2.0 (1.8) | -1.9 (1.7) | -1.8 (1.8) | 0.6 (1.8) |
| Leisure (total score of 6): | -0.8 (1.4) | -1.4 (2.0) | -1.7 (1.9) | -1.6 (2.0) | 0.1 (1.8) |
| Work/School (total score of 3): | -0.4 (0.8) | -0.9 (1.1) | -0.6 (1.1) | -0.9 (1.0) | -0.2 (1.3) |
| Personal Relationships (total score of 6): | -0.8 (1.7) | -1.3 (1.8) | -1.3 (1.7) | -1.3 (1.6) | -0.8 (1.1) |
| Treatment (total score of 3): | -0.6 (0.9) | -0.9 (1.1) | -0.9 (1.1) | -0.8 (1.1) | 0.3 (1.1) |
| **Overall Mean (95% CI) Changes**[*,**]** | | | | | |
| Overall DLQI | -4.9 (-7.0, -2.8) | -9.2 (-10.6, -7.7) | -8.5 (-9.9, -7.1) | -8.8 (-10.3, -7.4) | 1.0 (-1.1, 3.0) |

*based on observed data
** based on constrained longitudinal data analysis (cLDA)

**Conclusions:** Treatment of chronic plaque psoriasis with tildrakizumab was associated with clinically important changes in DLQI including improvements in symptoms/feelings, daily activities, leisure, work/school, personal relationships, and treatment categories that were correlated with improvements in PASI scores.

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## FRI0447 LONG-TERM (156-WEEK) EFFICACY AND SAFETY PROFILE OF APREMILAST, AN ORAL PHOSPHODIESTERASE 4 INHIBITOR, IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A PHASE III, RANDOMIZED, CONTROLLED TRIAL AND OPEN-LABEL EXTENSION (PALACE 1)

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**Background:** Long-term data on the efficacy and safety of therapies is vital for treatment decision making in chronic diseases such as psoriatic arthritis (PsA). Three-year treatment data from the PALACE 1 (NCT01172938) study of apremilast (APR) in patients with active PsA despite previous conventional disease-modifying antirheumatic drug (DMARD) or biologic therapy has recently become available.
**Objectives:** Using data from 3 years of treatment, examine the longer term efficacy/safety of APR.
**Methods:** Patients were randomized (1:1:1) to placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID (APR20) stratified by baseline DMARD use (yes/no). The PBO-controlled phase continued to Wk 24, with an early escape option at Wk 16. At Wk 24, all remaining PBO patients were re-randomized to APR30 or APR20. Double-blind APR treatment continued to Wk 52; patients could continue APR for up to 4 additional years. Efficacy assessments in years 2 and 3 were conducted at Wks 65, 78, 91, 104, 117, 130, 143, and 156.
**Results:** 504 randomized patients received ≥1 dose of study medication (PBO: n=168; APR30: n=168; APR20: n=168). In an "as observed" analysis, 53.2% (APR30) and 59.6% (APR20) of patients achieved a modified ACR20 response at Wk 52 (Table), regardless of when APR was started (baseline, Wk 16, or Wk 24). Of the patients entering year 2, 65.3% (APR30) and 60.9% (APR20) attained these responses at Wk 104. A total of 92% (260/284) of the patients starting the third year of the trial completed the Wk 156 visit; overall, this is 52% (260/504) of patients randomized at baseline. Patients receiving APR30 at Wk 156 demonstrated sustained improvements, as shown by ACR20 response rates of 65%, swollen/tender joint count mean percent improvements of -81.2% and 73.2%, and HAQ-DI mean change of -0.37, and 41.9% of patients reaching DAS (CRP) <2.6. Similarly, the proportion of patients with HAQ-DI exceeding the minimal clinically important difference (MCID) ≥0.30 threshold, mean change in DAS-28 (CRP), and PASI-75/PASI-50 responses were maintained (Table). No new safety concerns were identified with up to 156 wks of APR treatment. During Wks >104 to ≤156 of APR exposure, the only adverse event (AE) occurring in ≥5%

| | Outcomes at Wk 52 and Wk 156 | | | |
|---|---|---|---|---|
| | Wk 52 | | Wk 156 | |
| | APR30 n=193* | APR20 n=186* | APR30 n=139* | APR20 n=129* |
| ACR20, n/m† (%) | 101/190 (53.2) | 109/183 (59.6) | 69/137 (65.0) | 85/125 (68.0) |
| ACR50, n/m† (%) | 49/191 (25.7) | 45/180 (25.0) | 56/136 (40.6) | 55/125 (44.0) |
| ACR70, n/m† (%) | 27/191 (14.1) | 21/179 (11.7) | 32/135 (23.2) | 22/124 (17.7) |
| SJC, mean % change | -50.5 | -51.6 | -51.2 | -50.6 |
| TJC, mean % change | -45.1 | -59.9 | -73.2 | -74.2 |
| HAQ-DI (0-3), mean change | -0.31 | -0.33 | -0.37 | -0.35 |
| HAQ-DI MCID, ≥0.30, n/m† (%) | 85/193 (44.0) | 81/184 (44.0) | 71/139 (51.1) | 60/127 (47.2) |
| DAS-28 (CRP), mean change | -1.26 | -1.42 | -1.90 | -1.92 |
| DAS-28 (CRP) <2.6, n/m† (%) | 41/189 (21.7) | 56/185 (30.3) | 57/136 (41.9) | 64/129 (49.6) |
| PASI -75, n/m† (%)‡ | 31/95 (32.6) | 17/78 (21.8) | 24/67 (35.8) | 15/47 (31.9) |
| PASI -50, n/m† (%)‡ | 52/95 (54.7) | 39/78 (50.0) | 38/67 (56.7) | 25/47 (53.2) |

Data as observed. n/m=number of responders/number of patients with sufficient data for evaluation. †The n reflects the number of patients treated with APR30 and APR20, regardless of when APR was started (baseline, Wk 16, or Wk 24) and who had data available at the specific time point; actual number of patients available for each end point may vary. ‡Denominators vary slightly due to availability of sufficient data for each level of ACR response assessment. §Examined among patients with psoriasis involvement of ≥3% body surface area at baseline and having data at the specific time point

of patients was upper respiratory tract infection; most AEs were mild/moderate in severity. Serious AEs occurred in 6.9% (APR30) and 6.4% (APR20) of patients, similar to rates seen for the earlier study periods, few discontinuations due to AEs (0.7%) occurred over Wks >104 to ≤156.

**Conclusions:** Over 156 wks, among patients remaining in the study, APR demonstrated sustained and clinically meaningful improvements in PsA signs/symptoms, including physical function and associated psoriasis. APR continued to demonstrate an acceptable safety profile and was generally well tolerated.

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## FRI0448 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE PSORIATIC ARTHRITIS: 2-YEAR EFFICACY AND SAFETY RESULTS FROM THE PHASE 3 RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL, FUTURE 1

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**Background:** Secukinumab, an anti–interleukin-17A monoclonal antibody, provided rapid and significant improvements in multiple clinical domains of psoriatic arthritis (PsA) including, signs and symptoms, joint structural damage, physical function, and quality of life, through 52 weeks (wks) in the Phase 3 FUTURE 1 study (NCT01392326).[1]

**Objectives:** To assess the long-term efficacy and safety of secukinumab in patients (pts) with PsA treated for up to 104 wks in FUTURE 1.

**Methods:** 606 adults with active PsA were randomised to secukinumab or placebo (PBO). Secukinumab pts received a 10 mg/kg i.v. loading dose at baseline (BL), Wks 2 and 4, followed by 150 mg s.c. (IV→150 mg) or 75 mg s.c. (IV→75 mg) every 4 wks from Wk 8. PBO was given on the same dosing schedule. At Wk 16, PBO-treated pts were re-randomised to receive secukinumab 150 or 75 mg s.c. from either Wk 16 or Wk 24, based on clinical response. Clinical assessments at Wk 104 included: ACR 20/50/70, PASI 75/90, DAS28-CRP, SF-36 PCS, HAQ-DI, mTSS, dactylitis, and enthesitis. Efficacy variables are presented from those pts originally randomised to secukinumab. Multiple imputation (binary variables) and a mixed-effect model repeated measures (continuous variables) were used for analyses at Wk 104. mTSS data are as observed.

**Results:** Overall, 476 pts (78.5%) completed 104 wks of study (167 [82.7%] pts in IV→150 mg group; 155 [76.7%] in IV→75 mg group). At Wk 104, ACR 20/50/70 response rates were 66.8/39.0/22.4% with IV→150 mg and 58.6/29.7/17.6% with IV→75 mg, respectively. Sustained clinical improvements with secukinumab through Wk 104 were observed across other clinically important domains of PsA (Table). Responses were sustained through Wk 104 in pts naïve to anti-TNF therapy and in those with an inadequate response or intolerance to these agents (anti-TNF-IR). ACR20 response rates at Wk 104 in anti-TNF-naïve pts were 75.2% and 63.7% with IV→150 mg and IV→75 mg, respectively; corresponding rates in anti-TNF-IR pts were 48.0% and 46.9%. No radiographic disease progression (≤0.5 change in mTSS) was observed between BL and Wk 104 in 84.6% of x-ray completers in the IV→150 mg and 83.9% in the IV→75 mg groups. Over the entire study period (mean exposure to secukinumab of 627.1 days) the type, incidence and severity of AEs were consistent with that reported previously. Infections and infestations were the most common AEs observed with secukinumab (67.9 per 100 pt-years). No cases of TB were reported. Malignant/unspecified tumours and major adverse cardiac events occurred at a rate of 0.6 and 0.7 per 100 pt-years, respectively with secukinumab. No suicides were recorded in secukinumab-treated patients.

Table. Summary of Efficacy Results at Wk 104 (intent-to-treat analysis*)

| Variable | Secukinumab IV → 150 mg N = 202 | Secukinumab IV → 75 mg N = 202 |
|---|---|---|
| ACR 20/50/70 (% responders) | 66.8/39.0/22.4 | 58.6/29.7/17.6 |
| PASI 75/90 (% responders)† | 74.6/61.0 | 63.0/44.6 |
| DAS28-CRP, LS mean change from BL | −1.66 | −1.64 |
| SF-36 PCS, LS mean change from BL | 4.89 | 4.67 |
| HAQ-DI, LS mean change from BL | −0.38 | −0.39 |
| Resolution of dactylitis (%)‡ | 82.6 | 84.6 |
| Resolution of enthesitis (%)‡ | 73.7 | 76.8 |

*Multiple imputation (binary variables) or mixed-effect model repeated measures (continuous variables)
†Data evaluated in pts with psoriasis affecting ≥3% body surface area at BL (n = 108 in treatment arm)
‡Data from pts with these symptoms at BL
ACR, American College of Rheumatology response criteria; BL, baseline; DAS28-CRP, Disease Activity Score 28 using C-reactive protein; HAQ-DI, Health Assessment Questionnaire Disability Index; i.v., intravenous; LS, least squares; N, number of pts randomised; PASI, psoriasis area-and-severity index; SF-36 PCS, Short Form 36 Physical Component Summary

**Conclusions:** Secukinumab provided sustained improvements in signs and symptoms and multiple clinical domains of active PsA in pts who completed 2 years of therapy. Secukinumab was well tolerated with a safety profile consistent with that previously reported.

**References:**

[1] Mease P et al. N Engl J Med 2015; 373:1329–39

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## FRI0449 INCIDENCE AND PREVALENCE OF PSORIATIC ARTHRITIS IN SOUTH EAST ASIA

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**Background:** There is under reporting of prevalence of Psoriatic Arthritis among patients with psoriasis in India. The data on prevalence of PsA among patients of the psoriasis varies from 6.25% to 48% in western countries. [1],[2] A relatively low figures are reported from Asian countries.

**Objectives:** To determine the reporting of psoriatic arthritis from dermatology point of view

**Methods:** In this observational study, we identified subjects from hospital recordswho were diagnosed with psoriasisand psoriatic arthritis between 1/07/2010till 31/05/2014and 01/01/2015 till 31/12/2015 inDepartment Dermatologyin a tertiary care Hospital.Age-and sex-specific incidence rates were recorded.In order to sensitize dermatologists about the aspect of psoriatic Arthritis series of close group meetings between dermatologists and Rheumatologists were conducted in order to pick up Arthritis in patients of Psoriasis. Six months post educational intervention, observation of the hospital records regardingdiagnosis of psoriasis and psoriatic Arthritis were recorded.

**Results:** A total of 16842 patients were reviewed during the pre-education intervention period between 01/07/2010 till 31/05/2014. Out of these 771 (4.57%) patients were recorded as psoriasis but none of the patients were recorded as psoriatic arthritis. The mean± SD age of patients with psoriasis was 43.34± 16.72 years, 50.1% were males.A total of 6012 patients were reviewed during the post- education intervention period between 01/01/2015 till 31/12/2015. Out of these 331 (4.92%) patients were recorded as psoriasis and 35 (0.58%) patients were recorded as both psoriasis and psoriatic arthritis. The psoriatic arthritis patients were referred to rheumatologists and all were found to have PsA according to classification of psoriatic arthritis (CASPAR) criteria.The prevalence rate of psoriasis and psoriatic arthritis with age $\leq$10 years, 11–25 years, 26–50 years, 51–70 years, and $>$70 years was found to be 2.06% and 0%, 9.98% and 0.01%,52.9% and 0.9%, 29.8% and 0.8% and 5.2% and 0.6% respectively. The highest prevalence rate of psoriasis and psoriatic arthritis both was between 26–50 years of age

**Conclusions:** Psoriatic Arthritis is underreported from dermatology registries. Rheumatologist and dermatologist should share a platform regarding the concept of Psoriatic Arthritis in patients with psoriasis

**References:**

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## FRI0450 TUMOR NECROSIS FACTOR INHIBITOR TREATMENT IN PSORIATIC ARTHRITIS: NEED FOR CO-MEDICATION?

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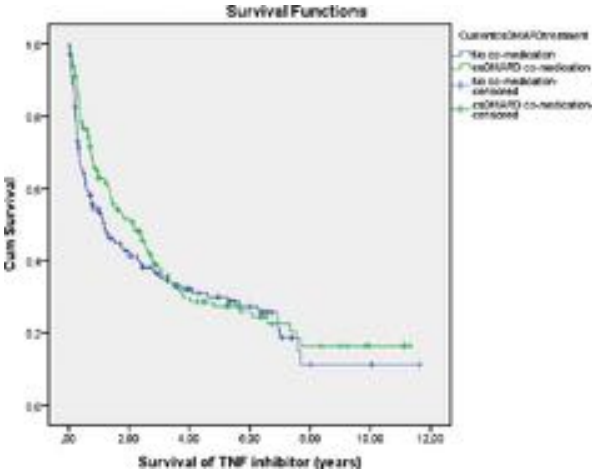
**Background:** Different than for rheumatoid arthritis, the potential benefits of conventional synthetic disease modifying drug (csDMARD) co-medication among psoriatic arthritis (PsA) patients receiving tumor necrosis factor inhibitors (TNFi) remain unclear.[1]

**Objectives:** This study aimed to investigate the role of concomitant csDMARDs on survival of subcutaneous TNFi in Norwegian PsA outpatients between 2000 and 2015.

**Methods:** We included all the PsA patients who initiated first time treatment with adalimumab, etanercept, golimumab and certolizumab in the years 2000–2015 in a Norwegian outpatient clinic. Baseline characteristics and drug survival were compared between patients with and without csDMARD co-medication. The $X^2$ test, independent t-test and Mann-Whitney U test were applied as appropriate for group comparisons. Drug survival was explored by Kaplan-Meier analysis, and patients receiving versus not receiving co-medication were compared using the log rank test. Additional analyses for each of the TNFi were performed. Univariable and multivariable Cox regression analysis were used to identify predictors of discontinuation.

**Results:** Among 371 PsA patients being treated with TNFi, 145 received csDMARD co-medication; 58/118 with etanercept, 48/106 with adalimumab, 21/47 with certolizumab and 18/47 with golimumab, respectively. Mean (SD) age was 54.0 (11.5) years, disease duration 13.1 (9.1) years, years of education 12.9 (3.4), body mass index (BMI) 27.1 (4.3) kg/m$^2$, baseline DAS28 4.1 (1.4), 45.7% were female. Baseline characteristics were similar for patients with and without co-medication, except for a higher percentage of first time TNFi users (67.6%) compared to previous TNFi users (32.4%) in the co-medication group, p=0.001. Drug survival of TNFi was similar for patients receiving versus not receiving concomitant csDMARDs (log rank test p=0,181, figure). In the Cox regression analysis identified predictors for TNFi discontinuation were previous use of TNFi (HR 1.68, 95% CI 1.25–2.26, p$<$0.001) and TNFi type (p$<$0.001). Separate analyses for first time TNFi users did not change the primary outcome. Separate analyses for different TNFi types showed similar drug survival with and without co-medication, except for certolizumab for which a trend toward better drug survival with co-medication was seen.

**Conclusions:** In our population of TNFi treated PsA patients, we found similar drug survival for patients with and without csDMARD co-medication. Identified predictors for TNFi discontinuation were previous use of TNFi and TNFi type.




**References:**

[1] Behrens F et al. Tumour necrosis factor inhibitor monotherapy vs combination with MTX in the treatment of PsA: a systematic review of the literature. Rheumatology. 2015; 54: 915–26.

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## FRI0451 SECUKINUMAB PROVIDES RAPID AND SUSTAINED REDUCTIONS IN DACTYLITIS AND ENTHESITIS IN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS OF DATA FROM THE PHASE 3 RANDOMISED, MULTICENTRE, DOUBLE-BLIND, PLACEBO-CONTROLLED FUTURE 2 STUDY

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**Background:** Dactylitis and enthesitis are common debilitating manifestations of psoriatic arthritis (PsA).[1] Secukinumab has previously been reported to reduce the number of dactylitic digits and enthesitis sites in patients (pts) with PsA, with a greater proportion of pts achieving complete resolution of dactylitis and enthesitis than placebo (PBO) at Week (Wk) 24.[2,3]

**Objectives:** To evaluate the effects of secukinumab on dactylitis and enthesitis through Wk 52 in FUTURE 2 (NCT01752634).

**Methods:** The study design from FUTURE 2 has been reported previously.[2] The proportions of pts with resolution of dactylitis and enthesitis at Wk 24 and Wk 52 were secondary and exploratory endpoints, respectively; additional measures were dactylitic digit and enthesitis counts. Post-hoc analyses included Kaplan Meier (KM) analysis to achieve resolution of enthesitis and dactylitism and proportion of pts with resolution of dactylitis and enthesitis by baseline (BL) severity.

**Results:** Of the 397 pts randomized, 138 (35%) and 253 (64%) had dactylitis and enthesitis, respectively, at BL. KM curves indicate that median time to resolution in dactylitis and enthesitis was Wk 4 for secukinumab 300 and 150 mg. At Wk 24, a greater proportion of secukinumab-treated pts achieved complete resolution of dactylitis and enthesitis than PBO (P$<$0.05); more secukinumab-treated pts had

Table 1. Dactylitis and Enthesitis Data at Wks 24 and 52

| Variable | Secukinumab 300 mg N=100 | Secukinumab 150 mg N=100 | Secukinumab 75 mg N=99 | PBO N=98 |
|---|---|---|---|---|
| Dactylitis at BL, n (%) | 46 (46.0) | 32 (32.0) | 33 (33.3) | 27 (27.6) |
| Dactylitis count at BL, mean | 3.6 | 4.4 | 3.0 | 2.7 |
| Dactylitis count, mean change from BL [95% CI] | | | | |
| Wk 24 | –2.56 [–2.32, 0.89] | –2.53 [–3.16, 0.04] | –1.68 [–2.32, 0.89] | –0.97 |
| Wk 52 | –3.08 [–1.06, 1.11] | –3.11 [–2.31, –0.15] | –1.85 [–2.44, –0.07] | – |
| Enthesitis at BL, n (%) | 56 (56.0) | 64 (64.0) | 68 (68.7) | 65 (66.3) |
| Enthesitis count at BL, mean | 2.82 | 3.19 | 3.16 | 3.06 |
| Enthesitis count, mean change from BL [95% CI] | | | | |
| Wk 24 | –1.68 [–1.27, 0.12] | –1.83 [–1.40, –0.04] | –1.38 [–0.95, 0.40] | –1.11 |
| Wk 52 | –1.68 [–0.38, 0.84] | –1.91 [–0.78, 0.43] | –1.50 [–1.00, 0.19] | – |

Symptoms in those patients with dactylitis/enthesitis at BL; dactylitis count from 20 digits (score of 0–20) and enthesitis count from 6 sites (score of 0–6); mixed-effect model repeated measures (MMRM) data.

complete resolution of symptoms at Wk 52 than Wk 24. Improvements at Wk 24 and 52 were observed regardless of BL severity. A sustained decrease in mean changes from BL to Wk 24 and 52 in dactylitis and enthesitis count were shown in those pts with symptoms at BL (Table), with improvements versus PBO observed by Wk 4 ($P<0.05$).

**Conclusions:** Secukinumab demonstrated a rapid resolution of dactylitis and enthesitis as early as Wk 4 and this was sustained up to Wk 52. A higher proportion of pts achieved complete resolution and reduced mean counts of dactylitis and enthesitis at Wk 52 than Wk 24.

**References:**

[1] Gladman et al. Ann Rheum Dis 2005;64:14–7;
[2] McInnes et al. Lancet 2015;386:1137–46;
[3] Kirkham et al. Ann Rheum Dis 2015;74:351

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## FRI0452 ARE GM-CSF-PRODUCING TH17 CELLS IMPORTANT IN THE PATHOGENESIS OF PSORIATIC ARTHRITIS?

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**Background:** Psoriasis [Ps] is a common chronic inflammatory skin condition affecting about 1–2% of the world population; approximately 20–30% of patients have psoriatic arthritis [PsA]. PsA can affect peripheral and axial joints, eyes, ileum, colon and skin. Genetic studies reveal common candidate genes including *IL23R*, *IL12B*, *STAT3*, and *CARD9*, all associated with IL-23 signalling. We demonstrated increased frequencies of $Th_{17}$ cells in patients with Ps and PsA and the clinical importance of IL-23/$Th_{17}$ is revealed by the efficacy of biologics targeting this pathway. Whilst IL-17 was thought to be pathogenic in inflammatory conditions such as experimental autoimmune encephalomyelitis, the redundancy of IL-17 but essential requirement for GM-CSF release by $Th_{17}$ cells was shown. GM-CSF$^+$ T cells were identified in cerebrospinal fluid from patients with multiple sclerosis but a role in the aetio-pathogenesis of PsA has not been established.

**Objectives:** 1) Are GM-CSF$^+$ T cells enriched in peripheral blood and synovial fluid obtained from patients with PsA?
2) Is GM-CSF co-produced with IFN-g?
3) Do CD4$^+$GM-CSF$^+$ T cells express surface markers characteristic of $Th_{17}$?
4) Is GM-CSF release augmented by exogenous IL-23 and/or IL-12?

**Methods:** PBMC or synovial fluid derived from patients with PsA, or healthy donor (HD) PBMC, were stimulated with anti-CD3/anti-CD28 +/– recombinant IL-23 or IL-12. Supernatants were harvested and analysed by ELISA for IL-17, IFN-$\gamma$ or GM-CSF. Alternatively, cells were activated with phorbol myristate acetate (PMA) and ionomycin, and evaluated for the expression of the $Th_{17}$-associated cell surface markers CCR6, CD161 & IL-23R plus IL-17A, IFN-g and GM-CSF by flow cytometry.

**Results:** GM-CSF release from PsA PBMC was higher than that of HD, whereas IFN-g levels were higher in HD. This was most significant on comparing the ratio of IFN-g to GM-CSF. On examining the co-expression of GM-CSF and IFN-g in CD4$^+$ T cells, PsA patients had higher proportions of GM-CSF$^+$ single positive and fewer GM-CSF$^+$IFN-g$^+$ relative to HD. There was also marked enrichment of CD4$^+$GM-CSF$^+$ cells in synovial fluid. On evaluating the expression of the $Th_{17}$-associated markers CCR6, CD161 and IL-23R, we demonstrated that whereas almost all CD4$^+$IL-17$^+$ cells expressed CCR6, approximately 50% of CD4$^+$GM-CSF$^+$ cells expressed this chemokine receptor. Surprisingly, there were fewer PsA patient CD4$^+$GM-CSF$^+$ peripheral blood T cells co-expressing CCR6, CD161 and IL-23R relative to HD. Finally, IL-23 has been shown to render Th17 cells more pathogenic, hence we examined the effect of this cytokine on GM-CSF release. We showed that whilst IL-17 release was enhanced by exogenous IL-23, GM-CSF release was significantly downregulated with little effect on IFN-g. In contrast, IL-12 increased IFN-g and GM-CSF, and reduced IL-17.

**Conclusions:** IL-23 and $Th_{17}$ cells are therapeutic targets in PsA, and mouse models of inflammation suggest that pathogenic $Th_{17}$ cells release GM-CSF. We reveal that GM-CSF release is elevated in patients with PsA, and GM-CSF$^+$ cells are enriched in diseased joints. However, only a proportion of GM-CSF$^+$ cells exhibited features of $Th_{17}$. Furthermore, IL-23 downmodulated GM-CSF whilst enhancing IL-17. Given that GM-CSF was mainly produced by cells *not* co-expressing IFN-g in PsA patients [in contrast to healthy donors], this subset may be pathogenic in PsA and warrants further investigation.

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## FRI0453 THE INCREASED PREVALENCE OF NAFLD IS WORRISOME AMONG PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Non-alcoholic fatty liver disease (NAFLD) affects 20–30% of general population and a wide range of 14–59% patients with cutaneous psoriasis (PsO). Psoriatic arthritis (PsA) has been linked to comorbidities including diabetes, arterial hypertension, dyslipidemia and metabolic syndrome (MetS) though data on NAFLD in PsA is lacking. In fact, in PsA, NAFLD has been evaluatedin only one Italian study affecting 28% patients.

**Objectives:** To evaluate the prevalence of NAFLD in our cohort of patients with PsA.

**Methods:** All patients with PsA regularly followed-up during a 6 month period at our outpatient rheumatology clinic were studied. They were evaluated byabdominal ultrasound (US) and NAFLD was defined in the presence of hepatic steatosis (US = Grades I to III).The occurrence of associated comorbidities, includingarterial hypertension, diabetes and dyslipidemia was recorded and the NCEP-ACT III criteria were applied to identify subjects with metabolic syndrome (MetS). DAS 28, BASDAI and ASDAS were used to assess PsA disease activity, while HAQ was performed to assess functional impairment. Student's t, Chi-square and Fisher's exact tests were performed for statistical analyses and P values $\leq 0.05$ were considered significant.

**Results:** Fifty six PsA patients were initially enrolled, but 3 were excluded due to the presence of alcoholic cirrhosis in 2 and a positive serology for hepatitis C in 1. Among the remaining 53 patients, 26 were males and 27 females, with mean age = 54,8±13 yrs (27–76) and mean disease duration = 14,4±8,1 yrs (04–40). US revealed NAFLD in 33/53 (63%) patients with PsA, confirmed by liver biopsy in 2. Arterial hypertension, diabetes and dyslipidemia affected 81%, 42%, 75% of patients with NAFLD respectively ($P<0.001$). MetS was present in 58,5% (31/53) individuals, significantly more prevalent in patients with compared to those without NAFLD: 26/33 (78.8%) vs. 05/20 (25.0%), $P<0.001$, despite of gender. All disease activity indices (% patients with DAS28$>$2.6), mean BASDAI and mean ASDAS) and HAQ scores were similar among patients with or without NAFLD (55.6% vs 46.7%; 3.1 vs 3.7; 1.9 vs 2.3; 1 vs 0.9 respectively, $P>0.05$).

**Conclusions:** NAFLD is very common in our cohort of PsA patients occurring in over 2/3 regardless of disease activity and associated to MetS in most subjects, suggesting a relationship between these conditions. Moreover, screening for NAFLD inPsA patients is warranted in order to avoid increased overall liver morbidity.

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## FRI0454 ENDOTHELIAL DYSFUNCTION IN PSORIATIC ARTHRITIS: EVALUATION BY ENDOTHELIAL-DEPENDENT FLOW-MEDIATED DILATION AND CORONARY FLOW RESERVE

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**Background:** Patients with psoriatic arthritis (PsA) are at an increased risk for premature cardiovascular disease (CVD) independent of traditional risk factors [1]. Endothelial dysfunction plays a central role in the development of accelerated atherosclerosis.

**Objectives:** To evaluate endothelial dysfunction by assessment of artery endothelial-dependent flow-mediated dilation (FMD) and coronary flow reserve (CFR).

**Methods:** 20 patients (12 males and 8 females – age 57,5 ±10,8 years) affected by PsA according to CASPAR criteria [2] were enrolled. The 10-years cardiovascular Framigham risk score was calculated. Ultrasound assessment of brachial artery FMD was performed according to Corretti et al. [3]. CFR was evaluated by contrast-enhanced Doppler echocardiography and dipyridamole administration as previously described [4].

**Results:** The 10-years cardiovascular Framingham risk score of PsA patients (mean 3.84 ± 3.22) was in the low risk range. The assessment of brachial artery FMD showed a significant reduction of post-ischemic vasodilation in PsA patients (mean -17.70 ± 16%) as compared with normal population (mean +15.00 ± 5%). Coronary flow reserve was under the normal range (CFR $>$2.5) [5] in 15/20 PsA patients.

**Conclusions:** The present results demonstrate that PsA patients with low cardiovascular Framingham risk score have increased arterial stiffness and

decreased coronary arteries flow reserve. These data suggest that endothelial dysfunction may underlie premature atherosclerosis in PsA patients

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**Disclosure of Interest:** None declared

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## FRI0455 ALL CARDIOVASCULAR (CV) RISK SCORES SIGNIFICANTLY UNDERESTIMATED CV RISK DEFINED BY CAROTID ULTRASOUND IN PSORIATIC ARTHRITIS- CAN WE IMPROVE THEIR PERFORMANCES?

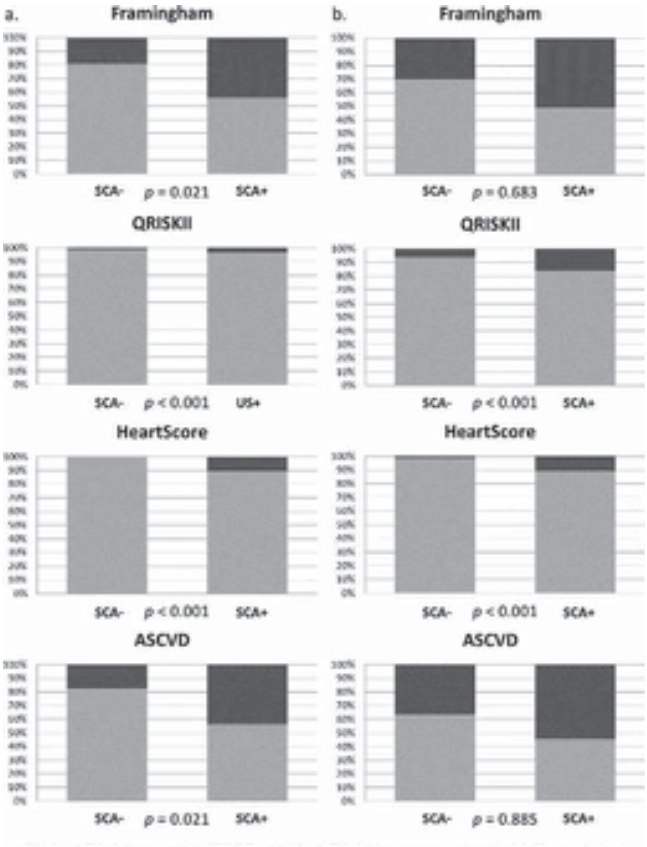
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**Background:** Psoriatic arthritis (PsA) is associated with higher cardiovascular (CV) risk. The performances of established CV risk scores for general population in PsA patients have not been fully evaluated yet. Meanwhile, European League Against Rheumatism (EULAR) recommended to introduce a 1.5 multiplication factor to the CV risk scores for certain patients with rheumatoid arthritis. Whether the multiplication factor could improve the performances of the risk scores in PsA is unknown.

**Objectives:** To evaluate the performances of different CV risk scores and their EULAR modified versions in detecting high CV risk in PsA patients defined as the presence of subclinical atherosclerosis (SCA) determined by carotid ultrasonography.

**Methods:** Four different CV risk scores namely Framingham risk score (FRS), QRISK II, HeartScore and American College of Cardiology and American Heart Association (ACC/AHA) 10-year atherosclerotic cardiovascular disease (ASCVD) and their EULAR recommended modified versions were calculated. Sonographic evaluation measuring carotid intima-media thickness (IMT) and plaque was used to determine SCA. IMT>0.90 mm and/or the presence of plaque were classified as SCA+.

**Results:** 162 patients [49.27±11.9 years, male: 95 (58.6%)] underwent carotid ultrasound were recruited. 142, 137, 128 and 118 patients were eligible to calculate FRS, QRISKII, HeartScore and ASCVD, respectively. 69 (34.3%) patients were considered to have high CV risk based on the presence of SCA. The SCA+ patients were significantly older (55±10 vs 45±12 years; $p<0.001$) and more diabetic [11 (15.9%) vs 12 (12.9%); $p<0.001$]. They also had higher systolic blood pressure (SBP: 138±25 vs 128±17 mmHg; $p=0.003$) and total cholesterol (TC: 5.3±0.9 vs 4.9±0.9 mmol/L, $p=0.005$). All CV risk scores were significantly higher in SCA+ patients (FRS: 17±14 vs 8±8%, $p<0.001$; QRISKII: 13±9 vs 7±7%, $p=0.002$; HeartScore: 3±3 vs 1±2%, $p=0.001$; ASCVD: 14±14 vs 8±8%, $p=0.002$). Areas under the receiver operating characteristic (ROC) curves discriminating SCA+ for FRS, QRISKII, HeartScore and ASCVD were 0.71 (0.63–0.80, $p<0.001$), 0.67 (0.58–0.76, $p=0.001$), 0.67 (0.58–0.77, $p=0.001$), and 0.67 (0.58–0.77, $p=0.001$), respectively. 42 (29.6%), 3 (2.2%), 6 (4.7%) and 35 (29.7%) patients were classified as having high CV risk scores according to FRS>10%, QRISK II>20%, HeartScore>5% and ASCVD>7.5%, respectively. By McNemar's test, all scores significantly underestimated the risk of SCA+ (all $p<0.05$, Figure 1a). By applying the EULAR multiplication factor, 55 (38.7%), 14 (10.2%), 7 (5.5%) and 53 (44.9%) patients were reclassified as having high CV risk, respectively. SCA+ risk was still significantly underestimated by the modified QRISKII and HeartScore, but not by the modified FRS ($p=0.683$) and ASCVD ($p=0.885$) (Figure 1b). EULAR modification increased the sensitivity of FRS and ASCVD in predicting SCA from 44% to 51%, and from 44% to 55%, respectively.




a. Original CV risk scores; b. EULAR modified CV risk scores; p value by McNemar's test. Dark grey: High risk, Light grey: low risk, according to risk scores.

**Conclusions:** All CV risk scores significantly underestimated the risk defined by carotid ultrasonography. EULAR recommended modification improved the sensitivity of FRS and ASCVD to a moderate level.

**Disclosure of Interest:** None declared

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## FRI0456 ASSOCIATION BETWEEN IMPROVEMENT IN ENTHESOPATHY AND QUALITY OF LIFE: RESULTS FROM ANTI-TNF-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS IN TWO PHASE 3 USTEKINUMAB TRIALS

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**Objectives:** To assess the relationship between changes in enthesopathy and in function/health-related quality of life (HRQoL) in anti-TNF-naïve patients (pts) with psoriatic arthritis (PsA) receiving treatment with ustekinumab (UST).

**Methods:** Adult pts in 2 Phase 3 trials (n=747 anti-TNF naive) with active PsA (≥5 SJC and ≥5 TJC;CRP≥0.3mg/dL) despite DMARD and/or NSAIDs were randomized to UST45mg, 90mg, or PBO at weeks 0, 4, and q12weeks. Stable concomitant MTX was permitted but not mandated. At week16, pts with <5% improvement in TJC & SJC entered blinded early escape (PBO→UST45mg; UST45mg→90mg; 90mg→90mg). Presence or absence of enthesopathy, HAQ-DI, and SF-36 were assessed at baseline and week 24. In this post-hoc analysis, enthesopathy of the Achilles tendon and plantar fascia was assessed as present or absent. Pts were categorized thereafter as follows: improved (enthesopathy present at baseline, but not at week 24), worsened (enthesopathy present at week 24, but not at baseline), and unchanged. Pts with an enthesopathy assessment missing at either time point were included in the unchanged category; those with enthesopathy data missing at both time points were excluded. Early escape pts were also excluded from this analysis. Improvements in HRQoL (assessed by the SF-36 PCS and MCS and physical function (HAQ-DI) were assessed by enthesopathy response category.

**Results:** A total of 591 anti-TNF-naïve pts from both trials were included in the analysis; 45% of pts were female, mean age was 47 years, mean PsA duration was 6.7 years, and 74% had ≥3% body surface area affected at baseline. The proportion of pts with enthesopathy at baseline was similar in the combined UST (46.5%) and placebo (49.4%) groups. At week 24, the proportions of pts with enthesopathy were 22.8% and 35.9% for the combined UST and placebo groups, respectively. Across all pts, those who had an improvement in enthesopathy had

Table 1

| | Enthesopathy Status | | |
|---|---|---|---|
| | Worsened | Unchanged | Improved |
| Overall | | | |
| % improvement in HAQ-DI | n=25 | n=407 | n=136 |
| | 14.0 (34.7) | 23.1 (63.9) | 35.5 (49.5) |
| Change in SF-36 PCS | n=27 | n=395 | n=139 |
| | 2.8 (7.4) | 5.0 (8.7) | 6.6 (8.8) |
| Change in SF-36 MCS | n=27 | n=395 | n=139 |
| | –0.9 (8.1) | 3.4 (10.2) | 6.9 (10.4) |
| ACR 20 responders | | | |
| % improvement in HAQ-DI | n=9 | n=184 | n=88 |
| | 31.3 (31.5) | 52.2 (37.1) | 51.2 (38.7) |
| Change in SF-36 PCS | n=10 | n=189 | n=90 |
| | 7.6 (7.1) | 8.6 (8.9) | 9.2 (8.4) |
| Change in SF-36 MCS | n=10 | n=189 | n=90 |
| | 3.4 (7.0) | 5.1 (10.6) | 7.9 (10.7) |

a greater improvement in functioning and HRQoL, compared with those who did not ($p<0.05$; Table). When the analysis was restricted to those who achieved an ACR 20 response, pts with an improvement in enthesopathy showed a trend of greater improvement in functioning and HRQoL compared to those who had worsened (Table).

**Conclusions:** There is an association between improvement in enthesopathy of the Achilles tendon and plantar fascia and improvement in physical function and quality of life in anti-TNF-naïve pts with PsA in 2 UST trials. Some, but not all, of this improvement may be explained by improvements in peripheral arthritis.

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## FRI0457 RECOMMENDATIONS FOR THE MANAGEMENT OF COMORBIDITIES IN PSORIATIC DISEASE

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**Objectives:** To establish recommendations for the management of comorbidities in patients with psoriatic disease (PsD).

**Methods:** A multidisciplinary panel drafted the recommendationsin a nominal group session. Evidence from four systematic reviews was added. Agreement was assessed by two-rounds Delphi technique. Recommendations with an agreement $\geq$7/10 by at least 70% of participants were kept in.

**Results:** A total of 19 recommendations on three key topics were issued: 1) screening of specific comorbidities, 2) specific preventive or therapeutic actions, and 3) general management.

**Conclusions:** Disease control coupled with the management of comorbidities is critical to ensure optimal patient care. These recommendations suggest actions on detection, management and integration of care in PsD.

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**Abstract FRI0457** – Table 1

| |
|---|
| **Recommendations for the screening of specific comorbidities** |
| CV disease and risk factors should be screened early and periodically; if present, they must be controlled. LE 3, A 9.8 |
| Adequate control of obesity and overweight should be a priority. LE 3, A 9.3 |
| Psycho-affective disorders should be investigated. LE 4, A 8.9 |
| Inquiring about sexual dysfunctions is recommended. LE 5, A 7.7 |
| Pts with ocular symptoms should be referred rapidly to ophthalmology. LE 5, A 8.8 |
| Uric acid and gouty symptoms should be periodically monitored. LE 4, A 8.8 |
| If new skin lesions, skin cancer should be screened, especially if pt. received PUVA, CsA or biological treatment. LE 5, A 8.5 |
| **Therapeutic and preventive actions** |
| Drugs with potential negative effect on comorbidities should be avoided. LE 5, A 9.5 |
| Even in absence of risk factors, it is recommended to inform about CV risk. LE 5, A 8.4 |
| It is advisable to include dietary recommendations, adapted to pt preferences, to prevent overweight and obesity. LE 2, A 8.8 |
| Regular aerobic exercise should be recommended. LE 2, A 9.1 |
| Smoker pts should be encouraged to cease smoking on each visit. LE 3, A 9.8 |
| Pts should be encouraged to cease or reduce alcohol intake. LE 4, A 9.1 |
| It is advised to follow standard guidelines for the prevention of osteoporosis, especially in pts on chronic GC therapy. LE 5, A 8.8 |
| **Recommendations on the management of chronic patients with PD** |
| The management of pts with PsD must be holistic; rheumatologists or dermatologists will play a key role coordinating with other specialists. LE 5, A 9.8 |
| For monitoring and control of comorbidities associated with PsD, it is essential to involve GPs and other specialists, as well as to promote pt empowerment. LE 5, A 9.3 |
| Comorbidities should be assessed at the time of diagnosis, upon Tx changes, and during follow-up*. LE 5, A 8.8 |

CV, cardiovascular; PsD, psoriatic disease; LE, level of evidence; A, agreement/over 10. *Specific timings are proposed.

## FRI0458 ASSESSMENT OF COMORBIDITY IN PSORIATIC DISEASE: HOW OFTEN SHOULD BE PERFORMED?

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**Background:** Psoriatic disease (PsD) is associated with multiple comorbidities. When establishing management protocols, the periodicity for detection and evaluation of such comorbid conditions needs to be specified.

**Objectives:** To establish guidelines for the follow-up of selected comorbidities in patients with PsD.

**Methods:** An expert panel with specialists in Rheumatology, Internal Medicine, Dermatology and General Practitioners defined the comorbidities with higher impact on PsD based on the existing literature and their experience. The periodicity for detection and monitoring of comorbidities in the Rheumatology setting was established by consensus after iterations and systematic review.

**Results:** The expert panel agreed to evaluate comorbidities as part of routine clinical practice at the time of diagnosis, upon changes in systemic treatment and at follow-up visits (evidence level 5, level of agreement 8.8). In any case, monitoring must be customized depending on the risk profile, morbidity, comorbidities and patient preferences. The following table shows the proposed periodicity for detection, assessment, and monitoring of the most important comorbidities in PsD.

**Conclusions:** This proposal for a periodic assessment of comorbidities in patients

**Abstract FRI0458** – Table 1

| At first visit | At all visits | Annually | Every 2 years | Before any change in treatment |
|---|---|---|---|---|
| Personal and family history<br>Allergies<br>List of treatments<br>CV assessment and CV risk score.<br>Screening of:<br>Obesity and metabolic syndrome (waist circumference, BMI)<br>Diabetes (blood glucose and HbA1c)<br>HTN<br>Dyslipidemia<br>Smoking<br>Cancer<br>Alcoholism Depression<br>Liver or kidney problems | Interrogation of new onset symptoms and corresponding examinations.<br>Liver and kidney function. | CV risk SCORE:<br>Total cholesterol, LDL and triglycerides<br>Glucemia<br>Smoking<br>Blood pressure<br>BMI<br>Waist circumference<br>lymphadenopathy screening<br>Evaluation of the psycho-emotional state<br>Questioning for addictions (alcohol/smoking) | Dermatology and Rheumatology recommendation:<br>Dietary<br>Exercise<br>Check for lipid-lowering antihypertensive treatment if altered (by Dermatology, Rheumatology and GPT). | CV risk<br>Infection risk<br>Latent Tuberculosis<br>Vaccinations<br>Working and living conditions |

CV: Cardiovascular; HbA1c: Glycated hemoglobin; BMI: Body Mass Index; HTN: arterial hypertension; GP: General Practitioner.

with PD allows systematic clinical monitoring of the patient by the Rheumatologist and Dermatologist, and can contribute to the early detection and management of these comorbidities

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**Disclosure of Interest:** None declared

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## FRI0459 LONGITUDINAL EVOLVEMENT OF PASDAS AND CPDAI AND ITS ASSOCIATIONS WITH PATIENTS CHARACTERISTICS AND TREATMENT IN INCIDENT PSORIATIC ARTHRITIS: RESULTS FROM THE DEPAR STUDY

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**Background:** Psoriatic Arthritis (PsA) is a multi-features disease requiring disease activity measures that capture not only joint disease, such as the Composite Psoriatic Disease Activity Index (CPDAI) and the Psoriatic Arthritis Disease Activity Score (PASDAS). Although both are well validated in clinical trials, little data exists on their evolvement in daily clinical care.

**Objectives:** to describe the longitudinal evolvement of CPDAI and PASDAS and its associations with demography, disease, and DMARDs.

**Methods:** Newly diagnosed consecutive PsA patients were recruited in 8 hospitals in the Netherlands from August 2013 to November 2015. Demographic and disease characteristics were registered. Data was analysed in the first 3 months by linear regression and over 12 months using linear mixed model with random intercept for CPDAI (0–15) and PASDAS (0–10)

**Results:** In November 2015 281 patients had had a baseline assessment, of which 234, 198, 157 and 129 had had resp. a 3, 6, 9 and 12 month assessment. The mean age was 50.6 (SD 13.6) and 50.5% were male. In terms of arthritis subtypes, 56 (20%) had monoarthritis, 108 (39%) oligoarthritis, 80 (29%) polyarthritis and 35 (12%) were diagnosed with axial disease, dactylitis or enthesitis only.

PASDAS evolved from a mean of 4.0 points (SD 1.2, n=174) at baseline, to 3.3 (SD 1.1, n=160) at 3 months, and 2.6 (SD 1.1, n=94) at 12 months. CPDAI evolved from 5.5 (SD 2.1, n=229), to 4.4 (SD 2.0, n=213) to 2.97 (SD 1.8, n=113) resp. Associations and their course over time are described in table 1. In summary: MTX had a lowering effect on both the CPDAI and PASDAS in the multivariate analysis, while baseline scores and disease duration had a raising effect. Higher baseline PASDAS and CPDAI values in the multivariate analysis were associated with being female, the presence of oligo- or polyarthritis and tender enthesis, for CPDAI also with the presence of morning stiffness. Similar results were observed in the 3-months linear regression.

Table 1. Univariate and multivariate regression analysis of CPDAI and PASDAS

| | T0-T3 | | | | | | T0-T12 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | univariate | | | multivariate | | | univariate | | | multivariate | | |
| | B | 95% CI | | B | 95% CI | | B | 95% CI | | B | 95% CI | |
| CPDAI | | | | | | | | | | | | |
| age | -0.01 | -0.03 | 0.01 | | | | -0.01 | -0.02 | 0.01 | | | |
| gender: male vs female | *0.74 | 0.23 | 1.25 | | | | *0.90 | 0.47 | 1.34 | | | |
| diagnosis: oligo vs mono | *0.90 | 0.18 | 1.61 | *0.76 | 0.08 | 1.45 | 0.44 | -0.08 | 0.97 | | | |
| poly vs mono | *1.64 | 1.03 | 2.25 | *1.04 | 0.29 | 1.79 | *1.23 | 0.67 | 1.80 | | | |
| other vs mono | *1.59 | 0.62 | 2.56 | | | | *1.59 | 0.72 | 2.45 | | | |
| symptom duration (months)* | *0.002 | 0.000 | 0.003 | | | | *0.001 | 0.000 | 0.002 | *0.001 | 0.000 | 0.002 |
| morning stiffness (y/n) | *1.21 | 0.54 | 1.88 | | | | *1.11 | 0.68 | 1.58 | | | |
| baseline CPDAI | *0.54 | 0.42 | 0.66 | *0.47 | 0.34 | 0.60 | *0.37 | 0.28 | 0.48 | *0.33 | 0.21 | 0.44 |
| average MTX dose (mg) | -0.01 | -0.04 | 0.01 | *-0.07 | -0.12 | -0.01 | *-0.03 | -0.04 | -0.01 | *-0.04 | -0.07 | -0.01 |
| ever MTX use# | 0.23 | -0.33 | 0.78 | *1.18 | 0.17 | 1.99 | 0.01 | -0.45 | 0.48 | | | |
| other DMARDs (y/n) | 0.79 | -0.17 | 1.75 | | | | -0.18 | -0.70 | 0.34 | | | |
| PASDAS | | | | | | | | | | | | |
| age | -0.01 | -0.02 | 0.01 | | | | -0.00 | -0.01 | 0.01 | | | |
| gender: male vs female | 0.25 | -0.18 | 0.39 | | | | *0.36 | 0.10 | 0.62 | | | |
| diagnosis: oligo vs mono | 0.28 | -0.19 | 0.75 | | | | 0.05 | -0.30 | 0.40 | | | |
| poly vs mono | *0.58 | 0.10 | 1.06 | | | | *0.49 | 0.12 | 0.87 | | | |
| other vs mono | 0.39 | -0.21 | 0.99 | | | | 0.29 | -0.15 | 0.74 | | | |
| symptom duration (months)* | 0.06 | -0.06 | 0.18 | | | | 0.06 | -0.00 | 0.13 | *0.09 | 0.01 | 0.17 |
| morning stiffness (y/n) | 0.20 | -0.29 | 0.69 | | | | *0.32 | 0.01 | 0.63 | | | |
| baseline PASDAS | *0.61 | 0.47 | 0.75# | *0.62 | 0.48 | 0.76 | *0.60 | 0.34 | 0.19 | *0.48 | 0.33 | 0.62 |
| average MTX dose (mg) | 0.00 | -0.02 | 0.02 | *-0.04 | -0.07 | -0.01 | *-0.02 | -0.03 | -0.01 | *-0.01 | -0.04 | -0.01 |
| ever MTX use# | 0.22 | -0.13 | 0.57 | *0.56 | 0.01 | 1.11 | 0.14 | -0.14 | 0.41 | | | |
| other DMARDs (y/n) | *0.82 | 0.01 | 1.23 | | | | -0.02 | -0.36 | 0.32 | | | |

CPDAI: Composite Psoriatic Disease Activity Index, PASDAS: Psoriatic Arthritis Disease Activity Score. Covariates: * disease duration is the log of number of months #ever MTX use: MTX used during follow up

**Conclusions:** PASDAS and CPDAI decrease over time associated with the use of Methotrexate, while higher baseline values and longer disease duration affected this negatively.

**Disclosure of Interest:** None declared

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## FRI0460 SECUKINUMAB SHOWS SIGNIFICANT EFFICACY IN NAIL PSORIASIS: WEEK 32 RESULTS FROM THE TRANSFIGURE STUDY

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**Background:** Nail psoriasis is associated with decreased finger mobility, functional impairment, pain and reduced quality of life [1] and is often resistant to available therapies.[2] It correlates with more severe psoriatic disease and is an important predictor of psoriatic arthritis (PsA).[3] The incidence of nail psoriasis in PsA patients is up to 80%.[4]

**Objectives:** We assessed superiority of secukinumab 300 mg and/or 150 mg vs. placebo (PBO) in treating subjects with moderate to severe psoriasis and significant nail involvement, as assessed by NAil Psoriasis Severity Index (NAPSI) at Week (Wk) 16 and Wk 32 and Psoriasis Area and Severity Index (PASI) at Wk 32. Impact on quality of life was assessed by Nail Assessment in Psoriasis and Psoriatic Arthritis (NAPPA) Patient Benefit Index (-PBI) and Quality of Life (-QOL) at Wk 16.

**Methods:** TRANSFIGURE is a double-blind, randomized, PBO-controlled, parallel-group multicentre phase 3b study. Subjects (N=198) were randomized 1:1:1 to receive either secukinumab 300 mg, secukinumab 150 mg or PBO subcutaneously up to Wk 128. At Wk 16, all subjects receiving PBO were re-randomized 1:1 to receive 300 mg or 150 mg secukinumab.

**Results:** The primary objective of this study was met. Both doses of secukinumab were superior to PBO at Wk 16 with a mean percentage NAPSI improvement from Baseline of -45.3%, -37.9%, and -10.8%, for secukinumab 300 mg, 150 mg and PBO, respectively ($P < 0.0001$). Responses improved further by Wk 32 with a NAPSI change of -63.2% and -52.6%, for secukinumab 300 mg and 150 mg, respectively. At Wk 32, PASI 90 responses were achieved in 72.1% and 61.4% of subjects, and PASI 100 responses in 36.9% and 28.1% for secukinumab 300 mg and 150 mg, respectively. At Wk 16, subjects on secukinumab showed significant improvements in NAPPA-QOL with a median decrease in total score of 60.9%, 49.9% and 15.8% for secukinumab 300 mg, 150 mg and PBO, respectively. The percentage of subjects achieving a weighted NAPPA-PBI global score of 2 and above (i.e. at least moderate benefits) was 75.4%, 61.3% and 8.6% for secukinumab 300 mg, 150 mg and PBO, respectively. The most common adverse events were nasopharyngitis, headache and upper respiratory tract infections, similar to previous studies.

**Conclusions:** In the prospective, placebo-controlled TRANSFIGURE trial, secukinumab demonstrated significant and clinically meaningful efficacy, quality of life improvement and patient-reported benefit in nail psoriasis.

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**Disclosure of Interest:** K. Reich Grant/research support from: K Reich has participated in clinical trials sponsored by AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Leo, Lilly, Medac, MSD, Novartis, Pfizer, Takeda, and Vertex, Consultant for: K Reich has served as a consultant for AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Leo, Lilly, Medac, MSD, Novartis, Pfizer, Takeda, and Vertex, J. Sullivan Grant/research support from: J Sullivan has received educational grants from Novartis, Abbvie and Pfizer., Consultant for: J Sullivan has received consultancy fees from Novartis, Abbvie, Pfizer and Eli Lilly. P. Arenberger Grant/research support from: P Arenberger has received grants from Novartis. U. Mrowietz Grant/research support from: U Mrowietz has received grants and/or participated in clinical trials for Abbott/AbbVie, Almirall, Amgen, BASF, Biogen Idec, Celgene, Centocor, Eli Lilly, Forward Pharma, Galderma, Janssen, Leo Pharma, Medac, MSD, Miltenyi Biotech, Novartis, Pfizer, Teva, VBL, and Xenoport. Consultant for: U Mrowietz has served as advisor and/or received speaker honoraria and/or received grants for Abbott/AbbVie, Almirall, Amgen, BASF, Biogen Idec, Celgene, Centocor, Eli Lilly, Forward Pharma, Galderma, Janssen, Leo Pharma, Medac, MSD, Miltenyi Biotech, Novartis, Pfizer, Teva, VBL, and Xenoport. S. Jazayeri Grant/research support from: S Jazayeri has received a grant from Novartis and personal fees outside of the submitted work., M. Augustin Grant/research support from: M Augustin has received grants and/or participated in clinical trials for Abbvie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Celgene, Centocor, Eli Lilly, Janssen-Cilag, Leo, Medac, MSD (formerly Essex, Schering-Plough), Mundipharma, Novartis, Pfizer (formerly Wyeth), Pohl Boskamp, Sandoz, Xenoport. Consultant for: M Augustin has served

as advisor and/or received speaker honoraria from Abbvie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Celgene, Centocor, Eli Lilly, Janssen-Cilag, Leo, Medac, MSD (formerly Essex, Schering-Plough), Mundipharma, Novartis, Pfizer (formerly Wyeth), Pohl Boskamp, Sandoz, Xenoport. A. Parneix Employee of: A Parneix is a full time employee of Novartis, P. Regnault Employee of: P Regnault is a full time employee of Novartis, R. You Employee of: R You is a full time employee of Novartis, M. Milutinovic Employee of: M Milutinovic is a full time employee of Novartis

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## FRI0461 HIGHER BURDEN OF DISEASE IN FEMALE PSA PATIENTS COMPARED TO MALE PATIENTS. DATA FROM THE BEPAS COHORT

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**Background:** Psoriatic arthritis impacts significantly function and quality of life. Although radiographic damage may be more important in rheumatoid arthritis both disability and quality of life are similarly impaired in both groups. Only few data in large cohorts are available to evaluate the impact of the articular and skin involvement in PsA. The BEPAS cohort is a unique opportunity to study cross-sectionally and longitudinally these aspects and their effect on disability and quality of life.

**Objectives:** (1) to estimate the severity of disease based on disease activity scores and active inflammation (2) to estimate the impact in terms of health-related quality of life of PsA in Belgium

**Methods:** A cross-sectional analysis at the inclusion visit was performed among all patients included in the BEPAS cohort and subsequently differences between male and female patients were studied. They were evaluated for the demographics, the disease activity at inclusion. Inflammatory parameters were captured at inclusion. HAQ and SF36 patient global assessment and physician global assessment were collected. Gender differences were evaluated by one way ANOVA or Chi –square testing.

**Results:** 461 patients including 263 male patients and 198 female patients with mean age: 52.79 years (±12.29) were recruited in the 17 centers from December 2012 to July 2014.

| | Male | | Female | | M vs F |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | P |
| TJ78 | 3.71 | 6.75 | 4.55 | 7.79 | 0.215 |
| SJ76 | 2.30 | 5.19 | 1.88 | 3.32 | 0.318 |
| No. sites w/ enthesitis | 0.73 | 2.51 | 1.63 | 4.09 | 0.004 |
| No. digits w/ dactylitis | 0.35 | 1.20 | 0.20 | 0.66 | 0.114 |
| BSA | 4.88 | 11.12 | 3.03 | 6.67 | 0.074 |
| PTGAVAS | 36.90 | 26.75 | 46.15 | 26.20 | 0.001 |
| PGAVAS | 21.60 | 19.61 | 25.20 | 20.64 | 0.065 |
| BMI | 27.85 | 4.52 | 26.94 | 5.44 | 0.060 |
| CRP | 4.09 | 11.41 | 4.34 | 7.30 | 0.792 |
| ESR | 10.78 | 12.93 | 14.15 | 12.65 | 0.010 |
| DAS28_CRP | 2.53 | 1.17 | 2.84 | 1.08 | 0.012 |
| PASDAS | 3.46 | 1.46 | 4.02 | 1.48 | 0.001 |
| HAQ (<0.3) | 105 (40.1%) | | 45 (22.7%) | | 0.002 |
| SF36 Σ phys comp | 41.40 | 10.55 | 38.27 | 9.68 | 0.001 |
| SF36 Σ mental comp | 46.58 | 12.42 | 42.48 | 13.65 | 0.001 |
| Actual use anti-TNF | 130 (50.2%) | | 74 (37.8%) | | 0.008 |
| Any use of anti-TNF | 142 (54%) | | 86 (43.4%) | | 0025 |

**Conclusions:** The differences in disease activity and consequently the burden of disease between male and female patients with PsA in the BEPAS cohort seem mainly based on the patient global assessment and enthesitis score. Swollen and tender joint counts as well as inflammatory parameters are not responsible for these differences

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## FRI0462 GENDER DIFFERENCES IN THE DISEASE EXPRESSION AND ARTICULAR MANIFESTATIONS AMONG PATIENTS WITH PSORIATIC ARTHRITIS. DATA FROM THE BEPAS COHORT

K. De Vlam[1], R. Lories[1], S. Steinfeld[2], F. Van Den Bosch[3], A. Nzeusseu Toukap[4], M. Malaise[5], V. Taelman[1], F. Van Bruwaene[6], M. Van Den Berghe[7], J. Lenaerts[8], R. Joos[9], P. Geusens[10], S. Dall'Armellina[11], I. Peene[12], G. De Brabanter[13], M. Van Den Berghe[14], J. Qu[15], M. Maertens[16], H. Leroi[17] on behalf of BEPAS. *[1]Rheumatology, University Hospitals Leuven, Leuven; [2]Clinique St Jean, Bruxelles; [3]Ugent, Gent; [4]Rheumatology, UCL St Luc, Brussels; [5]Rheumatology, CHU Sart Tilman, Liege; [6]Rheumatology, Heilig Hart Ziekenhuis, Roeselaere; [7]Rheumatology, Algemeen Stedelijk Ziekenhuis, Aalst; [8]Reuma instituut, Hasselt; [9]Rheumatology, ZNA, Antwerpen; [10]ReumaClinic, Genk; [11]Rheumatology, Clinique Notre Dame de Grace, Gosselies; [12]AZ St Jan; [13]Rheumatology, AZ St Lucas, Brugge; [14]Rheumatology, Grand Hopital de Charleroi, Charleroi; [15]Rheumatology, Iris Sud, Brussels; [16]AZ Damiaan, Oostende; [17]Medical Affairs Immunology, MSD Belgium, Brussels, Belgium*

**Background:** Psoriatic arthritis (PsA) is a common form of chronic arthritis strongly associated with the skin disease psoriasis. The gender distribution is considered equal but it is suggested that their might be gender related differences in disease expression, disease activity and outcome. The BEPAS cohort (Belgian Epidemiological Psoriatic Arthritis Study) is a large prospective multicenter real life cohort set up in 17 Belgian large academic and non academic rheumatology practices that offers a unique opportunity to study the disease patterns with their respective articular and skin involvement in this patient group

**Objectives:** (1) To assess gender-related differences in disease patterns and articular manifestations of psoriatic arthritis

**Methods:** A cross-sectional analysis at the inclusion visit was performed among the male and female patients included in the BEPAS cohort. They were evaluated for the demographics, the disease patterns at diagnosis and the presence of clinical articular and extra–articular manifestations at inclusion. Gender differences were evaluated by one way ANOVA or Chi –square testing.

**Results:** 461 patients including 263 male patients and 198 female patients with mean age: 52.79 years (±12.29) were recruited in the 17 centers from December 2012 to July 2014.There was no gender difference in rheumatoid factor, anti–CCP and extra-articular manifestations such as uveitis and inflammatory bowel disease

| | Male (263) | | Female (198) | | P |
|---|---|---|---|---|---|
| | mean | SD | mean | SD | |
| Age of onset PsA | 45.023 | 13.2 | 44.15 | 15 | 0.507 |
| Age of onset PsO | 35.38 | 14.06 | 33.69 | 17.95 | 0.286 |
| PsA disease duration at inclusion | 8.45 | 8.74 | 8.79 | 9.99 | 0.701 |
| HLA B27 (n=112) (%) | 9.8 | | 9.8 | | >0.5 |
| BMI | 27.85 | 4.52 | 26.94 | 5.43 | 0.06 |
| Psoriasis type 1 | 165 (62.7) | | 122 (61.6) | | >0.5 |
| Numbers of DMARDS | 1.62 | 0.95 | 1.59 | 1.017 | 0.735 |
| Actual use of anti TNF | 130 (50.2) | | 74 (37.8) | | 0.008 |
| Oligo at diagnosis (%) | 93 (20.2) | | 61 (13.2) | | 0.305 |
| Poly at diagnosis (%) | 134 (29.1) | | 78 (16.9) | | 0.014 |
| Clinical articular and skin manifestations at inclusion | | | | | |
| IBP (Rudwaleit criteria ≥2/4) | 76 (28.9) | | 81 (40.9) | | 0.007 |
| TJ78 | 3.71 | 6.75 | 4.55 | 7.78 | 0.215 |
| SJ76 | 2.3 | 5.19 | 1.88 | 3.31 | 0.318 |
| Number of enthesitis | 0.73 | 2.13 | 1.63 | 4.08 | 0.004 |
| Number of dactylitis | 0.35 | 1.2 | 0.2 | 0.66 | 0.114 |
| BSA | 4.87 | 11.12 | 3.03 | 6.66 | 0.074 |
| Nail involvement | 85 (32.3) | | 37 (18.9) | | 0001 |

**Conclusions:** The disease patterns and clinical manifestations differ in several aspects between male and female PsA. They have a different clinical articular presentation at diagnosis: male patients have more polyarticular disease while female patients have more entheseal disease. Skin involvement is comparable except for male patients having more nail involvement. These differences might have impact on the disease evolution, severity and treatment decisions.

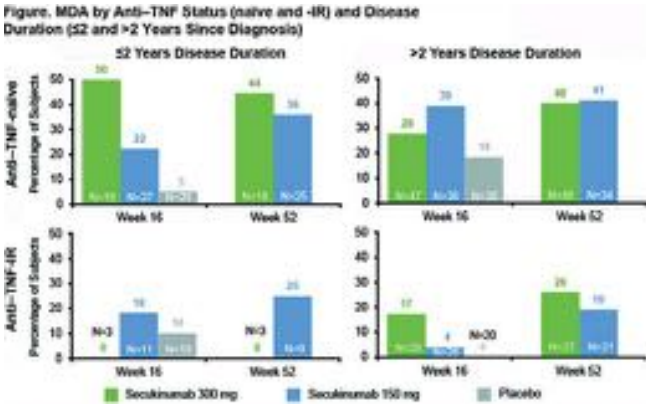
**Disclosure of Interest:** K. De Vlam: None declared, R. Lories Grant/research support from: MSD Belgium, S. Steinfeld Grant/research support from: MSD Belgium, F. Van Den Bosch Grant/research support from: MSD Belgium, A. Nzeusseu Toukap Grant/research support from: MSD Belgium, M. Malaise Grant/research support from: MSD Belgium, V. Taelman Grant/research support from: MSD Belgium, F. Van Bruwaene Grant/research support from: MSD Belgium, M. Van Den Berghe Grant/research support from: MSD Belgium, J. Lenaerts Grant/research support from: MSD Belgium, R. Joos Grant/research support from: MSD Belgium, P. Geusens Grant/research support from: MSD Belgium, S. Dall'Armellina Grant/research support from: MSD Belgium, I. Peene Grant/research support from: MSD Belgium, G. De Brabanter Grant/research support from: MSD Belgium, M. Van Den Berghe Grant/research support from:

MSD Belgium, J. QU Grant/research support from: MSD Belgium, M. Maertens Grant/research support from: MSD Belgium, H. Leroi Employee of: MSD Belgium
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## FRI0463 SECUKINUMAB IMPROVES MINIMAL DISEASE ACTIVITY RESPONSE RATES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: DATA FROM THE RANDOMIZED PHASE 3 STUDY, FUTURE 2

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**Background:** Minimal disease activity (MDA), a validated composite measure in PsA, is gaining acceptance as a target for achieving substantial disease control.
**Objectives:** Secukinumab (SEC), an anti–IL-17A monoclonal antibody, significantly improved the signs and symptoms of PsA over 52 wks in the FUTURE 2 study. This post-hoc exploratory analysis assessed MDA response rates through 52 wks.
**Methods:** 397 patients (pts) with active PsA were randomized to subcutaneous (SC) SEC (300 mg, 150 mg, or 75 mg) or placebo (PBO) at baseline (BL), Wks 1, 2, and 3, and every 4 wks (q4w) from Wk 4. PBO pts were re-randomized to SEC 300 or 150 mg SC q4w from Wk 16 or 24, depending upon clinical response. Pts were considered in MDA when they met at least 5 of the following 7 criteria: 1) tender joint count $\leq$1; 2) swollen joint count $\leq$1; 3) Psoriasis Activity and Severity Index $\leq$1 or psoriasis affecting $<$3% body surface area at BL; 4) pt pain VAS $\leq$15; 5) pt global disease activity VAS $\leq$20; 6) HAQ-DI $\leq$0.5; 7) tender entheseal points $\leq$1. MDA was assessed in the overall population and in pts stratified by prior anti-tumor necrosis factor (anti-TNF) therapy use (anti–TNF-naïve and inadequate response/intolerance to these agents [anti–TNF-IR]) and disease duration ($\leq$2 yrs vs $>$2 yrs since diagnosis). Observed data are shown. 75 mg data are not reported as this was not considered an effective dose (no secondary endpoints were met).
**Results:** In the overall population, 23/100 (23%) and 27/97 (28%) pts achieved MDA at Wk 16 with SEC 150 mg and 300 mg, respectively, vs 9/88 (10%) pts with PBO; these response rates were sustained through Wk 52 (150 mg: 29/88 [33%]; 300 mg: 33/93 [35%]). In the anti–TNF-naïve cohort, a higher proportion of pts achieved MDA at Wk 16 with SEC 150 mg (20/63 [32%]) or 300 mg (22/65 [34%]) vs PBO (8/58 [14%]), with response rates sustained through Wk 52 (150 mg: 23/59 [39%]; 300 mg: 26/63 [41%]). Lower rates were observed in anti–TNF-IR pts (SEC vs PBO at Wk 16: 150 mg, 3/37 [8%]; 300 mg, 5/32 [16%]; PBO, 1/30 [3%]; Wk 52: 150 mg, 6/29 [21%]; 300 mg, 7/30 [23%]). The proportion of pts achieving MDA at Wk 16 and Wk 52 in the overall population was greater for those $\leq$2 yrs since diagnosis vs those $>$2 yrs since diagnosis for both SEC 150 mg and 300 mg. The proportion of pts achieving MDA with SEC at Wk 16 was higher in anti–TNF-naïve pts with low disease duration vs pts with longer disease duration, and higher in the anti–TNF-naïve cohort than the anti–TNF-IR cohort at all times (Figure).




**Conclusions:** SEC pts had higher MDA response rates vs PBO pts at Wk 16, with response rates sustained through Wk 52. Response rates were consistent with those previously reported with anti-TNF therapies in comparable pt populations.[1] This study is the first to report MDA in anti–TNF-IR pts. The finding that greater MDA can be achieved in early anti–TNF-naive PsA pts warrants further research.
**References:**
[1] Mease et al. J Rheumatol 2013;40:647–52
**Acknowledgement:** The study was sponsored by Novartis Pharma AG.
**Disclosure of Interest:** L. Coates Grant/research support from: Abbvie, Pfizer, Janssen, Consultant for: Abbvie, Celgene, Pfizer, UCB, MSD, Boehringer Ingelheim, Novartis, Lilly, P. Mease Grant/research support from: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, B. Kirkham Grant/research support from: Abbvie, Novartis and Roche, Consultant for: Abbott, BMS, Chugai, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: Abbott, BMS, Chugai, MSD, Novartis, Pfizer, Roche and UCB, L. McLeod Consultant for: Novartis through employment at RTI Health Solutions, Employee of: RTI Health Solutions, S. Mpofu Shareholder of: Novartis, Employee of: Novartis, C. Karyekar Shareholder of: Novartis, Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis
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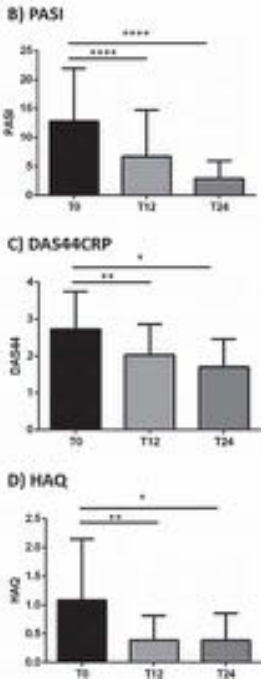
## FRI0464 LONG-TERM EFFICACY OF USTEKINUMAB TREATMENT IN PATIENTS AFFECTED BY PSORIATIC ARTHRITIS PREVIOUSLY TREATED WITH TNF INHIBITORS

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**Background:** IL12 and IL23 are two main cytokines involved in the pathogenesis of immune-mediated diseases. IL-12 is produced by macrophages and B lymphocytes and mediates differentiation of Th1 lymphocytes, while IL-23 is a pro-inflammatory cytokine essential for the differentiation of Th17 cells. Ustekinumab is a human monoclonal antibody directed against the p40 protein subunit shared by IL-12 and IL-23, blocking the signal transmission of both cytokines involved in the pathogenesis of both Psoriasis (PsO) and Psoriatic Arthritis (PsA)
**Objectives:** Evaluate the long-term efficacy of treatment with Ustekinumab in PsA patients previously treated with TNF inhibitors (TNF-i) in real life
**Methods:** We prospectively evaluated patients with PsO and moderate-severe PsA, who were treated with Ustekinumab after the failure of previous TNF-i therapies, in the period January 2013 -December 2015. Clinimetric scores (PASI, DAS44CRP, Pain VAS, Clinicians' VAS, and HAQ) were assessed and biochemical values (ESR, CRP, glucose, cholesterol, uric acid) were measured at baseline (T0) and after 6 (T6), 12 (T12) and 24 (T24) months. Differences between variables were analysed with paired T test ($P<0.05$ as significant)
**Results:** 36 patients (61% men; age (mean±DS): 49.7±11.4) treated with ustekinumab were evaluated (Figure 1A). In 6/36 (16.7%) patients treated with ustekinumab for $<$12 months (mean duration: 7.5 months), a significant reduction of PASI (P=0.02) and Pain VAS (P=0.04) was observed after 6 months of treatment. In patients treated continuously for 12 months, a significant reduction

**A) Table I**

| Demographic and clinical data | Patients (n=36) |
|---|---|
| Male sex (n/%) | 22/61 |
| Age (yrs) | 49.7±11.4 |
| Tobacco smokers (n/%) | 15/41.7 |
| PsO (n/%) | 36/100 |
| Onicopathy (n/%) | 20/55.6 |
| Age at PsO onset | 33.6±12.5 |
| Age at diagnosis | 38.1±10.1 |
| Height (cm) | 170.9±8.4 |
| Weight (kg) | 79.1±17.9 |
| BMI | 27.3±7 |
| Abdominal circumference (cm) | 90.8±14.8 |
| Comorbidities (n/%) | 20/55.6 |
| Cardiovascular (n/%) | 11/30.6 |
| Metabolic (n/%) | 7/19.4 |
| Inflammatory bowel disease | 5/13.9 |
| BPCO (n/%) | 1/2.8 |
| Ustekinumab therapy | |
| 1st line (n/%) | 6/16.7 |
| 2nd line (n/%) | 11/30.6 |
| 3rd line (n/%) | 9/25 |
| 4th line (n/%) | 8/22.2 |
| 5th line (n/%) | 2/5.6 |
| Concomitant DMARDs (n/%) | 30/83.4 |
| PASI | 14.7±11 |
| Pain VAS | 54.0±26.5 |
| Clinician's VAS | 57.1±19 |
| DAS44 | 2.8±1 |
| HAQ | 1.3±1.2 |
| ESR (mm/h) | 29±23.4 |
| CRP (mg/l) | 6.9±6.7 |
| Glucose (mg/dl) | 94.7±14.4 |
| Triglycerides (mg/dl) | 122.6±47.5 |
| Total Cholesterol (mg/dl) | 202.8±35.3 |
| HDL (mg/dl) | 53.4±9 |
| LDL (mg/dl) | 121.1±47 |
| Uric acid (mg/dl) | 2.8±2.7 |



of PASI (P<0.0001), DAS44 (P=0.008), ESR (P=0.03), CRP (P=0.04), and HAQ (P=0.002) was achieved. At T24, a persistent reduction of PASI (P<0.0001), DAS44 (P=0.04), and HAQ (P=0.02) with the rspect to T0 (Figure 1B,C,D) was maintained. Prevalence of patients on DMARDs was higher at T0 (83%) compared to the prevalence after the beginning of the ustekinumab therapy (36%). No significant differences in metabolic parameters were observed during the follow-up while a trend in reduction of uric acid resulted (2.8±2.7 at T0 vs 1±2 at T24).

**Conclusions:** Ustekinumab offers a therapeutic benefit in PsO/PsA patiens who failed TNF-i providing good clinical response both at the skin and joint level.

**Disclosure of Interest:** None declared

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## FRI0465 DOES SKIN MATTER IN INCIDENT PSORIATIC ARTHRITIS?

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**Background:** Psoriatic arthritis (PsA) is a disease with musculoskeletal and skin inflammation (psoriasis). Attempts are being made to develop comprehensive disease measures to capture global disease activity. However very little is known on how much psoriasis actually affects quality of life (QOL) in patients with PsA.

**Objectives:** In this study we aim to determine to what extent psoriasis affects quality of life in incident Psoriatic Arthritis patients.

**Methods:** Data collected at baseline in the Dutch south west Psoriatic Arthritis Registry (DEPAR) study were used. The DEPAR includes newly diagnosed PsA patients from 8 hospitals in the South-West of the Netherlands. PsA core measurements were collected: Swollen and Tender join count (66/68), enthesitis (LEI and MASES), dactylitis (LDI) and psoriasis (PASI). In addition 3 patient reported measures of quality of life were administered. Short Form-36 (SF-36) is a self-administered 36-item health survey questionnaire. The items are assigned to eight scales grouped in two factors: physical component summary (PCS) and mental component summary (MCS, score 0–100). Skindex-17 is a self-administered 17-item dermatology questionnaire that explores functioning, emotions and symptoms in a Symptoms Subscale (SS; range 0–10) and a Psychosocial Subscale (PS; range 0–24).The DLQI is a self-administered 10-item questionnaire, score 0–30 with higher scores resulting in poorer quality of life. It covers Symptoms and feelings, Daily activities, Leisure, Work and school, Personal relationships and Treatment

**Results:** In total 281 patients were included: mean age was 50.6 (SD 13.6) and 50.5% were male. In terms of arthritis subtypes, 56 (20%) had mono-arthritis, 108 (39%) oligo-arthritis, 80 (29%) poly-arthritis and 35 (12%) were diagnosed with axial disease, dactylitis or enthesitis only. The Median PASI score was 2.3, ranging from 0 to 22.5. Divided in PASI categories (1) this resulted for 12% in no skin disease, 72% mild (>0–7), 11% moderate (7–12) and 5% had severe (>12) psoriasis. Median PASI scores were different for mono, oligo to polyarthritis group: 2.7 (0–12.3), 3.4 (0–22.5) and 4.4 (0–21). Skin related quality of life measured by DLQI showed a median 1 (QR 0–5) and the two subscales of the skindex resulted in a median SS 4 (IQR 2–6) and a PS of 2 (IQR 0–8), and a SF-36 PCS of 40.3 (8.3) and SF-36 MCS of 47.7 (10.4).(table 1) Comparing none and mild psoriasis to moderate and sever psoriasis resulted in median scores for DLQI: 1 vs 5 (p<0.01) and Skindex-17 SS: 4 vs 7 and skindex-17 PS: 2 vs 7 (p<0.01)while significant difference was observed for the bodily pain an emotional role subscales of the SF-36. (P<0.05)




**Conclusions:** Skin involvement in incident Psoriatic Arthritis is in the majority of patients mild with median PASI score of 2.3. About 15% suffered from moderate to severe psoriasis. Skin quality of life measures showed poorer health states for these patients, which was also reflected in the emotional role and bodily pain subscale of more generic QOL questionnaire: SF-36.

**Disclosure of Interest:** None declared

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## FRI0466 INCREASED RISK OF CANCER IN PATIENTS WITH PSORIASIS: A NATIONWIDE POPULATION STUDY

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**Background:** Psoriasis is a chronic inflammatory disease that involves hyper-proliferation of keratinocytes in the epidermis. Several studies have reported the relationship between psoriasis and cancer. Population-based estimates for cancer risks in patients with psoriasis is rare

**Objectives:** This study estimated the standardised incidence ratio (SIR) of cancer in patients with psoriasis in Taiwan.

**Methods:** The primary data source was the National Health Insurance database of Taiwan. We identified patients with psoriasis based on a rheumatologist or dermatologist diagnosis. Incident cases who were free or cancers in 2000 were identified. Incidence of cancer was estimated in both incident psoriasis patients and the general population in 2000. To measure the relative risk of cancer in psoriasis patients, we calculated a SIR for all types of cancers and also each cancer type. SIRs were computed as ratios of observed numbers of cancers to the expected number of cancers on the basis of age-specific incidence rates in 5-year age intervals of the entire NHI covered population in 2000.

**Results:** A total of 6,835 incident psoriasis patients (4,472 men, 2,363 women) were identified from 21,226,181 cancer-free beneficiaries of NHI in 2000. Mean age was 46.96 years in men and 41.27 years in women. After a median follow-up of 11 years, cancer was diagnosed in 527 patients with psoriasis and 860,084 in the general population. The most common cancers sites were gastrointestinal tract, oral cavity and pharynx in patients with psoriasis. The overall incidence of cancer was higher in psoriasis patients than the general population (6.92 vs. 3.34 cases per 1,000 patient-years, P<0.001). Psoriasis was associated with an SIR of 1.15 (95% confidence interval [CI], 1.06–1.25) for cancer of all sites. The SIR was 1.95 (95% CI, 1.21–3.14) for skin cancers, 1.59 (95% CI, 1.26–2.02) for oral cavity and pharynx cancers and 1.14 (95% CI=1.00–1.30) for gastrointestinal tract cancers, respectively.

**Conclusions:** Compared with the general population, psoriasis patients have an increased risk for cancer.

**Disclosure of Interest:** None declared

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## FRI0467 PREDICTORS OF EARLY MINIMAL DISEASE ACTIVITY IN PSA PATIENTS TREATED WITH ANTI-TNF IN A REAL-WORLD REGISTRY

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**Background:** Early achievement of minimal disease activity (MDA) is recommended as a valid treat-to-target approach in psoriatic arthritis (PsA).

**Objectives:** The purpose of the current analysis was to evaluate predictors of MDA achievement in PsA patients treated with anti-TNF agents in Canadian routine clinical care.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis, ankylosing spondylitis, or PsA with Infliximab (IFX) or Golimumab (GLM). Eligible people for this analysis included PsA patients treated with IFX who were enrolled since 2005 or with GLM enrolled since 2010 and with available MDA information at baseline, 6 months, and/or 12 months. MDA was defined as the fulfillment of ≥5 of the following criteria: TJC28≤1, SJC28≤1, PASI≤1, Pain (VAS)≤15mm, PtGA (VAS)≤20mm, HAQ ≤0.5, tender entheseal points ≤1. Independent predictors of MDA achievement were assessed with logistic regression.

**Results:** A total of 196 patients (51.4% male and 87.2% bionaive) were included with a mean (SD) age and disease duration of 49.8 (11.1) and 5.4 (6.3) years, respectively. The proportion of patients with MDA was 11.7% at baseline, 43.5% at 6 months, 44.8% at 12 months, and 49.1% at either 6 or 12 months. Among patients with MDA at 6 months, 75.7% had sustained MDA at 12 months. Patients achieving MDA during follow-up had significantly lower disease activity at baseline; mean (SD) disease parameters were: SJC28: 3.24 (3.58) vs. 5.47 (4.31), P<0.001; TJC28: 3.75 (4.00) vs. 8.66 (6.53), P<0.001; pain: 35.39 (25.11) vs. 55.70 (22.93), P<0.001; PtGA: 38.51 (25.00) vs. 56.15 (25.13), P<0.001; HAQ-DI: 0.71 (0.61) vs. 1.33 (0.57), P<0.001; MDGA: 4.25 (2.38) vs. 5.84 (2.07), P<0.001); enthesitis count: 2.62 (1.60) vs. 4.97 (3.48), P=0.008.

Multivariate logistic regression analysis showed that lower baseline HAQ (OR=0.243; P<0.001), lower TJC28 (OR=0.889; P=0.008), and lower enthesitis count (OR=0.817; P=0.817) were significant predictors of MDA achievement over 12 months of treatment.

**Conclusions:** The results of the current analysis have shown that 50% of patients treated with IFX or GLM in routine clinical care achieve MDA within the first year of treatment. Lower baseline HAQ, lower TJC28, and lower enthesitis count were identified as significant predictors of MDA achievement.

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## FRI0468 HIGH PREVALENCE OF US DETERMINED SUBCLINICAL SYNOVITIS IN EARLY PSORIATIC ARTHRITIS CORRELATES BETTER WITH THE SJC RATHER THAN TJC: RESULTS FROM THE LEEDS SPARRO COHORT

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**Background:** Ultrasound (US) is known to be more sensitive than clinical examination in detecting synovitis in psoriatic arthritis (PsA). However, some studies found disparity between the US and clinical findings

**Objectives:** To assess the prevalence of synovial involvement in early PsA using clinical and sonographic assessments.

**Methods:** A total of 49 subjects with early PsA (CASPAR criteria) recruited in the Leeds Spondyloarthropathy Register for Research and Observation (SpARRO) study, a prospective longitudinal observational cohort, was assessed. The mean disease duration is 1.6 ±0.5 years; F:M ratio is 1.3; median SJC76 is 2 (1–2), median TJC78 is 6 (3–17); 90% of subjects had current skin psoriasis. Baseline US scan was performed on 1274 joints including bilateral wrists, MCP2–3, PIP2–3, elbows, knees, ankles & MTP 1–5. Grey Scale (GS) and Power Doppler (PD) were scored on a 0–3 semi-quantitative scale for each joint. Joints were considered clinically active if tender or swollen, and sonographically active if GS≥2 and/or PD≥1. We compared US active (yes/no) against tender (yes/no) and swollen (yes/no). The majority of the patients (88%) were DMARD naive

**Results:** US identified a higher proportion of subclinical synovitis among swollen rather than tender joints in subjects with early PsA. The agreement between clinical examination (tender & swollen) and US findings was high (73 & 87%) respectively. The most common sites for subclinical synovitis were MTP joints. In contrast, wrist tenderness and MTP2 swelling were the highest overestimated joints among the physical examination.

Table 1. Agreement between tender or swollen and US synovitis by joint type

| | Tender | | | | | Swollen | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | PEA % | Sp0 % | Sp1 % | US>CE % | CE>US % | PEA % | Sp0 % | Sp1 % | US>CE % | CE>US % |
| Elbow | 93 | 96 | 22 | 2 | 5 | 97 | 98 | 0 | 3 | 0 |
| Wrist | 60 | 69 | 46 | 2 | 38 | 96 | 98 | 75 | 0 | 4 |
| MCP2 | 83 | 90 | 26 | 2 | 15 | 92 | 96 | 50 | 2 | 6 |
| MCP3 | 82 | 89 | 31 | 1 | 17 | 92 | 96 | 60 | 1 | 7 |
| PIP2 | 77 | 87 | 0 | 1 | 22 | 89 | 95 | 0 | 1 | 9 |
| PIP3 | 72 | 84 | 7 | 2 | 26 | 85 | 92 | 0 | 3 | 12 |
| Knee | 69 | 82 | 12 | 7 | 24 | 85 | 91 | 40 | 3 | 12 |
| Ankle | 82 | 90 | 0 | 2 | 16 | 93 | 96 | 36 | 0 | 7 |
| MTP1 | 52 | 65 | 23 | 28 | 20 | 67 | 0 | 33 | 80 | 11 |
| MTP2 | 64 | 75 | 41 | 22 | 13 | 63 | 4 | 33 | 77 | 14 |
| MTP3 | 76 | 85 | 37 | 13 | 11 | 97 | 98 | 77 | 0 | 3 |
| MTP4 | 65 | 77 | 29 | 14 | 20 | 81 | 86 | 39 | 14 | 5 |
| MTP5 | 78 | 87 | 21 | 5 | 18 | 92 | 96 | 43 | 5 | 3 |
| Total | 73 | 83 | 23 | 8 | 19 | 87 | 73 | 37 | 15 | 7 |

*PEA = percentage exact agreement; CE = clinical examination; Sp0 = agreement specific to a score of 0; Sp1 = agreement specific to a score of 1.

**Conclusions:** The prevalence of subclinical synovitis is high in early PsA. Joint swelling is more likely to correlate with PD or GS in PsA when compared to joint tenderness. As opposed to RA, where clinical tenderness correlates with subclinical synovitis, the tender joint count may not be a reliable clinical measure to assess synovitis in PsA. Possible reasons for the over-estimation of TJC in clinical examination may be the concomitant occurrence of fibromyalgia. Larger studies are needed to confirm our results.

**Disclosure of Interest:** None declared

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## FRI0469 MEASURING OUTCOME IN PSORIATIC ARTHRITIS (MOPSA), A NEW WEB-BASED TOOL FOR ASSESSMENT OF PSORIATIC ARTHRITIS SHOWING INITIATION OF TREATMENT CHANGE IN PATIENTS ACHIEVING MINIMAL DISEASE ACTIVITY

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**Background:** Psoriatic arthritis (PsA) is a heterogeneous disease that includes features of peripheral arthritis, spondylitis, dactylitis, enthesitis, and skin and nail disease. PsA affects about 30% of patients with psoriasis.[1]

Minimal Disease Activity (MDA) is defined as a patient acceptable disease state which is validated and increasingly recognised as a treatment target. MDA is defined when a patient has 5 of the following 7 criteria: tender joint count ≤1, swollen joint count ≤1, tender entheseal point ≤1, PASI ≤1 or body surface area ≤3%, Pain Visual analogue score (VAS) ≤15, patient global ≤20, Health Assessment Questionnaire ≤0.5.[2]

Composite Psoriatic Disease Activity Index (CPDAI) assesses the five domains in PsA. Within each domain a score (range 0–3) is assigned according to predefined cut-offs. The scores for each domain are then added together to give a final score range of 0–15, 0 for no disease and 15 for severe disease.[3]

Recently, Measuring Outcome in Psoriatic Arthritis (MOPsA), a new web-based tool for assessment of PsA was developed and is freely available to use (see https://mopsa.ie). MOPSA will calculate all the scores and determine both MDA and CPDAI. MOPSA provides a graphic representation of CPDAI in the form of a spidergram that can be compared with subsequent visits.

**Objectives:** Our aim was to assess, (1) disease activity using CPDAI and the percentage of patients reaching MDA, in consecutive cohort of established PsA patients attending our unit; and (2) whether treatment change was initiated based on MDA state.

**Methods:** 137 patients with PsA, fulfilling CASPAR criteria, were included in this study. 68 tender joint counts (TJC) and 66 swollen joint counts (SJC) were recorded. Skin scores included Dermatology Quality of Life Index (DLQI), Body Surface Area (BSA) and Psoriasis Area Severity Index (PASI). Patient reported outcome measures (PROMs) included: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Health Assessment Questionnaire (HAQ), Ankylosing Spondylitis Quality of Life (ASQoL). CPDAI was calculated and MDA status was assessed.

**Results:** The mean age was 46.1 (± 11.6) and 72 (52.6%) were females. Clinical outcome measures and PROMs are shown in table 1. The mean CPDAI score was 3.75 (±2.94); 52 (37%) patients reached MDA. Of the 85 patients not in MDA, CPDAI was 5.94±3 in the 37 who had a treatment change and 4.54±2.49 in the 48 who did not. Of those undergoing treatment changes, 7 patients started on biologics, 4 switched to another biologic and 3 had their dose increased. 6 were started on synthetic DMARD, 2 had a second DMARD added to their regimen, and 8 had their dose increased. 6 patients had a short course of systemic steroids while 12 patients had intra-articular steroids injections.

| | |
|---|---|
| Dactylitis, number of patients (%) | 20 (14.6) |
| Dactylitis score | 0.27 (0.71) |
| Enthesitis, number of patients (%) | 38 (27.7) |
| Enthesitis score | 0.49 (0.83) |
| TJC | 4.48 (6.7) |
| SJC | 1.37 (3.2) |
| HAQ | 0.72 (0.77) |
| BASDAI | 1.55 (2.3) |
| ASQoL | 2.47 (4.5) |
| PsAQoL | 4.18 (4.9) |
| DLQI | 3.03 (4.9) |
| PASI | 2.66 (4.0) |
| BSA | 4.02 (7.9) |

Table 1 shows the raw scores for each of the instruments scored. Results are shown as mean (±SD)

**Conclusions:** MOPsA gives a comprehensive assessment of psoriatic disease that can be followed longitudinally. One third of patients in our cohort achieved MDA. CPDAI was higher in those patients not achieving MDA status where treatment was changed.

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## FRI0470 LONG-TERM (156-WEEK) SAFETY PROFILE OF APREMILAST, AN ORAL PHOSPHODIESTERASE 4 INHIBITOR, IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED SAFETY ANALYSIS OF 3 PHASE III, RANDOMIZED, CONTROLLED TRIALS

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**Background:** Apremilast (APR), a phosphodiesterase 4 inhibitor, acts to regulate immune activity in psoriatic arthritis (PsA) patients. PALACE 1 (NCT01172938), 2 (NCT01212757), and 3 (NCT01212770) compared the efficacy and safety of APR with placebo (PBO) in patients with active PsA despite prior conventional DMARDs and/or biologics.
**Objectives:** Assess the long-term safety of APR treatment for patients treated for up to 3 years with APR.
**Methods:** Patients were randomized (1:1:1) to PBO, APR 30 mg BID (APR30), or APR 20 mg BID (APR20) stratified by baseline DMARD use (yes/no). The PBO-controlled phase continued to Week 24; PBO patients were re-randomized to APR30 or APR20 at Week 16 (early escape) or Week 24. Double-blind APR treatment continued to Week 52; patients could continue to receive APR during an open-label, long-term treatment phase. Visits in years 2 and 3 were scheduled at 13-week intervals.
**Results:** 1493 patients were randomized and received ≥1 dose of study medication (PBO: n=495; APR30: n=497; APR20: n=501). At the studies' 3-year data cut, a total of 1441 (1209.3 patient-years), 1028 (937.8 patient-years), and 865 (790.4 patient-years) patients received APR in the Weeks 0 to ≤52, Weeks >52 to ≤104, and Weeks >104 to ≤156 periods, respectively, relative to the start of APR. During the Weeks 0 to ≤52 APR-exposure period, adverse events (AEs) occurring in ≥5% of APR-exposed patients were diarrhea, nausea, headache, upper respiratory tract infection, and nasopharyngitis (Table). Most diarrhea and nausea events were reported within the first 2 weeks of treatment and usually resolved in 4 weeks without medical intervention. The frequency of gastrointestinal AEs decreased with longer exposure (i.e., Weeks >52 to ≤104 or >104 to ≤156; Table); occurrence >5% of other common AEs either decreased in frequency or remained stable with prolonged exposure (Table). Most AEs were mild or moderate in severity up to 156 weeks of APR-exposure. Rates of depression remained very low, consistent with earlier findings. The rate of serious AEs (SAEs) was 8.1% during Weeks >104 to ≤156 of APR exposure; most SAEs occurred in 1 patient each. For SAEs of special interest (major cardiac events, malignant neoplasm, opportunistic infection), rates were very low and comparable to those in the first year of treatment. Discontinuation due to AEs was 1.6% during Weeks >104 to ≤156 of APR exposure. Marked laboratory abnormalities were infrequent, and most returned to baseline with continued treatment.

| | APR Exposure Period* Weeks 0 to ≤52 | | APR Exposure Period* Weeks >52 to ≤104 | | APR Exposure Period* Weeks >104 to ≤156 | |
|---|---|---|---|---|---|---|
| | APR30 n=721 | APR20 n=720 | APR30 n=520 | APR20 n=508 | APR30 n=443 | APR20 n=422 |
| Patients, n (%) | | | | | | |
| ≥1 AE | 524 (72.7) | 507 (70.4) | 315 (60.6) | 324 (63.8) | 276 (62.3) | 267 (63.3) |
| ≥1 SAE | 47 (6.5) | 40 (5.6) | 35 (6.7) | 40 (7.9) | 37 (8.4) | 33 (7.8) |
| AE leading to drug withdrawal | 56 (7.8) | 52 (7.2) | 13 (2.5) | 12 (2.4) | 6 (1.4) | 8 (1.9) |
| Death | 0 (0.0) | 1[a] (0.1) | 1[a] (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| AEs in ≥5% of patients, any treatment group, n (%) | | | | | | |
| Diarrhea | 112 (15.5) | 88 (12.2) | 20 (3.8) | 10 (2.0) | 11 (2.5) | 13 (3.1) |
| Nausea | 108 (15.0) | 69 (9.6) | 11 (2.1) | 8 (1.6) | 10 (2.3) | 4 (0.9) |
| Upper respiratory tract infection | 60 (8.3) | 71 (9.9) | 27 (5.2) | 40 (7.9) | 23 (5.2) | 29 (6.9) |
| Headache | 75 (10.4) | 61 (8.5) | 17 (3.3) | 14 (2.8) | 12 (2.7) | 11 (2.6) |
| Nasopharyngitis | 41 (5.7) | 48 (6.7) | 31 (6.0) | 29 (5.7) | 19 (4.3) | 30 (7.1) |
| Select marked abnormalities in clinical laboratory parameters, n/m (%) | | | | | | |
| ALT >3× ULN | 9/713 (1.3) | 8/713 (1.1) | 2/518 (0.4) | 1/502 (0.2) | 2/442 (0.5) | 2/419 (0.5) |
| Creatinine >1.7× ULN | 1/713 (0.1) | 1/713 (0.1) | 0/518 (0.0) | 0/502 (0.0) | 0/442 (0.0) | 1/419 (0.2) |
| Leukocytes <1.5, 10⁹/L | 0/713 (0.0) | 0/712 (0.0) | 0/517 (0.0) | 0/503 (0.0) | 0/442 (0.0) | 0/419 (0.0) |
| Neutrophils <1, 10⁹/L | 2/713 (0.3) | 4/712 (0.6) | 3/517 (0.6) | 2/502 (0.4) | 2/442 (0.5) | 1/419 (0.2) |
| Platelets <75, 10⁹/L | 0/713 (0.0) | 0/712 (0.0) | 0/517 (0.0) | 1/503 (0.2) | 1/441 (0.2) | 1/419 (0.2) |
| Hemoglobin, male <10.5 g/dL, female <8.5 g/dL | 5/713 (0.7) | 5/712 (0.7) | 4/517 (0.8) | 0/503 (0.0) | 5/442 (1.1) | 2/419 (0.5) |

*Includes all patients who received APR during the time interval relative to the start of APR. [a]Autoorgan failure not suspected to be treatment-related. [b]Motor vehicle accident on Study Day 489.

**Conclusions:** APR demonstrated a favorable safety profile and was well tolerated for up to 156 weeks. These data continue to support the lack of accumulation of immunosuppression and a need for specific laboratory monitoring with APR. The incidence of AEs remained stable or decreased with long-term exposure to APR.
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## FRI0471 CERTOLIZUMAB PEGOL FOR THE TREATMENT OF PSORIATIC ARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-PSA TRIAL

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**Background:** The RAPID-PsA trial (NCT01087788) has investigated the efficacy and safety of certolizumab pegol (CZP) for the treatment of patients (pts) with psoriatic arthritis (PsA). Previous reports have demonstrated CZP to be safe and efficacious over 96 weeks (wks) of treatment.[1]
**Objectives:** To report 4-year efficacy and safety data from the RAPID-PsA trial of CZP in PsA pts.
**Methods:** RAPID-PsA was double-blind and placebo-controlled to Wk24, dose-blind to Wk48 and open-label (OL) to Wk216. Pts had active PsA and had failed ≥1 DMARD. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks 0, 2, 4) continued on their assigned dose in the OL period. Outcomes assessed included: ACR20/50/70 and PASI75/90 responses, minimal disease activity (MDA), HAQ-DI, pain and patient's global assessment of disease activity (PGADA). Efficacy data are presented for all pts originally randomized to CZP. Data are shown as observed case and with imputation: NRI for categorical and LOCF for continuous measures. The safety set consisted of all pts treated with ≥1 dose of CZP to Wk216.

**Table: A)** Clinical outcomes to Week 216 of the RAPID-PsA trial

| | CZP 200 mg Q2W (n=138) | | | CZP 400 mg Q4W (n=135) | | | CZP dose-combined (n=273) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Wk24 (NRI) | Wk216 (NRI) | Wk216 (OC) | Wk24 (NRI) | Wk216 (NRI) | Wk216 (OC) | Wk24 (NRI) | Wk216 (NRI) | Wk216 (OC) |
| Outcome, % | | | | | | | | | |
| ACR20 | 63.8 | 54.3 | 76.5 [a] | 56.3 | 54.8 | 85.1 [b] | 60.1 | 54.6 | 80.5 [c] |
| ACR50 | 44.9 | 42.0 | 59.2 [a] | 41.5 | 44.4 | 69.0 [b] | 43.2 | 43.2 | 63.8 [c] |
| ACR70 | 28.3 | 34.8 | 49.0 [a] | 24.4 | 34.8 | 54.0 [b] | 26.4 | 34.8 | 51.4 [c] |
| MDA | 34.8 | 37.7 | 53.1 [a] | 34.8 | 40.7 | 63.2 [b] | 34.8 | 39.2 | 57.8 [c] |
| PASI75 [d] | 62.2 | 60.0 | 81.8 [e] | 60.5 | 42.1 | 76.2 [f] | 61.4 | 51.8 | 79.6 [g] |
| PASI90 [d] | 46.7 | 44.4 | 60.6 [e] | 35.5 | 35.5 | 64.3 [f] | 41.6 | 40.4 | 62.0 [g] |
| PASI100 [d] | 30.0 | 32.2 | 43.9 [e] | 13.2 | 23.7 | 42.9 [f] | 22.3 | 28.3 | 43.5 [g] |

**B)** Patient-reported outcomes to Week 216 of the RAPID-PsA trial

| | CZP 200 mg Q2W (n=138) | | | CZP 400 mg Q4W (n=135) | | | CZP dose-combined (n=273) | | |
|---|---|---|---|---|---|---|---|---|---|
| | BL | Wk24 (LOCF) | Wk216 (LOCF) | BL | Wk24 (LOCF) | Wk216 (LOCF) | BL | Wk24 (LOCF) | Wk216 (LOCF) |
| Outcome, mean | | | | | | | | | |
| HAQ-DI | 1.3 | 0.8 | 0.8 | 1.3 | 0.9 | 0.8 | 1.3 | 0.8 | 0.8 |
| Pain | 59.7 | 31.1 | 29.1 | 61.1 | 32.7 | 27.3 | 60.4 | 31.9 | 28.3 |
| PGADA | 60.2 | 31.1 | 28.3 | 60.2 | 32.5 | 27.0 | 60.2 | 31.7 | 27.7 |

All patients received CZP loading dose of 400mg at Weeks 0, 2 and 4. [a] n=98; [b] n=87; [c] n=185; [d] PASI response rates reported in patients with ≥3% body surface area skin involvement at baseline (CZP 200mg Q2W, n=90; CZP 400 mg Q4W, n=76); [e] n=66; [f] n=42; [g] n=108. BL: baseline; LOCF: last observation carried forward; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; PGADA: patient's global assessment of disease activity.

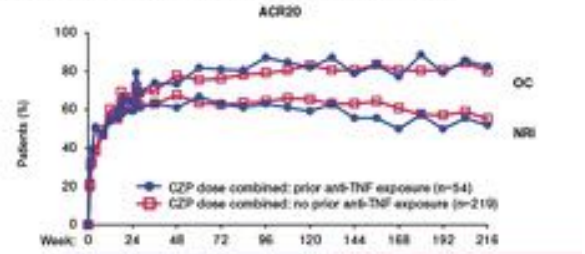
**Results:** 409 pts were randomized, of whom 273 received CZP from Wk0. Of CZP-randomized pts, 91% completed to Wk24, 87% to Wk48 and 67% to Wk216. In the OL period, 17 pts (6.2%) withdrew due to an adverse event (AE) and 5 pts (1.8%) due to loss of efficacy.
ACR responses were sustained in both dose regimens from Wk24 to Wk216 (Table A). In those 166 CZP pts (60.8%) with ≥3% body surface area skin involvement at baseline (BL), PASI75/90/100 responses were maintained to Wk216 (Table A). Improvements in patient-reported outcomes were also maintained through Wk216 (Table B). Pts had further improvements from Wk24 to Wk216 in high-threshold outcomes (ACR70, MDA and PASI100) when either observed case or conservative imputation methods (NRI) were used (Table A).
Pts in the safety set (N=393) had total CZP exposure of 1321 patient-years (PY) with an AE rate (ER) per 100 PY of 258.0. No new safety signals were identified from Wk96 to Wk204, and no additional deaths were reported.
**Conclusions:** CZP efficacy was maintained in PsA pts over 4 years of treatment, with no new safety signals identified. Additional improvements in high-threshold outcomes were seen from Wk24 to Wk216.
**References:**
[1] Mease P. RMD Open 2015;1:e000119
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## FRI0472 IMPROVEMENTS IN JOINT OUTCOMES OF PSORIATIC ARTHRITIS OVER 4 YEARS OF TREATMENT WITH CERTOLIZUMAB PEGOL IN PATIENTS WITH AND WITHOUT PRIOR ANTI-TNF EXPOSURE

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**Background:** Previous reports of the RAPID-PsA trial (NCT01087788) have demonstrated the efficacy of certolizumab pegol (CZP) in improving joint outcomes of psoriatic arthritis (PsA) over 96 weeks (wks) of treatment in patients (pts) with and without prior anti-TNF exposure.[1,2]
**Objectives:** To report the efficacy of CZP over 4 years for the treatment of joint outcomes in PsA pts with and without prior anti-TNF exposure.
**Methods:** The RAPID-PsA trial was double-blind and placebo-controlled to Wk24, dose-blind to Wk48 and open-label (OL) to Wk216. Pts had active PsA, had failed ≥1 DMARD, and ≤40% pts could have received 1 prior anti-TNF. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks 0, 2, 4) continued on their assigned dose in the OL period. Joint disease activity was assessed in all pts using tender joint count (TJC), swollen joint count (SJC) and DAS28(CRP), as well as the composite disease activity measures ACR20/50/70. Data are shown as observed case (OC) and with imputation: NRI for categorical and LOCF for continuous measures. Data are presented for all pts originally randomized to CZP with and without prior anti-TNF exposure.
**Results:** 409 pts were randomized and 273 received CZP from Wk0 (54/273 pts had prior anti-TNF exposure). Of pts randomized to CZP at baseline, 91% completed to Wk24, 87% to Wk48 and 67% to Wk216.
CZP treatment was associated with improvements in all measures of joint disease activity to Wk24. Improvements in outcomes including TJC, SJC and DAS28(CRP), as well as the composite measures ACR20/50/70, were sustained through to Wk216 of the trial and were similar in pts with and without prior anti-TNF exposure (Figure). Greater improvements were observed in those pts completing to Wk216, as expected (Figure, OC data). Pts experienced further improvements from Wk24 to Wk216 in the high-threshold outcome ACR70 when either OC or NRI was used (Table).
At Wk216, ACR20 responses were similar regardless of dose regimen in pts with and without prior anti-TNF exposure (pts with anti-TNF exposure [OC]: 200mg Q2W: 81.8%; 400mg Q4W: 83.3%; pts without prior anti-TNF exposure [OC]: 200mg Q2W: 75.0%; 400mg Q4W: 85.3%).

**Figure:** Joint outcomes in patients with or without prior anti-TNF exposure




| | Pts with prior anti-TNF exposure CZP dose combined (n=54) | | | Pts without prior anti-TNF exposure CZP dose combined (n=219) | | |
|---|---|---|---|---|---|---|
| | Wk24 (NRI) | Wk216 (NRI) | Wk216 (OC; n=34) | Wk24 (NRI) | Wk216 (NRI) | Wk216 (OC; n=151) |
| **Outcome, %** | | | | | | |
| ACR20 | 59.3 | 51.9 | 82.4 | 60.3 | 55.3 | 80.1 |
| ACR50 | 44.4 | 40.7 | 64.7 | 41.6 | 43.8 | 63.6 |
| ACR70 | 25.9 | 29.6 | 47.1 | 26.0 | 36.1 | 52.3 |

| | BL | Wk24 (LOCF) | Wk216 (LOCF) | Wk216 (OC) | BL | Wk24 (LOCF) | Wk216 (LOCF) | Wk216 (OC) |
|---|---|---|---|---|---|---|---|---|
| **Outcome, mean** | | | | | | | | |
| TJC | 21.4 | 11.1 | 9.5 | 4.9 (n=34) | 20.3 | 8.4 | 6.4 | 3.7 (n=151) |
| SJC | 12.6 | 3.4 | 2.4 | 1.4 (n=34) | 10.3 | 3.0 | 1.9 | 1.1 (n=151) |
| DAS28(CRP) | 5.2 | 3.1 | 2.9 | 2.4 (n=34) | 4.9 | 3.0 | 2.6 | 2.3 (n=145) |

BL: baseline; LOCF: last observation carried forward; NRI: non-responder imputation; OC: observed case.

**Conclusions:** Improvements in measures of joint disease activity were observed in PsA pts to Wk24 and efficacy was sustained over 4 years. Efficacy remained similar in pts with and without prior anti-TNF exposure in all joint outcomes assessed.
**References:**
[1] Mease P. RMD Open 2015;1:e000119;
[2] Gladman D. Arthritis Rheum 2015;67(S10)
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## FRI0473 WHAT PROPORTION OF PATIENTS WITH PSA FAIL TO ACHIEVE MDA BASED ON PATIENT REPORTED OUTCOMES? AN ANALYSIS FROM A PROSPECTIVE, OBSERVATIONAL REGISTRY

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**Background:** Recent treat-to-target guidelines in PsA recommend that minimal disease activity (MDA) is achieved as early as possible. Patient reported outcomes (PROs) have been criticized for not accurately assessing PsA disease activity as they may reflect aspects not directly related to PsA such as fibromyalgia, depression or other comorbidities.
**Objectives:** The aim of this analysis was to assess the proportion of patients failing to achieve MDA based on PROs in a real-world, routine clinical care setting in Canada.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis, ankylosing spondylitis, or PsA with infliximab (IFX) or golimumab (GLM). Eligible participants for this analysis included those with PsA treated with IFX who were enrolled since 2005 or with GLM enrolled since 2010 and with available MDA information at baseline, 6 months, and/or 12 months. MDA was defined as the fulfillment of $\geq$5 of the following criteria: TJC28$\leq$1, SJC28$\leq$1, PASI$\leq$1, pain (VAS)$\leq$15 mm, PtGA (VAS)$\leq$20 mm, HAQ$\leq$0.5, tender entheseal points $\leq$1. Near MDA was defined as fulfillment of 4 criteria.
**Results:** A total of 196 PsA patients (51.4% male) were included with a mean (SD) age of 49.8 (11.1) years and disease duration since diagnosis of 5.4 (6.3) years. The majority (62.2%) received concomitant DMARD therapy. The proportion of patients with MDA at baseline, 6 months and 12 months was 11.7%, 43.5%, and 44.8%, respectively. Overall, achievement of each individual MDA criterion was: TJC28: 43.0% of cases; SJC28: 51.3%; PASI 68.7%; pain: 27.7%; PtGA: 34.9%; HAQ: 36.8%; entheseal points: 79.4%. Among the 309 instances of non-MDA, 51 (16.5%) were near MDA cases. The most common reason for non-MDA in near MDA cases was patient-reported pain (82.4%) followed by PtGA (68.6%), and HAQ-DI (60.8%). Assuming that these criteria were met (i.e., not included in the MDA formula), the total number of MDA instances would increase from 29.6% to 36.7% (HAQ), 37.6% (PtGA), and to 39.2% (pain).
**Conclusions:** The results of the current analysis have shown that, similar to prior analyses in RA, the most common limiting factors in achieving MDA in PsA are PROs, including PtGA, pain, and HAQ-DI, accounting for as many as 82.4% of near MDA cases. Further analyses are required to identify the determinants of the differences in PROs and clinical outcomes.
**Disclosure of Interest:** P. Rahman: None declared, A. Avina-Zubieta: None declared, R. Arendse: None declared, W. Bensen: None declared, P. Baer: None declared, J. Kelsall: None declared, M. Starr: None declared, J. Stewart: None declared, D. Sholter: None declared, M. Zummer: None declared, L. Picard: None declared, E. Rampakakis: None declared, E. Psaradellis: None declared, K. Masolova Employee of: Janssen, A. Lehman Employee of: Janssen, F. Nantel Employee of: Janssen, C. Tkaczyk Employee of: Janssen, B. Osborne Employee of: Janssen
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## FRI0474 SERUM LEVEL OF IL-23 AND IL-23R POLYMORPHISMS IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Interleukin (IL) - 23 is one of the of cytokines involved in systemic inflammation. Interaction between this cytokine and its receptor (IL-23R) that plays an important role in pathogenesis of psoriatic arthritis (PsA).
**Objectives:** The present study aimed to assess the associations between polymorphisms within gene coding IL-23R, IL-23 serum levels and disease activity in patients with PsA.
**Methods:** Fifty-two PsA patients (diagnosed by the criteria recommended by CASPAR group) were genotyped for the IL-23R (rs11209026 and rs7530511) polymorphisms. The nuclear factor kappa (NF-kB1 (rs28362491; ins/del)) polymorphism (associated with the promoter activity of this gene and cytokine gene expressions, including IL-23) was also analyzed in PsA patients group. IL-23 serum levels were assessed by ELISA in patients with PsA, and for comparison, 10 healthy individuals. These laboratory data were further related with clinical characteristics of the patients. Disease Activity Score was measured (swollen and tender joints, ESR, CRP) in addition to BASDAI, BASFI, VAS, and PASI scores.
**Results:** Significantly ($p<0.05$) elevated levels of IL-23 cytokine were observed in PsA patients (126.5 pg/ml) when compared to control group (24.9 pg/ml). Moreover, IL-23 serum levels were associated with the IL-23R rs7530511 polymorphism. Patients carrying the IL-23R T allele characterized with higher concentrations of IL-23 in serum (299.1 vs 86.8, $p<0.05$). Interestingly, patients with the IL-23R T allele were also more frequently carrying the ins/ins homozygous NF-kB1 genotype (associated with a better promoter activity and higher expression of cytokines) (7/17 vs 4/34, distribution of the T allele among ins/ins vs del allele positive patients, p=0.03). No association was found between for IL-23 levels or IL-23R polymorphisms and disease activity.
**Conclusions:** Patients with PsA characterize with higher serum levels of IL-23 than healthy individuals. IL-23 concentrations in serum of PsA patients are associated with the polymorphism (rs7530511) of IL-23 receptor encoding gene.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5538

## FRI0475 FREQUENCY AND PREDICTORS OF CARDIOVASCULAR EVENTS IN A BICENTRIC COHORT OF PSORIATIC ARTHRITIS FROM SPAIN

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**Background:** Cardiovascular (CV) comorbidity is frequent in psoriatic arthritis (PsA). This population shows a higher frequency of traditional CV risk factors (CVRF) when compared to normal population. However, additional traits related to the inflammatory nature of the disease may also suppose an additional risk beyond that attributable to classic CVRF.
**Objectives:** To analyze the prevalence and predictors of CV events in a wide cohort of PsA patients recruited at two rheumatology departments from Spain.
**Methods:** We included (cross-sectional) 340 PsA patients (CASPAR criteria) from two different rheumatology departments in Spain. There were 190 males and 150 females (mean age: 55 ± 13 yrs). Both subpopulations were similar in terms of age, sex distribution and disease duration. Prevalence and predictors of CV events (coronary heart disease, ictus and/or ischemic peripheral vascular disease) were analyzed. Initially, a univariate analysis was performed to examine unadjusted associations of potential risk factors. Significant variables in the univariate analysis were then introduced in a multivariate analysis with a backward stepwise approach. The statistical analysis software package used was SPSS v.19.0. Patients gave their informed consent and an institutional ethics committee approved the final version of the study.
**Results:** Distribution of classic CVRF was as follow: Diabetes 14%, hypertension 36%, dyslipidemia 31%, tobacco 27%, obesity 35% and 24% had overweight. Thirty two out of 340 subjects (9.4%) developed 41 CV events: 15 coronary events, 15 ictus and 11 events of ischemic peripheral vascular disease. Compared to men, women had more diabetes (29.5% vs. 18%, p=0.049) and obesity (44% vs. 29%, p=0–010), even though the frequency of CV events did not differ between sexes. In multivariate analysis, an age of psoriasis onset $\geq$40 yr (OR 4.1, 95%CI: 1.04–16.2, $p<0.001$) and dyslipidemia (OR 5.8, 95%CI: 1.5–22.8, $p<0.001$) were found independently related to the risk of coronary events. Hypertension was an independent predictor of ictus (OR 8.0, 95%CI: 1.7–38.1, $p<0.001$). When analyzing CV events as a whole, an age of psoriasis onset $\geq$40 yr (OR 3.4, p=0.03), a polyarticular pattern during evolution (OR 2.9, p=0.04), hypertension (OR 5.3, p=0.007) and dyslipidemia (OR 2.6, p=0.07), were found independently associated to the risk of CV events in multivariate analysis.
**Conclusions:** In our context, CV comorbidity of PsA may be explained by a conjunction of classic CVRF, late onset of psoriasis, and the inflammatory burden of joint disease. A better management of these factors should be the basis for improvement of CV health of these patients
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4084

## FRI0476 COMORBIDITIES IN PSORIATIC ARTHRITIS: PATIENT EDUCATION COUNTS

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**Background:** Comorbidities are frequent in Psoriatic arthritis (PsA) and can have an impact on morbidity and mortality.
**Objectives:** We aimed to investigate the frequency of different comorbidities in

PsA, how comorbidities have an impact on PsA features and which factors were associated with the occurrence of comorbidities in a large number of patients, using PsART (Psoriatic Arthritis Registry of Turkey)registry.
**Methods:** PsART is a national, web-based registry where consecutive patients with PsA are recruited and demographic, clinical and therapeutic information are collected as well as comorbidities. The following comorbidities are questioned: Hypertension (HT), hyperlipidemia, depression, diabetes mellitus (DM), hyperuricemia, coronary arterial disease, liver disease, cerebrovascular accident, cancer, and depression. BMI more than 30 is recorded as obesity. Patients with or without comorbidities were compared for their demographic features and outcome tools.
**Results:** One thousand and sixty-nine patients whom comorbidity data were available were analyzed. Within these 693 (64.8%) were women. Mean (SD) age was 46.9 (12.8), with a median (range) PsA duration 45 (0–545) months. The number of patients with 1, 2 and 3 comorbidities were 642 (60.1%), 345 (32.3%), and was 191 (17.9%), respectively. Frequency of comorbidities was obesity in 327 (30.6%), HT in 256 (23.9%), hyperlipidemia in 199 (18.6%), depression in 188 (17.6%), DM in 161 (15.1%), hyperuricemia in 74 (6.9%), coronary artery disease in 39 (3.6%), liver disease 38 (3.6%), cerebrovascular event in 19 (1.8%), and cancer history 16 (1.5%). Patients with at least one comorbidity were older (51.1 (11.8) vs 40.9 (11.7), $p<0.001$) and had a higher disease activity (according to tender joint count (3.9 (5.2) vs 2.9 (4.2), p=0.001), pain (4.6 (2.6) vs 4.0 (2.6), p=0.006), patient global assessment (4.5 (2.4) vs 4.0 (2.5), p=0.014), fatigue (4.9 (2.5) vs 4.0 (2.6), $p<0.001$)). Education was found to contribute on comorbidities as patients with at least one comorbidity had less education in terms of school years (7.6 (4.4) vs 9.7 (4.4) years, $p<0.001$). This was also found separately for some of the comorbidities: Patients with DM (mean (SD) years of education 6.7 (4.2) vs 8.8 (4.5), $p<0.001$), HT (6.7 (4.3) vs 8.9 (4.5), $p<0.001$), cerebrovascular event (5.5 (2.9) vs 8.4 (4.5), p=0.012) and depression (7.5 (4.1) vs 8.6 (4.6), p=0.004) had less education compared to patients who don't have those comorbidities.
**Conclusions:** Our registry supported that comorbidities are frequent in PsA increasing the complexity of the disease and have an impact on the disease severity. Patients with comorbidities are less educated showing that education and awareness are important to improve patient outcomes in PsA in long term.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3716

## FRI0477 A MODIFIED VERSION OF THE PSORIATIC ARTHRITIS DISEASE ACTIVITY SCORE (MPASDAS) USING SF-12 AS A MEASURE OF QUALITY OF LIFE MAY BE MORE FEASIBLE IN CLINICAL PRACTICE

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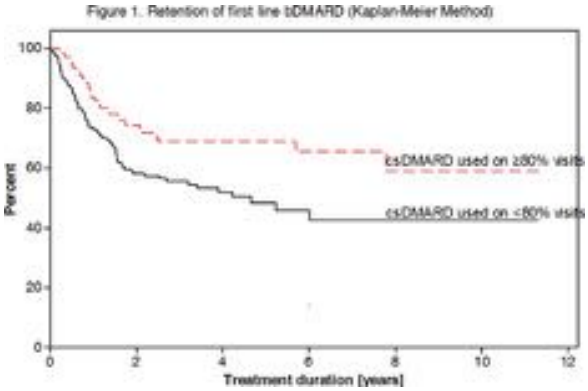
**Background:** The Psoriatic Arthritis Disease Activity Score (PASDAS) is a newly developed composite disease activity measure that summarizes psoriatic arthritis (PsA) disease activity with a score ranging from 0–10. PASDAS captures articular and extra-articular manifestations of the disease and the impact of the disease on the patient via the following variables: swollen and tender joints, dactylitis, Leeds enthesitis index, C-reactive protein, Health Assessment Questionnaire, physician and patient global disease activity, and the physical component summary score (PCS) of the medical outcomes survey Short Form 36 (SF-36). A limitation of PASDAS is that the score depends on the patient completing the SF-36, which requires a significant amount of time to complete. A shorter 12-question subset of SF-36, the SF-12, with the same range of values, agrees well with the SF-36 in many patient populations.
**Objectives:** The objective was to measure the agreement between PASDAS calculated using the standard scoring formula and mPASDAS calculated by replacing the SF-36-PCS with SF-12-PCS.
**Methods:** 100 PsA patients attending the University of Toronto PsA clinic for follow-up visits were consecutively recruited in June and July 2015. All variables required to calculate PASDAS were collected and PASDAS was calculated for each patient. The 12 item responses for SF-12 were extracted from the SF-36 questionnaires. A mPASDAS score was subsequently calculated based on the PASDAS scoring formula where SF-36-PCS is replaced by SF-12-PCS. A Bland-Altman plot of the differences in scores calculated via PASDAS and mPASDAS measured agreement between the two sets of scores. The rate of missclassification when categorizing the patient's disease activity state as high, moderate or low using the mPASDAS instead of PASDAS was also examined.
**Results:** The analysis [N=100, 53% male, mean (SD) age 57.3 (11.9) years, mean (SD) disease duration 16.9 (11.7) years] revealed that the mean (SD) PASDAS was 3.29 (1.39) and the mean (SD) mPASDAS was 3.24 (1.27). The Bland-Altman plot showed a mean difference (95%CI) between mPASDAS and PASDAS of -0.05 (-0.07, -0.03). The lower limit and upper limits of the difference was (-0.24 [95%CI -0.21, -0.28]) and 0.14 [0.10, 0.17]), respectively. Five (5%) patients were misclassified (4 to the lower disease activity category) when mPASDAS was used instead of PASDAS.
**Conclusions:** mPASDAS and PASDAS shows strong agreement without clinically significant systematic bias in mPASDAS scores. In clinical settings, the mPASDAS may replace PASDAS in disease activity assessment given the strong agreement and low misscalssification rate along with significantly reduced questionnaire burden.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3677

## FRI0478 DOES CO-MEDICATION WITH CSDMARDS HAVE AN IMPACT ON THE RETENTION OF BDMARDS IN PSORIATIC SPONDYLOARTHRITIS? DATA FROM BIORX.SI

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**Background:** In clinical practice we often extrapolate experience and evidence from patients with RA to patients with PsA. The body of evidence supporting the use of csDMARD co-medication in PsA patients treated with bDMARDs is weak.
**Objectives:** Our aim was to determine whether co-medication with csDMARDs has an impact on the retention of bDMARDs in PsA.
**Methods:** In December 2015 we extracted data of patients with PsA treated with the first bDMARD with at least one follow-up visit from the mandatory national registry BioRx.si. Appropriate descriptive statistics methods were used to describe the cohort. Where applicable appropriate post hoc tests were used to compare the baseline characteristics. We used the unadjusted Kaplan-Meier method with log rank test as the post hoc test to assess the retention of the bDMARDs depending on co-medication with csDMARDs (i.e. methotrexate or leflunomide or sulfasalazine).
**Results:** At the time of extraction 276 (44% female) patients with a median (IQR) age of 49.5 (42.0–56.6) years treated for 733 person years satisfied the inclusion criteria. Median follow-up time was 1.5 years (0.6–3.2) years. 50%/20%/18%/12% were treated with adalimumab/etanercept/golimumab/infliximab, respectively. Methotrexate/leflunomide/sulfasalazine were predominantly used as co-medication in 70%/9%/5% of patients while 16% never received csDMARD co-medication. There was no significant difference in the retention of the initial bDMARD depending on csDMARD use at the initiation of the bDMARD or when the csDMARD was used on <50% of follow-up visits. However, the bDMARD retention was significantly longer when csDMARD was used on more than 80% of follow-up visits (p=0.005; Figure 1).

Figure 1. Retention of first line bDMARD (Kaplan-Meier Method)




**Conclusions:** Regular co-medication with csDMARDs seems to improve the retention of the first line bDMARDs in PsA in daily clinical practice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3600

# Other orphan diseases

## FRI0479 EFFICACY OF COLCHICINE AND IL-1 INHIBITORS IN AMYLOIDOSIS ASSOCIATED WITH FAMILIAL MEDITERRANEAN FEVER: A RETROSPECTIVE ANALYSIS

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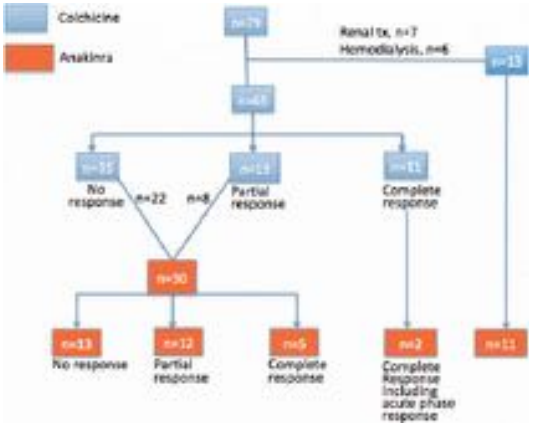
**Background:** Familial Mediterranean fever (FMF), the most common form of hereditary autoinflammatory diseases, is associated with increased risk for secondary (AA) amyloidosis
**Objectives:** We herein aimed to investigate the features of FMF patients with amyloidosis with respect to their responses to current therapies
**Methods:** We enrolled FMF patients with amyloidosis who were regularly followed-up for at least 6 months between 1978 and 2015 into the study. Starting times for colchicine, anakinra or canakinumab and treatment responses were noted. Proteinuria (spot urine protein/creatinine ratio) and C-reactive protein (CRP) levels were measured in every three months of follow-up. Partial response

was defined as ≥50% decrease in baseline proteinuria accompanied by a normal serum creatinine level, whereas complete response was defined as <0.3 gr/d baseline proteinuria and stable serum creatinine. Correlations between treatment responders and continuously elevated or normalized CRP levels were tested by using a chi-square test

**Results:** We identified 79 FMF patients with documented secondary amyloidosis, and all were on colchicine treatment. Their demographic features are shown in Table 1. Mean time to diagnosis after the first symptom was 10 years. Patients were evaluated for partial and complete response after mean follow-up period of 66±85 months. Response to colchicine was observed in 30/65 patients [partial response in 19 (29%), complete response in 11 (17%)]; and 54% was non-responder to colchicine. Anakinra was added to treatment in 22 patients with inadequate response to colchicine, which resulted in partial response in 12, and complete response in 2. Eight patients with partial response to colchicine also received anakinra for better control of attacks and/or elevated acute phase response, and a complete response was achieved in 3 patients. In 3 patients, anakinra was switched to canakinumab because of local injection site reaction (1 patient) and persistence of proteinuria (2 patients). Among those, two patients had partial response, and another underwent hemodialysis due to progressive kidney failure. No significant association was observed between normalized CRP levels and response to treatment with respect to proteinuria and creatinine levels (colchicine; p=0.67, anakinra/canakinumab;p=0.82). No serious infection requiring hospitalization was detected in association with IL-1 blockade.

Table 1. Demographic features of FMF patients with amyloidosis

| | |
|---|---|
| Male/Female | 40/39 |
| Age of onset (mean ± SD, range) | 16±12 (2–68) |
| Age of diagnosis (mean ± SD, range) | 27±13 (7–70) |
| Family history of FMF | 47% |
| Disease follow-up duration (mo) | 66±85 (6–480) |
| Time to diagnosis (mo) | 121±136 (2–576) |
| Family history of amyloidosis (%) | 18% |
| Arthritis at presentation (%) | 60% |
| MEFV variations (n=46) | M694V, 68%<br>V726A, 10%<br>M680I, 15%<br>Others, 7% |
| IL-1 inhibitors n (%) | 43 (54%) |
| Patients on hemodialysis | 7 (9%) |
| Renal Transplantation n (%) | 17 (21%) |
| High CRP levels in attack-free periods n (%) | 31 (39%) |




**Conclusions:** Amyloidosis still remains as an important complication of FMF, and a satisfactory response to colchicine could be observed in an important proportion of patients. Treatment with IL-1 inhibitors seems to be an effective and safe option for those patients with an inadequate response to colchicine

**Disclosure of Interest:** None declared

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## FRI0480 THIOL/DISULPHIDE HOMEOSTASIS IN FAMILIAL MEDITERRANEAN FEVER

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**Background:** Familial Mediterranean fever (FMF) is an autoinflammatory disease that include recurrent episodes of peritonitis, pleuritis, and arthritis, with accompanying fever. FMF is caused by mutations in MEFV and typically diagnosed during childhood. Thiol/disulphide homeostasis, marker of oxidative stress, is associated with an increased in inflammatory cytokines in many inflammatory diseases.

**Objectives:** We aimed to investigate the dynamic thiol/disulphide homeostasis in patients with FMF during attact free period.

**Methods:** Fifty five patients with FMF during attact free period, 55 patients with Ankylosing Spondylitis (AS) during inactive period and 55 age-and sex matched controls were included in the study. Native thiol, total thiol and disulphide levels were studied by the Erel and Neşelioğlu method.

**Results:** Total thiol and disulphide levels were significantly lower in FMF group compared to healthy controls. Native thiol levels were detected to be significantly increased in FMF groups compare to AS group. However, total thiol levels were similar in FMF and AS group. Ratios obtained using plasma native thiol, total thiol, and disulphide levels differed significantly between the FMF, AS and the control group.

Table 1. Plasma thiol–disulphide levels of FMF, AS and control group

| Parameter | FMF (n=55) | AS (n=55) | Control (n=55) | P* |
|---|---|---|---|---|
| Native thiol, μmol/L | 328.99±56,92 | 308.07±40.49 | 336.52±40.44 | 0.005 |
| Total thiol, μmol/L | 351.51±56.03 | 337.75±44.69 | 371.86±42.22 | 0.001 |
| Disulphide, μmol/L | 11.25±6.4 | 14.83±6.99 | 17.67±6.43 | 0.001 |
| Disulphide/native thiol, % | 3.61±2.56 | 4.85±2.40 | 5.35±2.15 | 0.001 |
| Disulphide/total thiol, % | 3.27±2.09 | 4.34±1.91 | 4.77±1.72 | 0.001 |
| Native thiol/Total thiol, % | 93.45±4.19 | 91. 31±3.82 | 90.45±3.45 | 0.001 |

Values are presented as mean ± standard deviation. *P values are comparing the native thiol, total thiol, disulphide, disulphide/native thiol, disulphide/total thiol, native thiol/total thiol in each group.

**Conclusions:** Thiol levels, an important anti-oxidant, was found to be significantly lower. Subclinical inflamation may be continued in FMF patients during attact free period. Randomised controlled trials with large patient populations might help clarify this issue.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.6041

## FRI0481 NO CHANGE IN SELF-REPORTED PAIN FROM PRE-PREGNANCY TO SIX MONTHS POSTPARTUM IN WOMEN WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** There are no previous studies on health related quality of life (HRQL) related to pregnancy in women with juvenile idiopathic arthritis (JIA). One study on a small population with rheumatoid arthritis (RA) using the short form 36 (SF-36) to measure HRQL, has shown that RA women reported a worsening in the aspect of bodily pain 12 and 24 weeks postpartum compared to pre-pregnancy (1).

**Objectives:** To study the impact of pregnancy on the aspect of bodily pain aspect in self- reported HRQL using SF-36 from pre-pregnancy to six months postpartum on women with JIA.

**Methods:** 25 women with JIA were followed from pre-pregnancy to six months postpartum. HRQL was measured using the SF-36 form resulting in eight multi-item subscales. In this study the aspect of bodily pain in SF-36 was explored. Registrations were recorded pre-pregnancy (within one year before conception), 1st trimester (1–12 weeks), 2nd trimester (13–27 weeks), 3rd trimester (28–40 weeks), six weeks and six months postpartum. The Wilcoxon test for related samples was performed.

**Results:** Mean age of the JIA women was 29 years (range 20–36) and mean disease duration 21 years (range 4–32). The mean number of DMARDs used before pregnancy was 0.64 (range 0–2). Correspondingly, the mean number of DMARDs were 0.68 (range 0–1) six months postpartum. The pre-pregnancy scores were tested to each of the other time points.

There was a statistically significantly improvement in self-reported pain from pre-pregnancy to six weeks postpartum (p=0.019), but no difference was observed at six months postpartum.

Table 1. SF-36 aspect of bodily pain from pre-pregnancy up to six months postpartum presented with mean scores and 95% confidence interval (CI)

| | Pre-pregnancy | 1st trimester | 2nd trimester | 3rd trimester | 6 weeks postpartum | 6 months postpartum |
|---|---|---|---|---|---|---|
| Mean BP | 55 | 63 | 60 | 57 | 66 | 61 |
| 95% CI | (42–67) | (51–74) | (51–68) | (47–68) | (55–76) | (46–73) |

**Conclusions:** There was a no statistically significant change in self-reported pain from pre-pregnancy to six months postpartum, but a significantly improvement was seen from pre-pregnancy to six weeks postpartum in this study population of JIA women.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4953

## FRI0482 ANTI-TNFα THERAPY AND SWITCHING IN SEVERE UVEITIS OF VOGT-KOYANAGI-HARADA SYNDROME. REPORT OF TWO CASES AND LITERATURE REVIEW

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**Background:** Vogt-Koyanagi-Harada disease is a multisystem autoimmune disorder mediated by T-cells directed against antigens of tissues that contain melanin. Clinically it's characterized by diffuse bilateral granulomatous panuveitis. Although conventional immunosuppresive therapy such as cyclosporine (CsA), azathioprine (AZA) or methotrexate (MTX) the disease can remain active and complicated by blindness.
**Objectives:** Our aim was to review the cases of VKH syndrome uveitis in a reference unit for the past five years especially those patients with anti-TNFα therapy.
**Methods:** We reviewed all the cases of posterior uveitis or panuveitis in a reference unit between January 2010 to December 2015. VKH syndrome was diagnosed by international standard criteria [(1).] The treatment was reviewed particularly those with anti-TNFa therapy refractory to conventional immunosuppresives. In addition we reviewed the literature of anti-TNF α therapy in a VKH uveitis syndrome
**Results:** 104 were assessed. 5 cases (4 wome /1 man) met criteria VKH syndrome, mean age was 45 years. In all cases the initial treatment was high doses of corticosteroids and conventional immunosuppressive therapy CyA (4 cases), AZA (2 Cases) CsA + AZA (2 cases). In two patients with failure to AZA + CsA, infliximab (IFX) was prescribed Weeks 0, 2 and 6 and each 8 weeks. In both cases (intorelancy and ineffectiveness to infliximab), "switch" to adalimumab 40 mg/sc biweekly achieving an adequate clinical response and remission of uveitis. In addition to the two cases in our series in the literature review we found 9 articles related to anti-TNF α therapy in VKH syndrome (Table). We found 9 series with 25 patients (14 with ADA/11 IFX). In most of them remission of intraocular inflammation was observed, 13 patients with ADA (92.8%)/10 IFX (90.9%). There are no published cases of "Switching" between anti-TNF agents in VKH.
**Conclusions:** In VKH syndrome uveitis refractory to conventional immunosuppressive, anti-TNF therapy may be a treatment option. In cases of inadequate response to the first anti-TNFa "switching" to another anti-TNFa is an option, however, these preliminary data should be tested in randomized prospective studies with larger numbers of patients.
**References:**
[1] Autoimmunity reviews. 2013; 12: 1033–1038.
Rest of references in the table (2–10).
**Disclosure of Interest:** None declared
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## FRI0483 IS THERE A DIFFERENCE IN AUTOIMMUNE MYOPATHIES WITH AND WITHOUT RAYNAUD'S PHENOMENON? A CAPILLAROSCOPY STUDY

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**Background:** The autoimmune myopathies (IM) comprise a broad spectrum of acquired muscular disorders characterized by autoimmune damage of skeletal muscle and complex visceral involvement, leading to chronic dysfunction and disability.
**Objectives:** The aim of our study was to assess the association between Raynaud's phenomenon (RP) and capillaroscopic findings in patients with polymyositis (PM), dermatomyositis (DM) and anti-synthetasic syndrome (ASS), and to identify possible correlation with clinical and serological pattern.
**Methods:** Nailfold videocapillaroscopy (Optilia 200x) was performed in a cohort of 27 patients diagnosed with IM, 12 with RP and 15 age-, sex-, and disease-duration-matched without RP, and 19 healthy controls. Total number of capillaries, enlarged and giant capillaries, ramified capillaries, haemorrhages, haemosyderin deposits were each scored by a semiquantitative assessment, while the disorganization of the vascular array and avascular area were scored as present/absent.
Data about IM activity (Myositis Disease Activity Assessment Tool), severity (Myositis Damage Index) and physical function (Stanford HAQ) were also collected.
Findings were analysed using linear and logistic regression, adjusted for age and sex (SPSS-19 software).
**Results:** Patients with IM were frequently abnormal, with significant lower capillary density, higher dimensions, enlarged capillaries, haemorrhages and haemosyderin deposits as compared with healthy controls ($p<0.001$).
80% of cases reported RP as the first manifestation of their disease, with frequently nailfold capillary abnormalities as compared to non-RP patients ($p<0.01$). Enlarged capillaries ($p<0.01$), avascular areas ($p<0.05$) and capillary hemorrhages ($p<0.05$) were typically described in DM and most of ASS patients, but not in PM without RP.
In addition, a scleroderma-like capillaroscopy pattern was identified in RP-positive patients, either DM or ASS. On the other hand, either normal or nonspecific capillaroscopy findings were found in RP-negative and PM.
Pulmonary involvement ($p<0.01$) and arthritis/arthralgia ($p<0.01$) were significantly more common in ASS with RP, especially in those who developped RP years before myositis, while digestive (proximal dysphagia) manifestations ($p<0.01$) were more common in DM with RP, particularly in those with late-onset RP.
We found an association between the presence of either active or late scleroderma pattern, elevated serum CK and disease activity: capillary loss was significantly associated high muscle and global disease activity, as well ($p<0.05$).
Anti-Jo-1 and anti-PL12 antibodies were associated with reduced capillary density ($p<0.05$), whereas anti-SRPs associated with reduced capillary density, enlarged capillaries and hemorrhages ($p<0.05$).
**Conclusions:** RP is associated with particular capillaroscopic findings in different IM subsets, suggesting that prognostic relevance of RP in myositis should be evaluated.
Significant changes in the capillary pattern reported in IM, particulary reduced density, size abnormalities, haemorrhages, indicating that nailfold videocapillaroscopy may be useful as an outcome measure of microvascular disease in IM
**Disclosure of Interest:** None declared
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## FRI0484 IGG4 RELATED HYPERTROPHIC PACHYMENINGITIS: DIAGNOSTIC APPROACH AND THERAPEUTIC OUTCOMES

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**Background:** IgG4 Related Disease (IgG4-RD) is a fibro-inflammatory condition characterized by IgG4 positive lymphoplasmacytic infiltrate of affected tissues. Meningeal involvement, typically of the dura mater, represents one of the most challenging manifestations of IgG4-RD in terms of diagnostic and therapeutic approach (1). Case reports have suggested the potential utility of cerebrospinal fluid (CSF) IgG4 measurement in the differential diagnosis of IgG4 Related Hypertrophic Pachymeningitis (IgG4-RHP) (2).
**Objectives:** To assess the usefulness of CSF analysis in the diagnosis of IgG4-RHP. To describe the clinical, serological and radiological response of IgG4-RHP to different therapeutic regimens.
**Methods:** Five pts (3 females and 2 male) with biopsy-proven IgG4-RHP were evaluated through serological, radiological, and microbiological studies before and after immunosuppressive treatment. CSF analysis for intrathecal IgG4 production was performed in all pts before therapy, and in 3 pts after therapy. Serum and CSF IgG subclasses were measured through ELISA assays. Intrathecal IgG

**Abstract FRI0482** – Table 1

| | Present series. Flores Robles et al. Spain | Martínez et al. Spain (2) | Díaz-Lagares et al. Spain (3) | Zmuda et al. France (4) | Khan et al. USA (5) | Díaz-Llopis et al. Spain (6) | Nicolli et al. Italy (7) | Jeroudis et al. USA (8) | Díaz-Llopis et al. Spain (9) | Yosuf et al. USA (10) |
|---|---|---|---|---|---|---|---|---|---|---|
| Number of Cases | 2 | 3 | 4 | 2 | 2 | 1 | 2 | 1 | 8 | 2 |
| Age (mean in years) | 43.5 | 40 | Not specified (NS) | 35.5 | 14.5 | 36 | 39.5 | 15 | NS | 11 |
| Previous immunosuppressive or biologic | CYA and AZA | MTX (2 cases) CyS (3 cases) | CyS (4 cases) MTX (2 cases) AZA (1 case) | MTX | MTX (1 case) CyS (1 case) Tacrolimus (1 case) AZA (1 case) MMF (1 case) | CyS | AZA (2 cases) CyS (2 cases) | MTX | NS | MTX (2 cases) MMF (1 case) CyS (1 case) |
| Biologic used | IFX (n=2), ADA (n=2) | IFX | ADA | IFX | IFX | ADA | IFX | ADA | IFX | IFX |
| Reason for initiating anti-TNFα | Immunosuppressant failure (IF) | IF | IF | First-line | IF | CyS failure | IF | MTXfailure | IF | First-line |
| Patients with clinical response | 2 | 3 | 3 | 2 | 2 | 1 | 2 | 1 | 8 | 1 |
| Adverse effects due to anti-TNFα | 1 | None | None | (1 case) | None | None | None | None | Not specified | None |
| Duration of response | 18 months | Not specified | 9.5 months | 7 months | 17 months | 8 months | 27 months | 26 months | NS | 12 months (1 patient) |

subclasses production was assessed through the IgG Index and the IgG-LOC.
**Results:** Cranial nerve deficit was the common clinical presentation of HP. Magnetic resonance imaging showed thickening of the dura mater in all pts. Serological and CSF results are reported in Table 1. CSF analysis before treatment revealed increased IgG4 values, IgG4 Index, and IgG4-LOC in all pts with an average value of 9.64 mg/dL (normal 0.01–0.33 mg/dL), 4.14 (normal <0.7) and 8.15 (normal <0) respectively. Pt 1 was treated with intravenous (i.v.) methylprednisolone, oral prednisone, i.v. cyclophosphamide, and, rituximab; Pt 2 was treated with oral prednisone and methotrexate; Pt 3 was treated with oral prednisone; Pt 4 was treated with oral prednisone, methotrexate, azathioprine, and oral cyclophosphamide; Pt 5 was treated with i.v. methylprednisolone, cyclophosphamide, and rituximab. Patient 2, 3 and 4 responded to therapy with a marked clinical improvement and an almost complete resolution of the meningeal thickening. Pt 1 had a minimal response to therapy with only a partial reduction of the meningeal thickening. Patient 5 had a poor response to therapy with no improvement of the meningeal thickening. CSF IgG4 (0.07 mg/dL), IgG4 Index (0.23) and IgG4-LOC (0) normalized after treatment in Patient 4, and decreased without normalization in Pts 1 and 5 (CSF IgG4 0.54 and 3.99 mg/dL, IgG4 Index 0.81 and 5.1, and IgG4-LOC 0.09 and 3.46, respectively).

| | Reference Values | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | |
|---|---|---|---|---|---|---|---|
| Age | | 54 | 69 | 76 | 64 | 30 | |
| Sex | | F | M | M | F | F | |
| **Serum** | | | | | | | **Median** |
| Total IgG | 767 - 1590 mg/dL | 651,99 | 930,36 | 1490,00 | 907,35 | 1390,00 | 930,36 |
| IgG1 | 490 - 1140 mg/dL | 295,13 | 524,06 | 1020,00 | 616,75 | 6,30 | 524,06 |
| IgG2 | 150 -640 mg/dL | 167,60 | 217,35 | 587,00 | 170,00 | 193,00 | 217,35 |
| IgG3 | 150 - 640 mg/dL | 39,09 | 36,45 | 96,00 | 74,00 | 9,00 | 39,09 |
| IgG4 | 8 - 140 mg/dL | 210,17 | 152,50 | 268,00 | 46,50 | 151,00 | 152,50 |
| Albumin | 3500- 5000 mg/dL | 3350,00 | 3430,00 | 4250,00 | 2370,00 | 2950,00 | 3350,00 |
| ANCA and ANA | | Negative | Negative | Negative | Negative | Negative | |
| ACE | 17 - 137 U/L | 29,00 | 68,1 | 14,00 | 19,2 | negative | 24,10 |
| ESR | 1- 20 mm/hr | 50,00 | 24,00 | 46,00 | 60,00 | 18,00 | 46,00 |
| CRP | < 6 mg/dL | 26,90 | 6,90 | 13,00 | 32,50 | 14,70 | 26,90 |
| **Cerebrospinal fluid** | | | | | | | |
| Appearance | | Clear | Clear | Clear | Clear | Clear | |
| Albumin | 10 - 30 mg/dL | 24,90 | 17,90 | 69,00 | 85,30 | 23,30 | 17,90 |
| Proteins | 12 - 60 mg/dL | 44,00 | 82,00 | 194,00 | 76,00 | 54,00 | 76,00 |
| Glucose | 40 - 80 mg/dL | 59 | 75 | 61 | 42 | 80 | 61,00 |
| Cells | 0 - 3 / microL | 2 | 1 | 87 | 12 | 15 | 12,00 |
| Tumoral Cells | | Negative | Negative | Negative | Negative | Negative | |
| Microbiology | | Negative | Negative | Negative | Negative | Negative | |
| Total IgG | 0.8 - 3.8 mg/dL | 8,73 | 18,84 | 78,90 | 127,43 | 23,50 | 23,50 |
| Link Index (IgG) | nv < 0.7 | 1,80 | 1,83 | 3,26 | 3,90 | 2,14 | 2,14 |
| Tourtellotte Index (IgG) | nv< 3.3 | 30,51 | 68,18 | 336,23 | 563,12 | 88,05 | 88,05 |
| Reiber Index (IgG) | nv < 0 | 5,54 | 11,80 | 61,69 | 102,79 | 16,22 | 16,22 |
| Barrier Damage | nv < 0.7 | 1,27 | 1,10 | 1,62 | 1,60 | 0,79 | 1,27 |
| IgG4 | 0.01 - 0.33 mg/dL | 4,94 | 5,17 | 26,40 | 5,36 | 6,34 | 5,36 |
| Link Index (IgG4) | nv < 0.7 | 1,16 | 1,07 | 6,07 | 1,20 | 5,20 | 1,20 |
| Tourtellotte Index (IgG4) | nv < 3.3 | 20,46 | 21,58 | 121,52 | 22,98 | 27,90 | 22,98 |
| Reiber Index (IgG4) | nv < 0 | 3,91 | 4,02 | 23,30 | 4,09 | 5,44 | 4,09 |

**Conclusions:** CSF analysis of intrathecal IgG4 production represents a useful tool for orienting the differential diagnosis of idiopathic HP especially when meningeal biopsy is not feasible. The variability in the responses to immunosuppressive therapies might be due to differences in the disease phenotypes and drug penetration in meningeal layers.
**References:**
[1] Della-Torre E, Lu LX, Stone JH, et al. IgG4-Related Hypertrophic Pachymeningitis: Clinical Features, Diagnostic Criteria, and Treatment. JAMA Neurol. 2014 Apr 14.
[2] Della-Torre E, Galli L, Franciotta D, et al. Diagnostic value of IgG4 Indices in IgG4-Related Hypertrophic Pachymeningitis. J. Neuroimmunol. 2013 Oct 22.
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## FRI0485 COMPARATIVE STUDY ON ADALIMUMAB VS INFLIXIMAB FOR TREATMENT OF UVEITIC CYSTOID MACULAR EDEMA DUE TO BEHCET'S DISEASE. MULTICENTRE STUDY OF 34 PATIENTS

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**Objectives:** Cystic macular edema (CME) is the most serious complication of uveitis and the most common cause of blindness. Our objective was to compare the efficacy and safety of adalimumab (ADA) vs infliximab (IFX) as the first biological drug in uveitic cystoid macular edema (CME) due to Behçet's disease (BD) during 1 year follow-up.
**Methods:** In a multicentre study of 175 patients with BD and uveitis refractory to conventional therapy, 34 patients had CME, defined by (OCT >300μ) at baseline. IFX (3–5 mg/kg 0,2, and 6 weeks and then every 4–8 weeks) was used in 12 cases and ADA (40 mg/2 weeks) in 22 cases. The main objective was the absence of CME. Secondary objectives: improvement in visual acuity (VA) (increased AV >20% in at least one of two eyes), inactive anterior chamber inflammation, vitritis, retinitis and retinal vasculitis. A bivariate analysis was performed to compare the response to biological therapy (ADA and IFX).
**Results:** We studied 34 patients (63 affected eyes). No statistically significant baseline differences were observed between both groups (IFX vs ADA) sex (men/women 4/6 vs 11/11; p=0.35), mean age (37.3±10.1 vs 41.5±8.3; p=0.2) HLAB51 positive (70% vs 80.9%; p=0.5), duration of uveitis before anti TNF alpha treatment [median (IQR]; 36 [10–82] vs 33 months [15.5 to 83]; p=0.8), VA (0.4 ± 0.33 vs 0.46±0.29; p=0.44); retinal vasculitis (75% vs 77%; p=0.87); retinitis (46% vs 30%; p=0.2); macular thickening (140.9±410.13 vs 409.46±138.55; p=0.98); combined treatment (58.33% vs 59.1%; p=0.96). We found differences in the presence of cells in the anterior chamber (Median [IQR]; 1 [0–1.2] vs 1 [0–3]; p=0.02) and vitritis (median [IQR], 1 [0–2] vs. 3 [0.5 -3]; p=0.002). Regarding the main objective, the improvement of CME is higher in patients treated with ADA during first month of treatment maintained at a year, although the difference is not statistically significant (table). With IFX we observed an improvement during the first month of treatment in vitritis, that became inactive, in the disappearance of the anterior chamber cells, and in retinitis and vasculitis that also became inactive. In no case statistically significant differences are reached. When adjusting for duration of illness, age and sex these differences remain. After a year of treatment all patients with retinitis and vasculitis in its baseline improve (ADA and IFX).

| | Ada/IFX (%) | crude odds ratio | CI 95% | p | adjusted* odds ratio | CI 95% | p |
|---|---|---|---|---|---|---|---|
| **After one month treatment** | | | | | | | |
| No CME (OCT <300) | 38,9%/18,2% | 2,86 | 0,473-17,35 | 0,252 | 3,88 | 0,384-39,25 | 0,25 |
| Visual acuity improvement | 80%/ 72,7% | 1,5 | 0,268-8,383 | 0,644 | 3,003 | 0,342-26,40 | 0,321 |
| Inactive anterior chamber inflammation | 36,2%/71,4% | 0,514 | 0,076-3,488 | 0,496 | 0,174 | 0,00-1,98 | 0,199 |
| Inactive vitritis | 23,5%/50% | 0,308 | 0,052-1,829 | 0,151 | 0,385 | 0,053-2,807 | 0,346 |
| Inactive retinitis | 57,1%/71,4% | 0,533 | 0,058-4,912 | 0,579 | - | - | - |
| Inactive retinal vasculitis | 50%/63,6% | 0,571 | 0,123-2,658 | 0,476 | 1,036 | 0,177-6,321 | 0,932 |
| **After one year treatment** | | | | | | | |
| No CME (OCT <300) | 88,9%/66,7% | 4 | 0,53-30,14 | 0,179 | 7,03 | 0,511-96,91 | 0,145 |
| Visual acuity improvement | 66,2%/66,7% | 1,071 | 0,239-4,794 | 0,928 | 1,1 | 0,171-7,086 | 0,92 |
| Inactive anterior chamber inflammation | 93,8%/100% | 1,467 | 1,102-1,951 | 0,99 | - | - | - |
| Inactive vitritis | 87,5%/100% | 1,5 | 1,109-2,03 | 0,99 | - | - | - |
| Inactive retinitis | - | - | - | - | - | - | - |
| Inactive retinal vasculitis | - | - | - | - | - | - | - |

**Conclusions:** Our study suggests that ADA and IFX don't show statistically significant differences in treatment of CME due to refractory uveitis in BD after 1 year follow-up.
**Disclosure of Interest:** None declared
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## FRI0486 TOCILIZUMAB TREATMENT FOR UVEITIC CYSTOID MACULAR EDEMA REFRACTORY TO OTHER SYNTHETIC AND BIOLOGICAL IMMUNOSUPPRESSIVE DRUGS. MULTICENTRE STUDY OF 23 PATIENTS

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**Objectives:** Cystoid macular edema (CME) is the leading cause of blindness in uveitis, which often requires more aggressive treatment based on associating corticosteroids and synthetic and biological systemic immunosuppressive drugs. Our objective was to evaluate the efficacy and safety of Tocilizumab (TCZ) in a series of patients with refractory CME.
**Methods:** A Multicentre study of 23 patients with CME secondary to non-infectious uveitis who had inadequate response or intolerance to traditional treatment with corticosteroids and at least one conventional immunosuppressive drug including in some cases biological therapy. CME was defined by (OCT>300μ). The outcome variables were the degree of inflammation of the anterior chamber and vitreous, visual acuity and macular thickness. The results are expressed as mean ± SD for normally distributed variables, or as median [interquartile range] when are not. Comparison of continuous variables was performed using theWilcoxon test.
**Results:** 23 patients (16 females/7 males) with CME were studied. With a mean age of 33.5±17.7 years. Associated disease were: juvenile idiopathic arthritis (n=9), Behçet's disease (n=6), Birdshot retinochoroidopathy (n=4) and idiopathic

(n=4). Ocular pattern was: panuveitis (n=8), anterior uveitis (n=6), posterior uveitis (n=5) and intermediate uveitis (n=4). Most patients had bilateral involvement (n=22). Prior to TCZ patients received: intraocular corticosteroids (n=20), intravenous methylprednisolone (n=6), methotrexate (MTX) (n=18), cyclosporine A (CsA) (n=16), mycophenolate (n=4), azathioprine (n=2), cyclophosphamide (n=1), sulfasalazine (n=1), daclizumab (n=1), acetazolamide (n=1), thalidomide (n=1), leflunomide (N=1), infliximab (n=8), adalimumab (n=17), etanercept (n=2), golimumab (n=2), rituximab (N=2), abatacept (n=3), anakinra (n=1). TCZ administration schedule was 8 mg/kg/4 weeks iv. in all patients except in one that administration was every 2 weeks. Monotherapy (n=11) and in combination with conventional immunosuppressive: MTX (n=6), CsA (n=5) and leflunomide (n=1). A statistically significant reduction was observed in macular thickness from 418.84±177.14 to 240.00±54.73 m; p=0.00009 during the first year of treatment with TCZ. Most of intraocular inflammation parameters showed also a rapid improvement after initiation of TCZ. (TABLE) Visual acuity improved in a statistically significant way from 0.4±0.32 at baseline to 0.59±0.30 after a year of treatment p=0.0002. Prednisone dose was reduced from 15.69±14 to 2.92±2.46 after a year of treatment. After 13.1±8.55 months minor side effects were observed: nausea (n=1), viral conjunctivitis (n=1) and bullous impetigo (n=1). Remission was achieved in 13 patients.

**Conclusions:** TCZ seems an effective and safe treatment in patients with uveitic CME refractory to other synthetic and biological immunosuppressive drugs.

**Disclosure of Interest:** None declared

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## FRI0487 ASSOCIATION BETWEEN FEVER PATTERN AND CLINICAL MANIFESTATIONS IN ADULT ONSET OF STILL'S DISEASE: UNBIASED ANALYSIS OF FEVER PATTERN USING HIERARCHICAL CLUSTERING

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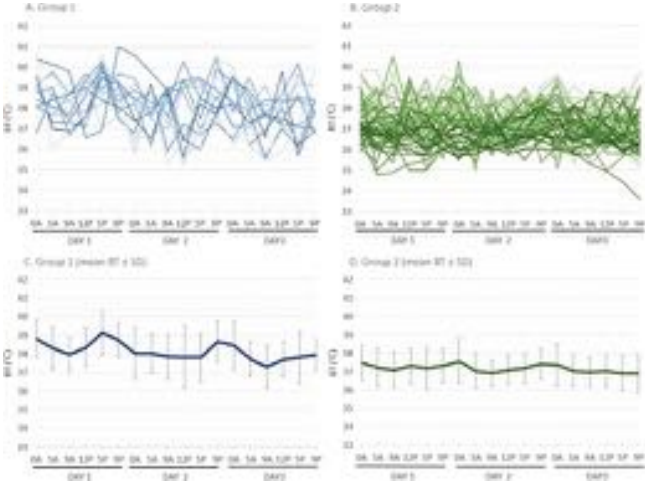
**Background:** Adult onset of Still's disease (AOSD) is a systemic inflammatory disease characterized by fever, arthritis, salmon pink rash and elevated serum inflammatory markers. The classical fever of AOSD is intermittent with a quotidian or double-quotidian pattern. However, a significant subset of AOSD exhibits persistently high fever with little temperature fluctuation. It remains unclear as to whether the certain fever pattern is associated with specific clinical manifestations.

**Objectives:** To investigate the association between fever pattern and clinical characteristics in patients with AOSD.

**Methods:** A total of 70 patients with AOSD who were treated as inpatient at Seoul National University Hospital from 2004 through 2015 were enrolled. Patients were grouped based on the fever curves on days 2, 3 and 4 using hierarchical clustering. The clinical and laboratory characteristics of the groups were compared.

**Results:** 70 patients were divided into 2 groups based on the fever curves. The group 1 with 14 patients had a higher mean temperature (38.1±0.4℃ vs. 37.2±0.5℃, p<0.001) with wider daily variation (2.7±0.9℃ vs. 1.9±0.7℃, p<0.001) as compared to 56 patients in the group 2.

Group 1 tended to be younger (38.4 ± 14.7 years vs. 46.1 ± 17.6 years, p=0.141) (Figure). Fever, arthritis, arthralgia and rash did not differ between them. However, group 1 tended to have more pericardial and lung involvement (42.9% v.s 23.2%, p=0.181). Group 1 had significantly lower platelet count (198,900 ± 68,000/μl vs. 312,900 ± 156,900/μl, p=0.0001), higher LDH (816.6 ± 376.4 IU/L vs. 477.5 ± 327.1 IU/L, p=0.002), higher mean ferritin level (27,004.1 ± 48,891.5 ug/mL vs. 6,852 ± 10,628.2 ug/mL, p=0.072) and d-dimer (9.5 ±7.9 ug/mL vs 3.3 ± 3.4 ug/mL) as compared to group 2, whereas white blood cell count, hemoglobin levels, CRP levels did note differ between the both groups. Group 1 tended to require longer time to a clinical remission (455.5 ± 850 days vs. 9.4 ± 115.7 days, p=0.137).



**Conclusions:** The unbiased analysis of fever reveals the presence of at least 2 distinctive fever patterns in AOSD. Spiking fever with higher daily variation was more often associated with higher inflammatory markers and coagulopathy and required longer treatment. Thus, fever pattern might be a prognostic factor in AOSD and AOSD patients with spiking fever might need more intensified treatment.

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## FRI0488 A PHASE III PIVOTAL UMBRELLA TRIAL OF CANAKINUMAB IN PATIENTS WITH AUTOINFLAMMATORY PERIODIC FEVER SYNDROMES (COLCHICINE RESISTANT FMF, HIDS/MKD AND TRAPS)

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**Background:** Periodic fever syndromes (PFS) are a group of rare autoinflammatory conditions, which includes, among others, cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD), TNF-receptor associated periodic syndrome (TRAPS). Canakinumab (CAN), a fully human, highly specific anti-IL-1β neutralising monoclonal antibody, is effective in CAPS.[1] IL-1β has been shown to be involved in the pathogenesis of FMF, HIDS/MKD and TRAPS, for whom no approved treatment exists. A series of small open label studies suggested efficacy of CAN in colchicine resistant/intolerant FMF (crFMF), HIDS/MKD and TRAPS.[2,3] We report the efficacy and safety of CAN from the randomised treatment epoch of a phase III trial in patients (pts) with crFMF, HIDS/MKD or TRAPS.

**Objectives:** Primary objective of this phase III pivotal trial was to demonstrate that CAN 150 mg (or 2 mg/kg for pts ≤40 kg) sc q4w is superior to placebo (PBO) in achieving a clinically meaningful response defined as resolution of the index flare at Day 15 and no new disease flares over 16 wks of treatment. Secondary objectives were: % pts who achieved a physician global assessment of disease activity (PGA) <2 (minimal/none); % pts with C-reactive protein (CRP) ≤10 mg/L; serum amyloid A level (SAA) ≤10 mg/L at Wk 16.

**Methods:** The trial (NCT02059291) consists of 3 disease cohorts (crFMF, HIDS/MKD and TRAPS) and 4 study epochs (E1–4): a screening epoch (E1) of up to 12 wks, a randomised treatment epoch (E2) of 16 wks, a randomised

**Table. Primary and secondary endpoint results at Week 16 and summary of safety**

| | Cohort | CAN (150 mg q4w) | Placebo | p-value |
|---|---|---|---|---|
| Proportion of responders, n (%) | crFMF | 19 (61.29) | 2 (6.25) | <0.001* |
| | HIDS/MKD | 13 (35.14) | 2 (5.71) | 0.0020* |
| | TRAPS | 10 (45.45) | 2 (8.33) | 0.0050* |
| Patients with PGA <2, n (%) | crFMF | 20 (64.52) | 3 (9.38) | <0.001* |
| | HIDS/MKD | 17 (45.95) | 2 (5.71) | 0.0006* |
| | TRAPS | 10 (45.45) | 1 (4.17) | 0.0028* |
| Patients with CRP ≤10 mg/L, n (%) | crFMF | 21 (67.74) | 2 (6.25) | <0.001* |
| | HIDS/MKD | 15 (40.54) | 2 (5.71) | 0.0010* |
| | TRAPS | 8 (36.36) | 2 (8.33) | 0.0149* |
| Patients with SAA ≤10 mg/L, n (%) | crFMF | 20 (64.52) | 3 (9.38) | <0.001* |
| | HIDS/MKD | 17 (40.95) | 2 (5.71) | 0.0006* |
| | TRAPS | 10 (45.45) | 1 (4.17) | 0.0028* |
| Patient exposure (median, days)# | crFMF | 113.0 | 113.0 | – |
| | HIDS/MKD | 113.5 | 111.5 | – |
| | TRAPS | 114.0 | 114.0 | – |
| Patients with any AE, n (%) | crFMF | 16 (76.2) | 4 (80.0) | – |
| | HIDS/MKD | 14 (77.8) | 4 (100.0) | – |
| | TRAPS | 9 (18.8) | 3 (100.0) | – |
| Patients with infections and infestations, n (%) | crFMF | 8 (38.1) | 1 (20.0) | – |
| | HIDS/MKD | 10 (55.6) | 2 (50.0) | – |
| | TRAPS | 2 (27.3) | 2 (66.7) | – |
| Patients with any SAE, n (%) | crFMF | 2 ( 9.5) | 1 ( 20.0) | – |
| | HIDS/MKD | 0 (0.0) | 2 (50.0) | – |
| | TRAPS | 0 (0.0) | 0 (0.0) | – |

n = number of patients who achieved primary or secondary endpoint; AE, adverse event; SAE, serious adverse event. *Indicates statistical significance (one-sided) at the 0.025 level based on Fisher exact test/logistic regression model for the primary endpoint/for the secondary endpoint. #Patients who had no new flare over the 16 weeks of treatment.

withdrawal epoch (E3) of 24 wks and an open-label treatment epoch (E4) of 72 wks. Pts (age ≥2 years) with crFMF, HIDS/MKD or TRAPS with a flare during E1 were randomised (1:1) in E2 to receive CAN or PBO. Safety assessments included adverse events (AEs).

**Results:** Of 181 pts (crFMF, n=63; HIDS/MKD, n=72; TRAPS, n=46) randomised in E2, 6 pts discontinued (5 PBO; 1 CAN). In all 3 disease cohorts, the proportion of pts who were responders for the primary outcome at Wk 16 was significantly higher with CAN vs PBO (Table). At Wk 16, a significantly higher proportion of pts achieved PGA score <2, CRP ≤10 mg/L and SAA ≤10 mg/L in the CAN group vs PBO in all 3 cohorts (Table). No new safety findings were reported in the CAN-treated pts through E2 (Table).

**Conclusions:** These results demonstrated superior efficacy of canakinumab at dose level of 150 mg q4w after a 16 weeks treatment period compared to placebo. The overall safety profile was not distinct from previous controlled studies and expectations in an auto-inflammatory patient population.

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## FRI0489 CANAKINUMAB IMPROVES PATIENT REPORTED OUTCOMES IN PATIENTS WITH PERIODIC FEVER SYNDROMES

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**Background:** Periodic Fever Syndromes (PFS) are rare autoinflammatory conditions including Familial Mediterranean Fever (FMF), Hyper-IgD Syndrome/ Mevalonate Kinase Deficiency (HIDS/MKD), and TNF-Receptor Associated Periodic Syndrome (TRAPS).[1] It has been shown that colchicine-resistant FMF (crFMF), HIDS/MKD and TRAPS considerably impact physical and emotional aspects of patients' lives.[2–4] Open label studies suggested that canakinumab (CAN), a fully human and highly specific anti-IL-1β monoclonal antibody, is efficacious in crFMF, HIDS/MKD and TRAPS.[5–7] To date, there is no data showing the effect of CAN on Health-Related Quality of Life (HRQoL) in PFS patients.

**Objectives:** To evaluate the effect of CAN on HRQoL using Child Health Questionnaire – Parent Form 50 (CHQ-PF50) and SF-12 Health Survey (SF-12) in PFS patients.

**Methods:** In a Phase 3 randomised placebo controlled study of CAN in PFS (NCT02059291), SF-12 Physical Component Summary (PCS) and Mental Component Summary (MCS) were assessed in adults. For children (>5–<18 years), CHQ-PF50 Physical (PhS) and Psychosocial (PsS) Summary scores were assessed.

**Results:** 181 patients were randomised to CAN or placebo in 3 cohorts (63 crFMF, 72 MKD/HIDS, 46 TRAPS). 71 adults ≥18 years and 110 children (age range ≥2–<18 years). Patients reported early clinically meaningful improvement in SF-12 PCS scores reported at Week (Wk) 5 which were sustained and increased to a large effect size by Wk 16 for all indications (Table). Similarly, clinically meaningful improvements in SF-12 MCS, CHQ-PF50 PhS and PsS was observed in all indications, with the exception of PsS in HIDS/MKD and TRAPS patients (Table).

Table 1. Patient reported outcomes

| | Mean change from baseline (n/N) | | | | | |
|---|---|---|---|---|---|---|
| | crFMF | | HIDS/MKD | | TRAPS | |
| | Week 5 | Week 16 | Week 5 | Week 16 | Week 5 | Week 16 |
| SF-12 PCS | 7.9 (29/30) | 9.55 (30/31) | 13.81 (15/15) | 13.81 (14/14) | 9.63 (16/17) | 11.64 (13/14) |
| SF-12 MCS | 4.83 (29/30) | 4.27 (30/31) | 6.41 (15/15) | 8.14 (14/14) | 5.65 (16/17) | 5.51 (13/14) |
| CHQ-PF50 PhS | 13.2 (21/24) | 20.1 (18/21) | 5.5 (32/34) | 9.9 (27/29) | 7.4 (16/18) | 14.9 (13/14) |
| CHQ-PF50 PsS | 4.1 (21/24) | 7.2 (18/21) | 1.8* (32/34) | 5.2 (27/29) | 0.9* (16/18) | 1.2* (13/14) |

N = total number of patients; n = patients who received at least one dose of canakinumab. *Minimal important difference[8,9] from baseline was *not* achieved.

**Conclusions:** Canakinumab showed rapid improvement by Week 5 in patient reported outcomes in adults and children with PFS, which was sustained through Week 16.

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## FRI0490 INFERTILITY AND PREGNANCY IN RHEUMATIC DISEASES: THE UTILITY OF A MULTIDISCIPLINARY PROTOCOL FOR THE MANAGEMENT OF THESE PATIENTS

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**Background:** Pregnancy in rheumatic diseases is a process that requires careful handling, beginning with proper planning. Infertility and chronic use of teratogenic drugs are some common situations in these patients, giving them a high-risk obstetrics.

**Objectives:** To established a protocol for planning and monitoring pregnancies in patients with rheumatic diseases

**Methods:** Retrospective review of a follow-up protocol for patients with rheumatic diseases and pregnancy wishes. This protocol includes: preconception consultation to asses fertility of the couple, as well as pregnancy couselling and establishment of a appropriate pharmacological treatment; after pregnancy period start, monthly consultations by a multidisciplinary team; and finally, a postpartum consultation after delivery

**Results:** A total of 51 patient with different rheumatic diseases were included: Sistemic Lupus Erythematosus (8 patients), Sjogren'S Syndrom (10 patients), Rheumatoid arthritis (13 patients), Psoriatic arthritis (5 patients), Behcet's disease (3 patients), Spondiloarthritis (2 patients), Familial Mediterranean Fever (2 patients), Conective mixed Tissues Disease (1 patient), Primary Antiphospholipi Syndrom (2 patient) an Hyper IgD Syndrome (1 patient). The results were: Infertility was detected in 8 couples and assisted reproductive techniques was requieres in 7 (6 IVF and 1 insemination). Safe Pharmacological treatments were used: sulfasalazine (4), hydroxychloroquine (13), azathioprine (2). Biological DMARDs in 3 patients (1 infliximab and Certlizumab in 2). Other treatments were: steroids (12) and intravenosus immunoglobulins for fetal heart block (2). All patients with thrombophilia have been treated with LMWH alone or plus aspirin. The course of pregnancy was:delivery at term (28), delivery pre-term (3)**, miscariages (3)*, pregnancy on course (7), neonatal death (1) and 8 patients are plannig the pregnancy. The abortions have occurred in 2 patients with lupus erythematosus and in 1 patient with rheumatoid arthritis. Postpartum care of newborns with mothers with positivity anti-Ro has objectified a neonatal transfer of Acs in 100% of cases;only 8 of them developed neonatal SLE.

**Conclusions:** A satisfactory evolution of pregnancy was observed in 87% of our patients, a fact that supports our impression that this process should be approached in a multidisciplinary team. Infertility is a situation that should be considered and treated at an early stage in this patients, preferably before preconceptional period.

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## FRI0491 ETIOLOGY AND CLINICAL FEATURES OF UVEITIS IN A TERTIARY CENTER IN TURKEY

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**Background:** Uveitis is inflammation of uvea (iris, ciliary body, choroid). Uveitis is classified as anatomically (anterior, intermediate, posterior, panuveitis) and etiologically (infectious, non-infectious and masquerade) (1).
**Objectives:** The aim of this study was to investigate etiology and clinical properties of uveitis in a tertiary center in Turkey.
**Methods:** Uveitis patients who admitted to our hospital from 2013 to 2015 were evaluated. Age, gender, type of uveitis, course of the attacks and etiology were noted.
**Results:** One hundred patients with uveitis (54% men, 46% women; age 40.01±14.1 years) were included in the study. The course of the disease was mostly acute (42%) followed by recurrent (36%) and chronic form (22%). Specific diagnosis was established in 68% of patients; whereas 32% of patients were evaluated as idiopathic. Etiology was spondiloartropathy (SpA) in 30%, Behçet's disease in 16%, infectious in 13%, connective tissue disease associated in 6%, sarcoidosis in 2% and malignancy associated uveitis in 1% of the patients. 67% of the patients had unilateral and 33% of patients had bilateral uveitis.
The characteristic properties of patients with SpA were as 56% men and 43% women; aged 43.57 ± 16.45 years. 60% of the patients with SpA had anterior, 40% had panuveitis. 46% of SpA patients had recurrent, 43% had acute and 10% had chronic uveitis. HLA B27 was positive in 50% of SpA patients. Sacroiliitis on MRI was detected in 76% of patients.
There were 32 idiopathic uveitis patients (53.1% women). Panuveitis was the most common type (37.5%) among idiopathic uveitis patients, followed by posterior uveitis (34.4%), anterior uveitis (21.9%) and intermediate uveitis (6.2%), respectively.
There were 16 patients with Behçet's disease, 62.5% of them were men. 62.5% of patients with Behçet's disease had panuveitis, 18.8% had anterior and 18.8% had posterior uveitis.
**Conclusions:** According to the literature posterior segment involvement is a rare presentation of SpA associated uveitis (2).The results of this study are noteworthy that higher incidence of panuveitis can be seen in SpA patients.
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## FRI0492 LONG-TERM SAFETY AND EFFICACY OF CANAKINUMAB IN PATIENTS WITH CAPS: FINAL RESULTS FROM THE BETA-CONFIDENT REGISTRY

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**Background:** Cryopyrin-associated periodic syndrome (CAPS), is a rare autoinflammatory disease encompassing a spectrum of 3 phenotypes with an estimated population frequency ranging from 1–3 per million.[1,2] The β -confident Registry (NCT01213641) is a multicenter, long-term, prospective, observational study with an enrollment period of 5 years (yrs) to monitor the long-term safety and efficacy of canakinumab (CAN) for CAPS. Here we report the overall final results.
**Objectives:** The primary objective of the Registry was to monitor the safety of CAN, focusing on SAEs including serious infections, vertigo, malignancies and hypersensitivity reactions.
**Methods:** Cumulative safety data were reported as incidence rate per 100 patient-yr (IR/100 pyr) from the enrollment of the first patient (November 2009) until end of study (December 2015). The registry protocol did not mandate any visits or procedures; however, all observed and reported AEs and SAEs or AEs potentially related to CAN were recorded. Efficacy was measured using physician global assessments (PGA).
**Results:** Overall, 288 patients were enrolled at 39 sites across 13 countries with mean patient exposure duration of 3.6 yrs. Of these, 22 (8%) discontinued CAN: 5 due to AEs, 10 due to poor efficacy and patient preference; and 7 due to unknown reasons. The IR/100 pyr for overall AEs was 100.0. Among the phenotypes of CAPS, patients with familial cold autoinflammatory syndrome (FCAS) had the lowest IR/100 pyr (78.0) compared to patients with Muckle–Wells syndrome (MWS) (IR/100 pyr 113.4) and neonatal onset multisystem inflammatory disease (NOMID) (IR/100 pyr 119.0). The most common AEs were infections and infestations (IR/100 pyr, 39.1). Overall, 161 SAEs were reported by 86 patients (IR/100 pyr, 16.3), most commonly, infections (IR/100 pyr, 5.0). One death (metastatic rectal adenocarcinoma in 76-yr-old MWS patient) was reported. Of 23 patients that received pneumococcal vaccination (PPV), 15 (65%) reported local post-PPV injection site reactions, of which 5 were considered as serious. Based on PGA, 50% of patients had no disease activity, whereas most of the others experienced mild/moderate disease activity up to Month 48. Similarly, disease activity was absent or mild/moderate in patients with *NLRP3* mutation negative CAPS (n=13) treated with CAN.
**Conclusions:** The β-confident Registry is the largest CAPS cohort documented in a registry. This registry demonstrated that safety profile of canakinumab was consistent with previous findings and efficacy was sustained for more than 5 years. Canakinumab therapy was also effective in patients with *NLRP3* mutation negative CAPS.
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## FRI0493 CLINICAL FEATURES OF THE VOGT-KOYANAGI-HARADA SYNDROME

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**Background:** Vogt-Koyanagi-Harada's disease (VKHD) is a bilateral, diffuse and chronic granulomatous panuveitis characterized by serous retinal detachment. This disease is often associated with neurological, auditory and dermatological disorders. The incidence of appearance is low, affecting mainly young women between 30 years approximately.
**Objectives:** The objective of the present study was to describe and to analyze the characteristics of patients with VKHD, followed in a third level hospital.
**Methods:** Retrospective and descriptive study of patients with EVKH. A large number of clinical, epidemiological variables and treatment were recorded. Statistical analysis was performed with SPSS19.0 program. The qualitative variables were expressed as frequencies and percentages, quantitative variables in mean.
**Results:** In the last 5 years, 3727 clinical records were reviewed and 8 patients were included. Of these, 5 (62.5%) were women with a mean age at diagnosis of 43 years old. All patients referred decreased visual acuity, 100% with bilateral panuveitis and 75% were associated with serous retinal detachment. Dermatological disorders was found in 25% (i.e. vitiligo, poliosis and alopecia), neurosensorial hearing loss in 25% and 12.5% of patients presented asthenia and fever. Neurological symptoms (ie epilepsy, meningismus, confusion, impaired balance) were found in 37.5%. About treatment, all patients received high doses of systemic glucocorticoids and 25% also received non-steroidal anti-inflammatory drugs (NSAIDs). 37.5% of patients received cyclophosphamide, 62.5% azathioprine and 12.5% methotrexate. Visual acuity improved in 75% of cases. Ocular complications were seen in 50% of patients, 12.5% with cataracts, 25% synechiae and glaucoma and band keratopathy in 12.5%. No patients required vitrectomy, nor developed ocular hypertension. Currently only 1 patient has active disease.
**Conclusions:** In our series of VKHD patients, we found that all required immunosuppressive therapy due to the severity of the disease and with this aggressive treatment, the prognosis of this disease was favorable.
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## FRI0494 ARTHRITIS POST CHIKUNGUNYA FEVER: CLINICAL PROFILE OF A POPULATION OF PATIENTS IN A SECONDARY CARE HOSPITAL

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**Background:** Chikungunya fever is a viral disease caused by an alphavirus that belongs to the Togaviridae family, it is transmitted by mosquitoes of the gender Aedes. Acute symthomps manifests with high fever, skin rash and arthritis. A high percentage of patients can develop severe and disabling poliarthritis. In 2015 there was an outbreak of this desease in outskirts of the capital city, presenting several cases of arthritis of chikungunya fever
**Methods:** Retrospective, descriptive and cross-sectional study of patients who consulted in a secondary care hospital from Villa Elisa city, for persistent joint pain after chikungunya's fever in the period from March to June of 2015. It was conducted describing the characteristics of clinical state, demographic, treatment and patient outcomes. Statistical analysis was performed with SPSS19.0 program. The qualitative variables were expressed as frequencies and percentages, quantitative variables in mean.

**Results:** 26 patients from the capital city and outskirts were included, 92% of females with the average age of 47.2 years old. The average duration of acute fever was 2.86 days. The predominant symptoms were headache (76.9%), joint pain (92.3%). 92.3% had skin rash in the acute stage, with an average duration of 4.5 days. The joint symptoms began after an average of 14 days after the fever started. The metacarpal phalangeal and interphalangeal joints were affected in 73% of patients, the radiocarpal joints and knees in 76.9%, shoulders in the 50% and feet in 92.3%.
All patients were treated with NSAIDs and 20/26 patients (76.9%) was added prednisone at a dose of 40 mg/day with fast and gradual tapering treatment in two weeks, with 92.3% with partial or total relief of symptoms. In 2 patients (7.6%) was decided to add methotrexate for recurrence of the arthritis, whit the decrease of corticosteroids doses.
**Conclusions:** Chikungunya's fever is a major public health problem with increasing cases reports in urban areas, especially for its ability to generate medium and long-term rheumatological complications. It is important to mention the high frequency of hand and feet involvement, leading to several degrees of disability as well impairments, even laboral absenteeism because of the intensity of the pain.
Even though the follow-up period is short, it is highlighted the excellent response to this treatment with short time of corticosteroids, although it is needed a longer follow up to define the appropriate treatment according to the evolution and outcome of cases, and with this develop protocols for such cases.
**Disclosure of Interest:** None declared
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## FRI0495 THE COMBINED PREVALENCE OF RARE DISEASES IN RHEUMATOLOGY DEMONSTRATES A SUM MORE THAN DOUBLE TO THAT OF ANKYLOSING SPONDYLITIS

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**Background:** Rare diseases (RD) in rheumatology are heterogeneous and thus lack a systemic classification. By definition, prevalences of RD range up to 5/10 000 in Europe. Clinical courses comprise a vast variety of musculoskeletal symptoms such as arthritis, myositis, vasculitis, autoimmune organ involvement and bone diseases. The impact of RD for health care systems is widely unknown and individual patients are prone to unsatisfactory diagnoses and/or treatments.
**Objectives:** The objective of this study was to identify and classify RD in rheumatology and estimate their combined prevalence. The data may give a better understanding for this area of rheumatology, may aid specified centers for RD, and perhaps sharpen the overall perception of health care systems.
**Methods:** Databases (pubmed.org, abstract archives of the European League Against Rheumatism and the American College of Rheumatology, and Orpha.net) were searched for the following terms: rare in combination with arthritis, arteritis, connective tissue disease, rheumatic and vasculitis. Furthermore, terms were used in various combinations including arthralgia, autoimmune, fever, inflammation, joint pain, muscle pain, myalgia and swollen joint. Identified syndromes were then classified according to the following terms and data: differential diagnosis, etiology, genetics, prevalence, principal symptom, prognosis, and therapy. The overall total point prevalence for all RD in rheumatology was estimated by adding up all single point prevalences available.
**Results:** A total of 82 syndromes and diseases were identified. Classification was as follows: arthritis (n=17) and vasculitis (n=18), fever syndromes (n=13), collagen diseases (n=10), myositis (n=9), and overlaps/others (n=15). Fifty-two diseases showed a chronic progressive course. The mortality was variable in many diseases and thus could not be determined precisely. Point prevalence data were available for 49 syndromes and diseases, and added up to a total point prevalence of 49/ 10 000. Forty-nine of these in part pathophysiologically quite distinct RD are treated with corticosteroids.
**Conclusions:** Rare diseases in rheumatology are most often chronic or progressive. Symptoms are variable, they include arthritis, organ and skin involvement. The estimated combined prevalence of all RD in rheumatology is significant with 49/10 000: it is double or more than that of ankylosing spondylitis with 18/10 000 [(1)]. Treatment options are often restricted to corticosteroids presumably because of the scarcity of randomized controlled trials. Health care systems should assign RD the same importance as any other common disease in rheumatology.
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## FRI0496 LONG TERM SAFETY AND EFFICACY OF ANAKINRA IN ADULT PATIENTS WITH REFRACTORY RECURRENT IDIOPATHIC PERICARDITIS

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**Background:** Our previous open label study has shown that IL-1 inhibition with anakinra was an efficacious, safe and steroid-sparing agent for the short term treatment of refractory recurrent idiopathic pericarditis in adults. However long term data are not available in such patients.
**Objectives:** The aim of this study, which is a follow-up of the initial cohort of patients, was to assess the long term safety and efficacy of Anakinra in adult patients with refractory recurrent idiopathic pericarditis.
**Methods:** Eleven patients with treatment-resistant idiopathic recurrent pericarditis were included (a new patient was added to the initial cohort of 10 patients). All patients were resistant and/or intolerant to previous treatment with aspirin and/or NSAIDs, colchicine and corticosteroids (CS) while two (18%) had failed azathioprine therapy. Initially all were treated with daily subcutaneous injections of Anakinra (100 mg) with gradual tapering of the administered dose (daily for 6 months, followed by every other day for 6 months). Recurrences as well as adverse events were recorded in all patients.
**Results:** Among the 11 patient included there were 6 males with a mean age of 42 ± 16.8 years and a median disease duration of 37 months. Patients had a median of 8 recurrences prior to Anakinra initiation and were CS-resistant (mean daily prednisolone dose at baseline: 14.7 ± 7.6 mg). Patients were followed for a period of approximately 3 years (median follow-up time: 35 months). All patients responded initially to Anakinra and all were able to discontinue CS rapidly (median time to discontinuation: 6 weeks). During the long term, follow-up, 3 patients discontinued anakinra (27.5%) and remain free of recurrences without any treatment ever since. Five patients (45%) remain on a reduced dose of Anakinra (once a week n=1, twice a week n=1, three days a week n=1, four days a week n=2). Most recurrences occurred while the dose of Anakinra was reduced from three to two injections per week (mean number of recurrences: 2.2 ± 1.4). Three patients continue on full dose Anakinra (one had started therapy 3 months ago). None of these patients had restarted CS. No significant side effects were seen during the long term follow up of these patients and no patient discontinued therapy due to side effects.
**Conclusions:** During long term follow-up, Anakinra remains a highly efficacious and safe medication for the treatment of refractory recurrent idiopathic pericarditis in adults. All patients remain CS-free and more than a quarter (27.5%) of them were able to discontinue all therapies. Approximately half remain on a reduced dose Anakinra with excellent disease control.
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**Disclosure of Interest:** None declared
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## FRI0497 THE INTERLEUKIN-1 INHIBITOR CANAKINUMAB FOR FAMILIAL MEDITERRANEAN FEVER: LONG-TERM BENEFICIAL EFFECT IN A COHORT OF 14 PATIENTS

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**Background:** Interleukin-1 (IL-1) is a major mediator of the inflammatory cascade in Familial Mediterranean Fever (FMF) and an established therapeutic target (1).
**Objectives:** To assess the efficacy and safety of the IL-1 inhibitor Canakinumab in adult and adolescent patients with refractory FMF.
**Methods:** Fourteen patients (7 men) with genetically confirmed FMF, fulfilling the Tel Hashomer criteria, aged 38.5 years (median, range 13–70), with median disease duration of 14 years and active disease despite colchicine (n=9) or both colchicine and anakinra (n=5), received Canakinumab 150mg subcutaneously (sc) every 4 (n=7) or 6 (n=2) or 8 weeks (n=5) for a median of 18 months (range 7–53). Canakinumab was given as monotherapy in 8; 6 patients received concomitant treatment with colchicine and/or corticosteroids.
**Results:** Eleven out of 14 patients (79%) achieved complete clinical remission (median time 2 months), while normalization of all laboratory parameters associated with inflammation occurred in 92% of patients (median time 3 months). The remaining patients achieved partial responses. Response was maintained until the last visit in all but 4 patients. Reducing the Canakimumab administration

interval led to suppression of disease activity in three cases, whereas in another two patients drug administration intervals could be increased without disease exacerbation. The corticosteroid dose was significantly reduced during follow up. The FMF50 score (2) was achieved by 50% and 86% of patients at 1 and 12 months, respectively. Canakinumab was well tolerated; one patient experienced an urinary tract infection and another one a viral gastroenteritis.

**Conclusions:** The rapid and sustained response to Canakinumab in the majority of our patients, together with the favorable safety profile, encourages its further use in FMF.

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## FRI0498 CLINICAL CHARACTERISTICS OF IGG4-RELATED DISEASE: A RETROSPECTIVE ANALYSIS OF 166 CHINESE PATIENTS

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**Background:** Since the initial recognition of autoimmune pancreatitis (AIP), elevated serum IgG4 levels and increased numbers of IgG4-positive plasma cells in tissues have been regarded as diagnostic hallmarks of the disorder. However, the role of the IgG4 level in other non-AIP IgG4-RD is unclear.

**Objectives:** To investigate the clinical features and factors associated with IgG4 test positivity over an 8-year period in 166 patients with IgG4-related diseases (IgG4-RD).

**Methods:** The medical records of 2,968 adult subjects who underwent serum IgG4 level tests conducted between December 2007 and August 2014 were reviewed.

**Results:** Among 2,968 patients, 166 (5.6%) were diagnosed with IgG4-RD and 2,802 (94.4%) were determined to have other diseases (non-IgG4-RD group). The mean IgG4 level in subjects with IgG4-RD was 1087.5 mg/dL (median: 597.0, range: 15–6790 mg/dL), which was significantly higher than that of subjects with non-IgG4-RD (mean: 104.1, median: 75.0, range: 1–4400 mg/dL; $p<0.0001$). Among the 166 IgG4-RD patients, the mean age was 58.5 ± 15.9 years (range: 21–87). Of 166 patients with IgG4-RD, 87 (52.4%) had an IgG4-RD other than autoimmune pancreatitis (non-AIP IgG4-RD). Twenty-seven out of 166 IgG4-RD (16.3%) patients had other organ involvement (OOI) outside of the pancreatobiliary system. IgG4 levels were elevated (>135 mg/dL) in 143 (86.1%) of 166 patients with IgG4-RD and in 652 (23.3%) of 2,802 patients with non-IgG4-RD ($p<0.001$). The present study showed that the best IgG4 cutoff was 222 mg/dL for the diagnosis of IgG4-RD.

**Conclusions:** In the present study, we demonstrated that more than half of the diseases associated with IgG4-RD were non-AIP IgG4-RD. Among the 166 IgG4-RD patients, the manifestations covered the full range of organ system involvement. Moreover, the best IgG4 cutoff (measured with nephelometry using a Siemens BN ProSpec instrument and Siemens reagent) was 222 mg/dL for IgG4-RD.

**Disclosure of Interest:** None declared

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## FRI0499 LONG TERM SURVIVAL OF IMMUNOSUPPRESSIVE THERAPIES IN UVEITIS PATIENTS

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**Background:** Uveitis encompasses a diverse group of inflammatory diseases associated with a significant risk of substantial and sometimes permanent visual loss. Although corticosteroids are the initial treatment, immunosuppressive therapy (IST) may be needed in case of inadequate response and/or side-effects. Most of the data regarding efficacy, tolerability and discontinuation rates of ISD in uveitis patients comes from clinical trials, as data from observational studies in uveitis are scarce. However, it is important to take into account that the trial settings are different from day-to-day clinical practice, which limits the validity of the extrapolated data to patients in daily practice.

**Objectives:** To assess the long-term survival of ISTs in uveitis patients in real-life clinical practice. Factors associated with discontinuation were also analyzed.

**Methods:** An observational retrospective longitudinal study of uveitis patients taking ISTs from 1989 to 2014 was conducted. The primary endpoint was IST discontinuation due to: clinical improvement, inefficacy, adverse drug reaction (ADRs), and other causes. Incidence rates of discontinuation (IR) per 100 patient-years were estimated. Variables associated with specific causes of discontinuation were analyzed using Cox bivariate and multivariate models.

**Results:** We included 225 courses of IST in 95 patients (565.3 patient-years of observation). Cyclosporine [62 patients (65.3%)], methotrexate [44 (46.3%)], azathioprine [28 (29.5%)], and anti-TNFs [30 (31.6%)] were the most frequently used. Treatment was suspended in 116 cases (IR 20.5 with 95% confidence interval [17.1 to 24.6]). In the first year of therapy 75% continued on IST, and after ten years, the retention rate was 16%. The IRs due to clinical improvement, inefficacy and ADRs were 8.0 [5.9 to 10.7], 5.1 [3.6 to 7.4], and 4.4 [3.0 to 6.5], respectively. The IRs of all cause discontinuation for cyclosporine, methotrexate, azathioprine, and anti-TNFs were 21.7 [16.3 to 28.8], 10.9 [7.3 to 16.3], 18.7 [12.4 to 28.2], and 24.1 [16.0 to 36.2] per 100 patients-year, respectively.

In the multivariate analysis, combined therapy was associated with a higher rate of discontinuation, regardless the cause. Presence of vasculitis was associated with a higher rate of discontinuation due to clinical improvement, and presence of macular edema was associated with higher risk of discontinuation due to inefficacy.

**Conclusions:** The major causes of IST discontinuation in cohorts of uveitis patients were clinical improvement and inefficacy. Methotrexate showed the lowest rate of discontinuation, while anti-TNFs showed the highest rate.

Combine therapy with IST was associated with higher discontinuation rate regardless the cause. Presence of vasculitis and macular edema were associated with a higher risk of discontinuation due to clinical improvement and inefficacy, respectively.

**Disclosure of Interest:** None declared

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## FRI0500 IDIOPATHIC GRANULOMATOUS MASTITIS: A SINGLE CENTER EXPERIENCE

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**Background:** Idiopathic granulomatous mastitis (IGM) is a rare benign inflammatory disease of the breast. Difficulties can be experienced in the treatment of IGM due to the lack of a common consensus in the literature. Treatment options include corticosteroids, surgical treatment, immunosuppressive drugs and conservative treatment with antibiotics.

**Objectives:** To present our experience about patients with IGM on immunosuppressive therapy.

**Methods:** The data of patients with a diagnosis of IGM under immunosuppressive therapy followed in the rheumatology outpatient clinic of a tertiary center enrolled between September 2010 and August 2015 were evaluated retrospectively. 16 histopathologically diagnosed patients receiving immunosuppressive therapy were evaluated for their treatments and treatment responses.

**Results:** The mean age of the patients, the average duration of immunosuppressive therapy and the average follow-up period were 35.9±6.5 years, 19.6±14.1 months and 28.3±17.8 months, respectively. Initially, 15 patients received (93.8%) steroids and methotrexate, and 1 patient (6.2%) was treated only with steroids. All patients responded well to initial therapy. Eight (53.3%) patients achieved remission with steroid + methotrexate. 2 of the other 7 patients relapsed after discontinuation of steroids and 1 after discontinuation of steroid + methotrexate. A positive response was obtained after the restart of treatment with steroids and methotrexate in these patients. Of these 7 patients, no recurrence was observed in 3 (42.9%) patients with only methotrexate and in 4 (57.1%) patients in the maintenance treatment with steroids and methotrexate. Lowered dose of steroid was associated with recurrence during follow-up of the patient taking only steroids as the initial treatment. 5 patients (33.3%) taking methotrexate had drug side effects, not necessitate stopping the treatment.

**Conclusions:** Systemic immunosuppressive therapy is safe and effective in IGM. Azathioprine and methotrexate have been the most frequently used immunosuppressive drugs in the literature. Our experience with methotrexate-based regimen allows the rapid reduction of the steroid dose and leads to remission.

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**Disclosure of Interest:** None declared

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## FRI0501 INVESTIGATION OF JOINT HYPERMOBILITY IN INDIVIDUALS WITH INDIRECT HYPERBILIRUBINEMIA AND ACROCYANOSIS

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**Background:** Hypermobility represents the excessive mobility of the joints. Joint hypermobility syndrome (JHS) is defined as the musculoskeletal symptoms in individuals with hypermobility in the absence of any systemic rheumatic disease, and the incidence in the general population is about 0.5%. A biochemical or structural disorder affecting collagen synthesis is assumed as an underlying mechanism in hypermobility syndrome. In animal studies, bilirubin has been shown to reduce fibrosis induced by bleomycin. In these studies, it is suggested that bilirubin leads to hypermobility by affecting the structure or function of

collagen. In addition, our observation in clinical practice is that hypermobility and acrocyanosis is more common in patients with indirect hyperbilirubinemia.
**Objectives:** This study aimed to evaluate the frequency of hypermobility and acrocyanosis in patients with indirect hyperbilirubinemia.
**Methods:** The study recruited 120 consecutive patients with indirect hyperbilirubinemia examined in gastroenterology outpatient clinics of a university hospital and 107 healthy individuals as a control group with normal bilirubin levels. Patients were examined for the presence of hypermobility and acrocyanosis. Hypermobility was determined by using Beighton scoring (Score, 0–9). To conclude whether the JHS was present, Brighton criteria were used. Acrocyanosis was identified by history and compatible physical examination.
**Results:** The mean age of the patients and the control group enrolled in the study were 33.4 ± 12.9 and 36.2 ± 11.2 years, respectively (p=0.09). 100 of the patients (83%) and 78 (73%) of the control group of were males (p=0.075). The average indirect bilirubin levels of the study and control groups were 1.44 ± 0.66 mg/dL and 0.37 ± 0.18 mg/dl, respectively. By Beighton scoring, 23 patients (19.2%) in the study group and 3 (2.8%) individuals in the control group had joint hypermobility. The difference between groups was statistically significant ($p<0.001$). 4 patients in the study group and 1 individual in the control group had JHS, and the difference was not statistically significant (p=0.220). In 35 (29.2%) of study patients and 12 (11.2%) individuals in the control group had acrocyanosis. The difference between groups was statistically significant (p=0.001). Joint hypermobility did not have any significant relationship with the presence of acrocyanosis (p=0.441).



Image 1. Beighton scoring system. Each of these movements can be made is regarded as one point.

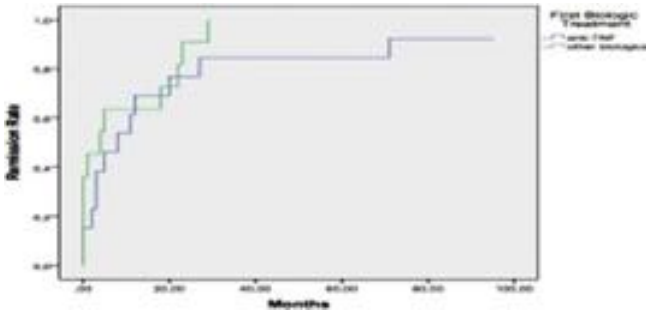
**Conclusions:** According to the results of our study, joint hypermobility and acrocyanosis is more frequent in patients with indirect hyperbilirubinemia compared to controls. This finding suggests that bilirubin has a role in both diseased. It should be determined whether they share a common or difference pathogenic pathway.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5418

## FRI0502 BIOLOGIC AGENTS IN REFRACTORY ADULT STILL'S DISEASE: BETTER RESPONSE RATES AND ACCEPTABLE SAFETY WITH ANAKINRA AND TOCILIZUMAB

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**Background:** There is no randomized controlled trial data to guide us for the management of Adult Still's Disease (AOSD) patients refractory to conventional treatments.
**Objectives:** We herein aimed to analyze retrospectively the treatment results of a series of refractory AOSD patients, who received different biologics.
**Methods:** We screened our database for patients diagnosed with AOSD between 1987–2015, and reviewed charts of those patients refractory to corticosteroid and DMARD combination and received biologics including TNF, IL-1 and IL-6 inhibitors. Patients were grouped according to their first biologics as TNF-inhibitors (TNF-i) or others [anakinra (ANK) or tocilizumab (TCZ)]. We also analyzed the patient responses according to their disease course characteristics as polycyclic or chronic patients. Time to remission were analysed by Kaplan-Meier method, and the association of response with first biological treatment was analysed by regression analysis
**Results:** Twenty-four patients with refractory AOSD (chronic=9 and polycyclic=15),who received biologic treatments with a mean duration of 41±27 months. The first biological treatment was TNF-i in 14 and other agents in 10 (ANK in 7 and TCZ in 3).Of the patients,50% were switched from TNF-i to ANK or TCZ. Comparison of the patients according to their first biologic therapy is given in Table 1. The patients who received other biologics were associated with a better response as the first treatment and tended to achieve remission earlier compared with those who received TNF-i as their first biological treatment (median time to remission 4 vs, 8 months, log-rank p=0.44). Joint involvement was more common and skin involvement tended to be more common in the chronic course group (100% vs 50%,78% vs 36%, respectively). While the duration of biologic treatment tended to be longer in the chronic course group (51 mo vs 28 mo,p=0.04), duration of remission was similar between the groups (26 mo vs 20 mo, p=0.4). The remission rate tended to be higher in the polycyclic group, whereas CRP and ESH tended to be lower in the chronic group. Complete remission rates under biologics course were as follows: 63% with TCZ 8mg/kg (7/11), 61% with ANK 100–200mg (11/18), 27% with etanercept (3/11), and 9% with infliximab (1/11) treatments. Regression analysis showed that selection of TCZ or ANK biologics as the first biologic was associated with a better response independent of the disease course type (estimate 2.5, 95% CI 0.3–4.7, p=0.026).No serious infection was observed in patients treated with biologics. In two patients severe skin reactions occurred with ANK and infliximab and, in one patient an immune thrombocytopenia developed under TCZ treatment.

| | TNF inhibitors (n=14) | Anakinra ( n=7) or Tocilizumab (n=3) |
|---|---|---|
| Current age (years) | 37±13 | 35±10 |
| Age at diagnosis (years) | 26 (20–59) | 26 (5–46) |
| Follow up (months) | 72 (18–252) | 54 (26–288) |
| Gender (% males) | 31 | 46 |
| Sore throat (%) | 54 | 73 |
| Skin involvement (%) | 54 | 46 |
| Joint involvement (%) | 85 | 55 |
| Hepatotoxicity (%) | 31 | 46 |
| CRP (mg/L) | 115±88 | 131±78 |
| ESR (mm/h) | 101±30 | 102±32 |
| Ferritin (ng/ml) | 1000 (281–29979) | 1280 (424–5181) |



**Conclusions:** This case series of AOSD patients suggest that ANK and TCZ seem to be better treatment choices in terms of remission rate and time to remission in patients refractory to conventional treatments
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4994

## FRI0503 EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH CRYOPYRIN ASSOCIATED PERIODIC SYNDROMES: AN OPEN-LABEL, PHASE-III, EXTENSION STUDY

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**Background:** Cryopyrin-Associated Periodic Syndrome (CAPS), a rare hereditary auto inflammatory disorder, constitutes 3 phenotypes: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and chronic infantile neurologic cutaneous and articular syndrome/neonatal onset multisystem inflammatory disease (CINCA/NOMID).[1] Canakinumab (CAN), a fully human monoclonal anti-human interleukin-1β (IL-1β) antibody is indicated for the treatment of CAPS patients (either ≥2 years or ≥4 years with body weight ≥7.5 kg.[2] Here, we present longer-term efficacy and safety of CAN in patients with CAPS aged >24 months.
**Objectives:** To assess long-term efficacy of CAN with respect to relapse in CAPS patients who completed the core (CACZ885D2307) study
**Methods:** CAPS pts (aged ≥1 years), who completed the core study, received a starting dose of 2 mg/kg s.c. of CAN every 8 weeks, in continuation with the core study. Patients who received a dose adjustment in the core study were allowed to continue same dose in the extension trial. Efficacy was evaluated by physician's global assessment (PGA), C-reactive protein (CRP) and serum amyloid A (SAA) levels. Safety was assessed in terms of adverse events (AEs).
**Results:** Of 17 pts enrolled, 12 (70.6%), 4 (23.5%) and 1 (5.9) were of MWS, NOMID and FCAS phenotypes, respectively. All 17 pts were complete responders; 16 (94.1%) had no relapse and 1 (5.9%) NOMID patient had a relapse at the end of study (EOS). PGA improved over the extension study with decline in severity

till EOS. The number of pts with absent autoinflammatory disease improved from 23.5% (4 pts) to 64.7% (11 pts). This improvement was also observed in the assessment of skin rash; proportion of patients with absent skin disease increased from 29.4% (5 pts) to 94.1% (16 pts). The mean decrease in CRP and SAA levels from baseline were -10.4mg/L and -54.36/L respectively. Overall, 10 (58.8%) pts had AEs suspected to be related to study drug; the most common were diarrhoea, pneumonia, rhinitis and cough (3 pts each). Eight (47.1%) pts experienced at least 1 Serious AE (4 MWS and 4 NOMID pts); with pneumonia being the most common 2 (11.8%). No deaths were reported during the study.

**Conclusions:** CAN effectively maintained clinical and serological efficacy in CAPS pts. No new safety findings were observed and the safety profile of CAN was consistent with previous studies, which corroborates the long-term use of CAN in the treatment of CAPS patients.

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## FRI0504 PROGNOSTIC FACTORS OF ADULT ONSET STILL'S DISEASE: ANALYSIS OF 100 CASES IN 3 TERTIARY REFERRAL CENTERS

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**Background:** Adult onset Still's disease (AOSD) is rare inflammatory disease [1]. Three different patterns of AOSD have been identified: i. monocyclic pattern, characterized by a systemic single episode; ii. polycyclic pattern, associated with multiple flares, separated by remissions; iii. chronic pattern, related to a persistently active disease with associated polyarthritis [2]. Until now, the treatment of AOSD remains largely empirical, lacking controlled clinical trials [1].

**Objectives:** We aimed to investigate clinical data of AOSD patients and any possible correlation among these features and the outcome of patients.

**Methods:** Clinical data of 100 AOSD patients were recorded. All patients fulfilled the Yamaguchi AOSD diagnostic [3]. Gender, age, clinical features, disease activity Pouchot's score [4], complications, serum ferritin, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), treatments, comorbidities, patterns and AOSD-associated death, were reported. Furthermore, we evaluated any possible correlation among these clinical features and the outcome of patients, by using linear regression analysis.

**Results:** One hundred consecutive AOSD patients (66 men, 34 women), whose age at diagnosis was 45.35±16.23 (mean±SD), were enrolled. All patients experienced fever, 86 patients showed joints involvement, 79 patients showed splenomegaly, skin rash was present in 78 patients, 62 patients showed hepatic involvement, 57 patients showed enlargement of lymph nodes. The Pouchot's score, 6.11±2.02 (mean±SD), confirmed the activity of the disease. Sixteen patients experienced different complications, mainly the macrophage activation syndrome. A strong increase of inflammatory markers (mean±SD) was observed: serum ferritin was 2560.07±3726.64 ng/mL, ESR was 67.28±26.65 mm/hr, CRP was 78.35±72.76. All the patients received steroids at different dosages, and 55 patients were treated with steroids and immunosuppressive drugs, mainly methotrexate and ciclosporin. Thirty-two patients were treated with biologic agents: 5 with anakinra, 8 with tocilizumab, and 19 with TNF inhibitors. Twenty-nine patients showed the monocyclic pattern, 22 patients showed the polycyclic pattern, 33 patients showed the chronic pattern. AOSD-associated death occurred in 16 patients. Regression analysis showed that Pouchot's score ($p=0.011$), the presence of any complication ($p<0.0001$) and associated comorbidities ($p<0.0001$) correlated with the unfavorable outcome.

**Conclusions:** This study provides information on the clinical, laboratory, therapeutic, and prognostic features in a large cohort of AOSD patients. The Pouchot's score, the presence of complications and comorbidities were significantly associated with the AOSD-associated death.

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## FRI0505 UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE: A 121 PATIENTS AUDIT FOCUSING ON INITIAL DIAGNOSIS AND CHANGES OVER TIME

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**Background:** The diagnosis of Undifferentiated Connective Tissue Disease (UCTD) has raised controversy over the years regarding making the diagnosis, evolution and prognosis. Le Roy et al[1] in 1980 and most recently Mosca et al[2] in 2014 proposed classification criteria for UCTD, but confusion still exists regarding making the diagnosis of UCTD, evolution and prognosis of the syndrome and how the patient should be followed up over time.

**Objectives:** Evaluate disease evolution, treatment and follow up plan in patients with UCTD diagnosis. Assess whether there are any factors that may predict disease evolution and should require regular follow up.

**Methods:** This was a retrospective study of patients followed up in a specialist clinic in a tertiary referral centre (University College London Hospitals) with a diagnosis of UCTD, focusing on clinical and serological features, treatment, follow up and disease evolution over time.

**Results:** A total of 121 patients were included in the study: 93% were females; the mean age at disease onset was 39 years (range 20 to 80); and the patients were followed up for at least 1 year (mean 12 years, range 1 to 40). 78% of these patients had a stable diagnosis of UCTD, while in 22% diagnosis changed over time: 9% evolved into a specific connective tissue disease (CTD) - 4 Systemic Lupus Erythematosus, 3 Sjogren's Syndrome, 1 Rheumatoid Arthritis, 1 Systemic sclerosis and 1 Anti-synthetase Syndrome -, 7% had a change of diagnosis from a specific CTD to UCTD, 4% evolved into an overlap syndrome and 2% of the patients were no longer diagnosed as having any CTD at the end of the study. The most prevalent manifestations were joint pain (arthralgia/arthritis) in 89% of the patients, fatigue 80%, Raynaud's phenomenon 63%, skin rashes 49% and sicca symptoms 45%. Lung involvement was observed in 11% of the patients within which 8% had a nonspecific interstitial pneumonia (NSIP) and 3% had a usual interstitial pneumonia (UIP) pattern. 36% of the patients were noted to have associated gastro-oesophageal reflux disease. Serological features included positive ANA in 98%, anti-RNP 33%, anti-Ro 32%, Rheumatoid Factor 20% and hypocomplementemia was observed in 19% of the patients. 7% of the patients did not require any treatment for their UCTD, but the majority of patients were treated with Hydroxychloroquine only (75%), and the rest with other immunosupressants/immunomodulators.

**Conclusions:** In our study the majority of patients initially diagnosed with UCTD kept this diagnosis over time but 13% of patients evolved to a defined CTD or an overlap syndrome and in 2% of patients, symptoms and serological features eventually resolved. Although, UCTD is often mild, significant major organ involvement such as interstitial lung disease can occur[3], as well as evolution to a defined CTD or overlap syndrome. This should guide follow up of these patients in clinic.

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## FRI0506 PREGNANCY IN PATIENTS WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE: CLINICAL OUTCOMES IN 78 CASES

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**Background:** Pregnancy is considered to be an important factor that may affect the course of autoimmune diseases; few data are currently available in the literature on pregnant patients with diagnosis of undifferentiated connective tissue disease (UCTD).

**Objectives:** To assess the outcome of pregnancy and evaluate the percentage of disease flare in a cohort of patients with UCTD.

**Methods:** We conducted a prospective study on 78 pregnancies in 64 UCTD patients, regularly monitored from the positive pregnancy test until the postpartum period by a multidisciplinary team including rheumatologists and obstetricians at our unit from 2000 to 2015.

**Results:** The mean age of patients at pregnancy was 34.1 (range 21–43) and the mean disease duration was 7.26 years. Only 3 patients presented hematologic disease activity at the beginning of pregnancy and none of the patients had experienced previous renal involvement. 20.8% of UCTD patients presented antiphospholipid (aPL)-antibodies positivity (only 2 cases of triple positivity of LAC, anti-β2GPI and ACLA) and the same percentage had anti-Ro positivity.

At the beginning of pregnancy 38.5% of patients was taking treatment: 20 hydroxychloroquine, 13 low doses of steroids and 11 aspirin. On average, the duration of pregnancy was 39 weeks (range 34–42), the mean birth weight was 3118.3 g (range 2122–4500 g). Eight pregnancies (10.5%) ended in miscarriage in the first trimester; the following obstetric complications occurred in 34.7% of the remaining successful deliveries: preterm delivery, small or large for gestational age (SGA/LGA), preeclampsia, premature membrane ruptures (PROM), increased transaminases. Six patients experienced a disease flare, 3 during pregnancy and 3 in puerperium: of these patients, 3 had a major flare progressing to SLE with the occurrence of lupus nephritis. No correlations were found between the incidence of obstetric complications and the positivity of aPL-antibodies, the use of steroids, the alterations of uterine artery Doppler velocimetry. The only variable correlated with the incidence of flare was the positivity of anti ds-DNA at the beginning of the pregnancy ($p<0.001$).

**Conclusions:** Our data suggest that UCTD as other connective tissue diseases should be carefully monitored during pregnancy as these patients present with obstetric complications. As in non pregnant UCTD patients anti-dsDNA are predictors of possible evolution to SLE, therefore these patients need careful monitoring during pregnancy.

**Disclosure of Interest:** None declared

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## FRI0507 ANAKINRA TREATMENT IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: A SINGLE-CENTER EXPERIENCE

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**Background:** Approximately 5 to 10% of FMF patients do not respond to colchicine treatment and/or intolerant to colchicine because of side effects. Several case reports and case series have pointed out the efficacy of IL-1 blockade in colchicine resistant FMF subgroup.

**Objectives:** To review the patients followed in our center with FMF who received Anakinra, an anti IL-1 receptor antagonist, in terms of outcome and side effects.

**Methods:** 36 FMF patients who were treated with Anakinra were retrospectively reviewed with regard to indication, effect on disease activity and acute phase response, adverse events. Patient global assessment was recorded before and after Anakinra treatment. Nine patients were pregnant at the time of the treatment and reported previously (1).

**Results:** There were 27 FMF patients with FMF who were treated with Anakinra for various indications (colchicine resistant recurrent febrile attacks in 21, colchicine related side effects in 6). The mean age of the 27 patients was 33.16±10.29 years. The mean duration of the disease was 19.29±10.94 years. There were various co-existing pathologies among this study group like Ankylosing Spondylitis (1), SLE (1), Behçet's disease (1) and Gout (1). The mean colchicine dose was 2.03±2.031 mg/d. The mean duration of anakinra treatment was 14,18± 18.39 months. Nine teen patients reported no attacks after anakinra treatment whereas 5 patients reported at least 50% decrease in the attack frequency and 3 patients reported less than 50% decrease in attack frequency. Mean patient global assessment decreased from 8,57±2,23 to 2,61±2,82 under Anakinra treatment ($p<0.001$)

As for the adverse events, four patients had allergic reactions under Anakinra treatment (severe disseminated rash in 1 patient and severe injection site reaction in 2 patients and tolerable injection side reaction in 1) therefore the treatment was terminated for 3 patients with severe allergic reactions. One patient had genital warts and urinary tract infection after the injections and Anakinra was stopped. One of our patients reported that her psoriatic lesions got worse on Anakinra. Twenty one patients reported no adverse events during the course of treatment.

Anakinra treatment was terminated in overall 11 patients for various reasons: Inadequate response in 3, allergic reactions in 3, flare in psoriatic plaques in 1, infection and genital warts in 1, full recovery in 2 and patient's preference in 1. Sixteen patients are still on Anakinra treatment.

**Conclusions:** Colchicine resistance or intolerance in FMF, although not very common, is an issue in daily rheumatology practice. During our experience with Anakinra, we reported remarkable decrease in the frequency of attacks in many patients with relatively tolerable side effects. Among patients whom Anakinra treatment was terminated, the most common reason was injection site reaction. We state that Anakinra is an effective alternative in patients with inadequate response or intolerance

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## FRI0508 EXPERIENCE WITH INTERLEUKIN-1 INHIBITOR CANAKINUMAB IN AUTO-INFLAMMATORY DISEASES AND SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN CLINICAL PRACTICE

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**Background:** Interleukin-1 inhibitor Canakinumab (a humanized anti- Il-1β monoclonal antibody) is gaining wider use in Russian clinical practice recently for treatment of auto-inflammatory diseases (AIDs). Experience with Canakinumab for systemic juvenile idiopathic arthritis (SoJIA), considered as AIDs, is being accumulated as first and second line *biologic agents* therapy. In Russia Canakinumab was initially marketed in 2011 for cryopyrin-associated periodic syndromes (CAPS), in 2013 – for SoJIA.

**Objectives:** To assess efficacy and tolerability of Canakinumab in AIDs and SoJIA patients in clinical practice.

**Methods:** Use Canakinumab at our Institute was commenced in 2012 y. The study included 19 pts, among them 12 had AIDs (including CAPS – in 8 pts: MWS – in 6, and CINCA/NOMID- in 2 pts; TRAPS - in 3 pts; Schnitzler syndrome – in 1), 7 pts had SoJIA. Among AIDs pts there were 7 females and 5 males, 9 pediatric and 3 adult pts, 2 pts from pediatric population getting adult by the time of analysis. Mean AIDs pts age at inclusion was 18,6 y (3–44), infantile disease onset was recorded in 9 pts, in 6 out of them – it was a neonatal onset from the moment of birth. Two familial MWS cases were included. Disease duration ranged from 3 to 44 years. Genetic mutations were established in 9 pts, including: gene NLRP3- 6 (Thr436Ile, Thr438Ile, Thr350Met – in 4 pts (two familial cases)), gene TNFRSF1A - 3 (His51Tyr, Cys59Arg, Cys99Arg). All AIDs pts presented with rash, fever, conjunctivitis or uveitis (8), neurosensory deafness (4), arthritis symptoms (9), lymphadenopathy (7), CNS involvement in 2, abdominal pain (5), stomatitis (4), physical retardation in CINCA/NOMID pts, intellectual retardation and cognitive impairment in 1 patient. SoJIA pts were aged 3,5 -17,5 y.o. predominantly males (5), with disease duration 1 - 16 y. All pts presented with systemic manifestations, 4 pts had severe polyarthritis. Increased levels of acute phase markers were documented in all pts. Canakinumab efficacy was estimated based on changes in ESR, CRP and WBC count vs baseline.

**Results:** Canakinumab was administered s/c at 2–4mg/kg (max 150 mg) once every 8 weeks in AIDs pts, and at 4–6mg/kg (max 300mg) once in every 4 weeks in SoJIA pts. Canakinumab therapy duration in AIDs pts varied from 3mo to 2,5y, in SoJIA pts – from 9mo to 4y. Rapid clinical improvement was documented in all pts, with resolution of systemic manifestations and normalizing levels of acute phase markers. Prolonged ESR and CRP normalization was observed in one CINCA/NOMID patient. In 4 SoJIA pts arthritis manifestations were not sufficiently controlled. Canakinumab tolerability was satisfactory in all AIDs and SoJIA pts. No serious adverse reactions were documented. Canakinumab discontinuation in one SJIA patient was associated with secondary drug failure and onset of macrophages activation syndrome (MAS).

**Conclusions:** The single Federal Center experience with Canakinumab in clinical practice in AIDs and SoJIA pts demonstrated high efficacy and good tolerability of this medication. No serious adverse events were noted. In SoJIA pts Canakinumab use should be viewed as possible option at early stages of the disease with systemic and initial joint involvement, whilst efficacy in pts with advanced arthritis turned out to be insufficient.

**Disclosure of Interest:** None declared

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## FRI0509 PREVALENCE OF SARCOIDOSIS AND AUTOINMUNE DISEASE IN NOT NECROTIZING GRANULOMATOSIS

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**Background:** The diagnosis of not necrotizing granulomatosis (NNG) is very frequent in clinical practice. Physicians often focused their attention on sarcoidosis. However, there are many conditions that can cause this histological diagnosis, including infectous diseases, neoplasms or inflamatory diseases. There ara a few studies into the spectrum of pathologies that cause NNG; consequently, except for sarcoidosis, little information is available (1,2).

**Objectives:** This study has been designed to determine the prevalence of sarcoidosis and autoinmune diseases in not necrotizing granulomatosis.

**Methods:** We recolected all the tissue samples described as not necrotizing inflammation from 1 January 2010 to 31 december 2014 in the University Hospital of Santiago de Compostela. We recolected socio-demographic, analytical and tissue characteristics. We followed these patients and we described the final diagnosis.

**Results:** During the study period, a total of 290 samples of 207 patients were involved. The 50.7% were women, their mean age was 51,23 years. Concerning the sample origin, the distribution was as follows: skin 68 (32,9%), lymphadenopathy 55 (26,6%), Transbronchial biopsy 30 (14,5%), lung 12 (5,8%) and others 42 (20,2%). Concerning to final diagnosis, we found sarcoidosis 124 (59,9%); infectous diseases 16 (7,7%), including tuberculosis infection 8 (4,0%) and nontuberculous mycobacterial infection 3 (1,4%); Foreign body granulomatosis 13 (6,3%); neoplasms 12 (5,9%); autoinmune disease 6 (3,1%),

2 of them Wegener granulomatous (0,9%), 1 chronic polyarticular arthritis (0,5%), 1 Autoimmune hepatitis (0,4%), 1 systemic lupus erythematosus (0,5%) and 1 alopecia (0,5%); rosacea 3 (1,4%); Crohn disease 2 (0,9%); cheilitis 2 (0,9%) and amyloidosis 1 (0,5%). The diagnosis was not determinated in 12 patients (5,9%).
**Conclusions:** The prevalence of sarcoidosis in NNG is almost 50%. However, the autoinmune disease is considerably lower (2,5%), being Wegener granulomatous the most frequently reported autoinmue disease as it has been described in the literature. The alternative diagnosis most frequent was infectous diseases, including tuberculosis. In 90% of cases, final diagnosis was realized.
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## FRI0510 LONG-TERM POST PARTUM FOLLOW-UP OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASES NEWLY DIAGNOSED DURING PREGNANCY

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**Background:** Undifferentiated connective tissue disease (UCTD) is a group of systemic autoimmune conditions not fulfilling the classification criteria for a definite connective tissue disease (CTD). While an average of 20–40% of UCTD patients develop a defined CTD during follow-up, the remaining patients maintain an undefined diseases.
**Objectives:** The objective was to assess flare or differentiation into well-defined CTD of UCTD newly diagnosed during pregnancy and to evaluate the prevalence of obstetric complications in the context of the new diagnosis.
**Methods:** We examined 54 patients with UCTD newly diagnosed during pregnancy, followed during pregnancy and after delivery at our rheumatologic unit. Diagnosis of UCTD was made at the time of pregnancy. Women in their first trimester ($T_0$) were screened using a two-step approach using a self-administered 10-item questionnaire, a subsequent testing for rheumatic autoantibodies (ANA, anti-dsDNA, ENA, anticardiolipin antibodies, anti-β2-glycoprotein I antibodies and lupus anticoagulant) and evaluation by a rheumatologist, who made the final diagnosis. The same questionnaire was re-administered at least one year after delivery ($T_1$) and the same rheumatic autoantibodies were tested at the same time.
**Results:** Fourty-two patients (77.77%) showed persistence or worsening of symptoms and 45 (83.33%) had at least one positivity for autoantibodies at $T_1$. The diagnosis of UCTD was confirmed in 29 patients (53.70%). Sixteen (16/54) women (29.62%) received a final diagnosis of another rheumatic disease: 12 patients with systemic lupus erythematosus (22.22%), 2 (3.70%) antiphospholipid syndrome, 1 (1.85%) spondyloarthritis and 1 (1.85%) Behçet disease. Amelioration of symptoms with a resulting unconfirmed diagnosis was seen among 9/54 (16.67%) of them. We then focused on the pregnancy that was ongoing at $T_0$. We observed some obstetrical complications: 3 miscarriages, 3 fetal loss, 6 hypertensive disorders, 4 intrauterine growth restriction, 6 preterm deliveries and 8 small for gestational age babies. These major obstetrical complications were not significantly different in the three different groups of new diagnoses. Also in the univariate analysis performed through Fisher's test for each single obstetric complication there was no significant difference between groups.
**Conclusions:** The questionnaire is an optimal screening method to detect undiagnosed rheumatic diseases in pregnancy, in particular UCTDs. Furthermore, in spite of their evolution or remission, UCTDs are always associated with negative effects on the outcome of pregnancy.
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## FRI0511 THE EFFECT OF ATTACK FREQUENCY ON QUALITY OF LIFE (QOL) AND MENTAL HEALTH IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)

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**Background:** FMF is an inherited autoinflammatory disease characterized by recurrent episodes of fever, acute serosal inflammation and pain. The QoL and mental health of FMF patients may be affected due to life-long disease, attack frequency, resistance of the disease, and severe complications such as amyloidosis.
**Objectives:** In this study, we investigated the effect of attack frequency on QoL and mental health (MH) in FMF patients.
**Methods:** A total of 149 patients (79 F, 70 M) diagnosed with FMF in Ankara Numune Education and Research Hospital Rheumatology Clinic, and 100 healthy controls (HC) (54 F, 46 M) were included in the study. Patients diagnosed with FMF according to Tel-Hashomer criteria. Mean±SD age of FMF patients is 36±10 year, and mean±SD age of HC is 35±8 year, NS. Mean±SD at onset of FMF patients is 17±4 year, and mean±SD age of disease duration is 107±71 months. FMF patients were classified as the ones that had >2, 1–2, and no attacks in the previous 3 months. The QoL was determined with SF-36, and MH was analyzed with Hospital Anxiety and Depression Scale (HADS). Student t test was used to compare FMF and HC groups for HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D) scores, and physical component summary scores (PCSS), mental component summary scores (MCSS), and subscale scores of SF-36. One Way Anova was used to analyze FMF patients for HADS-A and HADS-D, and PCSS and MCSS of SF-36 in relation with attack frequency. The associations of age, gender, SF-36 and HADS scores in both groups, and comparisons of SF-36 and HADS scores in relation with age at diagnosis and duration of disease in FMF patients were analyzed with Pearson's correlation. $p<0.05$ was regarded as significant.
**Results:** The summary scores of SF-36, and HADS-A and HADS-D of FMF patients and HC are presented in Tables 1. SF-36 summary scores, and HADS scores of FMF patients in relation with attack frequency, and SF-36 subscale scores of FMF patients and HC are presented in Table 2 and Figure 1. There were no significant correlations among age and gender, and QoL and mental health scores in either group. PCSS and MCSS of SF-36 were significantly lower, and HADS-A and HADS-D scores were significantly higher in FMF patients compared to HC ($p<0.001$). In addition, attack frequency showed negative correlations with PCSS and MCSS, and positive correlations with HADS-A and HADS-D in FMF patients ($p<0.001$). PCSS and MCSS showed negative correlations with HADS-A and HADS-D in FMF patients ($p<0.001$). Age at diagnosis and duration of disease were not correlated with QoL or MH scores.

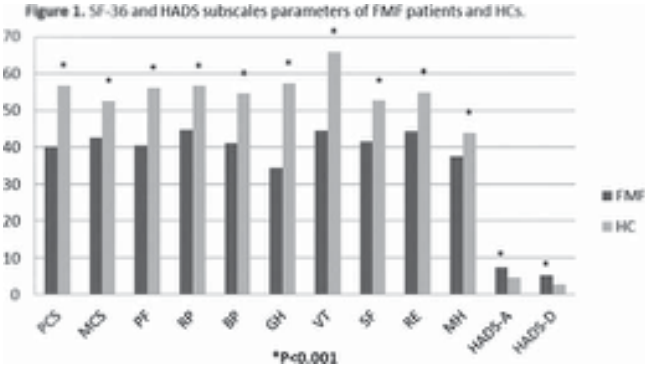
Table 1. Comparison of PCS, MCS, HADS-A and HADS-D in FMF patients and HC

| | FMF patients (n=149) | HC (n=100) | P values |
|---|---|---|---|
| PCS | 40±7* | 56±3* | <0.001 |
| MCS | 43±8* | 52±2* | <0.001 |
| HADS-A | 7.4±1.6* | 4.5±1.5* | <0.001 |
| HADS-D | 5.3±2.1* | 2.8±1.5* | <0.001 |

Table 2. PCS, MCS, HADS-A and HADS-D scores of FMF patients according to frequency of attacks in the last 3 months

| | >2 attack (n=32) | 1–2 attack (n=41) | No attack (n=76) |
|---|---|---|---|
| PCS | 28±5* | 34±7* | 42±6* |
| MCS | 32±5* | 33±5* | 46±6* |
| HADS-A | 8.5±1.5* | 8.2±1.0* | 7.2±1.7* |
| HADS-D | 8.8±0.7* | 7.6±0.8* | 4.5±1.8* |

*Mean ± SD. SD: Standart deviation, NS: Not significant.




**Conclusions:** In this study, we found lower QoL scores, and higher anxiety and depression scores in FMF patients compared to HC. Attack frequency determined this effect independent of age and gender.
**Disclosure of Interest:** None declared
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FRI0512 **IGG4-RELATED DISEASE IS ASSOCIATED WITH A HISTORY OF MALIGNANCY**

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**Background:** IgG4-related disease (IgG4-RD) is a fibroinflammatory disease of unclear etiology[1]. Some studies suggest that IgG4-RD predisposes patients to malignancy or is a *forme fruste* of cancer[2], but we have frequently observed IgG4-RD patients with a history of malignancy preceding the clinical onset of IgG4-RD.
**Objectives:** We sought to determine whether a history of malignancy was more common among patients at the onset of IgG4-RD compared to controls.
**Methods:** We identified IgG4-RD patients with a history of invasive malignancy from a well-defined cohort of 125 patients and compared their malignancy history to those of two reference groups. First, we calculated a standardized prevalence ratio against general US population estimates from the Surveillance, Epidemiology, and End Results (SEER) database. Second, we identified up to five age- and gender-matched controls for each case and calculated the odds of malignancy among those with IgG4-RD compared to controls using conditional logistic regression.
**Results:** The mean age at IgG4-RD onset was 50.3±14.9 years and 61% of the patients were male. Twenty (16%) had been diagnosed with 21 malignancies before the diagnosis of IgG4-RD. The observed prevalence of malignancy in this cohort was 2.5 times higher (95% CI:1.1–3.6) than expected compared to the SEER database. Compared with matched controls, a history of malignancy was more than three-fold higher in IgG4-RD (OR 3.1;95% CI:1.6–6.2).
**Conclusions:** Our findings suggest that malignancy is associated with the subsequent development of IgG4-RD in a subset of patients with IgG4-RD. Potential explanations include shared risk factors for both IgG4-RD and cancer, the triggering by cancer of autoantigen expression leading to IgG4-RD, and an increased risk of IgG4-RD resulting from cancer treatment.
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## Diagnostics and imaging procedures

FRI0513 **VALIDATING MRI-DETECTED INFLAMMATION THRESHOLDS PREDICTIVE OF STRUCTURAL DAMAGE PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A RANDOMIZED PLACEBO-CONTROLLED TRIAL**

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**Background:** In rheumatoid arthritis (RA), the concept that subclinical inflammation causes damage progression is now well established, but there is little work on how much inflammation is safe.[1] A previous study established RA MRI Scoring (RAMRIS) synovitis and osteitis thresholds (≤3 each and ≤9 [≤3 plus 2*≤3] as a total inflammation score) that correlated with a low risk of structural damage progression.[2] Further validation of these thresholds may guide physicians in clinical practice more reliably to identify individuals with a low likelihood of structural damage progression.
**Objectives:** To validate the performance of RAMRIS synovitis, osteitis and combined total inflammation thresholds in the prediction of structural damage progression.[1]
**Methods:** AVERT (Assessing Very Early Rheumatoid arthritis Treatment) was a Phase IIIb, randomized, active-controlled, 24-month trial, with a 12-month, double-blind treatment period. Patients with early RA received abatacept + MTX, abatacept monotherapy or MTX. Contrast-enhanced MRIs of the dominant hand and wrist were performed. MRI data were pooled from all three treatment arms (intent-to-treat population) for this *post hoc* analysis. Inflammation (synovitis, osteitis and combined) and erosion were scored by two central readers at baseline, Month 6 and Month 12. Structural damage progression was defined as erosion change >0.5. Patients were stratified into "low" and "not low" risk groups for MRI structural progression based on their inflammation scores at the start of the observation period: low: ≤3 for synovitis, ≤3 for osteitis and ≤9 when combined (with osteitis double-weighted due to its strong correlation with progression), as suggested by Baker et al.[2] Log odds ratio of probability of progression were compared between subgroups.
**Results:** 351 patients were randomized and treated, with MRIs at baseline; 276 (78.6%) and 235 (67.0%) also had MRI data available at Month 6 and Month 12, respectively. The percentage of patients with structural damage progression at follow-up was significantly higher in the "not low" versus "low" risk subgroup for all comparisons (Table). The probability of progression from Month 6 to Month 12 was significantly lower among patients with synovitis score ≤3, osteitis score ≤3, and total inflammation score ≤9 at Month 6.

| MRI progression from 0 to 12 months by MRI scores at baseline | | | | | | |
|---|---|---|---|---|---|---|
| | Synovitis | | Osteitis | | Synovitis + (2*Osteitis) | |
| Score category | Low (≤3) (n=85) | Not low (n=150) | Low (≤3) (n=155) | Not low (n=80) | Low (≤9) (n=130) | Not low (n=105) |
| MRI progression, % | 21.2 | 50.0 | 31.0 | 56.3 | 26.2 | 56.2 |
| Odds ratio (95% CI) | 0.27 (0.15, 0.49) | | 0.35 (0.20, 0.61) | | 0.28 (0.16, 0.48) | |
| p value | <0.0001 | | 0.0002 | | <0.0001 | |
| **MRI progression from 0 to 12 months by MRI scores at Month 6** | | | | | | |
| | Synovitis | | Osteitis | | Synovitis + (2*Osteitis) | |
| Score category | Low (≤3) (n=95) | Not low (n=136) | Low (≤3) (n=179) | Not low (n=52) | Low (≤9) (n=155) | Not low (n=76) |
| MRI progression, % | 18.9 | 53.7 | 29.6 | 73.1 | 24.5 | 69.7 |
| Odds ratio (95% CI) | 0.20 (0.11, 0.37) | | 0.16 (0.08, 0.31) | | 0.14 (0.08, 0.26) | |
| p value | <0.0001 | | <0.0001 | | <0.0001 | |
| **MRI progression from 6 to 12 months by MRI scores at Month 6** | | | | | | |
| | Synovitis | | Osteitis | | Synovitis + (2*Osteitis) | |
| Score category | Low (≤3) (n=108) | Not low (n=147) | Low (≤3) (n=200) | Not low (n=55) | Low (≤9) (n=175) | Not low (n=80) |
| MRI progression, % | 11.1 | 28.6 | 18.0 | 32.7 | 16.0 | 32.5 |
| Odds ratio (95% CI) | 0.31 (0.16, 0.63) | | 0.45 (0.23, 0.88) | | 0.40 (0.21, 0.73) | |
| p value | 0.0011 | | 0.0197 | | 0.0033 | |

**Conclusions:** The applied inflammation thresholds distinguished between patients with RA at lower or higher risk of structural damage progression, validating the previously proposed thresholds. This provides further support for the clinical value of measuring inflammation via MRI, as well as its role in predicting structural damage progression.
**References:**
[1] Gandjbakhch F, et al. J Rheumatol 2014;41:398–406.
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**Disclosure of Interest:** H. A. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, J. F. Baker: None declared, M. Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Janssen, Merck, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer-Ingelheim, Celgene, Eli Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, Wyeth, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, P. Emery Grant/research support from: AbbVie, Merck, Pfizer, Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, Lilly, Novartis, Samsung Bioepis, P. G. Conaghan Consultant for: AbbVie, Lilly, Novartis, Pfizer, Speakers bureau: AbbVie, Janssen, Roche
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FRI0514 **ADDING MRI OF THE SPINE TO THE ASAS CLASSIFICATION CRITERIA FOR AXIAL SPONDYLOARTHRITIS, REDUNDANT OR BENEFICIAL? DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE)-COHORT**

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**Background:** The ASAS definition of a positive MRI is solely based on inflammation in the sacroiliac joints (SIJ), although spinal inflammatory lesions on MRI suggestive of axial Spondyloarthritis (axSpA) may also occur. It is not well known how often inflammation in the spine occurs in absence of inflammation in the SIJ and consequently what the utility is of including inflammation in the spine in the definition of a positive MRI.
**Objectives:** To analyze the prevalence of spinal inflammation on MRI in patients with chronic back pain (CBP) at baseline and one-year follow-up, and to evaluate the yield of adding MRI-spine as imaging criterion to the ASAS classification criteria for axial SpA.
**Methods:** The SPACE-cohort includes patients with CBP (≥3 months, ≤2 years, onset <45 years) from five participating centres in Europe. All available baseline (BL) and one-year follow-up (FU) MRI of SIJ and spine were scored by 2 well-calibrated readers. MRI-SI were scored according to the ASAS definition. Bone marrow oedema suggestive of axSpA was assessed in the entire spine and only counted if visible on ≥2 consecutive slices. To define a positive MRI-spine, two cut-off values were used: ≥3 inflammatory lesions (ASAS consensus definition) and ≥5 inflammatory lesions (defined as the best cut-off in earlier analyses). Adjudication for the ASAS definition by an experienced reader was performed in case of disagreement and all modalities were considered positive if 2/3 readers agreed.
**Results:** All patients with both MRI-spine and MRI-SIJ available at BL (n=329) and FU (n=168) were included in the analyses. At BL 43/329 (13.1%) of patients

had a positive MRI-SIJ, of which 7/43 (16.3%) patients had a positive MRI-spine (ASAS consensus definition, ≥3 inflammatory lesions) and 2/43 (4.7%) if defined by ≥5 inflammatory lesions. Positive MRI-SIJ at FU was seen in 28/168 (16.7%) patients, 14 of which were also positive at BL; MRI-spine positivity was identified in 2/28 (7.1%) and 1/28 (3.6%) patients for the ASAS definition defined by ≥3 and ≥5 inflammatory lesions, respectively. In total, 4 patients had a positive MRI-spine and a negative MRI-SIJ: at BL 2 patients according to the ASAS definition of whom 1 also fulfilled the alternative definition. At FU this was 2 (different patients than at baseline) and 0 patients, respectively. Addition of MRI-spine to the classification criteria by the ASAS definition of ≥3 inflammatory lesions would lead to classification of 3 additional patients via imaging arm, with 1 patient already fulfilling the clinical arm.

**Figure 1.** Prevalence of positive MRI-SI according to ASAS definition and positive MRI-Spine at baseline and one-year follow-up using two different cut-off values; ≥3 inflammatory lesions (ASAS consensus definition) and ≥5 inflammatory lesions, respectively.

| BASELINE | | MRI of the SI joints | | |
|---|---|---|---|---|
| | | Positive | Negative | |
| MRI of the Spine, cut-off ≥3 inflammatory lesions | Positive | 7 | 2 | 9 |
| | Negative | 36 | 284 | 320 |
| | Total | 43 | 286 | 329 |
| | | MRI of the SI joints | | |
| | | Positive | Negative | |
| MRI of the Spine, cut-off ≥5 inflammatory lesions | Positive | 2 | 1 | 3 |
| | Negative | 41 | 285 | 326 |
| | Total | 43 | 286 | 329 |

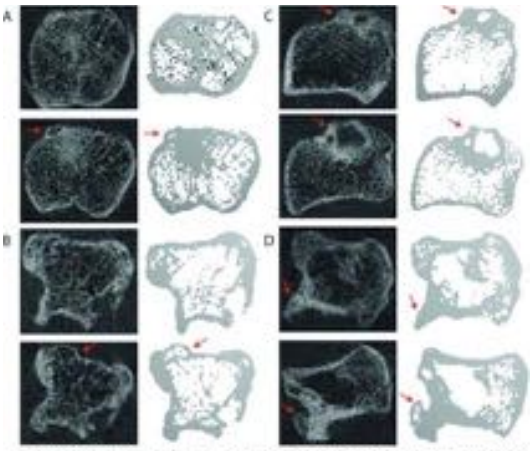
| FOLLOW-UP | | MRI of the SI joints | | |
|---|---|---|---|---|
| | | Positive | Negative | |
| MRI of the Spine, cut-off ≥3 inflammatory lesions | Positive | 2 | 2 | 4 |
| | Negative | 26 | 138 | 164 |
| | Total | 28 | 140 | 168 |
| | | MRI of the SI joints | | |
| | | Positive | Negative | |
| MRI of the Spine, cut-off ≥5 inflammatory lesions | Positive | 1 | 0 | 1 |
| | Negative | 27 | 140 | 167 |
| | Total | 28 | 140 | 168 |

**Conclusions:** In this cohort, a positive MRI-spine in the absence of sacroiliitis on MRI was rarely seen Addition of MRI-spine as an imaging criterion to the ASAS criteria had a low yield in number of classifications. Therefore, performing MRI of the spine at either baseline or one-year follow-up is of little value in patients with short duration of CBP and suspicion of axial SpA.
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## FRI0515 QUANTIFICATION AND IMPACT OF SECONDARY OSTEOARTHRITIS IN PATIENTS WITH ANTI-CITRULLINATED PROTEIN ANTIBODIES POSITIVE RHEUMATOID ARTHRITIS

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**Background:** Erosions have been described as the hallmark of bone damage in RA, resembling catabolic changes [1]. Usually bone erosions in RA are not accompanied by proliferative bone changes, which are typically found in psoriatic arthritis and spondyloarthritis [2]. Although such changes are much less pronounced in RA than in other diseases, RA patients may not be completely spared from bony proliferations, which likely resemble the development of secondary osteoarthritis.
**Objectives:** To search for evidence of secondary osteoarthritis in patients with rheumatoid arthritis (RA) in a cross-sectional and longitudinal setting and to relate osteophyte formation to functional outcome.
**Methods:** Anti-citrullinated protein antibody positive (ACPA+) RA patients underwent high-resolution peripheral quantitative computed tomography (HR-pQCT) of the hand. Cross-sectional and longitudinal measurements were performed. Number and size of osteophytes as well as bone erosions were documented. Relation of osteophytes to bone erosions and to demographic and disease specific data was evaluated by multiple logistic regression models.
**Results:** 202 ACPA+ RA patients were enrolled in the cross-sectional and 77 subjects in the longitudinal analysis (interval: 1.5 years). The mean number and size of osteophytes was 1.3±2.3 and 9.4±23.9 $mm^3$ respectively. Osteophyte number was significantly ($p<0.001$) correlated to erosion number and osteophyte size to erosion size ($p<0.001$). Moreover, presence and size of osteophytes were related to age ($p<0.001$), disease duration ($p<0.001$) and health assessment questionnaire (HAQ) ($p=0.013$). Multivariate regression analyses showed an independent association between osteophytes and erosions. In the longitudinal analysis the mean number ($p=0.033$) and size ($p<0.001$) of osteophytes significantly increased in RA patients during their disease course (Figure 1).



Transversal sections of metacarpal heads at baseline (upper image in A-D) and follow-up measurement (lower image in A-D). Red arrows indicate osteophytes.

**Conclusions:** Age, disease duration and bone erosions are associated with osteophytes indicating development of secondary osteoarthritis in patients with RA.
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## FRI0516 ULTRASONOGRAPHIC ASSESSMENT OF NEWLY DEVELOPED ELDERLY-ONSET RHEUMATOID ARTHRITIS: A COMPARISON WITH YOUNGER-ONSET RHEUMATOID ARTHRITIS

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**Background:** Elderly-onset RA (EORA) is defined as the onset of RA at 65 years of age or older and Patients with EORA frequently present with acute onset of the disease dominated by stiffness and pain in the shoulder and their daily activities are generally impaired. However, specific knowledge on sonographic findings in patients with newly-developed EORA remains limited.
**Objectives:** The aim of the present study was to clarify specific sonographic features in patients with new-onset EORA.
**Methods:** We included consecutive patients who were diagnosed with RA according to the 2010 ACR/EULAR classification criteria. EORA was defined as a RA onset at ≥65 years of age and YORA as an onset at <65 years. Prior to the initiation of therapy, we evaluated positivity for anti-CCP antibodies as well as DAS28-ESR and HAQ score. Musculoskeletal ultrasonography was performed at the initial visit and the investigation sites included the dominant side of the shoulder (long head biceps tendon, subacromial-subdeltoid bursa, and glenohumeral joint), wrist, metacarpophalangeal (MP) joints, and knee joint. Gray scale (GS) and power Doppler (PD) signals were subjectively graded for each site using a semi-quantitative scoring method, which consisted of a scale of 0–3, and the sum of the GS scores of a single joint was calculated as the total GS score for each joint and the sum of PD scores as the total PD score. We investigated sonographic differences between EORA and YORA and the relationships between disease activity variables and ultrasonographic findings were analyzed in patients with EORA using Spearman's correlation coefficient. Proportions were calculated by Fisher's exact test.
**Results:** EORA was diagnosed in 47 patients (mean age 79.4 ± 7.3 years) and YORA in 35 patients (age 48.1 ± 12.5 years). The positive ratios of GS and PD signals were 91.3% and 83.1%, respectively, at the shoulder joint in EORA patients, and both proportions were significantly higher than those in YORA patients (61.2% for GS [$p<0.01$] and 50.0% for PD [$p<0.01$]). The remainder of the examined joints including the wrist, MP and knee joints showed no significant differences in the GS or PD positive ratios between the two groups. We subsequently stratified EORA patients according to anti-CCP antibody positivity.

The t-GS score of the shoulder joint was significantly higher in the anti-CCP negative group than in the positive group (4.6 ± 2.0 and 2.8 ± 2.5, respectively, $p<0.05$). However, the remainder of the examined joints showed no significant differences. Furthermore, no significant differences were observed between the two groups in terms of the t-PD scores of all joints. In EORA patients, the t-GS and t-PD scores of the shoulder joint strongly correlated with the HAQ score ($r=0.72$, $p<0.0001$, $r=0.68$, $p<0.0001$, respectively) and, among the shoulder joint components, long head biceps tendon showed the strongest correlation both in the t-GS and t-PDS scores ($r=0.64$, $p<0.0001$, $r=0.55$, $p<0.001$). The t-PD scores of the shoulder, wrist, and MP joints correlated with DAS 28-ESR ($r=0.62$, $p<0.0001$, $r=0.43$, $p<0.05$, $r=0.38$, $p<0.05$).

**Conclusions:** Shoulder joint involvement was a specific feature in patients with EORA and contributed to functional disability and increased disease activity.

**References:**

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**Disclosure of Interest:** None declared

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## FRI0517 THE OMERACT ULTRASONOGRAPHIC CRITERIA FOR ELEMENTARY LESIONS IN CALCIUM PYROPHOSPHATE DEPOSITION DISEASE: RESULTS OF A DELPHI PROCESS BY ULTRASOUND WORKING GROUP

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**Background:** In the last years, the role of Ultrasound (US) for the diagnosis of calcium pyrophosphate deposition disease (CPPD) has been extensively growing. However, some issues have still to be resolved, being one of the most important the heterogeneity of the criteria used for the identification of calcium pyrophosphate crystals (CPP) deposits.

**Objectives:** The aim of this study was to define the US elementary lesions in CPPD

**Methods:** The panel of experts was compound by 18 members of the Omeract US group, especially interested in microcrystalline arthritides.

The first step was a systematic literature review aimed to select the studies regarding US and CPPD in order to collect all the definitions about US elementary findings in CPPD. The definitions retrieved by the literature were used for drawing up a first group of propositions. The experts evaluated these definitions, adding any further preposition according to their experience that could improve the initial set. According to the systematic review, the propositions about US elementary lesions were divided by anatomical structure: fibrocartilage, hyaline cartilage, tendons and synovial fluid. For each structure were defined: shape, echogenicity, localization and behaviour at dynamic scanning.

In the next rounds, the experts voted their level of agreement for each proposition according to the Likert scale (1 strongly disagree 5:strongly agree) with the possibility to add comments. After each round, a facilitator modified the prepositions according to the comments received. The consensus for each preposition was considered achieved if the agreement was equal or more than 75%

| Structure | Shape | Echogenicity | Localization | Behavior at Dynamic scanning |
|---|---|---|---|---|
| Fibrocartilage | deposits of variable shape | hyperechoic (similar to the bone cortex) | localized within the fibrocartilage structure | remain fixed and move together with the fibrocartilage during dynamic assessment (i.e. joint movement and probe compression) |
| Hyaline cartilage | deposits varying in size and shape | hyperechoic (similar to the bone cortex echogenicity) that do not create posterior shadowing | Localized within the hyaline cartilage | the deposits remain fixed and move together with the hyaline cartilage (i.e. joint movement and probe compression) |
| Tendon | multiple, linear (parallel to the tendon fibrillar structure and not in continuity with the bone profile) deposits | Hyperechoic (in relation to the tendon echogenicity), that generally not create posterior shadowing. The deposits maintain their high degree of echogenicity even at very low levels of gain and are not affected by anisotropy as the surrounding tendon. | Localized within the tendon | remain fixed and move together with the tendon during movement and probe compression. |
| Synovial fluid | deposits of variable size (from punctuate to large) | hyperechoic (similar to the bone cortex echogenicity), that generally not create posterior shadowing. | Localized within the synovial fluid | are mobile according to joint movement and probe pressure. |

**Results:** Three Delphi rounds were necessary in order to reach agreement. After the first round, 20 of the 93 definitions retrieved by the literature reached the consensus. During the second one, 23 propositions achieved the agreement while, after the last Delphi round, the number of propositions increased to 27. All the members responded to all the phases of the survey.

Final definitions for US identification of CPPD are illustrated in Table 1

**Conclusions:** To our knowledge this is the first set of definitions for US identification of CPPD created according to a consensus procedure between experts. These definitions should help sonographers to classify correctly patients with suspected CPPD thus giving the possibility to organise multicentre studies. However, the reliability and the diagnostic accuracy of this set has to be assessed before they become integral part of the daily clinical practice

**Disclosure of Interest:** None declared

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## FRI0518 ULTRASOUND DEFINITIONS FOR VASCULITIS IN CRANIAL AND LARGE VESSEL GIANT CELL ARTERITIS: RESULTS OF A DELPHI SURVEY OF THE OMERACT ULTRASOUND LARGE VESSEL VASCULITIS GROUP

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**Background:** In a systematic literature review (SLR), we identified halo sign, stenosis, occlusion, compression sign and a decreased vessel wall pulsation as elementary ultrasound (US) lesions in giant cell arteritis (GCA).

**Objectives:** To establish consensus-based definitions for the key elementary US lesions in GCA.

**Methods:** We invited 25 rheumatologists from 13 countries experienced in musculoskeletal and vascular US to participate in a Delphi exercise. Based on the results from the SLR and international expert consensus a questionnaire was developed including 12 statements on the definitions of normal temporal and extra-cranial large arteries, arteriosclerosis, halo sign, stenosis, occlusion, compression sign, and vessel wall pulsation. The experts were asked to express their level of agreement or disagreement with the proposed statements. A consensus was defined as agreement of $\geq$75% of participants.

**Results:** The response rate was 24/25 (96%) in round 1 and 24/24 (100%) in round 2. A consensus was achieved for 9/9 Delphi statements [normal temporal and extra-cranial large arteries, arteriosclerosis, halo sign, stenosis of temporal and extra-cranial large arteries, occlusion, compression sign (temporal arteries), US assessment of compression sign (temporal arteries) in round 1. In round 2, 3/3 Delphi statements (arteriosclerosis, halo sign, stenosis of temporal arteries) were redefined. The statements on vessel wall pulsation (definition and assessment) and measurement of vessel wall thickness did not reach the threshold for consensus. The halo and compression signs were deemed to be the most important US signs for GCA with 100% and 83.3% expert agreement, respectively.

**Conclusions:** This is the first international consensus on definitions for elementary US lesions in GCA. The next steps of the OMERACT project will be web- and patients based exercises testing the reliability of the new definitions.

**Disclosure of Interest:** None declared

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## FRI0519 ULTRASOUND DEFINITION OF CARTILAGE CHANGE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RELIABILITY STUDY BY THE OMERACT ULTRASONOGRAPHY

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**Objectives:** To produce ultrasound (US) consensus-based definitions of cartilage change in rheumatoid arthritis (RA) and assess its intraobserver and interobserver reliability in a web-based exercise.
**Methods:** We conducted a Delphi study on US defined cartilage change and a proposed semiquantitative (SQ) US scoring system for cartilage change in RA. A written Delphi questionnaire was developed based on a systematic literature review and expert international consensus and was distributed via consecutive written questionnaires by email to a group 35 rheumatologists from 17 countries with experience in musculoskeletal US. Taskforce members performed US B mode examination of the metacarpal cartilage in metacarpophalangeal joints 2–5 in RA patients and the images were collected in an electronic database. A reference image atlas of cartilage changes was developed for scoring 123 anonymized images including 25 duplicate images. These were sent to the participants who independently scored the images. Intraobserver reliability was assessed by Cohen's kappa and interobserver reliability by Fleiss' kappa.
**Results:** Group agreement (76–100%) was reached for 6 statements concerning: i) MSUS definition and assessment of normal hyaline cartilage, ii) elementary cartilage lesions in MSUS and iii) grading of elementary cartilage lesions in patients with RA in a two-round Delphi consensus process. A three-grade SQ (0–2) scoring system (grade 0, normal cartilage; grade 1, minimal change: blurring of outer and/or subchondral margin, focal thinning or incomplete loss of homogeneity of echostructure; grade 2, severe: diffuse thinning or complete loss of homogeneity of echostructure) was agreed for scoring cartilage damage in RA. Both intra- and inter-observer reliability were good (κ value of 0.87 and 0.64 respectively).
**Conclusions:** This study demonstrates that US is a reliable tool for evaluating cartilage in RA and strongly supports the use of a new reliable semiquantitative MSUS scoring system for cartilage change.
**Disclosure of Interest:** None declared
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## FRI0520 COMPARISON OF 18F-FLUORO-DEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY AND COMPUTED TOMOGRAPHY ANGIOGRAPHY FOR THE DIAGNOSIS OF GIANT CELL ARTERITIS: A PROSPECTIVE, CASE-CONTROL STUDY

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**Background:** Diagnosis of giant cell arteritis (GCA) is still a challenge. 18F-fluoro-deoxyglucose positron emission tomography scan (FDG-PET) and computed tomography angiography (CTA) are promising imaging techniques for the detection of GCA
**Objectives:** To compare the diagnostic performance of FDG-PET and CTA in patients with giant cell arteritis (GCA).
**Methods:** FDG-PET and CTA were acquired in 24 consecutive patients in whom temporal artery biopsy (TAB) was performed for suspected GCA. Results of FDG-PET and CTA were compared with the final clinical diagnosis based on a) the American College of Rheumatology GCA criteria set, b) clinical judgment including outcome under corticosteroids, and c) the absence of an alternative diagnosis after a 6 months follow-up. Sensitivity, specificity, and positive and negative predictive values (PPV, NPV) were calculated for each method.
**Results:** Fifteen of the 24 patients (62.5%) were ultimately diagnosed as having GCA. Strong FDG uptake in large vessels was found in 10 patients who all had GCA. Mean maximal standard uptake values (SUVmax) per patient measured at all the arterial territories were of 3.7 [range: 2.8–4.7]. FDG uptake was negative in 14 patients including 9 and 5 patients without and with GCA, respectively. Mural thickening suggestive of aortitis or branch vessel arteritis was observed on CTA in 11 patients with and 2 patients without GCA. No mural thickening was observed in 11 patients including 7 patients without and 4 patients with GCA. Overall, sensitivity of FDG-PET and CTA was 66.7% and 73,3%, respectively; specificity was 100% and 84.6%, NPV was 64.3% and 64.6%, and PPV was 100% and 84.6%, respectively.
**Conclusions:** Both FDG-PET and CTA have a strong diagnostic yield for the diagnosis of GCA. FDG-PET appeared to have a higher PPV as compared to CTA and may be the preferred noninvasive technique to evaluate patients with suspected GCA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2651

## FRI0521 RELIABILITY OF AN OMERACT RHEUMATOID ARTHRITIS TENOSYNOVITIS SCORING SYSTEM FOR WRIST AND HAND

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**Background:** Tenosynovitis in the hand occurs frequently and early in rheumatoid arthritis (RA) and sensitive outcome measures are important to assess and monitor the inflammatory activity. Magnetic resonance imaging (MRI) can visualize tenosynovitis and a semiquantitative scoring system for tenosynovitis in the hand has previously been suggested[1]. However, it did not include the metacarpophalangeal (MCP) flexor tendons. Furthermore, each increment of the scale covered a broad interval of tenosynovitis severity, potentially improving reliability but with a risk of reducing sensitivity to change over time.
**Objectives:** To assess the intra- and inter-reader agreement of a proposed OMERACT tenosynovitis scoring system in the wrist and MCP flexor tendons in the hands of RA patients.
**Methods:** Axial T1-weighted pre- and post-contrast fat-suppressed MR image sets (0.8mm slice thickness) of the hand of 43 patients receiving rituximab were obtained at baseline and after 3 (n=5), 6 (n=8), 9 (n=15) or 12 (n=15) months. The images were read and scored twice on separate days with intermediate re-randomization and re-anonymization by 4 readers blinded to patient data but not to chronology. The tendons of 6 extensor and 3 flexor tendon compartments of the wrist and 4 flexor tendon compartments of the 2nd to 5th MCP joints were assessed. Tenosynovitis was defined as peritendinous effusion (PE) or post-contrast enhanced tenosynovial proliferation (ETP) on 3 consecutive slices.

**Table 1** Intra- and inter-reader agreement for the wrist, metacarpophalangeal (MCP) flexor tendons and total score

| INTRA-READER | | Wrist | | | MCP flexor tendons | | | Total score | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline | Follow-up | Change | Baseline | Follow-up | Change | Baseline | Follow-up | Change |
| Reader 1 | SimICC | 0.91 | 0.82 | 0.82 | 0.89 | 0.89 | 0.81 | 0.90 | 0.90 | 0.88 |
| | PEA | 82.46 | 78.0 | 79.33 | 75.58 | 78.49 | 75.0 | 80.34 | 78.84 | 78.0 |
| | PCA | 99.48 | 99.22 | 99.48 | 100 | 100 | 99.42 | 99.64 | 99.46 | 99.66 |
| | SDC | | | 1.77 | | | 1.07 | | | 2.07 |
| Reader 2 | SimICC | 0.93 | 0.84 | 0.80 | 0.88 | 0.91 | 0.83 | 0.94 | 0.92 | 0.83 |
| | PEA | 81.90 | 76.92 | 80.25 | 73.84 | 80.81 | 78.49 | 79.42 | 78.12 | 79.71 |
| | PCA | 97.67 | 97.04 | 97.29 | 97.67 | 96.35 | 97.67 | 97.67 | 96.52 | 97.41 |
| | SDC | | | 1.98 | | | 1.15 | | | 2.70 |
| Reader 3 | SimICC | 0.84 | 0.81 | 0.76 | 0.79 | 0.86 | 0.68 | 0.87 | 0.86 | 0.84 |
| | PEA | 61.74 | 63.17 | 65.05 | 62.21 | 67.44 | 57.56 | 61.89 | 64.48 | 63.75 |
| | PCA | 97.60 | 96.59 | 96.27 | 100 | 99.42 | 96.51 | 98.34 | 97.46 | 96.34 |
| | SDC | | | 2.93 | | | 1.77 | | | 3.04 |
| Reader 4 | SimICC | 0.94 | 0.91 | 0.84 | 0.92 | 0.92 | 0.87 | 0.95 | 0.94 | 0.80 |
| | PEA | 80.62 | 83.37 | 76.94 | 81.98 | 79.07 | 70.35 | 81.03 | 82.04 | 74.91 |
| | PCA | 98.45 | 98.67 | 96.46 | 100 | 100 | 98.26 | 98.93 | 99.08 | 97.01 |
| | SDC | | | 2.34 | | | 1.13 | | | 2.86 |
| INTER-READER | AvmICC | 0.94 | 0.90 | 0.91 | 0.96 | 0.97 | 0.94 | 0.96 | 0.96 | 0.94 |
| | PEA | 42.51 | 48.06 | 50.26 | 40.99 | 48.71 | 42.44 | 42.04 | 48.57 | 47.85 |
| | PCA | 81.14 | 82.17 | 83.98 | 86.92 | 89.83 | 87.21 | 82.92 | 84.53 | 84.97 |
| | SDC | | | 1.65 | | | 0.87 | | | 1.82 |

Single measure intra-class correlation coefficients (SimICC) and average measure intra-class correlation coefficients (AvmICC) were calculated for intra-reader and inter-reader agreement respectively. An ICC ≥0.50 was considered good and an ICC ≥0.80 was considered very good. Percentage of exact agreement (PEA) was defined as the percentage of tendons given the same score within and between the readers (expressed as the average percentage for wrist, MCP tendons and total scores). Percentage of close agreement (PCA) was defined as the percentage of tendons given scores that differed ≤1 within and between the readers (expressed as the average percentage for wrist, MCP tendons and total scores). Smallest detectable change (SDC) was calculated for change scores and expresses the minimal amount of change that can be discriminated from the measurement error of the scoring system.

Pathologies were measured perpendicularly to the tendon at the thickest point of the effused or enhanced tenosynovium. Tenosynovitis was scored as follows: 0: no PE or ETP, 1: >0 but <1.5mm PE or ETP, 2: ≥1.5 but <3mm PE or ETP, 3: ≥3mm PE or ETP. Change in tenosynovitis over time was assessed using descriptive statistics and the Wilcoxon signed-rank test. Intra- and inter-reader agreement was calculated using single measure and average measure intra-class correlation coefficients (ICC), percentage of exact and close agreement (PEA and PCA) and the smallest detectable change (SDC).

**Results:** The mean (SD) change in tenosynovitis score between baseline and follow-up was -1.38 (2.84) for wrist, -0.94 (1.85) for MCP flexor tendons and -2.31 (4.63) for total score (all $p<0.01$). Intra- and inter-reader ICC for status scores were very good in all readers for all parameters (except baseline scores in the MCP region in 1 reader). Intra-reader ICC for change scores were good to very good in all readers for all parameters, and inter-reader ICC for status and change scores were very good in all readers for all parameters. Intra-reader PEA for status and change scores was above 57% and PCA was above 95% for all parameters. Inter-reader PEA was above 40% and PCA was above 81% for all parameters. Intra-reader SDC was below 3.0 for all parameters, except for total score in 1 reader (3.04). Inter-reader SDC was below 2.0 for all parameters (table 1).

**Conclusions:** The proposed OMERACT tenosynovitis scoring system showed high intra- and inter-reader agreement for wrist and MCP tendons and is a reliable tool for MRI-assessment of tenosynovitis in the RA hand, underpinning its likely responsiveness in subsequent randomized controlled trials.

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**Disclosure of Interest:** None declared

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## FRI0522 ULTRASOUND-DETECTED SYNOVITIS MAY PREDICT RADIOGRAPHIC DAMAGE PROGRESSION IN RHEUMATOID ARTHRITIS OVER THE NEXT FIVE YEARS – A PROSPECTIVE COHORT STUDY NESTED IN THE SWISS QUALITY MANAGEMENT PROGRAM (SCQM)

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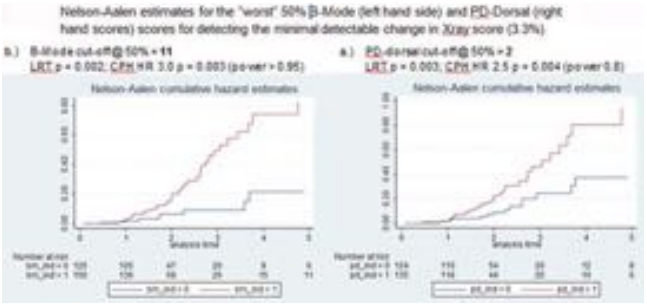
**Background:** Ultrasound and MRI are novel diagnostic imaging tools for evaluating rheumatoid arthritis (RA) disease activity in clinical research settings, but their use in daily practice is still limited. Since 2010, standardized grey scale ultrasound (GSUS) and Power Doppler ultrasound (PDUS) assessments, which are reimbursed by the Swiss health insurances, were included as an optional tool in the regular SCQM program work-up for RA patients.

**Objectives:** To study the predictive value of GSUS and PDUS for radiographic damage progression in RA patients in an observational real life setting.

**Methods:** For this study, all patients in the SCQM registry with at least one X-ray before and one X-ray after their first ultrasound assessment, with at least 20 of the recommended 22 joints evaluated in the SONAR score [] were included. Ultrasound-skilled rheumatologists which have attended a half-day ultrasound standardization workshop performed optional protocol-guided ultrasound examinations at their own discretion. GSUS and PDUS were scored in accordance with OMERACT standards in a semi-quantitative manner from 0 to 3 for all but the shoulder and thumb joints for a 28 joint status). Radiographic damage of hands and feet were centrally assessed by an assessor blinded to clinical and sonographic data. The present analyses were restricted to hand data. Radiographic damage progression was defined as an increase in the Ratingen Score (range 0–190) beyond the smallest detectable change of 3.3 score points. Univariate and multivariate cox-proportional hazard ratios were calculated for different arbitrary cut-off points in GSUS and PDUS.

**Results:** In total 377 patients were included for separate analyses of PDUS or GSUS scores, Median (mean±SD) disease duration at inclusion was 6.4 (9.5±9.8) years, median Ratingen score was 9.0 and median DAS-28(ESR) at inclusion was 3.4. Thus, the majority of patients had longstanding erosive disease and at least moderate inflammatory disease activity, despite synthetic DMARDs being used in 66%, biological DMARDs in 49% and corticosteroids in 33% of patients. Using cut-off levels for definition of the "worst" 20% (GSUS=18/66, PDUS=6/66), 30% (GSUS=16/66, PDUS=4 /66) or 50% (GSUS=11/66, PDUS=2/66) in GSUS or PDUS scores, a significantly higher proportion of patients ($p<0.05$) with GSUS or PDUS scores higher than each of these GSUS and PDUS thresholds had radiographic damage progression in univariate analyses (power 0.7–0.9).

**Conclusions:** Using PDUS as well as GSUS in routine care may provide valuable information to indicate increased risk for radiographic damage progression on a




long-term basis in established RA. Potential effects of US examinations on later treatment decisions remained in this study unaddressed.

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## FRI0523 RELATIONSHIP BETWEEN ULTRASOUND-DETECTED SYNOVITIS, QUALITY OF LIFE AND WORK PRODUCTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS OF WORKING AGE

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**Background:** Rheumatoid arthritis (RA) is a debilitating disease and can affect both quality of life (QOL) and work productivity (WP) [1]. Ultrasound (US) is an important imaging technique increasingly used as a reliable tool in evaluating and monitoring RA patients [2]. US-detected subclinical synovitis (SS) has been detected in patients in clinical remission [3].

**Objectives:** To investigate the relation between US-detected synovitis, clinically detected synovitis and US-detected SS and QOL and WP.

**Methods:** RA patients, aged between 18 and 59 years, with stable paid employment, were recruited. Clinical aseessment included 42 tender joint count (TJC) and 40 swollen joint count (SJC), Disease Activity Score (DAS) 28 and Health Assessment Questionnaire (HAQ). US assessment included 42 joints. At the joint level subclinical B mode synovitis (SSB) was defined as: absence of tenderness and swelling and presence of B mode score for synovitis ≥1 with or without power Doppler (PD) signal. Subclinical PD synovitis (PSS) was defined as absence of tenderness and swelling and presence of a PD score for synovitis ≥0. Global BM and PD scores for synovitis were assessed using the following scores: TS_B = total score of B-mode synovitis, TS_D = total score of PD synovitis, JS_B = count of joints with B-mode synovitis, JS_D =count of joints with PD synovitis, TSS_B = total score of SSB, TSS_D = total score of PSS, JSS_B = count of joints with SSB, JSS_D = count of joints with PSS. QOL [3] was described using 2 main domains: PCS (physical health) and MCS (mental health). WP was assessd using WPAI (work productivity and activity impairment) questionnaire [4].

**Results:** 104 patients, with a mean age of 49±8 years and a mean disease duration of 141±103 months were included. At the assessment point, most of the patients had long-standing, low activity disease and a low functional impairment, as assessed by the DAS28-ESR and the HAQ, respectively. With the exception of TSS_B, most of the parameters that significantly correlated with QOL and WP were clinical variables. However, these correlations were weak (r ≤0,39), being the highest with TJC.

**Conclusions:** Neither clinical and US detected synovitis nor US detected SS showed a consistent relation with QOL and WP in our population of RA patients. TJC seems to be the clinical parameter that better correlates with QOL and WP.

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**Disclosure of Interest:** None declared

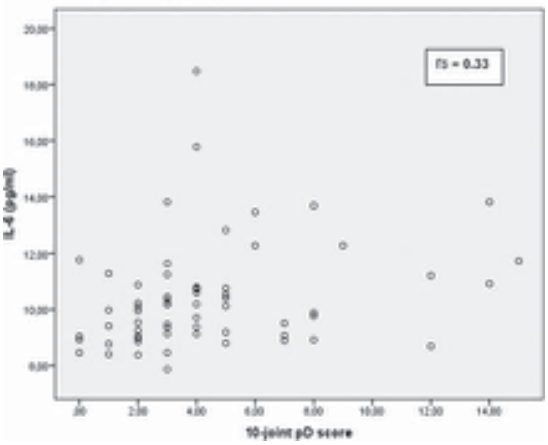
**DOI:** 10.1136/annrheumdis-2016-eular.3008

## FRI0524 ULTRASOUND POWER DOPPLER SYNOVITIS IS ASSOCIATED WITH PLASMA IL-6 IN ESTABLISHED RHEUMATOID ARTHRITIS

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**Background:** Cytokines have an important role in the pathogenesis of rheumatoid arthritis (RA). Muskuloscketalultrassound (MSUS) is a very useful tool in RA clinical management (1). In the last decades, it has been increasingly used in clinical rheumatology practice worldwide as it has demonstrated consistent and reproducible results among trained rheumatologists (2). Although plasma levels of IL-6 have been related to muskuloscketalultrassound (MSUS) synovitis in early DMARD-naïve RA (3), there are no similar studies in established disease.
**Objectives:** To investigate a possible association of MSUS synovitis and plasma citokines in patients with established RA.
**Methods:** 64 RA patients treated with non-biological DMARDs and 30 healthy controls were included in this prospective cross-sectional study. A blood sample was taken before evaluation of disease activity (DAS28) and ultrasonography (all tests performed in a blinded fashion). MSUS was performed by one of two ultrassound-trained rheumatologists on 10 joints of both hands (wrists, 2nd and 3rd metacarpophalangeal and 2nd and 3rd proximal interphalangeal joints) using high resolution equipment (My Lab 60, Esaote and 18mHZ linear tranducer). Gray scale (GS) and pD (power Doppler) synovitis were evaluated using a semi-quantitative scale (0–3) in individual joints, and their sum (score 10) was calculated. Plasma cytokines (IL-2, IL-4, IL-6, IL-10, IL-17, TNF, IFN-γ, and VEGF) were quantified by flow cytometry (Cytometric Bead Array kit - CBA; BD Biosciences).
**Results:** Levels of all cytokines, excepting VEGF, were significantly higher in RA patients than in controls ($P \leq 0.05$). In RA patients, IL-6, but not other cytokines, correlated positively with DAS28 and swollen joint count ($P \leq 0.01$), as well as with 10-joint pD score (figure 1), and GS and pD of both wrists ($P < 0.01$ for all tests). In multiple linear regression, the association of IL-6 with 10-joint pD score was mantained even after adjustment for DAS28. On the other hand, there was no correlation of IL-6 with tender joint count, 10-joint GS score, or presence of erosions.

Figure 1. Correlation of the 10-joint pD score with IL-6 levels ($r_S$= 0.33, 95%CI[ 0.06 to 0.56, P=0.008). $r_S$= Spearman correlation coefficient.

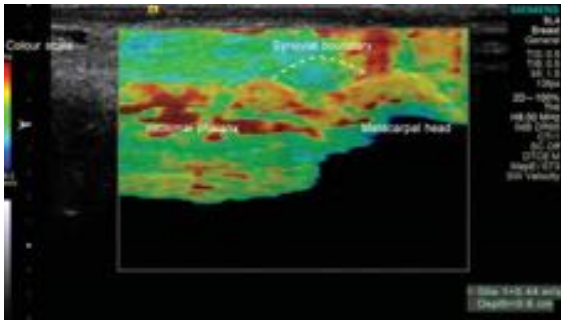



**Conclusions:** To the best of our knowledge, we report here, for the first time, an association of power Doppler sinovitis and plasma IL-6 independently of DAS28 in patients with established rheumatoid arthritis.
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## FRI0525 ELASTOGRAPHIC ULTRASOUND OF METACARPOPHALANGEAL (MCP) SYNOVIUM IN RHEUMATOID ARTHRITIS (RA)

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**Background:** Shear wave elastographic ultrasound (SW-EUS) assesses the stiffness of human tissues. It is used in liver, thyroid and breast imaging but has never before been studied in synovium. Soft tissues have a slower shear wave velocity (SWV) than stiff tissues. We hypothesised that rheumatoid arthritis (RA) patients would have softer synovium and thus slower SWV than controls.
**Objectives:** The aim of the project was to establish a reproducible scoring system for synovial SW-EUS and use it to compare RA patients with controls. We also set out to assess if SWV varied with disease activity.
**Methods:** A cross sectional study was conducted including nine RA patients and five age and sex matched controls. RA patients were recruited consecutively from a single rheumatology practice. Participants underwent a questionnaire, clinical examination, blood sampling, grey scale ultrasound (GSUS), power doppler ultrasound and SW-EUS ultrasound examination of MCP joints 2 - 5 on the dominant hand. Ultrasound was performed and scored by two blinded musculoskeletal trained sonographers.
**Results:** The average age of participants was 60. The mean RA disease activity score (DAS28-ESR) was in the low to moderate range of 3.65 (range 2.4–7.4). Patients with RA had significantly lower maximum SWV than controls (6.38 m/s vs 6.99 m/s p=0.042). Negative Pearson's correlation coefficients (PCC) were observed between maximum SWV and a range of disease activity markers including GSUS graded synovial thickness (PCC = -0.57, p=0.03) and ESR (PCC = -0.46, p=0.095). SW-EUS had good intra- and inter-observer reliability with intraclass correlation coefficients of 0.66 and 0.58 for maximum SWV and >0.80 for colour scale rated average and minimum SWV.




**Conclusions:** This is the first reported study of SW-EUS in synovial tissue. Maximum SWV was significantly lower in the synovium of RA patients compared with controls. There was a negative correlation between maximum SWV and GSUS graded synovial thickening suggesting that SWV may be lower in more active patients. SW-EUS may have a role in the diagnosis and assessment of disease activity in RA.
**Disclosure of Interest:** None declared
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## FRI0526 QUALITY OF ULTRASOUND-GUIDED SYNOVIAL BIOPSIES PERFORMED IN CLINICAL PRACTICE

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**Background:** Synovial tissue is the principal target and end organ involved in the pathogenesis of multiple articular disease processes. Histological and bacteriological analyses of synovial tissue (ST) are useful in clinical practice for the diagnosis of undifferentiated arthritis. Ultrasound (US) allows an evaluation of the synovial thickness and inflammation. It also helps to perform real-time synovial biopsy and detect nearby structures such as tendons, nerves and vessels.
**Objectives:** The aim of this study was to assess quantity and quality of synovial tissue obtained by ultrasound guided synovial biopsies, in clinical practice.
**Methods:** We retrospectively analysed all synovial biopsies performed between January 2007 and December 2014 in the Rheumatology Department of Nantes University Hospital. Synovial biopsies were performed under real-time US guidance (Philips HD11 XE) using a core biopsy needle with a 14 or 16G calibre semi-automatic Tru-cut needle. This technique allows to collect multiple synovial samples during a single procedure. Hematoxylin and eosin stained slides were analysed by one operator (AN), blindly from clinical data. Size, area, presence/absence of synovial tissue, presence/absence of lining layer, other types of tissues were assessed and compared to pathologist's analysis (gold standard).
**Results:** 75 biopsy procedures were analysed (73 patients). 125 samples were

available for analysis corresponding to a median number of samples taken per patient of 1 (IQR 1–3). Mean length and width of the biopsy samples were 6.34 millimetres (mm) (±3.60) and 1.70 mm (±0.77) respectively. The mean total area of the samples was 8.77 $mm^2$.
Biopsies showed synovial tissue at the histological examination in 102 samples (80.1%). The average area of synovial tissue in these samples was 6.36 $mm^2$ corresponding to 72.5% of the total area of biopsied tissue. The other types of tissue present on these biopsies were connective tissue in 101 cases (80.8%), adipose tissue in 42 cases (33.6%), tendon in 14 cases (11.2%) and fibrin in 24 cases (19.2%). The 23 sample retrieving no synovial tissue were composed of fibrin in 15 cases (12%), conjunctive and adipose tissue in 17 cases (13.6%), tendon in 3 cases (3.15%), cartilage in 3 cases (3.15%) and muscle in one case (0.8%).
Synovial lining layer was found in 92.6% of the successful biopsies.
Interobserver reliability for presence/absence of synovial tissue between AN and the pathologist was high with a kappa coefficient of 0.90 (95%CI =0.763 to 1).
**Conclusions:** Our study is the first to assess quality and quantity of synovial tissue obtained by ultrasound guided biopsy, in the clinical setting. In 80% of the biopsy procedures, quantity and quality of the synovial tissue were high enough to allow a proper histological examination. Given the fact that conjunctive and adipose tissues as well as fibrin were frequently seen on histological examination, retrieving a minimal number of 2 samples per patient appears to be required for appropriate pathology assessment in the clinical setting.
**Disclosure of Interest:** None declared
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## FRI0527 IMPACT OF ULTRASOUND IN TREATMENT DECISION OF RHEUMATOID ARTHRITIS ASSESSED IN ROUTINE CLINICAL PRACTICE

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**Background:** Remission or low disease activity is the therapeutic target of rheumatoid arthritis (RA). There is a consistent body of evidence supporting the value of ultrasound (US) findings in the diagnosis, disease activity and treatment monitoring of RA patients. In spite of these pieces of information, the real impact of US in treatment decisions in patients has not yet sufficiently studied.
**Objectives:** To explore the impact of US findings, in terms of proportion of patients in whom treatment recommendation differed after the US examination, in RA outpatients. We also tested the variations of US impact according to the level of patient's disease activity or the physician's experience.
**Methods:** Thirty-five consecutive outpatients were included. In the 1st step a senior rheumatologist (SR) and a trainee in rheumatology (TR), blinded to each other evaluations performed a clinical evaluation including DAS28, then, they independently proposed a treatment recommendation. In the 2nd step, all patients underwent an US examination using the 7-joint US score (2) by an experienced rheumatologist blinded to clinical evaluation, in order to established the sonographic disease activity. In the final step, all the patients returned to both, the SR and the TR, who integrated the US findings to their previous evaluation and reviewed their prescription. Potential changes of treatment (pre- and post-US) between both physician's (SR and TR) were recorded on standardized formats. Patients received final recommendation only from the SR. US usefulness was separately evaluated by the SR and the TR according to a Likert scale (0= not useful at all, 10= very useful).
**Results:** Patients were mainly female (91.4%), with (mean±SD) 44.8±10.1 years of age and (median, Q25-Q75) disease duration of 6.5 years (2.9–11.2). Fifty-one (73%) patients were in DAS28-remission and 29 (27%) showed some disease activity. In 17 clinical evaluations (25%), data from US evaluation modified treatment and it was most frequently increased (64.7%). Interestingly, DAS28 was higher in clinical evaluations where US impacted treatment than in those where US did not: (median [Q25-Q75] DAS28: 2.6 (1.6–3.2) vs. 1.6 (1.1–2.2), p=0.009. Also, there was a higher proportion of active patients among the first group: 47% vs. 20.7%, p=0.06. Twelve of the 17 clinical evaluations where US modified treatment recommendation, were performed by TR vs. 5 performed by the SR: 71% vs. 29%, p=0.09; nonetheless, US usefulness was equally scored by both physicians: 3 (2–7) vs. 3 (2–5), p=0.5.
**Conclusions:** US was an important technique for the treatment decision in routine clinical practice of patients with RA; the impact of US was more frequent in patients with active disease and in TR.
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## FRI0528 EPIDEMIOLOGICAL AND CLINICAL RELATIONSHIP OF ULTRASONOGRAPHIC FEATURES OF ACUTE ANSERINE SYNDROME

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**Background:** Anserine syndrome (AS) includes two pathological presentarions: The anserine bursitis and the anserine enthensytis. Most diagnostics of anserine syndrome are made considering topographic semiotics. It is logical to assume that treatment of different physiopathological features are associated with different clinical history but not necessary with differences in the clinical exam.
**Objectives:** To find relationships between ultrasonographic (US) findings and epidemiological data in patients with anserine syndrome
**Methods:** All the images of ultrasonographic studies of patients from 2013 to 2014 who were clinically assessed due to AS were reviewed. For that purpose we use the electronic database of the A&E department. Gender, age, and time from onset of symptoms were used to find correlation with US findings. US assessments were performed by two trained rheumatologist using standard Eular definitions as part of common clinical practice during the period selected. Findings considered positive were: bursitis and enthesitis.
**Results:** 113 registries which fulfilled the clinical diagnostic criteria were analyzed with their corresponding ultrasonographic images. 38 cases were unrelated to any particular ultrasonogrpahic finding, 20 were compatible with bursitis and 56 with enthesitis. Average age in the three groups were 69 SD 8, 46 SD 7 and 55 SD 9 years old ($P<0.0001$). Patients with bursitis where significantly younger than patients with enthesitis ($P=0.0001$). Also, patients without findings were significantly older than both other groups ($P<0.0001$ for both comparisons). Proportion of female gender was 58.9%, 65,0% and 53.6%, in enthesitis, bursitis and no-findings group, respectively ($P=0.647$). According to time since onset of symptoms, patients with less than a week presented bursitis and enthesitis in 55.17% and 34.48%, respectively. Patients with symptoms within 7 to 14 days presented bursitis and enthesitis in a proportion of 6.67% and 46.67%, respectively. Finally patients with symptoms within 15 days and less than a month presented bursitis in 2.56% and enthesitis in 64.10%. Bursitis was significantly higher in patients with acute symptomps compared to the other two groups ($P<0.001$). In the other hand, most patients with enthesitis were classified into the groups with a longer time since onset of symptoms ($P<0.05$)
**Conclusions:** Our results point as Follows: (1) The probability of identify no US findings is higher in older patients than younger. It is possible that mechanical issues related with the collateral ligament could cause a pain that suggest an anserine syndrome. (2) As earlier the symptoms are, is more factible the finding of bursitis. It could suggest that bursitis is a sign of acuteness. This finding could have relevance in terms of infiltration indication.
**Disclosure of Interest:** None declared
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## FRI0529 INITIAL VALIDATION OF THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

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**Background:** A range of clinical symptoms can be present in people at risk of rheumatoid arthritis (RA). However, information on location, timing, severity and predictive value of symptoms is still largely lacking. The Symptoms in Persons At Risk of Rheumatoid Arthritis (SPARRA) questionnaire has been developed with support of EULAR to provide more insight into these symptoms[1,2].
**Objectives:** To validate the SPARRA questionnaire in an international group of arthralgia patients at risk of RA.
**Methods:** Questions on presence, severity, impact and location of 13 symptoms were derived from a qualitative study in seropositive arthralgia patients[1]. The items are: joint pain or swelling, joint stiffness, burning and tingling sensations, numbness, change in skin colour, muscle cramps, weakness, fatigue, emotional distress, concentration difficulties and sleep problems. Answers are given on an ordinal scale. The number of days with a symptom per month (0, 1–5, 6–15, 16–30 days), severity (none, mild, moderate and severe) and influence on daily activities (no, small, moderate or high impact) were recorded. Finally, patients were asked to describe the pattern of symptom development over time. For this initial analysis of validity, patients were selected from the Dutch arthralgia cohort. We first administered the questionnaire to 30 patients to ask for ambiguities. Thereafter, 46 patients did a test-retest within one week to assess intra-rater agreement using the % agreement and the kappa score.
**Results:** Feedback on the questionnaire was received from 5/30 patients. There were only minor comments that did not lead to adaptations, such as difficulty distinguishing pain from stiffness (n=1) and difficulty describing muscle cramps (n=1). 46 arthralgia patients were assessed at 2 time points. The rater agreement was moderate to good for most items with kappa's of 0.42 to 0.93. We also found acceptable percentages of agreement of 65 to 91 (Table 1). Only tingling sensations and numbness scored low in agreement, with kappa's of 0.37 and 0.15, respectively. The kappa's were good across the presence, severity and impact

Table 1. Test-retest analysis of the SPARRA questionnaire (N=46)

| Items | % agreement[1] | Prevalence of the complaint[2] |
|---|---|---|
| Joint pain | 78% | 83% |
| Joint swelling | 91% | 37% |
| Joint stiffness | 76% | 74% |
| Burning sensations | 78% | 33% |
| Tingling sensations | 65% | 43% |
| Numbness | 74% | 30% |
| Change in skin colour | 87% | 20% |
| Muscle cramps | 78% | 28% |
| Weakness or loss of strength | 83% | 54% |
| Fatigue | 87% | 72% |
| Emotional distress | 83% | 37% |
| Concentration difficulties | 83% | 33% |
| Sleep problems | 83% | 57% |

[1]Retest analysis per item of duration of the complaint during the past month (0, 1–5, 6–15 or 16–30 days). [2]Percentage of patients that had the complaint at least 1 day in the past month in the first questionnaire.

of the item categories. Data on clinical variables and follow-up questionnaires to assess the construct and criterion validity will be presented at the congress.
**Conclusions:** The SPARRA questionnaire seems to be a reliable scale for evaluating symptoms in persons at risk for RA. More follow-up and data from collaborating centers within Europe is necessary for assessment of the construct, criterion and external validity.
**References:**
[1] Stack, Rheumatology 2014;
[2] van Tuyl, Musculoskel Care 2015
**Disclosure of Interest:** None declared
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## FRI0530 INTRA-AND INTER-OBSERVER RELIABILITY OF NAILFOLD VIDEOCAPILLAROSCOPY – A POSSIBLE OUTCOME MEASURE FOR SYSTEMIC SCLEROSIS-RELATED MICROANGIOPATHY?

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**Background:** Nailfold videocapillaroscopy (NVC) has been proposed as an outcome measure for systemic sclerosis [SSc] related microvascular disease.
**Objectives:** To assess the reliability of both measure availability and measured value of 4 parameters extracted from NVC images: capillary density, capillary (apex) width, overall image grade (normal, early, active, late), and the presence of giant capillaries.
**Methods:** 173 subjects were recruited in the study (101 with SSc, 22 with primary Raynaud's phenomenon and 50 controls). Panoramic NVC imaging was performed on all 10 digits using a 300x magnification microscope with green LED illumination for best capillary contrast.
Ten capillaroscopy experts ("raters") from 7 centres assessed images using custom software. Raters were asked to: (1) assess overall image grade ("Normal", "Early", "Active", "Late", "Non-specific", or "Ungradeable"), (2) mark the location of capillary apices (capillary density calculated from distal vessel locations), (3) categorically grade the distal vessels in terms of size and shape, and (4) measure the apical width of distal vessels using a click-and-drag tool.
**Results:** The 10 raters analysed a median (range) of 129 (98–1641) images, returning 3401 evaluations of 1650 images, including a sub-sample analysed twice by the same rater to measure intra-rater reliability. Of these, 2731 evaluations (80%) satisfied the criteria to allow vessel density to be measured (at least 2 distal vessels identified).
The reliability (intra- and inter-rater) of both measure availability and measured value for the 4 parameters are shown in the table. Overall image grade was available in only around 45% of observations due to the exclusion of "non-specific" gradings from the analysis.

Table 1

| | Intra-rater reliability (95% CI) | Inter-rater reliability (95% CI) |
|---|---|---|
| Measure availability | | |
| Distal vessel density | 0.71 (0.62, 0.79) | 0.14 (0.09, 0.21) |
| Mean distal apical width | 0.73 (0.65, 0.79) | 0.26 (0.19, 0.34) |
| Overall image grade | 0.56 (0.48, 0.64) | 0.22 (0.17, 0.27) |
| Presence of giant capillary | 0.69 (0.59, 0.78) | 0.13 (0.08, 0.20) |
| Measure (conditional on availability) | | |
| Distal vessel density | 0.90 (0.88, 0.92) | 0.64 (0.55, 0.71) |
| Mean distal apical width | 0.91 (0.89, 0.92) | 0.85 (0.81, 0.88) |
| Overall image grade | 0.93 (0.92, 0.95) | 0.78 (0.72, 0.82) |
| Presence of giant capillary | 0.71 (0.66, 0.76) | 0.41 (0.33, 0.48) |

**Conclusions:** Capillary density and (especially) apical width, parameters likely to be helpful in quantifying temporal change, were reliable measures in evaluable nailbeds. The reliability of measured values is generally high, but is conditional on measure availability. This must be accounted for when considering the applicability of outcome measures to clinical trial situations. With standardised training (and potentially increased automation of analysis), high magnification NVC has strong potential as an outcome measure of SSc-related microangiopathy.
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**Disclosure of Interest:** None declared
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## FRI0531 DIFFERENCES IN ULTRASONOGRAPHIC DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS WHO ARE IN CLINICAL REMISSION ACCORDING TO DIFFERENT REMISSION CRITERIA

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**Background:** At the present time remission is the target for treatment of rheumatoid arthritis (RA). Various composite indices are available that can be used to define remission. Although the new ACR/EULAR Boolean criteria is more stringent than others, it is difficult to achieve and even more difficult to sustain this Boolean remission.
**Objectives:** In this study we aimed to determine the differences of the ultrasonographically (US) assessed actual disease activities of the patients in remission according to different remission criteria.
**Methods:** RA patients in clinical remission (DAS28-ESR<2.6) for at least 3 months were included to this cross-sectional study. All patients' remission status according to DAS28-ESR-3, DAS28-CRP, SDAI, CDAI and Boolean based definitions were assessed. A standard gray scale (GS) and power Doppler (PD) US examination of 28 joints (included in DAS28) for the presence of synovitis was performed by an experienced sonographer (NI) blinded to clinical data. US synovitis GS and PD signals were semiquantitatively graded from 0 to 3. Total PD and GS synovitis scores of all sites are recorded as sum scores of PD and GS, respectively.
**Results:** A total of 88 out of 389 RA patients (22.6%) in DAS28 remission were enrolled (F/M=55/33, mean age 53.4±12.0, disease duration 10.5±6.3 years, bDMARDs 44.3%, RF/Anti-CCP positivity 72%). Of the 88 patients, 82 (93.2%), 72 (81.8%), 49 (55.7%), 40 (45.5%) and 33 (37.5%) fulfilled the DAS28-CRP, DAS28-ESR-3, SDAI, CDAI and Boolean remission criteria, respectively. PD synovitis scores which have shown to be associated with erosion development and worse functional outcome were lowest in CDAI, Boolean and SDAI remission. However despite that, those differences in US disease activity parameters (both PD and GS synovitis sum scores and percentages of patients without PD and GS signals [with both omitting and including grade 1 signals]) in remission patients according to different criteria were not statistically significant (*Table 1*). In comparison of US disease activity parameters of remission vs nonremission groups, only patients with Boolean and CDAI remission had significantly lower PD scores compared to their counterpart nonremission group (for both, 1 [0–4] vs 3 [1–7], *P*=0.015).

Table 1. Ultrasonographic disease activities of patients according to different remission criteria*

| | DAS28-ESR REM (n=88) | DAS28-CRP REM (n=82) | DAS28-ESR-3 REM (n=72) | SDAI REM (n=49) | CDAI REM (n=40) | Boolean REM (n=33) |
|---|---|---|---|---|---|---|
| PD sum score (0-84) | 2 (0-5) | 2 (0-5) | 2 (0-5) | 1 (0-4.2) | 1 (0-4) | 1 (0-4) |
| GS sum score (0-84) | 4 (2-8) | 3 (1-8) | 3 (2-8) | 4 (2-8) | 2.5 (0-7) | 2 (0-6.2) |
| PDGS sum score (0-168) | 6.5 (2-13) | 5 (2-13) | 5 (2-13) | 5 (2.5-11) | 4 (0.25-11) | 3 (0-8.2) |
| US joint count with PD signal (0-28) | 2 (0-3) | 1.5 (0-3) | 2 (0-3) | 1 (0-3) | 1 (0-2) | 1 (0-2.2) |
| US joint count with GS signal (0-28) | 2.5 (1-4) | 2 (1-4) | 2 (1-4) | 2 (1-4) | 2 (0-4) | 2 (0-4) |
| PD=0† | 34 (42.2) | 34 (28.6) | 19 (26.4) | 14 (28.6) | 14 (35) | 13 (39.4) |
| PD≥1† | 42 (47.7) | 42 (51.2) | 38 (52.8) | 28 (57.1) | 24 (60) | 21 (63.6) |
| GS=0† | 15 (17) | 15 (18.3) | 11 (15.3) | 10 (20.4) | 11 (27.5) | 10 (30.3) |
| GS≥1† | 36 (40.9) | 36 (43.9) | 31 (43.1) | 22 (44.9) | 20 (50) | 16 (48.5) |
| PD=0 and GS=0† | 14 (15.9) | 14 (17.1) | 11 (15.3) | 9 (18.4) | 10 (25) | 9 (27.3) |
| PD≥1 and GS≥1† | 32 (36.4) | 32 (39) | 27 (37.5) | 20 (40.8) | 19 (47.5) | 16 (48.5) |
| US/C with PD=0† | 34 (42.2) | 34 (28.6) | 19 (26.4) | 14 (28.6) | 14 (35) | 13 (39.4) |
| US/C with PD≥1† | 42 (46.8) | 42 (50) | 38 (48.6) | 28 (57.1) | 24 (60) | 21 (63.6) |
| US/C with GS=0† | 15 (17) | 15 (18.3) | 11 (15.3) | 10 (20.4) | 11 (27.5) | 10 (30.3) |
| US/C with GS≥1† | 36 (40.9) | 36 (43.9) | 31 (43.1) | 22 (44.9) | 20 (50) | 16 (48.5) |

*The values were presented as median (IQR) unless indicated otherwise. †The values were presented as n (%). All P values >0.05

**Conclusions:** US verified joint inflammation is the lowest in RA patients who are in remission according to Boolean and CDAI criteria. However, the clinical significance of this statistically nonsignificant inflammatory activity compared to other clinical remission criteria should be assessed in prospective studies. Till then, in clinical practice if Boolean remission could not be achieved, CDAI or SDAI could also be preferred as the remission target.
**Disclosure of Interest:** None declared
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## FRI0532 ASSOCIATION BETWEEN THE 7-JOINT ULTRASOUND SCORE (US7S) AND PHYSICAL FUNCTION IN RHEUMATOID ARTHRITIS

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**Objectives:** To investigate the longitudinal relationship between physical disability and US7S in a prospective cohort of patients with RA.
**Methods:** A cohort of 205 RA pts (49 incident/156 prevalent) (mean±SD age 55±14 years, 47% RF+, 63% ACPA+, DAS28-CRP 3.7±1.5, mHAQ 0.43±0.52, disease duration in incident vs. prevalent pts. 0.9±0.7 vs. 8.1± 8.3 resp.) was followed up longitudinally for 29±9 months. Assessments at baseline and at month 3 and 6, and then every 6 months comprised DAS28-CRP, functional evaluations using the modified Health Assessment Questionnaire (mHAQ) and an ultrasound assessment of the clinically dominant hand and foot by US7S[1]. US7S consists of 5 subscores for synovitis (syn) and tenosynovitis (ten) assessed by grey-scale (GS) and Power-Doppler (PD), and an erosions score (ES). A linear mixed model was used to assess the longitudinal relationship between US7 subscores and mHAQ. Univariate analyses with an interaction term for incident vs. prevalent disease, and a multivariate analysis (with age, sex, BMI, RF and ACPA status, and DAS28-CRP entered as covariates) were performed.
**Results:** In univariate analyses (table) mHAQ was longitudinally associated with GSsyn, PDsyn, PDten and GSten US7 subscores (with resp. β coefficients significantly higher in incident patients), while erosions score was a significant predictor of mHAQ only in prevalent pts. In a multivariate model the US7 subscores were individually no longer significant predictors of mHAQ, although the $R^2$ of the model was improved by addition of US7 items from 43.6 to 46.9 ($p<0.001$ for improvement of $R^2$).

Table 1. Univariate analyses and interaction with incident (i)/prevalent (p) RA (predicted variable – mHAQ)

| Predictor | RA | β (95% CI) | p-value* | p-value** | % variability explained – $R^2$ |
|---|---|---|---|---|---|
| DAS28-CRP | all | 0.112 (0.100; 0.123) | **<0.001** | 0.510 | 44.5 |
| | i | 0.120 (0.093; 0.146) | **<0.001** | | |
| | p | 0.110 (0.097; 0.123) | **<0.001** | | |
| GSsynUS | all | 0.008 (0.004; 0.011) | **<0.001** | **0.038** | 3.2 |
| | i | 0.014 (0.007; 0.021) | **<0.001** | | |
| | p | 0.006 (0.002; 0.010) | **0.002** | | |
| PDsynUS | all | 0.012 (0.008; 0.016) | **<0.001** | **0.018** | 4.3 |
| | i | 0.021 (0.012; 0.029) | **<0.001** | | |
| | p | 0.009 (0.004; 0.014) | **<0.001** | | |
| GStenUS | all | 0.018 (0.002; 0.035) | **0.032** | 0.078 | 1.7 |
| | i | 0.045 (0.011; 0.080) | **0.010** | | |
| | p | 0.010 (0.000; 0.020) | 0.316 | | |
| PDtenUS | all | 0.024 (0.012; 0.037) | **<0.001** | **0.032** | 2.0 |
| | i | 0.053 (0.024; 0.083) | **<0.001** | | |
| | p | 0.017 (0.010; 0.024) | **0.013** | | |
| ES | all | 0.009 (–0.003; 0.021) | 0.145 | 0.062 | 0.3 |
| | i | –0.021 (–0.055; 0.013) | 0.216 | | |
| | p | 0.013 (0.001; 0.026) | **0.047** | | |

*p-value of significance of given β. **p-value of significance of difference between incident and prevalent RA.

**Conclusions:** This study provides evidence that RA related activity and damage reflected by US7S contribute to impaired physical function in RA, and their impact differs in early and established disease. When combined with conventional clinical parameters, the additional explanatory value of US7 for mHAQ was only minor.
**References:**
[1] Backhaus M. et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum. 2009 Sep 15;61(9):1194–201
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## FRI0533 THE DIAGNOSTIC PERFORMANCE OF POST-CONTRAST 3-D ULTRASHORT ECHO TIME SEQUENCE OF SACROILIITIS IN PATIENTS WITH AXIAL SPONDYLOARTHROPATHY COMPARING WITH CONVENTIONAL POST-CONTRAST FAT SUPPRESSED T1 WEIGHTED SEQUENCE

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**Background:** Axial spondyloarthropathies (axSpA) are chronic inflammatory diseases affecting the sacroiliac joint, spine, peripheral joint, and entheses. Entheses are emphasized as one of the primary targets of axSpA, but they show little signal on conventional clinical magnetic resonance (MR). Recently, the ultrashort echo time (UTE) sequence has been reported to be useful in detecting a signal from the tissues with short T2 such as the ligaments, periosteum, and cortical bone. Contrast enhancement study of UTE sequence showed increased enhancement as a consequence of angiogenesis in a diseased tendon and fibrocartilage. To our knowledge, no prior study has compared the diagnostic performances of post-contrast 3D UTE and conventional post-contrast fat suppressed T1 weighted sequence (FST1WI) for sacroiliitis in patients with axSpA.
**Objectives:** To compare the diagnostic performance of post-contrast 3D UTE and conventional FS1WI for sacroiliitis.
**Methods:** Total 16 patients with axSpA (asSpA group: 10 men, 6 women, mean age: 35.56 years [range: 24–52 years], human leukocyte antigen B 27 positivity 81.25%,) and 10 patients with mechanical back pain (control group: 2 men, 8 women, mean age: 58.6 years [range 34–74 years]) were enrolled in this prospective study. All patients underwent oblique coronal short tau inversion recovery sequence (STIR), pre/post contrast fat suppressed (FS) 3D UTE, and post contrast FST1WI. Active inflammation of the sacroiliac joint was quantitatively analyzed and scored on post-contrast FS 3D UTE and post contrast FST1WI for inflammatory findings, such as osteitis, synovitis, capsulitis, and enthesitis, by two musculoskeletal radiologists with a consensus. The score per active inflammatory finding of 3D UTE and post contrast FST1WI was compared between axSpA group and control group using Wilcoxon rank test.
**Results:** The axSpA group showed higher scores for osteitis and synovitis on both post-contrast FS 3D UTE ($P$ =0.018, 0.025, respectively) and post-contrast FST1WI ($P$ =0.003, 0.005, respectively) and for enthesitis on post-contrast FS 3D UTE with a statistical significance ($P$ =0.004). Post-contrast FS 3D UTE showed statistically significant lower scores for all inflammatory findings than enhanced FS T1 WI sequences did ($P$ <0.05).




Figure 1. Oblique coronal image of the SI joint of a 23-year-old man with ankylosing spondylitis. Bone marrow edema (black arrow) is better visualized on FST1WI (A). However, the erosions (white arrow) and synovial enhancement (white dashed arrow) are more clearly visualized on FS 3D UTE with and without enhancement (B,C).

**Conclusions:** Post contrast 3D UTE can differentiate axSpA and mechanical back pain, especially when considering enthesitis. Although it showed slightly lower diagnostic performance for the active inflammatory finding than post contrast FST1WI did, post contrast 3D UTE might play a supplementary diagnostic role for early diagnosis of axSpA.
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## FRI0534 STUDYING BONE MINERAL DENSITY LOSS IN CLINICALLY SUSPECT ARTHRALGIA, ASSOCIATIONS WITH SUBCLINICAL INFLAMMATION AND PROGRESSION TO CLINICAL ARTHRITIS

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**Background:** Peripheral bone mineral density (BMD) can be decreased in early rheumatoid arthritis but it is unknown if BMD loss emerges already before arthritis is clinically apparent.
**Objectives:** We aimed to study if BMD loss occurs in patients with clinically suspect arthralgia (CSA), if it is associated with progression to clinical arthritis and if it is associated with MRI-detected subclinical inflammation.
**Methods:** Patients with CSA had arthralgia for <1 year and were suspect to progress to RA according to their rheumatologists. At baseline a 1.5T MRI was performed of unilateral MCP, wrist and MTP-joints and scored on synovitis, bone marrow edema and tenosynovitis;. summing these features yielded the MRI-inflammation score. Digital X-ray radiogrammetry (DXR) was used to measure BMD on two sequential conventional hand radiographs (mean interval between radiographs 4.4 months). The change in BMD was studied; BMD loss was defined as decrease of ≥2.5 mg/cm$^2$/month. Patients were followed on arthritis development for median 18.4 months.
**Results:** In CSA-patients (n=108) change in BMD was negatively associated with age (β=-0.03, p=0.007). Within CSA-patients BMD loss was associated with arthritis development (adjusted for age HR=6.1, 95%CI=1.7;21.4) and was most frequently measured in the months before clinical arthritis development. The MRI-inflammation scores were associated with the change in BMD (adjusted for age β=-0.05, p=0.047). The MRI-inflammation score and BMD loss were both independently associated with arthritis development (HR=1.1 95%CI=1.1;1.2 and HR=4.6 95%CI=1.2;17.2 respectively).

**Conclusions:** In CSA-patients BMD loss is associated with MRI-detectable subclinical inflammation and with progression to clinical arthritis.
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## FRI0535 HAND BONE LOSS IN EARLY RHEUMATOID ARTHRITIS IS INDEPENDENT OF ADALIMUMAB TREATMENT. A SUBSTUDY OF THE OPTIMIZED TREATMENT ALGORITHM IN EARLY RA (OPERA) TRIAL

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**Background:** Rheumatoid arthritis (RA) is characterised by progressive destruction of joint bone and loss of periarticular bone mineral. Hand bone loss (HBL) measured by Digital X-ray Radiogrammetry (DXR) has been proposed as a sensitive outcome measure for treatment effect and as a potential predictor of subsequent radiographic progression in RA patients.
**Objectives:** To investigate the effect of adding adalimumab to a methotrexate and intra-articular triamcinolone treat-to-target strategy on one-year HBL ($HBL_{one\text{-}year}$) in early RA and to determine if $HBL_{6months}$ is associated with radiographic progression after two years.
**Methods:** In a clinical trial (OPERA) of 180 treatment-naive early RA patients (1), bone mineral density (BMD) was estimated from hand radiographs with Digital X-ray radiogrammetry (DXR) at baseline, after 6 months (n=90) and 12 months (n=70) of follow-up. Baseline and two-year radiographs were scored according to the Sharp/van der Heijde method. Baseline characteristics and $HBL_{6months}$ (0–6 months changes in DXR-BMD) were investigated as predictors of structural damage by univariate linear ($\Delta$Total Sharp/van der Heijde Score (TSS) as dependent variable) and logistic (+/– radiographic progression ($\Delta TSS>0$) as dependent variable) regression analyses. Variables with $p<0.10$ were included in multivariable models.
**Results:** In 70 patients with available $HBL_{one\text{-}year}$ data, $HBL_{one\text{-}year}$ was median (InterQuartileRange (IQR)) -1.9 (-3.3; -0.26 mg/cm$^2$) in the placebo-group and -1.8 (-3.6; 0.06) mg/cm$^2$ in the adalimumab-group, p=0.98,Mann Whitney. Increased HBL (compared to general population reference values (2)) was found in 26/37 and 23/33 patients in the placebo- and adalimumab-groups, Chi-sq=0.99. In 90 patients with $HBL_{6months}$ data and two-year radiographic data, $HBL_{6months}$ was independently associated with $\Delta$TSS after two years ($\beta$=-0.086 (95% Confidence Interval= -0.15; -0.025) TSS unit/mg/cm$^2$ increase,p=0.006), and borderline associated with presence of radiographic progression ($\Delta TSS>0$) (OR 0.96 (0.92–1.0), p=0.10).
**Conclusions:** In early RA, adding adalimumab to a methotrexate-based treat-to-target strategy had no impact on $HBL_{one\text{-}year}$, which was increased in both treatment groups. $HBL_{6months}$ was independently associated with $\Delta$TSS after two years.
**References:**
[1] Hørslev-Petersen et al. Ann Rheum Dis. 2015 doi: 10.1136/annrheumdis-2015-208166.
[2] Ørnbjerg LM et al. [abstract]. Arthritis Rheumatol. 2015; 67 (suppl 10).
**Disclosure of Interest:** L. Ørnbjerg: None declared, M. Østergaard Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, T. Jensen: None declared, K. Hørslev-Petersen Grant/research support from: Abbvie, Meda, Roche, K. Stengaard-Pedersen Grant/research support from: Meda, Abbvie, Roche, Speakers bureau: UCB, Pfizer, P. Junker: None declared, T. Ellingsen: None declared, P. Ahlquist: None declared, H. Lindegaard Grant/research support from: Boehringer Ingelheim, A. Linauskas: None declared, A. Schlemmer Grant/research support from: Abbvie, Roche, MSD, M. Dam: None declared, I. Hansen: None declared, T. Lottenburger: None declared, C. Ammitzbøll: None declared, A. Jørgensen: None declared, S. Krintel: None declared, J. Raun: None declared, M. Hetland: None declared
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## FRI0536 A NEW SYSTEM FOR INVESTIGATING CAPILLARY MORPHOLOGY AND BLOOD FLOW IN SYSTEMIC SCLEROSIS

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**Background:** Nailfold videocapillaroscopy (NVC) captures high-magnification images of capillaries, allowing non-invasive assessment of systemic sclerosis [SSc] related microvascular disease. We have developed a state-of-the-art NVC system to enable faster and easier acquisition of high quality static images and produce video sequences in which red blood cell velocity can be measured. The system uses novel software to make fully automated quantitative estimates of capillary morphology and blood flow velocity, eliminating the need for (subjective) clinician input to image interpretation.
**Objectives:** To apply the new system in a case-control study to: 1) assess system usability 2) test how well automated measures of capillary morphology differentiate between healthy controls (HC), subjects with primary Raynaud's phenomenon (PRP) and patients with SSc 3) investigate capillary blood flow velocity as a new quantitative measure for NVC.
**Methods:** 112 participants were recruited into the study (50 HC, 12 PRP, 50 SSc). Panoramic video sequences were taken for all 10 digits, each comprising 10,000 – 20,000 frames (size: 640x480 px, spatial resolution: 1$\mu$m/px, frame rate: 120 frames/s). The frames were processed and registered to produce a static panorama of the whole nailfold ($\sim$2–5mm wide). The analysis software automatically detected and measured capillary structural properties in this image[1], before using in-focus frames at each capillary to create video sequences for blood flow velocity estimation (Fig 1). Capillary-level measurements were averaged across all 10 nailfolds to produce subject-level parameters: capillary density, mean capillary width, maximum capillary width, shape score, derangement and mean flow velocity. For each parameter one-way ANOVA and Tukey's range test were used to check for group differences, and the area under ROC curve ($A_z$) used to measure separation between HC/PRP and SSc.
**Results:** ANOVA tests showed significant group-wise differences for all parameters. Table 1 shows group means and $A_z$ for each parameter.

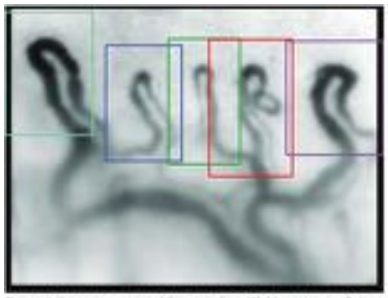


**Figure 1:** Segment extracted from whole nailfold panorama. Coloured boxes show capillaries detected by analysis software. Within each box the width and shape of the capillary is measured using the static image. A video sequence of in-focus frames is then extracted for each box and used to estimate capillary blood flow velocity.

**Conclusions:** The new system successfully generated high-quality video sequences, and allowed fast panoramic imaging of the whole nailfold. Automatically extracted capillary morphology parameters matched both clinical expectations and previous study results[1,2] and show considerable promise as outcome measures for SSc. Preliminary flow results suggest reduced blood velocity is associated with abnormal morphology and thus lower in SSc patients, further work is needed to corroborate this.
**References:**
[1] Berks et al, MICCAI, 8673, 658–665, 2014
[2] Murray et al, Arthritis Care Res, 61(8), 2009
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**Disclosure of Interest:** None declared
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**Abstract FRI0536** – Table 1. Group means and $A_z$ for each parameter

| Parameter | Group means (95% CI) | | | ROC Az (95% CI) HC, PRP vs SSc |
|---|---|---|---|---|
| | HC (n=50) | PRP (n=12)† vs HC | SSc (n=50)‡ vs HC, PR | |
| Capillary density (mm$^{-1}$) | 6.73 (6.40, 7.06) | 7.28 (6.76, 7.80) | 5.52‡ (5.11, 5.94) | 0.77 (0.68, 0.86) |
| Mean width ($\mu$m) | 11.8 (11.5, 12.0) | 12.7† (12.0, 13.4) | 15.0‡ (14.3, 15.7) | 0.87 (0.8, 0.95) |
| Max width ($\mu$m) | 16.5 (15.6, 17.4) | 21.4† (18.6, 24.2) | 27.4‡ (25.0, 29.7) | 0.84 (0.75, 0.92) |
| Shape score (no units, range [0, 1]) | 0.31 (0.30, 0.33) | 0.32 (0.30, 0.35) | 0.25‡ (0.24, 0.26) | 0.85 (0.77, 0.92) |
| Derangement (no units, range [0, 1]) | 0.65 (0.61, 0.68) | 0.69 (0.64, 0.74) | 0.54‡ (0.51, 0.573) | 0.76 (0.67, 0.85) |
| Mean flow velocity (mms$^{-1}$) | 0.26 (0.22, 0.29) | 0.30 (0.23, 0.36) | 0.19‡ (0.17, 0.22) | 0.75 (0.65, 0.84) |

†,‡denote pair-wise means significantly different at 95% level on Tukey's test.

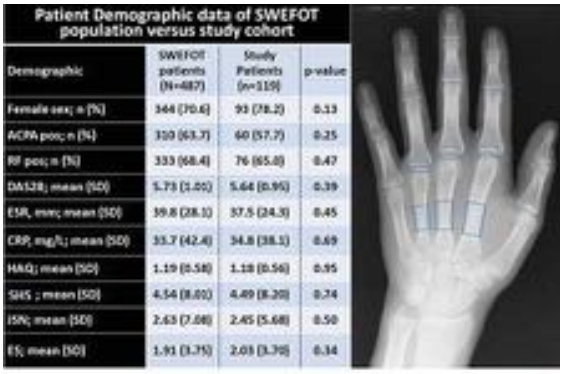
## FRI0537 AUTOMATED JOINT SPACE WIDTH MEASUREMENT AND DIGITAL X-RAY RADIOGRAMMETRY IN EARLY RA

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**Background:** Despite technological advancements and the availability of ultrasound and magnetic resonance imaging modalities, conventional radiography still remains the main imaging tool in Rheumatoid Arthritis (RA) patient management (1). One of the validated methods of radiographic scoring in RA, the modified Sharp van der Heijde (SHS) method, has much strength but is time-consuming, observer-dependent, and requires training, and is therefore seldom used in clinical practice (1, 2). Automated digital methods have been developed for analysing radiographs and may provide useful information on Joint Space Width (JSW) and/or Bone Mineral Density (BMD).
**Objectives:** To assess the feasibility and correspondence of fully automated digital measurements of JSW with conventional methods in early RA.
**Methods:** Patient characteristics and radiographic reports scored by the SHS method of 119 early RA patients were acquired from the SWEFOT database. From this cohort, 96 patients had both baseline and follow-up JSW and BMD measurements. Fully automated bilateral BMD of metacarpal diaphyses 2–4 and JSW of MCP joints 2, 3 & 4 (Sectra, Linköping, Sweden) were assessed. Additionally, JSW was compared to the joint space narrowing (JSN) score. Multilevel mixed models taking into account correlations between joints of the same hand, contralateral hand and repeated visits were used. Furthermore, these models were adjusted for height, age, gender and BMI.
**Results:** We studied 119 early RA patients (78% female), with an average age of 54 ±14.4 years. In 576 joints, patients with both baseline and follow-up JSW and BMD measurements, a significant reduction from baseline to 1 year was shown in the mean JSW (0.169 ±0.019cm to 0.166 ±0.019cm, $p<0.01$) and mean BMD (0.583 ±0.068g/cm$^2$ to 0.566 ±0.074g/cm$^2$, $p<0.01$). Significant correlations between JSW and BMD were observed at baseline ($r=0.32$, $p<0.01$) and 12-months ($r=0.35$, $p<0.01$). Inverse correlations emerged between automated JSW and SHS Joint Space Narrowing (JSN) assessments at baseline ($r=-0.29$, $p<0.01$) and 12-months ($r=-0.24$, $p=0.014$). JSWs of undamaged (JSN=0) joints were wider than damaged joints (0.168cm [95% CI: 0.170–167] versus 0.154cm [95% CI: 0.163–0.146]). Similarly the unadjusted multilevel model showed significant differences in JSW between undamaged (0.168cm [95% CI: 0.172–0.164]) and damaged joints (0.163cm [95% CI: 0.168–0.158cm]), $p<0.01$. This difference remained significant in the adjusted model (0.166cm [95% CI: 0.170–0.161] versus 0.162cm [95% CI: 0.168–0.156], $p<0.05$).

**Patient Demographic data of SWEFOT population versus study cohort**

| Demographic | SWEFOT patients (N=487) | Study Patients (n=119) | p-value |
|---|---|---|---|
| Female sex; n [%] | 344 (70.6) | 93 (78.2) | 0.13 |
| ACPA pos; n [%] | 310 (63.7) | 60 (57.7) | 0.25 |
| RF pos; n [%] | 333 (68.4) | 76 (65.0) | 0.47 |
| DAS28; mean (SD) | 5.73 (1.01) | 5.64 (0.95) | 0.39 |
| ESR, mm; mean (SD) | 39.8 (28.1) | 37.5 (24.3) | 0.45 |
| CRP, mg/l; mean (SD) | 33.7 (42.4) | 34.8 (38.1) | 0.69 |
| HAQ; mean (SD) | 1.19 (0.58) | 1.18 (0.56) | 0.95 |
| SHS ; mean (SD) | 4.54 (8.01) | 4.49 (8.20) | 0.74 |
| JSN; mean (SD) | 2.63 (7.08) | 2.45 (5.68) | 0.50 |
| ES; mean (SD) | 1.91 (3.75) | 2.03 (3.70) | 0.34 |




**Conclusions:** Digital JSW may have potential as a quick and observer-independent measure of cartilage damage in early RA.
**References:**

[1] Boini S, Guillemin F. Radiographic scoring methods as outcome measures in rheumatoid arthritis: properties and advantages. Annals of the rheumatic diseases. 2001;60(9):817–27.
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## FRI0538 VALIDATION OF A SEMI-AUTOMATIC ALGORITHM FOR DEFINING CORTICAL BREAKS IN FINGER JOINTS USING HIGH-RESOLUTION PERIPHERAL QUANTITATIVE CT BY MICROCT

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**Background:** High-Resolution peripheral QCT (HR-pQCT) imaging has a higher sensitivity in the detection of breaks compared to conventional radiography (1). Cortical bone in the finger joints is very thin (≈100μm) and it is therefore possible that the HR-pQCT is not able to detect these thin structures. An automatic algorithm that is based on binary images can therefore falsely identify these regions as breaks. To investigate the extent of this error, cortical break detection on HR-pQCT was compared to that on μCT with a higher resolution.
**Objectives:** To investigate the proportion of falsely detected breaks with a semi-automatic algorithm on HR-pQCT compared to μCT.
**Methods:** Nineteen finger joints of ten human female cadaveric index fingers (mean age ± SD; 85.1 ± 9.6 years) with unknown medical history were imaged by HR-pQCT and μCT (82 and 18μm isotropic voxel sizes, respectively). A semi-automatic algorithm was applied to HR-pQCT and μCT for the detection of cortical breaks. First, the outer margin of the bone structure was contoured. Second, the bone within 0.25mm from this contour was selected as cortical region. Last, different sizes for defining a cortical break (>0.50mm, >0.66mm and >0.82mm) were applied and evaluated. μCT images were registered to HR-pQCT in order to compare the locations of the detected breaks. The false discovery rate (FDR) of breaks detected on HR-pQCT was calculated, with μCT as reference.
**Results:** The number of breaks depended on the image modality and chosen break size, and varied between 0.8 and 20.8 breaks per joint (table 1).

Table 1. Comparison of the breaks detected on HR-pQCT and μCT by the algorithm using different break sizes

| Minimal break size | Number of breaks per joint[1] (n=19 joints) | | FDR of HR-pQCT[2] | |
|---|---|---|---|---|
| | HR-pQCT | μCT | μCT same break size | μCT break size of >0.50mm |
| >0.50mm | 14.2±11.6 | 20.8±19.4 | 37.9% | 37.9% |
| >0.66mm | 4.9±4.7 | 4.1±4.8 | 50.0% | 6.4% |
| >0.82mm | 2.4±2.5 | 0.8±1.1 | 86.7% | 4.4% |

[1]Mean ± SD; [2]μCT as reference.

The locations of the detected breaks on HR-pQCT and μCT generally correspond well (Fig 1-I). On HR-pQCT, however, breaks may be detected as large breaks, whereas on μCT these large breaks appear to represent a combination of several small breaks (Fig 1-II). With larger break diameters as a cut-off for both techniques, this resulted in the detection of breaks on HR-pQCT which were not detected on μCT. Therefore, the FDR for the detection of a break of the

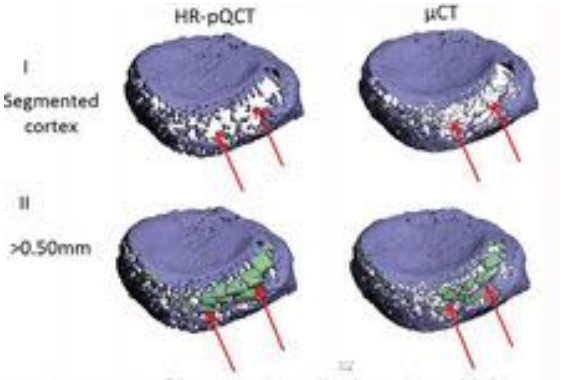



*Figure 1.* Binary images of the segmented cortex (I) and a visual output (II) of the phalangeal base of the algorithm as performed on HR-pQCT (left) and μCT (right). The cortex is shown in purple (I-II), cortical breaks are shown in white (I-II), and cortical breaks >0.50mm are shown in green (II). The red arrows indicate regions of which the μCT detects thin cortices which were not detected on HR-pQCT (I). This led to the detection of large breaks on HR-pQCT and multiple smaller breaks on μCT (II)

same size was sufficient for small breaks (37.9%), but poor for large break sizes (86.7%). However, when comparing a larger break on HR-pQCT with the smallest minimal break size on μCT it was found that only 4.4% of the detected breaks on HR-pQCT were falsely detected (table 1).

**Conclusions:** Because of its limited resolution, a single break region detected on HR-pQCT can appear as several smaller breaks on μCT. When accounting for this effect, however, excellent agreement is found between cortical break detected with the algorithm using HR-pQCT and μCT. We thus conclude that the use of HR-pQCT in combination with our semi-automatic algorithm is a promising tool for early detection and monitoring of the number of small cortical breaks in finger joints.

**References:**

[1] Stach CM, A&R.2010 Feb; 62(2):330–339

**Disclosure of Interest:** M. Peters: None declared, A. Scharmga: None declared, A. van Tubergen: None declared, B. van Rietbergen Consultant for: Scanco Medical AG, R. Weyers: None declared, D. Loeffen: None declared, J. Van den Bergh: None declared, P. Geusens: None declared

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## FRI0539 RELIABILITY OF A SEMI-AUTOMATIC ALGORITHM IN THE DETECTION OF CORTICAL BREAKS IN FINGER JOINTS USING HIGH RESOLUTION PERIPHERAL QUANTITATIVE CT

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**Background:** Conventional radiography (CR) is considered the gold standard for diagnosis and monitoring of erosions in rheumatoid arthritis (RA). However, CR is less sensitive in the detection of erosions than high resolution peripheral quantitative CT (HR-pQCT) in hand joints (1). The visual scoring of these erosions is, however, laborious. Therefore an automatic method could be timesaving. We previously developed a semi-automatic algorithm for HR-pQCT that is able to detect cortical breaks. However, the intra-operator reliability of our algorithm was not yet tested on the joint level for different break sizes, and neither on a single break level.

**Objectives:** To test the intra-operator reliability of the algorithm on HR-pQCT images on the joint level and on a single break level for different break sizes.

**Methods:** Nineteen finger joints of ten human female cadaveric index fingers (mean age ± SD; 85.1 ± 9.6 years) with unknown medical history were imaged by HR-pQCT (82μm voxel size). A semi-automatic algorithm was developed for the detection of cortical breaks, taking into account various break sizes. First, the automatically detected contours were manually adapted twice by the same operator several weeks apart. Second, bone within 0.25mm from this contour was selected as the cortical region. Last, different sizes for defining a cortical break (>0.50mm, >0.66mm and >0.82mm) were applied. Breaks that were detected by the algorithm using both contours, and overlapped with at least 30 voxels were counted as matching breaks. The proportion of matching breaks was calculated as a measure of reliability for a single break. Intraclass correlation coefficients (ICCs) were calculated as a measure of reliability on the joint level.

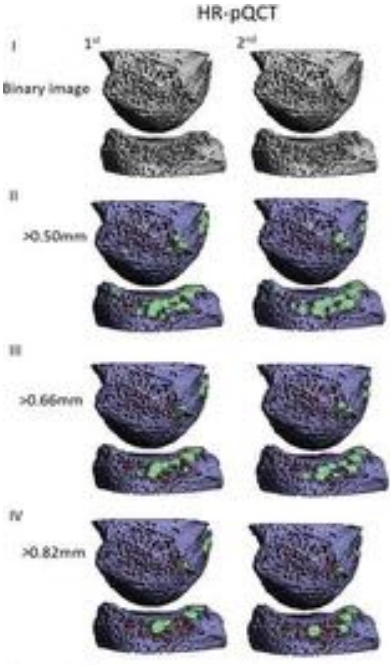



Figure 1. Binary images (I) and the visual outputs (II-IV) of an MCP joint of the designed algorithm as performed on the HR-pQCT after the first and second time contouring. The cortex is shown in purple, the trabecular bone in red, and the cortical breaks are shown in green (II-IV).

**Results:** The number of breaks depended on the chosen break size, and varied between 2.4 and 14.2 per joint. The locations of the detected breaks from the first and second time contouring generally corresponded well for all break sizes (Fig. 1). The agreement on a single break level was substantial for all break sizes (≥67.7%), with the highest agreement for breaks >0.66mm (80.9%).The agreement on the joint level was high for all break sizes (ICC≥.84, p<0.01) and excellent for breaks >0.66mm (ICC ≥.95, p<0.01) (table 1).

Table 1. Number of breaks and intra-observer reliability of breaks detected on the HR-pQCT images

| Minimal break size | HR-pQCT 1st* (n=19 joints) | HR-pQCT 2nd* (n=19 joints) | ICC# | Proportion of matching breaks$ |
|---|---|---|---|---|
| >0.50mm | 14.9±12.6 | 14.2±11.6 | 0.91 (0.79–0.97) | 67.7% |
| >0.66mm | 5.1±5.2 | 4.9±4.7 | 0.95 (0.87– 0.98) | 80.9% |
| >0.82mm | 2.6±3.2 | 2.4±2.5 | 0.84 (0.62–0.93) | 73.3% |

Number of breaks detected for different break sizes. *Mean ± SD, #ICC (95% CI), and $ with HR-pQCT 2nd as reference. SD = Standard Deviation, ICC = Intraclass Correlation Coefficient, 95% CI =95% Confidence Interval.

**Conclusions:** The intra-operator reliability of the algorithm was excellent at the joint level and very good of the single break detection for all break sizes. Therefore, the use of HR-pQCT in combination with our semi-automatic algorithm is a promising tool for early detection and monitoring of the number of small cortical breaks in finger joints.

**References:**

[1] Stach et al., A&R.2010 Feb; 62(2):330–339

**Disclosure of Interest:** M. Peters: None declared, A. Scharmga: None declared, J. de Jong: None declared, A. van Tubergen: None declared, R. Weijers: None declared, D. Loeffen: None declared, B. van Rietbergen Consultant for: Scanco Medical AG, J. van den Bergh: None declared, P. Geusens: None declared

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## FRI0540 EVALUATION OF NAILFOLDVIDEOCAPILLAROSCOPY IN CENTRAL SEROUS CHORIORETINOPATHY

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**Background:** Nailfold videocapillaroscopy (NVC) is a diagnostic tool to evaluate micro-vasculature. Presence of choroidal vasculopathy is apparent in central serous chorioretinopathy (CSCR).

**Objectives:** In this study, it was aimed to assess capillaroscopic findings of nailfold in patients with CSCR. To best of our knowledge, there is no study assessing NVC findings in CSCR in the literature.

**Methods:** Sixty-one patients with CSCR who met inclusion criteria and 82 age- and sex-matched healthy controls were included to the study. A videocapillaroscopy device with 200x magnification was used for capillaroscopic assessment.

**Results:** The mean age was 48.79 ± 11.146 years in the patient group (13 female, 48 male) whereas 49.38 ± 9.02 years in the control group (17 female, 65 male). The age and gender were comparable in the patient and control groups (p=0.727 and p=0.933, respectively). The capillary count was found to be decreased in the patient group compared to control group. No significant correlation was found between capillary count and choroidal thickness (p=0.551; r=-0.081). In the patient group, the frequencies of major capillaroscopic findings including capillary ectasia, aneurysm, micro-hemorrhage, avascular area, tortuosity, neo-formation, bizarre capillary, bushy capillary, meander capillary and extravasation were found to be increased in the patient group. However, no significant correlation was detected between capillaroscopic findings and disease type and presence of attacks.

Table 1. Capillaroscopic findings of patient and control groups

| Parameter | Patients (n=61) | Controls (n=82) | p |
|---|---|---|---|
| Capillary count, median (min-max) | 10 (7–12) | 11 (9–13) | <0.001 |
| Capillary ectasia, n (%) | 12 (19.7) | 0 (0) | <0.001 |
| Aneurysm, n (%) | 3 (4.9) | 0 (0) | 0.023 |
| Mega-capillary, n (%) | 1 (1.6) | 0 (0) | 0.427 |
| Micro-hemorrhage, n (%) | 6 (9.8) | 0 (0) | 0.001 |
| Tortuosity, n (%) | 47 (77) | 4 (4.9) | <0.001 |
| Avascular area, n (%) | 5 (8.2) | 0 (0) | 0.003 |
| Neo-formation, n (%) | 30 (49.2) | 0 (0) | <0.001 |
| Bizarre capillary, n (%) | 33 (54.1) | 3 (3.7) | <0.001 |
| Bushy capillary, n (%) | 30 (49.2) | 0 (0) | <0.001 |
| Meander capillary, n (%) | 6 (9.8) | 0 (0) | 0.001 |
| Extravasation, n (%) | 9 (14.8) | 0 (0) | <0.001 |

**Conclusions:** This is first study in which nailfold capillary assessment was

performed in patients with CSCR and we detected major capillaroscopic changes. These findings suggest that CSCR can be systemic microvasculopathy. Further studies are needed to clarify the diagnostic and prognostic value of capillaroscopy in CSCR.

**Disclosure of Interest:** None declared

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## FRI0541 A CROSS-SECTIONAL, INTERNATIONAL SURVEY ON NON-INVASIVE TECHNIQUES TO ASSESS THE MICROCIRCULATION IN PATIENTS WITH RAYNAUD'S PHENOMENON (SUNSHINE SURVEY)

N. Ughi[1], G. Dinsdale[2], V. Smith[3], Y. Allanore[4], I. Foeldvari[5], A. Sulli[6], M. Cutolo[6], A.L. Herrick[2], F. Ingegnoli[1] on behalf of SUNSHINE Study Group and the EULAR Study Group on Microcirculation in Rheumatic Diseases.
*[1]Division of Rheumatology, Gaetano Pini Institute, Department of Clinical Sciences & Community Health, University of Milan, Milan, Italy; [2]Centre for Musculoskeletal Research, Salford Royal NHS Foundation Trust, The University of Manchester, Academic Health Science Centre, Manchester, United Kingdom; [3]Department of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium; [4]Paris Descartes University and Cochin Hospital, AP-HP, Paris, France; [5]Hamburger Zentrum für Kinder- und Jugend Rheumatologie, Klinikum Eilbek, Hamburg, Germany; [6]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy*

**Background:** Microcirculatory impairment in patients with Raynaud's phenomenon (RP) may be assessed by different techniques, but real-life data concerning their roles and current usage are not available.
**Objectives:** To obtain an overview of the specific techniques which may be used for the assessment of adult patients with RP in clinical and research settings: nailfold videocapillaroscopy (NVC), dermoscopy, stereomicroscopy, and digital USB microscopy, laser Doppler flowmetry, imaging, and anemometry/velocimetry, laser Speckle Contrast Analysis (LASCA), thermographic imaging, upper limb arterial Doppler ultrasound.
**Methods:** This survey was conducted online between October and December 2015 on behalf of EULAR study group on Microcirculation in Rheumatic Diseases (SG_MC/RD). Emails with a link to the survey were sent to physicians from the European Scleroderma Trials and Research group (EUSTAR) and SG_MC/RD mailing lists. Of those e-mailed, 418 were physicians looking after adult patients, and this group was considered in the following descriptive analysis.
**Results:** Of the 418 eligible physicians, 107 completed the survey, giving an overall response rate of 25.6%. Among the respondents 89 (83.2%) were rheumatologists, 74 (69.2%) European; 87 (81.3%) were practising for more than 10 years and 50% looked after between 31 and 60 patients per year with primary and/or secondary RP. The most routinely performed technique was NVC (63/107, 58.9%) both by rheumatologists and non-rheumatologists (54/89, 60.7% and 9/18, 50.0%). NVC was reported as the most available technique (93/107, 86.9%), and available in the place of work in 78/107 (72.9%) among both rheumatologists and non-rheumatologists. Nailfold capillaroscopy was the most frequently performed by the physician him/herself by using different types of equipment relating to availability: NVC 64/94 (68.0%), dermoscopy 38/63 (60.3%), stereomicroscopy 31/42 (73.8%), and digital USB microscopy 34/39 (87.1%). Most rheumatologists reported high levels of "appropriateness" for NVC in both clinical and research settings for global assessment (86/88, 97.7% clinical setting, 87/88, 98.9% research setting), and differential diagnosis of primary and secondary RP (clinical and research setting both 84/87 96.5%). In clinical setting NVC showed the highest percentage of appropriateness for monitoring primary RP (84/88, 95.4%), RP secondary to connective tissue diseases other than systemic sclerosis (82/87, 94.2%) and to systemic sclerosis (87/87, 100%). All techniques other than capillaroscopy reached a consensus lower than 2/3 of respondents based on their knowledge/experience. In research setting, all techniques were judged as potentially useful with a consensus more than 2/3 of respondents.
**Conclusions:** Of all the different techniques upon which opinion was sought, nailfold capillaroscopy was the one most used by physicians looking after adult patients in both clinical and research settings, the majority of whom use NVC in their everyday practice. The low proportion of clinicians using other techniques suggests that these are currently confined to specialist centres.

**Disclosure of Interest:** None declared

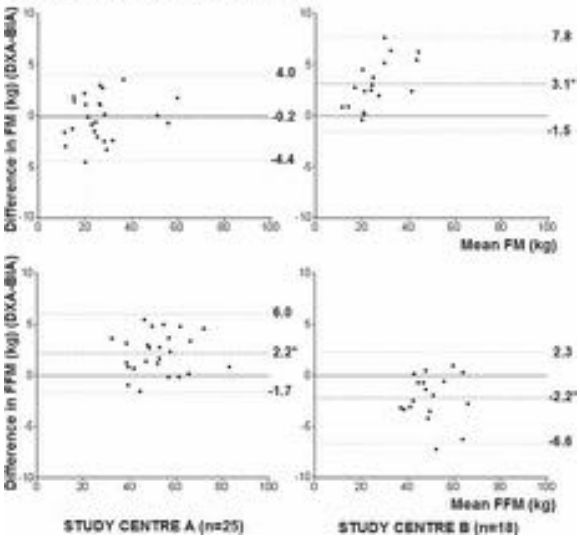
**DOI:** 10.1136/annrheumdis-2016-eular.3102

## FRI0542 BIOELECTRICAL IMPEDANCE ANALYSIS IS NOT A VALID METHOD FOR THE ASSESSMENT OF BODY COMPOSITION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid cachexia (i.e. loss of fat free mass (FFM) and gain in fat mass (FM)) is often observed in chronic rheumatoid arthritis (RA) patients, with deleterious effects on morbidity and functional capacity [1,2]. In addition, the use of glucocorticoids is associated with increase in FM. Therefore, careful assessment of body composition is important in RA patients. Dual-energy X-ray absorptiometry (DXA) is a valid and reliable method to assess body composition, but is also expensive, time-consuming, invasive and thus not feasible for everyday use. Bioelectrical impedance analysis (BIA) is a relatively cheap, rapid, and non-invasive method to assess body composition in clinical practice, however BIA has not been validated in RA patients.
**Objectives:** To validate BIA against two different, widely used DXA devices for the assessment of body composition in patients with RA.
**Methods:** This cross-sectional validation study was performed in RA patients who visited study center A or B in the context of the COBRA-light extension studyl. Body composition was assessed by DXA (study center A: Hologic Delphi; study center B: GE Lunar IDxa) and BIA (Quadscan 4000) on the same day, and recorded as FM, FM%, FFM and FFM%. Agreement between both methods was assessed by paired t-tests, Bland-Altman plots and intra-class correlation coefficients (ICC), in which DXA was used as reference method.
**Results:** Of the 149 extension study patients, 43 patients (63% women, mean age 56 years, mean disease duration 5 years) were assessed by both DXA and BIA at the same day, and were included in this validation study. In study center A (n=25), BIA overestimated FM by 0.2 kg (p=0.71), and significantly underestimated FFM by 2.2 kg ($p<0.001$). FM% and FFM% were respectively over- and underestimated by 1.1% (both p=0.05). In study center B (n=18), BIA systematically underestimated FM by 3.1 kg, and overestimated FFM by 2.2 kg; FM% and FFM% were respectively under- and overestimated by 3.6% (all: $p<0.001$). Bland-Altman plots showed wide limits of agreement for all assessments in both study centers (Figure 1). These limits of agreement, indicating measurement error on individual level, were approximately 8 kg for FM and FFM assessments in both study centers. The ICC's, indicating measurement error on group level, showed good agreement in study center A (>0.90) and moderate-to-good agreement in study center B (>0.85).

Figure 1. Bland Altman plots of the assessment of Fat Mass and Fat Free Mass by DXA and BIA per study center in RA patients (n=43)




**Conclusions:** This study showed that BIA is an invalid method for the assessment of body composition in RA patients, both at individual and group level, and that errors depend on the DXA device used as reference method.

**References:**

[1] Walsmith, Int J Cardiol 2002, 85:89–99
[2] Summers, Nat Rev Rheumatol 2010, 6:445–51

**Disclosure of Interest:** None declared

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## FRI0543 RAMIFICATIONS IN NAILFOLD CAPILLAROSCOPY, RISK FACTORS AND PROGNOSTIC IMPLICATIONS

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**Background:** Presence of ramifications (RM) (capillaries from whose central axis lateral branches emerge) in the nailfold capillaroscopy is generally seen in patients with advanced microvascular damage and is a characteristic feature of scleroderma and dermatomyositis. Nevertheless they are also seen in patients without defined disease, so that it can be an inespecific finding whose potential role in the evolution of the patient is unclear.

**Objectives:** To analyze the risk factors and the prognostic implications associated with the presence of RM in the capillaroscopy. Analyze the risk factors associated with RM in patients who we perform a capillaroscopic in our hospital.
**Methods:** We reviewed all the capillaroscopies performed in our systemic autoimmune diseases outpatient between January 2013 and December 2015. We reviewed the clinic and epidemiological characteristics, capillary pattern, diagnosis and evolution of all the patients and we analyzed their relation with the presence of RM.
**Results:** In this period we performed a capillaroscopy to 226 patients, 48 (21.2%) of which had RM. In the RM group (39 women, 9 men), mean age was 51.38 years, with no significant differences in gender distribution and in age compared to the no-RM group (p 0.394 and 0.694 respectively). 78 of our patients were smokers (34.5%), 61 (27%) had history of arterial hypertension, 71 (31.4%) had hypercholesterolemia and 13 (5.8%) diabetes mellitus, with no differences between both groups (p 0.380, 0.265, 0.501 and 0.867 respectively).
We found 6 patients with digital ulcers, any of them with RM (p 0.197). Patients with idiopathic thromboembolic disease were 5 (2.21%), only 1 with RM (p 0.466). 182 patients (80.5%) presented Raynaud's phenomenon (RP) with a mean duration of 8.59 years, 37 of which had RM (p 0.497). Among patients with RP in which the final diagnosis was primary RP (46, 20.53%) only 3 (6.25%) had RM (p 0.006). Patients that finally were diagnosed with any collagen vascular disease were 135 (59.73%), 37 of wich had RM (p 0.01). In this group 6 patients had systemic lupus erythematosus, 32 systemic sclerosis, 5 antiphospholipid syndrome, 6 Sjögren syndrome, 2 mixed connective tissue disease and 67 undifferentiated connective tissue disease. We found no differences between RM and no-RM groups separately analyzing each of these diagnoses (p 0.426, 0.466, 0.223, 0.191, 0.293 and 0.148 respectively).
With respect capillaroscopic findings we found no correlation with the presence of dilatations (p 0.193), megacapilaries (p 0.418) or hemorrhages (p 0.888) but we did with other suggesting advanced microvascular damage as capillary loss (p 0.018) and presence of tortuosities ($p<0.001$) and with the sclerodermic capillaroscopic pattern (p 0.003).
**Conclusions:** Presence of RM identifies patients at risk of secondary RP, especially with underlying connective tissue diseases. So, the presence of RM in patients with not clear diagnostic force us to have specially attention with them because they have risk to develop a connective tissue disease in the future.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2502

## FRI0544 IMPACT OF EDUCATION IN MUSCULOSKELETAL ULTRASONOGRAPHY: GOOD TO EXCELLENT RELIABILITY RESULTS IN MODIFIED US7 SCORING SYSTEM AFTER ONE YEAR OF CONTINUING EDUCATION SINCE BASIC OR INTERMEDIATE LEVEL OF TRAINING

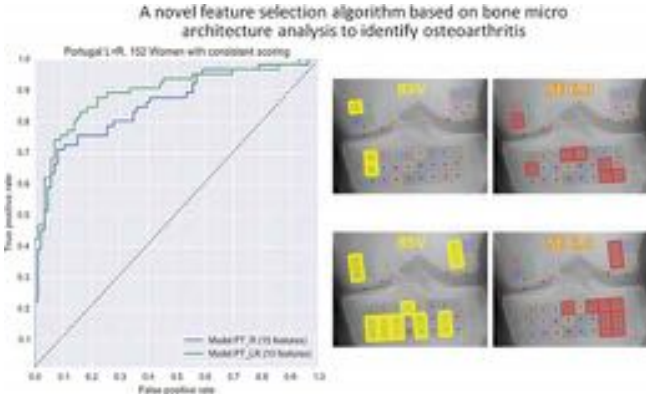
P. Hanova[1], J. Zavada[1], J. Hurnakova[1], H. Mann[1], M. Klein[1], O. Sleglova[1], M. Olejarova[1], O. Ruzickova[1], S. Forejtova[1], M. Komarc[2], J. Gatterova[1], K. Pavelka[1]. *[1]Instit. of Rheumatology; [2]Instit. of Biophysics and Informatics, Prague, Czech Republic*

**Objectives:** To estimate the time to reach reliable results in a larger group of rheumatologists at onset of their musculoskeletal ultrasound (MSUS) training in modified 7-joints scoring system (US7).
**Methods:** US7 has been shown a useful tool to estimate activity of rheumatoid arthritis (RA) in daily clinical practice. The system has been extensively described including an atlas. Targets of the US7 include synovitis (in B-mode and Power Doppler (BM+PD)), tenosynovitis (BM+PD) and erosive changes of 7 joints (wrist, MCP II+III, PIP II+III, MTP II+V) on the dominant site. We used a modification of the original US7 published, assessing both palmar and dorsal view of MCP and PIP joints. 9 rheumatologists with basic/intermed. level of MSUS underwent a training in general MSUS+US7. At month 1, reliability testing in scoring of static pictures was performed. At months 3 and 12, two reliability-testing sessions were organized. 4 patients with various stages of activity and disease progression of RA were repeatedly scanned, in 2 rounds per session. Sonographers were blind to all patients' data. 2 US machines were used for each session and the setting was fixed before the start. Smoking or drinking alcohol was not allowed. Each patient was investigated by the same US machine in the same daytime in each round of a testing session. Inter-/intra-observer agreement was calculated for each modality of US7 (synovitis score in BM+PD, tenosynovitis score in BM+PD, erosion score) by using non-weighted Cohen kappa (intra-observer agreement) and Light's kappa (inter-observer agreement).
**Results:** At month 1, mean intra- and inter-observer agreement in scoring of static images was reached; $\kappa$=0,61 and 0,60 respectively (good). At month 3, mean inter-observer reliability was low ($\kappa<0.2$), intra-observer reliability varied within interval $\kappa$(0.02;1). As the education continued, mean inter-observer agreement achieved $\kappa$=0,6 (good), intra-observer agreement varied within interval $\kappa$ (0.6;1) (good-excellent).
**Conclusions:** Ultrasound is an operator dependent technique. The level of experience necessary to obtain reliable results in modified US7 (as an example of easy and well determined US method) was achieved after 12 months of low intensity training with direct supervision of a specialist on demand. Low intensity training is in the authors' experience the most frequently used method among beginners in MSUS. Scoring of static images was reliable already after 1 month. Although the probe positions in US7 are well defined, the inter-/intra-observer reliability in scoring of self-obtained images was none in month 3 and the difference leading to good results in month 12 must have been achieved in this later period of training. The difference between higher intra-observer and none inter-observer agreement in month 3 suggests that direct supervision of a specialist in MSUS in this stage of education would lead to quicker progress and better results in achieving reliability among the group members.
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**Disclosure of Interest:** None declared
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## FRI0545 A NOVEL FEATURE SELECTION ALGORITHM BASED ON BONE MICRO ARCHITECTURE ANALYSIS TO IDENTIFY OSTEOARTHRITIS

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**Background:** Texture information of the subchondral bone area of 2D radiographs represents a promising possibility for evaluating the state of osteoarthritis (OA) in addition to traditional clinical means such as visual and semi-quantitative assessments.
**Objectives:** Algorithms based on fractal analysis have shown to be capable of identifying differences in trabecular bone structure. However such features are likely to vary within the subchondral bone area and therefore the appropriate selection of the region of interest (ROI) plays a crucial role for the result of the analysis. Thus, a feature selection algorithm is being applied in order to determine ROIs that enable an optimum discrimination between patients with and without OA.
**Methods:** The study included 152 standardized knee radiographs from 66 female patients with OA, and 86 controls. Subchondral bone micro architecture was assessed by using both fractal analysis and a Shannon Entropy (SE) algorithm at predefined regions of the proximal tibia and the distal femur. For fractal analysis the distinct parameter Bone Structure Value (BSV) was defined. The selected area of the proximal tibia involved a matrix of 3x8 ROIs, whereas a 2x2 matrix was defined for each condyle of the distal femur. SE and the BSV were calculated for each of the 32 ROIs, respectively. Based on these 64 variables, a feature selection algorithm was applied to determine the variables that showed the best discrimination power between Case and Control subjects.
**Results:** By combining the BSV and SE, the odds ratio increased significantly from 3.08 (95% CI: 1.78–5.30) to 14.82 (95% CI: 6.69–32.83) when using 15 features, and to 39.75 (95% CI: 15.41–102.51) based on 10 features. By using the selected 10 features the accuracy was found to be 0.86. This showed to be a significant improvement compared to the accuracy achieved when calculating a single mean value for the 3x8 ROIs of the proximal tibia alone (0.62 vs. 0.86).




**Conclusions:** The application of a feature selection algorithm in accordance with the combination of the two texture analysis methods shows a significant improvement with respect to the discrimination power between subjects with and without OA. The high odds ratios confirm that reliable results can be achieved by combining the BSV and the SE. This novel algorithm for the assessment of bine micro architecture may not only be useful in osteoarthritis subjects but also for the early prediction and assessment of other degenerative bone diseases like osteoporosis and rheumatoid arthritis.
**Disclosure of Interest:** R. Ljuhar Employee of: Braincon Technologies, B. Norman Employee of: Braincon Technologies, D. Ljuhar Employee of: Braincon Technologies, T. Haftner Employee of: Braincon Technologies, J. Hladuvka: None

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## FRI0546 THE POWER DOPPLER RESULT IN RHEUMATOID ARTHRITIS DEPENDS ON THE POSITION OF HANDS DURING ULTRASOUND EXAMINATION

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**Background:** Power Doppler (PD) ultrasound is used to assess joint inflammation in rheumatoid arthritis (RA). The extent of PD signals is influenced by several factors such as technical settings, room temperature and other variables.
**Objectives:** The aim of this study was to examine the relevance of the position of hands (extended versus neutral position) for PD ultrasound results in RA using a 2D semi-quantitative and a 3D quantitative analysis method.
**Methods:** Cross-sectional study of 42 consecutive RA patients with active disease according to clinical ($\geq$1 tender and/or swollen joint) and ultrasound examination ($\geq$1 joint with PD grade $\geq$1). Ultrasound examination was performed at dorsal sites of wrists and MCPs (bilaterally) by 1 (out of 2) investigators blinded to clinical results. An Esaote MyLab Twice ultrasound device was used with an 18-MHz linear transducer (2D-US) and a 4–13 MHz volumetric three-dimensional ultrasound probe (3D-US). For 2D-US, PD abnormalities were subjectively graded from 0 to 3. For 3D-US, the probe was placed at MCPs in a longitudinal direction over the extensor tendon and the joint space and at wrist over the lunate bone. Automatized image acquisition was conducted and the percentage of PD pixels within the region of interest (ROI, 100 slides, total width 8.5 mm) was calculated using the integrated 3D software.
Ultrasound examination was first performed with patients' hands in a neutral position (i.e. slight flexion of the fingers - only the wrist, thumb and finger tips touching the table), subsequently in an extended position (i.e. all palm and inner finger area touching the table).
**Results:** Out of the 42 RA patients, 66.7% were female. Median age was 57.5 (range 19–86) years. Patients had a median of 6 (0–23) swollen and 8 (0–45) tender joints, median SDAI was 22.1 (5.1–48.3).
In neutral position, a positive 2D-US PD result was found in 192/420 (45.7%) joints. A score of 1, 2 and 3 was observed in 42 (21.9% of all PD positive joints), 139 (72.4%) and 11 (5.7%) joints, respectively. 3D-US PD findings correlated well with 2D results, with median pixel values being 0.4 (range 1.0–1.9), 1.1 (0.2–7.4) and 2.3 (0.3–7.2) in joints with 2D-US scores of 1,2 and 3, respectively.
Changing the position from neutral to extended resulted in the disappearance of PD signals in 55/192 joints (28.7%, $p<0.001$, assessed with 2D-US). In detail, 29/42 joints with a PD score 1 in neutral position became PD negative in extended position (minus 69%, $p<0.001$). Out of those 139 joints with a PD score 2 in neutral position, 26 (18.7%) and 78 (56.1%) changed to scores of 0 and 1 in extended position, respectively. A PD score 3 was found to change to score of 1 and 2 at 4 (36.4% out of 11) and 5 (45.5%) joints, respectively.
Median 3D-US count was reduced from 0.9 (range 0.1–7.4) in neutral position to 0.2 (0.0–1.7, $p<0.001$) in extended position.
Inter-reader agreements for 2D-US and 3D-US results were good [ICC 0.82 (95%CI 0.69 to 0.90)] and [ICC 0.75 (0.27–0.93)] as was the intra-reader reliability for 3D-US [ICC 0.79 (0.38–0.94)].
**Conclusions:** A standardized approach for the ultrasound examination of RA patient is essential to produce reliable results. Our study demonstrates a significant reduction of PD scores by extended vs. neutral position of hands.
**Disclosure of Interest:** None declared
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## FRI0547 MAGNETIC RESONANCE IMAGING JOINT SPACE NARROWING IS AN INDEPENDENT PREDICTOR OF RADIOGRAPHIC AND MRI DAMAGE PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Magnetic Resonance Imaging (MRI) osteitis and synovitis have been identified as predictors of structural damage progression in rheumatoid arthritis (RA)[1,2], but the predictive value of MRI joint space narrowing (JSN, a measure of cartilage damage) and tenosynovitis (TS) needs further investigation.
**Objectives:** To investigate the predictive value of baseline MRI inflammatory and damage parameters on 2 year MRI and X-ray damage progression in an early RA (eRA) cohort following a non biologic treat-to-target strategy.
**Methods:** In 129 eRA (<6months) patients from the double-blind randomized CIMESTRA trial (methotrexate, intraarticular betamethasone and cyclosporine (CYA)/placebo CYA) contrast-enhanced MRIs of the non-dominant wrist and X-rays of hands and feet were performed at baseline and after 2 years. MRIs were evaluated according to the RAMRIS scoring system for osteitis, synovitis, erosion (ES), JSN, for TS[3] and X-rays according to the Sharp/van der Heijde method, with known chronology by two experienced radiologists. Potential predictive baseline variables (MRI osteitis, synovitis, TS, ES, JSN, X-ray ES and JSN, DAS28, gender, age, anti-CCP, smoking status) were tested in univariate linear regression analyses with 2-year change in MRI total damage score, Total Sharp Score (TSS), and MRI and X-ray JSN and ES scores as dependent variables. Significant variables ($p<0.05$) were included in multiple regression analyses with backward selection.
**Results:** Independent predictors of structural damage progression are presented in table 1.
If MRI JSN was not included in the model, MRI osteitis score was statistically significant independent predictor of X-ray progression (coefficient 0.32, p=0.001, vs TSS progression).
**Conclusions:** This trial is the first to report that MRI JSN independently predicts both X-ray and MRI damage progression in early RA. Further studies are needed to confirm early MRI-determined cartilage damage as predictor of progressive joint destruction in RA.
**References:**
[1] Hetland et al, Ann Rheum Dis 2009
[2] Boyesen et al, Ann Rheum Dis 2011
[3] Haavardsholm et al, Ann Rheum Dis 2007
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3452

**Abstract FRI0547** – Table 1

| Final models | Dependent variables | | | | | |
|---|---|---|---|---|---|---|
| | MRI variables | | | X-ray variables | | |
| Explanatory variables | MRI ES Coeff (CI) | MRI JSN Coeff (CI) | MRI total damage score Coeff (CI) | X-ray ES Coeff (CI) | X-ray JSN Coeff (CI) | TSS Coeff (CI) |
| MRI synovitis | 0.23 (0.06–0.31) p=0.006 | | 0.18 (0.03–0.36) p=0.023 | | | |
| MRI JSN | 0.39 (0.27–0.68) p<0.001 | 0.66 (0.35–0.54) p<0.001 | 0.54 (0.66–1.17) p<0.001 | 0.41 (0.89–2.15) p<0.001 | 0.24 (0.12–0.83) p=0.009 | 0.39 (1.10–2.82) p<0.001 |

MRI total damage score: sum score of MRI erosion and JSN; Coeff: Coefficient; CI: Confidence Interval.

## FRI0548 RESPONSIVENESS OF A NEW MRI SCORING METHOD BASED ON THE CANADA-DENMARK DEFINITIONS OF LESIONS IN THE SPINE AND THE SPARCC MRI SPINE INFLAMMATION INDEX IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** The Spondyloarthritis Research Consortium of Canada (SPARCC) Spine Inflammation Index is a well-established MRI scoring system for vertebral body inflammation.(1) It does not take the exact anatomical location of lesions into account. The Canada-Denmark (CanDen) MRI definitions were developed to allow detailed anatomical evaluation of inflammatory and structural lesions of the vertebral bodies as well as the posterior segments in patients with axial spondyloarthritis (axSpA).(2–3)
**Objectives:** The aim of this study was to assess the distribution of scores and the responsiveness of this new method, which combines the CanDen MRI definitions into a scoring system, as compared with the SPARCC Spine Inflammation Index in an axSpA randomized controlled trial.
**Methods:** For each disco-vertebral unit, inflammatory lesions of vertebral bodies (VB) in the anterior and posterior corners on central sagittal slices were scored

as 1 (small) or 2 (large). Non-corner lesions were scored as 2 (small) or 4 (large). Antero-lateral and postero-lateral inflammatory corner lesions in lateral sagittal slices were scored as 1. Inflammatory lesions in the posterior segments (PS) were each scored as 1. Fat (4), erosion and new bone formation were scored in a comparable way (details not shown due to length restrictions).
49 patients with axSpA and indication for TNFα inhibitor were randomized to placebo or adalimumab 40 mg sc. eow for 6 weeks. MRI of the spine was scored according to CanDen definitions and SPARCC by an experienced reader blinded to the clinical data. Responsiveness was assessed by standardized response mean (SRM) and Guyatt's responsiveness index (GRI). Values ≥0.8 represent a large degree of responsiveness.
**Results:**

Table 1. The distribution of CanDen and SPARCC scores at baseline as median, range, and inter-quartile range (IQR) is shown

| Measure (range) | Median | Range | IQR | SRM | GRI** |
|---|---|---|---|---|---|
| CanDen inflammation (total) (0–582) | 5 | 0–72 | 2–12 | 0.6 | 1.4 |
| CanDen inflammation (VB) (0–456) | 5 | 0–64 | 2–12 | 0.6 | 1.5 |
| CanDen inflammatory lesions (PS) (0–126) | 0 | 0–14 | 0–0 | 0.3 | 0.8 |
| CanDen fat infiltration (0–502) | 2 | 0–35 | 0–8 | 0.1 | 0.4 |
| CanDen bone erosion (0–480) | 0 | 0–8 | 0–0 | 0.2 | NA* |
| CanDen bone spurs (0–460) | 0 | 0–137 | 0–0 | NA* | NA* |
| SPARCC MRI Spine Inflammation Index | 6 | 0–65 | 2–14 | 0.6 | 1.5 |
| BASDAI | 6.3 | 4.2–9.8 | 5.3–7.2 | 1.1 | 1.3 |

SRM and GRI for changes week 0 to 6. *Not computable due to SD=0 in denominator. **Mean change score in adalimumab group divided by the SD of change scores in placebo group.

**Conclusions:** A new anatomy-based scoring system for spine inflammatory and structural lesions was described, demonstrating similar responsiveness as the SPARCC method. Further studies are needed to investigate the additional value of assessing posterior segments.
**References:**
[1] Maksymowych et al. Arthritis Rheum 2005;53:502–9;
[2] Lambert et al. J Rheumatol 2009;36-S84:3–17;
[3] Østergaard et al. J Rheumatol 2009;36-S84:18–34;
[4] Pedersen et al. Arthritis Res Ther 2013;15:R216
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1386

### FRI0549 CONE-BEAM CT, A NEW LOW-DOSE 3 D IMAGING TECHNIQUE FOR ASSESSMENT OF BONE EROSIONS IN RHEUMATOID ARTHRITIS: RELIABILITY ASSESSMENT AND COMPARISON WITH CONVENTIONAL RADIOGRAPHY

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**Background:** Early and accurate detection of erosive joint changes is important when validating and monitoring rheumatoid arthritis (RA). Magnetic resonance imaging (MRI) and ultrasound (US) have shown to be more sensitive than conventional radiography (CR) but have the drawbacks of being expensive (MRI) or difficult to learn (US). In several studies these methods have been compared to multidetector computed tomography (MDCT), which can be considered a reference method for detecting erosions but has several disadvantages, for example the exposure to ionising radiation. With the newly developed cone-beam CT (CBCT) which is dedicated for imaging of the extremities, these disadvantages can be minimized. The radiation dose is low, about 10% of the effective dose of MDCT, comparable to an extra CR exposure.
**Objectives:** To assess the intra-and interobserver agreement of erosions detected and scored with CBCT. To compare CBCT with CR for assessment of bone erosions in patients with established rheumatoid arthritis.
**Methods:** 30 patients (23 females, 7 males) with established RA – median disease duration (min-max) 15 (14–15) year – who had CR performed according to the Better AntiRheumatic PharmacOTherapy (BARFOT) study protocol were examined also with extremity CBCT (hands and feet) at the same occasion. Bone erosions were scored twice according to RA MRI score (RAMRIS), on digital images in three planes from the CBCT by two observers. The radiographs were scored by a third observer with Sharp van der Heijde Score (SHS). Disease activity was assessed with disease activity score of 28 joints (DAS28). Remission was defined as DAS28<2.6. Comparisons between groups was performed using Mann-Whitney U test. Correlations were performed with Spearman correlation test and intra class correlation coefficient (ICC) was calculated.
**Results:** The median age (min-max) was 54 (27–75) and median DAS28 (min-max) 2.25 (0.63–6.49). All 30 patients showed erosions on CBCT and 26 on CR. The correlation between CBCT and CR was 0.77 (p<0.001). Intra-and interobserver reliability for erosions scored by CBCT was excellent for both hands and feet for the two observers (ICC 0.90–0.97).The CBCT erosion scores of 16 patients in remission was median RAMRIS (min-max) 9 (1–67) vs. 21 (2–224), p=0.077 for 11 patients not in remission. The results for CR were for patients in remission median SHS (min-max) 12 (0–97) and those not in remission 40 (6–151), p=0.034. The median (min-max) numbers of eroded joints were 8 (1–40) with CBCT vs. 2 (0–20) with CR for patients in remission and for those not in remission 16 (2–68) with CBCT, vs. 7 (0–34) with CR. There were significantly more eroded joints detected by CBCT, p=0.002.
**Conclusions:** CBCT is a new low-dose 3 D imaging technique, which has high reproducibility and is more sensitive than CR in detecting erosions. CBCT has a potential to become a useful tool in detecting and follow up of erosions in patients with RA.
**Disclosure of Interest:** None declared
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## Epidemiology, health services and outcome research

### FRI0550 REAL-WORLD TREATMENT PATTERNS AMONG RHEUMATOID ARTHRITIS PATIENTS WHO SWITCH FROM A TUMOR NECROSIS FACTOR INHIBITOR TO ANOTHER MEDICATION

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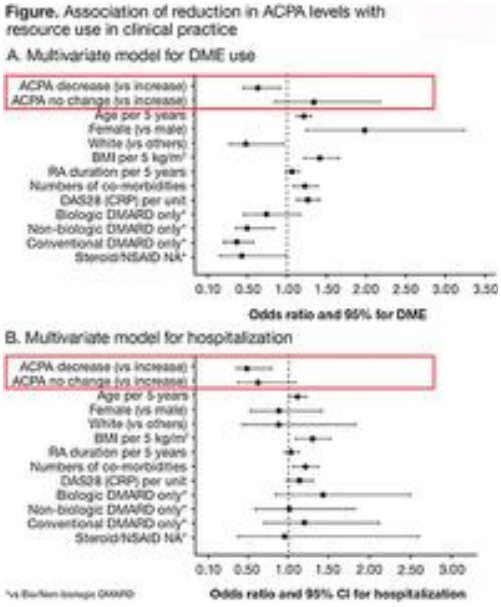
**Background:** When a patient with rheumatoid arthritis (RA) fails initial treatment with a tumor necrosis factor inhibitor (TNFi) because of inadequate response or lack of tolerability, switching to another TNFi or to a non-TNFi is recommended, but this is based on limited evidence.[1,2]
**Objectives:** This study examined real-world treatment patterns between patients with RA who switched from a TNFi to another TNFi (TNFi cyclers) compared with those who switched from a TNFi to a non-TNFi (non-TNFi switchers).
**Methods:** The data source was an administrative claims database from a large managed care organization of commercial and Medicare Advantage patients in the United States. The "index claim" was the first TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab) claim between January 2010 and February 2014 after ≥6 months of continuous enrollment pre-index. Eligible patients were aged ≥18 years at index with RA and no other autoimmune condition for which the study drugs could be used. The study included patients who subsequently switched either to another TNFi or to a non-TNFi (abatacept, tocilizumab, or tofacitinib) within 12 months post-index and had ≥12 months of additional follow-up. Each patient had 1 of 4 treatment patterns in the 12 months after the initial switch: (1) switched to a third TNFi or non-TNFi; (2) restarted the second therapy after a treatment gap of ≥45 days without switching; (3) discontinued the second therapy without switching or restarting; or (4) persisted with the second therapy without switching, restarting, or discontinuing. Adherence was defined as a proportion of days covered (PDC) of ≥80% for the second therapy.
**Results:** Of 32,272 adult patients with RA who received ≥1 biologic, 1432 met all study criteria, including 379 non-TNFi switchers and 1053 TNFi cyclers. Most patients (81%) were female. Non-TNFi switchers were older (54.0 vs 51.1 y; $P<0.001$) and less likely than TNFi cyclers to be commercially insured (82% vs 90%; $P<0.001$). In the 12 months after the initial switch, non-TNFi switchers were significantly more likely than TNFi cyclers to persist on the second medication (51% vs 44%; $P=0.021$) and significantly less likely to switch to a third TNFi or non-TNFi (29% vs 37%; $P=0.006$); non-TNFi switchers and TNFi cyclers had similar rates of restarting therapy after a ≥45-day treatment gap (6% vs 8%; $P=0.325$) and discontinuation without restarting or switching therapy (14% vs 11%; $P=0.185$). In the 12 months after the initial switch, non-TNFi switchers were significantly more likely than TNFi cyclers to have high adherence (≥80% PDC) to the second medication (45% vs 38%; $P=0.021$).
**Conclusions:** Among patients with RA, those who switched from a TNFi to a non-TNFi were more likely than TNFi cyclers to be persistent on the second medication in the first year, had greater adherence to the second medication, and were less likely to switch therapy again in the first year. The implications for clinical treatment outcomes deserve further study.
**References:**
[1] Singh et al. Arthritis Care Res (Hoboken). 2012;64:625–639.
[2] Smolen et al. Ann Rheum Dis. 2014;73:492–509.
**Acknowledgement:** This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. Jonathan Latham assisted with preparation and submission of the abstract.
**Disclosure of Interest:** B. Chastek Employee of: Optum, which was hired by Sanofi and Regeneron Pharmaceuticals to conduct the research, J. Curtis Consultant for: Sanofi and Regeneron Pharmaceuticals, L. Becker Employee of: Optum, which was hired by Sanofi and Regeneron Pharmaceuticals to conduct the research, P. Mahajan Shareholder of: Sanofi, Employee of: Sanofi, C. Chen Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc.
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## FRI0551 EVALUATION OF CHANGE IN ANTI-CITRULLINATED PEPTIDE AUTOANTIBODY LEVELS IN CLINICAL PRACTICE AND ASSOCIATION WITH RESOURCE USE

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**Background:** Testing for anti-citrullinated peptide antibodies (ACPA) has become standard in RA diagnosis in clinical practice, partly due to improved assay specificity compared with detection techniques for antibodies against RF.[1] ACPA concentration, beyond ACPA positivity, is indicative of more aggressive radiographic progression.[2] However, there is limited information on the association between changes in ACPA levels in clinical practice and resource use measures.
**Objectives:** To evaluate the association of changes in ACPA levels with resource use (durable medical equipment [DME] use/hospitalizations) in clinical practice.
**Methods:** Patients enrolled in the Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study (BRASS) Registry, established in 2003, were analysed. BRASS primarily comprises patients with established RA who were evaluated semi-annually for multiple, clinical patient-reported outcomes and resource utilization parameters. The current analysis is based on patients enrolled in the BRASS registry who had ACPA values at baseline and at follow-up visits. ACPA levels were measured by well-documented and validated ELISAs from Inova Diagnostics (San Diego, CA), until its discontinuation in 2011, and Euro-Diagnostica (distributed by IBL-America, Minneapolis, MN) thereafter. Annual mean ACPA change from baseline (CFB) to 12 months was calculated and categorized as decrease (1+ unit decrease), no change (>–1 to <1 unit change) or increase (1+ unit increase). DME use of canes, wheelchairs, walkers and commodes as well as hospitalizations were assessed every 6 months. Multivariate regression analyses controlling for baseline covariates were conducted to evaluate associations between ACPA CFB and resource use measures defined by DME and hospitalizations.
**Results:** A total of 840 patients (64%) in BRASS had ACPA values at baseline and follow-up and were included in the current analysis. A decrease in ACPA levels was observed in 42.6% (n=358) of patients, 18.1% (n=152) had no change and 39.3% (n=330) had an increase. There were no significant differences in baseline characteristics between the three groups, except for BMI; patients with RA with an increase in ACPA levels had significantly lower BMI at baseline. In univariate analyses, the percentages of patients with DME use were 23.8, 30.5 and 29.8% in the groups with a decrease, no change and an increase in ACPA levels, respectively. Similarly, the percentages of patients with hospitalizations were 13.7, 13.9 and 21.3%, respectively. After controlling for baseline covariates, the odds ratio for DME use over 12 months in patients who had an ACPA decrease (vs increase) was 0.60 (95% CI 0.41, 0.89; p=0.011), and the odds ratio for hospitalization was 0.49 (95% CI 0.32, 0.75; p=0.001; Figure).

**Figure.** Association of reduction in ACPA levels with resource use in clinical practice

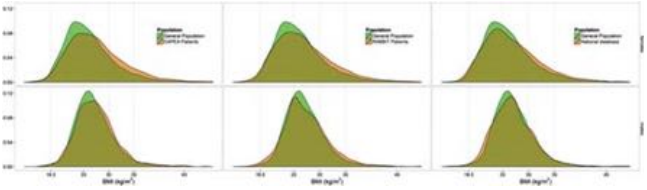



**Conclusions:** A reduction in ACPA levels was associated with a reduction in DME use and hospitalizations.
**References:**
[1] Whiting PF, et al. Ann Intern Med 2010;152:456–464; W155–466.
[2] Ronnelid J, et al. Ann Rheum Dis 2005;64:1744–9.
**Disclosure of Interest:** E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, C. Iannaccone: None declared, M. Frits: None declared, N. Shadick Grant/research support from: Bristol-Myers Squibb, Crescendo Biosciences, Amgen, UCB, Questcor, M. Weinblatt Grant/research support from: Bristol-Myers Squibb, Crescendo Bioscience, UCB, Amgen, Consultant for: Bristol-Myers Squibb, Crescendo Bioscience, UCB, AbbVie, Roche, Janssen, Pfizer, Lilly, Amgen
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## FRI0552 PATIENTS WITH RHEUMATOID ARTHRITIS ARE MORE OBESE THAN THE GENERAL POPULATION ALREADY AT DISEASE ONSET: A COLLABORATIVE ANALYSIS FROM THREE LARGE GERMAN RA DATABASES

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**Background:** METARTHROS (Metabolic impact on joint and bone disease) is a nation-wide German network to investigate the interaction between inflammatory and metabolic diseases.
**Objectives:** To compare the distribution of the body mass index (BMI) in early and established rheumatoid arthritis (RA) with representative data from the general population.
**Methods:** The distribution of the BMI was determined with baseline data from the early arthritis cohort CAPEA and the biologics register RABBIT as well as with data of patients enrolled in the National database of the Collaborative Arthritis Centers in 2013. BMI categories of <18.5 kg/m$^2$ (underweight), 18.5 to <25 kg/m$^2$ (normal weight), 25 to <30 kg/m$^2$ (overweight), and ≥30 kg/m$^2$ (obesity) were used. The results were stratified by age and sex and were compared to the German Ageing Study. The association of the BMI with sociodemographic features and markers of disease activity were analysed with non-parametric tests and linear models.
**Results:** The data of 1,207 (CAPEA), 12,230 (RABBIT) and 3,424 (National database) patients were evaluated. The mean age was 56/56/62 years, the mean disease duration 13 weeks/9.9 years/13.5 years and the mean DAS28 score 5.1/5.2/3.1 units, respectively. In all cohorts, obesity was more frequent (23.8%/23.4%/21.4%) than in the general population (18.2%), remaining in the age groups <70 years, independent of disease duration and more prominent in females (Fig.1). Current smoking was inversely associated with BMI. Linear analyses revealed no significant association between BMI and DAS28.
Fig.1 Distribution of the BMI in CAPEA, RABBIT and the National database



**Conclusions:** A higher prevalence of obesity, already seen at disease onset, supports a pathogenic role of obesity in the development of RA. This difference is more pronounced in females than in males. Patients in the cohorts with longer disease duration did not show a higher prevalence of obesity than those with recent onset RA, indicating that obesity may rather be a risk factor than a consequence of RA.
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**Disclosure of Interest:** None declared
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## FRI0553 OBESITY AND THE RISK OF SYSTEMIC LUPUS ERYTHEMATOSUS IN THE NURSES' HEALTH STUDIES

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**Background:** Obesity in the U.S. has increased to an alarming extent over the past four decades. Obesity is related to risk of several autoimmune diseases, possibly via generation of adipokines and inflammatory cytokines. Prospective studies of obesity and systemic lupus erythematosus (SLE) risk are lacking however.
**Objectives:** To prospectively evaluate the association between obesity and SLE risk
**Methods:** We conducted a prospective cohort study of women in the U.S. Nurses' Health Studies (NHS, 1976–2012, age 30–55 at baseline; NHSII, 1989–2013, age 25–42 at baseline). Incident SLE was confirmed by American College of Rheumatology 1997 criteria. Body mass index (BMI, kg/m$^2$) was reported at baseline and on biennial questionnaires. Cumulative average BMI (18.5 to <25 [normal (ref)], 25 to <30 [overweight], ≥30 [obese]) was the primary exposure. Cox proportional hazards models estimated hazard ratios (HR) and 95% confidence intervals (CI) for SLE by cumulative average BMI category, adjusting for covariates (Table). Analyses were conducted in each cohort; results were meta-analyzed with a DerSimonian-Laird random effects model. Sensitivity analyses: 1) excluded

women with cancer, and 2) started in 1988 (NHS)/1989 (NHSII) when obesity prevalence in the U.S. was most steeply increasing.
**Results:** We identified 154 SLE cases in NHS and 113 cases in NHSII. At baseline, obesity was present in 8.4% (NHS) and 11.8% (NHSII); mean age was 42.7 (SD 7.1) years (NHS) and 34.4 (SD 4.6) years (NHSII); 92% were White in each cohort. Obesity was significantly associated with SLE risk among women in NHSII, but not NHS (Table). In NHSII, a strong dose-dependent relationship between BMI and SLE risk was observed. After meta-analysis, obese women had a non-significantly elevated SLE risk compared to normal weight women (p trend 0.02). Results were similar in sensitivity analyses excluding women with cancer (HR 1.48, 95%CI 0.93–2.37, p trend 0.03). In analyses starting in 1988/1989, obese women had an increased SLE risk (meta-analyzed HR 1.76, 95%CI 1.19–2.58) compared to normal weight women (p trend <0.01).

Risk of SLE by cumulative average BMI category among 114,536 women in the Nurses' Health Study (NHS, 1976–2012) and 109,245 women in the Nurses' Health Study II (NHSII, 1989–2013)

| | Cumulative average BMI, kg/m$^2$ | | | p trend |
|---|---|---|---|---|
| | 18.5 to <25 | 25 to <30 | ≥30 | |
| NHS (n=154 cases) | | | | |
| Cases/P-Y | 89/1,989,864 | 47/897,609 | 18/381,108 | |
| Adjusted HR (95% CI)* | 1.00 | 1.28 (0.89–1.84) | 1.14 (0.67–1.92) | 0.37 |
| NHSII (n=113 cases) | | | | |
| Cases/P-Y | 65/1,368,032 | 19/577,955 | 29/393,325 | |
| Adjusted HR (95% CI)* | 1.00 | 0.75 (0.45–1.26) | 1.88 (1.19–2.98) | 0.02 |
| NHS + NHSII meta-analysis | | | | |
| Cases/P-Y | 154/3,357,896 | 66/1,475,564 | 47/774,433 | |
| Adjusted HR (95% CI)* | 1.00 | 1.02 (0.61–1.71) | 1.49 (0.91–2.43) | 0.02 |

P-Y: person-years.*Adjusted for age, questionnaire cycle, race, household income, smoking, alcohol intake, oral contraceptive use, age at menarche, menopausal status and post-menopause hormone use p for heterogeneity = 0.039.

**Conclusions:** Obesity was associated with a significant 88% increase in SLE risk in the younger cohort, NHSII, but did not significantly elevate SLE risk in NHS subjects. Meta-analysis revealed a non-significant 49% increased risk of SLE in obese women. We observed a stronger obesity-associated SLE risk when analyses started in 1988/1989 in both cohorts. The discrepant results between the cohorts are not fully understood and deserve further study.
**Disclosure of Interest:** None declared
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## FRI0554 POVERTY MODIFIES THE EFFECT OF RACE ON TOTAL KNEE ARTHROPLASTY OUTCOMES

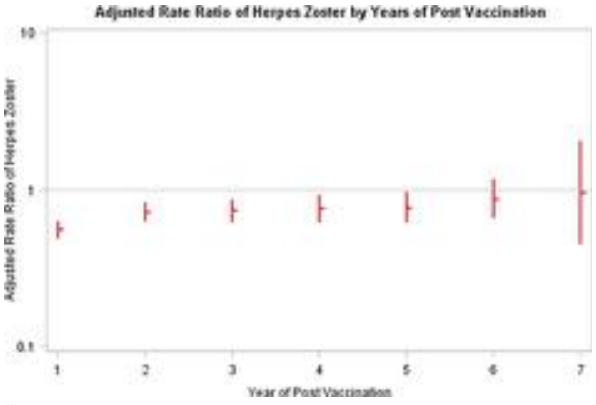
S.M. Goodman[1], M.L. Parks[2], M.H. Bogardus[1], M. Zhang[3], J.T. Nguyen[3], Y.-Y. Lee[3], M.P. Figgie[2], L.A. Mandl[1], A.R. Bass[1]. *[1]Rheumatology; [2]Orthopedics; [3]Biostatistics, Hospital for Special Surgery, New York, United States*

**Background:** Race is an important predictor of total knee arthroplasty (TKA) outcomes in the United States; however analyses of race can be confounded by socioeconomic factors.
**Objectives:** To analyze the interaction between race and community poverty as it effects patient reported outcomes after TKA.
**Methods:** We identified all patients undergoing TKA enrolled in a hospital based registry between 2007 and 2011, living in three adjacent states. Using geocoding we linked individual-level registry data including WOMAC pain and function to U.S. census tracts (CT) data. We constructed a multivariate linear mixed effect model within multilevel frameworks to assess the interaction between race and CT poverty on 2-year WOMAC outcomes.
**Results:** Of 4225 TKA patients, 194 (4.6%) were black. Baseline WOMAC scores were statistically but not clinically significantly worse for blacks than for whites (WOMAC Pain 49 vs. 55, p<0.0001; WOMAC Function 47 vs. 54, p<0.0001; 100=best). Fewer blacks had a college education or above (45% vs. 62%, p<0.0001), and blacks had higher BMI (33 vs. 30, p<0.001) and more comorbidities than whites (44% >1 comorbidity vs. 27%, p<0.0001). More blacks lived in high poverty neighborhoods (37% vs. 3.5%, p<0.0001). Controlling for multiple potential confounders, our model demonstrated that whites and blacks from census tracts with <10% poverty have similar 2-year WOMAC scores. With increasing community poverty, pain and function worsened; from census tracts with >50% poverty blacks had clinically meaningful worse pain and function compared to whites (Table 1).
**Conclusions:** We have found a significant differential effect of poverty on 2-year outcomes after TKA when stratified by race. Overall WOMAC scores are minimally but not significantly worse for blacks than whites. However, while outcomes among whites do not vary much between high and low poverty census tracts, the effect of high poverty levels was disproportionally associated with worse TKA outcomes among black Americans. Since a higher proportion of blacks live in high poverty areas, this finding has important implications. Efforts to improve TKA outcomes among U.S. blacks will need to investigate both the impact of individual patient-level factors and community-level poverty.
**Disclosure of Interest:** None declared
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## FRI0555 LONG TERM EFFECTIVENESS OF HERPES ZOSTER VACCINE AMONG PATIENTS WITH AUTOIMMUNE AND INFLAMMATORY DISEASES

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**Background:** Recent results from long-term follow-up of healthy older participants of the Shingles Prevention Study (SPS) demonstrated that the herpes zoster (HZ) vaccination lost most of its benefit after approximately 10 years. However, the duration of protection among patients with autoimmune or inflammatory (AI) diseases is unclear.
**Objectives:** Current study aimed to evaluate the duration of HZ vaccine effectiveness in preventing HZ among older patients with autoimmune diseases.
**Methods:** Using Medicare data from 2006–2013 for patients with AI diseases, this retrospective cohort study identified patients who had HZ vaccination. To control for confounding, patients without HZ vaccination were matched 2:1 to vaccinated patients on year of vaccination, age, gender, race, type of AI diseases, and use of biologics, DMARDs and glucocorticoids. Follow up began one month after vaccination and ended at: HZ, death, loss of coverage or 12/31/2012. We calculated HZ incidence rates for each year and used Poisson regression to calculate the adjusted risk ratio of HZ for each year.
**Results:** Of 59,627 vaccinated patients with AIs matched to 119,254 unvaccinated AI patients, we identified 1,242 and 3,183 HZ events during follow-up respectively. Incidence rates among vaccinated increased from 0.75 per 100 person years (PY) during the first year post vaccination to 1.36 during the 6th year post. After multivariable adjustment, vaccinated patients had a significantly lower risk of HZ compared to unvaccinated patients through 5 years but not beyond.




Figgure 1

**Conclusions:** Among patients with autoimmune diseases, the effectiveness of HZ vaccination waned over time, and a significant benefit to reduce HZ risk compared to non-vaccinated patients was found only through 5 years post vaccination.
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**Abstract FRI0554** – Table 1. WOMAC pain and function 2 years after total knee arthroplasty: interaction between race and census-tract poverty level

| Census tract poverty level* | Race | WOMAC pain at 2 years | | | WOMAC function at 2 years | | |
|---|---|---|---|---|---|---|---|
| | | Estimate (standard error) | Estimated difference (standard error) | p-value | Estimate (standard error) | Estimated difference (standard error) | p-value |
| 10% | Black | 85.64 (1.55) | –1.09 (1.59) | 0.49 | 82.16 (1.53) | –2.32 (1.56) | 0.14 |
| | White | 86.74 (0.39) | | | 84.48 (0.38) | | |
| 20% | Black | 82.85 (1.36) | –2.89 (1.53) | 0.06 | 79.59 (1.35) | –4.02 (1.52) | 0.009 |
| | White | 85.74 (0.74) | | | 83.61 (0.74) | | |
| 30% | Black | 80.05 (1.77) | –4.69 (2.11) | 0.03 | 77.03 (1.77) | –5.72 (2.12) | 0.007 |
| | White | 84.74 (1.19) | | | 82.74 (1.19) | | |
| 50% | Black | 74.47 (3.34) | –8.28 (3.94) | 0.04 | 71.89 (3.34) | –9.11 (3.94) | 0.02 |
| | White | 82.74 (2.13) | | | 81.00 (2.14) | | |

*Percentage of population in census tract below poverty level. Estimation based on linear mixed effect model using the following assumptions: WOMAC pain = 53.73; age = 66.51; BMI = 29.99; expectation score = 78.49; gender = female; comorbidities = 0.

Amgen, Pfizer, BMS, Crescendo, AbbVie, Consultant for: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, AbbVie
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## FRI0556 DOES LEAVING POVERTY REDUCE NEWLY ACCUMULATED DAMAGE IN SLE?

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**Background:** Several studies indicate that persons with SLE in poverty experience increased levels of accumulated damage compared to the non-poor. However, it is unknown as to whether leaving poverty reduces the amount of newly accumulated damage and over what time frame.
**Objectives:** Describe impact of permanently leaving poverty on newly accumulated damage and the duration of time until the effects of poverty are attenuated.
**Methods:** We used the UCSF Lupus Outcomes Study (LOS), a national longitudinal sample of persons with SLE interviewed annually. The survey collects data to assess whether individuals are ≤125% of the US Federal poverty level as well as a validated self-report battery of accumulated damage, the Brief Index of Lupus Damage (BILD)[1]. We used linear regression to analyze the impact of having left poverty permanently versus having remained in poverty or never having been in poverty and effect of # of years out of poverty on change in BILD between the 2009 and 2014, with and without adjustment for covariates. Covariates are listed in the footnote to Table 1, below.
**Results:** 2009 LOS interviews included 750 persons with SLE, of whom 587 were interviewed through 2014. Of the 587, 461 (80%) were never in poverty between 2009 and 2014, 51 (9%) remained poor throughout, and 67 (12%) left poverty permanently. In 2009 mean BILD was 1.95 (std dev, 2.00), range 0–13; by 2014, mean BILD increase was 1.44 (std dev 1.71), range 0–13, a clinically meaningful increment in damage. Table 1 summarizes change in BILD as a function of having left poverty and for how long and shows that persons who left poverty experience similar levels of accumulated damage as those never in poverty; this occurs by 2–3 years after leaving poverty.
**Conclusions:** Leaving poverty is associated with reduced levels of newly accumulated damage as soon as 2–3 years later, even when taking into account disease, demographics, medical care, and health behaviors. These results indicate that clinicians should be attentive to the burdens associated with poverty and that public policies to alleviate poverty not specifically geared to persons with SLE may contribute to the reduction of new damage in SLE.
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**Acknowledgement:** Robert Wood Johnson Investigator Award in Health Policy and NIAMS P60-AR-053308 and 5R01AR56476
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## FRI0557 THE ASSOCIATION BETWEEN BODY MASS INDEX AND MRI-DETECTED INFLAMMATION; PARADOXICAL EFFECTS IN RHEUMATOID ARTHRITIS, OTHER ARTHRITIDES AND SYMPTOM-FREE CONTROLS

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**Background:** Generally, an increased body mass index (BMI) is associated with higher inflammatory markers. Within rheumatoid arthritis (RA) it has been observed that a high BMI is associated with less severe radiographic joint damage.[1–4] The biologic mechanism underlying this association is unidentified.
**Objectives:** As joint damage is the consequence of inflammation, and because MRI is sensitive in detecting local inflammation, this study aimed to explore the association between BMI and MRI-detected inflammation in patients with RA, other arthritides and symptom-free persons recruited from the general population.
**Methods:** We studied 202 RA patients, 170 patients with other inflammatory arthritides from the Leiden Early Arthritis Clinic cohort and 193 symptom-free persons from the general population.[5] At baseline, all participants underwent a contrast-enhanced 1.5T MRI of the dominant or most painful MCP, wrist and MTP joints. Each MRI-scan was scored by two readers on synovitis, BME and tenosynovitis. The sum of the scores yielded the total MRI- inflammation score. Linear regression models (on log transformed MRI-data) were used for associations with the total MRI-inflammation score and Spearman's correlations for correlations with separate inflammatory features as they were non-normally distributed.
**Results:** A higher BMI was associated with higher MRI-inflammation scores in symptom-free persons ($\beta$=1.029, p=0.040) and arthritides other than RA ($\beta$=1.082, p<0.001). These $\beta$'s indicate an 1.029 fold and an 1.082 fold increase in MRI-inflammation with every point increase in BMI (Figure). However, in RA patients a higher BMI was associated with lower MRI-inflammation score ($\beta$=0.969, p=0.005). Similar results were seen when correcting for age and gender. Evaluating the different inflammatory features separately showed that BMI was correlated with higher synovitis and tenosynovitis scores in symptom-free persons (respectively $\rho$=0.17, p=0.016 and $\rho$=0.16, p=0.027) and in arthritides other than RA (respectively $\rho$=0.40, p<0.001 and $\rho$=0.26, p<0.001). This is in contrast to RA where a higher BMI was correlated with lower synovitis scores ($\rho$=-0.18, p=0.010) and was not correlated with tenosynovitis ($\rho$=-0.10, p=0.15). Similarly, BMI was positively correlated with BME in other arthritides ($\rho$=0.16, p=0.048)) and negatively correlated with BME in RA ($\rho$=-0.23, p=0.001).

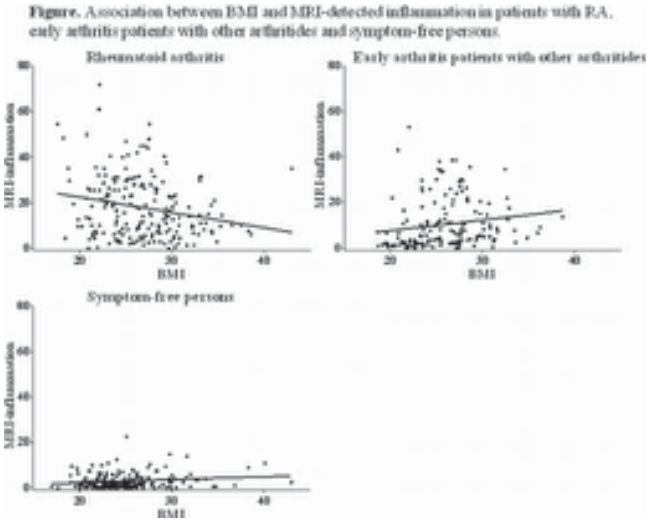


**Figure.** Association between BMI and MRI-detected inflammation in patients with RA, early arthritis patients with other arthritides and symptom-free persons

**Conclusions:** The association between BMI and MRI-detected inflammation differs in patients with RA compared to patients with other arthritides and symptom-free controls. Within RA a higher BMI is associated with less MRI-detected synovitis and BME; this might explain the previously observed association of BMI with less radiographic damage.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2035

**Abstract FRI0556** – Table 1. Effect of leaving poverty and years out of poverty on change in BILD damage index between 2009 and 2014 in SLE, with and without adjustment for disease, demographic, and health care characteristics and health behaviors

| Leaving poverty | | Never in poverty | Left poverty permanently | Remained in poverty | |
|---|---|---|---|---|---|
| | | Data in cells represent level of newly accumulated damage (BILD) between 2009 and 2014 | | | |
| | Unadjusted* | 1.33 | 1.41 | 2.08 | |
| | Adjusted* | 1.24 | 1.08 | 1.90 | |
| Years out of poverty | | 5–11 years | 2–3 years | 1 year | Remained in poverty |
| | Unadjusted* | 1.24 | 1.44 | 2.43 | 2.31 |
| | Adjusted* | 1.04 | 1.26 | 2.31 | 2.06 |

Variables in adjusted models include age, gender, race/ethnicity, level of educational attainment, disease duration, specialties of principal and other physicians for SLE, managed care vs. fee-for-service insurance, pass rates of ≥85% in SLE quality indicators, smoking status (past, current, never), and body mass index. *Leaving poverty and # of years out of poverty significantly related to level of new damage accrual between 2009 and 2014 (p<0.05).

## FRI0558 RHEUMATOID ARTHRITIS PREVALENCE IN EUROPE, A EULAR-ENDORSED SURVEY

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**Background:** Various rheumatoid arthritis (RA) prevalence estimates have been reported across Europe, but differences in methodology made it difficult to disentangle true heterogeneity (1). A unique RA prevalence survey method, comprising similar sampling and results interpretation, was needed.
**Objectives:** to estimate the RA prevalence in France, Turkey, Lithuania and Serbia using a unique methodology and to use direct method for standardization of results with reference to the European Standard Population.
**Methods:** In a first detection phase, a unique Questionnaire covering signs, symptoms, self-reported diagnosis and classification criteria for RA (ACR 1987) (2), previously translated and validated for each of the participating countries, was conducted on population sample. Two-stage random sampling was implemented on seven areas covering 20 counties in France, seven geographical regions covering 25 administrative provinces in Turkey, two largest cities- Vilnius and Kaunas in Lithuania and two geographical regions covering four counties in Serbia. In a second confirmation phase, diagnoses were confirmed by rheumatologists. Results were standardized by age and sex using the European Standard Population, defined as EU-27+EFTA, based on the 2010 estimates.
**Results:** Detection Questionnaire was administered by telephone on 15219 persons in France (3), 6558 in Lithuania (4) and 6213 in Serbia (1), with 64.7%, 64.7% and 63.3% response rate, respectively. In Turkey, Questionnaire was administered face-to-face on 4012 persons. Diagnoses were confirmed for 32 cases in France (93.7% female), 25 in Turkey (92.0% female), 39 in Lithuania (100.0% female) and 23 in Serbia (82.6% female). Overall standardized RA prevalence estimates are given in Table 1.

Table 1. Age- and sex-standardized RA prevalence, % (95% CI) for France, Lithuania, Turkey and Serbia, 18 years and older

| | Men | Women | Total |
|---|---|---|---|
| France | 0.15 (0.02–0.29) | 0.42 (0.26–0.58) | 0.29 (0.17–0.40) |
| Lithuania | 0.00 (0.00–0.00) | 1.01 (0.68–1.34) | 0.50 (0.38–0.63) |
| Turkey | 0.13 (0.00–0.31) | 1.02 (0.59–1.45) | 0.57 (0.31–0.84) |
| Serbia | 0.19 (0.00–0.38) | 0.52 (0.27–0.76) | 0.35 (0.18–0.53) |

**Conclusions:** Age- and sex-standardized RA prevalence estimates in France were in line with Serbia, but lower than in Turkey and Lithuania. Standardized RA prevalence estimates in men were similar for all countries, up to 0,19%. Standardized women RA prevalence was largely heterogenous, resulting in diverse overall European RA prevalence, from 0,29% to 0,57%. The use of a unique survey method with similar sampling and case ascertainment has shown genuine heterogeneity of the RA prevalence in women across Europe.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4940

## FRI0559 LATITUDE GRADIENTS INFLUENCE THE AGE OF ONSET OF RHEUMATOID ARTHRITIS: A WORLDWIDE SURVEY

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**Background:** The effects of latitude gradients on diseases serve as surrogates for environmental factors to generate hypotheses for further testing. The age of onset in rheumatoid arthritis (ao-RA) is one important outcome predictor. Some reports suggest that ao-RA may be different depending on latitude gradients.
**Objectives:** To assess the ao-RA at preselected cities worldwide.
**Methods:** A proof-of-concept, worldwide survey. We selected major cities in each 15° quadrant (latitude and longitude) worldwide and found rheumatologists' contact information through rheumatology associations (e.g. ACR, PANLAR). An invitation e-mail was sent to rheumatologists requesting to directly interview 20 consecutive RA patients (ACR criteria) who attended their clinics about ao-RA. A second e-mail with instructions and a data-log sheet was sent to those who accepted. The information was limited to patient ID (initials or consecutive numbers), date of birth (month and year), date of RA diagnosis and date of RA onset (when the patient first noted a swollen joint). This data was considered nonsensitive, so no informed consent was required as per local regulations. Our goal was to have 3 participating rheumatologists in each selected city from 40 countries around the world. Statistical analysis: intra-city consistency was considered if no significant differences in ao-RA among rheumatologists' data were found (non-parametric tests). Then the ao-RA was compared per latitudes (each 10°) and longitudes by continents, and worldwide (one-way ANOVA with post-hoc Scheffé for multiple comparisons). Frequency distribution per ao-RA etary groups (10 year intervals) was also analyzed by country and quadrant. Significant differences were set at $p<0.05$.
**Results:** Data from 2,481 patients were obtained from 126 rheumatologists in 78 cities in 42 countries. Intra-city variability could be assessed in 29 (37%) cities, and consistency was ascertained in 72.5% of these. The overall frequency distribution by age group showed that in 28% of patients the disease started before 35 yrs of age, 23% between 36 and 45, 26% between 46 and 55, 15% between 56 and 65, and 8% after 65 yrs of age; the mean ao-RA was 44±14 years (95% CI 44 to 45) and 84% were women. The linear chart of the mean ao-RA by worldwide latitudes showed a U shape, with the first peak in southern latitudes (>30°), the second peak in northern latitudes (>41°) and the base at the Tropic of Cancer. The ao-RA was 9 years older in northern latitudes when compared to the Tropic of Cancer (48 ± 15 vs. 39 ± 12 years, $p<0.001$), and the proportion of patients with ao-RA after the age of 55 was also higher (38% vs. 20%, $p<0.001$); these figures were consistent when analyzing data by continent.
**Conclusions:** RA should be considered a disease mainly affecting young people, with almost one-third beginning before age 36 and half before the age of 45 worldwide. ao-RA appears to be influenced in some way by latitudes, mainly in the Tropic of Cancer (younger) and northern latitudes (older). Studies to assess environmental factors in these latitudes may be worth pursuing further.
**Disclosure of Interest:** None declared
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## FRI0560 THE INCREASE IN THE NATIONWIDE INCIDENCE OF INFLAMMATORY RHEUMATIC DISEASES IN FINLAND DURING THIS MILLENNIUM

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**Background:** With the growing knowledge, the diagnostic and therapeutic opportunities of most inflammatory rheumatic diseases have intensified during the recent decades. This has led to improved functional outcomes in the vast majority of patients, but also to a certain dependency of specialist care in these patients, which, in the face of the current decreasing numbers of practicing rheumatologists raises concerns about the abundance of the health care resources. Some earlier reports have shown a decreasing incidence of rheumatoid arthritis (RA) in Eastern Finland; however there is no data on other diagnoses, and the experience from clinical practice contradicts these findings. Thus, to be able to optimally meet the future needs of rheumatological therapy, the total burden of new inflammatory rheumatic diseases needs to be assessed.
**Methods:** From the Finnish nationwide register maintained by the Social Institute of Insurance (SII) we collected data on all patients granted a new special reimbursement on medications for various inflammatory rheumatic diseases from January 1st 2000 to December 31st 2014. The diagnoses were: juvenile arthritis (all patients aged 0–16 years with ICD-10 diagnosis M02-M46), and for patients >16 years, seropositive rheumatoid arthritis (RA) (M05), seronegative RA (M06), spondylarthritis (M45-M46), unspecified arthritis (M13) and psoriatic arthritis (L40.5). The total number of new patients and the incidences for each diagnosis /100 000 patient years in these age groups were counted in 3-year cohorts.
**Results:** During the observation time altogether 54 658 patients (61.7% female) with a new diagnosis of a rheumatic disease and an initiated treatment were identified. The total incidence of inflammatory rheumatic diseases increased linearly from the first cohort's 63/100 000/patient years to the last cohort's (2012–14) 76/100 000/patient years, and the absolute yearly number of newly

| | Juvenile arthritis | Rheumatoid arthritis | | Spondyl-arthritis | Unspesified arthritis | Psoriatic arthritis |
|---|---|---|---|---|---|---|
| | | Sero+ | Sero– | | | |
| Female, % | 62.3 | 66.9 | 68.6 | 48.2 | 66.4 | 49.0 |
| Mean age (SD) years | 7.9 (4.6) | 57.4 (14.7) | 55.3 (16.4) | 38.1 (12.2) | 48.4 (16.0) | 48.5 (12.9) |
| Annual incidence/100 000 patients (Absolute number) | | | | | | |
| Total | 28 (4088) | 28 (18014) | 15 (9750) | 13 (8492) | 12 (7738) | 10 (6576) |
| Period 2000–02 | 23 (679) | 27 (3445) | 18 (2304) | 11 (1337) | 9 (1106) | 8 (985) |
| Period 2003–05 | 26 (758) | 28 (3515) | 16 (2057) | 11 (1417) | 12 (1493) | 9 (1144) |
| Period 2006–08 | 27 (774) | 28 (3656) | 14 (1825) | 12 (1512) | 13 (1625) | 10 (1298) |
| Period 2009–11 | 31 (898) | 27 (3571) | 14 (1805) | 14 (1902) | 13 (1669) | 11 (1496) |
| Period 2012–14 | 34 (979) | 28 (3827) | 13 (1759) | 17 (2324) | 14 (1845) | 12 (1653) |

diagnosed patients increased 1.39-fold during the follow-up. The characteristics of each diagnosis group are presented in the Table.
**Conclusions:** The total burden new of rheumatic diseases has increased during this millennium. The incidence of seropositive RA has remained stable and only that of seronegative RA has decreased slightly. However, the incidence unspecified and psoriatic arthritis, as well as spondylarthritis has increased clearly. Thus, with increasing numbers of new patients the recourses for rheumatological treatment should increase accordingly to face their needs.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2465

## FRI0561 HEALTHCARE RESOURCE UTILIZATION AND INFECTION RISK IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT COMORBIDITIES

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**Background:** Rheumatoid Arthritis (RA) patients have increased risk of infection and comorbidities[1]. Understanding healthcare resource utilization (HRU) and infection risk associated with comorbidity burden in RA may facilitate awareness of outcomes and development of care coordination strategies in RA.
**Objectives:** To estimate the differences in HRU and odds of an all-cause infection claim in RA patients with comorbidities compared to RA patients without comorbidities.
**Methods:** RA patients identified by ICD-9 CM codes (714.xx) were identified in a transactional U.S. healthcare claims database (Symphony Health) between years 2003 to 2013. RA patients with continuous clinical activity for 1 year after the first observed RA diagnosis (index date) were included. HRU and all-cause infection claim occurrence were measured 1 year post- index. The proportion of patients with ≥1 comorbidity (Comorbidity Cohort; CC) and those without any comorbidities (No Comorbidity Cohort; NC) were summarized using descriptive statistics. The odds of developing an infection and magnitude of HRU were estimated using multivariable logistic and gamma log-link regression models, respectively. Additional independent variables used in the models included age, gender, race, region, household income, medical payer and biologic medication use.
**Results:** 645,158 RA patients were identified using the inclusion criteria (30% NC; 70% CC). The average age for the NC group was 56 years at RA index and 75% were female. The CC group was similar in age and gender –mean age was 58 years at RA index and 77% were female. On average, the CC group had 3 comorbidities per patient (range 1 to 18). CC patients with ≥4 comorbidities were more than 2 times as likely to have an infection claim compared to NC patients ($p<.0001$). Patients with ≥10 comorbidities had the highest odds ratio (OR) for an all-cause infection claim (9.81 OR $p<.0001$) compared to NC patients. The risk for an infection claim increases by an average of 61% for each additional comorbidity. Females were more likely to develop infection compared to males (1.41 OR $p<.0001$). Furthermore, the odds of an infection claim increased as comorbidity burden increased ($p<.0001$). Biologic use did not significantly increase the odds of an infection claim in CC patients when comorbidities were controlled for in the model (OR 1.01; p=0.1938). HRU models estimated that each additional comorbid condition was associated with approximately 43% higher total costs and 41% increase in outpatient days.
**Conclusions:** Comorbidity burden in RA patients is associated with higher total healthcare resource and costs and higher odds of having a medical billing claim for infection. While controlling for comorbidity burden, biologic use did not significantly increase the odds of all cause infection healthcare claims.
**References:**
[1] Gullick, N.J., Scott, D.L. co-morbidities in established rheumatoid arthritis. Best Practice & Research Clinical Rheumatology 2011; 25: 469–483
**Disclosure of Interest:** A. Teeple Employee of: Janssen Scientific Affairs, LLC, M. Ryan Consultant for: Janssen Scientific Affairs, LLC, L. Muirheid Consultant for: Janssen Scientific Affairs, LLC, L. Ellis Employee of: Janssen Scientific Affairs, LLC
**DOI:** 10.1136/annrheumdis-2016-eular.3746

## FRI0562 ATTRITION AND PARTICIPANT CHARACTERISTICS IN A RHEUMATOID ARTHRITIS COHORT

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**Background:** The generalizability and validity of longitudinal observational studies is contingent on participant characteristics. If attrition is not random, it is important to identify any systematic differences between patients who continue to participate versus those who drop out.
**Objectives:** The purpose of this analysis was to compare characteristics of rheumatoid arthritis (RA) patients who continue to participate in the Ontario Best Practices Research Initiative (OBRI) to those of patients who have dropped out prior to reaching their 3 yr follow up.
**Methods:** Currently, 61 rheumatologists in Ontario (51% of active rheumatologists in Ontario) recruit patients into the OBRI. As of January 2015, 1533 patients had consented and were eligible to participate. 175 (11.4%) patients dropped out before reaching their 3 yr follow up assessment.
Among the drop outs, 109 (7.1%) withdrew consent, 38 (2.5%) were lost to follow up, and 28 (1.8%) refused to reconsent after 2 yrs of follow up. In addition to the drop outs, 38 (2.5%) patients had died. 1320 (86.1%) patients remained active participants. Patient characteristics and disease activity at enrollment were compared in the 175 patients who dropped out versus the 1320 patients who continued to participate. A survival curve was generated to look at time of drop out over the 3 year follow up period.
**Results:** Compared to patients who dropped out, patients who continued to participate had higher household incomes, lower disease activity scores, and were more likely to be taking a biologic at the time of enrollment (Table 1). The survival curve shows that the majority of patients drop out within the first two years (Figure 1).

Table 1. Patient Characteristics and Disease Activity at Time of Enrollment into OBRI

| | Patients who dropped out (N=175) | Active patients (N=1320) |
|---|---|---|
| Age, mean (SD) | 57.1 (15.4) | 56.9 (12.6) |
| Female, N (%) | 125 (75%) | 1041 (79%) |
| White, N (%) | 140 (88%) | 1133 (91%) |
| Education, N (%) | | |
| > High school | 146 (87%) | 1191 (92%) |
| *Household income, N (%) | | |
| ≥50,000 | 48 (28%) | 515 (39%) |
| Employment (full time), N (%) | 75 (45%) | 615 (52%) |
| Having private insurance, N (%) | 101 (60%) | 848 (68%) |
| Duration of disease (yrs), mean (SD) | 7.8 (9.9) | 9.2 (9.8) |
| *DAS28 (0–9.4), mean (SD) | 4.9 (4.4) | 4.4 (1.6) |
| *HAQ (0–3), mean (SD) | 1.44 (0.78) | 1.22 (0.76) |
| *Pain Score (0–3), mean (SD) | 1.76 (0.89) | 1.48 (0.87) |
| *RADAI (0–10), mean (SD) | 4.8 (2.2) | 4.0 (2.2) |
| Number of co-morbidities, mean (SD) | 2.3 (1.9) | 2.5 (2.1) |
| *RA medications | | |
| Biologic therapy, N (%) | 13 (8%) | 200 (15%) |

*$p<0.05$.

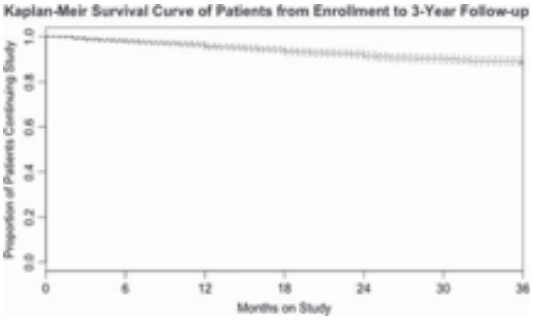



Figure 1

**Conclusions:** Patients with higher disease activity at enrollment were more likely to drop out. The OBRI attrition rate was 11.4% during the first three years of follow up, with 4.7% of patients dropping out in the first year, 3.5% in the second year and 3.2% in the third year. OBRI attrition rates were lower than those reported in the BRASS cohort (4.31% per 6 month follow up cycle) 1 and the ARAMIS cohort (6% per year) 2. The lower number of drop outs in the OBRI cohort could be attributed to the time invested in rheumatologist site visits by our study monitors and the biannual followup by our OBRI telephone interviewers.
**References:**
[1] Iannaccone et al., Arthritis Care &Research, July 2013
[2] Reisine et al., American College of Rheumatology, February 2000
**Acknowledgement:** OBRI Investigators
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4093

## FRI0563 IT'S MORE THAN DRYNESS AND FATIGUE: THE PATIENT PERSPECTIVE ON HEALTH-RELATED QUALITY OF LIFE IN PRIMARY SJÖGREN SYNDROME - A QUALITATIVE STUDY

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**Background:** Patients with primary Sjögren Syndrome (PSS) are affected by glandular and extraglandular manifestations leading to physical and mental impairment. How these factors affect the health related quality of life (HRQL) of these patients is largely unexplored.
**Objectives:** This qualitative study was conducted to investigate patients' perspectives and needs influencing HRQL in PSS.
**Methods:** We recruited 20 consecutive PSS patients fulfilling the American-European consensus classification criteria out of the PSS cohort of the Medical University Graz, Austria. A total of 6 focus group sessions were performed.

A discussion guide with four open-ended questions was developed containing all elementary components of HRQL (physical, mental, social, daily life). All interviews were audio-recorded and transcribed verbatim. A modified meaning condensation procedure was used to analyse the data.

**Results:** All patients were female, the mean age was 61 (SD ±8) years and mean disease duration was 5 (±2) years. The focus group sessions took on average 58 ±13 minutes. The number of patients in each group ranged from three to four.

The interview analysis resulted in 484 meaning units, 254 subconcepts and 87 concepts. The identified concepts were grouped into three dimensions: physical dimension, psychological & emotional challenges and social life & daily living. An inter-dependency of the three dimensions was identified.

The concepts most commonly reported belonged to the physical dimension: pain, dryness and complaints related to these two symptoms. Patients frequently mentioned consequences of dryness including recurrent inflammation of eyes and ears, loss of sense of smell and taste, sleeping disturbances and the inability to eat and chew.

In the dimension psychological & emotional challenges, the most frequently mentioned concepts were "being worried about the future", "a long symptom to diagnosis lag" and "the feeling of being an encumbrance for their families". Concepts like dependency on relatives in daily life, difficulties at work and financial burden were classified within the dimension of social life & daily living.

**Conclusions:** We found that three interrelated dimensions (physical dimension, psychological & emotional challenges and social life & daily living) best reflected patients' experiences and feelings related to PSS. HRQL in PSS patients was influenced not only by dryness rather psychological and social burden clearly impacted the patients.

**Disclosure of Interest:** None declared

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## FRI0564 SERUM URIC ACID TESTING PRACTICES OVER FIVE YEARS AMONG INCIDENT GOUT CASES

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**Background:** Gout is a chronic inflammatory disorder associated with elevated levels of serum uric acid (sUA), resulting in urate crystal deposits in soft tissues. Uncontrolled gout can lead to bone erosion and joint destruction, kidney stones, and uric acid nephropathy. Gout is treatable with medication and lifestyle change. Long-term sUA monitoring is needed to confirm that patients are achieving target levels (≤6 mg/dL, or <5 mg/dL in more severe cases).[1–3]

**Objectives:** To describe incident gout cases and characterize these patients by subsequent sUA testing practices during 5 consecutive years.

**Methods:** Data from Clalit Health Services were used to identify incident cases of gout (1/1/2003–31/12/2009) among members ≥25 years old with continuous enrollment in Clalit for 1 year prior to and 5 years subsequent to diagnosis (index date). Cases were identified based on the following criteria: a) 1 diagnosis of gout from a hospital or specialist visit; or b) ≥2 diagnoses of gout from a general practitioner (GP) visit and either elevated sUA (>6 mg/dL) or a purchase of colchicine or allopurinol. Cases were excluded if a member was concurrently diagnosed with a disease known to affect sUA (eg, renal insufficiency, cancer, Familial Mediterranean Fever). sUA testing practices during the 5-year follow-up period were defined as: full (≥1 test per year), moderate (≥1 test per year for 3 or 4 years), poor (≥1 test per year for 1 or 2 years) and no testing (no tests performed). Demographics, clinical characteristics, comorbidities, concurrent medications, and healthcare utilization were examined and stratified by testing practices. Chi-square tests and one-way ANOVAs were used to test for differences by testing practices.

**Results:** We identified 15,598 incident gout cases meeting the inclusion criteria. Mean age was 59.3±14.5 years, 79.7% were male, and 35.7% were of higher socioeconomic status. Patients' clinical history indicated that 15.2% were current smokers and 32.4% were obese. Prevalence of pre-existing comorbidities including CVD, diabetes and hypertension was 26.8%, 20.8%, and 52.5% respectively, and mean Charlson Comorbidity Index was 0.9±1.3. The distribution of annual sUA testing over the 5-year follow up in this cohort was: 5,445 (34.9%) patients had full testing, 6,678 (42.8%) had moderate testing, 3,196 (20.5%) had poor testing, and 279 (1.8%) had no testing. At the end of follow-up, 25.6% of patients' last documented sUA was ≤6 mg/dL. Among patients in the groups with sUA ≤6 or ≥10 mg/dL, close to 39% had full testing, while among those with sUA between 6.1–9.9 mg/dL, full testing ranged from 31.6%–35.7%.

**Conclusions:** Consistent with previous findings, gout patients in Clalit were on average older adults, predominately men and with concurrent comorbidities. Over three-quarters of newly diagnosed gout patients performed an annual sUA testing during at least 3 of the 5 years of follow-up. Further study is required to assess the association between regular testing and health outcomes.

**References:**

[1] Khanna, et al. Arthritis Care Res. 2012;64(10):1431–46;
[2] Zhang et al. Ann Rheum Dis 2006;65:1213–24;
[3] Jordan et al. Rheumatology 2007;46(8):1372–4.

**Acknowledgement:** Study funded by AstraZeneca.

**Disclosure of Interest:** A. Benis Employee of: Clalit Health Services, D. Jaffe Employee of: Kantar Health, N. Flores Employee of: Kantar Health, H. Gabay Employee of: Clalit Health Services, R. Morlock Employee of: Ardea Biosciences, A. Klein Employee of: AstraZeneca, D. Teltsch Employee of: Evidera, J. Chapnick Employee of: Kantar Health, B. Feldman Employee of: Clalit Health Services, M. Leventer-Roberts Employee of: Clalit Health Services

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## FRI0565 INFLUENCE OF ROUTE OF ADMINISTRATION/DRUG FORMULATION AND OTHER FACTORS ON COMPLIANCE WITH TREATMENT IN RHEUMATOID ARTHRITIS AND DYSLIPIDAEMIA

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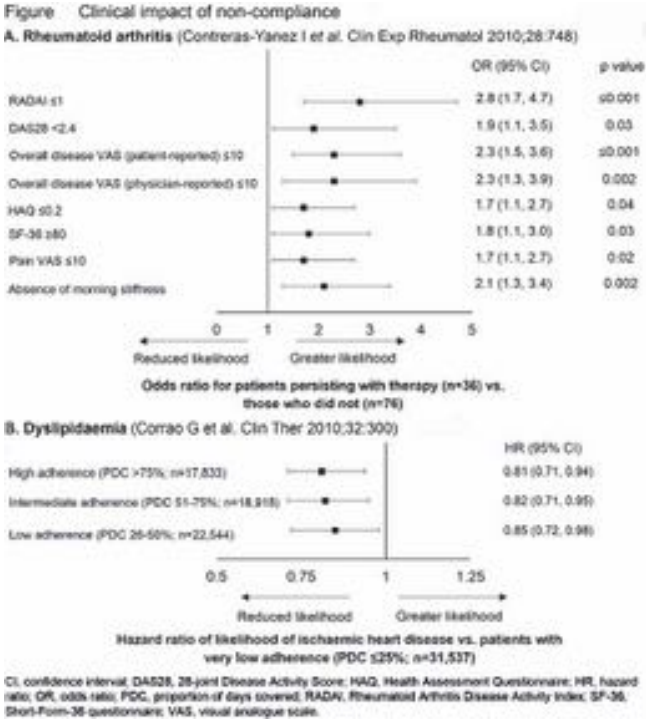
**Background:** Poor compliance with drugs for rheumatoid arthritis (RA) can lead to treatment failure, delayed recovery, disease progression and a need for more aggressive therapy. Understanding factors associated with poor compliance has potential to improve treatment outcomes.

**Objectives:** A comprehensive review was performed to investigate: the effect of route of administration on drug compliance in RA; compliance with oral drugs in RA compared with that in a non-pain-related disease (dyslipidaemia); the effect of poor compliance on clinical outcomes; the relationship between compliance and economic outcomes, such as healthcare resource utilisation and costs; and the impact of patient education/support programmes on compliance.

**Methods:** Comprehensive database searches and searches of the reference lists of relevant publications were performed to identify studies investigating drug compliance in adults with RA being treated with conventional synthetic or biologic agents. Similar searches were performed for studies of patients with dyslipidaemia being treated with statins. Studies had to be published after 1998 and in English, and had to involve ≥6 months of follow up. Compliance data were extracted and compared between the different routes of drug administration in RA, and between the two diseases for oral agents.

**Results:** A total of 33 and 22 papers underwent data extraction for RA and dyslipidaemia, respectively. The definitions and range of compliance values across studies was wide, making comparisons between drug formulations and diseases difficult. Within the constraints of the analysis, compliance and persistence rates were broadly similar for the different routes of drug administration in RA (compliance for intravenous [i.v.], subcutaneous [s.c.] and oral drugs, respectively: 68%, 59–73% and 33–107% [some patients took extra doses] at 6 months; 38–64% [i.v.] and 16–97% [s.c.] at 1 year; and 58–71% [oral] at 2 years). Compliance with oral drugs was also broadly similar across the two diseases (for RA: 33–107% at 6 months, 58–71% at 2 years; for dyslipidaemia: 40–100% at 6 months, 72–75% at 2–3 years). Poor compliance had clinical consequences

Figure Clinical impact of non-compliance



in both diseases: greater disease activity, pain and functional disability in RA, and increased serum cholesterol levels and risk of ischaemic heart disease in dyslipidaemia (Figure). The only factors associated with compliance/persistence across both diseases were age, race and the extent of copayment/out-of-pocket expenses. Over 1–3 years, poor compliance with biologic RA drugs led to increased resource use and medical costs but lower total direct costs due to reduced biologic (s.c. and i.v.) drug costs. By contrast, poor compliance with dyslipidaemia drugs resulted in increased total direct costs. For RA, compliance improved with patient education/support.

**Conclusions:** The route of drug administration and the symptomatic (pain) nature of the disease do not appear to be dominant factors for drug compliance in RA.

**Disclosure of Interest:** B. Fautrel: None declared, A. Balsa: None declared, P. Van Riel: None declared, M. Casillas Employee of: Employee of Eli Lilly and Company, J.-P. Capron Employee of: Employee of Eli Lilly and Company, C. Cueille Employee of: Employee of Eli Lilly and Company, I. De La Torre Employee of: Employee of Eli Lilly and Company

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## FRI0566 ATTRIBUTES OF THE SUBCUTANEOUS BIOLOGIC THERAPY PREFERRED BY PATIENTS WITH RHEUMATIC DISEASE AND SATISFACTION WITH THE TREATMENT. RHEU LIFE SURVEY

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**Background:** Preferences of patients and satisfaction with the medication are important to improve adherence and outcomes.

**Objectives:** In patients with rheumatoid arthritis (RA), axial spondyloarthritis (SpA) and psoriatic arthritis (PsA), we explored the attributes of drugs preferred by them, and the degree of satisfaction with the current medication.

**Methods:** RHEU-LIFE was a survey to patients >18 years-old with RA axial SpA or PsA treated with subcutaneous (SC) biological drugs, from 50 outpatient rheumatology hospital clinics. Patients responded anonymously to the survey. They ranked 5 treatment attributes from 1 (the most important) to 5 (the least important), and expressed their satisfaction with each one from "very satisfied" to "very dissatisfied".

**Results:** The survey was given to 1000 patients, 592 responded (59.2%, mean age 51.7 years, 42.4% men and 57.6% women; underlying disease RA: 304 (54.2%), axial SpA: 141 (25.1%), PsA: 116 (20.7%), not identified: 31. The biological drug was first (60.4%), second (26.8%) and third or more (13.5%). The attributes mentioned most frequently as "the most important" were normalization of quality of life (QoL) and symptoms control (43.6% and 32.5%, table). The importance was similar in patients with different diseases or treated with first, second or third biologic. The percentage "satisfied" or "very satisfied" was high for every attribute (80% or higher, table) and similar between patients with different conditions. The percentage "satisfied" or "very satisfied" with symptoms control and normalization of QoL was greater in those receiving the first biologic (87.8% and 85.7%) and lower with the third or more (78.4% and 72.0%, both $p<0.05$). No differences were found for the rest of the attributes.

Treatment attributes. Importance and satisfaction reported by patients with rheumatic diseases

| Treatment attributes | Importance* | | | | | % satisfied or very satisfied |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | |
| Continuous symptom control | 35.2% | 20.1% | 19.2% | 14.4% | 11.1% | 85.7% |
| Well tolerated | 21.5% | 20.2% | 27.9% | 18.2% | 12.2% | 81.0% |
| Rapid action | 19.2% | 20.6% | 21.2% | 22.5% | 16.5% | 79.8% |
| Convenience /ease of administration | 19.1% | 12.6% | 14.9% | 19.1% | 34.4% | 86.5% |
| Normalisation of quality of life | 43.6% | 19.9% | 13.6% | 8.9% | 14.0% | 81.7% |

*1 = the most important; 5 = the least important. The sum of percentages is not 100% because some patients scored various attributes as importance "1".

**Conclusions:** Patients with rheumatic diseases treated with SC biological drugs give more importance to normalization of the quality of life and symptom control than to tolerability, speed of action and the comfort or easeness of use, and express a high degree of satisfaction with their current treatment, especially those receiving therapy with a first biologic.

**Acknowledgement:** Financed by Merck Sharp & Dohme of Spain and endorsed by the patients' association ConArtritis (Arthritis National Coordinator).

**Disclosure of Interest:** None declared

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## FRI0567 TRENDS IN ANNUAL CONSULTATION INCIDENCE OF CLINICAL OSTEOARTHRITIS BETWEEN 1992-2013 IN UK PRIMARY CARE: ANALYSIS OF THE CLINICAL PRACTICE RESEARCH DATALINK

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**Background:** Recent trends and future projections in the population burden of osteoarthritis and primary joint arthroplasty rates across Europe point to a growing challenge for population health and health services. However there are few studies on whether the rate of new cases presenting to primary care is also increasing, and no published national studies in the UK.

**Objectives:** To determine the temporal trend in annual consultation incidence of clinical OA in UK primary care between 1992–2013.

**Methods:** We used the Clinical Research Practice Datalink (CPRD), a nationally representative database of primary care electronic health records (650 practices, 5 million population) to estimate the annual consultation incidence of clinical OA. To allow for known variation in codes used in primary care for coding osteoarthritis we using established Read codelists to define a new case of clinical OA as a recorded diagnosis of OA or, in adults aged over 45 years, a recorded non-specific peripheral joint pain code likely to reflect OA. Incident cases of OA in each calendar year had a coded record of clinical OA during the year, and no such record in the previous 3 years. Additionally we excluded cases with a record of a systemic inflammatory disease, spondyloarthropathy, or crystal disease in the previous 3 years or following 1 year, or a record of another specific non-OA diagnosis (soft-tissue disorders, other bone/cartilage diseases) at the same joint in the six months period before or after the recorded OA consultation. Prevalent OA cases identified in the previous 3 years were excluded from the denominator for each year to establish the at-risk population. Incidence density based on exact person time was applied to estimate annual incidence. Annual incidence was estimated for each year between 1992–2013 for any OA and for joint-specific (knee, hip and hand) OA, overall (all ages) and stratified by gender and age). Overall and gender estimates were age-standardised to the population of England in 2013. Sensitivity analyses included restricting the analysis to practices continuously registered with CPRD between 1992 and 2013, and to diagnosed OA only.

**Results:** Annual consultation incidence of clinical OA decreased from 30.7 per 1000 person-years (95% CI: 30.7–30.8) in 1992 to 28.4 (28.4–28.5) in 1999, then increased to 41.2 (41.1–41.2) in 2009 before decreasing to 32.8 (32.8–32.9) in 2013. The corresponding estimates among females were 36.2 (1992), 33.8 (1999), 48.7 (2009) and 39.2 (2013); for males, 25.3 (1992), 23.2 (1999), 34.1 (2009), and 26.8 (2013). Similar temporal trends in annual incidence were observed within each age-stratum and for knee and hip. There was a different pattern for incidence of hand OA which continuously increased from 1.9/1000 in 1992 to 4.9 in 2013. Similar trends were seen when restricting analysis to practices continuously registered with CPRD. Incidence of diagnosed OA decreased steadily from 2004.

**Conclusions:** We found no evidence of a sustained increase in the age-standardised consultation incidence of clinical osteoarthritis in UK primary care over recent years, a finding that held across a range of case definitions and sensitivity analyses.

**Acknowledgement:** We would like to thank Keele University and Public Health England for financially supporting this research.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4354

## FRI0568 DISEASE ACTIVITY STATES OF THE DAPSA, A PSORIATIC ARTHRITIS SPECIFIC INSTRUMENT, ARE VALID AGAINST THE CONSTRUCTS OF FUNCTIONAL STATUS AND STRUCTURAL PROGRESSION

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**Background:** The Disease Activity index for PSoriatic Arthritis (DAPSA) was developed and validated. It is a composite measure of swollen and tender joint counts, patient global and pain assessment and an acute phase reactant. Recently, also DAPSA disease activity states were developed using clinical trial data and observational data (1). However, the validity of these states in regards to important outcomes of the disease has not yet been determined.

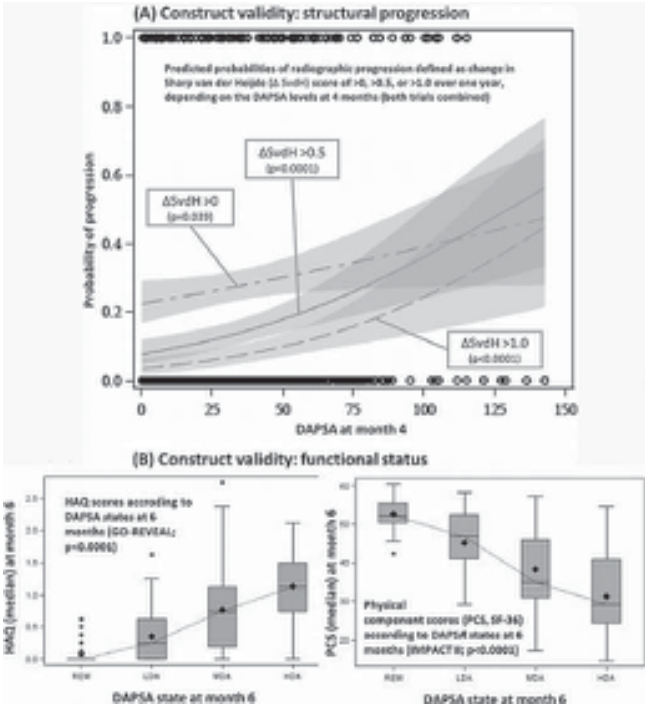
**Objectives:** To assess if different DAPSA disease activity states are associated with different degrees of functional impairment and/or different extents of joint damage progression in patients with psoriatic arthritis (PsA).

**Methods:** We used data from two pivotal trials of TNF-inhibitors in PsA, the IMPACT II (n=134) and the GO-REVEAL (n=313) trials. At 4 months, we identified patient in DAPSA remission (REM, ≤4), low disease activity (LDA, ≤14), moderate disease activity (MDA, ≤28), and high disease activity (HDA, >28). We then determined the rate of structural progression (defined as Sharp van der Heijde, SvdH, score increase of >0, >0.5, and >1 point from baseline to end of year 1) across these four disease activity groups. We also correlated DAPSA levels at 4 months with changes in SvdH change scores from baseline to year 1.

We also studied functional construct validity of the DAPSA states by assessing median scores of the Health Assessment Questionnaire Disability Index (HAQ; GO-REVEAL study only), and of the physical component scale of the Short Form-36 (PCS, SF-36; IMPACT II study only), across the different DAPSA states at 6 months.

**Results:** We identified 313 from GO-REVEAL and 134 from IMPACT II, with a mean (SD) baseline DAPSA of 44.7 (17.8) and 48.7 (26.3). The probability of progression according to different DAPSA scores is depicted in panel A of the Figure, separately for three cutpoints of progression. For all three analyses, the link between DAPSA and the probability of progression was significant

(progression >0: p=0.039; progression >0.5 and >1.0: p=0.0001 for both). This association was also seen when we compared patients in the four disease activity states at four months for their actual rate of progression, e.g., the proportion of patients with progression of >1 over one year was 3.7% among DAPSA remitters and 15.1% among patients with DAPSA HDA (p=0.0004).
We also confirmed functional construct validity by using HAQ scores in one trial (GO-REVEAL), and the SF-36 PCS in the other (IMPACT II). As can be seen in panel B of the Figure, the HAQ and PCS scores across the four groups were highly significantly different (p<0.0001 for both).




**Conclusions:** The definition of traditional disease activity states on the scale of the DAPSA, a PsA specific disease activity instrument, shows high validity against important constructs in PsA. This is important, and validates these DAPSA endpoints for future use in clinical trials, or as targets in clinical practice.
**References:**
[1] Schoels M et al. Ann Rheum Dis. 2015 Aug 12. [Epub ahead of print]
**Acknowledgement:** We thank Janssen/Centocor for providing data from their trials for the current analysis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4690

## FRI0569 REMISSION AND LOW DISEASE ACTIVITY MATRIX TOOL: RESULTS IN REAL-WORLD RHEUMATOID ARTHRITIS PATIENTS UNDER GOLIMUMAB

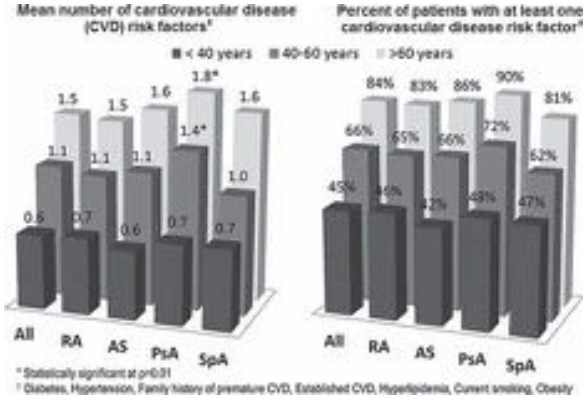
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**Background:** Cost-effectiveness of treatments in rheumatoid arthritis (RA) is of growing importance thus, the ideal is to have a tool that help us to select patients most likely to respond to biotechnological drugs.
**Objectives:** To assess the relationship between predicted disease states and the observed amount of improvement applying the remission and low disease activity (LDA) matrix tool presented by MSD as a poster at EULAR 2015[1] to our patients receiving golimumab (GLM).
**Methods:** We identified RA patients who had done GLM as first biological therapy in our hospital. Demographic and clinical data at baseline and at 6 months were collected. The calculation of remission or LDA rates at 6 months of GLM treatment was made based on the proposed prediction matrix tool. Patients were divided into 2 groups by their predicted remission rate at 6 months: lowest chance if <30% and greatest if ≥30%. Thereafter, we compared the amount of improvement in DAS28-4v, tender joint count (TJC), HAQ and Patient Global Assessment of Disease Activity Visual Analog Scale (PGA-VAS) scores observed in each group during 6 months of treatment with GLM.
**Results:** At our hospital, 239 patients with RA are under biological therapy. Of these, 20 had GLM as the first biological agent. Most patients were females (n=16, 80%) and mean age (SD) at start of biological therapy was 50 (11.8) years. Most were non-smoking (n=15, 78.9%). Only 2 patients had rheumatoid factor and anti–citrullinated protein antibodies negative and mean disease duration was 9.5 (5.6) years. The mean of DAS28 4v was 5.71 (1.16). At 6 months we found that only one patient had inactive disease, the remaining showed moderate (n=12) or high (n=4) disease activity; 6 patients did not have EULAR response. When we applied the matrix tool, we found that in these cases only three and one case had less than 20% predicted rate of remission and LDA, respectively. We observe that patients with lowest chance of remission had greater improvement in DAS28-4v, TJC, HAQ, and PGA-VAS scores than those with highest chance, during 6 months of treatment: 1.80 vs 0.54, 8.13 vs 0.27, 0.44 vs 0.26 and 19.63 vs 15.91, respectively (p<0.05 only for DAS28-4v and TJC).
We found 9 cases (45%) of drug discontinuations at 6 months, 8 of which for primary failure and 1 for adverse event (at 1 month). Of the patients that remained under GLM at 6 months, 9 remained beyond 12 months of treatment, 4 of which have achieved remission.
**Conclusions:** The application of the remission and LDA matrix tool in our sample showed contradictory results with regard to the predictive ability of remission or LDA rate at 6 months. On the other hand, our results reinforce that EULAR response may be a more appropriate goal of treatment than LDA or remission in a subgroup of patients.
**References:**
[1] Vastesaeger N, et al. EULAR 2015 (SAT0360)
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4835

## FRI0570 PRESENCE OF CARDIOVASCULAR DISEASE RISK FACTORS ACROSS DIFFERENT INFLAMMATORY JOINT DISEASE ENTITIES: RESULTS FROM THE NOCAR PROJECT

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**Background:** EULAR recommendations for cardiovascular disease (CVD) risk management in inflammatory joint diseases (IJD) advocate annual CVD risk assessment. Knowledge of the most prevalent CVD risk factors in the different IJD diagnoses may enable tailoring of efficient CVD preventive strategies for these high risk patients.
**Objectives:** 1) Evaluate prevalence of CVD risk factors in IJD patients and estimate 10-year risk for fatal CVD using the Systemic COronary Risk Evaluation (SCORE). 2) Investigate possible differences in CVD risk factor distribution across IJD entities.
**Methods:** In the nationwide NOrwegian Collaboration on Atherosclerosis in patients with Rheumatic joint diseases (NOCAR) project, annual CVD risk assessment is implemented in clinical practice of 11 rheumatology centres. IJD patients ≥30 years of age are eligible for inclusion. CVD risk factors and established CVD are recorded. The estimated CVD risk by SCORE was compared across IJD diagnoses for males and females individually, using analysis of variance, stratified by decennial age. Number of CVD risk factors, determined by presence of diabetes, hypertension, family history of premature CVD, hyperlipidemia (total cholesterol >8 mmol/L and/or low-density lipoprotein cholesterol >6 mmol/L), current smoking or obesity (body mass index ≥30kg/m$^2$), was counted for each patient. Frequency of CVD risk factors for the whole cohort was estimated and compared across the four major entities, using age and sex adjusted logistic regression analyses.
**Results:** Of the 2647 patients included in the 3 initial centres (Rheumatoid arthritis [RA]: n=1696, ankylosing spondylitis [AS]: n=445, psoriatic arthritis [PsA]: n=376, other spondyloarthritides [SpA]: n=130), 58.0% were females and the median (inter-quartile range [IQR]) age and disease duration were 57.4 (46.8–66.8) and 8.0 (3.8–15.9) years, respectively. The median (IQR) SCORE estimate was 1.4% (0.4–2.9) for the total population. The calculated CVD risk by SCORE was comparable across diagnoses, apart from male AS patients with a lower estimated CVD risk (p=0.01). Prevalence of CVD risk factors were comparable across all the IJD diagnoses, except for PsA patients who had significantly more CVD risk factors in the two oldest age groups (p=0.01). The percentage of patients



with at least one CVD risk factor and the mean number of risk factors for each patient are presented in the Figure. In detail, CVD risk factor rates were: family history of premature CVD: 17.5%, established CVD: 9.8%, current smoking: 19.6%, hypertension: 53.2%, obesity: 17.9%, diabetes: 6.7% and hyperlipidemia: 1.3%. PsA patients were more obese (p=0.001), more often hyperlipidemics ($p<0.05$), had more diabetes ($p<0.001$) and hypertension ($p<0.0001$), and were less frequently smokers (p=0.04). RA patients were more often smokers (p=0.02) and hypertensive (p=0.01).

**Conclusions:** In a large, multicentre cohort of IJD patients, a high prevalence of CVD risk factors was revealed, also in young patients. Interestingly, the risk factor burden was comparable in the 3 age categories across all IJD. Hence, CVD risk factor recording is essential in all IJD, and especially for PsA patients who had the largest CVD risk factor burden compared to the other IJD diagnoses.

**Disclosure of Interest:** None declared

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## FRI0571 THE ASSOCIATION BETWEEN COMORBIDITIES AND DISEASE ACTIVITY, FUNCTIONAL ABILITY AND QUALITY OF LIFE IN PATIENTS WITH SPONDYLOARTHRITIS: RESULTS FROM THE MULTI-NATIONAL ASAS-COMOSPA STUDY

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**Background:** Comorbidities in rheumatoid arthritis are known to add to the burden of disease and its complexity, with implications on disease outcomes and prognosis. In Spondyloarthritis (SpA), the impact of comorbidities on outcomes is less well studied; yet, their prevalence is high.

**Objectives:** To investigate the relationship between the comorbidity burden in SpA as measured by the Rheumatic Disease Comorbidity Index (RDCI) and: (1) disease activity; (2) function; (3) quality of life.

**Methods:** Analysis was based on data from the ASAS COMOrbidities SPA study, ASAS-COMOSPA, a cross-sectional, multinational study involving 22 countries across four continents. Patients fulfilling the ASAS SPA criteria were included. Comorbidities were computed according to the Rheumatic Diseases Comorbidity Index (RDCI), which includes ischaemic heart disease, stroke, hypertension, lung disease (COPD), malignancy, fractures, depression, diabetes and gastrointestinal disease; range 0–9 (higher score indicating higher comorbidity burden). Univariable, followed by multivariable multilevel mixed-effects linear regression models were used to investigate the relationship between the RDCI and ASDAS(CRP), BASDAI, patient global, BASFI, and EQ5D, adjusting for clinical confounders (table). Patients were nested into their country of origin, which formed the basis of the multilevel analysis.

**Results:** A total of 3558 patients were included in the study; 66% males, mean age 43 (SD 14), median disease duration 5 years (IQR 11) and mean RDCI 0.72 (1.08). An increase in RDCI was associated with higher BASFI, BASDAI, ASDAS and patient global score and lower EQ5D (all $p<0.001$) (see table). For instance a patient with an RDCI score of 2 compared to 0 had on average 0.7 point higher on the BASFI, one point higher on the BASDAI and patient global, 0.24 units higher on the ASDAS and a 0.06 points lower on the EQ-5D.

Table 1. Relationship between comorbidities and disease outcomes

| OUTCOME | RDCI (β [95% CI]) |
|---|---|
| BASFI[$] | 0.34 [0.27–0.40] |
| BASDAI[£] | 0.53 [0.45–0.61] |
| ASDAS^ | 0.12 [0.09–0.16] |
| Patient's Global Assessment of Disease Activity^ | 0.45 [0.36–0.53] |
| EQ5D** | –0.03 [–0.04 to –0.02] |

*All models adjusted for age; gender; the presence of axial vs peripheral disease. [$]Model also adjusted for disease duration; level of education; BMI; smoking status; ASDAS. [£]Model also adjusted for level of education; BMI; CRP. ^ Model also adjusted for level of education; BMI. **Model also adjusted for BASFI, ASDAS.

**Conclusions:** Higher comorbidity burden is independently associated with worse outcomes in SpA as reflected by higher disease activity, worse functional and quality of life measures. The results highlight the need for promptly identifying and treating comorbidities in SpA. As with emerging evidence in RA suggesting failure to achieve treat-to-target principles in the presence of comorbidities, it is possible that comorbidities also hinder the achievement of therapeutic goals in SpA.

**Disclosure of Interest:** None declared

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## FRI0572 SOCIAL AND EMOTIONAL IMPACT OF RHEUMATIC DISEASES IN PATIENTS TREATED WITH SUBCUTANEOUS BIOLOGICAL THERAPY. RHEU LIFE SURVEY

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**Background:** Rheumatic diseases impair patients' everyday life but this is rarely assessed in clinical studies.

**Objectives:** To describe the social and emotional impact perceived, as a consequence of the disease, by patients with rheumatoid arthritis (RA), axial spondyloarthritis (SpA) and psoriatic arthritis (PsA) treated with biological drugs.

**Methods:** RHEU-LIFE was a survey to patients with RA, axial SpA and PsA from Spain. Rheumatologists from 50 outpatient hospital clinics handed the survey to 20 consecutive patients >18 years-old who attended the clinic, they completed the survey at home and returned by pre-paid post mail. Patients were surveyed on the perceived impact of their rheumatic disease on five areas: 1) quality of life in general; 2) emotional state; 3) work or daily activity; 4) personal relations and 5) life of their families, responding with the options "no impact", "some", "moderate" or "severe".

**Results:** The survey was given to 1000 patients; 592 responded (response rate 59.2%, mean age 51.7 years [SD 13.2], 42.4% men and 57.6% women). Patients' disease were RA (n=304, 54.2%), axial SpA (n=141, 25.1%) and PsA (n=116, 20.7%). 31 patients did not identify their disease. The percentage of patients who considered that the disease moderately or severely affected the different areas is shown in the table. A higher percentage of women vs men declared that the disease moderately or greatly affected all the areas (table). Similarly, aged patients described a greater impact than those who were younger (table). No differences were observed with regard to the disease, with similar percentages of patients with RA, axial SpA or PSA declaring "moderate" or "severe" impact in all areas (all, $p>0.1$).

Percentage of patients who declared that the impact of the disease is "moderate" or "severe" effect in the different areas

| | All | Gender | | | Age | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Men | Women | p | <43 | 43–52 | 53–61 | >61 | p |
| Quality of life | 52.1% | 45.3% | 56.7% | 0.007 | 34.1% | 51.1% | 60.5% | 58.5% | <0.001 |
| Emotional | 41.0% | 36.2% | 44.6% | 0.004 | 30.4% | 44.6% | 45.4% | 39.7% | 0.018 |
| Work or daily activity | 49.2% | 40.5% | 55.9% | <0.001 | 33.3% | 47.5% | 59.8% | 55.0% | <0.001 |
| Personal relations | 26.0% | 19.6% | 30.4% | 0.014 | 15.6% | 28.3% | 30.8% | 27.5% | 0.017 |
| Life of family | 32.3% | 25.5% | 37.7% | 0.001 | 17.0% | 34.5% | 40.0% | 36.2% | 0.003 |

**Conclusions:** Patients with RA, axial SpA and PsA treated with biological drugs describe a significant impact in their quality of life, work or daily activity, emotional state, personal relations and life of their families, especially women and elderly patients. The impact was ranked similarly regarding the baseline disease.

**Acknowledgement:** This survey was financed by Merck Sharp & Dohme of Spain and endorsed by the patients' association ConArtritis (Arthritis National Coordinator).

**Disclosure of Interest:** None declared

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## FRI0573 INTEGRATION OF TIME-AVERAGED DAS28 FITS BETTER JOINT DESTRUCTION IN RHEUMATOID ARTHRITIS THAN ONE-TIME DAS28 AND IDENTIFIES A SIGNIFICANT JOINT-DESTRUCTIVE ASSOCIATION OF HLA-DRB1*04:05 WHICH IS INDEPENDENT OF ACPA AND DAS28

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**Background:** Disease Activity Score 28 (DAS28) is one of correlates of joint destruction in rheumatoid arthritis (RA) as well as genetic components, RA-related autoantibodies, and disease duration. Joint destruction is considered to reflect the cumulative history of the disease activities, but one-time DAS28 is used in many studies. Relationship among the correlates is still unclear, while we previously showed that HLA-DRB1*04:05 is associated with joint destruction independently of anti-citrullinated protein antibody (ACPA).

**Objectives:** We hypothesized the superiority of time-averaged DAS28 to one-time DAS28 to fit the model to assess joint destruction. We also hypothesized that DRB1*04:05 might be associated with joint destruction independently of ACPA and DAS28.

**Methods:** We recruited RA patients in the KURAMA (n=204) and IORRA cohort (n=557) whose data of modified Sharp/van der Heijde score (SHS), consecutive DAS28, and other correlates of SHS were available. We calculated time-averaged DAS28 and modeled SHS using time-averaged DAS28 and the other covariates. We randomly picked up DAS28 in each patient and constructed 1000 sets of DAS28 to model SHS. We empirically evaluated fitting of the model using time-averaged DAS28 among the 1000 models using one-time DAS28. Next, we analyzed an association between DRB1*04:05 and SHS of ACPA (+) patients in KURAMA (n=100) and IORRA (n=472).
**Results:** In conditioned for the autoantibodies and disease duration, the time-averaged DAS28 showed significant improvement of model fitting in comparison with one-time DAS28 ($R^2$ in KURAMA: p=0.037, $R^2$ in IORRA: p=0.001). Generalized linear regression model in ACPA (+) patients showed a significant association between DRB1*04:05 and SHS (overall p=0.0002) in conditioned for time-averaged DAS28 and the other covariates. We observed this significant association even in patients whose time-averaged DAS28 was in low disease activity or remission.

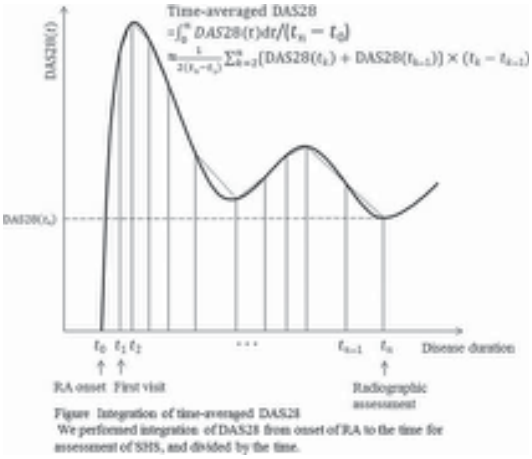


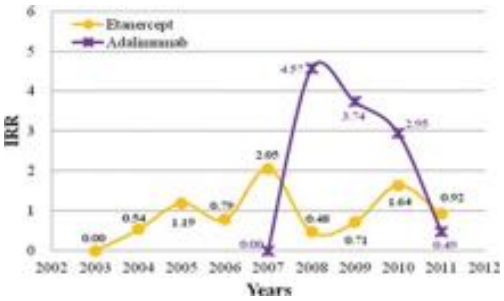
Figure Integration of time-averaged DAS28
We performed integration of DAS28 from onset of RA to the time for assessment of SHS, and divided by the time.

**Conclusions:** Time-averaged DAS28 fits SHS better than one-time DAS28 and usage of time-averaged DAS28 as a covariate would increase the power of studies to identify novel correlates of SHS. DRB1*04:05 demonstrates an association with joint destruction which is independent of ACPA and even DAS28 by using time-averaged DAS28, suggesting necessity of strong treatment for RA patients carrying DRB1*04:05 even when they are in low disease activity or remission.
**References:**
[1] Navarro-Compán V, et al. Rheumatology. 2015 54(6):994–1007.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3201

## FRI0574 ONE-YEAR TUBERCULOSIS RISK IN RHEUMATOID ARTHRITIS PATIENTS INITIATING TUMOR NECROSIS FACTOR-α INHIBITOR FROM 2003 TO 2011 IN TAIWAN: A NATIONWIDE POPULATION-BASED COHORT STUDY

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**Background:** Use of tumor necrosis factor-α inhibitor (TNFi), especially monoclonal antibody, may increase the risk of tuberculosis (TB) infection in patients with rheumatoid arthritis (RA). The emergence of active TB in RA patients receiving TNF-α inhibitor showed a biphasic pattern. The strategy of latent TB infection (LTBI) screening and treatment theoretically may reduce TB reactivation, which mainly contributes to the first phase of TB emergence. In Taiwan, etanercept and adalimumab were approved for RA treatment in 2003 and 2007 respectively.
**Objectives:** To examine the 1-year risk of TB infection in RA patients initiating TNFi therapies as compared to RA patients not treated with TNFi in Taiwan stratified by treatment initiation year (2003 to 2011).
**Methods:** Data was collected retrospectively using the 2003–2012 claim data from the Taiwanese National Health Insurance Research Database. We enrolled all treated RA patients initiating TNFi therapy as the study cohort, and those who never received TNFi therapy as the comparison cohort from 1st January 2003 to 31st December 2011. All patients were followed up for one year after starting treatment. The diagnosis of TB was identified using ICD-9-CM and the prescription of at least 2 anti-TB drugs within 6 months of TB diagnosis made. The 1-year TB risk of TNFi users compared with non-TNFi users was shown as incident rate rations (IRR) with 95% confidence intervals (CI) and adjusted hazard ratios (aHRs) using Cox's regression analysis after adjustment of potential confounders including age, sex, disease duration, TB history, comorbidities and concomitant medications, further stratified by the year of treatment initiation.
**Results:** A total of 46,668 RA patients were included; 40,678 (87.2%) in non-TNFi and 5,990 (12.8%) in TNFi group. A total of 163 1-year TB events were reported; 136 in non-TNFi group and 27 in TNFi group with 1-year TB incidence rate of 369 and 504 per 100,000 patient-years respectively. The 1-year TB risk was higher in TNFi users compared with non-TNFi users (IRR, 1.37; 95% CI, 0.71–2.07; aHR, 7.27; 95% CI, 3.65- 14.48). As shown in Figure 1, the IRR of TB within one year in adalimumab users compared with non-TNFi users peaked in 2008 (IRR, 4.57) and was lowest in the 2011 group (IRR, 0.49). Other significant risk factors of 1-year TB infection included age≥65 years (aHR, 1.52, 95% CI, 1.09–2.10), male (aHR, 1.81, 95% CI, 1.31–2.51) and prior TB infection (aHR, 29.28; 95% CI, 18.62–46.05).




**Conclusions:** The 1-year risk of TB in RA patients initiating TNFi was significantly higher than non-TNFi users. During 2008–2011, the 1-year TB IRR in adalimumab users compared with non-TNFi users dropped from 4.57 to 0.49, which might be explained by increasing physician/patient awareness with LTBI screening and treatment.
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[1] Chen DY, Shen GH, Chen YM, Chen HH, Hsieh CW, Lan JL. Biphasic emergence of active tuberculosis in rheumatoid arthritis patients receiving TNFalpha inhibitors: the utility of IFNgamma assay. Annals of the rheumatic diseases. 2012;71(2):231–7.
**Disclosure of Interest:** H.-H. Chen Grant/research support from: AbbVie Biopharmaceuticals GmbH Taiwan Branch, Y.-M. Chen: None declared, K.-L. Lai: None declared, C.-H. Lin: None declared, D.-Y. Chen: None declared, C.-H. Lim: None declared, C.-J. Tsai: None declared
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## FRI0575 THE UNMET NEED IN THE NORWEGIAN DISEASE-MODIFYING ANTIRHEUMATIC DRUG REGISTRY

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**Background:** Until 2012, the Norwegian disease-modifying antirheumatic drug (NOR-DMARD) registry included patients (pts) initiating treatment (trt) with conventional synthetic DMARDs (csDMARDs) and biologic DMARDs (bDMARDs). The revised NOR-DMARD protocol, implemented 2012–2013, includes bDMARDs only.
**Objectives:** Describe the outcomes of methotrexate (MTX) therapy and define the unmet need for further trt options for RA pts after MTX failure in the NOR-DMARD registry.
**Methods:** These analyses are based on data from two phases (P) of the NOR-DMARD registry: P1 – pts on csDMARDs and bDMARDs (2007–2011); P2 – pts on bDMARDs only (2012–2015). Using different selection criteria from P1 pts, MTX trt outcomes were assessed as follows: % of pts with inadequate response (IR) to MTX (defined as disease activity score 28–4 erythrocyte sedimentation rate [DAS28]>3.2 at 6 months [mo]); reasons for MTX discontinuation (D/C); % of MTX-IR pts remaining on trt despite DAS28>3.2 or DAS28>5.1. ACR20/50/70 and EULAR good/moderate response rates were assessed using P1 and P2 data in pts receiving bDMARDs as monotherapy (mono), +MTX or +other csDMARDs. Results are presented using descriptive statistics from non-imputed observations.
**Results:** P1 and P2 included a total of 2698 and 709 RA trt courses, respectively. Of 780 MTX-naïve pts starting MTX mono in P1, 429 (42.9%) had DAS28>3.2 at 6 mo; 381 of the 780 pts had available DAS28 data at Mo 12, and 30.9% pts had DAS28>3.2 at 12 mo. Furthermore, 58.2% of pts who had DAS28>3.2 at 6 mo remained at DAS28>3.2 at 12 mo. 1364 pts were treated with any csDMARDs in P1, 28/1364 pts had DAS28>5.1 for two consecutive visits and remained on trt.
In P1 pts previously exposed to MTX starting any trt other than MTX mono (N=1388), 1005 pts had a reason for MTX D/C listed; 489/1005 (48.7%) pts D/C due to side effects.
P1 included 1331 bDMARD trt courses: 279 (21.0%) as mono, 938 (70.5%) +MTX and 114 (8.6%) +other csDMARD. In P2 there were 709 trt courses with

bDMARDs: 229 (32.3%) as mono, 413 (58.3%) +MTX and 67 (9.3%) +other csDMARD. In P1, bDMARD mono pts had slightly higher baseline disease activity and slightly worse patient-reported outcomes. In P2, baseline demographics and characteristics were generally similar across trt groups (gps). EULAR and ACR responses at Mo 6 were generally comparable across trt gps in P1, although the bDMARD+other csDMARD gp had numerically higher ACR70 and lower EULAR good responses vs other gps. In P2, ACR20 and ACR50 responses were generally similar between bDMARD trt gps at Mo 6. At Mo 6, numerically more pts on bDMARD mono (18.4%) achieved ACR70 vs bDMARD+MTX (10.7%) and bDMARD+other csDMARD (5.9%); similar results were also observed for EULAR good/moderate responses. % of pts with DAS28 remission at Mo 6 were 54.4% for bDMARD mono; 45.7% for bDMARD+MTX; and 50.0% for bDMARD+other csDMARD (Table).

Efficacy endpoints at Month 6 in Phase 1 and Phase 2 populations for patients with RA treated with bDMARDs

| | bDMARD monotherapy | bDMARD + MTX | bDMARD + other csDMARD | All |
|---|---|---|---|---|
| *Phase 1 data (2007–2011)* | | | | |
| ACR70, n/N (%) | 20/160 (12.5) | 91/610 (14.8) | 11/64 (17.2) | 122/846 (14.4) |
| EULAR good/moderate, n/N (%) | 80/122 (65.6) | 331/487 (68.0) | 31/48 (64.6) | 442/657 (67.3) |
| EULAR good, n/N (%) | 57/122 (46.7) | 164/487 (33.7) | 11/48 (22.9) | 232/657 (35.3) |
| *Phase 2 data (2012–2013)* | | | | |
| ACR70, n/N (%) | 9/49 (18.4) | 27/253 (10.7) | 1/17 (5.9) | 37/319 (11.6) |
| EULAR good/moderate, n/N (%) | 34/44 (77.3) | 140/218 (64.2) | 8/11 (72.7) | 182/273 (66.7) |
| EULAR good, n/N (%) | 22/44 (50.0) | 89/218 (40.8) | 6/11 (54.6) | 117/273 (42.9) |
| Change in DAS28-4(ESR), mean (SD), [n] | -2.0 (1.7) [44] | -1.2 (1.4) [198] | -1.6 (1.2) [11] | -1.3 (1.5) [253] |
| DAS28-4(ESR) categories, n (%) | | | | |
| In remission (<2.6) | 25 (56.8) | 111 (45.7) | 7 (58.8) | 143 (47.2) |
| LDA (≥2.6 to ≤3.2) | 5 (10.9) | 42 (17.3) | 4 (28.6) | 51 (16.8) |
| MDA (>3.2 to ≤5.1) | 13 (28.3) | 74 (30.5) | 2 (14.3) | 89 (29.4) |
| HDA (>5.1) | 3 (6.5) | 16 (6.6) | 1 (7.1) | 20 (6.6) |
| Sustained remission: in remission at both Month 3 and Month 6 | 12/51 | 53/220 | 4/20 | 73/291 |

bDMARD, biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS, disease activity score; ESR, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; HDA, high disease activity; LDA, low disease activity; MDA, moderate disease activity; MTX, methotrexate; SD, standard deviation

**Conclusions:** Data from the NOR-DMARD registry showed that >40% of MTX-treated pts had not achieved DAS28 low disease activity 6 mo. Despite pts advancement to bDMARDs, almost 50% failed to reach DAS28 remission at follow-up. This demonstrates substantial unmet medical need for pts with moderate to severe RA. Trt grp comparisons will be further explored.

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## FRI0576 ECONOMIC IMPACT OF LOWER-LIMB OSTEOARTHRITIS WORLDWIDE: A SYSTEMATIC REVIEW OF COST-OF-ILLNESS STUDIES

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**Background:** Lower limb osteoarthritis (OA) is an expanding public health problem owing to the aging of the population and increase in obesity prevalence. Knowledge of the economic burden is limited.

**Objectives:** An overview of the economic consequences – overall costs as well as cost breakdown (direct and indirect) – of hip and knee osteoarthritis (OA) worldwide.

**Methods:** A systematic literature search of EMBASE, MEDLINE, Scopus and Cochrane databases for articles was performed independently by 2 rheumatologists who used the same predefined eligible criteria. Papers without abstracts and in languages other than English or French were excluded. Extracted costs were converted to an annual cost and to 2013 euros (€) by using the Consumer Price Index of the relevant countries and the 2013 Purchasing Power Parities between these countries and the European Union average.

**Results:** A total of 45 abstracts were selected, and 32 articles were considered for the review. The studiedpopulations were heterogeneous: administrative, hospital and national health survey data. Annual total costs per patient ranged from 0.7 to 12 k€, direct costs per patient from 0.5 to 10.9 k€ and indirect costs per patient from 0.2 to 12.3 k€. The weighted average annual costs per patient living with knee and hip OA were 11.1, 9.5 and 4.4 k€ for total, direct and indirect costs, respectively.

**Conclusions:** This review highlights the heterogeneity of studies and lack of methodologic consensus to obtain reliable cost-of-illness estimates for lower-limb OA. However, costs induced by the disease seem substantial and deserve to be more extensively explored.

**Disclosure of Interest:** None declared

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## FRI0577 A NATIONAL ELECTRONIC HEALTH RECORD-ENABLED REGISTRY IN RHEUMATOLOGY: THE ACR'S RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE)

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**Background:** In 2014, the ACR launched the Rheumatology Informatics System for Effectiveness (RISE), a national electronic health record (EHR)-enabled registry. RISE passively collects data from EHRs of participating practices, provides advanced quality measurement and data analytic capacities, and can be used to fulfill national quality reporting requirements. Here we detail the characteristics of practices participating in RISE, patient characteristics and performance on several nationally endorsed quality measures.

**Methods:** RISE is a national Qualified Clinical Data Registry (QCDR), allowing collection of data on quality of care without individual patient informed consent.

| Characteristic | Total N (N = 239,302) |
|---|---|
| Age at last encounter, mean (SD) | 59 (± 16.1) |
| Sex | |
| Female, n (%) | 179,069 (74.8) |
| Male, n (%) | 60,225 (25.2) |
| Missing, n (%) | 8 (0.003) |
| Race, n (%) | |
| White | 145,944 (60.9) |
| Black | 18,339 (7.7) |
| Asian | 3,408 (1.4) |
| American Indian/Alaskan Native | 974 (0.2) |
| Native Hawaiian/Pacific Islander | 116 (0.05) |
| Other | 23,901 (10.0) |
| Missing | 40,573 (17.0) |
| Insurance/Payer type (at last encounter), n (%) | |
| Medicare | 70,804 (29.6) |
| Medicaid | 3,914 (1.6) |
| Commercial | 114,269 (47.8) |
| Other | 4,220 (1.8) |
| Missing | 46,115 (19.3) |
| U.S. Region, n (%) | |
| Midwest | 29,114 (12.2) |
| Northeast | 32,085 (13.4) |
| Southeast | 91,727 (38.3) |
| Southwest | 50,239 (21.0) |
| West | 11,022 (4.6) |
| Missing | 25,064 (10.5) |
| Selected Diagnoses (ICD9 code at last encounter), n (%) | |
| Rheumatoid arthritis (ICD 9 714.0, 714.1, 714.2, 714.3x | 60,364 (25.2) |
| Sjogren's syndrome (710.2) | 15,800 (6.6) |
| Systemic lupus erythematous (ICD9 710.0) | 13,940 (5.8) |
| Psoriatic arthritis (696.0) | 13,550 (5.7) |
| Gout (ICD9 274.xx) | 9,887 (4.1) |
| Spondyloarthropathy (ICD9 720.xx) | 8,890 (3.7) |
| Systemic sclerosis (ICD9 710.1) | 2,754 (1.2) |
| Vasculitis (ICD9 446.0, 446.1, 446.2x, 446.4, 446.5) | 2,845 (1.1) |
| Dermatomyositis or polymyositis (710.3, 710.4) | 2,366 (1.0) |
| Sarcoidosis (ICD9 135) | 1,548 (0.6) |
| Smoking, n (%) (last encounter) | |
| Never | 142,962 (59.6) |
| Current | 24,913 (10.4) |
| Former | 47,879 (20.0) |
| Missing | 23,548 (10.5) |
| Blood pressure, mmHg, mean (SD) (last encounter) | |
| Systolic | 125.4 (±16.5) |
| Diastolic | 78.2 (±9.7) |
| Diastolic>90 OR Systolic>140, n (%) | 34,961 (14.6) |

Participating practices enter a Data Use Agreement with the ACR, after which local data are mapped, validated and uploaded regularly to the central registry. Practices can access an analytics dashboard that allows review of up-to-date information on quality measures by provider and practice as well as national benchmarks. RISE currently includes data on numerous quality measures regarding rheumatoid arthritis (RA), drug safety, osteoporosis prevention and treatment, low back pain, and preventive health care (e.g. smoking, blood pressure management). We analyzed data between October 1, 2014 and September 30, 2015 to characterize practices and patients captured in RISE. We also calculated performance on several RA quality measures endorsed by the National Quality Forum (DMARD use, disease activity measurement, functional status measurement).

**Results:** During the dates examined, RISE included data on 239,302 patients, including 60,354 with RA (Table). Three hundred twelve clinicians across 55 sites contributed data to RISE. Characteristics of patients in RISE are summarized in the Table. For the subset of patients with RA, 50.7% of patients had a disease activity score recorded, 53.2% had a functional status score recorded, and 82.1% were taking a DMARD, as defined by national quality measures. For DMARDs, 34.4% of patients with RA were on brand name biologic or small molecule drug at their last encounter, and 67.0% were receiving a non-biologic DMARD.

**Conclusions:** The ACR's national EHR-enabled registry will provide critical infrastructure for improving quality of care in rheumatology and will serve as a unique data source to generate new knowledge regarding rheumatic disease. Data validation and mapping is ongoing and RISE will be available to both the research and clinical community to use to advance rheumatology.

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## FRI0578 PATIENT AND CLINICIAN REPORTED OUTCOMES FOR PATIENTS WITH NEW PRESENTATION OF INFLAMMATORY ARTHRITIS: OBSERVATIONS FROM THE UK NATIONAL CLINICAL AUDIT

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**Background:** Early inflammatory arthritis (EIA) services have undergone substantial reconfiguration in recent years with the recognition of a window of opportunity early on in the disease course as well as the introduction of treat-to-target disease modifying anti-rheumatic drug strategies. As part of a national UK audit into the management of EIA data were collected on patients presenting with inflammatory arthritis for the first 3 months of specialist care.

**Objectives:** Here we report the response to treatment at a national level in terms of clinical outcomes.

**Methods:** All individuals >16 years presenting to specialist rheumatology services in England & Wales with suspected new onset IA were recruited. Clinician & patient derived assessments of outcome were collected with consent at baseline and after 3 months of specialist care. Data collected included the Disease Activity Score (DAS28), the Rheumatoid Arthritis Impact of Disease (RAID) questionnaire (a validated patient reported outcome measure assessing pain; functional capacity; fatigue; physical/ emotional wellbeing; quality of sleep and coping) and impact upon work status.

**Results:** 97% of hospital trusts in England and Wales participated. 6,354 patients with suspected early inflammatory arthritis were recruited between 1st February 2014 to 31st January 2015. Of these 2896 were diagnosed with RA (defined by the presence of polyarticular disease (>5 joints involved) or pauciarticular disease with positive cyclic citrullinated peptide antibody); this represented >40% of estimated expected incident RA cases. At first specialist assessment DAS28 was reported for 91% of RA patients: mean DAS28 was 5.0 (44% of patients a DAS28>5.1 indicating severe disease). The mean RAID score was 5.6 (range 0 not affected to 10 (most affected).

After 3 months of specialist care mean DAS28 reduced to 3.5 with 62% achieving a meaningful reduction in DAS28 of >1.2 units. 24% of patients achieved DAS remission. The mean RAID score after 3 months was 3.6; the mean reduction in RAID score was 2.6 and did not meet the minimum clinically important level of 3. Of the working patients aged 16–65 years providing data 7%, 5%, 16% and 37% reported that they were unable to work, needed frequent time off work, occasionally and rarely needed time off work due to their arthritis respectively. 19% reported never being asked about their work by clinicians.

**Conclusions:** Although there are data that suggest the severity of RA has diminished in recent years, this audit confirms that at presentation RA remains a disease with significant patient burden. Acknowledging that this audit only captures the first 3 months of care, the results demonstrate important achievements in RA care in contrast to what might have been expected for RA in previous decades. However, less than a quarter of patients achieved remission and improvements in RAID scores were below the accepted minimum clinically important difference within the first 3 months.

**Disclosure of Interest:** None declared

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## FRI0579 WHAT IS THE VARIABILITY OF HAQ OVER TIME IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ANTI-TNF?

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**Background:** The Health Assessment Questionnaire (HAQ) remains the gold standard for measuring patient-reported functional status in rheumatoid arthritis (RA) and is included among the measures suggested by the American College of Rheumatology for making treatment decisions in routine care. We have previously shown that significant variability exists in the correlation of individual HAQ questions with patient-reported and clinical outcomes.

**Objectives:** The aim of this analysis was to assess, in routine care, the timelines of HAQ improvement as compared to clinical improvement and to examine possible differences in the improvement of individual questions.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, ankylosing spondylitis, or psoriatic arthritis with infliximab (IFX) or golimumab (GLM). Eligible people for this analysis included RA patients treated with IFX who were enrolled since 2002 or with GLM enrolled since 2010. Time to achieving minimal important difference (MID; $\Delta \geq 0.22$) in HAQ, HAQ$\leq$1, minimal disease (MD) in individual HAQ questions (no or some difficulty), CDAI low disease activity (LDA), or CDAI remission was assessed with the Kaplan-Maier estimator of the survival function and cox regression.

**Results:** 1205 patients (75.3% female) were included with mean (SD) age of 56.0 (13.6) years and disease duration of 8.4 (8.9) years at baseline. Mean (SD) HAQ and CDAI were 1.55 (0.72) and 33.8 (17.4), respectively. Statistically significant and clinically meaningful improvements in both HAQ and CDAI were observed over time. The cumulative probability of achieving HAQ MID, HAQ$\leq$1, CDAI LDA, and CDAI remission by 12 months was 69.5%, 54.5%, 54.1%, and 18.1%, respectively. Time to achieving HAQ MID [Hazard Ratio (95% CI): 3.6 (3.2–4.2)], HAQ$\leq$1 [2.9 (2.6–3.4)], and CDAI LDA [3.1 (2.7–3.6)] was significantly lower as compared to CDAI remission.

With respect to individual HAQ questions, at baseline, the most predominant usual activities that patients were unable to do were taking a tub bath (27.9%), reaching and getting down a 5-pound object from the head (21.8%), and doing chores such as vacuuming or yard work (23.2%). In accordance, time to having no or some difficulty in these activities was significantly higher compared to the remaining HAQ items.

**Conclusions:** The results of this analysis show that the timelines for achieving HAQ targets in routine care is comparable to that of achieving CDAI LDA. Significant differences were observed in terms of improvement in individual HAQ items with the inability to take a tub bath, getting heavy overhead objects down, and doing chores being the most persistent.

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## FRI0580 COMORBIDITY BURDEN AND MEDICATION USE BETWEEN PSORIATIC ARTHRITIS PATIENTS WITH MODERATE-TO-SEVERE PSORIASIS VS. THOSE WITH MINIMAL SKIN PSORIASIS IN THE US

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**Background:** Psoriatic arthritis (PsA) is often presented with psoriasis (PsO). However, the severity of PsO among PsA patients varies, which may affect the comorbidity burden in this population.

**Objectives:** This study aimed to assess the comorbidity burden and medication use between PsA patients with moderate-to-severe PsO vs. those with minimal skin PsO.

**Methods:** Adults (18–64 years) with $\geq$2 claims for PsA (ICD-9-CM: 696.0) that were $\geq$30 days apart were selected from the Truven Health MarketScan claims database (data cut period 07/2009–06/2014). The index date was a randomly selected date after the first PsA claim. All patients were required to have $\geq$12-month continuous eligibility before (baseline period) and after (study period) the index date. Patients in the PsA+moderate-to-severe PsO group were required to have 1) $\geq$2 claims for PsO (ICD-9-CM: 696.1) that were $\geq$30 days apart, *and* 2) $\geq$1 PsO claim and $\geq$1 systemic therapy/phototherapy in the study period. PsA patients were classified into the PsA+minimal skin PsO group if they did not have any PsO claim or phototherapy in the data cut period, *or* had $\geq$1 PsO claim but

no evidence of systemic therapy or phototherapy in the data cut period. Patient demographics as of the index date, comorbidities, and medication use during the study period were compared between these two groups. Wilcoxon rank sum tests were used to compare continuous variables and Chi-square tests were used to compare binary variables. Bonferroni correction was used to adjust for multiple comparisons.

**Results:** A total of 10,495 patients with PsA+moderate-to-severe PsO and 15,503 patients with PsA+minimal skin PsO were included in this study. Mean age and percent male were comparable (48.46±10.29 vs. 49.92±10.05 years; 48.2% vs. 46.7%). Compared to patients with PsA+minimal skin PsO, those with PsA+moderate-to-severe PsO had slightly higher rates of chronic pulmonary disease (23.6% vs. 21.4%) and liver disease (excluding fatty liver) (15.1% vs. 10.7%), but lower rates of co-prevalent rheumatic disease (5.1% vs. 7.0%) and rheumatoid arthritis (32.2% vs. 35.7%). Patients with PsA+moderate-to-severe PsO also had significant higher rates of several PsA-associated comorbidities, including anxiety (18.8% vs. 15.8%), depression (23.2% vs. 20.1%) and obesity (21.5% vs. 15.9%) (all $p<0.0001$). Patients with PsA+moderate-to-severe PsO had significantly higher rates of all-cause medication use (99.9% vs. 94.7%) and larger number of unique medications filled (13.38 vs. 11.28) than patients with PsA+minimal skin PsO (both $p<0.0001$). Significant differences were also observed in the mean number of unique medications filled between these two groups for PsA-related medications (2.78 vs. 2.14), non-PsA-related medications (10.60 vs. 9.14), antidepressants (0.60 vs. 0.55), and antidiabetics (0.30 vs. 0.25) (all $p<0.0001$).

**Conclusions:** PsA patients with moderate-to-severe PsO had a higher comorbidity burden compared to those with minimal skin PsO, and also incurred significantly more medication use overall and related to PsA and specific comorbid conditions.

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## FRI0581 VALIDATION OF THE DANISH VERSION OF THE STANFORD HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX AND DETERMINATION OF THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS USING THE RASCH MEASUREMENT MODEL

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**Background:** The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a widely used patient reported outcome for functional disability measurement in rheumatoid arthritis (RA). Minimal clinically important differences (MCIDs) have previously been calculated based on the original ordinal HAQ-DI scores resulting in a dependence of the MCIDs on baseline scores (1). This causes limited generalizability and validity of the proposed MCIDs. The Rasch measurement model provides a transformation of these ordinal scores to an underlying latent scale with interval scale properties. This requires adequate fit of HAQ-DI data to the model.

**Objectives:** 1) To examine the internal construct validity of the Danish version of the HAQ-DI (scored without correction for devices) and 2) to determine a MCID of the HAQ-DI in a cohort of RA patients initiating anti-rheumatic treatment in clinical practice based on the transformed linear logit scale of the HAQ-DI.

**Methods:** RA patients registered in the DANBIO registry at the out-patient clinic at Center for Rheumatology and Spine Diseases, Copenhagen, Denmark were included in the study if HAQ-DI and Patient Global Visual Analogue Scores (PtGl) scores were available at a baseline visit and after > three months of follow-up after initiation of a) first synthetic Disease Modifying Anti Rheumatic Drug (sDMARD) (if disease duration <12 months) or 2) first biological drug (if disease duration >12 months). The Rasch model was fitted to HAQ-DI data at baseline and follow-up and item fit evaluated in separate analyses by comparing observed and expected item-restscore correlations (2). MCID was calculated as the median changes of A) the original and B) logit HAQ-DI score in the group of patients who had improved by 15–30 mm (ie. minimal improvement) on a 0–100 mm PtGl scale.

**Results:** 362 RA patients were included in the study (Table 1). HAQ-DI data showed acceptable fit to the Rasch model as no significant evidence of misfit was disclosed at the first time-point and only a single misfitting item (the "Grip" sub-item, p=0.01) was identified at the second time-point. Consistent item ranking across time indicated instrument invariance. Changes in ordinal and logit HAQ-DI scores were strongly correlated (Spearmans rho =0.935, $p<0.001$), but the association between them is not completely linear. Sixty-one patients had an improvement > MCID on the logit scale (0.48), but no improvement on the ordinal scale (MCID 0.250), while no patients had the opposite pattern.

**Conclusions:** The Danish version of the HAQ-DI scored without correcting for devices showed acceptable internal construct validity and thus a MCID based on a linear transformed scale could be calculated for this study (0.48). Application of the logit MCID classified an additional 17% of patients as having achieved a MCID compared to the MCID calculated on the ordinal scale. This finding has potential implications for the use of ordinal-based MCID and the powering of future studies.

Clinical characteristics of the study population grouped by change in Patient Global VAS from baseline to follow-up.

| | Worsened ΔPtGl > 15 | Unchanged ΔPtGl >-15 < 15 | Minimal improved ΔPtGl <-15 > - 30 | Improved ΔPtGl<-30 |
|---|---|---|---|---|
| No. of patients | 47 | 149 | 61 | 105 |
| Female gender, % | 88 | 77 | 78 | 80 |
| Age, years | 54 (46-65) | 58 (48-67) | 61 (49-68) | 60 (46-59) |
| Disease duration, years | 4.8 (2.5- 9.1) | 7.6 (2.5-14.6) | 7.6 (3.2 – 18.1) | 4.2 (2.1 – 12.7) |
| IgM-RF positive, % | 57 | 70 | 75 | 62 |
| PtGl, mm | 43 (23-56) | 51 (18-80) | 57 (37-74) | 77 (60-88) |
| Baseline DAS28 | 4.0 (3.21-4.75) | 4.1 (2.85-4.8) | 4.7 (3.6-5.2) | 5.1 (4.4-5.7) |
| ΔDAS28 | -0.1 (-0.5 -0.75) | -0.5 (-1.0 – 0.1) | -1.4 (-1.9- -1.0) | -2.2 (-3.4 - -1.5) |
| Initiated bDMARD, % | 69 | 82 | 80 | 63 |
| Baseline HAQ-DI – original scale | 0.875 (0.5-1.31) | 1.0 (0.5-1.5) | 1.0 (0.5-1.625) | 1.25 (0.875-1.625) |
| ΔHAQ-DI – original scale | 0.25 (0.0 - 0.5) | 0.0 (-0.218 – 0.125) | -0.250* (-0.375 - 0.0) | -0.625 (0.875 – -0.25) |
| Baseline HAQ-DI – Logit scale | 0.09 (-0.71 – 0.63) | 0.07 (-0.71 – 0.73) | 0.07 (-0.71 – 0.73) | 0.36 (-0.15 - 0.73) |
| ΔHAQ-DI – Logit scale | 0.26 (-0.03 – 1.02) | 0.0 (-0.33 – 0.24) | -0.48** (-1.07 – 0.0) | -0.98 (-1.96 – -0.42) |

Values are median (Inter Quartile Range). * Study specific MCID based on original scale; ** Study specific MCID based on logit transformed scale. IgM-RF: IgM Rheumatoid Factor, PtGl: Patient Global Visual Analogue Scale, DAS28: Disease Activity Score in 28 joints, HAQ-DI: Health Assessment Questionnaire Disability Index.

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## FRI0582 FLUCTUATING LEVELS OF RHEUMATOID FACTOR PREDICT PROGRESSION OF RHEUMATOID ARTHRITIS, BUT NOT INDEPENDENT OF DISEASE ACTIVITY

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**Background:** The presence of rheumatoid factor (RF) is associated with progression of joint damage in patients with rheumatoid arthritis (RA). RF levels may change during the course of therapy[1], but it is not clear, if such changes also reflect a change in prognosis of RA.

**Objectives:** Here, we aimed to investigate whether fluctuation of RF levels is an independent marker of progression of RA.

**Methods:** We identified 239 RA outpatients based on classifiable RA by the 2010 ACR/EULAR classification criteria, the presence of at least two available radiographs of hands and feet (2–4 years apart), the availability of repeated measurements of RF (at least two/year), and positive initial RF levels (≥50 IU/ml; for the possibility of fluctuation). Radiographic images were scored using the modified Sharp/van der Heijde (SvH) method. A total of 375 radiographic intervals could be included, since some of the patients had more than one included observation periods.

Logistic regression analysis was used to examine the effect of fluctuating RF levels (expressed as standard deviation of all RF measurements between the two radiographs) on significant damage progression (defined by an average increase of ≥3 on the SvH score per year); results were adjusted for mean RF levels over time, disease activity (expressed as Simplified Disease Activity Index – SDAI), percentage time on biologics and already existing radiographic damage.

**Results:** Mean (SD) RF levels were 351.4 (618.7) IU/ml at baseline and 253.7 (424.2) IU/ml at the time of the second radiograph ($p<0.001$). Mean and standard deviation of RF levels within each patient were on average 298.9 (515.0) and 128.7 (233.8), respectively. Mean time-integrated levels of disease activity (SDAI) were of 9.7 (7.0), and patients received biologic therapy over 32.4 (40.8) % of the observed time. Pre-existing damage was 41.1 (52.4) points on the SvH score.

Univariate logistic regression showed a clear association of higher standard deviations of RF levels with radiographic progression (p=0.015). When adjusting this effect for mean RF levels, disease activity (time-integrated levels of SDAI), percentage time on biologics and already existing radiographic damage, the association of standard deviation of RF levels on radiographic progression was lost (p=0.087), whereas disease activity ($p<0.001$) and pre-existing damage (p=0.001) showed high significance.

When adjusting for each of these predictors individually, the association remained unchanged when tested against time on biologics only (p=0.016), or pre-existing damage only (p=0.048). Even adjusting for mean RF levels only left a significant independent association (p=0.032), while the mean RF levels were not significant (p=0.146). Only when adjusted for time-integrated disease activity, standard deviation of RF lost significance on the association with radiographic progression (p=0.126; Table).

**Conclusions:** Fluctuations of RF levels are associated with radiographic progres-

| Predictors of Progression | | Wald | Sig. |
|---|---|---|---|
| Crude | SD of RF | 5.890 | 0.015 |
| Adjusted for Mean of RF, Disease Activity, Time on Biologics, Pre-existing damage | SD of RF | 2.922 | 0.087 |
| | Mean of RF | 1.848 | 0.174 |
| | SDAI (AUC) | 12.770 | <0.001 |
| | Bio Time % | 0.802 | 0.370 |
| | Damage | 11.688 | 0.001 |
| Adjusted for Mean of RF | SD of RF | 4.600 | 0.032 |
| | Mean of RF | 2.116 | 0.146 |
| Adjusted for Disease Activity | SD of RF | 2.336 | 0.126 |
| | SDAI (AUC) | 17.349 | <0.001 |
| Adjusted for Time on Biologics | SD of RF | 5.840 | 0.016 |
| | Bio Time % | 0.108 | 0.742 |
| Adjusted for Pre-existing Damage | SD of RF | 3.915 | 0.048 |
| | Damage | 16.178 | <0.001 |

sion in RA. This effect is independent of mean RF levels over time, but seems to be associated with, or a consequence of, disease activity. Further studies need to explore the direction of causality of these observations.

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## FRI0583 THE DECLINING BURDEN OF ABSENTEEISM DUE TO RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS IN SLOVENIA

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**Background:** In Slovenia, evidence on the indirect costs of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) is scarce.

**Objectives:** To analyse changes in sick leave for RA and AS patients in Slovenia in the 2000–2014 period.

**Methods:** National Institute of Public Health collects absenteeism data. Sick leave data for the entire population of Slovenia was used to conduct a comparative analysis of sick leave indicators (number of cases, share of lost working days, index of temporary disability measuring the number of lost days relative to the number of employees, frequency of spells reflecting the number of absenteeism cases relative to the number of employees and severity indicating the average length of absence from work) for RA and AS patients in Slovenia in the 2000–2014 period. Data were analysed using t-tests for equality of means and Chi-Squared tests of distribution uniformity. Chain indexes were used to determine average annual changes of the studied indicators.

**Results:** Over the period 2000–2014, the number of days lost per employed worker for RA declined by over 13% and by nearly 82% for AS. For all musculoskeletal disorders (MSDs) this indicator declined by nearly 20% while for all diseases combined by nearly 16%. For RA, the average annual decline in temporary disability and severity equalled 1%. The index of temporary disability for all MSDs also declined by slightly over 1% annually on average, severity on the other increased on average by 0.32% annually. For all diseases combined temporary disability declined annually by 1.6% and severity by 1.3% on average. The changes were considerably better for AS given that temporary disability and severity declined for 11.5% and 4.7% annually on average, respectively. The frequency index for RA increased after economic crisis in 2009 while the average annual decline for AS reached 7%. The average annual declines for all MDSs and all diseases combined were much lower reaching 1.5% and 0.3%, respectively.

For both RA and AS the mean values of all studied sick leave indicators with the exception of severity statistically significantly differ between genders ($p<0.001$). For RA sick leave indicators are higher for women while for AS absenteeism indicators are less favourable for men. This result is in line with the gender structure of RA and AS diagnosed patients (1:3 male to female ratio for RA and 3:1 male to female ratio for AS). There are also statistically significant differences ($p=0.000$) in the number of absenteeism cases between three age brackets (20–34, 35–49 and 50–64 years) for both RA and AS. For RA differences between age groups in severity are not statistically significant. For AS the younger population has statistically significantly lower severity indicators while for the upper two age brackets differences are not statistically significant.

**Conclusions:** Results indicate that indirect costs of RA and AS are declining. A more comprehensive estimation of indirect costs requires, however, also the assessment of presenteesim costs. The decline in the burden of absenteeism was larger for AS in comparison to RA. Patients diagnosed with AS are on average notably younger than RA patients. This implies that innovative treatment and disease management practices can prevent larger productivity losses created by absenteeism.

**Disclosure of Interest:** None declared

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## FRI0584 THE VICIOUS CIRCLE OF EDUCATIONAL LEVEL, RHEUMATOID ARTHRITIS, AND RISK OF POVERTY - RESULTS OF A CROSS-SECTIONAL MULTICENTER STUDY IN GERMANY

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**Background:** Compared to the general population, patients with rheumatoid arthritis (RA) are threatened by poverty due to treatment-related expenses, disability, and early retirement. Also, lower socio-economic state is associated with increased prevalence and severity of RA. The underlying mechanisms are still unclear.

**Objectives:** To evaluate the risk of poverty of RA-patients in an unselected community-based cohort in the German states of Brandenburg and Saarland, and to investigate interrelationship between educational level, socio-economic state and disease severity.

**Methods:** Cross-sectional multicenter study consecutively recruiting RA-patients in outpatient-clinics in Brandenburg and Saarland. Inclusion criteria were written consent and diagnosis of RA fulfilling ACR/EULAR-criteria. Using anonymised questionnaires, equivalised disposable income (EDI = total net income of a household divided by the number of equalised household members) was calculated. Risk of poverty was defined as <60% of the median EDI in Germany. Additionally, treatment-related expenses and effects of RA on social life were evaluated.

**Results:** Of all 910 returned questionnaires (return rate 88%), 882 (97%) were evaluable (666 from Brandenburg and 215 from Saarland). The mean±SD age of all patients was 61±12 years, 71% were female, mean functional capacity (FFbH) was 72±23%, rate of biologic treatment was 41%, and 21% were active smokers. Median monthly EDI of RA-patients was 1239€ (IQR 869–1654), 88% of the median EDI in Germany (1413€). The rate of RA-patients at risk of poverty was significantly higher compared to the population in Germany (27% vs. 16%, $p<0.001$). Of the RA-patients, 414 (52%) had approved disability and 136 (21%) got early retirement at a mean age of 55±11 years. Of all patients, 25% waved a drug prescription at some point due to financial reasons. The RA-subgroup at risk of poverty waived prescriptions even more often (37% vs. 18%, $p<0.001$), had a higher rate of active smokers (27% vs. 19%, $p=0.009$) with more pack-years (5.1±10.9 vs. 3.5±9.6, $p=0.034$), had worse functional scores (FFbH 64±25% vs. 75±22%, $p<0.001$) and higher rates of early retirement (30% vs. 17%, $p<0.001$) compared to the patients without poverty risk. Patients with an university degree had less functional impairment (mean FFbH 84±18% vs. 71±23%, $p<0.001$), lower early retirement rates (7% vs 22%, $p=0.004$) and older age at retirement (59±7 vs. 55±12years, $p=0.023$) than patients without a degree. These findings were not associated with different smoking rates, nutrition type, oral hygiene, exposure to agricultural or silica dust, or early diagnosis of RA.

**Conclusions:** RA-patients in this study had an almost doubled risk of poverty compared to the general population. Poverty reduces compliance to treatment resulting in a vicious circle. Lower educational level is associated with more severe disease course of RA, but the underlying mechanisms need further elucidation.

**Disclosure of Interest:** None declared

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## FRI0585 IMPORTANCE AND LEVEL OF IMPLEMENTATION OF THE EULAR/EUMUSC.NET STANDARDS OF CARE FOR RA IN THE NETHERLANDS: SIMILARITIES AND DISCORDANCE BETWEEN PATIENTS AND HEALTH CARE PROFESSIONALS

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**Background:** To harmonize care, the core concepts of RA care have been formulated in the 16 EULAR/EUMUSC.net standards of care (SOC). To further empower RA patients and help them to monitor their disease, SOC have been converted into a patient checklist. Yet, the SOC have never been applied to patients and health care professionals (HCP) in a daily practice setting.

**Objectives:** To assess the importance, level of implementation and implementation gap of the 16 EULAR/EUMUSC.net SOC among patients with RA and HCPs in the Netherlands.

**Methods:** Dutch patients with RA from two hospitals, rheumatologists as well as nurses of the Dutch Society of Rheumatology completed a questionnaire on the importance and level of implementation (0–10 numeric rating scale (NRS);

10=highest, best) of each SOC. An implementation gap, identifying the SOC with a higher need for implementation, was calculated for all individual SOC: (maximal implementation (10) – reported implementation) X reported importance. Patients completed a NRS on global disease activity. Comparisons across subgroups were analysed with Mann-Whitney test.
**Results:** Overall, 217 patients and 91 HCPs (52 rheumatologists and 39 nurses) were included. The 3 SOC with the highest importance and implementation scores were similar for patients and HCPs, and showed almost no implementation gap (table). While for both patients and HCPs the implementation gap for alternative therapies was high, it should be noted that its perceived importance was relatively low (patients: 6.5 (3.2) and HCPs 6.2 (2.2)). The remaining important implementation gaps referred to SOC with a low implementation, but a high importance, for both patients and HCPs (table). Within patients, perceived level of implementation of most of the SOC was lower in those with higher disease activity. No important differences were found between subgroups according to gender, age, disease duration, education or health literacy.

**Table: The top three Standards of Care in RA for importance, implementation and implementation gap**

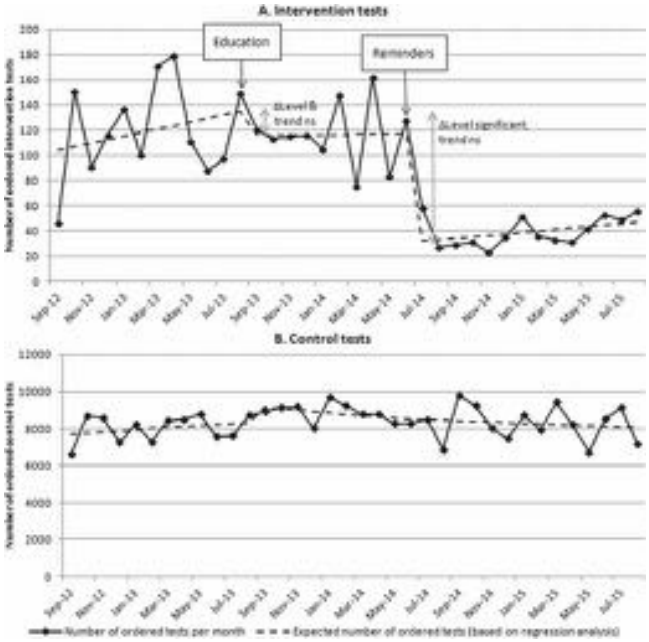
| | Patients (N=217) | Health Care Professionals (N=91) |
|---|---|---|
| **Age in years** *(mean ± SD)* | 60 ± 11 | 49 ± 9 |
| **Gender** *(% female)* | 69 | 72 |
| **Top 3 ranked SOCs** Level of importance *(mean ± SD) (0-10)* | 1. Informed on contact if disease worsens *(9.3 ± 1.1)*<br>2. Treatment with DMARDs *(9.2 ± 1.4)*<br>3. Regular re-appraisal if treatment target not achieved (9.1 ± 1.4)<br>3. Self-management of pain (9.1 ± 1.4) | 1. Treatment with DMARDs (9.2 ± 0.8)<br>1. Information on contact if disease worsens (9.2 ± 1.0)<br>2. Informed on treatments, benefits and risks (9.1 ± 0.8) |
| Level of implementation *(mean ± SD) (0-10)* | 1. Treatment with DMARDs (9.3 ± 1.2)<br>2. Regular re-appraisal if treatment target not achieved (9.1 ± 1.4)<br>3. Informed on contact if disease worsens (9.0 ± 1.6) | 1. Informed on contact if disease worsens (9.1 ± 1.3)<br>2. Treatment with DMARDs (8.9 ± 1.1)<br>3. Regular re-appraisal if treatment target not achieved (8.7± 1.3) |
| Implementation Gap different calculation *(mean ± SD) (0-100)* | 1. Informed on alternative therapies (and limited evidence) (30.2 ± 18.3)<br>2. Informed on personalised physical exercise (21.9 ± 20.1)<br>3. Access to trustful sources of information (21.5± 16.1) | 1. Treatment plan for patients (25.7 ± 18.7)<br>2. Informed on alternative therapies (and limited evidence) (23.6 ± 13.4)<br>3. Early diagnosis by specialist (22.3 ± 16.2) |

**Conclusions:** In the Netherlands, patients and HCPs share similar opinions on the most important aspects of RA care and agree these SOC are appropriately implemented. However, HCPs identified a need for improvement with regard to early diagnosis and providing a treatment plan to the patient. Patients experienced an unmet need in personalized exercise and access to trustful information. This audit of care using SOC identified areas for improvement for care that should be addressed.
**Disclosure of Interest:** None declared
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## FRI0586 THE EFFECTS OF AN EDUCATIONAL MEETING AND SUBSEQUENT COMPUTER REMINDERS ON THE ORDERING OF LABORATORY TESTS BY RHEUMATOLOGISTS: AN INTERRUPTED TIME SERIES ANALYSIS

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**Background:** Excessive use of diagnostic laboratory does not only constitute a waste of resources, it may also result in an increased rate of false positives which may lead to further unnecessary testing, unnecessary treatment, and increased anxiety in both patients and physicians. Still, many clinicians order irrelevant laboratory tests despite the available information about unnecessary test utilization.
**Objectives:** To examine the effects of an educational meeting and subsequent computer reminders on the number of ordered laboratory tests.
**Methods:** Using interrupted time series analysis we assessed whether trends in the number of laboratory tests ordered by rheumatologists between September 2012 and September 2015 at the Sint Maartenskliniek (the Netherlands) changed following an educational meeting (September 2013) and introduction of computer reminders into the Computerized Physician Order Entry System (July 2014). The reminders functioned as follows: whenever a clinician tried to order one of the intervention tests a pop-up message appeared explaining in which specific rheumatology-related situation the test was indicated or not, and asked for a reason for ordering the test. The analyses were done for the set of tests on which both interventions had focussed (intervention tests; complement, cryoglobulins, immunoglobins, M protein) and for a set of tests unrelated to the interventions, included as a control (alanine transferase, anti-cyclic citrullinated peptide, C-reactive protein, creatine, haemoglobin, leukocytes, mean corpuscular volume, rheumatoid factor and thrombocytes). Secondary outcomes were the percentage of abnormal intervention test results and the percentage of valid reasons provided with the intervention test orders, as judged by two experts.
**Results:** At study start 101 intervention tests and 7660 control tests were ordered per month by the rheumatologists. After the educational meeting both the level and trend of ordered intervention and control tests did not change significantly. After implementation of the reminders, the level of ordered intervention tests decreased with 85 tests (95%>CI -133 to -37, p<0.01), though the trend did not change significantly (1.06, 95%>CI -6.2 to 8.3, p=0.77). The level and trend of control tests did not change following the introduction of reminders. Of the reasons given for ordering the intervention tests after the introduction of reminders, only 34% was deemed valid by two experts. Interestingly, the percentage of abnormal results in the intervention tests did not change significantly after the introduction of the reminders (17.4% before introduction of reminders compared 18.4% after introduction (p=0.73)), nor was it different in those cases were the reason for ordering the test was judged as valid (18.8%).




**Conclusions:** The educational meeting alone was not effective in decreasing the number of ordered intervention tests, but subsequent introduction of computer reminders did result in a large decrease of those tests. Therefore, we recommend using computer reminders additionally to education if reduction of inappropriate test use is aimed for.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3213

## FRI0587 EVALUATION OF THE IMMUNE RESPONSE TO VACCINES IN PATIENTS ON BIOLOGICAL THERAPY. PRELIMINARY DATA OF RIER STUDY

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**Background:** Patients with rheumatic diseases on biological therapy have a greater risk of infections. Vaccination recommendations have been established, but, the effectiveness of vaccines in these patients is not well known, and it seems to depend on the different types of treatment used.
**Objectives:** To evaluate the response of vaccines against A and B Influenza, hepatitis B and pneumococcus in patients on biological treatment.
**Methods:** Patients with inflammatory arthopathies, psoriasis (Pso), inflammatory bowel disease (IBD) or connective tissue diseases (CTD) that were on or were going to initiate biological therapy, were included. A and B influenza antibodies (Ab) were measured by ELISA. A good response was achieved when base-line titer was increased by four. Hepatitis B surface antibody (Hep B sAb) was measured by ELISA and considered positive with a final titer >10m IU/ml. Protection against pneumococcus serotypes 1, 3, 7F, 14, 19A and 19F was measured by an opsonophagocytosis killing assay (OPKA). Opsonization titers (OT) were defined as the serum dilution that kills 50% of bacteria.
**Results:** 280 subjects were included, 167 women (59.6%), with a average age of 49.5±13.2 years. 35% were Rheumatoid Arthritis patients, 33.9% had spondiloarthropathies, 16.8% Psoriatic Arthritis, 5.4% Pso, 2.9% IBD and 6% other diagnostics. 84% of patients were on anti-tumor necrosis factor therapies, 8.9%

on Rituximab, 5% on tocilizumab, 1.4% on abatacept and 1.4% received other biologics. 45.4% of subjects were also on DMARDs and 18% on corticosteroids. A good response to influenza A vaccine was achieved in only 3.7% of patients for A influenza and 3.2% for type B, even though the majority of patients showed detectable titers of Ab in sera. 75% of patients had been vaccinated against hepatitis B before beginning the biological therapy. More than 90% of patients vaccinated against hepatitis B during the study achieved a good response. 40% of subjects showed OT against 3 or more pneumococcal serotypes.

**Conclusions:** The response from patients on biological therapy to the influenza vaccine is lower than expected. Comparative studies between these patients and those without biological treatment and healthy people are needed. There is a considerable amount of patients that have not received hepatitis B vaccine before the beginning of the biological treatment, although the response to this vaccine is good. Pneumococcal vaccine is successful in a considerable proportion of subjects. It is worth insisting on its administration.

**Disclosure of Interest:** None declared

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## FRI0588 COMPARING THE BURDEN OF ILLNESS OF PATIENTS WITH TOPHACEOUS AND NON-TOPHACEOUS GOUT IN FRANCE, GERMANY, ITALY, SPAIN, AND THE UK

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**Background:** Gout is a common inflammatory arthritis and its worldwide prevalence is increasing. EULAR and American College of Rheumatology guidelines recommend a target sUA <6 mg/dL, with a target of <5 mg/dL in those with more severe symptomatic disease. Patients with significant crystal burden are assumed to have higher humanistic and economic burden of illness.

**Objectives:** To describe patient and treatment characteristics and resource utilization in gout patients with and without tophi.

**Methods:** Data were assessed from a survey of physicians and in-depth patient chart audits from France, Germany, Italy, Spain and the UK. Severity of gout was measured by physician global assessment. Flares, organ/joint damage and tophi were abstracted from the clinical chart. Type/dose of xanthine oxidase inhibitor, length of current treatment, physician type and patient sociodemographic factors were identified. Anonymized patients were included. Patients with a diagnosis of tophaceous gout were compared to all other gout (non-tophaceous) patients. Demographic characteristics and comorbidities, sUA levels, and use of colchicine for acute flares during the 12-month study period were compared using chi-square or Fisher's exact tests.

**Results:** Of the 1260 patients identified with gout, 327 (25.95%) had physician-confirmed tophaceous gout and 933 (74.05%) had non-tophaceous gout. Patients with tophi were older (62.3 vs 58.6 years old; $p<0.001$), had gout for a slightly longer period of time (2.8 vs 2.5 years; $p<0.001$), reported more flares (3.4 vs 1.7 per year; $p<0.001$), and were more likely to have joint damage (45.3% vs 10.5%; $p<0.001$). There were significantly higher levels of comorbidities in patients with tophi including cardiovascular disease ($p<0.001$), chronic obstructive pulmonary disease ($p<0.001$), congestive heart failure ($p<0.001$), diabetes ($p=0.011$), depression ($p=0.001$), hypertension ($p<0.001$), osteoarthritis ($p<0.001$) and Stage III ($p<0.001$) and Stage V ($p=0.016$) chronic kidney disease. Patients with tophi were more likely to be treated with a urate-lowering therapy (87.5% vs 78.6%; $p<0.001$). Patients with tophi were less likely to be using allopurinol (56% vs 68%; $p<0.001$) and more likely to be treated with febuxostat (22.9% vs 7.9%). There was no difference in the use of NSAIDs; however, patients with tophi were more likely to take colchicine (46.5% vs 33.7%; $p<0.001$) and steroids (27% vs 10%; $p<0.001$). Patients with tophi were less likely to reach the ideal treatment goal of sUA targets of <6 mg/dL and no flares (17% vs 27%; $p<0.001$) or <5 mg/dL and no flares (6% vs 14%; $p<0.001$). Patients with tophi made more gout-related office visits (6.07 vs 4.51; $p<0.001$) and a greater proportion made ≥1 gout-related emergency visit (27.2% vs 9.5%; $p<0.001$), hospitalization (12.8% vs 3%; $p<0.001$) or had a gout- related surgery (3.1 vs 1.2; $p=0.022$).

**Conclusions:** Patients with tophaceous gout have significantly greater burden of disease and greater frequency of comorbidities than patients with non-tophaceous gout. Preventing the development of tophi or resolving crystal burden by treating to guideline targets remains a rarely achieved goal for patients with and without tophi.

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## FRI0589 THE IMPACT OF GOUT FLARES ON PATIENT-REPORTED ASSESSMENTS OF PAIN AND DISABILITY

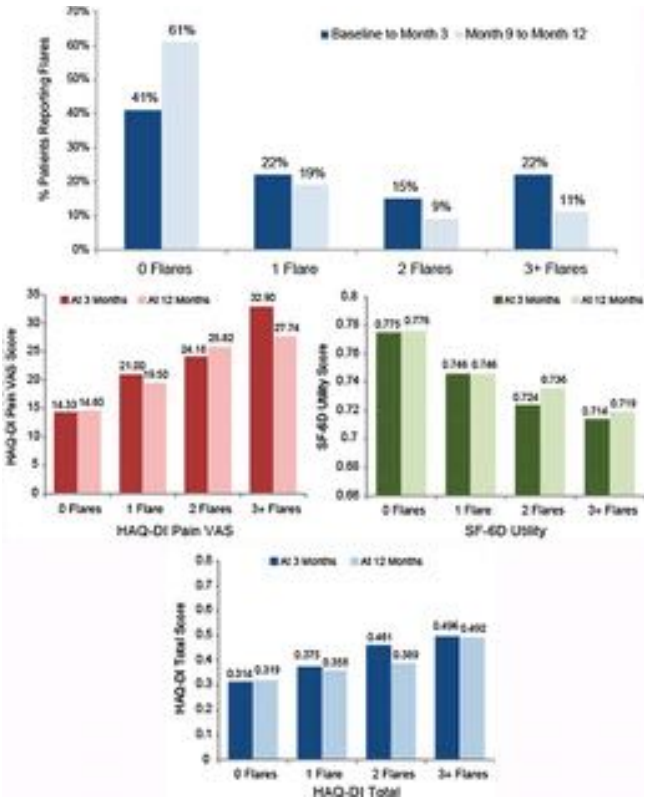
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**Background:** Lesinurad (RDEA594) is a selective uric acid reabsorption inhibitor (SURI) investigated for the treatment of gout in combination with xanthine oxidase inhibitors. In two Phase 3 clinical trials examining lesinurad in combination with allopurinol, patients with non-tophaceous gout demonstrated a reduction in gout flares over the 12-month study periods.

**Objectives:** Investigate the relationship between gout flares and patient-reported assessments of pain and disability during the first 3 and last 3 months of two 1-year clinical trials assessing lesinurad in non-tophaceous gout patients with inadequate response to standard of care (NCT01510158 and NCT01493531).

**Methods:** CLEAR 1 and CLEAR 2 were 12-month, randomized, double-blind, phase III trials to evaluate lesinurad (200 mg or 400 mg oral, daily) in combination with allopurinol (ALLO) vs ALLO + placebo. Gout flares were collected using an electronic patient diary and all flares reported in the diary were assessed. Patient-reported assessments of pain and disability included a Global Pain Scale and the HAQ-DI. A global measure of health utilty, the SF-6D, was derived from the SF-36v2. A pooled analysis of non-tophaceous patients in CLEAR 1 and CLEAR 2 assessed patient-reported measures for those with 0 flares, 1 flare, 2 flares and 3 or more flares, across treatment arms, during the first 3 months of the study (months 1 to 3) and during the final 3 months of the study (months 10 to 12), irrespective of treatment.

**Results:** Patients in the CLEAR 1 and CLEAR 2 clinical trials (N=1062) were primarily male (94.8%), mean±SD age was 51.5±11.1 years and duration since gout diagnosis was 11.1±9.1 years. Most patients (87.8%) received ALLO 300 mg (range: 200–900 mg) daily. Irrespective of treatment, during the first 3 months of the study 41%, 22%, 15% and 22% patients reported 0, 1, 2 and 3 or more flares, respectively. During the final 3 months of the study 61%, 19%, 9% and 11% patients reported 0, 1, 2 and 3 or more flares, respectively. For both the HAQ-DI and Pain VAS, during the first 3 months and last 3 months of the study, the best (lowest) HAQ-DI and Pain VAS scores were reported in patients with 0 flares and the worst (highest) scores were reported in patients with 3 or more flares. The best (highest) SF-6D health utility scores, during the first 3 months and last 3 months of the study, were found in patients with no flares and the worst (lowest) scores were found in those with 3 or more flares.




**Conclusions:** Non-tophaceous patients with the lowest number of flares, during the first and last 3 months of treatment, reported the most favorable HAQ-DI, pain and health utility measures. A majority of patients experiences zero flares during the final 3 months of the study period.

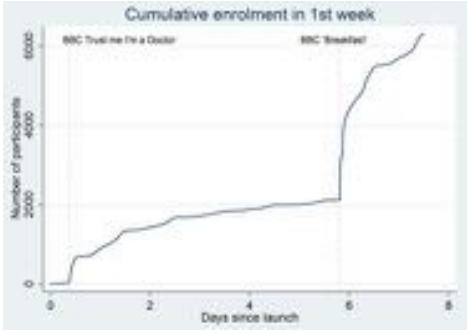
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**Disclosure of Interest:** P. Khanna Grant/research support from: AstraZeneca, S. Baumgartner Employee of: Ardea Biosciences, Inc., a member of the AstraZeneca Group, J. Robinson Employee of: Ardea Biosciences, Inc., a member of the AstraZeneca Group, E. Tafesse Employee of: AstraZeneca, R. Morlock Employee of: AstraZeneca
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## FRI0590 EARLY RECRUITMENT TO "CLOUDY WITH A CHANCE OF PAIN"; FROM WEBSITE HITS TO SMARTPHONE APP DOWNLOADS

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**Background:** Traditionally, participant recruitment for observational studies occurs by clinical teams identifying and approaching eligible patients. The current digital age, with increasing access to the web via PCs, tablets and smartphones provides an exciting alternative recruitment strategy. However, it is not clear whether studies can successfully recruit large numbers of participants in this way. "Cloudy with a Chance of Pain" is a national prospective population study which utilises participant's own smartphones to connect daily symptoms and hourly local weather using global positioning system (GPS) and is recruiting participants without the involvement of their clinical teams.
**Objectives:** To describe website activity and subsequent participant enrolment in the first week of recruitment following two national television broadcasts featuring the study.
**Methods:** Cloudy with a Chance of Pain was featured on BBC Two's "Trust Me I'm a Doctor" (20th January 2016) and BBC One's "Breakfast" (26th January 2016). Potential participants were directed to the study website www.cloudywithachangeofpain.com. The landing page described the project in text and video, after which interested visitors were directed to click through each item of an eligibility questionnaire (age ≥17 years, have arthritis or other chronic pain, resident in the UK, own a smartphone). If eligible in all 4, they were instructed to download the study app. Following download, participants were required to consent and then complete a baseline questionnaire. Google Analytics was used to evaluate the pattern and frequency of website traffic since launch. Enrolment data was provided by the data custodians and app developers, uMotif. Results are reported as mean (SD) or number (%).
**Results:** Within one week of launch, there were 84,494 visits from 22,732 visitors to the landing page of the website. There were 22,046 views of the "Take Part" page. The "take part" eligibility questionnaire was completed on 18,631 occasions. Of those, 15,836 (85%) were determined eligible. 5,683 participants successfully enrolled after following instructions to download the app and provide consent. 4,433 (78%) participants were female. The mean age was 49 (13). Figure 1 demonstrates cumulative enrolment within the first 7 days of launch. 48% of all enrolees registered within 3 hours of either the first or second TV broadcast.




**Conclusions:** Early recruitment to this study has been highly successful without any involvement of clinical teams. Although high website activity has been enabled by national media coverage, we have noted an excellent conversion rate (>33%) from website activity to app downloads without offering personal support or incentives. This confirms that direct participant recruitment using website information and smartphones is a novel and potentially successful approach to patient recruitment to observational studies.
**Acknowledgement:** Arthritis Research UK and uMotif Ltd.
**Disclosure of Interest:** None declared
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## FRI0591 HYPERURICEMIA AND THE RISK FOR CARDIOVASCULAR DISEASE: INDIVIDUAL PATIENT META-ANALYSIS OF 77,045 INDIVIDUALS ENROLLED IN 15 EPIDEMIOLOGIC STUDIES

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**Background:** Even though well-designed literature-based meta-analyses have confirmed the link between hyperuricemia and the risk for cardiovascular disease (CVD), it is known that study-level analyses can lead to biased assessments, and use of aggregated summary values has some limitations for explaining the heterogeneity. An individual patient data (IPD) meta-analysis offers several advantages including more accurate adjustment for confounders and better accounting of study heterogeneity.
**Objectives:** To perform unadjusted and risk-adjusted IPD meta-analysis of the association between hyperuricemia and prevalent CVD using data from diverse epidemiologic populations in the United States.
**Methods:** Baseline subject level data from 15 epidemiologic studies evaluating CVD risk conducted by the US National Heart Lung and Blood Institutes were pooled. Individuals who reported gout and using gout medications were excluded. Unadjusted and adjusted logistic regression analyses were performed. CVD was defined by self-reported physician diagnosis of myocardial infarction or stroke. Multivariable analyses adjusted for age, sex, sex-urate interaction, body mass index, smoking, total cholesterol, blood pressure, and diabetes mellitus.
**Results:** Overall, 50,966 men (66.1%) and 26,082 women (33.9%) were studied. The mean (standard deviation) age and serum urate (sUA) concentration were 49 (14) years and 5.9 (1.6) mg/dL, respectively. The overall proportion of participants with sUA >6.0 mg/dL was 44.3% and those with sUA >7 mg/dL was 22%. The prevalence of CVD was 7.7% among those with sUA ≤6 mg/dL and 9.8% among those with sUA >6 mg/dL ($p<0.001$). The unadjusted (77,045 observations) and adjusted (age-gender adjusted, 77,045 observations; multivariable adjusted, 66,234 observations) logistic regression models indicated significant association between hyperuricemia and the risk for CVD. For sUA >6.0 mg/dL compared to ≤6.0 mg/dL, odds ratios (95% confidence intervals) were 1.31 (1.24, 1.37), 1.37 (1.20, 1.56), and 1.60 (1.42, 1.81) in the adjusted, age-gender adjusted, and multivariable adjusted models, respectively. For each mg/dL increase in sUA, odds ratios were 1.13 (1.12, 1.15), 1.24 (1.20, 1.28), and 1.20 (1.15, 1.24), respectively.
**Conclusions:** These IPD meta-analyses confirm the results of literature-based meta-analyses that hyperuricemia is associated with elevated risk for CVD. Although the results of individual epidemiologic studies may vary due to differences in the risk profile, age, gender, and other risk factors, overall, the association between hyperuricemia and CVD appears to be robust.
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## FRI0592 MAINTAINING MENTAL HEALTH IN OLDER PEOPLE WITH MUSCULOSKELETAL PAIN: A LONGITUDINAL COHORT STUDY

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**Background:** Reporting troublesome pain doubled the risk of the onset of depression in older people[1]. However the majority (84%) of those with troublesome pain remained free of depression. Social participation (SP) (i.e. recreational and functional activities involving interaction with others) has been linked to good mental health. Whether SP (and its associated pathways; social support (SS), eudaimonic wellbeing (EW; a sense of purpose and meaningfulness in life) and physical activity (PA)) is associated with maintaining mental health in older adults with troublesome pain is not known.
**Objectives:** To test the hypothesis that among older people with troublesome pain higher levels of SP explain why some older people maintain good mental health, and if any role of SP remains once that through SS, PA and EW is accounted for.
**Methods:** Data were from a nationally representative population-based prospective (baseline, 2 and 4 year follow up) cohort study of community-dwelling people aged ≥50 years; the English Longitudinal Study of Ageing (ELSA; n=2654). At baseline participants were asked "are you often troubled with pain?" (response options yes/no). Mental health was classified at baseline and 4 years using the 8-item Centre for Epidemiologic Studies Depression scale (CESD-8) with scores <4 indicating "good mental health". SP at 2 years was defined using a multidimensional latent class model and coded as low or high participation. Path analysis assessed the total, direct and indirect (via SP) effects of pain at baseline on CESD-8 score at 4 year follow-up adjusted for age, gender, socioeconomic status, baseline CESD-8, self-rated health and limiting illness. In a multiple parallel pathways analysis EW (derived from CASP-19), SS and PA (using established ELSA measures) were then entered into the model. Not being troubled by pain was the referent category and results were expressed as odds ratios (OR) with 95% confidence intervals (95% CI).
**Results:** 1475 (55.6%) were female, median age 62 years (interquartile range: 57–69) and 863 (32.5%) reported being often troubled by pain at baseline. Having pain at baseline was associated with a 70% decreased odds of good mental health (total effect OR 0.30; 95% CI (0.23, 0.38)). Among those with pain at

baseline those with high SP at 2 years were 3 times more likely to have good mental health at 4 years (2.97; (2.29, 3.86)). After adjusting for confounders there was no indirect effect for SP (1.00; (0.98, 1.01)). In a multiple parallel pathways analysis there was a strong indirect effect for EW (0.53; (0.36, 0.73)) and no indirect effect through PA or SS.
**Conclusions:** In older people with pain high EW was associated with good mental health 4 years later. Interventions that aim to increase EW may improve mental health outcomes in older people with pain.
**References:**
[1] Arola H-M et al. E J Pain 2010;14:966–971.
**Disclosure of Interest:** None declared
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## FRI0593 A SYSTEMATIC LITERATURE REVIEW OF THE PREVALENCE OF PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a heterogeneous multifaceted inflammatory arthritis associated with psoriasis (PsO). PsA causes a substantial disease burden and has a significant societal health impact. Accurately determining the prevalence of PsA can be difficult due to variations in disease presentation over time, changes in disease classification and specialty of the treating physician.
**Objectives:** To perform a systematic literature review of the prevalence of PsA and to identify potential determinants of the prevalence of PsA.
**Methods:** A systematic literature search of English-language articles was conducted in October 2015 using MEDLINE, EMBASE and CINAHL, and was limited to articles published between 2009 and 2015. The systematic literature review was conducted by two independent reviewers in compliance with the PRISMA Statement.
**Results:** Thirty-nine studies (23 clinical studies, 10 database analyses, and 6 population-based surveys) were included. In most of the studies (n=38), the diagnosis of PsA was made by physicians using different classification criteria: Classification Criteria for Psoriatic Arthritis (CASPAR) criteria (n=14), CASPAR and Moll and Wright (M&W) criteria (n=2), CASPAR and Gladman modification of M&W criteria (n=1), CASPAR and Assessment of Spondyloarthritis International Society criteria (n=1), classification criteria for PsA not reported (n=20). In the reviewed articles, only point prevalence rates for PsA were reported. The point prevalence of PsA ranged between 0.02% to 0.67% in the adult population, and 3% to 42% in patients with PsO, with rates differing across countries. PsA seemed to be most prevalent in the 50–59 years age-group. PsA was more common among first-degree relatives of patients with PsA and also showed marked differences between different ethnic groups (showing the highest prevalence in the Caucasian population). The results of studies on gender differences were conflicting: some reported that PsA was more frequent in men and others that it occurred more frequently in women. In the studies reviewed, the majority of PsA patients had peripheral symptoms without axial involvement; polyarthritis seemed to be more prevalent than oligoarthritis. Findings of studies estimating the prevalence of PsA in PsO patients suggested that 29% to 41% of PsO patients attending dermatology clinics had undiagnosed PsA.
**Conclusions:** The high variance of prevalence rates can be explained with the differences in study populations, diagnostic methods and classification criteria of PsA. The prevalence of PsA seemed to be mostly affected by age and genetic factors. Findings of the epidemiological studies measuring the prevalence of PsA in PsO patients suggested that a large proportion of patients with PsO seen in dermatology centers might have PsA that had not been previously diagnosed. Given that untreated PsA may result in irreversible joint damage, increased awareness of this condition among PsO patients may be a critical step in reducing disability in this patient population. Further research is needed to better understand the occurrence of PsA.
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## FRI0594 ASSOCIATION OF GOUT DIAGNOSIS WITH INCREASED RISK OF JOINT REPLACEMENT: A POPULATION-BASED COHORT STUDY OF OVER 250,000 PATIENTS

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**Background:** Gout is the most common cause of inflammatory arthritis in men and older women, and there are very few studies on the rate of joint replacement among patients with diagnosed gout compared to those without gout.
**Objectives:** To assess the risk of joint replacement among patients with diagnosed gout compared to patients without gout diagnosis, and the predictors.
**Methods:** This was a population-based study with cohort study design in a cohort of older adults. We first identified all subjects aged >66 years between January 1, 1995 and December 31, 2009. A study cohort of 252,255 individuals was reconstructed using the Quebec RAMQ and MedEcho administrative databases. Patients with gout diagnosis were defined only if they met *all* of the following criteria: 1) gout defined by *ICD-9 or ICD-10 or exposure of specific gout treatment*. The date of cohort entry of patients with gout was defined as the first date of established gout during follow-up. The primary outcome was incident joint replacement rate defined by a composite endpoint representing patients with a medical procedure in the hip, femur and basin, knee, ankle/foot, hand/finger, shoulder and humerus, forearm and elbow, or wrist. Potential predictive factors examined included gout diagnosis, cardiovascular diseases, cerebrovascular disease, peripheral vascular disease, diabetes, kidney disease, pulmonary disease, dementia, rheumatic disease, and gastrointestinal disease.
**Results:** The incident rate of joint replacements was at 2.67 (95% CI: 2.57–2.77) and 1.92 (1.90–1.94) per 100 person-years among patients with diagnosed gout and those without a gout diagnosis, respectively ($p<0.0001$). Major predictors of total joint replacements were gout diagnosis (31%), advanced age (42%), cerebrovascular disease (13%), acute renal failure (10%), respiratory disease (12%), rheumatic disease (43%), and gastrointestinal disease (10%). Significant predictors of drug exposure are NSAIDs, intra-articular corticosteroids and narcotic use. Noted limitations included the limited ability to adjust for clinical severity and the potential of residual confounding factors.
**Conclusions:** Gout disease was associated with a significant, 31% increase risk of joint replacement in older adults. Further research should be conducted to confirm this potential associated risk.
**Acknowledgement:** This study was funded by AstraZeneca.
**Disclosure of Interest:** S. Perreault: None declared, A. Klein Employee of: AstraZeneca, R. Morlock Employee of: Ardea Biosciences, Inc., a member of the AstraZeneca Group
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## FRI0595 RESPONSIVENESS AND TEST-RETEST RELIABILITY OF NEW DISEASE ASSESSMENT INSTRUMENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS IN RELATION TO SLEDAI-2K

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**Background:** Several new simplified Disease Assessment Instruments/Indices (DAIs) in Systemic Lupus Erythematosus (SLE) are in different stages of development to aid easy use in daily clinical practice, including SLE Activity Tracking Evaluation Tool (LAST; 14 items; includes medications, Physician Global Assessment (PhGA) 0–10 scale, Patient Global Assessment (0–10 scale), C3/C4/anti-dsDNA measures), Clinical LAST (C-LAST; 11 items; similar to LAST, without lab measures), Total Lupus Activity Score (TLAS; 30 items on lupus symptoms, with 15 each of physician clinical & patient self-assessments), and Simple Disease Assessment for People with Lupus Erythematosus (SIMPLE; 17 items; includes patient self-assessment of lupus symptoms, Lupus Impact Tracker, steroid medication, C3/C4/proteinuria).
**Objectives:** To assess responsiveness and test-retest reliability of the DAIs between baseline (BL) and 3mo assessments.
**Methods:** This is a prospective real-world observational cohort study of SLE patients receiving standard care in two private and two academic sites in the US. Respective portions of DAIs (incl. SLEDAI-2K & PhGA (0–3 scale) (in all sites) & BILAG-2004 (in academic sites)) are completed by physicians and patients at four time points: BL/3mo/6mo/12mo. Responsiveness was assessed by analyzing within-person change in scale scores and effect size (mean change divided by standard deviation of BL score) between BL and 3mo in relation to change in clinical status, as measured by SLEDAI-2K scores, categorized as “improved”, “no change”, or “worsened”, and test-retest reliability was assessed by Spearman correlation coefficient ($r_s$) comparing BL and 3mo scores among those with “no change” in SLEDAI-2K scores. Correlations ($r_s$) between BILAG-2004 and other DAI scores were assessed.
**Results:** In total, 201 patients (mean age: 45 yrs; female: 91%; Black/African American: 56%; Hispanic: 10%) were enrolled in the study; 149 patients with BL baseline and 3mo data were evaluated. Within-person change/effect size among the *Improved* group (n=54): LAST = -6.4/-0.537, C-LAST = -5.6/-0.536), TLAS

= -1.7/-0.234, SIMPLE = -4.1/-0.359, PhGA (0–10) = -1.3/-0.655, PhGA (0–3) = -0.7/-0.915; *No change (n=55):* LAST = -0.7/-0.055, C-LAST: -0.5 /-0.049, TLAS: 1.7/.159, SIMPLE: -1.3/-0.114, PhGA (0–10) = -0.2/-0.080, PhGA (0–3): -0.02/-0.025; *Worsened (n=40):* LAST = 4.1/0.323, C-LAST = 2.9/0.265, TLAS = 4.8/0.449, SIMPLE = 1.9/0.170, PhGA (0–10) = 1.0/0.495, PhGA (0–3) = 0.4/0.480. Test-retest reliability was ($r_s$; all $p<0.0001$): LAST = 0.713, CLAST = 0.684, TLAST = 0.778, SIMPLE = 0.757, PhGA (0–10) = 0.639, PhGA (0–3) = 0.503). At 3mo, BILAG-2004 correlated with DAIs as (r/n): LAST = 0.465/59 (p=0.0002), C-LAST = 0.391/59 (p=0.0022), TLAS = 0.280/56 (p=0.0366), SIMPLE = 0.627/56 ($p<0.0001$), PhGA (0–10) = 0.553/59 ($p<0.0001$), PhGA (0–3) = 0.507/71 ($p<0.0001$).

**Conclusions:** Test-retest reliability showed moderate-to-strong correlations between baseline and 3mo assessments. For the "improved" and "worsened" groups (per SLEDAI-2K change), effect sizes indicated a small to medium effect, whereas the "no change" group had effect sizes indicative of no change; mean within-person change scores were directionally responsive to clinical change. Most DAIs had moderate correlation to BILAG-2004.

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## FRI0596 RHEUMATOID ARTHRITIS RISK ALLELES, HLA-DRB1 HAPLOTYPES, AND RESPONSE TO TNFI THERAPY – RESULTS FROM A SWEDISH COHORT STUDY

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**Background:** Tumour necrosis factor inhibitors (TNFi) have proven successful in suppressing both inflammation and joint damage in rheumatoid arthritis. Still, predictors of response are largely lacking, to increase our understanding of the disease-driving biology and response to treatment. Several pharmacogenetics studies, including five GWAS, have been conducted to identify genetic predictors to TNFi response, but few markers have reached genome-wide significance or withstood replications.

**Objectives:** By taking a genetic risk score approach, combining information contained in individual RA risk markers, amino acids, and haplotypes, we may be able to better predict treatment response to TNFi.

**Methods:** We linked recent onset RA patients from the Swedish EIRA study (genotyped with the Illumina Immunochip array) to prospectively recorded data on treatment and clinical characteristics in the nationwide Swedish Rheumatology Register (SRQ). The cohort was defined as those who started TNFi as first biological DMARD treatment 2000–2012, and had at least one return visit with recorded DAS28 within 2–8 months after TNFi start (N=867). Based on previous reports, we identified established RA genetic risk factors: 76 RA risk loci, 4 amino acid polymorphisms at *HLA-DRB1* (position 11, 13, 71, 74), and calculated 16 haplotypes based on the amino acids. We calculated risk scores for the 76 SNPs, the 4 amino acids, and the haplotypes, by weighting SNP alleles/amino acid residues/copies of haplotype by their published log-odds. The association of RA risk scores and individual established genetic risk factors with DAS28-based EULAR response and a number of clinical disease activity measures at the evaluation visit closest to 5 months after initiation was estimated using logistic and linear regression models.

**Results:** All risk scores were good predictors for RA, in particular for ACPA-positive RA. We found, however, no association for any of the risk scores, or SE, in achieving good/moderate EULAR response in RA overall, nor in any RA subset. When evaluating each of the 76 SNPs, individual amino acid residues and haplotypes separately, we found that the number of SNPs with significant associations to response for TNFi was not higher than expected by chance (5/76 SNPs had $p<0.05$ in ACPA-positive RA, 4/76 in ACPA-negative RA). Similarly, despite the borderline significant association for some residues in ACPA-positive RA (glycine at position 11, serine and tyrosine at position 13) and in ACPA-negative RA (proline at position 11, arginine at position 13), none survived correction for multiple testing. In addition, none of the haplotypes, neither those based on 4 amino acids (11/13/71/74) nor those based on 3 amino acids (11/71/74), were significantly associated with EULAR response. With regard to the changes in individual disease activity measures, no associations were identified except that the risk scores may explain a small proportion of variance in HAQ changes.

**Conclusions:** Identified RA risks genes, amino acids, and haplotypes in our study do not predict response to TNFi therapies, neither individually nor when groups together into scores.

**Disclosure of Interest:** None declared

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## FRI0597 SYSTEMATIC REVIEW OF CONSUMER PERCEIVED HEALTH INFORMATION NEEDS REGARDING BACK PAIN

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**Background:** Low back pain (LBP) is very common. Being one of the most common presenting complaints for doctor visits, in the Global Burden of Disease study, it was ranked highest in terms of causing disability, and 6th in terms of overall burden, despite current available guidelines to manage LBP [1,2]. As optimal management requires coordination with patient expectations, understanding the consumer's perceived health information needs is important to optimize health outcomes for LBP.

**Objectives:** To identify consumer perceived health information needs regarding LBP.

**Methods:** A comprehensive search of MEDLINE, EMBASE, CINAHL and PsycINFO was performed (1990 to December 2014). Core search terms were developed around consumers' perspective of needs relating to health information relating to LBP. Data regarding design and methodology were extracted. Emergent themes were identified to provide a systematic review of the existing literature.

**Results:** 2638 papers were identified, of which 37 articles were relevant (Fig 1); 33 used qualitative methods, 7 used quantitative methods, and 3 used mixed methods. Participants, mainly with chronic LBP, were mostly recruited from primary practice but also from pain clinics, hospital, rehabilitation centers, specialist spine clinics and the general public. The quality of the literature was variable, with few studies specifically addressing the review question. However, many results were consistent. The 2 major areas of need, identified in at least 2 studies, related to

1) Information content: Consumers wanted general information about LBP to better understand it, with emphasis on obtaining a specific diagnosis and cause for LBP, which underscored the perceived need for imaging to acquire a diagnosis. Patients also wanted information regarding prognosis, including future disability and effect on work capacity, potential precipitation of flares. General information on LBP management, including pharmacological and non-pharmacological strategies, pain management, flare management and prevention, self-management strategies and support services for LBP were desired. They valued individualized information that did not conflict with their lived experience, life goals and beliefs.

2) Information delivery: Patients valued high quality information that was valid and trustworthy. Information needed to be delivered in a suitable tone and in understandable language, without medical jargon. They wanted to know how to find information about LBP.




**Conclusions:** This review highlights the mismatch between consumer health information needs and current health care providers' management. Widespread community wide interventions may be required to address community beliefs and expectations about back pain in order to improve consumer understanding of LBP. Addressing consumer perceived needs more effectively and integrating this into the management of LBP may improve patient outcomes regarding LBP.

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FRI0598 **RELATIONSHIP OF JOINT HYPERMOBILITY WITH LOW BACK PAIN AND LUMBAR SPINE OSTEOARTHRITIS: A COHORT STUDY**

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**Background:** Low back pain (LBP) and osteoarthritis (OA) of the lumbar spine are common causes of disability. The contribution of joint hypermobility (range of motion greater than normal at most joints) to LBP and lumbar spine OA is not well known.
**Objectives:** This cross-sectional study examined the relationship of joint hypermobility with LBP and lumbar spine OA in a large cohort in the United States.
**Methods:** Of the 2146 participants with Beighton (hypermobility) data collected from 2003 to 2010, 1864 had complete LBP and lumbar spine radiographic data available for analyses. For the Beighton criteria, one point was given for each completed maneuver: passive dorsiflexion right/left fifth finger 90+ degrees, passive apposition right/left thumbs to forearm, right/left elbow hyperextension 10+ degrees, right/left knee hyperextension 10+ degrees, and palms on floor during forward trunk flexion with knees extended. The total score ranged from 0 (unable) to 9 (performed all maneuvers). A Beighton score $\geq$4 was defined as hypermobility. Presence of LBP was based on pain, aching or stiffness of the low back on most days. Each lumbar spine radiographic level was graded for disc space narrowing (DSN) and osteophytes (OST) in a semi-quantitative fashion (0–3) according to the Burnett Atlas. Radiographic lumbar spine OA (rOA) was defined as the presence of DSN and OST grade 1+ at the same lumbar level. Symptomatic lumbar spine OA (sxOA) was defined as presence of rOA with LBP. Associations of LBP and lumbar spine OA with hypermobility (Beighton $\geq$4) and each individual Beighton maneuver were estimated using separate logistic regression models, controlling for gender, race, age, body mass index (BMI), and history of low back injury. Interactions were examined between hypermobility and each covariate ($p<0.10$ considered statistically significant).
**Results:** Participant characteristics were: mean age 66 years (standard deviation [SD]±10), mean BMI 31 (SD±7) kg/m$^2$, 65% women, 33% African American, 2% low back injury, 6% hypermobility, 40% LBP, 59% rOA, and 25% sxOA. Adjusted results are summarized in the Table. Although not statistically significant, the adjusted odds of rOA were 18% lower among participants with vs. without hypermobility, while the odds of LBP and sxOA were 30% and 20% higher, respectively. Fifth finger dorsiflexion was inversely associated with LBP (35% lower odds) and sxOA (21% lower odds). The elbow maneuver was positively associated with LBP (41% higher odds), but inversely associated with rOA (28%); a similar, but not statistically significant, pattern was seen for the knee maneuver. The trunk flexion maneuver was inversely associated with LBP, rOA, and sxOA. No interactions of hypermobility and covariates were noted.

**Table. Adjusted* odds ratios (aOR) and 95% confidence intervals (CI) for association of hypermobility and lumbar spine outcomes.**

| | Lumbar Spine Outcome | | |
|---|---|---|---|
| **Hypermobility Measure** | Back Pain | Radiographic Osteoarthritis | Symptomatic Osteoarthritis |
| | aOR (95% CI) | aOR (95% CI) | aOR (95% CI) |
| Beighton Score, ≥4 / <4 | 1.30 (0.89, 1.90) | 0.82 (0.56, 1.22) | 1.20 (0.78, 1.84) |
| Fifth finger dorsiflexion, yes/no | 0.65 (0.54, 0.79) | 1.17 (0.96, 1.43) | 0.79 (0.63, 0.98) |
| Thumb apposition, yes/no | 0.80 (0.42, 1.52) | 0.88 (0.46, 1.66) | 0.86 (0.41, 1.84) |
| Elbow hyperextension, yes/no | 1.41 (1.05, 1.90) | 0.72 (0.53, 0.98) | 1.20 (0.86, 1.68) |
| Knee hyperextension, yes/no | 1.29 (0.79, 2.09) | 0.85 (0.52, 1.39) | 1.28 (0.75, 2.18) |
| Trunk flexion, yes/no | 0.38 (0.23, 0.63) | 0.67 (0.43, 1.03) | 0.38 (0.20, 0.73) |

*Adjusted for age, gender, race, low back injury, and body mass index

**Conclusions:** Joint hypermobility (specifically elbow and knee maneuvers) appears to be positively associated with LBP but inversely related to lumbar spine rOA. The trunk maneuver may reflect the musculotendinous (hamstring) flexibility more than ligamentous laxity, suggesting that greater hamstring flexibility is linked to a reduced occurrence of LBP and lumbar spine OA. Longitudinal studies may elucidate the role of joint hypermobility in lumbar spine outcomes.
**Disclosure of Interest:** None declared
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## Education

FRI0599 **CLINICIAN TRAINING IN MOTIVATIONAL COMMUNICATION SKILLS: THE IMPACT OF THE LANGUAGE OF CHANGE PROGRAM AMONG RHEUMATOLOGISTS FROM ACROSS CANADA**

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**Background:** Motivational communication (MC) is an evidenced-based communication style designed to enhance patients' intrinsic motivation to engage in a healthy lifestyle and adhere to treatment. Due to its efficacy and popularity, the demand for physician training has risen markedly over the past decade. Despite the widespread dissemination of these programs, there is little empirical data on the extent to which they impact physician knowledge and attitudes.
**Objectives:** This study assessed the impact of a 1.5 hour introduction to MC workshop (phase I of Language of Change) on MC attitudes among rheumatologists.
**Methods:** This was a single group pre-post intervention trial. The MC training program, called *The Language of Change*, was developed by rheumatology and behavior change experts. The program being assessed consisted of 1 live workshop (a 1.5 hour introductory session) delivered by an MC expert alongside a dermatologist/nurse, to 53 rheumatologists from across Canada. Participants completed a battery of validated questionnaires measuring MC motivation, self-efficacy, outcome expectancies, and short term (30 day) intention to change, at baseline and after the session. T-tests were conducted to assess the effects of the introductory workshop on each questionnaire.
**Results:** Analyses revealed significant post introductory workshop effects on motivation to use MC (+.87, $p<.0001$), MC self-efficacy (+1.37, $p<.001$), outcome expectancies (including perceived program usefulness [+.73, $p<.002$], pertinence [+.65, $p<.001$], effectiveness [+.94, $p<.0001$], potential to benefit physicians [+.72, $p<.0001$] and potential to benefit patients {+.82, $p<.0001$]), and short term (30 day) intention to change (pre=42%, post=66%).
**Conclusions:** This study indicates that a 1.5 hour introductory workshop on MC significantly increased motivation to use MC and MC self-efficacy, and had a uniformly positive impact on outcome expectancies and intention to use MC in practice. Results suggest that even low doses of MC training may impact healthcare professional attitudes and intention to change.
**Disclosure of Interest:** K. Lavoie: None declared, M. Bell: None declared, T. Taylor: None declared, R. Arendse: None declared, M. Saum Employee of: Janssen Canada Inc., D. Faucher: None declared, M. Shawi: None declared, M. Camerlain: None declared
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FRI0600 **FEARS AND BELIEFS OF PEOPLE LIVING WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS OR PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW**

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**Background:** Despite the growing interest of rheumatologists into the patients' perspective in the last decade (1) and the wide use of patient-reported outcomes in the assessment of Rheumatoid Arthritis (RA) (2,3) and Spondyloarthritis (SpA) (4), the main fears and beliefs of these group of patients and their consequences on treatment outcomes are unclear.
**Objectives:** To assess the main fears and beliefs of people with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) from different continents and their effect on treatment outcomes;
**Methods:** A systematic literature review was conducted in Pubmed/Medline. All original articles published up to December 2014, reporting fears and/or beliefs of adult patients with RA, AS or PsA were analyzed. Fears and beliefs were collected by two independent researchers and grouped in categories.
**Results:** Of the 293 publications identified, 70 were analyzed, corresponding to 19,161 RA, 1,693 AS/Spondyloarthritis and 202 PsA patients. No article reported fears and/or beliefs of people living in Latin America, Africa or Oceania. Fears were reported in 19 articles of which 9 (47.4%) reported fears related to pharmacological therapy. Beliefs were reported in 59 articles: beliefs about the rheumatic disorder were found to affect the impact of disease (in N=24 articles, 40.7% of articles assessing beliefs), beliefs about therapy were sometimes linked to adherence (N=11, 18.6%) and beliefs about cause of disease influenced coping strategies and adherence (N=5, 8.5%). Beliefs mediated the emotional impact of disease in RA (N=9, 15.2%) and influenced functioning in AS and RA (N=4, 6.8%).
**Conclusions:** Patients' beliefs are linked to impact of disease and non-adherence

in RA, AS and PsA. Further research is needed on fears of PsA and AS patients and on fears/ beliefs of patients living outside Europe and North America.

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## FRI0601 ROLE OF GROUP LEARNING TO IMPROVE REPRODUCIBILTY OF DAS-28 AMONGST HEALTHCARE PROFESSIONALS

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**Background:** Interprofessional group learning is a valuable educational tool in multidisciplinary settings as it helps improve clinical care and encourages professionals to learn with, from and about each other (CAIPE, 2006). Disease activity in rheumatoid arthritis is assessed using the DAS28 scoring system; and changes in treatment are influenced by the result of the DAS28 score. In our Rheumatology Department DAS28 assessment is carried out by many members of our multidisciplinary team including doctors, nurses and pharmacists. This necessitates checking of, and ensuring reproducibility of DAS28 scoring amongst our team, to enable appropriate management of patients.

**Objectives:** We utilised educational theory to organise a group learning exercise to assess reproducibility of DAS-28 score and identify areas for improvement amongst multidisciplinary rheumatology healthcare professionals, based at a large general hospital in South West England.

**Methods:** Four patients with rheumatoid arthritis were selected for the exercise based on availability. All members of the multidisciplinary team assessed the patients using the DAS28. 13 professionals participated in this activity: six rheumatology consultants (two academics), three rheumatology specialist registrars, three rheumatology specialist nurses and one rheumatology specialist pharmacist. Median scores and coefficient of variation expressed as a percentage (CV, calculated by standard deviation/mean x 100) were calculated for each patients overall DAS28 score and the constituent parts. CRP levels were fixed for each patient.

**Results:**

| Patient | Tender Joint Count Median (CV) | Swollen Joint Count Median (CV) | VAS Median (CV) | DAS-28 Median (CV) |
|---|---|---|---|---|
| 1 | 17.5 (19.2) | 5.5 (42.0) | 75.5 (5.5) | 5.85 (5.5) |
| 2 | 6.0 (39.8) | 1.5 (138.9) | 24.0 (5.4) | 3.21 (17.3) |
| 3 | 0 (143.0) | 3.0 (52.9) | 34.5 (69.1) | 2.36 (20.1) |
| 4 | 0 (128.7) | 2.0 (38.5) | 9.0 (15.1) | 3.09 (14.2) |

**Conclusions:** Reproducibility of overall DAS28 scores and its constituent parts were generally poor according to the CV. No differences in reproducibility were seen when stratifying by professional group. All subcomponents of the DAS28 showed equally poor reproducibility. This may have important clinical implications for patient care, particularly when deciding on treatment escalation. This interprofessional learning exercise, deliberately bringing together all members of the rheumatology multidisciplinary team, has enhanced learning for all by identifying the following points: (1) no professional group is "better" than another when assessing DAS28; (2) standardisation of how we ask about the VAS subcomponent will be introduced immediately; (3) tender joints are to be classed as ones with any tenderness from reasonable palpation; and (4) clinical judgement should be used when assessing rheumatoid disease activity.

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## FRI0602 BELIEFS ABOUT SUBCUTANEOUS BIOLOGICAL AND ORAL MEDICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS. ARCO STUDY

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**Background:** Patients' perception on the usefulness of their medicines is important to implement actions that increment confidence and minimize concerns.

**Objectives:** To describe the beliefs that patients with rheumatoid arthritis (RA) treated with subcutaneous (SC) biological drugs have on their oral and SC biological medications for RA.

**Methods:** ARCO is a cross-sectional study in RA patients >18 years-old on SC biological drugs from 42 Spanish hospitals. The beliefs on medication was assessed with the Spanish version of the Beliefs About Medicines Questionnaire (BMQ), obtaining their agreement with each statement through a Liker scale from 1 (strongly disagree) to 5 (strongly agree). The BMQ score was obtained subtracting the "concerns subscale" score from that of the "necessity scale"

**Results:** 364 patients were included (mean age 54.9 years [SD 12.5]; 77.5% women, median RA duration 7.8 years). The mean scores of the BMQ for the oral and SC biological medication were 5.60 (SD 5.03) and 5.22 (SD 5.43) respectively; the median for both was 5 (p = NS). For the oral medication, 84.4% of the patients scored higher in the necessity subscale than in the concerns subscale, whereas for the SC biological the percentage was 78.3%. Some 73.3% scored necessity > concerns for both drugs, whilst 4.4% scored necessity < concerns for. In the necessity subscale, the highest score for the oral medications was "My health, at present, depends on my medicines" and for SC "My medicines protect me from becoming worse" (table). In the concerns subscale, the highest score was "I sometimes worry about the long-term effects of my medicines" for both groups of drugs (table).

Percentage who responded "agree" or "strongly agree" to the BMQ statements (%)

| | Oral | SC biological |
|---|---|---|
| Necessity scale | | |
| My health, at present, depends on my medicines | 92.2 | 87.5 |
| My life would be impossible without my medicines | 86.5 | 76.6 |
| Without my medicines I would become very ill | 89.3 | 78.8 |
| My health in the future will depend on my medicines | 82.6 | 69.9 |
| My medicines protect me from becoming worse | 88.4 | 88.9 |
| Concerns scale | | |
| Having to take medicines worries me | 58.3 | 48.8 |
| I sometimes worry about the long term effects of my medicines | 77.5 | 73.0 |
| My medicines is mystery to me | 43.4 | 50.2 |
| My medicines disrupts my life | 24.2 | 19.8 |
| I sometimes worry about becoming too dependent on my medicines | 50.6 | 45.6 |

**Conclusions:** RA patients show strong positive beliefs about the necessity of their medicines for RA, although a substantial percentage also describes concerns. The beliefs are similar for oral and SC biological medicines. Rheumatologists should contribute to improve aspects related to specific patients' concerns.

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## FRI0603 PATIENTS' PRIORITIZATION OF PATIENT-CENTERED EDUCATION AND RESEARCH TOPICS IN RHEUMATIC DISEASE

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**Background:** While healthcare provider priorities often coalesce around clinical concerns, little has been done to explore the most pressing educational concerns among rheumatic disease patients.

**Objectives:** To identify healthcare education topics most important to patients with inflammatory arthritis and other rheumatic conditions.

**Methods:** Participants were recruited from within the membership registry of the rheumatology patient community, CreakyJoints, to participate in one of six nominal groups held in June 2015. Each of the six groups generated a set of educational topics or questions ("items"), and then rank-ordered them within each focus group. Items were aggregated into common topic groups, redundant items de-duplicated, and then categorized into common topic groups and themes. Based on the qualitative work, a survey describing items from all nominal groups was created and deployed more widely to the CreakyJoints membership. Demographics and other disease-related features were captured.

**Results:** From the nominal groups, 8 educational themes emerged that were related to 28 unique educational topics (see Table 1). Overall, "Lifestyle changes

and patient environment modifications" was the most valued theme, receiving 14% of votes. Medication data (drug dosing, interactions, performance, etc.), physician selection, and knowledge of disease/disease progression were also strongly emphasized at 12%, 11%, and 10%, respectively. Themes of least interest included friend/family/community support, financial concerns (including insurance), and social interactions, with nominal group vote percentages of 3%, 2%, and 1%, respectively.

Among 400 participants who completed the survey, mean (SD) age was 55 (11.5) years with 86% being women and 82% being white. Participant health conditions (not mutually exclusive) included rheumatoid arthritis (74%), osteoarthritis (45%), fibromyalgia (26%), osteoporosis (18%), psoriatic arthritis (8%), lupus (5%), and ankylosing spondylitis (5%). The top 10 items rated as "Extremely Important" by a majority of patients were: How arthritis affects more than just your joints (86%); What are the signs that the medication is not working (84%); Importance of knowing about how the disease will progress, even if the news is bad (83%); What are the side effects of available drugs, and how do the drugs interact with each other (82%); What are the available medications and treatments for your case (80%); How to understand the results of tests used to monitor your condition (79%); How to find the right rheumatologist (76%); How to take an active role in decisions about your care (76%); How your life will change as your disease progresses (74%); and How to speak up and help manage your care when your perspective is different from your doctor's (73%).

**Table 1:** Top-ranked rheumatic disease educational concern themes, topic group and items.

| Theme | Topic Group Example | Item Example |
|---|---|---|
| Lifestyle Changes & Patient Environment Modifications | Dietary Choices | What would be good food alternatives for reducing flares |
| Medication Data (Dosing, Effects, Limitations) | Drug Effects | Drugs take a couple of months to work; don't expect an immediate fix |
| Physician Selection | Finding the Right Specialist | Make sure to have a proper diagnosis by a rheumatologist |
| Knowledge of Disease & Disease Progression | Disease Progression | What to look for that indicates the condition is getting worse |
| Reliable Resources | Individual Research Resources | It is important to educate yourself and do your own research |
| Asking for Help & Extent of Limitations | Asking for Help | Don't be afraid to ask for help when you are having a flare |
| Coping | Emotional | Dealing with the mental and emotional problems that come with the condition |
| Personalized Disease needs Personalized Treatment | Individualized Treatment Options | What are all medications/treatments available to you for your case in particular |
| Alternative Treatments | Alternative Treatments | What alternative therapies that might be helpful (i.e. acupuncture and biofeedback) |
| Self-Advocation and Voicing Concerns | Self-Advocation | Be your own advocate in your disease; trust your instincts and speak up |

**Conclusions:** Patients with rheumatic diseases are concerned about a variety of topics, which include lifestyle changes/patient environment modifications, medication data, and physician choice. Patient-centered research should maximally respond to addressing questions of importance to patients, and this survey is a first step in identifying and prioritizing the topics that matter most to patients.

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**Disclosure of Interest:** None declared

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## FRI0604 THE EFFECT OF AN EDUCATIONAL INTERVENTION BASED ON CLINICAL SIMULATION IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS DIAGNOSIS BY GENERAL PRACTITIONERS: A RANDOMIZED CLINICAL TRIAL

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**Background:** Clinical simulation is a teaching strategy generally used in the medical field that has not been used in rheumatology education yet. This innovative idea will enable the basis of models designed hands-size providing a very accurate way to study the most important semiological findings, such those of the rheumatoid arthritis and its main distinction diagnoses (osteoarthritis - OA); the most challenging to evaluate among general practitioners. Clinical simulation models are protected under the patent certificate number 50152 of the Superintendency Industry and Trade of the Republic of Colombia

**Objectives:** To evaluate the effectiveness of a rheumatology educational tool based on clinical simulation designed for general practitioners, professionals who will improve the diagnosis of rheumatoid arthritis and osteoarthritis

**Methods:** Randomized clinical trial. The research subjects were randomly assigned to two different groups: The experimental group, and the control group. A) The experimental group: educational intervention in rheumatoid arthritis based on clinical simulation, B) Control group: educational intervention on basic aspects of diagnosis and treatment of osteoporosis. After four weeks of the educational intervention, members of the two groups faced an evaluation process that included four cases with real patients (two patients with rheumatoid arthritis and two patients with osteoarthritis), two cases with two clinical simulation models (a case of rheumatoid arthritis and an osteoarthritis case), and six virtual clinical cases (three rheumatoid arthritis cases and three osteoarthritis cases). At that point participants ascertained the detected semiological findings, establishing a complete diagnosis very helpful in order to corroborate the diagnosis if it is required.

**Results:** 160 physicians (80 from the active group and 80 from the control group), 89 were women (56%). The average age was 35.0 years (standard deviation 7.7 years). Clinical stimulation was considered to work successfully when a practitioner diagnosed accurately at least 10 out of 12 cases submitted under his examination. A difference of 81.3% (confidence interval 95% 72–90%) was found successfully, amount statistically significant in favor of the active group (88.8% vs 7.5%) ($p = <0.001$). A greater number of hits were found in the detection of the semiological findings in the active group compared with the control ($p<0.001$)

**Conclusions:** The present study showed the effectiveness of an educational intervention based on clinical simulation to improve the diagnostic approach in rheumatoid arthritis and osteoarthritis; this innovative idea opens the gate for a new horizon in the teaching of modern rheumatology. Moreover, the clinical simulation is a meaningful benefit for patients representing an improvement in the quality and use of health system resources.

**Disclosure of Interest:** None declared

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## FRI0605 EFFECT OF AN EDUCATIONAL INTERVENTION BASED ON CLINICAL SIMULATION IN THE DIAGNOSIS OF SPONDYLOARTHRITIS (SPA) FROM GENERAL PRACTITIONERS, A STUDY BEFORE AND AFTER

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**Background:** This paper wants to quantify the rate of improvement in the diagnosis of SPA among a group of general practitioners who receive an educational intervention based on clinical simulation in the rheumatology field

**Methods:** Intervention study before and after

**Results:** 102 general practitioners received an educational intervention based on clinical simulation. The topic of this educational intervention was Spondyloarthritis. A workshop that includes clinical simulation models of feet, fingers and a mannequin created for this purpose was created, based on the strategy of problem-based learning. The workshop lasted 5 hours, it was divided into two parts: the first was about the of the clinical approach of joint pain and lumbar pain diagnosis and relevant aspects of SPA. In this first part, besides the theoretical support for the diagnosis of SPA, participants viewed pictures of patients with spondylitis and peripheral involvement (enthesitis, dactylitis, arthritis) seeking to achieve awareness of their sense of sight with respect to the diagnostic approach to patients with suspected SPA and sought to strengthen the logical approach to be implemented when approaching this type of patients. The second part focused on clinical cases applied to clinical simulation models, applying the knowledge acquired during the theoretical phase. Participants made a several stations where they where they could appreciate for periods of 15 minutes each simulators of 3 feet, 6 simulators simulated fingers and a mannequin where they can identify entheses and psoriasis lesions, improving visual and tactile sensitivity in each semilogic findings for tehe diagnosis of SPA. The participants filled out an pre and post test, which included clinical cases with simulators and photographs of hands and feet of patients with suspected EAS. 102 participants (59% women), average age 32.3 years (SD 7.1). Improvement in the correct diagnosis of EAS of 47% (the correct diagnosis increased from 39% to 86%). Paraclinical application in the cases presented decreased significantly, from an average of 8–4 paraclinical requested by each clinical case presented. 98.5% of participants would recommend to other colleagues to make this workshop. 97.7% believe that this educational intervention will improve the diagnostic approach to patients with suspected SPA

**Conclusions:** The usefulness of clinical simulation in the field of rheumatology has been shown, given by an improvement in the diagnostic sensitivity for the diagnosis of EAS demonstrated

**Disclosure of Interest:** None declared

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## FRI0606 THE METHOD USED TO SET PASS MARKS IN AN OBJECTIVE STRUCTURED CLINICAL EXAMINATION (OSCE) DETERMINES THE OVERALL PERFORMANCE OF CANDIDATES DURING AN ACCREDITATION PROCESS

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**Background:** The assessment of clinical competences during a national accreditation is a high-stakes process, and the pass mark needs to be settled through

robust methods [1]. Since 2012, the MACR certifies trainees in Rheumatology (TR) using both written (multiple-choice questions –MCQ- test) and clinical (OSCE) examinations [2]. For 2013 and 2014 accreditations, OSCE pass mark was set by absolute criterion referencing (APM), while a global rating of borderline performance (BPM) was added for the 2015 process.

**Objectives:** To compare the performance of TR during an OSCE according to APM and BPM, and to examine whether correlations between MCQ and OSCE evaluations are affected by OSCE pass mark selection.

**Methods:** Forty-three TR presented a MCQ test and an OSCE circuit including 15 stations. Each station (8 minutes long) was assigned to an evaluator who rated candidate performance as "fail", "borderline" or "above range" using a Likert scale and additionally filled a tailored-checklist. Mean checklist scores (maximum score of 10) from those TR rated as borderline was defined as the BPM for each station. Average of all BPM defined the overall OSCE BPM. A composite OSCE score was obtained for each candidate. Descriptive statistics was used and correlations were examined using Pearson's test and Mann Whitney U test.

**Results:** For MCQ test, pass mark was set by criterion as >5.7; OSCE-APM was defined as >6 and composite OSCE-BPM was calculated as >7.4. TR's performance varied depending on the pass mark selected. Mean MCQ test score was 6.6±0.6 with 5 candidates receiving a failing score; mean composite OSCE score was 7.4±0.6 and no candidate received a failing score according to CPM, while 21 (48.8%) received a failing score according to BPM.

The BPM score widely varied among stations, ranging from 4.5 to 9.5; candidate's performance also varied across stations and within each station depending on the pass mark; station 2 showed the lowest percentage of TR with APM-passing score (26%) or BPM-passing score (42%); the opposite figure was true regarding station 10 who showed the highest percentage of TR with a passing score (100% and 72%, respectively).

MCQ test score correlated with composite OSCE score (r=0.67, P=0.001). Those TR who obtained a passing score according to BPM had higher MCQ scores than those with a failing OSCE score: (median, Q25-Q75) 7.1 (6.4–7.3) vs. 6.3 (5.9–6.7), p=0.001. There were more candidates with a passing OSCE-BPM score distributed in the upper MCQ quartiles than TR with a failing OSCE score (P<0.001).

**Conclusions:** The way to set a pass mark for an OSCE strongly impacts the performance of TR during a national accreditation process but poorly affects correlations between clinical and written examinations.

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**Disclosure of Interest:** None declared

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## FRI0607 RHEUMATOLOGY TRAINING IN INDIA – A REFLECTION AND COMPARISON WITH UNITED KINGDOM

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**Background:** Indian subcontinent is one of the largest growing economy in the world.The burden of rheumatic musculoskeletal disease among Indian population is overwhelmimg.Clearly,there is a demand for specialist rheumatology work force in India.In this era of biologics and biosimilars,rheumatology is an attractive speciality among aspirant doctors.Our previous observational studies have explored and identified the strength and weakness in the rheumatology training programme in UK,Canada[1] and South Asian countries[2]. We aim to explore the perception of rheumatology training among specialist and current trainees in India,and compare with UK training.

**Objectives:** 1.To explore the perception of rheumatology training in India.

2.To identify the strength and weakness and the areas of improvement in training programme in India.

**Methods:** This is an observational questionnaire based study. A pilot study was conducted with 32 questions during APLAR conference 2015 in India. The re-designed questionnaire was circulated electronically to rheumatology trainees across India through their training leads. Our survey was directed towards exploration of rheumatology curriculum including content, training and research opportunities and job prospect. The results were analysed through smart survey.

**Results:** Total respondents were n=77, 16% (40/240)from UK and 49% (37/75) from India. There were female predominance (55%) in UK and male predominance (71%) in India. Noted a wide variation in application process, structure and duration of training. In India, training duration is 6 years (3 yrs in GIM and 3 yrs in rheumatology), whereas it is 5 years for combined and 4 years for pure rheumatology in UK.The national rheumatology curriculum was designed by JRCPTB in UK, but multiple regional syllabus were followed in India with lack of adherence to national curriculum.

Trainees from both countries received weekly institutional teaching. UK trainees received structured supervision for joint injections, whereas Indian trainees received more training for crystal identification and immunological studies. Fewer cross speciality clinics were practised in India. Less exposure to MSK ultrasound skills was noted among the trainees, however the concept of MSK Ultrasound was clearly evolving in India.

Postgraduate research programmes and opportunities were available in UK, whereas Indian trainees need to complete a formal supervised dissertation project as a part of postgraduate qualification.

Mandatory training for generic skills were lacking in India. Training records were maintained electronically in UK and by paper log book in India. Although speciality exit exam was mandatory in both countries, the format was different including MCQ based in UK and theoretical and practical based in UK.

**Conclusions:** 1. This is the first study comparing rheumatology training between UK and India.

2. Lack of structured Curriculum and homogenous rheumatology training exist in India.

3. Harmonisation of rheumatology training in India is essential, matched with developed nations.

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## FRI0608 SIMULATION FOR JOINT INJECTION AND ASPIRATION. COLLABORATING OUR EXPERIENCES, WHAT HAVE WE LEARNT?

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**Background:** We present a knee injection and aspiration course, with simulated rheumatology clinical scenarios targeting core medical trainees. Simulation should be a core part of the curriculum, providing a safe learning environment, as hands on rheumatology exposure is often limited.

**Objectives:** 1. To review and compare two different rheumatology practical teaching courses.

2. To highlight important rheumatology cases presenting on the acute medical take, and achieve the requirements on the core medical training curriculum.[1]

3. With training emphasis on service provision, to provide organised targeted teaching.[2]

**Methods:** Eight core medical trainees were recruited to a knee aspiration and injection course at a cardiothoracic specialist centre (no on-site rheumatology). There was a pre-course assessment, pre-course handout, followed by a practical demonstration on a knee manikin[3] by a competent teacher. Each trainee underwent assessement: Directly Observed Procedures – DOPs assessment. Pre- and post- course surveys evaluated confidence. Six months later, a second cohort of eight trainees were recruited, and the session was delivered by a rheumatology registrar. There was a brief lecture, followed by a demonstration. Trainees also underwent one-to-one assessment with SimMan® (scenarios: prosthetic joint septic arthritis and haemoptysis secondary to TB reactivation following anti-TNF treatment).

**Results:**

– Trainee experience prior to teaching: Cohort 1: 12.5% no experience. 37.5% seen but not attempted. 50% performed with supervision only. Cohort 2: 25% no experience. 37.5% seen but not attempted. 37.5% performed with supervision only.
– Confidence pre- and post teaching: Cohort 1: Initially only 40% had confidence in aspirating a knee joint. *Increased to 80%.* Cohort 2: Initially 34% had confidence in aspirating a knee joint. *Increased to 85%.*
– 100% trainees identified correct anatomical landmarks, proving that clinicians possess the knowledge but are limited by experience and resources.
– Outcomes were suprisingly largely unchanged despite involving a rheumatology registrar.

**Conclusions:** - Opportunities to gain practical experience are infrequent. This affects trainees rotating through multiple training centres. Trainee confidence is increased through simulation, however simple organised teaching sessions are currently not readily available.

– Limitations: Small cohorts, inconsistent outcomes due to two sessionsbeing delivered by different people. It is dfficult to directly compare the cohorts, as cohort 2 included SimMan®. However confidence was slightly increased with this, showing that simulation is an effective learning tool.
– This program may be targeted at rheumatology specialist trainees too.

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## FRI0609 FIFTEEN-YEAR TREND IN INFORMATION ON THE INTERNET FOR PATIENTS WITH RHEUMATOID ARTHRITIS: EVOLVING, BUT WITH OPPORTUNITIES FOR IMPROVEMENT

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**Background:** Rheumatoid arthritis (RA) may lasts for decades, so patient education is very important. There has been an increase in RA patients seeking information on the Internet during the last 15 years.
**Objectives:** a) To assess the content, authorship, scope, readability and quality of the information currently available on the Internet in relation to RA; b) To compare it with a report published in 2001 [1] (2001-referent study); c) To assess the current positioning of websites posted by universities, hospitals, and medical associations.
**Methods:** We recreated the method used for the 2001-referent study assessing information on the Internet using the phrase "rheumatoid arthritis" in WebCrawler. All websites and pages were critically assessed for relevance, scope, authorship, type of publication, and financial objectives. Differences between studies were considered significant if 95% confidence intervals did not overlap. Additionally, we added a Google search following the same method, with a particular assessment of Internet pages posted by medical institutions regarding content quality (DISCERN instrument), readability (Flesch-Kincaid Grade Level test), and accessibility (the order of appearance).
**Results:** The search returned 316 hits using WebCrawler (85% were considered relevant). There were significant differences between the current studies and the 2001-referent studies (WebCrawler). There were increases in information sites (82% vs. 36%) and RA-specific discussion pages (59% vs. 8%), and decreases in advertisements (2% vs. 48%) and alternative therapies (27% vs. 45%). Google searches had significantly lower relevance (58% vs. 85%), more news articles (18% vs. 7%), more "only RA discussed" pages (76% vs. 59%), and less "alternative therapy" pages (19% vs. 27%) when compared with WebCrawler. Concerning the content quality of Internet pages, 37% were rated as good and 36% unbiased. Among the first 300 hits, 30 (10%) were posted by medical institutions, 17 from the United States, five from the United Kingdom, four from Australia, and one each from Canada, Malaysia, Spain and the Netherlands. The Mayo Clinic appeared as the top result, the Arthritis Foundation (United States) 3rd, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (United States) 7th, the American College of Rheumatology 8th, and the Arthritis Research (UK) in 14th position. Regarding readability, 7% of these Web pages required six years of schooling, 27% between seven and nine years, 27% between 10 and 12 years, and 40% 12 years of schooling or more.
**Conclusions:** It seems that information on the Internet has evolved in this fifteen-year period. Medical institutions are better positioned now. However, there are still areas for improvement, such as content quality, leadership from medical institutions, and readability of information.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3024

## Genomics, genetic basis of disease and HLA/T cell recognition

### SAT0001 IDENTIFICATION OF SJÖGREN'S SYNDROME RISK LOCI NEAR TNFAIP3 AND PRDM1

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**Background:** Sjögren's syndrome (SS) is a complex autoimmune disease with both environmental and genetic factors playing important roles in its etiology.
**Objectives:** The goal of this study was to replicate 8 suggestive loci that failed to exceed the genome-wide significance (GWS) threshold of 5x10E-8 in our previously published work: *TNFAIP3*, *PTTG1*, *PRDM1*, *DGKQ*, *FCGR2A*, *IRAK1BP1*, *ITSN2*, and *PHIP*.
**Methods:** Our previous study included 1638 SS cases and 6754 population controls. In the current study, we genotyped an additional 282 SS cases and 2576 population controls yielding a total of 1920 SS cases and 9330 controls. Analysis was done using logistic regression accounting for ancestry and gender.
**Results:** Two regions exceeded the GWS threshold. Association has been previously established with SS to a risk haplotype spanning the *TNFAIP3* coding region described in lupus; however, we identified a novel independent effect ~230kb 5' of *TNFAIP3* (rs6933404 $P_{meta}$=6.85x10E-9, OR=1.28) originally described in rheumatoid arthritis. Association was observed for the haplotype spanning the *TNFAIP3* coding region peaking at rs58721818 (P=4.77x10E-4), which is not correlated with rs6933404 ($r^2$=0.02; D'=0.49). Bioinformatics data provided limited support that rs6933404 is the functional variant in this region; however, another variant on this haplotype also surpassing GWS, rs6927172, modifies 8 transcription factor binding sites, and is located within an enhancer element in $CD4^+CD25^-IL17^+$ PMA-Ionomycin stimulated Th17 primary cells by the Epigenetics Road Map Project. A variant in the region of *PRDM1* also surpassed the GWS threshold (rs526531 $P_{meta}$=1.70x10E-8, OR=1.25). Two additional variants on this haplotype exceeded GWS, but no clear candidate functional variant has emerged based on bioinformatics data. Of the 6 remaining suggestive regions, *PTTG1*, *DGKQ*, and *FCGR2A* continue trending towards GWS.
**Conclusions:** These data now establish 2 new SS risk loci, *TNFAIP3* and *PRDM1*. *TNFAIP3*, which codes for the protein A20, is a negative regulator of NF-kB. *PRDM1*, which codes for the protein BLIMP1, is a transcription factor that regulates interferon-beta locus and plasma cell differentiation. Additional studies are needed to determine how these association signals function in the human genome and contribute to SS etiology.
**Disclosure of Interest:** None declared
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### SAT0002 SPECIFIC PREMATURE EPIGENETIC AGING OF CARTILAGE IN OSTEOARTHRITIS

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**Background:** Accelerated aging may be a component of osteoarthritis (OA) as shown by changes observed at the level of cartilage (local) in multiple studies. Systemic changes of biological aging have been much less studied, but accelerated telomere shortening (a biomarker of biological aging) has been described in the blood of patients with hand OA (1). In addition, some studies report increases in age-related comorbidities, frailty and mortality in patients with OA, which are consistent with sytemic premature aging. The recent discovery of an epigenetic biomarker of biological age consisting in DNA methylation age measures (DmAM) provides a new opportunity to address these questions.
**Objectives:** We aimed to explore the local and the systemic components of biological aging in OA using epigenetic DmAM biomarkers.
**Methods:** Three tissues were investigated: blood with 890 samples (182 controls without OA, 206 clinical hand OA, 229 severe knee OA and 273 severe hip OA), bone from femoral heads (45 controls without OA and 33 severe hip OA) and cartilage from tibial plateau or femoral heads (31 controls without OA and 36 severe OA). Two DmAM were used: a novel DmAM based on 8 CpG selected from previous work (2) and analyzed by quantitative minisequencing for blood; and the multi-tissue age estimator by Horvath (3), which is based on 353 CpGs analyzed with Illumina Methylation arrays, for bone and cartilage. Accuracy of the 8 CpG DmAM was evaluated with correlation and mean absolute difference (MAD) to age. Differences in DmAM (ΔDmAM) between OA patients and controls were evaluated with ANOVA adjusting for age and sex.
**Results:** OA cartilage showed an accelerated epigenetic aging of 3.7 years in relation with cartilage from controls without OA (Table 1). By contrast, no significant difference was observed in bone from OA patients (Table 1).
The new DmAM for blood based on 8 CpG was accurate as shown in data sets from controls, two from previous studies and the 182 controls without OA from the current study ($R^2 \geq 0.52$, $p < 10^{-16}$, MAD≤7.3 years). Therefore, it was applied to compare the controls without OA with the OA patients. None of the three groups of patients, hand OA, knee OA or hip OA, showed accelerated aging in blood (Table 1).

Table 1. Specific accelerated DmAM in OA cartilage compared with control cartilage

| Tissue | OA set | ΔDmAM (95% CI) | *P*-value |
|---|---|---|---|
| Cartilage | Knee/hip | 3.66 (1.06 to 6.26) | 0.008 |
| Bone | Hip | 0.04 (–1.80 to 1.87) | 0.34 |
| Blood | Hand | 0.01 (–1.10 to 1.12) | 0.98 |
| | Knee | 0.04 (–0.94 to 1.02) | 0.93 |
| | Hip | –0.72 (–1.70 to 0.25) | 0.11 |

**Conclusions:** OA cartilage showed premature biological (epigenetic) aging according to DNA methylation changes. This effect was cartilage-specific, excluding a systemic component, since it was not observed in bone tissue or in blood.
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**Disclosure of Interest:** None declared
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### SAT0003 THE ROLE OF 12/15-LIPOXYGENASE IN THE PATHOGENESIS OF OSTEOPOROSIS IN MICE

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**Background:** The pathogenesis of osteoporosis is complex and involves age-related factors and inflammation. 12/15-lipoxygenase (12/15-LOX) plays a key role in the regulation of inflammatory response and has been shown to contribute in bone metabolisms. However, the exact role of 12/15-LOX in the pathogenesis of osteoporosis is not clear.
**Objectives:** We aimed to investigate the impact of genetic deletion of *12/15-LOX* on 1) bone mineral density (BMD) and 2) serum balance between osteoprotegerin (OPG) and RANK ligand (RANKL), the two proteins known to be involved in bone remodelling, in mice.
**Methods:** The whole body BMD was measured using dual-energy X-ray absorptiometry (DEXA) bone densitometer equipped with software for evaluation of small animals (Hologic Discovery, USA) in 40-weeks old 12/15-LOX knockout mice and their age- and sex-matched wild-type littermates (C57Bl mice). Serum concentrations of OPG and RANKL were measured using commercially available ELISA kits (R&D Systems and USCN Life Science Inc., respectively).
**Results:** The mean whole body BMD was significantly lower in female 12/15-LOX knockout mice as compared with age-matched female C57Bl mice ($p < 0.01$). No significant differences were found in the mean whole body BMD of male 12/15-LOX knockout mice as compared with their age-matched male wild-type littermates.
No significant difference could be found in the mean serum concentration of OPG between 40-weeks old female 12/15-LOX knockout and C57Bl mice. However, in younger (8-weeks old) female C57Bl mice the mean serum concentration of OPG was significantly higher as compared with female 12/15-LOX knockout mice of the same age as well as compared with female 40-weeks old C57Bl or 12/15-LOX knockout animals ($p < 0.01$ for all comparisons).
There were no significant differences in the mean serum concentration of RANKL between female 12/15-LOX knockout mice and their wildtype littermates.
**Conclusions:** The results of our study indicate that 12/15-LOX plays a role in age-related osteoporosis in female mice, possibly through regulation of OPG-RANKL balance. Further studies should address the role of hormonal status on 12/15-LOX interactions with OPG-RANKL pathway.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5884

## SAT0004 GENOMIC STRATIFICATION BY HLA-DRB4 EXPRESSION IDENTIFIES INNATE AND ADAPTIVE IMMUNE PATTERNS AS DIFFERENTIAL PREDICTORS OF RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS

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**Background:** Variability of clinical course and response to therapy in RA suggests differences in molecular mechanisms depending on stage and sub-entity of the disease. Most dominant molecular discriminators are HLA-DR4 shared epitope (SE), and the status of rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA) development, all indicating subentities with influence on severity and outcome.
**Objectives:** Early RA prior to methotrexate (MTX) treatment was investigated to exclude major therapeutic influence. By comparing whole blood transcriptomes between subsequent responders and non-responders we aimed to unravel molecular mechanisms with influence on MTX outcome of RA.
**Methods:** Whole blood of 52 patients with early RA was obtained in the HITHARD and in the ArthroMark study. Clinical characteristics assessed at baseline and after 16 weeks included RF, ACPA, DAS28 and EULAR response for classification in good (GR), moderate (MR) and non-responders (NR). Total RNA was globin reduced and processed according to standard protocols for hybridization to U133 Plus 2.0 microarrays. Biostatistical methods included MAS5.0 and RMA algorithms with limma, lasso and Wilcoxon tests. For functional interpretation, expression of candidate genes was tested in various blood cell types and stimulation conditions using own and GEO reference transcriptomes. Marker selection was validated by qPCR with commercial primers and four different housekeeping genes.
**Results:** Different biostatistical approaches favored MAS5.0 algorithms for marker selection. Comparison between good and non-responders in unselected patients revealed insufficient discriminatory power. Generating different subgroups defined by gender, status of RF, ACPA, SE, HLA-DRB4 or DQA1 identified molecular patterns with a strong discrimination between GR and NR in HLA-DRB4$^-$ patients. All other subgroups did not improve pattern selection. In HLA-DRB4$^-$ patients, genes increased in GR were related to phagocytes and bone marrow activation whereas genes increased in NR were associated with lymphocyte activity. In HLA-DRB4$^+$ patients, patterns of adaptive immunity were again related to non-response but frequently combined also with innate patterns. Receiver-operating-characteristics (ROC) with the top 20 markers in HLA-DRB4$^-$ and DRB4$^+$ subgroups revealed AUC<0.96 and AUC<0.91 for response and AUC<0.98 and AUC<0.99 for non-response associated genes, respectively. Technical validation by qPCR with the 16 top candidates confirmed AUC-values up to 0.97 for prediction in the HLA-DRB4$^-$ group and reached AUC up to 0.89 in HLA-DRB4$^+$ patients.
**Conclusions:** Genetic stratification revealed transcriptional patterns that indicate different molecular pathomechanisms in RA depending on response to MTX therapy. Interestingly, the group responding to MTX was dominated by phagocyte but not lymphocyte activity, which may indicate an important contribution of innate triggers to the pathomechanisms in RA.
**Disclosure of Interest:** None declared
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## SAT0005 A META-ANALYSIS AND A FUNCTIONAL STUDY WITH TRANSMITOCHONDRIAL CYBRIDS CONFIRM THE ROLE OF THE MTDNA HAPLOGROUPS IN THE DEVELOPMENT OF INCIDENT KNEE OSTEOARTHRITIS. DATA FROM CHECK AND OAI

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**Background:** In the last years the study of the mitochondria in the context of osteoarthritis (OA) attracted much attention. In the present work we aim to analyze the role of the mtDNA haplogroups in the development of incident knee OA in well-characterized study cohorts
**Objectives:** To analyze the influence of the mtDNA haplogroups in the rate of incident knee OA in the prospective cohorts of CHECK and OAI and to perform functional analysis with transmitochondrial cybrids to explore the consequences of the mitochondrial background in the pathogenesis of Osteoarthritis
**Methods:** The influence of the haplogroups in the development of incident knee OA at eight years in 2579 subjects from the Osteoarthritis Initiative (OAI) and 635 subjects from the Cohort hip and Cohort knee (CHECK) was assessed. A subsequent meta-analysis was conducted to strengthen the association of these individual studies.
Transmitochondrial cybrids carrying the haplogroups J and H were constructed to study the influence of the mitochondrial background in different OA-related features.
**Results:** The haplogroup J significantly associates with a decreased risk of incident knee OA in subjects from the OAI (HR=0.680;95%CI=0.470–0.968;p<0.05) and CHECK (HR=0.728;95%CI=0.469–0.998;p<0.05). The subsequent meta-analysis including 3214 cases showed that the haplogroup J significantly associates with a lower risk of incident knee OA (HR=0.702;95%CI=0.541–0.912;p=0.008) (Figure 1).

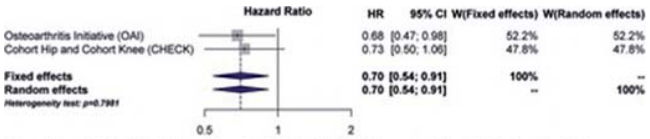


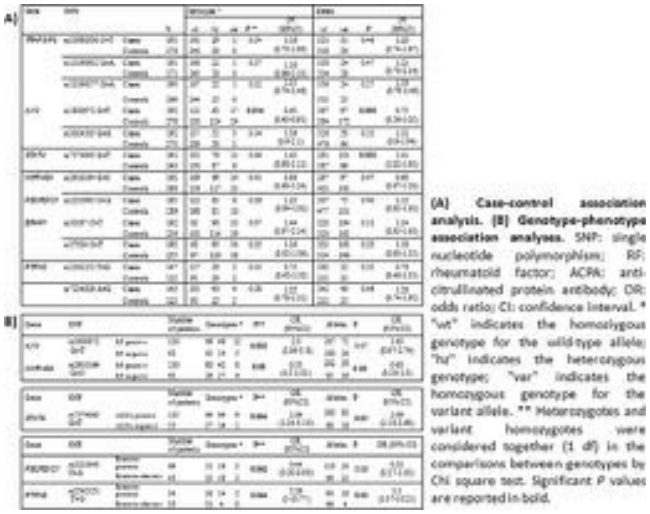

Figure1. Forest plot of individual associations involving the mtDNA haplogroup J and the risk of incident knee OA

Compared with the haplogroup H, haplogroup J shows a lower free radical production, specially peroxide/peroxynitrite (52.51±11.34 vs 41.26±7.48;p<0.05) and superoxide (8.58±3.0 vs 4.25±0.9;p<0.05), a higher cell survival under oxidative stress conditions (29.63±3.3 vs 56.45±7.36;p<0.05), a lower grade of apoptosis (7.35±3.78 vs 4.69±1.68;p<0.05) as well as a lower expression of the mitochondrially-related pro-apoptotic gene BBC3 (3.3-fold;p<0.05), a higher lactate production (64.22±10.76mg/dl vs 51.42±6.85mg/dl;p<0.05) and a lower expression of the mitochondrial biogenesis-related gene PGC1-α (2-fold;p<0.05)
**Conclusions:** The haplogroup J reduces the risk of incident knee OA. This mitochondrial variant constitute a protective phenotype against the development of OA, emerging as a powerful OA biomarker and even leading to the consideration of the mitochondrion as a potential therapeutic target in OA
**Acknowledgement:** We'd like to acknowledge to the participants of CHECK and OAI cohorts
**Disclosure of Interest:** None declared
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## SAT0006 POLYMORPHISMS IN STAT4, IL10, PSORS1C1, PTPN2 AND MIR146A GENES ARE DIFFERENTLY ASSOCIATED WITH NEGATIVE PROGNOSTIC FACTORS IN ITALIAN PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid Arthritis (RA) is a systemic autoimmune disease resulting in chronic inflammation of the synovium and consequent cartilage and bone erosion. RA is strongly associated with the presence of rheumatoid factor (RF) and consists of clinical subsets of anti-citrullinated protein antibody (ACPA)-positive and negative patients. Several genes have been proven to contribute to the disease susceptibility and they may be associated with a particular pattern of disease and with the response or toxicity to therapy. It is important to identify novel genomic biomarkers associated not only with disease susceptibility but also able to detect early those patients with negative prognostic factors who may benefit from a more aggressive therapeutic approach.
**Objectives:** This study was designed to evaluate whether the most relevant single nucleotide polymorphisms (SNPs) associated with RA and other autoimmune disorders are related to RF, ACPA, and clinical phenotype in a cohort of biologic-naïve Italian RA patients.
**Methods:** A total of 192 RA patients [female n=147 (76.5%), age 54.1 ± 13.2



**(A) Case-control association analysis. (B) Genotype-phenotype association analyses.** SNP: single nucleotide polymorphism; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibody; OR: odds ratio; CI: confidence interval. * "wt" indicates the homozygous genotype for the wild-type allele; "hz" indicates the heterozygous genotype; "var" indicates the homozygous genotype for the variant allele. ** Heterozygotes and variant homozygotes were considered together (1 df) in the comparisons between genotypes by Chi square test. Significant *P* values are reported in bold.

years, disease duration 7.8 ± 9 years, positive RF n=130 (67.7%), positive ACPA n=137 (71.7%), 28 joint count disease activity score (DAS28) 5.2 ± 1.3, bone erosions at diagnosis n=69 (60%), disease modifying anti-rheumatic drugs (DMARDs) n=148 (77.1%)] were enrolled. 278 age-matched healthy controls were included. We analyzed a total of 12 SNPs in STAT4, IL10, PSORS1C1, PTPN2, ERAP1, TRAF3IP2 and MIR146A genes by allelic discrimination assays. Case-control association studies and genotype/phenotype correlation analyses were performed (Figure 1A-B).

**Results:** A higher risk to develop RA was observed for rs7574865 in STAT4 gene (P=0.035, OR=1.41). We observed a significant association between the variant alleles of rs1800872 in IL-10 gene and RA susceptibility. Subjects carrying the variant alleles (in heterozygous and homozygous status) showed a lower risk to develop RA in comparison with wildtype individuals (P=0.014, OR=0.63). The presence of RF resulted significantly associated with rs1800872 variant in IL10 (P=0.032, OR=2) while rs2910164 in MIR146A was protective (P=0.05, OR=0.55). ACPA were significantly associated with rs7574865 in STAT4 (P=0.004, OR=2.64). The SNP rs2233945 in PSORS1C1 gene was protective regarding the presence of bone erosions (P=0.042, OR=0.44) while rs2542151 in PTPN2 gene was associated with joint damage (P=0.044, OR=3.26).

**Conclusions:** Our results confirm that polymorphisms in STAT4 and IL10 genes confer susceptibility to RA. For the first time we described that SNPs in PSORS1C1, PTPN2 and MIR146A genes were differently associated with a severe disease phenotype in terms of autoantibody status and radiographic damage in an Italian RA population.

**Disclosure of Interest:** None declared

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## SAT0007 GENETIC POLYMORPHISMS OF HLA-DRB1 ARE ASSOCIATED WITH DERMATOMYOSITIS AND ANTI-MDA5 ANTIBODIES IN CHINESE

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**Background:** Risk alleles at genome loci containing interferon induced with helicase C domain 1 (IFIH1) and human leukocyte antigen (HLA) genes closely associated with dermatomyositis (DM) in European population [1–3]. Autoantibody targeted to melanoma differentiation associated protein 5 (MDA5), a protein encoded by IFIH1, was associated with rapidly progressive interstitial lung disease (RP-ILD) and high mortality in DM [4].

**Objectives:** To estimate the associations between HLA and IFIH1 rs1990760 polymorphisms and susceptibility to DM and anti-MDA5 antibody expression in Chinese population.

**Methods:** HLA-DRB1and IFIH1 rs1990760 polymorphisms were determined in 102 DM patients and 400 healthy controls. Anti-MDA5 antibodies and ILD were evaluated by ELISA and high-resolution computed tomography (HRCT), respectively.

**Results:** Frequencies of HLA-DRB1*04:01 were significantly higher in DM (4.41% *vs* 0.63%, OR 7.34, 95%CI 2.84–18.95, *P* 0.00004, *Pc* 0.001), but the frequency of HLA-DRB1*14 (0.98% *vs* 5.88%, OR 0.16, 95%CI 0.05–0.55, *P* 0.004, *Pc* 0.049) was significantly lower than that of healthy controls. Compared with the healthy controls, HLA-DRB1*04:01 was associated with the development of ILD in DM (7.14% *vs* 0.63%, OR 12.23, 95%CI 4.97–30.10, *P* $5.03\times10^{-8}$, *Pc* $1.81\times10^{-6}$). The frequency of HLA-DRB1*09 (5.36% *vs* 18.48%, OR 0.25, 95%CI 0.10–0.63, *P* 0.003, *Pc* 0.042) was significantly lower in DM patients with ILD than in DM patients without ILD, suggesting it is a protective allele for ILD in DM. The frequencies of HLA-DRB1*04:01 (8.51% *vs* 0.63%, OR 14.79, 95%CI 6.17–35.45, *P* $1.53\times10^{-9}$, *Pc* $5.49\times10^{-8}$) and HLA-DRB1*12:02 (21.28% *vs* 10.00%, OR 2.43, 95%CI 1.43–4.14, *P* 0.001, *Pc* 0.037) were significantly increased in anti-MDA5 positives than in controls. Compared with anti-MDA5 negatives, the frequency of HLA-DRB1*12:02 (21.28% *vs* 4.55%, OR 5.68, 95% CI 2.22–14.48, *P* 0.0003, *Pc* 0.010) were significantly increased in anti-MDA5 positives. No association was observed between the IFIH1 rs1990760 and DM, anti-MDA5 antibody expression and ILD status.

**Conclusions:** HLA-DRB1 alleles, but not IFIH1 polymorphisms, may be associated with the susceptibility to DM, ILD involvement and anti-MDA5 expression in Chinese population.

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## SAT0008 IL-17A GENE IMPLICATION IN SPANISH PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an autoimmune pathology associated with increased risk of cardiovascular (CV) disease and subclinical atherosclerosis[1]. Consequently, both inflammatory diseases share common molecules involved in its pathogenesis. In this sense, interleukin 17A (IL-17A) is a pro-inflammatory cytokine involved in the regulation of immune responses and chronic inflammation[2].

**Objectives:** To evaluate the potential association between different IL-17A polymorphisms and CV events, as well as subclinical atherosclerosis, in a large cohort of Spanish RA patients.

**Methods:** Five IL-17A polymorphisms (rs4711998, rs8193036, rs3819024, rs2275913 and rs7747909) were genotyped by TaqMan assays in a 7900 HT Real-Time polymerase chain reaction system in 1,974 Spanish patients diagnosed with RA (fulfilling the 2010 American College of Rheumatology classification criteria for RA[3]), recruited from different Spanish hospitals. 318 patients (16.1%) had experienced CV events, and 822 had undergone carotid ultrasonography studies to assess subclinical atherosclerosis (presence/absence of plaques and carotid intima media thickness [cIMT]). The relationship between IL-17A alleles, genotypes and haplotypes and CV events, presence/absence of plaques and cIMT values was assessed. Results were adjusted for sex, age at diagnosis and traditional CV risk factors.

**Results:** No statistically significant differences were observed when allelic/genotypic frequencies of each IL-17A polymorphism were assessed regarding presence/absence of CV events, plaques or cIMT values. This was also the case when the five polymorphisms were combined to form haplotypes.

**Conclusions:** Our results do not confirm an association between the five IL-17A polymorphisms studied and the development of CV events or subclinical atherosclerosis in our cohort of Spanish RA patients.

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## SAT0009 INVESTIGATION OF DIFFERENTIAL METHYLATION AS A POTENTIAL BIOMARKER OF METHOTREXATE RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) is the first-line disease modifying anti-rheumatic drug (DMARD) for the treatment of rheumatoid arthritis (RA). By two years of treatment only 55% of patients remain on the drug, implying that many do not respond adequately or experience adverse effects (1,2). Therefore, identifying blood-based biomarkers that predict treatment response is an important research priority. DNA methylation is an epigenetic marker that modifies but does not alter DNA sequence, and should be considered for evaluation as potential biomarkers for treatment response. The mechanisms of action of MTX are unclear. However, it is thought that MTX promotes adenosine release and interferes with the intracellular methyl donor status leading to DNA hypomethylation (3).
**Objectives:** To identify differential DNA methylation signatures in whole blood, which may act as biomarkers predictive of response to MTX in patients with RA.
**Methods:** Epigenome-wide DNA methylation levels were measured using the HumanMethylation450 BeadChip (Illumina) in whole blood-derived DNA samples from individuals recruited to the Rheumatoid Arthritis Medication Study (RAMS), a one year observational study including patients with RA starting MTX for the first time, who had EULAR good response (n=36) or EULAR poor response (n=36) to MTX. DNA was taken from blood samples pre-treatment and following four weeks on therapy. Response was determined at six months using the DAS28 score. Differentially methylated positions (DMPs) were identified using linear regression, adjusting for gender, age, cell composition, and baseline DAS28 score.
**Results:** Although no probe reached study-wide significance, 16 DMPs suggestive loci were associated with MTX response in the pre-treatment samples (arbitrary $p<10^{-4}$), including a DMP close to the *IL6R* gene (cg15633035, $p=5.24x10^{-5}$). At four weeks, 20 DMPs were associated with response, with no overlap with the DMPs reported in the pre-treatment sample. In good responders, 10 DMPs were differentially methylated between pre-treatment and four week samples. In poor responders, 17 DMPs were differentially methylated between time-points. There was no overlap of DMPs between good and poor responders
**Conclusions:** These preliminary results suggest DNA methylation may provide a useful source of biomarkers of MTX response and now require replication in an independent dataset. Furthermore, investigation of differential methylation between baseline and four weeks reveals the potential of DNA methylation in pharmacodynamic modelling of MTX response. Further analysis is being conducted and significant findings will be validated in the total RAMS population using pyrosequencing.
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## SAT0010 A TARGETED NEXT-GENERATION SEQUENCING GENE PANEL FOR AUTOINFLAMMATION

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**Background:** Monogenic autoinflammatory diseases (AID) are severe lifelong systemic inflammatory disorders with dysregulated innate immunity, causing significant morbidity, mortality, and economic burden. The number of AID is rapidly expanding. Securing a molecular diagnosis is of major importance for treatment, prognosis, and genetic counselling. Routine genetic screening is time-consuming, costly, and lacks sensitivity since only common disease harbouring exons of a minority of the known AID genes are currently tested using Sanger sequencing. Next-generation sequencing (NGS) offers the ability to rapidly and cost-effectively screen all exons of a gene panel containing hundreds of genes. This approach has not yet been routinely introduced in the UK for AID.
**Objectives:** To develop and evaluate the performance of a NGS gene panel for AID.
**Methods:** The Agilent SureDesign tool was used to design an NGS panel targeting 113 genes, grouped into 9 broad clinical phenotypes: AID; monogenic vasculitis/vasculopathy; complement defects; monogenic lupus; hemophagocytic lymphohistiocytosis (HLH); early-onset inflammatory bowel disease; autoimmune lymphoproliferative syndromes; monogenic stroke; and hereditary amyloidosis. The targeted region includes coding exons, conserved non-coding exons, upstream promoter regions, and splice sites. Captured and indexed libraries (QXT Target Enrichment System) were sequenced as a multiplex of 16 samples on an Illumina MiSeq sequencer in paired-end mode. Positive controls for panel validation comprised 19 DNA samples from patients with confirmed mutations in a variety of genes on the panel. We then applied the panel to test 29 prospective samples with suspected but unconfirmed monogenic inflammation. Read alignment, variant calling, and annotation were performed using Agilent SureCall v3.0 software.
**Results:** In the validation stage, our targeted panel detected all known mutations in the 19 positive control samples with an average read depth of 244X (+/–29X) across the captured genes. The panel was effective at detecting different types of variants, including rare and common single nucleotide variants (SNVs), insertion/deletions, splice-junction variants, upstream promoter region variants, and somatic mosaicism. Prospective testing of the panel in 29 patients revealed potential pathogenic variants in 14 of the 29 patients giving a detection rate of 48%. These included atypical patients with novel mutations in specific exons/genes, not currently routinely available for testing by Sanger sequencing in the NHS.
**Conclusions:** This study demonstrates the clinical utility of a comprehensive NGS-based targeted gene panel which was both highly sensitive and specific in detecting different sequence variants of clinical significance. We are currently integrating this panel into a routine diagnostic laboratory testing strategy for monogenic inflammation. This will facilitate accurate and timely molecular diagnosis, more targeted treatment, and ultimately better outcomes for our patients.
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## SAT0011 REPLICATION OF A DISTINCT PSORIATIC ARTHRITIS RISK VARIANT AT IL23R

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**Background:** Psoriatic arthritis (PsA) is an inflammatory arthritis that is associated with psoriasis. Although the majority of PsA genetic risk loci identified also confer risk for psoriasis, we have recently reported evidence of loci that are associated with PsA and not psoriasis, including an association at the *IL23R* locus which is also independent of a psoriasis variant at the same locus.
**Methods:** The PsA-specific SNP rs12044149, and the psoriasis SNP rs9988642 at the *IL23R* locus were genotyped in a cohort of 914 PsA cases and 6,945 controls from Spain, Crete, Germany and the UK, with the Life Technologies QuantStudio genotyping platform. Association testing was carried out using PLINK, and a meta-analysis was performed with PsA Immunochip data (1,962 cases, 8,923 controls). Genotype data was also available from the psoriasis WTCCC2 study (excluding known PsA, n=1,784) to compare effect sizes between PsA and psoriasis using multinomial logistic regression in Stata, and to directly compare PsA and psoriasis genotypes. Credible SNP sets were calculated for the PsA and psoriasis *IL23R* associations using the Bayesian refinement method, and functionally annotated.
**Results:** We replicated the association rs12044149 with PsA ($P=4.03x10^{-6}$), which remained significant when conditioning upon the psoriasis variant, rs9988642 ($P_{cond}=4.86x10^{-6}$), and reached genome-wide significance during

meta-analysis of the combined PsA dataset ($P_{meta}$=4.76x10$^{-20}$). Only a modest association was found for rs9988642 ($P$=0.04), with no genome-wide significance found during meta-analysis ($P$=4.61x10$^{-4}$). Within the psoriasis dataset, this association remained significant when conditioning upon rs12044149 ($P$=1.0x10$^{-07}$ vs. $P_{cond}$=1.63x10$^{-5}$). Effect estimates for rs12044149 were significantly different between PsA and psoriasis ($P$=2.0x10$^{-3}$), and direct comparison of genotypes for PsA and psoriasis found the risk allele to be significantly increased in PsA ($P$=4.52x10$^{-4}$, OR=1.3). Credible SNPs for rs12044149 mapped to promoter and enhancer regions within memory CD8$^+$ T cells, which we have previously reported to be critical for PsA.

**Conclusions:** We have successfully replicated a PsA-specific (associated with PsA but not psoriasis) risk variant at the *IL23R* locus in an independent cohort, confirming rs12044149 to be distinct from rs9988642 ($r^2$=0.02). This gives five PsA-specific associations that have now been identified.

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## SAT0012 GENETIC ANALYSIS OF ABCG2 IN PRIMARY HYPERURICEMIA AND GOUT

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**Background:** The urate transporter *ABCG2* is one of the genetic determinants of serum uric acid concentrations[1].

**Objectives:** In the present study, we describe the identification and functional analysis of allelic variants in the *ABCG2* gene, a physiologically important urate transporter whose dysfunction plays a major role in pathogenesis of gout, in a cohort with primary hyperuricemia and gout.

**Methods:** The cohort consisted of 150 individuals: 32/118 primary hyperuricemics/gout. The definition of hyperuricemia was as follows: >420/360 μmol/l at two repeated measurements at intervals of at least 4 weeks in men/women. Gouty arthritis was diagnosed according to the 1977 preliminary criteria of the American College of Rheumatology for acute arthritis of gout. Patients suffering from secondary gout were excluded. We analyzed 15 exons of *ABCG2* gene by PCR amplification and sequenced directly. The functional analysis of identified allelic variants is in process (HEK cells).

**Results:** In the *ABCG2* gene, 16 intronic sequence variants were detected. In the case of c.689+1G>A, related to an individual with severe gouty phenotype, two abnormal splicing variants were identified: a) r.[532_689del]; b) r.[532_689del], r.[944_949del]. Identified deletions lead to frameshift and premature stop codon introduction[2].

From the nine exon variants detected, there were seven non-synonymous: p.V12M (*rs2231137*), p.Q141K (*rs2231142*), p.R147W (*rs372192400*), p.T153M (*rs753759474*), p.F373C (*rs752626614*), p.T434M (*rs769734146*) and p.D620N (*rs34783571*). Heterozygous p.V12M variant was detected in seven individuals. Heterozygous variant p.R147W, p.T153M, p.F373C and p.D620N was detected once, variant p.D620N was detected twice also in heterozygous state. Variants p.R147W, p.T153M, p.F373C and p.T434M were *in silico* predicted using Polyphen, Sift and Provean program as a probably damaging. The p.Q141K, previously functionally characterized allelic variant with a strong effect on uric acid secretion impairment, was in cohort of hyperuricemic/gout patients presented with significantly higher allele frequency MAF=0.19 (42 heterozygotes/5 homozygotes), than in population of European origin (MAF=0.09) and world-wide population (MAF=0.12).

**Conclusions:** Our results show that genetic factor *ABCG2* should be considered as one of the common risks for hyperuricemia/gout. In clinical practice, *ABCG2* dysfunction can be estimated easily by genotyping and these findings will help to recognize a trait of hyperuricemia at a very early stage.

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## SAT0013 JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATION OF PTPN22 RS2476601 SNP IS SPECIFIC TO FEMALES IN A GREEK POPULATION

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**Background:** Juvenile idiopathic arthritis (JIA) is an autoimmune disease characterized by persistent chronic arthritis [1] and is believed to be influenced by both genetic and environmental factors. *PTPN22* single nucleotide polymorphism (SNP) rs2476601 has been recently reported in an Australian study to be restricted to females and to not be observed in males [2].

**Objectives:** Considering that a significant source of inconsistency amongst the literature on autoimmune disease susceptibility genes stems from an inability to replicate genetic findings across different racial or ethnic groups, we attempted to confirm the female-specific association of rs2476601 in a homogeneous Greek population.

**Methods:** The sample set consisted of 128 (70.3% female) Caucasian JIA patients and 221 (28.1% female) healthy controls from Northern Greece. Genotyping for the *PTPN22* rs2476601 (*Xcm*I) was performed by restriction fragment length polymorphism (RFLP) analysis [3]. Logistic regression or the Gart (Woolf) method were used to estimate ORs and 95% CIs. Analyses were performed using Stata v13 (StataCorp, College Station, TX, USA).

**Results:** The rs2476601 was genotyped in 128 Caucasian JIA patientsand 221 healthy controls from Northern Greece. Overall, *PTPN22* was associated with increased risk of JIA in this Greek sample (OR =2.3, 95% CI 1.1 – 5.1, p=0.038). Sex-stratified analyses showed that, once again, the risk association was restricted to females (Female: OR =19.9, 95% CI 1.2 – 342, p=0.0016; Male: OR =1.1, 95% CI 0.3 – 3.1, p=0.94) confirming the prior findings. Given that the sex bias differs by JIA subtype, ideally we would have liked to test for these associations in individual subtypes; however, small sample size prevented us from performing these analyses with any statistical certainty.

**Conclusions:** This data demonstrated that the sex-specific pattern of association detected is broadly applicable to different populations, and provided further impetus to undertake studies to understand the crucial role of rs2476601 in the mechanisms leading to disease's development preferentially in females. Our work is of interest given the importance of comparative studies in populations of differing ethnic and/or racial origin in any attempt to conclusively define the genetic architecture of JIA and the magnitude of the effects of specific risk alleles globally.

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## SAT0014 ASSOCIATION OF HLA GENES IN SYSTEMIC SCLEROSIS WITH INTERSTITIAL LUNG DISEASE

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**Background:** Interstitial lung disease (ILD) is associated with a significant morbidity and mortality in systemic sclerosis (SSc). Many studies have reported the association between human leukocyte antigen (HLA) alleles and increased risk of SSc, but the associated between ILD in SSc and HLA alleles remains unclear.

**Objectives:** The aim of this study was to investigate the association of HLA class I and HLA class II with ILD in Korean SSc cohort.

**Methods:** A total of 170 SSc patient (105 SSc patients with ILD and 65 SSc patients without ILD) were enrolled at Seoul National University Hospital from 1988 to 2014. Two hundred one healthy participants from Korean Marrow Donor Program (KMDP) were recruited as controls. Demographic information, clinical skin subset (limited vs. diffuse), SSc-specific autoantibodies (anti-topoisomerase I (ATA), anti-centromere (ACA), anti-ribonucleoprotein (RNP)), and internal organ involvement (ILD, pulmonary arterial hypertension, gastrointestinal, renal involvement) of the enrolled patients were characterized. ILD were diagnosed based on the findings of the chest computed tomography. HLA-A, -B, -C,-DQB1,-DRB1, and -DPB1 typing were performed PCR amplification with directly sequencing from extracted genomic DNA.

**Results:** HLA-B*52:01, C*12:02, DRB1*15:02, DPB1*09:01, and DPB1*13:01 alleles were more frequent in SSc patients with ILD than healthy controls. However, the frequencies of these genes did not differ between SSc patients with and without ILD (Table). ATA positive SSc was associated with HLA-B*52:01,

C*12:02, DRB1*15:02, DPB1*09:01, and DPB1*13:01 alleles compared to ATA negative SSc and DPB1*09:01 showed the highest odds ratio for ATA (OR =23.08).

Table 1. HLA frequencies in patient with systemic sclerosis with ILD and without ILD compared to healthy controls

| HLA alleles | SSc_Total (N=170) | ILD(+)SSc (n=105) | ILD(–)SSc (n=65) | Control (N=201) | SSc Total vs. Control $P_c$ | ILD(+)SSc vs. Control $P_c$ | ILD(–)SSc vs. Control $P_c$ |
|---|---|---|---|---|---|---|---|
| B*52:01 | 23 (13.5) | 20 (19.0) | 3 (4.6) | 9 (4.5) | 0.076 | <0.001 | 1.000 |
| C*12:02 | 23 (13.5) | 20 (19.0) | 3 (4.6) | 9 (4.5) | 0.046 | <0.001 | 1.000 |
| DRB1* 15:02 | 29 (17.1) | 24 (22.9) | 5 (7.7) | 14 (7.0) | 0.074 | <0.001 | 1.000 |
| DPB1* 09:01 | 22 (12.9) | 18 (17.1) | 4 (6.2) | 9 (4.5) | 0.045 | <0.001 | 1.000 |
| DPB1* 13:01 | 52 (30.6) | 38 (36.2) | 14 (21.5) | 25 (12.4) | <0.001 | <0.001 | 1.000 |

Abbreviation: HLA, human leukocyte antigen; SSc, systemic sclerosis; ILD, interstitial lung disease; OR, odds ratio; $P_c$, corrected $P$ by Bonferroni correction. $P_c$ of ILD(+)SSc vs. ILD(–) SSc: HLA-B*52:01 ($P_c$=0.304), C*12:02 ($P_c$=0.184), DRB1*15:02 ($P_c$=0.407), DPB1*09:01 ($P_c$=0.570), DPB1*13:01 ($P_c$=0.660).

**Conclusions:** SSc patients with ILD have several specific HLA genes compared with healthy controls and the frequencies of these HLA genes were significantly higher in ATA-positive SSc as well. Therefore, ATA positivity and ILD are associated with ceratin HLA class I and II in SSc patients.

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## SAT0015 NOVEL AND RARE MUTATIONS LINKED TO POLYAUTOIMMUNITY

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**Background:** Polyautoimmunity (i.e., the presence of two or more autoimmune diseases in a single patient) and familial autoimmunity (i.e., diverse autoimmune diseases in a nuclear family) represent extreme phenotypes ideal for identifying major genomic variants contributing to autoimmunity (1–3). Whole Exome Sequencing (WES) and linkage analysis are well suited for this purpose due to its strong resolution upon familial segregation patterns of functional protein coding and splice variants (3).

**Objectives:** The primary objective of this study was to identify potentially autoimmune causative variants using WES data from extreme pedigrees segregating polyautoimmunity phenotypes.

**Methods:** DNA of 47 individuals across 10 extended and multigenerational pedigrees, ascertained from probands affected with polyautoimmunity and familial autoimmunity, were selected for WES. Variant calls were obtained through Genome Alignment Tool Kit (GATK) algorithm; filters for prioritizing major functional were applied and later implemented for genetic linkage analysis. Sanger sequencing corroborated variants with significant linkage.

**Results:** Novel and mostly rare variants harbored in *SRA1, MLL4, ABCB8, DHX34* and *PLAUR* genes showed significant linkage (LOD scores are >3.30). The strongest signal was in *SRA1*, with a LOD score of 5.48. Network analyses indicated that *SRA1* and *PLAUR* both contribute to regulation of apoptotic processes.

**Conclusions:** Novel and rare variants in genetic linkage with polyautoimmunity were identified throughout WES. Genes harboring these variants might be major players of autoimmunity.

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## SAT0016 ROLE OF PCR, GCKR, HNF1A, LEPR, ASCL1 AND NLRP3 IN ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an autoimmune inflammatory disease associated with accelerated atherosclerosis and increased cardiovascular (CV) disease. Elevated levels of the C-reactive protein (CRP) are related to an increase risk of coronary artery disease [1] and stroke [2]. Recently, PCR, GCKR, HNF1A, LEPR, ASCL1 and NLRP3 have been associated with CRP levels in non-rheumatic population [2].

**Objectives:** We aimed to determine the potential role of these genes in the development of CV disease and subclinical atherosclerosis in patients with RA.

**Methods:** Genotyping was performed in 2,384 Spanish RA patients by TaqMan assays. Subclinical atherosclerosis was determined by carotid ultrasonography (US) in 1,193 patients.

**Results:** No statistically significant differences were found when PCR, GCKR, HNF1A, LEPR, ASCL1 and NLRP3 were assessed according to the presence/absence of CV disease. It was also the case when patients were stratified according the presence/absence of subclinical atherosclerosis.

**Conclusions:** Our results do not confirm an association between these genes and the development of CV disease and subclinical atherosclerosis in patients with RA.

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## SAT0017 SYNOVIAL FLUID MIR-223 EXPRESSION LEVELS IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS PATIENTS

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**Background:** Synovial hypertrophy and synovitis could be seen in both rheumatoid arthritis (RA) and inflammatory osteoarthritis (OA) as a consequence of deregulated pro-inflammatory cytokine production. Abnormal local microribonucleic acids (miRNAs) production that regulate the inflammatory milieu in the synovial joints has been reported in several studies. Due to their stability miRNAs are widely explored as potential diagnostic biomarkers for both diseases as well as for disease activity and treatment response.

**Objectives:** The objective of our study was to evaluate the role of expression levels of miR-223 in the synovial fluid (SF) of RA and OA patients as diagnostic biomarker in the clinical practice.

**Methods:** Total RNA including miRNAs was isolated from SF of 48 RA, 16 OA and 11 healthy controls (HCs) by using RNeasy Protect Cell Mini kit (according to manufacturer's protocol). Reverse transcription was performed in order to synthesize cDNA by using miScript II RT kit. Expression of miR-223 was analyzed by relative quantitation method $2^{\wedge-(\Delta\Delta Cq)}$. As reference control for normalization RNU6B gene was used. Data were analyzed by SPSS. The results were compared to HCs as well as between the two disease groups.
**Results:** In SF miR-223 was overexpressed in 79.17% of the RA ($p=1.64 \times 10^{-3}$) and in 62.50% of OA patients (p=0.885) when compared to HCs. SF miR-223 levels were upregulated in 77.08% of the RA when compared to OA patients ($p=6.2 \times 10^{-3}$). In order to evaluate the diagnostic accuracy of miR-223 expression levels in SF to distinguish patients with RA or OA from HCs as well as between the two diagnostic groups receiver operating characteristic (ROC) curve analysis was constructed using RQ values. Expression levels of miR-223 in SF could discriminate RA patients from HCs with high diagnostic accuracy since area under the curve (AUC) was 0.841 (95 CI: 0.724–0.958; $p=4.6 \times 10^{-4}$) with 87.5% sensitivity and 72.7% specificity. ROC curve analysis showed that OA patients could not be well distinguished from HCs (AUC =0.631; 95 CI: 0.417–0.845) probably due to the small sample size but SF miR-223 levels could be used to discriminate OA from RA with the following AUC =0.693 (95% CI: 0,493–0.893) and with 68.8% sensitivity and 66.7% specificity.
**Conclusions:** SF miR-223 level could serve as potential diagnostic biomarker for RA as it could distinguish RA from both HCs as well as inflammatory OA. Larger sets are needed to confirm the diagnostic accuracy of miR-223 in RA.
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## SAT0018 PRELIMINARY ANALYSIS REVEALS AN INTERFERON SIGNATURE IS ASSOCIATED WITH NON-RESPONSE TO ETANERCEPT IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The treatment of rheumatoid arthritis (RA) has changed considerably over the last couple of decades, particularly since the introduction of biological therapies; however, a considerable proportion of patients fail to respond satisfactorily (30–40%). Early and effective treatment is known to correlate with better long-term outcomes and there is an unmet clinical need for predictors of response which can be used to stratify patients prior to treatment; so that those prone to non-response can be offered alternative options. We hypothesis that gene expression profiles of RA patients about to commence treatment with the biological drug etanercept will provide such a biomarker.
**Objectives:** To identify gene expression biomarkers which discriminate between good-responders (R) and non-responders (NR) to etanercept in RA patients.
**Methods:** 72 RA patients about to commence treatment with etanercept were chosen for analysis from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS) longitudinal cohort. Using the established EULAR classification criteria this equated to 34 R (28-joint disease activity score (DAS28) of $\leq$3.2 and improvement of $>$1.2) and 38 NR (DAS28 $>$5.1 and improvement $<$0.6 or between 0.6–1.2) patients at 3-months follow-up. Total RNA was extracted from pre-treatment whole blood previously collected into TEMPUS/PaxGene blood tubes upon recruitment to BRAGGSS. Following biotin labelling and RNA amplification (Illumina TotalPrep RNA Amplification Kit), cRNA was hybridised to Illumina HumanHT-12 v4 Expression BeadChips targeting over 47,000 probes. GenomeStudio software summarised the bead level data, followed by QC and differential expression analysis using the Bioconductor package Limma.
**Results:** Using a fold-change (FC) cut-off of $>$1.2 between R and NR and p-value $<$0.05, 82 probes were differentially expressed; 33 up-regulated in NR and 49 up-regulated in R prior to treatment with etanercept. Interestingly, of the probes up-regulated in NR, an interferon (IFN) signature was observed, including the type-I IFNs, *IFITM3* (FC 1.53, p-value=0.01), *MX1* (FC 1.45, p-value=0.02) and *IFI44L* (FC 1.28, p-value=0.04) and a type-II IFN, *BTN3A2* (FC 1.38, p-value $9.6 \times 10^{-05}$). Of note, expression of *PTPRC*, a previously reported treatment response gene, was found to be up-regulated in R as compared to NR prior to treatment (FC 1.24, p-value=0.03).
**Conclusions:** The preliminary results suggest that an IFN signature prior to etanercept treatment is indicative of non-response in RA patients. These results are encouraging in that an IFN signature has consistently been associated with RA and clinical outcome to biological therapies. However, to the best of our knowledge this is the first study to observe an IFN signature correlating with response to etanercept. More in-depth analysis is ongoing using packages such as WGCNA (weighted correlation network analysis) and Matrix eQTL to further explore these associations.
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## SAT0019 TUMOR NECROSIS FACTOR-α -308 A/G GENE POLYMORPHISM IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: RELATION TO DISEASE ACTIVITY, DAMAGE AND DISABILITY

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood and an important cause of disability[1]. Its cause remains unknown, but likely includes complex interactions between genes and environmental exposures resulting in dysregulation of the immune system[2]. TNF-α is a cytokine with an important role in inflammation and immune function[3]. Several single nucleotide polymorphisms (SNPs) have been identified within the region of the TNF-α gene but only very small minority have proven functional consequences and were associated with JIA susceptibility[4]
**Objectives:** To evaluate the clinical significance of serum levels of tumor necrosis factor alpha (TNFα) and -308 A/G promoter polymorphism in JIA patients and find any association to the subsets, clinical and laboratory features, disease activity and damage as well as functional disability
**Methods:** Forty-eight JIA children and 30 controls were included in the present study. Juvenile arthritis disease activity score in 27 joints (JADAS-27) was calculated, juvenile arthritis damage index (JADI) assessed and Childhood Health Assessment Questionnaire (CHAQ) to measure the functional status. Serum TNF-α was assayed by ELISA and gene (-308) promoter polymorphism determined by polymerase chain reaction.
**Results:** The 48 JIA children (mean age: 11.5±2.8 years) were 13 systemic, 17 oligoarticular and 18 polyarticular onset. The serum TNF-α was significantly higher in patients (90.4±6.3 ng/ml) compared to control (3.5±2.6 ng/ml) ($p<0.0001$) with a tendency to be higher in the polyarticular subtype. All controls had TNF-α -308GG alleles. The frequency of GG genotype tended to be higher in systemic onset compared to oligoarticular and polyarticular subtypes. The serum TNF-α significantly correlated with JADAS-27 (r=0.32, p=0.03) and CHAQ (r=0.37, p=0.01) and negatively with the presence of GG alleles (r=-0.48, p=0.001). The GG alleles were significantly negatively associated with C-reactive protein (r=-0.32, p=0.03) with a tendency to negatively correlate with JADAS-27, CHAQ and JADI-extrarticular (r=-0.28, p=0.06; r=-0.25, p=0.09 and r=-0.25, p=0.09 respectively).
**Conclusions:** There is evidence of a possible influence of the –308 SNP promoter position on the production of TNF-α, the severity of JIA which may consequently influence the response to anti-TNF-α treatment.
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SAT0020 **ASSOCIATION OF HLA-DP/DQ AND STAT4 POLYMORPHISMS WITH ANKYLOSING SPONDYLITIS IN A CHINESE POPULATION**

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**Background:** Ankylosing spondylitis (AS) is a highly heritable complex inflammatory arthritis disease. Genetic factors are thought to be crucial in the pathogenesis of ankylosing spondylitis. However, few studies were performed to investigate the relationship between HLA-DP/DQ and STAT4 polymorphisms and AS susceptibility.
**Objectives:** To further explore the associations of the four SNPs (HLA-DP rs3077, HLA-DP rs9277535, HLA-DQ rs7453920 and STAT4 rs7574865) with the risk and clinical characteristics of AS in a Chinese Han population. And also to analyze the linkage disequilibrium (LD) in HLA gene and the association between the HLA haplotypes and the susceptibility to AS.
**Methods:** 400 patients with AS and 379 age- and sex-matched healthy controls in a Chinese population were included. All the four SNPs were genotyped using polymerase chain reaction high resolution melting (HRM) analysis. Allele, genotype, and haplotype frequencies were compared between AS patients and controls. Besides, stratification analyses of HLA-DP/DQ and STAT4 polymorphisms and risk for AS were also performed.
**Results:** No significant difference was observed between AS patients and healthy controls in the allele frequency of rs3077, rs9277535 and rs7574865. However, there was a significant association between the HLA-DQ rs7453920 G/A variant and AS patients, with minor allele A correlated with a reduced risk of AS (allelic frequency, OR=0.44, 95% CI: 0.31–0.62, p=3.0E-06; dominant model, OR =0.42, 95% CI: 0.29–0.62, p=7.0E-06). Moreover, the haplotypes block AAA and GGA in the HLA gene significantly correlated with reduced risk of AS (AAA: OR =0.38, 95%CI: 0.22–0.66, p=0.0004; GGA: OR=0.41, 95% CI: 0.24–0.69, p=0.0006).




**Conclusions:** This is the first study demonstrating the relationship between HLA-DQB2 rs7453920 and the risk of AS in a Chinese population. Besides, this study revealed that LD blocks around HLA–DP/DQ are strongly associated with AS susceptibility. This research sheds new light on the significant relationship between the SNPs in the HLA gene and the risk of AS.
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## Innate immunity in rheumatic diseases

SAT0021 **TYPE 2 INNATE LYMPHOID CELLS ARE RAPIDLY AND PERSISTENTLY RECRUITED IN EXPERIMENTAL FIBROSIS AND THEIR COUNTS CORRELATE WITH THE SEVERITY OF SKIN AND LUNG FIBROSIS IN SYSTEMIC SCLEROSIS**

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**Background:** Type 2 innate lymphoid cells (ILC2s), are recently identified as population of cells with lymphoid morphology lacking re-arranged antigen-specific receptors.
**Objectives:** We aimed to evaluate the contributive role of ILC2s in the pathogenesis of systemic sclerosis (SSc), in particular their levels and correlations with fibrotic manifestations in SSc and various fibrotic mouse models.
**Methods:** Human blood samples and skin sections (69 patients with SSc and 47 healthy controls) as well as skin and lung tissue of various fibrotic mouse models were analyzed by flow cytometry and immunohistochemistry using two complementary panels of markers each. ILC2s were further phenotyped for activation and homing parameters. ILC2 counts were correlated with clinical manifestations of SSc
**Results:** Significantly elevated numbers of ILC2s were detected in the skin (10-fold increase) and blood (4-fold increase) of SSc patients by two independent established sets of ILC2 markers compared to healthy controls. In contrast to circulating ILC2s, skin-resident ILC2s express various activation markers and stained positive for skin homing markers. Furthermore, our data suggest that ILC2s might be involved in the pathogenesis of fibrosis in SSc by showing multiple associations of ILC2 counts with fibrotic manifestations in SSc patients. Significantly higher frequencies were observed in diffuse cutaneous (dc)SSc patients compared to limited cutaneous SSc (lcSSc). The modified Rodnan Skin Score (mRSS) positively correlated with ILC2 counts and pulmonary involvement. In parallel, we detected significantly elevated numbers of ILC2s in the fibrotic skin of bleomycin-induced and DNA topoisomerase I-induced mice compared to control mice. Moreover, in the tight-skin (Tsk)-1model of fibrosis resembling less inflammatory stages of SSc significantly increased ILC2 counts were detected compared to control mice. Kinetic analyses revealed an early upregulation of ILC2s in experimental models of fibrosis. In contrast to lineage positive lymphocytes that peak at early inflammatory stages of fibrosis, however disappear over time, ILC2s persist also in later stages of established fibrosis.
**Conclusions:** Here, we provide first evidence for a role of ILC2s in the pathogenesis of SSc by demonstrating increased ILC2 counts in the skin and blood of human SSc patients. These findings were indirect supported by elevated numbers of ILC2s in the fibrotic skin and lung sections of various mouse models for SSc, reflecting different pathophysiological aspects of the disease. Proliferation of ILC2s in the fibrotic skin, the activated state of dermal ILC2s and correlations of ILC2 counts with dermal and pulmonary fibrosis together with supporting findings of these cells in fibrotic areas of murine skin and lung samples suggest a central role of ILC2s in the pathogenesis of fibrosis.
**Disclosure of Interest:** None declared
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SAT0022 **S100A8/A9 IS A POTENT SERUM AND IMAGING BIOMARKER TOOL FOR ASSESSING JOINT INFLAMMATION AND DESTRUCTION IN SERONEGATIVE EXPERIMENTAL ARTHRITIS**

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**Background:** Seronegative joint diseases, including psoriatic arthritis and juvenile idiopathic arthritis, are characterized by the lack of autoantibodies, which are relevant biomarkers for predicting disease activity in rheumatoid arthritis. Promising alternative biomarkers are the Damage Associated Molecular Patterns (DAMPs), S100A8, S100A9 and the heterodimer S100A8/A9. These proteins are specifically expressed and released by infiltrating phagocytes and may therefore serve as relevant biomarkers for joint inflammation and destruction in seronegative arthritis.
**Objectives:** In this study we determined the biomarker potential of serum S100A8/A9 and in vivo imaging of synovial S100A8 to asses joint inflammation and damage in the IL-1 receptor antagonist deficient (IL-1Ra$^{-/-}$) mice, a mouse model for seronegative arthritis in which serum autoantibodies are not correlated to disease activity.
**Methods:** Serum levels of S100A8/A9 and various cytokines were monitored during arthritis development in IL-1Ra$^{-/-}$ mice using ELISA and Luminex and were correlated to macroscopic and microscopic parameters for joint inflammation and

damage. Local S100A9 expression and matrix metalloproteinase (MMP) mediated cartilage damage in the ankle joints were investigated by immunohistochemistry. In addition local S100A8 and activated MMPs were monitored in vivo by optical imaging using anti-S100A8-Cy7 and AF-489-Cy7, a specific tracer for activated MMPs.

**Results:** Starting at week 8, serum levels of S100A8/A9 were significantly increased (1640 ± 1008 ng/ml at week 16) in IL-1Ra$^{-/-}$ mice compared to WT BALB/c control mice (429 ± 191 ng/ml, $P$ =0.005) and strongly correlated to joint swelling (r =0.766, $P$<0.0001), while serum levels of IL-1β, IL-6, TNFα, IL-17, IL-4 or IFN-α did not. In addition, high serum S100A8/A9 levels at week 10 were predictive for increased joint swelling at week 16 (r =0.576, $P$ =0.0002). Next to macroscopic swelling, increased serum S100A8/A9 also correlated to microscopic cell influx (r =0.794, $P$ <0.0001) and was reflected by local expression of S100A9 within the synovium, indicating the activated synovial lining as the source of increased serum S100A8/A9. Local expression of S100-DAMPs could also be monitored non-invasively by in vivo optical imaging using anti-S100A8-Cy7. Next to a biomarker for inflammation, S100-DAMPs may also be used for assessing joint damage. Indeed, arthritic IL-1Ra$^{-/-}$ mice showed increased cartilage damage (r =0.687, $P$ <0.0001) which coincided with MMP-mediated neoepitope (VDIPEN) expression and in vivo imaging of activated MMPs.

**Conclusions:** These findings underline the potential of S100-DAMPs as a systemic and local biomarker in seronegative arthritis, not only for assessing inflammation but also joint damage.

**Disclosure of Interest:** None declared

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## SAT0023 ARTERY TERTIARY LYMPHOID ORGANS OCCUR IN GIANT CELL ARTERITIS

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**Background:** Arteries are immuno-privileged sites. In advanced atherosclerotic lesions, however, adventitial lymphoid infiltrates, sometimes aggregated in lymphoid follicles (the so called artery tertiary lymphoid organs, ATLO), occur together with marked neoangiogenesis and lymphangiogenesis, and with the extensive induction of high endothelial venules.

**Objectives:** To investigate if tertiary lymphoid organs (TLO) are present in GCA and their formation is associated with the ectopic expression of constitutive lymphoid tissue-homing chemokines.

**Methods:** RT-PCR, immunohistochemical and immunofluorescence analysis were used to determine the presence of ectopic TLO in GCA and the expression of chemokines/chemokine receptors and cytokines involved in lymphoneogenesis in the artery samples obtained from 50 GCA patients and 30 controls. The presence of lymphatic conduits, of follicular dendritic cells (FDC) precursors and lymphoid tissue inducer cells was also investigated. Finally, expression of CXCL13 and BAFF by isolated vascular smooth muscle cells was evaluated before and after stimulation with toll like receptors agonists and cytokines.

**Results:** Artery TLO (ATLOs) were observed in the media layer of 60% of GCA patients in close proximity to neo-formed PNAD+ high endothelial venules. Pesence of ATLOs was independent by the number of infiltrating mononuclear cells, the age of patients and the presence of atherosclerosis. ATLO formation was also accompanied by the expression of CXCL13, BAFF, APRIL, IL-7 and IL-17. CXLC13 and BAFF expression was manily observed in the context of ATLOs, in VSMC and endothelial cells of neo-formed high endothelial cells. IL-7 and IL-17 expression levels were significantly correlated with the levels of CXCL13 and BAFF. The presence of follicular dendritic cells (FDC) precursors and of lymphoid conduits was demonstrated by confocal microscopy analysis and immunohistochemistry, respectively. Stimulation of VSMC with TLR agonists (LPS and poly-IC) and pro-inflammatory cytokines (IL-1b, IL-6, IFN-g and IL-17) resulted in the up-regulation of BAFF and CXCL13.

**Conclusions:** ATLOs occur in the inflamed arteries of GCA patients possibly representing the immune sites where immune responses toward unknown arterial wall-derived antigens may be organized.

**Disclosure of Interest:** None declared

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## SAT0024 EPIGENETIC ANALYSIS OF LPS-INDUCED TOLERANCE IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS AND MACROPHAGES

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**Background:** In macrophages, repeated stimulation of Toll-like receptor (TLR) 4 leads to a tolerant state of the cell which protects inflamed tissues from damage. We have recently shown that rheumatoid arthritis (RA) synovial fibroblasts (SF) lack these protective mechanisms and maintain the secretion of inflammatory cytokines and matrix degrading metalloproteinases (MMPs) after repeated LPS stimulation.

**Objectives:** To investigate mechanisms behind LPS tolerizable and non-tolerizable effects in RASF and macrophages.

**Methods:** RASF, and *in vitro* differentiated peripheral blood derived macrophages from healthy donors were treated with LPS (100 ng/ml) for 24h and then re-stimulated with low doses of LPS (10 ng/ml) for another 24h. The expression levels of interleukins (IL), chemokines, MMPs, retionoic acid-inducible gene 1 (RIG1), melanoma differentiation associated protein-5 (MDA5) and 2'-5'-oligoadenylate synthetase (OAS1) were analyzed by multiplex immunoassays on the Luminex®200 platform, ELISAs or quantitative Real-time PCR. Nuclear factor-κB (NF-κB) and activator protein-1 (AP-1) promoter activities in RASF (n=4) were evaluated by Dual-Luciferase reporter assays after repeated stimulation with LPS. The levels of histone 3 (H3) and H4 acetylation (H3ac, H4ac) as well as H3 lysine 4 trimethylation (H3K4me3) in promotor regions of tolerizable (OAS1, RIG1) and non-tolerizable (IL6, IL8) genes in SF (n=6–7) and macrophages (n=5) were analyzed by Chromatin Immune precipitation (ChIP).

**Results:** Multiplex protein platform and ELISAs revealed that most of the IL and chemokines were tolerizable in macrophages and non-tolerizable in supernatants from RASF after repeated LPS stimulation. A lack of tolerizable effects of RASF was also found for MMP1 and MMP3, whereas the anti-viral response genes OAS1, RIG1 and MDA5 were tolerizable in RASF and macrophages. Reporter gene activities for NF-κB and AP-1 were similar in single and double stimulated RASF, excluding potential differences in the activation of these transcription factors as underlying mechanisms for tolerizable/non-tolerizable effects in RASF. The levels of the activating histone marks H3ac and H3K4me3 were decreased by LPS double compared to single stimulation of SF and macrophages in promoter regions of OAS1 and RIG1. These chromatin marks were not changed or even increased in promoter regions of IL6, IL8 and MMP1 in RASF. Interestingly, AcH3 levels in an IL6 (-525/-349) and an IL8 (-80/-25) promoter region were increased in RASF (IL6: single LPS: 1.38; double LPS: 1.5; IL8: single LPS: 0.17 double LPS: 0.24) but decreased in macrophages (IL6: single LPS: 1.55; double LPS: 1.14; IL8: single LPS: 0.61 double LPS: 0.51).

**Conclusions:** Epigenetic modifications on gene promoters contribute to differences in tolerization between RASF and macrophages. Since many pro-inflammatory cytokines and MMPs are *non*-tolerizable genes in RASF, epigenetic enzymes that maintain the aggressive phenotype of RASF in persistent inflammation are future therapeutic targets.

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## SAT0025 ENHANCED CAPACITY OF MPO-ANCA COMPARED TO PR3-ANCA FOR INDUCING NEUTROPHIL EXTRACELLULAR TRAPS

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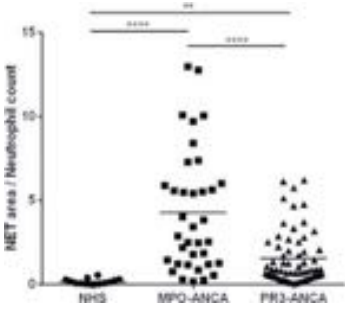
**Background:** Neutrophil extracellular traps (NETs) are hypothesized to play an important role in the pathogenesis of ANCA associated vasculitis (AAV). On the one hand NETs can be part of the antigenic load in ANCA patients because NETs are covered with proteinase 3 (PR3) and myeloperoxidase (MPO) proteins (1). Presence of PR3 and MPO in a proinflammatory environment can induce ANCA autoantibody formation. On the other hand PR3- and MPO-ANCA autoantibodies by themselves have NET-inducing capabilities (1–3). The latter common pathway to induce NET release is intriguing taking into account the diverse clinical phenotype of granulomatosis with polyangiitis (GPA) versus microscopic polyangiitis (MPA).

**Objectives:** The present study aimed to better characterize the NET-inducing capabilities of PR3-ANCA and MPO-ANCA by using a novel assay to quantify NET release. This assay uses highly sensitive, 3-dimensional confocal laser scanning microscopy (3D-CLSM) to quantify in vitro NET release upon incubation with PR3- and MPO-ANCA.

**Methods:** Sera from 62 PR3+ patients, 36 MPO+ patients and 14 healthy subjects were collected. To induce and quantify NET release, healthy PKH-labelled neutrophils were seeded in a 96-well plate and stimulated with 10% sera. After 3¾ hours, cells were incubated with Sytox green for 15 minutes to stain NETs. NET release was imaged by automated 3D-CLSM and quantified with digital image analysis. NET release was represented as NET area corrected for neutrophil count. NET release was correlated with PR3- and MPO-ANCA titers as well as with clinical disease characteristics.

**Results:** Both MPO-ANCA and PR3-ANCA sera induced significant NET release (mean ± SEM for MPO-ANCA 4.29 ± 0.60, p<0.0001 and 1.56 ± 0.20 for

PR3-ANCA, $p<0.01$) as compared to NHS (0.17 ± 0.04). Moreover, MPO-ANCA induced significantly higher NET release than PR3-ANCA ($p<0.0001$) (Figure 1). NET release did not correlate with either MPO-ANCA titers ($r=0.17$, $p=0.35$) or PR3-ANCA titers ($r=-0.04$, $p=0.79$). We, then, categorized according to ANCA serotype and NET release.




**Conclusions:** We here demonstrate that MPO-ANCA has significantly enhanced NET-inducing capabilities compared to PR3-ANCA, which is independent of ANCA serum titers. These data point to a direct pathogenic role of ANCA autoantibodies in the perpetuation or relapse of AAV disease. Future studies will need to investigate whether ANCA-induced NET release can be a functional test to identify pathogenic from non-pathogenic ANCA in AAV patients.

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## SAT0026 PRO-RESOLVING AND CARTILAGE-PROTECTIVE ACTIONS OF RESOLVIN D1 IN INFLAMMATORY ARTHRITIS

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**Background:** Dietary supplementation with fish oils has proved efficacious in reducing joint pain, swollen joint count and NSAID usage in RA patients, yet there is an unmet need to determine how they act. Omega-3 PUFA, which are abundant in fish oils are precursors to a new genus of protective bioactive lipids comprised of lipoxins, resolvins, protectins and maresins (collectively termed specialised pro-resolving mediators (SPM)).

**Objectives:** We hypothesised that SPM may offer a molecular mechanism for the beneficial effects of omega-3 consumption in RA patients. We tested the anti-arthritic potential of a specific SPM; Resolvin D1 (RvD1), in an inflammatory polyarthritis model and investigated novel mechanisms of action.

**Methods:** Metabololipidomic profiling on murine arthritic joints or human synovial fluids was performed by LC-MS/MS. Murine arthritis was induced by transfer of K/BxN serum. Mice were treated with 100ng AT-RvD1 daily either prophylactically or therapeutically ensuing overt signs of arthritis. Histology and flow cytometry was performed to assess joint leukocyte infiltrate. Human chondrocyte micromasses were cultured to assess chondroprotective actions of RvD1.

**Results:** Arthritic joints obtained from mice supplemented with an omega-3 rich diet contained elevated levels of protective SPM, and human RA synovial fluid analyses with LC-MS/MS revealed physiologically active levels of RvD1. Mice treated with a stable epimer of RvD1 (17*R*-RvD1) exhibited significantly attenuated arthritis severity, cachexia, hind-paw oedema and paw leukocyte infiltration and shortened the remission interval. Mechanistically, metabololipidomic profiling in arthritic joints revealed AT-RvD1 significantly reduced $LTB_4$, $TXB_2$ and prostaglandin biosynthesis, whilst selectively enhancing levels of protective SPM. AT-RvD1 stimulated genes associated with cartilage matrix synthesis, exhibited chondroprotection *in vitro* and direct intra-articular treatment prevented arthritis induced cartilage degradation. Joint protective actions of AT-RvD1 were abolished in ALX *(fpr2/3)* null mice, indicating the essential role of this receptor in mediating AT-RvD1 actions.

**Conclusions:** These studies indicate that this SPM offers a valuable therapeutic approach for inflammatory joint diseases including RA.

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**Disclosure of Interest:** None declared

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## SAT0027 INHIBITION OF TLR7 AND TLR8 SIGNALING BY ANTAGONIZING MICRO-RNA DERIVED FROM EXTRACELLULAR VESICLES SUPPRESSES INFLAMMATION IN A NOVEL HUMAN-MOUSE CHIMERIC MODEL OF LUPUS

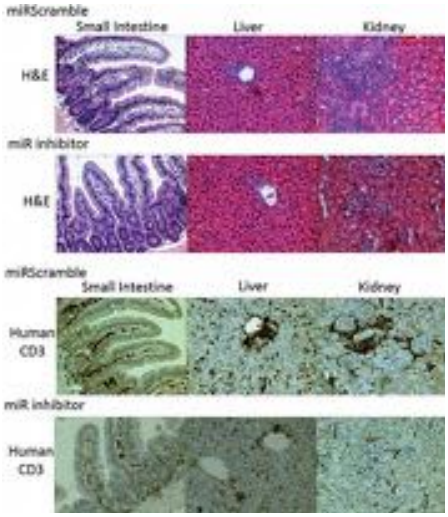
N.A. Young, G. Valiente, J. Hampton, H. Steigelman, W. Jarjour. *Rheumatology and Immunology, The Ohio State University Wexner Medical Center, Columbus, United States*

**Background:** Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease affecting multiple organs and displaying a heavy female predominance during reproductive years. Our previous studies have demonstrated that toll-like receptor (TLR)7 and TLR8 are significantly up-regulated in peripheral blood mononuclear cells (PBMCs) of SLE patients and induced with estrogen treatment. While the conventional role of TLR7 and TLR8 involves binding to single-stranded RNA of viral origin to stimulate innate inflammatory responses, recent work has identified specific micro-RNAs (miRs) capable of activating these receptors that are packaged and secreted in exosomes.

**Objectives:** The goal of this study was to explore the therapeutic potential of using a cocktail of miR antagonists to block TLR7 and TLR8 inflammatory pathways induced by extracellular vesicle (EV)-derived miRs in SLE.

**Methods:** PBMCs from active SLE patients were adoptively transferred into immunodeficient NOD-scid IL-2rγ (null) mice to produce chimeras using a similar protocol we have previously established for Sjöjren's syndrome. PBMCs were treated with a cocktail of locked nucleic acid miR antagonists or nonsense, scrambled RNA control prior to injection. Blood was collected for both flow cytometry and cytokine analysis and tissues were processed for histopathological examination by H&E and immunohistochemistry.

**Results:** 21 days after adoptive transfer, human T-cells (CD4+ and CD8+), B-cells, monocytes, and NK cells were all successfully recovered from whole blood of chimeric mice at similar levels in both treatment groups. However, miR inhibition reduced levels of human IL-2, IL-6, IL-10, and TNF-α when compared to scramble (control) treatment. Although histopathological analysis revealed little to no inflammation in the skin and ear, miR inhibition blocked the robust responses detected in the small intestine, liver, and kidney with scramble RNA (control) treatment. Immunohistochemical analysis of the infiltrates confirmed the presence human CD3+ T-cells in these tissues and further demonstrated the suppression of inflammation following miR inhibition.




**Conclusions:** These results establish a novel chimeric model to study SLE and provide a platform to further explore the therapeutic efficacy of suppressing EV-encapsulated miRs that bind to TLR7 and TLR8 to induce autoimmune-mediated inflammatory responses.

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**Disclosure of Interest:** None declared

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## SAT0028 CIRCULATING SURFACTANT PROTEIN-D (SP-D) MOLECULAR SIZE PROFILE DIFFERS BETWEEN PATIENTS WITH UNTREATED AXIAL SPONDYLOARTHRITIS AND HEALTHY CONTROL SUBJECTS

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**Background:** Surfactant protein-D (SP-D), an innate immune defence molecule of the collectin family has immune modulatory and anti-microbial effects and is expressed in lungs and on mucosal surfaces. The molecule consists of subunits ordered as trimers, dodecamers and even higher multimers. In healthy adults genes are responsible for the majority of the quantitative variation of SP-D in serum as well as its molecular size distribution[1]. High Molecular weight (HMw) SP-D is suggested to have anti-inflammatory properties, while low Mw (LMw) variants lack this capacity. In spondyloarthritis (SpA) SP-D correlates negatively with hsCRP and positively with patient global assessment. LMw variants have been shown to prevail in serum during inflammatory flares in chronic obstructive pulmonary disease.

**Objectives:** To investigate the distribution of SP-D HMw and LMw variants in serum among patients with SpA and controls according to the Met11Thr polymorphism.

**Methods:** 34 patients with SpA (age 22–63) according to the ASAS criteria, receiving NSAIDs only and 57 healthy controls (age 10–75) were included (Table 1). Total SP-D in serum was measured by ELISA and SNP rs721917 was genotyped. SP-D molecular size distribution was assessed using gel filtration chromatography. Integration of the area under the curves was performed to determine the ratio between HMw and LMw SP-D in serum.

**Results:** SP-D in SpA was in the normal range, 1092 ng/ml (725;1541) vs. controls, 910 ng/ml (494; 1682). Whereas the ratio of HMw:LMw serum SP-D was lower in SpA patients, 0.38 (0.18;0.53) compared to controls 1.49 (0.37; 3.24) even when adjusting for the Met11Thr polymorphism, gender, age, BMI and smoking (Table 2).

Tabel 1. Characteristics of patients and controls

| | SpA (n=34) | Control (n=57) | P-value |
|---|---|---|---|
| Sex (% male) | 71% | 42% | <0.0001 (Fisher test) |
| Age (y) | 36.4 (33.3- 39.6) | 39.7 (35.8–43.6) | 0.13 (Unpaired t-test) |
| Smoker | 32% | 51% | 0.006 (Fisher test) |
| BMI (kg/m$^2$) | 25.3 (23.7–26.9) | 25.6 (24.0–27.3) | 0.69 (Mann-Whitney test) |
| HLA-B27 | 82% | – | – |
| NSAID | 88% | – | – |
| Met11/Met11 | 8 (24%) | 21 (37%) | |
| Met11/Thr11 | 19 (58%) | 18 (32%) | |
| Thr11/Thr11 | 6 (18%) | 18 (32%) | |
| SP-D (ng/ml) | 1092 (725; 1541) | 910 (494; 1682) | 0.35 |
| H/L Mw SP-D ratio | 0.38 (0.18; 0.53) | 1.49 (0.37; 3.24) | 0.0004 |

Age, BMI: mean with 95% CI. SP-D and H/L Mw SP-D ratio: median with 25 and 75% percentile. Mann-Whitney test was used to compare SP-D levels and H/L Mw SP-D ratios.

Tabel 2. Ratio of HMw and LMw serum SP-D ratio between controls and SpA according to Met11Thr polymorphism

| H/L Mw SP-D ratio | Control | SpA | Difference | 95% CI | P-value |
|---|---|---|---|---|---|
| Met11/Met11 | 4,14 | 1,38 | –2,76 | –3.60 to –1.93 | P<0.001 |
| Met11/Thr11 | 1,51 | 0,36 | –1,15 | –1.84 to –0.46 | P<0.001 |
| Thr11/Thr11 | 0,22 | 0,06 | –0,16 | –1.15 to 0.83 | P>0.05 |

**Conclusions:** The molecular size distribution of circulating SP-D in patients with SpA is skewed towards preponderance of small size molecular variants. SpA related disease mechanisms may disrupt the multimeric state of SP-D, thereby amplifying the inflammatory burden of the disease.

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**Disclosure of Interest:** None declared

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## SAT0029 DECTIN-1 MEDIATES ABERRANT INNATE AND ADAPTIVE IMMUNE RESPONSE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Dectin-1 is a c-type lectin receptor that signals via syk and is involved in anti-fungal immunity. Dectin-1 was found to trigger experimental inflammatory arthritis, and likely play a role in the pathogenesis of some autoimmune diseases.

**Objectives:** To examine (1) dectin-1 expression on circulating CD14+ monocytes in patients with systemic lupus erythematosus (SLE), (2) the effects of dectin-1 stimulation in ROS production by lupus monocytes and (3) syk signaling and cytokine profile of dectin-1 stimulated lupus monocyte-derived dendritic cells (MDDCs).

**Methods:** SLE patients with active and inactive diseases and healthy subjects were recruited. MDDCs were derived from peripheral monocytes in the presence of IL-4 and GM-CSF. Dectin-1 agonists including curdlan, zymosan and toll-like receptor agonists $Pam_3CSK_4$ (TLR2) and LPS (TLR4) were used to stimulate monocytes and/or MDDCs. Dectin-1, ROS and phosphorylated-syk (p-syk) were measured by flow cytometry. Cytokine profile was measured by and multi-bead immunoassay.

**Results:** The percentage of dectin-1 expressing monocytes was significantly lower in active SLE patients (64.5±24.3%) compared to inactive patients (89.6±7.2%) and healthy controls (91.7±9.5%) (both $p<0.001$). The absolute count of dectin-1 expressing monocytes correlated significantly and inversely with SLEDAI (r=-0.40, $p<0.001$), anti-dsDNA antibody level (r=-0.29, p=0.004), C3 (r=0.35, p=0.001) and C4 (r=0.24, p=0.02). Despite this, ROS production upon stimulation by dectin-1 agonists was comparable between these 3 groups. Stimulation of dectin-1 led to activation and maturation of MDDCs with upregulation of HLA-DR and CD86 (all $p<0.001$). SLE MDDCs showed higher p-syk activation compared to normal MDDCs upon dectin-1 stimulation (6.0±2.0 vs 2.8±1.0%, $p<0.001$). Curdlan-stimulated MDDCs produced higher levels of IL-1β, IL-23 and TNF-α. Adding TLR2 agonist to curdlan, SLE MDDCs produced significantly higher level of IL-1β (327.1±51.5 vs 125.3±88.5, p=0.009) and IL-6 (median 39.8 vs 21.7, p=0.03) compared to normal MDDCs. Combination of TLR4 agonist and curdlan induced IL-12 and TNF-α in normal MDDCs whereas lupus MDDCs produced predominant IL-6 and TNF-α.

**Conclusions:** Active SLE patients had significantly lower circulating dectin-1 expressing CD14+ monocytes which produced comparable level of ROS upon stimulation compared to inactive patients and healthy subjects. Dectin-1 agonists led to activation, maturation and higher p-syk activation in SLE MDDCs. Concomitant dectin-1 and TLR2 stimulation induced production of Th17 promoting cytokines, among which IL-1β and IL-6 were significantly higher in SLE compared to normal MDDCs.

**Disclosure of Interest:** None declared

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## SAT0030 ACTIVE PMR AND GCA IS ASSOCIATED WITH CHANGES IN MONOCYTE SUBSET COMPOSITION

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**Background:** Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two closely related syndromes affecting older people. Pro-inflammatory cytokine IL-6 is found increased in both GCA/PMR patients and in the aged healthy population [1]. Pro-inflammatory monocytes, identified by CD16 and CD14 expression, increase with age and are potent producers of IL-6 [2]. Importantly, monocyte-derived macrophages have been identified in the inflamed arteries of GCA and contribute to the immunopathology of GCA [3]. Yet, peripheral monocyte subsets are less well studied in GCA and PMR patients.

**Objectives:** To assess the distribution of different monocyte subsets in newly diagnosed GCA and PMR patients before and after glucocorticoid (GC) treatment as well as the presence of CD16+ monocytes/macrophages in GCA temporal artery biopsies.

**Methods:** Peripheral blood samples of 24 newly-diagnosed GCA patients, 22 newly-diagnosed PMR patients and 24 age-matched, healthy controls (HCs) were studied. In a prospective, longitudinal study design, samples were obtained from 17 GCA and 15 PMR patients who were in remission after 3 month of treatment with GCs. Absolute numbers of total monocytes and non-classical ($CD14^{dim}CD16^{bright}$), intermediate ($CD14^{bright}CD16^{dim}$) and classical ($CD14^{bright}CD16^{-}$) monocytes were determined by truecount and flow cytometry. Immunohistochemical staining for detection of CD16 and CD68 was performed on sections of TAB from 15 GCA patients. Co-localization of CD16 and CD68 cells was performed using immunofluorescence.

**Results:** Total numbers of circulating monocytes were increased in newly-diagnosed GCA and PMR patients compared to age-matched HCs. Following 3 months of GC treatment, monocyte numbers normalized in PMR patients. When analysing absolute numbers of non-classical, intermediate and classical monocytes, we found the classical monocytes increased in newly-diagnosed GCA and PMR. GC treatment in GCA and PMR decreased numbers of non-classical

and intermediate monocytes but not classical monocytes. CD16 + cells were readily identified in GCA TABs. CD16 staining was detected in macrophage rich area's as evidenced by CD68 staining. Double Immunofluorescence using CD16 and CD68 showed the presence of double positive CD16+ CD68+ macrophages in GCA lesional tissue.
**Conclusions:** We show that peripheral monocyte numbers are modulated in active GCA and PMR. Treatment with GCs decreased CD16+ monocytes in GCA/PMR. CD16+ macrophages were readily detected in inflamed temporal artery biopsy tissue. The data may suggest a role for CD16+ monocytes in the pathogenesis of GCA/PMR.
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**Disclosure of Interest:** None declared
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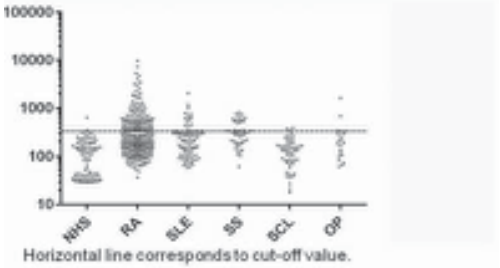
## Rheumatoid arthritis - etiology, pathogenesis and animal models

### SAT0031 PREVALENCE, SENSITIVITY AND SPECIFICITY OF ANTIBODIES AGAINST CARBAMYLATED PROTEINS IN A LARGE COHORT OF ITALIAN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Beside Rheumatoid Factor (RF) and anti-citrullinated peptide antibodies (ACPA), crucial biomarkers in the diagnosis of Rheumatoid Arthritis (RA), antibodies against carbamylated proteins (anti-CarP) have been recently identified in the sera of RA patients [1, 2]. Despite the interesting data presented up to now regarding anti-CarP in the sera of RA patients, the specificity and sensitivity of these new autoantibodies have not been addressed yet [3].
**Objectives:** To evaluate prevalence, sensitivity and specificity of anti-CarP compared to ACPA and RF, in a large cohort of RA patients, normal healthy subjects (NHS) and other disease controls.
**Methods:** A total of 607 frozen stored sera from 309 patients with established RA diagnosed according to the 2010 ACR/EULAR criteria, 98 NHS and 200 patients with other rheumatic conditions were evaluated. Sera were collected from consecutive unselected patients attending outpatient clinics of our department for clinical evaluation. The disease control group included patients with Systemic Lupus Erythematosus (SLE) (n=83), Sjögren's syndrome (SS) (n=45), systemic sclerosis (SCL) (n=51), and osteoporosis (OP) (n=21). Anti-CarP antibodies were detected by a modified solid phase "home-made" ELISA as described by Shi et al. using carbamylated foetal calf serum (FCS) as antigen [4]. ACPAs were detected using a second-generation ELISA (anti-CCP) kit (Delta Biologicals) while IgM RF was determined as part of routine analysis by immunonephelometry (Behering, Marburg, Germany).
**Results:** Anti-CarP antibodies were detected in 117 (34.4%) of RA patients, ACPA in 190 (61.4%) while RF in 202 (65.3%) of them. Two (2.04%) of the NHS were positive for anti-CarP, one (1.02%) for ACPA and three for RF (3.06%). Among disease controls, anti-CarP antibodies were detected in 14 (16.8%) of the SLE patients, 14 (31.1%) of SS patients, 3 (5.8%) of SCL patients and 2 (9.5%) of patients with OP. ACPAs resulted positive in 15 (18.07%) of the SLE patients, 11 (24.4%) of SS patients, 1 (1.9%) of SCL patients and 2 (9.5%) of patients with OP. On the other hand RF was detected in 19 (22.8%) of the SLE patients, 23 (51.1%) of SS patients, 18 (35.2%) of SCL patients and 4 (19.04%) of patients with OP. All data are summarised in Figure 1. To note, the sensitivity of anti-CarP, ACPAs and RF was 46.8%, 61.8% and 64.4% respectively while specificity was recorded as 91.95%, 89.93% and 76.51% respectively.

**Figure 1.** Anti-CarP antibodies in the sera of patients with rheumatoid arthritis, normal healthy subjects and disease control group.




Horizontal line corresponds to cut-off value.

Anti-CarP = antibodies against carbamylated proteins; NHS= normal healthy subjects; RA=rheumatoid arthritis; SLE=systemic lupus erythematosus; SS=Sjogren Syndrome; SCL= scleroderma; OP=osteoporosis.

**Conclusions:** Anti-CarP antibodies determined by the reactivity to carbamylated FCS, are predominantly present in RA but can also be detected in other rheumatic conditions. The prognostic relevance of anti-CarP antibodies in these latter patients should be further determined. Among the three autoantibodies studied, anti-CarP antibodies showed a slightly higher specificity but a relatively low sensitivity.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3909

### SAT0032 PRO-RESOLVING MEDIATORS ISSUED FROM APOPTOTIC CELL EFFEROCYTOSIS (SUPERMAPO) MODULATE APC PROPERTIES TOWARD A TOLEROGENIC PROFILE: EFFICACY IN THE TREATMENT OF COLLAGEN- INDUCED ARTHRITIS

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**Background:** Pro-resolving mediators produced by macrophages eliminating apoptotic effector cells during the resolution of inflammation have been shown to stop inflammation, favor tissue repair and return to homeostasis. In immune-mediated inflammatory diseases such as rheumatoid arthritis (RA), one may believe that reintroducing pro- resolving mediators would allow the control of the disease. We have developed a cell culture system of macrophages and apoptotic cells that mimics this phase of resolution. The supernatant of this cell culture system called SuperMApo (SUPERnatant issued from Macrophage APOptotic cell culture) is enriched in pro-resolving factors including anti- inflammatory cytokines like TGF-b.
**Objectives:** to evaluate the effects of SuperMApo in the treatment of collagen-induced arthritis (CIA).
**Methods:** SuperMApo is obtained after 48h of culturing macrophages from peritoneal cavity with apoptotic cells obtained from thymus after X-ray irradiation. CIA was used as a model of RA. SuperMApo (200 μL of 5x concentrated SuperMApo, IV, for 2 days) was injected in score 8 CIA mice. The effect of SuperMApo was first evaluated on APC and T cells from naive mice in terms of phenotype, profile and properties such as maturation of APC before or after TLR-ligand stimulation and T cell polarization assays. Then, SuperMApo was evaluated in vivo in CIA mice.
**Results:** Macrophages, cDC and pDC submitted to SuperMApo demonstrated robust insensitivity to TLR ligand-induced activation, particularly in terms of co-stimulatory molecules expression. Spleen cells cultured with SuperMApo demonstrated a strong Treg increase. This was confirmed using naive CD4+CD25– T cells cultured in the presence of SuperMApo showing Foxp3 expression. CIA mice received 2 injections of SuperMApo (over 48h) and demonstrated a significant long term decrease of CIA (joint score before and after SuperMApo: 8–10 and 1–4, respectively; sustained response to 60 days). This clinical improvement was associated with a higher suppressive function of Treg. Treg transfer from mice treated by SuperMApo to arthritic mice induced joint improvement. Finally, we tested SuperMApo effect on PBMC issued from 4 patients with RA, with and without TLR ligand activation. Our results were that monocytes from 3 patients showed a decreased inflammatory phenotype after overnight exposure to SuperMApo (CD80, CD86, CD40 and HLA-DR expression).
**Conclusions:** these data demonstrated that macrophages eliminating apoptotic cells produced pro-resolving mediators affecting APC properties therefore allowing the control of arthritis in the CIA model.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4715

### SAT0033 CIRCULATING PLATELETS IS ACTIVATED AND ASSOCIATED WITH DISEASE ACTIVITY OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Physiologically, platelets can distribute systemically by circulation and contribute to hemostasis after activation [1]. Activated platelets acquire functional abilities of adhesion, and morphological changes, and releasing ingredients or small vesicles called microparticles (MP) [2]. On the other hand, recent reports have been shown that platelets include a lot of humoral factors such as chemokines, cytokines and growth factors [3], suggesting that platelets

and MPs can be vectors for transferring these factors to the lesions and contribute to disease processes such as inflammation [4].
**Objectives:** To examine the hypothesis that platelets is involved in the pathogenesis of Rheumatoid arthritis (RA), we investigated the activation status of circulating platelets and the association with clinical characteristics using a brief evaluation system.
**Methods:** Fifty-seven patients with RA were involved and 7 primary Sjogren's syndrome (pSS), 4 systemic lupus erythematosus (SLE), and 16 healthy controls were examined as controls. Fractions of platelets and microparticles were determined by the size less than 1mm in diameter using forward and side scatter of flow cytometry with Megamix® beads. Activated platelets were detected by $CD41^+CD62P^+$ population in the platelet fraction. Platelet-derived MPs were determined $CD41^+annexinV^+$ population in microparticle fraction. Activation status of platelets was examined by the ratio of CD62P-positive to negative platelet population. Proportion of platelet-derived MPs was examined by the ratio of platelet-derived MPs to platelets population. Correlation of activation status of platelets, MP and clinical parameters of patients with RA were also examined.
**Results:** Proportion of activated platelets and that of MPs were higher in RA compared to HC ($P<0.001$, $P<0.00001$, respectively). Serial analysis of 6 patients, who were treated with methotrexate and/or biologics and achieved improvement of disease activity at 12 week after the treatment, revealed significant decrease of these proportions ($P<0.03$). On the other hand, these parameters were comparable between HC and pSS or SLE. In patients with RA, proportion of activated platelets and those of MPs were correlated each other ($P<0.0001$). Interestingly, proportion of activated platelets and MPs were positively correlated with clinical parameters of patients with RA such as serum CRP ($P<0.05$, $P<0.05$, respectively), erythrocyte sedimentation rate ($P<0.03$, $P<0.05$, respectively), and CDAI ($P<0.05$, $P<0.05$, respectively), which were markers of disease activity. Whereas, no correlation was observed with age, sex, tender- and swollen-joint count, HAQ, nor MMP-3.
**Conclusions:** In patients with RA, platelets are activated and their activation status is correlated with the inflammatory markers and disease activity, suggesting that activation of platelets can contribute to the process of systemic chronic inflammation in the pathogenesis of RA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4004

## SAT0034 NICOTINE IS A POTENT DRIVER OF NETOSIS AND ACCELERATES COLLAGEN-INDUCED ARTHRITIS

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**Background:** Cigarette smoking is a major risk factor for rheumatoid arthritis (RA). The contribution of nicotine, the most ubiquitous and addictive component in the traditional as well as electronic cigarettes (e-cigarettes), to the development of RA remains unclear. Recent evidences implicate aberrant Neutrophil Extracellular Trap (NET) formation in the pathogenesis of RA.
**Objectives:** This study was undertaken to investigate the effect of nicotine on NETosis and its ability to potentiate arthritis in a murine model of RA.
**Methods:** Human neutrophils were incubated with nicotine in the presence of DNA-binding dye (Sytox) to quantify NETosis. In parallel, levels of NET-associated myeloperoxidase (MPO)/DNA complexes were measured using a novel NET-specific ELISA. Immunofluorescent staining was used to perform microscopic kinetic analysis of NETosis and to assess the presence of nicotinic acetylcholine receptors (nAChRs) in these neutrophils. NETosis were measured after stimulating neutrophils with GTS-21 ($\alpha$7-specific nAChR agonist) or mecamylamine (an AChR antagonist). Finally, the effect of systemic nicotine exposure on arthritis development and progression was investigated using subcutaneous osmotic nicotine pumps in the collagen-induced arthritis (CIA) mouse model.
**Results:** Neutrophils derived from current smokers displayed significantly higher level of spontaneous- and PMA-induced NETosis as measured by Sytox assay and by NET-specific ELISA. In line with this, nicotine enhanced NETosis in a dose-dependent manner in vitro. Furthermore, incubation with APCA-immune complexs or TNF-$\alpha$ facilitated priming of neutrophils to undergo nicotine-induced NETosis. Immunofluorescent staining revealed that nicotine induced robust formation of NET-like structure in these neutrophils. Cell surface staining with an $\alpha$7-specific agonist ($\alpha$-bungarotoxin) and anti-$\alpha$7-specfic antibody demonstrated co-localization on the plasma membrane. Nicotine-induced NETosis was reproduced when stimulated with GTS-21 and was abrogated when neutrophils were pretreated with mecamylamine. A significantly increased arthritis score as measured by paw swelling and thickness was observed in CIA mice treated with nicotine compared with vehicle treated controls.
**Conclusions:** Our data indicate that nicotine is a potent inducer of NETosis and may play an important role in the initiation and propagation of RA. Furthermore, our study provides molecular evidence for public awareness and clinical guidance against the use of nicotine-containing products including e-cigarettes in patients with RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4399

## SAT0035 REGULATORY CD4+ T-CELL LEVELS AND ANTI CITRULLINATED PROTEIN ANTIBODY REPERTOIRE AS BIOMARKERS FOR ARTHRITIS DEVELOPMENT IN SEROPOSITIVE ARTHRALGIA PATIENTS

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**Background:** Early diagnosis and treatment of rheumatoid arthritis (RA) is of paramount importance for achieving a better disease outcome. Seropositive arthralgia patients (SAP), positive for anti citrullinated protein antibody (ACPA) and/or rheumatoid factor (RF) with (a history of) arthralgia, have a "high risk" of developing RA. Therefore it is necessary to understand which preclinical immunological factors play a role in the progression towards RA in SAP since this could help identify individuals earlier and result in early intervention.
**Objectives:** This prospective study aimed at identifying whether altered regulatory T-cells (Tregs) levels and subsets, besides a broadened ACPA response, are biomarkers for RA development in SAP.
**Methods:** Thirty-four consecutive SAP were prospectively assessed every 6 months for at least 2 years. Every visit, peripheral blood mononuclear cells (PBMCs) were isolated and stored. At inclusion, peripheral Treg ($CD4^+CD25^+FoxP3^+$) levels and Treg subsets, defined as $CD45RA^+FoxP3^{low}$ naive Treg cells (Fr I), $CD45RA^-FoxP3^{high}$ activated Treg cells (Fr II) and cytokine producing $CD45RA^-FoxP3^{low}$ non-Treg cells (Fr III), were compared to age and sex matched healthy controls (HC, n=16) and treatment naive RA patients (n=12). SAP that developed RA during follow-up were compared to non-switchers on Treg levels and functional Treg subsets. To assess broadening of the IgG and IgA ACPA repertoire in serum, reactivity was measured against citrullinated peptides from fibrinogen, $\alpha$-enolase and vimentin.
**Results:** Total Treg levels were similar between HC, SAP and RA patients. Although functional Treg subsets Fr I and Fr II were comparable between groups, Fr III was increased in SAP compared to HC ($p=0.01$). Fourteen (41%) SAP developed RA during follow-up. Their Treg levels were comparable to those of non-switched SAP. At RA diagnosis, Treg levels in switched SAP were not changed compared to 6 months before. Switched SAP displayed an extended IgG ACPA repertoire compared to non-switched SAP ($p=0.046$).
**Conclusions:** Total and functional Treg levels do not indicate development of RA in SAP, in contrast to an extended IgG and IgA ACPA repertoire. Hence, there is presumably no contribution of altered Treg levels leading to the loss in suppression of autoimmunity in RA pathology.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4035

## SAT0036 BRAIN IGF1 RECEPTOR SIGNALING CONTROLS BEHAVIOR OF ARTHRITIC MICE

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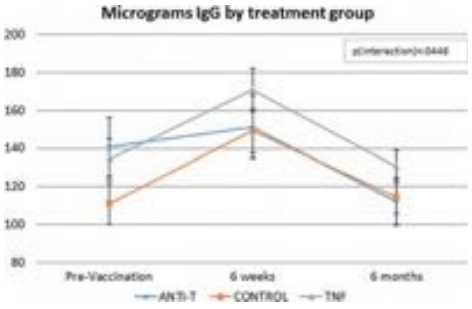
**Background:** Insulin-like growth factor (IGF-1) signaling is essential for development and function of the brain. It helps to improve neuronal plasticity in response to stress, and recently it has been reported to mediate depression [1]. In rheumatoid arthritis (RA), depression is a serious comorbidity with a tight connection to functional disability and early mortality [2]. The serum levels of IGF-1 and the local expression of its receptor (IGF-1R) in inflamed joints are affected in RA [3]. However, the brain IGF-1R signaling in arthritis and its consequences for behavior has not been studied previously.
**Objectives:** In this study we analyze how arthritis affects IGF-1R expression and activity in the brain and its relation to behavioral changes.
**Methods:** Arthritis was induced in DBA/1 mice by immunization with collagen type II. Development of arthritis was followed clinically. One group was treated with shRNA targeting IGF1R, second group obtained control shRNA, and naïve healthy siblings comprised the control group. Behavioral pattern of each mouse was registered by filming at different stages. Protein and mRNA levels of IGF-1R, CD68 and IL-1b were measured in different parts of the brain with IHC and real-time PCR. Serum IGF-1 and IL6 were analyzed with a sandwich ELISA. We

validated the findings from experimental arthritis with a cohort of 235 patients with established RA.
**Results:** In RA patients, the arbitrary measure of pain (VAS) was mainly associated with depression index (FIQ, r=0.46), fatigue (r=0.44), and disability index (r=0.68) rather than to RA activity (DAS28, r=0.36). In mice, arthritis decreased locomotion and rearing, corresponding to the depressive-like behavioral pattern. Severity of arthritis and decreased mobility correlated with the increased mRNA levels of inflammatory cytokine IL-1, and a marker of activated microglia CD68. We observed a decreased expression of IGF-1R and a remarkable reduction in the number and regularity of the Purkinje cells in the cerebellum accompanied by an accumulation of phosphorylated tau along these cells. Arthritis increased serum levels of IGF-1, which correlated with behavioral pattern in arthritic mice. When the IGF1R signaling was inhibited with shIGF1R-treatment, the arthritic mice showed aggravation of the depressive-like behavior, including increased immobility time, which was no longer correlated to severity of arthritis.
**Conclusions:** Depression and functional disability aggravate pain experience in RA patients. Arthritis-induced inhibition of IGF-1R expression and signaling provide molecular mechanism of depression in RA.
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## SAT0037 DURATION OF IMMUNE RESPONSE TO INFLUENZA VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICAL AGENTS

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**Background:** After influenza vaccination, limited data is available to prove effective anti-influenza status at the end of the season[1].
**Objectives:** To assess the strength and duration of response to trivalent influenza vaccine (A-California/07/2009(H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/02/2012) in patients with rheumatoid arthritis (RA) receiving biological agents.
**Methods:** Sera were collected prior to vaccination, and 4–6 weeks and 5–6 months thereafter. The vaccine was given in the age-appropriate dose recommended by the manufacturer. Antibody response to vaccination was measured by detection of vaccine-specific IgG using ELISA. Hemagglutination inhibition assay (HIA) was used to determine patients who were seroprotected (titer>1:40) prior to vaccination, and patients seroconverted (≥4-fold increase) post-vaccination[2].
**Results:** Study comprised of 88 subjects, 16 in Anti-T cell agent (abatacept) group, 35 in anti-TNF (adalimumab, certolizumab, etanercept, golimumab, infliximab) group and 37 were age-matched healthy controls. When tested by HIA, all subjects fulfilled the criteria for seroprotection prior to vaccination and only one patient failed to seroconvert by the end of the season. Levels of vaccine-specific IgG (mean±SE) for each of the groups with respect to each time point were: control group pre-vaccination 111.07±11.05 μg, 6 weeks post-vaccination 149.19±11.76 μg and 6 months post-vaccination 114.62±8.94 μg; Anti-T-cell group pre-vaccination 140.93±15.41 μg, 6 weeks post vaccination 151.33±16.4 μg and 6 months post vaccination 112.22±12.47 μg; Anti-TNF group pre-vaccination 134.33±10.63 μg, 6-weeks post vaccination 170.96±11.31 μg and 6-months post vaccination 130.67±8.6 μg. The three-way ANOVA model produced a statistically significant two-way interaction of diagnostic group*time (p=.0446) indicating a differential pattern of antibody response across the groups, with a more moderate slope between pre-vaccination and 6 weeks post-vaccination among the Anti-Tcell group as compared to the other two groups. Statistically significant positive correlations were found between baseline titer and titer at 6 weeks and 6 months post-vaccination for each of the three diagnostic groups tested individually. There was no correlation between RA and treatment duration with antibody titers at 6 weeks and 6 months post-vaccination.




**Conclusions:** The study suggests that anti-Tcell therapy may affect the strength and duration of IgG-mediated immune response and protection may fade away before the end of the influenza season. At the same time, response of patients on anti-TNF therapy was comparable to the control group. HIA results indicated all patients were seroprotected at the baseline and nearly all seroconverted whereas ELISA analysis helped reveal the more subtle dynamics of the immune response.
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## SAT0038 CONFIRMATION OF SEROLOGICAL ANTIBODIES AGAINST NOVEL CITRULLINATED PROTEINS IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid Factors (RF) and autoantibodies against citrullinated proteins (ACPA) are part of the diagnosis of rheumatoid arthritis (RA). Unfortunately these analytes lack sensitivity especially in early phases of RA. By way of screening proteins from a human protein library of over 7,000 proteins we discovered over 20 novel citrullinated antigens targeted by ACPAs in CCP positive as well as in 5–10% of CCP negative RA patients suggesting added diagnostic potential.
**Objectives:** To challenge novel human proteins as biomarkers for early RA which exhibited reactivities in citrullinated format against early and late RA patient serum samples we set to analyze sufficiently large, new cohorts of patients with early and established RA against the candidate proteins both in their citrullinated and non-citrullinated form. We also planned to veify single antigen performance by comparison to established benchmark proteins and marketed assays.
**Methods:** 34 novel citrullinated antigens were analyzed in serum samples from independent cohorts of 300 CCP positive and 151 CCP negative patients with early RA, 100 healthy volunteers and 50 patients with established RA. All samples were analyzed in a multiplexed, bead-based array on Luminex FlexMAP3D, compared to reactivities against known citrullinated proteins (vimentin, fibrinogen, enolase) and subsequently in 3 commercially available anti-CCP-assays.
**Results:** We confirmed novel citrullinated antigens targeted by ACPAs as markers of RA. The citrullinated antigens are highly reactive compared to their non-citrullinated forms in mature RA and in CCP positive samples of patients with early RA. 4 single antigens reach high overlap to established CCP-Assays each with >75% sensitivity at 97% specificity. Increased reactivity of novel antigens was identified in up to 10% of CCP negative samples suggesting the presence of additional citrullinated epitopes not present in commercial CCP assays used in this study.
**Conclusions:** Novel citrullinated antigens discovered by large scale "omics" screening via Luminex bead based arrays were confirmed in novel samples of early and established RA, especially in CCP positive samples. Reactivity in 10% CCP negative samples suggests added diagnostic value.
**Disclosure of Interest:** P. Schulz-Knappe Employee of: Protagen AG, P. Budde Employee of: Protagen AG, A. Lueking Employee of: Protagen AG, P. Schriek Employee of: Protagen AG, H. Goehler Employee of: Protagen AG, H.-D. Zucht Employee of: Protagen AG, J. Detert: None declared, G.-R. Burmester: None declared, M. Schneider: None declared, J. Richter: None declared, S. Vordenbäumen: None declared
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## SAT0039 ENDOGENOUS GLUCOCORTICOID PRODUCTION BY THE ENZYME 11BETA-HYDROXYSTEROID DEHYDROGENASE TYPE 1 IS INCREASED WITH INFLAMMATION IN MUSCLE, WHERE IT SUPPRESSES INFLAMMATORY CYTOKINE OUTPUT AND PROTECTS AGAINST MUSCLE WASTING IN VIVO

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**Background:** Local generation of endogenous glucocorticoids (GCs) by the enzyme 11beta-Hydroxysteroid Dehydrogenase Type 1 (11beta-HSD1) with inflammation has been shown to be an important anti-inflammatory pathway in both

acute and chronic inflammatory disease. Whilst beneficial within inflamed tissues such as the rheumatoid synovium (through suppression of pro-inflammatory pathways), the inflammatory regulation and impact of 11beta-HSD1 on neighbouring tissues such as muscle remain poorly defined.
**Objectives:** To characterise the inflammatory regulation of 11beta-HSD1 in muscle during systemic inflammation and examine its functional consequences on muscle inflammation and wasting in vitro and in vivo using primary human tissue and a transgenic murine model of polyarthritis.
**Methods:** Inflammatory regulation of 11beta-HSD1 was examined in primary myotube culture and ex vivo muscle biopsies isolated from human donors and from transgenic TNF overexpressing (TNF-tg) mice, as a model of systemic polyarthritis. Inflammatory cytokine output, myotube viability and markers of inflammatory muscle wasting were measured following exposure to endogenous GCs activated by 11beta-HSD1. The contribution of 11beta-HSD1 to muscle status in vivo was examined in the TNF-tg mouse on an 11beta-HSD1 global null background.
**Results:** In both human and murine primary muscle culture, 11beta-HSD1 mRNA and activity were significantly increased in response to the pro-inflammatory cytokine TNFa (mRNA; 7.6 fold, $p<0.005$, activity 4.1 fold, $p<0.005$). 11beta-HSD1 mRNA and activity were evident in ex vivo biopsies of murine and human muscle from tibialis anterior and quadriceps. This expression was augmented in response to TNFa and in muscles harvested from TNF-tg mice relative to wild type controls. Endogenous GCs activated by 11beta-HSD1 suppressed pro-inflammatory cytokine output of IL-6, TNFa, and IFNg, but had little impact on markers of muscle wasting and cell viability in myotube culture. To delineate the contribution of 11beta-HSD1 to suppression of inflammation and muscle wasting in vivo, we generated a TNF-tg mouse on an 11beta-HSD1KO background. These animals had more marked muscle wasting with reduced muscle weight relative to body weight (TNF-tg; 13.45%; TNF/11bKO, 36.2%; $p<0.005$), smaller compacted muscle fibres and increased pro-inflammatory gene expression.
**Conclusions:** This study demonstrates that in muscle, as observed in tissues such as the rheumatoid synovium, 11beta-HSD1 and endogenous glucocorticoid activation are markedly increased in response to inflammation. Whilst concerns have been raised that excess levels of GCs may contribute to factors such as muscle wasting, in this model, local endogenous glucocorticoid activation appears to be overwhelmingly anti-inflammatory in nature and protective in regards to inflammatory muscle wasting in vivo.
**Disclosure of Interest:** None declared
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## SAT0040 THE ACTIVE METABOLITE OF LEFLUNOMIDE, A77 1726, ATTENUATES ARTHRITIS SEVERITY IN MICE WITH SPONTANEOUS ARTHRITIS VIA INDUCTION OF HEME OXYGENASE-1

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**Background:** Rheumatoid arthritis (RA) is a debilitating, chronic autoimmune polyarthritis, characterized by synovial hypertrophy and inflammatory cell infiltration. Although the pathogenesis of RA is not understood clearly, altered oxidative stress is considered to play a critical role during the development and perpetuation of the disease. Although the pathogenesis of RA is not understood clearly, altered oxidative stress is considered to play a critical role during the development and perpetuation of the disease. Over the course of evolution, defensive mechanisms against oxidative stress have been developed. One major mechanism in the cellular defense against oxidative stress is activation of the nuclear-related factor 2 (Nrf2), a key transcription factor that contributes to the maintenance of cellular redox homeostasis. One of the major stress-responsive players regulated by Nrf2 is the antioxidant enzyme heme oxygenase-1 (HO-1). Nrf2 signaling has received recent attention as a participant in the pathogenesis of RA. Leflunomide is an oral drug that inhibits de novo pyrimidine synthesis by inhibiting dihydroorotate dehydrogenase. Leflunomide exerts immunoregulatory properties and is useful in RA treatment. Despite the clinical usefulness of the drug, the underlying mechanisms of the drug remain elusive.
**Objectives:** We investigated the antiarthritis effects and mechanisms of action of the active metabolite of leflunomide, A77 1726, in interleukin-1 receptor antagonist-knockout mice (IL-1Ra-KO mice).
**Methods:** To assess the therapeutic effect of A77 1726 on symptom severity in the IL-1Ra-KO mouse model, 14–15-week-old male IL-1Ra-KO mice were treated with 10 mg/kg or 30 mg/kg A77 1726. On day 42 after the first A77 1726 injection, the spleen was removed from each mouse in the different groups. Histologic analysis of the joints was performed using Safranin O, toluidine blue, and immunohistochemical staining. Sandwich ELISA kits were used to measure the amounts of IL-1β, TNF-α and malondialdehyde in sera obtained from the mice. The epxression of HO-1 in splenocytes was analyzed by immunostaining and western blotting.
**Results:** A77 1726 reduced the arthritis severity and cartilage destruction. The joints isolated from A77 1726-treated mice showed decreased expression of inducible nitric oxide synthase, nitrotyrosine, TNF-α, and IL-1β. Interestingly, HO-1 expression was significantly higher in splenic CD4+ T cells isolated from A77 1726-treated mice compared with those from vehicle-treated mice. A77 1726 treatment in Jurkat cells significantly increased nuclear HO-1 activity. Proteome profiler array revealed that A77 1726 slightly activated the phosphorylation of Akt in Jurkat cells. The ability of A77 1726 to induce HO-1 was diminished when Akt activity was blocked.
**Conclusions:** We suggest that the inhibitory effects of A77 1726 on joint inflammation and oxidative stress occur through Akt-dependent HO-1 induction in CD4+ T cells.
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## SAT0041 MICRORNA-146A AN IMPORTANT REGULATOR OF LOCAL BONE DESTRUCTION IN INFLAMMATORY ARTHRITIS

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**Background:** MicroRNA (MiR-) 146a plays an important role in the regulation of the innate immune response and has also been shown to suppress cancer development in myeloid cells. Although in late stages of arthritis elevated expression of miR-146a in synovial tissue of rheumatoid arthritis patients was detected, the level of this miRNA was found to be down regulated in early disease, but its role in the development of inflammatory arthritis is still elusive.
**Objectives:** To analyse the role of miR-146a in arthritis using two different disease models hTNFtg and K/BxN serum transfer arthritis and the regulatory function of this miRNA in fibroblasts and immune cells.
**Methods:** We induced K/BxN serum transfer arthritis in wild type and miR-146a$^{-/-}$ mice. As a second inflammatory arthritis model we crossed miR-146a deficient into hTNFtg mice. Disease severity was assessed clinically and histologically in both arthritis disease models. Blood of arthritis animals was analysed by flow cytometry. Serum cytokine levels were measured by Elisa. RNA expression levels were measured by qPCR. Proliferation of fibroblasts was analysed histologically and by $^{3}$[H]thymidine incorporation.
**Results:** Absence of miR-146a leads to increased clinical signs of the induced serum transfer arthritis. In line, higher serum levels of the proinflammatory cytokines IL-12 and IL-6 were measured in miR-146a deficient compared to wt mice. When we crossed miR-146a$^{-/-}$ into hTNFtg mice, histological examination revealed a significant increase in synovial inflammation and even more striking a more than twofold increase in local bone destruction due to increased generation of osteoclasts in the tarsal joints in miR-146a$^{-/-}$/hTNFtg mice compared to hTNFtg mice. Interestingly, systemic bone loss was comparable in hTNFtg compared to miR-146a$^{-/-}$/hTNFtg mice, suggesting an important local role of miR-146a. Indeed, we detected increased levels of IL-1β, TRAF6 and RANKL and decreased expression of OPG locally in the paws of miR-146a$^{-/-}$/hTNFtg compared to hTNFtg mice. Analysing the content of myeloid cells in the blood of arthritis diseased mice, revealed significantly increased numbers of circulating CD11b$^{+}$ as well as CD11c$^{+}$ cells in mice lacking miR-146a. Bone marrow transplants demonstrated a pivotal role for miR-146a in mesenchymal cells in controlling local osteoclast generation and bone destruction. Moreover loss of miR-146a leads to enhanced proliferation of synovial fibroblasts *in vitro* and *in vivo*.
**Conclusions:** These data demonstrate an important mitigating role of the miR-146a in inflammatory arthritis, most importantly in local bone destruction, by controlling mesenchymal expression of osteoclastogenic factors. This shows an important anti-inflammatory role of miR-146a, which might possibly be exploited for therapeutic purposes.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4910

## SAT0042 DISENTANGLING THE ROLE OF HYPOXIA-INDUCIBLE FACTOR 1 AND 2 IN THE ADAPTION PROCESS OF HUMAN MICROVASCULAR ENDOTHELIAL CELLS TO PATHOPHYSIOLOGICAL HYPOXIA

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**Background:** Angiogenesis is a prominent feature of the pathogenesis of RA. Although new blood vessels deliver oxygen to the augmented inflammatory cell mass, the neovascular network is dysfunctional and fails to restore tissue oxygen

homeostasis, so that the inflamed joint remains markedly hypoxic. At a cellular level, hypoxia is detected by a mechanism that regulates the amount of hypoxia-inducible factor (HIF)-1α and -2α. After translocation to the nucleus, HIF-1α or HIF-2α subunit bind its partner HIF-1β to form a functional, heterodimeric transcription factor, HIF-1 and HIF-2, which activate a gene program associated with angiogenesis, glycolysis, and adaptation to pH.
**Objectives:** The distinct functions of HIF-1 and HIF-2 in the hypoxia-induced angiogenesis and metabolic switch of endothelial cells are still unknown and therefore aim of this study.
**Methods:** Therefore, we investigated the adaption of Human Microvascular Endothelial Cell (HMEC)-1 to pathophysiologic hypoxic conditions (1% $O_2$). Angiogenesis assay and cytokine analyses were conducted to describe angiogenesis. Gene expression and ATP/ADP measurements were performed to visualize the bioenergetic switch under hypoxia. shRNA-technology enabled a specific knockdown of either HIF-1α or HIF-2α or the combination of HIF-1α and HIF-2α, in order to identify distinct functions of both transcription factors, which were assessed via microarray analysis.
**Results:** Hypoxia induced angiogenesis and a bioenergetic switch from oxidative phosphorylation towards glycolysis. Knockdown of either HIF-1α or HIF-2α leads to a reduced angiogenesis *in vitro*. Although HIF-1α and HIF-2α show overlapping functions during adaption of HMEC-1 towards hypoxia reduction of HIF-1α resulted in a diminished cellular energy supply due to a reduction in hypoxia-induced glycolytic enzyme gene expression thereby not altering pro-angiogenic factors VEGF, VEGF receptor 1 and 2, and IL8. In contrast, reduction of HIF-2α resulted in a reduction of hypoxia induced pro-angiogenic VEGF and IL8 gene and protein expression but induction of VEGFR1 without altering glycolytic enzyme gene expression. Finally, the results of HIF-1α/HIF-2α combined knockdown demonstrate that the lack of both factors significantly reduced cell survival as compared to the scramble control thereby diminishing both gene expression of pro angiogenic factors and glycolytic enzymes.
**Conclusions:** Our results indicate distinct but also overlapping functions of HIF-1α and HIF-2α in ECs which are of high interest regarding the intervention of tumour growth but also the chronicity of the inflammatory process in RA. Finally we clearly demonstrate a major impact of HIF-1α and HIF-2α on angiogenesis mediated either via the expression of pro-angiogenic factors in case of HIF-2α or via the glycolytic switch in case of HIF-1α. At least both are essential for endothelial cellular function. These findings open new possibilities for therapeutic approaches by targeting the specific hypoxia induced factors.
**Disclosure of Interest:** None declared
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## SAT0043 INHIBITORY POTENTIAL OF SPECIFIC MONOCLONAL ACPAS IN TWO MOUSE SUBSPECIES GENETICALLY SEPARATED ABOUT ONE MILLION YEARS AGO

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**Background:** Rheumatoid arthritis is believed to be induced by environmental, genetic and immunological factors. Monoclonal Anti-citrullinated protein autoantibodies ACPA target different proteins and their role in RA is still largely unknown
**Objectives:** As a prerequisite to identify genetic factors involved in rheumatoid arthritis, we analyzed the susceptibility of PWD Mus musculus musculus subspecies, separated from Mus musculus domesticus about one million years ago to collagen antibody-induced arthritis (CAIA) and the role of ACPA antibodies in the CAIA model of arthritis.
**Methods:** Collagen antibody-induced arthritis (CAIA) was induced by administration of collagen antibodies followed by lipopolysaccharide injection. Two genetically distinct mouse strains, representatives of the subspecies *Mus musculus domesticus* and *Mus musculus musculus* as well as their F1 hybrids, and consomis strains thereof were analyzed for the development of clinical and histological signs of arthritis upon CAIA treatment. ACPA antibodies were tested by adding it to the CAIA cocktail and their autoantigenic profile was generated using protein macroarrays previously described (Leidinger et al., 2009; Lin et al, 2007; Ludwig et al. 2008).
**Results:** The wild-derived mouse strain PWD/Ph was highly susceptible to CAIA induced arthritis, whereas the classical laboratory strain C57BL/6J was resistant. Mice carrying chromosomes 5 or 12 from PWD on a B6 background display a B6-like phenotype in the CAIA model as well as the F1 hybrids (B6xPWD and PWDxB6) implicating the presence of dominant resistance modifiers in the C57BL/6J genetic background. The two mouse strains differ highly in their autoantigenic profile and the PWD strain show decrease of B-cells and IgA, IgG, IgM levels. Injecting specific monoclonal ACPAs reactive with the citrullintated H1 and H4 were able to block the CAIA induced arthritis. This inhibition can be explained in part by the inhibition of osteoclasts via a Toll 9 activation. DNAse treatment of ACPA immune complex blocks the the osteoclast inhibition in vitro in a dose dependent manner. Moreover TLR2 activation via P. gingivalis LPS and lipomannan treated animals show a 80% reduction of arthritis score compared to E. coli LPS in a C57BL/6J CAIA model. Anti-collagen specific antibodies are increased in both strains B6 and PWD when arthritis is induced.Rheumatoid factor RF was not detected in PWD or B6 mice before and after the CAIA-treatment nor in the LPS-treated control animals. Interestingly, the commercial CCP2 ELISA detected ACPA in some animals regardless of the treatment. Using the arginine and citrulline containing peptides as control shows that this response is directed to the arginine containing peptide and in most of the animals citrullination downregulates the antigenicity of the autoantibody targeted peptides.
**Conclusions:** The *Mus musculus musculus* derived mouse strain PWD/Ph is highly susceptible to arthritis development in the CAIA model. TLR2 activation blocks CAIA and specific ACPAs are able to block Osteoclast activation via TLR9 activation and may be used as therapeutic antibodies in the future that protect from RA development.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2974

## SAT0044 ROBUST THERAPEUTIC EFFICACY OF MATRIX METALLOPROTEINASE-2 CLEAVABLE FAS-1-RGD PEPTIDE COMPLEX ON CHRONIC INFLAMMATORY ARTHRITIS

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**Background:** Transforming growth factor-β-inducible gene-h3 (βig-h3) is an ECM protein, which consists of integrin-interacting structures including four homologous fas-1 domains and an Arg-Gly-Asp (RGD) motif, is abundantly found within synovial tissues and fluid of rheumatoid arthritis (RA). In the pathogenesis of RA, βig-h3 intensifies inflammatory processes by facilitating adhesion and migration of fibroblast-like synoviocyte (FLS) via binding to αvβ3 integrin. Based on these functions, fragmented peptides of βig-h3 have been developed as therapeutic agents for chronic inflammatory arthritis. Expression of MMP-2 is highly upregulated within the invasive pannus and associated with radiographic erosions in RA. Therefore, therapeutic agents that are transformable via introducing cleavable linkage by locally enriched MMP-2 within the pannus tissue would enhance targetability and therapeutic efficacy on chronic inflammatory arthritis.
**Objectives:** To investigate whether MMP-2 cleavable peptide complex consisted of fas-1 domain and RGD peptide blocks the interaction between βig-h3 and resident cells and leads to the amelioration of inflammatory arthritis.
**Methods:** We designed βig-h3-derivatives, including the fourth fas-1 domain truncated for H1 and H2 sequences of mouse (MFK00) and MMP-2-cleavable peptide complex (MFK902). MMP-2 selectivity was examined by treatment with a series of proteases. MFK902 efficacy was determined by the adhesion and migration assay with NIH3T3 cells *in vitro* and collagen-induced arthritis (CIA) model *in vivo*. The mice were treated intraperitoneally with MFK902 at different dosages (1, 10, or 30 mg/kg).
**Results:** MFK902 was specifically cleaved by active MMP-2 in a concentration-dependent manner. Both MFK00 and MFK902 revealed a dose-dependent inhibition of βig-h3-mediated adhesion of fibroblasts and were similarly effective at a lower concentration (1 μM), compared with RGD peptide. In the migration assay, a very high concentration of RGD peptide (500 μM) reduced fibroblast migration by less than 50%. The lowest effective concentration of MFK00 for inhibition was 1 μM with the $IC_{50}$ of 13.56 ± 1.28 μM. The $IC_{50}$ of cell migration for MFK902 was 4.56 ± 0.25 μM with the degree of inhibition higher than 2 fold at 1 μM and higher than 5 fold at 20 μM. In *in vivo* assay with a murine CIA model, treatment with all dosages of MFK902 resulted in a slower onset of arthritis, followed by less steep increase of clinical arthritis index up to day 50 with significantly lower scores, compared with controls. On day 50, the incidence of arthritic paws for the control group was 94%, whereas those for 1, 10, and 30 mg/kg groups with MFK902 treatment were 54, 41, and 38%, respectively. MFK902 ameliorated histopathologic deterioration and reduced the expression of inflammatory mediators in parallel with improvement of clinical features. In addition, a favorable safety profile of MFK902 was demonstrated *in vivo*.
**Conclusions:** The present study reveals that the MMP-2-cleavable peptide complex, based on βig-h3 structure, was a potent and safe therapeutic agent for chronic inflammatory arthritis and provides a reliable evidence for the MMP-2-cleavable mechanism as a tissue-targeted strategy to treat rheumatoid arthritis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4539

## SAT0045 ANTIBODIES DIRECTED AGAINST ENDOGENOUS AND EXOGENOUS CITRULLINATED ANTIGENS PRE-DATE THE ONSET OF RHEUMATOID ARTHRITIS

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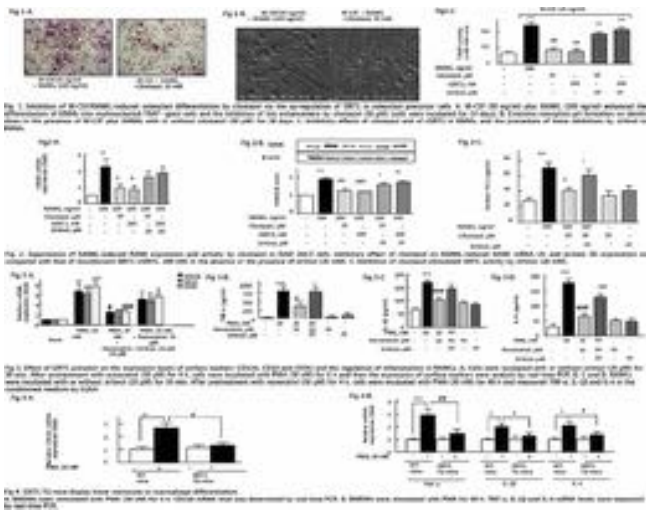
**Background:** Anti–citrullinated-peptid/protein antibodies (ACPA) have been detected in individuals pre-dating symptom onset of rheumatoid arthritis (RA), with an initial limited spectrum of reactivities that gradually broadens to different citrullinated substrates typical of RA (1,2). The recent discovery of NETs as source of citrullinated antigens, and namely citrullinated histones H3 and H4 (3). We have previously described deiminated sequences contained in EBV-derived

proteins EBNA1 and EBNA2 as specific targets of ACPA in sera from patients with RA (4).
**Objectives:** The aim was to analyze the evolution of the antibody response predating the symptom onset using citrullinated exogenous (viral peptides) and self (H4 peptides) antigens as substrates to detect ACPA.
**Methods:** A cohort of 521 individuals sampled before symptoms of RA, and 272 population controls were identified as being donors to the Medical Biobank of Northern Sweden; 241 plasma samples from early RA-patients were also collected. ACPA were detected by ELISA on viral citrullinated peptides derived from Epstein-Barr-virus-encoded protein (EBNA1) and EBNA2 (VCP1 and VCP2) and on histone 4 derived peptides (HCP1 and HCP2).
**Results:** Anti-VCP1 antibodies were detected in 10.4% of the pre-symptomatic individuals as compared with 36.1% in early RA; anti-VCP2 in 17.1% vs. 52.3%; anti-HCP1 in 10.2% vs. 37.3%; anti-HCP2 in16.3% vs. 48.5%. Anti-VCP and -HCP concentrations were significantly increased in pre-symptomatic individuals as compared with controls ($p<0.001$) and increased approaching symptom onset. ACPA specific for HCP or VCP appeared simultaneously (median (Q1-Q3) 5.3 (2.9–8.9) years before symptom onset). Combination of anti-VCP1, -VCP2 and–HCP2 and negativity for -HCP1 yielded a high risk ratio (OR=18.70; 95%CI 2.53–138.47; $p<0.004$). Anti-VCP2 and -HCP2 antibodies were associated in pre-symptomatic individuals with HLA-SE in particular DRB1*0401 but not with the *PTPN22* T-allele. Three PADI3/PADI4 single nucleotide polymorphisms (rs3003444, rs7542629 and rs11800688) were significantly associated with anti-HCP1 antibodies after Bonferroni corrections.
**Conclusions:** Anti-VCP and -HCP antibodies predate symptom onset and predict disease development, but no hierarchy of citrullinated epitopes is clear of the ACPA response. These results suggest that no inciting citrullinated antigen so far described is common to all RA patients; rather data suggest a stochastic mechanism in ACPA production. Anti-HCP1 antibodies were associated with PADI polymorphisms.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2118

## SAT0046 REGULATION OF SIRT1 MAYBE A PIONEERING STRATEGY IN TREATMENT OF RHEUMATOID ARTHRITIS

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**Background:** Monocyte maybe a dual role in rheumatoid arthritis (RA) development, because of differentiation to macrophages in joint and osteoclasts in bone so, blocking of monocyte differentiation maybe effective target in RA treatment.
**Objectives:** In this study, we interrupted monocyte differentiation to macrophages and osteoclasts via SIRT1 blocking and proposed pioneering treatment of RA.
**Methods:** In this study, monocytes from synovial fluid of RA patients (RAMCs), THP-1 monocytes, bone marrow–derived monocytes (BMDCs) from mice and RAW 264.7 cells were studied. PMA-induced expression of macrophages surface markers (CD11b, CD14 and CD36), proinflammatory cytokines (TNF-α, IL-1β and IL-6) secretion and differentiation of BMDCs from SIRT1 TG mice were measured after administration of resveratrol, which was reversed by sirtinol, an inhibitor of sirtuin proteins. In addition, RANKL [receptor activator of nuclear factor kappa B (RANK) ligand]-induced RANK expression in bone marrow–derived monocyte/macrophage precursors (BMMs) and RAW 264.7 cells were treated cilostazol and this was blocked by sirtinol (a SIRT1 inhibitor) in vitro and in a mouse model of collagen-induced arthritis (CIA).



**Results:** PMA-induced expression of macrophages surface markers (CD11b, CD14 and CD36) and proinflammatory cytokines (TNF-α, IL-1β and IL-6) secretion was inhibited by resveratrol. BMDCs from SIRT1 TG mice were inhibited differentiation by PMA than control BMDCs from C57BL/6 mice. These effects were associated with decrease in proinflammatory cytokines (TNF-α, IL-1β and IL-6) secreation by decreasing mRNA expression in BMDCs from SIRT1 TG mice. Further, resveratrol suppressed the PMA-induced PU.1 activation, which is critical transcription factor for macrophages differentiation. SIRT1 inhibits monocytes to macrophages differentiation through the down-regulates PU.1 activity and cilostazol elevated SIRT1 mRNA and protein levels in 12–24 h and increased SIRT1 activity, and these effects were also inhibited by sirtinol. Furthermore, the RANKL-induced nuclear expression of PU.1 was suppressed by cilostazol. In addition, marked RANKL-induced RANK immunofluorescence staining in Raw264.7 cells was strongly attenuated by cilostazol and by rSIRT1, and these attenuations were prevented by sirtinol. Extensive RANK staining of knee synovial tissues in a mouse model of collagen-induced arthritis (CIA) was also markedly reduced by cilostazol (30 mg/kg/day), and in BMMs both RANKL- and M-CSF-induced differentiation of BMMs to multinucleated $TRAP^+$ giant cells and resorption pit formation were inhibited by cilostazol in association with a decrease in TRAP (a marker enzyme of osteoclasts) activity.
**Conclusions:** SIRT1 have dual a role in anti-osteoclast formation BMMs of RA bone and inhibiting differentiation monocyte to macrophage in RA synovium. so, SIRT1 maybe a perfect strategy for RA treatment.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2213

## SAT0047 LOCAL CRYOTHERAPY DOWN-REGULATES LOCAL AND SYSTEMIC IL-6 AND IL-17 PATHWAYS IN ADJUVANT-INDUCED ARTHRITIS

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**Background:** Cryotherapy is widely and empirically used in an adjuvant and symptomatic setting in inflammatory rheumatic diseases, with a low level of evidence [1].
**Objectives:** The aim of this work was to evaluate local and systemic anti-inflammatory effects of local cryotherapy (LC) in adjuvant-induced arthritis (AIA), comparing 2 techniques (ice and cold gas spray). We considered clinical (arthritic score and ankle diameter) and biological effects on IL-6, IL-17A, IL-1β, TNF-α local and systemic levels.
**Methods:** Arthritis was induced by a single Mycobacterium butyricum injection in male Lewis rat tails (day 0). At the onset of arthritis (day 11), rats were treated either by 30 minute-ice applications on hind paws (in cages lined with ice pops – n=10) or by 2 minute-cold gas pulverizations on both hind paws (n=9) twice a day for 14 consecutive days. Ten non-treated AIA rats were used as controls. At day 24 (the day after the last cold application), hind paws were grinded in order to measure cytokine gene expression levels by Q-RT-PCR. Plasmatic levels of the same cytokines were also measured in plasma by cytometry (Multiplex Magpix® ebioscience). IL-6 plasma levels were measured by ELISA (rat IL6 platinum ELISA, BMS625®, ebioscience).
**Results:** Ice application significantly reduced the mean arthritic score and ankle diameter from day 6 to day 14 ($p<0.001$) and globally throughout the 14 day treatment period (2-way ANOVA: $p<0.001$) compared to non-treated AIA controls. Cold gas first aggravated arthritis at days 11–12 ($p<0.01$) then improved clinical inflammation at days 21–24 ($p<0.001$). Skin temperature after LC didn't differ between treatment groups. Both techniques significantly reduced IL-6, IL-1β, IL-17A gene expression levels in hind paws at day 24 compared to non-treated AIA (by 60%, 87% and 50% respectively, $p<0.001$, $p<0.001$ and $p<0.05$). Cytokine gene expression levels correlated positively with hind paw arthritic score and ankle diameter. Conversely, LC had no effect on TNF-α gene expression in hind paws. LC also significantly reduced IL-17A plasmatic protein levels at day 24 (Ice: 47±3pg/ml versus 132±15pg/ml; n=9; $p<00001$ – cold gas: 89±12pg/ml versus 132±15pg/ml; $p<0.02$) and IL-17A plasmatic levels correlated positively with arthritic score, ankle diameter and negatively with weight gain. Ice also reduced IL-6 plasmatic levels (118±20pg/ml versus 197±60pg/ml; $p<0.05$). LC had no effect on TNF-α nor IL-1β plasmatic levels.
**Conclusions:** These results demonstrate in vivo previously unknown therapeutic and anti-inflammatory effects of 14 day-LC in AIA. We observed both local (at the gene level in treated hind paws) and systemic (at the protein level in plasma)

down-regulation of key cytokine pathways critically involved in the pathogenesis and severity of inflammatory rheumatic diseases. LC local and systemic anti-inflammatory effects were mainly IL-6/IL-17A-driven and TNF-α-independent in this model.

**References:**
[1] Guillot X, et al. Cryotherapy in inflammatory rheumatic diseases: a systematic review. Expert Rev Clin Immunol. 2014;10(2):281–94.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1779

## SAT0048 OVEREXPRESSION OF CCL18 PROMOTES MIGRATION AND ACTIVATION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS

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**Background:** CC chemokine ligand 18 (CCL18) has been reported overexpressed in numerous inflammatory disorders since 1997. However, its functional receptor, phosphatidylinositol transfer membrane-associated phosphatidylinositol transfer protein 3 (PITPNM3), has not been discovered until 2011 by our colleagues. Multiple functions of CCL18 besides its chemotactic activity were then identified, including promoting cytokine production, migration/invasion of cancer cells, type I collagen production by human fibroblasts of lung or skin. The effect on the pathogenesis of rheumatoid arthritis (RA) remains unclear.
**Objectives:** To explore the expression of CCL18 in RA patients and its effect on RA fibroblast-like synoviocytes (FLS).
**Methods:** CCL18 in serum and synovial fluid was measured by ELISA. Synovial tissue was obtained by closed-needle biopsy for H&E and immunohistochemistry staining, and FLS culture *in vitro*. Expression of PITPNM3 on cell membrane was detected by western blot. Cell proliferation was identified by cell counting kit (CCK-8) and migration ability was analyzed by transwell assay. Cytokines (IL-1β, IL-6, IL-17A, TNF-α, GM-CSF), chemokines (CCL2, CCL3, CCL5, CCL8) and MMP3 in culture supernatant were measured by Cytometric Bead Array (CBA) or ELISA.
**Results:** (1) Serum CCL18 of 51 active RA patients was 112 ng/mL (IQR, 85–132), which was significantly higher than healthy controls ($n$=11, 64 ng/mL (IQR, 36–70), $p<0.001$, Figure 1A). Eighteen RA patients had synovial fluid and CCL18 in synovial fluid was 1229 ng/mL (IQR, 934–1540) which was significantly higher than corresponding serum level ($p<0.001$) and synovial fluid CCL18 of osteoarthritis patients ($n$=7, 33 ng/mL (IQR, 25–229), $p$=0.001). (2) Immunohistochemistry staining showed CCL18-positive cells in lining and sublining area of RA synovium (n=48), which were significantly greater than osteoarthritis synovium (both $p$=0.001, Figure 1B∼D). Double-immunocytofluorescent staining showed vimentin-positive RA-FLS *in vitro* expressed PITPNM3 (Figure 2A) and western blot of membrane protein showed the expression of PITPNM3 protein on RA-FLS. (3) RA-FLS was incubated with different concentrations of CCL18 (0, 100, 250, 500 ng/mL) and CCK-8 proliferation assay showed no significant impact throughout 9 days (Figure 2B). Transwell assay showed that the migration ability of RA-FLS was significantly enhanced after stimulation of CCL18 (500 ng/mL) for 48 hours (Figure 2C). IL-6, CCL2 and MMP3 in culture supernatant were significantly increased after stimulation of CCL18 (500 ng/mL) for 48 hours (Figure 2D∼F).



Figure 1 CCL18 expression of rheumatoid arthritis (RA) patients and the control groups in serum (A), synovial fluid (A) and synovium (D). CCL18 expression in representative synovium from a RA patient (B, according to a 4-scale semiquantitative score, 4 scores for lining and 3 scores for sublining) and an OA patient (C, 3 scores for lining and 2 scores for sublining). In panels B and C, immunohistochemical stains of CCL18 with DAB as chromogen (brown), with original magnification of ×400.

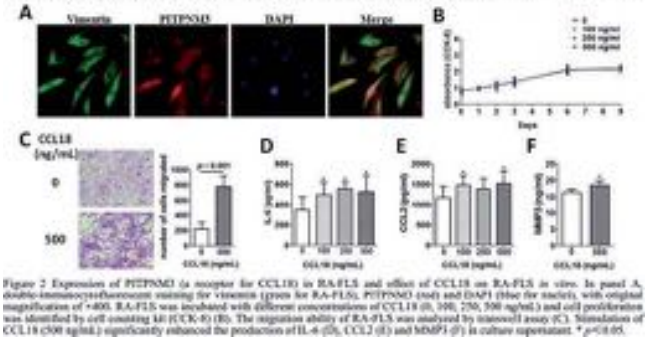


Figure 2 Expression of PITPNM3 (a receptor for CCL18) in RA-FLS and effect of CCL18 on RA-FLS *in vitro*. In panel A, double-immunocytofluorescent staining for vimentin (green for RA-FLS), PITPNM3 (red) and DAPI (blue for nuclei), with original magnification of ×400. RA-FLS was incubated with different concentrations of CCL18 (0, 100, 250, 500 ng/mL) and cell proliferation was identified by cell counting kit (CCK-8) (B). The migration ability of RA-FLS was analyzed by transwell assay (C). Stimulation of CCL18 (500 ng/mL) significantly enhanced the production of IL-6 (D), CCL2 (E) and MMP3 (F) in culture supernatant. * $p<0.05$.

**Conclusions:** Our preliminary results show overexpression of CCL18 in synovial tissue and fluid of RA patients can stimulate migration and activation of RA-FLS probably through the interaction between CCL18 and PITPNM3.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5384

## SAT0049 CIRCULATING CD45+ CD34+ CD11B+ CELLS ARE IMMATURE FIBROCYTES AND THE LEVEL CORRELATES WITH THE NUMBER OF MONONUCLEAR CELLS THAT IN VITRO DIFFERENTIATE TO MATURE FIBROCYTES: A POTENTIAL NEW MARKER FOR INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS

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**Background:** Circulating fibrocytes express both hematopoietic (CD45+ CD34+), and mesenchymal markers (Collagen+). The circulating "immature" fibrocytes can differentiate to "mature" fibrocytes in the target organ and there produce fibrosis components. Chronic inflammatory stimuli mediate differentiation of fibrocytes in diseased organs as observed in idiopathic pulmonary fibrosis (IPF) and asthma, where the levels of circulating fibrocytes correlated to disease severity. In Rheumatoid Arthritis (RA), interstitial lung disease (ILD) is an fibrotic disease manifestation with limited treatment options.
**Objectives:** 1) To demonstrate that circulating CD45+ CD34+ CD11b+ cells can express Procollagen and thereby show that these markers can be used to identify circulating fibrocytes. 2) To measure the levels of CD45+, CD34+, CD11b+ cells in patients with RA, Fibrotic ILDs, severe asthma and in healthy controls (HC). 3) To compare the levels with number of peripheral blood mononuclear cells (PBMC) that differentiate to mature fibrocytes *in vitro*.
**Methods:** CD45+, CD34+, CD11b+ cells from 4 patients were isolated by cell sorting, and stained for Procollagen. 30 patients (10 of each RA, fibrotic ILDs: IPF or non-specific interstitial pneumonitis, severe asthma) and 10 HC were included. Current medication, disease activity, lung function and radiographic data were collected. In 100 μL of lysed blood cells were enumerated by flowcytometry. Further, PBMC were isolated and cultured for 5 days. Coverslips from two wells were stained and mature fibrocytes counted and reported as fibrocytes per $10^6$ PBMC originally added to the well.
**Results:** A higher fraction of sorted CD45+ CD34+ CD11b+ cells stained positive for Procollagen, compared to CD45+ CD34+ CD11b- cells. All groups had higher level of CD45+ CD34+ CD11b+ cells compared to HC (all $p<0.05$). HC had a median of 1.02 cells/μL (IQR 0.71–1.32), RA 2.38 (IQR 1.93–4.39), asthma 3.45 (IQR 2.25–8.08) and fibrotic ILDs 5.89 (IQR 2.86–10.2). The number of CD45+ CD34+ CD11b+ cells correlated to number of PBMC that *in vitro* differentiated to mature fibrocytes, overall (r=0.62, p=0.0006), notably in the RA group (r=0.92, p=0.0005), the level of CD45+ CD34+ CD11b- cells did not.
**Conclusions:** This study supports that the markers CD45+ CD34+ CD11b+ can be used to identify immature fibrocytes, as they can express Procollagen and are more abundant in fibrotic diseases compared to HC. Further, the level correlates to the number of PBMC that differentiate to mature fibrocytes *in vitro*. The results indicate that circulating CD45+, CD34+, CD11b+ cells could be involved in the development of organ fibrosis, and thereby be a biomarker of early fibrosis development in RA ILD. Associations to inflammatory markers, pulmonary function and disease activity will be presented at the conference.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5943

## SAT0050 RESIDENT NON-CLASSICAL MONOCYTES ARE CRITICALLY IMPORTANT FOR TISSUE DESTRUCTION IN ARTHRITIS

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**Background:** Bone destruction in rheumatoid arthritis is mediated by osteoclasts, which are derived from precursor cells of the myeloid lineage. Although there is much known about mature osteoclasts, the identity of osteoclast precursor populations during arthritis is poorly understood. Blood monocytes can be subdivided in classical inflammatory monocytes ($CD115^+Ly6C^{high}CCR2^+$) and non-classical resident monocytes ($CD115^+Ly6C^{-/low}CCR2^-$) and especially classical monocytes have been implicated in mediating tissue damage in autoimmunity.
**Objectives:** To investigate the role of different monocyte populations in joint destruction.

**Methods:** HTNFtg mice were clinically scored once per week for grip strength and swelling. In addition, blood was collected every other week starting on week 4. Mice were sacrificed at week 10 - blood, spleen and bone marrow were collected for flow cytometry analysis. K/BxN Arthritis was induced in wild type mice, blood and spleen were collected 14 days after disease induction. HTNFtg/CCR2$^{-/-}$ and hTNFtg mice were analyzed histologically. Different monocyte subsets were Facs-sorted and cultured in the presence of RANKL and MCSF to induce osteoclasts. RNA sequencing of RANKL stimulated osteoclast precursor cells was performed.
**Results:** Here we show that hTNFtg mice lacking CCR2, which lack circulating classical inflammatory monocytes, show enhanced local bone erosion and osteoclast generation in chronic TNF driven arthritis. When we correlated the number of the two monocyte subsets in blood with histological signs of joint destruction the number of inflammatory monocytes did not correlate at all with those parameters. In contrast, the number of non-classical monocytes in blood significantly correlated with the extent of tissue damage in both hTNFtg arthritis and also K/BxN serum transfer arthritis. Histological examination revealed that while all infiltrating monocytes express CD115, only a small fraction of these cells express Ly6C, suggesting that the synovial infiltrate predominantly consists of Ly6C$^{-/low}$ monocytes. Upon sorting resident and from blood, we demonstrate that resident Ly6C$^{-/low}$ monocytes are more potent to form osteoclasts *ex vivo* than classical Ly6C$^{high}$ monocytes. Genome-wide transcriptome profiling revealed increased expression of genes which are required for pre-osteoclast fusion in RANKL-stimulated resident Ly6C$^{-/low}$ monocytes.
**Conclusions:** Non classical resident monocytes possess particular osteoclastogenic potential and their numbers in blood correlate with histological parameters of joint destruction in two different models of inflammatory arthritis. Therefore these cells may provide a biomarker for erosive inflammatory arthritis and even a possible target for therapeutical intervention.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4109

### SAT0051 TRANSCRIPTION FACTOR SOX5 PROMOTES RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLAST MIGRATION AND INVASION BY REGULATING MMP9 EXPRESSION VIA DOWNREGULATED MIR-15A/MIR-16

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**Background:** SOX5 is known as a transcription factor which primarily involved in the regulation of embryonic development, cell fate, and chondrogenesis. To date, little is known the effect of SOX5 on rheumatoid arthritis (RA). We previously reported association between younger age at onset of rheumatoid arthritis (RA) and a RANKL promoter SNP that conferred an elevated promoter activity after stimulation via binding to a transcription factor SOX5 (Arthritis Rheum 2010; 62(10):2864–75.). Subsequently, we confirmed that SOX5 could up-regulate RANKL expression in RA synovial fibroblast (SF) and participate in the bone erosion of RA.
**Objectives:** Here, we examine the effect of SOX5 on the migration and invasive characteristics of RA synovial fibroblasts.
**Methods:** Rheumatoid synovial fibroblasts cell line MH7A were treated with SOX5 small interfering RNA (SOX5-siRNA) and recombinant Adenovirus SOX5 expression vectors (Ad-SOX5). Migration and invasion and of RASF was assessed by transwell matrigel™ invasion chambers and collagen gel assays. Modulation of MMP9 expression in RASF was analyzed by real-time PCR, western blot, luciferase assay and Chromatin immunoprecipitation (ChIP). Collagen-induced arthritis (CIA) DBA/1 mouse locally injected with lentivirus-shSOX5 was used to examine the effect of SOX5 on MMP9 expression in vivo.
**Results:** Overexpression of SOX5 significantly induced cell migration, invasion and MMP-9 expression in RASF. Migration and invasion of RASF could be markedly decreased by silencing SOX5 expression but could be reverted by added the recombinant MMP9 cytokine into RASF. Overexpression of SOX5 enhanced the promoter activity of MMP9 in Hela cell. Chromatin immunoprecipitation (ChIP) showed approximately 3-fold enrichment of MMP9-specific DNA in anti-SOX5 immunoprecipitate in IL-6 treated MH7A, as compared to untreated cells. Silencing SOX5 resulted in significantly increased miR-15a/miR-16 expression in MH7A. The enhanced MMP-9 expression induced by Ad-SOX5 transfection could be inhibited by miR-15a/miR-16 mimics. Local silencing SOX5 in CIA mice inhibited the synovitis and bone erosion in CIA mice and accompanied by the markedly reduced MMP9 expression in synovium.
**Conclusions:** These findings indicated transcription factor SOX5 plays an important role in regulating the migration and invasion and production in RA SF by modulation MMP9 expression via downregulated miR-15a/miR-16, suggesting SOX5 as a potential therapeutic target for the treatment of RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3167

## Rheumatoid arthritis - prognosis, predictors and outcome

### SAT0052 IS INFORMATION ABOUT THE REASON FOR PREVIOUS BIOLOGICS DISCONTINUATION USEFUL TO PREDICT THE EFFECTIVENESS OF A BIOLOGIC WITH A DIFFERENT MODE OF ACTION?

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**Background:** With more biological disease modifying antirheumatic drugs (bDMARDs) in rheumatoid arthritis (RA), switching between bDMARDs is becoming more frequent. Patients (Pts) discontinue bDMARDs for various reasons, including inadequate effectiveness (IE) and adverse events (AE). Observational data indicates that the reason for discontinuing a second TNF inhibitor is usually the same that led to the first TNFi discontinuation, suggesting that a change in bDMARD mode of action may be more favourable.
**Objectives:** To investigate the impact of specific reasons for discontinuing the previous bDMARD on the clinical response to abatacept (ABA), a bDMARD with a different mode of action.
**Methods:** This is a pooled observational database analysis of 10 prospective cohorts of RA pts treated with iv ABA. All pts with available information on the reason for discontinuation of the last bDMARD were included. Pts initiating ABA as a first bDMARD were excluded from the analysis. The predictor of interest was the reason for prior bDMARD discontinuation, categorized as IE, AE, or other. The primary endpoint was time to ABA discontinuation, defined as the time between drug initiation to last administration: 1) for any reason, and 2) specifically for AEs or IE. Cox regression was used to estimate hazard ratios (HRs) for drug discontinuation, adjusting for pts demographics, disease and treatment characteristics.
**Results:** Of the 2001 RA pts included, 1272 discontinued ABA during the 3639 patient-years of follow-up. 499 pts (24.9%) had stopped their last bDMARD for AEs, 1290 pts (64.5%) for IE, and 212 pts (10.6%) for other reasons. Pts who discontinued their prior bDMARD for IE were younger, more frequently RF positive, had lower BMI, shorter disease durations, higher baseline DAS28 and had less comorbidities than pts who stopped their previous bDMARD for other reasons.
There was no association between reason for discontinuing prior bDMARDs (AE, IE, or other) and overall ABA retention (log-rank p=0.78). ABA discontinuation for AEs was significantly associated with prior discontinuation of bDMARDs for AEs (log-rank $p<0.001$), and ABA discontinuation for IE was significantly associated with prior bDMARD discontinuation for IE (log-rank, p=0.02). In adjusted models, discontinuation of the prior bDMARD due to AE doubled the risk of AE-related discontinuation with ABA (HR 2.15, 95% CI: 1.63 – 2.84), compared to pts who had not discontinued their last bDMARD for AEs. IE on the prior bDMARD also tended to increase the risk of discontinuing ABA for IE (HR 1.15, 95% CI: 0.98 – 1.35), compared to pts without IE on their last bDMARD.
**Conclusions:** The same reason that led to discontinuing prior bDMARDs is likely to lead to the discontinuation of a new bDMARD with a different mode of action. Overall these results suggest that discontinuation is mostly explained by patient-specific characteristics (selection) and less by particular drug mechanism.
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**Disclosure of Interest:** A. Finckh Grant/research support from: BMS, D. Courvoisier: None declared, J. Gottenberg: None declared, M. Hernandez: None declared, F. Iannone: None declared, E. Lie: None declared, H. Canhão: None declared, K. Pavelka: None declared, M. Hetland: None declared, C. Turesson: None declared, X. Mariette: None declared, D. Choquette: None declared
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### SAT0053 C1M IS A SEROLOGICAL BIOMARKER FOR IDENTIFICATION OF STRUCTURAL PROGRESSORS IN RHEUMATOID ARTHRITIS; VALIDATION IN 3 PHASE III CLINICAL TRIALS

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**Background:** There is a need for reliable prognostic biomarkers in rheumatoid arthritis (RA) for identification of patients in urgent need of aggressive treatment. Serological assessment of type I collagen degradation (C1M) was demonstrated to be a biomarker for identification of RA disease progression in the phase 3[1] LITHE study. In the LITHE study C1M predicted JSN progression when corrected for confounders (including CRP and baseline level of joint space narrowing; JSN).
**Objectives:** To support serum C1M as a biomarker for RA structural progression.
**Methods:** Placebo groups were pooled (n=543) from the 24-week Phase 3, randomized, double-blind, placebo-controlled, parallel group studies of fostamatinib on a MTX background, OSKIRA 1, 2 and 3 (NCT01197521; NCT01197534;

NCT01197755). Patients who did not achieve ACR20 at week 12 were given active drug and were considered escapers. Radiographic progression was assessed by increase in JSN, erosion (ERN) or modified total sharp score (mTSS) after 24 weeks. Only 270 patients had radiographic assessment at both baseline and at 24 weeks. C1M was assessed in fasting serum at baseline (BL). One-way ANOVA was used to assess differences in BL demographics. Associations between BL demographics were investigated by Spearman's correlation. Multiple regression included age group, gender, disease duration, BMI, CRP and BL radiographic status. Non-normalized data was log-transformed.

**Results:** BL demographics of the 3 studies were comparable. 36% of patients were escapers, having BL elevated levels of C1M, CRP and disease activity compared to non-escapers (p=0.03, p<0.0001, p=0.006). 20% of all patients had radiographic progression by JSN, 24% by ERN and 31% by mTSS. BL CRP was significantly elevated in progressors compared to non-progressors (JSN p=0.02, mTSS p=0.005, ERN p=0.005). ERN progressors had a significantly increased level of C1M than non-progressors (p=0.02). JSN only progressors had significant increases in BL radiographic status compared to non-progressors (JSN p=0.003, mTSS p=0.007, ERN p=0.03).

At BL there was an association between C1M and radiographic status (JSN rho=0.14, mTSS rho=0.14, ERN rho=0.13,) and disease activity (DAS28 rho=0.44). In multiple regression the effect size β of C1M alone was -0.25, 0.90 and 1.18 for the association with the 24 week change in radiographic progression as determined by JSN, mTSS and ERN, respectively. Only for ERN the effect size reached statistical significance (p=0.0008). The beta value describes the effect of C1M on predicting the radiographic progression. The effect size decreased for JSN when adjusted for CRP (β=-0.68), but for both mTSS and ERN the effect was eliminated. When the other confounders were included the effect size decreased even further for JSN (β=-0.70).

| | Δ 24weeks | | | |
|---|---|---|---|---|
| **JSN** | | | | |
| | B | P | R2 | N |
| C1M | -0.25 | NS | 0.0008 | 270 |
| C1M, CRP | -0.68 | 0.044 | 0.008 | 270 |
| C1M, age group, gender, dis.dur, BMI, CRP | -0.71 | 0.036 | 0.01 | 270 |
| C1M, age group, gender, dis.dur, BMI, CRP, BL mTSS | -0.70 | 0.038 | 0.010 | 270 |
| **mTSS** | | | | |
| C1M | 0.90 | NS | 0.009 | 266 |
| C1M, CRP | -0.04 | NS | 0.02 | 266 |
| C1M, age group, gender, dis.dur, BMI, CRP | -0.01 | NS | 0.04 | 266 |
| C1M, age group, gender, dis.dur, BMI, CRP, BL mTSS | 0.17 | NS | 0.04 | 266 |
| **ERN** | | | | |
| C1M | 1.18 | 0.0008 | 0.04 | 266 |
| C1M, CRP | 0.64 | NS | 0.04 | 266 |
| C1M, age group, gender, dis.dur, BMI, CRP | 0.71 | NS | 0.06 | 266 |
| C1M, age group, gender, dis.dur, BMI, CRP, BL mTSS | 0.71 | NS | 0.08 | 266 |

Multiple regression analysis of the effect of C1M on predicting radiographic progression after 24 weeks. The beta-, p- and R2 and N value are given. Statistical significance was considered as p<0.05. C1M: MMP-degraded type I collagen. CRP: C-reactive protein, dis.dur: disease duration, BMI: body mass index, JSN: Joint space narrowing, mTSS: modified total sharp score, ERN: Erosion.

**Conclusions:** In this study we found that BL C1M was associated with structural status and disease activity and that BL C1M was a predictor of radiographic progression (JSN) after 24 weeks when adjusted for confounders. Secondly, escapers had higher level of C1M, CRP and disease activity indication a worse disease stage in escapers at baseline. This study provides supports C1M as an important emerging biomarker of progression in RA.

**References:**

[1] Arthritis Res Ther. 2013 Aug 14;15(4):R86.

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## SAT0054 FAVORABLE LONG-TERM OUTCOME OF EARLY INFLAMMATORY ARTHRITIS IN CLINICAL PRACTICE: HIGH BASELINE HAQ AND DAS28 AT 3 MONTHS PREDICT USE OF BIOLOGICS

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**Background:** The course and natural history of early inflammatory arthritis (EA) varies widely and partly depends on the level of disease control in the early stages. Dedicated EA clinics follow a systematic targeted approach to improve long-term outcome of patients.

**Objectives:** To assess the long-term outcome of EA following care in a dedicated early arthritis outpatient clinic.

**Methods:** The "Early Arthritis (EA) Cohort" of the Department of Rheumatology of the University Hospital of Crete is a prospective cohort, which follows patients with inflammatory arthritis [RA, spondylarthritis or undifferentiated (UA)] of less than 6 months duration. Patients are followed quarterly for 2 years with systematic documentation of disease activity and function (measured by the DAS28 and HAQ, respectively), as well as for changes in therapy based on physician judgment. For the purpose of this study, we assessed long-term outcome (disease activity and function at 2 years) and examined prognostic factors for subsequent initiation of biologic agent.

**Results:** Out of 559 patients referred to the EA Clinic, a total of 317 had a final diagnosis of RA or UA and were included in the present analysis [83.0% women, mean (SD) age at disease diagnosis 53.7 (15.1) years, 28.5% positive for RF or/and ACPA, mean (SD) number of tender and swollen joints at baseline 6.9 (6.0) and 5.5 (5.5), respectively. Mean (SD) DAS 28 at baseline was 4.59 (1.38) and mean HAQ was 0.59 (0.51), with 33.9% of patients having high disease activity (DAS28>5.1) and 18.3% reporting a HAQ≥1. At 2 years of follow-up, mean (SD) DAS28 and HAQ were 3.63 (1.3) and 0.49 (0.48), respectively (p<0.001 compared to baseline values for both). Nevertheless, 38.3% of patients still had moderate and 13.8% high disease activity at 2 years, while 19.3% reported a HAQ>0.75.

During the course of follow-up, 34 patients received a biologic agent due to persistent high disease activity. In multivariate regression analysis, factors associated with initiation of biologic were HAQ at baseline [adjusted RR (95% CI) 4.91 (3.54–6.81)] and DAS28 at 3 months [adjusted RR (95% CI) 1.49 (1.15–1.93)].

**Conclusions:** Routine care with regular, objective documentation of disease activity and function is associated with satisfactory long-term outcomes in early inflammatory arthritis. Baseline impaired function and persistent disease activity at 3 months predict need for biologic treatment during follow-up.

**Disclosure of Interest:** None declared

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## SAT0055 TREATMENT RESPONSE TO CONVENTIONAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS) AND BIOLOGICS IN SEROPOSITIVE AND SERONEGATIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RESULTS FROM CATCH (CANADIAN EARLY ARTHRITIS COHORT)

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**Background:** Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) status may affect treatment response in early rheumatoid arthritis (ERA).

**Objectives:** To investigate differences in treatment response to disease modifying anti-rheumatic drugs (DMARDs) and biologics in ERA in seropositive versus seronegative patients for RF and/or ACPA.

**Methods:** Data were obtained from The Canadian Early Arthritis Cohort (CATCH), a prospective multi-site study of patients with ERA who met 1987 or 2010 ACR/EULAR criteria for RA, had symptom duration <1 year, were not in remission at baseline and had RF or ACPA available, DAS28 scores at baseline and follow-up. Stratified multiple linear regression compared the effects of initial treatment with methotrexate (MTX) monotherapy, MTX combination therapy (defined as MTX plus one or more conventional DMARD), biologic therapy and other therapy on change in DAS28 (D DAS) at 3 and 6 month follow up in patients who were seropositive (RF + and/or ACPA+) and seronegative (RF- and ACPA-), patients who were RF positive and RF negative, and patients who were ACPA positive and ACPA negative, respectively. All multivariable models were adjusted for baseline age, gender, education, ethnicity, symptom duration, comorbidities, erosions and pain scores.

**Results:** 1068 patients had a baseline mean (SD) age of 53.3 (15.0), symptom duration of 5.8 (3.0) months, DAS28 of 5.2 (1.3) and 74% were female. A total of 867 (81.2%) patients were seropositive and 201 (18.8%) were seronegative (RF positive 759 [66%], RF negative 385 [34%], ACPA positive 539 [61%], and ACPA negative 349 [39%]). Relative to the other therapy group, better treatment response to methotrexate combination therapy at 3 months was observed for patients who were RF+ (β: 0.45 [95% CI -0.74 to -0.17]) vs. RF- (β: 0.29 [95% CI -0.14 to 0.71]) and the combined seropositive (β: -0.29 [95% CI -0.56 to -0.02]) vs. seronegative group (β: -0.12 [95% CI -0.69 to 0.44) but not patients who were ACPA+ (β: -0.06 [95% CI -0.41 to 0.30]) vs. ACPA- (β: -0.41 [95% CI -0.84 to 0.02]), after adjusting for covariates. Similar results were observed when analyses were repeated with change in DAS at 6-months as the outcome as patients

on methotrexate combination therapy who were RF+ (β: -0.47 [95% CI -0.81 to -0.13]) vs. RF- (β: 0.15 [95% CI -0.39 to 0.71]) and those that were seropositive (β: -0.32 [95% CI -0.65 to 0.00]) vs. seronegative (β -0.20 [95% CI -0.97 to 0.56]) responded better to treatment. Response to other treatment strategies did not significantly differ by antibody in any grouping (Table).

**Table**

| | Antibody | RF | | ACPA | | RF and ACPA | |
|---|---|---|---|---|---|---|---|
| | Treatment | Negative β (95% CI) | Positive β (95% CI) | Negative β (95% CI) | Positive β (95% CI) | Both Negative β (95% CI) | Either or Both Positive β (95% CI) |
| DAS28 over 3 months | MTX mono | 0.23 (-0.23, 0.70) | -0.14 (-0.44, 0.18) | -0.28 (-0.76, 0.21) | 0.17 (-0.23, 0.57) | -0.12 (-0.81, 0.57) | -0.05 (-0.35, 0.24) |
| | MTX combo | 0.29 (-0.14, 0.71) | -0.45 (-0.74, -0.17) | -0.41 (-0.84, 0.02) | -0.06 (-0.41, 0.30) | -0.12 (-0.69, 0.44) | -0.29 (-0.56, -0.02) |
| | Biologic | -0.30 (-1.75, 1.16) | -0.37 (-1.19, 0.45) | -0.64 (-2.43, 1.16) | -0.48 (-1.29, 0.33) | -1.65 (-4.74, 1.44) | -0.44 (-1.18, 0.29) |
| | Other | Reference | Reference | Reference | Reference | Reference | Reference |
| DAS28 over 6 months | MTX mono | 0.17 (-0.45, 0.80) | -0.05 (-0.42, 0.32) | -0.05 (-0.67, 0.57) | 0.08 (-0.40, 0.57) | 0.19 (-0.77, 1.16) | 0.00 (-0.36, 0.36) |
| | MTX combo | 0.16 (-0.39, 0.71) | -0.47 (-0.81, -0.13) | -0.27 (-0.83, 0.28) | -0.15 (-0.58, 0.28) | -0.20 (-0.97, 0.56) | -0.32 (-0.65, 0.00) |
| | Biologic | -1.71 (-3.47, 0.04) | -0.92 (-1.85, 0.01) | -2.32 (-4.64, 0.00) | -1.05 (-2.02, 0.08) | -2.24 (-5.74, 1.27) | -1.09 (-1.98, 0.21) |
| | Other | Reference | Reference | Reference | Reference | Reference | Reference |

**Conclusions:** In ERA, RF and ACPA status affected treatment response to MTX combination therapy, with better changes in DAS28 at 3 and 6-months in seropositive compared with seronegative patients. Given the complexity of rheumatoid arthritis management, the study findings potentially have implications for identifying prognostic indicators that may help inform therapeutic decision-making.
**Disclosure of Interest:** None declared
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## SAT0056 WHAT ARE THE REASONS OF DISCREPANCIES BETWEEN PATIENTS AND PHYSICIANS IN THEIR PERCEPTIONS OF RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND WHAT IS THE IMPACT OF THIS DISCORDANCE ON REMISSION, FUNCTION AND STRUCTURE AT 1 YEAR? RESULTS FROM THE ESPOIR COHORT

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**Background:** Patients and physicians often differ in their perceptions of rheumatoid arthritis (RA) disease activity, as quantified by the patient's global assessment (PGA) and by the evaluator's global assessment (EGA). The quest for understanding the reasons for discrepancies in evaluations of disease activity becomes particularly important in the context of recent recommendations that define Boolean-based ACR EULAR remission as the treatment target.
**Objectives:** The objectives of this study were:
1) to explore the extent and reasons for this discordance
2) to determine if this discordance at baseline is associated with RA outcomes at 1 year (remission, function and structure) in early RA in daily clinical practice.
**Methods:** *Patients:* from the French cohort of EA ESPOIR (at least 2 swollen joints for less than 6 months, DMARD naïve), fulfilling the ACR-EULAR criteria for RA at baseline
*Analyses:* At baseline, agreement between PGA and EGA (Bland-Altman plot) was assessed. Multivariate linear regression was used to determine the patient and EA features independently associated with discordance (calculated as PGA – EGA). Logistic regression was used to analyze discordance as |PGA – EGA| $\geq$20. Multivariate logistic models were used to determine if discordance at baseline is associated with remissions (Boolean, SDAI and DAS28), functional stability (HAQ $\leq$0.5 and deltaHAQ $\leq$0.25) and absence of radiographic progression (delta Sharp score $<$1) after 1 year of follow-up.
**Results:** In 645 patients with ERA (mean age=48.8±12.2 years, 77% female, 48.7% ACPA+) agreement was better at both ends of the spectrum, especially for patients with high disease activity. Evaluation of disease activity yielded discordant scores between the patients and their physicians in 30% of our cohort: 153 patients (24%) had higher PGA scores, 41 patients (6%) had higher EGA scores, and 451 patients (70%) had concordant PGA and EGA scores (|PGA – EGA| $<$20).
In multivariate linear regression center-adjusted, higher PGA has been found to be associated with absence of fulfilling ACR 1987 revised criteria for RA (p=0.0005), higher levels of fatigue (p$<$0.0001) and lower number of swollen joint counts (SJC) (p=0.0022). With logistic regression center-adjusted, low number of SJC (OR [95% CI]: 1.92 [1.26–2.91]), low mental component of the SF-36 (OR [95% CI]: 1.82 [1.23–2.69]) and living alone (OR [95% CI]: 1.68 [1.09–2.58]) were associated with discordance between PGA and EGA.
In multivariate analyses, discordance at baseline was not associated with remission, function and structural progression at 1 year.
**Conclusions:** In early RA, the discordance between PGA and EGA is multifactorial with objective measures like low SJC and absence of ACR 1987 revised criteria for RA, but also patient reported outcomes like high level of fatigue and low mental status, and environmental factor: living alone. Discordance between PGA and EGA at baseline was not associated with RA outcomes at 1 year. Understanding the reasons for a discordant view of disease activity will help to facilitate the sharing of decision-making in the management of RA.
**Disclosure of Interest:** None declared
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## SAT0057 LOW MORTALITY RATE IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS FROM SOUTH ITALY

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**Background:** Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder associated with increased mortality (1), (standardized mortality ratio for all causes–SMR, being 1.47 in the last 50 years) (2).
**Objectives:** To investigate the mortality rate and predictive factors as assessed at admission in a cohort of RA patients followed at a South Italy tertiary centre.
**Methods:** RA patients admitted to the outpatient Clinic of a tertiary centre from 01/01/2008 to 31/12/2015 were investigated. Table 1 shows patients features (age, sex, disease duration, Simplified Disease Activity Index-SDAI index, Health Assessment Questionnaire-Disability Index-HAQ-DI, Rheumatoid Factor-RF and/or Anti-Citrullinated Cyclic Peptides Antibody-ACPA, concomitant comorbidity) as detected at baseline, and treatment during follow-up. RA patients mortality incidence rate (event/100person year) was calculated, baseline predictors of mortality were analyzed by univariate and multivariate cox-regression analysis.
**Results:** A total of 608 RA patients were included (497 women), median age 56.8 years, range 15–89.5. On December 31 2015, 589 out of patient were alive, 19 were known to have died and 7,3% had been lost to follow up. Mortality Incidence rate (MIR) in our cohort was 0.79 deaths/100 person-year, SMR with respect to Italian population was 0.79 (MIR in Italy 1/100 person-year). This feature might depend on the low prevalence of RF/ACPA positivity (69.13%) in our series. Cox regression analysis (univariate analysis) pointed out age at first visit (HR 1.14; p$\leq$0.0001), diabetes (HR 4.395; p=0.004) and a HAQ value$>$1 (HR 6.02; p=0.02) as independent predictors of mortality. On the contrary, female sex resulted to have a protective role (HR 0.349, p=0.027). At multivariate analysis, the only baseline independent predictor of mortality was age at admission (HR 1.17, 95% CI 1.01–1.35, p=0.026).

**Table 1. Clinical and epidemiological features of 608 RA patients at baseline**

| | |
|---|---|
| Sex F/M ratio | 497/111 |
| Age (yrs : median, range) | 56.8 (15-89.5) |
| Disease duration (yrs: median, range) | 9 (0.5–41) |
| RF positivity | 270/432 (62.5%) |
| ACPA positivity | 188/360 (52.2%) |
| FR and/or ACPA positivity | 318/460 (69.13% |
| Biologic drug treatment (n) (%) | 354/608 (58%) |
| DAS 28 (median, range) | 3.97 (0.56-7.29) |
| Media ±DS | 4.03±1.21 |
| SDAI (median, range) | 12.19 (0.03-45) |
| HAQ –DI (median, range) | 1 (0-3) |
| Arterial Hypertension | 246/608 (40.5) |
| Metabolic syndrome | 63/608 (10.4) |
| Diabetes Mellitus | 51/608 (8.4) |
| History and/or follow-up Cardiovascular Events | 41/608 (6.7) |

**Conclusions:** The present study points out a South Italian RA SMR lower than that in general Italian population and significantly lower than that reported in RA patients from other countries (2). This result can depend on the lower percentage of RF/ACPA positive patients in our cohort in respect to general population. Epidemiological studies on the sierological profile of South Italian RA patients are needed.
**References:**
[1] Sokka T et al. ClinExpRheumatol. 2008;26(Suppl):S35–61.
[2] Dadoun S et al. Joint Bone Spine. 2013;80:29–33.
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SAT0058 **CONSISTENCY OF RADIOGRAPHIC RESPONSES WITH SARILUMAB PLUS METHOTREXATE ACROSS SUBPOPULATIONS OF PATIENTS WITH RHEUMATOID ARTHRITIS IN A PHASE 3 STUDY**

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**Background:** The investigational drug sarilumab is a human monoclonal antibody directed against the interleukin 6 receptor.[1] The phase 3 MOBILITY study (NCT01061736) examined sarilumab + methotrexate (MTX) vs placebo + MTX in a double-blind, 52-week, randomized trial of patients with active, moderate-to-severe rheumatoid arthritis (RA) with inadequate response to MTX.[1] Both sarilumab doses (150 and 200 mg subcutaneously every 2 weeks [q2w]) demonstrated statistically significant improvements in signs and symptoms of RA, in physical function, and inhibition of radiographic progression. The most common treatment-emergent adverse events were infections, neutropenia, injection site reactions, and increased transaminases.

**Objectives:** In the present study, radiographic efficacy of sarilumab across subpopulations from MOBILITY was assessed.

**Methods:** To explore the consistency of radiographic response, treatment-by-subgroup interactions were assessed by rank ANCOVA for change in van der Heijde modified total Sharp score (mTSS) at week 52. A total of 19 subgroups were investigated (listed in Table footnote); those with $P \leq 0.2$ for interaction are presented. Radiographic progression was defined as mean change from baseline mTSS.

**Results:** Both doses of sarilumab showed less progression relative to placebo across all subgroups. Change in mTSS across subgroups based on rheumatoid factor and anti–cyclic citrullinated peptide status and demographic characteristics such as age, sex, and ethnicity appeared to be consistent with overall study findings. Subgroups with interaction $P \leq 0.2$ were prior use of biologics and baseline C-reactive protein (CRP), body mass index (BMI), RA disease duration, median mTSS, and smoking history (Table). In some groups (lower BMI, no prior biologic use, higher baseline CRP, no history of smoking, and high mTSS), the treatment effect increased, because there was greater progression in the placebo group relative to the sarilumab groups. The progression with sarilumab 200 mg q2w was consistently lower compared with sarilumab 150 mg q2w. Progression was substantially greater in placebo patients with baseline mTSS >25 compared with those with baseline mTSS ≤25. These differences were not observed in sarilumab-treated patients. Joint space narrowing and erosion score showed patterns similar to the total score. Overall, sample sizes were limited in some subgroups.

**Conclusions:** Sarilumab generally inhibited radiographic progression to a similar extent across a wide spectrum of subgroups. Nonetheless, the treatment effect appeared to be greater in subgroups with poor prognostic markers such as high levels of CRP and more structural damage at baseline, as well as in nonsmokers and patients with low BMI.

**Table.** Radiographic Progression (Mean Change From Baseline mTSS at Week 52) in MOBILITY Subgroups[a] With Treatment by Subgroup Interaction *P*≤0.2

| | Placebo + MTX (n=398) | Sarilumab 150 mg q2w + MTX (n=400) | Sarilumab 200 mg q2w + MTX (n=399) |
|---|---|---|---|
| **Overall MOBILITY results, ITT population** | | | |
| Mean mTSS change (SD) | 2.78 (7.73) | 0.90 (4.64) | 0.25 (4.61) |
| **BMI, kg/m²; interaction *P*=0.09** | | | |
| <25 kg/m², n | 163 | 131 | 120 |
| Mean mTSS change (SD) | 3.95 (9.45) | 1.06 (4.63) | -0.08 (3.54) |
| ≥25 and <30 kg/m², n | 138 | 114 | 113 |
| Mean mTSS change (SD) | 3.06 (7.47) | 1.14 (5.14) | 0.58 (4.35) |
| ≥30 kg/m², n | 111 | 106 | 126 |
| Mean mTSS change (SD) | 1.33 (5.58) | 0.48 (4.14) | 0.26 (5.64) |
| **Prior biologic use; interaction *P*=0.57** | | | |
| No, n | 253 | 251 | 263 |
| Mean mTSS change (SD) | 3.23 (8.19) | 1.11 (4.75) | 0.22 (5.17) |
| Yes, n | 99 | 101 | 96 |
| Mean mTSS change (SD) | 1.63 (6.29) | 0.37 (4.41) | 0.33 (2.54) |
| **Baseline CRP levels; interaction *P*=0.29** | | | |
| ≤15 mg/L, n | 197 | 181 | 175 |
| Mean mTSS change (SD) | 1.62 (5.53) | 0.80 (4.61) | -0.46 (4.94) |
| >15 mg/L, n | 155 | 171 | 187 |
| Mean mTSS change (SD) | 4.25 (9.36) | 1.00 (4.72) | 0.90 (4.20) |
| **Duration of RA; interaction *P*=0.11** | | | |
| ≤3 years, n | 85 | 89 | 93 |
| Mean mTSS change (SD) | 2.69 (7.13) | 0.84 (3.96) | 0.17 (3.60) |
| >3 and ≤10 years, n | 142 | 130 | 144 |
| Mean mTSS change (SD) | 2.85 (8.23) | 0.53 (4.11) | 0.24 (4.12) |
| ≥10 years, n | 125 | 133 | 122 |
| Mean mTSS change (SD) | 2.62 (7.58) | 1.29 (5.53) | 0.32 (5.65) |
| **Smoking history; interaction *P*=0.04** | | | |
| No, n | 259 | 259 | 265 |
| Mean mTSS change (SD) | 2.94 (8.54) | 0.83 (4.38) | 0.11 (3.14) |
| Yes, n | 93 | 93 | 93 |
| Mean mTSS change (SD) | 2.31 (10.38) | 1.08 (5.35) | 1.18 (5.11) |
| **Baseline mTSS status; interaction *P*<0.01 (post hoc)** | | | |
| ≤25, n | 179 | 167 | 185 |
| Mean mTSS change (SD) | 1.49 (4.89) | 0.42 (2.67) | 0.41 (3.06) |
| >25, n | 173 | 185 | 174 |
| Mean mTSS change (SD) | 4.11 (9.68) | 1.33 (5.88) | 0.07 (5.83) |

BMI, body mass index; CCP, cyclic citrullinated peptide; CRP, C-reactive protein; DAS28-CRP, disease activity score by CRP; DMARD, disease-modifying antirheumatic drug; ITT, intent-to-treat; mTSS, modified total Sharp score; MTX, methotrexate; q2w, every 2 weeks; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation. [a]Subgroups investigated were based on sex, race, ethnicity, geographic region, age, baseline weight, BMI, prior biologic use, RF status, anti-CCP status, RF/anti-CCP seropositivity, baseline erosion, baseline CRP levels, baseline DAS28-CRP, duration of RA (cutpoint at median and categories), number of prior DMARDs, smoking history, and baseline mTSS status (≤ vs > median).

**Disclosure of Interest:** D. van der Heijde Consultant for: Sanofi, C. Fan Shareholder of: Sanofi, Employee of: Sanofi, H. van Hoogstraten Shareholder of: Sanofi, Consultant for: Sanofi, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. van Adelsberg Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, P. Miranda Grant/research support from: Sanofi, M. Genovese Grant/research support from: Roche, Sanofi, GSK, R-Pharma, RuiYi, and BMS, Consultant for: Roche, Sanofi, GSK, R-Pharma, RuiYi, and BMS

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SAT0059 **CRITERIA FOR CHOICE BY CLINCIANS OF THE THERAPEUTIC STRATEGY IN PATIENTS WITH INSUFFICIENT RESPONSE TO A FIRST ANTI-TNF: DATA FROM THE RANDOMIZED "ROC" CRITERIA**

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**Background:** Therapeutic strategy after failure of a 1st anti-TNF (TNF-IR) is not codified in rheumatoid arthritis (RA). Little is known about the criteria for choice of a second biologic by clinicians.

**Objectives:** To determine whether patient's or disease characteristics guide clinicians for their choice of a second biologic in TNF-IR patients with RA

**Methods:** The ROC trial randomized patients with an insufficient response to a 1st anti-TNF to receive either a second anti-TNF or a non-TNF targeted biologic. Before randomization, the clinician's preference for the second biologic (either a non-TNF targeted biologic or a second anti-TNF) was collected. After randomization, the choice of the molecule within each arm was left to the clinician.

**Results:** The clinician's preference for the second biologic could be collected before randomization for 281 out of the 292 patients analyzed in the ROC trial. 151 clinicians would have preferred to prescribe a non-TNF targeted biologic, 72 a second anti-TNF and 58 clinicians had no preference.

Among baseline characterics of disease, only disease duration was significantly associated with the preference for non-TNF targeted biologics (median 8 [3–17] years for patients for whom clinicians would have chosen a non-TNF biologic versus 5 [1–13] years for patients for whom clinicians would have chosen a second anti-TNF, p=0.001). Other parameters (such as age, sex, body mass index, number of previous conventional DMARDs, seropositivity for

RF/ACPA, extra-articular invovement, CRP, ESR, DAS28-ESR at inclusion) has no significant impact on the clinician's choice.Cotreatment either with glucocorticoids, methotrexate or anopther conventional DMARD had no significant impact on the choice of clinicians either.
With regards to the choice of the mechanism of action in the non-TNF targeted group, clinicians significantly more frequently prescribed abatacept in patients with cardiovascular risk factors (70% of patients treated with abatacept had cardiovascular risk factors compared to 44% of patients treated with rituximab or tocilizumab) p=0.03). Clinicians prescribed significantly more frequently tocilizumab in patients with a high C-reactive protein value (median baseline value of 10.5 mg/l versus 5 mg/l in patients who received abatacept or rituximab) (p=0.01).
**Conclusions:** There is no characteristic patient's profile explaining the preference of clincians for a non-TNF biologic or a second anti-TNF in TNF-IR patients. Among non-TNF biologics, abatacept was more frequently prescribed in patients with cardiovascular risk factors and tocilizumab was more frequently prescribed in patients with a high C-reactive protein value.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6141

## SAT0060 ACHIEVEMENT OF INDIVIDUAL IMPORTANT RESPONSE MEASURED BY DAS28DCRIT IN ACTIVE RHEUMATOID ARTHRITIS WHEN TREATED WITH TOCILIZUMAB: DATA FROM A LARGE PROSPECTIVE OBSERVATIONAL STUDY

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**Background:** Normal fluctuations in results of disease activity measurements due to short-term situational effects and measurement errors are issues for evaluation of individual clinically meaningful therapeutic response in daily practice in patients with rheumatoid arthritis (RA). To address this aspect, we established earlier a statistical approach to determine a critical difference (dcrit) that defines valid criterion for response as assessed by the Disease Activity Score-28 joints (DAS28)[1]. With this study DCRIT criterion was used to measure clinical meaningful response in RA-patients treated with Tocilizumab (TCZ) in routine care.
**Methods:** The patient population was derived from a prospective noninterventional study in patients with active RA treated with TCZ. A total of 635 patients were analysed. 310 patients with stable disease and stable therapy (no change in TCZ, cDMARD, NSAID and prednisolone) for at least one year (from month 12 to 24 after TCZ initiation) were used to evaluate the previous established $DAS28_{dcrit}$ cut-off of 1.8 for response. To evaluate individual variations in DAS28 scores despite stable mean DAS28 without treatment changes, we subjected DAS28 scores at 12, 18 and 24 months to an ANOVA model to establish a 95% one sided confidence interval (95% CI) for normal fluctuations; this value was used to define the dcrit for individual changes. The total cohort was used to calculate percentage of achieving DAS28 dcrit-response.
**Results:** The mean baseline disease activity (DAS28) from the stable cohort was 5.52 and decreased to 2.51 (month 12). For the next treatment year, the mean DAS of the entire cohort was stable (month 15 2.44, 18 2.40, 21 2.44 and 24 2.46). The calculation of the dcrit cut-off in TCZ-monotherapy results in 1.81 which is within the range of dcrit values in other treatment regimes; for the population including combinational therapy, result was slightly higher (1.9). 70.5% of the patients achieved $DAS28_{dcrit}$, reflecting meaningful clinical response only arised from the treatment intervention after 12 weeks. The responders increased up to 76.0% at week 24 and 78.9% at week 52 (calculated based on dcrit cut-off 1.8). After 2-years of treatment 80.6% of the patients reach a stable $DAS28_{dcrit}$ response. If using the more conservative (1.94) the result reads as follows: 64.5% week 12, 73.8% week 24, 77.3% week 52, 77.6% at week 104.
**Conclusions:** The established critical differences for DAS28 ($DAS28_{dcrit}$) of 1.8 was confirmed in an independent cohort of TCZ-treated patients. The slightly higher value of critical difference in TCZ treated patients (especially in TCZ+DMARD) might be due to the unique effect of TCZ on one variable of DAS28 (ESR/CRP). For both cut offs (1.8 and 1.9) high percentages of patients achieved this level of response after initiation of TCZ-treatment.
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**Disclosure of Interest:** F. Behrens Grant/research support from: Chugai, M. Köhm: None declared, M. Hofmann Employee of: Chugai, G. Fliedner Grant/research support from: Chugai, C. Specker Grant/research support from: Chugai, H. Burkhardt Grant/research support from: Chugai
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## SAT0061 CONCURRENT ULTRASOUND-DETECTED SYNOVITIS AND TENOSYNOVITIS PREDICT FLARE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION

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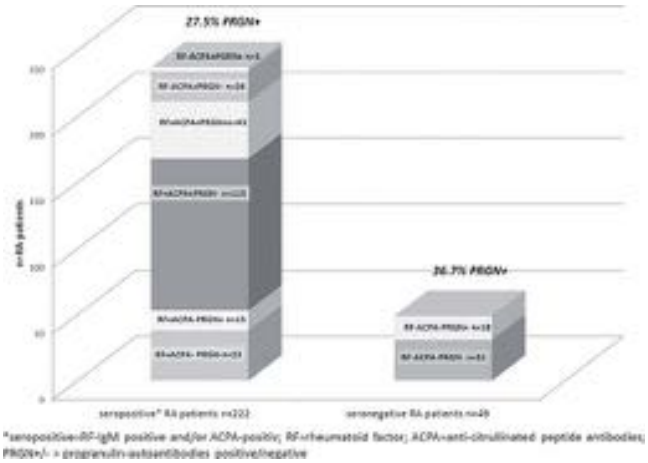
**Background:** Subclinical synovial inflammation detected by ultrasonography (US) in patients with rheumatoid arthritis (RA) in clinical remission relates to disease flare. The impact of tenosynovitis in this context is not known.
**Objectives:** To evaluate the association between US-detected tenosynovitis and synovitis in RA patients in clinical remission and flare over 12-months.
**Methods:** STARTER is a multicentre cohort study of the US Study Group of the Italian Society for Rheumatology. Participants were selected on the basis of a reliability exercise and the availability of high-end equipment. Patients with RA in clinical remission underwent clinical evaluation and US synovitis (-S) and tenosynovitis (-T) were assessed categorically for Grey Scale (GS) and power Doppler (PD) at 11 joints, extensor and flexor tendons in both hands and wrists. Patients were seen at 6 and 12 months. Flare within 12 months was defined as increase of $>1.2$ or $>0.6$ if final DAS28$>$3.2. The relationship between the presence of GS-T/-S, PD-T/-S was evaluated by logistic models, presented as odds ratios (OR) and 95% confidence interval (CI), adjusted for pre-specified confounders.
**Results:** 361 patients (72.3% f, mean age (sd) 56.1 (13.3), median disease duration (IQR) 7.1 years (3.6–13.5)) were included. 98/326 (30.6%) patients had a flare within 12 months. Considering US variables separately, only PD-S significantly predicted flare (OR 1.87 (1.12,3.14)). When the model included both –T and –S, only the concurrent presence of –T and –S predicted flare (PD-T+-S: OR 2.06 (1.04, 4.07); GS-T+-S: OR 2.27, (1.01,5.10)), while isolated –S and –T did not.
**Conclusions:** In patients with RA in clinical remission, US-detected synovial and tenosynovial inflammation identifies patients at risk of flare. US might help decisions on management in this population.
**Disclosure of Interest:** None declared
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## SAT0062 TEST FOR SERUM PROGRANULIN AUTOANTIBODIES CAN REDUCE THE SERONEGATIVE STATUS IN RHEUMATOID ARTHRITIS BY ONE THIRD

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**Background:** Progranulin autoantibodies (PGRNabs) have been previously described in sera of patients with different autoimmune diseases such as ANCA associated vasculitis, large vessel vaskulitis, Crohn's disease, polyarthritis including psoriatic arthritis and rheumatoid arthritis, whereas healthy controls and patients with different non-rheumatological disorders have shown a prevalence less than 1% [Ref.]. At primary diagnosis of rheumatoid arthritis as well as during the course of diseases at least 25% of RA patients have never developed serum RF or ACPA. Here we conducted a study on RA patients who were tested for RF, ACPA, and PRGNabs to evaluate the prevalence of serostatus in RA.
**Objectives:** Prevalence of serum PRGNabs in RA with stratification into seropositive RA patients with the proof of serum RF and/or ACPA and seronegative RA patients.
**Methods:** From Nov 2011 till Dec 2013 sera of 271 RA patients were collected and analyized for RF-IgM, ACPA-IgG, and PGRNabs with ELISA (as previously published) using a retrospective, blinded, non-randomized study design. All patients were on treatment with conventional DMARDS (n=165) or TNF inhibitors (n=106). All patients fullfilled the ACR criteria from 1987 and the revised diagnostic EULAR/ACR criteria from 2011. RA patients characteristics concerning age, gender, treatment history, radiological joint imaging, and duration of disease were availiable.
**Results:** The overall prevalence of PGRNabs in RA patients was 29,2%. 222

RA patients were seropositive for RF and/or ACPA, 49 RA patients were seronegative. Testing for PRGNabs resulted in significantly higher prevalence of PRGNabs in RF- and ACPA-seronegative RA patients compared to RA patients with seropositivity in at least one of serummarkers RF or ACPA (27.5% versus 36.7%, p=0.021, Chi2 test) [Figure]. The prevalence of PRGNabs in RF-positive RA patients were significant higher than in ACPA-positive RA (25.0% vs. 29,6%, p=0.019, chi2 test). The disease duration did not differ between in PRGNabs negative or positive RA patients (8.1 vs. 7.9 years).




**Conclusions:** PGRNabs are positive in more than 30% of sera of RA patients who are seronegative for RF-IgM and ACPA. These results suggest that testing for PRGNabs can reduce the seronegative status in RA patients. However, the data has to be confirmed by a larger validation cohort of RF and ACPA negative RA patients.

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**Disclosure of Interest:** None declared

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## SAT0063 REMOTE ASSESSMENT OF DAILY FLUCTUATIONS OF PATIENT-REPORTED DISEASE SYMPTOMS AND ACTIVITY IN RHEUMATOID ARTHRITIS: FEASIBILITY, COMPLIANCE AND ACCEPTABILITY

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**Background:** Existing clinical measures for Rheumatoid Arthritis (RA) patients, eg: Disease Activity Score (DAS)28 are labor-intensive and typically compiled once every three months by a physician. In contrast, wearable fitness activity trackers allow for continual measurement of activity and lifestyle events. If correlated to disease activity, use of data from "wearable" will provide an understanding of impact on activity on a more frequent basis than the physician-applied tests.

**Objectives:** The primary aim of this study was to determine feasibility, patient compliance and acceptance using an activity tracker together with a novel smartphone-based electronic Patient Reported Outcome (ePRO) app (Remote Access to RA [RA-RA] app developed in-house) for RA patients.

**Methods:** Smartphone users diagnosed with RA (n=15) were recruited to wear an activity tracker and use the RA-RA app daily for one week. The patients attended two study sessions. During the first session patients were dispensed the activity tracker. The investigator installed the activity tracker companion and the RA-RA apps on the patient's smartphone and provided instructions for their use. Patients wore the activity tracker for one week, and were asked to complete RA symptom questionnaires on a regular basis (eg:morning, evening, and weekly). During the study period, the activity monitor collected objective measures of patient activity while the RA-RA app collected patient reported outcome measures (eg: stiffness, sleep quality, joint pain). Blinded activity and RA symptom data were automatically transferred to and stored on a clinical electronic data capture system. During the second session, patients were interviewed regarding their experiences; likes, dislikes, difficulties, and provided feedback on the RA-RA app, activity tracker and its accompanying app. Patients also described any instances and reasons for non-compliance with using the app or wearing the activity tracker.

**Results:** Thirteen of fifteen patients successfully used the activity tracker and wore it for the duration of the study week.Overall, patients found the RA-RA app easy to use for tracking their RA symptoms and activity. Many patients reported that RA-RA accurately described their RA symptoms. Some patients experienced app errors and required assistance from study staff. Overall, patients liked the on-screen controls. Patients provided valuable feedback on interface design considerations (eg: keypad or the arrows for time entry). Preliminary analysis showed some correlation between duration of morning stiffness reported in the app and level of morning activity captured by the activity tracker.

**Conclusions:** Digital healthcare application, use of the activity tracker, and a smartphone-based ePRO is a feasible, easy to use and acceptable system for the collection of daily fluctuations of symptoms and activity in RA patients. Based on the results of this pilot study, the next trial will be in a clinical setting with RA patients receiving treatment. This study will establish correlation of patient's activity and ePRO information with the standard clinical information (ACR, DAS28, and HAQ), as well as serum and imaging biomarkers to determine disease activity and inflammation.

**Disclosure of Interest:** I. Gourley Employee of: Janssen R & D, LLC, C. Calderon Employee of: Janssen R & D, LLC, M. Beyer Employee of: Janssen R & D, LLC, L. Hamade Employee of: Janssen R & D, LLC, R. Margolies Grant/research support from: Janssen R & D, LLC, K. Gilmer Employee of: Janssen R & D, LLC, T. Messina Employee of: Janssen R & D, LLC, O. Fields Employee of: Janssen R & D, LLC, D. Tisdale Employee of: Janssen R & D, LLC, M. Curran Employee of: Janssen R & D, LLC, A. Rowe Employee of: Janssen R & D, LLC

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## SAT0064 THERAPY ADHERENCE, PRESCRIBED MEDICATIONS, DISEASE ACTIVITY AND PSYCHOSOCIAL CONSEQUENCES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Adherence to rheumatoid arthritis (RA) treatment is essential for therapeutic success.Factors contributing to therapy adherence and their consequences are under debate.

**Objectives:** To investigate the relationship between therapy adherence and disease activity as well as patients' quality of life.

**Methods:** The survey included a representative, nationwide sample of German physicians specialized in RA and patients with RA. The physician questionnaire assessed disease activity (DAS28), patients' adherence to therapy and medical prescriptions. The patient questionnaire assessed quality of life (SF-12), health education literacy (i.e., the understanding and use of medical information, HELP), activities of daily living (MDHAQ), fatigue (EORTC QLQ-FA13) and patients' listings of their medications. Adherence was assessed with a combined measure of physician rating (1= very adherent, 0 = less adherent) and the match between physicians' prescriptions and patients' accounts of their medications (1 = perfect match, 0 = no perfect match). Three groups of patients could be distinguished: high (very adherent according to physician and perfect medication match, n=180), medium (either high physician rated adherence or perfect medication match, n=279), and low (0 in both adherence criteria) (n=205). An ANOVA was used to analyze differences in continuous variables among the three groups.

**Results:** 671 pairs of patient and physician questionnaires were analyzed. Mean patients' age (73% female) was 60 years (SD=12). At the time of assessment, 67.2% the patients showed low disease activity (DAS28 <3,2), 28.8% moderate disease activity (DAS28 3,2 to 5,1), and 4.0% high disease activity (DAS28 >5,1). There was no relation between adherence and demographic variables. However, it was related to disease activity, numerous psychosocial variables and the number of prescribed medications (Table 1).

Table 1

| | Adherence | | | p |
|---|---|---|---|---|
| | High | Medium | Low | |
| DAS28* | 2.45 (1.11) | 2.80 (1.20) | 3.06 (1.26) | <0.001 |
| HAQ (Disability)* | 0.58 (0.62) | 0.76 (0.67) | 0.85 (0.74) | 0.001 |
| SF-12** | | | | |
| Physical | 43.20 (9.91) | 40.85 (10.95) | 39.61 (10.98) | 0.004 |
| Psychological | 50.42 (10.58) | 47.49 (11.37) | 46.47 (11.55) | 0.002 |
| Fatigue* | | | | |
| Physical | 2.18 (0.80) | 2.39 (0.85) | 2.45 (0.88) | 0.006 |
| Psychological | 1.71 (0.72) | 1.95 (0.85) | 2.02 (0.90) | 0.001 |
| Cognitive | 1.36 (0.46) | 1.50 (0.61) | 1.54 (0.68) | 0.011 |
| HELP* | | | | |
| Understanding medical information | 1.46 (0.54) | 1.54 (0.65) | 1.67 (0.78) | 0.008 |
| Use of medical information | 1.79 (0.70) | 1.94 (0.84) | 2.16 (0.91) | <0.001 |
| Communicative competence | 1.50 (0.53) | 1.58 (0.64) | 1.70 (0.75) | 0.012 |
| Number of prescribed medications | 3.71 (2.16) | 5.04 (2.74) | 5.69 (2.74) | <0.001 |

Data are presented using means and (standard deviations). *Lower values denote better performance, **higher values denote better performance.

**Conclusions:** This study showed that patient adherence to therapy was associated with less disease activity and higher levels of quality of life. Adherence was also dependent on the total number of prescribed medications. The effects were consistent across different psychosocial domains. The findings may help to detect patients who are at risk not to comply with treatment and eventually to optimize patient education and counseling.

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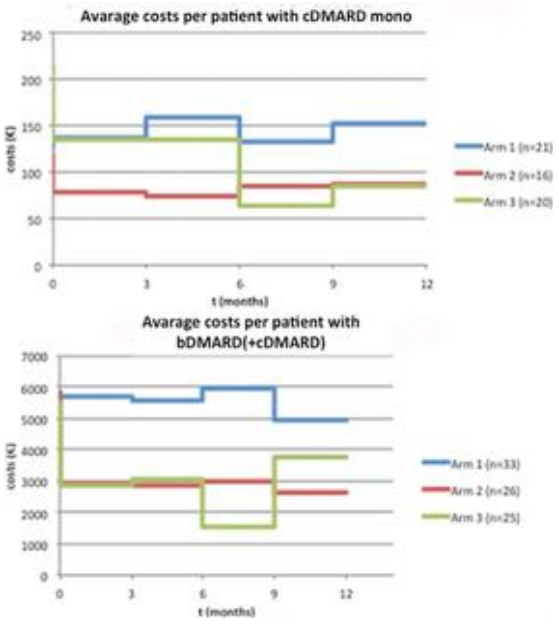
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**Disclosure of Interest:** None declared
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## SAT0065 EFFECTS OF DMARD TAPERING ON TREATMENT COSTS IN RHEUMATOID ARTHRITIS PATIENTS- AN ANALYSIS FROM THE PROSPECTIVE RANDOMIZED CONTROLLED RETRO-STUDY

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**Background:** Achieving remission is the most important treatment goal in patients with rheumatoid arthritis (RA). With the development and wider use of highly effective disease modifying anti-rheumatic drugs (DMARD) about half of RA patients reach a state of disease remission, raising the question about tapering or stopping anti-rheumatic treatment.
**Objectives:** To assess the effect of a controlled DMARD tapering regimen on treatment costs and work productivity in RA patients in remission
**Methods:** 101 RA patients in sustained remission (DAS28 <2.6 for more than 6 months) enrolled in the multicenter randomized controlled RETRO Study were analyzed (1). Patients either continued DMARDs (arm1), tapered dose by 50% (arm 2) or entire stopped DMARDs after tapering (arm 3) for one year. Assessment of DMARD costs and work productivity was done every three months in all 101 patients including those remaining in remission and those relapsing a re-starting their original DMARD regimen.
**Results:** In RA patients treated with conventional DMARDs, baseline quarterly treatment costs of 154€ remained stable in arm 1 (156€), while decreasing to 81€ in arm 2 and 75€ in arm 3. In patients treated with biologic DMARDs quarterly treatment costs were 5708€ at baseline. They remained stable in arm1 (5533€) and decreased to 2855€ in arm 2 and 2668€ in arm 3. Overall DMARD costs were reduced by 327.292€ within one year, while outcome was very good




with patients either remaining in remission or immediately regaining remission when exposed to original DMARD regimen after relapse.
**Conclusions:** Controlled tapering of DMARD treatment leads to effective reduction of treatment costs in RA patients in sustained remission.
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**Disclosure of Interest:** None declared
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## SAT0066 THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE IN METHOTREXATE INCOMPLETE RESPONDERS PREDICTS CLINICAL RESPONSES TO NON-BIOLOGICAL VERSUS BIOLOGICAL THERAPY IN EARLY RA

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**Background:** In rheumatoid arthritis (RA), biological medications are marginally better than combination of conventional non-biological drugs such as methotrexate (MTX) with sulfasalazine and hydroxychloroquine (triple therapy [TT]) at group level [1–3]. Previously we have reported that multi-biomarker disease activity (MBDA) score measured after MTX monotherapy in MTX incomplete responders (MTX-IR) or the change of the MBDA score (ΔMBDA) from baseline (BL) to month 3 (M3) was predictive for a subset of patients with low versus high likelihood of subsequent response to TT or TNF inhibitor (TNFi) [4, 5].
**Objectives:** To evaluate a combination of the MBDA score at M3 and ΔMBDA (BL-M3) as a predictor of response to TT or TNFi in MTX-IR in early RA patients from the SWEFOT trial.
**Methods:** In the SWEFOT trial, patients started MTX monotherapy for 3 months and MTX-IR were randomised to TT or TNFi. We analysed 157 MTX-IR patients with complete data on the MBDA score at BL and M3, and DAS28 at year 1. The MBDA score between BL and M3 was compared by Wilcoxon Signed Rank test. Proportions of clinical responders (DAS28≤3.2) at year 1 among patients with high (>44 [validated cut-off] or >38 [non-validated, ROC curve-based cut-off]) MBDA score at M3 AND non-big decrease from BL to M3 (ΔMBDA≤20) were compared with other patients (MBDA≤44/≤38 OR/AND ΔMBDA>20) by $\chi^2$ test. Overall difference of the responses in the two therapy arms was analysed by Breslow-Day test (for homogeneity of odds ratio).
**Results:** Median (interquartile range) of the MBDA score at BL and M3 were 59 (49–73) and 46 (37–60), respectively (p<0.001). For patients with a high MBDA score (>44 or >38) and ΔMBDA≤20, the likelihood of response to TNFi was significantly greater than to TT (60% vs 30%, p=0.006, Figure 1A and 60% vs 33%, p=0.006, Figure 1B), whereas for other patients the likelihood of response was greater for TT than TNFi (63% vs 46%, p=0.134, Figure 1A, and 69% vs 41%, p=0.035, Figure 1B). The overall differences of the responses to the treatments based on >44 or >38 cut-offs were highly significant (p=0.003 and p=0.001, respectively; Figure 1A, B).

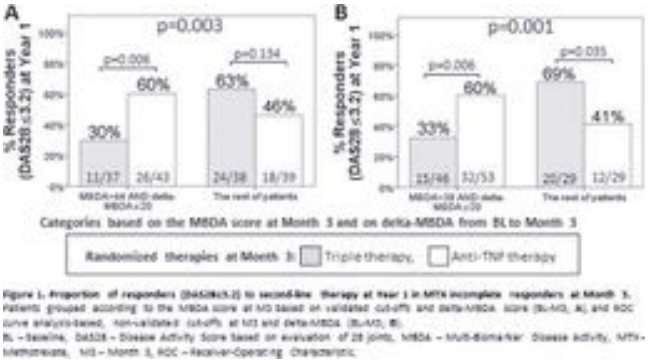



Figure 1. Proportion of responders (DAS28≤3.2) to second-line therapy at Year 1 in MTX-incomplete responders at Month 3. Patients grouped according to the MBDA score at M3 based on validated cut-offs and delta-MBDA score (BL-M3, A), and ROC curve analysis-based, non-validated (cut-offs) at M3 and delta-MBDA (BL-M3, B).
BL – baseline, DAS28 – Disease Activity Score based on evaluation of 28 joints, MBDA – Multi-Biomarker Disease Activity, MTX-IR – methotrexate, M3 – Month 3, ROC – Receiver-Operating Characteristic

**Conclusions:** In patients with early RA and incomplete response to MTX, MBDA score predicted the relative efficacy of subsequent treatment with triple therapy versus anti-TNF. Patients with high MBDA score after MTX monotherapy AND change in the MBDA score ≤20 had higher likelihood of responding to TNFi and the other patients had higher likelihood of responding to TT.

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**Disclosure of Interest:** K. Hambardzumyan: None declared, R. Bolce Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience, S. Saevarsdottir: None declared, K. Forslind: None declared, J. Wallman: None declared, R. van Vollenhoven Grant/research support from: Abb Vie, BMS, GSK, Pfizer, Roch, UCB, Consultant for: Abb Vie, Biotest, BMS, Crescendo Bioscience, GSK, Janssen, Lilly, Merck, Pfizer, Roch, UCB, Vertex
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## SAT0067 RADIOGRAPHIC DAMAGE AND DISABILITY IN PATIENTS WITH RA IN RELATION TO DISEASE DURATION IN THE ERA OF BIOLOGICS. LONG-TERM RESULTS FROM THE SCQM COHORT

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**Background:** Rheumatoid arthritis (RA) is an inflammatory disease with a chronic course over many years. Long-term observations in the late 90s have demonstrated that RA is associated with progressive articular destruction and increasing disability over the course of the disease. When biologic treatment was introduced, a lot of studies were able to show a favourable influence on disease activity, joint destruction, and disability. However, to our knowledge, no long-term studies have been conducted investigating the radiographic outcome and disability in this new era of treatment with biologics.
**Objectives:** To analyse patients with RA for radiographic damage, disability and disease activity dependent on disease duration.
**Methods:** We included all RA patients from the Swiss Clinical Quality Management in rheumatoid arthritis (SCQM) with at least one clinical visit and information on the disease duration available in the database. The primary endpoint was the association between the radiographic destruction, assessed by Ratingen erosion scores at the last clinical visit, and disease duration. This endpoint was investigated by a multiple negative binomial regression model which corrected for the effect of gender, age, rheumatoid factor (RF), ACPA and therapeutic status regarding the use of anti-TNF drugs and methotrexate (MTX), as possible confounding factors. Disease activity (DAS 28) and disability (HAQ DI) in dependence of disease duration served as secondary outcomes, analysed by using a multiple linear regression model with corrections for the same potential confounders as described for the primary endpoint.
**Results:** The original 52'753 records on 8'678 patients resulted in 6'526 evaluable observations for the Ratingen score. Disease duration ranged between less than 1 and more than 65 years, with a median disease duration of 8.3 years, and past or current use of anti-TNF drugs in 58.4% of patients. We found a significant association between disease duration and radiographic destruction with an average increase of Ratingen scores by 8.3% each year (95%CI from 8.1% to 8.6%). The most significant predictor for less radiographic destruction was a negative rheumatoid factor. During the first 5 years of the disease, clinical activity and disability decreased over time. While DAS 28-scores remained on a stable level in patients with a disease duration of more than 5 years (median DAS 28 of 2.8), HAQ-DI scores increased continuously by 0.018 for each additional year.
**Conclusions:** In this RA cohort, patients showed a continuous increase of articular destruction and physical disability in parallel to disease duration, despite treatment with biologics in the majority of patients. Even though in the era of biologics a satisfactory control of disease activity can be achieved in most patients, RA remains a progressive disease leading to joint destruction and physical disability.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4176

## SAT0068 CIRCULATING MIR-126 IS A MARKER OF DISEASE ACTIVITY IN PATIENTS WITH EARLY RA BUT DOES NOT DIFFERENTIATE PATIENTS AT RISK OF DEVELOPING RA

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**Background:** We have previously shown differential expression of some circulating miRNAs in patients with early RA (ERA) and their potential as markers of disease activity and treatment response.
**Objectives:** We aimed to investigate differentially expressed circulating miRNAs in clinically suspect arthralgia patients with positive antibodies to citrullinated peptide antigens (ACPA) who are at high risk of developing RA and compared them to ERA and established RA.
**Methods:** The study included 20 ACPA+ arthralgia patients, 25 treatment naïve ERA patients who met the 2010 ACR/EULAR criteria (disease duration $<$6 months), 26 patients with highly active established RA prior anti-TNF treatment initiation and 24 healthy controls (HC). Clinical disease activity assessments (DAS28, SDAI) were performed. Ultrasound of 28 small joints was performed in ACPA+ arthralgia patients to evaluate subclinical synovitis. Total RNA from plasma was isolated using phenol-chloroform extraction. A comprehensive analysis of miRNAs was performed using TaqMan® Low Density Array (TLDA) in 5–6 samples in each group. The expression of miR-126 was further validated by single assays in remaining samples and normalized to an average of 2 spike-in C. elegans controls. dCt was used for relative quantification.
**Results:** Patients with arthralgia showed no clinical and ultrasound evidence of arthritis (grey scale and power Doppler for single joint $\leq$1) Of these, all were ACPA+, CRP 7.4±19.2 mg/l. Treatment naïve ERA patients had active disease (DAS28 5.7±1.3, CRP 20.7±23.2 mg/l), 60% were ACPA+. Patients with established RA all had high disease activity (DAS28 6.6±0.9, CRP 28.1±31.3 mg/l), 73% were ACPA+, had failed DMARDs therapy and were due to commence anti-TNF treatment. Out of the 380 miRNAs analysed by TLDA, 128 miRNAs were detected in HC, 129 in arthralgia, 44 in ERA and 25 in RA patients. TLDA analysis revealed 1.7x higher levels of miR-126 in ACPA+ arthralgia patients compared to HC, and 27x and 63x lower levels in ERA and RA compared to HC, respectively. These data were suggestive of significant dysregulation of miR-126 in patients with active polyarthritis compared to ACPA+ arthralgia. However, further validation showed no difference in miR-126 levels among HC, arthralgia and ERA patients but the levels were 2.6x lower in RA patients compared to HC (p=0.0037). The levels of miR-126 significantly negatively correlated with DAS28 (r=-0.460; p=0.047), SDAI (r=-0.535; p=0.018), SJC (r=-0.504; p=0.028), and TJC (r=-0.517; p=0.023) in treatment naïve ERA patients, but not in those with established disease. There was no correlation with CRP in any patient group.
**Conclusions:** Higher miR-126 levels reflect lower disease activity in treatment naïve ERA patients. We hypothesize that significant downregulation of miR-126 levels in RA patients may be modified by previous exposure to multiple treatments.
**Acknowledgement:** MHCR 023728 project
**Disclosure of Interest:** None declared
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## SAT0069 THE VALIDATION ABOUT THE MEASUREMENT OF JOINT SPACE DISTANCE BY USING SUPER RESOLUTION IMAGE AND CURVE FITTING METHODS

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**Background:** Cartilage loss is irreversible progress, so physicians have to find the detection of joint space narrowing as early as possible. It is stated that physical disability in rheumatoid arthritis (RA) is associated with joint space narrowing rather than erosion [1], so early detection of progressive joint damage is the most important. But in DICOM which is the international standard for medical images, 1 pixel on radiographic images is 0.10 to 0.15 mm, so the detection of the change which is lower than that is impossible.To solve this problem, we previously developed new method measuring the joint space distance with the X-rays image which performed super-resolution image processing [2]. However, we did not validate the measured value by our methods.
**Objectives:** To validate the measurement of joint space distance by using super resolution image and curve fitting methods. We also evaluated whether the focus-film distance affected the measured value.
**Methods:** We producted phantom model (PM) of joint space that expressed metacarpophalangeal joint space 1mm by using 3D printer.The super-resolution images of PM with radiographs by using total variation regularization and shock filter were prepared (Fig. 1). We measured the distance of joint space by three methods, 1) conventional measurement; distance between two points, 2) measurement by using normal vector from the top of joint surface of phalanx bone, 3) measurement using joint space area calculated by integration method. Each method processed on MATLAB®. 2), 3) methods were processed by curve fitting method which create parabolic curve by choosing some points of joint surface.We measured the distance ten times to adjust the error of measurement.We took radiographs with the focus-film distance under conditions of 90cm, 100cm, 110 cm, respectively.
**Results:** Between the two points method, normal line method and integration method, the mean (standard deviation) of measured value under focus-film distance 90 cm was 1.033 (0.018), 0.964 (0.017), 0.939 (0.009), respectively. Under focus-film distance 100 cm, it was 0.963 (0.031), 0.969 (0.032) ,0.943 (0.025), respectively. Under focus-film distance 110 cm, it was 1.019 (0.026), 0.964 (0.018), 0.943 (0.015) , respectively. There were no significant differences with measured value between three methods under each focus-film distance. There were also no significant differences with each focus-film distance (Fig. 2).

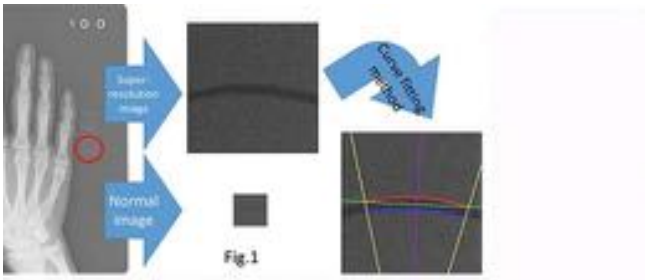



Fig.1

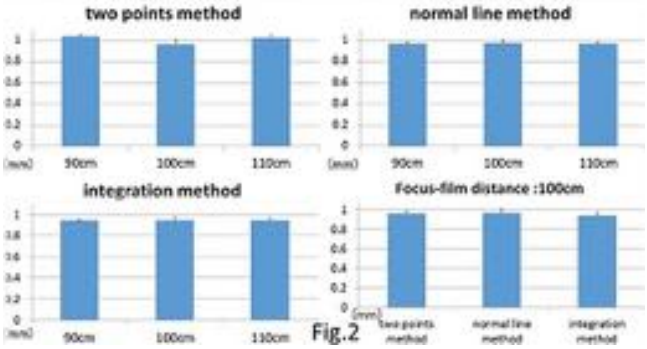



Fig.2

**Conclusions:** The measured value was not affected by a difference of the focus-film distance between 90cm to 110cm.We obtained the measured value, 0.937 – 0.970 by two methods, which were equal to 1mm of PM.The standard deviation was less than 0.032mm. We validated the measurement accuracy of curve fitting methods. We suggested that the possibility of early detection with joint space narrowing in rheumatoid arthritis patients by using super resolution image and curve fitting methods.

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## SAT0070 PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED WITH REMISSION INDUCTION TREAT-TO-TARGET REGIMENS REPORT IMPORTANT EARLY AND LASTING HEALTH IMPROVEMENT: RESULTS FROM THE CARERA TRIAL

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**Background:** Patients' and healthcare providers' perceptions about treatment success can differ. Patient-reported health is therefore an important parameter to consider in daily care, especially in early rheumatoid arthritis (ERA), a disease stage where major health improvements can be realized, and patient adjustment is fully in progress.

**Objectives:** To explore patient-reported health of persons with ERA within the first treatment year.

**Methods:** The CareRA trial is a RCT rooted in daily practice, comparing remission induction treat-to-target regimens in ERA patients stratified in risk groups based on classical prognostic markers: in the high-risk group, patients were randomized to 1/3 intensive combination therapies with moderate-to-high-dose glucocorticoid bridging; in the low-risk group, patients were randomized to MTX monotherapy or MTX with moderate dose glucocorticoid bridging. The Short-Form 36 (SF36) questionnaire was used to assess 8 health dimensions at treatment initiation (BL), 4 months (W16) and 1 year (W52) later. Missing data were handled according to the SF36 user's manual. Differences in patient-reported health between risk and treatment groups, and between patients in remission (DAS28-CRP $<2.6$) or not were tested with Mann-Whitney U or Kruskal-Wallis.

**Results:** Participants (n=379) shared characteristics with a typical ERA population; 66.2% was in remission at W16. The SF36 scores improved in all treatment groups at W16 and no differences between or within risk groups were observed, except for the general health dimension, which differed at W16 ($p<0.001$) and showed a different evolution (p=0.047) across the high-risk treatment arms. At W52, only the physical functioning score differed across the low-risk treatment arms (p=0.024). The largest health improvement was seen over the first 4 treatment months, while scores remained stable up to W52. The largest mean improvements were observed within physical health domains, e.g. "role physical" (30.84±45.07); but patients also reported progress in the mental health dimensions, e.g. "vitality" (10.44±19.39). Nevertheless, some participants did not report any improvement, e.g. 26 patients (8.52%) perceived no change in "physical functioning" after 4 months and 36 patients (11.80%) reported lower scores (mean change = -12.31±15.31), regardless of being in remission or not at W16 (p=0.93). Patients in remission at W16 scored significantly better for "mental health" ($p<0.001$) at W16, and for "role emotional" ($p<0.001$) at W16 and in terms of 4-month change (p=0.01).

**Conclusions:** In our ERA population, important improvement in patient-reported health was seen at W16 lasting up to W52. Perceived health hardly differed between risk and treatment groups, which could be expected within a treat-to-target approach. Despite substantial improvements at group level, some patients did not perceive progress. Our future research will explore this particular subset, including also psychosocial health determinants, as these patients are likely to benefit from more tailored care interventions.

**Disclosure of Interest:** None declared

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## SAT0071 NUMBER OF AUTOANTIBODIES ASSOCIATED WITH ALL-CAUSE MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Patients with rheumatoid arthritis (RA) show higher mortality rates than the general population (1). The increase has been correlated with several features as the long-term activity of the disease, corticosteroid use and autoantibody seropositivity. Regarding autoantibodies, an increase in mortality has been associated with rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), but there is not consensus on the relative role of them. Recently, the anti-carbamylated protein antibodies (anti-CarP) have also been associated with increased mortality in RA patients (2), but in the early RA patients that were studied only RF seemed to be independently associated with all-cause mortality.

**Objectives:** The aim of this study was to determine the association of RF, ACPA and anti-CarP autoantibodies with all-cause mortality in patients with established RA.

**Methods:** Patients with established RA were recruited from 2001 to 2009 and followed until November 2015. Full data were available for 274 patients and only this subset was included in the present analysis. Anti-CarP was assessed by homemade ELISA with in vitro carbamylated fetal bovine serum (3). Cox proportional hazards regression models for all-cause mortality were used adjusting for age, sex and smoking status, and hazard ratios (HR) of ACPA, anti-CarP and FR positivity were obtained in antibody-specific and -combination models.

**Results:** At recruitment, patients showed the following characteristics: age =68.6 years (SD=7.95), disease duration =16.1 years (11.28), RF =61.8%, ACPA =66.4%, anti-CarP =40.2%, ever smokers =19.7%. At the end of the study 171 patients have died (62.4%). Age and smoking at recruitment showed increased hazard ratios for all-cause mortality, whereas gender was not associated.

Each of the three RA autoantibodies was associated with increased all-cause mortality in antibody-specific analysis with very similar HR: RF =1.59 (1.03–2.44, p=0.036), ACPA =1.57 (1.01–2.45, p=0.046), and anti-CarP =1.60 (1.07–2.39, p=0.024). The similarity of effects was also observed in the combined analysis including a variable for each of the antibodies, with the following HR: RF =1.30 (0.79–2.14), ACPA =1.22 (0.72–2.05), and anti-CarP =1.37 (0.88–2.13), none of them significant. Therefore, it seemed appropriate to consider the three autoantibodies as additive factors: the additive showed HR for the number of autoantibodies =1.29 (1.08–1.56, P=0.007) per each additional antibody.

**Conclusions:** The three RA autoantibodies were associated with increased all-cause mortality without clear differences between them, making it appropriate to consider the antibodies as additive factors contributing to risk stratification. This additive contribution is similar to the described for other aspects of RA activity and severity where patients with the largest number of autoantibodies are the most affected.

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## SAT0072 ULTRASOUND IS ASSOCIATED WITH LATE PHASES PRECEDING THE CLINICAL ONSET OF RHEUMATOID ARTHRITIS IN INDIVIDUALS GENETICALLY AT RISK

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**Background:** Identifying pre-clinical phases of rheumatoid arthritis (RA) is challenging. Musculoskeletal ultrasound (US) is more sensitive than clinical assessment for the detection of synovitis. US abnormalities have been associated with subsequent joint inflammation in patients with anti-citrullinated peptide antibodies (ACPA) without clinical synovitis (SJ)[1].
**Objectives:** To identify US abnormalities associated with the recognized phases of RA development[2] in individuals at increased risk for RA.
**Methods:** This is a nested cohort study within an ongoing prospective study of individuals genetically at risk of developing RA, namely first degree relatives of patients with RA (FDR). Individuals without clinical evidence of RA were enrolled, and then followed-up yearly. We included in this analysis all individuals with available ACPA status (anti-CCP 2, 3.0, or 3.1) and US assessment. The US examination was conducted according to the validated SONAR score[3] and performed by US trained rheumatologists blinded to clinical and biological data. According to previous publications[4], inflammatory activity on US (active US) was defined as a Bmode score ≥9 and at least one synovitis of grade 2 or 3, or a Doppler score ≥2. We used logistic regression to analyze univariable and multivariable associations between US findings and specific phases preceding RA development and other patient characteristics.
**Results:** A total of 269 FDRs were analyzed, of which 97 (36%) had an active US as defined above. Individuals with an active US tended to be older (years median (IQR): 51 (41–59) vs 47 (35–57), OR: 1.0, 95% CI: 1.0–1.0, p<0.05), with no difference in sex, body mass index and tobacco smoking. In univariable analyses, there was a strong correlation between an active US and the presence of 'unclassified arthritis' (≥1 SJ on physical examination) (OR:2.6, 95% CI:1.4–4.9). No association was demonstrated with genetic risk factors (presence of shared epitope), systemic autoimmunity (ACPA positivity) or self reported symptoms in the absence of arthralgia or SJ (Table 1). In the multivariable analyses, the relation between US and 'unclassified arthritis' remained significant (OR:2.4, 95% CI:1.3–4.5).

Table 1. Phases of RA development[2]

| n(%) | Non-active US (n=172) | Active US (n=97) | Univariable OR (95%CI) |
|---|---|---|---|
| Shared epitope (1 or 2 copy) | 58 (34) | 27 (28) | 0.8 (0.4-1.3) |
| ACPA without arthralgia or SJ | 8 (5) | 6 (6) | 1.4 (0.5 – 4.0) |
| Arthralgia or CSQ+3 without SJ | 11 (6) | 6 (6) | 1.0 (0.3-2.7) |
| ACPA and arthralgia without SJ | 9 (5) | 6 (6) | 1.2 (0.4-3.5) |
| Unclassified arthritis (≥1 SJ) | 23( 13) | 28 (29) | 2.6 (1.4-4.9)[a] |

SJ: swollen joint, CSQ: Connective Tissue Disease Screening Questionnaire, (a) P<0.05

**Conclusions:** In individuals at risk of RA, active US was strongly associated with the presence of "unclassified arthritis". There was no association between US findings and earlier identified phases of RA development. These data suggest that in individuals at increased risk for RA, without obvious disease, US may identify imminent RA. These findings support the usefulness of US in a screening strategy for imminent RA.
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## SAT0073 GOOD THERAPEUTIC RESPONSE WITH BIOLOGICS BUT PATIENTS' AND PHYSICIANS' OPINION ARE DIFFERENT. DATA FROM THE AUSTRIAN BIOREG REGISTRY

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**Background:** The discordance between patients and physicians in estimation of patients' global health is well known especially from RA patients. We tried to find out whether differences in global health estimation are the same in patients with different diseases using data of the Austrian biologic registry.
**Objectives:** The aim of this evaluation was to elucidate the amount of differences between PGA (Patient Global disease Activity) and EGA (Evaluator's Global disease Activity) in patients with rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA) at baseline and at control visits every six months after inclusion in *BioReg*.
**Methods:** Data were extracted from the Austrian *BioReg* registry (http://www.bioreg.at) which was initiated in 2009 to document patients treated with one of the nine biologics (abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab, tocilizumab) approved in Austria. Patients with ongoing biologic therapy as well as biologic-naïve patients starting biologic therapy can be included (baseline, BL). Further documentation is recommended about every six months (V1, V2 up to V11). Meanwhile, 1663 patients (rheumatoid arthritis (RA) n=948, ankylosing spondylitis (SpA) n=400, psoriatic arthritis (PsA) n=267, other disease n=48) have been documented. Estimation of global health is done using a visual analogue scale (VAS with 100 mm, 0 = no disease) by patients (PGA) and by physicians (EGA) at every visit.
**Results:** VAS (median values of BL; V1; V2; V3; V4; V5) of patients with RA showed differences between PGA (30; 20; 22; 20; 20; 20) and EGA (15; 7; 10; 10; 10) as well as in SpA (PGA 39; 30; 26; 30; 30; 20 and EGA 20; 10; 10; 10; 10; 10) and in PSA (PGA 30; 10; 12; 20; 20; 10 and EGA 20; 10; 5; 10; 10; 10). Median values of inflammation's laboratory markers (ESR in mm/1st hour and CRP in mg/l) were always within the normal range (ESR and CRP in RA 5; 12; 14; 12; 14; 14 and 2,0; 2,0; 2,2; 2,0; 2,0; 2,0; in SpA: 7; 7; 7; 8; 7; 7 and 1,5; 1, 5; 1,7; 1,4; 1,2; 1,1 and in PsA 8; 8,5; 9; 9; 10; 10 and2,0; 1,7; 1,4; 1,0; 1,0; 1,0).
**Conclusions:** As described for RA we also saw in patients with RA but also in SpA and PsA, that physicians' estimation of global health is always better than patients' values at all visits. We suppose that physicians focus primarily on signs of active inflammation and less on general feeling. The normal values of ESR and CRP support this assumption.
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## SAT0074 NO NEED TO DETECT ANTI-DRUG ANTIBODIES IN PATIENTS TREATED WITH TNF INHIBITORS

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**Background:** Formation of anti-drug antibodies (ADA) might be responsible for sub-therapeutic serum drug levels resulting in a lack of clinical response. The need to test ADA levels in patients treated with a TNF inhibitor is the subject of discussion (1, 2).
**Objectives:** ADA levels were measured in patients treated with ADL or ETN or IFX to check immunogenicity in patients receiving various TNF inhibitors and clarify whether ADA measurement reflects treatment output.
**Methods:** Frozen serum samples from patients with rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriasis arthritis (PsA) and treated with adalimumab (ADL; n=41) or etanercept (ETN; n=42) or infliximab (IFX; n=42) were selected. All patients were receiving continuous care of one of the authors. Anti-ADL, anti-ETN or anti-IFX levels were tested with commercially available assays (*Grifols Deutschland GmbH*) according to the manufacturer's instructions. Drug levels were also determined with assays from the same manufacturer.
**Results:** Among ADL-treated patients we found 8/41 (20%) to be positive for ADA. In the ETN group elevated ADA levels were found in 3/42 (7%) patients; in the IFX group 8/42 (19%) patients had positive ADA levels. High ADA concentrations did not always correlate with diminished therapeutic response. Among ADA positive patients 3/8 in the ADL group (1 of each disease), 3/3 in the ETN group (RA 2, SpA 1) and 5/8 in the IFX group (RA 1, PsA 3, SpA 2) continued the given therapy

with good response. The three positive ETN patients showed only borderline elevated ADA levels.
**Conclusions:** ADA levels were more often found in patients treated with ADL or IFX than with ETN. These results agree with those of previous studies (3) and might indicate differences in immunogenicity between these three TNF inhibitors. Nevertheless positive ADA levels did not always indicate failure of therapy. The low incidence of ADA levels, the high cost of ADA assays and the absence of a need to change therapy based on ADA levels have to be considered before ADA analysis is ordered within a routine control.
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## SAT0075 VALIDATION OF THE RHEUMATOID ARTHRITIS PREDICTION RULES FOR THE DISEASE DEVELOPMENT IN PATIENTS WITH JOINT PAIN FROM WEST SWEDEN

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**Background:** Rheumatoid arthritis (RA) is a joint destructive disease, which leads to physical disability. There is no cure of RA today. Thus, recognition of RA at preclinical stages is essential for successful treatment.
**Objectives:** To validate and improve known prediction rules aiming at early recognition of clinically suspect arthralgia and diagnosis of RA.
**Methods:** Medical records of 241 first-time patients with clinically suspect joint pain were evaluated for RA diagnosis by the 2010 EULAR/ACR criteria (1) and by the RA prediction rules (13-points, Amsterdam (2)); and 16-points clinical assessment (Leiden (3)) and prospectively followed during 29–47 months. All the patients were a part of the inception cohort of 5455 patients whose samples were tested for RF and/or ACPA during 12 consecutive months at the Laboratory of Clinical Immunology at the University Hospital of Gothenburg. Patients with known diagnosis of RA, other rheumatic disease and chronic pain conditions were excluded. The utility of arthritis-specific autoantibody status (ACPA and/or RF) and the family history for RA prediction were analyzed.
**Results:** The RA criteria applied to the records of the first visit identified 24% of patients as RA (EULAR score mean 7.6), 30% as undifferentiated arthritis (UA, EULAR score mean 3.6), while the remaining 45% of the patients were characterized as arthralgia (EULAR score mean 2.3). The 13-point and 16-point prediction rules allocated RA patients to the high-risk group with comparable sensitivity of 78% and 91%. The significant correlation between the two models was present in UA (r=0.398; p=0.0005) and arthralgia (r=0.411; $p<0.0001$) groups, but not in RA (r=0.0007, ns). Specificity for RA diagnosis at the first visit was higher in the 13-point rule (90.5%), however it was not discriminative between the arthralgia and UA groups. The clinical 16-point assessment discriminated successfully between RA/UA and between UA/arthralgia groups. The 16-point assessment allocated 50% of patients with UA to the high-risk group, which affected specificity. During the follow-up period, 23 cases of new RA and 5 UA were registered. The sensitivity of the 16-point assessment at the first visit was 60%, similar for the antibody-positive and for antibody–negative cases. The sensitivity of the 13-point rule was 21% (p=0.003), and was selective for the antibody-positive cases. At the first visit, subjects with family history of RA were over-represented in the arthralgia group (p=0.022). At follow-up only 1 of them developed UA.
**Conclusions:** Both prediction rules are shown to be sensitive identify RA patients at assessment. The clinical 16-point assessment has prospective sensitivity for new cases. This is shown independently of autoantibody status and family history of RA.
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## SAT0076 UTILITY OF SURVIVIN MEASUREMENTS FOR EARLY RECOGNITION OF CLINICALLY SUSPECT ARTHRALGIA AND DIAGNOSIS OF RHEUMATOID ARTHRITIS IN WEST SWEDEN

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**Background:** Recognition of rheumatoid arthritis (RA) at preclinical stages is essential for successful treatment, long-term functional ability and survival. Available serological markers of the disease are restricted to acute-phase reactants and presence of autoantibodies - rheumatoid factor (RF) and ACPA. Although specific, these markers cover less than a half of the patients with RA. Oncoprotein survivin has been recently identified as a marker of severe RA frequently associated with progressive joint damage and poor response to antirheumatic treatment (1). A pilot study on the samples from the Nordic Biobank showed that survivin could predict development of RA several months ahead of clinical symptoms (2).
**Objectives:** To validate the utility of survivin measurements for early recognition of clinically suspect arthralgia and diagnosis of RA in the epidemiological setting.
**Methods:** The first-visit patients with joint pain from the inception cohort of 5455 subjects tested for RF and/or ACPA during 12 consecutive months at the Laboratory of Clinical Immunology at the University Hospital of Gothenburg, were evaluated for RA diagnosis by the 2010 EULAR/ACR criteria (3). Patients with known diagnosis of RA, other rheumatic disease and chronic pain conditions were excluded. The subjects not fulfilling RA diagnosis at the first visit were prospectively followed during 29–49 months. The utility of survivin measurement and arthritis-specific autoantibody status (ACPA and/or RF) for RA diagnosis were analyzed.
**Results:** The total of 385 patients were included in the study. RA criteria applied to the records of the first visit identified 17% of patients as RA. Additional 21% of patients were recognized as undifferentiated arthritis (UA), while the remaining 62% of the patients were characterized as arthralgia. Majority of the RA patients were survivin positive (52%) with an overlap for antibodies (RF and/or ACPA) in 88%. The UA and arthralgia groups had low prevalence of patients positive for survivin (p=0.018) and for autoantibodies (p=0.002). During the follow-up period, 23 cases of new RA and 5 new UA were registered. The incidence of new cases was significantly higher among the survivin-positive patients and corresponded to the increased risk compared to survivin-negative (p=0.008). The combination of survivin and autoantibodies increased further the risk for development of the disease compared to negative patients (RR 4.05[ 1.73–9.20], p=0.002). The presence of isolated survivin was also associated with higher risk of RA (RR 2.55 [1.14–5.71], p=0.028), while no increase in RA risk could be shown for the isolated presence of autoantibodies.
**Conclusions:** This prospective study showed in the epidemiological setting that the presence of survivin was associated with an increased risk of RA. Combination of survivin and autoantibodies further increased this risk.
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## SAT0077 PROGNOSTIC FACTORS FOR ABATACEPT RETENTION IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A JAPANESE MULTICENTER REGISTRY

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**Background:** In recent years, it has been reported that baseline anti-cyclic citrullinated peptide (CCP) antibody positivity is associated with a better response and retention rate in patients with rheumatoid arthritis (RA) [1,2]. However, there have been few reports describing the association of prognostic factors with the long-term clinical results represented by drug retention rate.
**Objectives:** The aim of this study was to identify prognostic factors for abatacept (ABT) retention in clinical routine practice using data from a Japanese multicenter registry system for RA patients treated with biological DMARDs.
**Methods:** All eligible RA patients who underwent ABT therapy from October 2010 through to March 2015 (n=513) were prospectively registered in the Tsurumai Biologics Communication Registry (TBCR). Potential prognostic factors such as

baseline demographics and disease characteristics were analyzed using Log-rank test. Variables with a p value of <0.20 were included in the multivariable analysis using a Cox proportional hazard model.
**Results:** The overall retention rate was 58.2% (95% CI; 0.49 - 0.66) at 4 years. Based on Log-rank test, previous biologics treatment (naïve vs. switch), Steinbrocker stage (1–2 vs. 3–4), RF status (negative vs. positive), anti CCP antibody status (negative vs positive) and concomitant MTX use (user vs. non-user) were eligible to enter the multivariate model (Table 1). Multivariable analysis revealed that patients had a significantly lower risk of ABT discontinuation if they were biologic-naïve (HR; 0.57, 95%CI; 0.35 - 0.91) and anti-CCP antibody positive (HR; 0.57, 95%CI; 0.32 - 0.99) (Table2). Furthermore, we divided anti-CCP antibody status into three categories (<4.5; negative, 4.5 - <100; low titer, ≥100; high titer) and examined the relationship between titer and retention rate. Kaplan-Meier curve indicated that the retention rate in high titer group was lower than that in low titer group (Figure 1).

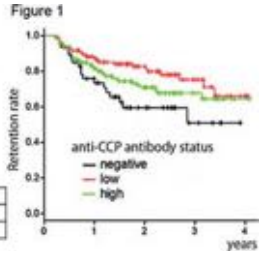
Table 1

| Variables | Log-rank |
|---|---|
| naïve vs. switch | p<0.001 |
| stage (1-2 vs.3-4) | p=0.086 |
| RF (negative vs. positive) | p=0.159 |
| anti CCP antibody (negative vs. positive) | p=0.035 |
| MTX (user vs.non-user) | p=0.060 |

Table 2

| Variables | adjusted HR (95% CI) | p-value |
|---|---|---|
| naïve vs. switch | 0.568 (0.354 - 0.912) | 0.019 |
| anti CCP antibody (negative vs. positive) | 0.567 (0.323 – 0.995) | 0.048 |

Figure 1




**Conclusions:** This study demonstrated that baseline anti-CCP antibody positivity is associated with a better long-term retention of ABT therapy. But additional therapeutic intervention would be necessary for patients with high titer to improve the short- and long-term clinical results of ABT.
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## SAT0078 PROSPECTIVE OBSERVATIONAL STUDY TO EVALUATE THE USE OF MUSCULOSKELETAL ULTRASONOGRAPHY TO IMPROVE RHEUMATOID ARTHRITIS MANAGEMENT: CANADIAN EXPERIENCE (ECHO)

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**Background:** Musculoskeletal Ultrasound (MSUS) has been shown to be superior to clinical examination in the detection of synovitis in patients with Rheumatoid Arthritis (RA), and can be used to improve diagnostic accuracy [1] and potentially monitor disease changes in order to make treatment decisions aimed at optimizing patient care. Since the creation of the Canadian Rheumatology Ultrasonography Society (CRUS) in 2010, an increasing number of rheumatologists has been trained in the use of MSUS.
**Objectives:** The overall study objective is to compare the effectiveness of MSUS to Routine Care (RC) as a disease management tool in patients with moderate-to-severe RA for whom a change in treatment is indicated. The study also assessed the predictive power of US assessments.
**Methods:** Descriptive interim analysis of the "Echo" study, a prospective two-cohort, quasi-experimental study of patients diagnosed with active moderate-to-severe RA managed either with MSUS or as per RC. In order to be eligible for the study patients must require a change in treatment as per the judgment of the treating physician. Patients are followed for 1 year with assessments at baseline, 3, 6, 9, and 12 months. Outcome measures of interest include CDAI Remission, DAS-28 Remission and DAS-28 Low Disease Activity (LDAS).
**Results:** A total of 339 patients (70.1% female) with a mean (SD) age of 58.7 (11.79) years and disease duration of 7.4 (10.2) years were enrolled, without any significant differences between treatment groups. There were no differences between the two treatment groups with respect to the study outcomes. However, higher total US Erosion Scores at baseline were associated with lower rates of LDAS at 9 months (OR =0.810; P=0.047) and 12 months (OR =0.808; P=0.078) and lower rates of DAS-28 Remission at 9 months (OR =0.811; P=0.60); higher total synovitis GREY scale at baseline was associated with a lower rate of LDAS at 6 months (OR =0.913; P=0.014) and DAS – 28 Remission at 3 months (OR =0.911; P=0.074)
**Conclusions:** MSUS assessments can be useful predictors of future disease remission in patients with RA. The impact of MSUS on disease management and clinical outcomes requires further study.
**References:**
[1] Colebatch AN et al. Ann Rheum Dis 2013, 72:804–814.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4230

## SAT0079 CHARACTERIZATION OF RA PATIENTS WITH A DAS28 RESPONSE TO ADALIMUMAB THERAPY BY IMPROVEMENT IN PAIN: A GERMAN NONINTERVENTION STUDY

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**Background:** In daily clinical practice, therapeutic responses (eg, Disease Activity Score-28 joints [DAS28]) are not always associated with improvements in pain in patients with rheumatoid arthritis (RA).
**Objectives:** To evaluate pain responses in RA patients with a DAS28 response to adalimumab (ADA) therapy.
**Methods:** We analyzed data from two large German multicenter observational studies of patients with active RA who initiated ADA therapy during routine clinical care. Patients were classified on the basis of significant responses in DAS28 and pain (on a scale of 0=best; 10=worst), as determined by statistical analyses of the critical difference for individual improvement.[1] Patients with a significant DAS28 improvement at month 12 (≥1.8 points from baseline) and significant pain improvement (≥3 points from baseline) were compared with patients with a significant DAS28 response, but no significant reduction in pain. Outcomes included fatigue, patient global assessment (PGA), and physician global assessment (MDGA) (all on a scale of 0=best to 10 = worst) and function as assessed by the Funktionsfragebogen Hannover questionnaire (FFbH; % remaining function).
**Results:** Of 5745 patients in the full analysis set, 1509 patients had available data on pain and a significant DAS28 response at month 12. Of these patients, 1038 had a significant improvement in pain and 471 did not. Baseline characteristics and concomitant medications were similar between the two groups (Table). After 24 months of ADA therapy, both groups had similar swollen and tender joint counts and levels of inflammatory markers. Patients with both DAS28 and pain responses had better functional status at month 12 than patients without an improvement in pain (mean FFbH=76.0% vs 68.8%; $P<0.0001$), despite lower mean baseline values (56.8% vs 63.8%). Significant differences ($P<0.0001$ for all) in favor of patients with pain responses were also observed in mean values for fatigue (2.8 vs 4.2), PGA (3.0 vs 4.5), and MDGA (2.3 vs 2.9) at month 12.
**Conclusions:** Approximately two-thirds of patients with a significant therapeutic response to ADA at month 12 also have a significant improvement in pain. There were no obvious differences in baseline characteristics between patients with or without improvements in pain. Patients with improvements in both DAS28 and pain have significantly less fatigue and significantly improved function and global disease activity at month 12 compared with patients who have a DAS28 response, but no improvement in pain.
**References:**
[1] Behrens F et al. Arthritis Care Res. 2013;65:1608–16.
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## SAT0080 EQUIVALENCE OF DIFFERENT VERSIONS OF THE HEALTH ASSESSMENT QUESTIONNAIRE (HAQ) ACROSS SOCIO-ECONOMIC FACTORS IN THE MULTI-NATIONAL QUEST-RA STUDY

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**Background:** Several studies reported socio-economic (SE) gradients in physical function as assessed by HAQ. It is however not known whether this reflects true differences in physical function among socio-economic groups, or whether differential interpretation of HAQ items across SE groups biases item responses.
**Objectives:** To investigate differential item functioning (DIF) across SE factors (age, gender, education and work status) when assessing physical function in RA patients across the different composite HAQ scores.
**Methods:** Data from the Questionnaires in Standard Monitoring of Patients with Rheumatoid Arthritis (QUEST-RA), comprising 8,891 patients from 30 countries (mean age 55 years, 81% females) were used. Physical function in daily activities

was assessed using a set of 30 individual items from the different HAQ versions (Stanford HAQ, HAQ-II, modified HAQ (MHAQ) and multi-dimensional HAQ (MDHAQ)). SE factors comprised age, gender, education (years), and work status (yes or no).

DIF was investigated using item response theory models implemented in a latent variable modelling framework, with models equivalent to ordinal logistic regressions having answers on each HAQ as outcome and SE factors as well as the latent trait function as predictors. Scores for 4 composite HAQs were recalculated and adjusted for DIF by methods similar as above, but simultaneous modelling all previously identified items exhibiting DIF. To assess the impact of DIF on associations between SE factors and composite HAQ scores, multilevel mixed effect linear regression models were estimated with individuals nested in country. Models were adjusted for SE factors, disease activity score in 28 joints (DAS28)) and a comorbidity index (Rheumatic diseases comorbidity index (RDCI)). Changes in the strength of association between SE-factors and HAQ or for DIF-adjusted HAQ were investigated by comparing β-coefficient of the SE factors in the models.

**Results:** Relevant DIF (defined as OR $>1.1$ or $<0.90$, ($\Delta \geq 10\%$)) in HAQ items was found for the SE factors age (n=13 items), gender (n=26 items) and work status (n=20 items), whereas education influenced only few items (n=7) (table) (table). Adjustment of composite HAQs for DIF resulted in an increase of HAQ scores, indicating influence of individual item DIF on the composite scores (table). In regression models all SE factors remained significantly related to all composite HAQ before or after adjusting for DIF. Changes in coefficients of regression models were overall negligible, except for gender (all HAQ versions). β-coefficients for gender increased by up to 0.07 (70% coefficient change), indicating several items have for women a different meaning, independent of their underlying level of functional limitation.

Table: Differential item functioning (DIF) of health assessment questionnaire across socio-economic factors

| | Health Assessment Questionnaire HAQ version | | | | DIF (Odds Ratio (OR), 95% CI) | | | |
|---|---|---|---|---|---|---|---|---|
| HAQ item, short description | HAQ | MHAQ | MDHAQ | HAQ-II | Age (per 10 years) | Education (standardized OR, SD=4.1 years) | Gender (reference: male) | Employment status (reference: not working) |
| dress | ✓ | ✓ | ✓ | | | | | |
| shampoo | ✓ | | | | | | | |
| stand up | ✓ | | | ✓ | | | | |
| get in/out of bed | ✓ | ✓ | ✓ | | | | | |
| cut meat | ✓ | | | | | | | |
| lift cup | ✓ | ✓ | ✓ | | | | | |
| open milk | ✓ | | | | | | | |
| walk outdoor | ✓ | ✓ | ✓ | ✓ | | | | |
| climb 5 step | ✓ | | | | | | | |
| wash body | ✓ | ✓ | ✓ | | | | | |
| take bath | ✓ | | | | | | | |
| get on/off toilet | ✓ | | | ✓ | | | | |
| reach objects | ✓ | | | ✓ | | | | |
| bend down | ✓ | ✓ | ✓ | | | | | |
| open car | ✓ | | | ✓ | | | | |
| open jars | ✓ | | | | | | | |
| turn faucets | ✓ | ✓ | ✓ | | | | | |
| run errands | ✓ | | | | | | | |
| get in/out of car | ✓ | ✓ | ✓ | | | | | |
| do chores | ✓ | | | | | | | |
| walk 2 miles | | | ✓ | | | | | |
| run 2 miles | | | ✓ | | | | | |
| climb stairs | | | ✓ | | | | | |
| climb 2+25ins | | | | ✓ | | | | |
| lift heavy object | | | | ✓ | | | | |
| move heavy object | | | | ✓ | | | | |
| drive 5 miles | | | ✓ | | | | | |
| wait in line 15 min | | | | ✓ | | | | |
| outside work | | | | ✓ | | | | |
| sports | | | ✓ | | | | | |
| Composite HAQ (mean (SD)) | 0.66 (0.66) | 0.58 (0.59) | 0.76 (0.62) | 1.01 (0.74) | | | | |
| Composite HAQ adjusted for DIF (mean (SD)) | 0.74 (0.62) | 0.63 (0.59) | 0.76 (0.62) | 1.06 (0.72) | | | | |

In bold: relevant DIF (OR $>1.1$ or $<0.90$, $\Delta \geq 10\%$). *False discovery rate (5%) adjusted p-value $<0.001$

HAQ=Stanford HAQ, MHAQ=Modified HAQ, MDHAQ=Multidimensional HAQ, DIF=Differential Item Functioning, SD=Standard Deviation

**Conclusions:** Relevant measurement bias across SE factors was found for a number of individual HAQ items. In composite HAQ scores, some evidence for measurement issues remains. Although not having a major impact in terms of measurement of physical function, there is some need for caution when comparing HAQ between males and females.

**Disclosure of Interest:** None declared

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## SAT0081 THE DIAGNOSTIC AND PREDICTIVE VALUE OF ANTI-ACETYLATED PEPTIDE ANTIBODIES (AAPA) IN RHEUMATOID ARTHRITIS PATIENTS STARTING THEIR FIRST DMARD TREATMENT ON METHOTREXATE

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**Background:** Anti-acetylated-peptide antibodies (AAPA) have recently been described in rheumatoid arthritis (RA) patients and may be used as a further diagnostic marker in patients with undifferentiated arthritis (1).

**Objectives:** To determine the prevalence of AAPA in a cohort of RA patients starting their first conventional synthetic DMARD treatment (csDMARD). In addition, we aimed to evaluate the usefulness of AAPA as potential predictors of clinical response to methotrexate (MTX) therapy.

**Methods:** We measured IgG and IgA AAPA by ELISA using two acetylated peptides derived from vimentin. We tested by regression, parametric and non-parametric analyses of disease activity measures if AAPA show potency for predicting response to MTX.

**Results:** Among 110 patients starting treatment on MTX, 74.5% were positive for IgG and/or IgA AAPA: 49% were positive for either IgA or IgG antibodies and 25.5% were IgA/IgG double positive. In comparison, 63.6% of the patients were positive for either RF or ACPA (measured by the CCP assay). In the AAPA positive patients; in total, 26.4% of the patients showed IgA antibodies and 73.6% were positive for IgG AAPA. Importantly, of the 36.4% of patients negative for both RF and ACPA (double negative), 55% were positive for IgG and/or IgA AAPA, and the remaining 45% (i.e. 16% of the total cohort) were completely seronegative (triple-negative; see table). When comparing triple negative patients with the AAPA positive double-negative ones, no significant difference in baseline characteristics was found but a trend that patients with more seroreactivities showed higher composite disease activity scores. Analyzing the clinical response to MTX, AAPA positive double-negative patients showed a significantly greater relative SDAI change after 6 months compared to triple-negative patients (p=0.028; median (IQR): -44.6% (-58.5 - -28.90) vs. 5.26% (-23.9 - 55.5%). In addition, there was a significantly greater relative change in CRP and erythrocyte sedimentation rate in AAPA positive double-negative patients.

In a backward regression model only RF could significantly be associated with the SDAI response, leading to + 30% relative change in SDAI (p=0.024). Status of ACPA and AAPA as potential predictors had to be excluded. Furthermore, RF positive patients showed larger relative changes in CRP, ESR, SDAI, CDAI and DAS after 6 months of MTX treatment

Table 1. Crosstable of status of RF, ACPA and anti-acetylated peptide antibodies (AAPA)

| | Anti-acetylated peptide antibodies | | | Total |
|---|---|---|---|---|
| | Negative | IgA or IgG positive | IgA and IgG positive | |
| Negative | 16.4% | 16.4% | 3.6% | 36.4% |
| RF | 3.6% | 3.6% | 2.7% | 10% |
| ACPA | .9% | 1.8% | 0.9% | 3.6% |
| RF+ACPA | 4.5% | 27.3% | 18.2% | 50% |
| Total | 25.5 | 49.1 | 25.4 | 100% |

**Conclusions:** AAPA commonly occur in RA patients and were, in fact, the most prevalent autoantibodies in our cohort. Measuring AAPA in addition to RF and ACPA reduced the prevalence of seronegative patients by more than 50%. These AAPA positive but RF and ACPA negative patients responded significantly better to MTX. Therefore, AAPA positivity in RF and ACPA negative patients identifies a subgroup of patients with a more favourable response to MTX.

**References:**

[1] Juarez M, Bang H, Hammar f et al. Ann Rheum Dis 2015 Jul 9; Epub ahead of print.

**Disclosure of Interest:** P. Studenic: None declared, S. Blüml: None declared, H. Bang Employee of: has developed the assay, M. Unger: None declared, K. Raza: None declared, D. Aletaha: None declared, J. Smolen: None declared, G. Steiner: None declared

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## SAT0082 BIOLOGICAL THERAPY AND IMPROVEMENT OF DISEASE ACTIVITY IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS IN A SPECIALIZED CENTER

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**Background:** Biological therapy is useful to prevent clinical and radiological progression in patients with rheumatoid arthritis (RA) when there is a failure with conventional DMARD therapy. Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA). On the other hand a multidisciplinary care team (MCT) model was generated in order to improve outcomes.

**Objectives:** The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 24-month period in patients with biological DMARD therapy in a large cohort of patients from a Colombian specialized in RA center with a MCT model.

**Methods:** A descriptive retrospective study was performed. Records of patients using biologics from specialized in RA center were reviewed; those patients were followed-up under T2T standards. Clinical follow-up was according to DAS28: every 3–5 weeks (DAS28 $>5.1$), every 7–9 weeks (DAS28 $\geq 3.1$ and $\leq 5.1$), and every 11–13 weeks (DAS28 $<3.1$). Therapy had to be adjusted with DAS28 $>3.2$ unless patient's conditions don't permit it. A MCT model means that a patient should be seen by other specialties such as physiatrist, physical and occupational therapy, nutritionist and psychologist at least 3 times a year. We divided patients in three groups: low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission (REM). Descriptive epidemiology was

done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson's statistics.
**Results:** 370 patients were included in this study, 310 (83%) women and 60 (17%) men. Average age was 59 ± 9 years. The biological therapy was distributed: Infliximab 57 (15%), Abatacept 53 (14%), Adalimumab 53 (14%), Etanercept 52 (14%), Rituximab 46 (12%), Tocilizumab 46 (12%), Certolizumab 41 (11%), Golimumab 19 (5%). At 24 months was observed an increase in percentage of patients (up to 71%) in REM/LDA and a decrease in percentage of patients in MDA/SDA disease activity statistically significant. At beginning mean DAS28 was 4.3 ± 1.23 and after 24 months of follow-up mean DAS28 was 3.02 ± 0.72; the median was analyzed using t-Student assuming normality for DAS28 distribution; it showed improvement ($p<0.00$).

| ACTIVITY LEVEL | TIME 0 n (%) | 6 MONTHS n (%) | 12 MONTHS n (%) | 24 MONTHS n (%) |
|---|---|---|---|---|
| REM | - | 72 (19) | 137 (37) | 145 (39) |
| LDA | 73 (19) | 85 (23) | 73 (20) | 118 (32) |
| MDA | 195 (53) | 178 (48) | 142 (38) | 103 (28) |
| SDA | 102 (28) | 95 (9) | 17 (5) | 4(1) |

**Conclusions:** There was a global improvement of DAS28 in a cohort of RA patients receiving biological therapy followed and treated under recommendations of T2T strategy and MCT model; this revision shows the importance of T2T follow-up and treatment for this disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5528

## SAT0083 ON THE RELATIONSHIP BETWEEN RHEUMATOID FACTORS, MONOCYTE SUBSETS AND FC RECEPTOR FUNCTION IN EARLY RA

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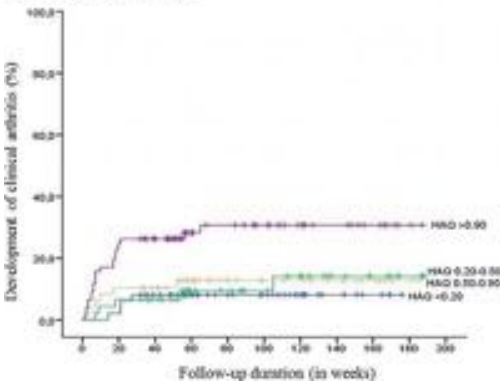
**Background:** Immunoglobulins (Ig) and immune complexes (ICs) intervening with complement and Fc receptors (FcR) are important for the pathogenesis of rheumatoid arthritis (RA). Thus, B-cells are interesting targets for controlling chronic inflammation and autoantibody production (rheumatoid factors (RF) and ACPAs), especially in seropositive disease. In inflamed RA joints, accumulated FcR bearing monocytes/macrophages contribute to inflammation by cytokine release and antigen presentation. These cells consist of subpopulations with different features and may be defined by the composition of specific membrane receptors. However, the association between RA-specific antibodies and monocyte function in early RA is poorly studied.
**Objectives:** We have previously reported on altered monocyte FcR expressions, FcγR function and IgG load in an early RA cohort which reflected joint disease activity (ref). Here we were interested in evaluating the systemic B-cell activity in the same patients and related these findings to monocyte subpopulations, the FcγR function and to treatment response.
**Methods:** The sera of 20 early DMARD- and steroid naïve RA patients and 33 matched HCs were analyzed for Ig isotypes, IgG subclasses, the IgM, IgG and IgA RF isotypes and ACPA-IgG with standardized methods or with ELISA kits. Correlations of the Ig measurements with available data on the patients' monocyte FcγR function (eq. IgG1/IgG3 IC binding and TNFα production after IgG1/IgG3 stimulation) and monocyte subpopulations (defined by CD14/CD16 expression) were performed. The patients were evaluated before and after 3 months of treatment with methotrexate (MTX) and prednisolone (PRED). At follow up the individual treatment effect was determined using the EULAR response criteria. The distribution and the amount of the 3 RF isotypes among the responder groups were determined.
**Results:** The RA patients presented higher levels of total IgG, the IgG1 and IgG3, and all tested RF isotypes than the HCs. These findings correlated negatively with the monocyte FcγR function; high levels of all 3 RF isotypes reflected low IgG1-IC binding capacity, and high IgA-RF titers were associated with low monocytic TNFα release after IgG1- and IgG3-IC stimulation. These findings did not apply to the ACPA-IgG titers. A general observation of higher pre-treatment levels of Igs and auto-antibodies in the non responders was made, these individuals also maintained high levels of IgG3 and IgM-RF at follow up. Interestingly, an increase in the classical monocyte subset was seen in the non responders compared to the HC. And these non responders also had fewer non classical monocytes compared with the good responders. A good treatment response was observed in those patients who initially presented with few concurrent RF isotypes and low titers thereof.
**Conclusions:** In early naïve seropositive RA elevated specific IgG subclasses and RFs reflect an immune state of decreased monocyte FcγR function. An altered distribution of the monocyte subpopulations can be observed which may reflect the patients' treatment response. A good response to a combined MTX/PRED therapy is more likely to be observed in those patients who present low systemic B-cell activity.
**References:**
[1] P Matt et al: Elevated Membrane and Soluble CD64: A Novel Marker Reflecting Altered FcγR Function and Disease in Early Rheumatoid Arthritis That Can Be Regulated by Anti-Rheumatic Treatment. DOI: 10.1371/journal.pone.0137474
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4818

## SAT0084 EVALUATION OF FUNCTIONAL DISABILITY IN PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA

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**Background:** A phase of arthralgia precedes the emergence of rheumatoid arthritis (RA). This phase is not yet well characterized. The presence of MRI-detected subclinical inflammation has been identified in this phase and is correlated with RA development. However, it is unknown if patients with arthralgia at risk for RA (with and without subclinical inflammation) have functional limitations.
**Objectives:** This study assessed functional disability in patients with clinically suspect arthralgia (CSA) and the associations with MRI-detected inflammation and progression to clinical arthritis.
**Methods:** Between April 2012 and April 2015 patients were included in the CSA cohort. Patients with CSA were defined as having no clinical arthritis, with symptoms of hands or feet for <1 year and were considered to be at risk for RA by their rheumatologists based on their clinical presentation. At baseline, functional disability was assessed using HAQ scores and unilateral 1.5 T extremity MRIs of wrist, MCP and MTP joints were made. MRIs were scored on synovitis, tenosynovitis and bone marrow edema (BME) by two independent readers. The sum of these features yielded the total MRI-inflammation score. Pearson correlation coefficients, linear regression models, paired t-tests and Cox proportional hazards regression analyses were used.
**Results:** Of the 255 patients included, 77% were female and the mean age was 44.2 years. Median HAQ score was 0.50 at baseline and median duration of follow-up was 61 weeks. In univariable linear regression, a higher total inflammation score was significantly associated with a higher HAQ score (β=0.01, p=0.019). Of the individual types of inflammation, tenosynovitis showed the strongest correlation (β=0.04, p=0.003). When evaluating subclinical inflammation at specific hand joints in relation to HAQ-questions measuring hand function, significant correlations were observed. For instance, difficulties with opening previously opened jars was associated with MRI-inflammation score at the wrists (Pearson r=0.18, p=0.011). Patients that progressed to clinical arthritis had higher HAQ scores at presentation, than CSA-patients that did not progress (median HAQ scores 0.90 and 0.50 respectively). HAQ scores above 0.90 in particular were associated with arthritis development (HR=2.62, 95% CI: 1.06–6.47, p=0.036) as shown in the Kaplan-Meier plot (figure 1). An analysis of the patients that did develop arthritis revealed that median HAQ-scores were the same both at initial presentation with CSA and at conversion to clinical arthritis (median HAQ scores 0.90 and 0.68 respectively, paired t-test p-value = 0.751).

Figure 1. Kaplan -Meier One Minus Survival plot showing cumulative progression to clinical arthritis for CSA patients divided in four groups based on their baseline HAQ score.




**Conclusions:** CSA-patients already have functional limitations. The severity of functional disability is associated with the severity of local subclinical inflammation. CSA-patients that progressed to clinical arthritis had high HAQ scores at baseline and these HAQ scores did not increase when arthritis became clinically evident.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4047

## SAT0085 DO SPECIFIC ACPAS OR OTHER AUTOANTIBODIES MEASURED BY A NOVEL ASSAY PREDICT RESPONSE TO METHOTREXATE MONOTHERAPY IN PATIENTS WITH EARLY DMARD-NAÏVE RA?

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**Background:** Antibodies against citrullinated peptide antigens (ACPAs) strongly predict the risk of developing RA. ACPA also seem to predict a more severe RA phenotype.
**Objectives:** Little is, however, known about the predictive value of specific ACPAs, or other autoantibodies (AAbs), in terms of response to methotrexate treatment.
**Methods:** A total of 20 AAbs were measured by a custom-made microarray assay based on the ImmunoCAP ISAC system (*Phadia AB, Uppsala, Sweden*), in baseline samples from patients participating in two randomized controlled trials (RCTs): Swefot, n=340; Improved, n=450). Validation was performed in two large inception cohorts (EIRA linked to the SRQ register, n=1481; Glasgow, n=384). All patients started methotrexate in monotherapy as their first DMARD. Response to methotrexate was defined as EULAR response at first follow-up visit (3–6 months). The likelihood of EULAR good or moderate (vs. no) response was calculated by logistic regression adjusted for potential confounders, and the proportion of patients positive for each AAb is provided (adj. OR, 95%CI; *% positive*).
**Results:** For the RCTs, 5 out of 20 AAbs were significantly associated with response in Improved, and 1 out of 17 in Swefot (fewer peptides on an earlier version of ISAC). *Fib36_52_cit* (citrullinated fibrinogen) was significantly associated with good/moderate response in both RCTs (Improved: adj.OR=2.27 (1.19–4.31), *32% positive*; Swefot: adj.OR=1.87 (1.06–3.29), *44% positive*). *Fib591_cit* (also citrullinated fibrinogen) was associated with good/moderate response in Improved (adj.OR=3.70 (1.27–10.76), *15% positive*) and a non-significant trend was observed in Swefot (adj.OR=1.65 (0.89–3.06), *30% positive*). *Vim60_75_cit* (citrullinated vimentin) was associated with response in Improved (adj.OR=1.85 (1.06–3.21), *46% positive*) but not in Swefot (adj.OR=1.06, *63% positive*). For *CEP_1*, a borderline significant association was observed in Improved (adj.OR=1.70 (0.96–3.00), *40% positive*) but not in Swefot (adj.OR=0.90, *51% positive*). Further, AAbs against citrullinated peptides named pept_Z2 and pept_5 were associated with response in Improved (adj.OR=1.81 (1.02–3.23), *41% positive*; and 2.25 (1.27–4.01), *44% positive*, respectively), while no association was observed in Swefot (adj.OR=0.98 and 1.17). Interestingly, none of the above associations were replicated in the inception cohorts (EIRA-SRQ, Glasgow), nor did we observe any trend for a dose-response association with response for the total number of positive AAbs.
**Conclusions:** Whilst two AAbs against citrullinated fibrinogen predict response to methotrexate in both early RA RCTs, neither these nor any other of the AAbs tested predicted response in the real-life population-based inception cohort setting. The reasons for the discrepant results are not yet clear, but our results highlight the importance of testing in multiple study populations and settings when identifying predictors to be used for clinical prediction.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4451

## SAT0086 THE SHORT-TERM AND LONG-TERM OF HUMERAL IMMUNE RESPONSES TO HEPATITIS B VACCINATION ARE IMPAIRED IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING CONVENTIONAL AND BIOLOGICAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

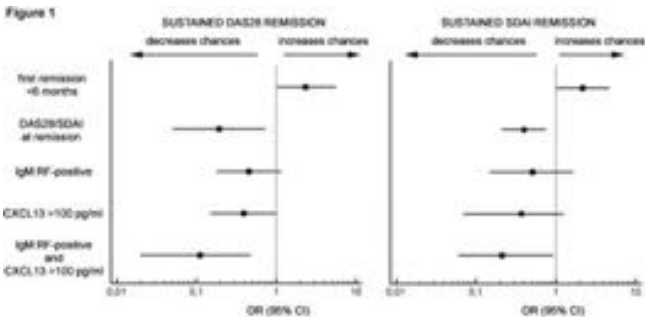
S. Intongkam, M. Muthanugulwong, R. Pakchotanon, P. Narongroeknawin, P. Asavanabodee, S. Chaiamnuay. *Medicine, Phramongkutklao Hospital, Bangkok, Thailand*

**Background:** Hepatitis B vaccination is recommended for rheumatoid arthritis (RA) patients in many international guideline. However, the short-term and long-term efficacies of hepatitis B vaccination in RA patients that recieved conventional and/or biological disease-modifying anti-rheumatic drugs (cDMARDs and/or bDMARDs) are not clearly established.
**Objectives:** To assess the long term of immunogenicity of the hepatitis B vaccination in rheumatoid arthritis (RA) patients receiving cDMARDs and/or bDMARDs.
**Methods:** The study comprised 45 patients with RA, of whom 33 received cDMARDs and 12 received bDMARDs therapy (study group), and 9 subjects with age- and sex-matched healthy controls (control group). All subjects were vaccinated with 20 $\mu$g of recombinant hepatitis B vaccine (Euvax B®) at weeks 0, 4, and 24. Blood samples were collected 8 weeks and 12 months after receipt of the third vaccine dose to test for antibody to hepatitis B surface antigen (anti-HBs). Responders (seroprotection) were defined as anti-HBs level $\geq$10 mIU/mL. The study was approved by the ethic committee and institutional review board.
**Results:** Baseline characteristics of study and control groups were similar. Patients receiving cDMARDs tended to has lower proportion of seroprotection than control group (69.7% vs 100%, p=0.09) at 2 months and (57.57% vs 100%, p=0.016) 12 months after receipt of the third vaccine dose. Patients receiving bDMARDs had a significantly lower proportion of seroprotection compared with control group (50% vs 100%, p=0.02) at both 8 weeks and 12 months after receipt of the third vaccine dose. The proportion of seroprotection is significantly decreased between 2 months and 12 months in patients receiving cDMARDs (69.7% vs 57.57%, p=0.044) after completion of the third dose vaccine.
**Conclusions:** DMARDs both conventional and biological DMARDs therapy impaired short-term and long-term immunogenic response to hepatitis B vaccine.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5505

## SAT0087 SERUM LEVELS OF CXCL13 REFINE THE PREDICTIVE ABILITY OF AUTOANTIBODIES TO IDENTIFY UNSTABLE REMISSION IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Early achievement and maintenance of disease remission improve long-term outcomes in patients with rheumatoid arthritis (RA), and eventually allow therapeutic withdrawal. Better knowledge of the prevalence and prognostic factors for sustained remission might improve patient care according to their individual profile. RA-specific autoantibodies are associated with a less favorable disease course, but their impact on the achievement and sustainability of remission upon treatment in early RA remains controversial.
**Objectives:** To evaluate whether additional B cell-related markers, such as serum levels of the B-cell chemoattractant CXCL13, predict different remission outcomes in patients with early RA.
**Methods:** We evaluated 205 RA patients from the Pavia early arthritis inception cohort not in remission at baseline with at least 2 years of follow-up, for whom baseline serum was available. Patients had arthritis of short duration ($<$12 months) and were treatment-naïve at presentation. After diagnosis, patients were initiated a treat-to-target regimen with methotrexate aiming at low disease activity and were seen at 2-months intervals for the first six months and then trimestrally. Levels of rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA) and CXCL13 were determined on baseline sera. Point remission was defined as the achievement of DAS28 remission ($<$2.6) or SDAI remission ($\leq$3.3) at any time within the first 12 months. Mean DAS28 $<$2.6 and mean SDAI $\leq$3.3 in the 3 visits following first remission (7–9 months) were regarded as sustained remission.
**Results:** 95/205 (46.3%) patients achieved point DAS28 remission and 69/205 (33.7%) point SDAI remission, with a median (IQR) time to remission of 6 (2–9) and 6 (4–9) months respectively. Male gender, younger age, a lower TJC28, better functional status, absence of radiographic erosions and use of prednisone were independent predictors of point remission. No significant effects of the autoantibody status and CXCL13 levels, alone or in combination, were seen. Irrespective of the remission criterion, more than half of the patients lost remission at follow-up (54.7% for DAS28, 62.3% for SDAI). Shorter time to remission and deeper remission were independent predictors of sustained remission (Figure 1). The ACPA status did not significantly impact the chance of sustaining remission. In contrast, both DAS28 and SDAI remission showed a trend to be less frequently maintained in RF-positive patients and in patients with baseline serum levels of CXCL13 $>$100 pg/ml (Figure 1). The combination of RF-positivity and high CXCL13 independently predicted failure to sustain remission with an adjusted OR (95% CI) of 8.49 (1.95 to 36.91) for DAS28 and 4.61 (1.01 to 24.67) for SDAI (Figure 1).




**Conclusions:** Disease remission is unfrequently maintained in early RA patients despite steered treatment strategies. B-cell autoimmunity does not significantly impact the chance of ever achieving remission. However, RF-positivity in combination with high CXCL13 identify a subgroup of patients at particularly high risk of losing remission in the short-term, irrespective of how early and how stringent remission is achieved.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5176

SAT0088 **ANTI-JAK IS ANTI-FIBROTIC IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Objectives:** To quantify connective tissue turnover from type III collagen in response to 4 different types of intervention in rheumatoid arthritis (RA); methotrexate (MTX) combined with or without either tocilizumab (TCZ), tofacitinib (TOFA) or adalimumab (ADA) in RA.
**Methods:** 149 RA patients were treated with 1) MTX; 23, 2) ADA+MTX; 49, 3) TOFA+MTX; 27 or 4) TCZ+MTX; 50. Four specific neo-epitopes biomarkers were measured in the serum samples; C3M and PRO-C3 markers of type III collagen degradation and formation respectively.
**Results:** Tissue destruction measured by C3M increased in RA patients and was significantly correlated with total sharp score (SHS) as well as disease activity (DAS28) at baseline even after adjustment for covariates (rho=0.20, 0.33, p=0.018, <0.0001, respectively). PRO-C3 was also increased and the levels correlated with both SHS, and DAS28 (rho=0.22, 0.43, p=0.0067, <0.0001, respectively). Tissue destruction measured by C3M was reversed to healthy levels in all treatment after the treatment with MTX, ADA+MTX, TOFA+MTX or TCZ+MTX. However, JAK inhibition resulted in a decrease of PRO-C3, a sign of fibrogenesis, whereas MTX increased PRO-C3 in RA. (Figure)

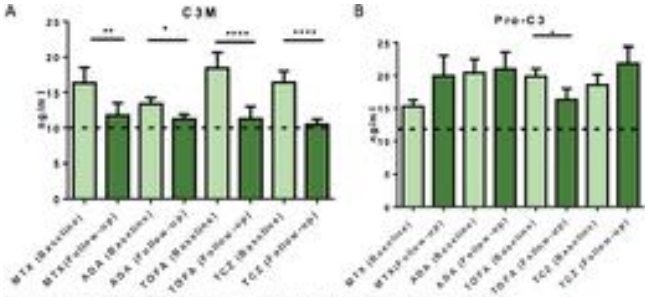



Figure: Evaluations of biomarker levels at baseline and follow-up: A) Type III collagen degradation evaluated by C3M. B) Type III collagen formation evaluated by PRO-C3. Difference between baseline and Follow-up was evaluated by mean of Wilcoxon match pairs signed rank test. The dashed line represents a reference level of healthy controls as provided by the manufacturer. *p≤0.05, ** p≤0.01, ***p≤0.001, ****p≤0.0001. Error bars are illustrated as SEM.

**Conclusions:** Interstitial tissue remodeling was increased in RA as compared to healthy controls. All four different intervention inhibited inflammation-driven tissue destruction to the same level, whereas only TOFA blocked fibrogenesis in RA patients, indicating that JAK inhibition could attenuate tissue fibrosis.
**Disclosure of Interest:** S. Hirata Speakers bureau: AbbVie, Eisai, Bristol Meyers Squibb, N. Gudmann Employee of: Nordic Bioscience A/S, S. Kubo: None declared, M. Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, A. Bay-Jensen Employee of: Nordic Bioscience A/S, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Chugai, MSD, Astellas, Novartis, Speakers bureau: Abbvie, Chugai, Astellas, Takeda, Santen, Mitsubishi-Tanabe, Pfizer, Janssen, Eisai, Daiichi-Sankyo, UCB, GlaxoSmithKline, Bristol-Myers
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SAT0089 **ANXIETY AND DEPRESSION AMONG RHEUMATOID ARTHRITIS PATIENTS, AND ASSOCIATION WITH CLINICAL MEASUREMENTS AND PATIENT REPORTED DISABILITY AND TREATMENT SATISFACTION**

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**Background:** Rheumatoid arthritis (RA) has a substantial negative impact on patients' (pts) lives and is marked by pain and reduced mobility. In addition to RA articular manifestations, RA is often associated with important extra-articular manifestations, including anxiety and depression.[1]
**Objectives:** To describe pt self-reporting of anxiety and depression in pts with RA and to better characterize the association of anxiety/depression with disease activity, disability, and satisfaction with current treatment.
**Methods:** Descriptive analyses and multivariate linear and logistic regression analyses were performed using mood disorder data from the EU5 and US Adelphi RA Disease Specific Program. Presence of anxiety and depression was reported by pts that completed the EQ-5D anxiety/depression domain in the Patient Self Completion form. Multivariate models were run, controlling for pt age, gender, body mass index, and current disease severity, for each of the following measures: WPAI, HAQ-DI, DAS28 (ESR), and pt satisfaction with current treatment. WPAI, HAQ-DI, and DAS28 (ESR) data were evaluated using linear models, and pt-reported satisfaction were evaluated using logistic regression models.
**Results:** For the sample of pts included in the analysis (n=1,015), 38.4% of pts reported moderate or extreme anxiety/depression as their current health state. Pts with self-reported moderate (n=349) or extreme (n=41) anxiety/depression had greater work impairment, higher scores on the HAQ-DI, higher scores on the DAS28 (ESR), and a higher likelihood of being dissatisfied with their current treatment than those without stated depressed mood or anxiety. (n=625; Table). In multivariate analyses, significant differences were observed between the presence of pt-reported moderate anxiety/depression and higher WPAI scores ($P<0.001$), higher HAQ-DI scores ($P<0.001$), and lower pt-reported satisfaction with current treatment ($P<0.001$); significant differences were also observed between the presence of pt-reported extreme anxiety/depression and poorer results on the DAS28 (ESR) ($P=0.004$), HAQ-DI ($P<0.001$), and pt-reported satisfaction with current treatment ($P=0.001$), all compared to pts without anxiety or depression.

Table 1. Disease activity, disability, and treatment satisfaction in pts by self-reported anxiety and depression and severity

| Measure | No reported anxiety/depression (n=625) | Moderate anxiety/depression (n=349) | Extreme anxiety/depression (n=41) |
|---|---|---|---|
| Mean (SD) percent overall work impairment[a] | 18.3 (21.7) | 37.6 (26.4) | 36.4 (28.4) |
| Mean (SD) HAQ-DI score[a] | 0.6 (0.6) | 1.1 (0.7) | 1.5 (0.8) |
| Mean (SD) DAS28 (ESR)[a] | 3.4 (1.3) | 3.8 (1.5) | 4.8 (1.5) |
| Proportion dissatisfied with current treatment, % (n/n)[a] | 16.6 (96/579) | 36.0 (113/314) | 56.4 (22/39) |

[a] *P*-value for global test <0.0001.

**Conclusions:** Anxiety and depression represent a significant burden for pts with RA. In this analysis, pt-reported mood disorders were independently associated with work impairment, disability, pt satisfaction with current treatment, and clinical disease activity. These findings highlight the multi-dimensional impact of anxiety and depression as a key extra-articular manifestation of RA. Further research on optimal management of this key unmet medical need is warranted.
**References:**
[1] Isik A, et al. Clin Rheumatol. 2007;26(6):872–878.
**Disclosure of Interest:** S. Peterson Shareholder of: Janssen, Employee of: Janssen, N. Li Employee of: Janssen, S. Blackburn Employee of: Adelphi Real World, D. Kielar Shareholder of: Janssen, Employee of: Janssen
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SAT0090 **THREE OUT OF EVERY FOUR PATIENTS WITH DMARD-NAIVE EARLY RHEUMATOID ARTHRITIS MEET DAS28 REMISSION AT 12 MONTHS IN FINLAND**

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**Background:** Finnish national combination treatment trials [1,2] have demonstrated excellent outcomes in patients with early rheumatoid arthritis (RA)

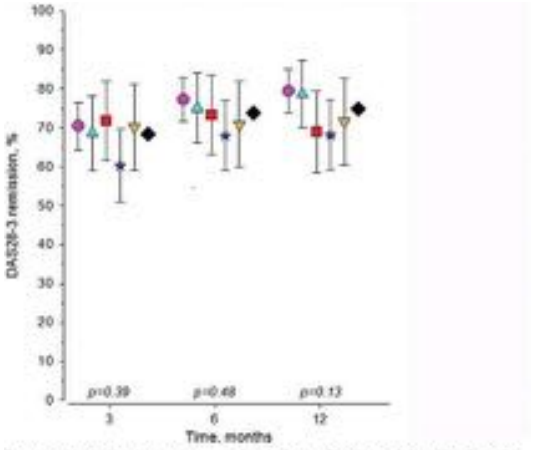



Figure 1. Remission proportions at 3, 6 and 12 months visits at 5 FIN-ERA clinics by DAS28-3 remission criteria.
*Values are percentage of RA patients with 95% CIs. Pink ball = Site A; Blue star = Site B; Turquoise triangle = Site C; Orange triangle = Site D; Red square = Site E. Black diamond = Entire cohort.

including 90% of patients reaching 28-joint Disease Activity Score (DAS28) remission. Whether similar results are reached in clinical praxis is not known.
**Objectives:** To assess what proportion of patients with dmard-naïve early rheumatoid artritis (RA) reach DAS28 remission over one year and remission variability across clinics in Finland
**Methods:** Patients with dmard-naïve inflammatory arthritis diagnosed as new early RA were recruited. Comparison among sites were made in proportion of patients in 28-joint Disease Activity Score with 3 variables (DAS28–3) remission. Repeated measures were analyzed using mixed models approach with appropriate distribution and link function.
**Results:** 611 patients were recruited at 5 sites: 67% female; the mean age (SD) at diagnosis was 57 (16) years; respective 71% and 68% were RF and AntiCCP positive; 23% had radiographic erosions. A total of 506 (83%) fulfilled the ACR/EULAR 2010 classification criteria for RA for further analyses. DAS28–3 remission was met by 68% and 75% at 3 and 12 mo, respectively. Clinic had no effect in remission when adjusted for confounders (Figure 1). At baseline, a total of 68% used MTX based combination therapy, and 31% used triple therapy with methotrexate, hydroxychloroquine and sulphasalazine. In multivariate analysis, the only independent predictors of DAS28–3 remission at 12 mo were lower baseline DAS28–3 (odds ratio 0.6, 95% confidence interval 0.4–0.7, $P<0.001$) and triple therapy as the initial treatment (odds ratio 1.8, 95% confidence interval 1.0–3.3, $P=0.048$).
**Conclusions:** Three out of every four dmard-naïve early RA patients are in remission in Finland after 1 year of diagnosis. High remission rates were achieved with use of csDMARDs in combinations for majority of patients. Treatment with triple therapy is a predictor of DAS28–3 remission also in real-life rheumatology settings.
**References:**
[1] Möttönen T, Hannonen P, Leirisalo-Repo M, Nissilä M, Kautiainen H, Korpela M, et al. Comparison of combination therapy with single-drug therapy in early rheumatoid arthritis: A randomised trial. FIN-RACo trial group. Lancet 1999; 353:1568–73
[2] Leirisalo-Repo M, Kautiainen H, Laasonen L, Korpela M, Kauppi MJ, Kaipiainen-Seppänen O, et al. Infliximab for 6 months added on combination therapy in early rheumatoid arthritis: 2-year results from an investigator-initiated, randomised, double-blind, placebo-controlled study (the NEO-RACo Study). Ann Rheum Dis 2013;72:851–7
**Acknowledgement:** We would like to thank study nurses. This study was supported by Pfizer.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4894

## SAT0091 MAJOR CLINICAL CHARACTERISTICS OF CHINESE RHEUMATOID ARTHRITIS (RA) PATIENTS WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) UNDER TREAT-TO-TARGET (T2T) RECOMMENDATIONS

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**Background:** Treat-to-target (T2T) is a widely accepted management strategy for rheumatoid arthritis (RA) to achieve defined outcomes (remission or low disease activity). Moreover, mobile applications of patient-centered care created by multidisciplinary teams have been used for disease management in rheumatology. Smart System of Disease Management (SSDM) is a series of applications system for chronic diseases management.
**Objectives:** To describe major clinical characteristics of Chinese RA patients using SSDM under T2T recommendation in real world.
**Methods:** The SSDM includes doctors' application system and patients' application system. The patient application system includes self-assessment (DAS28, HAQ), medication management, adverse events management and laboratory records. After data entry, patients can synchronize data to the authorized doctor. The data were collected online from 173 rheumatology centers that cover 27 provinces in China. All patients fulfilling the 1987 ACR (formerly the American Rheumatism Association) criteria for RA were recruited. The median of each variable was analyzed using t-test assuming normality for DAS28 distribution and the level disease activity was analyzed using Pearson's statistics.
**Results:** Since December 14th, 2014 to January 25th, 2016, 2,585 patients, 1,854 (71.7%) women and 731 (28.3%) men, participated in this study. Average age was 49.4 ±12.86 (15–90) years with mean disease duration of 8.9 years. The mean DAS28 scores was 4.03±1.54 (0.62–8.84) and the mean HAQ scores was 2.80±4.33 (0–24). At the Baseline, 19.5% of patients got remission, 12.9% low disease activity (LDA), 43.5% moderate disease activity (MDA) and 24.1% high disease activity (HDA). Clinical remission rate was negatively correlated with HAQ scores. For the entire cohort, the most commonly used treatment were conventional DMARDs (92.7%) include leflunomide (65.52%), hdroxychloroquine (48.52%), methotrexate (39.00%) and sulfasalazine (5.77%).
**Conclusions:** SSDM has provided demographic and clinical data of Chinese RA patients in real world practice. Clinical data and biologic samples would be valuable resources for future national and international studies.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5352

## SAT0092 PREVALENCE OF SUBCLINICAL INFLAMMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAVE LOW DISEASE ACTIVITY

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**Background:** Studies using ultrasound (US) showed that a significant proportion of patients thought to be in clinical remission actually exhibited different grades of synovitis, and a subgroup of these patients suffered from flares and/or joint damage during follow-up[1].
**Objectives:** Evaluate joint inflammation by ultrasound in patients with different stages of rheumatoid arthritis as the primary endpoint measure.
**Methods:** Gray scale and power Doppler ultrasound were performed on the dorsal radio-scaphoid, dorsal radio-lunae, ulnar-triquetrium, and palmar radio-lunate joints of both wrists. The presence of synovitis, comorbidities, and use of disease modifying anti-rheumatic drugs were recorded. Patient with a bilateral wrist score sum (GSUS + PDUS) equal or greater than 4 was considered to have sonographic inflammation. A logistical regression model was used to identify factors associated with inflammation.
**Results:** There were 1248 patients (1010 females, 238 males; mean age: 59.61 ± 12.19 years). Synovitis was most common at the dorsal radio-lunate joint. Patients with high disease activity (DAS28 $>5.1$) had more sonographic inflammation than those with moderate or low disease activity. Most patients (57.4%) in complete remission (DAS28 $<2.6$) had subclinical synovitis (Table). Logistical regression analysis indicated that male sex, smoking, and liver disease are positively associated with inflammation and that advanced age, alcohol consumption, hypertension, gastrointestinal disease, and use of MTX, glucocorticoid, or a biological therapy are negatively associated with inflammation. Use of biological agents decreased the risk of inflammation by 40.9%.

Table 1

| DAS28 | 0 | 1 | 2 | 3 | ≧4 | Total |
|---|---|---|---|---|---|---|
| Complete remission, n (%) | 2 (1%) | 12 (5.9%) | 28 (13.9%) | 44 (21.8%) | 116 (57.4%) | 202 (100%) |
| Low disease activity, n (%) | 2 (0.9%) | 14 (6.5%) | 20 (9.3%) | 42 (19.6%) | 136 (63.5%) | 214 (100%) |
| Moderate disease activity, n (%) | 4 (0.6%) | 20 (3.1%) | 75 (11.5%) | 123 (18.8%) | 431 (66%) | 653 (100%) |
| High disease activity, n (%) | 10 (5.6%) | 8 (4.5%) | 20 (11.2%) | 21 (11.7%) | 120 (67%) | 179 (100%) |
| Total, n (%) | 18 (1.4%) | 54 (4.3%) | 143 (11.5%) | 230 (18.48%) | 803 (64.3%) | 1248 (100%) |

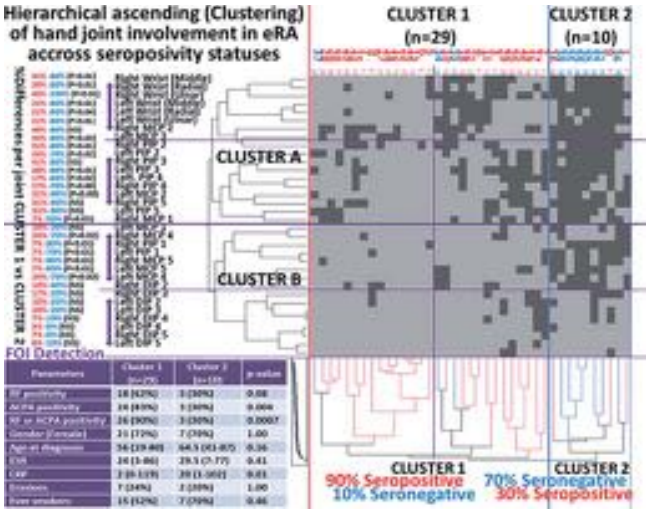
**Conclusions:** There was sonographic evidence of synovitis in most patients who were in complete remission. Regular monitoring of rheumatoid arthritis patients with ultrasound and DAS28 may help prevent disease flare-ups and joint destruction.
**References:**
[1] Brown AK, et al. Arthritis and Rheumatism 2006;54:3761–3773.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5332

## SAT0093 HAND JOINT INFLAMMATION ON FLUORESCENCE OPTICAL IMAGING REVEAL DISTINCT PATTERNS IN SEROPOSITIVE AND SERONEGATIVE EARLY RHEUMATOID ARTHRITIS

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**Background:** Detection of abnormal Rheumatoid Arthritis (RA) related autoantibodies, Rheumatoid Factor (RF) and Anti-Citrullinated Peptide Antibody (ACPA), along with Musculoskeletal ultrasound (MSUS) play a critical role in the diagnosis of early RA (eRA). Fluorescence optical imaging (FOI) is an emerging modality designed for the hands and wrists that detects subclinical hand joint inflammation[1] and may therefore prove valuable in the assessment of eRA.
**Objectives:** Here, we analyzed the FOI results of eRA patients and investigate whether patterns of hand joint inflammation may distinguish seropositive from seronegative RA.
**Methods:** In FOI, Inflammation is considered positive, when altered microcirculation (capillary leakage/perfusion) is seen as abnormally increased focal optical signal intensities by visual inspection of the entire image series in real-time (360 seconds all 34 joints: 3 wrists, 5 MCPs, 5 PIPs and 4 DIPs, bilaterally are evaluated

using post-processing imaging techniques). Unsupervised ascending hierarchical clustering was used to identify clusters of patients with different patterns of joint involvement in FOI. The robustness of the clustering was verified using another clustering method (k-means), and agreement between the 2 methods was assessed using Cohen's kappa. Baseline clinical and biological characteristics of patients were compared between the clusters using non-parametric tests.
**Results:** Out of 1326 joints of 39 eRA patients (26 females; 9 with erosive RA; 54% RF+; and 69% ACPA+), 400 (30%) were considered positively inflamed by FOI. The mean (±SD) number of active joints detected by FOI was 10.3 ± 7.2. Clustering of joint involvement according to the FOI distinguished 2 separate clusters of patients: Cluster1 (n=29) and Cluster2 (n=10). The proportion of seropositive patients was significantly higher in cluster 1 versus cluster 2 (26/29 versus 3/10, $p<0.01$) (figure). The distribution of inflammation throughout the joints, except for right MCP2, PIPs 5, left MCP1 & DIPs in cluster 2 displayed distinguishable patterns ($p<0.05$) compared to cluster 1, which showed joint inflammation to be largely concentrated around wrists, right MCP2, bilateral MCP3, and to a lesser degree around PIPs 2–4, and left MCP2. The DIPs showed no significant differences between clusters.




**Conclusions:** Two separate patterns of inflammatory joint involvement may be distinguished in early RA, using fluorescence optical imaging. The proportion of seropositive patients was significantly different between these patterns, suggesting that FOI identifies patterns of joint involvement that are different for seropositive and seronegative RA.
**References:**
[1] Kisten Y, Györi N, af Klint E, et al. 2015 Detection of clinically manifest and silent synovitis in the hands and wrists by fluorescence optical imaging. RMD Open 2015;1: e000106. doi:10.1136/ rmdopen-2015-000106 (http://rmdopen.bmj.com/content/1/1/e000106.full.pdf+html)
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4502

## SAT0094 THE ASSOCIATION BETWEEN METHOTREXATE USE AND EFFECTS OF TREATMENT WITH A SECOND BIOLOGIC AGENT IN RHEUMATOID ARTHRITIS

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**Background:** In general, the concomitant use of methotrexate (MTX) and biologic disease-modifying antirheumatic drugs (DMARDS) plays an important role in treatment for bio-naïve patients with rheumatoid arthritis (RA). However, it remains unclear whether concomitant use of MTX is related to the effects of treatment with second biologic DMARDS in RA patients for whom first biologic DMARDS therapy have failed.
**Objectives:** The objective of the current study was to determine whether, and if so to what extent, concomitant use of MTX was associated with the effects of treatment with second biologic DMARDS, especially in the context of whether or not tumor necrosis factor inhibitor (TNFi) had been used.
**Methods:** We used demographic and clinical data from the Tsurumai Biologics Communication Registry, which comprises Nagoya University and 20 affiliated hospitals in Japan. Patients aged 20–80 years who fulfilled the ACR 1987 revised classification criteria or the 2010 ACR/EULAR classification criteria for RA were selected; only those switching to second biologic DMARDS therapy were included. Multivariate logistic regression analysis was used to assess the association between MTX use and the possibility of sufficient response to second biologic DMARDS treatment, as defined by good response at week 16 in the EULAR response criteria, based on DAS28. Crude and adjusted odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs) were calculated. Adjustment variables included sex, age, disease duration, whether or not TNFi had been used in RA treatments with first and second biologic DMARDS, use of MTX in first biologic treatment, and use of glucocorticoids in treatment with second biologic DMARDS. We determined the statistical significance of potential subgroup effect of whether or not TNFi had been used as second biologics by testing the significance of the interaction terms added to our multivariable models.
**Results:** The demographic and disease characteristics of the patients at baseline were comparable except for the proportion of TNFi between patients not using MTX (n=49) and those treated concomitantly with MTX (n=122). The mean age was 59 years; 86% were women. Patients had longstanding RA (mean 10.6 years), and the baseline DAS28 was 5.2. Among the patients, 68% received glucocorticoids. The mean dose of MTX was 8.0 mg/week in patients using MTX. The proportion of TNFi was 26.5% in patients not using MTX and 62.3% in those using MTX, respectively. A good response as per EULAR response criteria was identified in 14 (28.6%) patients not using MTX and 58 (47.5%) patients treated concomitantly with MTX. The crude OR for the association between concomitant use of MTX and the possibility of good response as per EULAR response criteria was 2.27 (95% CI 1.11–4.63) compared with nonuse of MTX. After adjustment for the aforementioned covariates, concomitant use of MTX was associated with an increased possibility of good response to biologic DMARDS compared with nonuse of MTX (OR 2.77, 95% CI 1.04–7.36). This multivariable adjusted effect estimate was not modified by whether or not TNFi had been used (P value for interaction greater than 0.05).

**Table 1.** Association between MTX use and the possibility of good response as per EULAR response criteria, as determined by binary logistic regression analysis*

| | Crude OR (95% CI) | Adjusted OR (95% CI)† |
|---|---|---|
| MTX not using | 1.00 (referent) | 1.00 (referent) |
| MTX using | 2.27 (1.11–4.63) | 2.77 (1.04–7.36) |

* OR = Odds ratio; 95% CI = 95% confidence interval. MTX = methotrexate
† Adjusted for sex, age, disease duration, whether or not tumor necrosis factor inhibitor had been used in treatments with first and second biologics, use of MTX in first biologic treatment, and use of glucocorticoids in treatment with second biologics.

**Conclusions:** This study demonstrated that concomitant use of MTX was independently associated with an increased possibility of good response to second biologic DMARDS regardless of whether or not TNFi had been used in RA treatment.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5520

## SAT0095 LEUCINE-RICH ALPHA2-GLYCOPROTEIN IS A USEFUL BIOMARKER TO EVALUATE THE CLINICAL DISEASE ACTIVITIES OF RHEUMATOID ARTHRITIS UNDER TREATMENTS

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**Background:** Acute phase biomarkers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are usually used for the evaluation of the disease activity of rheumatoid arthritis (RA). However, these biomarkers are sometimes not useful in evaluating the disease activity of RA patients in daily clinical practice, because they often become within normal range after the initiation of treatments. Thus, new biomarker which reflects the disease activity of RA under the treatment is required. Leucine-rich-α2-glycoprotein (LRG) is a newly identified biomarker that reflects inflammation and is correlated with the 28-joint Disease Activity Score even in patients treated with IL-6 receptor antagonist.
**Objectives:** To assess whether serum LRG levels could be a biomarker to evaluate the disease activity of RA under treatments in daily clinical practice.
**Methods:** Serum LRG levels were measured by enzyme-linked immunoabsorbant assay in 370 consecutive RA patients who were under treatments in our facility in 2012. Disease activity was evaluated by Clinical Disease Activity Index (CDAI) that does not include ESR or CRP as components. Radiological joint destruction was evaluated by modified Total Sharp Score (mTSS). Multivaiate analysis of covariance (MANOVA) was used to assess the association between CDAI and LRG, ESR, CRP levels and the association between mTSS and LRG, ESR, CRP, disease duration, and anti-CCP antibody level.
**Results:** Among 370 patients, 71% were treated by methotrexate and 29% by biological DMARDs and average CDAI was 7.8±6.2 (low disease activity). After MANOVA analysis, LRG but not ESR or CRP showed the significant correlation with CDAI (LRG; effect size 0.034, p=0.0007, CRP; effect size 0.010, p=0.055, ESR; effect size 0.0053, p=0.18). LRG significantly correlated with the disease activities in RA patients, even when ESR or CRP levels were within normal range.

In addition, LRG showed the significant correlation with mTSS as well as disease duration and anti-CCP antibody level (LRG; effect size 0.019, p=0.017, disease duration; effect size 0.769, p<0.001, and anti-CCP antibody; effect size 0.036, p=0.0011), while ESR and CRP did not (ESR; effect size 0.0038, p=0.28, CRP; effect size 0.00073, p=0.64).
**Conclusions:** LRG is useful marker to evaluate the disease activity and to estimate the joint damage of RA patients under treatments in daily clinical practice independent of CRP and ESR levels.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4567

## Rheumatoid arthritis - comorbidity and clinical aspects

### SAT0096 INDICATORS AND FREQUENCY OF HIP SYNOVITIS DETECTED BY ULTRASOUND IN RA

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**Background:** Large joints affection including the hip in RA has significant impact on patient's activity. Unfortunately, clinical detection of hip synovial hypertrophy and effusion is difficult, while Ultrasound is reliable and effective to compensate for such problem[1].
**Objectives:** Identify clinical and Laboratory characteristics associated with Ultrasonographic hip synovitis among RA Patients
**Methods:** We conducted an observational cohort study on 60 RA adult patients fulfilling the 1987 ACR classification Criteria for RA. Exclusion criteria include those with non- RA related Hip Arthritis (Degenerative, Traumatic, Metabolic and referred pain from the back). Grouping: Group I, 30 patients complaining of hip pain and Group II 30 without hip pain. All patients had full history and clinical examination including DAS28, SJC66, TJC68, Patient and Physician Global Assessment of disease activity (PTGA, PGA); and Lab includes ESR, CRP and RF. Ultrasound examination was done according to the standard EULAR guidelines.
**Results:** The following table shows the demographic, clinical and lab characteristics of both groups.

| | Group I | Group II | P-value |
|---|---|---|---|
| Female, n (%) | 22 (73) | 27 (90) | NS |
| Age, mean (SD), years | 32.7 (5.4) | 32.1 (5.9) | NS |
| RA Duration, (SD), years | 5.3 (3.1) | 4.8 (2) | NS |
| SJC 66, mean (SD) | 6.6 (2.5) | 5 (4.8) | NS |
| TJC 68, mean (SD) | 13.7 (4.9) | 10 (7.25) | 0.026 |
| VAS, mean (SD) | 6.6 (0.8) | 5.8 (1.1) | 0.003 |
| PTGA, mean (SD) | 7 (0.7) | 6.2 (1.2) | 0.001 |
| PGA, mean (SD) | 6 (0 .8) | 5 (1.2) | 0.002 |
| SJC 28, mean (SD) | 5.5 (2) | 3.3 (2.1) | <0.001 |
| TJC 28, mean (SD) | 10.5 (3.5) | 7 (3.5) | <0.001 |
| ESR, mean (SD) | 41.8 (13.6) | 35.4 (11.8) | NS |
| CRP, mean (SD) | 7.6 (5.9) | 5.2 (5.2) | NS |
| DAS 28, mean (SD) | 5 (0.65) | 4.2 (0.85) | <0.001 |

The initial intra-group analysis showed no statistically significant difference in all the measurable demographic, clinical and laboratory data between patients with Normal and Abnormal US. Except for duration of symptoms of hip pain in Group I (16.3±9.6 weeks in those with abnormal US vs 4.4±2.3 weeks in those with normal US Scan (P<0.001) by using point Biserial correlation. Regarding US, Synovial Hypertrophy/ effusion (Abnormal US) was found in 14 out of 30 patients (46.7%) in Group I and 10 out of 30 (33.33%) in group II with no significant difference (P=0.29).
Further whole group analysis showed that CRP was statistically significantly higher in patients with abnormal Hip US (24/60 patients) 8.25±5.25 mg/dl than those with normal Hip US (36/60 patients) 5.17±5.58 mg/dl (P=0.036). In addition, Knee effusion and synovial thickening detected by clinical examination was more frequent in patients with abnormal Hip US (than those with normal hip US, 41.7% vs 13.8% (P=0.015).
**Conclusions:** Hip joint is frequently affected in RA and searching for hip joint involvement should not be limited to those complaining of hip pain to exclude subclinical hip involvement.
Apart from CRP, duration of hip symptoms and knee affection, there was no significant correlation between abnormal US and demographics or laboratory data.
**References:**
[1] Di Geso L1, Filippucci E, Riente L, et al. (2012) Ultrasound imaging for the rheumatologist XL. Sonographic assessment of the hip in rheumatoid arthritispatients. Clin Exp Rheumatol. 30(4):464–8.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4566

### SAT0097 EFFECTIVE CONTROL OF RHEUMATOID ARTHRITIS DISEASE ACTIVITY PREVENTS DEVELOPMENT OR ACCELERATION OF SUBCLINICAL ATHEROSCLEROSIS OVER 3 YEARS

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**Background:** Rheumatoid arthritis (RA) associates with increased cardiovascular disease (CVD) morbidity and mortality due to accelerated atherosclerosis, attributed to both classical risk factors and chronic inflammation.
**Objectives:** To examine whether effective inflammation control prevents development and/or modifies acceleration of subclinical atherosclerosis in RA.
**Methods:** Consecutive, non-diabetic RA patients (n=139), aged 61.3 (52.9–67.9) years, with RA duration 10 (5–17) years, followed-up at least every 4 months in our center and previously examined by ultrasonography for subclinical atherosclerosis, were prospectively re-evaluated after 3.2 (3.1–3.3) years. None had known CVD, malignancy, chronic renal failure, or other chronic or acute inflammatory disease at baseline. The only inclusion criterion in the prospective study was effective disease control during the follow-up period, determined arbitrarily as the presence of remission or of low disease activity (DAS28<3.2) for at least 75% of this period. Non-diabetic control individuals without CVD at baseline (n=251, aged 56.1 (44.9–56.1) years) were studied in parallel (median follow-up of 3.2 (3.1–3.3) years). Preclinical atherosclerosis was assessed as described in detail elsewhere [1,2].
**Results:** Formation of new atheromatic plaques in carotid and femoral arterial beds, reflecting atheromatosis, was evident in 22% of RA patients versus 28% of controls. Carotid intima-media thickness, reflecting arterial wall hypertrophy, increased per year by 0.010 (0.002–0.023) in RA versus 0.011 (0.002–0.023) in controls for the left common carotid artery and by 0.010 (0.002–0.023) in RA versus 0.011 (0.000–0.025) for the right common carotid artery. Pulse wave velocity, reflecting arterial stiffness, changed per year by 0.071 (-0.149- 0.275) in RA versus -0.015 (-0.247–0.184) in controls. Two of 139 patients versus 1 of 251 controls developed clinical CVD during follow-up. By multivariate analysis after correcting for age, gender, smoking, body mass index, hypertension, hyperlipidemia, as well as anti-hypertensive and lipid lowering therapies, no statistically significant differences for any of the evaluated markers of subclinical atherosclerosis were found between patients and controls.
**Conclusions:** Effective inflammation control seems to abrogate any RA-specific effect on the progression of atherosclerosis. Whether early and sustained disease control translates to the expected for the general population rates of cardiovascular morbidity and mortality in RA patients remains to be proven by large prospective cohort studies.
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[1] Arida A, Zampeli E, Konstantonis G, et al. Rheumatoid arthritis is sufficient to cause atheromatosis but not arterial stiffness or hypertrophy in the absence of classical cardiovascular risk factors. ClinRheumatol. 2015:34(5):853–9.
[2] Zampeli E, Protogerou A, Stamatelopoulos K, et al. Predictors of new atherosclerotic carotid plaque development in patients with rheumatoid arthritis: a longitudinal study. Arthritis Res Ther. 2012:14(2):R44
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5258

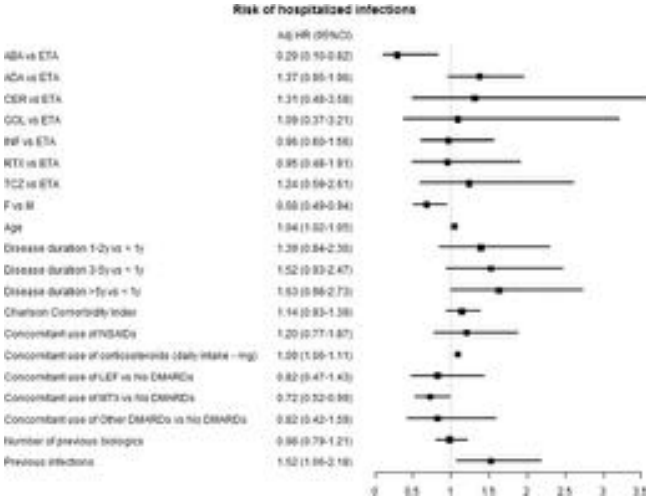
### SAT0098 RISK OF HOSPITALIZATION FOR SERIOUS BACTERIAL INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS. ANALYSIS FROM THE RECORD STUDY OF THE ITALIAN SOCIETY FOR RHEUMATOLOGY

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**Background:** Biological disease modifying antirheumatic drugs (bDMARDs) are widely used in treating rheumatoid arthritis (RA). There are concerns regarding the risk of serious infections related to these treatments, and scarce information on the impact of co-treatments.
**Objectives:** To define the risk of serious infections in patients receiving bDMARDs, evaluating the effect of specific biologic agents and co-treatments in a large population-based sample of RA deriving from the administrative health database of the Lombardy region in Italy.
**Methods:** Data were extracted from health databases of the Lombardy Region in the period between 1/1/2004 and 31/12/2013. Patients with RA, identified through a rheumatologist certified diagnosis (exemption code 006.714.0) and treated with bDMARDs (abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab) were included. Hospitalizations for bacterial infections were evaluated by the hospital discharge forms in the period of exposure to each biologic drug with the following diagnosis ICD9CM: 049.* or 320.*, 054.3 or 323.*, 681.*682.*, 421.*, 481.*482.*, 590.*, 711.*, 730.0*730.2*, 038.* or 790.7. The association between biologic drugs exposure and hospitalization for bacterial infections was assessed by survival models for competing risks, with time-dependent covariates. Results were presented as hazard ratios (HR) and 95% confidence intervals (CI), crude and adjusted for pre-specified confounders

(sex, age, disease duration, Charlson comorbidity index, concomitant use of methotrexate, leflunomide, corticosteroids, NSAIDs, number of previous biologics and previous infections).

**Results:** 4656 RA patients who had at least one bDMARD prescription for a total of 7601 exposures were included. 3603 were women (77.4%) with a mean age at first bDMARD exposure of 55.7 years (12.7 ± SD) and with a modal disease duration over 5 years. The factors associated with hospitalization with a definite bacterial infection are shown in figure. Considering etanercept as reference, the adjusted HR for infection was equal to 0.29 (95% IC 0.10 - 0.82) for abatacept, while it was not significantly different compared to other bDMARDs.




**Conclusions:** Treatment with bDMARDs was not associated with an increase in hospitalized infection. The risk was lower with abatacept that confirmed to have a better safety profile.

**Disclosure of Interest:** None declared

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## SAT0099 ADVOCATING FOR RHEUMATOID ARTHRITIS AND CARDIOVASCULAR HEALTH (ARCH): A SYSTEMS-BASED SCREENING INITIATIVE IN A US TERTIARY REFERRAL CENTER

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**Background:** Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease (CVD) as compared to the general population. Furthermore, RA patients have a comparable increased risk of CVD to that of diabetics and yet are not screened as well. The European League Against Rheumatism (EULAR) recommends that rheumatologists engage in assessing the CVD risks in RA patients, but there are currently no specific recommendations from the American College of Rheumatology (ACR). Multiple barriers such as limited time and lack of familiarity of CVD screening guidelines challenge the feasibility of this practice. Furthermore, recent data suggest that primary care providers fail to assess RA patients consistently or aggressively.

**Objectives:** The project aimed to increase RA patient awareness of CV risks, improve the process for screening and documenting CV risk factors. At National Jewish Health, a tertiary referral center, we implemented an integrated system to provide RA patients direct access to evaluation by a cardiologist for CVD risk assessment.

**Methods:** We reviewed the medical records of all RA patients presenting to our hospital for new or follow up appointment in 2015 when the rheumatology CVD risk assessments began. Charts were reviewed for: baseline characteristics, a chest commuted tomography (CT) scan that included cardiac imaging information and medication use. A board certified cardiologist reviewed the cardiac CT information for the presence or absence of coronary calcifications.

**Results:** There were 683 RA patients seen during the study interval and 251 were screened and referred for CV risk assessment. A significant number of patients are current or past smokers. (Table) The majority are seropositive and have normal lipid and hemoglobin A1C levels. We have recorded an MDHAQ on 75% of the RA patients and 39% have an ASCVD risk score. Prior to this project, we had not done routine assessments or recorded them in our electronic medical records. We found 104/251 (41%) of the patients had a chest CT available for review. 41/104 (39%) had some presence of coronary calcifications on chest CT and 39/104 (37%) were either on or started a statin.

**Conclusions:** RA patients seen in our tertiary hospital were effectively screened for CVD risk and aggressively treated, but we found that not all patients could be screened. Our institution was amenable to the practice changes and implementation among other hospitals may be a feasible option.

| | Total N = 251 | Women N =189 | Men N = 62 |
|---|---|---|---|
| Age, years | 56.5 | 55.8 | 58.7 |
| Average BMI | 30.4 | 31.6 | 29.0 |
| BMI > 25 | 197 (78%) | 148 (78%) | 49 (79%) |
| Current or past smoker, no (%) | 155 (62%) | 108 (57%) | 47 (76%) |
| Never smoker, no (%) | 96 (38%) | 81 (42%) | 15 (24%) |
| RF positive (>14 IU/mL) | 154 (61%) | 113 (60%) | 41 (66%) |
| CCP positive (>20 units) | 164 (65%) | 120 (64%) | 44 (71%) |
| Hemoglobin A1C | 5.71 | 5.71 | 5.72 |
| Lipids ordered, no (%) | 189 (75%) | 141 (75%) | 48 (77%) |
| 10 yr ASCVD score calculated | 61 (24%) | 42 (22%) | 19 (31%) |
| Statins, no (%) | 92 (37%) | 65 (35%) | 27 (44%) |

**References:**

[1] Peters MJ et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis. 2010 Feb;69(2):325–31.

[2] Gossec L et al. Challenges of cardiovascular risk assessment in the routine rheumatology outpatient setting: an observational study of 110 rheumatoid arthritis patients. Arthritis Care Res. 2013 May;65(5):712–7.

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**Disclosure of Interest:** None declared

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## SAT0100 ASSOCIATION BETWEEN CHRONIC PERIODONTITIS AND CLINICAL PROFILE OF RHEUMATOID ARTHRITIS

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**Background:** Recent clinical data show a clear association between periodontitis (P) and rheumatoid arthritis (RA). However, the literature is inconsistent whether severity of P is associated with RA activity; some studies haven't shown any or negative association.Nevertheless, there is one study[1] that has found a positive association between severity of P and activity of RA.

**Objectives:** 1) To describe if the severity of P affects the clinical expression and activity of RA.2) To define the characteristics of P in RA patients with high clinical activity.

**Methods:** Observational, cross-sectional, case-control study of adult RA patients (ACR/EULAR 2010) in a hospital Rheumatology Service,with at least 4 teeth, no dental prophylaxis or antibiotic intake 6 months before. Sociodemographic/anthropometric variables including smoking status, Graffar scale and stress level. RA variables: DAS28 (ESR & CRP), SDAI, titles RF/ACPA, extraarticular manifestations and comorbidities:o steoporosis (OP), diabetes mellitus (DM), dyslipidemia (DS), ischemic cardiovascular disease (ICD); glucocorticoid (GC),synthetic and biological therapy (DMARDs/BT). Periodontal Variables: plaque index (PI), bleeding on probing (BoP), probing pocket depth (PPD), recession (REC), clinical attachment level (CAL). Dental team: 2 periodontists/2 general dentists. Full mouth CAL, PPD and periapical x-rays were taken. CAL was classified according to the European Workshop in 2005 (Tonetti), into level 0 (absence), N 1T (mild), N2 T (severe). Statistical Analysis: t-student, Kruskal Wallis, Chi-square. Statistical program: Stata 13.1.

**Results:** 187 RA patients, F/M 78,6%/21,4%, mean age 54,4 yo, follow-up: 8,8 y. Early RA 18,72%. Positive F/ACPA: 74,19%/67,86%. Mean clinical activity: DAS28(ESR) 3,81/DAS28(CRP) 3,18/SDAI 14,49. Disease activity: remission 20, 86%, low 24,06%, moderate 45,45%, high 9,63%; RA treatment: GC therapy 47,06% (pred 2,85 mg/d)l; DMARDs monotherapy/combined: 53%/11,76%, BT 30%. Smoking: Current smoker (19,25%)/former smoker (24,6%); low socioeconomic status (36,36%), relative poverty (33,69%); annual dental prophylaxis: 43%; dyslipidemia: 53,47%, OP/osteopenia: 55,86%. P N2T in 69, 05% of patients with moderate/high activity vs 30,95% remission/low activity; 55,34% patients with P N1T showed RA remission/low activity ($p<0,001$). It has been found a strong association between severe P and moderate/high RA activity, with OR 57,649±37,403 (CI 95% 16,163–205,620). Patients with moderate/high RA activity presented increased values of all periodontal parameters compared to those with low activity ($p<0,005$). It has been observed an association between rheumatoid nodes, pleuritis and OP with severe P ($p=0,028$).

**Conclusions:** 1. High-activity RA is associated with severe P. 2. Patients with moderate and high activity RA have higher prevalence of both number and percentage of probing pocket depth ≥ de 5mm. 3. Presence of rheumatoid nodes and osteoporosis are related to severe P. 4. These results prompt an independent relationship between severe P and RA patients with high clinical disease activity.

**References:**

[1] Mikuls,et al. Arthritis Rheum 2014

**Disclosure of Interest:** None declared

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## SAT0101 COULD THE FUNCTIONAL DISABILITY OF RHEUMATOID ARTHRITIS PATIENTS INFLUENCE IN THE DEVELOPMENT OF PERIODONTITIS?

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**Background:** It has been suggested that functional disability in patients with rheumatoid arthritis (RA) could influence in hygiene procedure performance,promoting the development of periodontitis (P).However, this factor has been tested in few studies, with inconsistent data[1,2]. Hence, it has been implied both that functional disability has a possible role in P process risk (13,4%)[2],and that there is no higher plaque index[3] (PI) or no association between P severity and functional index by HAQ[4].
**Objectives:** 1)To test whether the functional ability of RA patients is associated with the presence of a more severe P.2) To describe the possible influence of functional disability on the development of P in terms of RA activity.
**Methods:** Observational,cross-sectional,case-control study,performed in adult RA patients (ACR/EULAR 2010) in a Rheumatology Service; and a control group with a non-inflammatory joint pathology,with at least 4 teeth,without dental prophylaxis or antibiotic intake 6 months before. RA activity was evaluated:DAS28 (ESR), DAS28(CRP) and SDAI, and patients were categorized by activity and functional disability (HAQ index).Periodontal parameters:PI (Silness and Löe,1964)[5],4 surfaces/tooth (0–3);bleeding on probing (BoP), probing pocket depth (PPD), clinical attachment level (CAL). Dental team:2 periodontists/2 general dentists (inter-observer variability<30%). Full mouth CAL,PPD and periapical x-rays were taken. CAL was classified according to the European Workshop 2005 (Tonetti):level 0 (absence), N1 T (mild), N2 T (severe). Statistical Analysis:t-student, Kruskal Wallis, Chi-square. Statistical program: Stata 13.1.
**Results:** 344 patients:187RA (147 F/40 M)and 157 control (101F/56M),mean age 54,9 (17,9), follow-up 8,8 years;18,72% patients with early RA. 83/187 (44,39%) RA patients presented a remission/low disease activity and 55,61%, moderate/high activity. 69,05% patients had P N2 T. Mean HAQ index was 0,76 (0,62), finding differences between patients with varied disease activity:p50 [p25-p75] 0,250 (0–0,750) in RA patients with remission/low activity vs 1,125 (0,625–1,5) those with moderate/high activity, p=0,000. There was no association between HAQ values and presence of P (OR 1,0003 IC 95% 0,999–1,001). Nevertheless, there was a gradually increase in PI values from control patients 0,56 (0,40), to remission/low RA activity 0,59 (0,37), RA moderate/high 0,86 (0,53), with statistically significant differences between consecutive categories (p<0,001 and p=0,001, respectively).
**Conclusions:** 1. No association was found between functional ability of RA patients measured by HAQ index and presence of a more severe P.2. An ascendant gradient in PI is observed related to RA clinical activity with significant difference, despite an acceptable preserved functional ability.3. These findings could strenghten an classic risk factor independent relationship between RA and P.
**References:**
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[2] Pischon N,et al. J Periodontol 2008;
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5763

## SAT0102 INFLUENCE OF VACCINATION PROGRAM TO PREVENT ACUTE RESPIRATORY INFECTION IN RHEUMATOID ARTHRITIS

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**Background:** Patients with autoimmune rheumatic diseases such as rheumatoid arthritis (RA) are at increased risk for infections, especially respiratory type. Immunization is a recommended measure to reduce these complications.
**Objectives:** Assess the incidence of acute respiratory infections (ARI), defined as one that causes hospitalization, before and after inclusion in a systematic vaccination program.
**Methods:** Prospective study in a cohort of 294 patients diagnosed with RA, were included in the vaccination program. This program includes: seasonal flu vaccine (october to april), pneumococcal (combined regimen 13-valent and 23-valent) and Haemophilus influenzae B.
Only 7 patients (2.94%) refused vaccination.
The follow-up time was from October 1st, 2011 (starting date) to June 30th, 2015. Information on ARI episodes before and after immunization was collected from the Hospital Information System, reviewing hospital records.
**Results:** 287 RA patients (225 women/62 men) were vaccinated, with an average age of 58.1 ± 12.7 years. RA was characterized at the time of vaccination by the time of evolution of RA 93 ± 95.9 months; 154 (53.65%) positive RF, 97 (33.8%) erosive and 40 (13.9%) with extra-articular manifestations (7 with pulmonary fibrosis).

TABLE: SERIUS INFECTIONS POST-IMMUNIZATION

| | Age | sex | Biological Therapy At vaccination | Biological Therapy previus | Others Theraphys | Rheumatoid Factor | Serius Respiratory infections |
|---|---|---|---|---|---|---|---|
| 1 | 72 | W | No | Yes | Prednisone 30 mg/24h | - | Pneumonia(E. coli) |
| 2 | 45 | W | No | - | LFN | + | LRTI (Microbial culture negative) |
| 3 | 66 | M | No | Yes | CQ | - | Pneumonia (microbial culture negative) |
| 4 | 67 | W | No | No | - | - | LRTI (Microbial culture negative) |
| 5 | 48 | W | No | No | MTX Prednisone 10 mg/24h | + | LRTI (Microbial culture negative) |
| 6 | 63 | W | No | Yes | MTX Prednisone 10 mg/24h | + | LRTI (aspergillus fumigatus) |

Abreviatures: W: Woman; M: Man; LFN: leflunomide; CQ: chloroquine; MTX: methotrexate; LRTI: Lower Respiratory Tract Infections

Only 42 (14.6%) were not taking any immunosuppressive or immunomodulatory therapy at the time of immunization. 147 patients were treated with Disease Modifying Antirheumatic Drugs (DMARD's), mainly methotrexate, and 98 patients (34.1%) were with a TNFa inhibitor.
Regarding the ARI, before inclusion in the vaccination program, 20 (7%) patients in the cohort studied had been admitted into the hospital for this reason.
During follow-up, and subsequent immunization, only 6 of the 287 patients (2.1%) had ARI (Table 1). One of them had an ARI prior to vaccination program.
This reduction from 7% to 2.1% achieved statistically significant difference (p=0.0017).
**Conclusions:** Incorporating a program of systematic vaccination in RA patients appears to be an effective prophylactic measure to prevent the ARI.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5211

## SAT0103 RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN A SWISS COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLARTHRITIS

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**Background:** Rheumatoid arthritis (RA) has been associated with an increased risk of cardiovascular (CV) morbidity and mortality. Recent data indicated that this could also be the case in psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA) patients.
**Objectives:** To compare the risk of major adverse cardiovascular events (MACE) in RA, PsA and AxSpa as of disease onset.
**Methods:** A mixed retrospective and prospective cohort study was conducted using data from patients included in the Swiss Clinical Quality Management (SCQM) registry. Patients diagnosed with RA, PsA, or AxSpA at an age of ≥18 years without a history of MACE (i.e., non-lethal myocardial infarction, non-lethal stroke and death from cardiovascular event) at the time of first articular symptoms or, if not available, at the time of diagnosis were included. The primary outcome was the incidence of first MACE, using self-reported or physician-reported data. For each patient we recorded the time in years from disease onset until either occurrence of first MACE or end of follow-up. The exposure of interest was the type of rheumatic disease: RA, PSA or AxSpA. In addition to sex and age at disease onset, we assessed traditional CV risk factors: known familial history of MACE before age 50, and presence of ever-hypertension, ever-diabetes, ever-hyperlipidemia, and ever-smoking. We applied Poisson regression to estimate and compare the incidence rates for MACE.
**Results:** 5311 patients (3068 RA, 1462 AxSpA, and 781 PsA patients) were eligible and contributed a total follow-up time of 37'459 years for RA, 19'818 for AxSpA, and 9'159 for PsA. Diseases started between 1950 and 2014 and differed significantly with respect to assessed CV risk factors (Table 1). A total of 98 RA, 28 AxSpA, and 11 PsA patients had experienced at least one MACE since disease onset. The unadjusted incidence rate of MACE per 1000 person-years was 2.62 for RA, 1.41 for AxSpA, and 1.20 for PsA (p=0.0011). After adjusting for traditional CV risk factors, age at disease onset, sex, and year of disease onset (categorized as: <1985, 1985–2000, or >2000) the significant difference between PsA and RA persisted (MACE incidence rate ratio (IRR): 0.45, 95% confidence interval (CI): 0.22- 0.91), while the difference between AxSpA and RA was decreased and no longer significant (IRR: 0.86, 95% CI: 0.5 -1.49). Because ever-hypertension, ever-diabetes, ever-hyperlipidemia, and ever-smoking may not reflect the status at time of disease onset, we analyzed the risk of MACE also with only adjusting for sex, age at disease onset, disease onset and family history of early MACE. The results (n=5311) were very similar, suggesting that especially age and sex are important confounders when comparing incidence rates across diseases. Male sex, older age at disease onset, a known family history of early MACE, ever-hypertension, and ever-hyperlipidemia were also significantly positively associated with the risk of MACE.

Table 1

| | AxSpa (n= 1462) | PsA (n=781) | RA (n=3068) | P-value |
|---|---|---|---|---|
| Age in yrs at disease onset, median (IQR) | 29 (23-39) | 39 (30-49) | 47 (37-56) | 0.0000 |
| Sex (male), n (%) | 804 (55) | 418 (54) | 768 (25) | 0.0000 |
| Family history of early MACE (< 50 yrs), n (%) | 173 (12) | 116 (15) | 357 (12) | 0.048 |
| Ever-hypertension, n (%) | 346 (26, n = 1326) | 276 (37, n=738) | 1141 (39, n= 2940) | 0.0000 |
| Ever-diabetes, n (%) | 63 (4, n=1417) | 50 (7, n= 759) | 214 (7, n= 3068) | 0.0021 |
| Ever-hyperlipidemia, n (%) | 208 (18, n=1185) | 163 (24, n = 668) | 663 (25, n=2668) | 0.0000 |
| Ever-smoking, n (%) | 892 (62, n = 1450) | 450 (58, n= 775) | 1700 (56, n= 3048) | 0.0012 |

IQR = Interquartile range
P-values are from a Kruskal-Wallis test for continuous or discrete variables and from a Fisher's exact test for categorical variables.

**Conclusions:** Taking into account traditional CV risk factors, age and sex, the type of rheumatic disease remained associated with risk of MACE. RA seems to convey a larger CV risk than PsA, while the difference between RA and AxSpA remains unclear.
**Disclosure of Interest:** None declared
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## SAT0104 DEPRESSION AND ANXIETY IN PATIENTS WITH AN EARLY ARTHRITIS – A PILOT STUDY

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**Background:** The depression is with an average of 16% to 38% one of the most prevalent co-morbidities in rheumatoid arthritis (RA) as well as heart diseases or diabetes mellitus. Few studies investigate the clinical relevance of psychiatric disorders in an early disease stage of the RA and as if they may affect future outcomes in chronicity process.
**Objectives:** The aim was to evaluate the prevalence rates of depression and anxiety in an early arthritis (EA) cohort and the distribution across diagnosis groups and gender. Furthermore, we wanted to investigate whether certain disease parameters of an EA show differences between patients (pts) with normal scores versus (vs) pts with high scores in depression and anxiety to construe strategies for everyday practice by gathering such diseases at an early stage.
**Methods:** In a prospective cross-sectional survey, 176 pts with EA answered the Hospital Anxiety and Depression Scale (HADS). The suspicion of an EA was defined by at least one fluid joint and a disease duration from six weeks to maximum 12 months. We compared the standardized clinical routine assessment with disease activity score 28 (and clinical investigation of 68 joints), visual analogue scale (VAS) for pain and disability according the health assessment questionnaire (HAQ) with results of HADS in different diagnostic groups.
**Results:** The mean age of EA cohort was 50.4±16.1 years (♀ 69.3%, mean disease duration: 4.2±3.4 months). Pts assigned to the following groups: "Rheumatic diseases" (RD, n=108) with subgroups "Rheumatoid Arthritis" (RA, n=55) and "Non-rheumatoid arthritis" (NRA, n=53) and "Non-rheumatic diseases" (NRD, n=68). We found a positive global distress in 47.7% of EA pts. The score in RD group was 50.9% vs 42.6% in NRD group. In RA pts it was 49.1% vs 52.8% in NRA pts. The HADS average was as similar in all groups and if compared to gender. We found out that a positive distress score accompanied with significantly higher means of the tender joint count-68 (TJC, p=0.032), the VAS for pain ($p<0.000$) and HAQ ($p<0.000$). RA pts with positive distress score showed higher rates in HAQ (p=0.004) and pain-VAS (p=0.001). NRD pts with positive distress scores had also significant higher means of pain-VAS (p=0.033). Only the NRA group didn't show statistically significant differences.
**Conclusions:** There is an extremely high point prevalence, with almost 50%, of anxiety and depression for EA pts. If EA pts had positive HADS, three established standardized EA measurement instruments (HAQ, VAS for pain, TJC68) showed significantly higher average as if they had negative scores. To improve the treat-to-target concepts in clinical practice with a particular focus on comorbidities, further studies are required. The importance of early psychiatric-psychological interventions in the early stages of RA disease is unclear.
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## SAT0105 INFLAMMATORY MARKERS IN RHEUMATOID ARTHRITIS – WHAT IS THE ROLE OF SERUM AMYLOID A PROTEIN?

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**Background:** Dissociation between the responses of a number of acute-phase proteins (APP) is well known. C reactive protein (CRP) levels have been used extensively to model disease activity in rheumatoid arthritis (RA). However, biologic therapy reduce CRP levels, even without associated reductions in RA disease activity. Serum amyloid A (SAA) also models RA disease activity and has been suggested as a better biomarker for RA disease activity.
**Objectives:** To determine if SAA levels had better correlation with conventional clinical and serological assessments in RA than CRP and ESR.
**Methods:** A cross-sectional study was performed. Samples were analyzed from RA patients under biologic therapy of a reference hospital in northern Portugal. We compared the correlation between SAA, CRP and ESR levels with swollen and tender joints counts (SJC and TJC), DAS28-4v, SDAI, CDAI, HAQ and visual analogue scale for pain (VAS-P). Correlation was calculated using the Spearman rank correlation (r). P-values $<0.05$ were regarded as significant.
**Results:** 173 patients were evaluated, 86.7% (n=150) were women. The mean (SD) age was 56 years (10.75). Mean disease duration was 16.31 years (8.87). Most of patients had positive serology (rheumatoid factor and/or anti-CCP antibody) (n=146, 84.4%). Ninety eight patients (56.6%) were under TNF antagonists, 23.7% (n=41) were under rituximab and the remaining under tocilizumab (TCZ).
SAA levels were moderately correlated with CRP levels ($r=0.49$, $p<0.001$) but there was no statistically significant correlation with ESR (r=0.03, p=0.75).
Correlation analysis of SAA and CRP levels with several conventional assessments showed (SAA and CRP, respectively): SJC - 0.17 vs 0.08, TJC - 0.18 vs 0.09, DAS28-4v - 0.32 vs 0.41, SDAI - 0.23 vs 0.18, CDAI - 0.18 vs 0.11, ESR – 0.32 vs 0.55; all p values $<0.05$ except SJC, TJC and SDAI for CRP values. There was no statistically significant correlation of these acute-phase protein with HAQ and VAS-P. ESR levels showed very weak correlation with all parameters ($p>0.05$), except with DAS28-4v ($r=0.58$, $p<0.001$).
We also noted that SAA levels were raised ($>6.4$mg/L) in 37.6% (n=65) of patients in which the CRP concentration was normal ($<0.3$mg/dL). However, only 6% (n=11) with normal SAA levels had raised concentrations of CRP. When evaluated SAA and CRP levels in patients with active disease (DAS28-4v $^3$2.6, SDAI$>$3.3 and CDAI$>$2.8) we found more patients with normal CRP values than SAA (62 vs 26, 82 vs 32, 84 vs 33, respectively).
Interestingly, when comparing the effects of biological therapy on APP we noted that in TCZ group the CRP, ESR and SAA levels were lower than in group under TNF antagonists and rituximab ($p<0.001$ for all, Mann-Whitney test).
**Conclusions:** The lack of a strong correlation between SAA and CRP or ESR levels coupled with their better correlation with markers of RA activity suggests that changes in their levels may provide a more sensitive indicator of disease activity, especially during treatment with biologic therapy.
**Disclosure of Interest:** None declared
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## SAT0106 VALVULAR HEART DISEASE IN A MEXICAN MESTIZO COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY

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**Background:** Rheumatoid arthritis (RA) is associated with a higher rate of cardiovascular mortality. The prevalence of valvular heart disease (VHD) varies greatly in the published reports. Data in Mexican mestizo patients with RA is scarce.
**Objectives:** We aimed to evaluate the presence of VHD in a cohort of RA Mexican mestizo patients and compare it to matched controls.
**Methods:** An observational, comparative, case control study was designed. Patients with RA aged 40 to 75 years that fulfilled the 2010 ACR/EULAR criteria were included. Exclusion criteria included prior atherosclerotic cardiovascular disease (myocardial infarction, stroke and peripheral arterial disease) and overlap syndromes.
Patients were matched using age, sex and comorbidities. A standard transthoracic echocardiography was performed according to the American Society of Echocardiography guidelines. Valvular regurgitation was classified as mild, moderate or severe according to the European Association of Echocardiography and American Society of Echocardiography recommendations.
**Results:** A total of 56 patients and 28 controls were included in the final analysis. Characteristics of both groups are shown in Table 1. There was no statistical difference in sex, age, type 2 diabetes mellitus and body mass index between the two groups. VHD was reported in 45 (80.4%) RA-patients and 13 (46.4%) individuals in the control group ($p<0.003$). Statistical difference was found in mitral and tricuspid regurgitation ($p<0.001$ and $p<0.003$, respectively) in RA-patients when compared with the control group.
In the RA group, 5 (8.9%) showed mild aortic regurgitation; 28 had mild and 1 had moderate (50% and 1.8%, respectively) mitral regurgitation; 8 (14.3%) showed mild pulmonary regurgitation; 39 had mild and 4 had moderate (69.6% and 7.1%, respectively) tricuspid regurgitation. In the control group, 1 (3.6%) showed mild

aortic regurgitation; 3 (10.7%) had mild mitral regurgitation; 1 (3.6%) showed mild pulmonary regurgitation; 12 (42.9%) had mild tricuspid regurgitation.

Table 1. Clinical and Demographic characteristics

| | RA group (n= 56) | Control group (n=28) | P value |
|---|---|---|---|
| Women, n (%) | 54 (96.4%) | 27 (96.4%) | .845 |
| Age, mean ± SD | 56.01 ± 9.38 | 53.15 ± 6.27 | .922 |
| Hypertension, n (%) | 22 (39.3%) | 4 (14.3%) | .024 |
| Type 2 Diabetes mellitus, n (%) | 8 (14.3%) | 4 (14.3%) | > 999 |
| Smoking, n (%) | 6 (10.7%) | 0 (0.0%) | <.004 |
| Body mass index, mean ± SD | 28.51 ± 4.61 | 28.49 ± 4.54 | .538 |
| Valvular heart disease, n (%) | 45 (80.4%) | 13 (46.4%) | < 0.003 |
| Mitral valve regurgitation, n (%) | 29 (51.8%) | 3 (10.7%) | < 0.001 |
| Tricuspid valve regurgitation, n (%) | 43 (76.8%) | 12 (42.9%) | < 0.003 |
| Aortic valve regurgitation, n (%) | 5 (8.9%) | 1 (3.6%) | .658 |
| Pulmonary valve regurgitation, n (%) | 8 (14.3%) | 1 (3.6%) | .260 |

**Conclusions:** In our cohort, 80.4% of the RA-patients had VHD, with the tricuspid valve being the most affected (76.8%). Prospective studies are needed to evaluate the role of VHD in RA-patients morbi-mortality.

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## SAT0107 SIMPLE PREDICTORS OF ABNORMAL 2H POSTLOAD GLUCOSE IN RA PATIENTS WITH NORMAL FASTING GLUCOSE

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**Background:** Rheumatoid arthritis (RA) is characterized by an excess of cardiovascular diseases (CVD) risk, similar to type 2 diabetes (T2DM). A recent meta-analysis confirmed an elevated prevalence and incidence of T2DM in RA [1]. In this context, the necessity to recognize early T2DM in RA is driven by the evidence that CVD risk factors tends to act synergistically, thus increasing the risk conferred by each single factor [2]. However, it's still difficult to select patients that need to underwent extensive diabetes investigation in the rheumatology setting.

**Objectives:** Aim of our work was to identify useful predictors of impaired glucose tolerance (IGT) and T2DM in RA patients with normal fasting glucose values in the rheumatology outpatient setting.

**Methods:** 100 RA patients satisfying ACR/EULAR 2010 criteria [3] were screened with FPG. Of these, 78 had normal (<100 mg/dL) FPG values and therefore were recruited. All patients underwent a 75g oral glucose tolerance test (OGTT) following World Health Organization (WHO) recommendations. According to 2-hours postload glucose values (2h-pG), patients were classified as normal (NGT) if 2h-pG <140 mg/dL, impaired glucose tolerance (IGT) if 2h-pG 140–200 mg/dL or T2DM if 2h-pG ≥200 mg/dL. Age, sex, body mass index (BMI), waist circumference (WC) and blood pressure were recorded. After overnight fasting, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), total and HDL cholesterol, triglycerides (TG) and uric acid were measured. The homeostasis model assessment of insulin resistance (HOMA-IR)[4] was calculated with the formula: glucose (mg/dL) x insulin (mU/L)/405. The triglycerides and glucose index (TyG index)[5] was calculated with the formula: *ln* (TG [mg/dL] x glucose [mg/dL]/2). The lipid accumulation product (LAP)[6] was calculated with the formula [WC (cm) – 58 for women or 65 for men] x TG (mmol/L). The visceral adiposity index (VAI) was calculated with the formula proposed by Amato et al [7].

**Results:** Of the 78 RA patients recruited 57 were NGT, 18 were IGT and 3 were T2DM. After correction for age, sex, BMI, and systolic blood pressure, 2h-pG correlated with diseases duration (R=0.25, p=0.04), ESR (R=0.27, p=0.02), lnTG/HDLc (R=0.24, p=0.04), HOMA-IR (R=0.29, p=0.01), LAP (R=0.28, p=0.02) but not with lnCRP, lnTG, fasting glucose, uric acid, TyG index or VAI. In addition 2h-pG category correlated only with LAP (R=0.33, p=0.005). When A1c% was set as dependent variable, it correlated with lnTG (R=0.26, p=0.03), fasting glucose (R=0.29, p=0.0), uric acid (R=0.26, p=0.03), TyG index (R=0.25, p=0.04), LAP (R=0.30, p=0.01).

**Conclusions:** In RA patients with normal fasting glucose, LAP correlates significantly with 2hPG and predicts abnormal glucose tolerance.

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## SAT0108 METHOTREXATE AND ANTI-TNF TREATMENT IMPROVE ENDOTHELIAL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

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**Background:** Inflammatory rheumatic diseases (IRD) are associated with accelerated atherosclerosis, which progression is related to inflammation. One of the first stages in atherogenesis is endothelial dysfunction (ED).

**Objectives:** We wanted to examine the effects of methotrexate (MTX) and anti-tumor necrosis factor (TNF) treatment (with or without MTX co-medication) on endothelial function (EF) in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

**Methods:** From the data registry from PSARA (an observational study), we evaluated patients with RA (n=64), PsA (n=30) and AS (n=20) who completed a 6 month follow-up. All patients required treatment with either MTX monotherapy or anti-TNF±MTX, due to clinical indication. EF was assessed by finger plethysmography (RH-PAT): reactive hyperemia index (RHI) <1,67 was considered as ED. In patients with ED at baseline (n=40), we searched for change in EF after 6 weeks and 6 months of anti-rheumatic therapy.

**Results:** In IRD patients with ED, RHI improved from baseline to 6 weeks (mean change=0.56, p<0.005) and 6 months (mean change=0.46, p<0.005), with the greatest improvements within the RA subgroup in whom RHI significantly improved at both control visits. In PsA, RHI improved at both control visits, but the change was statistically significant only at the 6 months visits. AS patients had a statistically non-significant trend towards RHI improvement at both control visits. At 6 months, RHI improved more in the MTX group than in the anti-TNF±MTX group (mean change 0.74 vs. 0.24; p=0.010), and this difference remained statistically significant after adjustments for potential confounders. There was no significant difference between the treatment regimens at 6 weeks.Id significantly greater thhe The improvement in RHI was independent of changes in disease activity and of traditional CV risk factors.

**Conclusions:** Treatment with MTX and anti-TNF±MTX appears to relatively fast improve EF in IRD patients with ED, independently of improvement of disease activity. After 6 month, the EF improvement was more pronounced in the MTX users than in the anti TNF±MTX users. Among other factors, this might be due to a better effect of MTX on the vasculature, or due to differences in the MTX and anti-TNF±MTX populations.

It remains to be examined in further studies if the lack of significant effect of the treatment on ED in AS is due to specific features of vascular disease in AS, or due to other factors, such as Type-2 error.

**Disclosure of Interest:** None declared

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## SAT0109 SUBCLINICAL ECHOCARDIOGRAPHIC CHARACTERISTICS IN PATIENTS WITH RHEUMATOID ARTHRITIS WITHOUT OVERT CARDIAC DISEASE

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**Background:** Patients with rheumatoid arthritis (RA) have an increased risk for cardiovascular (CV) disease, despite preserved left ventricular (LV) ejection fraction (EF). Changes in LV geometry, LV systolic dysfunction (LVSD) and the development of excessive left ventricular mass (LVM) are closely and consistently

associated with CV disease in several settings of patients such as those with arterial hypertension or type 2 diabetes mellitus, with preserved LVEF.
**Objectives:** The aim of this study was the evaluation of this subclinical parameters in patients with RA.
**Methods:** 198 outpatients with RA without overt cardiac disease were prospectively analyzed with echocardiography and compared with 198 matched controls. In all patient LV geometry (concentric remodeling or hypertrophy), LVEF, circumferential and longitudinal LVSD (respectively by stress-corrected midwall shortening [sc-MS] and Tissue Doppler mitral annular peak systolic velocity [S']) and the presence of inappropriately high LVM (iLVM)were evaluated.
**Results:** The patients with RA present higher prevalence respect to controls ofconcentric remodeling or hypertrophy, circumferential or/and longitudinal LVSD and iLVM as reported on table.

Table 1

| | RA | Controls | p |
|---|---|---|---|
| Concentric remodeling (%) | 74 | 18 | <0.001 |
| Hypertrophy (%) | 37 | 16 | <0.001 |
| LVEF (%) | 1 | 3 | NS |
| iLVM (%) | 64 | 15 | <0.001 |
| Circumferential LVSD (%) | 55 | 14 | <0.001 |
| Longitudinal LVSD (%) | 45 | 20 | <0.001 |
| C&L LVSD (%) | 28 | 6 | <0.001 |

By multiple logistic regression analysis, rheumatoid arthritis emerged as independent predictor of all this echocardiography alterations.
**Conclusions:** The patients with RA without overt cardiac disease have the same echocardiographyc characteristics what are associated with CV disease in hypertension and in diabetes mellitus. These findings may be clinically useful for identifying a subgroup of patients with RA at very high risk for adverse CV events (mostly heart failure). Longitudinal studies are needed to assess the prognostic role of this conditions in these patients and to test conceivable and useful pharmacological and/or non-pharmacological treatments.
**Disclosure of Interest:** None declared
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## SAT0110 PREVALENCE OF SELF-REPORTED COMORBIDITIES IN RHEUMATOID ARTHRITIS OUT-PATIENT CLINIC PATIENTS

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**Background:** Patients with rheumatoid arthritis (RA) has been shown to be at increased risk for other diseases, in particular for osteoporosis, infections, cardiovascular diseases and malignancy. There are limited data on prevalence of comorbidities in unselected RA patient outpatient cohorts reflecting the magnitude of comorbidities in RA patients.
**Objectives:** To explore the prevalence of comorbidities in RA patients followed at outpatient clinics in Norway.
**Methods:** The RA patients were recruited from two outpatient clinics in Norway, one located in the southern and one in the western part of Norway. As part of clinical routine the RA patients at these two centers were monitored at ordinary visits by the use of the computer software tool GoTreatIT® Rheuma. Standardized data collection for disease activity measures, patient reported outcome measures (PROM) and treatment was registered as part of clinical routine. Patients also self-reported their comorbidities using the computer system. Patients with at least one visit in 2015 at the outpatient clinics were included.
**Results:** A total of 2437 RA patients were assessed, 1065 from the southern and 1372 from the western located center. Only minor differences were found between the two centers, for demographic, disease and treatment variables. Patient demographic and disease characteristics: mean age 62.7 (SD 14.1) years, BMI 25.9 (4.5) kg/m$^2$, education 11.8 (3.6) years, 70% females, current smoker 16.0% and 66.8% were RF+ and 73.5% were anti-CCP+. Measures reflecting disease activity: mean ESR 18.2 (14.4) mm/hr, CRP 7.0 (13.8) mg/dl, DAS28 2.4 (1.2) and CDAI 6.6 (7.0). Mean values for PROMs: Pain 32.7 (25.3) mm, fatigue 37.8 (29.8) mm. MHAQ 0.18 (0.42). Current user of mono synthetic disease modifying anti-rheumatic drugs (sDMARDs) 45.5%, mono biologic DMARDSs (bDMARDs) 10.4% and combination sDMARDs and bDMARDs 25.5%. Prednisolone was used by 40.8% of the patients.
Self-reported comorbidity data was available in 1616 of the 2437 (66.3%) patients. The percentage of patients reporting to have myocardial infarction was 3.9%, arterial hypertension16.5%, heart failure 1.2%, peripheral artery disease 1.7%, cerebrovascular disease 1.8%, osteoporosis 12.8%, chronic infections 3.7%, lymphoma 0.7%, melanoma 0.9%, other skin cancer 0.5%, other cancers 5.8%. Among the 123 patients who reported to have cancer 6.5% reported to have metastasis and 58.1% reported to have had ca treatment the last 5 years. Thyroid gland disease was reported by 8.0%, diabetes mellitus by 4.4% and peptic ulcer disease by 5.0%.
**Conclusions:** Our data gives an estimate of the prevalence of the most frequent comorbidities in RA patients seen in Norwegian outpatient rheumatology clinics. Osteoporosis and cardiovascular disease was the most frequent comorbidities. Both of these comorbidities have been shown to be more frequent in RA patients compared with the background population. Data on prevalence of comorbidities may contribute to an increased awareness improving overall patient care in RA.
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## SAT0111 INCREASED INSULIN RESISTANCE AND IMPAIRED BETA-CELL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: COULD INFLAMMATION FULLY EXPLAIN THESE METABOLIC DISTURBANCES?

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**Background:** Chronic inflammation, the basic feature of rheumatoid arthritis (RA), plays a major role in accelerated atherosclerosis through its influence on insulin resistance (IR), lipid status, and other risk factors.
**Objectives:** To investigate the level of IR and β-cell function in RA pts compared to healthy controls and evaluate whether inflammation can explain these metabolic disturbances.
**Methods:** The study population included 127 nondiabetic subjects (90 RA pts and 37 matched healthy controls). We determined body mass index (BMI), waist circumference (WC), presence of hypertension and metabolic syndrome (MetS). All pts were on disease modifying antirheumatic drugs (93.3% on methotrexate), 65.6% on steroids (median 5 mg/day, range 5–10, none on steroids >10 mg/day), and 27.8% on biologic therapy. Laboratory analyses included inflammation markers (SE, hsCRP, IL-6), glucose, insulin, and C peptide (as a marker of insulin secretion). IR was calculated using the updated-computer Homeostasis Model Assessment (HOMA2-IR), based on fasting plasma glucose and specific insulin concentrations. Serum specific insulin was measured by a sensitive ELISA, which employs a monoclonal antibody to insulin. The output of the HOMA2 model was calibrated to give IR of 1 as normal. Therefore, values were considered abnormal when HOMA2-IR was >1.
**Results:** Insulin resistance (HOMA2-IR>1) was detected in 67/90 (74.4%) of RA pts and in 20/37 (54.2%) of controls, p=0.025. RA pts had significantly higher concentration of specific insulin, C peptide and HOMA2-IR than healthy controls, while HOMA2-B was not statistically different. Importantly, both groups were comparable regarding all other factors known to affect glucose metabolism in the general population (age, WC, presence of hypertension or MetS). As it was expected we found significant differences in inflammation markers between RA pts and controls: ESR 29.5 (14–44) vs. 16.0 (10.0–20.0); hsCRP 5.5 (2.8–15) vs. 3.0 (1.8–3.9); IL-6; 7.4 (2.0–18.8) vs. 2.0 (2.0–2.4); p<0.000 for all. In logistic regression analysis, after adjustment for inflammation markers, statisticaly significant differences for HOMA2-IR and insulin became less important but still persisted (Table), while significance for C peptide disappeared.

Table 1. Impact of inflammation markers on the level of IR and β cell function

| Laboratory parameters | RA pts (N=90) | Controls (N=37) | P | P adjusted for ESR | P adjusted for CRP | P adjusted for IL-6 |
|---|---|---|---|---|---|---|
| Glucose (mmol/l) | 4.8±0.6 | 4.7±0.8 | ns | – | – | – |
| Insulin (pmol/L) | 68.5 (50.2–102.7) | 55.3 (36.0–69.1) | 0.008 | 0.030 | 0.048 | 0.035 |
| HOMA-S | 70 (46–100) | 84 (71.0–132) | 0.010 | 0.063 | 0.074 | 0.095 |
| HOMA2-IR | 1.4 (1.0–2.3) | 1.2 (0.8–1.4) | 0.008 | 0.028 | 0.046 | 0.031 |
| HOMA-B | 148 (116–190) | 141 (114–158) | 0.186 | – | – | – |
| C peptide (pmol/L) | 785 (520–1010) | 600 (450–880) | 0.046 | 0.199 | 0.078 | 0.058 |

**Conclusions:** RA pts had higher IR and impaired β-cell function in comparison to healthy controls. The persistence of statistical significance for IR after correction for inflammation markers, may implicate that the influence of inflammatory disease burden is important but not the only risk factor for IR in RA.
**Disclosure of Interest:** None declared
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## SAT0112 THE EFFECT OF CARDIAC REHABILITATION PROGRAM ON DISEASE ACTIVITY, FUNCTIONAL OUTCOME AND CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by symmetric peripheral synovial joint involvement. The most common mortality cause in rheumatoid arthritis (RA) is cardiovascular diseases. Recent guidelines recommend assessment of cardiovascular risk, however the management of cardiovascular risk is not clear.
**Objectives:** The aims of the study were to find effect of cardiac rehabilitation on

**Abstract SAT0112** – Table 1

| Parameters | Groups | Baseline | 10th weeks | 24th weeks | F time | P value | F group | P value |
|---|---|---|---|---|---|---|---|---|
| MET value | Cardiac rehabilitation | 3.76±0.92 | 4.75±1.05 | 4.26±0.79 | 12.57 | <0.001 | 17.35 | <0.001 |
| | Home exercise | 3.66±0.87 | 3.58±0.85 | 3.57±0.93 | | | | |
| VO2 maximum | Cardiac rehabilitation | 13.17±3.26 | 16.6±3.69 | 14.90±2.75 | 12.26 | <0.001 | 16.24 | <0.001 |
| | Home exercise | 12.76±3.08 | 12.52±3.03 | 12.5±3.28 | | | | |
| Maximum energy consumption | Cardiac rehabilitation | 5.13±1.28 | 6.42±1.20 | 5.81±1.30 | 13.06 | <0.001 | 16.60 | <0.001 |
| | Home exercise | 5.10±1.31 | 5.03±1.36 | 4.96±1.32 | | | | |
| Maximum load | Cardiac rehabilitation | 61.75±17.28 | 81.65±18.28 | 72.00±18.79 | 12.56 | <0.001 | 15.58 | <0.001 |
| | Home exercise | 59.65±20.00 | 58.60±20.12 | 57.90±19.70 | | | | |
| 6 minute walking test | Cardiac rehabilitation | 499.20±61.99 | 587.95±58.27 | 581.05±67.39 | 38.54 | <0.001 | 34.46 | <0.001 |
| | Home exercise | 468.95±71.77 | 474.10±80.83 | 467.85±73.91 | | | | |
| HAQ scores | Cardiac rehabilitation | 1.32±0.68 | 0.78±0.43 | 0.86±0.48 | 2.701 | 0.08 | 8.727 | <0.001 |
| | Home exercise | 1.13±0.65 | 1.27±0.66 | 1.29±0.64 | | | | |
| Beck depression inventory | Cardiac rehabilitation | 17.25±9.94 | 11.50±7.08 | 14.55±8.70 | 5.79 | 0.005 | 3.85 | 0.025 |
| | Home exercise | 15.20±9.18 | 14.60±9.05 | 14.55±7.81 | | | | |
| DAS 28 score | Cardiac rehabilitation | 4.02±0.47 | 3.14±0.54 | 3.51±0.58 | 10.49 | <0.001 | 17.30 | <0.001 |
| | Home exercise | 4.04±0.60 | 4.14±0.59 | 4.20±0.56 | | | | |

disease activity, functional status, fitness and cardiovascular risk score in patients with moderate disease activity.

**Methods:** Forty seven patients with RA who had filled ACR/EULAR 2010 classification criteria were enrolled to the study. The patients were randomized to cardiac rehabilitation (25 patients) and home based exercise program (22 patients) groups. The intervention in cardiac rehabilitation group included warming, bicycle ergometer, upper and lower extremity stregthening, cooling and stretching exercises. The patients had received cardiac rehabilitation three times a week for 10 weeks. Individualized home exercise program was given to cardiac rehabilitation group after 10th week. The patients in home exercise program were encouraged to do aerobic and strengthening exercises. The patients were evaluated at baseline, 10th and 24th week with exercise tolerance test, 6 minute walking test, DAS28 score, analysis of mSCORE risk profile, HAQ (Stanford Health Assessment Questionnaire), SF36 (Short Form-36) and Beck Depression Scale.

**Results:** There were significant improvement in the VO2 max, MET level, DAS28, HAQ, SF36- pain, Beck Depression Scale parameters in cardiac rehabilitation group when compared to home exercise group. There was no effect on mSCORE risk profile.

**Conclusions:** Cardiac rehabilitation improved physical fitness, functional outcomes and decreased disease activity but did not affect mSCORE risk profile. mSCORE risk analysis was seemed to be useful to evaluate cardiovascular risk for 10 years but not for appropriate tool for follow up of cardiac risk.

**Disclosure of Interest:** None declared

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## SAT0113 IMPLEMENTATION OF THE TREAT-TO-TARGET STRATEGY LEADS TO DRAMATICALLY REDUCTION OF N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE LEVEL IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Objectives:** to study the effect of antirheumatic therapy administered in accordance with "treat-to-target" principles on NT-proBNP level in early rheumatoid arthritis (RA) patients (pts) during 18-month follow-up

**Methods:** A total of 66 early RA pts (ACR/EULAR criteria, 2010) were included in the study: 71% of women, age 56 [46;61] years, disease duration 6 [4;8] months; DAS28 5.3 [5.0;6.2], positive for ACCP (100%), RF (87%), without prior administration of DMARDs and glucocorticoides. The control group consisted of 27 healthy subjects, which were matched by sex and age. Methotrexate (MT) therapy was started in all pts with an escalation of the dose up to 30 mg/week subcutaneously. Incase of no remission 3 months (mon) later, MT was added with biologic therapy (BT): Adalimumab, Certolizumab pegol, Abatacept. After 18 mon 27 (41%) pts achieved remission. Antihypertensive therapy was administered in 51 (77%) pts: ACE inhibitors, ARBs, beta-blockers, calcium antagonists, diuretics. The normal range for NT-proBNP was less than 125 pg/ml.

**Results:** At baseline the concentration of NT-proBNP in early RA pts (125 [65;208] pg/ml) was higher than in control group (52 [40;69] pg/ml), $p<0,05$. In 32 (49%) RA pts NT-proBNP level were higher than normal. Pts with elevated NT-proBNP level compared to pts with normal one were older (60 [56;65] vs 50 [35;55] years), have a higher frequency of carotid atherosclerosis (85% vs 43%), coronary artery calcinosis (69% vs 22%), chronic heart failure (CHF) (20% vs 0%), ischemic heart disease (28% vs 5%), as well as a higher BMI (28 [24;31] vs 24 [22;29] kg/m$^2$), CRP (34 [13;78] vs 14 [3;41] mg/l), $p<0,05$ for all cases. The frequency of dyslipidemia, abdominal obesity, diabetes mellitus were not obtained between the groups. After 18 mon NT-proBNP level decreased from 125 [65;208] to 68 [33;115] pg/ml, $p<0,05$. There were also reduction in the number of pts with high NT-proBNP level from 49% to 21%, $p<0,05$. Pts who achieved remission showed a decrease in the number of pts with high NT-proBNP level (from 41% to 7%), $p<0,05$, and those who disease activity remained showed a decrease in the number of pts with high NT-proBNP level (from 54% to 31%), $p<0,05$. In group of MT+BT revealed a more pronounced decrease in NT-proBNP level (from 50% to 15%), $p<0,05$, than in group MT (46% vs 31%), $p>0,05$. The most pronounced decrease NT-proBNP level was in pts who achieved remission on MT+BT therapy (Tabl.1). There were correlation between $\triangle$NT-proBNP and $\triangle$CRP ($r=0,4$;$p<0,05$).

Table 1. The elevated NT-proBNP level depending on achieved RA activity and therapy

| | DAS28<2,6 (n=27) | | | | DAS≥2,6 (n=39) | | | |
|---|---|---|---|---|---|---|---|---|
| | MT (n=15) | | MT+BP (n=12) | | MT (n=11) | | MT+BP (n=28) | |
| | 0 mon | 18 mon | 0 mon | 18mon | 0 mon | 18 mon | 0 mon | 18 mon |
| NT-proBNP, n (%) | 5 (33%) | 2 (13%) | 6 (50%) | 0 (0%) | 7 (64%) | 6 (55%) | 14 (50%) | 6 (21%) |

**Conclusions:** At baseline NT-proBNP concentration in early RA pts were higher than in control group and its level correlated with age, traditional risk factors of cardiovascular disease (CVD), CVD, disease activity, markers of inflammation. Achieved remission especially in case of MT+BP therapy leads to a more pronounced reduction in NT-proBNP level. That can contribute to reduce the risk of CHF.

**Disclosure of Interest:** None declared

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## SAT0114 THE IMPACT OF EDUCATION ON ADHERENCE TO TREATMENT WITH DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disorder that typically affects small and medium sized joints in a symmetric manner. In RA joint damage with loss of function can occur. To reduce the risk of joint damage and functional impairment a high degree of adherence by patients to their prescribed regimen is necessary for optimal outcomes. However, poor adherence to drug is suspected in many patients.

**Objectives:** Identify potential determinants of adherence to disease modifying anti-rheumatic drugs (DMARDs) including the level of education in RA patients.

**Methods:** This survey was conducted in the outpatient Rheumatology department. 232 consecutive adult RA patients were included in a survey during their routine rheumatology appointments. RA patients fulfilled EULAR/ACR 2010 or ARA criteria for RA. Survey was designed to record adherence to different RA treatments using two questionnaires, one for a rheumatologist and one for a patient. The data from both questionnaires was entered into a database and statistically evaluated. All the analyses were performed in the R statistical software, version 3.2.2. (R Foundation for Statistical Computing, Vienna, 2015).

**Results:** The surveyed patient population was mostly female (79.7%) with a mean age of 59.3 years (SD=10, range 26–83). 64.3% of patients were rheumatoid factor (RF) positive. According to DAS-28, 7.5% of patients had high disease activity, 34.6% moderate, 21.1% low, and 36.8% patients were in remission. 62.8% of patients had secondary, 20.8% primary and 16.5% university degree of education. At the time of survey, 10% of patients were unemployed, 24% were working and 65.9% were retired. There were 63%, 73% and 88% patients with primary, secondary and university education, respectively, adherent to cs-DMARDS. Considering education there's borderline statistically significant difference in adherence in DMARDs' treatment ($p=0.0517$). The adherence to folic acid treatment was somewhat lower: 38%, 37% and 48% in patients with primary, secondary and university education, respectively. No impact of education on adherence was found in corticosteroid treatment group. No significances in adherence considering education were found in corticosteroid and folic acid treatment ($p=0.937$ in $p=0.629$). There seems to be no clear trend in adherence with respect to patient age, gender and marital status, while the unemployed patients seem to be less adherent in all therapies. We observed the lowest adherence in patients with high disease activity.

**Conclusions:** Education degree seems to be important factor considering adherence in RA patients treated with cs-DMARDS. The best adherence was observed in patients with highest education degree.

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## SAT0115 CORRELATIONS BETWEEN RHEUMATOID ARTHRITIS ACTIVITY INDICES AND FACTORS AFFECTING ACUTE PHASE REACTANTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Assessment of disease activity is a key part of clinical decision in rheumatology care. High disease activity presented by DAS28 >5.1 is used as a cutoff for biologic use in many countries include Korea, while remission (DAS28 <2.6) is considered as a goal of therapy.
**Objectives:** We compared the DAS28ESR and DAS28CRP to other RA activity measures and were to find confounding factors affecting acute phase reactants to patients with rheumatoid arthritis to find best tool to access RA disease activity.
**Methods:** A cross-sectional study was conducted in 1120 patients with RA, using initial registration data from Korean Biologics Registry (KOBIO).
**Results:** In comparison of composite indices, DAS28CRP showed excellent correlation with SDAI (r =0.926, p<0.001), CDAI (r =0.901 p<0.001). DAS28ESR also showed good correlation with SDAI (r =0.875, p<0.001) and CDAI (r =0.886, p<0.001). In defining high disease activity, DAS28CRP showed an excellent agreement with DAS28ESR (kappa 1.000). However, in defining remission, DAS28CRP showed a fair agreement with DAS28ESR (kappa 0.317, 95%CI 0.137 to 0.497). Compared CDAI remission (≤2.8), DAS28ESR showed a fair agreement (kappa 0.331, 95%CI -0.014 to 0.675) and DAS28CRP showed a poor agreement (kappa 0.104, 95%CI -0.031 to 0.238).
In comparison of acute phase reactants to other disease activity measures, CRP showed low but significant correlation with SJC (r =0.132, p<0.001), TJC (r =0.087, p=0.004), SDAI (r =0.441, p<0.001), CDAI (r =0.134, p<0.001) and RAPID3 score (r =0.139, p<0.001). ESR also showed significant correlation with SJC (r =0.132, p<0.001), TJC (r =0.063, p=0.035), SDAI (r =0.233, p<0.001), CDAI (r =0.145, p<0.001) and RAPID3 score (r =0.166, p<0.001).
In correlation analysis using CDAI as controlled variable, ESR increased with age (r =0.110, p<0.001) and serum rheumatoid factor (r =0.105, p=0.001) but was not correlated with BMI, disease duration, and anti-CCP Ab titer. There was no difference in ESR according to the gender, smoking status, presence of diabetes mellitus, obesity (BMI ≥30) or low body weight (BMI <20).
In the same analysis, CRP was not correlated with age, BMI, disease duration, RF and anti-CCP antibody. It was higher in male compared to female (3.41 ± 3.60 vs 2.42 ± 4.08 mg/dL, p=0.001) and higher in ever-smoker compared to never-smoker (3.23 ± 3.46 vs. 2.48 ± 4.10 mg/dL, p=0.027). There was no difference in CRP according to the presence of diabetes mellitus, obesity (BMI ≥30) or low body weight (BMI <18.5).
**Conclusions:** Both DAS28CRP and DAS28ESR were well correlated with other activity indices and showed an excellent agreement in defining high disease activity. ESR increased with age but was less susceptible to gender or smoking status compared to CRP, suggesting DAS28ESR to be a more useful marker for inter-patient-comparison of RA disease activity.
**Disclosure of Interest:** None declared
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## SAT0116 MORTALITY PROFILE OF PATIENTS WITH RHEUMATOID ARTHRITIS IN FRANCE AND ITS CHANGE IN 10 YEARS

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**Background:** Rheumatoid arthritis (RA) is associated with an excess of mortality. This risk depends on disease activity, severity and associated comorbidities.
**Objectives:** Our objective was to study the mortality profile of RA patients in France using multiple-cause-of-death analysis.
**Methods:** Data were collected between 2000 and 2011 in the French Epidemiological Center for the Medical Causes of Death database, and death certificates issued upon the death of an adult for whom RA was an underlying cause of death (UCD) or a non-underlying cause of death (NUCD) were evaluated using multiple-cause-of-death analysis. Sex, age, sex ratio, standardized mortality rates, as well as frequency of the various causes of death were assessed. For the main causes of death, the observed number of deaths in relation to the expected number of deaths (O:E ratio) was calculated.
**Results:** During the study period, 13,208 deaths related to RA were identified. RA was identified as the UCD in 4597 (35%) certificates. The number of certificates mentioning RA as the UCD decreased from 38 to 27% between 2000 and 2011. The mean±SD age at death was 79 ± 9 years (51% with ≥80 years). The female: male ratio was 3.2 and remained stable during the follow-up period. This ratio was significantly higher in the population where RA was the UCD (4.1 vs. 2.8 p<0.001). The mean standardized mortality rate was 0.25 per 1 million people (range 0.21–0.28), and remained stable throughout the period. When RA was the UCD (n=4,597), the main NUCDs were cardiovascular diseases (29%) and infectious diseases (22%). When RA was a NUCD (n=8,611), the most common UCDs were cardiovascular diseases (35% of certificates, including 877 patients with ischemic heart disease), neoplasms (15%), respiratory diseases (10%) and infectious diseases (7%). The overall O:E ratio was >1 for infectious (3.56), respiratory (1.40) and cardiovascular diseases (1.24), but was <1 for neoplasms.
**Conclusions:** This is the first national study using a multiple-cause-of-death analysis to study the mortality profile of patients with RA. Our results show that cardiovascular diseases are the most common UCD and NUCD associated with RA in France. These data strengthen the need to develop specific strategies for cardiovascular prevention to improve survival of patients with RA.
**Disclosure of Interest:** None declared
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## SAT0117 QUALITY ASSESSMENT IN THE MANAGEMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS. IMPLEMENTATION OF THE "TREAT TO TARGET" STRATEGY

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**Background:** The current paradigm of optimal clinical management of patients with rheumatoid arthritis (RA) recommends reaching a state of remission or low activity of the disease, assessed by composite indexes of activity, by means of a tight control and a dynamic adjustment of available therapeutic options, using a "treat to target" strategy.
**Objectives:** The aim of this study is to assess the level of implementation of the "treat to target" strategy and other parameters of medical quality in clinical records (CRs) of RA patients in Spanish rheumatology departments.
**Methods:** Adult RA patients fulfilling 2010 ACR-EULAR criteria for RA and diagnosed between January 1st, 2010 and December 31st, 2013 in Spanish rheumatology departments were included. From every centre, 19 patients were randomly chosen from a computerized anonymized list provided by every department. Independent auditors assessed the CRs, verifying the fulfilling of the quality criteria included in an assessment tool specifically developed for this project. The study was approved by the ethic committees of every participant hospital. Descriptive statistics was used for the presentation of the results.
**Results:** A total of 856 CRs from 46 rheumatology departments were included. Patients' mean age was 54 years and 71% of patients were women. Mean duration of RA was 2 years. During the follow-up, 38% of patients reached a state of low disease activity, defined by DAS28 and/or SDAI. An explicit assessment of the disease activity as a determinant element considered to choose the therapy was recorded in 32% of the CRs. An optimal escalation of methotrexate dose was registered in 72% of the cases. Use of a composite disease activity score (DAS28, SDAI, CDAI) was reported in 61% of the cases. Disease activity monitoring every 6–8 months after reaching the therapeutic target was recorded in 73% of the cases. In 99% of the cases, the clinicians had registered patient's comorbidities and these associated conditions had been considered in planning the therapeutic approach and objective. In only 4% of the CRs, visits every 4 weeks using a composite activity score had been reported during the early stage while trying to reach remission after diagnosis. Starting a DMARD in the first two weeks after the first appointment with the rheumatologist was recorded in only 35% of the cases.
**Conclusions:** Currently, the implementation of the "treat to target" strategy is scarcely registered in clinical records of patients diagnosed with RA in Spanish rheumatology departments. A minority of patients is treated according to the "Treat to target" recommendations.
**Disclosure of Interest:** None declared
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## SAT0118 DYSLIPIDEMIA IS UNDERTREATED IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM A LARGE COHORT OF RA PATIENTS IN DAILY CLINICAL PRACTICE

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**Background:** Existing guidelines advocate aggressive management of dyslipidemia in rheumatoid arthritis (RA) patients according to cardiovascular disease (CVD) risk scores generated for the general population (SCORE). More specific RA scores such as the ERS-RA score have not been extensively studied.
**Objectives:** To evaluate the use of lipid-lowering agents for CVD prevention (primary/secondary) in RA patients according to different CVD risk scores (SCORE, ERS-RA).
**Methods:** Prospective, multicenter (12 hospitals, 6 private offices), cross-sectional, epidemiological study in Greece (06/2015–01/2016, RA Study Group). Demographics, disease characteristics, treatment and comorbidities were collected and SCORE/ERS-RA were calculated.
**Results:** Among 1475 patients, 178 (12%) had CVD (44% coronary artery disease, 44% peripheral vascular disease, 27% stroke) and 43% were not receiving any hypolipidemic therapy. From those on therapy, only 12% achieved an LDL-cholesterol (LDL-C) level <70 mg/dl while 48% had LDL-C<100 mg/dl. 859 patients without CVD, diabetes or hypolipidemic therapy were further analyzed (79% women, mean age 59.5 yrs, mean disease duration 3.4 yrs, mean DAS28-ESR 3.4, mean HAQ 0.45). Complete data for SCORE calculation were available in 225/859 patients (26%). When stratified according to CVD risk, 31.5%, 66%, 2% and 0.5% of patients had a SCORE of <1% (low risk), ≥1 to <5% (moderate), ≥5 to <10% (high) and ≥10% (very high), respectively. In moderate risk (1–5%) patients, 78% had an LDL-C>100 mg/dl while among high or very high risk (≥5%) patients, 100% had an LDL-C>70 mg/dl (target groups for drug therapy). Among 996 patients (40–75 yrs old), without CVD events, there were 99 diabetic patients (10%) and less than half (48%) were on hypolipidemic therapy. For the rest, the ERS-RA score was calculated (619/897, 69% with available data); 50% of them (308/619) had a 10-year risk of ≥7.5% (therapeutic cutoff) but only 40% of patients in this group were being treated.
**Conclusions:** A substantial proportion of RA patients with established CVD or diabetes do not receive lipid-lowering therapy or they do not achieve therapeutic targets. Among those without CVD or diabetes, more than half belong to moderate to high CVD risk groups and are not receiving appropriate hypolipidemic therapy.
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## SAT0119 COMPARISON BETWEEN CAROTID PLAQUE AND CAROTID INTIMA MEDIA THICKNESS TO DETECT SUBCLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS

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**Background:** Carotid plaque (CP) detected by ultrasonography and carotid intima-media thickness (cIMT) are useful surrogate markers for subclinical atherosclerosis and good predictors of cardiovascular disease in the general population and rheumatoid arthritis (RA).
**Objectives:** Our aim was to determine if cIMT may predict the presence of carotid plaques.
**Methods:** We evaluated 670 RA patients from NW Spain without previous history cardiovascular events. Carotid ultrasonography was performed by a MyLab 70 scanner (Esaote; Genoa, Italy), equipped with 7–12 MHz linear transducer and the *automated software guided technique radiofrequency – Quality Intima Media Thickness* in *real-time* (*QIMT*, *Esaote*, *Maastricht*, *Holland*). The cIMT was determined as the average of three measurements in each common carotid artery. The final cIMT was the largest average cIMT (left or right). Carotid plaque was defined according to the Manheim Consensus Conference criteria. Based on studies reported in non-rheumatic patients, a cIMT was considered as associated with high cardiovascular risk if it was ≥0.90 mm.
**Results:** Unilateral and bilateral carotid plaque frequency and cIMT values are summarized in table 1.
cIMT values were 0.619±0.105 mm in patients without plaques and 0.774 ± 0.161 mm in those with plaques (p<0.001).
Using 0.90 mm as the cIMT cut-off value for high cardiovascular risk, the sensitivity to detect carotid plaques was 21.2% and the specificity 99%. A ROC curve comparing the presence of carotid plaque and cIMT was performed, being the area under the curve 0.795.
The best cIMT cut-off point to determine the presence of plaques was considered as the one with the highest sensitivity and specificity. According to that, 0.670 mm was found to be the best cut-off point, being sensitivity and specificity for plaque detection 71.9% and 74% respectively. Positive predictive value for a cIMT ≥0.670 mm was 78.3% in our population, being 66.8% the negative predictive value.
Regarding bilateral plaques, a cIMT cut-off value of 0.90 mm had sensitivity of 27.7% and specificity of 96.6%. The ROC curve showed that the best cut-off point for bilateral plaque detection was also 0.670 mm with sensitivity 79.1% and specificity 64.2%.

Table 1

| Variable | | Variable | |
|---|---|---|---|
| Carotid plaque, n (%) | 379 (56.8) | Bilateral plaque, n (%) | 251 (37.6) |
| Unilateral plaque, n (%) | 128 (19.2) | cIMT (mean ±SD) mm | 0.71±0.16 |

**Conclusions:** In Spanish RA patients cIMT ≥0.670 mm is a good predictor of carotid plaques. Our study suggests the possibility of considering a cIMT lower than 0.90 mm as a predictor of high cardiovascular risk in RA.
**Disclosure of Interest:** None declared
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## SAT0120 COMPARISON BETWEEN CAROTID ULTRASONOGRAPHY AND CORONARY ARTERY CALCIFICATION SCORE TO DETECT SUBCLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS

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**Background:** Carotid ultrasonography (CU) and coronary artery calcification score (CAC) evaluated by multidetector computed tomography (MDCT) scanner are useful in detecting subclinical atherosclerosis and are good surrogate markers of cardiovascular morbidity and mortality in general population and in rheumatoid arthritis (RA). In RA, a good correlation between both diagnostic methods has been demonstrated, being CU more sensitive for detecting subclinical atherosclerosis.
**Objectives:** Our aim is to determine the association between the presence of carotid plaque and CAC quantification, and, using the presence of carotid plaque as a reference, to determine the cut-off value of CAC score that better predicts subclinical carotid atherosclerosis.
**Methods:** We evaluated 127 RA patients without previous cardiovascular events. Carotid ultrasonography was performed by a MyLab 70 scanner (Esaote; Genoa, Italy), equipped with 7–12 MHz linear transducer and the *automated software guided technique radiofrequency – Quality Intima Media Thickness* in *real-time* (*QIMT*, *Esaote*, *Maastricht*, *Holland*). Carotid plaque was defined according to the Manheim Conference Consensus criteria. To determine CAC score, a CT Imaging of coronary arteries using a 32-slice MDCT scanner (Lightspeed, Pro 32, GE Healthcare, USA) was performed. A CAC score ≥100 was considered as a surrogate marker of very high cardiovascular risk.
**Results:** Unilateral and bilateral carotid plaque frequency and the mean CAC score in the different groups are summarized in table 1. Patients without carotid plaques had a mean CAC value of 23 ±49 [range 0–250], being 50 ±116 [0–569] in patients with unilateral plaque and 192± 302 [0–1205] in patients with bilateral plaques, being these differences statistically significant (p<0.001). Using a CAC score ≥100 as a marker of very high cardiovascular risk, the sensitivity to detect carotid plaques was very low (28%).
A ROC curve comparing the presence of carotid plaque and CAC quantification was performed, being the area under the curve 0.692. When we used CAC score value score ≥1 as the cut-off value to predict high cardiovascular risk, the sensitivity and specificity for the presence of carotid plaques increased (69.3% and 64.1%, respectively). Positive predictive value for CAC ≥1 was 81.3% in our population, being 48.1% the negative predictive value.
Regarding bilateral carotid plaques, the CAC score ≥100 had a sensitivity of 40%. ROC curve showed an area under the curve of 0.712. Using a CAC score value score ≥1 as the cut-off value to predict high cardiovascular risk, the sensitivity to determine the presence of carotid plaques increased to 76.4% but the specificity decreased to 54.2%.

| Variable | | Variable | |
|---|---|---|---|
| Age (mean ± SD) | 58, 57±9,7 | Bilateral plaque, n (%) | 55 (43,3) |
| Female, n (%) | 92 (72,4) | CAC (media ± DE) | 103,4±222,6 |
| Plaque No, n (%) | 39 (30,7) | CAC ≥1, n (%) | 75 (59) |
| Plaque Yes, n (%) | 88 (69,3) | CAC ≥100, n (%) | 26 (20,5) |
| Unilateral plaque, n (%) | 33 (26) | | |

**Conclusions:** A CAC score value score ≥1 is good predictors of carotid plaques, showing sensitivity close to 70%. Our data support the use of a CAC score

value score ≥1 instead of a CAC score ≥100 as the cut-off value to predict high cardiovascular risk in patients with RA.
**Disclosure of Interest:** None declared
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## SAT0121 THE EFFECT OF TYPE 2 DIABETES ON DISEASE ACTIVITY IN MALE AND FEMALE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) patients with comorbidities are likely to have higher disease activity (DAS28) scores than patients without comorbidities[1–3]. Diabetes has been recently suggested to associate with higher disease activity in a large group of RA patients[4]; however, it is still uncertain how baseline diabetes affects RA disease activity and remission percentages in RA[5]. This is important and information might be used to improve treatment strategies.
**Objectives:** To investigate the effect of having type 2 diabetes on DAS28 scores and RA remission percentages in male and female RA patients during the first year after RA diagnosis.
**Methods:** Data were retrieved from the prospective Nijmegen Early RA cohort. Patients fulfilled the ACR or ACR-EULAR classification criteria. The course of disease activity (DAS28) over the first year after RA diagnosis was the primary outcome. Secondary outcome was RA remission one year after diagnosis (DAS28 score <2.6)[6]. Presence of diabetes was defined by physician diagnosis. Statistical analyses comprised mixed linear models and logistic regression. Potential confounders included smoking, BMI, alcohol intake, age, HAQ score and rheumatoid factor at baseline. Gender was treated as effect modifier.
**Results:** 35 (4.2%) out of the 840 included patients had DM2 at baseline. Mean DAS28 values at baseline were 5.33 (SE 0.20) for diabetic and 5.04 (SE 0.05) for non-diabetic patients (p<0.21). At baseline only age was relevantly different between non-diabetic and diabetic patients in univariable analyses (53.8 (SE 0.50) versus 56.0 (SE 2.44) years, p=0.04), and was therefore included as confounder in the analyses. The difference in DAS28 scores during the first year after RA diagnosis between diabetic and non-diabetic patients is presented in Table 1.The parameter estimate of the interaction between gender and DM2 was -0.08 (SE 0.41), indicating no statistically significant interaction (p=0.85). Moreover, after one year, four (11.8%) diabetic and 186 (23.1%) non-diabetic patients were in remission. Table 1 presents the effect of DM2 on achieving remission one year after RA diagnosis, which was not statistically significantly different for males and females (parameter estimate 1.36, SE 1.24, p=0.28).

Table 1. Differences in DAS28 scores and OR for achieving RA remission during the first year after RA diagnosis between diabetic and non-diabetic patients

| | Crude effect | P | Adjusted effect* | P |
|---|---|---|---|---|
| Difference in DAS28 score (SE) | | | | |
| DM2 versus no DM2 | 0.00 (0.00) | 0.89 | 0.00 (0.00) | 0.95 |
| OR for achieving remission at 1 year after RA diagnosis (95% CI) | | | | |
| DM2 versus no DM2 | 0.44 (0.15–1.28) | 0.13 | 0.21 (0.03–1.59) | 0.13 |

*Adjusted for gender, age, and interaction between gender and DM2. α=0.05. CI, confidence interval; DM2, diabetes mellitus type 2; SE, standard error.

**Conclusions:** There was no large influence of having DM on baseline DAS28, response in DAS28 scores and remission percentages during the first year after RA diagnosis; this was the same for male and female patients.
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## SAT0122 COMORBIDITIES IN A MEXICAN MESTIZO COHORT OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Patients with rheumatoid arthritis (RA) are at an increased risk of comorbidities and it has been linked to a decrease in life expectancy in comparison with the general population. Early recognition and treatment of comorbidities is important.
**Objectives:** We aimed to evaluate the presence of comorbidities in a Mexican mestizo cohort of patients with early-RA.
**Methods:** A descriptive, cross-sectional study of patients with early-rheumatoid arthritis (disease duration <12 months) was designed. Information on comorbidities, weight, height and body mass index (BMI) was collected.
**Results:** Data of fifty patients was included in the final analysis, 46 (92.0%) of them were women. Patient's characteristics are shown in Table 1. Mean age was 44.3 ± 13.12 years. Mean disease duration was 6.09 ± 2.91 months. Tuberculosis (TB) infection was found in 12 (24.0%) patients, 7 (58.3%) of them were latent tuberculosis infection. Four cases of extra-pulmonary TB were reported. Hypertension was the second most prevalent comorbidity, being reported in 11 (22.0%) patients.

| Table 1. Patient's characteristics | |
|---|---|
| Women, n (%) | 46 (92.0%) |
| Age (yo), mean ± SD | 44.30 ± 13.12 |
| Disease duration (months), mean ± SD | 6.09 ± 2.91 |
| Body mass index, mean ± SD | 28.60 ± 5.48 |
| Type 2 diabetes mellitus, n (%) | 6 (12.0%) |
| Smoking, n (%) | 9 (18.0%) |
| Dyslipidaemia, n (%) | 4 (8.0%) |
| Hypertension, n (%) | 11 (22.0%) |
| Tuberculosis infection, n (%) | 12 (24.0%) |
| | n= 50 |

**Conclusions:** In this cohort of Mexican mestizo patients with early-RA, TB infection was found in 24.0% of the patients. Hypertension was the second most prevalent comorbidity in our cohort, being reported in 22.0% of the patients. Other cardiovascular heart disease risk factors were also reported. Early recognition of these comorbidities is needed because of the higher risk of cardiovascular heart disease in RA-patients in comparison to the general population.
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## SAT0123 RADIOGRAPHIC SEVERITY OF RHEUMATOID ARTHRITIS IN LATIN AMERICAN PATIENTS: RESULTS FROM THE GLADAR COHORT

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**Background:** More radiographic damage occurs within the first year of rheumatoid arthritis (RA). Erosions occurring preferentially in feet and joint space narrowing (JSN) in wrists have been described in early RA. Little is known of radiographic progression in Latin American patients with early RA.
**Objectives:** To describe radiographic changes in a Latin American (LA) early rheumatoid arthritis (RA) multinational inception cohort at baseline, a multicenter observational study.
**Methods:** Patients were enrolled in GLADAR (*Grupo Latino Americano de estudio De Artritis Reumatoide)*, the largest longitudinal cohort of early RA (<1 year from onset) in LA, from 2004/2005–2008. Demographic and clinical data were obtained and sets of hand/wrist and foot radiographs were scored using the modified Sharp/ Van der Heijde scoring system.
**Results:** A total of 507 patients with radiographic readings were evaluated. The mean radiographic score was 23.37 at baseline visit; 56.2% had erosions and 97.8% joint space narrowing (JSN). Among patients with JSN, the mean score was 20.97. JSN occurred in hands/wrists (97%) and feet (72%), while erosions were observed in hands/wrists (42.8%) and feet (28.8%). X-rays of 253 patients were assessed after at one-year of follow-up; of 132 without erosions, 14.4% developed erosions; and 100% JSN. No significant differences were observed among patients who progressed according to socio-demographic features, use of DMARDS, use of prednisone and rheumatoid factor positivity.
**Conclusions:** This is the largest radiographic study of Latin American RA patients. Damage occurs early in the disease. Surprisingly, JSN is the most common radiographic change and occurs more often in hands/wrist. Further studies are needed to understand the meaning of the greater breakdown in cartilage compared to erosions in this population.
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## SAT0124 RISK FACTORS OF VENOUS THROMBOEMBOLIC EVENTS IN PATIENTS WITH RHEUMATHOID ARTHRITIS (RA)

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**Background:** Venous thromboembolic events (VTE) such as deep vein thrombosis, thrombophlebitis and thromboembolism of pulmonary artery are an important clinical problem that concerns all spheres of medicine. Patients with chronic inflammatory diseases including RA have an increased risk of venous thromboembolism. It is important to determine risk factors of VTE in patients with RA (standard and associated with disease) for prevention of thrombosis.
**Objectives:** To determine prognostic risk factors of venous thromboembolic events in patients with rheumathoid arthritis.
**Methods:** 362 patients (F:302, M:61) with definite diagnosis of rheumathoid arthritis were analyzed, 53,7 ± 13,3 years old, duration of disease 12,4 ± 10,9 years. All patients were hospitalized in V.A. Nasonova Reasearch Institute of Rheumatology. Doppler ultrasound of lower limbs veins were done to patients with suspected thrombosis or with thrombosis in past history. Patients were divided in 2 groups: 1st Gr included patients with thrombosis in a moment or in past history – 34/362 (9,9%) and 2nd Gr - patients and without thrombosis – 328/362 (90,1%). Analysis of risk factors was done according to questionnaire survey and medical history. Disease activity was expressed as DAS28 score which is a composite score derived from tender joint count, swollen joint count, ESR and patient's global assessment of disease activity. Possible prognostic risk factors included age (>40 years, >60years, >75 years), body mass index (BMI) >30, smoking, pregnancy and childbirth, taking antifertility agents, immobilization, surgical treatment, traumas, fractures, diabetes mellitus, pulmonary diseases, cardiac failure, varicose vein disease, cancer, oral and intra-articular (<5 and >5 injections) introduction of glucocorticoids (GCs). In order to identify predictors of venous thromboembolic events we used multivariance analysis (discriminant function classification).
**Results:** Multivariance analysis showed that the thrombosis is mainly influenced by following factors: immobilization, cardiac failure, varicose vein disease, oral and intra-articular (>5 injections) introduction of GCs; weighted coefficients: 1,0; 0,92; 3,13; 0,02; 0,52. Function of prediction of thrombosis is suggested:
Z =1,0 * immobilization (Yes-1/No-0) + 0,92* cardiac failure (Yes-1/No-0) + 3,13* varicose vein disease (Yes-1/No-0) + 0,02* oral GCs (yes-1/No-0) + 0,52* intra-articular (>5 injections) introduction of GCs (Yes-1/No-0).
The value of function Z=1,65 divides patients with and without venous thromboembolic events, sensitivity 64%, specificity 82%, positive predictive relevance 80%.
**Conclusions:** Adverse prognostic factors of venous thromboembolic events in patients with rheumathoid arthritis are immobilization, cardiac failure, varicose vein disease, oral and intra-articular (>5 injections) introduction of GCs.
**Disclosure of Interest:** None declared
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## SAT0125 TOCILIZUMAB ACHIEVES RAPID REDUCTION OF DISEASE ACTIVITY AND HAS BENEFICIAL EFFECTS ON BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS – RESULTS OF A PROSPECTIVE 5- YEAR STUDY

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**Background:** Tocilizumab (TCZ) leads to a rapid improvement of the clinical course in patients with highly active rheumatoid arthritis (RA). However, a residual rheumatic activity can still be detected.1 RA is a known risk factor for osteoporosis related bone fractures.2 It is well established that TCZ has beneficial effects on bone remodeling.3
**Objectives:** The aim of this analysis was to investigate the effects of TCZ on bone mineral density in a real world patient population.
**Methods:** 50 rheumatoid factor positive patients with RA (17 male, age 20–72 years) who received TCZ as monotherapy since 2008 were prospectively investigated. At baseline and the following 4–6 clinical visits, DAS28 was determined and ultrasound performed. At baseline and every 6 months thereafter, biochemical parameters for bone metabolism and protein diagnostics were recorded. Once a year, the subjects underwent MRI, CT and DXA scan.
**Results:** In all 50 patients the DAS28 normalized at the latest by the 3rd infusion cycle of TCZ. The initial RAMRIS score of >5 was reduced to <2 after 6–18 months. Ultrasound revealed a decline of synovialitis and tenodynovialitis after 8 weeks and 12 months, respectively. At baseline in 22 women with early RA, axial QCT/DXA values and lateral DXA values were within reference. 3 patients with early RA had osteopenia, 2 had osteoporosis. Patients with manifest RA had a BMD in the reference range, 3 had osteopenia and 2 were diagnosed with osteoporosis. In 6 male patients, BMD values were within the reference range. 2 men with early RA had osteopenia and 2 had manifest osteoporosis. In 1 male patient with manifest RA, normal BMD values were documented. 2 men with manifest RA hat osteopenia and 4 had osteoporosis. 10 patients had vitamin D3 deficiency and were treated with vitamin D3. 2 patients with osteoporosis were treated with antiresorptive medication. In all patients, BMD values were within the reference range after 1 year of treatment with TCZ, despite 18% of patients presenting with a DAS score >2.7. 2 patients presented with pustular dermatosis in the palms. No allergic reactions were observed.
**Conclusions:** Treatment with TCZ leads to a rapid decline of inflammatory activity of the affected joints in patients with RA and minimizes cartilage destruction. TCZ showed a positive effect on bone remodeling and therefore BMD. Thus, the risk for the development of osteoporosis and its related fractures can be minimized by TCZ treatment. Furthermore, TCZ has a positive effect on BMD in manifest RA thus preventing sarcopenia. Temporary elevations of DAS28 during TCZ therapy do not negatively affect BMD.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4890

## SAT0126 COMORBIDITIES AFTER DAILY CONCOMITANT TREATMENT WITH 10MG PREDNISONE OR PLACEBO IN THE 2-YEAR COMPUTER ASSISTED MANAGEMENT IN EARLY RHEUMATOID ARTHRITIS TRIAL-II

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**Background:** In the second Computer Assisted Management in Early Rheumatoid Arthritis (CAMERA–II) trial, patients initiated treatment with methotrexate (MTX) with randomized 10 mg/d prednisone (pred) or placebo (plac), given for 2 years [1]. Significantly more patients in the MTX+pred strategy arm than in the MTX+plac arm were erosion free at 2 years, and disease activity improved faster. The frequency of adverse events (AE) during the 2 year trial was comparable between the groups. There is paucity of data on long-term AEs after treatment with medium dose of glucocorticoids, however.
**Objectives:** To investigate the incidence of long-term AEs/comorbidities in early rheumatoid arthritis patients, who had been treated additionally with pred10 mg/day or plac in CAMERA-II.
**Methods:** After the 2 year trial, patients were followed according to a protocol in clinical care. The occurrence of AEs/comorbidities and the use of pred (it was the strategy to taper and stop it) was collected retrospectively from the medical charts. The incidence of long-term AEs/comorbidities in the former MTX+pred group was tested versus that in the former MTX+plac group using Fisher's Exact tests.
**Results:** Of the 236 patients included in the CAMERA-II trial, follow-up data was available of 218 patients: MTX+pred N=107, MTX+plac N=111; no longer followed according to protocol N=18. The median follow-up time after the end of the 2-year trial period was 6 (range 0–9) and 6 (0–11) years, respectively. 86 (80%) patients treated with pred could discontinue it after a median of 9 months after the end of the trial end. The percentage of patients with AEs/comorbidities is shown in Table 1. No statistically significant differences between the two groups were found.

Table 1. Percentage of new onset AEs/comorbidities after the trial in the former pred vs former plac group

| Comorbidity | MTX + pred (N=107) | MTX + plac (N=111) | p-value |
|---|---|---|---|
| ≥1 comorbidity | 36 | 36 | 1.00 |
| Hypertension | 4 | 10 | 0.11 |
| Diabetes Mellitus type II | 3 | 2 | 0.68 |
| Cardiovascular disease | 13 | 8 | 0.27 |
| Peptic ulcer | 1 | 0 | 0.49 |
| Cataract | 8 | 7 | 0.80 |
| Glaucoma | 0 | 1 | 1.00 |
| Fracture | 11 | 14 | 0.55 |
| Osteonecrosis | 0 | 0 | – |
| Mortality | 10 | 6 | 0.33 |

**Conclusions:** Of patients in the MTX+pred group during CAMERA-II, 80% could discontinue pred after the trial. There was no increased incidence of long-term AEs/comorbidities in the former MTX+pred group.

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## SAT0127 CHILD OUTCOME AFTER CERTOLIZUMAB PEGOL EXPOSURE IN RHEUMATOID ARTHRITIS PREGNANCIES: A CASE SERIES REPORT

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**Background:** About 25% of pregnant RA patients remain active during pregnancy and need continuation of effective therapy to maintain low disease activity [1]. Recent evidence supports the use of TNF inhibitors (TNFi) to achieve these goals [2]. The overall safety of TNFi exposure during pregnancy has been demonstrated [3–4]. Certolizumab pegol (CZP) has received particular interest because of its low transplacental transfer, an advantage compared to several other TNFi [5]. A recent study analyzing CZP exposure during gestation has not shown harmful effects on pregnancy outcomes [6]. Since there are few data on child outcome, our case series adds observations on the safety of CZP in pregnancy.
**Objectives:** The study purpose consists in assessing CZP exposure safety during pregnancy in a group of RA patients.
**Methods:** During a 48 months period, we retrospectively evaluated 8 RA patients exposed to CZP in the 1st and/or the 2nd trimester of pregnancy. All patients had signed an informed consent regarding the potential risk of biologic agents for the fetus. Details regarding demographic and clinical presentation as well as pregnancy outcome and child health were collected. Data on child development during the first 6 months of life were obtained.
**Results:** The eight enrolled patients had been treated with CZP for 6 to 18 months. Three patients received methotrexate (MTX) and other TNFi (infliximab or etanercept) before pregnancy, which were discontinued 6–24 months before conception.
During pregnancy all patients were treated with the standard dose of CZP 200 mg every 2 or 3 weeks. In addition, all patients received low-dose prednisone ranging from 5±2.5 mg daily. Two subjects were in addition on sulfasalazine 500 mg x 3/day, and three others on hydroxychloroquine (HCQ) 200 mg twice daily. In 6/8 patients, CZP treatment was continued throughout the first trimester. In 2 cases high disease activity required continuation of CZP until the end of the second trimester.
No obstetric, neonatal or perinatal severe complication was observed. Except for one SGA child all neonates were healthy at birth. One child was hospitalized at the age of 4 months for disseminated Candida albicans infection, but recovered completely with amphotericin B treatment. All other children developed normally during the first 6 months of life. None of the newborn was breastfed, due to the lack of data on safety. All babies were vaccinated according to the mandatory Italian schedule (includes no live vaccine during the first 6 months of life); one child had the 5th month dose postponed to the 6th month of life.
**Conclusions:** The limits of our case series consist in the small numbers and the lack of measuring CZP levels in cord blood. However, our data add to the experience that CZP might be considered in pregnant RA patients when disease activity requires continuation of therapy throughout pregnancy.
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## SAT0128 SECONDARY SJÖGREN'S SYNDROME IN RHEUMATOID ARTHRITIS: CHARACTERISTICS AND ASSOCIATION WITH JOINT DAMAGE

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**Background:** Rheumatoid Arthritis (RA) is often associated with secondary Sjögren's syndrome (SSs) with a prevalence ranging from 10 to 30 percent.
**Objectives:** The aim of this study was to evaluate the prevalence of SSs, characterize sSS patients and study the association between sSS and joint damage.
**Methods:** We conducted a cross-sectional study of RA patients, according to ACR/EULAR 2010 classification criteria, followed up at the Department of Rheumatology. Demographic characteristics and RA features of disease were collected. Pain was measured using a visual analogue scale (VAS). Disease activity was assessed by the Disease Activity Score (DAS 28). Functional disability was evaluated by the Health Assessment Questionnaire (HAQ). Joint destruction was assessed by the van der Heijde-modified Sharp Score. The diagnosis of SSs was made by a rheumatologist or confirmed by chart review. Data analysis was carried out using the SPSS 20 Software. $p<0.05$ was considered statistically significant.
**Results:** One hundred and four patients with a mean±SD age of 49.37 ± 13.21 years were enrolled. Eighty-nine percent were females. Mean±SD duration of symptoms was 10.88 ± 9.17 years. Rheumatoid factor was present in 75% of patients with RA. Seventeen patients (16.3%) had SSs. RA subjects with sSS had longer RA disease duration and higher sharp scores. VAS pain and functional disability were significantly higher in patients with sSS ($p<0.05$). The multivariate analysis showed that factors associated with joint destruction in patients with SSs were disease duration of RA (p=0.0001) and seropositivity by ACPA (P=0.006).
**Conclusions:** In our study, RA patients with sSS had worse joint damage, suggesting that sSS is a marker of a more aggressive disease. Therefore, it is important to screen sSS symptoms in patients with RA.
**Disclosure of Interest:** None declared
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## SAT0129 VITAMIN D STATUS AND ITS ASSOCIATION WITH DISEASE ACTIVITY, SEVERITY AND PHYSICAL DISABILITY IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Vitamin D has immunomodulatory effects in a wide range of human autoimmune diseases; including Rheumatoid Arthritis (RA). Vitamin D deficiency is common in RA.
**Objectives:** The objective of this study was to evaluate vitamin D status in RA patients and assess the relationship between vitamin D levels, disease activity, severity and physical disability.
**Methods:** We included in this cross-sectional study patients with RA according to ACR/EULAR classification criteria, followed up at the Department of Rheumatology. Demographic characteristics and disease specific variables were collected. Disease activity was assessed by the Disease Activity Score (DAS 28). Functional disability was evaluated by the Health Assessment Questionnaire (HAQ). Joint destruction was assessed by the van der Heijde-modified Sharp Score. Serum concentrations of 25(OH) Vitamin D were measured. According to the GRIO recommendations, 25(OH)D insufficiency was defined as 25(OH)D ranging from 10 to 30 ng/mL, and deficiency as 25(OH)D $<10$ ng/mL. Data analysis was carried out using the SPSS 20 Software. $p<0.05$ was considered statistically significant.
**Results:** Seventy-tree patients with a mean±SD age of 52.04 ± 12.26 years were enrolled. Sixty-nine percent were females. Mean±SD duration of symptoms was 11.61 ± 8.43 years. The prevalence of 25(OH)D insufficiency and deficiency was 69.9% and 17.8% successively. The univariate analysis showed a significant correlation between 25(OH)D serum concentration, number of swollen joints (p=0.024) and disease activity (p=0.012). In multivariate analysis adjusted for age, Sharp score, and C-Reactive Protein, there was a significant correlation between 25(OH)D serum concentration and disease activity (p=0.048).
**Conclusions:** Vitamin D deficiency is highly prevalent and is associated with higher disease activity in our RA patients. Therefore, Vitamin D measurement and possibly vitamin D supplementation should be considered in the management of RA patients.
**Disclosure of Interest:** None declared
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## SAT0130 DRUG USAGE ANALYSIS AND COMPARATIVE MEDICATION EXPENSES IN PATIENTS WITH RHEUMATOID ARTHRITIS USING CONVENTIONAL OR BIOLOGICAL THERAPY

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**Background:** In the last years it has seen a marked improvement in the treatment of rheumatoid arthritis (RA) by using conventional DMARDs and more recently with the introduction of biologics; biological therapy is useful to prevent clinical and radiological progression in patients with RA but is associated with high costs and has impacted budget in Colombian health system.
**Objectives:** The purpose of this study was to assess drug usage of conventional treatment and biologic agents in terms of reduction of the Disease Activity Score 28 (DAS28) and comparative medication expenses associated in patients with moderate-severe RA during a 24 month period.
**Methods:** We conducted a real-world, retrospective, cross-sectional study, based on information from a specialized in RA center in Colombia where there is a model with therapeutic goals like T2T and a multidisciplinary approach. Subjects with moderate-severe disease activity received conventional treatment or biologic

therapy, and were followed-up and treated according to DAS28; therapy had to be adjusted with DAS28 >3.2 unless the patient's conditions did not allow it. Descriptive epidemiology was done and the overall drug costs were assessed and compared between the two types of therapies.
**Results:** 526 patients using conventional treatment were included, mean age 63.5 ± 11.8, 424 (80%) female and 102 (20%) male. These patients had a DAS28 on average 4.5 ± 1 at beginning and after 24 months 410 patients (78%) got remission/low disease activity status with a mean DAS28 2.57 ± 1. On the other hand, 303 patients using biologics were included, mean age 58.5 ± 9.4, 251 (82%) female and 52 (18%) male; after 24 months of observation 154 patients (50%) obtained remission/low disease activity status with a mean DAS28 of 2.6 ± 1. Cost of conventional DMARD treatment for RA in Colombia was about 850 US dollars/patient/year because mostly of patients have more than one DMARD; use of biologics cost $7,725 US dollars/year/patient, ranging between the cheapest biological and the most expensive ($4,878 and $12,774 US dollars/year respectively); that means conventional treatment is nine times cheaper in comparison with costs of biological therapy and possibly more effective.
**Conclusions:** This study showed that it is possible to decrease disease activity and obtain a significant cost-reduction in treatment of RA by using conventional DMARDs in a model with therapeutic goals like T2T and optimizing a multidisciplinary approach; the use of biologic therapies in the treatment of RA continues being evaluated but is associated with high costs; we show real-world data on drug utilization in patients with moderate-severe RA in a low income developing country. These observations could be used by decision makers in order to consider health decisions; nonetheless, further research based on cost-effectiveness analysis and cost-comparison is needed to verify these results.
**Disclosure of Interest:** None declared
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## SAT0131 A LOOK TO THE WRONG DIAGNOSIS OF RHEUMATOID ARTHRITIS

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**Background:** There is a lack of expertise in rheumatoid arthritis (RA) diagnosis in primary level of Colombian medical centers, leading to misdiagnosis; many times osteoarthritis (OA) and another rheumatic diseases are misdiagnosed as RA which derives in wrong treatment for patients with clinical and health economics implications.
**Objectives:** The aim of this study was to describe demographic and clinical characteristics of a cohort of patients with misdiagnosis of RA in a specialized center in Colombia.
**Methods:** A descriptive, cross sectional study. Were included patients who were referred from primary care centers to a RA specialized center in a 48 month period with presumptive diagnosis of this disease. Each patient was evaluated to confirm or rule-out diagnosis of RA as follows: a rheumatologist fulfilled a complete medical record including all previous data; it was assessed rheumatoid factor and anti-citrullinated antibodies, and other laboratories depending on each case. Also were made x-rays of hands and feet, and in some cases of persistent doubt about the diagnosis was requested comparative MRI of hands or/and feet. Frequencies and percentages were calculated for the demographic and clinical characteristics of the cohort of patients in which the diagnosis of RA was ruled-out.
**Results:** In 5176 patients was found a wrong diagnosis of RA. Of these misdiagnosed patients, 4.385 (85%) were women, and 791 (15%) men, with an average age of 59 ± 13 years old. Between differential diagnosis which were found in this cohort of misdiagnosed patients: osteoarthritis in 2930 patients (56.6%), systemic lupus erythematosus (SLE) in 369 patients (7.1%), Sjögren syndrome in 237 patients (4.6%), spondyloarthropathies in 135 patients (2.6%), gout in 95 patients (1.8%), and in 28.3% of cases other diagnoses including all kinds of soft tissue rheumatism.
**Conclusions:** Almost half patients with presumptive RA diagnosis in primary care centers in Colombia are misdiagnosed. The most important cofounding diagnosis was osteoarthritis and many patients were receiving DMARDs for treatment. For this reason there is an urgent need of education strategies for primary care physicians and the implementation of centers of excellence in RA, in order to conduct a proper diagnose and avoid clinical and health economics consequences of misdiagnosis.
**Disclosure of Interest:** None declared
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## SAT0132 PRESENCE OF PSYCHOLOGICAL, SEXUAL AND SLEEP DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The rheumatoid arthritis (RA), as known, causes inability in various performance areas mostly in the musculoskeletal, but few is known about psychological, sleep and sexual problems.
**Objectives:** The aim of this study is to describe the socio-demographic profile of patients with RA in specialized RA clinic in Colombia, where we identified disorders in areas besides the physical or musculoskletal, like psychological, sexual and sleep.
**Methods:** A descriptive study was performed in a specialized clinic dedicated to care patients with RA. 1298 RA patients were included in the study, which were seen by the area of psychology; information was collected through semi-structured interviews and non-probability sampling, also using classificatory criteria of pathologies described in CIE 10 diagnostic manual, applying descriptive epidemiology for continuous variables, measure of central tendency and dispersion for qualitative and categorical variables through percentages and averages.
**Results:** Total sample of patients was 1298, 1048 (80%) were women and 250 (19%) were men. Patients had a DAS28 2.6 in average ± 1.1; mean age was 55.1 ± 8.8 years; 58% of patients were medium socio-economical level and the 34% were low socio-economical level; 59% were married, 18% were divorced, 14% is single and 6% were widowed. Related with the occupation, 25% were retired because age and 10% had handicap retirement pay; 24% were dedicated to housekeeping and 35% were working. Related to education 6% were illiterate, 44% had elementary school, 33% high school, 8% had a technical degree and only 7% had college level. According to CIE-10 739 patients (57%) had psychological disorders, 279 patients (21%) had sexual and 373 (28%) had sleep disorders.
**Conclusions:** According to these findings there is a high prevalence of patients with low-medium socio-economical levels in RA which shows a possible correlation of a socio-demographic unfavorable situation with presence of disease. Also there are high rates of psychological, sexual and sleep comorbidities, which implies that measures must be implemented in order to improve these areas of performance in patients with RA.
**Disclosure of Interest:** None declared
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## SAT0133 MANAGEMENT OF CARDIOVASCULAR RISK FACTORS IN RHEUMATOID AND PSORIATIC ARTHRITIS: THE AUSTRALIAN RHEUMATOLOGY ASSOCIATION DATABASE (ARAD) HEART HEALTH SURVEY

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**Background:** Chronic inflammatory arthritis is associated with increased cardiovascular (CV) morbidity and mortality [1]. Furthermore, obesity is associated with a reduced chance of achieving low or minimal disease activity in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) [2,3]. EULAR guidelines recommend that patients with chronic inflammatory arthritis should receive screening and management for traditional CV risk factors [4]. Previous analysis showed that diabetes mellitus (DM) and high cholesterol were more common in patients with PsA than RA [5].
**Objectives:** To describe and compare current treatment patterns for CV risk factors in patients with RA and PsA in ARAD.
**Methods:** ARAD is a voluntary national registry. Participants with inflammatory arthritis complete questionnaires every 6 -12 months in online or paper format. An additional Heart Health Survey was sent to online participants, including questions about pharmacological management of CV risk factors, dietary modification and physical activity. Results from the survey were linked with ARAD.
**Results:** Out of 1973 online ARAD participants, 1254 (64%) responded to the Heart Health Survey. Unlike earlier analysis of the whole ARAD cohort, there were no significant differences in the prevalence of CV risk factors between the RA and PsA responders. Pharmacological or dietary management was utilised by all patients with DM. Most patients with hypertension received pharmacological treatment (RA 93%, PsA 94%). The majority of patients with hypercholesterolaemia also received pharmacological management (RA 69%, PsA 73%). However, utilisation of lifestyle modification for management of obesity was low. In obese patients, only 34% had made any dietary change for their health. 12% of obese patients with RA and 8% of obese patients with PsA had attended an exercise program. 63% of RA and 61% of PsA patients who were obese reported being physically inactive; undertaking less than 30 minutes of

moderate physical activity on 3 or more days of the week. In obese patients, 79% with RA and 62% with PsA reported that their arthritis limited their ability to engage in physical activity.

**Conclusions:** CV risk factors are common in this Australian cohort. Management of CV risk factors was similar between patients with RA and PsA. The majority of patients receive pharmacological management. However, lifestyle modifications appear to be underutilised in the management of obesity. Arthritis is reported as the main factor limiting respondents' physical activity.

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## SAT0134 PERIODONTAL CONDITION AS A EARLY MANIFESTATION OF UNDIFERENCIATED ARTHRITIS

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**Background:** Periodontal disease (PD) and rheumatoid arthritis (RA) are two common chronic inflammatory diseases globally destructive. Recently, there has been increasing evidence that periodontal disease and rheumatoid arthritis share many biological and pathological features like the significant increase in acute phase reactants. It is important to demonstrate that periodontal inflammation can affect clinical index and variability of the patients with RA.

**Objectives:** To evaluate the association between clinical indices of PD and markers of activity in Colombian RA patients and individuals with first-degree relatives of patients with RA.

**Methods:** The rheumatologic condition and periodontal status of 73 individuals with rheumatoid early arthritis and 164 individuals first degree relative with RA patient were evaluated. *Porphyromona gingivalis (Pg),* IgG1, and IgG2 to *Pg* were determined. The C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor-RF, anti-citrullinated protein antibodies, RA 33 antibodies and scales of RA activity were measured. The rheumatologic Scores and periodontal condition were evaluated by two experienced and calibrated periodontists and rheumatologist. The chi-square test was used to evaluate association between periodontal variables and RA activity indices. The study was approved by the Ethics Committee of the Universidad El Bosque and the Hospital Militar Central, Bogotá, Colombia.

**Results:** RA group showed 67.1% of periodontitis, of which 43.8% were classified as moderate and 15.1% as severe, positive RF in 49 patients (67.2%) and ACPAs (52%), RA patients had association between dental Plaque >30% with activity clinical index DAS28ESR (p=0.05), SDAI (p=0.008), Bleeding of probing with DAS28ESR (p=0.05), ESR (p=0.03) and CRP (p=0.03) and association between clinical attachment level with ACPAs (p=0.05), Furthermore first-degree relatives of patients with RA showed periodontal disease in a 70.1% classified as moderate 43.9% and 12.8% as severe, positive RF 18 (18%), and ACPAs (7.1%), was finding association between gingival index with activity clinical index DAS28ESR (p=0.05), CRP (p=0.03), ESR (p=0.005) and RAPID3 (p=0.05), association periodontal pocket deep with HAQ-DI score (p=0.05) and bleeding of probing with SDAI (p=0.05).

**Conclusions:** RA and PD share pathophysiological mechanisms that explain how greater commitment periodontal dental plaque index and periodontal pocket deep are directly related to indices of clinical activity of the joint disease. This would explain the persistence of elevated acute phase reactants with minimal or absent joint clinical manifestations.

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## SAT0135 ACHIEVING FREEDOM FROM GLUCOCORTICOIDS MIGHT DECREASE RISK OF CLINICAL FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS: FIVE-YEAR FINDINGS OF THE TOMORROW STUDY

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**Background:** Patients with rheumatoid arthritis (RA) who have muscle weakness and stiff or painful joints might be at increased risk of falls and fractures.

**Objectives:** The present study prospectively investigates correlations between decreasing doses of glucocorticoid (GC) and the incidence of clinical fractures in patients with RA based on the five-year findings of the TOMORROW study (UMIN000003876) that started in 2010.

**Methods:** We evaluated anthropometric parameters, bone mineral density, disease activity, RA medication, and the incidence of clinical fractures over a period of five years in 202 patients with RA (mean age, 58.6 years; mean disease duration, 14.0 years). We also assessed the effects of GC doses on the incidence of clinical fractures over the same period in patients with RA using multivariate regression analysis.

**Results:** The incidence of clinical fractures in patients with RA was 0.042/person-years (py). There were 87 RA patients (41.8%) treated with GC whose incidence rate and number of clinical fractures were significantly higher than those without GC treatment (27.4% vs. 11.9%; p=0.008; 0.063 vs. 0.012 py; p=0.012, respectively). After adjusting for fracture risk factors including age, sex, smoking, and body mass index, multivariate logistic regression analysis revealed that GC administered within the five-year period was a significant risk factor for clinical fractures (odds ratio [OR], 2.58; 95% confidence interval [CI], 1.22–5.44, p=0.013). A mean GC dose during the 5-year period of ≥2 mg/day increased risk for fractures in patients with RA (OR 3.48; Table 1). Although only reducing the GC dose did not decrease the risk of clinical fractures in patients with RA, risk was significantly lowered when the dose was reduced to zero within the five-year period (OR 0.21; Table 1).

Table 1. Odds ratios for fractures determined by multivariate logistic regression analysis in 87 patients with RA treated by GC

| | OR | 95% CI | *p* |
|---|---|---|---|
| History of fractures | 1.99 | 0.95–4.16 | 0.069 |
| Average GC dose (≥2 mg/day/5 y) | 3.48 | 1.19–10.21 | 0.023 |
| Only reducing GC within 5 y | 0.61 | 0.21–1.78 | 0.362 |
| Reducing GC to zero within 5 y | 0.21 | 0.07–0.65 | 0.006 |
| Bisphosphonate medication | 3.37 | 1.51–7.54 | 0.003 |
| Low BMD at thoracic vertebrae (<0.7 g/cm$^2$) | 4.44 | 1.69–11.64 | <0.001 |

RA, rheumatoid arthritis; GC, glucocorticoid; OR, odds ratio; CI, confidence interval; BMD, bone mineral density.

**Conclusions:** Medication with GC was a significant risk factor for clinical fractures, and low doses are apparently significantly associated with an increased frequency of fractures among patients with RA. However, reducing the GC dose to zero among RA patients within five-years could lower the risk for clinical fractures. We concluded that GC medication should be tapered to zero over a period of five years in patients after RA activity is controlled.

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## SAT0136 PATIENTS WITH RHEUMATOID ARTHRITIS AND HIGH LEVELS OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY UNDER TREATMENT WITH HIGH-DOSE GLUCOCORTICOID FREQUENTLY FALL: FIVE-YEAR FINDINGS OF THE TOMORROW STUDY

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**Background:** Patients with rheumatoid arthritis (RA) who have muscle weakness and stiff or painful joints might be at increased risk for falls. However, previous prospective studies have not included controls to clarify whether RA per se represents a risk factor for falls.

**Objectives:** The present study prospectively compares the five-year incidence of falls and risk factors influencing falls between patients with RA and controls based on the findings of the TOMORROW study (UMIN000003876) that started in 2010.

**Methods:** We compared anthropometric parameters, bone mineral density, disease activity, and the incidence of falls in 202 patients with RA (mean age, 58.6 years; medication with biological agents, 54.9%) and in 202 age- and sex-matched healthy volunteers (controls; mean age, 57.4 years) over a five-year

period. We also analyzed risk factors for falls in the patients using multivariate regression analysis.
**Results:** The rate of individuals who fell did not significantly differ between patients with RA (n=101, 50%) and Controls (n=91, 45%) within the five-year period. However, the incidence of falls was significantly higher in the patients than the controls (0.39 vs. 0.21/person-years (py); $p$ =0.002). Multivariate linear regression analysis adjusted for fall risk factors including age, sex, smoking, and body mass index, revealed the association of a history of falls at entry into the study and RA morbidity with the number of falls in all participants ($\beta$ =0.248, 0.144, $p$ <0.01, respectively). In addition, anti-cyclic citrullinated peptide antibody (CCP), matrix metalloproteinase (MMP)-3 levels, a history of falls at entry, mean MMP-3 values, disease activity score 28 (DAS28-CRP), modified Health Assessment Questionnaire (mHAQ) score and glucocorticoid dosage (GC) over five years were related to the number of falls among the patients (Table 1).

Table 1. Multivariate linear regression analysis of risk factors associated with number of falls sustained by patients RA

| | | RA | N=202 |
|---|---|---|---|
| | Number of falls | $\beta$ | $p$ |
| At the entry | Anti-CCP antibody (U/mL) | 0.295 | <0.001 |
| | MMP-3 (ng/mL) | 0.197 | 0.005 |
| | History of falls | 0.248 | <0.001 |
| | DAS28-CRP | 0.108 | 0.129 |
| | mHAQ | 0.137 | 0.061 |
| | Dose of GC (mg/day) | 0.009 | 0.900 |
| 5 years | Average MMP-3 (ng/mL) | 0.162 | 0.026 |
| | Average DAS28-CRP | 0.157 | 0.033 |
| | Average mHAQ | 0.150 | 0.043 |
| | Average dose of GC (mg/day) | 0.160 | 0.024 |

RA, rheumatoid arthritis; CCP, cyclic citrullinated peptide; MMP-3, matrix metalloproteinase-3; DAS28-CRP, disease activity score 28 with C-reactive protein; mHAQ, modified Health Assessment Questionnaire; GC, glucocorticoid.

**Conclusions:** The rate of individuals who fell did not significantly differ between the patients and controls, but the incidence of falls was significantly higher in the patients within the five-year period. A higher titer of anti-CCP, higher doses of GC, and a high anti-CCP level were the most significantly associated with an increased frequency of falls among patients with RA.
**Disclosure of Interest:** None declared
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## SAT0137 HIGH DISEASE ACTIVITY AND GLUCOCORTICOID USE ARE ASSOCIATED WITH INCREASED RISK OF MYCOBACTERIUM TUBERCULOSIS INFECTION IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) increased risk of Mycobacterium Tuberculosis Infection (TB). Risk of TB infection in RA patients from Thailand, the country with moderate prevalence of TB infection (137/100,000 in general population) has not been studied.
**Objectives:** The aim of this study was to determine incidence and factors related TB infection in RA patients from Thailand.
**Methods:** All patients were diagnosed with RA according to American College of Rheumatology (ACR) 1987 and/or ACR and European league of Rheumatology 2010 between 2000 and 2015. Twenty Cases of TB infection diagnosed after having RA were identified. TB infection was diagnosed by WHO 2013 revision definition and confirmed by physicians. Four age and sex matched controls were selected from 355 RA patients from Thai Army Rheumatoid Arthritis Cohort. Demographic data, RA disease associated factors and risk factos for TB infection were collected. Incidence rate was calculated by incidence density. Univariable and multivariable analyses were performed to identify factors associated with TB.
**Results:** Twenty-nine TB cases and 116 controls were included and 85.60% were female. The mean age ± SD was 64.75±11.06 years and mean disease duration ± SD was 12.79±7.15 years. Rheumatoid factor and anti-citrullinated protein antibody were positive in 75.23 and 68.95%, respectively. Most patients (93.18%) were treated with synthetic DMARDs. The combination of biologic and synthetic DMARDs was used in 7.58% of the patients. Incidence of TB infection was 2,180/100,000 person-year. Cases were more likely to have higher disease activity, use higher dose of methotrexate, use higher dose of leflunomide and use higher dose of glucocorticoid than controls. The means ± SD of Disease activity28 score (DAS28), dose of methotrexate, dose of leflunomide and dose of glucocorticoid in cases and control were 5.26 ±1.73 vs 4.45 ±1.51 (p=0.027), 9.84 ±6.02 vs 6.47 ±5.62 mg/week (p=0.03), 15±9.26 vs 6.55±7.53 mg/day (p=0.06) and 6.17±5.18 vs 1.15±2.06 mg/day (p=0.005), respectively. In multivariate regression analysis, only high DAS28 and current use of prednisolone were independently associated with TB infection (Odd ratio, 95% CI of 4.95, 1.15–8.36 and 1.23, 1.04–1.44, respectively).
**Conclusions:** Incidence of TB infection in RA in this study was very high compared to general population in Thailand and other Asian countries such as Hong Kong and Korea. High RA disease activity and the use of glucocorticoid are independently associated with TB infection.

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## SAT0138 LEFT VENTRICULAR FUNCTION AT 2-YEAR FOLLOW-UP IN TREATMENT-NAIVE RHEUMATOID ARTHRITIS PATIENTS IS ASSOCIATED WITH ANTI-CCP STATUS: A COHORT STUDY

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**Background:** In patients with rheumatoid arthritis (RA) the role of autoimmunity and especially auto antibody status and the time-course of left ventricular (LV) function is unknown.
**Objectives:** To assess LV function as well as the amount of coronary calcium by coronary computer tomography (CCT) in relation to anti-cyclic citrullinated peptide antibody (anti-CCP) status in a cohort of treatment-naive RA patients. Furthermore to assess changes in these parameters during a 2-year follow-up period.
**Methods:** Sixty-six steroid- and DMARD-naive RA patients (42 women) were included and treated with methotrexate according to the national guidelines. We assessed both the LV function by conventional echocardiography and speckle-tracking echocardiography. Furthermore, we performed CCT to estimate the amount and progression of coronary calcium. Patients were examined at he time of diagnosis and after 2-years of efficient anti-inflammatory treatment.
**Results:** All patients fulfilled the international criteria for RA. We found no clinical significant differences in LV function parameters during the 2-year follow-up period in the total population. However, we found that patients with a persistently elevated anti-CCP both had a significantly lack of improvement in S'(1±1.4 cm/s versus 0.2±0.9 cm/s; p=0.04) and had a worsening in global longitudinal systolic strain (GLS) (0.6±1.8% versus -1±2.8%; p=0.04) compared to patients with non-persistently elevated anti-CCP over a 2-year time period. Furthermore, we observed a significant correlation between ΔGLS over 2 years and anti-CCP at 2-year follow-up (r=0.36;p=0.006). It remained significantly correlated (p=0.008) after correction for relevant cofounders (age, gender, blood pressure, heart rate, and baseline GLS). The circumferential strain improved in the group with non-persistently elevated anti-CCP compared to the group with persistently elevated anti-CCP (-4.2±3.8% versus 0.3±1.9%; p=0.009). We observed a mean progression of calcium score during the 2-year follow-up period of 22.4±68.9. We observed no differences in progression in calcium score in patients with persistently elevated anti-CCP (n=12) versus not persistently elevated (n=32) (23.8±40.3 versus 22.6±68.9; p=0.96).
**Conclusions:** LV function and deformation is reduced in treatment-naive RA patients with persistently elevated anti-CCP. Deformation abnormalities is associated with the degree of anti-CCP positivity in a 2-year follow-up period. No differences in the amount of coronary calcium was observed according to inflammatory burden.
**Disclosure of Interest:** None declared
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## SAT0139 MAXIMUM METHOTREXATE DOSE SEEM TO BE AN ONLY RISK FACTOR FOR DEVELOPMENT OF MTX-ASSOCIATED LYMPHOPROLIFERATIVE DISORDERS

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**Background:** Since February 2011, an approved Methotrexate (MTX) dose for rheumatoid arthritis: RA treatment has been raised from 8mg/wk to 16mg/wk in Japan. Recently, we have an impression that incidence of MTX-associated lymphoproliferative disorders (MTX-LPD) are increasing.
**Objectives:** To investigate incidence and etiology of MTX-LPD.
**Methods:** All of adult patients receiving MTX for treatment of autoimmune diseases (n=244) in our hospital from May 2012, to August 2015 are surveyed. In each case, the possible risk factors for development of MTX-LPD including minimum MTX dose, maximum MTX dose, administration period, and cumulative dose were investigated in detail. In order to detect the important risk factors, Cox proportional hazards regression analysis (Cox model) were carried out.
**Results:** At baseline, the background of the patients were as follows: male-

to-female ratio was 4:3, age was 72.3±8.5 years, minimum MTX dose was 5.4±1.0mg/wk, maximum MTX dose was 10.9±3.6mg/wk, administration period was 274.4±379.7wk, and all cumulative dose was 1842.3±1358.1mg. By the end of 2015, seven of patients developed (six RA, one psoriatic arthritis: PsA). The incidence was accounted for 2.9% in all amenable patients by following up for 119 weeks on average. By Kaplan-Meier plots, incidence of MTX-LPD was 0.85% at up to 52weeks and 9.2% at up to 260weeks. Cox model analysis revealed that maximum MTX dose was the only independent risk factor for MTX-LPD development. The annual incidence of MTX-LPD increases 1.58 times with 1mg increment of MTX (p=0.009, 95%CI 1.12–2.25). The seven MTX-LPD cases include three DLBCL, two indeterminable, and one Hodgkin's lymphoma. The last one had both Follicular and Hodgkin's lesions. The EBV in blood level was significantly elevated in all checked cases, and EBER was positive in six specimens of five cases by histopathological inspection. All of the lymphoproliferative lesions regressed spontaneously after MTX was withdrawn.

**Conclusions:** In our cohort, the incidence of MTX-LPD was quite frequent as compared to previous Japanese report (0.5%; before 2011) or reports from worldwide (0.05–0.3%). It is of particular interest that the annual incidence of MTX-LPD increases 1.58 times with only 1mg increment of MTX a week. It is also notable that all of the lesions regressed spontaneously so far after cessation of MTX, and the connection with EBV infection was found in all investigated cases. Although our cohort is rather small, we believe that it is worth to survey why the incidence of MTX-LPD are increasing in Japan with a larger cohort study. It may reveal the etiology of MTX-LPD in detail.

**Disclosure of Interest:** None declared

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## SAT0140 PREVALENCE OF REACTIVATION OF HEPATITIS B VIRUS (HBV) IN PATIENTS WITH RESOLVED HBV HEPATITIS ON IMMUNOSUPPRESSIVE THERAPY FOR RHEUMATIC DISEASE: MULTICENTRE PROSPECTIVE OBSERVATIONAL STUDY IN JAPAN

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**Background:** Although the reactivation of hepatitis B virus (HBV) is recognized as a serious complication in patients with connective tissue disease (CTD) receiving immunosuppressive drugs (ISDs), the incidence and risk factors of reactivation remain controversial.

**Objectives:** We performed a multicentre, observational, prospective study across 16 Japanese Red Cross hospitals to clarify the prevalence and pathophysiology of HBV reactivation in patients with CTD. We report the results of 2-year observations in patients with resolved HBV infection.

**Methods:** Patients with CTD, treated with a dose of ≥5 mg/day prednisolone, and/or synthetic or biological ISDs, with negative HBs antigen and positive anti HBs and/or HBc antibody (Ab), were enrolled. HBV-DNA (RT-PCR) and related data were registered regularly.

**Results:** Among 1040 patients, including 950 rheumatoid arthritis, HBV-DNA was detected in 32 patients (1.75/100 person-years), and >2.1 log copy/ml was observed in 9 cases (0.49/100 person-years) over 1–2 years of observation. None of the reactivated patients, including six treated with a nucleic acid analogue, showed overt hepatitis. Low HBs Ab titres and advanced age seemed to be risk factors for HBV reactivation; however, reactivation was observed in 3 patients with positive HBs Ab and negative HBc Ab. The risk of reactivation among the different types of ISDs was not statistically different. The intervals from the start of ISD to reactivation were longer than previous reports (4–157 months, average 58.9 months).

**Conclusions:** HBV reactivation with ISD was 1.75/100 person-years in CTD patients with resolved HBV infection. Overt hepatitis was observed in none of the reactivated patients, and low HBs antibody titres and advanced age were risk factors for reactivation. Patients with positive HBs Ab and negative HBc Ab are not free from the risk of reactivation of HBV.

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## SAT0141 CHANGES OF BONE DENSITY AND MICROARCHITECTURE IN RHEUMATOID ARTHRITIS PATIENTS WITH EARLY DISEASE: A ONE-YEAR STUDY WITH HR-PQCT

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**Background:** Periarticular and systemic osteoporosis is a major feature in patients with rheumatoid arthritis (RA). Bone loss in RA is considered to be a result of chronic inflammation, particularly at the early stage of the disease. High Resolution peripheral Quantitative Computed Tomography (HR-pQCT) is an in vivo 3D imaging modality dedicated to peripheral skeleton imaging. Whether a better controlling of the disease inflammation could lead to a preservation of vBMD and microarchitecture is to be determined.

**Objectives:** This one-year cohort study in RA patients with early disease (onset <2 years) aimed to compare changes of vBMD and bone microarchitecture indices at the distal radius and tibia between patients who achieved and those who did not achieve disease remission.

**Methods:** Forty-seven RA patients (age: 54.5±11.8 years) with disease onset <2 years and with active disease (Disease Activity Score in 28 joints [DAS28] ≥3.2) were recruited for this one-year study. Disease remission at 12 months was assessed as Simplified Disease Activity Score ≤3.3. HR-pQCT imaging of the distal radius and tibia was performed at baseline and 12 months.

**Results:** At 12 months, 20 patients achieved disease remission and 27 patients remained with activity disease. There was no significant difference in baseline DAS28 score (4.93 vs. 4.92, p>0.05) and age between the two groups. In patients who did not achieve disease remission, particularly at the distal radius, there were decreases in cortical and trabecular vBMD, cortical thickness and trabecular number, and increase in trabecular separation (Table 1). Increase in cortical porosity presented as the most prominent deterioration of bone microarchitecture (20%). Only changes in trabecular separation (2.87%) and cortical vBMD (-1.12%) achieve statistical significance. In patients who achieve disease remission, decrease in vBMD and deterioration in bone microarchitecture were in general to a lesser extent than their counterparts. In particular, there appeared to be a decrease in cortical porosity in these patients (-6.62%). However, there was no significant group-wise difference in changes of vBMD and microarchitectural indices (all p>0.05).

Table 1. Percentage changes of all HR-pQCT indices between two groups

| Variables | No remission (n=27) | Remission (n=20) | p-value |
|---|---|---|---|
| Radius | | | |
| Cortical vBMD | –0.19±1.76 | 0.63±3.19 | 0.269 |
| Trabecular vBMD | –2.41±7.30 | –3.06±7.22 | 0.765 |
| Cortical thickness | –1.12±4.51 | –0.11±3.43 | 0.407 |
| Cortical pore volume | 20.1±105 | –6.22±25.8 | 0.282 |
| Cortical porosity | 19.7±95.0 | –6.62±25.9 | 0.236 |
| Trabecular number | –2.21±8.34 | –0.55±7.31 | 0.483 |
| Trabecular thickness | 0.21±2.28 | –0.51±1.50 | 0.227 |
| Trabecular separation | 2.87±8.42 | 1.21±6.90 | 0.475 |
| Tibia | | | |
| Cortical vBMD | –1.12±3.07 | –0.90±1.58 | 0.773 |
| Trabecular vBMD | –0.13±2.69 | 0.11±1.57 | 0.718 |
| Cortical thickness | –0.34±3.49 | 0.39±2.51 | 0.432 |
| Cortical pore volume | 6.27±17.28 | 5.05±11.6 | 0.785 |
| Cortical porosity | 7.89±18.5 | 4.95±12.4 | 0.542 |
| Trabecular number | 2.20±7.71 | 1.72±8.85 | 0.843 |
| Trabecular thickness | –0.58±1.80 | –0.24±1.47 | 0.494 |
| Trabecular separation | –1.37±7.29 | –0.92±8.89 | 0.847 |

RA, rheumatoid arthritis; CCP, cyclic citrullinated peptide; MMP-3, matrix metalloproteinase-3; DAS28-CRP, disease activity score 28 with C-reactive protein; mHAQ, modified Health Assessment Questionnaire; GC, glucocorticoid.

**Conclusions:** There was a trend towards a preservation of vBMD and bone microarchitecture in RA patients who achieve disease remission. An early and better control of disease activity might reduce the future risk of osteoporosis in RA patients.

**Disclosure of Interest:** None declared

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SAT0142 **TREAT-TO-TARGET PRACTICE USING ONLINE ASSESSMENT OF DISEASE ACTIVITY WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS: A COHORT STUDY OF RHEUMATOID ARTHRITIS PATIENTS IN CHINA**

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**Background:** There are more than 5 million RA patients in China, but only 4,000 rheumatologists. T2T strategy are critical for the treatment of RA, but the Chinese doctors can hardly provide patients with a complete assessment in the clinic due to limited time. We have confirmed in a validation study that Chinese RA patients can master the use of SSDM for accurate DAS28 self-assessments after training[1].
**Objectives:** To explore the effectiveness of applying SSDM in improvement of disease activity after repeated self-assessment in Chinese RA patients.
**Methods:** The SSDM includes both doctors' and patients' application. After entry of lab test, treatment regiments, and executing DAS28 assessment by patients, all data can be synchronized to the authorized doctor' mobile tool. They can adjust treatment regiments base on these data. Since Aug. 2014 to Jan. 2016, 31 rheumatologists from 25 hospitals participated in the study. Patients were educated to measure DAS28 with SSDM on the baseline, and were asked to repeat the assessment once a month.
**Results:** 636 RA patients with repeated self-assessment of DAS 28 were recruited, 448 (70.4%) women and 188 (29.6%) men. Mean age was 45.26±13.17 (18 to 83) years, median duration of disease was 2.92 (0.08 to 50.42) years. Mean duration of self-assessment was 67.00±66.50 (2 to 371) days. Mean assessment times were 4.38±3.36 (2–20). Mean DAS28 score was 3.96±1.46 (0.62 to 8.29) at baseline and 3.58±1.45 (0.60 to 9.07) at the last assessment. Proportion of patients in remission, low, moderate and severe disease activity (Rem, LDA, MDA and SDA) was 19.03%, 13.36%, 45.28% and 22.33% respectively at baseline, and changed into 26.57%, 13.68%, 45.28% and 14.47% at the last assessment. The rate of T2T (DAS28$\leq$3.2) at the last assessment was higher than that of baseline significantly ($P<0.01$). The rate of SDA patients for last assessment was also significantly lower than baseline ($P<0.01$). To explore whether the frequency of self-assessment could influence disease activity, we stratified the times of DAS28 assessment among those who did not achieve clinical remission (DAS$>$2.6). 65 patients made only two assessments within 151.41±86.72 (48–372) days, whose mean DAS28 was 4.20±1.28 (2.64–7.39) at baseline and improvement of that was 0.49±1.46 (-4.31–4.25) at their last assessment. There were 61 patients making more than 5 times of self-assessment during 159.98±88.10 (28–343) days. Their mean DAS28 score was 4.27±1.13 (2.61–7.19) at baseline and improvement of that was 1.12±1.34 (-1.86–4.51) at the last assessment, which was significantly better than patients who had only two self-assessments (T=2.52, P=0.013).
**Conclusions:** Under regular self-assessment of DAS28 using SSDM, RA patients achieved better T2T result. SSDM can assist rheumatologists to rationally adjust treatment for RA patients.
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**Disclosure of Interest:** None declared
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SAT0143 **THE EFFECT OF TOTAL KNEE ARTHROPLASTY ON THE ARTHRITIS OF OTHER JOINTS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** There have been some reports that total arthroplasty can improve the disease activity in RA patients. The RA disease activity is commonly assessed using composite measures. These include five components: inflammation markers, the swollen joint count, tender joint count, patient's global VAS and evaluator's global VAS. Therefore, total arthroplasty can improve all of these components if there is improvement of arthritis, even if it is only in the surgical site. It is still unclear whether the improvement of disease activity is only at the surgical site or includes other joints.
**Objectives:** The aim of this study was to assess the arthritis of systemic large joints at baseline and 12 weeks after TKA using 18FDG-PET (PET)/CT in patients with RA.
**Methods:** Seventeen RA patients who underwent TKA were included this study. We assessed the FDG-PET, CRP, ESR, MMP-3, DAS28-ESR, DAS28-CRP, CDAI, SDAI, HAQ-DI, HSS score and Knee ROM at baseline (just before TKA) and 12 weeks after TKA.
**Results:** The median age of the patients was 68 years old, and the disease duration was 23 years. Concomitant MTX and PSL treatment was being administered to 71% of the patients. One patient was treated with infliximab, two used etanercept, one used tocilizmab and two used abatacept. The CRP, MMP-3, all of the composite measurements, the HAQ and the knee function improved significantly 12 weeks after TKA. These data show the changes in the SUV of each joint. The SUV of the bilateral wrist joints decreased significantly 12 weeks after TKA. However, the SUV of other large joints were unchanged.
**Conclusions:** TKA can improve not only the ADL and knee function, but also the disease activity in RA patients. However, TKA has limited effectiveness against the arthritis of the joints not undergoing surgery.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5995

## Rheumatoid arthritis - other biologic treatment

SAT0144 **SOLUBLE FORM OF GP130 MOLECULE, AN IL-6 INHIBITOR, CONTRIBUTES THE EFFICACY ON RA TO TOCILIZUMAB (AN ANTI-IL-6 RECEPTOR ANTIBODY) THERAPY**

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**Background:** IL-6, one of the causes of key molecule in RA pathogenesis, is signaling through the two receptor systems, one is IL-6 binding molecule (IL-6R) and the other is gp130 molecule (gp130), a signal transducer. And we know the presence of soluble form of IL-6 receptor (sIL-6R) and gp130 (sgp130). SIL-6R is an IL-6 functional accelerator; however less is known about the function of sgp130.
**Objectives:** We want to know whether sgp130 is a regulator of IL-6 both in vitro and vivo. Tocilizumab, an anti-IL-6 receptor antibody, shows good effect as well as TNF-a inhibitors for the treatment of RA. However the efficacy is variable to each of patient. We want to know the reason of this variety caused by sgp130 molecule.
**Methods:** [In vitro] Hep3B, a hepatoma derived cell line, was stimulated with IL-6 or Hyper IL-6 (complex of IL-6/sIL-6R) and co-cultured with tocilizumab or complex of gp130-Fc. CRP mRNA induction was accessed after two days culture by real-time RT-PCR.
[In vivo] We performed with observation study. 88 RA patients (48 biologics naïve, 40 biologics non-naïve) were treated with tocilizumab over 16 weeks by every 4 week injection at dose 8mg/kg. 41 biologics in pretreatment serum was measured by Bio-Prex27 and Milliplex. The disease activity at 16 week was scored on DAS28-CRP. Multiple linear regression analysis were used to determine if any relationship existed between biologics and patient's week 16 DAS 28-CRP score.
**Results:** [In vitro] Gp130-Fc did not inhibited the IL-6 induced CRP, however inhibited the Hyper IL-6 induced CRP productions. This means, gp130-Fc specifically inhibited the stimulation with complex of IL-6/sIL-6R which stimulation could not be inhibited with tocilizumab.
[In vivo] 7 biomarker including sgp130 were predictive of the week 16 DAS28-CRP in naïve tocilizumab patients ($R2=0.646$, $P<0.0001$) while gp130, GM-CSF, IP-10 were predictive in non-naïve patients ($R2=0.486$, $P<0.001$). The most reliable marker is sgp130 (Estimated value -5.34).
**Conclusions:** 1) Sgp130 is a natural IL-6 inhibitor both in vitro and in vivo.
2) Higher level of sgp130 predicts the better outcome to tocilizumab therapy
3) Clinical efficacy might be resulted in the additive effects by the inhibition with tocilizumab (IL-6 binding inhibition on IL-6R) and the inhibition with sgp130, (IL-6/sIL-6R binding inhibition on gp130).
4) Prediction of individual RA patient's outcome to tociizumab therapy can be recognized by measuring biologics including sgp130 (most reliable marker) in pretreatment serum.
5) Opening the personalized medicine in RA field by measuring biomarker before therapy.
**References:**
[1] non
**Disclosure of Interest:** None declared
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## SAT0145 EFFICACY AND SAFETY OF SIRUKUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE DISEASE-MODIFYING ANTI-RHEUMATIC DRUG TREATMENT: RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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**Background:** Sirukumab, a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, is under development for rheumatoid arthritis (RA) and other diseases.
**Objectives:** To evaluate efficacy and safety of sirukumab in patients (pts) with RA refractory to conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs).
**Methods:** In this Phase 3 global study, 1,670 pts with active RA and inadequate response to DMARDs were randomized (1:1:1) to sirukumab subcutaneous (SC) 50mg q4w, sirukumab SC 100mg q2w, or placebo SC q2w. Pts on placebo with insufficient improvement (<20%) at Wks 18 or 40 or still on placebo at Wk 52 were re-randomized to receive blinded treatment in 1 of the 2 sirukumab doses. Co-primary endpoints were the proportion of pts achieving ACR20 at Wk 16 and change from baseline in modified van der Heijde/Sharp (vdH-S) radiographic damage mean score at Wk 52.
**Results:** For both co-primary endpoints, sirukumab 50mg q4w and 100mg q2w showed significant improvement vs placebo (Table; all $P<0.001$). All major secondary endpoints were met for both sirukumab doses. Significantly greater improvements were also observed in both the physical and mental component summary scores of the Short Form-36 (SF-36) Health Survey with both sirukumab doses vs placebo at Wk 52 (all $P<0.001$). Significantly more pts on sirukumab did not experience radiographic progression from baseline to Wk 52 (50mg q4w, 59.0%; 100mg q2w, 62.4%) than on placebo (45.5%; both $P<0.001$). Through Wk 52, incidences of treatment-emergent adverse events (AEs) and serious AEs, respectively, were numerically higher with sirukumab 50mg q4w (79.6% and 11.0%) and 100mg q2w (80.2% and 9.8%) vs placebo (65.5% and 6.8%). The most common AEs (≥8%) with sirukumab were elevated liver enzymes, upper respiratory tract infection, and injection site erythema, and nasopharyngitis.

Table 1. Key endpoints

| Endpoints | Placebo (n=556) | Sirukumab 50mg q4w (n=557) | Sirukumab 100mg q2w (n=557) |
|---|---|---|---|
| Primary endpoints | | | |
| ACR20 at Wk 16, n (%) | 147 (26.4) | 305 (54.8)[a] | 298 (53.5)[a] |
| vdH-S mean (SD) change from baseline at Wk 52 | 3.69 (9.25) | 0.50 (2.96)[a] | 0.46 (3.26)[a] |
| Major secondary endpoints | | | |
| HAQ-DI mean (SD) change from baseline at Wk 24 | −0.22 (0.53) | −0.43 (0.58)[a] | −0.46 (0.57)[a] |
| ACR50 at Wk 24, n (%) | 69 (12.4) | 168 (30.2)[a] | 185 (33.2)[a] |
| DAS28 (CRP) remission at Wk 24, n (%) | 31 (5.6) | 145 (26.0)[a] | 142 (25.5)[a] |
| Major clinical response at Wk 52, n (%) | 10 (1.8) | 30 (5.4)[a] | 50 (9.0)[a] |

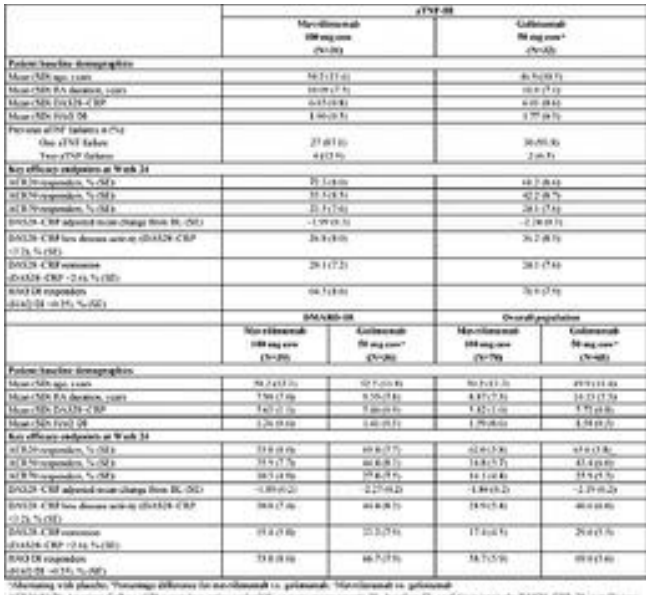
[a] $P \leq 0.001$ vs placebo.

**Conclusions:** In DMARD-inadequate responders, sirukumab SC 50mg q4w and 100mg q2w reduced signs/symptoms of RA, inhibited radiographic progression, and improved health-related quality of life. The safety profile of sirukumab was consistent with the known safety profile of anti-IL-6 treatment.
**Disclosure of Interest:** T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahikasei Pharma Corp., and Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., and Asahi Kasei Medical K.K.,abbivie GK, Daiichi Sankyo Co.,Ltd., Bristol–Myers K.K., Nipponkayaku Co.Ltd., Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co,. Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Astellas Pharma, and Diaichi Sankyo Co., Ltd., Celtrion, Nipponkayaku Co. Ltd, C. Thorne Grant/research support from: Abbvie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant for: Abbvie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: Medexus/Medac, G. Karpouzas Consultant for: Janssen, Speakers bureau: Janssen, S. Sheng Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, W. Xu Employee of: Janssen Research & Development, LLC, R. Rao Shareholder of: GSK, Employee of: GSK, K. Fei Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC
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## SAT0146 EARTH EXPLORER 2, A PHASE IIB EXPLORATORY STUDY EVALUATING EFFICACY AND SAFETY OF MAVRILIMUMAB, A FULLY HUMAN GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR RECEPTOR-ALPHA MONOCLONAL ANTIBODY, AND THE TUMOR NECROSIS FACTOR ANTAGONIST GOLIMUMAB IN RHEUMATOID ARTHRITIS

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**Background:** Mavrilimumab, a fully human monoclonal antibody targeting the granulocyte-macrophage colony-stimulating factor receptor-α, has demonstrated efficacy and safety in disease-modifying antirheumatic drug (DMARD)-inadequate responder (IR) patients (pts) with rheumatoid arthritis (RA).[1]
**Objectives:** Few head-to-head studies in tumor necrosis factor antagonist (aTNF)-IR assess alternative aTNFs vs. other agents; this Phase IIb exploratory study (NCT01715896) evaluates the efficacy and safety of mavrilimumab and golimumab in aTNF-IR and DMARD-IR pts.
**Methods:** This 24-week study enrolled pts with active RA (28-joint Disease Activity Score [DAS28]–C-reactive protein [CRP]/erythrocyte sedimentation rate ≥3.2); ≥4 swollen joints; inadequate response to ≥1 DMARDs and/or 1–2 aTNFs receiving concomitant methotrexate (MTX; 7.5–25.0 mg/week). Pts received subcutaneous mavrilimumab 100 mg every other week (eow), based on data from the Phase IIa study,[2] or golimumab 50 mg alternating with placebo eow. Key endpoints were ACR20/50/70 responses, DAS28–CRP <3.2 and <2.6, Health Assessment Questionnaire Disability Index improvement >0.22 at Week 24 and safety/tolerability. Treatment estimates for mavrilimumab and golimumab are presented with standard errors.
**Results:** Pts were randomized to mavrilimumab or golimumab (1:1) (Table). Data for pts receiving mavrilimumab 100 mg eow and golimumab 50 mg at Week 24 are shown for the aTNF-IR, DMARD-IR and overall strata (Table). The most common treatment-emergent adverse events (TEAEs) for mavrilimumab 100 mg and golimumab 50 mg were nasopharyngitis (5.7%, 1.5%), headache (4.3%, 2.9%), upper respiratory tract infection (4.3%, 2.9%), viral upper respiratory tract infection (4.3%, 2.9%), and hepatic enzyme increase (4.3%, 2.9%), respectively. Related serious TEAEs were pneumocystis pneumonia (n=1) and lung disorder (n=1) [both in golimumab-treated pts]. No deaths were reported and no significant pulmonary safety signals were identified.



**Conclusions:** In this exploratory study, mavrilimumab 100 mg eow and golimumab 50 mg demonstrated efficacy and an acceptable safety profile in DMARD-IR and aTNF-IR pts. The study was not powered to demonstrate statistical significance between mavrilimumab and golimumab. As mavrilimumab 100 mg eow has previously been shown to be suboptimal compared with 150 mg eow in DMARD-IR pts (EARTH EXPLORER 1),[1] additional studies are needed to establish the benefit of a higher dose in pts with moderate to severe RA and inadequate response to aTNF agents.
**References:**
[1] Burmester G, et al. Arthritis Rheum. 2014;66:S1231

[2] Burmester G, et al. Ann Rheum Dis. 2013;72:1445–1452
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Joint senior authors: D. Close and G. Burmester
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## SAT0147 SAFETY AND EFFICACY OF BI 655064, AN ANTAGONISTIC ANTI-CD40 ANTIBODY IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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**Background:** Blocking the CD40-CD40L pathway may be a new emergent treatment for patients with RA. BI 655064 is a humanized, purely antagonistic anti-CD40 monoclonal antibody. In healthy volunteers, BI 655064 was well tolerated in doses up to 240 mg q1w s.c. for 4 weeks. Doses ≥120 mg resulted in persistent >90% CD40 receptor occupancy and >90% inhibition of CD40L-induced CD54 upregulation.
**Objectives:** BI 655064 was investigated in RA patients with prior inadequate response (IR) to a stable dose of MTX at ≥15 mg.
**Methods:** In this double-blind, randomized trial, RA patients (n=67) were treated with either 120 mg BI 655064 or placebo q1w (2:1, respectively) for 12 weeks as add-on to MTX. Patients were stratified based on region (Eastern Europe vs. Western Europe/New Zealand). Inclusion criteria were ≥6 swollen and ≥6 tender joints, CRP ≥8 mg/L or ESR ≥28 mm/1h. The primary efficacy endpoint was ACR20 response at week 12.
**Results:** Baseline variables of the 2 groups were comparable except mean baseline CRP, which was substantially lower in patients treated with BI 655064 (9.8 mg/L) vs. placebo (23.6 mg/L). Treatment was prematurely discontinued by 4 patients (9.1%) in the BI 655064 group and 4 (17.4%) in the placebo group. Adverse events (AE) were reported in 65.9% of BI 655064-treated patients vs. 78.3% of placebo-treated patients. Two SAEs were reported in each group, neither was considered drug-related. The most frequently reported AEs were nasopharyngitis (BI 655064: 13.6%, placebo: 21.7%) and headache (BI 655064: 6.8%, placebo: 13.0%). There were no relevant changes in safety-related laboratory parameters. Efficacy results of all patients (FAS), including a subgroup of patients with CRP > median (7.5 mg/L; upper limit of normal: 6.0 mg/L), are listed in the table.

Table 1

| | BI 655064 (N=44) | Placebo (N=22*) |
|---|---|---|
| ACR20 response % | 68.2 | 45.5 |
| ACR50 response % | 36.4 | 18.2 |
| Mean change† in DAS28-CRP @wk12 | –1.65 | –1.42 |
| **Subgroup with CRP > median** | **BI 655064 (N=17)** | **Placebo (N=16)** |
| Mean change† in DAS28-CRP @wk12 | –1.83 | –1.38 |
| CRP change from baseline, mean (SE) | –10.45 (3.54) | –3.90 (3.65) |

*1 patient excluded from efficacy analysis due to early use of i.v. steroids. †Adjusted for region, anti-TNF history and baseline CRP.

All 6 patients who had previously received anti-TNF therapy were in the BI 655064 group; 4 achieved an ACR20 and 2 achieved an ACR50 response. There was a median decrease in ESR and total rheumatoid factor in the BI 655064-treated group by 16 mm/h and 81.5 IU/mL, respectively, compared with a decrease of 9 mm/h and 0.2 IU/mL in the placebo group.
**Conclusions:** In this relatively small proof-of-clinical-concept trial, treatment of MTX IR RA patients with BI 655064 did not indicate a relevant safety concern and showed moderate efficacy, which might have been impacted by the relatively high placebo response rate and the imbalance in baseline CRP.
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## SAT0148 IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES WITH OLOKIZUMAB TREATMENT IN PATIENTS WITH ACTIVE, MODERATE TO SEVERE RHEUMATOID ARTHRITIS WHO HAD FAILED PREVIOUS ANTI-TNF THERAPY: RESULTS FROM THE RA0056 DOUBLE-BLIND, RANDOMIZED CONTROLLED STUDY, AND RA0057, ITS OPEN-LABEL EXTENSION

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**Background:** Rheumatoid arthritis (RA) has a high patient (pt) burden with significant impact on health-related quality of life. Here we report the effect of treatment with olokizumab (OKZ), an interleukin-6 (IL-6)-targeting monoclonal antibody in development for the treatment of RA, on pt-reported outcomes (PROs) in the phase 2 randomized controlled trial (RCT) RA0056 and its open-label extension (OLE) RA0057.
**Objectives:** To assess the effect of OKZ treatment on PROs in pts with moderate to severe RA who have previously failed anti-TNF therapy.
**Methods:** RA0056 was a dose-ranging, multicenter, double-blind RCT (NCT01242488) that enrolled pts with active, moderate to severe RA (meeting 1987 ACR classification criteria and/or ACR/EULAR diagnostic score ≥6; ≥6 swollen and ≥6 tender joints; CRP ≥1.2x upper limit of normal). Pts were receiving stable dose MTX 12.5–25mg/week (wk) for ≥6 wks and were intolerant to, or had a previous inadequate response to, ≥1 anti-TNF ≤2 years prior to screening. Pts received 1 of 9 treatments: subcutaneous (sc) placebo (PBO) every 4 weeks (Q4W) or every 2 weeks (Q2W), intravenous (iv) tocilizumab (TCZ) 8mg/kg Q4W, or sc OKZ 60/120/240mg Q2W or Q4W. Pts who completed the 12-wk study were eligible for entry into the RA0057 OLE (NCT01296711), in which all pts received sc OKZ 120mg Q2W+MTX. Pts with ongoing serious adverse events were excluded. PROs included change from baseline in: Health Assessment Questionnaire-

**Table: Patient-reported outcomes in the RA0056 and RA0057 studies (observed data)**

| | Treatment (RCT→OLE) | | | | | |
|---|---|---|---|---|---|---|
| | PBO→OKZ [a] | | OKZ→OKZ [b] | | TCZ→OKZ | |
| | RCT Week 12 | OLE Week 48 | RCT Week 12 | OLE Week 48 | RCT Week 12 | OLE Week 48 |
| **Mean change from baseline (SD)** | | | | | | |
| HAQ-DI | 0.07 (0.52) [n=40] | -0.15 (0.66) [n=21] | -0.32 (0.48) [n=114] | -0.45 (0.49) [n=70] | -0.35 (0.28) [n=36] | -0.43 (0.50) [n=23] |
| PtGADA | -0.1 (29.1) [n=40] | -15.6 (29.8) [n=20] | -18.8 (27.0) [n=111] | -24.0 (28.1) [n=69] | -26.5 (25.5) [n=35] | -30.0 (22.6) [n=22] |
| PAAP | -0.4 (29.6) [n=39] | -13.9 (35.4) [n=20] | -20.2 (27.3) [n=113] | -26.8 (30.1) [n=69] | -27.1 (23.4) [n=36] | -35.6 (22.0) [n=23] |
| BRAF-MDQ | -3.7 (13.3) [n=41] | -8.4 (15.3) [n=20] | -11.3 (12.7) [n=115] | -13.3 (13.2) [n=68] | -12.3 (13.3) [n=40] | -13.3 (12.5) [n=23] |
| EQ-5D VAS | -6.4 (24.6) [n=41] | 5.9 (30.1) [n=21] | 10.1 (27.6) [n=115] | 17.5 (20.2) [n=69] | 17.0 (22.6) [n=41] | 24.8 (21.8) [n=23] |
| **Patient acceptable symptomatic state, shift from baseline n/N (%)** | | | | | | |
| No → Yes | 6/41 (14.6) | 9/21 (42.9) | 38/116 (32.8) | 31/68 (45.6) | 10/41 (24.4) | 12/24 (50.0) |
| No change | 34/41 (82.9) | 12/21 (57.1) | 75/116 (64.7) | 35/68 (51.5) | 30/41 (73.2) | 10/24 (41.7) |
| Yes → No | 1/41 (2.4) | 0/21 | 3/116 (2.6) | 2/68 (2.9) | 1/41 (2.4) | 2/24 (8.3) |
| **Patient's global impression of change, change from baseline n/N (%)** | | | | | | |
| Any improvement | 30/37 (81.1) | 18/20 (90.0) | 86/102 (84.3) | 65/70 (92.9) | 29/34 (85.3) | 20/24 (83.3) |
| No change | 4/37 (10.8) | 0/20 | 10/102 (9.8) | 4/70 (5.7) | 3/34 (8.8) | 3/24 (12.5) |
| Any worsening | 3/37 (8.1) | 2/20 (10.0) | 6/102 (5.9) | 1/70 (1.4) | 2/34 (5.9) | 1/24 (4.2) |

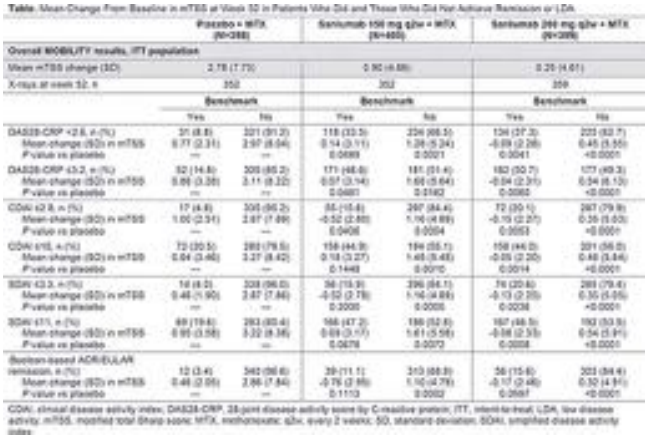
[a] Both PBO dosing arms from the RCT are presented as combined data; [b] All OKZ dosing arms from the RCT are presented as combined data
BRAF-MDQ: Bristol Rheumatoid Arthritis Fatigue-Multi-Dimensional Questionnaire; EQ-5D VAS: EuroQoL-5 Dimensions Visual Analogue Scale; HAQ-DI: Health Assessment Questionnaire-Disability Index; OLE: open-label extension; PAAP: Patient's Assessment of Arthritis Pain; PtGADA: Patient's Global Assessment of Disease Activity; RCT: randomized controlled trial; SD: standard deviation

Disability Index, Pt's Global Assessment of Disease Activity, Pt's Assessment of Arthritis Pain, Pt Acceptable Symptom State, Pt's Global Impression of Change, Bristol Rheumatoid Arthritis Fatigue-Multi-Dimensional Questionnaire and EuroQoL-5D Visual Analogue Scale. All missing data were left as missing.
**Results:** 198 pts completed RA0056; 190 (114 OKZ, 40 PBO, 36 TCZ) enrolled in RA0057. At Wk12 of the RCT, OKZ-treated pts reported greater improvements in PROs compared to PBO pts, similar to TCZ pts (Table). These changes were maintained to Wk48 of the OLE both in pts receiving OKZ throughout (OKZ→OKZ) and in TCZ-pts switching to OKZ at OLE entry (TCZ→OKZ). PBO-pts reported improvements in PROs following switch to OKZ (PBO→OKZ).
**Conclusions:** Treatment with OKZ resulted in improvements in PROs in patients with moderate to severe RA, which were maintained up to Wk48 of OLE.
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## SAT0149 RADIOGRAPHIC OUTCOMES IN PATIENTS ACHIEVING CLINICAL REMISSION OR LOW DISEASE ACTIVITY IN A PHASE 3 STUDY OF SARILUMAB PLUS METHOTREXATE IN PATIENTS WITH ACTIVE, MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS

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**Background:** Clinical remission is an important treatment target of rheumatoid arthritis (RA), and it is important to understand its role as a surrogate for radiographic inhibition.[1,2] In the phase 3 MOBILITY study (NCT01061736), sarilumab (150 or 200 mg subcutaneously every 2 wks [q2w] + methotrexate [MTX]) demonstrated clinical and radiographic efficacy in adults with active, moderate-to-severe RA with inadequate response to MTX.[3] The most common treatment-emergent adverse events were infections, neutropenia, injection site reactions, and increased transaminases.
**Objectives:** The objective of this post hoc analysis was to examine differences in radiographic progression between patients in MOBILITY who did and those who did not achieve different definitions for remission or low disease activity (LDA).
**Methods:** Remission and LDA categories included CDAI $\leq$2.8 and $\leq$10, SDAI $\leq$3.3 and $\leq$11, and Boolean-based ACR/EULAR remission, which included tender joint count and swollen joint count (28-joint count) $\leq$1, CRP $\leq$10 mg/L, and patient global visual analog scale $\leq$10. Cutoffs for 28-joint disease activity score by C-reactive protein (DAS28-CRP) were $<$2.6 and $\leq$3.2. Differences in radiographic progression, defined as the mean change from baseline in modified total Sharp score (mTSS), between the treatment and placebo groups in these benchmarks were assessed using a 2-sided Cochran-Mantel-Haenszel test stratified by prior biologic use and region. Missing or postrescue radiographic data were imputed by a linear extrapolation approach for any patient with $\geq$1 postbaseline radiograph, but these patients were not counted as in remission or with LDA for clinical outcomes.
**Results:** Overall, a greater proportion of patients receiving either dose of sarilumab + MTX achieved remission or LDA and had significantly less radiographic progression than patients receiving placebo + MTX (Table). Regardless of treatment group, patients who achieved remission or LDA showed less radiographic progression at wk 52 than patients who did not (Table). In general, the progression in patients achieving remission was lower than in patients achieving LDA. Even if patients did not achieve remission or LDA, patients receiving sarilumab + MTX had less radiographic progression than those receiving placebo + MTX. Smaller mean changes in mTSS were observed with sarilumab 200 mg q2w compared with sarilumab 150 mg q2w. Similar findings were observed for erosion score and joint space narrowing.
**Conclusions:** Remission or LDA was associated with less radiographic progression irrespective of treatment, and remission was associated with less radiographic progression than LDA. Irrespective of whether patients achieved remission or LDA, sarilumab + MTX was associated with less radiographic progression than placebo + MTX.



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## SAT0150 COMPARATIVE RISK OF MALIGNANCY WITH INITIATON OF ABATACEPT AND OTHER BIOLOGICS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A COHORT ANALYSIS OF A UNITED STATES CLAIMS DATABASE

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**Background:** Patients with RA may be at an increased risk for malignancies compared with the general population, and treatment with TNF inhibitors have been reported to further increase this risk.[1] Abatacept, the first selective co-stimulation modulator for the treatment of RA, has a mechanism of action that is fundamentally different from that of other biologic agents.
**Objectives:** This cohort study aimed to compare the risk of malignancy between patients initiating abatacept and patients initiating other biologic treatments.
**Methods:** Adult patients diagnosed with RA in the MarketScan® Commercial and Supplemental Medicare database who initiated treatment with abatacept or another biologic treatment between 1 July 2006 and 30 September 2014 were eligible for inclusion in the analysis. Patients were required to have at least 180 days of continuous health plan enrolment prior to, and $\geq$1 day following, initiation of the qualifying RA treatment. Patients were presumed to have initiated a treatment if there was no claim for that particular drug in the 180 days prior to the index date. Therefore, patients initiating abatacept or another biologic treatment may be initiating a biologic for the first time or switching from one biologic to another. Malignancies were identified by International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes. Patients were followed from 180 days after the date of initiation of abatacept or another biologic treatment until occurrence of a malignancy (identified by ICD-9 code), end of enrolment in the database or end of data collection, whichever occurred first. Patients who had an ICD-9 code for a malignancy in the 6 months prior to or after the date of initiation were excluded. Crude incidence rates were calculated for each cohort. After matching each initiator of abatacept with 1 or 2 initiators of other biologic treatments on the propensity score, a Cox regression analysis was performed to estimate the hazard ratio.
**Results:** A total of 17,670 patients initiating abatacept and 50,641 initiating another biologic were identified. During an average follow-up of 1.4 years for abatacept initiators and 1.6 years for other biologic initiators, there were 1132 and 2933 patients with an incident event of malignancy, respectively. This resulted in incidence rates of 44 (95% CI: 42, 47) and 36 (35, 38) per 1000 person-years in abatacept initiators and other biologic initiators, respectively. The propensity score analysis resulted in 17,517 patients initiating abatacept matched with 32,277 patients initiating another biologic. After adjusting for prior biologic treatment, the hazard ratio of malignancy with abatacept relative to other biologic agents was

1.10 (0.98, 1.23). Hazard ratios for lung cancer, lymphoma, breast cancer and non-melanoma skin cancer were also similar between the two.
**Conclusions:** In this large, real-world study of patients treated for RA, the risk of malignancy was not significantly different for those who initiated abatacept compared with those who initiated other biologic agents.
**References:**
[1] Mercer LK, et al. Ann Rheum Dis 2015;74:1087–93.
**Disclosure of Interest:** S. Suissa Consultant for: Bristol-Myers Squibb, Genentech, Roche, N. Baker Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, H. Kawabata Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, N. Ray: None declared, T. Simon Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb
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## SAT0151 IMAGING AND HISTOPATHOLOGICAL CHANGES TO TOCILIZUMAB IN PATIENTS WITH MODERATE TO SEVERE RA: A SINGLE CENTRE RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED STUDY

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**Background:** Tocilizumab (TCZ) is a well-established biologic therapy in the treatment of rheumatoid arthritis (RA). There is limited data on imaging and synovial tissue histology changes.
**Objectives:** To evaluate level of response as defined by power Doppler (PD) ultrasound (US) and synovial tissue histology changes.
**Methods:** Patients with RA, inefficacy to minimum one DMARD +/– TNFi, with DAS28≥3.2 and knee synovitis amenable to synovial biopsy were recruited to this open-label 48-week study. Patients randomised to TCZ/methotrexate (MTX) for 48 weeks or placebo (PBO)/MTX for the first 16 weeks followed by TCZ/MTX until week 48. Clinical and US hand, wrist and knee assessments with US-guided knee synovial biopsy at baseline (BL), weeks 12 and 48 (biopsy optional). US was scored accrording to OMERACT 0–3 grey scale and PD synovitis scoring system. Synovial tissue was assessed for synovial inflammatory infiltrate, stromal cell density, synovial lining on 0–3 scale and overall synovitis (0–9 scale) determined.
**Results:** 15 patients recruited: 12 (80%) females; 9 received TCZ/MTX, 6 PBO/MTX. 2 patients withdrew at each arm, one due to TCZ infusion reaction. Week 16: 33% (3/9) TCZ/MTX achieved DAS28ESR-rem vs 0 PBO+MTX, latter remaining in moderate/high disease activity. Week 48: 92% (12/13) whole group in DAS28ESR-rem. US response: 38% (3/8) TCZ/MTX group who had BL PD synovitis in hand/wrist had absence of PD synovitis at week 16 vs none PBO/MTX group. All patients with abnormal BL PD in knees (median (IQR) PD score of 2 (0–9)) had improved week 48 PD score (median (IQR) PD score of 0 (0–1)). 13 patients (8 TCZ/MTX, 5 PBO/MTX) had synovial biopsies obtained weeks 0 & 12; 21/26 samples (80%) samples useable. No difference between pre- and week 12 synovitis score in both groups. Median (IQR) total synovitis score at BL and after week 12 respectively of 3 (2.75, 4.25) and 3 (2.5–4) in the TCZ/MTX group vs 6 (4,7) and 6 (4,6) in PBO/MTX group. BL total synovitis score did not predict early or late response.
**Conclusions:** TCZ/MTX was associated with significant clinical and imaging improvement compared to MTX alone. An absence of change in synovial infiltrate with TCZ/MTX at 12 weeks suggests a different mechanism for response compared to other anti-cytokine therapies such as the TNFi. Further histochemistry analysis and investigation may potentially determine mechanism and indicators of response on a tissue level.
**Disclosure of Interest:** None declared
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## SAT0152 SAFETY OF SURGERY IN PATIENTS TREATED WITH TOCILIZUMAB FOR RHEUMATOID ARTHRITIS: DATA FROM THE REGATE REGISTRY

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**Background:** Rheumatoid Arthritis (RA) patients have a higher risk of post-operative complications compared with the general population, especially considering the risk of infection. It remains unclear whether use of biological DMARDs, including Tocilizumab (TCZ), is an independent risk factor for post-operative complications.To date, there is no evidence pointing to delayed wound healing or increased risk of post-operative infection in patients receiving TCZ.
**Objectives:** To evaluate safety and predictive factors of complications after surgery in rheumatoid arthritis patients receiving Tocilizumab in routine care.
**Methods:** Patients treated with TCZ for RA included in the French REGATE registry were included if they underwent surgery. When TCZ was interrupted more than 12 weeks prior to surgery, patients were excluded. Post-operative complications were defined as an adverse event occurring in the 12 weeks after surgery. Frequency of post-surgery complications was collected and compared in patients with and without complications in order to identify factors associated with complications. A second analyze was achieved in patients with post-operative infection (local or general). Qualitative variables were compared by Fisher's test and quantitative variables were compared by the Mann-Whitney test.
**Results:** Out of 1499 patients from the REGATE registry, a total of 167 patients underwent 175 surgical procedures: 103 orthopedic surgeries (58.9%) and 29 abdominal surgeries (16.6%). These patients were mainly women (84%), the mean age was 58.11±12.83 years, and the disease duration of 14.96±11.29 years. The mean delay between surgery and the last TCZ infusion was 4.94±1.74 weeks (median 4 weeks). Thirty-eight surgical procedures happened whereas the last TCZ infusion was less than 4 weeks ago. Fifteen patients experienced 15 complications (8.9%) with 10 severe infections, 1 intestinal obstruction, 1 RA flare, 1 delayed wound healing, 1 thromboembolic disorder and 1 hemorrhagic complication. Postoperative complications occurred after 7.8% of orthopedic surgeries (8 of 103) and 2.9% of abdominal surgeries (2 of 29). The 10 severe infections occurred mostly after orthopedic surgery (7/10). There was 7 surgical site infections (46.7%) and 3 general infections. In 5 patients, TCZ treatment was definitely stopped. In univariate analysis, leflunomide dose was significantly associated with postoperative complications (p=0.04). Steroids and previous Rituximab treatment in the year before surgery, tended to be associated with peri-operative complications (p=0.09 and 0.07 respectively). In multivariate analysis, considering patients with infectious complications, diabetes was significantly associated with an increased risk of infection (P=0.03, OR 8.01, 95%CI 1.29–49.71).
**Conclusions:** In routine practice, the postoperative period in TCZ treated patients seem to be safe when TCZ is stopped 1 month before surgery. Diabetes was significantly associated with an increased risk of post-operative infection in RA patients treated with TCZ.
**Disclosure of Interest:** None declared
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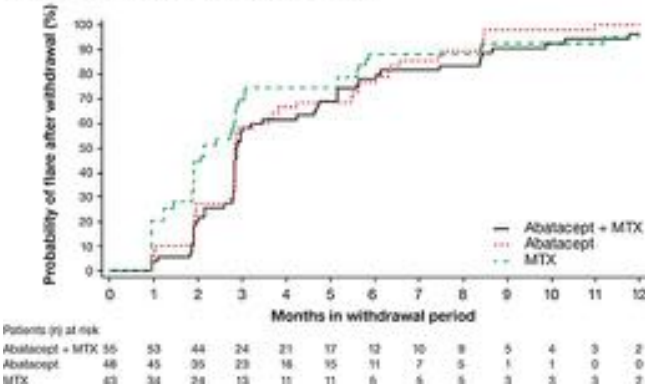
## SAT0153 ABATACEPT PLUS METHOTREXATE CAN EFFECTIVELY AND SAFELY REGAIN THE TARGET OF REMISSION FOLLOWING RE-TREATMENT FOR FLARES AFTER DRUG-FREE WITHDRAWAL IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** AVERT was a Phase IIIb, randomized, active-controlled study to evaluate the efficacy and safety of abatacept (ABA) treatment in three phases: treatment period (TP), withdrawal period (WP) and re-exposure period (RP). The TP and first 6 months (M) of the WP have previously been reported.[1]
**Objectives:** To describe efficacy and safety of re-treatment with ABA + MTX following RA disease flare after all treatment withdrawal.
**Methods:** MTX-naïve, anti-cyclic citrullinated peptide-2-positive patients (pts) with early RA (active synovitis in ≥2 joints for ≥8 weeks, DAS28 [CRP] ≥3.2 and symptom onset within ≤2 years) were randomized to 12M of weekly SC ABA 125 mg + MTX, ABA 125 mg monotherapy (mono) or MTX alone. Pts with DAS28 (CRP) <3.2 at M12 entered a 12M WP with no treatment, including corticosteroids. All pts with protocol-defined flare after 15M could receive open-label weekly SC ABA 125 mg + MTX 10–20 mg (RP) for 6M. Baseline for the RP was the last assessment within 30 days before the first re-exposure dose. For pts who entered the RP, time to first flare after withdrawal (Kaplan–Meier [KM] curves) and predictors of shorter times to flare (Cox proportional hazard model), and DAS28 (CRP) remission during re-exposure (adjusted logistic regression), were modeled.
**Results:** Most pts entered the WP (225/351); of 176 pts with DAS28 (CRP) <2.6 at 12M, only 12.3, 14.0 and 11.3% for ABA + MTX, ABA mono and MTX alone, respectively, maintained DAS28 (CRP) <2.6 free of all drugs at 24M. The KM curves for time to first flare during WP for pts entering the RP are shown (Figure). Corticosteroid use at study entry was associated with shorter time to flare. In total, 146 pts from all three groups entered the RP; baseline characteristics were similar to those of pts at study entry (mean RA duration ~0.5 yrs). Mean (SD) DAS28 (CRP) was 5.28 (1.37) at RP baseline and 2.41 (0.94) at the end of RP (mean change: –2.87 [0.13], n=120). In total, 76.6% (95/124) of evaluable pts had low disease activity (DAS28 [CRP] <3.2) on RP Day 169, with 62.9% (78/124) in remission (DAS28 [CRP] <2.6). Mean (SD) HAQ at RP entry was 1.40 (0.63), and 0.64 (0.57) at the end of the RP. Pt assessment of disease activity was significantly associated with DAS28 (CRP) remission during the RP. Over the 12M WP, the numbers (%) of serious AEs were 2 (2.4), 0 (0) and 5 (6.7), respectively; only one serious infection was reported (MTX alone; pyelonephritis; 337.4 pt-yrs). In the RP, no pts discontinued due to AEs and no serious infections were reported (292.2 pt-yrs). Overall rates of infections were 8.1 and 16.1 (incidence rate/100 pt-yrs) in the WP and RP. In the TP, incidence rates of infections were 116.6,

126.1 and 110.7/100 pt-yrs from 0–6M, and 64.6, 66.5 and 72.8/100 pt-yrs from 6–12M for ABA + MTX, ABA mono and MTX alone.

**Figure.** Time to first flare after study medication withdrawal
All treated patients entering the re-exposure period




**Conclusions:** Re-treatment with abatacept + MTX can effectively recapture prior remission following flare after complete withdrawal of therapy. The lower rate of infections in the RP versus initial TP suggests re-treatment is well tolerated.

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## SAT0154 REASONS FOR DISCONTINUATION THE BIOLOGICAL TREATMENT IN CHRONIC INFLAMMATORY ARTHROPATHY

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**Objectives:** To analyze the reasons for discontinuation the biological treatment in a cohort of patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PA), ankylosing spondylitis (AS) and other spondyloarthropathies (O) that have been treated with at least a biotech drug.

**Methods:** Retrospective observational study. All patients who had been treated with a biological drug for at least six months during the period between 01/01/2009 and 31/08/2014, for any of the previously specified indications were included. In addition to demographic data, all lines of treatment received from the diagnosis, and the reasons for discontinuation of those lines were analyzed. The adverse events categorized as reasons to treatment discontinuation were collected. The relationship between the reasons for discontinuation and the biological treatment was explored.

**Results:** We studied 484 patients with a mean age of 56 years (SD 14.4), 54.3% women. Disease distribution: 49% RA,21.5% PA, 22.6% AS and 6.9%O.Drug distribution:adalimumab 45.7% of patients,etanercept 29%,infliximab 12.7%,golimumab 2.6%,certolizumab 0.8%, abatacept 2.6%, rituximab 3.4% and tocilizumab 3%.Of a total of 765 lines of treatment, were analyzed all the finished lines:365.The reasons for discontinuation were:42.5% secondary failure,22.7% side effects,10.7% primary failure,6% clinical remission,1.9%, exitus, nonadherence 0.3% and other reasons for discontinuation 15.9%.Significant differences ($p<0.05$) were observed in the distribution of reasons for discontinuation based on biological treatment used.All comparisons between different drugs 2–2 were performed for each of the reasons for discontinuation, and the following differences were found.When adalimumab versus etanercept and versus infliximab is compare, it is more frequent the reason for discontinuation “clinical remission” in adalimumab than in etanercept or infliximab ($p<0.05$).When comparing etanercept versus infliximab is more often the reason for discontinuation “primary failure” with etanercept ($p<0.01$).

In the 50% of patients (P) with rituximab and in the 38.5% of P with abatacept the reason for discontinuation was an adverse event (AE), compared with 19% in adalimumab, 19.6% etanercept and 26.3% infliximab. Regarding the AE that were a cause for discontinuation:infusion reaction in 19P,general symptoms in 16P,bacterial infection in 12P,other types of skin toxicity 11P,anaphylaxis in 8P,liver toxicity in 4P,hematologic tumor in 2P,tuberculosis in 2P,psoriasiform reaction 2P,viral infectión 2P,interstitial disease 1P,solid tumor in 1P,psychiatric disorders in 1P,lipid abnormalities 1P,hematologic toxicity 1P and not collected in history in 2P.

**Conclusions:** The most common reason for discontinuation was "secondary failure" followed by “AE”,highlighting the infusion-related reactions and bacterial infections.The frequency of several of the reasons for discontinuation of treatment is different depending on the biological drug used.

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**Disclosure of Interest:** None declared

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## SAT0155 SIGNATURE OF INFLAMMATORY GENES IN B-CELLS AND DOUBLE NEGATIVE MEMORY PHENOTYPE AS BIOMARKERS OF RESPONSE TO TOCILIZUMAB

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**Background:** Tocilizumab (TCZ) is an effective treatment in Rheumatoid Arthritis (RA) inducing modifications of B cell subsets in vivo.[1–3]

**Objectives:** To define whether the study of circulating B cell subsets could represent a possible tool to understand the pharmacological action of TCZ, helping the clinician to identify the best responders to IL6R blockade.

**Methods:** 70 RA patients (age 52.3±15.2 years, disease duration 8.5±10.1 years, 74.3% female) not responder to previous cDMARDs (n=39) and/or bDMARDS (n=31) were enrolled in the study, of which 19 (27.1%) with early RA (ERA) and 51 (72.9%) with a long-standing disease (LSRA). All patients were treated with TCZ at a dose of 8 mg/kg every 4 weeks. At each visit remission was evaluated according to ACR/EULAR criteria[4] and peripheral blood (PB) derived B cells were collected for the analysis of B-cell subsets distribution by FACS using IgD-CD27 classification[5]. Among them, PB-derived B cells from 13 bDMARDs naïve RA patients were analyzed for specific genes expression through RT-PCR.

**Results:** In RA cohort, 16.7% and 19.3% of TCZ-treated RA patients reached ACR/EULAR remission (SDAI$\leq$3.3) at 6th and 12th months FU. At TCZ baseline, a higher percentage of post-switched memory B-cells (p=0.005) together with plasmablasts ($p<0.001$) and a lower percentage of pre-switched memory B cells (p=0.01) were observed in RA patients compared to Healthy Controls (HC, n=45) mainly in bDMARDs naïve patients. After TCZ treatment, we showed an increase of pre-switched memory and a reduction of post-switched memory and double negative (DN) B cells in responders, more evident in patients reaching remission. In particular, patients reaching SDAI remission at 6 and 12 months of TCZ-treatment had a higher reduction of DN B cell subsets already after 3 months reaching a comparable value as in HC ($p<0.05$). At the multivariate analysis, a disease duration less than 12 months [OR (95%CI): 18.0 (1.6–203.9)], a moderate disease activity (SDAI$\leq$26) at baseline [OR (95%CI): 20 (1.7–250)] and a higher reduction of DN B cells at 3 months of FU [OR (95%CI): 1.05 (1.01–1.08)] arose as significant independent predictors of ACR/EULAR remission (SDAI$\leq$3.3) at 6th months of TCZ treatment. Finally, TCZ-treatment seems to influence B-cell genes expression inducing an up-regulation of proinflammatory molecules (TNF-alpha, IL6) genes, together with the related STAT3, SYK and ZAP-70 genes, in the earlier treatment phases (3 and 6 months respectively) and the subsequent down-regulation of their receptors (TNF-RII and IL6R). Interestingly, the expression of JAK1 decreased significantly at the 12th month, whereas that of JAK3 did not change at the different time points.

**Conclusions:** In our cohort of TCZ-treated RA patients, a significant reduction of DN memory B cells at the 3th month of FU has emerged as an early biomarker of remission afterwards. At the same time, profound effects at the JAK1 gene level occurred in B cells after TCZ treatment, even if an increase of Syk and ZAP-70 genes expression was observed, suggesting that B cells are not fully deactivated even after 6–12 months of treatment.

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**Disclosure of Interest:** None declared

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## SAT0156 ABATACEPT IN RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE: A MULTICENTRE STUDY IN 34 PATIENTS

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**Background:** Rheumatoid arthritis (RA) may associate with Interstitial Lung Disease (ILD). Disease-modifying anti-rheumatic drug (DMARD) or TNF alfa inhibitors (iTNF), had been involved in the ILD development as well as exacerbation of an existing one. Nowadays there is no consensus related to treatment.
**Objectives:** The aimed of this study is to evaluate efficacy and safety of Abatacept (ABA) treatment in patients with AR and ILD.
**Methods:** Multicentre study in patients with RA and ILD associated were treated with ABA. ILD was diagnosed by High Resolution Computed Tomography (HRCT). ABA was used at dose of 10 mg/kg/4 weeks iv or 125 mg/week sc. Its efficacy was evaluated according to the following measures:

a) Dyspnea classified by the Modified Medical Research Council (MMRC); Significant variability of 1 point and asymptomatic MMRC=0;
b) Pulmonary function test (PFT); Significant oscillations >10% in Forced Vital Capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) >10%;
c) Imaging technique (HRCT);
d) Joint assessment (DAS28).

Quantitative variables were expressed as mean ± SD or as median (interquartile range) and compared with (Wilcoxon test) (Test Fisher) between the baseline and 3, 6 and 12 months.
**Results:** 34 individuals were included (19 women /15 men), patients with ILD associated to RA, with a mean age of 61,4 ± 9,8 years. The median duration of RA before ADA was initiated was 4,8 [0,86–13,12] (0–25) years, and had previously received an average 1,29±0,90 DMARDs. RA was seropositive in 24 cases (71%). ILD was associated with a DMARD: MTX (n=3), Etanercept (n=3), Adalimumab (n=3) y Certolizumab (n=1).
ABA was used in monotherapy in 14 patients and combined with other immunosuppressors in 20 patients: Leflunomide (LFD) (n=7), LFD and cyclosporine (n=1), Sulfasalazine (n=1), MTX (n=2), MTX with LFD (n=1), hydroxychloroquine (n=5), Hydroxychloroquine with LFD (n=2), Azathioprine (n=1).
A significant improvement of dyspnea was observed; patients who didn't have dyspnea, kept asymptomatic. FVC and HRCT showed a significant improvement during 6 to 12 months period. DLCO remained stable in the majority of the patients. RA (DAS28) activity also improved.
After follow up of 12,82±7,48 months, the most significant adverse effects were: pulmonary Infection (n=2), urinary infections (n=1), infusion reactions (n=1).
ABA was discontinued due to: Serious infections (n=2); join inefficacy (n=2), pulmonary inefficacy (n=1), infusion reaction (n=1).
**Conclusions:** ABA seems to be an effective and relatively safe treatment in patients with RA and associated ILD. This data should be verified again in prospective and randomized studies.

TABLE

| | 3 months | 6 months | 12 months |
|---|---|---|---|
| MMRC, available data, n<br>- Stable<br>- Improvement<br>- worse | n= 34<br>26 (76,5%)<br>7 (20,6%)*<br>1 (2.9%) | n= 25<br>18 (72%)<br>7 (28%)**<br>0 (0%) | n= 22<br>14 (63,7%)<br>7 (31,8%)**<br>1 (4,5%) |
| CVF, available data, n<br>- Stable<br>- Improvement<br>- Worse | n= 10<br>7 (70,0%)<br>2 (20,0%)<br>1 (10,0%) | n=11<br>5 (45,5%)<br>4 (36,4%)**<br>2 (18,1%) | n=12<br>7 (58,3%)<br>3 (25,0%)*<br>2 (16,7%) |
| DLCO, available data, n<br>- Stable<br>- Improvement<br>-worse | n=9<br>4 (44,4%)<br>4 (44,4%)**<br>1 (11,2%) | n=7<br>3 (42,9%)<br>1 (14,2%)<br>3 (42,9%) | n=8<br>5 (62,5%)<br>1 (12,5%)<br>2 (25,0%) |
| HRCT, available data, n<br>- Stable<br>- Improvement<br>- worse | n=3<br>2 (66,7%)<br>1 (33,3%)<br>0 (0.0%) | n=8<br>2 (25.0%)<br>6 (75.0%)**<br>0 (0.0%) | n=8<br>3 (37,5%)<br>3 (37,5%)**<br>2 (25.0%) |
| Join., DAS28,available data, n<br>- average [IQR] # | n= 30<br>3,9 [2,4-4,5]* | n=25<br>3,3 [2,3-4,4]** | n= 21<br>3,7 [2,4-4,6]** |

Comparisons were linked in relationship with baseline * p<0.05; **p<0.01.
# At baseline we have 33 data,with a median 5,1 [3,8-5,8].

**Conclusions:** The presence of low serum Tocilizumab levels correlates with a

**Disclosure of Interest:** None declared
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## SAT0157 TOCILIZUMAB SERUM TROUGH LEVELS CORRELATE WITH CLINICAL ACTIVITY IN RHEUMATOID ARTHRITIS

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**Background:** Tocilizumab (TCZ), a humanized anti-IL-6 receptor antibody, represents a new treatment strategy for RA patients.Several studies have demonstrated the association between high serum levels of TNF-inhibitors and a good clinical response in patients with RA. Little evidence exists on this relationship for other biological therapies.
**Objectives:** To evaluate the association between TCZ serum through levels and disease activity in a cohort of RA patients after one year of treatment with TCZ.
**Methods:** 34 RA patients treated with Tocilizumab were included. Clinical activity was assessed using the Disease Activity Score 28 (DAS28-ESR) and the Clinical and Simplified Activity Index (CDAI and SDAI), serological improvement by C-Reactive Protein- CRP- and Erythrocyte Sedimentation Rate-ESR, clinical improvement by the delta-DAS 28 and response to treatment using EULAR criteria at baseline and after one year of treatment. We stratified all patients into quartiles according to the tocilizumab levels (μg/ml) as follows: IQR1: <3,4, IQR2: 3,4–11,2, IQR3: 11,2–18,5 and IQR4 >18.5. A last observation carried forward analysis (LOCF) was performed at the first year of treatment, so patients that dropped out of the therapy before this period were included. Blood samples were collected just before intravenous (i.v) infusion. Serum drug levels were determined by a capture enzymelinked immunosorbent assay (ELISA).
**Results:** The baseline demographic and clinical characteristics are shown in Table 1. When patients were categorised into quartiles, IQR1 comprised 8 (24,2%) patients; IQR2, 7 (21,2%); IQR3, 8 (24,2%) and IQR4, 10 (30,3%). Clinical activity (DAS28, CDAI and SDAI) was statistically significant higher in patients with lower serum through levels at the first year [DAS28 (IQR1: 4,46 ±1,5, IQR2: 2,58 ± 0,87, IQR 3: 3,6± 0,79; IQR4: 2,17 ± 0,74; p=0,001), CDAI (IQR1: 23±13,9, IQR2: 7,72 ± 4,44, QIR 3: 13,38± 4,35, IQR4: 6,33 ± 4,62; p=0,003) and SDAI (IQR1: 19,46 ±15,5, IQR2: 9,51± 7,4, IQR3: 12,59 ± 6,31, IQR4: 4,55 ± 3,73; p=0,005)] and also was the number of swollen joints (IQR1: 7,5 ± 6,6, IQR2: 2,29 ±2,06, IQR3: 5,63 ± 4,3, IQR4: 1,1 ± 1,6, p=0,013) and tender joints (IQR1: 5,5 ± 5,7, IQR2: 1,71 ± 2,06, IQR3: 3,13 ± 2,8, IQR4: 0,8 ± 0,9, p=0,014). In addition, the EULAR reponse was worse in those patients with lower serum drug levels [non-responders: 4 (66,7%) in IQR1 vs 1 (16,7%) in IQR2 vs 1 (16,7%) in IQ3 vs 0 (0%) in IQR4, moderate responders: 3 (37,5%) in IQR1 vs 0 (0%) in IQR2 vs 4 (50%) in IQR3 vs 1 (12,5%) in IQR4 and good responders: 1 (5,3%) in IQR1 vs 6 (31,6%) in IQR2 vs 3 (37,5%) in IQR3 vs 9 (47,4%) in IQR4, p=0,006]. In terms of acute-phase reactants, the mean ESR tended to be higher in patients with lower TCZ levels (IQR1: 22,6±14,8 vs IQR2: 5,6±1,6 vs IQR 3: 9,4 ±3,5 vs IQR4: 6,4 ± 3,5, p=0,005), and also CRP levels (RIQ1: 10,2±17,4 vs RIQ2: 2,3 ± 3,4 vs RIQ3 0,56 ± 0,4 vs RIQ 4: 0,42 ± 0,66, p=NS)].

| | |
|---|---|
| Age, years ± SD | 58,44 ± 13,9 |
| Female [n/N (%)] | 30/34 (88,2%) |
| BMI (kg/m2) ± SD | 26,6 ± 5,4 |
| Smokers<br>Ex-smokers<br>Non smokers | 8/34 (23,5%)<br>5/34 (14,7%)<br>20/34 (58,8%) |
| Erosive Arthritis [n/N (%)] | 24/32 (70,6%) |
| Disease duration ±SD | 12,06 ±7 |
| DAS 28-ESR, mean ± SD<br>CDAI, mean ± SD<br>SDAI, mean ± SD | 5,66 ± 1,14<br>32,7 ± 13,4<br>34,6 ± 15,3 |
| SJC/TJC, mean ± SD | 11,8 ± 6,7/ 8,71 ± 5,1 |
| CRP/ESR, mean ± SD | 18,1 ± 22,8/ 30,8 ± 21,9 |
| RF/ ACPA + [n/N (%)] | 28/34 (82%); 30/34 (88%) |
| Prev DMARD, mean ± SD | 0,56 ± 0,7 |
| Previous biol. n/N (%): | 19/34 (55,8%) |
| Baseline Co-therapy, [n/N (%)] | Monotherapy:4/34(11,8%);<br>MTX: 25/34 (73,5%);<br>Other DMARD:15/34 (44%)<br>MTX+oDMARD:10/34(29%) |

worse clinical disease activity. Consequently, measurement of Tocilizumab levels is a valuable tool that might help in the clinical management of patients with Rheumatoid Arthritis.

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## SAT0158 RESPONSE AND RADIOGRAPHIC PROGRESSION IN BIOLOGIC-NAÏVE AND BIOLOGIC-EXPERIENCED PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SIRUKUMAB

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**Background:** Efficacy and safety of sirukumab, a selective, high-affinity human monoclonal antibody to IL-6, have recently been evaluated in a global Phase 3 study in patients (pts) with active rheumatoid arthritis (RA) refractory to conventional disease-modifying anti-rheumatic drugs (DMARDs).

**Objectives:** To compare efficacy and radiographic progression of sirukumab in subgroups of pts with active RA despite DMARD treatment who previously received biologic therapy (biologic-experienced) and who previously only received synthetic DMARDs (biologic-naïve).

**Methods:** Pts were randomized (1:1:1) to sirukumab subcutaneous (SC) 50mg q4w, sirukumab SC 100mg q2w, or placebo SC q2w. Pts on placebo with insufficient (<20%) improvement at Wks 18 or 40 or still on placebo at Wk 52 were re-randomized to sirukumab treatment (1 of the 2 doses). The co-primary efficacy endpoints were: Wk 16 ACR20 response and Wk 52 change from baseline (BL) in modified vdH-S radiographic score. This post-hoc analysis compared efficacy for biologic-naïve and -experienced pts within biologic experience category for sirukumab vs placebo, and across experience category within sirukumab dose group.

**Results:** Improvements were observed in all outcomes for sirukumab vs placebo, regardless of prior biologic use (all $P<0.001$ within biologic experience categories; Table). 34.9% (583/1,670) of pts were prior biologic-experienced; efficacy with sirukumab was comparable for pts who had taken 1 or ≥2 prior biologics. At BL, compared with biologic-naïve pts, biologic-experienced pts had longer disease duration (mean, 11 vs 7 yrs; $P<0.0001$) and worse HAQ-DI scores (mean, 1.58 vs 1.49; $P=0.02$). No differences between prior biologic-naïve and -experienced pts were observed in either sirukumab dose group for the co-primary endpoints (both $P\geq0.1$) as well as for Wk 24 ACR50 response, DAS28 (CRP) remission, or Wk 52 mean DAS28 change from BL (all $P\geq0.1$).

**Conclusions:** Both sirukumab doses significantly reduced RA signs/symptoms and inhibited radiographic progression vs placebo within prior biologic use categories, with comparable efficacy observed between biologic-naïve and -experienced pts for both sirukumab doses.

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## SAT0159 RESULTS OF A PHASE 1B STUDY OF THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF THE MMP9 INHIBITOR GS-5745 IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** Active matrix metalloproteinase-9 (MMP9) degrades matrix proteins and promotes inflammation. MMP9 knockout mice are also protected from collagen-induced arthritis disease progression. Furthermore, elevated levels of MMP9 are present in the synovial fluid of patients with RA suggesting that targeting of MMP9 may have therapeutic benefit. GS-5745 is a humanized $IgG_4$ mAb that inhibits MMP9 activity with picomolar specificity.

**Objectives:** To determine the safety and tolerability of GS-5745 in adult subjects with RA. Secondary objectives were to investigate the PK of GS-5745, and to assess the effect of GS-5745 on RA disease activity measures.

**Methods:** This multi-center, randomized, double-blind, placebo-controlled study enrolled 18 subjects who met the ACR criteria for RA and had a mean screening CRP ≥8.0 mg/L. Subjects were randomized 4:1 to receive GS-5745 400 mg or placebo (PBO) infusions every 2 weeks for a total of 3 infusions. Concurrent biologic DMARD use was excluded, but subjects continued their stable conventional DMARD therapy. A 28 swollen and tender joint count, patient assessment of pain, and patient and physician global assessment of health were obtained.

**Results:** Eighteen subjects (15 active and 3 PBO) were enrolled and received 3 doses of GS-5745 or PBO. The median plasma half-life of GS-5745 was 5.7 days. Mean free plasma MMP9 levels in the GS-5745 cohort were reduced by 90% from 126.1 ng/mL at Baseline to 13.2 ng/mL (2.18) at Day 43; compared to a 17% increase from 76 ng/mL at Baseline to 89 ng/mL at Day 43 in the PBO cohort. DAS 28-CRP low disease activity or remission at Day 43 occurred in 4/15 patients receiving GS-5745 versus 0/3 receiving PBO There were no SAEs. All adverse events were of Grade 1 or 2 severity. AEs occurring in ≥10% of active treated subjects included hypertension and nasopharyngitis, both 13%. Changes in additional RA disease activity measures are shown in the tab:

**Conclusions:** Short term treatment with GS-5745 in patients with RA was well tolerated. Improvement in selected measures of RA disease activity was observed after 3 doses of GS-5745. Mean free plasma MMP9 was reduced by 90% compared to baseline in the GS-5745 group at Day 43. These results support further studies evaluating GS-5745 in RA.

**Acknowledgement:** We would like to thank study investigators Drs. E. Peterfai,

**Abstract SAT0158** – Table 1. Key endpoints by prior biologic use[a]

| | Placebo | | Sirukumab 50mg q4w | | Sirukumab 100mg q2w | |
|---|---|---|---|---|---|---|
| | Bio-naïve (n=360) | Bio-experienced (n=196) | Bio-naïve (n=382) | Bio-experienced (n=175) | Bio-naïve (n=345) | Bio-experienced (n=212) |
| Primary endpoints | | | | | | |
| ACR20 at Wk 16, n (%) | 101 (28.1) | 46 (23.5) | 210 (55.0)[b] | 95 (54.3)[b] | 194 (56.2)[b] | 104 (49.1)[b] |
| vdH-S mean (SD) change from BL at Wk 52 | 3.38 (9.02) | 4.27 (9.65)[c] | 0.42 (3.00)[b] | 0.67 (2.88)[b] | 0.67 (3.41)[b] | 0.11 (2.98)[b] |
| Secondary endpoints | | | | | | |
| ACR50 at Wk 24, n (%)[d] | 69 (21.2) | 30 (17.1) | 129 (36.0)[b] | 53 (32.7)[b] | 134 (42.4)[b] | 68 (37.8)[b] |
| DAS28 (CRP) remission at Wk 24, n (%)[d] | 29 (9.0) | 15 (8.7) | 108 (30.6)[b] | 46 (28.6)[b] | 98 (31.2)[b] | 54 (30.5)[b] |
| DAS28 (CRP) mean (SD) change from BL at Wk 52[d] | –2.18 (1.37) | –2.23 (1.22) | –2.79 (1.25)[b] | –2.84 (1.28)[b] | –2.79 (1.29)[b] | –2.72 (1.23)[b] |

[a]n values reflect overall numbers of biologic-naïve and -experienced pts. [b]$P<0.001$ vs placebo within experience subgroup. [c]$P=0.04$ vs biologic-naïve (all other $P\geq0.1$ for biologic-experienced vs -naïve). [d]Observed values.

**Abstract SAT0159** – Table 1

| Subjects | Clinical Assessments | Day 43 # Subjects with a 50% Improvement | | | | | |
|---|---|---|---|---|---|---|---|
| | DAS28-CRP (mean Δ from baseline to Day 43) | Swollen joint count (28-joints) | Tender joint count (28-joints) | Subject pain score (VAS, 0–100) | Subject global assessment of health (VAS, 0–100) | Physician global assessment of health (VAS, 0–100) | CRP (mg/L) |
| GS-5745 (N=15) | –1.35 (1.393) | 9 (60%) | 7 (47%) | 7 (47%) | 6 (40%) | 6 (40%) | 4 (27%) |
| Placebo (N=3) | –0.77 (0.570) | 0 (0%) | 1 (33%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (33%) |

B. Rojkovich, P. Sramek, I. Varkonyi, their study staff and the study subjects who volunteered for this trial.
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## SAT0160 CLINICAL AND RADIOGRAPHIC OUTCOMES AFTER 2 YEARS OF SARILUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Sarilumab, an investigational human IL-6 receptor mAb, demonstrated statistically significant improvements in signs and symptoms of RA, physical function, and inhibition of radiographic progression in combination with MTX in the 1-year phase 3 MOBILITY study (NCT01061736).
**Objectives:** This analysis examined 2-year clinical and radiographic outcomes and safety in patients completing the MOBILITY study who continued in the open-label, long-term extension (OLE) study EXTEND (NCT01146652) and were treated with sarilumab 200 mg q2w.
**Methods:** Patients who participated in MOBILITY were initially randomized to placebo or sarilumab 150 or 200 mg subcutaneously for up to 1 year. Early rescue with open-label sarilumab 200 mg was allowed in case of insufficient response after wk 16. Following MOBILITY patients were eligible for enrollment in EXTEND, where all patients received active treatment (sarilumab 200 mg q2w after final dose selection) + MTX. Radiographs of patients who had a radiograph available at baseline and in the first and second year were centrally read by 2 readers independently. Linear extrapolation was performed if a patient had 2 postbaseline radiographs but was missing a radiograph at year 2. Analysis of clinical endpoints was based on all available data. Clinical endpoints were set to missing after early treatment discontinuation but not after rescue with open-label sarilumab. Statistical analysis was performed on the basis of patients' original randomized treatment assignment (placebo, or sarilumab 150 or 200 mg), regardless of whether the patient was rescued during the double-blind period (MOBILITY).
**Results:** Of the 1197 randomized patients enrolled in MOBILITY, 901 patients participated in EXTEND (Table). At year 2, disease activity (DAS28-CRP and CDAI) reached the same level regardless of initial treatment. In addition, at year 2, percentages of patients achieving DAS28-CRP $<2.6$ were similar in the 3 groups, and similar trends were observed for CDAI remission (CDAI $\leq 2.8$) (Table). Two-year radiographic data were available for 800 patients; linear extrapolation was used in 56 of these patients. mTSS scores at year 1 in initial placebo and sarilumab 150 and 200 mg groups were maintained through year 2 in the OLE (Table). TEAEs occurred in 86.3% of patients over 2 years, and SAEs occurred in 16.3% of patients. Over 2 years, death occurred in 7 patients (0.6%). Five deaths were classified as unrelated to treatment. Two deaths were assessed as possibly associated with sarilumab (streptococcal sepsis, possible stroke). The most common TEAEs ($\geq$5% in $\geq$1 treatment group) were neutropenia (17.8%), increased ALT (11.6%), and upper respiratory tract infections (11.1%).
**Conclusions:** Once active treatment with sarilumab 200 mg q2w was initiated after year 1, clinical response at year 2 was similar irrespective of prior treatment, and radiographic progression stabilized. Adverse events were consistent with the anticipated effects of IL-6 inhibition and the known safety profile of sarilumab.
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**Disclosure of Interest:** D. van der Heijde Consultant for: Sanofi, J. van Adelsberg Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Fay Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, H. van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, N. Graham Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Fan Shareholder of: Sanofi, Employee of: Sanofi, A. Spindler: None declared, M. Genovese Grant/research support from: Roche, Sanofi, GSK, R-Pharma, RuiYi, and Bristol-Myers Squibb, Consultant for: Roche, Sanofi, GSK, R-Pharma, RuiYi, and Bristol-Myers Squibb
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**Table.** Clinical and Radiographic Data at Baseline, Year 1, and Year 2 for Patients With RA Enrolled in the EXTEND Study, Where All Patients Received Active Treatment (Sarilumab 200 mg q2w After Final Dose Selection) + MTX

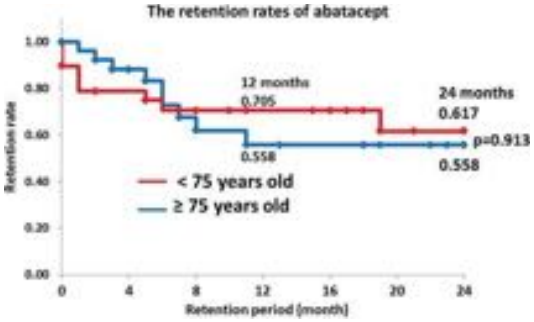
| | Placebo + MTX→ sarilumab 200 mg + MTX | Sarilumab 150 mg + MTX → sarilumab 200 mg + MTX | Sarilumab 200 mg + MTX |
|---|---|---|---|
| Randomized population | 398 | 400 | 399 |
| OLE population,* n | 307 | 300 | 294 |
| DAS28-CRP, mean ± SEM | | | |
| Baseline (at randomization into MOBILITY) | 5.9 ± 0.0 | 6.0 ± 0.0 | 6.0 ± 0.0 |
| Year 1 (randomized period) | 3.6 ± 0.1 | 2.9 ± 0.1 | 2.8 ± 0.1 |
| Year 2 (completers) | 2.5 ± 0.1 | 2.5 ± 0.1 | 2.4 ± 0.1 |
| Incidence of DAS28-CRP <2.6, yes, n/N (%) | | | |
| Year 1 (randomized period)† | 89/398 (22.4) | 156/400 (34.0) | 143/399 (35.8) |
| Year 2 (randomized population)‡ | 162/398 (40.7) | 159/400 (39.8) | 163/399 (40.9) |
| Year 2 (entered OLE)‡ | 162/307 (52.8) | 159/300 (53.0) | 163/294 (55.4) |
| Year 2 (completers) | 162/270 (60.0) | 159/258 (61.6) | 163/262 (62.2) |
| CDAI, mean ± SEM | | | |
| Baseline (at randomization into MOBILITY) | 40.6 ± 0.6 | 40.4 ± 0.6 | 40.4 ± 0.6 |
| Year 1 (randomized period) | 14.7 ± 0.6 | 11.0 ± 0.6 | 11.0 ± 0.6 |
| Year 2 (completers) | 8.9 ± 0.6 | 8.7 ± 0.6 | 8.6 ± 0.6 |
| CDAI remission (CDAI ≤2.8), yes, n/N (%) | | | |
| Year 1 (randomized period)† | 37/398 (9.3) | 65/400 (15.0) | 75/399 (18.8) |
| Year 2 (randomized population)‡ | 73/398 (18.3) | 73/400 (18.8) | 81/399 (20.3) |
| Year 2 (entered OLE)‡ | 73/307 (23.8) | 73/300 (25.0) | 81/294 (27.8) |
| Year 2 (completers) | 71/271 (26.9) | 71/259 (29.0) | 81/262 (30.9) |
| mTSS score, mean ± SEM | | | |
| Baseline (at randomization into MOBILITY) | 45.8 ± 3.8 | 49.2 ± 3.6 | 43.2 ± 3.4 |
| Year 1 (randomized period) | 48.4 ± 3.9 | 49.6 ± 3.6 | 43.1 ± 3.4 |
| Year 2 (completers) | 48.3 ± 3.9 | 50.4 ± 3.7 | 43.3 ± 3.4 |
| Erosion score, mean ± SEM | | | |
| Baseline (at randomization into MOBILITY) | 22.4 ± 2.0 | 22.2 ± 1.8 | 19.7 ± 1.7 |
| Year 1 (randomized period) | 23.6 ± 2.0 | 22.5 ± 1.8 | 19.6 ± 1.7 |
| Year 2 (completers) | 23.6 ± 2.0 | 22.9 ± 1.8 | 19.7 ± 1.7 |
| Joint space narrowing score, mean ± SEM | | | |
| Baseline (at randomization into MOBILITY) | 23.4 ± 1.9 | 26.9 ± 2.0 | 23.5 ± 1.8 |
| Year 1 (randomized period) | 24.8 ± 2.0 | 27.1 ± 2.0 | 23.5 ± 1.8 |
| Year 2 (completers) | 24.7 ± 2.0 | 27.5 ± 2.0 | 23.6 ± 1.8 |
| mTSS change from baseline, mean ± SEM | | | |
| Δ Baseline - year 1 (randomized period) | 2.4 ± 0.3 | 0.4 ± 0.2 | 0.2 ± 0.2 |
| Δ Baseline - year 2 (completers) | 2.5 ± 0.3 | 1.0 ± 0.4 | 0.2 ± 0.2 |

*Patients were tabulated according to their randomized treatment in MOBILITY.
†Year 1 incidence of DAS28-CRP <2.6 or CDAI remission based on the number of patients who enrolled in MOBILITY (randomized population).
‡Year 2 incidence of DAS28-CRP <2.6 or CDAI remission based on the number of patients who enrolled in MOBILITY (randomized population).
§Year 2 incidence of DAS28-CRP <2.6 or CDAI remission based on the number of patients who rolled over from MOBILITY into EXTEND (OLE).

## SAT0161 THE RETENTION RATE OF ABATACEPT IN VERY ELDERLY PATIENTS (75 YEARS AND ABOVE) WITH RHEUMATOID ARTHRITIS, SINGLE-CENTER, RETROSPECTIVE, OBSERVATIONAL STUDY

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**Background:** There are few data about the safety of biologics for very elderly rheumatoid arthritis patients.
**Objectives:** To analyze the retention rate of abatacept in very elderly patients with rheumatoid arthritis (RA).
**Methods:** Data was collected retrospectively from medical records of RA patients in our center. Abatacept was administered in 58 patients. We divided them into two groups of the very elderly group (over 75 years old) and the remaining group (under 75 years old). We analyzed the retention rate of each group by Kaplan-Meier curves and log-rank test.
**Results:** In *the very elderly group* (29 cases: 81.6±3.3 years, women: 89.7%, ACPA-positive: 86.2%, MTX use: 48.3%, oral steroid use: 31.0%), the cumulative retention rates in 12 and 24 months were both 0.558.
In *the remaining group* (29 cases: 63.4±10.7 years, women 89.7%, ACPA-positive: 86.2%, MTX use: 58.6%, oral steroid use: 37.9%), the cumulative retention rates in 12 and 24 months were 0.705 and 0.617 respectively.
There was no significant difference in the retention rates in the two groups (log-rank test, p=0.913). Abatacept was administered as the first biologics in 58.6% of the very elderly group, 31.0% of the remaining group respectively.
The main reasons for discontinuation of abatacept were hospitalization for infection (elderly: 3 cases, remaining: 2 cases) and hospitalization for gastrointestinal symptoms (elderly: 2, remaining: 0).

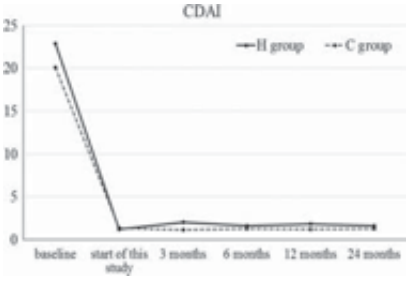



**Conclusions:** Our data suggested that abatacept can be used for a long period even for very elderly RA patients.
**References:**
[1] Lahaye C, et al. Rheumatology (Oxford). 2016 Jan 27. pii: kev437. [Epub ahead of print]
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5204

## SAT0162 BIOLOGICAL AGENT HOLIDAY THERAPY FOR RHEUMATOID ARTHRITIS IN PATIENTS WITH CLINICAL DISEASE ACTIVITY INDEX REMISSION

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**Background:** The advancement in biological agents (Bio) and improvement in treatment strategy enabled patients with rheumatoid arthritis to achieve remission or to achieve low disease activity. On the other hand, the cost of Bio has become a major problem in health economics and for some patients Bio therapy is not affordable. In this situation, it is important for us to consider whether we should discontinue or extend the interval of Bio.
**Objectives:** To investigate Bio-holiday therapy for rheumatoid arthritis patients with clinical disease activity index (CDAI) remission.
**Methods:** Thirty seven rheumatoid arthritis (RA) patients with CDAI remission were included in this study. The patients were classified into two groups. Bio-holiday group (group H) consisted of 17 patients (etanercept (ETA) 5, golimumab (GLM) 8, tocilizumab (TCZ) 4 patients) where the patients were off from Bio if they achieved CDAI remission. Methotrexate was combined for all patient. They had to visit our clinic at least once in every two months, and were treated with Bio within 3 months after falling out of CDAI remission. They could be off from Bio again once they've reached CDAI remission. Bio group (group C) consisted of 22 patients (ETN 7, GLM 9, TCZ 6 patients). The mean ages of the two groups were 55.6 for H and 58.3 years old for C group and the mean disease duration were 4.45 and 4.96 years. There were no statistical differences between the backgrounds of both groups. CDAI, the van der Heijde-modified total sharp scores [1] (mTSS) and health assessment questionnaire [2] (HAQ) were compared between both groups.
**Results:** The mean withdrawal periods were 11.8 (GLM), 6.5 (ETN) and 10.0 months (TCZ) respectively. Two patients in group H and 3 patients in group C dropped out due to financial reasons. One patient in each group dropped out due to flare-up. None of the patients discontinue their therapy for adverse events in both groups. Except for one patient who dropped out from CDAI remission due to flare-up in H group, all the other patient were able to achieve CDAI remission without delay. There were no statistical differences in CDAI throughout the period of study (Figure). There were no statistical differences in ∆mTSS (group H -0.18/year and group C -0.24/year) and HAQDI (group H; 0.12, 0.08 and group C; 0.10, 0.08 at baseline and at final evaluation respectively).




**Conclusions:** We conclude that it is possible to keep disease activity, radiographic progression and physical function by Bio-holiday for RA patients with CDAI remission under tight control strategy. As the flare-up rate of RA patients with deep remission is not so severe, it is not difficult for us to restart Bio therapy and gain CDAI remission. In addition it is financially durable and thus we recommend bio-holiday therapy.
**References:**
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[2] Siegert CE, et al. Clin Rheumatol. 1984;3:305–9
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4453

## SAT0163 LONG TERM TREATMENT WITH ABATACEPT OR TOCILIZUMAB DOES NOT INCREASE EPSTEIN-BARR VIRUS LOAD IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Epstein-Barr Virus (EBV) is a widely disseminated lymphotrophic herpes virus implicated in a lot of benign and malignant disorders. In transplant patients, EBV load is enhanced because of immunosuppressive drugs (cyclosporine) and in a few cases, it can lead to lymphoproliferative disorders (LPD). An EBV load higher than 500 copies per 500 ng of DNA is a predictive factor of post transplant lymphoma [1,2] Similarly, immunity against EBV is particular in RA patients: the level of antibodies against EBV is higher in RA than in healthy controls [3], RA patients have a defective EBV specific supressor T cell function [4].The risk to develop a lymphoma is higher in RA patients than in controls. We have previously shown that: 1/ EBV load is 10 fold higher in RA patients than in controls [5] and 2/ Methotrexate and TNF alpha antagonists (immunosuppressive drugs used in RA patients) do not increase EBV load in RA [6].
**Objectives:** Here, we monitored EBV load over 3 years in patients with RA treated by 2 more recent biologics, Abatacept (CTLA4 Ig) a T cell activation inhibitor, or Tocilizumab, an anti IL6 receptor antibody.
**Methods:** EBV load in the peripheral blood mononuclear cells (PBMCs) from 55 patients under Abatacept (+/– Methotrexate) and 35 patients under Tocilizumab (+/– Methotrexate) was monitored from 6 months up to 3 years, by real time PCR. The influences of treatment duration and disease activity score 28 (DAS28) index on EBV load were analyzed.
**Results:** Neither Abatacept nor Tocilizumab significantly enhanced EBV load over time. None of our patients developed EBV associated lymphoma.
**Conclusions:** Long term usage of Methotrexate with Abatacept or Tocilizumab in patients with RA does not significantly influence EBV load in PBMCs.
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## SAT0164 IMMUNE RECONSTITUTION 20 YEARS AFTER TREATMENT WITH ALEMTUZUMAB IN A RHEUMATOID ARTHRITIS COHORT: IMPLICATIONS FOR LYMPHOCYTE DEPLETING THERAPIES

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**Background:** Alemtuzumab, an anti-CD52 monoclonal antibody, was administered (cumulative dose range 1–420mg) to a cohort of patients with severe RA between 1991–94[1]. We previously reported significant delays in immune reconstitution detectable 12 years after administration[2].
**Objectives:** To perform the 20 year follow-up of our unique cohort with regards to morbidity, mortality, lymphocyte reconstitution, circulating cytokines and response to vaccination.
**Methods:** Mortality and morbidity data (Mar 2006–Jan 2015) were collected from death certificates, case notes or interview. Alemtuzumab patients were age, sex and disease duration matched with RA controls. For both groups circulating lymphocyte subsets ($CD4^+$ and $CD8^+$ naïve, central memory and effector memory T cells; naïve, memory and $CD5^+$ B cells and $CD19^+CD24^{hi}CD38^{hi}$ Bregs; NK Cells and NK T Cells) were quantified by multicolour flow cytometry. Serum IL-15 and IFN-$\gamma$ were measured by ELISA (MSD) and antigenic responses by generation of protective titres (as conventionally defined) following vaccination with influenza, Pneumovax II and combined diphtheria/tetanus/poliovirus vaccines
**Results:** 16 patients were alive at the time of this study, 9 agreed to interview, vaccines and peripheral blood analysis, a further 4 had case note review only and 3 were uncontactable. 8 matched RA controls were also recruited. Since our last review 10 patients had died with causes of death consistent with a population with long-standing RA. There was no suggestion of compromised immune function with no increase in new autoimmune conditions or severe infections in living patients. Alemtuzumab patients continued to demonstrate abnormalities in their lymphocyte compartment with persistent significant reductions in $CD4^+$ and $CD8^+$ central memory cells, $CD5^+$ B Cells and a new finding of significantly reduced naïve B cells when compared with previous analysis[2]. For the first time we examined $CD19^+CD24^{hi}CD38^{hi}$ Bregs which were also significantly reduced. Nonetheless vaccine responses were comparable between alemtuzumab recipients and controls. In addition, there were significantly higher IL-15 and IFN-$\gamma$ levels in the

serum of the alemtuzumab cohort. IL-15 levels inversely associated with $CD4^+$ total memory and central memory T cells.
**Conclusions:** In this unique patient cohort, after 20 years the effects of alemtuzumab treatment persist. Despite lymphocyte abnormalities, satisfactory vaccine responses are mounted and opportunistic infections remain absent. We hypothesise the reduced T-cell compartments trigger IL-15 via homeostatic mechanisms which, as a bystander effect, may activate NK cells causing IFN-$\gamma$ release. An activated NK compartment could explain the lack of opportunistic infections in patients with lymphocyte abnormalities for 20+ years.
As lymphodepleting therapies, including alemtuzumab, continue to be administered this work is important with regard to long term drug safety and stages of immune recovery.
**References:**
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[2] Anderson AE et al. Rheumatology (Oxford) 2012;51(8):1397–406
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4019

## SAT0165 TOFACITINIB VERSUS BIOLOGIC TREATMENTS IN MODERATE TO SEVERE RHEUMATOID ARTHRITIS PATIENTS WHO HAVE HAD AN INADEQUATE RESPONSE TO NONBIOLOGIC DMARDS: SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS

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**Background:** Rheumatoid Arthritis (RA) patients who are intolerant, show an inadequate response, or experience moderate/high disease activity despite traditional, non-biologic disease-modifying antirheumatic drugs (inadequate response [DMARD-IR] or second-line therapy patients) are often treated with a biologic agent (or "novel DMARDs") in Europe. Other treatments of interest, such as Janus kinase (JAK) inhibitors (a new class of DMARDs) are currently in development. Tofacitinib is an oral JAK inhibitor for the treatment of RA.
**Objectives:** The overall objective of this study was to compare the efficacy, and safety/tolerability of tofacitinib as monotherapy and combined with a DMARD relative to biological DMARDs (bDMARDs) and other novel DMARDs currently approved or being considered for approval by the European Medicines Agency (EMA) for second-line moderate-to-severe RA patients by means of a systematic literature review (SLR) and network meta-analysis (NMA) of randomized clinical trial (RCT) evidence.
**Methods:** MEDLINE®, EMBASE®, and Cochrane Central Registry of Controlled Trials databases were searched simultaneously to identify RCTs published in English between 1990 and March 2015. Population of interest included adults with moderate to severe RA who had responded inadequately or failed treatment with at least one traditional, non-biological DMARD. Treatments approved by the EMA for moderate-to-severe RA and investigational therapies were of interest and included: abatacept, adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, tocilizumab, baricitinib (investigational), and tofacitinib (investigational). Outcomes of interest were: American College of Rheumatology (ACR) response criteria (20/50/70), change from baseline in the Health assessment questionnaire (HAQ-DI), the Disease activity score (DAS-28) (change from baseline and categorical), and safety outcomes. Bayesian NMA models were simultaneously synthesized to obtain treatment effects for the outcomes of interest.
**Results:** 68 full-text articles and 11 conference abstracts corresponding to 45 RCTs were identified, the majority of which demonstrated a low risk of bias. Based on evidence synthesis of monotherapies, tofacitinib 5 mg twice daily (BID) and 10 mg BID monotherapy exhibited comparable efficacy, and safety/tolerability to other monotherapies. Based on evidence synthesis of combination therapies, tofacitinib 5 mg BID and 10 mg BID + DMARDs or methotrexate (MTX) were mostly comparable to other combination therapies in terms of efficacy based on DAS28 and ACR. In terms of safety, tofacitinib 5 mg BID + MTX or DMARDs was mostly comparable to other combination therapies, but less favorable versus some (with respect to withdrawals, infections, serious adverse events), and tofacitinib 10 mg BID + MTX or DMARDs was comparable to most, but less favorable in terms of withdrawals versus a few treatments.
**Conclusions:** Tofacitinib 5 mg BID and 10 mg BID, either as monotherapy or combined with DMARDs or MTX is comparable to other monotherapies and combination therapies respectively, based upon DAS28 and ACR response criteria. While monotherapies were also comparable in terms of safety, further research is recommended to firmly establish the comparative safety of the combination therapies.
**Disclosure of Interest:** E. Bergrath Consultant for: Paid consultant for Pfizer, G. Wallenstein: None declared, R. Gerbert: None declared, D. Gruben: None declared, C. Makin: None declared
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## SAT0166 AN ANALYSIS OF LABORATORY RESULTS FROM 2 RANDOMIZED, DOUBLE-BLIND STUDIES OF SIRUKUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS REFRACTORY TO DISEASE-MODIFYING ANTI-RHEUMATIC DRUG TREATMENT

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**Background:** Agents intercepting the IL-6 pathway have been associated with abnormalities in liver enzymes, neutrophils, and platelets.
**Objectives:** To evaluate laboratory results from 2 Phase 3 studies (1 global, 1 Japanese) of sirukumab, a selective human anti-IL6 monoclonal antibody, in patients with active rheumatoid arthritis (RA), and to compare patients using concomitant methotrexate (MTX) or not.
**Methods:** In the global study, patients with active RA and inadequate response to disease-modifying anti-rheumatic drugs were randomly assigned (1:1:1) to sirukumab SC 50mg q4w, sirukumab SC 100mg q2w, or placebo SC q2w. Approximately 86% were taking MTX at baseline in the global study. In the Japanese study, 122 patients with active RA refractory to MTX or sulfasalazine were assigned (1:1) to monotherapy with sirukumab SC 50mg q4w or sirukumab SC 100mg q2w. Descriptive hematology and chemistry results through Wk 24 were summarized for the 2 sirukumab dose groups, and results were stratified by MTX use. No inferential statistical testing was conducted.
**Results:** As has been observed with other IL-6 pathway inhibitors, sirukumab was associated with increases in alanine transaminase (ALT) and aspartate transaminase (AST) and decreases in neutrophil and platelets. The proportion of patients with maximum toxicity grade $>1$ at Wk 24 for lab results of interest were similar across the sirukumab dose groups (Table). The proportion with increased ALT and AST grade $\geq 2$ ($>3$x Upper Limit of Normal) through Wk 24 was numerically greater for patients on concomitant MTX in the global study vs those not on MTX. Similarly, continued MTX exposure numerically amplified the effect of sirukumab treatment on liver test abnormalities in the 121 Japanese patients in the global study (on MTX), vs the Japanese monotherapy study. Neutrophil and platelet decreases were similar between groups with and without MTX.

Table 1. Proportion of patients (n [%]) on sirukumab with key lab abnormalities through Wk 24

| Sirukumab dose | CTCAE grade | Global study – with MTX | | Global study – no MTX | |
|---|---|---|---|---|---|
| | | 50mg q4w (n=562) | 100mg q2w (n=564) | 50mg q4w (n=86) | 100mg q2w (n=85) |
| ALT increased | 1 | 330 (58.7) | 312 (55.3) | 27 (31.4) | 33 (38.8) |
| | 2 | 32 (5.7) | 46 (8.2) | 2 (2.3) | 5 (5.9) |
| | 3 | 9 (1.6) | 20 (3.5) | 1 (1.2) | 0 |
| | 4 | 0 | 0 | 0 | 0 |
| AST increased | 1 | 266 (47.3) | 283 (50.2) | 22 (25.6) | 28 (32.9) |
| | 2 | 15 (2.7) | 20 (3.5) | 2 (2.3) | 1 (1.2) |
| | 3 | 1 (0.2) | 5 (0.9) | 0 | 0 |
| | 4 | 0 | 0 | 0 | 0 |
| Neutrophils decreased | 1 | 104 (18.5)[a] | 113 (20.1)[b] | 17 (19.8)[c] | 15 (17.6) |
| | 2 | 66 (11.8)[a] | 63 (11.2)[b] | 9 (10.5)[c] | 11 (12.9) |
| | 3 | 20 (3.6)[a] | 13 (2.3)[b] | 2 (2.3)[c] | 3 (3.5) |
| | 4 | 0 | 1 (0.2)[b] | 0 | 0 |

[a]n=561. [b]n=563. [c]n=85.

**Conclusions:** Numeric differences in abnormally elevated liver enzyme tests for RA patients treated with sirukumab were observed between patients on MTX and not on MTX, including patients from the global and Japanese studies. In these 2 Phase 3 studies, there was no clear dose-dependent effect on ALT, AST, neutrophils, or platelets between the 2 sirukumab doses.
**Disclosure of Interest:** G. Karpouzas Consultant for: Janssen, Speakers bureau: Janssen, C. Thorne Grant/research support from: Abbvie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant for: Abbvie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: Medexus/Medac, T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahikasei Pharma Corp., and Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., and Asahi Kasei Medical K.K.,abbivie GK, Daiichi Sankyo Co.,Ltd., Bristol–Myers K.K., Nipponkayaku Co.Ltd., Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co,. Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Astellas Pharma, and Diaichi Sankyo Co., Ltd., Celtrion, Nipponkayaku Co. Ltd, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-

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## SAT0167 HEALTH-RELATED PHYSICAL AND EMOTIONAL WELL-BEING AND FATIGUE IMPROVE SIGNIFICANTLY WITH SIRUKUMAB TREATMENT: RESULTS OF A PHASE 3 STUDY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS REFRACTORY TO CONVENTIONAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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**Background:** Rheumatoid arthritis (RA) may have a substantial negative impact on physical and emotional well-being and fatigue. Sirukumab, a selective, high-affinity human anti-IL6 monoclonal antibody, is being evaluated for RA treatment.

**Objectives:** To evaluate the effects of sirukumab on health-related physical and emotional well-being (based on Short Form-36 [SF-36] health survey) and fatigue (Functional Assessment of Chronic Illness Therapy [FACIT]-Fatigue scale) in patients (pts) with RA refractory to Disease-Modifying Anti-Rheumatic Drugs (DMARDs).

**Methods:** This Phase 3 study evaluated 2 sirukumab doses in pts with active RA and inadequate response to DMARDs. Pts were randomized (1:1:1) to double-blind treatment with sirukumab subcutaneous (SC) 50 mg q4w, sirukumab SC 100 mg q2w, or placebo SC q2w. In the placebo group, pts with <20% improvement at Wks 18 or 40 or still on placebo at Wk 52 were re-randomized to treatment with 1 of the 2 sirukumab doses. Pts completed the SF-36 and FACIT-Fatigue at baseline (BL) and Wks 8, 16, 24, 36, and 52. Clinically meaningful improvements from BL were defined as ≥5-point increase for the SF-36 physical and mental component summary (PCS and MCS) scores and ≥4-point increase for the FACIT-Fatigue score.

**Results:** Significantly greater mean increases (improvements) from BL in mean SF-36 PCS and MCS, all 8 SF-36 domain scores, and the FACIT-Fatigue score were observed for sirukumab 50mg q4w and 100mg q2w vs placebo at Wks 8, 16, 24, 36, and 52 (all $P<0.02$; Table). Also, significantly more pts achieved clinically meaningful improvements from BL in the SF-36 PCS and MCS scores (≥5-point increase) and the FACIT-Fatigue score (≥4-point increase) on sirukumab (both doses) vs placebo at Wks 8, 16, 24, 36, and 52 (all $P<0.05$).

Table 1. SF-36 and FACIT-Fatigue Outcomes at Wk 52[a]

| Outcome | Placebo (n=556) | Sirukumab 50 mg q4w (n=557) | Sirukumab 100 mg q2w (n=557) |
|---|---|---|---|
| Mean (SD) change from BL | | | |
| SF-36 PCS | 2.42 (6.81) | 5.66 (7.74)[b] | 6.16 (7.23)[b] |
| SF-36 MCS | 2.69 (9.57) | 5.35 (9.64)[b] | 4.77 (9.80)[b] |
| SF-36 domain scores | | | |
| Bodily pain | 3.91 (8.58) | 7.77 (8.41)[b] | 7.83 (8.70)[b] |
| General health | 2.04 (7.12) | 5.08 (7.86)[b] | 4.35 (7.49)[b] |
| Physical function | 1.44 (8.20) | 4.72 (9.20)[b] | 5.49 (8.68)[b] |
| Role-physical | 2.98 (8.40) | 5.79 (8.59)[b] | 6.09 (8.10)[b] |
| Vitality | 3.03 (8.87) | 6.17 (9.22)[b] | 6.49 (9.18)[b] |
| Mental health | 2.47 (9.24) | 5.20 (9.71)[b] | 4.67 (9.81)[b] |
| Role-emotional | 2.62 (11.34) | 5.70 (10.85)[b] | 5.16 (11.77)[b] |
| Social function | 2.80 (9.84) | 5.72 (10.07)[b] | 5.86 (9.47)[b] |
| FACIT-Fatigue score | 2.7 (9.6) | 6.7 (9.5)[b] | 6.8 (9.5)[b] |
| Proportion of pts achieving clinically meaningful improvement from BL | | | |
| SF-36 PCS[c] | 173 (31.1) | 272 (48.8)[b] | 277 (49.7)[b] |
| SF-36 MCS[c] | 191 (34.4) | 260 (46.7)[b] | 246 (44.2)[b] |
| FACIT-Fatigue score[d] | 228 (41.0) | 329 (59.1)[b] | 337 (60.5)[b] |

[a]n based on initial treatment assignment. [b]$P<0.001$ vs placebo. [c]Increase ≥5 points. [d]Increase ≥4 points.

**Conclusions:** Sirukumab treatment yielded early, durable, statistically significant and clinically meaningful improvements in health-related physical and emotional well-being and fatigue in patients with DMARD-refractory RA compared to placebo throughout Wk 52.

**Disclosure of Interest:** G. Karpouzas Consultant for: Janssen, Speakers bureau: Janssen, C. Thorne Grant/research support from: Abbvie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant for: Abbvie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: Medexus/Medac, T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahikasei Pharma Corp., and Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., and Asahi Kasei Medical K.K.,abbivie GK, Daiichi Sankyo Co.,Ltd., Bristol–Myers K.K., Nipponkayaku Co.Ltd., Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co,. Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Astellas Pharma, and Diaichi Sankyo Co., Ltd., Celtrion, Nipponkayaku Co. Ltd, K. McQuarrie Employee of: Janssen Research & Development, LLC, S. Sheng Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, W. Xu Employee of: Janssen Research & Development, LLC, S. Peterson Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, C. Han Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, K. Fei Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC

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## SAT0168 CLINICAL REMISSION OUTCOMES WITH SARILUMAB PLUS CSDMARDS IN ACTIVE, MODERATE-TO-SEVERE RA PATIENTS WITH INADEQUATE RESPONSE TO TUMOR NECROSIS FACTOR INHIBITORS

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**Background:** Clinical remission is an important treatment goal in rheumatoid arthritis (RA) and is associated with improved physical function and quality of life.[1,2] In the phase 3 TARGET study (NCT01709578), sarilumab (150 or 200 mg subcutaneously every 2 weeks + conventional synthetic disease-modifying antirheumatic drugs [csDMARDs]) demonstrated efficacy in adults with active, moderate-to-severe RA and inadequate response to tumor necrosis factor (TNF) inhibitors.[3] Infections, neutropenia, injection site reactions, and increased transaminases were among the most common treatment-emergent adverse events.[3]

**Objectives:** This analysis assessed the proportions of patients achieving clinical remission measured by 4 different disease activity measures in a difficult-to-treat patient population with active RA and inadequate response or intolerance to ≥1 prior TNF inhibitor(s).

**Methods:** Four definitions of remission were used: 28-joint disease activity score by C-reactive protein (DAS28-CRP) <2.6, clinical disease activity index (CDAI) ≤2.8, simplified disease activity index (SDAI) ≤3.3, and Boolean-based ACR/EULAR remission (tender and swollen joint counts [28 joints] ≤1, CRP ≤10 mg/L, and patient global visual analog scale ≤10 mm/100 mm). Differences in incidence of these benchmarks between the active treatment groups and placebo were assessed using 2-sided Cochran-Mantel-Haenszel tests stratified by geographic region and number of prior TNF inhibitors. Patients who started rescue medication or discontinued the study were considered not to be in remission (nonresponder imputation).

**Results:** Baseline demographic and disease characteristics were balanced among the 3 treatment groups. At week (wk) 12 and wk 24, the proportion of patients achieving DAS28-CRP <2.6, CDAI, SDAI, and Boolean-based remission was higher in the sarilumab-treated groups than in the placebo group (Table). At wk 24, a significantly greater proportion of sarilumab patients achieved DAS28-CRP <2.6 compared with placebo. In comparison with placebo patients, a greater proportion of sarilumab patients who achieved DAS28-CRP <2.6 or Boolean-based remission also had clinically meaningful improvements in Health Assessment Questionnaire–Disability Index (HAQ-DI) and Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) at wk 24 (Table).

**Conclusions:** Sarilumab induced remission (using a broad range of definitions) as early as 12 weeks after initiation of therapy in patients with an inadequate response to TNF inhibitors. Patients with remission generally had improvements in physical function and fatigue as well.

**Table.** Incidence of Clinical Remission in Patients With Inadequate Response to ≥1 Prior TNF Inhibitor at Weeks 12 and 24

| | Placebo + csDMARDs (n=181) | Sarilumab 150 mg q2w + csDMARDs (n=181) | Sarilumab 200 mg q2w + csDMARDs (n=184) |
|---|---|---|---|
| **DAS28-CRP <2.6** | | | |
| Week 12, n (%) | 7 (3.9) | 31 (17.1) | 33 (17.9) |
| *P* value vs placebo[a] | — | <0.0001 | <0.0001 |
| OR, CI vs placebo | — | 5.41 (2.29, 12.79) | 5.71 (2.43, 13.44) |
| Week 24, n (%) | 13 (7.2) | 45 (24.9) | 53 (28.8) |
| *P* value vs placebo[a] | — | <0.0001 | <0.0001 |
| OR, CI vs placebo | — | 4.42 (2.34, 8.13) | 5.00 (2.65, 11.41) |
| DAS28-CRP <2.6 at week 24 and decrease in HAQ-DI ≥0.30 | 11 (6.1) | 37 (20.4) | 38 (20.7) |
| DAS28-CRP <2.6 at week 24 and mCID in FACIT-F all points | 11 (6.1) | 40 (22.1) | 46 (25.0) |
| **CDAI remission** | | | |
| Week 12, n (%) | 1 (0.6) | 6 (3.3) | 9 (4.9) |
| *P* value vs placebo[a] | — | 0.0551 | 0.0106 |
| OR, CI vs placebo | — | 6.36 (0.75, 54.12) | 9.18 (1.18, 71.62) |
| Week 24, n (%) | 9 (5.0) | 17 (9.4) | 15 (8.2) |
| *P* value vs placebo[a] | — | 0.0971 | 0.2134 |
| OR, CI vs placebo | — | 2.05 (0.87, 4.84) | 1.72 (0.73, 4.09) |
| **SDAI remission** | | | |
| Week 12, n (%) | 0 | 11 (6.1) | 10 (5.4) |
| *P* value vs placebo[a] | — | 0.0007 | 0.0014 |
| OR, CI vs placebo | — | NC | NC |
| Week 24, n (%) | 5 (2.8) | 18 (9.9) | 16 (8.7) |
| *P* value vs placebo[a] | — | 0.0044 | 0.0146 |
| OR, CI vs placebo | — | 4.13 (1.47, 11.67) | 3.41 (1.21, 9.59) |
| **Boolean-based remission[b]** | | | |
| Week 12, n (%) | 0 | 6 (3.3) | 5 (2.7) |
| *P* value vs placebo[a] | — | 0.0129 | 0.0252 |
| OR, CI vs placebo | — | NC | NC |
| Week 24, n (%) | 5 (2.8) | 10 (5.5) | 11 (6.0) |
| *P* value vs placebo[a] | — | 0.1794 | 0.1109 |
| OR, CI vs placebo | — | 2.10 (0.70, 6.33) | 2.27 (0.77, 6.73) |
| Boolean-based remission at week 24 and decrease in HAQ-DI ≥0.30 | 5 (2.8) | 10 (5.5) | 8 (4.3) |
| Boolean-based remission at week 24 and mCID in FACIT-F all points | 5 (2.8) | 10 (5.5) | 10 (5.4) |

CDAI, clinical disease activity index; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-CRP, 28-joint disease activity score by C-reactive protein; FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; mCID, minimum clinically important difference; NC, not calculated; OR, odds ratio; q2w, every 2 weeks; SDAI, simplified disease activity index; TNF, tumor necrosis factor. [a]DAS28-CRP <2.6 at week 24 was part of the controlled hierarchical testing strategy at the 5% level. All other *P* values are nominal. [b]Boolean-based remission was defined as tender joint count and swollen joint count (28-joints) ≤1, CRP ≤1.0 mg/L, and patient global visual analog score ≤10.

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## SAT0169 SUCCESSFUL EXTENSION OF TOCILIZUMAB INFUSION INTERVALS FROM 4 WEEKS TO 6 OR 5 WEEKS IN 90% OF RA PATIENTS WITH GOOD RESPONSE TO 4 WEEKS INTERVALS

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**Background:** A period of 4 weeks (w) has been recommended as the interval between tocilizumab (TCZ) infusions. The cost of TCZ is very high, which makes it difficult for all patients to receive TCZ because of the associated expenses.
**Objectives:** Treating the patients with TCZ, we experienced that longer intervals than 4w were also effective. We examined whether the intervals between TCZ infusions could extend from 4w to 6w or 5w.
**Methods:** The RA patients who had shown good response and maintained low disease activity (LDA) with 8mg/kg of TCZ infusions at 4w intervals were enrolled in the study. To the eligible patients, the intervals between TCZ infusions were extended to 5w at the same TCZ dose (8mg/kg). For the patients who could maintain LDA for 6 months and more at 5w interval of TCZ infusion, the intervals between TCZ infusions were extended to 6w. We followed the patients up for 2 years and more. Good response and LDA was defined as DAS-28CRP EULAR criteria.
**Results:** One hundred patients were enrolled in the present study, and 96 patients completed the study. 93 patients maintained LDA with 8mg/kg of TCZ infusion every 5w for 6 months and more and the rest of 7 patients could not keep LDA and the intervals between TCZ infusions were shortened to 4w. The 93 patients who maintained LDA with 8mg/kg of TCZ infusion every 5w were received 8mg/kg of TCZ infusion every 6 weeks, and 62 patients maintained LDA with 6w-interval. After 2 years follow-up, 96 patients could maintain LDA and 4 patients were dropped from the study. Among 96 patients who could maintain LDA, the intervals between TCZ intervals were 6w in 62 patients, 5w in 28 patients, and 4w in 6 patients, indicating that 90% of patients who had shown good response with 4w intervals could extend the intervals between TCZ infusions from 4w to 5w or 6w. The mean baseline DAS28-CRP score in patients who could maintain LDA with TCZ infusions at 6w intervals were 2.2 and was significantly lower than that at 4 weeks interval (2.6). The frequency of adverse events with TCZ infusions at 6 weeks intervals was lower than that at 4 weeks intervals.
**Conclusions:** The present study provides evidence that most of RA patients who showed good response to TCZ infusions at 4w could extend the intervals to 6w or 5w. This finding should be of great interest for both financial and labor reasons.
**Disclosure of Interest:** None declared

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## SAT0170 BDMARDS MONO VS COMBO THERAPY IN RHEUMATOID ARTHRITIS. ANALYSIS OF A RHEUMATOLOGICAL SINGLE TERTIARY CENTER REAL-LIFE EXPERIENCE

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**Background:** Despite adavantages of biological combo therapy over biological mono for RA treatement and the limited approval of biologics as monotherapy (etanercept, adalimumab, certolizumab, tocilizumab), real life registries data revealed that approximately one-third of patients taking biologic agents are using them as monotherapy.
**Objectives:** To assess the prevalence of bDMARDs use as monotherapy (bDMARDs-mono) in a cohort of RA patients treated with bDMARDs attending a tertiary rheumatological center.To characterize the clinical profile of these patients, and to investigate factors related to monotherapy.
**Methods:** All patients with Rheumatoid Arthritis attending our center and receiving bDMARDs up to 31th january 2015 were retrospectively analyzed. Demographic, and clinical characteristics of each patient were recorded: age, gender, disease duration, drugs history and clinical disease activity (DAS28) at last visit.
**Results:** 341 RA patients receiving bDMARDS were included. F 160, M 123, mean age 59.98 ±12.54, disease duration 178.69±101.81 months. 197 patients were taking bDMARD as first line bio-therapy, 144 had been previously treated with one or more bDMARDs. 52% (n=179) of patients were receving bDMARD-mono with a mean disease duration 187.4±125.1 month; 48% (n=162) were bDMARDs-combo, 65% of them with MTX; mean disease duration 168.9±42.4 m. Biologic agents used as mono or combo are shown in table 1. 32% of bDMARDs-mono had discontinued csDMARDs before starting biological therapy, 68% after an average 50,4 months after starting bDMARDs ($p<0.001$). The most common

reasons for discontinuing csDMARDs were toxicity (55% of cases), with significant difference between those who stopped before and after starting bDMARDs (66% vs 48% respectively, p<0,02). 11% of patients discontinue csDMARDs because of nonspecific bad tolerance, 9% for inefficacy, 11% for others unspecified reasons. 25 patients (14%) on bDMARDs-mono stopped csDMARDs for clinical remission. Overall, 57% of RA patients were in clinical remission (DAS28 PCR <2.6) at the time of the inclusion in the study, without significant differece between the two groups (bDMARDs-mono vs combo). The use of bDMARDs-mono was more frequently observed in those patients with disease duration longer than 10 years (p<0,0001).

| | pz 341 | pz 179 | pz 162 |
|---|---|---|---|
| Biol | pz Bio | BioMT | BioCT |
| ETA * | 126 (37%) | 67 (53%) | 59 (47%) |
| ADA* | 61 (15%) | 27 (44%) | 34 (56%) |
| IFX | 15 (4%) | 8 (53%) | 7 (47%) |
| TCZ* | 50 (17%) | 31 (62%) | 19 (38%) |
| RTX | 46 (16%) | 29 (63%) | 17 (37%) |
| ABA | 25 (9%) | 16 (64%) | 9 (36%) |
| CTZ* | 10 (1%) | 1 (10%) | 9 (90%) |
| GOL | 7 (1%) | 0 | 7 (100%) |
| KIN | 1 (0%) | 1 (100%) | 0 |

Tab 1. *Biologic approved in monotherapy for RA treatment

**Conclusions:** Biologic monotherapy for managing RA is widely used in our clinical practice especially in patients with long term disease. The proportion of patients (1/3) who start bDMARD-mono is quite similar to that reported in literature. On the other hand, most of patients arrive to bDMARDs-mono after starting biologic agent as the result of csDMARD witdrawal due to AE or intollerance to DMARDs and to a lesser extent because achieving good control of the disease since patient's preference is strongly oriented to csDMARD discontinuation rather than bDMARDs withdrawal or tapering.

**References:**

[1] Emery P, et al. Ann Rheum Dis 2013:Dec:72 (12):1897–904.

**Disclosure of Interest:** None declared

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## SAT0171 SERUM IL-33 INDEPENDENTLY PREDICTS RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS: DATA FROM THE SMART AND REPLICATION COHORTS

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**Background:** In a transcriptomic study, we found that whole blood interleukin-33 (IL-33) mRNA expression is increased in patients with rheumatoid arthritis (RA) responding to rituximab (RTX) (1). Using one ELISA IL-33 kit (DuoSet, R&D) for protein assessment, we previously reported an association between serum IL-33 level and RTX response in a single cohort, but additional experiments have recently raised caution about accuracy of this kit for sera measurements (2). Recommendations from the manufacturer advice to use for human sera another assay (Quantikine, R&D).

**Objectives:** To replicate in different cohorts and with a more accurate ELISA assay the possible association between detectable serum level of IL-33 and response to RTX in RA patients.

**Methods:** Serum IL-33 level and B-cell biomarkers known to be associated with RTX response (rheumatoid factor [RF], anti-citrullinated cyclic peptide [anti-CCP] antibodies, high serum IgG level above upper limit normal >12.7 g/L) were assessed in 111 RA patients receiving a first course of 2 grams RTX in the SMART cohort (85% of patients with RF or anti-CCP) as well as, for replication, in 74 RA patients (including 32 patients from Leeds, UK and 42 from Clermont-Ferrand, France) treated with the same schedule in routine care (97% of patients with RF or anti-CCP). We performed uni- and multivariate analyzes to identify factors associated with a EULAR response at 24 weeks.

**Results:** At week 24, 84 (76%) and 54 (73%) patients reached EULAR response in SMART and in replication cohort, respectively. Serum IL-33 was detectable in 27/111 (24%) and 35/74 (47%) patients from SMART and replication cohort, respectively. In SMART, multivariate analysis indicated that auto-antibodies status (positive RF or anti-CCP) were associated with RTX response (OR 3.47 95%CI 1.04–11.60; p=0.04). The same trend was observed for high serum IgG (OR 2.82 95%CI 0.97–8.14; p=0.056) but not for serum IL-33. In the replication cohort, detectable serum IL-33 was independently associated with RTX response (OR 3.73, 95%CI [1.12–12.38]; p=0.03) with the same trend for auto-antibodies status (OR 32, 95%CI [0.69–999]; p=0.08), but without significant result for high serum IgG. When we combined both cohorts (n=185), the 3 parameters were associated with RTX response in multivariate analysis: presence of RF or anti-CCP (OR 3.27 95%CI 1.13–9.46; p=0.03), high serum IgG (OR 2.32, 95%CI 1.01–5.33; p=0.048) and detectable IL-33 (OR 2.40 95%CI 1.01–5.72; p=0.047). There was synergy between the 3 predictive factors since detection of IL-33 in patients having positive auto-antibodies and high IgG level improved likelihood of response (100% EULAR responders) compared with patients having only positive auto-antibodies and high IgG level (77% responders) or compared with those without any of these factors (55% responders) (Figure 1).

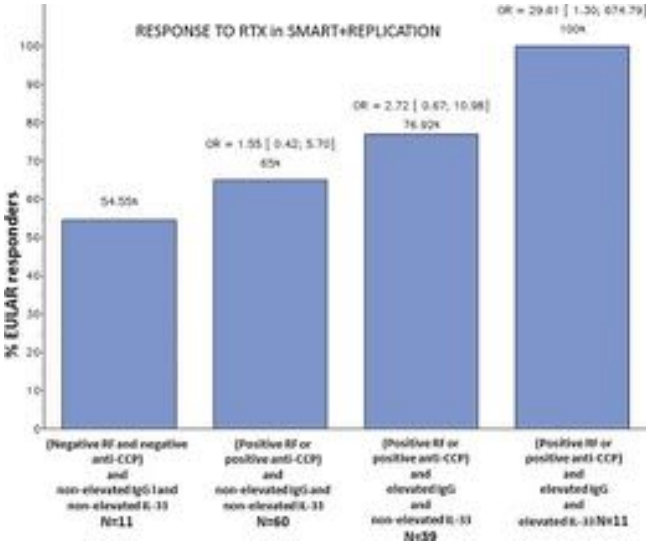



Figure 1

**Conclusions:** Using an accurate ELISA kit, serum IL-33 may predict clinical response to RTX, independently of and synergistically with auto-antibodies and serum IgG level

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## SAT0172 COMPARISON OF EFFICACY AND SAFETY OF BIOLOGIC AGENTS BETWEEN ELDERLY-ONSET AND YOUNGER-ONSET RHEUMATOID ARTHRITIS

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**Background:** There are pathogenetic and clinical differences between elderly-onset rheumatoid arthritis (EORA) and young-onset rheumatoid arthritis (YORA).

**Objectives:** To compare the efficacy and safety of biologic agents between patients with EORA and those with YORA.

**Methods:** A total of 61 patients with RA, who started biologic agents after the age of 65 years, have been enrolled from April 2011 to August 2015, and divided into two groups according to the age at disease onset; i.e. EORA ≥65 years and YORA <65 years. Biologic agents were grouped into 3 classes; the TNF-alpha inhibitors (TNFi) including infliximab, etanercept, adalimumab, golimumab and certolizumab pegol, the CTLA4-Ig abatacept (ABT) and the IL-6 inhibitor tocilizumab (TCZ). Forty-four patients with EORA have received 64 biologic agents (36 women and 8 men; average ± SD age, 76.1 ± 5.7 years; disease duration, 2.0 ± 3.4 years; rheumatoid factor (RF)/anti-cyclic citrullinated peptide antibody (ACPA) positive, 63.6%/65.9%), and 17 patients have received 29 biologic agents (13 women and 4 men; average age, 71.2 ± 4.9 years; disease duration, 17.8 ± 13.9 years; RF/ACPA positive, 76.5%/70.6%). The disease activity was measured according as simplified disease activity index (SDAI), and the efficacy was determined by the induction rate of remission (SDAI ≤3.3) and low-disease activity (3.3 < SDAI ≤11).

**Table** SDAI in EORA or YORA patients during 6-month observation of biologic therapy.

| SDAI | Month 0 | | Month 3 | | Month 6 | |
|---|---|---|---|---|---|---|
| | EORA | YORA | EORA | YORA | EORA | YORA |
| ABT | 21.8±1.8 | 18.3±3.1 | 8.8±0.8 | 8.8±1.9 | 5.3±0.7 | 9.1±3.7 |
| TCZ | 28.6±4.0 | 30.1±4.8 | 8.3±1.4 | 13.1±2.7 | 4.0±0.9 | 11.5±1.8 |
| TNFi | 20.7±2.0 | 21.6±2.7 | 11.1±2.6 | 17.9±3.9 | 4.8±0.7 | 8.9±2.3 |
| Total | 23.5±1.6 | 21.8±2.0 | 9.5±1.1 | 13.4±2.0 | 4.7±0.4 | 9.6±1.9 |

SDAI: simplified disease activity index; EORA:elderly-onset rheumatoid arthritis; YORA: young-onset rheumatoid arthritis; ABT: abatacept; TCZ: tocilizumab; TNFi: TNF-alpha inhibitor.

**Results:** The EORA patient group did respond better to biologic agents than the YORA patient group; the SDAI was significantly lower in the former than in the latter. At present, there were no significant differences in responses to TNFi, ABT and TCZ between the 2 patient gourps (Table 1). Both patient groups developed adverse events during biologic therapy, and severe adverse events including cholecystitis, pulmonary cryptococcosis, diverticulitis, malignant lymphoma, Pneumocystis pneumonia, organizing pneumonia and so on.
**Conclusions:** The results indicate that biologic agents are similarly effective for both EORA and YORA patients, irrelevant to different classes, but patients with EORA appears to be more responsive to biologics than YORA patients, presumably due to their shorter disease duration.
**Disclosure of Interest:** None declared
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## SAT0173 LIPOPROTEIN(A) CONCENTRATIONS IN RHEUMATOID ARTHRITIS ON BIOLOGIC THERAPY: RESULTS FROM THE CARDIOVASCULAR IN RHEUMATOLOGY [CARMA] STUDY PROJECT

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**Background:** Plasma concentrations of lipoprotein (a) [Lp(a)], a lipoprotein with proatherogenic and thrombogenic properties, have a strong genetic basis, although high concentrations of Lp(a) have also been reported in the context of inflammation, as rheumatoid arthritis (RA) (1). There are few studies that evaluate the impact of biologic therapies on Lp(a) in RA (2), taking into account that with these new therapies a better control of inflammation is achieved.
**Objectives:** Evaluate the plasma concentrations of Lp(a) in Spanish RA patients on biologics therapy attending rheumatology outpatient clinics.
**Methods:** Baseline analysis of the CARMA project (CARdiovascular in rheuMAtology), a 10-year prospective study evaluating the risk of cardiovascular events in RA patients and other forms of inflammatory arthritis who attended rheumatology outpatient clinics at 67 hospitals in Spain. RA patients were classified into four categories: no biologic therapy, undergoing anti-TNF therapy, receiving anti-IL-6 receptor tocilizumab (TCZ), and other biologic therapies (rituximab or abatacept). A model of linear multivariate regression was built in which the dependent variable was Lp(a) concentration and the explanatory variable was biologic therapy. The model was adjusted for confounding factors.
**Results:** Seven hundred and seventy-five RA patients were analyzed. Total cholesterol and triglycerides concentrations were significantly higher in TCZ-treated patients. Nevertheless, no significant difference in the atherogenic index (TC/HDL-c) between TCZ-treated patients and patients without biological therapy was found. After adjusting for confounding factors, patients treated with biologic therapy had lower plasma concentrations of Lp(a) than those not undergoing biologic therapy. However, only TCZ-treated patients achieved statistically significant differences when compared with those not undergoing biologic therapy (β-coefficient: -0.303, 95% confidence interval: -0.558 to -0.047; p=0.02).
**Conclusions:** RA patients treated with tocilizumab, an inhibitor of interleukin 6 receptor, show lower plasma concentrations of Lp (a) compared to patients without biological therapy.
**References:**
[1] Garcia-Gomez C et al. J Rheumatol 2009, 36:1365–1370.
[2] McInnes IB et al. Ann Rheum Dis 2015, 74:694–702.
**Disclosure of Interest:** None declared
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## SAT0174 EFFICACY OF SARILUMAB PLUS CSDMARDS IN RHEUMATOID ARTHRITIS PATIENTS WHO HAD AN INADEQUATE RESPONSE TO ONE OR MORE THAN ONE PRIOR TNF INHIBITOR

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**Background:** In the phase 3 TARGET study (NCT01709578), sarilumab (150 or 200 mg subcutaneously [SC] every 2 weeks [q2w] plus conventional synthetic disease-modifying antirheumatic drugs [csDMARDs]) demonstrated efficacy in adults with active, moderate-to-severe rheumatoid arthritis (RA) and inadequate response to tumor necrosis factor inhibitors (TNFis).[1] Consistent with IL-6 inhibition and the safety profile of SC sarilumab, infections, neutropenia, injection site reactions, increased lipids, and increased transaminases were among the most common treatment-emergent adverse events.
**Objectives:** This prespecified analysis examined whether the efficacy of sarilumab plus csDMARDs was affected by the number of prior TNFis.
**Methods:** Adults with active, moderate-to-severe RA with inadequate response or intolerance to ≥1 TNFi were randomized to receive placebo (n=181), sarilumab 150 mg q2w (n=181), or sarilumab 200 mg q2w (n=184) SC plus csDMARD(s) for 24 weeks.[1] Efficacy by number of prior TNFis (1 vs >1) was analyzed for the coprimary endpoints of ACR20 response at week 24 and mean change from baseline in Health Assessment Questionnaire–Disability Index (HAQ-DI) at week 12. Additional post hoc analyses evaluated the secondary endpoints of ACR50/70. Treatment-by-subgroup interactions were analyzed using a logistic regression model for ACR20 at week 24 and a mixed-effect model for repeated measures for HAQ-DI at week 12; treatment-by-subgroup interaction with $P<0.05$ was considered significant.
**Results:** A majority of patients (76.8%) reported prior use of only 1 TNFi; 23.2% of patients used >1 TNFi. Most patients discontinued TNFi treatment because of inadequate response (92.3%). ACR20 responses were numerically greater in patients receiving either dose of sarilumab in both the 1 and the >1 prior TNFi groups at week 24 relative to placebo patients (Table). Responses in placebo and sarilumab groups were numerically higher in the group that failed 1 TNFi. Similar results were observed with ACR50/70 responses. The mean change from baseline in HAQ-DI at week 12 was greater in sarilumab patients than in placebo patients in both prior TNFi exposure groups. Interaction test analyses indicated no significant treatment-by-subgroup effect in the proportion of patients with 1 or >1 prior TNFi who achieved ACR20 at week 24 ($P$=0.1215) or in mean change from baseline in HAQ-DI at week 12 ($P$=0.1767).

Table. Efficacy of Sarilumab Plus csDMARDs in Patients With 1 or >1 Prior TNFi Failure

| | Placebo + csDMARDs (n=181) | Sarilumab 150 mg q2w + csDMARDs (n=181) | Sarilumab 200 mg q2w + csDMARDs (n=184) |
|---|---|---|---|
| **ACR20 at week 24, n/N (%)** | | | |
| 1 TNFi | 49/132 (37.1) | 83/132 (62.9) | 82/133 (61.7) |
| OR (95% CI vs placebo) | — | 3.11 (1.85, 5.25) | 2.90 (1.73, 4.86) |
| >1 TNFi | 12/49 (24.5) | 18/49 (36.7) | 30/51 (58.8) |
| OR (95% CI vs placebo) | — | 1.82 (0.75, 4.43) | 4.66 (1.94, 11.21) |
| **ACR50 at week 24, n/N (%)** | | | |
| 1 TNFi | 30/132 (22.7) | 56/132 (42.4) | 58/133 (43.6) |
| OR (95% CI vs placebo) | — | 2.71 (1.55, 4.75) | 2.76 (1.60, 4.78) |
| >1 TNFi | 3/49 (6.1) | 11/49 (22.4) | 17/51 (33.3) |
| OR (95% CI vs placebo) | — | 4.69 (1.18, 18.68) | 8.75 (2.25, 34.04) |
| **ACR70 at week 24, n/N (%)** | | | |
| 1 TNFi | 13/132 (9.8) | 39/132 (22.7) | 24/133 (18.0) |
| OR (95% CI vs placebo) | — | 2.93 (1.41, 6.08) | 2.06 (0.99, 4.32) |
| >1 TNFi | 0/49 | 6/49 (12.2) | 6/51 (11.8) |
| OR (95% CI vs placebo) | — | NC* | NC* |
| **HAQ-DI at week 12** | | | |
| 1 TNFi | | | |
| LS mean change from baseline ± SE | -0.29 ± 0.05 | -0.44 ± 0.05 | -0.50 ± 0.05 |
| LS mean difference vs placebo (95% CI) | — | -0.15 (-0.28, -0.01) | -0.21 (-0.34, -0.07) |
| >1 TNFi | | | |
| LS mean change from baseline ± SE | -0.17 ± 0.08 | -0.54 ± 0.09 | -0.40 ± 0.08 |
| LS mean difference vs placebo (95% CI) | — | -0.37 (-0.59, -0.14) | -0.23 (-0.45, -0.01) |

ACR20/50/70, American College of Rheumatology 20%/50%/70% response; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire–Disability Index; LS, least squares; NC, not computable; OR, odds ratio; q2w, every 2 weeks; SD, standard deviation; SE, standard error; TNFi, tumor necrosis factor inhibitor. *Odds ratios were not computable because no placebo patients with exposure to >1 TNFi achieved an ACR70 response.

**Conclusions:** Efficacy of sarilumab was observed in patients with inadequate response to TNFis, irrespective of the number of prior TNFi therapies. In harder to treat patients (ie, patients with prior exposure to >1 TNFi), sarilumab 200 mg was associated with a greater numerical trend in ACR20/50 when compared with sarilumab 150 mg.
**References:**
[1] Fleischmann et al. Presented at: ACR; Nov. 7–11, 2015; San Francisco, CA.

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## SAT0175 VALIDATION OF B CELL DEPLETION AS A PREDICTOR OF CLINICAL RESPONSE AND EFFICACY OF RETREATMENT OF NON-RESPONSE IN RHEUMATOID ARTHRITIS

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**Background:** Rituximab has been licensed for the treatment of Rheumatoid Arthritis (RA) for over a decade. We previously showed that the initial depth of B cell depletion was associated with clinical response; 96% complete versus 74% incomplete depletion at 6 months (p=0.02)[1] and that retreatment of initial non-responders with incomplete depletion led to 72% response rate in cycle 2 (C2)[2].
**Objectives:** To validate B cell depletion after the first infusion as a predictor of response to rituximab (Project 1) and assess outcome of retreatment of first cycle non-responders (Project 2) as a basis for B cell monitoring during rituximab treatment.
**Methods:** The published discovery cohorts included 60 patients in Project 1 and 25 patients in Project 2. For this validation study, we analysed the subsequent consecutive 180 patients with RA treated with rituximab at a single centre. Each cycle of rituximab consisted of 2×1000mg infusions, repeated on clinical relapse. B cell subsets (naïve, memory and plasmablast) were measured at baseline, after first infusion of rituximab (2 weeks) and at early B cell repopulation (6 months) using a flow cytometry protocol optimized to detect low numbers of B cell subsets and plasmablasts. Complete depletion was defined as total B cell count $<0.0001\times10^9$/L. First cycle non-responders who had incomplete depletion at C1 were retreated at 6 months.
**Results:** 180 patients (female=147 (81%), median age at rituximab initiation 62 (IQR 51–71) years and median disease duration 10 (IQR 5–18) years were studied. 72 (40%) patients were biologic-naïve. In C1, 126 (70%) achieved moderate-good EULAR response. The complete depletion rate for C1 was 54%. Complete depletion was associated with response; p=0.027 (Table 1). 30 patients who were C1 non-responders and had incomplete depletion were retreated at 6 months. Of these, 20 (67%) had complete depletion and 20 (67%) responded in C2. Non-responders in C2 had trend to higher plasmablast numbers at retreatment than responders (p=0.14).

Table 1. B cell depletion and response in validation cohort

| Cohort | Project A | | | |
|---|---|---|---|---|
| | Depletion | Non response | Response | p |
| Validation (n=180) | Incomplete | 32/82 (39%) | 50/82 (61%) | 0.036 |
| | Complete | 23/98 (23%) | 75/98 (77%) | |
| Combined discovery + validation (n=240) | Incomplete | 46/117 (39%) | 71/117 (61%) | 0.003 |
| | Complete | 26/123 (21%) | 97/123 (79%) | |

**Conclusions:** We have validated that the depth of B cell depletion after the first infusion is a predictor of response to rituximab in RA. A high degree of response in C2 was also confirmed when C1 non-responders who had incomplete depletion were retreated. B cell subsets therefore should be monitored in the routine care of RA patients receiving rituximab and repeat infusions considered if early depletion is incomplete and clinical response poor.
**References:**
[1] Dass S et al. A&R 2008
[2] Vital EM et al. A&R 2010
**Disclosure of Interest:** None declared
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## SAT0176 IL-6 BLOCKADE WITH TOCILIZUMAB DOES NOT SUPPRESS CD4+T CELL ACTIVATION AT 48 WEEKS OF THE TREATMENT

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**Background:** Rheumatoid arthritis (RA) is a common immflamatory autoimmune disease characterized by persistent synovitis and progressive destruction of cartilage and bone in multiple joints. The proportion of CD25+CD4+ T cells is increased in anti-citrullinated protein antibodies (ACPA) positive RA patients compared with ACPA negative RA patients. Abatacept (ABA), a biologic blocking T cell co-stimulation, decreased the proportion of CD25+CD4+ T cells and interleukin (IL)-6 levels in ACPA positive RA patients. It has been reported that CD25 expressions are increased by IL-6. Tocilizmab (TCZ) is a humanized anti-human IL-6 receptor antibody that has been developed to inhibit the IL-6 signal as a therapeutic agent.
**Objectives:** We aimed to investigate whether IL-6 blockade with TCZ decreases the proportion of CD25+CD4+ T cells.
**Methods:** Peripheral blood mononucleated cells (PBMCs) were obtained from 13 ACPA (+) RA patients at baseline, 24 and 48 weeks of TCZ treatment (male:female ratio = 0.077). Surface phenotypes and activation markers of T cells were analyzed with flow cytometory.
**Results:** DAS28-ESR and SDAI were significantly reduced at 24 and 48 weeks compared with those at baseline (DAS28-ESR: 4.87±1.25 at baseline; 1.99±1.13 at 24 weeks, $p<0.0001$; 1.61±0.70 at 48 weeks $p<0.0001$; SDAI: 20.75±9.56 at baseline; 6.30±7.0 at 24 weeks,$p=0.0008$; 3.20±2.86 at 48 weeks, $p<0.0001$). The serum levels of matrix metalloproteinase (MMP)-3 were significantly decreased at 48 weeks (250.5±311.0 ng/mL at baseline; 85.1±81.8 ng/mL at 24 weeks, $p=0.07$; 54.9±27.2 ng/mL at 48 weeks, $p=0.04$). The proportion of CD4+ cells was significantly increased at 24 and 48 weeks compared with those at baseline (29.7±18.2% at baseline; 37.3±12.9% at 24 weeks, $p=0.0094$; 37.7±14.1% at 48 weeks, $p=0.025$). The proportions of CD25+CD4+ cells in CD4+ cells were not significantly different (5.7±4.2% at baseline; 6.1±3.4% at 24 weeks, $p=0.795$; 7.1±2.1% at 48 weeks, *$p=0.247$*). Also, the proportions of regulatory T (Treg) cells (FoxP3+CD25+CD4+ in CD4+ cells) were not significantly different (0.68±0.67% at baseline; 0.58±0.52% at 24 weeks *$p=0.752$*; 0.61±0.53% at 48 weeks, $p=0.794$).
**Conclusions:** IL-6 blockade has therapeutic effects on RA patients. However, the blockade does not change proportions of CD4+CD25+ in CD4+ T cells as well as those of Treg cells. Some other mechanisms, besides a decrease in CD4+ activation or an increase in Treg cell proportion, contribute the therapeutic effect of IL-6 blockade.
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## SAT0177 BARICITINIB FOR RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** Baricitinib is a small molecule inhibitor of the Janus kinase (JAK) pathways that reduce and modulate the production of inflammatory mediators and cytokines.
**Objectives:** We conducted a systematic review to evaluate the efficacy and safety of baricitinib for the treatment of patients with rheumatoid arthritis.
**Methods:** A comprehensive search of the literature was conducted in the following electronic databases: Cochrane Library, MEDLINE, EMBASE and Web of Science. Also, we searched clinicaltrials.gov and hand searched conference proceedings through December 2015. Any randomized controlled trial (RCT) comparing baricitinib alone or in combination with any DMARD versus placebo or other traditional or biologic DMARDs for the treatment of patients with rheumatoid arthritis were included. Two independent reviewers performed study selection, data collection and risk of bias assessment using Covidence.org. Our primary outcome was the percent of patients achieving an American College of Rheumatology (ACR) 50% response. Secondary outcomes included: clinical remission (Disease Activity Score (DAS $<2.6$)), minimum clinical important difference (MCID) $\geq0.22$ in the Health Assessment Questionnaire (HAQ), total withdrawals and serious adverse events (SAEs).
**Results:** Out of 146 citations, 7 RCTs met our inclusion criteria. Most studies were published in abstract format and risk of bias assessment was judged unclear in most domains. Five studies compared more than two doses of baricitinib, however, we only report here results for the dose of 4 mg once daily. Four comparisons were included: i) baricitinib plus methotrexate (MTX) vs MTX, ii) baricitinib alone vs MTX, iii) baricitinib plus MTX vs adalimumab (ADA) plus MTX, and iv) baricitinib plus MTX vs baricitinib alone. For the combination of baricitinib plus MTX, more patients in the baricitinib group achieved an ACR 50 response and clinical remission compared to patients in the MTX group at 12 and 24 weeks

(at 12 weeks patients in the control group were re-assigned to baricitinib). The combination group reported lower withdrawal rates at 24 weeks (RR 0.61, (95% CI 0.47–0.81) and similar SAEs at 24 weeks compared to control. For baricitinib alone vs MTX, improvement rates were higher in the baricitinib group at 12 weeks (RR 1.7, 95% CI 1.3–2.1; 1.8, 95% CI 1.2–2.6; 1.3, 95% CI 1.2–1.4; for ACR50, clinical remission, and MCID HAQ rates, respectively). No differences were found in total withdrawals or SAEs. When baricitinib was compared to ADA, greater rates of ACR50 response were observed in the baricitinib group at 12 weeks (RR 1.3; 95% CI 1.1, 1.5); but also higher rates of SAEs compared to the ADA group at 24 weeks were reported (RR 2.5; 95% CI 1.0, 6.1). No significant differences were observed between baricitinib plus MTX compared with baricitinib alone.

**Conclusions:** Baricitinib alone or combined with MTX had better efficacy responses compared to MTX alone at 12–24 weeks. Total withdrawal rates were lower in the baricitinib combined group when compared to MTX. Baricitinib had similar effects compared to adalimumab, but higher rates of SAEs. Baricitinib can be considered an additional therapeutic option to treat patients with moderate to severe disease who have an inadequate response to other treatment agents.

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## SAT0178 CLINICAL RESPONSES OF SARILUMAB BASED ON RHEUMATOID FACTOR AND ANTI–CYCLIC CITRULLINATED PEPTIDE ANTIBODY STATUS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Sarilumab is a human investigational anti–IL-6 receptor mAb that has been studied in 2 randomized, double-blind, placebo-controlled, multicenter, phase 3 studies in patients with RA. Subcutaneous (SC) sarilumab q2w + MTX demonstrated efficacy in patients with inadequate response to MTX in the MOBILITY study (NCT01061736).[1] Sarilumab SC q2w + conventional synthetic DMARDs demonstrated efficacy in patients who were inadequate responders to or intolerant of TNFi in the TARGET study (NCT01709578).[2] The most common TEAEs in both studies were infections, neutropenia, injection site reactions, and increased transaminases.

**Objectives:** Negative autoantibody status has been associated with attenuated clinical response to biologic disease-modifying agents in RA.[3,4] This study assessed the clinical efficacy of sarilumab in subgroups of patients based on rheumatoid factor (RF) and anti-CCP antibody status in MOBILITY and TARGET.

**Methods:** Incidence of ACR20/50/70 response at wk 24, mean change from baseline in HAQ-DI at wk 12 (TARGET) or 16 (MOBILITY), and DAS28-CRP at wk 24 were evaluated by RF and CCP status.

**Results:** The majority of MOBILITY (78%) and TARGET (70%) patients were RF+/CCP+. Treatment-by-subgroup interaction ($P<0.05$) was observed for ACR20 response (CCP status in MOBILITY; RF and CCP in TARGET) and HAQ-DI (RF and CCP status in MOBILITY; RF in TARGET). Clinical and functional responses in RF/CCP single- and double-positive patients were generally similar to overall study results (Table). However, certain clinical measures, including HAQ-DI, showed a trend toward smaller effect sizes, particularly in double-negative patients, that was somewhat more pronounced with sarilumab 150 mg q2w (Table), though sample sizes were small. Comparable findings were observed for DAS28-CRP: mean change from baseline for placebo + MTX, sarilumab 150 mg q2w + MTX, and sarilumab 200 mg q2w + MTX was -1.56 (n=191), -2.75 (n=257), and -3.09 (n=246), respectively, for RF+/CCP+ patients and -1.97 (n=22), -2.10 (n=13), and -2.51 (n=20), respectively, for RF-/CCP- patients in MOBILITY. TARGET results were similar. Trends toward lower clinical and functional responses with RF or CCP negative autoantibody were not observed in radiographic measurements of structural progression; change from baseline in mTSS appeared to be similar regardless of autoantibody status (data on file).

**Conclusions:** Overall, within MOBILITY and TARGET, clinical responses with sarilumab were generally consistent among patients who were RF+ and/or CCP+. Regardless of autoantibody status, there was a more robust response with regard to clinical signs and symptoms with sarilumab 200 mg q2w.

Table. ACR20[a] Incidence and HAQ-DI Mean Change From Baseline in RF and CCP Subgroups in MOBILITY and TARGET Studies

| | MOBILITY | | | TARGET | | |
|---|---|---|---|---|---|---|
| | Placebo + MTX (N=398) | Sarilumab 150 mg q2w + MTX (N=400) | Sarilumab 200 mg q2w + MTX (N=399) | Placebo + csDMARD (N=181) | Sarilumab 150 mg q2w + csDMARD (N=181) | Sarilumab 200 mg q2w + csDMARD (N=184) |
| **ACR20 incidence at week 24** | | | | | | |
| RF+/CCP+ n/N (% responders) | 97/310 (31%) | 195/325 (60%) | 209/299 (70%) | 45/135 (33%) | 77/125 (62%) | 71/121 (59%) |
| RF+/CCP- n/N (% responders) | 14/26 (54%) | 16/20 (80%) | 19/28 (68%) | 1/6 (17%) | 7/9 (78%) | 9/10 (90%) |
| RF-/CCP+ n/N (% responders) | 8/30 (27%) | 18/32 (56%) | 21/37 (57%) | 8/14 (57%) | 5/10 (50%) | 10/16 (63%) |
| RF-/CCP- n/N (% responders) | 14/32 (44%) | 7/19 (37%) | 14/32 (44%) | 11/24 (46%) | 12/36 (33%) | 21/33 (64%) |
| **HAQ-DI mean change from baseline at week 16 (MOBILITY) and week 12 (TARGET)[b]** | | | | | | |
| RF+/CCP+ n, mean change (SD) | 295, -0.29 (0.56) | 295, -0.59 (0.56) | 278, -0.61 (0.62) | 126, -0.30 (0.53) | 115, -0.54 (0.66) | 112, -0.58 (0.63) |
| RF+/CCP- n, mean change (SD) | 23, -0.29 (0.70) | 19, -0.39 (0.47) | 26, -0.58 (0.56) | 6, 0.04 (0.20) | 8, -0.79 (0.41) | 9, -0.57 (0.30) |
| RF-/CCP+ n, mean change (SD) | 30, -0.20 (0.62) | 28, -0.33 (0.44) | 33, -0.50 (0.72) | 13, -0.16 (0.40) | 9, -0.36 (0.69) | 16, -0.29 (0.32) |
| RF-/CCP- n, mean change (SD) | 30, -0.52 (0.62) | 18, -0.19 (0.36) | 26, -0.34 (0.64) | 23, -0.48 (0.67) | 31, -0.30 (0.59) | 31, -0.28 (0.34) |

CCP, cyclic citrullinated peptide; CRP, C-reactive protein; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire–Disability Index; MTX, methotrexate; q2w, every 2 weeks; RF, rheumatoid factor; SD, standard deviation; VAS, visual analog score. [a]ACR20 response was defined as at least 20% improvement from baseline in both tender joint count and swollen joint count and in at least 3 of the HAQ-DI score, CRP, and 3 VAS assessments. [b]HAQ-DI coprimary endpoint was evaluated at week 16 in MOBILITY and at week 12 in TARGET.

**References:**

[1] Genovese et al. Arthritis Rheumatol. 2015;67:1424–1437
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## SAT0179 EXPERIENCES OF RITUXIMAB TREATMENT IN RF+ RHEUMATOID ARTHRITIS

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**Background:** Immunoglobulins (Ig) and immune complexes generate and fine-tune inflammation in rheumatoid arthritis (RA) by interacting with receptors on immune cells. After successful antirheumatic treatments, reductions of Igs are observed in many patients. Rituximab (RTX), a second line biologic anti-rheumatic drug, has proven efficacy in RA; by interacting with CD20, it causes lysis/apoptosis of B-cells. However, this may increase the patients' infection sensitivity and reduce their immune response to vaccines. Consequently, there is lack of information on the optimum level of B-cell depletion (and biomarkers thereof), and on rheumatics' exposure to infections in everyday clinical practice.

**Objectives:** To evaluate if the degree of RTX-mediated B-cell depletion in seropositive RA is correlated to joint disease activity and Ig serum levels. To review the extent, the nature, and risk factors of infectious diseases during RTX treatment in a non-selected RA cohort.

**Methods:** Sixty-nine patients (57 female/12 men, mean age 58.7 years) treated with at least one course of RTX at the Department of Rheumatology, University Hospital in Uppsala were included. A high proportion (71%) had erosive disease, 72% were on DMARD and 60% on steroid treatment. On average 1.2 other biologics had been tested prior to RTX. Analyses of Ig isotypes, IgG subclasses and IgM RF, and joint disease activity were evaluated just before the next RTX course was administered. Data were collected from medical records regarding occasions with leuco-/neutropenia, medications for concurrent diseases, admissions due to various infections, and the number of systemic or topical antibiotics prescribed.

**Results:** RA patients who were RF- at evaluation had acquired a higher total dose of RTX, had lower disease activity and lower serum IgA than RF+ patients. No difference in the number of infections or prescribed antibiotics was observed comparing RF+ with RF- patients. The total IgM levels correlated positively with the SJC and the IgG3 serum levels and negatively with the RTX total dosis. The HAQ score was negatively related to the IgG1 serum levels. In 4 patients

transient leuco-/neutropenia was observed; one of these was administered to hospital and was successfully treated for pneumonia. In the medical records, 244 systemic (1.21 per patient year) and 33 topical (0.20 per patient year) antibiotic prescriptions were observed; the most common infections were of airways (n=147), urinary tract (n=87), and skin (n=49). One case of hepatitis B reactivation was observed in a patient who voluntarily had paused prophylactic antiviral treatment. A total of 10 in-patient admissions was observed, and one death occurred due to tick borne virus encephalitis (TBE). At encephalitis onset this patient had no detectable levels of anti-TBE antibodies although she had been immunized according to guidelines. RA patients with concurrent treatments for diseases with increased risk of developing infections had more infections and antibiotic therapies than non-risk patients.

**Conclusions:** A good response to RTX-treatment is followed by conversion to seronegativity in initially RF+ individuals. During RTX treatment, an increased risk of infections is seen especially in RA patients with concomitant diseases. These patients should be recommended to review their vaccination-status, to optimize their non-RA treatments, and to seek medical care in case of infection symptoms. In endemic areas TBE vaccination before RTX start should be mandatory.

**Disclosure of Interest:** None declared

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## SAT0180 ONSET OF ACTION OF SARILUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN 2 PHASE 3 STUDIES

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**Background:** The investigational human anti–interleukin 6 receptor monoclonal antibody sarilumab plus methotrexate (MTX) has demonstrated efficacy in patients with rheumatoid arthritis (RA) and inadequate response to MTX (MOBILITY; NCT01061736),[1] while sarilumab plus conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) demonstrated efficacy in patients with RA and inadequate response or intolerance to tumor necrosis factor (TNF) inhibitors (TARGET; NCT01709578).[2] Among the most common treatment-emergent adverse events in both studies were infections, neutropenia, injection site reactions, and increased transaminases.

**Objectives:** This analysis of MOBILITY and TARGET study data assessed the time to onset of clinical efficacy of sarilumab and the durability of response over 24 weeks.

**Methods:** Adults with active, moderate-to-severe RA were randomized to 1 of 3 groups receiving subcutaneous sarilumab 150 or 200 mg or placebo every 2 weeks (q2w) plus background MTX (MOBILITY) or csDMARDs (TARGET). Clinical efficacy was evaluated in these patients at weeks 2, 4, 8, 12, and 24 in a post hoc analysis. ACR20/50/70 response rates were analyzed using the 2-sided Cochran-Mantel-Haenszel test stratified by prior biologic use and region (MOBILITY) or by region and number of prior TNF inhibitors (TARGET); nonresponder imputation was applied for patients who started rescue medication or discontinued the study. Changes from baseline in Health Assessment Questionnaire–Disability Index (HAQ-DI), 28-joint disease activity score by C-reactive protein (DAS28-CRP), and clinical disease activity index (CDAI) were analyzed with a mixed model for repeated measures; no data were imputed.

**Results:** Baseline demographic and disease characteristics were similar between treatment groups in both studies.[1,2] Improvements in ACR20 responses were observed as early as week 2 in both studies, with nominal $P<0.05$ observed at week 8 for all sarilumab-treated groups in both studies. Similar trends were observed for ACR50 and ACR70 responses. Greater reductions in DAS28-CRP mean change from baseline vs placebo were observed with both doses of sarilumab by week 2 in both studies (nominal $P<0.05$). Similarly, numerical improvements in HAQ-DI and CDAI were observed with both doses of sarilumab vs placebo by week 4 in both studies (nominal $P<0.05$; Table). Improvements in all efficacy parameters were sustained through the end of each study (ie, week 52 for MOBILITY and week 24 for TARGET). The most common treatment-emergent adverse events at week 12 were infection and neutropenia, consistent with the safety profile previously reported for the entire study periods.

Table. Effect of Sarilumab at Weeks 2, 4, 8, 12, and 24 After Treatment Initiation in the ITT Population

| | MOBILITY | | | TARGET | | |
|---|---|---|---|---|---|---|
| | | Sarilumab | | | Sarilumab | |
| | Placebo + MTX (N=398) | 150 mg q2w + MTX (N=400) | 200 mg q2w + MTX (N=399) | Placebo + csDMARD (N=181) | 150 mg q2w + csDMARD (N=181) | 200 mg q2w + csDMARD (N=184) |
| **Incidence of ACR20 responses, %** | | | | | | |
| Week 2 | 12.3 | 20.5[‡] | 20.8[‡] | 12.2 | 22.1[‡] | 15.8 |
| Week 4 | 22.9 | 36.3* | 47.4* | 25.4 | 32.6 | 44.0* |
| Week 8 | 33.2 | 54.0* | 60.7* | 35.4 | 49.1[‡] | 57.1* |
| Week 12 | 34.7 | 54.0* | 64.9* | 37.6 | 54.1[‡] | 62.5* |
| Week 24 | 33.4 | 58.0* | 66.4* | 33.7 | 55.8* | 60.9* |
| **DAS28-CRP; LS mean change from baseline ± SE** | | | | | | |
| Baseline ± SD | 5.93 ± 0.87 | 5.95 ± 0.91 | 5.97 ± 0.87 | 6.23 ± 0.86 | 6.09 ± 0.93 | 6.29 ± 0.96 |
| Week 2 | -0.45 ± 0.04 | -0.88 ± 0.04* | -1.09 ± 0.04* | -0.39 ± 0.07 | -0.81 ± 0.07* | -0.98 ± 0.07* |
| Week 4 | -0.69 ± 0.05 | -1.38 ± 0.05* | -1.68 ± 0.05* | -0.68 ± 0.08) | -1.44 ± 0.08* | -1.62 ± 0.08* |
| Week 8 | -0.88 ± 0.06 | -1.85 ± 0.06* | -2.17 ± 0.06* | -0.94 ± 0.10 | -1.91 ± 0.10* | -2.15 ± 0.10* |
| Week 12 | -1.05 ± 0.07 | -2.01 ± 0.07* | -2.40 ± 0.07* | -0.97 ± 0.10 | -2.13 ± 0.10* | -2.45 ± 0.10* |
| Week 24 | -1.16 ± 0.08 | -2.44 ± 0.08* | -2.81 ± 0.08* | -1.38 ± 0.12 | -2.35 ± 0.11* | -2.82 ± 0.11* |
| **HAQ-DI; LS mean change from baseline ± SE** | | | | | | |
| Baseline ± SD | 1.61 ± 0.66 | 1.63 ± 0.63 | 1.69 ± 0.64 | 1.80 ± 0.64 | 1.72 ± 0.62 | 1.82 ± 0.62 |
| Week 2 | -0.09 ± 0.02 | -0.15 ± 0.02[‡] | -0.14 ± 0.02[‡] | -0.08 ± 0.03 | -0.20 ± 0.03[‡] | -0.12 ± 0.03 |
| Week 4 | -0.16 ± 0.02 | -0.27 ± 0.02[†] | -0.29 ± 0.02* | -0.09 ± 0.03 | -0.27 ± 0.03[†] | -0.22 ± 0.03[‡] |
| Week 8 | -0.22 ± 0.03 | -0.42 ± 0.03* | -0.43 ± 0.03* | -0.23 ± 0.04 | -0.37 ± 0.04[‡] | -0.37 ± 0.04[‡] |
| Week 12 | -0.26 ± 0.03 | -0.46 ± 0.03* | -0.54 ± 0.03* | -0.26 ± 0.04 | -0.48 ± 0.04[†] | -0.47 ± 0.04[†] |
| Week 24 | -0.32 ± 0.03 | -0.56 ± 0.03* | -0.57 ± 0.03* | -0.34 ± 0.05 | -0.52 ± 0.05[†] | -0.58 ± 0.05[†] |
| **CDAI; LS mean change from baseline ± SE** | | | | | | |
| Baseline ± SD | 40.60 ± 11.95 | 40.45 ± 12.51 | 40.40 ± 12.33 | 44.17 ± 12.27 | 42.53 ± 12.89 | 44.11 ± 13.93 |
| Week 2 | -6.88 ± 0.52 | -8.15 ± 0.52 | -7.74 ± 0.51 | -5.90 ± 0.79 | -8.61 ± 0.79[‡] | -7.18 ± 0.78 |
| Week 4 | -10.03 ± 0.57 | -13.56 ± 0.58* | -14.32 ± 0.57* | -10.06 ± 0.96 | -14.69 ± 0.99[†] | -13.61 ± 0.98[†] |
| Week 8 | -12.06 ± 0.63 | -18.53 ± 0.63* | -19.78 ± 0.63* | -12.36 ± 1.05 | -19.15 ± 1.07* | -18.93 ± 1.05* |
| Week 12 | -14.10 ± 0.69 | -19.49 ± 0.70* | -21.72 ± 0.69* | -12.53 ± 1.15 | -21.13 ± 1.17* | -21.96 ± 1.15* |
| Week 24 | -14.39 ± 0.81 | -23.78 ± 0.77* | -25.71 ± 0.76* | -16.35 ± 1.20 | -23.65 ± 1.14* | -26.08 ± 1.11* |

CDAI, clinical disease activity index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-CRP, 28-joint disease activity score by C-reactive protein; HAQ-DI, Health Assessment Questionnaire–Disability Index; ITT, intent to treat; LS, least squares; MTX, methotrexate; q2w, every 2 weeks; SE, standard error. *P<0.0001 vs placebo. [†]P<0.001 vs placebo. [‡]P<0.05 vs placebo.

**Conclusions:** Sarilumab rapidly improved signs and symptoms of RA in patients with inadequate response to MTX (MOBILITY) or TNF inhibitors (TARGET), and improvements were sustained through the end of treatment.

**References:**

[1] Genovese et al. Arthritis Rheumatol. 2015;67:1424–1437
[2] Fleischmann et al. Presented at: ACR; Nov. 7–11, 2015; San Francisco, CA

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## SAT0181 CXCL4 IS NOT A BIOMARKER IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT AND TOCILIZUMAB

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**Background:** CXCL4 (platelet factor4, PF4) is a pleiotropic α-granules chemokine, produced by platelets, dendritic cells, macrophages and neutrophils. Recently, CXCL4 levels have been found to increase under treatment with infliximab, in unresponsive Rheumatoid Arthritis (RA) patients [1]. At present, the influence of non TNFalfa blockers biological DMARDs (Abatacept and Tocilizumab) on CXCL4 serum levels not have been investigated in RA.

**Objectives:** To investigate CXCL4 serum levels in RA patients naïve for biological disease-modifying anti-rheumatic drugs (bDMARDs) at baseline and after 1-year treatment and look for associations with disease features at baseline and distinct biological therapy overtime.

**Methods:** Fifty-six RA were enrolled in the study at the time of initiating a treatment with a biological DMARD. CXCL4 serum levels were investigated by a multiplex suspension immunoassay at baseline and after 1 year and compared with those detected in 30 healthy controls. Epidemiological, clinical and serological features of RA patients at baseline are showed in table 1.

**Results:** Out 56 RA patients, 39 (70%) were assigned to an anti-TNF-α treatment (3 patients to Infliximab, 12 to Etanercept, 24 to Adalimumab); 10 to Abatacept and 7 to Tocilizumab.

At baseline, CXCL4 serum levels were found to be increased in RA patients as compared to controls but the difference was not significant (1,538 ng/ml vs 1.26 ng/ml, p=0.082). Moreover, CXCL4 levels were not found to be related to any disease feature. At baseline, 6 (10%) RA patients presented serum CXCL4 levels exceeding the 95th percentile of the values detected in controls (4.569 ng/ml). These patients did not differed from the remaining RA patients in any feature. After 1 year of treatment, CXCL4 levels increased with respect to basal values in the whole series (3.280 ng/ml vs 1.538 ng/ml, $p<0.0001$). However, a different trend was detected in patients undergoing distinct treatments: CXCL4 serum levels were found to increase after 1 year in patients treated with anti-TNF agents (3.595 ng/ml, vs 1,241 ng/ml, $p<0.0001$); on the contrary, CXCL4 levels

at 1-year remained unchanged in patients treated with Abatacept (4.160 ng/ml vs 2.030 ng/ml, p=0.21) and with Tocilizumab (3.310 ng/ml, vs 3.290 ng/ml, p=0.6). At 1-year follow-up, 32 patients could be considered responsive to the treatment (R); 24 (43%) were non-responder (NR). No difference was detected in the change of CXCL4 over time, comparing the 32 responsive to treatment with the 24 unresponsive patients.

**TABLE 1.** *Epidemiological, clinical and serological features at entrance of the investigated 56 RA patients.*

| Features | Whole cohort (n = 56) | Anti-TNF-α (n = 39) | Non Anti-TNF-α (n = 17) | p |
|---|---|---|---|---|
| Sex F:M ratio | 48:8 | 35:4 | 13:4 | ns |
| Age in years (median, range) | 54 (28-71) | 47 (34-71) | 54 (40-70) | ns |
| Disease duration (median, range) | 7.5 (1-32) | 7 (1-32) | 8 (2-26) | ns |
| RF+ | 42 | 30 | 12 | ns |
| ACPA+ | 29 | 22 | 7 | ns |
| ANA+ | 8 | 4 | 4 | ns |
| ESR (mm/h) (median, range) | 25 (4-88) | 26 (4-88) | 22 (4-70) | ns |
| CRP (mg/dl) (median, range) | 0.8 (0.03-8.68) | 0.7 (0.03-8.68) | 0.8 (0.2-6.9) | ns |
| HAQ (median, range) | 1.5 (0.125-3.0) | 1.25 (0.125-3.0) | 1.625 (0.25-2.625) | ns |
| DAS28 (median, range) | 4.73 (3.38-7.2) | 4.650 (3.38-7.2) | 4.790 (3.55-6.62) | ns |
| SDAI (median, range) | 23.5 (3.42-44.18) | 22.4 (11.7-44.18) | 24.2 (3.42-34.2) | ns |
| Tender Joints (median,range) | 8 (2-28) | 7 (2-28) | 10 (2-26) | ns |
| Swollen Joints (median,range) | 2 (0-11) | 2 (0-11) | 1 (0-6) | ns |

**Conclusions:** Similarly to previous studies (1) we found an increase in CXCL4 serum levels in patients undergoing an antiTNFa agent, but we failed to find differences between responsive and unresponsive patients. Moreover, we found that treatment with Abatacept and Tocilizumab did not modify CXCL4 serum level. Finally, we failed to detect any correlation between CXCL4 levels and any disease feature both at baseline and during follow-up.

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[1] Trocmé C., et al. Ann Rheum Dis. Aug 2009; 68(8): 1328–1333

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## SAT0182 CORRELATION BETWEEN POSITIVE BLOOD FLOW SIGNAL ON JOINT ULTRASONOGRAPHY AND PROGRESSION OF JOINT DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB FOR 4 YEARS

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**Background:** The goal of rheumatoid arthritis (RA) treatment is to achieve clinical, functional, and structural remission. Tocilizumab (TCZ), an anti-interleukin-6 receptor monoclonal antibody agent, has a high compliance rate and can maintain clinical and functional remissions. Imaging examination for structural remission is advanced; however, the accuracy of evaluation results is inconsistent. Joint ultrasonography is an important measurement tool to comprehensively evaluate synovitis according to the presence or absence of blood flow signal. However, only a few reports have evaluated the efficacy of TCZ by using joint ultrasonography.

**Objectives:** The objective of this study was to evaluate the correlation between positive blood flow signal on joint ultrasonography and progression of joint destruction in patients with RA treated with TCZ for 4 years.

**Methods:** Among 111 patients who were treated with TCZ in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA), 16 patients were receiving TCZ for 4 years or longer and enrolled this study. We examined age, sex, disease duration, C-reactive protein (CRP) level, MMP3 level, DAS28-ESR score, and clinical disease activity index (CDAI) at the start of TCZ administration and once a year. Moreover, we examined for blood flow signal (power Doppler signal) on joint ultrasonography at 4 years and modified total Sharp score (mTSS) on radiography at the baseline and once a year. Joint ultrasonography was performed in 34 joints, including bilateral proximal interphalangeal and metacarpophalangeal joints of the five fingers, wrists, knees, and metatarsophalangeal joints of the five toes in all of the patients, as well as other joints with symptoms. The subjects were divided into the P(+) and P(–) groups according to the presence or absence of blood flow signal on joint ultrasonography at 4 years. Eight patients were classified into the P(+) group and 8 were the P(–) group. Furthermore, progression of joint destruction by using mTSS were compared among both groups.

**Results:** The mean patient age was 52 (range, 38–63) years, and the mean disease duration was 92 (range, 30–159) months. Women accounted for 69% of the patients. At the start of TCZ administration, no significant differences in age, proportion of women, disease period, CRP, CMMP3, and CDAI were observed between both groups. However, the DAS28-ESR score was significantly higher in the P(+) group than in the P(–) group (p=0.0279). Before the start of TCZ therapy, the scores of mTSS/year were 3.9 in the P(+) group and 2.7 in the P(–) group, showing no significant difference. After the start of TCZ therapy, the scores of mTSS/4 years were 3.4 in the P(+) group and 0.2 in the P(–) group, showing a significant difference (p=0.0347).

**Conclusions:** The presence of positive blood flow signal on joint ultrasonography at 4 years was significantly correlated with progression of joint destruction in patients with RA treated with TCZ.

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## SAT0183 LONG-TERM EFFICACY, SAFETY, AND TOLERABILITY OF TOCILIZUMAB IN RITUXIMAB-REFRACTORY RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an inflammatory autoimmune process, and the dysregulated overproduction of interleukin-6 (IL-6) plays an important role in its pathogenesis. Tocilizumab (TCZ) is a humanized monoclonal antibody targeting the IL-6 receptor, and is recommended for use in RA. (1)

There is evidence demonstrating good outcomes with TCZ in patients who have disease refractory to B-cell depletion with rituximab (RTX), a chimeric monoclonal antibody targeting CD20 B-cells, with up to 18 months' follow-up. (2) Long-term data, however, on the efficacy, safety and tolerability of TCZ in RA that is refractory to sDMARDs, anti-TNF and RTX are lacking.

**Objectives:** To evaluate the long-term efficacy and safety of TCZ in real patients with RA refractory to synthetic DMARDs, anti-TNF agents and B cell depletion therapy with RTX, beyond 2 years.

**Methods:** We retrospectively studied 45 patients from two centres who received TCZ for median 48-months (range, 9–72) duration. All patients received anti-TNF and RTX previously. Efficacy and safety was evaluated according to the EULAR response criteria and EMEA guidance, respectively. Wilcoxon matched ranks test was used to assess changes in outcomes.

**Results:** Of 45 patients, 36 (80%) had previously discontinued RTX due to inefficacy and 9 (20%) due to intolerance. At most recent follow-up, median 48 months, 30 of 45 (67%) patients were continuing TCZ and 15 (33%) had discontinued, 7 due to inefficacy and 8 others due to intolerance.

Of 36 patients with RTX-refractory RA, 25 (69%) were continuing TCZ and 11 had discontinued due to, inefficacy in 6 (17%) and intolerance in 5 (14%): 2 patients due to diverticulitis, 2 due to upper respiratory tract infections and 1 due to discitis.

Of the 9 patients with RTX-intolerance, 5 (56%) were continuing TCZ and 4 (44%) had discontinued: 1 patient due to inefficacy and 3 due to intolerance, who had a prior history of hypogammaglobulinemia and infections associated with RTX.

There were no significant differences in lipid profile in 25 of 36 of patients continuing TCZ therapy whereas 11 required statin therapy.

**Conclusions:** A majority of patients with RA refractory to synthetic DMARDs, anti-TNF and RTX responded to TCZ. Lipid profile in a majority of patients was stable in the long-term.

Key messages:

1. The efficacy of TCZ is sustained in the long-term in patients with RTX-refractory RA.
2. TCZ appears to be safe in patients previously treated with RTX.

TCZ does not alter lipid profile in a majority of the patients with RTX-refractory RA.

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## Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

### SAT0184 SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION 3 (STAT3) INTEGRATES SEVERAL PROFIBROTIC PATHWAYS IN SYSTEMIC SCLEROSIS

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**Background:** Signal transducer and activator of transcription 3 (STAT3) is a transcription factor that is regulated by phosphorylation of key tyrosine residues. Phosphorylation of STAT3 triggers dimerization, nuclear translocation and transcriptional activation. STAT3 can be phosphorylated by JAK2, SRC, c-ABL and JNK kinases, all of which have been implicated in aberrant fibroblast activation in systemic sclerosis (SSc). We therefore hypothesized that profibrotic signals transmitted through those kinases may converge on STAT3 and that STAT3 may be an important molecular checkpoint for tissue fibrosis in SSc.
**Objectives:** The aim of this study was to investigate the role of STAT3 in fibroblast activation and to evaluate it as a potential molecular target for antifibrotic intervention.
**Methods:** Activation of STAT3, JAK2, SRC, c-ABL and JNK was analyzed in SSc patients and in experimental models of SSc by Western Blot and immunochemistry. Selective inhibitors in conjunction with knockdown and knockout strategies were used to target STAT3 signaling and its upstream kinases in cultured fibroblasts. The anti-fibrotic potential of STAT3 genetic and pharmaceutical inhibition was evaluated in two mouse models of SSc: bleomycin-induced fibrosis and fibrosis induced by overexpression of a constitutively active TGFβ receptor type I (TBRact).
**Results:** Accumulation of phosphorylated and thus active STAT3 (P-STAT3) was detected in fibroblasts in the skin of SSc patients as compared to healthy volunteers. Enhanced STAT3 signaling was also found in murine models of SSc. The accumulation of P-STAT3 was mediated by increased TGF-β signaling and inhibition of TGF-β normalized the levels of P-STAT3 in SSc fibroblasts and in experimental fibrosis. JAK2, SRC, JNK and to a lesser degree also c-ABL were activated in SSc patients and in experimental fibrosis. Functional in vitro studies identified SRC and JAK2 as major kinases phosphorylating STAT3 in response to TGF-β in fibroblasts. To further evaluate the role of STAT3, we analyzed the effects of STAT3 inactivation on collagen release and tissue fibrosis. STAT3-deficient fibroblasts were less sensitive to the pro-fibrotic effects of TGF-β with impaired collagen release and myofibroblast differentiation. Fibroblast-specific knockout of STAT3 also ameliorated experimental fibrosis in the models of bleomycin-induced fibrosis and TBRact-induced fibrosis. Pharmacological inhibition of STAT3 also exerted potent anti-fibrotic effects and inhibited TGF-β-induced fibroblast activation and bleomycin- as well as TBRact-induced experimental fibrosis.
**Conclusions:** We demonstrate that STAT3 integrates several profibrotic signals and might thus be a novel core mediator of fibrosis. Inhibition of STAT3 prevented fibroblast activation and demonstrated potent anti-fibrotic effect in different preclinical models of SSc. Considering these potent anti-fibrotic effects and the fact that several STAT3 inhibitors are currently tested in clinical trials, STAT3 might be an interesting candidate for molecular targeted therapies of SSc.
**Disclosure of Interest:** None declared
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### SAT0185 WNT5A PROMOTES FIBROBLAST ACTIVATION AND TISSUE FIBROSIS BY ROR2/ RYK DEPENDENT ACTIVATION OF PCP-SIGNALING

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**Background:** Canonical Wnt/beta-catenin signaling has been identified as a core pathway of fibrosis in SSc. However, the role of non-canonical Wnt signaling has not yet been investigated. A subset of Wnt proteins such as Wnt5a can bind to different cell surface receptors and activate non-canonical Wnt pathways which are independent of beta-catenin pathway.
**Objectives:** In this study we aimed to characterize the role of non-canonical Wnt signaling in fibrotic diseases and find out the major target receptor for further therapeutic antibody generation.
**Methods:** The expression of non-canonical Wnt ligands was analyzed by qPCR, IF and Western blot in patients with SSc, IPF and healthy controls as well as in experimental fibrosis. The effect of fibroblast-specific (col1a2; CreER) as ubiquitous (ubiquitin; CreER) knockout of Wnt5a was evaluated in bleomycin-induced fibrosis and in experimental cGvHD. Wnt5a was overexpressed in 3D human skin culture systems and in the skin and lungs of mice using adeno-associated vectors. Wnt5a-induced signaling pathways were analyzed in vitro and in vivo using small molecule inhibitors, siRNA mediated knockdown, Western blots and reporter assays.
**Results:** The mRNA and protein levels of Wnt5a, but not other non-canonical Wnt ligands, were increased in skin and lungs of patients with SSc and IPF as compared to healthy volunteers. Wnt5a was also upregulated in murine models of fibrosis. Co-staining with cell-type specific markers identified fibroblasts as a major cellular source of Wnt5a in fibrotic diseases. Wnt5a induced myofibroblast differentiation and collagen release *in vitro* and induced pulmonary and dermal fibrosis *in vivo*. In contrast, inducible fibroblast-specific knockout of Wnt5a ameliorated bleomycin-induced fibrosis and experimental cGvHD. The effects of fibroblast-specific knockout were comparable to those in mice with inducible ubiquitous knockout. The pro-fibrotic effects of Wnt5a were independent of Wnt/beta-catenin and Wnt/Calcium signaling, but were mediated by Wnt/PCP signaling via binding with Ror2 and Ryk receptors and subsequent phosphorylated JNK and cJun. Consistently, pharmacologic or genetic inactivation of JNK or cJun abrogated the pro-fibrotic effects of Wnt5a *in vitro* and *in vivo*. Co-incubation with neutralizing antibodies against TGFbeta and inhibitors of TGFbeta receptors demonstrated that the profibrotic effects of Wnt5a were partially mediated by rapid activation of latent TGFbeta with subsequent activation of classical downstream pathways such as Smad3.
**Conclusions:** We characterize Wnt5a as a novel mediator of fibroblast activation in fibrotic diseases. Wnt5a is upregulated in SSc and IPF and induces fibroblast activation and tissue fibrosis. The pro-fibrotic effects of Wnt5a are independent of canonical Wnt signaling and Wnt/Calcium signaling, but are mediated by PCP signaling via binding with Ror2 and Ryk receptor and JNK/cJun activation and by activation of latent TGFbeta.
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### SAT0186 THE HOMEOPROTEIN ENGRAILED-1 REGULATES CANONICAL TGF-β SIGNALING VIA FIBROBLAST DIFFERENTIATION AND TISSUE FIBROSIS

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**Background:** Systemic sclerosis (SSc) is a chronic fibrotic connective disease of unknown etiology that affects the skin and internal organs. Transforming growth factor-β (TGFβ) has been characterized as a key-mediator of fibroblast activation in SSc. However, the intracellular signaling cascades that control TGFβ signaling and the TGFβ-induced activation of fibroblasts are still incompletely understood. Homeobox containing transcription factor, Engrailed-1 plays a key role in embryonic development and has also been linked to disease, including cancer. EN-1 is induced by proinflammary cytokines and oxidative stress which play an important role in Systemic Sclerosis (SSc).
**Objectives:** The aim of this study was to determine the role of the embryonic homeoprotein EN-1 in fibroblast activation and tissue fibrosis in systemic sclerosis (SSc).
**Methods:** The expression of EN-1 in skin tissue and in human dermal fibroblasts was determined by real-time PCR, Western blot and immunofluorescence. Knock-down and overexpression strategies were used to evaluate the effect of EN-1 on fibroblast activation. The outcome of mice with fibroblast-specific knockout of EN-1 (EN1 fibKO) was evaluated in bleomycin-induced skin fibrosis; fibrosis induced by overexpression of a constitutively active TGF-β receptor I (TBRIact) and in the Tsk model which resembled the later stages of SSc. Co-IP and CAGA Reporter assay were performed to study the physical and functional interaction between EN-1 and Smad3.
**Results:** A five-fold increased expression of EN-1 was detected in the upper layer of the dermis of SSc patients on fibroblasts double stained for EN-1 and anti-prolyl-4-hydroxylase. EN-1 expression was induced by TGF-β in cultured fibroblasts and treatment with the TBR inhibitor SD-208 prevented the induction of EN-1 by two-fold decrease in experimental fibrosis. Fibroblasts lacking EN-1 were less sensitive to the pro-fibrotic effects of TGF-β with impaired induction of target genes mRNA and protein. Additionally, overexpression of EN-1 enhanced the profibrotic effect of TGF-β with myofibroblast differentiation and increased collagene release as well as mRNA and protein levels of target genes. Function studies demonstrated that EN-1 interacts with Smad3 to regulate the pro-fibrotic effects of TGF-β. Co-IP demonstrated that TGF-β induces binding of EN-1 to Smad3. Reporter study and analyses of the expression of classical Smad target genes such as PAI-1 demonstrated that the binding of EN-1 to Smad3 stimulates the transcriptional activity of Smad3. In the model of bleomycin-induced fibrosis dermal thickening, hydroxyproline content and myofibroblast counts were significantly decreased in EN1 fibKO mice as compared to wildtype littermates. EN1 fibKO also protected from TBRIact-induced fibrosis and ameliorated fibrosis in the Tsk1 model.
**Conclusions:** We demonstrate for the first time a role of EN-1 in fibroblast

activation and tissue fibrosis. Deficiency in EN-1 reduced the stimulatory effect of TGF-β on fibroblasts by interfering with canonical Smad and protected from experimental fibrosis in different mouse models. Considering the potent anti-fibrotic effects observed in this study, EN-1 might be a candidate for molecular targeted therapies of SSc.

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## SAT0187 THE ANTIMICROBIAL PEPTIDE LL-37 AND TYPE I INTERFERON IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** The human antimicrobial peptide LL-37, exhibits a variety of biological functions such as activation of plasmacytoid dendritic cells (pDC) to produce type I interferon and mediate tissue damage. In autoimmune diseases such as systemic lupus erythematosus, rheumatic arthritis, and psoriasis LL-37 released by neutrophils is overexpressed at inflammatory sites and may have a role in pathogenesis by induction of type I interferon pathway. Type I interferon pathway is activated in subgroups of patients with idiopathic inflammatory myopathies (IIM). The mechanisms that drive type I interferon in IIM is unclear. We hypothesized that LL-37 in muscle and/or skin may be a factor that can activate type I interferon in these conditions.
**Objectives:** The aim of our study was to investigate the expression of LL-37 and type I interferon related proteins (MxA) in the affected organs of patients with polymyositis (PM) and dermatomyositis (DM).
**Methods:** Twelve muscle and 5 skin biopsies were obtained from 6 PM and 6 DM patients. Additional 3 skin biopsies taken from non-affected skin in 3 of DM patients. Five muscle and 7 skin biopsies from healthy subjects were selected as controls (HC). Immunohistochemistry staining of LL-37, CD66b (neutrophil), MxA (type I interferon), BDCA-2 (pDC), CD68 and CD163 (both macrophage markers) were performed in all muscle and skin specimens. Western blot (WB) was utilized to confirm the expression of LL-37 in muscle and skin tissues. Co-localization of LL-37 and neutrophils in muscle and skin tissue was confirmed by double-staining. The relationship of the markers were analyzed and compared with the clinical features of PM/DM patients.
**Results:** The expression of LL-37, CD66b, BDCA-2, and MxA in muscle as well as in skin tissue was significantly higher in PM/DM patients when compared to HC ($P<0.05$). In addition, LL-37 expression in skin lesions of DM patients was higher than in non-affected skin from the same patient ($P<0.05$). WB confirmed LL-37 expression in muscle and skin tissues of PM/DM patients but was negative in HC. A positive correlation was found between expression of LL-37 and CD66b in muscle and skin tissues of PM/DM patients (R=0.89 and 0.69 respectively, $P<0.05$). Double-staining revealed co-localization of LL-37 and neutrophils in both muscle and skin tissues. The expression of CD66b correlated to MxA expression in muscle tissue in PM/DM patients (R=0.58, $P<0.05$). Expression of LL-37 and CD66b in muscle tissue correlated to serum CK levels (R=0.85 and 0.88 respectively, $P<0.05$). LL-37 and CD66b expression in skin tissue correlated with disease activity (physician global assessment score) in DM patients.
**Conclusions:** The presence of the antimicrobial peptide LL-37 in affected muscle and skin tissues of patients with PM and DM together with the correlation of expression of LL-37 to the type I inducible protein MxA might indicate a role of LL-37 as an inducer of interferon production in patients with PM and DM. Thus, LL-37 may be involved in the pathogenesis of these diseases.
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## SAT0188 SKELETAL MUSCLE FIBERS IN MYOSITIS ACTIVELY UPREGULATE IMMUNOPROTEASOME SUBUNITS

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**Background:** Idiopathic inflammatory myopathies (IIMs) are characterized by enhanced sarcolemmal expression of MHC class I molecules and infiltration of immune cells including $CD8^+$ T cells into skeletal muscle tissue. Immunoproteasome is a proteolytic complex that can efficiently produce peptides for antigen presentation via major histocompatability complex class I (MHC class I) molecules and is highly expressed in immune cells. Previously, we described upregulated expression of immunoproteasome subunits (β1i and β5i) within myositis muscle biopsies at the mRNA level suggesting its possible involvement in diseases pathogenesis [1].
**Objectives:** The aim of this study was to clarify, whether immunoproteasomes are expressed within the muscle fibers of patients with IIMs and therefore, could be associated with the increased MHC class I surface expression.
**Methods:** Cryosections of muscle biopsies from sporadic Inclusion body myositis (sIBM), Immune-mediate necrotizing myopathy (IMNM), Dermatomyositis (DM) patients and healthy controls were examined for expression of proteasome subunits and cellular infiltrates by western blot and double-immunofluorescence. Proteasome activity was measured and compared between the different groups using a proteolytic assay *in vitro*.
**Results:** Western blot analyses of muscle biopsies from IBM (n=9), IMNM (n=9), DM (n=9) patients showed a strong upregulation of β1i and β5i subunits. Of note, double immunofluorescence provided clear evidence for an expression of immunosubunits β1i and β5i especially in the infiltrated muscle fibers in all studied disease conditions, whereas healthy muscle (n=4) fibers showed no staining for β1i and β5i. Interestingly, expression of proteasome immunosubunits was accompanied by increased MHC class I expression on the same muscle fibers. Both $CD68^+$ and $CD14^+$ macrophages showed strong staining of β1i and β5i in all disease group. In IBM, among the infiltrating cells about 50% of CD8+ T cells stained positive for β1i and β5i. In agreement with these results, significant increase in proteasomal chymotrypsin-like (CTL) activity was observed.
**Conclusions:** These results suggest direct involvement of immunoproteasome subunits β1i and β5i in the pathogenesis of myositis through enhanced upregulation of MHC class I.
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## SAT0189 CHARACTERIZATION OF EXTRACELLULAR HISTIDYL-TRNA SYNTHETASE IN MYOSITIS

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**Background:** Histidyl-transfer RNA synthetase (HisRS) is a major autoantigen in myositis with lung involvement[1–4]. Simultaneous presence of anti-HisRS and anti-Ro52 antibodies has been demonstrated in patients with myositis[5–7].
**Objectives:** We investigated the presence of HisRS in the extracellular compartments plasma, sera and bronchoalveolar lavage fluid (BAL). In addition, the occurrence of anti-HisRS antibody isotypes as well as other auto-reactivities was evaluated in BAL and sera from patients with myositis.
**Methods:** HisRS was measured in sera, plasma and BAL from myositis (anti-HisRS antibody positive, anti-Jo1+ and negative, anti-Jo1-), sarcoidosis, rheumatoid arthritis (RA) patients and healthy controls (HC) by dot-blot, western-blot, immunoprecipitation and mass spectrometry. The presence in BAL and sera of anti-Jo1 isotypes and other ANA-associated autoantibodies was analysed by ELISA and addressable laser bead immunoassay.
**Results:** HisRS was detected in sera, plasma and BAL of patients with myositis, sarcoidosis and RA and in HC. HisRS systemic levels were elevated in anti-Jo1+ myositis (14 out of 20 sera) compared to anti-Jo1- myositis (10/18), sarcoidosis (0/8) and RA (3/15) patients, and HC (5/23). In BAL, significant levels of HisRS were detected in 6/8 HC and 5/8 sarcoidosis, compared to 4/8 myositis (2 anti-Jo1+ and 2 anti-Jo1-). Our results demonstrated the presence of a factor in BAL with high binding capacity for HisRS and HisRS complexed with anti-HisRS-N-terminal antibody. C1q-binding immune complexes (IC) containing HisRS were not the binding factor. However, anti-Jo1 isotypes as well as anti-Ro52 IgG were identified in both BAL (5/8 patients were positive for anti-Jo1 IgG, 3/8 for anti-Jo1 IgA, 3/8 for anti-Jo1 IgM and 4/8 for anti-Ro52 IgG) and sera (5/8 for anti-Jo1 IgG, 3/8 for anti-Jo1 IgA, 4/8 for anti-Jo1 IgM and 3/8 for anti-Ro52 IgG) from patients with myositis. Furthermore, a positive correlation between the presence of anti-Jo1 IgG and anti-Ro52 IgG in BAL was identified ($r^2$=0,881; p=0,007).
**Conclusions:** HisRS was detected both in blood and BAL fluid. The identification of extracellular HisRS, anti-Jo1 isotypes and anti-Ro52 in myositis BAL may provide additional clues for the development of autoimmunity in the lungs.
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## SAT0190 HISTOLOGICAL STUDY ON THE EXPRESSION OF TRANSCRIPTIONAL INTERMEDIARY FACTOR 1 (TIF 1) IN THE PATIENTS WITH INFLAMMATORY MYOPATHIES

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**Background:** Myositis-specific antibodies in patients with inflammatory myopathies are known to be associated with various clinical manifestations, classifications and diagnosis. Among them, recently found anti-transcriptional intermediary factor 1 (TIF1) α, β, or γ antibodies, has been reported to be associated with dermatomyositis (DM) accompanied by cancer.
**Objectives:** Although previous studies have evaluated the association of the antibodies in serum and clinical subtypes, the information about the target antigen is insufficient. The purpose of this study was to confirm the overexpression of TIF1s in the muscle and skin tissues of patients with inflammatory myopathies.
**Methods:** From February 2004 to November 2014, skin and muscle biopsies were performed on 45 patients diagnosed with dermatomyositis and polymyositis. We stained skin and muscle tissue by immunohistochemistry using anti-TIF1α, β, or γ and compared with the results of healthy control. We analyzed the association between the clinical manifestations and protein expression in each tissue.
**Results:** When compared with the control group, any antigens showed no significant overexpression in the muscle. However, TIF1α showed higher positive rate in the skin of DM (12/15 [80%]) than in the skin of healthy control (0/7 [0%]) (p=0.001). TIF1γ expression was higher in the muscle of patients with DM while there was no expression in the muscle of healthy controls (DM, 8/19 [80%] vs. healthy control 0/7 [0%], p=0.039).
In the tissues of inflammatory myopathies, TIF1α and TIF1γ demonstrated higher positive rates in the skin than in the muscle (TIF1α, muscle, 4/35 [11%] vs. skin, 12/15 [80%], p<0.001; TIF1γ, muscle, 10/35 [29%] vs. skin, 13/15 [87%], p<0.001). When analyzing DM patients only, the result was similar (TIF1α, muscle, 1/19 [5%] vs. skin, 12/15 [80%], p<0.001; TIF1γ, muscle, 8/19 [42%] vs. skin, 13/15 [87%], p=0.013). TIF1β showed strong positivity in all tissues of myositis or healthy control.
Analyzing the association with TIF1s expression and cancer, there was no significant difference in the positive rate of TIF1α or γ in the muscle or skin between the myositis patient with or without cancer.
**Conclusions:** TIF1α was expressed more in the skin of DM patients than that in that of control group and TIF1γ in the muscle of DM patients than in that of control. The expression of TIF1α in the skin and TIF1γ in the muscle of cancer associated DM was not higher than those of DM without cancer. Thus the expression levels of TIF1α in the skin and TIF1γ in the muscle may be associated with myositis rather than with cancer.
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## SAT0191 PLATELETS INDUCE THYMIC STROMAL LYMPHOPOIETIN PRODUCTION BY ENDOTHELIAL CELLS: CONTRIBUTION TO HUMAN SYSTEMIC SCLEROSIS FIBROSIS

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**Background:** Systemic sclerosis (SSc) is a complex systemic autoimmune disease characterized by microvascular dysfunction, immune activation and fibrosis affecting the skin and internal organs (1). Improved characterization of the fibrotic mechanisms involved in SSc is a keystone to developing biomarkers and effective disease-modifying therapies. The activation of endothelial cells (ECs) appears very early in the course of the disease, suggesting that chronic fibroblast activation may be at least partly the result of endothelial dysfunction (1,2). However, the ability of the platelet/EC interaction to induce the secretion of factors directly involved in fibroblast activation and subsequent fibrosis in SSc remains uncertain.
**Objectives:** The objective was to provide evidence of a new pathogenic loop implicating activated platelets, microvascular ECs and ECM production in SSc.
**Methods:** A total of 203 SSc patients and 30 healthy donors (HDs) were prospectively enrolled between March 2012 and January 2015 at the University Hospital of Bordeaux. Immunohistochemistry and immunofluorescence analysis were performed on skin biopsy specimens from 18 SSc patients and 5 HDs. Serum TSLP levels were measured (ELISA) in the entire cohort. Human dermal microvascular ECs and fibroblasts were purified from normal and SSc patients skin biopsies. Extracellular matrix production by cultured fibroblasts was assessed by RT-qPCR.
**Results:** Serum TSLP levels were significantly increased in SSc patients compared to HDs (p=0.0005) and were associated with a higher frequency of vascular damage (p=0.02). The proportion of dermal TSLP-positive cells was increased in the skin biopsies of SSc patients compared to HDs (p=0.0008) and was correlated with skin fibrosis (modified Rodnan skin score) (R=0.059, p=0.01). In SSc dermis, TSLP was mainly expressed by CD31-positive ECs. In vitro, activated platelets induced TSLP production by dermal microvascular ECs in an IL1β-dependent manner. Recombinant TSLP in normal fibroblasts reproducibly induced a pro-fibrotic profile as indicated by a significant increase in the collagen/collagenase ratio (p=0.03). Interestingly, this property was shared by fibroblasts purified from non-fibrotic TSLP-negative SSc skin, but lost with fibroblasts purified from TSLP-positive fibrotic skin.
**Conclusions:** Taken together, these results identify dermal microvascular ECs as new contributors to TSLP production in SSc and suggest a potential mechanism by which platelets may profoundly affect the fibrotic process in SSc.
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**Disclosure of Interest:** None declared
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## SAT0192 DECREASED INTERLEUKIN-6/STAT3, BUT INCREASED INTERFERON/STAT1 SIGNALLING IN LYMPHOCYTES OF PATIENTS WITH SYSTEMIC SCLEROSIS (SSC)

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**Background:** Increased interleukin-6 (IL-6) was found in SSc skin, and early studies suggest therapeutic efficacy of IL-6 receptor blockade in SSc. Similarly, an increased interferon (IFN) signature was found in SSc patients. Accordingly, both IL-6 and interferons may be upregulated in SSc, and both act via Stat (signal transducer and activator of transcription) molecules, namely Stat3, and Stat1, respectively.
**Objectives:** To analyze the interleukin-6 (IL-6) receptor-Stat3 axis, as well as Stat1 and phosphorylated Stat1, in lymphocytes of patients with SSc.
**Methods:** PBMC of 30 patients with SSc and 42 healthy individuals (HC) were prepared. CRP, ESR, modified Rodnan skin score (mRSS) and the EULAR activity score were recorded. For determining the percentages of CD126 and CD130 positive cells, PBMC were directly stained with PE-labelled or control antibodies. Ex vivo and after 15 minutes of incubation with or without recombinant human interferon-γ (IFNγ) or interleukin-6 (IL-6), PBMC were fixed with formaldehyde (2%), permeabilized with methanol (80%), and stained with PE-labelled control antibodies or antibodies to Stat1 or phosphorylated Stat1 (pStat1) or pStat3, respectively. Stained cells were immediately analyzed on a Becton Dickinson FACSCalibur fluorocytometer, gating for lymphocytes. As a semiquantitative measure of Stat and pStat contents, mean fluorescence intensity (mfi) was used. Data were expressed as mean±SD.
**Results:** Both chains of the IL-6 receptor, CD126 and CD130, were expressed on decreased percentages of SSc lymphocytes (50.2±18.1% vs. 60.0±7.9%, p=0.0086, and 52.6±15.1% vs. 59.6±9.5%, p=0.0212, respectively). This translated into a diminished increase of pStat3 in SSc lymphocytes upon IL-6 stimulation (Δmfi 17.2±12.1 vs. 20.5±9.3, p=0.03). In contrast, the IFNγ-induced increase in pStat1was more pronounced in SSc lymphocytes (Δmfi 10.5±11.2 vs. 4.8±3.7, p=0.0035), despite their increased Stat1 contents (mfi 51.2±27.4 vs. 16.7±9.1, p<0.0001), thus suggesting activity of the IFN system in SSc. Somewhat unexpectedly, no differences were found between diffuse cutaneous (or anti-topoisomerase positive) and limited cutaneous (or anti-centromere-positive) SSc.
**Conclusions:** In combination of increased Stat1 and Stat1 phosphorylation and decreased IL-6 receptors, our results suggest activity of both the IFN/Stat1 and the IL-6/Stat3 axis in SSc, with a shift towards phosphorylated Stat1.
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SAT0193 **MACROPHAGES RESPONDING TO MECHANICAL STRESS IN SCLERODERMA**

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**Background:** Inflammation, vasculopathy and tissue fibrosis are key features of scleroderma (SSc). While healthy forearm skin which has a Young's modulus of 4–12kPa, SSc fibrotic skin measures 50–80kPa with its increased mechanical stiffness[1]. We have shown that mechano-sensing properties of fibroblasts in SSc are mediated by myocardin-related transcription factor A (MRTF-A)[3]. Monocytes/macrophages are likely to be involved in SSc pathogenesis but the effect of mechanical stress on these cells remain to be elucidated[3,4].
**Objectives:** To investigate if a mechanically-stressed microenvironment like that in SSc tissue, promotes macrophages towards a pathogenic phenotype, and whether MRTF-A is involved in this process.
**Methods:** Control and scleroderma skin sections were immunostained with anti-CD68 and anti-MRTF-A antibodies (n=3). Human PBMC-derived macrophages were cultured in RPMI/M-CSF on 4kPa and 50kPa collagen-fibronectin-coated plates to mimic "soft"/healthy and "stiff"/fibrotic skin, and activated with LPS (10ng/ml) or IL-10 (10ng/ml) for macrophages designated M(LPS) and M(IL-10) (n=4). MRTF-A expression was assessed by qPCR and conditioned media profiled by Luminex array for inflammatory cytokines. Mouse bone marrow-derived macrophages (BMDMs) of wildtype and MRTF-A-null mice were maintained in RPMI/M-CSF on soft and stiff substrates. The data were analysed by two-way ANOVA and Tukey test ($p<0.05$, CI 95%).
**Results:** We observed a greater number of $CD68^+$ macrophages in diffuse SSc skin compared to control skin, mainly around perivascular regions. These macrophages also expressed MRTF-A. Human macrophages expressed MRTF-A mRNA and showed differential cytokine expression when cultured on soft and stiff substrates. M(LPS) on soft matrix expressed IFN-$\gamma$, which was undetectable with M(LPS) on stiff substrate (mean difference 0.2075±0.1576pg/ml, $p<0.01$). LPS- and IL-10 activation on soft substrate increased MCP-3 expression compared to controls (mean difference 68.51±49.19pg/ml, $p<0.01$, 92.88±49.22pg/ml, $p<0.0001$, respectively). M(LPS) on stiff compared to soft substrate showed lower MCP-3 expression (mean difference 57.01±49.22pg/ml, $p<0.05$). M(IL-10) on soft substrate showed higher MCP-1 expression compared to controls (mean difference 2448±2232pg/ml, $p<0.05$). M(IL-10) on stiff substrate decreased expression of MCP-1 (mean difference 2590±2233pg/ml, $p<0.05$) and increased fractalkine levels compared to soft substrate (mean difference 51.22±36.28pg/ml, $p<0.01$). Wildtype BMDMs on stiff compared to soft substrate displayed a more elongated morphology. MRTF-A-null BMDMs remained rounded on stiff substrate.
**Conclusions:** MRTF-A is a mechanical stress-responsive factor which co-activates transcription of cytoskeletal and extracellular matrix-modifying genes. MRTF-A may couple mechanical stress to macrophage activation in SSc, where stiff matrix promotes macrophage secretion of cytokines and growth factors that exacerbate fibrosis.
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SAT0194 **IL-6 SERUM LEVELS AND CORONARY MICROVASCULAR DYSFUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Functional impairment of coronary microcirculation is thought to be a pathway in the development of cardiac involvement in systemic sclerosis (SSc). The underlying mechanism is not fully understood. A reduction of coronary flow reserve (CFR) suggests a coronary microvascular dysfunction (CMD) and predicts adverse outcomes in several cardiovascular diseases. Interleukin-6 (IL-6) is involved in the pathogenesis of SSc and it is a marker of immune activation. High serum levels of IL-6 are correlated with the severity of skin lesions, pulmonary fibrosis and pulmonary hypertension, but the role of IL-6 in the development of cardiomyopathy in SSc is yet not clear.
**Objectives:** To assess the relationship between CFR values and IL-6 serum levels in SSc.
**Methods:** Forty SSc patients (32 female and 8 male, aged 55±11 years), classified according to the 2013 ACR/EULAR criteria, were enrolled. Disease activity was evaluated by EUSTAR score. Twenty-three patients were affected by diffuse cutaneous form and 17 by limited form. All patients had no clinical evidence of heart disease. Coronary flow velocity in the left anterior descending coronary artery was detected by transthoracic Doppler echocardiography at rest and during adenosine infusion. CFR was the ratio of hyperaemic diastolic flow velocity (DFV) to resting DFV. A CFR $\leq$2.5 was considered abnormal and marker of CMD. Serum levels of IL-6 and of cardiac biomarkers (pro-BNP and troponin I) were evaluated in all patients.
**Results:** CFR was reduced in 21 patients (52.5%). The average value was 2.08±0.29. Serum levels of IL-6 (n.v. <2.5 pg/mL), pro-BNP (n.v. <125 ng/L) and troponin I (n.v. <0.0017 $\mu$g/L) were increased respectively in 50%, 45% and 27.5% of cases. No significant correlation between CFR and subsets of SSc was found. Higher EUSTAR score were correlated with reduced CFR (*p=0.037*) and high values of IL-6 (*p=0.002*).
A significant correlation between the increase levels of IL-6 and the reduction of CFR (*p=0.039*) was found.
**Conclusions:** Our results showed that high serum levels of IL-6 are associated with CMD independently from the severity of SSc. A positive correlation between IL-6, EUSTAR score and the impairment of CFR in SSc patients may be suggest an implication of IL-6 in the cardiac pathogenesis of SSc. The evaluation of serum IL-6 might represent a tool for the prediction of CMD, suggesting a role in the increased cardiovascular risk in patients with SSc. Moreover they could open new possibilities for the treatment of SSc cardiomyopathy.
**Disclosure of Interest:** None declared
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## Scleroderma, myositis and related syndromes

SAT0195 **EARLY NAILFOLD CAPILLAROSCOPIC PATTERN PREDOMINATES IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE**

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**Background:** Mixed connective tissue disease (MCTD) is a rare connective tissue disease with clinical picture consisted of multiple organ manifestations, including skin changes resembling systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and/or dermatomyositis (DM). On the background of these manifestations are microvascular changes - alteration of endothelial function and impairment of endothelial progenitor cells. The most prevalent clinical manifestation is Raynaud's phenomenon, which is only partly caused by functional narrowing of small vessels. Nailfold capillaroscopy (NFC) is widely used as a simple, non-invasive technique for investigating microvascular involvement in rheumatic diseases[1].
**Objectives:** To describe the course of skin changes in MCTD and its relation to nailfold capillaroscopy patterns.
**Methods:** We analyzed clinical picture and nailfold capillaroscopy patterns (NFC) in 79 patients (pts) with MCTD recognized according to Kasukawa criteria. Clinical data achieved on the day of examination were compared with the data from beginning of the disease collected retrospectively. NFC was performed on the day of examination and analysed by one investigator. NFC changes were classified according to phases of NFC changes by Cutolo[2] as early, active or late pattern.
**Results:** Median of MCTD pts age was 44 (18–67) years, median of disease duration - 117,6 months (min-max: 10–420). A Raynaud's phenomenon was observed in 75 (94,9%) pts with similar frequency at disease onset and in follow-up. Skin changes were present in 64 (81%) pts, involving 22% SLE-like, 27% SSc-like, 32% SLE and SSc-like, and 1% DM-like phenotype. Totally NFC changes were observed in 55 (69,6%) pts. Majority of changes were in the spectrum of early pattern - 41 (51,9%) pts, active and late pattern were observed in 8 (10,1%) and 6 (7,6%) pts, respectively. No abnormalities were observed in 24 (30,4%) pts. According to skin changes phenotype, NFC changes were observed in 37, (86%) pts with SLE-like and in 32 (66,6%) pts with SSc-like. In pts with both main types of skin changes early pattern of NFC picture predominated. SLE-like early pattern was seen in 21 (48,8%) pts, active in 5 (11,6%) and late in 5 (11,6%) pts; SSc-like early pattern was present in 21 (43,8%) pts, active in 6 pts (12,5%) and late in 5 (10,4%) pts. We did not find any correlation between NFC pattern and any clinical and serological features.
**Conclusions:** Capillaroscopy abnormalities are independent feature from the skin manifestations in MCTD. In all patients changes of early pattern predominate, even if the phenotype is SSc-like. Meanwhile, opposite to systemic sclerosis, they did not correlate with severity of organ involvement or type of skin changes.
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**Disclosure of Interest:** None declared
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## SAT0196 IMPRESS 2 (INTERNATIONAL MULTICENTRIC PROSPECTIVE STUDY ON PREGNANCY IN SYSTEMIC SCLEROSIS). PROSPECTIVE, CASE-CONTROL STUDY OF PREGNANCY IN SYSTEMIC SCLEROSIS

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**Background:** Data on pregnancy in Systemic Sclerosis (SSc) are limited;we recently published IMPRESS,a retrospective multicenter study that compared 109 pregnancies from 99 SSc women with a general obstetric population (GOP).In SSc women preterm deliveries (PD, < W37: 25% vs.12%) and severe preterm deliveries (SPD,< W34: 10% vs. 5%),intrauterine growth restriction (IUGR, 6% vs. 1%) and very-low-birth-weight babies (VLBW, 5% vs. 1%) were significantly more frequent than GOP.Multivariable analysis found that corticosteroid use was associated with PD,while folic acid and anti-Scl70+ was protective.The disease remained stable in most SSc patients,but there were 4 cases of progression within 1 year from delivery

**Methods:** This is a fully prospective,multicenter case-control study of 3 groups of people: 1) 100 pregnant SSc patients, 2) 200 not-pregnant SSc women (matched for age, auto-antibody pattern, limited/diffuse/sine scleroderma – L/D/S – form and obstetric history), 3) 200 healthy pregnant women (matched for age and obstetric history).We will prospectively investigate disease activity during pregnancy and further year,pregnancy outcome and children health status at birth and at 1 year

**Results:** 39 pregnancies are currently ongoing,22 patients have already delivered:8 ACA+ (6 L,1 D,1 S),13 Scl70+ (7 L,4 D, 2 S),1 RNA-P3+ D, 2 L form without SSc-specific autoantibodies.We observed 4 miscarriages (1 ACA+, 2 Scl70+,1 RNA-P3+), 1 therapeutic abortion at W22 (ACA+ D in treatment with prednisone 15mg/d and cyclophosphamide),1 early voluntary termination,2 SPD in Scl70+ L (1 cesarean section at W30, due to IUGR and fetal heart rate alteration;1 spontaneous in twin pregnancy: one twin with VLBW and both of them with respiratory distress at birth), 2 PD (both of them in SCl70+ L disease at W 36), 1 pre-eclampsia at W 37 in Scl70+ limited disease, with pulmonary embolism during post-partum.

Till now,16 mothers and 28 SSc controls had completed one year surveillance after delivery.We observed disease progression in two cases: the ACA+D patient treated with prednisone and cyclophosphamide who underwent therapeutic abortion showed a kidney function worsening till hemodyalisis;the Scl70+L patient who underwent twin pregnancy showed significant worsening in pulmonary function testing,without specific findings at chest CT.

One child,born at W36 from Scl70+L mother, died at 3 months due to cardiac malformation and aesopaghus atresia;all other children showed a regular growth at 12 months pediatric evaluation

**Conclusions:** IMPRESS 2 is still going on,and we hope to answer to important questions: 1) are complications of SSc more frequent during pregnancy? 2) Are some autoantibodies protective for prematurity? 3) Which is the impact of prematurity on children development?

**Disclosure of Interest:** None declared

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## SAT0197 CAPILLAROSCOPY AND MACROVASCULAR DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Different studies and meta-analysis have shown that subclinical atherosclerosis (AS) and vascular complications (VC) are higher in patients with Systemic Sclerosis (SSc) than in healthy population. However, the relationship between macrovascular damage and microvascular affection has not been adequately studied by specific techniques such as capillaroscopy.

**Objectives:** To explore the possible relation between several macrovascular disease variables (carotid doppler ultrasound, ankle-brachial index [ABI]) and capillaroscopy findings in patients with SSc.

**Methods:** Transverse descriptive study with analytical components. Study population: a cohort of 115 patients with SSc controlled in the Rheumatology Department of a tertiary hospital. Variables: 1) *clinical variables*; 2) *capillaroscopy study:* findings of scleroderma pattern (megacapillaries, haemorrhages and avascular areas) and classification of evolving patterns according to Cutolo et. Al.; 3) *vascular study:* ankle-brachial index (ABI) and carotid doppler ultrasound (ESAOTE MyLab XV70, 7–12 MHz linear transducer, software $^{RF}$QIMT) measuring intima-media thickness (IMT) and presence of atheroma plaques (Mannheim Consensus). A vascular surgeon measured ABI and the capillaroscopy and carotid doppler ultrasound were done by a highly experienced rheumatologist, blind to the rest of findings, in a term of 3 months after the initial evaluation. Statistical analysis: IBM-SPSS Statistics v22.0 package.

**Results:** 115 patients where included consecutively, of which 108 were studied; with a mean age of 60,16 years (SD ±15.16); 99 women (91.7%) and 9 men (8.3%). Mean SSc evolution was 11.45 years (S*D* ±8.84). LSSc was most frequently diagnosed (50%), followed by SSc without scleroderma (18.5%) and, decreasingly, DSSc (16.7%), overlap syndrome (9.3%) and pre-SSc (5.6%). The mean right side IMT was 0,579 mm (S*D* ± 0,126), and the left side 0,657 mm (SD ± 0,158); 33,3% had atheroma plaques. In total, 37% had a pathological carotid ultrasound, and 39,8% had macrovascular damage (atheroma plaque and/or IMT >0,9 mm and/or ABI<0,9). In the capillaroscopy study, megacapillaries, haemorrhages and avascular areas were found in a 82,4%, 74,1% and 56,5% of patients, respectively. When re-classifying the findings according to Cutolo et al, 31,5% of patients showed an early pattern, 37% an active pattern and a 22,2% a late SSc pattern.

In the bivariate analysis, the existence of macrovascular affection showed an association with a capillary pattern with more avascular areas and fewer megacapillaries. Statistically, this association was significant between the presence of avascular areas and the macrovascular damage ($\chi^2$=4,412; *p*-value = 0,036) and the pathological carotid ultrasound ($\chi^2$=4,107; *p*-value = 0,043) variables. A tendency towards an association between these last two macrovascular variables and capillaroscopy patterns of major microvascular damage was seen.

**Conclusions:** Nailfold capillaroscopy might be a useful tool to predict the presence of AS and macro vascular damage in patients with SSc.

**Disclosure of Interest:** None declared

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## SAT0198 THE DESSCIPHER PROJECT IN SYSTEMIC SCLEROSIS (SSC): OBSERVATIONAL DATA ON DIGITAL ULCERS (DU) PREVENTION FROM THE EUSTAR GROUP

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**Background:** In SSc, the management of DU is a problem in clinical practice, therefore their prevention is highly warranted. Sildenafil, iloprost, calcium channel blockers (CCB), ACE inhibitors (ACEi) and bosentan, alone or in combination, are used for DU prevention without unanimous agreement.

**Objectives:** DeSScipher ("to decipher the optimal management of SSc") is an EC-funded FP7 research project that consists of five observational trials (OT) addressing different aspects of SSc. The aim of OT1 was to evaluate the efficacy of vasoactive and vasodilating drugs or a combination therapy for the management of DU in SSc.

**Methods:** Longitudinal data were collected for up to 24 months by 28 DeSScipher centres. In SSc patients, the efficacy of sildenafil, bosentan, sildenafil+bosentan, iloprost or CCB /ACEi for the prevention of new DU was evaluated. Clinical features, ulcer type and other drugs were also recorded. Time without new DU, proportion of patients without new DU, risk of developing new DU and the mean number of new DU per patient were evaluated at 6 months follow-up.

**Results:** In OT1, 1394 patients were enrolled. The history of DU was a significant risk factor for developing new DU (OR=3.146; (95%CI:1.19–8.31), p=0.021), therefore analysis was focused on secondary prevention (prevention of new DU in patients with DU history). 473/1394 (33.9%) had a history of DU and 268/473 (56.7%) had follow up data (58.2% limited and 41.8% diffuse SSc subset). 47/268 (17.5%) were on Bosentan, 33/268 (12.3%) on Sildenafil, 40/268 (14.9%) on Iloprost, 31/268 (11.6%) on Sildenafil and Bosentan combination and 117/268 (43.7%) on CCB/ACEi alone. In patients with history of DU in the last 24 weeks, the treatment with CCB/ACEi alone was associated with 7 fold increased risk of developing new DU compared to all other treatment arms (OR =7.313; 95%CI:1.248–42.85, p=0.027). Patients on concomitant immunosuppressive treatment had a trend towards faster DU recurrence.

**Conclusions:** History of DU in the past 24 weeks should prompt a more

aggressive preventive strategy other than therapy with CCB/ACEi alone due to its lower efficacy to prevent DU recurrence compared to the other treatment options.
**Acknowledgement:** The DeSScipher project was funded by the European Community's Framework Programme 7 (FP7-HEALTH-2012.2.4.4–2 - Observational trials in rare diseases) under grant agreement N° 305495.
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## SAT0199 NMR-BASED METABOLOMIC ANALYSIS FOR THE DIAGNOSIS OF SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a complex multi-organ autoimmune disease that is caused by inflammation, vasculopathy and fibrosis. Clinical heterogeneity, unpredictable course, high mortality and resistance to treatment make physicians still frustrated. Recently, there are unmet needs of useful biomarkers for diagnosis, disease activity and severity of SSc. Metabolomics is expected to be a useful tool for the identification of biomarkers and new therapeutic targets. Several researchers have applied metabolomics to autoimmune diseases such as systemic lupus erythematosus, and rheumatoid arthritis.
**Objectives:** To identify the biomarker candidates for the diagnosis of SSc using metabolomic analysis.
**Methods:** Fifty-five patients (48 females (87%); mean age 59.30 ± 11.44 years; disease duration 6.92 ± 4.36 years; 11 diffuse cutaneous SSc, 44 limited cutaneous SSc) and thirty age, gender matched healthy controls (HCs) were enrolled. Serum samples after 8 h of fasting were stored at -80° and analysed using nuclear magnetic resonance (NMR)-based metabolomics.
**Results:** Multivariate analysis showed metabolic differences between SSc and HCs using partial least squares discrimination analysis (PLS-DA: $R^2Y$=0.654, $Q^2$=0.482) and orthogonal partial least squares discrimination analysis (OPLS-DA: $R^2Y$=0.83, $Q^2$=0.674) (Figure 1). We identified nine discriminatory metabolites ($p$<0.05): isopropanol, lactate, 2-oxoisocaproate, glucose, and formate were increased and pyruvate, glutamate, methylguanidine, and methanol were decreased in SSc compared with those in the HCs. Using these metabolites for diagnosis of SSc, sensitivity was 96.36% and specificity was 80% by Leave-one-out analysis.

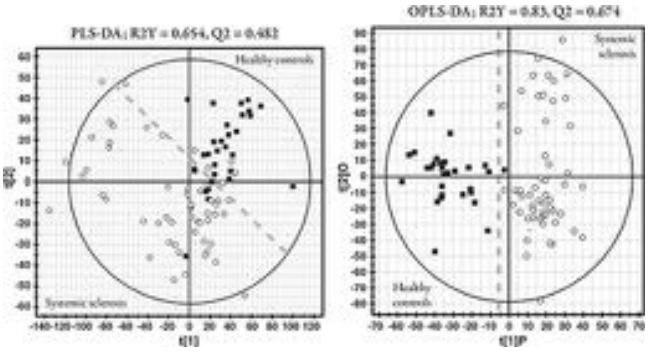



Figure 1. PLS-DA and OPLS-DA plots based on NMR analysis of systemic sclerosis (white dots) and healthy controls (black square). PLS-DA: partial least squares discrimination analysis, OPLS-DA: orthogonal partial least squares discrimination analysis.

**Conclusions:** There are considerable differences in the serum metabolomic characteristics between SSc and HCs. We expect that metabolomic analysis can be a useful tool for identification of potential diagnostic biomarkers of SSc.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3126

## SAT0200 SERUM BIOMARKERS OF COLLAGEN TURNOVER IN EARLY AND LATE DIFFUSE SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is characterized by vascular damage and excessive collagen deposition in the skin and internal organs. The excessive collagen deposition results from accelerated turnover, both formation and degradation, contributing to release of extracellular matrix (ECM) fragments to the circulation, where they may be quantified as biomarkers. Skin is rich in type I and III collagen, while type IV, V and VI collagen are present in a lesser amount. Thus, the turnover of these collagens is potentially altered in SSc.
**Objectives:** The objective was to investigate the level of collagen (type, I, III, IV, V and VI) turnover in early and late stage diffuse SSc patients compared to healthy controls (HC).
**Methods:** Diffuse SSc patients (n=40) were included together with HC (n=20). Twenty patients were early diffuse (<2 years of SSc symptoms) and twenty were late diffuse (>10 years of disease with stable skin for at least six months), all without progressive lung disease. Biomarkers of type I, III, IV, V and VI collagen formation (P1NP, Pro-C3, P4NP7S, Pro-C5 and Pro-C6, respectively) and type I, III, IV and VI collagen degradation (C1M, C3M, C3A, C4M2 and C6M, respectively) were assessed in serum. Statistical differences between the groups were tested by Kruskal-Wallis test with Dunn's multiple comparisons test. The potential discrimination capacity of these biomarkers were analysed by receiver operating characteristics (ROC) area under the curve (AUC) on HC, SSc, early and late diffuse SSc versus each other.
**Results:** In early diffuse SSc Pro-C3, P4NP7S, Pro-C5 and Pro-C6 ($p$<0.0001) levels were significantly increased compared to HC (figure). In late diffuse SSc compared to HC a significant increase in P4NP7S (p=0.005) and Pro-6 (p=0.006) levels were observed. Contrary, P1NP was significantly decreased in both early (p=0.016) and late (p=0.002) diffuse SSc compared to HC. Moreover, a significant increase in Pro-C3 (p=0.0006), Pro-C5 (p=0.003) and Pro-C6 (p=0.0043) levels were detected in early diffuse SSc compared to late diffuse SSc.
The degradation biomarkers were significantly increased in early SSc compared to HC (C1M, C4M2 and C6M: $p$<0.0001, C3M: p=0.001 and C3A: p=0.02). Increased levels were found in late diffuse SSc compared to HC in C3M (p=0.02), C3A (p=0.006), C4M2 (p=0.005) and C6M (p=0.003). A significant difference

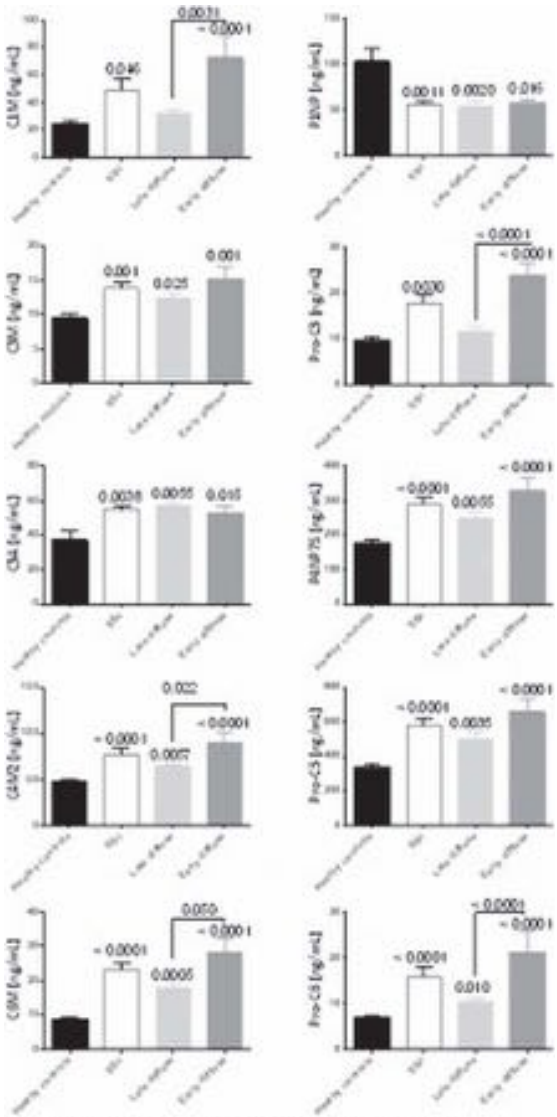


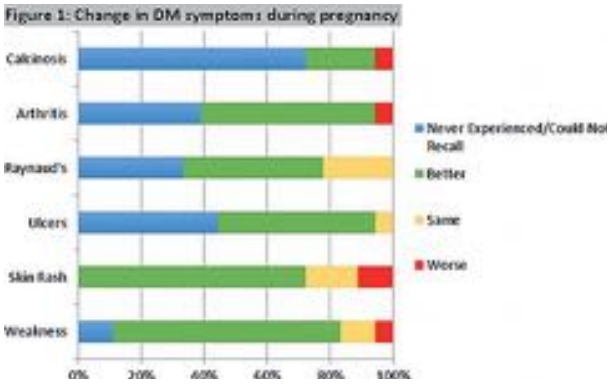
**Figure: Mean level of collagen turnover biomarker in healthy controls, diffuse SSc patients.** Kruskal-Wallis test with Dunn's multiple comparisons test was used to test differences between groups. Statistical significance was considered when p<0.05.

between early and late diffuse SSc was also observed for C1M (p=0.02), C4M (p=0.022) and C6M (p=0.05).
The best predictive value was found for Pro-C6 and C6M with AUC values of 0.92 and 0.93 for HC vs. SSc, 0.94 and 0.99 for HC vs. early diffuse, and 0.91 and 0.87 for HC vs. late diffuse, respectively. Pro-C6 had an AUC of 0.88 for early vs. late diffuse. In addition, C4M2, Pro-C3, P4NP7S and Pro C5 all had AUC values of more than 0.90 when assessing HC vs. early diffuse.
**Conclusions:** This pilot study showed that collagen turnover appears to be significantly different between HC and SSc, as well as between early and late stage diffuse patients. The discriminatory power of these biomarkers was high, especially C6M and Pro-C6. These data suggest that serological assessment of ECM turnover could be relevant in SSc, and offers an area of investigation of the pathogenesis.
**Disclosure of Interest:** P. Juhl: None declared, R. Domsic: None declared, A.-C. Bay-Jensen: None declared, M. Karsdal: None declared, A. Siebuhr: None declared, N. Franchimont Shareholder of: Biogen, Employee of: Biogen, J. Chavez Shareholder of: Biogen, Employee of: Biogen
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## SAT0201 DERMATOMYOSITIS AND PREGNANCY: ASSESSMENT OF DISEASE ACTIVITY AND PREGNANCY OUTCOMES COMPLICATED BY MATERNAL DERMATOMYOSITIS

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**Background:** The effect of pregnancy on Dermatomyositis (DM) disease activity and on maternal and fetal outcomes in patients with DM is unclear[1,2].
**Objectives:** Evaluate disease activity and pregnancy outcomes complicated by maternal dermatomyositis.
**Methods:** A total of 10 patients with 21 pregnancies from a cohort of 438 DM patients of child-bearing potential, diagnosed between 2006 and 2015 from two centers, were eligible for interview with a specific questionnaire regarding pregnancy and fetal outcomes.
**Results:** Weakness, rash and arthritis were the most common clinical symptoms that improved during pregnancy in affected patients (Figure 1). In 16 out of 18 pregnancies, patients experienced weakness. Weakness improved during 13 pregnancies (81.3%), stayed the same during 2 pregnancies (12.5%), and worsened during one (6.3%). All 10 patients experienced cutaneous rash during all 18 pregnancies carried to live birth. Cutaneous rash improved during 13 pregnancies (72.2%), remain unchanged during 3 (16.7%), and worsened during 2 (11.1%). Five patients experienced arthralgias or arthritis in a total of 11 pregnancies. Symptoms improved during 10 of these pregnancies (91%) and worsened during one (9%).There were no cases of interstitial lung disease, cancer or antiphospholipid antibody syndrome among the 10 patients studied. One patient suffered from pre-eclampsia while diagnosed with DM. 3 total pregnancy losses: two early miscarriages (<10 weeks gestation) one therapeutic abortion for an ectopic pregnancy. 3 neonates out of 18 live births went to the NICU after delivery – reasons for transfer: meconium aspiration; apnea and pre-term birth.




**Conclusions:** Pregnancy does not appear to carry a worse prognosis for DM patients and all but one of our patients experienced improvement in clinical symptoms during pregnancy.
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**Disclosure of Interest:** None declared
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## SAT0202 NAILFOLD MICROANGIOPATHY EXTENT AND CHOROIDAL VASCULAR THICKNESS EVALUATED BY NAILFOLD VIDEOCAPILLAROSCOPY AND OPTICAL COHERENCE TOMOGRAPHY IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Systemic sclerosis (SSc) is a connective tissue disease characterized by progressive microvascular involvement (1). Nailfold videocapillaroscopy (NVC) represents the best and safest method to detect and to follow the progression of morphological microvascular SSc abnormalities (2). Microvascular alterations in SSc are observed in several organs, including the choroidal plexus of the eye (3). Modern optical coherence tomography (OCT) imaging and analysis have allowed the choroid to become observable and measurable (4). An overall thinning of choroidal layer has been observed in SSc patients consistent with an impairment of choroidal perfusion; the process becomes progressively more severe and extensive in overt SSc (5).
**Objectives:** To compare severity of nailfold microvascular damage with the choroidal thickness, as assessed by NVC and OCT. To evaluate OCT plausibility in SSc staging.
**Methods:** Twelve SSc patients according to recent ACR/EULAR classification criteria (6) (disease duration 4.8 ± 2.8 years, age 58±13 years) underwent NVC (4 "early", 3 "active", 5 "late" scleroderma NVC pattern) and ophthalmologic examination by OCT. NVC patterns were scored by quantitative rating scale and the "microangiopathy evolution score (MES)" was calculated (7). OCT images were recorded by 3D-2000 OCT using protocol "line" that averages 50 B-scans and generates a horizontal 6 mm line. Choroidal thickness area measurements were performed manually using image J software. Statistical analysis was performed by non parametric tests.
**Results:** Despite the limited number of enrolled SSc patients, a statistically significant negative correlation was observed between the progressive severity of the microvascular damage score (MES) and the choroidal thickness values (OCT) (r=-0.39, p=0.05).
**Conclusions:** Nailfold microangiopathy evolution, as evaluated by NVC in SSc patients, seems to correlate with the choroid thickness, as assessed by OCT. Microangiopathy progression seems to involve the choroidal plexus by showing a thinner layer thickness in SSc patients. Therefore, OCT may be useful in the evaluation of possible retinal microvascularization damage in SSc patients.
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**Disclosure of Interest:** None declared
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## SAT0203 RITUXIMAB IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

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**Background:** Interstitial lung disease (ILD) is the most common internal organ manifestation of idiopathic inflammatory myopathies (IIM) that can severely affect the course of the disease. IIM patients with ILD often show resistance to conventional treatment with glucocorticoids (GC) and cytotoxic drugs so addition of biologic agents is an interesting possibility.
**Objectives:** To assess efficacy and tolerability of rituximab (RTM) in IIM patients with ILD.
**Methods:** IIM patients fulfilling Bohan and Peter criteria and having ILD were followed up in the Nasonova Research Institute of Rheumatology from 2009 to 2015. RTM was administered in case of intolerance or inadequate response to GC and other immunosuppressive drugs. Manual muscle testing (MMT), dyspnea assessment according to NYHA, creatinkinase (CK) and anti-Jo-1 antibodies (anti-Jo-1) assay; forced vital capacity (FVC) and carbon monoxide diffusion capacity (DLCO) evaluation as well as high-resolution computed tomography (HRCT) scanning of the chest were performed at baseline, 6–12 and 18–24 months after inclusion.
**Results:** 41 patients (34 females, 7 males) with median age 50 [44;56], median disease duration 24 months [7;108] were included. 28 from them had decreased MMT value and class 1–2 NYHA dyspnea was present in 19. 18 patients were positive for anti-Jo-1 and 15 had elevated CK level. HRCT showed ILD signs

including ground glass opacities (GGO) in all cases. FVC<80% was revealed in 16 and DLCO<80% - in 32 cases. All patients received GC 10–90 mg/day equivalent to prednisolone, 28 were treated with immunosuppressive agents (cyclophosphamide or mycophenolate mofetil). Patients received RTM courses consisted from 2 infusions of RTM 1000 or 500 mg at days 0 and 14. 1 RTM course was provided in 13, 2 – in 10, 3 – in 11, 4 – in 2, 5 – in 2, and 8 – in 3 patients. The follow up lasted for at least 12 months in 33, and for at least 24 months – in 15 patients. Dyspnea subsided and CK level decreased to normal values in all patients within 6–12 months after the first RTM infusion. 16 patients improved FVC by >10%, and 7 demonstrated DLCO increase by >10%. Worsening of pulmonary function tests was documented in 2 cases, while in the rest they were stable. After 18–24 months of follow up FVC remained +10% better vs baseline value in 10, DLCO – in 8 patients. In the rest patients these parameters remained stable. ILD was not progressing in 27 patients based on HRCT images in 6–12 months, moreover GGO lesions count was reduced in 10 patients, but there were cases of ILD worsening documented in 6 patients. Although, HRCT monitoring in 18–24 months showed ILD improvement in 7 patients and worsening – in 2, in remaining patients ILD was stable. Comorbid infections were documented in 18 patients, commonly manifesting in 2–3 months after the first RTM infusion.

**Conclusions:** RTM treatment allows to achieve stable disease without typical for this condition further progression of pulmonary lesions in the majority of IIM patients with ILD.

**Disclosure of Interest:** None declared

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## SAT0204 THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) SCORE – A NEW PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SYSTEMIC SCLEROSIS UNDER DEVELOPMENT

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**Background:** Patient reported outcome measures (PROM) are required as key outcomes in disease modifying therapeutic trials in systemic sclerosis (SSc) and could also improve the clinical care of patients with SSc. A PROM tool for clinical trials and practice in SSc, covering the different features of this multi-organ autoimmune disease, is lacking.

**Objectives:** To develop and validate a brief, disease-specific, patient-derived, composite disease impact score for scientific and clinical use in SSc.

**Methods:** This multi-center project involves SSc patients and experts from 11 European countries. Firstly, using the nominal group technique, patients with SSc selected the health dimensions where the disease has the most significant impact. The dimensions were subsequently given numeric priority by an international group of SSc patients. The dimensions with the top 10 median ranks, as ranked by the patients, were used to construct the ScleroID questionnaire using numeric rating scales. Further, the dimensions are currently weighted by distributing 100 points among the dimensions by a larger cohort of patients from all participating countries. The calculation of the score will be based on the ranking of the weights.

**Results:** 24 SSc patients selected 17 health dimensions in the nominal group exercise. The prioritization cohort included 108 SSc patients from 11 centers (female:male 82:25, limited:diffuse SSc subset 53:54). The top 10 health dimensions which were ranked most relevant by the patients were Raynaud's phenomenon, hand function, upper and lower gastrointestinal tract symptoms, pain, fatigue, limitation of life choices and activities, body mobility, breathlessness and digital ulcers (Figure 1).

**Conclusions:** The EULAR ScleroID score is a novel tool under development designed for use in clinical practice and clinical trials to display the disease impact of SSc. Further validation of this new instrument will be performed as soon as the weighting procedure is completed.

**Acknowledgement:** Contributing patients: Yanne Perriault, Susanne Tuppeck, Helene Kambourakis, Elisabeth Scheel, Stephan Houbertz, Anna Vegh, Beata Garay Toth, Barbara Zappitello, Grazia Tassini, Silvia Sandulescu, Ana Marcela Badea, Stefana Dumitru, Rachida Amrouch, Alicia García Oliva, Begoña María Gorricho Corta, Heleen Lever, Johanna Berglind, Mervat Gaafar, Natalie Perruchoud, Alice Martins Correia, Richard Dodds, Nicola Whitehill.

Figure 1. Results of the prioritization of the health dimensions' (N=108).

| No. | Health dimensions | Mean rank | Median rank | Order by median rank | %Patients giving rank 1 to the dimension | %Patients giving rank 1-3 to the dimension | %Patients giving rank 1-10 to the dimension |
|---|---|---|---|---|---|---|---|
| 1 | Raynaud | 5,78 | 5 | 1 | 19,4 | 36,1 | 84,3 |
| 2 | Hand function | 6,65 | 5 | 1 | 8,3 | 25 | 78,7 |
| 3 | Upper GI | 7,16 | 6 | 2 | 7,4 | 24,1 | 73,1 |
| 4 | Pain | 6,94 | 6 | 2 | 10,2 | 25,9 | 75,9 |
| 5 | Fatigue | 6,67 | 6 | 2 | 9,3 | 26,9 | 78,7 |
| 6 | Lower GI | 7,82 | 7 | 3 | 10,2 | 24,1 | 69,4 |
| 7 | Limitation of life choices and activities | 8,34 | 8 | 4 | 4,6 | 20,4 | 66,7 |
| 8 | Body mobility | 8,71 | 8,5 | 5 | 2,8 | 11 | 65,7 |
| 9 | Breathlessness | 8,57 | 9 | 6 | 12 | 27,8 | 52,8 |
| 10 | Digital ulcers | 9,45 | 10 | 7 | 1,9 | 17,6 | 54,6 |
| 11 | Anxiety | 10,18 | 10 | 7 | 2,8 | 9,3 | 50,9 |
| 12 | Dryness | 10,13 | 10 | 7 | 1,9 | 9,3 | 54,6 |
| 13 | Appearance | 10,31 | 11 | 8 | 3,7 | 9,3 | 49,1 |
| 14 | Concentration difficulties | 10,87 | 12 | 9 | 1,9 | 9,3 | 39,8 |
| 15 | Cough | 11,26 | 13 | 10 | 1,9 | 10,2 | 38,9 |
| 16 | Depression | 11,63 | 13 | 10 | 0,9 | 7,4 | 35,2 |
| 17 | Calcinosis | 12,52 | 14 | 11 | 0,9 | 6,5 | 31,5 |

'Patients were asked to rank the dimensions in order of their importance by giving a rank from 1(most important) to 17 (least important). Each rank could only be used once. The top 10 dimensions with the lowest median rank (highest importance) were selected for the questionnaire. The 10th dimension had an equal median rank but clearly higher role for more patients (% giving top rank, last 2 columns) and was consequently chosen in favor of dimensions 11,12.
Abbreviations: No, number; GI, gastrointestinal.

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## SAT0205 ULTRASONOGRAPHIC FEATURES OF THE HANDS IN PATIENTS WITH SYSTEMIC SCLEROSIS REFLECT VISCERAL MANIFESTATIONS OF THE DISEASE

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**Background:** In a recent EUSTAR study, joint synovitis and tendon friction rubs reflecting fibrotic tenosynovitis (fTS) have proven to be independent predictive factors for disease progression in patients with early systemic sclerosis (SSc). Power Doppler Ultrasonography (PDUS) of the hand can detect early asymptomatic joint synovitis or fTS and is a reliable tool to perform a vascular evaluation of the hand, especially to assess ulnar artery involvement.

**Objectives:** The objective of this study is to determine whether joint synovitis, fTS and ulnar artery occlusion (UAO) assessed by PDUS of the hand are associated with visceral manifestations of SSc and can thus be considered as severity markers of the disease.

**Methods:** 47 systemic sclerosis patients matching the 2013 EULAR/ACR classification criteria of SSc were consecutively included in this observational transversal study. Patients were also classified using 2008 LeRoy classification subsets. A bilateral US evaluation of both hands of every patients was performed assessing the presence of active synovitis, fTS or UAO. PDUS features were confronted to the visceral manifestations of the disease assessed by the annual standard investigations: pulmonary function tests (PFTs), thoracic CT-scan, echocardiographic evaluation. A right heart catheterization (RHC) was conducted if pulmonary arterial hypertension (PAH) was suspected based on the results of the previous tests. PDUS of the hand was performed blinded for the results of visceral investigations.

**Results:** A fibrotic TS was present in 17% of the patients. fTS was associated with an interstitial lung disease on CT-scan and a diffuse cutaneous involvement (respectively p=0,023; Odds ratio (OR)=10,06; 95% confidence interval (1,13–89,94) and p=0,018; OR=11,2; 95%CI (1,125–100,31). An active synovitis was present in 14,9% of the patients and was associated with pericarditis on the echocardiographic evaluation (p=0,05; OR=15,6; 95%CI (1,19–204,78)). There was a significant association between PAH on RHC and bilateral UAO on PDUS (p=0,008, OR non available because every patient with PAH had a bilateral UAO).

*Table 1.* Associations between PDUS features and visceral manifestations in 47 SSc patients

| Association between Tenosynovitis and fibrotic visceral manifestations | OR (95%CI) | p |
|---|---|---|
| ILD | 10,06 (1,128-89,94) | 0,023 |
| Diffuse cutaneous SSc | 11,20 (1,125-100,31) | 0,018 |
| **Association between active synovitis and inflammatory manifestations** | | |
| Pericarditis | 15,6 (1,189-204,78) | 0,05 |
| **Association between bilateral UAO and PAH** | | |
| PAH suspected on Echocardiography | 1,64 (0,403-6,705) | NS |
| PAH Confirmed on RHC* | NA | 0,008 |
| PAH Confirmed on RHC** | 1,27 (1,004-1,598) | 0,022 |

PDU=Power doppler ultrasonography; DU =Digital Ulcers; UAO=Ulnar Artery Occlusion; FPBF=Finger Pulp Blood Flow; dSSc=Diffuse Systemic Sclerosis; Pulmonary Fibrosis =PF ACA=anticentromere antibodies; NS=not significant; NA=not available Level of significance : p<0,05 . * among patients who had a RHC(n=9) ** among all patients (n=47)

**Conclusions:** The evaluation of the hand by Power Doppler Ultrasonography in SSc provides new evidence that vascular, joint and tendon involvements reflect visceral manifestations of SSc and therefore constitute severity markers of the disease. These results should be completed by prospective studies to determine whether these PDUS features are also independent predictive factors for disease progression, especially in patients with early SSc.

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**Disclosure of Interest:** None declared
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## SAT0206 VASCULAR EVALUATION OF THE HAND BY POWER DOPPLER ULTRASONOGRAPHY PROVIDES NEW PREDICTIVE MARKERS OF ISCHAEMIC DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

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**Background:** The consequences of the macrovascular disease on ischaemic digital ulcers (DUs) onccurence are still to be determined in systemic sclerosis (SSc) patients and power doppler ultrasonography (PDUS) is a simple and non-invasive efficient tool to evaluate ulnar artery and fingers pulp blood-flow (FPBF).
**Objectives:** Our aim was to evaluate in a longitudinal study the relevance of PDUS as a predictive tool of new ischaemic DUs in a cohort of unselected SSc patients.
**Methods:** 55 SSc unselected patients fulfilling the 2013 EULAR classification criteria of SSc underwent PDUS of both hands to evaluate the prevalence of ulnar artery occlusion (UAO) at baseline. Finger pulp blood flow (FPBF) of the third and fourth fingers were also assessed and considered as pathological if a defect of doppler signal on a finger pulp was observed. All patients were clinically re-evaluated 6 and 12 months later and new ischaemic DUs occurrence in the meantime was then retrospectively recorded. Patients were also asked to phone if new DUs occurred between the consultations. The main outcome measure was the first new ischaemic DU occurring after PDUS evaluation, defined as a new loss of epidermis with dermis exposure appearing on a finger pulp during follow-up and unoticed at the time of PDUS evaluation. We did not take into account traumatic and calcinosis related DUs.
**Results:** The mean age was 57,6 years, 76.4% of the patients were women, 64.6% had a limited cutaneous SSc, 34.2% had a history of multiple episodes of DUs.
The prevalence of UAO was 36.3% and was bilateral in 70% of the SSc cases. 56.4% of SSc patients had a pathological FPBF.
UAO and pathological FPBF were both associated with a history of multiple DU episodes (OR=8.98; 95%CI (2.52–32.01); p<0.001 and OR=4.69; 95%CI (1.30–16.93); p=0.014) and with the occurrence of new ischaemic DUs during the follow-up (OR=8.73; 95%CI (2.00–38.16); p=0.005 and OR=12.65; 95%CI (1.50–106.77); p=0.005).
Multivariate analysis revealed an independent association between PDUS parameters and a history of multiple DU episodes at baseline (p<0.05).
Kappa coefficients of inter-rater agreement were 0.94 for the presence of pathological FPBF and 0.97 for the presence of UAO on PDUS images. Kappa coefficients of intra-rater agreement were 0.90 for the presence of pathological FPBF and 0.93 for the presence of UAO.
**Conclusions:** UAO and pathological FPBF are associated with a history of multiple DU episodes and are predictors of new ischaemic DUs in SSc patients. These parameters could therefore be used as prognostic factors and considered in further studies evaluating DUs treatment strategies.



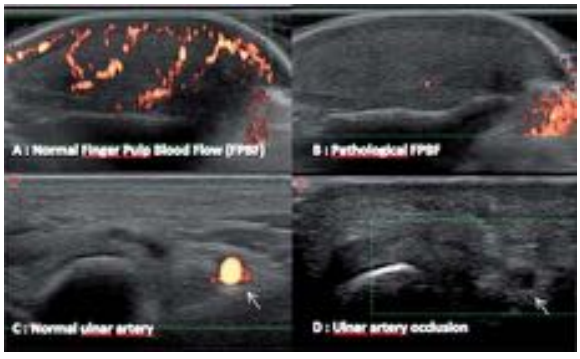

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## SAT0207 ULNAR ARTERY OCCLUSION EVALUATED BY POWER DOPPLER ULTRASONOGRAPHY IS ASSOCIATED WITH ACRO-OSTEOLYSIS IN SYSTEMIC SCLEROSIS

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**Background:** Acro-osteolysis and calcinosis are frequent clinical features in Systemic sclerosis (SSc). These manifestations are thought to have a vascular origin but there is still a lack of evidence to objectively support this hypothesis. Ulnar artery occlusion (UAO) is also a specific and frequent vascular feature in systemic sclerosis and Power Doppler Ultrasonography (PDUS) has proven to be a reliable tool to assess the permeability of the ulnar artery.
**Objectives:** The objective of this study is to determine whether calcinosis and acro-osteolysis (AO) are related to vascular features evaluated by PDUS.
**Methods:** A vascular Power Doppler Ultrasonographic evaluation of both hands and bilateral hand X-rays were systematically performed in 43 patients matching the ACR 2013 classification criteria of SSc. PDUS of both hands was performed to evaluate the prevalence of UAO. Finger pulp blood flow (FPBF) of the third and fourth fingers were also assessed and considered pathological if a defect of the doppler signal on a finger pulp was observed. Radiological assessment of calcinosis and acro-osteolysis was performed blinded for the results on PDUS features.
**Results:** 43 patients were consecutively recruited during a 6-month period. The mean age was 56,6 years, 70% of the patients were women, 44,2% had a limited cutaneous SSc, 37,2% had a history of multiple digital ulcers (DUs).
23 patients had a pathological FPBF (53,5%), 22 had a UAO (51,2). Patients with AO on X-rays were more likely to have a pathological FPBF or UAO (respectively p=0,029, Odds Ratio (OR) =4,36; 95% confidence interval (1,112–17,128) and p=0,002; OR=8,67; 95%CI (1,97–38,41)). There was no association between calcinosis on X-rays and pathological FPBF or UAO (p=0,362 and 0,076 respectively). UAO and FPBF were both associated with classical ischemic manifestations of the disease such as multiple DUs history (p=0,002 and p=0,029). Multivariate logistic regression analysis revealed an independent association between UAO and AO (p=0,003, OR=2,08; 95%CI (1,79–35,74)).
**Conclusions:** A study has recently shown that acro-osteolysis was independently



associated with the late nailfold videocapillaroscopic pattern (Morardet et al. Arthirtis Care Research, jul 2015). These results strengthened the link between this radiographic lesion and digital destructive vasculopathy. Our study reveals an association between UAO or FPBF assessed by PDUS and acro-osteolysis. These results suggest once again a vascular etiology to AO and provides new evidence of the link between micro and macro-vascular damages in SSc.

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## SAT0208 INFLAMMATORY MYOPATHIES ASSOCIATED WITH SJÖGREN'S SYNDROME DO NOT DIFFER FROM THOSE WITHOUT SJÖGREN'S SYNDROME ASIDE FROM OLDER AGE AT DIAGNOSIS AND LESS FREQUENT NORMAL MUSCLE BIOPSY

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**Background:** Prevalence of Sjogren's syndrome (SS) in inflammatory myopathies (IM) and whether IM patients with SS represent a distinct disease subset are currently unknown.
**Objectives:** To assess the signification of SS in IM with regard to phenotype and prognosis.
**Methods:** IM patients with SS (IM-SS group) were identified among a cohort of 270 patients with IM using European-American Consensus Group (EACG) classification criteria. Clinical, serological, muscle pathological features, management and outcomes of IM-SS patients were retrospectively studied and compared to the IM patients who had been assessed for SS but did not fulfill these criteria (IM-noSS group).
**Results:** EACG criteria were available in 63 IM patients of the total cohort and 29 (46%) were diagnosed as having SS. These IM-SS patients were older at IM diagnosis than the 34 IM-noSS patients (56±3.1 vs 47.7±2.8 years, p=0.05), sex ratio wasn't different.
SS was mostly diagnosed at the time of IM diagnosis (n=23, 79%) and less frequently preceded (n=3: 1, 3 and 4 years) or followed (n=3, 3, 6 and 30 years) IM diagnosis. IM-SS patients had subjective sicca syndrome (29/29, 100%) with objective dryness (10/12, 92%), anti-SSA/SSB antibodies (14/29, 48%) and/or focus score $\geq$3 in minor salivary glands biopsy (n=21/24, 88%).
Creatine kinase level was not different between IM-SS and IM-noSS (1400±320 vs 2538±214 UI/L, p=0.5). A normal muscle biopsy was less frequently found in IM-SS than in IM-noSS patient (7/28 vs 1/24 p=0.05). According to the ENMC criteria, DM was the more frequent muscle histological finding in IM-SS patients (n=10, 42%) but all histological patterns were represented (including nonspecific IM: 6 (25%), inclusion body myositis: 4 (17%), polymyositis: 2 (8%), necrotizing myopathy: 1 (4%). This distribution was not different from the IM-noSS group.
IM-SS patients also suffered from interstitial lung disease (n=10, 34%), arthralgia and/or arthrithis (n=17, 59%), skin involvement (n=14 48%) and Raynaud syndrome (n=14, 48%) which occurrence characteristics were not different from IM-noSS group.
Anti-SSA (n=13, 45% vs n=1, 3%, p=0.0001) and anti-SSB (n=6, 21% vs n=0, 0% p<0.01) were more frequent in IM-SS groups. Other auto-antibodies were found in 14 IM-SS patients (48%) and in 19 IM-noSS patients (56%, p=0.62) which specificities were not significantly different between the two groups. Cryoglobulin was also found with a similar frequency in both groups (n=3, 10% vs n=3, 9%; p=1.0). Six IM-SS patients (21%) were diagnosed with cancer versus 4 IM-noSS patients (12%) (p=0.49). Mean number of treatment was not different between the two groups (1.9±0.2951 vs 1.6±0.2616; p=0.41) and after a follow-up >7 years, 6 patients died in both groups, whithout any significant difference in survival (p=0.23).
**Conclusions:** SS is frequently observed in IM. No difference was found between IM-SS and IM-noSS with regards to phenotype, serotype and survival aside from older age at diagnosis and less frequent normal muscle biopsy.

**Disclosure of Interest:** None declared

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## SAT0209 IDIOPATHIC INFLAMMATORY MYOPATHIES: EVALUATION OF SKELETAL MUSCLE GLUCOSE METABOLISM BY PET-CT 18F-FDG

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**Background:** There is a need for tools to measure muscle disease activity in inflammatory myopathies (IM).
**Objectives:** To assess the contribution of metabolic imaging with positron emission tomography combined with computed tomography (PET-CT) 18F fluorodeoxyglucose-(18F-FDG) for muscle disease activity assessment in patients with IM.
**Methods:** The SMGM was higher in IM than in the control group in visual analysis ($p<0.001$) and quantitative analysis ($p<0.001$). No correlation was found between the SMGM and the muscle histological findings. In addition, the quantitative measurement of SMGM was significantly correlated with serum CK levels (Spearman $\rho$=0.47, $p<0.01$) and with the MITAX (Spearman $\rho$=0.72; p=0.001). Finally, in 9 patients who underwent two consecutive 18F-FDG PET-CT, the evolution of the SMGM was concordant with the clinical course according to the MITAX in 8.
**Results:** The SMGM was higher in IM than in the control group in visual analysis ($p<0.001$) and quantitative analysis ($p<0.001$). No correlation was found between the SMGM and the muscle histological findings. In addition, the quantitative measurement of SMGM was significantly correlated with serum CK levels (Spearman $\rho$=0.47, $p<0.01$) and with the MITAX (Spearman $\rho$=0.72; p=0.001). Finally, in 9 patients who underwent two consecutive 18F-FDG PET-CT, the evolution of the SMGM was concordant with the clinical course according to the MITAX in 8.
**Conclusions:** These data suggested that 18F-FDG PET-CT, which is useful for the screening of cancer associated IM, is also helpful for the measurement of IM muscle disease activity.

**Disclosure of Interest:** None declared

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## SAT0210 HIERARCHICAL CLUSTER STUDY OF PATIENTS WITH ANTI-KU ANTIBODIES IDENTIFIES TWO PHENOTYPICAL SUBGROUPS WITH DISTINCT PROGNOSIS RECOGNIZED BY ANTI-DNA STATUS

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**Background:** The presence of anti-Ku antibody is associated with a wide variety of clinical manifestations and various outcomes.
**Objectives:** We attended to refine anti-Ku associated disease by identifying subgroups of Ku-positive patients with similar clinico-biological features and prognosis.
**Methods:** We reviewed clinical, biological characteristics, diagnosis and management of 24 patients with anti-Ku antibody. A multidimensional analyze was performed to highlight homogeneous groups of patients. We search for features that most strongly match with each group.
**Results:** Anti-Ku positive patients had joint (n=19), muscle (n=10), lung (n=9), skin (n=9), renal (n=9), hematological (n=8), thrombotic (n=6), serous (n=6) and gastrointestinal (n=4) involvements. Associated antibodies were anti-DNA (n=7), -SSA (n=6), -RNP (n=4), -SSB (n=1), -Sm (n=1), rheumatoid factor (n=9) and ACPA (n=4). Diagnosis were overlap myositis (n=9), lupus erythematosus (n=8), Sjögren's syndrome (n=7), rheumatoid arthritis (n=3), undifferentiated connective (n=2), and systemic sclerosis (n=2). Many patients had criteria for several connectivite tissue diseases. Managements were heterogeneous.
Multidimensional analyze identified to groups that were mutually exclusive: (i) Patients characterized by scleroderma-like skin disease,myositis and ILD,frequently treated with high dose of corticosteroids, (ii) Patients with lupus like skin disease, haematological and renal involvements frequently receiving cyclophosphamide and mycophenolate mofetil.
Anti-DNA antibody, absent in the first group and present in the second was the most powerful criteria to distinguish these two subsets of the anti-ku associated disease (sensibility 93% and a sensitivity of 86%).
**Conclusions:** Anti-DNA status distinguishes patients at risk of muscle and lung involvement (anti-DNA negative) from patients at risk of renal involvement (anti-DNA positive). These data significantly refine anti-Ku associated disease and help to personalize monitoring and care of the patients.

**Disclosure of Interest:** None declared

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## SAT0211 RELIABILITY, VALIDITY, AND SENSITIVITY TO CHANGE OF THE DURUOZ HAND INDEX IN SYSTEMIC SCLEROSIS*

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**Background:** Hand involvement is observed in almost all patients with Systemic Sclerosis (SSc), and is due to skin and tendon fibrosis, arthritis and microvascular impairment, sometimes complicated with digital ulcers (DUs).
**Objectives:** The Duruoz's Hand Index (DHI) (or Cochin hand functional disability scale), is a reliable tool for hand function assessment and can be used in diseases like rheumatoid arthritis and SSc. The purpose of this study was to assess the reliability, validity and sensitivity to change of the DHI in SSc patients.
**Methods:** 66 patients with SSc according to the 2013 ACR/EULAR criteria, examined in our EUSTAR center from 1.10.2014 to 31.12.2015 were included. Patients completed the DHI, the Scleroderma Health Assessment Questionnaire (SHAQ) questionnaires and the Hand Mobility in Scleroderma (HAMIS) test. Three anthropometric measures to assess finger range of motion were also measured: the finger extension (FE), finger-to-palm distance (FTP) and $\Delta$ FTP (FE - FTP).
*Step 1:* In 38 patients the test-retest reliability, using intra-class correlation coefficients (ICC), and the internal consistency (Cronbach's alpha test) were examined. *Step 2:* In all 66 patients, the criterion validity by correlation coefficients with SHAQ, HAMIS and the anthropometric measures, and the discriminative capacity between different subsets of patients were examined. *Step 3:* 27 consecutive patients had a second evaluation at an interval of (mean±SD) 9.3±2.3 months; among them, only 4 patients had progressive early diffuse SSc. Sensitivity to change was assessed in these patients using the effect size (ES) (Cohen's d) and the standardized response mean (SRM).
**Results:** The study included 59 females/7 males with SSc, age 50.8±13.0 years, disease duration 6.2±6.0 years; 24 with diffuse cutaneous SSc (dcSSc) and 38 with limited cutaneous SSc (lSSc).
The DHI had a mean±SD score of 22.8±19.5, range 0–71 (with possible range 0–90) at baseline, and 24.3±21.1, range 0–73 at follow-up. The DHI presented an excellent test-retest reliability (ICC 0.98), a good internal consistency (Cronbach's alpha 0.960). Criterion validity of the DHI was proved by moderate to strong correlations with HAMIS, FE, FTP, $\Delta$ FTP and the SHAQ disability index (Spearman rho 0.57–0.85, $p<0.001$). The discriminative capacity of the DHI was proven by statistically significant differences between patients with and without: synovitis, flexion contractures of the fingers, and history of DUs. The sensitivity to change (ES of 0.27 and SRM of 0.52) was acceptable for detecting the minimally important difference.
**Conclusions:** The DHI is a reliable, valid and easy to apply tool for hand involvement assessment in patients with SSc. The preliminary results on sensitivity to change suggest DHI could be a sensitive measure to detect change in clinical status, however more early diffuse SSc patients are needed to confirm these findings.
**Acknowledgement:** **This abstract was realized as part of the "Development of a computer-based nailfold videocapillaroscopy (NVC) system for longitudinal evaluation of patients with systemic sclerosis" (QUANTICAP) project, financed by the UEFIS-CDI PN-II-PT-PCCA-2013–4-1589 grant.*
**Disclosure of Interest:** None declared
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## SAT0212 PERICARDIAL EFFUSION RELATED TO SYSTEMIC SCLEROSIS: A POSSIBLE CONTRIBUTION OF THE SERUM LEVELS OF ADIPOKINES AND INTERLEUKINES

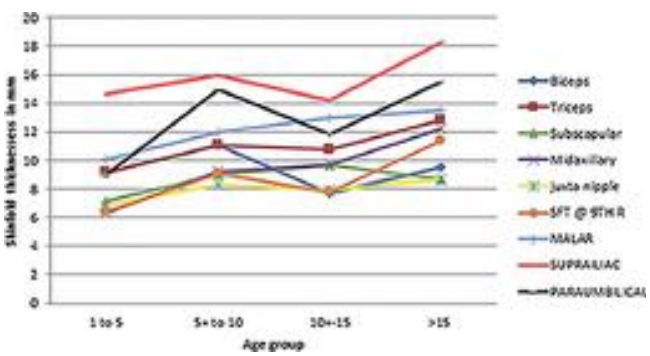
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**Background:** Pericardial effusion (PE) is a common clinical manifestation in systemic sclerosis (SSc). Few data are available about its pathogenesis. The role of adipokines and interleukins produced by the adipose tissue and the immune system in PE related to SSc had never been investigated.
**Objectives:** This study aimed at evaluating the differences in serum levels of adipokines and interleukins (IL) in systemic sclerosis (SSc) patients with and without PE.
**Methods:** A total of 87 outpatients (84 female, mean age of 52,6±14,2 ys, and disease duration of 8,2±6,7 ys), who fulfilled the ACR/EULAR 2013 SSc classification criteria, were recruited in this study. The anthropometric measures, as body mass index (BMI), demographic, clinical and laboratoristic characteristics and SSc related manifestations were assessed in each patient. The presence of PE was evaluated by means of echocardiographic techniques (the presence of fluid $\geq$5 cc was considered pathologic). Sera levels of adiponectin, leptin, resistin, visfatin, tumor necrosis factor $\alpha$ (TNF-$\alpha$), interferon g (INF-g), IL-2, IL-10 and IL-17 were measured in SSc patients, using Multiplex Immunoassay (Bioplex 200 System), by means of two kits (Bioplex ProTM Cytokine/Chemokine and Growth Factor Assay e Bioplex Pro Diabetes Assay). The data normality was verified using Kolmogorov-Smirnov Test; the comparisons between SSc patients groups were evaluated by Mann-Whitney U test and t-student test, where appropiate. Statistic significance was set at $p\leq0,05$. The results are expressed as median and interquartile range (IQR) or means±1standard deviation. The data analysis were assessed using IBM SPSS statistic 20.
**Results:** 11 SSc patients had PE. The SSc patients groups (with and without PE) did not differ in age, sex and BMI. 11 SSc patients were obese (BMI$\geq$30) (2 with PE and 9 without PE). We found significant differences between SSc patients with PE and without PE in sera levels of visfatin (1546,9 (8590,9) vs 388,8 (103); p=0,036), adiponectin (2845000 (4132900,0) vs 5272100,0 (8243600,0); p=0,027) and IL-17 (1,33 (3,5) vs 0,05 (0,56); p=0,45). Moreover higher adiponectin/leptin ratio was found in patients with PE than SSc patients without PE (569,2 (1415,3) vs 166,9 (504,9) p=0,032). The presence of interstitial lung disease, pulmonary arterial hypertension, limited or diffuse skin subset, the different nail fold videocapillaroscopy pattern and the modified Rodnan skin score did not influenced the serum levels of adipokines and IL. In the SSc patients with PE there is no differences in visfatin and adiponectin serum level and adiponectine/leptin ratio between patients that are in menopause and those who are not.
**Conclusions:** The visfatin and adiponectin could play an important role in pathogetic mechanism in pericardial effusion related to SSc. Further study are necessary to unravel a role of visfatin and adiponectin as biomarkers of SSc and a role of the adipose tissue and innate immune system in PE related to SSc pathology.
**Disclosure of Interest:** None declared
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## SAT0213 STUDY OF MUSCLE & SUBCUTANEOUS FAT MASS IN CHILDREN WITH JUVENILE DERMATOMYOSITIS

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**Background:** Juvenile dermatomyositis (JDMS) is a rare but serious inflammatory myositis of childhood with proximal muscle and skin involvement with lipodystrophy (LD) being an important complication. Most studies on JDMS are either on diagnostic or treatment aspects with a paucity of information on the pattern of muscle mass and subcutaneous fat depletion amongst these patients.
**Objectives:** To study the pattern of muscle mass assessed in terms of MUAMC (mid upper arm muscle circumference) & sub-cutaneous fat mass in terms of different skinfold thicknesses (SFT), and to see the correlation between selected anthropometric parameters and different components of lipid profile amongst children with JDMS.
**Methods:** Thirty-five patients (14 male, 21 female) aged between 1 to 22 years diagnosed as cases of JDMS were enrolled in a tertiary care institute in north India. Controls (35) were age and sex matched. All the study subjects underwent standardized anthropometric measurements and 9 different i.e. (biceps, triceps, subscapular, mid-axillary, juxta nipple, 9th rib SFT, malar, suprailiac and paraumbilical) skinfold thicknesses were measured using Harpenden skinfold calipers (Holtain, Dyfed, UK). All absolute skinfold thicknesses were transformed in to their logarithms by formula given Edwards et al. MUAMC was derived using the modified Jelliffe & Jelliffe formula. Lipid profile was measured only in patients
**Results:** Statistically significant ($p<0.05$) difference was obtained for mid axillary SFT in 1–5 years age group, biceps, triceps and juxta nipple SFT in 10–15 years age, triceps and 9th rib SFT in >15years of age, while none was noted in 5–10 years of age group. In pooled age group biceps, juxta nipple and paraumbilical SFT became statistically significant. Maximum (26.3%) fat loss was recorded for Juxtanipple SFT, while minimum was in suprailiac region (13.6%).The remaining skinfolds enjoyed an intermediate percentage fat loss. 63–71% reduction in c.v was observed for different SFT after log transformation. Overall 97% patients had muscle mass significantly lesser ($p<0.01$) with mean difference of 2.8±1.9 cm (10%) than controls. No significant correlation was noted between SFT and triglycerides or total cholesterol. Only moderate level significant associations between juxta nipple, malar SFT and LDL as well as between HDL and triceps and malar SFT, shows persistence of interdependence of these two biochemical parameters with only few selected anthropometric measurements of sub cutaneous fat despite influence of the disease.




**Conclusions:** The subcutaneous fat mass and muscle content was substantially

reduced in patients as compared to control subjects in our cohort which were site specific and of variable magnitude. Log transformed skinfold thickness to be preferred than absolute values to arrive at logical conclusions on dynamics of subcutaneous fat mass. Further studies are warranted with a larger sample size to arrive at scientifically more meaningful conclusions.

**Disclosure of Interest:** None declared

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## SAT0214 MACROPHAGE ACTIVATION AND BIGLYCAN AS DISEASE ACTIVITY AND DIAGNOSTIC BIOMARKERS IN SYSTEMIC SCLEROSIS

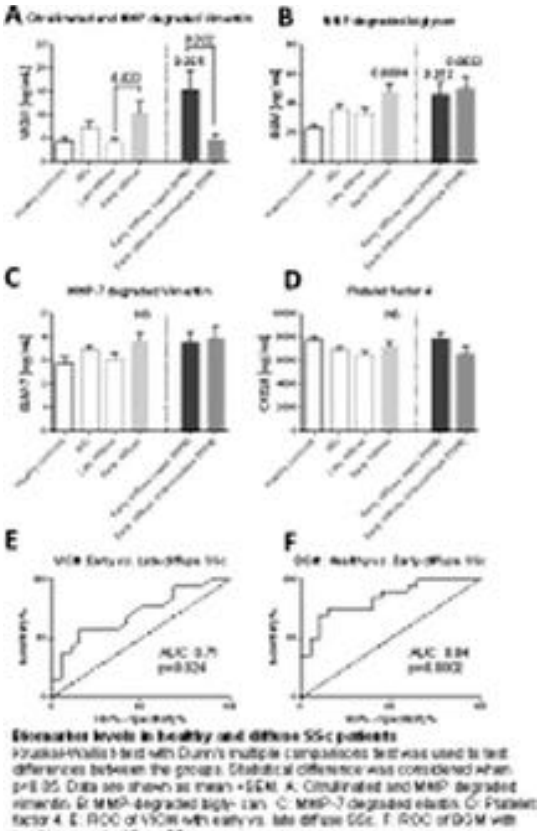
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**Background:** Systemic sclerosis (SSc) is a chronic disease characterized by vascular damage, immunologic activation and excessive extracellular matrix (ECM) deposition in the skin and internal organs. The excessive ECM deposition leads to the release of ECM fragments into circulation, where they may be quantified as biomarkers. Activation of macrophages is a hallmark of the immunologic activation in autoimmune diseases and the activation lead to uncontrolled ECM destruction. In addition, activated macrophages has been shown to secrete the intermediate filament vimentin, making it an ideal protein biomarker of activated macrophages.

**Objectives:** The objectives were to investigate 1) if biomarkers of ECM turnover and macrophage activation could seperate diffuse SSc patients and healthy and 2) the diagnostic power of these biomarkers.

**Methods:** Diffuse SSc patients (n=40) fulfilling the American College of Rheumatology criteria were included. Patients were divided into early and late diffuse based on disease duration (n=20 per group). Furthermore, early SSc patients were divided into intermediate and rapid skin thickness progression rate (STPR; n=10 in each). Twenty healthy controls were included. The macrophage activation biomarker citrullinated and MMP-degraded vimentin (VICM), the ECM biomarkers matrix metalloproteinase (MMP) degraded biglycan (BGM) and MMP-7 degraded elastin (ELM-7) were assessed in serum. The currently best diagnostic and prognostic biomarker (platelet factor 4; CXCL4) was furthermore investigated in serum. Statistical differences between the groups were tested by Kruskal-Wallis test with Dunn's multiple comparisons test. Diagnostic capacity was analysed by receiver operating characteristics (ROC) area under the curve (AUC) on healthy vs. diseased, healthy vs. early or late diffuse and between early and late diffuse.

**Results:** VICM level was significantly increased in early SSc compared to late SSc (p=0.023). The VICM level in the rapid STPR was significantly increased compared to healthy (p=0.025) and intermediate STPR (p=0.022). Of notice, the VICM level of intermediate STPR was at the level of healthy. BGM level was significantly increased in early diffuse SSc compared to healthy (p=0.0003). Both early SSc groups (rapid and intermediate STPR) was increased compared to healthy (p=0.012 and p=0.0022, respectively). There were no difference in the ELM-7 and CXCL4 levels between any groups.




The diagnostic capacity of the biomarkers were assessed. VICM did not reach significance, but reached an AUC of 0.71 for diagnosing early vs. late SSc. BGM had an AUC of 0.79 for healthy vs. SSc. The diagnostic power increased when only testing early SSc (AUC=0.84) and decreased when only testing late SSc (AUC=0.74).

**Conclusions:** VICM could identify the group with rapid STPR, whereas BGM was a possible diagnostic biomarker of early SSc. CXCL4 was in this study not a diagnostic tool of SSc as previously shown[A]. The current study illustrates that serological biomarkers of BGM could be a diagnostic tools in SSc and that macrophage activation (VICM) could be potential biomarkers of SSc disease activity (VICM).

**Disclosure of Interest:** A. S. Siebuhr Employee of: NORDIC BIOSCIENCE A/S, R. Domsic: None declared, P. Juhl Employee of: NORDIC BIOSCIENCE A/S, A.-C. Bay-Jensen Employee of: NORDIC BIOSCIENCE A/S, M. Karsdal Shareholder of: NORDIC BIOSCIENCE A/S, Employee of: NORDIC BIOSCIENCE A/S, N. Franchimont: None declared, J. Chavez: None declared

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## SAT0215 TWELVE YEAR FOLLOW-UP ON PROGRESSION OF NAILFOLD MICROANGIOPATHY DETECTED THROUGH TRANSITION BETWEEN DIFFERENT CAPILLAROSCOPIC PATTERNS OF MICROVASCULAR DAMAGE IN SYSTEMIC SCLEROSIS

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**Background:** Microangiopathy, which features may be detected by nailfold videocapillaroscopy (NVC), is an early aspect of systemic sclerosis (SSc). It is not a static event, but dynamic and may progress through different patterns of microvascular damage (named "early", "active" and "late") during follow-up (1,2). The time of transition is variable, and it was little investigated (2). Furthermore, only a few studies demonstrated correlations between microvascular damage extent and organ involvement over long time (2–4).

**Objectives:** Longitudinal study to investigate the transition of nailfold microangiopathy through different NVC patterns of microangiopathy in SSc, looking for associations with organ involvement and progression over long time.

**Methods:** Thirty-four SSc patients according to LeRoy criteria (mean age 57±11 years, mean disease duration from Raynaud's phenomenon onset 9±11 years) with the "early" pattern of nailfold microangiopathy at first capillaroscopic visit were enrolled and followed by both NVC and clinical assessment for a mean time of 12±3 years. Only SSc patients with fully complete documentation were included into the study. The proper pattern of microangiopathy was recorded by NVC at each visit as previously reported (1,2), as well as organ involvement and antinuclear antibody (ANA) profile.

**Results:** At the end of the twelve-year follow-up, 12 (35%) of patients were still showing the "early" scleroderma-pattern, while the NVC pattern of microangiopathy was changed in 65% of the patients. The NVC pattern was found "active" in 10 patients (30%) and "late" in 12 patients (35%). The median time of progression from the "early" to the "active" pattern was 31 months, from "active" to "late" 38 months, and from "early" to "late" 66 months. Interestingly, in the subgroup of patients whose microangiopathy progressed from the "early" to the "late" NVC pattern through the "active" pattern, the median time of progression from the "early" to the "active" pattern was only 14 months, while in the subgroup of patients whose microangiopathy progressed only from the "early" to the "active" NVC pattern it was 42 months. The median time of progression from "early" to "late" pattern was shorter in SSc patients with either nucleolar IIF ANA pattern or Scl70 autoantibodies. Organ involvement was found progressively larger in SSc patients with "early", "active" and "late" NVC pattern of microangiopathy, respectively.

**Conclusions:** The results confirm the progression of the SSc microvascular damage, quantified through the transition of different NVC patterns, in 65% of SSc patients. Patients showing either a fast progression from the "early" to the "active" NVC pattern of microangiopathy or positive ANA with a nucleolar IIF pattern should be strictly monitored as at risk of rapid progression to the "late" NVC pattern of microangiopathy which is associated to a larger risk of organ involvement.

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**Disclosure of Interest:** None declared

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## SAT0216 CHEST ULTRASOUND SIGNS OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS PATIENTS: A COMPARISON BETWEEN HIGH RESOLUTION CHEST COMPUTED TOMOGRAPHY FINDINGS

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**Background:** Interstitial lung disease (ILD) is a typical clinical manifestation in Systemic Sclerosis (SSc). The high resolution chest computed tomography (HRCT) is the gold standard to evaluate and grade ILD. The presence of fibrotic tissue in the lung, or other structures beside the air, allows obtaining specific sonography images (such as ultrasound lung comet, higher pleural line thickness, irregular pleural margins and subpleural cysts) by chest ultrasound. In previous studies it was demonstrated that the ultrasound comets number increases in SSc patients.
**Objectives:** We aimed at correlating the specific lung sonography signs with ground glass and honeycombing pattern detected by chest HRCT.
**Methods:** A total of 60 SSc outpatients (54 female, mean age 56,2 ± 13,8 ys and disease duration of 9,57±8,7 ys), who fulfilled ACR/EULAR 2013 SSc classification criteria, were recruited. All patients underwent chest HRCT and US examination. The US examination was performed with 7,5 Mhz probe and conducted with patients in sitting position from paraspinal line to anterior axillary line, for each intercostals space. The presence of typical ultrasound signs as lung comets (pathological if >35), higher pleural line thickness (pathological if >2mm), irregular pleural margins, subpleural cysts and pleural effusion was detected. The sensitivity, specificity and accuracy of US patterns (compared to chest HRTC) were evaluated by ROC analysis. Statistic significance was set at $p<0.05$. All results are expressed as mean ± 1 standard deviation.
**Results:** 23 patients had the CT honeycombing pattern, of which 92% had the US irregular pleural margins, 70% had US higher pleural line thickness and sub-pleural cysts, just 54% had US lung comets. 16 patients had the CT ground glass pattern, of these in 94% the US irregular pleural margins, in 87% US lung comets, in 60% US higher pleural line thickness were found. As regard the CT ground glass pattern the US sign with the highest specificity (91%), sensibility (85,7%) and accuracy (88%) was the lung comets; while regarding the CT honeycombing pattern the US sign with the highest specificity (92%), sensibility (69,6%) and accuracy (82%).
**Conclusions:** The lung US is a good diagnostic technique for its repeatability, low cost and risklessness. Although HRCT remains the best imaging technique to assess the ILD, in SSC the lung US could be a useful tool to detect the presence or the evolution of ILD and to improve the timing of HRTC without exposing the patients to high radiation doses over time.
**Disclosure of Interest:** None declared
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## SAT0217 AXON REFLEX VASODILATATION OF DIGITAL ARTERIES IN SYSTEMIC SCLEROSIS PATIENTS, EVALUATED BY LASER-DOPPLER FLUXMETRY

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**Background:** Systemic sclerosis (SSc) is a connective disease characterized by severe microvessels vasculopathy. The important role of endothelial dysfunction in SSc pathogenesis is widely demonstrated, but the SSc related autonomic nervous system impairment is controversial and rarely described. The dysregulation of axon reflex vasodilatation of fingertip microvessels in SSc has been reported in some studies, but the functional involvement of digital arteries in SSc patients had never been investigated.
**Objectives:** We aimed at evaluating the blood flux changes mediated by axon reflex response upon heating stimulus in SSc patients.
**Methods:** 87 SSc patients (SSc pt) and 22 healthy controls (HC) were recruited in this study. The SSc patients were aged 52,7±16,2 yrs, with disease duration of 8,23±7,8 yrs. The LD Flowmetry (Periflux System 5000, Perimed) with 4 LD heating probes was used to measure the skin blood flux of the middle phalanx of the 2nd, 3rd, 4th and 5th fingers of the left hand. The skin fingers flux was recorded at pre-heating period with probes temperature fixed at 34 °C (PHF) and after 5 min heating at 44 °C (IHF). Therefore, the heating test assesses the variation of digital artery flux in response to local heating stress at 44 °C. The ratio IHF/PHF evaluates the axon reflex mediated vasodilatation (ARMV). The results are expressed as average across 4 fingers at each time. The flux was expressed in perfusion unit (PU) and HC and SSc patients responses were compared by the t-student test. Statistic significance was set at $p\leq0,05$. The data analysis was performed using IBM SPSS statistic 20.
**Results:** The ARMV was significantly reduced in SSc patients (2,2±1,4) in comparison with HC (4,8±2,7, p=0,0001). IHF was lower in SSc patients (118,6±54,3) than HC (168±78, p=0,001). Dividing the SSc pts group by the presence of pitting scars (PS), digital ulcers (DU) and digital necrosis (DN), we observed a lower IHF in SSc pts with PS (103,2±48,6) than in SSc pts without (138,1±56, p=0,003), and in SSc pts with DU (97,8±47,6) than in SSc pts without (160,27±120,1, p=0,002). Moreover, SSc pts with ND showed a lower ARMV (1,8±1) than SSc pts without (2,6±1,5, p=0,006), and a lower IHF (98,3±49,1 vs 133,2±54,5, p=0,004). The age, sex, concomitant therapy with Ca-antagonist or Bosentan or cardioaspirin did not influence the digital artery flux.
**Conclusions:** This study provided evidence that a functional impairment of DA occurs in SSc, and it worsens with increasing severity of vascular clinical manifestations.
**Disclosure of Interest:** None declared
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## SAT0218 EFFICACY OF BOSENTAN FOR THE TREATMENT OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES

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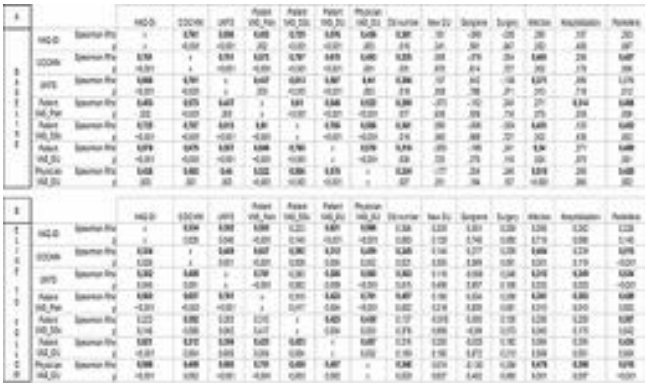
**Background:** Patients with Systemic Autoimmune Diseases (SADs), in particular, systemic sclerosis, are prone to suffer from severe Raynaud's phenomenon (RP), accompanied with digital ulcers secondary to ischemia and associated with a high rate of morbidity and mortality. Bosentan, a dual endothelin receptor antagonist, is a therapeutic option for refractory cases with an inadequate response to conventional management.
**Objectives:** The objectives of our study were: i) to assess safety and efficacy of bosentan in patients suffering from different kinds of SADs and active digital ulcers secondary to RP, ii) to determine predictive factors of response, and iii) to identify predictive factors for survival.
**Methods:** This is a retrospective observational study of patients suffering from SADs and digital ulcers secondary to RP, treated with bosentan in our department between January 1st, 2005 and December 31st, 2014. Patients with ischemic ulcers caused by other factors were excluded. The following baseline independent variables were considered: type of SAD, exposition to cold or to toxic substances, clinical and epidemiological characteristics, concomitant treatments, the coexistence of pulmonary hypertension, and number and location of digital ulcers. Therapeutic response, adverse effects, the need for amputation and death were considered as dependent outcome variables. Chi-square, Student t test, and Mann-Whitney U test were used to establish statistical significance in the univariate analysis between independent baseline variables and outcomes. A $p<0.05$ was considered significant.
**Results:** We included 31 patients (26 women, mean age 57 years). Twenty patients had systemic sclerosis (10 cases the limited form, and 10 cases the diffuse form). Eight patients had concomitant pulmonary hypertension. Mean follow-up after starting bosentan was 1470 days. Six patients had, at least, an adverse effect, being the most frequent alterations of liver function tests. In 87% of the cases, ulcers improved significantly, with a clinical response within the first 12 weeks of treatment in 77% of the cases. Ninety percent of the patients received concomitant treatment with calcium channel blockers and 45% had received previous treatment with prostaglandins. Despite bosentan therapy, amputation was done in 4 patients. Type of SAD, gender, or exposition to cold did not show any significant correlation with morbidity and mortality. Nine patients died. Smoking habit showed a correlation with death (p=0.05). There was a significant correlation between the duration of the disease and death (p=0.0235), as well as with the age of the patient (p=0.0013). Pulmonary hypertension was predictive of a poor therapeutic response (p=0.043) and mortality (p=0.015).
**Conclusions:** This open study suggests that bosentan is an effective agent for ischemic digital ulcers in patients with SADs, with a favorable safety profile. Age and associated pulmonary hypertension are predictors of mortality and poor outcome.
**Disclosure of Interest:** None declared
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## SAT0219 CORRELATION BETWEEN PATIENT-REPORTED OUTCOMES AND CHANGES IN DIGITAL ULCER STATUS IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Among various measures used to evaluate patients with systemic sclerosis (SSc), the Health Assessment Questionnaire (HAQ-DI) for disability, the UK scleroderma Functional Score (UKFS) and the Cochin Scale for hand functionality, the Visual Analogic Scale (VAS) to estimate pain, general disease activity and digital ulcers status are among the more frequently used [1]. Digital Ulcers (DU) are a major clinical complication in patients with Systemic Sclerosis (SSc), leading to a severe impairment of the quality of life and possibly determining important complication (from infections to amputation).

**Objectives:** this study aimed at evaluating the correlation between Clinician-Reported outcomes (CROs) and patient-reported outcome (PROs) and how changes in different parameters related to DU status in SSc patients may reflect changes in the above mentioned outcome measures.
**Methods:** SSc patients presenting at least one DU and attending the Rheumatology Wound Care Clinic of the Florence University Hospital or the London Royal Free Hospital were eligible for the study. Patients were assessed with HAD-DI, UKFS, Cochin scale, VAS for pain, DU status and general disease status (as PROs) and VAS for DU status (as CROs) at baseline and then every 4 weeks for a total of 16 weeks (or until DU healing, if occurred before). Number of DU, appearance of new DU, presence of gangrene, infection, need for hospitalization or surgery procedures, painkillers use were recorded at each visit. Correlations were tested through Spearman test.
**Results:** forty-four SSc patients were enrolled in the study. At baseline, all the PROs and CROs were positively correlated to each other, with most of the scales being also correlated with baseline DU number, presence of infection, need for hospitalization and painkillers use. When investigating baseline to mean follow-up changes, significant correlations were confirmed between CROs and PROs (except for VAS for general disease status), as well as between changes in PROs/CROs and changes of DU parameters being already significant at baseline.



**Conclusions:** PROs are useful outcome measures paralleling changes in clinical evaluation of DU status, which is influenced by changes in DU number, presence of infection, need for hospitalization and painkillers use.
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## SAT0220 RETROSPECTIVE AUDIT COMPARING BSR STANDARDS WITH DETECT CRITERIA FOR PAH-SCREENING IN SYSTEMIC SCLEROSIS PATIENTS AT A DGH

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**Background:** Pulmonary arterial hypertension (PAH) is a complication of Systemic Sclerosis (SSc). It is the lead cause of mortality and can affect up to 20% of SSc patients. The DETECT study developed an evidence-based screening algorithm to aid early detection and diagnosis; as well as guide management of those with SSc-PAH. Many studies, including DETECT have shown earlier detection, higher survival rates and improved outcomes in those enrolled to a screening programme. PAH is often diagnosed late, when symptoms are advanced and prognosis is poor. Therefore, screening is crucial to enhance patient safety and improve outcomes. In light of this; a retrospective audit of 29 SSc patients at a DGH in July 2015 was performed to compare adherence rates to the national BSR standards of annual pulmonary function testing (PFT) echocardiogram and DETECT criteria for PAH-screening.
**Objectives:** 1. Evaluation of current practice against the BSR standards.
2. Evaluation of current practice against DETECT criteria
**Methods:** Data was retrospectively collated from written medical notes, Medway and CVIS in accordance with a Microsoft Excel proforma of 30 variables, including annual echocardiography and PFT; and eight PAH-predictive variables identified by the DETECT study (FVC %predicted/DCLO %predicted, Telangiectasias, ECG Right Axis Deviation (RAD), Serum Urate, Serum Anti-Centromere Antibody (ACA) and Serum NTproBNP).
**Results:** Adherence to the BSR standard was 75.9% over the last 18 months. Stratification showed higher rates of adherence in those with more recent diagnoses; 70%, 83.3% and 100% for 0–4years, 5–8 years and 9–12 years disease duration respectively, compared to 50% and 0% for 17–20 years and 21–24 years respectively.
DETECT scores were calculable for 2/29 patients. Serum NTproBNP, serum urate and ECG RAD are not routinely tested for or documented in SSc patients. Furthermore, in this audit, less than 50% of patients had a documented serum ACA in their notes. As a result, DETECT scores were not calculable for most patients.
**Conclusions:** Adherence rates in the last 18 months are 75.9%. Adherence is highest in those with more recent diagnoses. Seven patients (24%) did not receive annual screening in the past 18 months. Adherence to BSR standards and patient safety could therefore be improved. As a result of this audit, a centralised patient list was uploaded to CVIS for automatic annual screening appointments.
The use of DETECT criteria is not currently applicable. However small, inexpensive changes in routine management of SSc patients would make this possibile.
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## SAT0221 DETERMINANTS ASSOCIATED WITH INTERSTITIAL PULMONAR INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS – A CROSS-SECTIONAL STUDY

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**Background:** Interstitial lung disease (ILD) is one of the major types of lung involvement in systemic sclerosis (SSc). Affected patients have a worse prognosis than patients with SSc who are free of pulmonary involvement. Therefore, it is important to explore determinants of this organ complication.
**Objectives:** To found possible determinants of ILD in SSc patients.
**Methods:** A cross-sectional study was conducted in 104 SSc patients (2013 ACR/EULAR criteria) from a university hospital of Portugal. The analyzed variables were: age, sex, age at disease onset, disease duration, antinuclear antibodies (ANA), topoisomerase I DNA (Scl70) and anticentromere antibodies (ACAs) status, Raynaud phenomenon, areas of skin sclerosis (limited was divided into sclerodactyly or proximal to the metacarpophalangeal (MCP) joints), digital ulcers (DU), digital pitting scar and telangiectasia status, diffusion capacity of carbon monoxide transfer/alveolar volume (DLCO/VA, % of the predicted value) at diagnosis and esophagus involvement. Descriptive statistics were calculated for several demographic and clinical characteristics. Pearson or Spearman correlation and chi-square or Fisher's exact test was used for the assessment of the correlation between ILD and the different continuous and categorical variables. Subsequently, binary logistic regression analysis (method enter) was carried out using the ILD as the dependent variable. As independent variables, were included variables that had clinical or statistical significance.
**Results:** Most (89.4%) of patients were women; mean (SD) age was 59 (±13) years. Mean age at diagnosis was 51 (±13) years with disease duration median (min;max) of 6 (0;38) years. Ninety-three (89.4%) patients had limited (lcSSc) scleroderma. Most (98.1%) patients had ANA positive (mainly centromere (n=61) followed by nucleolar pattern (n=15)), 61 (58.7%) patients were ACAs positive and 21 (20.2%) positive for Scl70 antibodies. DLCO/VA mean at SSc diagnosis was 74.8% (±13.6). Twenty-three (22.1%) patients had ILD (most NSIP pattern) and 64 (61.5%) had esophagus involvement. Correlation coefficients with statistical significance were noted for disease duration and age however, these were weak (rô=0.22, p=0.03 and r=0.29, p=0.004; respectively). For categorical variables we observed statistical significance for SSc subgroups (ILD prevalence of 15.1% in lcSSc vs 72.7% in diffuse SSc; $p<0.001$), ACAs and Scl70 serology (6.6% in ACAs vs 57.1% in Scl70 positive patients; $p<0.001$) and DU (33.3% if history vs 15.5% if without history of DU, p=0.02). Correlation of ILD with DLCO/VA at SSc diagnosis and sex had not statistical significance (p=0.064). In logistic regression the following variables were introduced: age, disease duration, SSc subgroups, ACAs and Scl70 serology, skin sclerosis proximal to the MCP joints, DU status and DLCO/VA at SSc diagnosis. The analysis showed that the age (OR=1.13,p=0.003), SSc subgroups (OR=22.95,$p<0.001$) and ACAs status (OR=0.08,p=0.001) influence the ILD in the model.
**Conclusions:** Our results suggest that higher age and diffuse sclerosis increased ILD risk and ACAs decreases. A prospective longitudinal study with a larger sample is desirable to confirm these results.
**Disclosure of Interest:** None declared
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## SAT0222 B CELL DEPLETION THERAPY IN SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE. A MULTICENTER, OPEN LABEL, COMPARATIVE STUDY WITH A FOLLOW UP OF 94 PATIENT-YEARS

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**Background:** We have previously shown that rituximab (RTX) may favorably affect lung function and skin fibrosis in patients with systemic sclerosis (SSc).
**Objectives:** To assess long term efficacy and safety of RTX in SSc compared to standard treatment.
**Methods:** Fifty one patients with SSc associated interstitial lung disease were recruited and treated with RTX (n=33) or standard treatment (n=18). RTX cycles were repeated every 6 months throughout follow up apart from 6 patients where RTX was discontinued following 2 years of continuous treatment. Mean follow up was 2.9 years (range 1–7). Standard treatment consisted of azathioprine (n=2), methotrexate (n=6) and mycophenolate (n=10).
**Results:** Patients in the RTX group showed an increase in FVC during the first year of treatment (mean ± SEM of FVC: 80.60 ± 3.69 vs 83.02 ± 3.37 at baseline vs 1-year, respectively, p=0.13); this beneficial effect was further augmented at 2 years (86.90 ± 4.72, p=0.04 compared to baseline). In sharp contrast, patients in the control group had no change in FVC during the first 2 years of follow up. At 2 years, the RTX group was numerically better than the control group; however, differences tended but did not reach statistical significance (p=0.063). At the 7 year time point patients in the RTX group had higher FVC compared to baseline (mean ± SEM of FVC: 91.60 ± 6.62, p=0.15 compared to baseline) in contrast to patients in the control group where FVC deteriorated ($p<0.01$, compared to baseline). Direct comparison between the 2 groups showed a significant benefit for the RTX group (p=0.013). DLCO also improved following 2 years of RTX treatment (mean ± SEM of DLCO: 59.22 ± 3.16 vs 61.51 ± 4.02 at baseline vs 2-years, respectively, p=0.05). In the standard treatment group DLCO constantly deteriorated throughout follow up. In 6 patients where RTX was stopped following 2 years of continuous treatment a decline in PFTs was evident. Improvement of skin thickening was found in both the RTX and the standard treatment group, however, direct comparison between groups strongly favored RTX at all time points (p=0.002, 0.015, 0.002, 0.053 0.029 for the 1, 2, 3, 4 and 5-year time point, respectively). In the RTX group, six cases of respiratory infection requiring hospitalization, one case of hepatitis B reactivation and one case of herpes zoster were recorded. Two patients were diagnosed with cancer (lung and prostate). Five deaths were recorded: end stage respiratory failure (n=2), lung cancer (n=1), sudden death (n=1), unknown (n=1). In the control group, five patients with respiratory and four patients with urinary infection were hospitalized. In four cases, infections were recurrent. Two deaths were reported due to respiratory infection.
**Conclusions:** Our data indicate that continuous treatment with RTX has a beneficial effect on lung function and skin fibrosis in patients with SSc. Treatment was well-tolerated. Randomized controlled studies are highly needed.
**Disclosure of Interest:** None declared
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## SAT0223 SOLUBLE SEMAPHORIN 3A AND NEUROPILIN-1: NEW MARKERS FOR DYSREGULATION OF ANGIOGENESIS IN SYSTEMIC SCLEROSIS?

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**Background:** Semaphorins, through interactions with their receptors- neuropilins, play critical roles in many biological processes such as the regulation of immunity, apoptosis, cell migration and angiogenesis. Systemic sclerosis (SSc) is an autoimmune disease, characterised by dysregulation of angiogenesis, leading to severe ischemia and loss of capillaries.
**Objectives:** The aim of the study was to investigate if soluble semaphorin 3A and neuropilin-1 could be involved in the dysregulation of angiogenesis in systemic sclerosis.
**Methods:** This was an investigator-initiated cross-sectional study. Serum samples obtained from 37 patients with systemic sclerosis (age 53 ± 9 years) and control serum samples obtained from 24 healthy individuals (age 51 ± 15 years) and 20 patients with Sjögren's syndrome (age 46 ± 9 years). Samples were analyzed for the presence of soluble semaphorin 3A and neuropilin-1 using enzyme-linked immunosorbent assays. The results were expressed as median and range and compared by Mann-Whitney U test. $P \leq 0.05$ were considered statistically significant.
**Results:** Serum semaphorin 3A levels were significantly higher in patients with systemic sclerosis (median 1.81 ng/mL; range 0.43–4.72 ng/mL) versus healthy controls (median 0.21 ng/mL; range 0.16–0.28 ng/mL) ($p<0.001$). Neuropilin-1 levels were significantly increased (median 844.26 pg/mL; range 556.80–1271.54 pg/mL) in comparison to those detected in healthy controls (median 58.60 pg/mL; range 33.75–80.00 pg/mL) ($p<0.001$) and patients with Sjögren's syndrome (median 278 pg/mL; range 137.50–443.70 pg/mL) ($p<0.001$). There was tendency to higher values of neuropilin-1 in patients with long lasting illness (Spearman's; r=0.29, p=0.075).
**Conclusions:** Our data show that semaphorin 3A and neuropilin-1 levels are significantly increased in patients with systemic scleroderma. Semaphorin 3A and neuropilin-1 may be involved in the modifications of neuro-vascular mechanisms leading to dysregulation of angiogenesis in systemic scleroderma.
**Disclosure of Interest:** None declared
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## SAT0224 NAILFOLD VIDEOCAPILLAROSCOPIC FINDINGS IN UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE (UCTD) AND THEIR RELATIONSHIP WITH RAYNAUD'S PHENOMENON (RP)

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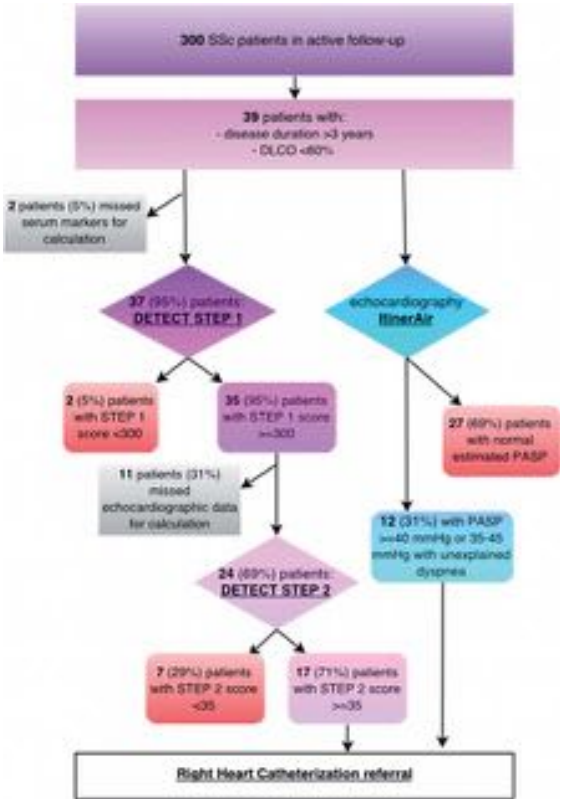
**Background:** The term undifferentiated connective tissue disease (UCTD) is used to describe a group of patients that lack definitive characteristics of any specific, well-defined connective tissue disease. The microcirculation may be affected and nailfold capillary abnormalities were sometimes described.
**Objectives:** The aim of the study was to evaluate and depict the capillaroscopic features in these patients, especially in combination with Raynaud's phenomenon (RP).
**Methods:** A consecutive cohort of 78 patients with UCTD and disease duration of at least one year was included in the study. Diagnosis of RP was based on a detailed history and/or observation of bilateral, cold-induced blanching and/or cyanosis of the fingers. Nailfold videcapillaroscopy (NVC) was performed blinded to disease group by the same investigator using a computerized videomicroscope at 200x magnification. The capillaroscopic findings were classified as normal, non-specific (tortuous, crossed, bizarre capillaries, haemorrhages, thrombotic capillaries), scleroderma pattern (SP) findings (definitely enlarged capillaries, giant loops/megacapillaries, bushy capillaries and angiogenesis, no, moderate or extensive loss of capillaries, architectural disruption of the nailfold capillary bed). Different data of continuous variables were described and compared using the Mann-Whitney U test. Comparison of categorical variables was performed using the $\chi^2$ test with continuity correction. Statistical significance was defined as $p<0.05$.
**Results:** The 78 patients consisted of 87% women (68/78) and we diagnosed RP in 41 (52.5%). The mean age was 45.1±14.7 (yrs±SD) and the mean disease duration 48.6±50.0 (months±SD). NVC abnormalities were present in 18/41 (43.9%) patients with UCTD+RP and in 1/37 (2.7%) without RP ($p<0.0001$). A considerable percentage of patients with RP (15%) had a normal NVC, compared to patients without RP (36.6%) (p=0.0004). Homogeneously enlarged loops were identified in 30/41 (73.1%) of UCTD+RP, in a higher percentage respect to patients without RP (27.0%) (p=0.0001). Irregularly enlarged loops and megacapillaries were found in 55% and 35% of UCTD+RP patients, respectively, in a significant high frequency respect to patients without RP. Bushy or angiogenetic capillaries and/or avascular areas were not found in both group. The combination of features suggestive for a SP without reduction in capillary density were present in 18/41 patients with UCTD+RP, and in 1/37 without RP (p=0.0003).
**Conclusions:** In our UCTD+RP patients, irregularly enlarged and giant loops were predominant. We found neither moderate capillary loss, nor avascular areas in any of our patients. Only the SP without capillary loss distinguishes patients with RP from those without. This fact would also be supported by other results, which failed to show any of the findings typical of a severe or "active' disease involving nailfold microcirculation, such as features suggesting capillary re-growth ("bushy" capillaries), and "destruction" of capillaries (capillary loss/avascular areas) The typology of microvascular damage found in our patients is consistent with the general profile of UCTD, commonly considered as a condition characterised by a mild clinical picture.
**References:**
[1] De Angelis R, et al. Raynaud's phenomenon: clinical spectrum of 118 patients. Clin Rheumatol 2003; 22:279–84.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4558

## SAT0225 SCREENING FOR PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS PATIENTS: SINGLE CENTER REAL-LIFE PERFORMANCE OF THE DETECT ALGORITHM

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**Background:** A new algorithm for early detection of PAH in Systemic Sclerosis (SSc) patients has been recently developed (1). However, the cost-effectiveness of this strategy has not yet been defined in a real-life setting.
**Objectives:** The aim of this study was to compare two methods of PAH screening among SSc patients for the referral to invasive tests (right heart catheterization (RHC)) in a single PH referral center.

**Methods:** Patients with SSc according to the ACR/EULAR 2013 classification criteria were enrolled in the study and prospectively followed in a Scleroderma Unit of a University Hospital which is also a PH referral center between Jan 2015 and Jan 2016 with at least 6-monthly visits. According to the ESC/ERS 2015 guidelines (2), annual screening with echocardiography, DLCO, ECG and serum biomarkers (including urate and NT-proBNP) was performed. Patients satisfying the two-steps DETECT score and/or with echocardiographically estimated Pulmonary Arterial Systolic Pressure (PASP) ≥45 mmHg or between 35–45 mmHg with unexplained dyspnea (3) were referred to an expert cardiologist to undergo RHC.
**Results:** Three-hundred patients with a diagnosis of SSc were screened and 39 patients (13%) met the criteria for the application of the DETECT algorithm (disease duration >3 years, DLCO <60%). The male:female ratio was 1:12; 16 patients (41%) were positive for anticentromere antibodies; 14 patients showed cutaneous teleangectasias (26%); 33 patients (85%) were classified as limited SSc, 4 (10%) as diffuse SSc and 2 as SSc without skin involvement (5%). For 2 of them (5%), STEP 1 score was not calculated due to missing serum biomarkers. Among the remaining 37 patients, 2 (5%) had a STEP 1 score <300; and 35 (95%) showed a STEP 1 score ≥300. Among the latter, for 11 (31%) echocardiographic measures for the calculation of the STEP 2 score could not be derived. In 7/24 (29%) the STEP 2 score was <35 while in 17/24 (71%) ≥35, thus needing referral to RHC according to the DETECT algorithm. In the same 39-patients group, 12 (31%) satisfied the ItinerAir criteria for RHC (p=0,0019, chi-squared).




**Conclusions:** Our results indicate that the feasibility in clinical practice of both PAH screening methods strongly depends on the performance of a correct echocardiographic screening, with a complete assessment and quantification of right heart parameters, which often lacks in outpatient practice. In addition, applying the DETECT algorithm, a larger number of patients should be sent to RHC than those identified by solely echocardiographic parameters. Further observational studies are needed to define the real-life sensivity and cost-effectiveness of this new algorithm.
**References:**
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[2] Galiè N et al, Eur Respir J 2015.
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**Disclosure of Interest:** None declared
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## SAT0226 CIRCULATING SERUM LEVELS OF CORTISOL ARE ASSOCIATED WITH THE PAIN THRESHOLD IN SYSTEMIC SCLEROSIS: CORRELATIONS WITH DEPRESSION

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**Background:** Previous studies on pain prevalence among systemic sclerosis (SSc) patients confirms its prominent role in disease outcomes[1]. Although pain perception is receiving more importance among patient-reported outcomes in SSc research, still its interface with mood disorders and immune system need to be further elucidated. The prevalence of clinically significant symptoms of depression or anxiety in SSc varies between 36% and 65% according to the evaluation used, and are rather associated with increased disability and altered HRQoL, than with disease-specific organ manifestations. An endocrine influence on pain perception and threshold is supported by robust evidences, more specifically related to sex, adrenal and thyroid hormones.
**Objectives:** To analyze the association between pain threshold, depression and cortisol serum levels in systemic sclerosis patients, major depression disorder patients and healthy controls.
**Methods:** Thirty SSc patients, 30 major depressive disorder (MDD) patients and 30 healthy controls completed the study. All participants underwent pressure pain threshold (PPT) assessment through an algometer in three anatomical surfaces, the ungula bed (UPPT) and the metacarpophalangeal joint (MPPT) of the second finger of the right hand and the anterior portion of the quadriceps muscle (QPPT), and depression evaluation, assessed by patient health questionnaire 9 (PHQ-9). Serum cortisol was measured in SSc and MDD patients for further analysis. Patients under treatment with corticosteroids were excluded.
**Results:** PHQ-9 values showed that 15% of SSc patients had no signs of depression, while 30% had mild and another 30% moderate signs of depression, 18% moderate/severe and 9% severe signs. Among MDD patients, PHQ-9 12% had mild depression, 45% moderate, 15 moderate to severe and 28% severe depression. PHQ-9 scores were significantly higher in SSc and MDD compared to controls ($p<0.0001$) and furthermore MDD patients had significantly higher than those reported by SSc patients ($p<0.005$). Pain threshold scores were significantly lower in SSc and MDD patients compared to healthy subjects in all sites ($p<0.0001$). In addition, SSc patients showed significant lower pain thresholds when compared to MDD, regardless the site of measurement (UPPT: p=0.0053; MPPT: p=0.0121; QPPT: p=0.0086). In addition, cortisol serum levels were significantly higher in MDD patients compared to SSc (17.1±5.7 vs 8.5±3.7 μg/dl; $p<0.0001$). Both in SSc and MDD a significant direct correlation was observed between cortisol serum levels and PPT in all sites.
**Conclusions:** The interface between pain, depression and cortisol could represent an additional complex aspect of care of patients with either SSc or MDD.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5015

## SAT0227 THE EFFICACY OF VASOACTIVE AND VASODILATING DRUGS ON DIGITAL ULCERS HEALING IN SYSTEMIC SCLEROSIS: DATA FROM THE DESSCIPHER OBSERVATIONAL STUDY OF EUSTAR GROUP

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**Background:** Digital ulcers (DU) are an important driver of poor quality of life

in Systemic Sclerosis (SSc). Real life clinical management of DU includes the use of vasoactive (Bosentan) and vasodilating (Sildenafil, Iloprost, CCB and ACE inhibitors) drugs in different combinations, without strong evidence for efficacy.
**Objectives:** One of the aims of the EC-funded FP7 research project DeSScipher (acronym for "to decipher the optimal management of SSc") was to determine the relative effectiveness of the above treatments for the healing of DU in SSc patients.
**Methods:** Twenty eight centres in Europe participated to the study. Longitudinal data were collected over 24 months in a specific web based EUSTAR database. The DU distal to PIP joints at the inclusion visit or developed over the follow-up were included. End-points included: mean number of healed ulcers/patient; proportion of patients with healed DU; and time to healing of at least one DU.
**Results:** Out of 1394 enrolled patients, 265 met inclusion criteria. Follow-up data were available for 156 patients. 57% of patients were on vasodilators (Sildenafil, Iloprost, CCB, alone or in combination), 5.8% were on single vasoactive drug (Bosentan) and 37.2% patients were on combination therapy. The mean number of DU/patient at the inclusion visit was comparable among the 3 treatment arms. At 12 and 24 months, the mean number of healed DU/patient was higher in the vasodilator group compared to the vasoactive and combination groups (1.8 vs 1 vs 1.2, p=0.013 and 2.4 vs 1.3 vs 1.3, p=0.018 respectively). No significant difference was observed at 6 months. The proportion of patients with all or at least one DU healed was not significantly different between treatment arms. Initial exploratory analysis also suggested that the estimated mean time to healing of at least one DU was 9.71±2.2 months in vasoactive arm, 8.7±0.5 in vasodilator arm and 7.9±0.6 in combination therapy arm. Further, when considered separately, patients on Sildenafil (±CCB) showed the highest healing rate at 6months follow-up, compared to other drug combinations. However, correction for concurrent treatment and confounding factors is still on going.
**Conclusions:** Vasodilating treatment achieved a major number of healed DU at 12 and 24 months. The combination treatment seems to be of help in obtaining a shorter time to healing and limiting observation at 6 months may bias overall interpretation of data. Further analysis is ongoing for different drug combination at different time-points.
**Acknowledgement:** The DeSScipher project was funded by the European Community's Framework Programme 7 (FP7-HEALTH-2012.2.4.4–2 - Observational trials in rare diseases) under grant agreement N° 305495.
**Disclosure of Interest:** None declared
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## SAT0228 EFFICACY OF RITUXIMAB FOR THE TREATMENT OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONNECTIVE TISSUE DISEASES – A RETROSPECTIVE ANALYSIS

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**Background:** Interstitial lung disease (ILD) is a notable complication of Connective Tissue Diseases (CTDs) characterised by lung inflammation and scarring, leading to a reduced functional capacity, shortness of breath and exercise-induced hypoxia. To date, the mainstay of treatment for this condition is Cyclophosphamide (CYC); some patients, however, fail to respond and recent reports have shown that Rituximab may be beneficial as a second-line option. Currently, no guidelines are available to direct the management of CYC-resistant patients and, at present, these individuals remain to be treated on a case-by-case basis.
**Objectives:** To retrospectively evaluate the efficacy of Rituximab treatment in patients with ILD associated with CTDs.
**Methods:** We retrospectively reviewed patients in our trust with CTD associated ILD, refractory to cyclophosphamide, in whom Rituximab has been used. Parameters assessed were lung function (forced vital capacity (FVC) and carbon monoxide transfer factor (TLCO)), radiographic changes and creatine kinase (CK) response (for myositis) both pre- and post-treatment.
**Results:** Our cohort included 7 patients (4 females, 3 males) – average age 42 years. 6 patients had underlying diagnosis of polymyositis (3 anti-Jo, 2 anti-Jo/Ro, 1 anti-Zo) and 1 had an undifferentiated CTD. Average disease duration of 70 months. On high resolution CT scan, 3 patients had non-specific interstitial pneumonia (NSIP) pattern, 2 had usual interstitial pneumonia (UIP), 1 organising pneumonia, and one had features of both cryptogenic pneumonia and NSIP. Of note, one patient had mild co-existant pulmonary arterial hypertension. Previous treatments included CYC, azathioprine and steroids.
Lung function results were available for 6 of 7 patients – 5 of these patients showed improvement in post-treatment FVC and TLCO (average improvement 11.2% predicted; 0.14L and 4.06% predicted, respectively). Two patients had CT scans following treatment – one showed no change from baseline scan, and one (who later died of disease progression) showed worsened fibrosis.
Regarding muscle involvement, 5 of 7 patients had pre-treatment CK values available – two of these patients had a normal CK prior to Rituximab treatment. Interestingly, in the 3 patients with elevated CK levels, an average 45.3% improvement in CK was noted following Rituximab therapy.
**Conclusions:** This study reports improvement in both lung function tests and CK response in the majority of a small cohort of patients with CTD associated ILD following Rituximab treatment. Similar results have been shown in other small cohort studies. Larger, randomised studies are needed to further assess the response to Rituximab therapy and determine whether these findings have statistical significance. Consideration of a formal treatment pathway for patients resistant to CYC treatment would be helpful on both a local and national level to determine which patients are likely to have poor response to CYC, when to trial Rituximab and to determine markers of response to Rituximab treatment, including patient reported outcomes.
**References:**
[1] Kier et al. Severe interstitial lung disease in connective tissue disease: rituximab as rescue therapy. The European Respiratory Journal 2012; 40(3): 641–8.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4661

## SAT0229 A NOVEL SERUM TEST BASED ALGORITHM TO AID IN VERY EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS (VEDOSS)

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**Background:** VEDOSS project relied on a specific set of inclusion criteria identifying patients in very early stage of systemic sclerosis (SSc) to be submitted to a tight follow up and unravel factors linked to the progression of the disease. The components of the ELF score (PIIINP, TIMP-1 and HA) have been shown to correlate with severity of skin and lung fibrosis in SSc.
**Objectives:** Our aim was to analyze the concentrations of ELF components in a subset of patients enrolled in the VEDOSS study and determine their potential diagnostic value.
**Methods:** Sera from 114 patients enrolled into the VEDOSS data base and 67 SSc controls fulfilling ACR/EULAR 2013 criteria (subsets: 33 diffuse; 34 limited) were obtained from 2 centres. Serum concentrations of ELF components were determined on Siemens Advia Centaur platform. Logistic regression analysis of the results was performed employing classification of SSc as state variable.
**Results:** Among the 114 patients enrolled from VEDOSS, 30 subjects had primary Raynaud's phenomenon (PRP); 54 had Raynaud's phenomenon (RP) and at least one of the following "red flags" (risk factors) for SSc: (Puffy fingers, ANA, SSc specific autoantibodies or SSc-specific capillaroscopic pattern) without fulfilling 2013 ACR/EULAR criteria (score $<9$). 30 VEDOSS patients fulfilled new ACR/EULAR criteria (score $>9$) despite having no evidence of skin involvement nor interstitial lung disease at lung high resolution CT or pulmonary arterial hypertension, left ventricular systolic impairment or renal involvement.
All serum biomarkers concentrations correlated with age ($p<0.05$ for all). Logistic regression analysis using the three biomarkers as variables identified a specific model (SSc score) ranging from -3.92 to 5.77. The new score showed good ability to discriminate between patients with SSc (VEDOSS patients already classified as SSc and SSc controls) versus VEDOSS patients not yet classified as SSc (AOUC under ROC curve: 0.853, 95%CI 0.797–0.910). Within the VEDOSS database, SSc score showed a fair ability to discriminate between VEDOSS patients fulfilling SSc classification criteria, despite lack of skin internal organ involvement (lung, heart and kidneys), and those not fulfilling the criteria (AOUC =0.756, 95%CI 0.646–0.865). Indeed, patients fulfilling SSc classification criteria, had average score of 0.44 vs -0.86 of patients not fulfilling the criteria and the score remained significant even after correcting for age (p=0.026). Furthermore, SSc controls had significantly higher SSc score compared to VEDOSS patients already classified as SSc, confirmed after age correction ($p<0.000$). No difference in SSc score has been observed between PRP and VEDOSS patients not yet classified as SSc.
**Conclusions:** Our data indicate that the SSc score is a simple serum test based model that can be used in patients with RP to aid in the very early diagnosis of SSc. Furthermore, the identification of VEDOSS patients with a high SSc score test and already classified as SSc even in the absence of internal organ involvement can be used in intervention trials aimed to prevent further disease progression.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5921

## SAT0230 PROGRESSION OF LEFT VENTRICULAR MYOCARDIAL DYSFUNCTION IN SYSTEMIC SCLEROSIS: USING SPECKLE TRACKING STRAIN ECHOCARDIOGRAPHY TO IDENTIFY PATIENTS AT RISK

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**Background:** Cardiac involvement is a main cause of mortality in systemic sclerosis (SSc)[1]. Its detection remains challenging using conventional echocar-

diographic parameters and little is known about which patients are at risk for deterioration of cardiac function. Speckle-tracking strain analysis of echocardiographic images can detect subtle myocardial dysfunction in patients with SSc, and decreased strain has been shown to associate with lower functional capacity and rhythm disturbances[2]

**Objectives:** This study evaluated: 1. changes in cardiac performance over time in SSc patients including echocardiographic myocardial speckle tracking strain analysis, and 2. baseline characteristics associated with deterioration of cardiac function.

**Methods:** 205 SSc patients (171 female, 52±14 years) were evaluated at baseline and follow-up (2.25years IQR1.3–3.8), including complete physical examination and screening for organ involvement with at least HRCT-thorax, pulmonary function test, cardiopulmonary exercise test, electrocardiography and echocardiography.

**Results:** Left ventricular (LV) ejection fraction did not change significantly (61%±7 vs 61%±8,p=0.148) while global longitudinal strain (LS) decreased significantly (-21%±2 vs -19%±3, p<0.001). 39 patients showed progression of LV dysfunction as defined by ≥15% decline in LS. These patients showed significant worsening of LV diastolic function (figure) and TAPSE (22mm±4 vs 19mm±4, p=0.003) and 8% developed pulmonary hypertension. Baseline parameters associated with progression of LV dysfunction were proximal muscle weakness (OR: 4.264 IQR: 1.473–12.342, p=0.007), diffusing capacity of carbon monoxide (DLCO, OR: 0.972 IQR: 0.948–0.995, p=0.020) and LV diastolic dysfunction (OR: 2.245 IQR: 1.019–4.946, p=0.045).

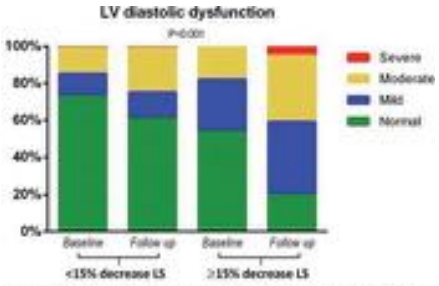



Figure 1: association of decrease in global longitudinal strain (LS) with degree of left ventricular (LV) diastolic dysfunction at baseline and follow-up; ≥ 15% decrease in LS is associated with worsening of LV diastolic function

**Conclusions:** In SSc patients, progression of LV systolic dysfunction was detected by speckle tracking strain analysis but not by LV ejection fraction. Proximal muscle weakness, DLCO and LV diastolic function may identify patients at higher risk and in need of closer cardiac monitoring.

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**Disclosure of Interest:** None declared
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## SAT0231 PHYSICAL ACTIVITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Due to involvement of the skin and vital organs systemic sclerosis (SSc) can affect physical activity (PA). For SSc, positive effects of exercise therapy have been reported.[1] To support SSc patients to improve the exercise capacity it is important to be informed about the overall level of PA of patients with SSc, and disease specific manifestations that might interfere with exercise.

**Objectives:** To gain more insight in the level of PA of Dutch SSc patients, this study assessed the self-reported levels of PA in SSc patients and compared these levels to data of the general Dutch population. In addition, factors associated with PA levels in SSc patients and needs and preferences of SSC patients regarding exercise were examined.

**Methods:** Fifty-nine SSc patients referred to a multidisciplinary health care program and fulfilling the ACR 1980[2] or LeRoy[3] criteria for systemic sclerosis filled in the Short QUestionnaire to ASess Health-Enhancing PA (SQUASH) comprising 10 questions about PA[4]. The proportion of patients meeting the Dutch public health recommendation for PA (i.e., moderate PA for 30 minutes on > or =5 days/wk) and the total number of minutes of PA per week were calculated. These data were compared with similar data from a representative sample of the general Dutch population. Characteristics of patients with high level of PA (defined as > mean PA in minutes/week for the Dutch population) were compared with patients with low level of PA (≤ mean PA in minutes/week for the Dutch population). The needs and preferences of patients with SSc regarding exercise were assessed.

**Results:** The proportion of SSc patients meeting the Dutch Recommendation for Health Enhancing PA was higher than the proportion of the general Dutch population (68% vs 59% for the total group; P not significant). The average number of minutes of PA per week was significantly lower in the SSc population compared with the general population (1729 vs. 2614, respectively, P<0.001). No significant association was found between specific disease characteristics and lower level of PA. SSc patients who did not meet the Dutch Recommendation for Health-Enhancing PA more often reported pain during exercise and a lack of energy interfering with exercise. Thirty percent of patients stated to need more information about exercising and depended on advices of the rheumatologist concerning exercise.

**Conclusions:** The proportion of SSc patients meeting the Dutch Recommendation for Health-Enhancing PA is not significantly different from the Dutch population. However, with respect to the average number of minutes of PA per week, SSc patients were less physically active. In patients not meeting the Dutch recommendation for Health Enhancing PA pain and lack of energy might interfere with proper exercising.

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## SAT0232 ANTI-CENTROMERE ANTIBODY POSITIVE DIFFUSE SCLERODERMA IS UNCOMMON BUT HAS A DISTINCT CLINICAL PHENOTYPE

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**Background:** Anti-centromere antibodies (ACA) typically associate with limited cutaneous disease subset (lcSSc) in scleroderma, and are protective for renal crisis (RC) and interstitial lung disease (ILD). Only 5–7% of ACA positive patients have the diffuse subset (dcSSc). Both antibody specificity and disease subset may influence disease phenotypic expression and organ manifestations.

**Objectives:** To describe demographic and clinical manifestations of ACA positive patients with dcSSc (ACA+diffuse), comparing with two other subsets: ACA positive with lcSSc (ACA+limited) and ACA negative with dcSSc (non-ACA diffuse).

**Methods:** Retrospective study of consecutive patients ACA+diffuse from a single large referral center between 2001–2015. Comparative analysis was made with 160 consecutive patients ACA+limited and 260 consecutive patients non-ACA diffuse. Data were obtained by medical records review.

**Results:** 1313 patients ACA+ were identified, 36 (2.7%) had dcSSc. The peak modified Rodnan skin score was lower in ACA+diffuse compared with non-ACA diffuse (24.0±9.9 vs 27.4±10.4, p=0.031), but occurred later in disease course (88.8±77.2 vs 30.7±33.1 months, p<0.001).

Survival in ACA+ was similar for both subsets with 5, 10 and 15 years survival rates of 96%, 84% and 73% in ACA+limited and 94%, 80% and 72% in ACA+diffuse. Non-ACA diffuse had lower survival of 85%, 72% and 55% at 5, 10 and 15 years respectively, although the difference from ACA+diffuse was not significant.

ACA+diffuse had higher incidence of ILD than ACA+limited (p=0.018), but significantly lower than non-ACA diffuse (p=0.003). During follow-up at 5 years, 15% of ACA+diffuse developed ILD (3% - ACA+limited; 36% - non-ACA diffuse). At 15 years, cumulative incidence of ILD was 26% in ACA+diffuse (5% - ACA+limited; 49% - non-ACA diffuse).

More patients developed pulmonary hypertension (PH) in ACA+diffuse group (27.8%), than in the other groups (12.5% - ACA+limited; 11.9% - non-ACA diffuse), though this was mainly due to longer follow-up of ACA+diffuse. Cumulative incidence of PH in ACA+diffuse was not different from the other groups. At 5 years, 8% of ACA+diffuse had PH (6% - ACA+limited, 6% - non-ACA diffuse), while at 15 years cumulative incidence was 24%, 20% and 18% respectively.

Similarly, cardiac involvement was more frequent in ACA+diffuse (8.3%) vs 1.9% in ACA+limited and 6.5% in non-ACA diffuse, but differences were not significant adjusting for time of follow-up. In contrast, incidence of RC was higher in non-ACA diffuse (13.9%), affecting only 2 patients in ACA+diffuse (5.6%) and none in ACA+limited.

**Conclusions:** This study confirms that ACA diffuse subset is infrequent, but has a distinct clinical phenotype. Despite the dcSSc, these patients have a more insidious onset of skin and major organ involvement, which may represent a therapeutic window for early intervention. We confirm that ACA+ has a protective role and is associated with lower incidence of ILD and RC and better survival than expected in dcSSc. The role of ACA in patients with dcSSc as a possible phenotype modifier needs to be explored further in larger prospective studies.

**Disclosure of Interest:** None declared
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## SAT0233 DESCRIPTIVE STUDY OF CARDIOVASCULAR RISK FACTORS AND ENDOTHELIAL DISFUNCTION IN PATIENTS DIAGNOSED WITH SCLERODERMA AND MIXED CONECTIVE TISSUE DISEASE

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**Background:** Cardiovascular complications are a common cause of morbidity in inflammatory arthritis and connective tissue diseases like several studies have shown.
**Objectives:** Detection of cardiovascular risk factors and endothelial dysfunction in patients diagnosed with Systemic Sclerosis (SSc) and Mixed Connective Tissue Disease (MCTD). Creation of a longitudinal cohort of patients.
**Methods:** Studies have been collected from April 2012 to December 2015. The data collection protocol included BMI, dyslipidemias, DM, HTN, previous or active smoking, thrombotic episodes, strokes and ischemic cardiopathy. ESR, CPR, cholesterol level, LDL, HDL, triglycerides, 25OH-D and homocysteine levels were requested to all patients. Vascular surgery's ultrasound protocol was: 1. Carotid study, intima-media thickness (IMT) and presence of plaques; 2. Ankel branquialindex (ABI), being pathological when ABI $\leq$0.9; 3. Endothelial dysfunction was assessed measuring abnormal brachial artery flow-mediated dilatation (FMD) after a four minutes transient ischemia period, being patologic if FMV $<$10% and severe if $<$5%.
**Results:** A total of 61 patients (95.1% women) were included: 28 SSc limited, 21 SSc diffuse, 2 SSc Sine Scleroderma, 4 MCTD, 3 overlap SSc-polymyositis and 3 Prescleroderma. The mean age at the time of the study and diagnosis were 49 (19–76) and 46 years (17–75). The average time of the disease was 5 years (0–37). 7 patients had HTN, 2 had DM, 18 hyperlipidemia (10 HCL, 2 HTG, 6 mixed hyperlipidemia), 9 active smokers, 18 ex-smokers, 2 patients with stroke, 2 have had thrombotic episodes and 1 had ischemic heart disease. The mean BMI was 24 (18–50) and 37.3% had a BMI$>$25.
The mean value of the different analytic parameters was: ESR: 15 mm/h (1–55), PCR: 2.7 mg/L (0,1–22), COL: 198 mg/dL (143–298), 25OH D Vitamin:23,6 ng/mL (12–118), homocystein 10.8 micromol/l (5,9–19,5) and 21.4% had pathological levels $\geq$15 micromol/l. The mean modified Rodnan skin score was 9 (0–42), 20% of patients had ILD and 3 patients had PAH. 64% patients were treated with steroids, 65% DMARDs and 13.1% biologic therapies.
The echographic findings were the following:
1. The mean right and left common carotid IMT were 0.6 (0.47–1.2) and 0.7 mm (0.44–1.3) respectively. 66% and 61.2% of the cases had an increase of right and the left IMT respectively and 43% of both when it was compared with age group of reference population.
2. 26% had unilateral plaques and 7% bilateral plaques.
3. Three patients had a pathologic ABI.
4. The average FMV was 4%, 80% cases had endothelial dysfunction, being severe in 51% of these.

**Conclusions:**
1. Nearly 40% of patients have overweight (BMI$>$25).
2. A high percentage of patients (16%) have hyperhomocyisteinemia.
3. The percentage of subjects with increased IMT is high, around 65%. The presence of plaques is less frequent (30%).
4. Endothelial dysfunction was found in 80% of the cases, and it was severe in almost 50%.

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## SAT0234 STUDY OF THE ROLE OF IL-6 IN THE DEVELOPMENT OF ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** IL-6 is one of the cytokines with greater presence in Systemic Sclerosis (SSc) and also one of the key cytokines in the development of atherosclerosis (AS). A recent study (Schiopu E, et al. Rheumatology 2014;53:704–713) has shown a relationship between IL-6 and carotid AS. However, the number of patients was scarce, the results were not confirmed in a multivariate analysis and whether these results are replicable in different populations in different geographical areas has not been tested.
**Objectives:** To assess the relation between plasma IL-6 and AS findings (carotid ultrasound, ankle-brachial index [ABI] and arterial pressure difference between arms) in patients with SSc.
**Methods:** Transverse descriptive study with analytical components. Study population: a cohort of 115 patients with SSc controlled in the Rheumatology Department of a tertiary hospital. Variables: 1) clinical variables; 2) determination of serum IL-6 (IMMULITE 2000; Siemens Healthcare Diagnostics, UK); 4) vascular study: ABI and carotid doppler ultrasound (ESAOTE MyLab XV70, 7–12 MHz linear transducer, software $^{RF}$QIMT) measuring intima-media thickness (IMT) and presence of atheroma plaques (Mannheim Consensus). A vascular surgeon measured ABI, and the doppler ultrasound was done by a highly experienced rheumatologist, blind to the rest of findings, in a term of 3 months. Statistical analysis: IBM-SPSS Statistics v22.0 package.
**Results:** 115 patients where included consecutively, of which finally 108 were studied; with a mean age of 60,16 years (SD ±15.16); 99 women (91.7%) and 9 men (8.3%). Mean SSc evolution time was 11.45 years (SD ±8.84). LSSc was most frequently diagnosed (50%), followed by SSc without scleroderma (18.5%) and, decreasingly, DSSc (16.7%), overlap syndrome (9.3%) and pre-SSc (5.6%). 38.9% of patients were hypertensive, 46.3% suffered a DL and 6.3% were diabetic. Mean concentrations of serum IL-6 were 4.34 pg/mL (SD ± 5). Mean right IMT was 0.579 mm (SD ± 0.126), and left 0.657 mm (SD ±0.158); 33.3% had atheroma plaque. In total, 37% had a pathological carotid ultrasound and 39.8% macrovascular damage (atheroma plaque and/or IMT$>$0.9 mm and/or ABI$<$0.9). In the bivariate analysis, serum IL-6 was associated to the IMT as well as the presence of atheroma plaque ($p$-value = 0.002).This association was maintained when jointly considering an ABI$<$0.9 ($p$-value = 0.003). Serum IL-6 was also related to the difference in systolic arterial pressure between both arms (r-Pearson =0.236; $p$-value = 0.022). In the multivariate analysis, the number of atheroma plaques and the macrovascular damage variable maintained statistical significance in the different models.
**Conclusions:** Serum IL-6 concentrations are independently related to the presence of AS and macrovascular disease in patients with SSc. Blocking the action of IL-6 by means of specific therapies could be a therapeutic option which could reduce macrovascular damage in patients with SSc.
**Disclosure of Interest:** None declared
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## SAT0235 SURVIVAL IN SYSTEMIC SCLEROSIS RELATED PULMONARY ARTERIAL HYPERTENSION IN THE MODERN TREATMENT ERA: RESULTS FROM A MULTICENTRE AUSTRALIAN COHORT STUDY

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**Background:** Pulmonary arterial hypertension (PAH) is the leading cause of mortality in patients with systemic sclerosis (SSc).
**Objectives:** To determine the cumulative survival rates and predictors of mortality in SSc- PAH
**Methods:** Patients enrolled in a SSc longitudinal cohort between 2007 and 2015 were included. PAH was diagnosed on right heart catheterization (RHC) (mPAP $>$25 and PAWP $<$15 mmHg). Patients with pulmonary hypertension secondary to interstitial lung disease (ILD) and co-existent PAH and severe interstitial lung disease (ILD) (defined as a HRCT scan demonstrating ILD with a FVC$<$60%) were excluded. Summary statistics, chi-square tests and survival methods including Kaplan-Meier survival curves and cox proportional hazards regression were used to determine survival rates and identify predictors of mortality.
**Results:** Among 132 SSc PAH, 84.9% were female, 68.9% had limited disease subtype (lcSSc), the mean age at diagnosis of PAH was 62.3 years and disease duration at PAH diagnosis was 14.1 years. Over a median follow-up of 3.7 years, 60 (45.5%) patients died with a median survival time from PAH diagnosis of 3.7 years. The standardized mortality ratio for patients with SSc-PAH compared with mortality in the general population is 5.8 (95%CI 4.3–7.8). The years of life lost overall for both males and females due to SSc-PAH was 15.22 years (95%CI 12.3–18.1). Kaplan-Meier survival curves showed a survival advantage with

Table 1. Independent predictors of mortality in SSc-PAH

| Characteristic | Hazard Ratio (95% CI) | p-value |
|---|---|---|
| Age at diagnosis of PAH, years | 1.05 (1.0–1.1) | 0.03 |
| ILD (FVC $>$60%) | 2.83 (1.4–5.6) | 0.01 |
| WHO functional class | 2.01 (1.1–3.9) | 0.03 |
| Pulmonary arterial pressure, mmHg | 1.06 (1.0–1.1) | 0.001 |
| Digital ulcers present | 3.12 (1.4–7.2) | 0.01 |
| Specific PAH therapies and anticoagulation | | |
| Vasodilator monotherapy only | reference | reference |
| Vasodilator monotherapy and anticoagulation | 0.39 (0.1–1.2) | 0.09 |
| Vasodilator combination therapy only | 0.49 (0.2–1.2) | 0.10 |
| Vasodilator combination therapy and anticoagulation | 0.28 (0.1–0.7) | 0.007 |

Abbreviations: PAH, pulmonary arterial hypertension; WHO, World Health Organization; ILD, interstitial lung disease; 6MWD, six minute walk distance; mRAP, mean right atrial pressure; mPAP, mean pulmonary arterial pressure; HCQ, Hydroxychloroquine.

combination therapy and anticoagulation. In cox proportional hazards regression analysis (table1), older age at PAH diagnosis, presence of mild ILD, worse WHO functional class, higher mean pulmonary arterial pressure at PAH diagnosis and presence of digital ulcers were predictive of PAH mortality. Combination PAH therapy together with anticoagulation, provided the most significant survival advantage with a 72% reduction in mortality compared with pulmonary vasodilator therapy alone.

**Conclusions:** Despite advanced therapy, the median survival in SSc PAH is only 4 years. In our study, the addition of anticoagulation to standard combination therapy was associated with a significant survival advantage, pointing to mechanisms involving endothelial abnormalities and small vessel thrombosis in the pathogenesis of PAH.

**Disclosure of Interest:** None declared

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## SAT0236 THE TRADITIONAL CARDIOVASCULAR RISK FACTORS AND THEIR RELATIONS TO HEART STRUCTURE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Cardiac involvement is one of the important factors of a poor prognosis in Systemic Sclerosis (SSc). Different pathogenetic mechanisms are involved in heart pathology in SSc, including microvascular disease and the atherosclerotic process. The relationship between primary cardiac involvement and atherosclerosis (AS) is under investigation.

**Objectives:** To evaluate frequency of the traditional cardiovascular disease risk factors (TRF) and their relations with the heart structure abnormalities in SSc

**Methods:** 125 pts with SSc (113 women, mean age 51±12 years, mean duration of the disease 8, 9±8) who met to ACR/EULAR criteria (2013). The limited type of the disease had 73% of pts. There were no cases of nephropathy, 18 pts (15%) had systolic pulmonary arterial pressure (PAP) >40 mmHg and 63 (50%) had interstitial lung disease. The assessed TRF were age, sex, overweight (a body mass index [BMI] >25 kg/m$^2$, arterial hypertension [AH] (>140/90 mmHg), DM, smoking, total cholesterol (TC). The ten-year risk of fatal cardiovascular disease (CVD) was evaluated by SCORE. 50 age- and sex matched volunteers were used as a control. Echocardiography (ECHO) was performed in 121 pts

**Results:** The increased BMI was detected in 60 (48%) of pts and 15 (30%) of controls (p=0, 03). The TC level was >5, 2 mmol/l in 69 (55%) of pts and 38 (76%) of controls (p=0, 01). Arterial blood pressure (ABP) was elevated in 33 (25%) of pts and in 16 (32%) of controls (p>0, 05), the frequency of others TRF was not significantly different from controls. The high/very high SCORE >5% had 36 (28, 8%) of pts and 4 (8%) of controls (p=0,003). Among them the very high risk (SCORE >10% or coronary heart disease and experienced a cardiovascular event) had 20% of pts and 6% of controls (p=0, 02). The low/moderate values of SCORE <5% had 89 (71%) of pts and 46 (92%) of controls (p=0,003). When compared pts >50 and ≤50 yrs. the higher prevalence of AH (36% and 12%, p=0,003) and hypercholesterolemia (62, 7% and 44%, p=0, 04) were demonstrated in older pts. The ECHO revealed abnormalities in 100 (83%) of pts. The prevalence of ECHO changes was significantly higher in pts with AH when compared to pts with normal level of ABP. The following changes had higher rate in pts with AH: the diastolic dysfunction of left ventricle (LV) (60,6% and 36,4%, p=0,016), thickened aortic (88% and 52%, p=0,0003) and/or mitral leaflets (69,7% and 36%, p=0,001); calcinosis of aortic (36% and 16%, p=0,015) and/or mitral leaflets (33% and 4,5%, p=0,000), dilatation of the left atrium (30% and 8%,p=0,0016). The rate of ECHO valvular abnormalities was higher in pts who were older 50 yrs compared with those <50 yrs. The LV hypertrophy was revealed in 10/58 of pts with overweight and in 3/63 of pts with normal weigh (p=0, 03). The prevalence of thicked aortic leaflets was higher in pts with elevated level of TC comparing with those who had normal values of TC in sera (p=0, 02).

**Conclusions:** Our study displayed the higher cumulative 10-year risk for CVD according to SCORE and indicated a higher prevalence of clinical AS (CHD) ischemic arterial events) in SSc comparing with controls. Presence of the TRF in patients was assosiated with more severe heart structure abnormalities. Appropriate management should be carried for high CVD risk categories of patients, especially in older ones in presence of systemic AH.

**Disclosure of Interest:** None declared

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## SAT0237 NAILFOLD CAPILLAROSCOPY FINDINGS IN SCLERODERMA PATIENTS – PROGNOSTIC IMPLICATIONS

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**Background:** Nailfold *capillaroscopy* (NCP) is a useful tool for the diagnosis and follow-up of systemic rheumatic diseases and represents one of the best methods to evaluate microvascular abnormalities.

**Objectives:** To characterize NCP findings of patients with Systemic Sclerosis (SSc), and understand how NCP associates with the presence of digital ulcers, gastrointestinal involvement, pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD).

**Methods:** NCP findings of adult patients with SSc followed-up in our center were reviewed. Demographic and clinical features were collected. Nonparametric tests were used to determine potential associations between capillaroscopy findings/patterns and the presence of digital ulcers, gastrointestinal involvement, PAH and ILD.

**Results:** In total, 52 out of 103 patients with SSc had at least one NCP result available. Forty five were female (86.5%) and seven male (13.5%), the age was 56.6 ±13.2 years and disease duration 10.9 ±10.5 years. Thirty one (59.6%) had limited cutaneous SSc, seven (13.5%) diffuse cutaneous SSc, ten (19,2%) VEDOSS, three (5.8%) overlap syndromes and one (1.9%) SSc sine scleroderma. (table 1). The most frequent NCP findings were hemorrhages (54.7%) megacapillaries (54.7%), and capillary dilatations (52.8%).

We found that digital ulcers were significantly associated with the existence of avascular areas (p=0.02), and with neoangiogenesis (p=0.03) in univariate analysis, but were not associated with any capillaroscopy pattern. Looking to interstitial lung disease, there is a trend for association with the presence of avascular areas (p=0.056). Only one patient had PAH confirmed by right heart catheterization. In this case NCP showed giant capillaries, neoangiogenesis and avascular areas. There was also a trend for association between avascular areas and higher values of NT pro BNP (p=0.078). Gastrointestinal involvement was not significantly associated with NCP findings (table 2).

Table 1. Distribution of patients according to NCP and disease subtypes

| | Diffuse cutaneous (n=7) | Limited cutaneous (n=31) | Overlap syndrome (n=3) | VEDOSS (n=10) | Sine scleroderma (n=1) |
|---|---|---|---|---|---|
| Early pattern n (%) | 0 (0) | 9 (29) | 1 (33) | 6 (60) | 0 (0) |
| Active pattern n (%) | 1 (14.2) | 5 (16.1) | 1 (33) | 2 (20) | 0 (0) |
| Late pattern n (%) | 3 (42.9) | 7 (22.6) | 0 (0) | 0 (0) | 0 (0) |
| Nonspecific n (%) | 3 (42.9) | 8 (25.8) | 1 (33) | 1 (10) | 1 (100) |
| Normal NCP n (%) | 0 (0) | 2 (6.5) | 0 (0) | 1 (11) | 0 (0) |

| | Digital ulcers n=14 | Interstitial lung disease n=14 | Pulmonary arterial hypertension * n=1 | Gastrointestinal involvement n=11 |
|---|---|---|---|---|
| **Tortuosities** (%) (p value) | 42.9 (3) (0.716) | 42.9 | 0 | 36.4 (0.643) |
| **Dilatations** (%) (p value) | 64.3 (0.451) | 42.9 (0.693) | 0 | 45.5 (0.647) |
| **Haemorrhages** (%) (p value) | 71.4 (0.233) | 42.9 (0.360) | 0 | 45.5 (1) |
| **Megacapillaries** (%) (p value) | 71.4 (0.124) | 57.1 (0.693) | 100 | 45.5 (0.647) |
| **Neoangiogenesis** (%) (p value) | 57.1 **(0.03)** | 42.9 (0.282) | 100 | 45.5 (0.390) |
| **Avascular areas** (%) (p value) | 0.5 **(0.02)** | 42.9 **(0.056)** | 100 | 36.4 (0.673) |

Table 2 – NCP findings and clinical manifestations of SSc (*Patients submitted to right heart catheterization).

**Conclusions:** In our study the presence of avascular areas and neoangiogenesis in NCP was significantly associated with the existence of digital ulcers. Also, ILD and higher values of NT-proBNP were more common in patients who present avascular areas. These results suggest that abnormalities detected in the NCP might help predict organ involvement, although long term follow up and greater numbers of patients are needed in order to confirm the prognostic value of NCP findings.

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**Disclosure of Interest:** None declared

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## SAT0238 SUBCLINICAL ATHEROSCLEROSIS IS LOWER IN PATIENTS WITH SYSTEMIC SCLEROSIS THAN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Different studies and meta-analysis have shown that subclinical atherosclerosis (AS) and vascular complications (VC) are higher in patients with Systemic Sclerosis (SSc) than in healthy population. A major intrahospital mortality because of VC in patients with SSc as to those with Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) has also been described (Dave AJ, et al. Arthritis Care Res 2014; 66: 323–7).

**Objectives:** To compare the presence of subclinical AS among patients with SSc, RA and a population of healthy people.

**Methods:** Transverse study including patients diagnosed with SSc and RA, controlled in a Rheumatology Department of a tertiary hospital. Patients with previous VC, renal failure and/or diabetes were excluded. The control group (healthy individuals) were volunteers from the same geographical area. We gathered demographic variables (age,gender,BMI), smoking status, clinical (blood pressure), and analytical variables (cholesterol fractions, atherogenic index [AI]). The extracranial branches of carotid artery were explored by ultrasonography

(US) using an ESAOTE MyLab XV70 with a 7–12 MHz linear transducer and an automated program measuring intima-media thickness (IMT) through radiofrequency ($^{RF}$QIMT). The presence of atheroma plaques as per the Mannheim consensus was registered. Statistical analysis was done using the IBM-SPSS Statistics v22.0 package.
**Results:** 266 patients were included, 23,7% (85) with SSc and 50,4% (181) with RA. The control group was conformed by 93 healthy individuals. Women proportion, arterial hypertension and age were greater in RA and SSc patients than in healthy subjects ($p<0,001$); but smoking status was higher in healthy subjects ($p<0,001$). BMI showed lower values in patients with SSc than RA (p=0,046) and the healthy group (p=0,008). No differences were found between groups in the rest of analyzed variables. Results of the vascular study, grouped by diagnosis, is shown in the table below.

| | AS plaques % (n) | IMT μ mean (SD) | Pathologic IMT % (n) | Pathologic US % (n) |
|---|---|---|---|---|
| SSc | 22,6 (19) | 643,1 (149,7) | 8,2 (7) | 27,1 (23) |
| RA | 42 (76) | 718,2 (158,0) | 12,7 (23) | 44,2 (80) |
| Healthy | 24,7 (23) | 590,3 (123,0) | 0 (0) | 23,7 (22) |

A major prevalence of atheroma plaque and pathologic US was seen in RA patients than in SSc patients (p=0,002 and p=0,007, respectively) and healthy subjects (p=0,005 and p=0,001, respectively), whereas no differences between SSc and healthy subjects were seen within these results. Patients with SSc, however, showed higher mean IMT values than healthy subjects (p=0,047) but less than patients with RA ($p<0,001$), with a higher percentage of patients with IMT>0,9 than healthy subjects (p=0,005) in the bivariate analysis. However, this association was lost in the multivariate analysis, and these differences might be due to age and arterial hypertension differences between groups.
**Conclusions:** RA is a more atherogenic disease than SSc, probably because of its higher inflammatory load. Higher mortality by VC in SSc could be attributed to a major multiorganic affection of the disease. In our serie we didn't find a higher prevalence of subclinical AS in patients with SSc than in healthy subjects.
**Disclosure of Interest:** None declared
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## SAT0239 THE CUMULATIVE NUMBER OF MICRO-HAEMORRHAGES AND MICRO-THROMBOSIS IN NAILFOLD VIDEOCAPILLAROSCOPY IS A GOOD PREDICTOR OF DISEASE ACTIVITY IN SYSTEMIC SCLEROSIS: A VALIDATION STUDY OF NEMO SCORE

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**Background:** In a previous study it has been shown shown that, in patients with systemic sclerosis (SSc), the cumulative number of micro-haemorrhages (MH) and micro-thrombosis (MT), computed in eight finger nailfold videocapillaroscopy (NVC), and called NEMO score, was strongly predictive of disease activity (DA) measured by means of European Scleroderma Study Group (ESSG) score. Even the number of giant capillaries (GC) was correlated to a lesser extent with the ESSG score, and then a modified (m) NEMO score was proposed in which the combined presence of a MH/MT and GC was considered [1].
**Objectives:** The present study was aimed at validating NEMO score in different cohorts of patients.
**Methods:** NEMO score and the total number of GC were assessed by eight finger NVC in 122 patients with SSc referring to the Rheumatic Disease Unit of the "Istituto G.Pini" of Milan, where the preliminary study had been carried out (internal validation). The same procedure was performed in 99 patients collected in a different centre, i.e., the Rheumatic Dept. of the II University of Naples (external validation). In all of the patients DA, measured by ESSG score, was assessed at the same time of NVC performance.

Table 1

| | Number of patients | Male/ female | Patients with lcSSc/dcSSc | Age (years), mean (range) | Years from diagnosis, mean (range) | Patients with a ESSG score ≥3 |
|---|---|---|---|---|---|---|
| Milan Cohort | 122 | 8/114 | 60/62 | 53 (17–82) | 6 (0–28) | 54 |
| Naples Cohort | 99 | 10/89 | 58/41 | 53 (20–80) | 8 (1–30) | 77 |
| All patients | 221 | 18/203 | 118/103 | 53 (17–82) | 7 (0–30) | 121 |

lcSSc = limited cutaneous SSc; dcSSc = diffuse cutaneous SSc.

Table 2

| | Correlation* of NEMO vs. ESSG score | Correlation* of GC vs. ESSG score | NEMO ROC curve for ESSG score ≥3 | Sens./spec. of NEMO >7 for ESSG score ≥3 |
|---|---|---|---|---|
| Milan Cohort | R=0.54; p<0.0001 | R=0.22; p<0.02 | AUC=0.81 | 75.9/79.7 |
| Naples Cohort | R=0.59; p<0.0001 | R=0.50; p<0.0001 | AUC=0.88 | 89.5/71.9 |
| All patients | R=0.58; p<0.0001 | R=0.31; p<0.0001 | AUC=0.83 | 83.2/77.1 |

*By Spearman Rank correlation; Sens./spec. = sensitivity/specificity.

**Results:** Demographic and clinical characteristics of the patients were summarised in Table 1. Table 2 shows the main statistical results obtained by the analysis of the two cohorts.
The mNEMO score does not add anything in terms of sensitivity and specificity to the performance of the simple NEMO score in predicting DA.
**Conclusions:** This validation study confirms that the presence of a certain number of MH plus that of MT in eight finger NVC may represent a simple screening method to predict the presence of DA in patients with SSc.
**References:**
[1] Sambataro D, et al. Arthritis Res & Ther 2014;16:462.
**Disclosure of Interest:** None declared
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## SAT0240 SNPS IN THE BAFF GENE ARE ASSOCIATED WITH INCREASED RISK OF ANTI-JO-1-POSITIVITY AND HIGH SERUM BAFF LEVELS IN PATIENTS WITH MYOSITIS

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**Background:** B-cell activating factor of the TNF family (BAFF) plays a role in (auto)antibody production. Elevated serum levels (sBAFF) were found in patients with myositis. Associations of elevated sBAFF with a SNP in the 5'regulatory region of the BAFF gene were reported in patients with autoimmune diseases, together with TTTT haplotype of the four SNPs located upstream of the BAFF gene. TTTT was associated with myositis in Czech patients, independently from the HLA-DRB1*03 allele.
**Objectives:** Here we evaluate associations of sBAFF with particular SNPs, anti-Jo-1-autoantibodies, HLA-DRB1*03, ILD and disease activity in myositis.
**Methods:** The SNPs (rs9514828:871C>T, rs9514827:-2841T>C, rs3759467:-2704T>C and rs1041569:-2701T>A) were analysed by direct DNA sequencing in 311 patients with myositis (age:58.0±14.5 (years), females=74%) and 113 healthy controls (age:40.6±14.3, females=70%). Levels of sBAFF were measured by ELISA. Autoantibodies were detected by immunoprecipitation. Multivariable logistic regression model for presence of anti-Jo-1-autoantibodies and nonparametric tests for group comparisons and correlation analysis were used.
**Results:** Analysed patients cohort included 150 DM, 139 PM, 51% ILD and 24% anti-Jo-1-positive patients. HLA-DRB1*03 was present in 45% of patients and 16% of controls. Higher s-BAFF levels were detected in: patients compared to healthy controls ($p<0.0001$), patients with anti-Jo-1-autoantibodies compared to autoantibody negative (p=0.02), patients with early (duration≤6 month; n=114) compared to late disease (p=0.038) and were associated with creatine kinase (CK) levels (rho=0.36; $p<0.0001$) and disease duration (rho=-0.2; p=0.0007).
Logistic regression model explaining 49% (McFadden $R^2$=0.49) of the data variability included, besides ILD (OR=27.24; $p<0.0001$) and HLA-DRB1*03 (OR=5.26; p=0.0009), significant additive effect of the BAFF gene SNPs: -2841T allele (OR=2.55; p=0.028) and a -871TT genotype (OR=7.75; p=0.007). The alternative substitution of CK concentration (OR=1.48; p=0.175) with sBAFF (OR=0.67; p=0.037) lowered model stability ($R^2$=0.38). However, the additive effect of -871T allele to sBAFF levels in anti-Jo-1-positive patients compared to autoantibody-negative (higher in -871TT: p=0.023 and -871CT: p=0.043) and the opposite association in -2841TT genotype (higher in -2841CC: p=0.033 and -2841CT: p=0.068) were seen.
**Conclusions:** In addition to ILD and HLA-DRB1*03 allele, SNPs of the promotor region of the BAFF gene, -871C>T and -2841T>C, increase the risk of having anti-Jo-1-autoantibodies and high sBAFF levels in patients with myositis.
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## SAT0241 OBSERVATIONAL STUDY OF SEASONAL MONTHLY INFUSIONS OF ILOPROST –EXPERIENCE FROM A REGIONAL CENTRE IN UK

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**Background:** Iloprost (Prostacyclin) is effective for resistant Raynaud's phenomenon. We describe our practice of seasonal once monthly infusion which is more cost-effective and flexible than the usual practice of giving iloprost for 3 to 5 days.
**Objectives:** To identify the characteristics, response and tolerance of patients on seasonal monthly infusions of Iloprost from a regional centre in Cannock, United Kingdom.
**Methods:** Retrospective data analysis of patients having monthly iloprost infusions before and during winter for 3–4 months a year (November to February) for resistant Raynaud's phenomenon in 2013 and 2014.
**Results:** There were 72 patients; 57 females and 15 males (F/M =3.8/1), with a mean age of 50.2 (±15.1) years at the start of the iloprost infusion.

Underlying diagnosis:

| | |
|---|---|
| Scleroderma – limited | 26 (36.1%) |
| Scleroderma – diffuse | 6 (8.3%) |
| Mixed connective tissue disease | 10 (13.8%) |
| Primary Raynaud's | 10 (13.8%) |
| Systemic lupus erythematosus | 7 (9.7%) |
| Rheumatoid arthritis | 5 (6.9%) |
| Undifferentiated connective tissue disease | 3 (4.1%) |
| Dermatomyositis | 2 (2.8%) |
| Others | 3 (4.1%) |

Sixty-four patients (88.9%) received calcium channel blockers like nifedipine prior to iloprost and 2 of them also had sildenafil. Thirteen (18.1%) patients had iloprost for 3 to 5 days before switching to seasonal monthly treatment; 8 of them had a digital ulcer or gangrene at presentation. Average follow up was 3.4 (± 2.3) years and mean number of infusions/patient/year was 3.28 ± 0.98.Iloprost improved Raynaud's symptoms in winter in all the patients and was well tolerated by most. Dose adjustment of the iloprost was necessary in 6 (8.3%) patients while 5 (6.9%) of them discontinued due to intolerance.
**Conclusions:** Monthly seasonal iloprost during winter is effective and well tolerated in patients with resistant Raynaud's phenomenon. It is also less expensive than longer courses of iloprost.
**Disclosure of Interest:** None declared
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## SAT0242 LUNG INVOLVEMENT IN UNDIFFERENTIATED CONNECTIVE TISSUE DISEASES (UCTD): RELATIONSHIP WITH CLINICAL AND CAPILLAROSCOPIC FEATURES

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**Background:** Patients with UCTD (1) have been reported to present lung involvement most frequently characterized by nonspecific interstitial pneumonia (NSIP) at High Resolution Computerized Assial Tomography (HR-CAT), FVC and DLCO values lower than predicted (2).
**Objectives:** To investigate UCTD patients for the presence of lung involvement and search for demographic, serological, capillaroscopic and organ involvement features associated with it.
**Methods:** Eighty-six patients consecutively admitted to the Rheumatology Unit of the Second University of Naples and satisfying criteria for the classification of UCTD (1) were enrolled into the study. Patients presenting with any major CTD marker autoantibody other than anti-Ro (SSA) and/or scleroderma capillaroscopic specific pattern were excluded. Each patient underwent a careful history, a complete physical examination, evaluation of serum Antinuclear (ANA) and anti Extraible Nuclear Antigens antibody (anti-ENA), videocapillaroscopy, echo-Doppler-cardiography with evaluation of Left ventricular E/A ratio. Those who consented also underwent HR-CAT and esophagotonometry. Interstitial lung disease (ILD) was defined by HR-CAT or, if unavailable, by FVC<80% plus DLCO<80%.
**Results:** The table lists the features detected in the patients subdivided according to the presence of lung involvement. DLCO <80% was found in 30/86 (34.8%) patients; FVC <80% in 3/86 (1.2%); HR-CAT was carried in 36/86 (41.8%) patients. It pointed a lung involvement NSIP pattern in 5/36 patients (13%).
An isolated reduction of DLCO resulted the be the most frequent finding and might depend on pulmonary vascular disease. Anti-SSA positivity and Capillaroscopic alterations were detected more frequently in patients with lung involvement (either isolated reduction of DLCO or ILD).

| FEATURE | Normal Findings (n=56) | Isolated DLCO < 80% (n=25) | ILD (n=5) | P |
|---|---|---|---|---|
| Sex (M/F) | 6/50 | 1/24 | 3/2 | 0.0004 |
| Age at admission (median;IQ range) | 38 (30- 46) | 42 (37.7- 48) | 52 (44-60) | >0.05 |
| ANA positivity (>1:160) | 56/56 | 25/25 | 5/5 | >0.05 |
| Anti SSA positivity | 9/56 | 6/25 | 2/5 | 0.01 |
| Capillaroscopic alterations | 22/56 | 15/25 | 5/5 | 0.03 |

**Conclusions:** We detected a prevalence of ILD in UCTD lower than previously reported (2) (80%). Nevertheless, we found an isolated reduction of DLCO in about 35% of the UCTD patients. Lung involvement resulted to be significantly associated with capillaroscopic alterations and anti-SSA positivity.
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## SAT0243 REDUCTION OF PULMONARY ARTERY PRESSURE IN SCLERODERMA PATIENTS: THE ROLE OF LONG-TERM, INTENSIVE IV ILOPROST TREATMENT

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**Background:** Cardiopulmonary involvement is recognized as a poor prognostic factor in systemic sclerosis (SSc). So, stabilizing the cardiopulmonary parameters as long as possible may represent an important therapeutic goal. Intravenous iloprost is a first-line option for the treatment of SSc-related digital vasculopathy to reduce the frequency and severity of SSc-Raynaud's phenomenon (RP) attacks and to heal active digital ulcers in patients with SSc.[1] Some studies have suggested its role in preventing the incidence of most severe vascular complications in long term treated patients.[2–3]
**Objectives:** The aim of our study is to evaluate the evolution of the disease, with particular focus on cardiopulmonary function, in a group of consecutive patients chronically treated with iloprost at the Rheumatology Unit of AOU Policlinico Vittorio Emanuele, Catania Italy, from 2006 to 2015.
**Methods:** 59 SSc patients (59F, 51.8±12.1 years). At baseline, 71.2%, 20.3% and 6.8% had a limited, diffuse and early SSc, respectively, and 23% had interstitial lung disease.Iloprost was administered for a mean duration of 31.1±18.9 months, with a regimen of 6 infusions per month (6 hours/day, 0.5–2.0 ng/kg/min) to treat secondary RP, diagnosed at an average age of 45.9±14.8 years.We evaluated: skin score (SS), systolic pulmonary arterial pressure (PAPs), plane tricuspid annular systolic excursion (TAPSE), lung diffusing capacity of carbon monoxide (DLCO), forced vital capacity (FVC), alveolar volume (VA), DLCO/VA, pro-brain natriuretic peptide (pBNP), and NYHA class.We analyzed the patients as whole group and in groups divided according to the length of treatment: <1 year (n=10), 1–2 years (n=9), 2–3 years (n=21), >3 years (n=19).
**Results:** In the whole group of patients, SS showed statistically significant improvement from baseline (4.6±6.2 vs 3.9±6.0, p=0.034) while the other parameters showed no significant changes: TAPSE (21.5±2.3 vs 23.1±8.1 mm), PAPs (31.3±6.4 vs 30.1±9.0 mmHg), DLCO (83.5±14.4 vs 81.1±14.2 mmol/kPa.min), FVC (108.2±15.1 vs 107.9±18.2 liters), VA (93.4±11.7 vs 92.2±13.1 liters), DLCO/VA (88.1±13.7 vs 87.6±15.8), pBNP (105.2±75.1 vs 90.8±64.0 pg/ml), and NYHA class (1.0±0.0 vs 1.1±0.4).Subgroup analysis indicates a significant improvement in the SS from >1 year follow-up on, and a significant reduction of the PAPs in the subgroup of patients treated for more than 3 years. We observed an inverse correlation (R=-0.97) between the duration of treatment and the reduction of the PAPs from baseline.
**Conclusions:** An intensive (6 inf/month) and chronic regimen of iv iloprost administration seems to stabilize and potentially improve the long term evolution of disease in SSc patients, as suggested by the stabilization of cardiopulmonary parameters and the significant improvement of SS and PAPs in patients treated for more than 3 years.Our results suggest a potential effect of iv iloprost on the evolution of the disease, with a role that goes beyond the mere treatment of SSc vasculopathy.
**References:**
[1] Ann Rheum Dis;68:620–8.
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**Disclosure of Interest:** None declared
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## SAT0244 ACTIVE SKIN DISEASE AT BASELINE DOES NOT PREDICT PROGRESSION OF SKIN FIBROSIS AT ONE YEAR FOLLOW UP – A EUSTAR ANALYSIS

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**Background:** In clinical trials of systemic sclerosis (SSc), there is an unmet need for better inclusion criteria to enrich for patients with progressive skin fibrosis [1,2]. Recent trials on skin fibrosis frequently used active skin disease at baseline as an enrichment parameter. However, there is little data available supporting such an approach.

**Objectives:** To investigate the relationship between active skin disease at baseline and progression of skin fibrosis after one year in patients with diffuse cutaneous SSc (dcSSc).
**Methods:** A longitudinal analysis of the EUSTAR registry was performed. The inclusion criteria were: dcSSc, fulfillment of ACR criteria, baseline mRSS≥7, available data for mRSS at 12±2 months. Skin progression was defined as increase in mRSS of >5 points AND ≥25% within 1 year [1]. Activity of skin fibrosis was assessed by patient-reported parameters (worsening of skin within the past month), by using a modified skin thickness progression rate (defined as MRSS at baseline visit/disease duration (years)) and by following patients with progression of mRSS in the recent 12 months for another 12 months. Additionally, non skin specific activity parameters such as the Valentini index, elevated serum inflammatory markers, and other patient reported activity parameters were also analyzed. The Mann-Whitney and the Chi-square tests were used.
**Results:** From the 637 patients included, 9.7% had progressive skin fibrosis after 1 year. The patient-reported worsening of skin fibrosis within the past month prior to baseline was not significantly associated with progressive skin disease after 1 year (p=0.774). Similarly, the modified skin progression rate at baseline did not differ between progressive and non-progressive patients at 1 year follow up (p=0.323). Most interestingly, patients with progression of skin fibrosis in the previous year were not significantly more likely to show progression of skin fibrosis in the following year (p=0.385, none of the initially progressive patients at one year showed further progression). In addition, other more general activity parameters at baseline including the Valentini activity index (p=0.673) and inflammatory markers (Erythrocyte sedimentation rate, p=0.287; C-reactive protein p=0.358) were also not associated with progression of skin fibrosis after one year (Figure 1).

Figure 1. Association of baseline parameters of active skin fibrosis and other activity parameters with skin progression at one year

| Parameter of disease activity* | Association with skin progression after one year (P-value**) |
|---|---|
| Worsening of skin in the last month (185/637) | 0.774 |
| Modified skin progression rate (590/637) | 0.323 |
| Progression of mRSS in the recent 12 months*** (377/637) | 0.385 |
| Erythrocyte sedimentation rate (175/637) | 0.287 |
| CRP elevation (177/637) | 0.358 |
| Worsening of finger vascularisation in the last month (185/637) | 0.100 |
| Worsening of cardiopulmonary symptoms in the last month (184/637) | 0.100 |
| Valentini activity index (139/637) | 0.673 |

Abbreviations: mRSS: modified Rodnan skin score
* (available cases/whole cohort)
** as by Mann-Whitney or Chi-square tests, as appropriate by variable type
*** Progression of the mRSS between the 2nd (1-year follow-up) and 3rd visit was computed only if the 3rd visit took place 12 ± 2 months after the 2nd visit.

**Conclusions:** dcSSc patients with recently active skin disease have a similar or even lower likelihood to show further progression of skin fibrosis in a 12 months trial – most likely because they have reached their peak skin score already. Recently active skin disease should not be used as an enrichment criterion in clinical trials targeting skin fibrosis.
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[1] Maurer B, Graf N, Michel BA, et al. Prediction of worsening of skin fibrosis in patients with diffuse cutaneous systemic sclerosis using the EUSTAR database. Ann Rheum Dis. 2015;74(6):1124–31.
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**Disclosure of Interest:** R. Dobrota: None declared, B. Maurer: None declared, N. Graf: None declared, O. Kowal-Bielecka Consultant for: Abbvie, Actelion, Bayer, Biogen, Pfizer, Roche, Speakers bureau: Abbvie, Actelion, Bayer, Biogen, Pfizer, Roche, M. Matucci-Cerinic: None declared, P. Airò: None declared, P. Caramaschi: None declared, P. Carreira: None declared, G. Riemekasten: None declared, E. Rosato: None declared, Y. Allanore Grant/research support from: Bristol-Myers Squibb, Roche/Genentech, Inventiva, Pfizer, Sanofi, and Servier, Consultant for: Actelion, Bayer, Roche/Genentech, Inventiva, Medac, Pfizer, Sanofi, Servier, and UCB, O. Distler Grant/research support from: Bayer, Sanofi, Ergonex, Boehringer Ingelheim, Actelion, Pfizer, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, EpiPharm, Ergonex, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Pharmacyclics, Pfizer, Serodapharm, Sinoxa
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## SAT0245 COMPARISON OF PAIN CHARACTERISTICS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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**Background:** Rheumatoid arthritis (RA) is a systemic inflammatory disease characterized by progressive destruction of inflamed joints leading to severe disability and functional loss. Systemic sclerosis is a multisystem autoimmune disease characterized by vasculopathy, diffuse fibrosis of skin and various internal organs. Pain is usually an overlooked entity in patients with SSc compared to RA.
**Objectives:** To compare pain characteristics particularly in terms of neuropathic pain (NeP) and to assess the possible impact of neuropathic component on functioning, physical and mental components of health related quality of life (HRQoL) in patients with RA and SSc.
**Methods:** Patients who met ACR/EULAR criteria for SSc and RA were recruited. Patients with prior diagnosis or taking medications for NeP, mood disorders, uncontrolled diabetes or neurological disorders or taking any biologic agents for their treatments were excluded. Patients were examined and evaluated for disease specific and generic outcome measures including disease activity parameters, physical functions, psychological status and health related quality of life measures (SF-36; HAQ; Hospital Anxiety and Depresson Scale, HADS). The DN4 interview and PainDetect questionnaire were applied by the same experienced physician who was blind to patients clinical and outcome data. Patients with a score ≥4 in DN4 were considered as "probable NeP"; between 13–18 or ≥19 in PainDetect were considered as "possible" or "likely NeP", respectively.
**Results:** Fifty patients (44 F, 6 M) with SSc and fifty-one (45 F, 6 M) with RA were included. Patients had similar age and similar gender, educational and smoking status, as well as functioning and HRQoL. However, patients with RA declared more severe pain on VAS-pain (p=0.012), and higher body mass index than patients with SSc (p<0.0001). NeP component was similar in patients with SSc vs RA. NeP component was detected 42.0% in SSc, and 47.1% in RA (p>0.05) according to DN4 scores. According to PainDetect questionnaire, possible NeP was detected in 12.0% vs 15.7%, whereas 16.0% vs 17.6% had likely NeP in SSc and RA, respectively (p>0.05). Neuropathic characteristics of pain were similar in SSc and RA defined as burning, electric shock, tingling, pins and needles, and itching except for numbness and painful cold which were significantly more prevalent in patients with SSc (%50.0 vs %25.5, p=0.011 and %50.0 vs %19.6, p=0.001; respectively). In SSc patients with or without NeP component had similar functioning and HRQoL measures. However, having NeP component revealed a heavier burden of disease regarding functioning, HRQoL and psychometric components patients with RA.

| | NeP +ve | NeP –ve | P |
|---|---|---|---|
| SSc | (n=21) | (n=29) | |
| Age | 53.43±9.58 | 43.55±13.82 | 0.004 |
| HAQ | 0.55±0.62 | 0.53±0.60 | 0.758 |
| SF-36 – PCS | 53.90±21.62 | 48.58±20.41 | 0.350 |
| SF-36 – MCS | 64.33±21.36 | 53.87±20.85 | 0.087 |
| HADS – depression | 7.76±3.45 | 7.10±3.63 | 0.636 |
| HADS – anxiety | 7.38±3.75 | 6.10±4.17 | 0.252 |
| 6-min walk, m | 408.95±67.16 | 433.21±82.46 | 0.336 |
| RA | (n=24) | (n=27) | |
| Age | 50.21±9.17 | 51.30±11.02 | 0.850 |
| HAQ | 0.48±0.62 | 0.57±0.64 | 0.727 |
| SF-36 – PCS | 40.55±17.63 | 59.77±20.37 | 0.0001 |
| SF-36 – MCS | 42.83±15.06 | 68.99±21.14 | 0.0001 |
| HAD – depression | 9.29±4.30 | 5.56±4.33 | 0.004 |
| HAD – anxiety | 10.08±3.78 | 5.67±4.37 | 0.0001 |
| 6-min walk, m | 378.33±77.27 | 368.15±69.74 | 0.690 |

**Conclusions:** The NeP component was similar in patients with RA and SSc. However NeP was associated a heavier burden of disease in patients with RA.
**Disclosure of Interest:** None declared
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## SAT0246 COMPARISON OF LEVEL OF FATIGUE AND DISEASE CORRELATES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC SCLEROSIS

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**Background:** Rheumatoid arthritis (RA) and systemic sclerosis (SScl) are two different forms of connective tissue diseases associated with significant morbidity. While fatigue is not required for a diagnosis of RA or SScl persistent fatigue is an important clinical problem which may interfere with loss of functioning and health related quality of life (HRQoL) and contribute to the increased disease burden. Several studies compared these two diseases in terms of clinical, laboratory and imaging aspects, however level of fatigue has not been evaluated comparatively.
**Objectives:** The aim of this study was to compare levels of fatigue in RA and SSc and to assess potential influence of fatigue on clinical variables.
**Methods:** Patients meeting the ACR/EULAR criteria for SSc and RA with an age more than 18 were consecutively recruited. Patients with a prior diagnosis of psychiatric disorders or fibromyalgia or taking medications for these disorders,

or with uncontrolled diabetes, neurological disorders or taking any kind of biologic agents were excluded. Patients were examined and evaluated for disease specific and generic outcome measures including disease activity parameters, physical functions, psychological status and health related quality of life (HRQoL) measures. Level of fatigue was assessed by Fatigue Severity Scale (FSS) and Multidimensional Assessment of Fatigue (MAF) scale. These were interviewed by the same experienced physician who was blind to clinical data.
**Results:** Fifty patients (44 F, 6 M) with SSc and fifty-one (45 F, 6 M) with RA were included. Patients had similar age and similar gender, educational and smoking status, as well as functioning and HRQoL. However, patients with RA declared higher levels on VAS-pain (p=0.012), and higher body mass index than patients with SSc (p<0.0001) and lower distances in 6-minute walking test (p=0.002). Levels of fatigue which were assessed by VAS, FSS and MAF were quite similar between patients with RA and SSc. Levels of fatigue, measured by different scales, were significantly correlated with physical functions and HRQoL measures and psychometric variables in both groups, however the correlation coefficients were relatively higher in patients with RA.

| | SSc, n=50 | RA, n=51 | P |
|---|---|---|---|
| Age | 47.70±13.07 | 50.78±10.11 | 0.189 |
| BMI, kg/m$^2$ | 26.26±5.95 | 30.96±6.17 | 0.0001 |
| Symptom duration, years | 10.10±7.04 | 11.06±8.01 | 0.525 |
| VAS – pain | 3.95±2.94 | 5.25±2.08 | 0.012 |
| HAQ | 0.54±0.60 | 0.53±0.63 | 0.946 |
| SF-36 – vitality | 48.40±20.26 | 51.76±21.54 | 0.421 |
| SF-36 – PCS | 50.81±20.88 | 50.72±21.27 | 0.983 |
| SF-36 – MCS | 58.27±21.49 | 56.68±22.60 | 0.719 |
| FSS | 4.67±1.77 | 4.39±1.94 | 0.439 |
| MAF – severity | 6.37±2.07 | 5.50±2.37 | 0.064 |
| MAF – distress | 5.80±2.74 | 5.56±2.56 | 0.656 |
| MAF – interference ADL | 4.78±2.25 | 5.07±2.17 | 0.534 |
| MAF – timing | 6.39±2.05 | 6.56±2.08 | 0.696 |
| MAF – global fatigue index | 27.77±12.22 | 25.27±12.77 | 0.317 |
| 6-min walk, m | 423.40±76.82 | 372.94±83.43 | 0.002 |
| VAS – F | 5.96±2.67 | 5.14±2.84 | 0.148 |

**Conclusions:** Fatigue is a major problem in patients with RA and SSc. This is the first report comparing these two diseases in terms of fatigue and its correlates. Patients with RA and SSc should be carefully evaluated for fatigue by using valid scales and the impact of fatigue on clinical measures should not be overlooked.
**Disclosure of Interest:** None declared
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## SAT0247 HIGHER FIBRINOGEN PLASMA LEVELS AT BASELINE ARE ASSOCIATED WITH A FASTER DEVELOPMENT OF NEW DIGITAL PITTING SCARS/ULCERS AT FOLLOW-UP IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** The -455 G>A polymorphism in the proximal promoter region of β-fibrinogen gene is known to increase fibrinogen plasma levels and to promote arterial and venous thrombosis in the general population (1). We previously showed that systemic sclerosis (SSc) patients with pitting scars and/or ulcers have a higher frequency of the β-fibrinogen -455 A allele and higher plasma levels of fibrinogen (2).
**Objectives:** We aimed to investigate fibrinogen plasma levels in a prospective cohort of SSc patients and to search for associations with features of vascular involvement at follow-up (FU).
**Methods:** SSc patients meeting the 2013 ACR/EULAR criteria for disease classification with measurement of fibrinogen plasma levels and at least one FU visit with complete clinical evaluation were enrolled. The comparison of fibrinogen levels in different patient groups was performed using the Mann-Whitney U test; differences between patients with fibrinogen levels higher or equal/lower than the median value were analyzed by Kaplan-Maier curves applying the log-rank test.
**Results:** One-hundred and thirty-three SSc patients, aged 51±13 years, were investigated (91% females; median disease duration 8 years, range 1–49). Seventy-six % of patients had a limited SSc subset (lcSSc); 24% had a diffuse subset (dcSSc). All patients were ANA positive (40% had anti-centromere antibodies, 35% anti-Scl70+; 3% anti-RNApolymerase III; 2.3% anti-PmScl; 1.5% anti-U1RNP). All patients were under low-dose aspirin and oral vasodilators. Forty-one % of patients had already pitting scars and/or ulcers at baseline; 13% developed new digital ischemic injury during observation (median FU 3 years; range 0.7–22). Baseline fibrinogen levels were higher in patients who developed digital ischemic lesions during FU (385 mg/dl, range 180–688 versus 344 mg/dl, range 81–765; p<0.05). SSc patients with levels higher than the median value developed new ischemic lesions in the digits faster than patients with values lower or equal to the median ($\chi^2$=4.3; p<0.05).
**Conclusions:** Consistently with our previous findings, here we first show that higher fibrinogen levels at baseline in SSc patients are associated with a faster development of new digital ischemic lesions over time. Of note, all our patients were taking aspirin, which, however, does not affect platelet-fibrinogen interaction. In addition, all of them were taking an oral vasodilator, that is recommended for the treatment of peripheral vasculopathy in SSc (3). Randomized controlled clinical trials in larger SSc cohorts to explore the potential benefit of gpIIb/IIIa inhibitors± low-dose aspirin in these patients are needed.
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## SAT0248 B CELL CHARACTERIZATION IN SYSTEMIC SCLEROSIS: CD19 CORRELATES INVERSELY WITH DISEASE ACTIVITY AND PLASMABLASTS DIRECTLY WITH DIFFUSE DISEASE AND LUNG INVOLVEMENT

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**Background:** B cells play an important role in Systemic Sclerosis (SSc).
**Objectives:** To determine the phenotypic characteristics of blood B cell subsets in patients with SSc and their possible association with organ involvement and disease activity.
**Methods:** 100 SSc patients (83.0% females; mean age 56.5±13.9 years; 49 (49.0%) with diffuse skin involvement-dcSSc) and 50 age and sex matched healthy controls (HC) were studied. Clinical, immunological and inflammatory characteristics were assessed for all the SSc patients. Peripheral blood samples were analyzed by flow cytometry for the distribution of circulating B cell subpopulations by staining with surface markers CD45, CD19, CD38, CD27 and IgD (1). For each patient at study entry, disease activity and severity were evaluated (2,3). Patients with an activity score ≥3.0 were considered to have an active disease.
**Results:** The distribution of circulating CD19+ cells of SSc patients and healthy controls was comparable. Considering the two main phenotypes of the disease, the percentage of CD19+ cells was lower in patients with dSSc versus HC (8.0±4.8%vsHC 10.6±3.3%, p=0.01), as well as versus patients with limited skin disease (lSSc) (11.3±5.3%, p=0.01). The percentage of CD19 cells inversely correlated with activity index (R=-0.36, p=0.001) and patients with active disease showed lower percentage of CD19 (8.1±4.2%) compared with patients with inactive disease (11.6±5.9%, p=0.001). ROC curve analysis showed a CD19 cut off of 5.5% as the one that identified patients with active disease (AUC=0.31, p=0.006). Patients with CD19 higher than 5.5% more frequently presented a diffuse disease (p=0.02) and a restrictive lung involvement (p=0.001). The analysis of B cell subsets showed a lower percentage of pre-switched memory B cells (IgD+CD27+: 7.9±8.3p<0.001) and an higher percentage of naïve B cells (IgD+CD27-: 70.7±16.9, p=0.001) in SSc patients with respect to HC (IgD+CD27+:13.3±8.3,p<0.001;IgD+CD27-:64.4±11.1,p=0.001). An higher percentage of naïve B cells and a lower percentage of pre-switched memory B cells were confirmed either for diffuse (IgD+CD27-:8.4±9.3%; IgD+CD27+: 69.5±18.9%) or the limited subset of the disease (IgD+CD27-: 7.4±7.5%; IgD+CD27+: 71.4±19.0%) with respect to HC (p<0.02 for all comparisons).Furthermore an higher percentage of plasmablasts (CD38+CD27+: 4.0±4.5%) was observed in dSSc patients compared to HC (2.0±2.6%, p=0.004) and compared with the limited disease (2.2±2.8%, p=0.003). Considering organ involvement, an higher percentage of plasmablast (3.9±3.4) characterized patients with restrictive lung disease (FVC<79%) with respect to patients with FVC>79% (2.9±3.9%, p=0.01).
**Conclusions:** Systemic sclerosis patients show an immune deregulation of B cell subset phenotypes in the peripheral blood. The difference in the percentage of CD19 population in the different subsets of the disease and when the disease is active suggests that the CD19 count may be a potential simple biomarker of the activity. Plasmablasts represent crucial biomarkers of dSSc with lung involvement.
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## SAT0249 PREDICTORS OF RESPONSE TO METHOTREXATE IN PATIENTS WITH EOSINOPHILIC FASCIITIS

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**Background:** Eosinophilic fasciitis (EF) is a rare scleroderma-like disorder

described in 1974 by Shulman. It is characterized by the acute onset of edema and induration of the skin and the subcutaneous tissue associated with peripheral blood eosinophilia. Deep skin biopsy shows characteristic alterations in the muscle fascia. There is no consensus regarding the treatment of the FE. Oral or intravenous glucocorticoids (GC) are usually the initial treatment with significant improvement in most cases. Immunosuppressive drugs may be associated when the response is insufficient and the most used is methotrexate (MTX). The response to MTX is usually favorable, especially in cases with concomitant morphea lesions. However, there are no studies that specifically analyze which factors predict response to treatment with this drug in EF.

**Objectives:** To determine which demographic, clinical and laboratory baseline features are associated with remission during treatment with MTX in patients with EF.

**Methods:** We performed an observational, retrospective (1983–2014) and multicentric study of patients with EF from 5 Spanish university hospitals. Inclusion criteria: 1) characteristic cutaneous manifestations; 2) deep biopsy with consistent changes in muscle fascia, and 3) treatment with MTX. Response to treatment with this drug is divided into: 1) complete remission (absence of symptoms and disappearance of lesions); 2) partial response (patients who develop limitation despite treatment); and 3) lack of response (persistence of symptoms and findings on examination). Statistical nonparametric tests were used for the data analysis, Kruskal Wallis for continuous variables and x2 for categorical variables.

**Results:** 33 patients were included, 18 women (54.5%), with a mean age of 54.6 years (range 22–81) and a median duration of disease until diagnosis of 4 months (range: 1–25). Most of these patients had previously been treated with GC (97%) with insufficient response, 8 (24.2%) had previously received other Immunomodulatory drugs (hydroxychloroquine, azathioprine, cyclosporine) and 5 (15.2%) with photochemotherapy (PUVA). The median MTX dose used was 15 mg/week (range: 10–25), 16 (48.5%) cases achieved complete remission with this drug, 15 (45.5%) partial response and 2 (6%) lack of response. Patients who achieved complete remission had a mean age at diagnosis slightly higher (64), presented more frequently induration $\geq$50% of body surface, myalgia and associated malignancies but C-reactive protein (CRP) levels were lower. Of all the variables analyzed, only low CRP level was significantly associated with complete remission (p=0.004). Two patients in remission relapsed after discontinuation of MTX, with a favourable response to re-treatment with GC.

**Conclusions:** The only variable that seems to be associated with remission during treatment with MTX in our series is the absence of elevated CRP. All other variables showed no significant differences, although the statistical power may be small due to the limited sample size.

**Disclosure of Interest:** None declared

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## SAT0250 SCREENING FOR SUBCLINICAL PULMONARY VASCULAR DISEASE OF SYSTEMIC SCLEROSIS: THE BEST NON-INVASIVE TEST AND WHAT WE FOUND BY GENE EXPRESSION ANALYSIS OF PERIPHERAL BLOOD

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**Background:** Pulmonary arterial hypertension (PAH) remains a leading cause of death in systemic sclerosis (SSc) in spite of current best treatments. As the better treatment effects is expected in the earlier PAH, current studies focus on early diagnosis. On the other hand, it is known that pulmonary vascular disease (PVD) can be well compensated for. Therefore, more than a half of the pulmonary circulation is considered to be obstructed by PVD before early PAH is detected. Recently, it has been reported that stress testing with exercise or infusion of dobutamine can reveal abnormal mean pulmonary artery pressure-cardiac output (mPpa-Q) responses, which may facilitate early diagnosis of PVD.

**Objectives:** We tried to detect changes at the stage of subclinical PVD in SSc with using non-invasive or invasive examinations including pulmonary function test, cold stress thermography, stress Doppler echocardiography (DE) or stress right heart catheterization (RHC). And then, gene expression profiles, including subclinical PVD of SSc, in peripheral blood were explored

**Methods:** Total of 58 cases categorized NYHA I with Raynaud symptoms (78.0%), puffy fingers (49.2%), or serological abnormality related to SSc including anti-centromere (44.8%), anti-topoisomerase I (1.7%), or anti-U1-RNP antibody positive (10.3%) were investigated. To find the best non-invasive index to screen for early PVD, correlation between mPpa-Q by dobutamine stress RHC and the result of clinical tests were evaluated (n=15). The tests includes serum BNP, %DLCO and %VC/%DLCO by pulmonary function test, thermography of hand with cold stress, resting tricuspid regurgitation pressure gradient (rest TRPG), maximum TRPG and mPpa-Q estimated by DE with Master's two-step stress. Then, the expressed genes in peripheral blood, which correlated with the best non-invasive index, were explored with using next-generation sequencing (n=58).

**Results:** The mPpa-Q by dobutamine stress RHC was found to correlate most strongly with maximum TRPG estimated by exercise DE (R=0.65, p<0.01, FDR<0.05). The analysis of gene expression profile revealed that expressions of 94 genes were highly correlated with maximum TRPG by exercise DE (p<0.0001, FDR<0.05). It includes fibroblast growth factor (FGF) 12 (R=0.59, P<0.000001, FDR<0.05) and FGF 23 (R=0.50, P<0.0001, FDR<0.05). It also contained the genes of bone morphogenetic protein (BMP) 10 (R=0.47, P<0.001, FDR<0.05) and endothelin 2 (R=0.47, P<0.001, FDR<0.05), that are reported to be directly implicated in the development of PAH[1)].

**Conclusions:** Although detection of early PVD in SSc patients remains a major challenge, maximum TRPG by stress DE seems to be an encouraging candidate for non-invasive screening. The results of gene expression analysis shed on changes in circulating blood cells at the early stage of SSc-associated PVD. By the analysis of gene expression, we found a very strong correlation between FGF12/23 and maximum TRPG by exercise DE. It is of particular interest that BMP-10 and endothelin-2 were also correlated significantly. As these factors were reported to be involved in the development of PAH, it is possible that theses factors could be candidates for therapeutic target to prevent the progression of SSc-associated PVD.

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**Disclosure of Interest:** None declared

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## SAT0251 VASCULAR INVOLVEMENT IN SCLERODERMA; PHENOTYPIC VARIABILITY WITH DIFFERENT MECHANISTIC PATHWAYS

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**Background:** Vascular involvement is an early feature of Systemic sclerosis (SSc) and has a major role in the phenotypic presentation of the disease. Recent data showed overlapping pathways between bone and vascular biology. OPG was shown to enhance neovascularization and protects micro-vascular endothelial cells (ECs) from apoptosis; Signaling studies on human umbilical vein endothelial cells (HUVECs) showed that OPG is a positive regulator of micro-vessel formation acting as a pro-angiogenic molecule, OPG is also increased in idiopathic pulmonary artery hypertension (iPAH). RANKL, has shown anti-angiogenic properties with subsequent inhibition of EC proliferation. Vinculin: in turn was shown to be over expressed in ECs and may have a role in the impaired angiogenic process seen in SSc. we hypothesize that overexpression of Vinculin in SSc may trigger anti-vinculin antibodies (abs) which may contribute to vasculopathic features in SSc.

**Objectives:** We wanted to investigate the role of OPG/RANKL, anti-Vinculin antibodies as biomarkers of vascular dysfunction such as PAH and ulcers in SSc.

**Methods:** Serum levels of OPG/RANKL and Anti-Vinculin abs were measured by ELISA in serum obtained from 70 SSc patients. Correlations between serum levels and clinical aspects of SSc patients (skin ulcers, PAH) were done by linear regression analysis. Clinical assessments, procedures, questionnaires and lab results were obtained from medical charts for clinical correlations.

**Results:** 70 SSc pts, mean age 56 yrs, 58females, 23 (32%) pts with PAH, active ulcer in 19 (28%) (table 1). Higher OPG was associated with older age (p=0.003), lower Ulcer visual analogue scale (VAS) (p=0.036), lower FEV1 (p=0.042). No association was found with PAH (p=0.50). Higher RANKL levels were associated with presence of skin ulcers (p=0.039). There was no evidence of differential prediction of OPG and RANKL for any of the clinical variables, given PAH status, using linear regression. In contrast, Linear regression analysis for anti-vinculin identified PAH (p value<0.052) as significant predictors of higher anti-vinculin in SSc patients. Further regression analysis for predictors of PAH with higher vinculin levels revealed smoking (current or former) as a significant (p value <0.01) predictor.

**Conclusions:** Higher RANKL correlated with the presence of skin ulcers while Higher OPG correlated Lower ulcer VAS regardless of the PAH status. Anti-vinculin antibodies correlated with PAH regardless the skin ulcer status of our SSc patients.

Although vascular dysfunction has a major role in driving the various morbidities in SSc (ulcer and PAH), Our Study Suggests that Different pathogenic pathways are involved in skin ulcer and Pulmonary artery hypertension.

**Disclosure of Interest:** None declared

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SAT0252 **LONG-TERM SURVIVAL ANALYSIS AND PROGNOSTIC OUTCOME FACTORS IN IDIOPATHIC INFLAMMATORY MYOPATHY**

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**Background:** Idiopathic inflammatory myopathy is a group of systemic connective tissue diseases, including dermatomyositis (DM), polymyositis (PM) and inclusion body myositis (IBM). PM/DM are characterized by chronic muscle inflammation and can affect other internal organs. Survival rate and prognostic factors of PM/DM vary widely. The 5-year survival rates for PM/DM range from 60% to 95%. Additionally, the long-term outcome of a large group of Chinese patients with PM/DM is absent. Although Interstitial lung disease (ILD) and coexistent cancer were indicated to be predictors of mortality, few studies conducted multivariate regression analysis to provide independent prognostic factors, as well as the calculation of Standardized Mortality Ratio for PM/DM patients.
**Objectives:** To analyze the survival rate, cause of death and the prognostic outcome factors in idiopathic inflammatory myopathy (IIM).
**Methods:** A total of 201 IIM patients treated in Peking University People's Hospital from January 1996 to September 2013 were included. Medical records were abstracted for clinical, laboratory and therapeutic data.
**Results:** The follow-up time of 201 IIM patients, including 121 with DM, 33 with PM and 47 with CADM, ranged from one to 492 months, and 56 cases were lost to follow up. Overall cumulative survival rate was 93.0%, 87.0%, 86.0% and 84.0% at 1, 3, 5 and 10 years respectively from the disease onset. The rates were similar in DM, PM and CADM. During the follow-up period, 26 (19.3%) patients died, among which 21 cases died within 3 years from the onset. Respiratory failure associated with ILD was the main cause of death, followed by cardiac involvement and coexistent malignancy. Rapidly progressive ILD, myalgia, fever, abnormal ECG, normal CKMB, lymphopenia and hypoalbuminemia, elevated LDH and CEA were associated with mortality ($P<0.05$). In multivariate Cox regression analysis, elevated CEA was the significant predictor of poor outcome. Therapy with glucocorticoids combined with immunosuppressants for more than one year was negatively correlated with mortality, as well as methylprednisolone pulse therapy for patients with rapidly progressive ILD. Intravenous cyclophosphamide therapy was associated with a better survival than MTX.
**Conclusions:** The ten-year survival rate shows no statistically significant difference among DM, PM and CADM. The survival rate of patients with rapidly progressive ILD is significantly lower than patients with chronic or without ILD. Elevated CEA acts as the independent risk factor for poor prognosis. Glucocorticoids combined with immunosuppressants for more than one year is associated with high survival rate. Intravenous cyclophosphamide therapy is associated with a better survival than MTX.
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## Paediatric rheumatology

SAT0253 **EVANS SYNDROME AT CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS DIAGNOSIS: A LARGE MULTICENTER STUDY**

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**Background:** Evans syndrome (ES) is an uncommon manifestation characterized by autoimmune destruction of red cells and platelets and concomitant or sequential appearance of immune thrombocytopenia (ITP) and autoimmune hemolytic anemia (AIHA). This involvement has been associated to severe disease activity in adult patients with systemic lupus erythematosus (SLE), particularly at disease onset. However, ES studies in childhood-onset SLE (cSLE) patients have been rarely reported and limited to small populations.
**Objectives:** The objective of the present multicenter study was to assess ES in a large cSLE cohort at diagnosis evaluating prevalence, clinical features, laboratory findings and outcomes.
**Methods:** A retrospective multicenter cohort study (Brazilian cSLE group) was performed in 10 Pediatric Rheumatology services including 850 patients with cSLE (ACR criteria). None of them had secondary etiologies of autoimmune cytopenias, such as infections, primary immunodeficiencies and malignancies. Patients were divided in two groups for the assessment of lupus manifestations, laboratory exams and treatment at cSLE diagnosis: patients with ES and patients without ES.
**Results:** ES was observed in 11/850 (1.3%) cSLE patients at diagnosis. The majority of them had hemorrhagic manifestations (58%) and active disease (82%). All patients with ES were hospitalized and none of them died. Comparisons of cSLE patients with and without ES at diagnosis revealed similar frequencies of female gender, multi-organ involvement, autoantibody profile and low complement levels ($p>0.05$). Patients with ES had a lower frequency of malar rash (9% vs. 53%, p=0.003) and musculoskeletal involvement (18% vs. 69%, p=0.001) than those without this complication. The median of hemoglobin [7.4 (5.4–9.4) vs. 10.3 (3.5–16.4)g/dL, $p<0.001$] and platelets [27 (15–54) vs. 231 (2–761)x$10^3$/mm$^3$, p=0.005] were significantly lower in ES compared to non-ES patients, whereas lymphocytes were significantly higher in ES patients [1.8 (1–2.38) vs. 1.16 (0.07–7)x$10^3$/mm$^3$, $p<0.001$]. The frequencies of intravenous methylprednisolone (82% vs. 43%, p=0.013) and intravenous immunoglobulin use (64% vs. 3%, $p<0.0001$) were significantly higher in the former group. Current prednisone dose between the two groups was similar [1.1 (0.76–1.5) vs. 1.0 mg/kg/day (0–30), 0.195].
**Conclusions:** Our large multicenter study identified that ES was a rare and severe cSLE manifestation with a difficult diagnosis due to the absence of typical lupus manifestations, often requiring hospitalization and intravenous treatment.
**Disclosure of Interest:** G. Lube: None declared, M. Ferriani: None declared, L. Campos: None declared, M. Terreri: None declared, E. Bonfá: None declared, C. Magalhães: None declared, N. Aikawa: None declared, D. Piotto: None declared, O. Peracchi: None declared, M. C. Santos: None declared, S. Appenzeller: None declared, V. Ferriani: None declared, R. Pereira: None declared, C. Silva Grant/research support from: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 302724/2011–7 to CAS), Federico Foundation (to CAS) and by Núcleo de Apoio à Pesquisa "Saúde da Criança e do Adolescente" da USP (NAP-CriAd) to CAS
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SAT0254 **THE ICEBERG IN JUVENILE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: SUBCLINICAL DETERIORATION OF CARDIAC FUNCTIONS ASSESSED WITH TWO-DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY AND CONTRIBUTING FACTORS OF SYSTOLIC DYSFUNCTION**

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by vasculitis and inflammation in various organs. Cardiovascular involvement, although not frequent in juvenile-onset SLE (j-SLE), if present, is a significant cause of morbidity and mortality (1). Particularly, involvement of the myocardium layer may lead to ventricular dysfunction since its progression is insidious (1,2). Speckle tracking echocardiography (STE) could demonstrate subclinical myocardial deformations (strain) that globally seems normal in conventional echocardiography (2).
**Objectives:** The aim of this study is early detection of subclinical systolic dysfunctions in j-SLE with STE and if present, then to investigate whether this is disease-related or it is a result of other predisposing conditions.
**Methods:** 35 patients with j-SLE and 30 healthy children as a control group were evaluated between January and August 2015 at outpatient clinics of Cerrahpasa Medical Faculty. STE was performed on all patients and controls. Medical records that are including age at diagnosis, duration of the disease, diagnostic criteria, laboratory tests and cumulative clinical manifestations were evaluated. SLE disease activity was assessed using the SLE Disease Activity Index (SLEDAI). A SLEDAI score >4 was arbitrarily designated as a sign of moderate/severe disease activity.
**Results:** j-SLE patients had lower EF values than control subjects. Left ventricular end diastolic dimension (LVEDD) and left ventricular end systolic dimension (LVESD) were significantly greater in j-SLE patients (42,278±4,530 vs. 37,314±5,535; 28,108±3,344 vs. 24,055±3,290 p=0.001, respectively) than in the control group. There was a significant reduction in systolic parameters of longitudinal strain in the j-SLE group ($p<0.05$) at all segments compared to control patients.
SLE patients were divided into two subgroups. Group 1 included patients having SLEDAI scores >8 at the beginning of the disease but who improved with therapy during follow up, with resulting SLEDAI scores less than or equal to 4 points. Group 2 included j-SLE patients with SLEDAI scores >8 at diagnosis but with SLEDAI scores still greater than 4 at the end of follow up.
In comparisons of two groups, mid inferior and mid inferolateral LV segment STE

strain measurements of Group 2 were significantly lower than those in Group 1, (15.9000±6.47130 vs. 20.0714±4.49725 mid inferior; 17.9000±7.23341 vs. 23.2308±3.87629 mid inferolateral, p=0.075, 0.055, respectively).
**Conclusions:** We can say that prevention of long-term cardiovascular complications in j-SLE begins with noticing the iceberg early, before irreversible changes take place. In this regard, STE is an accurate method for detecting subclinical systolic dysfunction.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2483

## SAT0255 PROSPECTIVE STUDY: THE ROLE OF URINARY HER2 AS A LUPUS NEPHRITIS BIOMARKER

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**Background:** Recently, a dramatic increase in HER2 expression in the glomeruli and in the tubular compartment of patients with lupus nephritis was observed. A similar pattern was not seen in patients with IgA nephropathy, post-streptococcal glomerulonephritis or granulomatosis with polyangiitis. HER2 overexpression was also found in NZM2410 mice and it correlated with disease activity. *In vitro*, IRF1 and α-interferon increased HER2 expression in human mesangial cells and HER2 regulated the levels of miR-26a and miR-30b. These miRNAs control mesangial cell proliferation, by regulating the expression of several genes, including those controlling cell cycle. It was also found that urinary HER2 levels were increased in patients with active lupus nephritis in an adult cohort and correlated with the urine protein:creatinine ratio and with the levels of MCP-1 and VCAM-1.
**Objectives:** Determine the role of HER2 as a urinary biomarker for lupus nephritis activity.
**Methods:** This is an interim analysis of a prospective, multicentric study, of patients with juvenile-onset systemic lupus erythematosus with biopsy-proven lupus nephritis. Urine samples were collected from patients at every clinical visit and also from age-sex matched controls. The samples were centrifuged and the supernatants were analyzed by enzyme-linked immunosorbent assays for HER2. Clinical data were also collected. The activity of lupus nephritis was measured using renal SLEDAI. Unpaired and paired t tests were used for the comparisons between samples. The relationship between HER2 and disease activity was defined by Pearson's correlation and linear regression.
**Results:** Urinary HER2 is significantly increased in children with lupus nephritis (N=15) when compared to controls (N=24) (p=0.003). Furthermore, our preliminary data from patients analyzed at different visits showed that HER2 levels tend to reflect disease activity.
**Conclusions:** HER2 was significantly increased in the urine of children with lupus nephritis and its levels changed between visits, reflecting disease activity. Further studies are necessary to determine if HER2 levels can be clinically useful, namely if they can predict the occurrence of a flare. These findings also support the study of anti-HER2 drugs for cell proliferation control in lupus nephritis.
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**Disclosure of Interest:** None declared
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## SAT0256 JUVENILE SYSTEMIC SCLEROSIS COHORT WITHIN THE CHILDHOOD ARTHRITIS AND RHEUMATOLOGY RESEARCH ALLIANCE (CARRA) LEGACY REGISTRY: BASELINE AND FOLLOW UP CHARACTERISTICS

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**Background:** Systemic sclerosis (SSc) is a rare multisystem autoimmune disease characterized by vasculopathy and organ fibrosis. From 2010–2013, the North American CARRA Legacy Registry enrolled and prospectively followed children with rheumatologic conditions including juvenile systemic sclerosis (jSSc).
**Objectives:** Describe disease manifestations, physician metrics, and patient quality of life (QOL) at enrollment and follow up of jSSc subjects.
**Methods:** Descriptive statistics were used for demographic and clinical features. We used McNemar's test for paired data and Fisher's exact for group comparisons.
**Results:** For the 64 children with SSc in the database, the majority were female (84%) and Caucasian (78%); 86% identified as non-Hispanic. Median age of onset was 10.3 yr while age at first pediatric rheumatology (PRH) evaluation was 11.8 yr, with 23% having a ≥2 yr delay to PRH. Baseline visit occurred a median of 3.6 yrs after disease onset and data obtained 1–2 yr from enrollment was analyzed for follow up (n=25, median 1.4 yrs).
For those with complete clinical data, 81% met ACR/EULAR 2013 adult criteria for SSc at baseline. Overlap with juvenile dermatomyositis was reported in 3 individuals, with mixed connective tissue disease in 1. Of those with documented testing for specific antibodies, 80% were ANA positive, 46% anti-Scl70 and 15% ACA. Three of 15 patients tested for anti-PM-Scl antibodies were positive.
At baseline, the most prevalent organ manifestations were dermatologic (93%) and vascular (92%), with Raynaud phenomenon as the most common feature. Multiple organs were affected in 93%, and 38% had ≥4 organ systems involved. Disease manifestations remained stable at follow up with the exception of decreased frequency of arthritis (4 to 1) and increased joint contractures (7 to 11). At conclusion of the study, no interval development of renal, cardiac, or pulmonary manifestations or mortalities occurred.
Frequency of disability, measured by ACR functional class, decreased from 44% at baseline to 25% at follow up. Median Physician Global Disease Activity scores improved from 3 (IQR 1–4) to 2 (1–3), with trending significance for those with <2 years of disease at enrollment (n=7, $p$=0.059). While there were no statistically significant differences in QOL measures over time, trends of improvement in pain scale (3.5 to 2) and global well-being scale (5 to 3) were appreciated in this early disease group.
**Conclusions:** Even with inclusion of overlap patients, baseline clinical data from this cohort are similar to the jSSc cohort described by Martini et al in 2006 and most met current ACR/EULAR adult SSc criteria. Most organ manifestations were stable with time and for the duration of the study observation period, there was no interval development of major organ involvement or mortality. While limited by the cross sectional nature of enrollment, trends of improvement in disability and disease activity were appreciated after 1–2 years of follow up.
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**Disclosure of Interest:** B. Stevens: None declared, K. Torok: None declared, S. Li: None declared, N. Hershey: None declared, M. Curran: None declared, G. Higgins: None declared, K. Moore: None declared, E. Rabinovich Grant/research support from: Abbie Vie; UCB Pharma; Hoffmann-La Roche Inc.; Janssen Research & Development, LLC, A. Stevens: None declared
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## SAT0257 UPDATE ON THE JUVENILE SYSTEMIC SCLEROSIS INCEPTION COHORT PROJECT. CHARACTERISTICS OF THE FIRST 74 PATIENTS AT FIRST ASSESSMENT

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**Background:** Juvenile systemic sclerosis (jSSc) is an orphan autoimmune disease. Currently just retrospective data exist regarding evolvement of organ involvement. In the retrospective studies assessment of the organ involvement is not standardized. Our project is the first one, where prospectively and with a standardized assessment data of jSSc patients are collected.
**Objectives:** to learn about the characteristics and evolvement of jSSc
**Methods:** Patients with jSSc were recruited worldwide and were prospectively assessed, using the proposed standardized patient assessment protocol.

**Results:** 26 centers from 17 countries applied to participate on the project. The assent and consent forms were translated into the local native languages. Up till now 74 patients were enrolled. Sixty (81%) of the 74 patients were female. The mean age of the onset of Raynaud symptomatic was 9.2 years (0.2 – 15.9). The mean age at the onset of the non-Raynaud symptomatic were 9,7 years (0.3 -15.9). 56 (76%) of the 74 have diffuse subtype, 10 (14%) of them have an overlap symptomatic. At the time of the inclusion the mean modified Rodnan Skin Score was 16.0. ANA positive were 55/71 (77%), 24/70 (34%) of them were anti-Scl 70 positive and 3/42 (7%) was anticentromere positive. 43/74 (58%) had already capillary changes and 36/72 (50%) inactive ulcerations, 13/72 (18%) had active ulceration at the time of the inclusion. 38/74 (51%) had cardiopulmonary involvement, 19/38 (50%) of had signs of interstitial lung disease on imaging, 18/42 (43%) had FVC <80% and 12/21 (57%) had DLCO <80%. 6/38 (16%) patients had pulmonary hypertension. 5/74 (7%) had renal involvement. 26/74 (35%) had gastrointestinal involvement, and 23/26 (88%) of them esophageal involvement. 46/73 (63%) had musculoskeletal involvement. 2/74 (3%) showed neurologic involvement. The mean CHAQ score was 0.4 (0–2.5). Patient global disease activity on VAS (0–100) was 44.9 and disease damage 41.6. Physician global of disease activity on VAS (0–100) was 39.7 and physician global of disease damage was 34.6.
**Conclusions:** The current recruitment data confirms that pediatric patients are different from the adult patients, there is a significantly higher proportion of diffuse subset patients with 81%. 14% of the patients have overlap features.
**Disclosure of Interest:** None declared
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## SAT0258 ASSESSING MYOCARDIAL DEFORMATION OF KAWASAKI PATIENTS WITH SPECKLE-TRACKING ECHOCARDIOGRAPHY ON LONG TERM FOLLOW UP

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**Background:** Myocardial dysfunction due to coronary arterial lesions is an important complication after Kawasaki disease in childhood (1,2). Speckle-tracking echocardiography (STE) is a recently developed technique for evaluation of myocardial deformation (3).
**Objectives:** Our objective was to examine myocardial deformation at long term follow-up of Kawasaki patients.
**Methods:** We assessed regional myocardial function in 32 asymptomatic Kawasaki patients and 30 age matched healthy child as control group. STE examination were recorded and the acquired raw data were saved for offline analysis The inferoseptal, anterolateral, inferior, anterior, and inferolateral (posterior) walls were investigated for longitudinal systolic peak values for strain (LV-SR) imaging.
**Results:** Mean age was 21±12 months, mean follow up time 61 months, Left ventricular ejection fraction was 57,373±8,338 in patients and 61,100±3,804 in control group. LV-SR of Kawasaki patients at basal-inferoseptal (20,000±6,046 vs 25,200±5,074), basal-anterolateral (19,595±5,713 vs 22,733±3,494), apical-septal (23,378±5,609 vs 26,267±4,334), apical-inferior (24,054±3,696 vs 25,200±2,396) segments had lower values than control group.
**Conclusions:** We demonstrated subclinical systolic impairment of function especially at left ascending artery territories with STE. STE has the potential to detect these subtle abnormalities, and help management during long term follow up.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3017

## SAT0259 DERMATOLOGICAL FEATURES OF KAWASAKI DISEASE: DATA EXTRACTED FROM THE FRENCH KAWASAKI DISEASE COHORT (KAWANET)

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**Background:** Kawasaki disease (KD) is a systemic vasculitis of unknown origin affecting mainly young children. The diagnosis criteria for KD described by the American Heart Association (AHA) include fever accompanied by five criteria, which are mainly mucocutaneous.
**Objectives:** Given the importance of dermatological manifestations in KD we aimed to describe their types and frequencies in a large French cohort of patients, and to analyze their possible association with coronary arteries abnormalities (CAAs).
**Methods:** Patients with complete and incomplete KD according to the AHA criteria and included between May 2011 and March 2013 in the French national database for KD (Kawanet), were analyzed. Consents were obtained for all included patients. Mucocutaneous signs of the disease were described (modification of the extremities detailed on erythema, edema and/or desquamation, diffuse exanthema, seat erythema and perineal desquamation, erythema or induration at BCG inoculation site, bilateral non purulent conjunctivitis, cheilitis (dry lips), raspberry tongue, erythema of oral mucosa) and their association with coronary artery abnormalities studied by multivariate analysis
**Results:** We analyzed 142 KD patients classified according to the AHA criteria. Their mean age was 2.9 years. One hundred and twenty four (87.3%) were complete KD and 18 (12.7%) were incomplete KD. Changes in lips and oral cavity were found in 132 children (93%), bilateral conjunctiva injection in 129 (92%), changes in extremities in 117 (82%), diffuse exanthema in 107 (79%), perinea involvement in 53 (41%), and erythema or induration at the site of previous BCG immunization in 10 vaccinated children (13%). This latest sign was significantly more frequent in patients less than 1 years than in older ones (36% vs 9% p=0.01). CAAs were detected in 25 patients with complete KD (22%) and in all patients with incomplete Kawasaki disease by definition. No significant associations were found between any type of mucocutaneous lesion and CAAs in this study.
**Conclusions:** Our study has underlined the importance of mucocutaneous symptoms for the definition of KD, and as expected, using the AHA criteria, they were associated with the phenotype of complete KD. In patients <1 year, modification on the site of previous TB immunization was significantly more reported than in older patients and so could be considered a diagnostic criterion. In addition, modification on the site of previous TB immunization and seat involvement were major and frequent dermatological clues for the diagnosis. Even frequent, none of the cutaneous symptoms were related to KD prognosis. Two limitations were present in this study: (i) some data were entered retrospectively; (ii) some groups of comparison were small and could explain the absence of association between mucocutaneous lesions and CAAs.
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## SAT0260 A NOVEL MRI-BASED ANALYSIS WORKFLOW FOR CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO)

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**Background:** Chronic recurrent multifocal osteomyelitis (CRMO) is an auto-inflammatory bone disorder affecting children and adolescents, characterised by sterile bone inflammation. There is a clinical spectrum, ranging from presentation with a single, non-recurrent bone lesion to a chronic relapsing course affecting multiple, often symmetrical bone sites. Whole body MR imaging may reveal multiple lesions and therefore is promising for assessing progression of CRMO and effectiveness of treatment. Nevertheless, no tool has been available for quantitative measurement of multiple lesions in whole body MRI scans, and a fast, reproducible scoring system for CRMO patient assessment is warranted.
**Objectives:** To test a novel postprocessing scoring method for the quantification of multiple lesions in CRMO patients from static whole body STIR MRI scans, using the normalized intensity ("NormI") parametric map function, in combination with the region of interest (ROI) tools built into the software Dynamika, a platform for quantitative MRI analysis (www.imageanalysis.org.uk).
**Methods:** Whole-body static MRI STIR images from 4 patients were analysed by 2 different readers. The workflow for each reading was: 1) Define reference/baselines in fat, bone and muscle region in both left and right side of the body, respectively. 2) Draw regions of interests (ROIs) around lesions defined as areas of marrow hyper intensity. 3) Compute, NormI parametric maps by comparison with corresponding baseline. NormI have previously shown to be useful in semi-automatic quantification of inflammatory lesions in the spine on STIR or DWI-MRI sequences [1]. 4) Group the selected 2D ROIs across slices into volume of interests (VOIs). 5) Generate and save report - automated generation of lesion ROI parameters, including the sum, maximum and mean of all positive pixel values in the VOIs (SumNormI,MaxNormI and MeanNormI). Inter-reader agreement for SumNormI and MeanNormI was calculated using the intraclass correlation coefficient for each VOI.
**Results:** Single or multiple lesions seen in whole body MRI scans of CRMO patients were identified and quantified using NormI parametric maps. As shown in figure, quantification parameters for the lesions identified in right femur and right clavicle have been computed by normalising to the baseline in muscle. Reproducibility assessed by ICC is shown in table.

| | Intraclass Correlation Coefficient (ICC) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Patient 1 | | Patient 2 | | Patient 3 | | Patient 4 | |
| | Single | Average | Single | Average | Single | Average | Single | Average |
| SumNormI | 0.95 | 0.98 | 0.98 | 0.99 | 0.63 | 0.79 | 0.34 | 0.51 |
| Mean NormI | 0.76 | 0.86 | 0.95 | 0.98 | 0.50 | 0.67 | 0.60 | 0.73 |

Single measure: reliability of raters is computed from a single measure. Average measure: reliability of raters is computed taking average of rater's measures.



**Conclusions:** The suggested workflow and postprocessing technique provides a relatively fast and reproducible scoring method for both single and multiple lesions in CRMO from wholebody STIR MRI scans. Larger trials to test day-to-day variation and sensitivity to change following treatment response are warranted and currently ongoing.

**References:**

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**Disclosure of Interest:** Y. Chu Employee of: Image Analysis Ltd., D. Roettger Employee of: Image Analysis Ltd., C. Trentin Employee of: Image Analysis Ltd., M. Hinton Employee of: Image Analysis Ltd., O. Kubassova Employee of: Image Analysis Ltd., R. Hargunani: None declared, M. Boesen Consultant for: Image Analysis Limited as Head of Clinical Advisory Board, P. O'Donnell: None declared

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## SAT0261 DIFFERENT TREATMENT STRATEGIES FOR CHRONIC NON-BACTERIAL OSTEOMYELITIS: THE EXPERINCE OF 52 PATIENTS

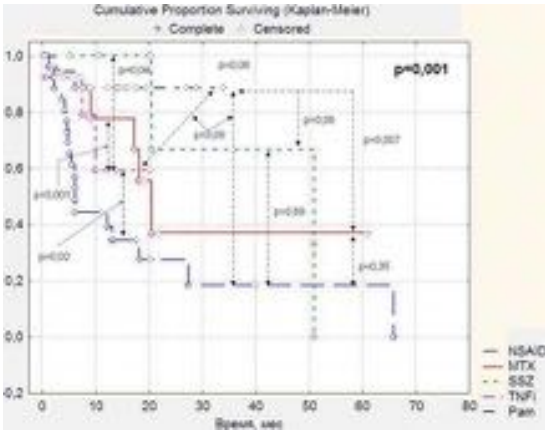
M.M. Kostik[1], O. Kopchak[1,2], I. Chikova[1], V. Masalova[1], M. Dubko[1], L. Snegireva[1], E. Isupova[1], O. Kalashnikova[1], A. Mushkin[3], V. Chasnyk[1]. *[1]Saint-Petersburg State Pediatric Medical University, Saint-Petersburg; [2]Kirov's regional children's hospital, Kirov; [3]Science research Institute of Phthisiopulmonology, Saint-Petersburg, Russian Federation*

**Background:** Chronic non-bacterial osteomyelitis (CNO) is a heterogenous group of immune-mediated inflammatory bone diseases, often co-exist with other rheumatic diseases. There are no approved treatments for CNO except non-steroid anti-inflammatory drugs (NSAID). The efficacies of methotrexate (MTX), sulfasalazine, pamidronate (PAM), anti-IL1 and TNFα-inhibitors (TNFα-inh) were shown in different reports.

**Objectives:** The aim of study: to compare the efficacy of non-randomized different treatment approaches in pediatric patient CNO cohort.

**Methods:** 52 children (25 M and 27 F) with CNO has average age at the onset of disease 8.4 years (5.4÷11.0), the number of foci - 3.0 (2.0÷6.0, incl. multifocal cases in 80.8%), fever at the onset – 38.5%, spine involvement - 34.6%, positive family autoimmune diseases (AID) history - 7.7%, concomitant AID - 67.3%. NSAID was the first-line treatment for non-vertebral cases, as well as PAM for vertebral involvement. Second-line treatment includes MTX, PAM and TNFα-inh. Dynamics of pain, patient's (PVAS) and physician's (MDVAS) assessment and ability to each medication to achieve remission of CNO activity we evaluated.

**Results:** According to the NSAID, MTX, SSZ, PAM and TNFα-inh groups next data were registered: PVAS: -14.2% (p=0.05), -50.0% (p=0.04), -23.1 (p=0.89), -83.3% (p=0.0001), -73.6% (p=0.0007); pain: -21.9% (p=0.01), -18.6% (p=0.13), +36,4 (p=0.89), -79.7% (p=0.00016), -74.1%, (p=0.0015);
MDVAS: -13.8% (p=0.13); -56.4% (p=0.09), +30.8% (p=0.89), -74.7%, (p=0.0001), -82.1 (p=0.0015) respectively.
The ability of each treatment strategy to achieve the CNO remission was 52.6%, 44.4%, 57,1%, 88.8% and 73.3% respectively (log-rank test, p=0,001, figure). TNFα-inh usually used as second-third line treatment in cases where other options, especially PAM were fall.




**Conclusions:** The most effective treatment approaches for CNO were PAM and TNFα-inh. The randomized controlled trials for assessment efficacy and safety of these medications is mandatory to confirm these results.

**Disclosure of Interest:** None declared

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## SAT0262 7 CASES OF CHINESE JUVENILE RELAPSING POLYCHONDRITIS AND SYSTEMIC REVIEW

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**Background:** Relapsing polychondritis (RP) is a rare systemic autoimmune disease characterized by recurrent episodes of inflammation and progressive destruction of cartilaginous tissues. Juvenile RP (<18 years) mentioned more severe than adult as previous reports.

**Objectives:** Our work is to study the clinical and prognostic features of Juvenile Relapsing polychondritis (RP).

**Methods:** 7 RP cases from 1994–2013 in our hospital were reviewed and compared with 51 international juvenile cases and 158 Chinese adult case series reported from 1985–2013 including clinical features, systemic involvement, differential diagnosis and prognosis.

**Results:** 1)Average age at the onset was 15.1 years old, the mean age at first symptoms was 15.1 months and female-male ratio was 0.4:1, 6 of 7 had been misdiagnosed. 2)The incidences of arthritis (100%: 53%), nasal chondritis (1%: 53%), laryngotracheal syndromes (86%: 68%), auricular chondritis (86%: 67%), cardiovascular involvement (14%: 10%) and autoimmune diseases (14%: 5%) were higher than in Chinese adult except skin (20%: 46%). 3) Our juvenile RP patients had more severe in respect toocular inflammation (57%: 40–47%), arthritis (100%, 71–90%), cardiovascular (14%: 3–10%) and skin involvement (20%:10–11%) than Caucasian juvenile RP.

**Conclusions:** Our juvenile RP series were more severe than Chinese adult RP as the same as in Caucasians and has its unique characteristics in spite of sharing most clinical features with case series in literature.

**Disclosure of Interest:** None declared

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## SAT0263 COHORT STUDY OF 80 PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS DURING TRANSITION FROM PEDIATRIC TO ADULT CARE

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatism in children. The International League of Associations for Rheumatology 2001 (ILAR) classification includes 7 subgroups: systemic JIA, polyarticular JIA, oligoarticular JIA, enthesitis related arthritis (ERA), psoriatic arthritis and undifferenciated arthritis. Most pediatric inflammatory rheumatism persist into adulthood. Therefore, a transition from pediatric to adult rheumatology is a necessary step. Transition is defined as an active process by which a young patient with a chronic disease develops skills and resources to gradually assume his pathology. The transition phase should be anticipated and structured because of the risk of failure in monitoring. However difference in classification criteria in pediatric and adult rheumatism represents a major difficulty for adult rheumatologist.

**Objectives:** The aim of this study was to determine the characteristics of juvenile-onset rheumatism seen during transition period and to compare pediatric classification criteria to adult criteria.
**Methods:** A retrospective single-center study was performed. Patients with JIA according to ILAR classification were included and had transition visit. JIA classification criteria were compared to ACR/EULAR 2010 criteria for rheumatoid arthritis (RA), Yamaguchi criteria for adult Still's disease and ASAS criteria for spondyloarthritis.
**Results:** 80 patients were included: 12 systemic JIA, 17 polyarticular JIA, 13 oligoarticular JIA, 29 ERA and 9 psoriatic arthritis. The median duration of disease was 7 years and the median age of transition was 19 years old. Six uveitis in oligoarticular JIA and 4 uveitis in ERA were observed as extra-articular manifestations. Radiographic structural damages were assessed and showed 12.5% of erosions and 7.6% of carpitis, mainly in polyarticular and systemic JIA patients. 39.3% of patients with ERA displayed sacroiliitis. In comparison with adult rheumatism 42% of patients with systemic JIA fulfilled Yamaguchi criteria and 29% of patients with polyarticular JIA fulfilled ACR/EULAR criteria for RA. 54% of patients with oligoarticular JIA, 76% with ERA and 100% with psoriatic arthritis fulfilled ASAS criteria for spondyloarthritis. In addition 78.75% of patients were in remission and 70% of patients were treated with biotherapy.
**Conclusions:** Our study confirmed an articular destructive potential of polyarticular and systemic JIA and an ocular risk of oligoarticular JIA. Comparison of JIA criteria to adult rheumatism criteria showed that polyarticular JIA with positive rheumatoid factor fulfilled ACR/EULAR criteria for RA. However, oligoarticular JIA and polyarticular JIA without rheumatoid factor did not fulfill any adult rheumatism criteria and seem to be pediatric entities. Finally, most of patients with ERA and psoriatic arthritis fulfilled ASAS criteria for spondyloarthritis.
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## SAT0264 A SINGLE CENTRE EXPERIENCE OF CHILDHOOD POLYARTERITIS NODOSA FROM NORTH INDIA

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**Background:** Polyarteritis nodosa (PAN) is a necrotizing vasculitis involving medium or small sized vessels. It is characterized by a variable clinical presentation, ranging from a benign cutaneous involvement to a more severe systemic disease with multisystem involvement
**Objectives:** We describe clinical and laboratory features, treatment and outcome of pediatric PAN patients
**Methods:** A retrospective case review of all children diagnosed as PAN at a single tertiary care hospital in north India between 1990 to 2014 was done. Diagnosis of PAN was based on European League against Rheumatism (EULAR)/Paediatric Rheumatology European Society (PRES)/Paediatric Rheumatology International Trials Organisation (PRINTO) classification criteria. (1)
**Results:** A total of 16 children (12 boys and 4 girls) with PAN were identified. Median age of symptom onset and diagnosis was 8 years (range 1–11 years) and 9 years, respectively. The presenting symptoms were fever (68%), CNS complaints [headache, seizures, altered sensorium, stroke or vision loss] (50%), fatigue (44%), myalgia (44%), gangrene (31%), weight loss (31%), gastrointestinal complaints [pain abdomen, bleed] (31%) and bluish black patches over body (19%). Hypertension was present in 88% patients at admission. Various neurological manifestations were seen in 62.5% patients. Skin involvement (digital gangrene, livedo reticularis, bluish black patches, erythema nodosum or necrotic ulcer) was seen in 50% patients. Renal and gastrointestinal involvements were seen in 38% patients each.
CT angiography was done in 13 patients. Aneurysmal dilatation of vessels was seen in 6 patients, while 3 patients showed features of renal infarcts. CT angiography was normal in 4 patients. In 2 such patients, digital subtraction angiography (DSA) showed aneurysmal dilatation of vessels. ANCA was positive in 4 patients (c-ANCA in 3 and p-ANCA in 1). HBsAg was positive in 3 patients (not treated as liver function remained normal). ASO was positive in 4 patients (2 patients were given penicillin; one patient had a relapse with high ASO titres on stopping penicillin).
Two patients had only a single visit to the clinic; hence their treatment details were not available. Treatment regimen included cyclophosphamide (78%), methylprednisolone pulses (43%), oral prednisolone (93%), maintenance azathioprine (36%), and IVIg and methotrexate (14% each). Mean follow up was for 4.8 years (range 0–25 years).
Five patients experienced relapses with more than 1 relapses seen in 2 patients. Relapses were noted as early as 6 months and as late as 22 years after diagnosis
**Conclusions:** We found a significant male preponderance in our cohort. Streptococcal infection can have a pathogenic role in the disease progression and relapse, and penicillin prophylaxis can prevent disease relapse in susceptible patients
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## SAT0265 EVALUATION OF BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS, SINGLE CENTER RESULTS

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**Background:** JIA is a chronic inflammatory joint disease with onset in children <16 years of age. Several biological agents (BAs) have become available for the treatment of JIA.
**Objectives:** To analyze trends in prescription patterns of biological agents and drug efficacy, achievement of inactive disease and reason for switching in JIA.
**Methods:** This was a retrospective study of children with JIA treated with biologic agent (BA) between 2006 and 2015. Efficacy was determined using the Juvenile Arthritis Disease Activity Score (JADAS)-27.
**Results:** We enrolled total 111 patients (61female, 50 male). The JIA type differentiated was systemic JIA (sJIA) (n=16), Extended Oligo (n=21); Poly JIA (n=33);Entezitis related arthritis (ERA) (n=32); psoriatic arthritis (n=4) and undifferentiated JIA (n=5). The median age of the patients at diagnosis of JIA was 94 months [interquartile range (IQR) 60–138), while the median age at the time of treatment with first BA was 141 months (IQR 83–177). The median disease duration prior to treatment with BA was 20 months (IQR 7–48). 94 patients (84.7%) received their BA in combination with mtx (alone or with another DMARD) while 15.3% had BA alone. Pretreatment steroids was higher in sJIA with 15 (94%), than in Poly (n=20,60%) and ERA (n=14,45%) patients (p=0.00).The JADAS 27 was available for 94% of patients at baseline, with a median score of 18.5 and no significant variation with the subtypes (p=0.68). The median JADAS27 after prior BA was 4 (IQR 2–8). No statistically significant differences was seen in baseline CHAQ across the subtypes (p=0.32). In ERA, the median JsPD score was 4,5 at baseline. The BAs were etanercept (ETA) (62%), adalimumab (ADA) (36%), tocilizumab (19%), infliximab (9%), canakinumab (7%), abatacept (7%) and anakinra (2.7%). ADA and ETA were preferred with equal in ERA while ETA was the first BA in other subtypes (p=0.00). 26% of patients (n=29) received more than one biologic during follow-up (2 agents, n=18; ≥3agents, n=11). Most of the switchers were in SJIA (38%, p=0.00), less often were in Poly (31%) and ERA (14%). In the switchers, median follow-up duration on BA was 13 months (range 1–69) under the first BA, 6.8 months (range 1–26) under the second and 6.5 months (range 1–19) under the third BA, (p>0.05). The reasons of switching was loss of response (58.6%, n=15), lack of effectiveness (27.5%,n=8), adverse event (13.7%, n=4), and convenience of use and patient's choice in 2 patients each (2%). At last follow up, 97 patients (87.4%) achieved inactive disease, in 78 (80%) of these patients with a first BA, 12 (12.3%) with a second BA, 4 (4%) with a third and 2 (2%) under a fourth BA. Minimal disease activity was seen in 11 patients while 3 patients were still in the active.A persisting limitation or loss of normal range of articular motion of ≥1 joint was recorded in 26 of patients (23.4%) at last follow-up. No case of cancer or death was recorded. 8 patients had developed short stature, 6 had osteoporosis, 2 had amyloidosis,2 had neuropathic pain and 2 had glaucoma at last examination. Two patients underwent surgical intervention (hip arthroplasty and wrist arthrodesis).
**Conclusions:** Biologic agents appear to be highly effective in children and adolescents with JIA who were resistant DMARDs. Reumatologists take into patient factors andnewly data in choosing the optimal BA
**Disclosure of Interest:** None declared
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## SAT0266 SAFETY ASSESSMENT OF BIOLOGICAL AGENTS USED IN PEDIATRIC RHEUMATIC DISEASES, SINGLE CENTER RESULTS

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**Background:** In recent years, the biologic drugs has led to a dramatic change in the management of rheumatic diseases in children. Currently available biologics include TNF-α blockers, agents that target IL-1 and IL-6, T-cell costimulation inhibitors and antibodies against the CD20 molecule present on B cells. The studies about the long term safety of biologic agents (BA) in pediatric patients with rheumatic diseases are still limited.

**Objectives:** The aim of this study was carry out a safety evaluation of biologic agents in patients with rheumatic disease
**Methods:** This was retrospective study in Erciyes University Faculty Medicine, the tertiary center for pediatric rheumatology in Turkey. We recruited the patients who were diagnosed a rheumatic disease and treated with a biologic agent (BA) between 2009 and 2015. Adverse events (AEs) were categorized and graded based on the Common Terminology criteria for AEs (CTCAE). Grades 3–5 were considered SAEs. The time until discontinuation of BA was counted as patient-years (PY).
**Results:** We included 127 consecutive patients: Juvenile idiopathic arthritis (n=102, 80.3%), Familial Mediterranean fever (n=9, 7.8%), Uveitis (n=7, 5.5%), sarcoidosis (n=3, 2.4%), Systemic lupus erythematosus (n=2, 1.6%), Hyperimmunglobulin D syndrome (HIDS) (n=2, 1.6%), Takayasu arteritis (n=1, 0.8%), Tumor necrosis factor receptor associated periodic syndrome (TRAPS) (n=1,0.8%). The median age of the patients at diagnosis was 91 months [interquartile range (IQR) 60–138), while the median age at the time of treatment with biologic therapy was 144 (IQR 90–184) months. The median disease duration prior to treatment with biologics was 22 months (IQR 8–49).
A total of 241.3 patient years (PY) were included: 132 py (72 patients) for etanercept, 44.5 (41) for adalimumab, 23 (20) for tocilizumab, 22 (13) for canakinumab, 7.7 (9) for infliximab, 4.2 (15) for anakinra, 6 (7) for abatacept and 1.9 (2) for rituximab.
A total of 113 patients (89%) were on methotrexate prior to biologics and 90 (71%) during biologics. A total of 38 patients (30%) had been on two or more biologics, 7 (5.5%) on three, 5 on four (3.9%) and 1 on five.
A total of 35 patients (27.6%) had at least one AE. Those with AEs 45 months (IQR 57) had a significantly longer median follow-up of 31 months (IQR 41) than those without an AE (p=0.01). Forty-five patients experienced 93 AEs (38.5/100 py). Of those AEs, 20 were reported as serious AEs (8.3 /100 py). The SAEs were lower with anti TNF alpha agents than others (6.8 for ETN, 21.7 for TOS, 4.5 for ADA, 25.9 for INF, 4.5 for CAN, 23.8 for ANK, 33.3 for ABT) (p=0.00).
Eight of the SAEs (40%) were classified as noninfectious (infusion reaction, anaphylaxis, vasculitis, macrophage activation syndrome, seizure and glomerulonephritis) were documented. Three patients on ETN developed reactivation of latent tuberculosis. No deaths, malignancies, opportunistic infections, demyelinating diseases, or lupus-like reactions were observed during biologic agents exposure.
**Conclusions:** Here in, we presented safety data comparing biologic drugs in pediatric patients retrospectively. The frequency of mild infections and latent tuberculosis was higher on Anti TNF alpha drugs, but sAEs were lower than others. To better define the safety profile of biologic drugs need for prospective studies and large cohorts.
**Disclosure of Interest:** None declared
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## SAT0267 ROLE OF MUSCULOSKELETAL ULTRASONOGRAPHY IN THE EVALUATION OF HEMOPHILIC ARTHROPATHY IN CHILDREN

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**Background:** Recurrent clinical and subclinical joint bleeding almost inevitably causes arthropathy with affected function up to severe loss of motion of elbows, knees and ankles. Diagnosis of hemophilia is essentially clinical and laboratory based, however, imaging is an important tool for evaluation of complications and therapeutic follow-up. Musculoskeletal Ultrasound (MSUS) is a useful method for frequent follow-up in pediatric patients being non-invasive, easy repeatable, painless, without ionizing radiation, relatively inexpensive, with no need for sedation.
**Objectives:** To investigate the role of MSUS as a tool for evaluation of joint affection in hemophilic arthropathy compared to clinical and functional assessment as well as conventional x-ray.
**Methods:** This study included 20 male children (a total of 120 joints) with severe hemophilia type A (6–15ys). Twenty age and sex matched non-hemophilic children served as controls. Patients underwent clinical examination, assessment of the Hemophilic Joint Health Score, functional assessment according to Functional Independence Score for Hemophilia, radiological evaluation using conventional X-ray according to Pettersson classification as well as qualitative ultrasongraphic scoring according to Klukowska et al., 2001, and Muca-perja et al., 2012. For more accurate quantitative values, we designed an MSUS index based on measurements of the cartilage thickness and joint space dimensions. All above was done at the knees, ankles and elbow joints.
**Results:** The knee joint was the principal joint affected among hemophilic patients. Cartilage thinning was the predominant pathological disorder with subsequent joint space narrowing especially at the medial condylar side of the knee. Using the designed quantitative score the cartilage thickness among patients, as well as the joint space, showed a highly significant negative correlation with age, clinical scores and the radiological score while no statistically significant relation was detected with the functional scoring. The ultrasonography qualitative scores failed to show statistically significant relation on correlating with clinical, functional and radiological scores. The prevalence of cartilage damage among patients according to Klukowska et al., score was 75% of the total 40 knee joints, 47.5% with synovial hypertrophy, 30% with synovial effusion and 20% with increased synovial vascularity. The prevalence of cartilage damage among patients according to Muca-perja et al., 2012 was 90% of the total 40 knee joints, 47.5% with synovial hypertrophy, 27.5% with bone erosions and 20% with synovial hyperemia.
**Conclusions:** MSUS successfully detected changes in the hemophilic joints even before functional affection started. MSUS provides accurate assessment, allowing early detection of hemophilic arthropathy as well as precise follow up of progression of damage by standardizing and simplifying the planes and landmarks for acquisition of the sonographic images using quantitative measurements in haemophilic joints
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## SAT0268 TOCILIZUMAB THERAPY IN CHILDREN WITH POLYARTHICULAR COURSE JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Patients with polyarticular-course Juvenile idiopathic arthritis (pcJIA) have risk for profound disability.Although these patients may respond to methotrexate (MTX) or biological agents approved for pcJIA, up to 30% continue to have active disease.Interleukin-6 (IL-6) is concentrations are positively correlated with the severity of joint involvement and with C-reactive protein (CRP) levels. Tocilizumab is effective drug for the treatment of JIA refractory to immunosuppressive drugs.
**Objectives:** To evaluate safety and efficacy of tocilizumab treatment in children with pcJIA
**Methods:** Analysis of efficacy and safety tocilizumab therapy was performed in 46 patients (4 - RF+, 3-enthesitis related arthritis, 1-psoriatic JIA) and in 24 patients, whom follow up period was 6 and 12 m. Median age was 9,8 y (range; 1,9 to 17,2 y) and median disease duration was 5,1y (range; 0.4 to 13,7 y). Tocilizumab was administrated intravenously at a dose of 8or 10 mg/kg every 4 weeks. 29 patients were treated by biologics previously. The majority of patients received concomitantDMARDs, 31 patients received methotrexate, 1-leflunomid, 1-sulfasalazin,5-cyclosporin and 8- prednisolone at dose 0.4 (0.2; 1) mg/kg/day. 14 patients had uveitis: 6-not active,1-subactive and 7-active. Efficacy end points included the American College of Rheumatology (ACR)for improvement 30 (ACR30), ACR50, ACR70, ACR90 and criteria of inactive disease andindex JADAS10. During the follow-up period, significant side-effects were sought.
**Results:** The ACR Pedi 30, 50, 70, 90 and 100 improvement were achieved by 92% (n=36), 82% (n=32), 56% (n=22), 23% (n=9),and 12% (n=5) of patients at Week 24 (n=39), by 100% (n=24), 87% (n=21), 83% (n=20), 54% (n=13), and 20% (n=5) of patients at Week 48 (n=24)respectively. Inactive disease was achieved by 14/39 (36%) of patients at week 24 and by 12/24 (50%) of patients at week 48. The JADAS10 decreased from 23,4 (14,8; 27,8) to 6,2 (1,6; 11,8) at week 24 ($p<0.001$) and to 2,0 (0,5; 4,9) at week 48 ($p<0.001$). The number of platelets decreased from 383 x109/l (302; 488) to 250 (220; 282) at week 24 ($p<0.001$) and to 258 (216; 284) at week 48 ($p<0.001$), number of leucocytes – from 8,8 x109/l (7,6; 9,9) to 6,5 (5,3; 7,3) at week 24 ($p<0.001$) and to 6,4 (4,7; 6,8)) at week 48 ($p<0.001$); level of hemoglobin increased from 112 (100; 123) g/l to 126 (118; 132) at week 24 ($p<0.01$) and to 129 (122; 136)) at week 48 ($p<0.001$).The frequently observed non-severe adverse events were nasopharyngitis, upper respiratory tract infections and gastroenteritis. No cases of opportunistic infections, malignancies or death were reported. 12 patients had incidences of neutropenia, 2 – thrombocytopenia,7-increased level of ALT and AST. Tocilizumab treatment was discontinued in 7 patients during the follow-up 48 weeks period. The causes for cancellation were lack of efficacy (n=6), infusion reaction (n=1), flare (n=1). 5patients were switched to antiTNF blockers and 2 – to abatacept.
**Conclusions:** Tocilizumab treatment provided clinically meaningful improvement for patients with pcJIA. Tocilizumab induced remission of the disease The safety profile of tocilizumab was consistent that seen in other studies
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## SAT0269 SURVIVAL OF THE SECOND TNF INHIBITOR IN PATIENTS WITH POLY-JIA

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**Background:** TNFα is one of the most important cytokine in the pathogeneses of poly-JIA. There are several TNF inhibitors for the treatment poly-JIA. Switching TNF-blockers is often strategy in the treatment of poly-JIA.
**Methods:** An open observational study in patients with poly-JIA taking the second TNFinhibitor. A total of 119 patients (46 boys and 73 girls) were included in this study. The mean age was 11 (7;14), disease duration was 5 (3;8) years. By the switching time 54/119 had active polyarthritis, 58/119 – olygoarthritis, 7/119 – active uveitis without arthritis. Infliximab was the first TNF inhibitor in 105/119, adalimumab – in 3/119, etanercept – 11/119. 81/119 were switched to adalimumab, 38/119 – to etanercept. Analysis of survival the second TNF blocker treatment was performed in all patients by Kaplan–Meier curve.
**Results:** The causes for cancellation of the first and second TNF blockers were second inefficacy (3,7% and 8%), adverse events (5,6% and 2,5%) and administration causes (7% and 8%). Infliximab was cancelled because of primary inefficacy (7/105, 6.7%), second inefficacy (57/105, 54.3%), adverse events (12/105, 11.4%), relapse of uveitis (7/105, 6.7%), disease remission (19/105, 18.1%), administration causes (3/105, 2.8%). Etanercept was discontinued because of primary inefficacy (1/11, 9%), second inefficacy (2/11, 18%), adverse events (2/11, 18%), relapse of uveitis (6/11, 55%). Adalimumab was cancelled because of primary inefficacy (1/3), adverse events (1/3), administration causes (1/3). The second TNF inhibitor treatment survival in patients with the primary inefficacy of the first TNF inhibitor at 1,2 year was 73%, at 1,8 year was 73%, at 2,4 year was 53%. The second TNF inhibitor treatment survival in patients with the second inefficacy of the first TNF inhibitor at 1,2 year was 82%, at 1,8 year was 82%, at 2,4 year was 69%. The second TNF inhibitor treatment survival in patients with the remission of the first TNF inhibitor and relapse of disease at 1,2 year was 82%, at 1,8 year was 82%, at 2,4 year was 72%. The number of AE was 32.2 and 24.5 per 100 p.y. on the 1st and 2nd TNF blocker treatment, accordingly ($p<0,0001$).
**Conclusions:** The highest percent of survival of the second TNF inhibitor treatment was registered in patients with poly-JIA whom the first TNF inhibitor was cancelled because of disease remission and the lowest percent – in patients with poly-JIA whom the first TNF inhibitor was cancelled because of the primary inefficacy of the first TNF inhibitor.
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## SAT0270 SUBCLINICAL INFLAMMATION IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER: MEASUREMENT OF SERUM AMYLOID A LEVELS

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**Background:** Familial Mediterranean Fever (FMF) is an autosomal recessive, inherited, autoinflammatory disease characterized by recurrent, self-limited febrile episodes of inflammation of serous membranes and marked elevation of acute phase proteins. In some patients with FMF, the laboratory markers of inflammation do not return to normal levels during attack-free periods, and complications related with persistent subclinical inflammation may occur.
**Objectives:** The aim of this study was to evaluate the clinical role of serum amyloid A (SAA) and other acute-phase proteins during the treatment and follow-up of children with FMF.
**Methods:** The children with the diagnosis of FMF were enrolled in the study. Information including clinical and laboratory findings, erythrocyte sedimentation rate (ESR), SAA and C-reactive protein (CRP) levels, type of MEFV mutation were collected from the hospital's records following approval by the local ethics committee. Children were divided into four groups according to the time of SAA determination: group I during diagnostic evaluation (before colchicine treatment), group II asymptomatic children treated with low-dose colchicine, group III asymptomatic compliant children treated with adequate dose colchicine according to the their body weight, group IV non-compliant children with colchicine treatment.
**Results:** A total of 141 children, 73 (51.8%) girls with a median age of 11 years (1.5–18) and a median follow-up period of 12 months (3–135) were included in the study. Thirty two children, (22.7%) had parental consanguinity and 79 children (56.0%) had family history of FMF. Thirty three children (23.4%) were homozygous, 66 children (46.8%) were compound heterozygous and 42 children (29.8%) were heterozygous for MEFV gene. Colchicine treatment was started in all patients. The main clinical characteristics of the children were: abdominal pain in 87.2%, fever in 61.7%, arthralgia/myalgia in 52.5%, arthritis in 15.6%, chest pain in 10.6%, erysipelas-like erythema in 4.3%, history of appendectomy in 6.2%, microalbuminuria in 15.6% and proteinuria 6.4%. There were 21 children in group I, 9 in group II, 84 in group III and 27 in group IV. Elevated SAA levels (>10 mg/L) found in 55 children (39.0%), elevated CRP levels (>0.5 mg/dl) in 45 children (31.9%) and elevated ESR (>20 mm/hour) in 42 children (29.8%). Comparison of the acute-phase proteins revealed significant differences between four groups as expected (Table 1). In group II, number of children who had elevated SAA levels was higher than the number of children with elevated CRP levels (88.9% vs 44.4%) and none of these children had elevated ESR.

Table 1. Number of patients with elevated acute phase protein levels on groups

| | Group I (n=21) | Group II (n=9) | Group III (n=84) | Group IV (n=27) | p |
|---|---|---|---|---|---|
| SAA levels (>10 mg/L), n (%) | 18 (85.7) | 8 (88.9) | 5 (6.0) | 24 (88.9) | 0.001 |
| CRP levels (>0.5 mg/dl), n (%) | 14 (66.7) | 4 (44.4) | 4 (4.8) | 23 (85.2) | 0.001 |
| ESR (>20mm/hour), n (%) | 15 (71.4) | 0 | 3 (3.6) | 24 (88.9) | 0.001 |

**Conclusions:** Our findings suggest that SAA level is important laboratory parameter for determination of subclinical inflammation especially in asymptomatic children treated with low-dose colchicine. Monitoring of SAA levels should be part of routine follow-up of children with FMF for the prevention of the development of FMF-related complications.
**Disclosure of Interest:** None declared
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## SAT0271 HEPATOSPLENOMEGALY: A COMPLICATION OF PERSISTENT SUBCLINICAL INFLAMMATION IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER?

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**Background:** Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disorder characterized by attacks of painful inflammation. Some patients with FMF have subclinical inflammation persisting between the attacks. This subclinical inflammation may leads to many important clinical complications such as anemia, splenomegaly, decreased bone density, and amyloidosis.
**Objectives:** The aims of this study were to evaluate sonographic findings in patients with familial Mediterranean fever (FMF) during attack-free periods and examine whether there is an association between hepatosplenomegaly and *inflammatory* markers in FMF.
**Methods:** Medical records of children with FMF were reviewed during attack-free periods. Demographic features, clinical and laboratory findings, hematological data (leukocyte, hemoglobin and platelet counts),er*ythrocyte* sedimentation rate (ESR), SAA and C-reactive protein (CRP) levels, type of MEFV mutation, family history of FMF were collected from the hospital's computerized database following approval by the local ethics committee.
**Results:** A total of 136 patients, 74 (54.4%) girls were included in this cross sectional study during non-attack period. Median age of 11.25 years (2–18 years) and median follow-up period were 18 months (3–129 months) at time of sonographic evaluation. Thirty one patients (22.8%) had parental consanguinity and 472 (52.9%) patients had family history of FMF. Thirty three patients (24.3%) patients were homozygous, 61 (44.9%) patients were compound heterozygous and 42 (30.9%) patients were heterozygous for MEFV gene. Hepatomegaly and splenomegaly were found in 22 (16.2%) and 32 patients (23.5%), respectively. Ten patients had both hepatomegaly and splenomegaly. Spleen size had a negative correlation with platelet count and a positive correlation with ESR, CRP and SAA (all $p<0.05$). Also, there was significant positive correlation between liver size and CRP levels ($p<0.05$). White blood cell count, hemoglobin, urinary protein-creatinine ratio were not associated with spleen and liver size. And also, patients with splenomegaly had significantly higher SAA, CRP and ESR levels than the patients with normal spleen size (Table 1).

Table 1. Laboratory findings of patients

| | SAA (mg/L) | CRP levels (mg/dl) | ESR (mm/hour) |
|---|---|---|---|
| Patients with splenomegaly | 11.02±9.10 | 2.3±3.4 | 19.06±12.32 |
| Patients without splenomegaly | 8.8±15.25 | 1.01±1.79 | 14.89±12.28 |
| P value | 0.03 | 0.03 | 0.01 |

**Conclusions:** Hepatomegaly and splenomegaly are not uncommon in FMF, which might be due to the chronic inflammatory characteristics of the disease. We speculate that FMF is a chronic inflammatory disease rather than episodic illness.
**Disclosure of Interest:** None declared
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## SAT0272 SURVIVAL OF BIOLOGICAL TREATMENT IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS NON-SYSTEMIC

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**Background:** Currently we have biological treatments for control juvenile idiopathic arthritis (JIA), we have specific protocols that help us to handle, and do not know the exact time they keep these treatment, which conducted this study survival the biological agent.
**Objectives:** The purpose this work is describe the survival time of biological drugs used in patients diagnosed with JIA, excluding the form systemic, in a pediatric unit of a children's hospital in the last 5 years.
**Methods:** Descriptive analytic study of patients diagnosed with JIA (non-systemic) (as proposed by ILAR nomenclature, Edmonton 2001), who received biological treatment from 1 January 2010 to 30 June 2015. It considered as an event end the suspension of treatment by state remission or change to regimen decrease. Statistical analysis performed using the Kaplan-Meier and log rank test with SPSS.19.0 program.
**Results:** Total 90 patients diagnosed with JIA with biological treatment in the last 5 years, 2/3 female (60 girls, 66.7%), 1/3 male (30 boys, 33.3%), mean age 5 years 2 months (minimum: 1 year 11 months, maximum: 15 years 6 months). The distribution of JIA: Oligoarticular arthritis 40% (42 patients). Polyarticular RF negative arthritis 22.9% (24 patients). Enthesitis-Related arthritis 15.2% (16 patients). Polyarticular RF positive arthritis 3.8% (4 patients). Psoriatic arthritis 3.8% (4 patients).
Total 100 treatments: 49% adalimumab, 46% etanercept, 5% Tocilizumab. Median time of 36 months overall monitoring (SD ± 21.8). Continue with the drug 45 patients, 45 achieved remission or regimen decrease (23 adalimumab, 20 etanercept, 2 tocilizumab), replaced by inefficiency 7, suspended for toxicity 3. Namely 45 and 55 censored events cases.
Medians for survival time: 56 months adalimumab (95% CI 46.5–65.5), 48 months etanercept (95% CI 38.8–57.2), Tocilizumab 46 months.
The comparison between the survival curves of etanercept and adalimumab (Logrank) was 0.092 (p=0.762).
**Conclusions:** The time when "survive" (remain) biological treatment are significantly prolonged, over 4 years, with little difference between the two treatments used (etanercept and adalimumab). In addition, it can be deduced that serious side effects are rare, since in this cohort were replaced only in three cases by significant adverse effects.
No significant differences in the comparison of the survival curves of the main biological treatments used were found.
**Disclosure of Interest:** None declared
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## SAT0273 CORTICOSTEROIDS AS RESCUE THERAPY FOR RESISTANT KAWASAKI DISEASE

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**Background:** Kawasaki Disease (KD) is one of the most common systemic vasculitidies in children today. IVIG is the mainstay of treatment, however, about 1/5 of patients do not respond (Teraguchi) resulting in an increased risk of Coronary Artery Abnormalities (CAA). Based on the current literature and from experience it is our preference to use Intravenous Methylprednisolone (IVMP) in the treatment of IVIG resistant Kawasaki Disease (rKD) patients.
**Objectives:** To examine the differences in CAA seen in patients who were treated with IVMP versus retreatment with IVIG
**Methods:** Demographic, clinical manifestations and echocardiogram data were collected and analyzed. Descriptive statistics were used to describe the data. Chi square/Fisher Exact Test were used to test association, student t test or Mann Whitney U were used to compare the data where appropriate. Kaplan Maier analysis was used to assess the time to CAA resolution. Significance was set at 0.05.
**Results:** Of the 78 rKD patients included (type of KD: complete 55, incomplete 23), 33 received 2nd IVIG and 45 received IVMP. 13 rKD patients who failed the 2nd IVIG treatment were excluded from the analysis (2nd IVIG failure 27.7%). Median age at onset was 1.5 years (IQR 0.76, 2.58) and 45 patients were male. There was no significant difference in regards to gender (p=0.63), age at onset (p=0.14), type of KD (p=0.89) or KD clinical manifestations between treatment groups (p=0.25–0.56). 88.9% of IVMP and 57.6% of 2nd IVIG patients had CAA prior to therapy (p=003). The median duration to completing CAA resolution was 1.19 years; 2nd IVIG group (IQR 0.62, 2.43) and IVMP (IQR 0.84, 3.27). Time to achieve CAA resolution was not different between treatment groups (p=0.11, Figure 1).
**Conclusions:** Between 2nd IVIG and IVMP as rKD rescue therapy, there was no difference in duration of achieving CAA resolution. Our group has described higher number of rKD with CAA prior to IVMP treatment. A larger, prospective randomized controlled trial is needed to confirm our preliminary observations for which this is underway in our region.
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## SAT0274 INDIRECT COMPARISON OF BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS: META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. Recent advances in biologics have greatly changed the prognosis of JIA.
**Objectives:** To evaluate the efficacy and safety of biological agents in patients with JIA.
**Methods:** We included all randomized controlled trials (RCTs) that compared biologics with placebo in JIA patients. According to the American College of Rheumatology Pediatric (ACR Pedi) criteria, the proportions of patients reaching 30%, 50% or 70% improvement (ACR Pedi 30/50/70) or suffering disease flare were used as the efficacy outcomes. Adverse events (AEs), infections and severe AEs were applied to evaluate the safety. The biological agents were pooled to perform comparison with placebo and among themselves, calculating odds ratios, probability of being best ($P_{best}$) and numbers needed to treat (NNT).
**Results:** Sixteen RCTs totaling 18 reports (1689 patients) were included in the analysis focusing on 4 different types of biologics, i.e. tumor necrosis factor (TNF) inhibitors (etanercept, infliximab, adalimumab and golimumab), anti-interleukin-1 agents (anakinra, rilonacept, canakinumab), anti-interleukin-6 agent (tocilizumab) and cytotoxic lymphocyte-associated antigen-4 agent (abatacept). All biological agents were efficacious in achieving ACR Pedi 30/50/70 responses and preventing disease flare compared with placebo but with a higher risk of infections. No significant differences in efficacy were found among biologics, except that tocilizumab had a higher rate of ACR Pedi 30 response than TNF inhibitors. And for ACR Pedi 30/50/70 responses, tocilizumab was ranked the most effective option with NNT of 2 ($P_{best}$ 89.9%, 82.3% and 48.4%, respectively).
**Conclusions:** Compared to placebo, biologics are all effective in the treatment of JIA but with a higher risk of infections. Tocilizumab is more likely to achieve ACR Pedi 30/50/70 responses.
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## SAT0275 KAWASAKI DISEASE – AN EASTERN INDIAN COHORT OF 7YEARS

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**Background:** Kawasaki disease (KD), an acute febrile childhood vasculitis can present with varying clinical features and the main complication is involvement of coronary arteries (1). The epidemiological pattern may be different in different geographical regions, even it can vary within a country. KD is not unusual in India but published series are infrequent (2). Here we present a series of 185 cases of KD diagnosed in our hospital in last 7 years to have a look in to the varied clinical manifestations, epidemiology, atypical features and complications.
**Objectives:** 1. To analyse the record of Kawasaki disease diagnosed in the study period.
2. Compare the epidemiology and clinical features of KD in our part of the country with that of the published series from northern India.
3. To note the atypical features and estimate the incidence of coronary involvement.
**Methods:** Clinical records of 185 children fulfilling the diagnostic criteria of Kawasaki Disease and admitted at the Institute of Child Health, Kolkata during the time period October 2008 to January 2016 were reviewed. The data collected included details of clinical and laboratory features, treatment and outcome.
**Results:** A total of 185 patients were diagnosed as KD (4.8 per 1000 hospital admission). Among these 185 patients,171 presented with typical features of KD, rest 14 were atypical including KD with erythroderma, KD with bilateral ptosis,

neonatal KD, KD with facial Palsy,KD with nephrotic syndrome etc. Average age of presentation was 22 months. Most patients presented with fever of an average duration of 9 days. Besides the typical features, we want to stress upon some special features of KD, like orange-brown chromonychia (orange brown discolouration of nails) in 65% of cases, BCG scar reactivation in 14%, extreme irritability in 86% and greenish loose stools in about 68%. Echocardiographic abnormalities (ectasia or aneurysm) were detected in 29% of cases. All patients received Intravenous Immunoglobulin of which 7 did not respond to a single dose of 2gram/kg.

**Conclusions:** 1. A bimodal seasonality has been seen with clustering of cases during March- April and September-October.
2. Mean age of onset (22 months) is lower than the north India series.
3. Most (94%) presented with typical form with a response rate of 96% with first dose ivIg.
4. Orange brown Chromonychia is a novel finding that has been seen in a significant number of patients.
5. Coronary abnormalities is on the higher side than the reported series from north India as well as other parts of the world.

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## SAT0276 CYCLOSPORINE IN RESISTANT SYSTEMIC JIA - A CHEAPER ALTERNATIVE TO BIOLOGICS FOR DEVELOPING COUNTRIES

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**Background:** Systemic juvenile idiopathic arthritis (sJIA), though well responsive to corticosteroids (1), but toxicity limit their prolonged usage. Other disease modifying anti rheumatic drugs (DMARDs) have been tried to limited effect (1). Only the newer biologic agents (Anakinra, Tocilizumab) are promising (1,2), but in a developing country like India, accessibility and prohibitive costs limit their use. We started trying Cyclosporine, a potent immunosuprressive agent for the cost benefit in steroid dependent or refractory sJIA specially in those who relapsed with predominant systemic symptoms. Here, we present a series of 15 cases refractory sJIA most of whom were successfully treated with oral Cyclosporine in conjunction with methotrexate ± low dose steroids.
**Objectives:** 1. To assess the efficacy of Cyclosporine in patients of steroid unresponsive or steroid dependent Systemic JIA. 2. To evaluate the optimum dosing and blood level to achieve and maintain remission.
**Methods:** Clinical records of children fulfilling the diagnostic criteria of sJIA admitted at the Institute of Child Health, Kolkata during the time period July 2009 to November 2015 were reviewed. The data collected included details of clinical and laboratory features, treatment and outcome. In this prospective study a total of 82 sJIA was diagnosed. 15 were refractory and included as a candidate for cyclosporine therapy.
*Criteria for initiating Cyclosporine:* sJIA relapsing frequently (at least 3 times) on withdrawing or attempting to taper off steroids, in spite of being on Methotrexate +/– Hydroxychloroquine.
**Results:** Among the 15 patients of frequently relapsing, steroid dependent sJIA, 13 responded to cyclosporine and Steroid could be withdrawn completely after a mean duration of 6.15 months of starting Cyclosporine.
Among this 13, 11 never relapsed after initiation of Cyclosporine and 2 relapsed but managed with a short course of steroid. So we achieved a permanent remission rate of 73% (P value0.02) with a mean follow up of 15 months after starting cyclosporine.
At present:
1. Off Steroid, off Cyclosporine -11 (9 never relapsed, 2 relapsed but responded to short course steroids)
2. Off Steroid, on Cyclosporine-2 (never relapsed)
3. Did not respond to Cyclosporine -2
The mean dose of Cyclosporine to achieve the remission was 3.9 mg/kg/day.
The mean blood level in which remission was induced was 138.4ng/ml.
There was no significant side effect noted except hirsuitism in one and another one developed transient hypertension.
**Conclusions:** 1. Cyclosporine was found to be effective in almost 75% of frequently relapsing steroid dependent sJIA to achieve and maintain remission.
2. Cyclosporine was found to be a cheaper alternative to Tocilizumab as the average cost of therapy for a 20kg patient on Cyclosporine was found to be 10,000 INR (143 EURO)/patient over a 6 months period; which would amount to 100,000 INR (1430 EURO)/patient with Tocilizumab for the same duration (Anakinra not available in India).

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## SAT0277 NEUROPSYCHIATRIC INVOLVEMENT IN JUVENILE-ONSET SYSTEMIC LUPUS

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**Background:** Neuropsychiatric involvement in systemic lupus erythematosus (NPSLE) includes the neurological syndromes of the central, peripheral or autonomic nervous systems and psychiatric disorders. Some studies suggests that juvenile systemic lupus erythematosus (jSLE) has a more serious course and a more frequent neuropsychiatric involvement than adult onset, coursing with significant morbidity and mortality. Its prevalence ranges from 22 to 50.9%.
**Objectives:** To assess neuropsychiatric manifestations in juvenile-onset SLE patients and study the predictors and association to disease characteristics.
**Methods:** Retrospective observational study was performed including consecutive patients with jSLE (disease onset before 16 years of age,) that fulfilled American College of Rheumatology (ACR) criteria followed in our Paediatric Rheumatology Unit. Clinical, demographic and laboratory characteristics were retrospectively collected by consulting the medical records. The neuropsychiatric manifestations were defined according to the nomenclature and classification of ACR. Patients with NPSLE were compared with others using Student t-test, Mann-Whitney test, Chi-square or Fisher test (SPSS 23.0). Significance level was set as $<0.05$.
**Results:** 38 patients were included, 92.1% (35) were female, with a mean age at diagnosis of 12.9 ± 3 years. Median period between onset of symptoms and diagnosis of SLE was 0.3 [0–1.2] years and median duration of follow-up was 14 [0.75–26]. Neuropsychiatric manifestations of the SLE were observed in 8 (21%) patients: chorea (n=1), psychosis (n=2), seizures (n=1), transverse myelitis (1), stroke and weakness (n=1), headache (n=2).
Among the 8 patients with NPSLE, 7 were female and 1 was male. The median time between diagnosis and NPSLE manifestation was 1.75 [0–3] years. The two patients with headaches were treated with oral glucocorticoid. The remaining patients were treated methylprednisole pulses, 3 were treated with cyclophosphamide and 1 with rituximab.
Full recovery was observed in almost patients, except for those with headaches that had many recurrences of symptoms during follow up.
Comparing patients that had NPSLE with the remaining, we found a statistically significant higher SLEDAI and SLICC scores in those with NPSLE (4 vs 2, p=00.04 and 1.5 vs 0, p=0.003, respectively).The age, sex and disease duration were comparable between the groups.
NPSLE was associated with more frequent lupus nephritis (75% vs 43.3%, p=0.03) and presence of antiphospholipide syndrome (APS) (20% vs 11.2%, p=0.04).
NPSLE patients also had higher lupus anti-coagulant prevalence (25% vs 10.7%) and anticardiolipine antibodies (23.3% vs 12.5%) %), yet none of the above reached statistical significance.
**Conclusions:** The neuropsychiatric manifestations are frequently observed in patients with jSLE and central nervous system manifestations were more frequently observed than manifestations affecting the peripheral nervous system. Our study suggests an association between NPSLE and lupus nephritis, higher disease activity and the presence of APS. We observed a good outcome with complete resolution in the majority of the cases.
**Disclosure of Interest:** None declared
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## SAT0278 ASSOCIATION BETWEEN MUCOCUTANEOUS MANIFESTATIONS AND CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS IN JUVENILE-ONSET SYSTEMIC LUPUS

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**Background:** Patients diagnosed with juvenile-onset systemic lupus erythematosus (jSLE) often have skin and oral lesions as part of their presentation. It is suggested, in literature, that mucocutaneous involvement in jSLE may be associated with some antibodies and systemic disease and often require treatment with systemic immunosuppressive drugs in order to achieve adequate disease control.
**Objectives:** To assess mucocutaneous manifestations in jSLE and to study it's associations with clinical and immunological characteristics.
**Methods:** Retrospective observational study was performed including consecutive patients with jSLE (disease onset before 16 years of age) followed in our Paediatric Rheumatology Unit. Clinical, demographic and laboratory characteristics were retrospectively collected by consulting the medical records. All patients fulfilled the clinical and laboratory criteria of the American College of Rheumatology (ACR). Patients with mucocutaneous manifestations were compared with others using Student t-test, Mann-Whitney test, Chi-square or Fisher test. (SPSS 23.0). Significance level was set as $<0.05$.

**Results:** 38 patients were included, 92.1% (35) were female, with a mean age at diagnosis of 12.9 ± 3 years. Median period between onset of symptoms and diagnosis of SLE was 0.3 [0–1.2] years and median duration of follow-up was 14 [0.75–26].
84.3% had mucocutaneous manifestations, (78.9% malar rash, 5.2% discoid rash, 70.3% photossensibility and 39.5% ulcers). 78.9% of the patients also had musculoskeletal symptoms, 63.2% haematological manifestations, 50% had renal involvement, 21% serositis and 13.2% neuropsychiatric involvement.
Patients with mucocutaneous involvement had more frequently renal involvement (58% vs 14.2%, p=0.001), haematological manifestations (70.9% vs 28.5%, p=0.02), positive lupus anticoagulant (13.8% vs 4.3%, p=0.012), positive coombs test (59% vs 14.2%, p=0.04) and positive anti-SSa (35.4% vs 3.3%, p=0.04). SLEDAI and SLICC scores were comparable between the two groups.
Analysing by type of skin involvement, patients with malar rash had also more frequently haematological involvement (76.7% vs 12.5%, p=0.002) and it was associated with the presence of anti-SSa (33.3% vs 12.5%, p=0.04).
Patients with photossensibility had more frequently positive anti-SSa (34.5% vs 11.1%, p=0.029).
Two patients (5.2%) had discoid lupus and 15 (39.5%) had ulcers but it was not associated with any other clinical or immunological manifestation.
**Conclusions:** Mucocutaneous are frequent manifestations in jSLE, and they are associated with active disease occurring frequently in patients with also haematological and renal manifestations. Anti-Ssa antibody is important in these patients as we have demonstrated it's association with some particularly skin manifestations.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4729

## SAT0279 CYTOKINE GENE POLYMORPHISMS (IL10, IL6, TNFα) IN CHILDREN WITH RHEUMATIC FEVER IN LATVIA

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**Background:** Rheumatic fever (RF) is an autoimmune disease which pathogenesis is based on the response of cellular and humoral immune system, that develops after Group A beta hemolytic Streptococci infection with following 45% obtained heart disease (Guilherme L, 2011). One of the most typical clinical manifestations is polyarthritis. So far it is found that genetic polymorphisms may affect the immune system functions and phenotype of RF clinical manifestations. Since cytokines are central immune system molecules, and cytokine gene promoter polymorphisms can affect cytokine production *in vitro*, the following polymorphisms are among the candidates to be studied in pathogenesis of rheumatic fever. The most frequently studied polymorphisms - TNFa-308G/A is associated with mitral valve (MV) damage and TNFa-238G/A - with myocarditis and aortal valve (AV) damage (Rajendranath R, 2007). Data are different and Hernandez-Pacheeco (2003) proved TNFa-238 as unrelated.
**Objectives:** To investigate the following cytokine gene promoter polymorphisms – TNFa-238G/A (ra361525), -308G/A (rs1800795), IL 1-592C/A (rs1800872)-819T/C (rs1800871), -1082G/A (rs1800896) and IL6-174G/C (rs1800795) in patients with rheumatic fever in Latvia.
**Methods:** Clinical and DNA material were analyzed of 70 rheumatic fever patients (born 1984–2002) and 254 healthy. Data and DNA from controls were obtained from the State Population Genome Database. To determine rs1800795 and rs1800896 polymorphisms, was used real time TaqMAn SNP genotyping. Other polymorphisms were analyzed performing polymorphism-containing region Sanger sequencing. Statistical analysis were done with Plink 1.06. All genotyped polymorphisms corresponded to Hardy-Weinberg equation and initial SNP genotyping efficiency was over 98.8%.
**Results:** 48 out of 70 RF patients (68.5%) were boys, 22 (33.4%) were girls. Up to 7 years of age were 23 (32.8%) and after - 47 (67.1%) patients. Acquired rheumatic heart disease developed in 47 (67.1%) patients, MV insufficiency in 24 (34.3%) patients, AV insufficiency in 3 (4.3%) patients and combined MV and AV damage in 20 (28.6%) patients. Polyarthritis were diagnosed in 34 (48.6%) patients. 8 (11.4%) patients suffered from *chorea minor* and 3 (4.3%) patients had *erythema annulare*. Analyzing TNFa and IL-10 genes SNP of promoters in different clinical patients groups and comparing them with controls, statistically significant differences in the frequency of alleles were not observed, but in patients with polyarthritis IL-6 genes rs1800795 alleles showed statistically significant differences comparing with other clinical groups p=0.04737, OR=0.4621.
**Conclusions:** 1. Inflammatory cytokine IL-6 gene promoter's-174G/C position (rs1800795) polymorphism is polyarthritis development affecting SNP in patients with rheumatic fever in Latvia. 2. There was no proven link between TNFa-238G/A and-308G/A SNP and acquired heart disease development.
**Disclosure of Interest:** None declared
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## SAT0280 RAYNAUD'S PHENOMENON AS AN EARLY SYMPTOM OF RHEUMATIC DISEASE IN CHILDHOOD

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**Background:** Raynaud's phenomenon (RP) can be an initial manifestation of rheumatic disease [1]. In 2013 PReS Congressnewe consensus standards for clinical practice for children with RP was presented [2]. In 2014 a panel of experts established new diagnostic criteria for RP [3]. Nailfold capillaroscopy is an easy test with a well defined diagnostic role in the management of rheumatic diseases [4].
**Objectives:** The aim of the study was the assessment of RP in children and adolescents with the evaluation of nailfold capillaroscopy and the relation of the clinical features to the capillaroscopic pattern.
**Methods:** 77 children aged 7 to 18 years with symptoms of RP diagnosed according to the new diagnostic criteria [3] in Department of Pediatric Pulmonology and Rheumatology Medical University of Lublin were included in the study. RP was differentiated into primary (PRP) and secondary (SRP) RP in accordance with the new criteria [3]. Patients were reviewed for Raynaud's and other clinical symptoms, antinuclear antibodies (ANA) titer and other features. Capillaroscopic patterns were assessed by qualitative and semiquantitative methods and defined as normal, nonspecific changes or scleroderma pattern. Images of the study were archived.
**Results:** 77 patients were included in the study (66 female and 11 male), average age of RP onset was 14,2 years. ANA and capillaroscopy were examined in all patients. Positive ANA (titer≥1/160) were found in 36 (46,75%) patients. Capillaroscopy results were normal in 33 (42,85%) cases, nonspecific changes in 25 (32,46%). The scleroderma patterns were recognized in 19 (24,7%) patients. According to diagnostic criteria for RP, 49 (63,6%) patients had secondary RP, among them systemic sclerosis was diagnosed in 1, juvenile dermatomyositis - 1, juvenile lupus erythematosus - 1, mixed connective tissue disease - 1, juvenile idiopathic arthritis in 3 patients and undifferentiated connective tissue disease in 16. Moreover, we recognized autoimmune thyroiditis in 7 patients, who had SRP. In patients with SRP: 19 (38,8%) had scleroderma pattern in capillaroscopy, 15 (30,6%) - nonspecific changes, 15 - 30,6% results were normal. In children with PRP: the results of capillaroscopy were normal in 18 cases (64,3%), nonspecific changes were observed in 10 (35,7%).
**Conclusions:** In the present group of patients, more than half had secondary RP recognized.
Typically, RP had a beginning in teenage years with marked female predominance.
Almost half of the patients with SRP was diagnosed with a rheumatic disease.
The new criteria and consensus standards for clinical practice in children with RP defined and the objective criteria for the assessment of the capillaroscopic exam significantly clarify the procedure of management of children or adolescents with RP.
A high percentage of secondary RP in our experience confirms the need for further follow up, even after the transition to adult age.
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**Disclosure of Interest:** None declared
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# SLE, Sjögren's and APS - clinical aspects (other than treatment)

## SAT0281 COMPENSATORY BRAIN MECHANISMS TO MAINTAIN COGNITIVE FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Cognitive dysfunction (CD) has been reported to affect up to 80% of systemic lupus erythematosus (SLE) patients. The cause of CD in SLE is unclear and studies examining structural brain abnormalities have been inconclusive. Functional magnetic resonance imaging (fMRI) is well used in other diseases and is now starting to be used in SLE. Preliminary studies have suggested that patients employ compensatory brain mechanisms to maintain adequate cognitive function but many questions remain unanswered.
**Objectives:** Our study aims to examine the effects of disease activity in SLE on

CD using fMRI, also considering potential confounding factors such as depression and medication.
**Methods:** 32 SLE participants (11 with active disease, SLE-F, and 21 stable, SLE-S) and 30 healthy controls (HC) undertook a working memory task (n-back) and a facial emotional recognition task (FERT) during fMRI. The n-back task had three levels (0-, 1- and 2-back) with the 2-back level being the most difficult. The FERT displayed faces expressing different emotions: happiness, sadness, fear and neutral. fMRI responses to both tasks were analysed using SPM12, the n-back using a cluster significance threshold of $p<0.05$ familywise error corrected and the FERT using a region of interest approach focusing on the amygdala. Demographic, mood and disease variables were analysed using SPSS 22.
**Results:** The three groups were matched on age, sex and handedness but varied on IQ and mood scores. The two SLE groups were well-matched on disease characteristics except, as expected, on the measure of current disease activity (SLEDAI) ($p<0.001$). During the n-back task, the SLE patients had an increased BOLD signal in lateral frontal areas compared to the HC group for the 2-back condition ($p<0.05$). This was more pronounced in the SLE-F group. Also, in the ventral anterior cingulate cortex (vACC), the SLE-S and HC groups had attenuated BOLD signals compared to the SLE-F group ($p<0.05$). For the FERT, there was a strong trend towards the SLE groups having a greater BOLD signal in the left amygdala compared to the HC group ($p=0.07$) (fig. 1).

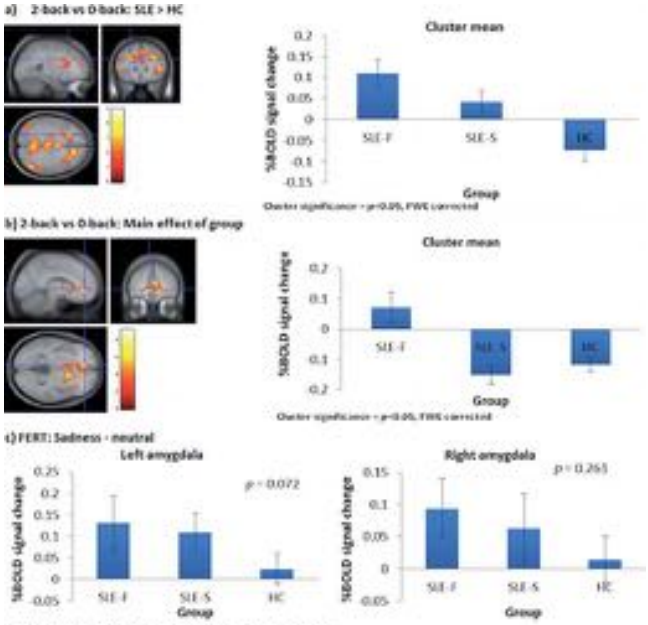



**Figure 1: Results from the n-back and FERT tasks**
N-back task, 2-0back condition:
a) Increased BOLD signal for SLE groups in lateral frontal areas (cluster co-ordinates: -24 23 30, 15 35 30).
b) Attenuated BOLD signal in the vACC for the SLE-S and HC groups (cluster co-ordinates: -9 44 0, 18 11 10, -21 38 -10).
FERT task:
c) BOLD response in the amygdala for the sadness minus neutral condition.

**Conclusions:** Our results in lateral frontal areas supported findings from previous studies that suggested SLE patients employ compensatory prefrontal mechanisms to maintain adequate cognitive function on effortful tasks. The vACC is part of a "default mode network", putatively involved in reflective self-focused processing and typically suppressed during cognitive tasks. The inability of the SLE-F to suppress signal in this region may negatively impact their cognitive function by allowing self-reflective processes to interfere with performance. The trend towards an increased BOLD signal in the left amygdala for the SLE groups is similar to that seen in depressed patients, which suggests that low mood in SLE has detectable neuronal effects. Overall, these results indicate that regardless of current disease activity, SLE affects cognitive and emotional function at a neuronal level. Some effects are more pronounced in SLE-F patients, in particular inability to suppress self-reflective "default mode" processing while undertaking cognitive tasks.
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## SAT0282 FREQUENCY AND PREDICTORS OF ATTAINMENT OF THE LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) IN A CROSS SECTIONAL STUDY OF SLE PATIENTS IN THE ASIA PACIFIC

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**Background:** Systemic lupus erythematosus (SLE) is a heterogeneous disease characterised by fluctuating disease activity. A low disease activity endpoint, the Lupus Low Disease Activity State (LLDAS), was recently reported and retrospective validation showed that time spent in LLDAS translated into reduced damage accrual (Franklyn, Ann Rheum Dis, 2015). A large prospective study to validate LLDAS in a multiethnic cohort of lupus patients from the Asia Pacific Region is underway.
**Objectives:** To describe the frequency and identify the predictors of fulfilling criteria for LLDAS in baseline visit data from a large multinational multiethnic cohort of patients with SLE in nine Asia Pacific countries.
**Methods:** Prospectively collected baseline visit data from 1846 SLE patients enrolled in a longitudinal study were analysed cross sectionally against the recently published definition of LLDAS, and patient characteristics associated with LLDAS attainment determined.
**Results:** LLDAS criteria were met by 44% of patients at a single baseline visit. Stepwise multivariable logistic regression revealed that patients with shorter disease duration were less likely to be in LLDAS (OR 0.31, 95% CI 0.19–0.49, $p<0.001$). Likewise, discoid rash (OR 0.66, 95% CI 0.49–0.89, p=0.006), renal disease (OR 0.60, 95% CI 0.48–0.75, $p<0.001$), elevated double stranded DNA (OR 0.65, 95% CI 0.53–0.81, $p<0.001$) or hypocomplementaemia (OR 0.52, 95% CI 0.40–0.67, $p<0.001$) were negatively associated with LLDAS attainment. Significant differences in LLDAS attainment between countries were observed, and higher national social wealth as measured by the Gross Domestic Product per capita was positively associated with LLDAS (OR 1.57, 95% CI 1.25–1.98, $p<0.001$).
**Conclusions:** Low disease activity was observed in less than half of SLE patients at a single point in time. Disease duration and phenotype, as well as national social wealth, were predictive of LLDAS attainment.
**Disclosure of Interest:** None declared
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## SAT0283 RELAPSES OF LUPUS NEPHRITIS - RISK FACTORS, INCIDENCE AND IMPACT ON OUTCOME

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**Background:** Lupus nephritis (LN) is one of the most severe complications of systemic lupus erythematosus (SLE). In recent years, the morbidity and mortality of LN have improved considerably owing to more appropriate use of traditional drugs, such as corticosteroids and cyclophosphamide, and the incorporation of new ones, such as mycophenolate mofetil and biologic agents. Renal relapses are part of the natural history of LN and represent a significant challenge not only because they are associated with an increased risk of decline in renal function, but also there is a cumulative toxicity of immunosuppressive treatments.
**Objectives:** The aim of this study was to review renal flare frequency, to identify potential risk factors for relapses, to assess the value of serological tests during flares and to analyse their impact on global outcome in LN patients.
**Methods:** Patients with biopsy proven LN diagnosed between 1985 and 2015 were identified from our database. All patients (pts) met the ACR criteria for SLE. LN classes based on glomerular pathology were defined according to the ISN/RPS classification. Clinical and laboratory data were obtained from the records of patients. According to the response to treatment, LN pts were divided into 3 groups of complete remission (CR), partial remission (PR) and no response (NR). Those in remission were divided into 2 groups of relapsing and non-relapsing during maintenance period. Associated factors for remission and relapse were analyzed. CR was defined as proteinuria less than 0.5 g/24 h and stable or improved serum creatinine, whilst PR was defined as more than 50% reduction in baseline proteinuria achieving less than 1,0 g/24 h with stable or improved creatinine. We defined proteinuric flares as proteinuria above 1 g/24 h in pts with CR, and doubling of proteinuria in cases of PR.
**Results:** 218 (70,64%) of 276 SLE pts (250 females and 26 males) with biopsy proven LN (class I ISN/RPS LN – 18 pts, class II – 45 pts, class III – 56 pts, class

IV – 75 pts, class V – 54 pts, class VI – 2 pts, mixed forms – 26 pts) achieved either CR (n=154; 55,8%) or PR (n=64; 23,2%). 47 pts (38 had preceding CR and 9 had PR) with LN had one flare, 36 (26 had preceding CR and 10 - PR) – two flares, 27 (14 had preceding CR and 13 - PR) – three flares, 17 (7 had preceding CR and 10 - PR) ≥4 flares. The median time between remission and relapse was 23,5 ± 21,9 months in pts with CR, and 11,4 ± 9,3 months in pts with PR. The maintenance immunomodulating drugs at the time of flare was low dose (<10 mg/24 h) corticosteroids and/or azathioprine. 123 LN pts (48%) had angiotensin blockers in therapy. Non-adherence to treatment at time of relapse was documented in 26 pts. At the time of first flare, the median proteinuria was 1,84 ± 0,97 g/24 h in pts with CR, and 2,78 ± 1,25 g/24 h in pts with PR. 42 LN pts had raised serum creatinine, 65 had raised anti-double stranded deoxyribonucleic acid, 94 had low complements at flare.

**Conclusions:** Renal flares in patients with LN are common, have a negative impact on outcome, but cannot be readily predicted. Our study shows that 58,83% of LN patients develop at least one relapse after reaching remission, usually within 2 years. The length of time to flare tends to be shorter in cases of preceding PR than in CR. Lack of adherence to long term immunosuppression was identified as a significant factor in LN flare (20,47%). Patients with LN in remission require close follow-up.

**Disclosure of Interest:** None declared

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## SAT0284 BOTH PROLONGED REMISSION AND LUPUS LOW DISEASE ACTIVITY STATE ARE ASSOCIATED WITH REDUCED DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Treat-to-target strategies in systemic lupus erythematosus (SLE) are thought to be the next step in improving outcome for SLE patients. Composing and validating treatment targets are therefore important. Recently, criteria for remission [1] and for Lupus Low Disease Activity State (LLDAS)[2] have been proposed.

**Objectives:** To identify predictors of organ damage and specifically the relationship between prolonged disease remission or LLDAS and damage accrual in a longitudinal cohort of SLE patients.

**Methods:** Patients from the Amsterdam SLE cohort were prospectively assessed including the occurrence of minor/major flares, and once a year: remission and LLDAS. To determine which variables were predictive of damage accrual (dependent variable), variables with p<0.10 in univariable analysis were entered into the respective multivariate logistic regression model in a backward stepwise elimination manner. Secondly, odds ratios (ORs) for damage accrual during follow-up were calculated for patients with or without prolonged remission during 5 years, and with or without LLDAS in ≥50% of observations.

**Results:** Data from 183 patients (90.2% female, 68.3% Caucasian) with a median follow-up duration of 5.0 years were analyzed. In univariable analysis, patients with damage accrual had higher SDI scores, number of fulfilled ACR criteria, frequency of nephrological manifestations and hypertension at baseline, higher mean SLEDAI-2K, mean daily doses of prednisone, and frequency of ≥1 major flare during follow-up, and lower frequency of remission at all visits and ≥50% of observations in LLDAS. The most important predictors for damage accrual were: occurrence of ≥1 major flare (OR 5.2, 95% CI 1.8 – 14.5, p=0.002), mean daily prednisone dose during follow-up (OR 1.1, 95% CI 1.0 – 1.2, p=0.03 per increase of 1 mg), and nephrological manifestations at baseline (OR 2.2, 95% CI 1.1 – 4.5, p=0.03). Prolonged remission was present in 32.5% (38/117) and LLDAS in ≥50% of observations in 64.5% (118/183) of patients. Both the presence of prolonged remission during 5 years and LLDAS in ≥50% of observations were associated with a reduced risk of damage accrual (OR 0.20, 95% CI 0.07 – 0.53, p=0.001 and OR 0.52, 95% CI 0.28 – 0.99, p=0.046, respectively).

**Conclusions:** In this observational study, we present for the first time longitudinal data regarding disease activity and damage accrual in our cohort. Prolonged remission and LLDAS were associated with an improved outcome, as determined by yearly assessments. Remission and LLDAS are therefore realistic targets as the respective criteria were fulfilled frequently in our cohort. In order to improve the outcome in SLE patients, future studies should investigate whether these targets can be reached actively with therapeutic strategies.

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**Disclosure of Interest:** None declared

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## SAT0285 VACCINATIONS IN SLE: COVERAGE AND REASONS FOR NON-VACCINATION - RESULTS FROM THE LULA-STUDY

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**Background:** Infections are an important factor for morbidity and mortality in patients with systemic lupus erythematosus (SLE). Vaccinations may prevent certain infections. In Germany vaccination recommendations have been released by the German Society for Rheumatology based on the recommendations of the German Standing Committee on Vaccination. Similar suggestions have been published by the European League against Rheumatism. Vaccination coverage in the general population often falls short of reaching its goal.

**Objectives:** Our objective was to assess vaccination rates and reasons for non-vaccination in a representative sample of German SLE patients.

**Methods:** The LuLa-Study is a longitudinal patient-reported cross-sectional survey of the German LE self-help community on a multitude of LE associated factors. It is being conducted annually by means of a self-reported questionnaire since 2001. Amongst others medication, health-related quality of life, damage and disease activity are surveyed. In 2012 we additionally inquired about vaccinations as a main topic using a compilation of questions regarding usage, monitoring, execution and physician' respectively patients' reservations against vaccinations.

**Results:** 579 patients (94.0% female) aged 52.3 ± 13.4 years (mean ± standard deviation) and disease duration of 16.8 ± 9.1 years completed the questionnaire. Their vaccination status is primarily checked by the general practitioner (GP) (57.3%) and only occasionally by an internal specialist (7.9%), their rheumatologist (7.6%) or others (8.5%). A quarter of patients (24.9%) reported that their vaccinations status is not checked by any of their attending physicians. Ninety-three participants (16.1%) stated that at least one of their attending physicians had generally advised against the use of vaccinations. Characteristics (clinical and demographic) did not differ significantly compared to participants that had never been advised against the use of vaccinations.

37.5% of the participants stated that they rejected vaccinations before. The two main reasons expressed for rejecting a vaccination were the fear of developing a lupus flare (21.8%) or developing adverse events after vaccination (13.5%). Only accrued damage was significantly different in univariable analysis between participants that rejected vaccinations before and participants who did not with more damage being reported by the latter ('Brief Index of Lupus Damage' 2.2 ± 2.0 vs. 1.9 ± 2.1; p=0.009). There was no evidence for differences in other demographic or clinical characteristics between the two groups. We observed vaccinations rates of 65.8% for tetanus (past 10 years), 45.2% for influenza (past year), 32.2% for pneumococcal (past 5 years) and 6.1% for meningococcal (past 5 years) vaccinations.

**Conclusions:** Standard vaccination (tetanus) as well as medically indicated vaccination (influenza, penumococcal, meningococcal) coverage in SLE patients is still low in Germany. Reasons for non-vaccination are physician-based, patient-based but also due to organizational deficits because of competing responsibilities (GP vs. rheumatologist). Patients' and physicians' education is of major importance to increase vaccination rates. The rheumatologist bears the responsibility for this process optimization.

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## SAT0286 RISK OF SEVERE HERPES SIMPLEX VIRUS INFECTION IN PATIENTS SLE: A NATIONWIDE POPULATION COHORT STUDY

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**Background:** Severe herpes simplex virus (HSV) infections, especially encephalitis and keratitis, often affect immunocompromised patients and result in severe sequela. However, only few attempts have been made at the association between systemic lupus erythematosus (SLE) and HSV.

**Objectives:** To identify the risk of severe HSV infection in SLE patients by means of a nationwide population-based cohort study.

**Methods:** We identified SLE patients from the National Health Insurance research database between 1997 and 2012. We compared the incidence rate (IR) of severe HSV infection, including viral septicaemia, CNS infection, ocular infection, visceral infection and those with complications after infection, with that of non-SLE cohort. A Cox multivariable proportional hazards model was applied to evaluate the risk of severe HSV infection in the SLE cohort.

**Results:** A total of 122,520 subjects (24,504 SLE patients and 98,016 age- and gender-matched subjects as control group) were analyzed and revealed a significantly higher IR of severe HSV infection in SLE (Incidence rate ratio =3.52, $p < 0.001$). Previous skin infection (HR=2.17, $p$=0.047), intravenous steroid pulse therapy (HR=4.48, $p<0.001$), oral daily steroid dose over 7.5mg prednisolone or equivalent (HR=1,60, $p$=0.010) were independent risk factors for severe HSV infection in SLE patients, while Age ≤18 (Hazard ratio [HR]=0.47, $p$=0.021) was a protective factor.

Table 1. Risk factors of severe HSV infection in patients with SLE[a]

| Variable | Univariate analysis | | Multivariable analysis[a] | |
|---|---|---|---|---|
| | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value |
| Age | 1.01 (1.00–1.03) | 0.017 | | |
| ≤18-year-old | | | 0.47 (0.24 – 0.89) | 0.021 |
| >18-year-old | | | 1.23 (0.54–2.82) | 0.612 |
| Male | 0.986 (0.57–1.71) | 0.974 | | |
| Diabetes mellitus | 0.56 (0.31–1.02) | 0.057 | | |
| End-stage renal disease | 0.96 (0.62–1.49) | 0.844 | | |
| Malignancy | 1.12 (0.28–4.54) | 0.871 | | |
| CHF | 0.79 (0.46–1.36) | 0.399 | | |
| Previous skin infection | 2.21 (1.03–4.73) | 0.042 | 2.17 (1.01–4.65) | 0.047 |
| Hydroxychloroquine | 1.05 (0.75–1.46) | 0.108 | | |
| Azathioprine | 1.60 (1.10–2.3.2) | 0.015 | – | – |
| Mycofenolate mofetil | 0.40 (0.06–2.89) | 0.367 | | |
| Cyclosporine | 1.58 (0.58–4.26) | 0.371 | | |
| Cyclophosphamide | 1.67 (0.87–3.18) | 0.122 | | |
| MTX | 1.32 (0.58–2.99) | 0.507 | | |
| Intravenous | 5.24 (3.52–7.79) | <0.001 | 4.48 (2.95–6.80) | <0.001 |
| Oral daily dose over 7.5mg[†] | 2.03 (1.44–2.86) | <0.001 | 1.60 (1.12–2.30) | 0.010 |

**Conclusions:** A higher risk of severe HSV infection was observed in SLE patients Risk factors for severe HSV infection were age over 18, previous skin infection, intravenous steroid pulse therapy and an oral daily steroid dose over 7.5mg.

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## SAT0287 ETHNIC DIFFERENCES STRONGLY INFLUENCE THE PHENOTYPIC EXPRESSION OF PRIMARY SJÖGREN: STUDY OF 7887 PATIENTS FROM 20 COUNTRIES ON 5 CONTINENTS (EULAR-SS TASK FORCE BIG DATA SJÖGREN PROJECT)

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**Objectives:** To analyse the influence of ethnicity on the clinical presentation at diagnosis in an international cohort of patients with primary Sjögren syndrome (pSS).

**Methods:** The Big Data Sjögren Project is a multicentre registry formed by international experts from the EULAR-SS Task Force. By January 2016, the database included 8315 consecutive patients fulfilling the 2002 AE criteria (20 countries, 5 continents). Ethnicity was classified according to FDA (White=W, Black/African American=B, Asian=A, Hispanic=H, Others=O).

**Results:** Ethnicity data was available in 7887 (95%) patients: 6177 W (78%), 1066 A (13%), 393 H (5%), 104 B (1%) and 147 O (2%). European patients were overwhelmingly white compared with Americans (96% vs 52%, $p<0.001$). The greatest differences between ethnicities ($p<0.001$) were observed for mean age at diagnosis (47yrs in B vs 54yrs in W), and the frequency of males (12% in B vs 4% in A), dry eyes (76% in A vs 98% in O), dry mouth (83% in A vs 99% in O), abnormal ocular tests (79% in O vs 90% in H), abnormal oral tests (65% in O vs 91% in H), positive minor salivary biopsy (75% in O vs 95% in H), positive anti-Ro (54% in O vs 84% in A) and positive anti-La (28% in O vs 50% in A).

**Conclusions:** White patients had the oldest age at diagnosis, Black/African Americans the highest frequency of men and the lowest mean age, Asians the highest frequency of women, the lowest frequency of sicca symptoms and the highest frequency of Ro/La and Hispanics the highest frequency of abnormal diagnostic tests. Ethnicity plays a capital role in the phenotypic expression at diagnosis of primary SS.

**Disclosure of Interest:** None declared
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## SAT0288 CLINICAL PHENOTYPING IN 608 PATIENTS FROM THE UNITED KINGDOM PRIMARY SJÖGREN'S SYNDROME REGISTRY

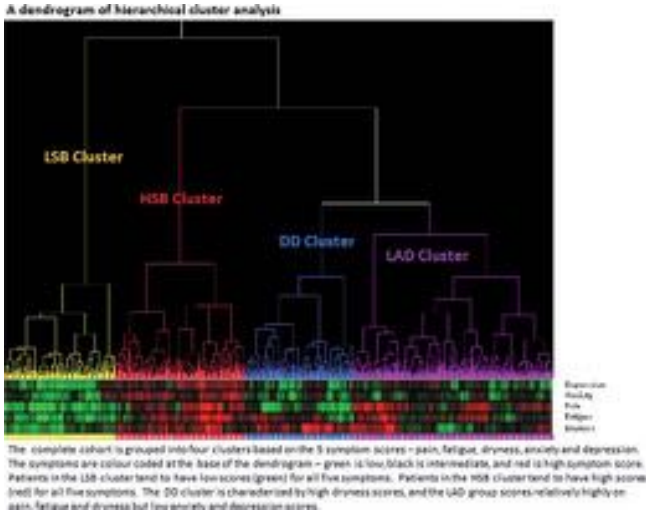
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**Background:** Primary Sjögren's Syndrome (pSS) is a chronic multi-system disease causing a wide-range of symptoms including dryness, pain and fatigue.[1,2] Individual experiences of pSS differ considerably resulting in a heterogeneous patient population.[3] These differences in disease-manifestation have not yet been characterised and the biological basis of varied patient-reported outcomes remains unclear.

**Objectives:** We aim to identify distinct clinical phenotypes within pSS, using patient-reported symptoms and to determine whether such clinical subgroups display differences in healthy utility values, and biological measures of disease activity.

**Methods:** Symptoms of 608 patients on the United Kingdom Primary Sjögren's Syndrome Registry (UKPSSR) were reviewed.[4] Phenotypes were identified using hierarchical cluster analysis of patient reported rating scales for pain, fatigue, dryness, anxiety and depression symptoms. Non-parametric analysis of variance was used to evaluate differences between clusters.

**Results:** Four phenotypic clusters were identified: High symptom burden (HSB), Low symptom burden (LSB), dryness dominant (DD) and Low Anxiety and Depression (LAD). Not surprisingly, there were significant differences between these groups in measures of health status and quality of life (EQ-5D $p<0.0001$, TTO $<0.0001$). More interestingly, objective measures of disease activity (ESSDAI $p=0.039$), objective dryness (salivary flow $p=0.007$, Schirmer's $p=0.014$), and biological parameters (IgG $p<0.0001$, lymphocytes $p=0.0005$, ESR $p=0.003$) suggest these subgroups may reflect different underlying endotypes.




**Conclusions:** Distinct biological differences may underlie pSS clinical phenotypes. The identification of these different clinical subsets of pSS could impact on the future study and management of the condition using a stratified approach.

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**Acknowledgement:** We would like to thank all the patients and healthy volunteers who have participated in the UKPSSR. This study received grant support from the Medical Research Council, British Sjögren's Syndrome Association and the Newcastle University.
**Disclosure of Interest:** None declared
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## SAT0289 SONOGRAPHIC ALTERATIONS DURING THE COURSE OF SJÖGREN'S SYNDROME – A FIVE-YEAR FOLLOW UP

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**Background:** Sonography in the evaluation of salivary gland alterations in suspected Sjögren's Syndrome (SS) and its benefit with regard to the diagnosis is part of continuing investigation. With most studies concentrating on the contribution to the diagnosis, few reports exist on longitudinal changes in the sonomorphology of salivary glands in SS. An improvement of salivary gland echostructure six months after rituximab infusion [1] and a decline of salivary gland stiffness evaluated with shear wave elastography after a two months period of a liposomal local therapy could be observed [2]. Despite intense research, many questions in ultrasound of salivary glands remain unanswered. Amongst other things it is unclear why not all patients with SS manifest sonographic abnormalities, when during the course of SS sonographic changes occur or if theses sonographic observations proceed the clinical symptomatic.
**Objectives:** Which variation of sonographic salivary gland alterations can be observed during the five-year follow up of patients with primary Sjögren's Syndrome (pSS)?
**Methods:** Patients with pSS diagnosed according to the AECG classification criteria were included in this study. The EULAR SS Patient Reported Index (ESSPRI) was applied for the evaluation of patient's symptoms and the EULAR SS Disease Activity Index (ESSDAI) for systemic features. During 2011 and 2016 the sonographic evaluation of salivary gland alterations in patients with primary Sjögren's Syndrome were evaluated. The echostructure of the parotid (PG) and submandibular glands (SMG) was graded on a scale of 0 to 4 (grade 0=normal, homogeneous gland; grade 1=mild parenchymal inhomogeneity (PIH), hypoechoic areas $<$2mm; grade 2=evident PIH, hypoechoic areas of 2–6mm; grade 3=gross PIH, hypoechoic areas $>$6mm; grade 4=adipose degeneration of the gland and parenchymal atrophy).
**Results:** Fifty patients diagnosed with pSS were included (45 female, age: 56y). In 2011 the mean ESSPRI score was 8.3 (SD=4.6) and the mean ESSDAI score was 5.6 (SD=7.5). The sonographic evaluation of the PG resulted in a mean score of 1.6 (SD=0.6) and in the SMG of 1.7 (SD=1.0). The sonographic score did not correlate with the time since onset of symptoms. Clinical examination and ultrasonographic evaluation was repeated after five years in 2016, revealing a mean ESSPRI score of 6.1 (SD=3.2, p=0.002) and a mean ESSDAI score of 4.6 (SD=7.0, p$<$0.001). The mean sonographic score of the PG was 1.4 (SD=0.7, p$<$0.001) and of the SMG was 1.9 (SD=1.0, p=0.034). There was a decline in the sonographic score of the PG of 0.27 (SD=0.5) and increase of the SMG of 0.1 (SD=1.1) on average. The mean time interval between onset of first symptoms and first sonographic examination in 2011 was 57.3 months (SD=60.8).
**Conclusions:** The five-year sonographic follow up of salivary gland alterations in patients with pSS revealed only minor alterations, even in patient with short illness duration. The relation to systemic or local therapeutic interventions is part of on-going analysis.
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## SAT0290 A HIGHER DISEASE ACTIVITY IN ANTI-SSA/SSB POSITIVE SJÖGREN'S SYNDROME IS EXPLAINED BY A HIGHER CLINICAL AND BIOLOGICAL B-CELL ACTIVATION

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**Background:** Anti-SSA/SSB positive Sjögren's syndrome is characterized by a higher risk for developing lymphoma (1), but no data already exist on systemic disease activity in subgroups of SS, as measured by validated scores for primary SS, such as the ESSDAI or ClinESSDAI.
**Objectives:** Primary objective of the study was to demonstrate the differences between anti-SSA/SSB positive and anti-SSA/SSB negative SS patients as regards systemic disease activity.
**Methods:** 955 patients affected by primary SS were included. All patients fulfilled the American-European Consensus Group Criteria for primary SS. Patients showing isolated anti-SSB positivity were excluded from these analyses. Patients were 911 female (95,4%), with a mean age of 52±14 years. ESSDAI and ClinESSDAI scores were measured (2, 3). Mann-Whitney U test was used to compare the ESSDAI and ClinESSDAI scores between anti-SSA/SSB positive and negative patients.
**Results:** Patients with anti-SSA with or without anti-SSB antibodies were 684 (71.6%), while anti-SSA and anti-SSB antibody negative patients were 271 (28.4%). Median (range) ESSDAI and median (range) ClinESSDAI were 5 (0–54) and 6 (0–53) in anti-SSA/SSB positive patients, and 4 (0–63) and 4 (0–60) in anti-SSA/SSB negative patients, respectively. Both the ESSDAI and the ClinESSDAI scores were significantly higher in anti-SSA/SSB positive patients (p$<$0.001 and p=0.021, respectively). Importantly, these differences were determined by a significant difference in the frequency of some domains, i.e., "lymphadenopathy" (p=0.034, Chi-square test), "glandular" (p=0.0004, Chi-square test), "cutaneous" (p=0.017, Chi-square test), "hematological" (p$<$0.0001, Chi-square test) and "biological" (p$<$0.0001, Chi-square test) (table 1). Notably, anti-SSA/SSB positive patients were younger than anti-SSA/SSB negative patients (50±14 vs. 57±11 years, p$<$0.0001 by t-test). Rheumatoid factor positivity (p$<$0.0001, Chi-square test), low C3 (p$<$0.0001, Chi-square test), low C4 (p=0.045, Chi-square test) and the presence of serum cryoglobulins (p=0.022, Chi-square test) were also significantly linked to the presence of anti-SSA/SSB positivity.

Table 1

| | Anti-SSA/SSB+ (%) | Anti-SSA/SSB– (%) | P value |
|---|---|---|---|
| Constitutional | 92 (13.5) | 30 (11.1) | 0.376 |
| Lymphadenopathy | 183 (26.8) | 54 (19.9) | 0.034 |
| Glandular | 196 (28.7) | 47 (17.3) | 0.0004 |
| Articular | 390 (57) | 150 (55.4) | 0.692 |
| Cutaneous | 102 (15.9) | 24 (8.9) | 0.017 |
| Pulmonary | 37 (5.4) | 24 (8.9) | 0.069 |
| Renal | 22 (3.2) | 6 (2.2) | 0.544 |
| Muscular | 6 (0.9) | 4 (1.5) | 0.482 |
| PNS | 39 (5.7) | 15 (5.5) | 0.920 |
| CNS | 8 (1.2) | 6 (2.2) | 0.239 |
| Hematological | 206 (30.1) | 43 (15.9) | $<$0.0001 |
| Biological | 434 (63.5) | 78 (28.8) | $<$0.0001 |

**Conclusions:** Clinical and biological signs of B-cell lymphoproliferation more specifically characterized anti-SSA/SSB positive patients, glandular, hematological and biological domains showing the most significant differences. This feature appears to clearly differentiate Sjögren's disease from Sjögren's syndrome.
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## SAT0291 INTIMA MEDIA THICKNESS AND ATHEROSCLEROTIC PLAQUES AS MARKERS OF SUBCLINICAL ATHEROSCLEROSIS AND CARDIOVASCULAR MANIFESTATION IN SLE PATIENTS

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**Background:** Cardiovascular diseases are the main cause of morbidity and mortality in SLE patients. Detection of risk factors can increase survival and improve quality of life.
**Objectives:** The aim of study was the detection of subclinical atherosclerosis

measured by ultrasound evaluation of intima media thickness and its correlatation to PVW (pulse velocity wave), traditional risk factor, and clinical profile of the disease, autoantibodies and selected laboratory markers.
**Methods:** From March 2015 to January 2016 we examined 42 patients with SLE (5 men, 37 women) by ultrasound of carotic arteries. Traditional risk factors, clinical manifestation, immunological profile and disease activity scores (SELENA-SLEDAI 2K, SLICC) were collected. Cumulative dose of glucocorticosteroids and duration of disease was calculated. History of cardiovascular events was recorded. Statistical tests (descriptive statistic, Student t-test, Spearman test, ANOVA) were performed, p-value $\leq$0.05 was considered as significant.
**Results:** Pathological IMT was detected in 10 patients (23.8%). IMT correlated with cumulative dose of glucocorticoids, levels of anti ds DNA (p=0.05), low levels of C3 (p=0.03), positivity of LA and high LSR (p=0.007,p=0.05), low levels of GF and serum creatinine (p=0.03, p=0.04), anti La antibodies (p=0.009), leucopenia (p=0.007), haematological manifestation (p=0.04), dyslipidemia (p=0.03) and PVW (p=0.01). The presence of plaques correlated with BMI (p=0.05), cardiac failure (p=0.03), anti ds DNA (p=0.03), LA (p=0.003), low levels of HDL (p=0.005), hsCRP (p=0.05), PWV (p=0.04). If groups with or without pathological IMT were compared, there was difference in age ($p\leq0.001$), smoking - packet-years (p=0.01), cardial failure (p=0.02), stroke and lupus CNS (p=0.02, resp. 0.003), cardiac manifestation (p=0.003) and hrCRP (p=0.02). There was no correlation in lipid profile. In this group 5 strokes, 5 cardiac failure, 2 myocardial infarction, 4 ischemic heart disease and 6 cardiac manifestation were present.
**Conclusions:** IMT and detection of plaques are very important markers of subclinical atherosclerosis. They correlated with traditional risk factors and are good prognostic factor of cardiovascular and ischemic CNS manifestation. It is important to evaluated both IMT and plaques. The result of the study highlights the necessity of active screening of cardiac involvement in SLE patients.
**Acknowledgement:** Grant support: MZ CR VES15–28659A
**Disclosure of Interest:** None declared
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## SAT0292 SERUM AND SALIVARY CYTOKINES AND CHEMOKINES LEVELS AS DISEASE ACTIVITY BIOMARKERS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Evidence suggests that levels of different cytokines in primary Sjögren's syndrome (pSS) are associated with cell infiltration degree within salivary and lacrimal glands and severity of the disease. Chemokines appear to contribute to the pathogenesis of pSS.
**Objectives:** To evaluate the association between serum and salivary Th1/Th2/Th17 cytokines and chemokines leves and disease activity in patients with pSS.
**Methods:** Case-control study, 18 patients with pSS and 13 healthy controls were included. Disease activity was assessed by EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI); serum and salivary IFN-$\gamma$, TNF, IL-2, IL-4, IL-6, IL-10, IL-17, IP10, MCP-1, MIG, RANTES and IL-8 levels were measured by bead-based assays following the sandwich immunoassay principle (BD Cytometric Bead Array; BD Biosciences). Differences between groups were analyzed using the Mann-Whitney U test, correlation was estimated by Spearman's correlation coefficient.
**Results:** IL-17, IL-2, IL-4, IFN$\gamma$, MIG and RANTES salivary levels were statistically different between controls and patients with pSS ($p<0.005$). Significant correlation ($p<0.005$) was showed in patients between serum IL-6 and serum IL-12 (r=0.004), IL-10 (r=0.006); serum IL-12 and serum RANTES (r=0.008); serum IP-10 and serum MIG (r=0.000), RANTES (r=0.003); serum MIG and serum RANTES (r=0.014); salivary IL-17 and salivary IL-2 (r=0.004), IL-4 (r=0.001), INF$\gamma$ (r=0.000), TNF (r=0.002), IL-10 (r=0.000); salivary IL-6 and salivary IL-2 (r=0.000), IL-4 (r=0.000), TNF (r=0.000), IL-10 (r=0.000), IL-8 (r=0.0003), MCP-1 (r=0.007); salivary IL2 and salivary IL4 (r=0.000), INF$\gamma$ (r=0.006), TNF (r=0.001), IL10 (r=0.000); salivary IL4 and sallivary TNF (r=0.001), IL10 (r=0.000), MCP-1 (r=0.009); salivary TNF and salivary INF$\gamma$ (r=0.002), IL-10 (r=0.000), IP-10 (r=0.006); salivary MCP-1 and salivary TNF (r=0.000), IL-10 (r=0.001), IL-8 (r=0.003).
**Conclusions:** Increased salivary Th1/Th2/Th17 cytokines and chemokines levels were found in pSS. No correlation was found between serum or salivary cytokines and chemokines levels and pSS disease activity.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5331

## SAT0293 SERUM AND TEAR CYTOKINES AND CHEMOKINES LEVELS AS DISEASE ACTIVITY BIOMARKERS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

A.A. Castillo Ortiz [1], R.E. Barbosa Cobos [1], L.T. Becerril Mendoza [1], G. Lugo Zamudio [1], V. Lima Gómez [2], M.A. Moreno Eutimio [3], N.G. Nieto Velázquez [3], A.A. Tzec Pérez [1]. *[1]Rheumatology; [2]Ofthalmology; [3]Inmunology, Hospital Juárez de México, Mexico, Mexico*

**Background:** Evidence suggests that levels of different cytokines in primary Sjögren's syndrome (pSS) are associated with cell infiltration degree within lacrimal and salivary glands and severity of the disease. Chemokines appear to contribute to the pathogenesis of pSS.
**Objectives:** To evaluate the association between serum and tear Th1/Th2/Th17 cytokines and chemokines leves and disease activity in patients with pSS.
**Methods:** Case-control study, 19 patients with pSS and 13 healthy controls were included. Disease activity was assessed by EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI); serum and tear IFN-$\gamma$, TNF, IL-2, IL-4, IL-6, IL-10, IL-17, IP10, MCP-1, MIG, RANTES and IL-8 levels were measured by bead-based assays following the sandwich immunoassay principle (BD Cytometric Bead Array; BD Biosciences). Differences between groups were analyzed using the Mann-Whitney U test, correlation was estimated by Spearman's correlation coefficient.
**Results:** TNF, IL-2, IL-4, IL-6, IL-10, IP-10, MCP-1, RANTES and IL-8 tear levels were statistically different between controls and patients with pSS ($p<0.005$). Significant correlation ($p<0.005$) was showed in patients between serum IL-6 and serum IL-2 (r=0.652), IL-4 (r=0.731); serum IL-2 and serum IP-10 (r=0.640); serum IL-2 and tear IL-2 (r=0.614), IL-8 (r=0.723), IP-10 (r=0.795), MIG (r=0.755); serum IL-4 and tear IL-8 (r=0.696), MIG (r=0.707); serum IP-10 and serum MIG (r=0.847), RANTES (r=0.626); serum IP-10 and tear IP-10 (r=0.619); serum MIG and serum RANTES (r=0.719); serum MIG and tear IL-17 (r=0.619); serum RANTES and tear IL-2 (r=0.628), IL-4 (r=0.619), IL-6 (r=0.736), IL-8 (r=0.770), IP-10 (r=0.687), MCP-1 (r=0.566), MIG (r=0.740).
**Conclusions:** Increased tear Th1/Th2 cytokines and chemokines levels were found in pSS. No correlation was found between serum or tear cytokines and chemokines levels and pSS disease activity.
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## SAT0294 CIRCULATING LIN1-DABP-CD34+CD133+CD309+ ENDOTHELIAL PROGENITOR CELLS (EPC) ARE REDUCED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) BUT NOT ASSOCIATED WITH BIOPHYSICAL MARKERS OF CARDIOVASCULAR DISEASE (CVD)

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**Background:** Dysfunctional EPC have been proposed to contribute to CVD in SLE patients. Due to various methodological flaws in identifying the rare EPC population in previous studies, how the true circulating EPC count is altered in SLE patients remains unclear. Furthermore, how the EPC population correlates with the biophysical markers of CVD in SLE patients has not been adequately addressed.
**Objectives:** To quantify and compare circulating EPC count between SLE patients and healthy controls (HC) based on a stringently modified EPC identification method proposed by the European League Against Rheumatism Scleroderma Trials and Research (EUSTAR) group that involves lineage-positive and dead-cell exclusion and fluorosphere calibration (1). To address the functional relevance of EPC by evaluating the relationship between EPC count and biophysical markers of CVD in SLE patients.
**Methods:** Peripheral blood (32ml) were obtained from SLE patients and HC

naïve of CVD, cerebrovascular disease, diabetes mellitus and antiphospholipid syndrome. Clinical and serological parameters of SLE patients were collected. The peripheral blood mononuclear cell (PBMC) fraction was prepared for flow cytometry. Singlets were gated from the PBMC population, followed by exclusion of the lineage-positive (Lin-1 FITC+) and dead cells (DAPI+). To mitigate the issue of autofluoresence, 3 fluorescence-minus-one (FMO) panels (panels stained all but one respective fluorochrome) were designed. From the Lin1-DAPI- population, CD309-APC, CD133-PE and CD34-PerCP-Cy5.5 were gated from the corresponding FMO panels. All the FMO gates were then applied on the all-stained samples to identify the true EPC population (Lin1-DAPI-CD34+CD133+CD309+). The absolute EPC counts were calculated by fluorosphere calibration. Endothelial reactivity, arterial stiffness and carotid atherosclerosis were assessed by brachial artery flow-mediated dilation (FMD), pulse-wave velocity (PWV) and carotid intima-media thickness (cIMT) respectively. Relationships between EPC count and disease-related factors, FMD, PWV and cIMT were studied by Spearman correlations.

**Results:** Thirty SLE patients and 22 HC (5 and 3 men in SLE and HC groups respectively, p=1.0) were studied. Mean±SD age of SLE patients and HC was 34.63±11.5 and 31.87±8.4 years respectively (p=0.34). The mean±SD disease duration, daily prednisolone dose, atherogenic index (AI) (total cholesterol/HDLc), SLEDAI and SLICC/DI were 60.17± 69.4 months, 14.77±16.5 mg, 3.49±0.9, 5.53± 5.4 and 0.10±0.3 respectively in SLE patients. Mean±SD EPC count in SLE patients was significantly lower than that of HC (3.93±4.4 vs. 9.24±8.5 cells/ml, p=0.014), despite ANCOVA adjustment for PBMC count (p=0.018). No significant relationships were found between EPC count and disease duration, daily prednisolone dose, AI, SLEDAI, SLICC/DI, FMD, PWV and cIMT in SLE patients.

**Conclusions:** Incorporating the FMO gating strategy into the EUSTAR recommendation of EPC identification confirmed significantly lower circulating EPC count in SLE patients as compared to HC, but the reduced EPC level was not associated with biophysical CVD markers in SLE patients. Prospective studies are needed to address the impact of reduced EPC on CVD in SLE patients.

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## SAT0295 AUTOIMMUNE HEMOLYTIC ANEMIA AND THROMBOCYTOPENIA IN A SINGLE CENTRE COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS FROM TURKEY: CLINICAL ASSOCIATIONS AND EFFECT ON DISEASE DAMAGE AND SURVIVAL

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**Background:** Hematologic involvement is common in patients with SLE. Thrombocytopenia and AIHA, prevalences of which have been reported as 10–40% and 5–10% respectively, have considerable impact on prognosis.

**Objectives:** Herein, we aimed to investigate the frequencies of these hemocytopenias, their clinical and serological associations and effect on disease outcome in a large single centre cohort of patients.

**Methods:** We analysed our cohort of 852 patients who fulfilled at least 4 of the ACR criteria for SLE. The data presented was the cumulative clinical and serological manifestations throughout the follow-up period. Hemolytic anemia was defined as a drop in hemoglobin accompanied by increased reticulocyte count, high serum lactate dehydrogenase and reduced haptoglobin levels in the presence of a positive Coombs' test. Thrombocytopenia was defined as a platelet count of $<100x10^9/mm^3$. Demographic characteristics, clinical features, autoantibody profiles, damage and mortality data retrieved from the database were compared between patients with and without each hematological abnormality. The $\chi^2$ test, logistic regression and Kaplan-Meier survival analyses were used.

**Results:** There were 93 (10.9%) patients with AIHA and 215 (25.3%) with thrombocytopenia. Patients with AIHA were significantly younger at diagnosis (27±13 vs 31±12, $p<0.05$) and had a significantly shorter disease duration (95±84 vs 118±85 mo, $p<0.05$). AIHA and thrombocytopenia were both associated with neuropsychiatric (NP) involvement ($p<0.05$) and associated with each other ($p<0.05$) and leukopenia ($p<0.05$). Comparison of patients with AIHA or thrombocytopenia to the rest of the cohort displayed significant associations with antiphospholipid syndrome (APS), anticardiolipin (aCL) antibodies and lupus anticoagulant (LA). In patients with thrombocytopenia the relationship with APS features, namely thrombosis and pregnancy morbidity, was stronger ($p<0.001$).

Compared to the rest of the cohort, more patients in both groups had organ damage and their mean SLICC damage score was significantly higher. Association to NP damage was discernible in both groups ($p<0.05$). In addition, damage in renal and cardiovascular domains and diabetes were more pronounced in patients with thrombocytopenia ($p<0.001$)

Kaplan Meier survival analysis showed that patients with AIHA had significantly reduced survival rates at 10 (94 vs 77%) and 20 (88 vs 77%) years ($p<0.001$). In the thrombocytopenia group, despite the lack of significant differences, there was a tendency for lower survival rates.

**Conclusions:** We demonstrated that both AIHA and thrombocytopenia were associated with aCL antibodies, coexisting APS and NP involvement and damage in our cohort. There was a strong link between AIHA and thrombocytopenia. Patients with AIHA had a younger age at disease onset with reduced survival. No significant reduction in survival rates was observed in patients with thrombocytopenia. However, besides NP involvement, thrombocytopenia delineated a subgroup of patients with a higher renal and cardiovascular damage which perceivably can affect prognosis. Overall, AIHA and thrombocytopenia may predict a poorer outcome in patients with SLE.

**Disclosure of Interest:** None declared

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## SAT0296 IS HYPERURICEMIA AN INDEPENDENT RISK FACTOR FOR ARTERIAL THROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS?

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**Objectives:** To evaluate whether hyperuricemia is independently associated with cardiovascular events in a cross-sectional study of Chinese patients with SLE.

**Methods:** Consecutive patients who fulfilled ≥4 ACR criteria for SLE were recruited. Fasting blood was taken for serum urate level, along with other atherosclerosis risk factors that included glucose, total, LDL, HDL cholesterol and triglyceride. Patients were assessed for body mass index (BMI), waist circumference and the presence of the metabolic syndrome (MetS) as defined by the updated joint consensus criteria, using the Asian criteria for central obesity. The 4-variable estimated glomerular filtration rate (eGFR) was also calculated. Patients were stratified according to different serum urate levels: <0.35mmol/L, 0.35–0.48mmol/L, 0.48–0.60mmol/L and >0.60mmol/L. Comparison of the prevalence of vascular risk factors, the MetS and arterial thrombotic events (acute coronary syndrome, stroke, peripheral vascular event) was made among patients with different levels of urate. Cox regression models were established to study whether hyperuricemia was independently associated with arterial events with adjustment of demographic variables, eGFR, vascular risk factors and the antiphospholipid (aPL) antibodies.

**Results:** 485 SLE patients were studied (93% women; mean age 46.2±14 years); 259 (53%) had renal involvement and 73 (15%) had chronic kidney disease (stage ≥3). Hyperuricemia (urate >0.35mmol/L) was present in 185 (38%) patients. The number of patients who had serum urate levels of 0.35–0.48, 0.48–0.60 and >0.60mmmol/L was 131 (27%), 40 (8.7%) and 14 (2.9%), respectively. Patients with hyperuricemia, compared with those without, were more likely to be men (14% vs 3%; $p<0.001$), have renal disease (72% vs 42%; $p<0.001$), hypertension (34% vs 15%; $p<0.001$), lower eGFR (73.4±34 vs 101±27; $p<0.001$) but longer SLE duration (14.3±8.7 vs 12.2±7.4 years; p=0.006). The LDL-cholesterol level (3.34±1.37 vs 2.89±1.51mmol/L; p=0.001), triglyceride level (1.62±0.77 vs 1.29±0.78mmol/L; $p<0.001$), BMI (23.2±4.5 vs 22.3±3.8kg/$m^2$; p=0.04) and occurrence of the MetS (22% vs 12%; p=0.007) were significantly higher in patients with hyperuricemia. Over an observation of 12.9±8.0 years, 50 acute arterial events (17 acute coronary syndrome; 24 stroke, 7 peripheral vascular event and 2 retinal artery thrombosis) developed in 47 patients. Acute coronary events were significantly more common in patients with hyperuricemia than those without (7.6% vs 1.0%; p=0.001). Cox regression analysis revealed that HDL<1.0mmol/L (HR 3.44 [1.62–7.27]; p=0.001], lupus anticoagulant (HR 3.84 [1.92–7.65]; $p<0.001$) and age of SLE onset (1.03 [1.004–1.05] per year; p=0.02) were independently associated with arterial thrombosis. In separate regression models, elevated urate levels (>0.35, >0.48 or >0.60mmol/L) were not significantly associated with arterial events after adjustment for age, sex, eGFR, smoking, LDL-cholesterol, HDL-cholesterol, triglyceride, BMI, diabetes mellitus, hypertension and the apL antibodies.

**Conclusions:** In patients with SLE, hyperuricemia was associated with atherosclerotic risk factors, the MetS and acute coronary events. However, in multivariate regression models, hyperuricemia was not an independent risk factor for any arterial events after adjustment for confounding factors.

**Disclosure of Interest:** None declared

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## SAT0297 PRIMARY SJOGREN SYNDROME: CLINICAL AND BIOLOGICAL FEATURES ACCORDING TO THE PRESENCE OF ANTI-SSA ANTIBODIES FROM A COHORT OF 176 PATIENTS

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**Background:** Since 2002, the European American Consensus Group criteria required the presence of 4 criteria among whom the presence either anti-SSA/anti-SSB antibodies or a focus score upper or equal to 1 at the labial salivary gland biopsy for the diagnosis of pSS. The direct consequence of such classification criteria is the constitution of two different immunological patterns in pSS: one with positive anti-SSA or anti-SSB antibodies, representing 60 to 70% of patients (called seropositive pSS) and the second with negative anti-SSA and anti-SSB antibodies (seronegative pSS).

**Objectives:** To analyze the clinical and biological differences between anti-SSA

seropositive patients and seronegative patients from a cohort of 176 pSS patients.
**Methods:** We included 176 patients fulfilling 2002-AECG criteria for pSS and retrospectively analyzed their clinical and biological features according to the presence or absence of anti-SSA antibodies.
**Results:** The median age at pSS diagnosis was 54 years; 79% were female; 68% Caucasian and 13% Black. The median follow-up time was 41 months.
pSS criteria included xerostomia for 89% of patients, xerophtalmia 96%; a positive minor salivary glands biopsy 83% of 151 patients and anti-SSA antibodies 62% (109 patients) and anti-SSB antibodies 32%. Cumulative extraglandular manifestations included arthralgia in 66%, purpura 13%, lung involvement 10%, peripheral neuropathy 36%, central nervous system involvement 6% and B-NHL 6%. Peripheral neuropathy was small fiber neuropathy (24%), large fiber sensory neuropathy (6%) and sensorimotor neuropathy (4.5%).
Seropositive patients (109 patients, 62%), when compared to seronegative patients (67 patients, 38%), were younger at pSS diagnosis (49 vs 58 years; P=0.00015), more frequently Black (18% vs 4.5%; P=0.010) and had less frequently xerostomia (84% vs 97%; P=0.006), peripheral neuropathy (28% vs 51%; P=0.002), mainly small fiber neuropathy (16% vs 39%; P=0.001) but more often purpura (20% vs 3%; P=0.01). There was no significant difference regarding, articular or lung involvement or B-NHL. Biologically, they were hallmarked by a higher prevalence of 1) B-cell chronic activation markers which included hypergammaglobulinemia (61% vs 25%; $P<10^{-5}$), rheumatoid factor (65% vs 32%; $P<10^{-5}$), and abnormal FLC ratio (31% vs 0%; $P<10^{-5}$), 2) peripheral cytopenia including anemia (27% vs 8%; P=0.003), leucopenia (17% vs 5%; P=0.03) and lymphopenia (50% vs 29%; P=0.01). There was no difference regarding mixed cryoglobulin (11% vs 6%) and monoclonal gammopathy (16%vs 16%).
**Conclusions:** Our results showed that the presence or the absence of anti-SSA antibodies are associated with two distinct clinical and biological faces of the "same disease". Anti-SSA positive patients are younger at diagnosis with a higher prevalence of purpura and B cell activation markers and cytopenia; inversely, anti-SSA negative patients are older at diagnosis with a lower prevalence of B cell activation and are more prompt to develop sensory neuropathies mainly small fiber neuropathies. These findings question the pSS clinical and biological homogeneity and the selection of patients for B cell targeting therapies.
**Disclosure of Interest:** None declared
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## SAT0298 RETROSPECTIVE EVALUATION OF BASAL LEPTIN LEVELS IN SLE PATIENTS WHO DEVELOPED DISEASE FLARES AND DAMAGE ACCRUAL

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**Background:** Adipokines are citkokines mainly secreted by adipose tissue and involved in a wide spectrum of processes including metabolism, insulin sensitivity, atherogenesis and immunity. Leptin is the first adipokine discovered and plays important immunological functions. Crescent scientific data confirm the leptin involvement in many human autoimmune diseases. We described leptin hyperexpression in sera of female SLE patients, especially in fertile age, in relation with metabolic parameters and disease activity
**Objectives:** To evaluate the basal leptin levels in SLE patients who develop disease flares and damage accrual in 3 years follow-up.
**Methods:** We performed a retrospective evaluation of basal serum leptin levels, metabolic parameters and SLE disease features in 20 female SLE patients. For all subjects, complete data concerning disease activity and damage were available over a period of almost 3 years after the baseline assessment. Metabolic parameters included basal insulin, glycaemia, HOMA-IR, plasma lipid profile, BMI, waist-hip ratio. SLE disease features were expressed as anti-dsDNA positivity, complement fraction C3 and/or C4 depletion, disease activity measured by SELENA SLEDAI and disease damage evaluated by SDI. SLE disease flares were assessed by revised SFI index. Number of disease flares was evaluated during the fist year of follow-up and at the end of a 3 years follow-up. SDI was measured at baseline and at the end of year 3.
**Results:** We found hyperexpression of basal leptin levels in SLE patients who developed almost 1 flare at year 1 compared to patients without flares (p 0.002). Basal leptin in subject with almost 1 flare at the end of the 3 years of follow-up was higher in comparison with patients who didn't develop disease flares (p 0.0003). Basal leptin was increased in patients who presented almost 1 new point of SDI at the end of the 3 years follow-up versus patients without SDI increase (p 0.0003). The survival curve of the time without a lupus flare in subjects with leptin above 50 percentile significantly differed compared to subjects with leptin levels below 50 percentile (p 0.003). Patients with almost 1 flare at year 1 and year 3 and subject with almost 1 new SDI point at year 3 presented increased basal HOMA-IR, BMI and basal SELENA-SLEDAI. At baseline, leptin levels positively correlated with HOMA-IR (r 0.8, $p<0.0001$), BMI (r 0.8, $p<0.0001$) and SELENA SLEDAI (r 0.8, $p<0.0001$).
**Conclusions:** We found basal leptin hyperexpression in SLE patients who developed disease flares and damage accrual in a 3 years follow-up period. These patients presented increased insulin-resistance and disease activity at baseline and leptin was tightly related to both these aspects. Further studies are required to evaluate the possible role of leptin as predictor of SLE prognosis
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## SAT0299 ANGIOGENESIS BIOMARKERS AND DOPPLER ULTRASOUND OF UTERINE ARTERIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND/OR ANTIPHOSPHOLIPID SYNDROME CAN BE HELPFUL IN DIFFERENTIAL DIAGNOSIS BETWEEN PREECLAMPISA AND DISEASE ACTIVITY

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**Background:** Preeclampsia (PE) is a specific pregnancy syndrome that affects 2–5% of healthy women. This risk increases up to 10–30% in patients with autoimmune diseases such as Systemic Lupus Erythematosus (SLE) and/or Antiphospholipid Syndrome (APS). Differential diagnosis between PE and disease flare during pregnancy is often difficult. Pulsatility index of uterine arteries (mPI-UtA), serum levels of endoglin and the ratio tyrosine kinase-like soluble receptor/placental growth factor (sFlt-1/PlGF) are useful markers for early diagnosis of PE, even in asymptomatic women.
**Objectives:** To analyse the utility of these markers among pregnant patients with SLE/APS.
**Methods:** We included patients consecutively followed in our high-risk pregnancy clinic from 2008 to the present. These patients had diagnosis of SLE (ACR criteria 1987), LES-like (<4 ACR-SLE 1987 criteria), APS (Sydney criteria) or antiphospholipid antibodies without fulfilling criteria APS (aPL). PE and its severity were diagnosed according to the International Society for the Study of Hypertension in Pregnancy criteria (ISSHP). Lupus activity was assessed with moderate considering SLEPDAI index $\geq$6 and APS according to the clinical activity. Follow-up visits were performed at 11–13, 22, 28 and 32 weeks and postpartum. We collected clinical data about autoimmune disease and pregnancy, treatments, toxic and cardiovascular risk factors, analytical data including endoglin and ratio and Doppler ultrasound (mPI-UtA). We performed a descriptive analysis, Chi-square or t-Student tests according to the type of variable. Odds ratio and confidence intervals were calculated by using simple logistic regression.
**Results:** We analysed 58 pregnancies. Lupus activity during pregnancy was detected in 6 patients (10.3%), 5 with SLE and one with LES-like diagnosis. Two patients developed moderate to severe activity (SLEPDAI 25 and 12, respectively) with worsening since 24th week (33.3%). Two patients with SLE +/– APS developed PE (3.4%). We found statistically significant association between PlGF and ratio values in week 32 and development of PE [(mean 151.76±118.85 with p=0.023) and (89.62±114.70 with p=0.020), respectively)]. In addition, the values of endoglin, ratio and mPI-UtA were higher in PE than in normal pregnancy or flares since 24 week (see Table). On the other hand, there not seems to be differences in scores between patients with lupus activity and normal development of pregnancy.
**Conclusions:** Despite the limited number of patients who develop complications in our cohort, it seems that the mPI-UtA, endoglin and ratio in patients with SLE and/or APS behaves as in the general population and may help in the differential diagnosis of preeclampsia and disease activity.
**Disclosure of Interest:** None declared
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## SAT0300 THE RELATIONSHIP BETWEEN GENETIC VARIATIONS OF ADAPTIVE IMMUNE SYSTEM INTRACELLULAR SIGNAL TRANSDUCTION PATHWAYS AND CLINICAL FINDINGS IN SYSTEMIC LUPUS ERYTHEMATOUS

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**Background:** In T-cells of the systemic lupus erythematosus (SLE), the gene expression of two variants of CD44; CD44v3 and CD44v6 are increased and their expression correlates with disease activity. Moreover, the existence of these two variants is related with kidney involvement and anti-DNA positivity. Increased CD44v3 and CD44v6 expressions were shown in cells that infiltrated the kidney in SLE. It was also revealed that the hyperactivity of the B-cells in the SLE were related to increased plasmablasts and naive B-cells, increased stimulation through

TLR9, activation and longer survival through BAFF, and decreased suppressor signals.
**Objectives:** Genetic variations related to signal cell transduction in the adaptive immune system were seen to be active in SLE in different studies, and their association with clinical findings in different populations should be known.
**Methods:** Eighty three SLE patients and 116 healthy control subjects were included into the study. The clinical features, organ involvements, laboratory values and outcome of SLE patients were obtained from hospital records. SLE patients' treatment modalities since diagnosis, their response to therapy and relapses were recorded. Polymorphisms of BANK1 gene (rs10516487 and rs10516483) –involved in B-lymphocyte intracellular signal transduction pathway-, and polymorphisms of CD44 gene (rs507230 and rs2732552) –playing a role in T-cell signal transduction- were studied from blood samples of patients by PCR method.
**Results:** In the SLE group, rs570230 (CD44) polymorphism CT genotype was significantly more frequent than in the control group (39.8% vs. 22.4%, p=0.014). SLE group had significantly less frequent rs10516487 (BANK1) polymorphism AA genotype (1.2% vs. 8.6%); and significantly more frequent GG genotype (59% vs. 44%) and A allele than controls (p values, 0.027, 0.036 and 0.013). No significant differences were found in terms of rs10516483 (BANK1) and rs2732552 (CD44) polymorphisms. In SLE patients with nephritis, rs570230 polymorphism TT genotype was significantly more frequent (50% vs. 20.7%, p=0.009), whereas the CT genotype was less frequent in the active disease group (31% vs. 61.4%, p=0.01). rs10516487 polymorphism GG genotype was significantly more frequent in SLE patients with arthritis (62.5% vs. 40%, p=0.045).
While SLE patients with neurologic involvement had more frequent rs2732552 polymorphism AA genotype (35.3% vs. 11.5%, p=0.038), GG genotype was more frequent in patients with lupus nephritis (57.7% vs. 29.6%) and anti-nucleosome positivity (78.6% vs. 31.3%) (p values, 0.023 and 0.004). rs10516483 polymorphism CC genotype was higher in patients with alopecia in contrast to others (77.8% vs. 34.8%, p=0.042).
**Conclusions:** In our SLE group, there is a significant association between BANK 1 (rs10516487) and rs570230 polymorphisms.
**Disclosure of Interest:** None declared
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## SAT0301 PREVALENCE OF ABORTIONS AND FETAL ATRIOVENTRICULAR BLOCK IN PATIENTS WITH POSITIVE ANTI-RO AND ANTI-LA ANTIBODIES

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**Background:** Anti-SSA/Ro and anti-SSB/La antibodies are present in inflammatory autoimmune disease patient sera, and there are related to different clinical manifestations. It is well known the association between the presence of these antibodies in maternal blood and fetal atrioventricular block. However, there are no much studies about infertility or repeated abortions and anti-SSA/Ro and anti-SSB/La antibodies in broad series.
**Objectives:** To characterise a cohort of patients with positive anti-SSA/Ro and/or anti-SSB/La antibodies and to evaluate the prevalence of abortions and neonatal mortality.
**Methods:** Observational descriptive study with 162 patients older than 15 years old with pregnancies history and positive anti-SSA/Ro and/or anti-SSB/La antibodies from February 2011 to July 2015. We consider healthy women with pregnancies history and with comparable characteristics as negative control group.
**Results:** We included 162 patients with positive anti-SSA/Ro and/or anti-SSB/La antibodies with a mean age of 50.5±14.2 years old. Main diagnosis were systemic lupus erythematosus (n=85), Sjögren syndrome (n=40), rheumatoid arthritis (n=16), systemic sclerosis (n=6), mixed connective tissue disease (n=3) and other diagnosis (n=12). Lupus anticoagulant was positive in 8 cases and 57 patients showed low complement values. 37% of patients had at least one pregnancy, and the 36.7% aborted during pregnancy.
There were no significant differences in the abortion incidence between our cohort of patients and the healthy control group considered.
We observed 4 cases of fetal atrioventricular block, all of them with positive anti-SSA/Ro and/or anti-SSB/La antibodies and only in one case also with positive lupus anticoagulant.
**Conclusions:** In our series, pregnant women with positive anti-SSA/Ro and/or anti-SSB/La antibodies did not show high prevalence of abortion. However, the positivity of these antibodies was statistically correlated with the presence of fetal atrioventricular block.
**Disclosure of Interest:** None declared
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## SAT0302 ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATES WITH CAROTID INTIMA-MEDIA THICKNESS PROGRESSION

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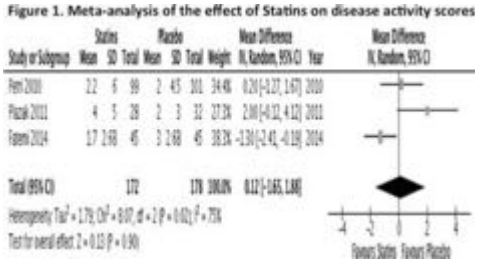
**Background:** A relationship between systemic inflammation and increased cardiovascular risk is often postulated. Simple and affordable clinical predictors of increased cardiovascular risk in patients with autoimmune disease, however, are not yet available in the clinical practice.
**Objectives:** To address the role of clinical, serological markers of disease activity, and of classical cardiovascular risk factors (CVRF) in predicting the carotid intima-media thickness (c-IMT) progression at 5 years (∆c-IMT) in patients with the prototypic autoimmune disease systemic lupus erythematosus (SLE).
**Methods:** Clinical and biochemical data including SLEDAI were collected at baseline and at five years of follow up from 50 patients with SLE and 50 age- and gender-matched healthy controls. C-IMT was also measured at baseline and at 5 years to evaluate progression.
**Results:** A higher SLEDAI score at baseline correlated with a faster ∆c-IMT (0.007 (0.006) mm/year vs 0.003 (0.001) mm/year when compared to controls, P=0.026), irrespectively of the presence of CVRF and of the serological profile. Patients with higher SLEDAI score at baseline also experienced disease flares more frequently (p=0.037) than those with milder disease at baseline. Patients with a higher disease activity during follow up had also a faster ∆c-IMT when compared to those with a persistently low disease activity (0.008 (0.004) mm/year vs -0.006 (0.004) mm/year, P=0.021). Elevated LDL-C levels were the only CVRF associated with disease flare-up; this might a consequence of the aggressive immunosuppressant therapy in those patients.
**Conclusions:** Patient with SLE show an increased cardiovascular risk as estimated by the c-IMT. Disease activity and in particular disease flares accelerate the progression of the vascular damage.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5698

## SAT0303 EFFECT OF HMG-COA REDUCTASE INHIBITOR DRUGS (STATINS) ON SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** Statins have a known effect in reducing the morbidity and mortality due to atherosclerosis. Recently, statins have been proposed to have anti-inflammatory and immunomodulatory effects. In in-vitro studies these drugs inhibit inflammatory cells like monocytes, macrophages, and lymphocytes, decrease the expression of major histocompatibility complex (MHC) and decrease adhesion molecules and inflammatory cytokines such as IL6 and IL10, that are also implicated in SLE pathogenesis. In terms of immunomodulary effects, animal studies demonstrated that statins exacerbate or trigger cellular apoptosis and induce a shift in the Th1/Th2 balance leading to B-cell reactivity and production of pathogenic autoantibodies. Also it has been found that Treg cells can be unstable in the periphery and may promote autoimmunity. These may promote preexisting autoimmune conditions to progress toward clinical disease, such as SLE.
Statins have not been widely studied in SLE. The existing studies mostly have primary endpoints on the evaluation of atherosclerosis, and in terms of disease activity, these studies showed contradicting results. Thus, we sought to determine the effect of statins on the disease activity of SLE based on the best available evidence.
**Methods:** To identify relevant publications on statins and SLE disease activity, a systematic literature search of PubMed, Scopus, and Cochrane databases was done with no date and language restrictions. Included studies were on adult SLE patients. Only randomized controlled trials that used statins as intervention and reported SLE disease activity as an outcome measure were included. Two reviewers did quality appraisal, risk bias assessment, and data extraction.
**Results:** Three studies have met the eligibility criteria and were included in this review. Quantitative synthesis was then done. The pooled analysis of these

**Figure 1. Meta-analysis of the effect of Statins on disease activity scores**



studies suggests that statins have no significant effect on disease activity on random effects model with an overall effect of 0.13 (P=0.90, 95% CI -1.65, 1.88).
**Conclusions:** Statins neither increased nor decreased SLE disease activity; therefore possibly it can be safely given to SLE patients without the risk of triggering or exacerbating a flare.
**Disclosure of Interest:** None declared
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## SAT0304 COAGULATION FACTOR XIII MIGHT BE A PROMISING MARKER FOR PREDICTING ATHEROSCLEROSIS IN SLE

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**Background:** Several traditional and non-traditional risk have been implicated in the development of atherosclerosis in systemic lupus erythematosus (SLE). However, while growing evidence demonstrates that blood coagulation factor XIII (FXIII) may play an essential role in atherothrombotic disease in patients with primary antiphospholipid syndrome, the role of this coagulation factor in atherothrombotic disease and overall disease activity in patients with SLE is still poorly understood. Plasma FXIII cross-links fibrin with itself and with the endothelium, making clots resistant to fibrinolysis. Intracellular FXIII in monocytes also cross-links Type I angiotensin receptor dimer, which increases monocyte adhesion to endothelial cells and accelerates atherosclerosis. We investigated whether FXIII was associated with intima media thickness (IMT) of carotid arteries or disease activity in patients with SLE.
**Objectives:** to evaluate clinical significance of FXIII in SLE.
**Methods:** the study involved 50 consecutive patients with SLE enrolled in a longitudinal study on atherosclerosis biomarker from 2008 through 2015 at UCLA. Plasma FXIII activity (FXIIIa) was measured in the blood samples by ELISA. B-mode and Doppler Scanning was performed to measure IMT at baseline and 24–36 month.
**Results:** Table1 shows the correlation with plasma level of FXIIIa and variables that were independently associated with SLE activity and atherosclerosis. There was a strong inverse correlation with the SLE Disease Activity Index (SLEDAI), physician global assessment (PGA), and dsDNA antibody, whereas there was a significant positive correlation between FXIIIa and C3 and IMT at the follow-up ultrasound (Figure1). In patients with high plasma FXIIIa (>143%), the mean SLEDAI was significantly lower, (2.17± 3.7 vs. 4.1 ± 3.2, p=0.009) and IMT at follow-up was significantly higher (0.61 ± 0.17 vs. 0.51 ± 0.14, p=0.009).

Table 1. Correlations between FXIII and variables in SLE

| Variable | Plasma level of XIII activity | |
|---|---|---|
| | Correlation | P-value (Spearman's) |
| SLEDAI | –0.378 | 0.007** |
| PGA | –0.311 | 0.028* |
| ds DNA antibody | –0.361 | 0.014* |
| C3 | 0.440 | 0.002** |
| C4 | 0.294 | 0.050 |
| Diagnosis of APS | –0.021 | 0.914 |
| Positive aCL | –0.118 | 0.463 |
| Hypertension | 0.110 | 0.466 |
| Diabetes | 0.255 | 0.090 |
| Dyslipidemia | 0.142 | 0.354 |
| Tobacco | 0.286 | 0.046* |
| IMT at follow up | 0.400 | 0.010* |

**p<0.01 (2-tailed), *p<0.05 (2-tailed).

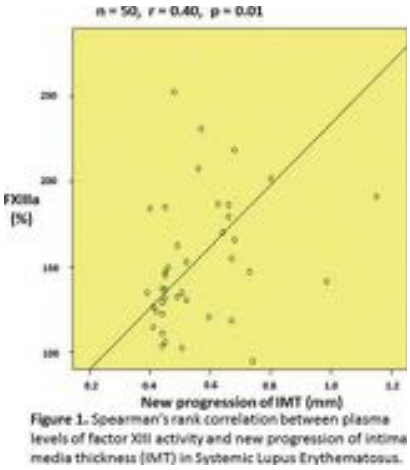


Figure 1. Spearman's rank correlation between plasma levels of factor XIII activity and new progression of intima media thickness (IMT) in Systemic Lupus Erythematosus.

**Conclusions:** Although further confirmatory testing is underway, FXIII might be a novel marker for increased IMT in SLE.

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**Disclosure of Interest:** None declared
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## SAT0305 NEUTROPHIL EXTRACELLULAR TRAPS MARKERS ARE ELEVATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Impaired removal of apoptotic waste in patients with systemic lupus erythematosus-SLE has been long known as important factor that trigger autoimmune response. Neutrophil extracellular traps could be another source of autoantigens in patients with SLE.
**Methods:** We analysed sera from 84 SEL patients (60 patients had one sample and 24 patients were followed 2 or 3 times) and 50 healthy blood donors. Serum levels of myeloperoxidase, B-cell activating factor-BAFF, cell free DNA, complement components C3 and C3, antibody to dsDNA by CLIFT end ELISA assays, netolitic activity and DNAse I were measured.
**Results:** Patients with SLE had higher cfDNA (1.69±0.23 vs. 1.42±031 ng/mL, p=0.0003), MPO activity (p<0.05) and BAFF levels (160735±2353.23 vs. 891.16±184.31, p<0.05). DNAse concentration was also lower in healthy controls (5.84±5.72 vs. 9.38±6.97 pg/mL, p<0.05). BAFF showed strong correlation with anti-dsDNA antibodies determined by ELISA method (ρ=0.564, p=0.000), MPO activity (ρ=0.256, p=0.021), DNAse I concentration (ρ=0.27, p=0.012) and cfDNA concentration (ρ=0.262, p=0.014). MPO activity showed correlations with cfDNA levels (ρ=0.386, p=0.001), DNAse concentration (ρ=0.501, p=0.000), and anti-MPO antibodies (ρ=0.293, p=0.006). Cell free DNA levels additionally correlated with DNAse activity (ρ=0.288, p=0.007) as well with netolytic activity (ρ=0.244, p=0.026).
**Conclusions:** Increased NETs' footprints (myeloperoxidase and cfDNA) are present in lupus sera. As probably compensatory mechanism increased DNAse I concentrations also were found in lupus sera. NET burden is followed by production of various antibodies recognizing different NET structures.
**Disclosure of Interest:** None declared
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## SAT0306 HOW DOES CIGARETTE SMOKING AFFECT SJÖGREN'S SYNDROME?

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**Background:** Cigarette smoking has been found to play a pathogenic role in several autoimmune diseases. However, data about its influence on Sjögren's syndrome (SS) is scarce [1,2].
**Objectives:** To assess the impact of cigarette smoking on patients with SS.
**Methods:** This was a cross-sectional study in which consecutive patients with SS (2002 AECG) followed at a single center were included. Smoking status (ever) together with additional environmental factors and clinical and laboratory characteristics were assessed. Bivariate analysis and the mixed-cluster methodology based on multivariate descriptive methods were employed to analyze data.
**Results:** Out of a total of 277 patients, 94% were women. The mean age of patients was 51.2 ± 12.5 years, and the mean duration of the disease was 7.1 ± 7.1 years. By Chisholm and Mason classification, 93% of patients were positive for a minor salivary gland biopsy. Anti-Ro and anti-La antibodies were present in 65% and 40% respectively (by ELISA). Polyautoimmunity was registered in 43% of patients. Smokers showed a longer duration of the disease and were mostly men. Cigarette smoking was associated with parotidomegaly (OR: 1.9; 95%CI 1.05–4.3; p=0.03), polyautoimmunity (OR: 1.9; 95%CI 1.2–3.3; p=0.009), acid peptic disease (OR: 2.3; 95%CI 1.4–4.0; p=0,0008), and coffee consumption (OR: 1.7; 95%CI 0.98–3.6; p=0.04). In order to clarify whether the observed associations were influenced by gender or coffee consumption, 4 clusters were built: 1) men with a high frequency of smoking and coffee consumption (5.6%), 2) women who exclusively reported coffee consumption (42%), 3) women who all drank coffee and smoked cigarettes (30%) and 4) women with no coffee consumption but a third had been exposed to tobacco (22.4%). Cluster 2 patients were statistically less prone to present factors found in the bivariate analysis suggesting that coffee consumption may counteract the harmful effects of smoking.

**Conclusions:** Our results indicate that cigarette smoking has significant effects on SS expression, which could be modified by coffee consumption.
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[1] Manthorpe R, et al. Ann Rheum Dis 2000;59(1):54–60.
[2] Karabulut G, et al. Mod Rheumatol 2011;21(6):602–7.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5129

## SAT0307 JACCOUD ARTHROPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS: ASSOCIATION BETWEEN ANTI-CITRULLINATED PROTEIN ANTIBODIES AND EROSIVE DAMAGE

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**Background:** Jaccoud arthropathy (JA) is a deforming, non-erosive arthritis, occurringin 2–35% of Systemic Lupus Erythematosus (SLE) patients. The deformities could be easily misdiagnosed as those identified in rheumatoid arthritis (RA), even though, unlike in RA, they are reducible. To date no specific markers for JA are available. The evaluation of Rheumatoid Factor (RF) and anti-citrullinated protein antibodies (ACPA) in JA patients demonstrated a higher frequency of RF in comparison with SLE patient without JA. No differences in ACPA positivity were found. Imaging techniques could be helpful in the assessment of JA: the traditional radiographic definition of non-erosive arthropathy has been modified in the last years thanks to the use of new imaging techniques such as ultrasonography (US). So far, small JA populations have been evaluated by US, identifying the presence of mild articular and peri-articular involvement.
**Objectives:** The aim of the present study was to evaluate the prevalence of JA in a wide monocentric cohort of SLE patients and to describe clinical, serological and ultrasonographic features in this subset of patients.
**Methods:** Consecutive SLE patients (ACR criteria 1997) were evaluated. JA index was applied for patients with reducible deformities. Patients with JA index $\geq$5 underwent physical examination, blood draws and US assessment. ACPA and RF was detected by using the commercial ELISA kit. We compared JA patients with a subgroup of 62 SLE patients, age and sex matched, with joint involvement without JA. A single rheumatologist performed the US assessment of bilateral wrist and hands. All abnormalities were evaluated according to the OMERACT definitions.
**Results:** Four hundred eighty SLE patients were evaluated: 17 (3.5%) showed a JA index $\geq$5 (M:F 1:16; mean age±SD 50.7±11.1 years; mean disease duration±SD 247.8±116.2 months). The most frequent deformity was *ulnar drift* of MCP joints (88.2%).RF resulted significantly more frequent in JA patients compared with ACPA (41.2% versus 23.5%, P=0.009). We compared the frequency of RF and ACPA in JA patients with a subgroup of 62 SLE patients, age and sex matched, with joint involvement without JA. JA patients showed a significantly higher frequency of RF than SLE patients without JA (41.2% *vs* 17.7%, respectively; P=0.0006). Conversely, no significant difference in ACPA frequency was found between these two groups of patients. No differences were found in the titre of ACPA and RF. Bone erosions, in at least one joint, have been found in 10 JA patients (58.8%) and the most frequent joints involved were I and II MCP (17.6% of the patients for both joints). Subgrouping JA patients according with ACPA status, ACPA+ patients showed significantly more frequent erosive damage compared with ACPA- (75% versus 53.8%, P=0.002).
**Conclusions:** The present study identified an association between ACPA positivity and erosive damage in JA patients. These results suggest the possibility to use ACPA as a marker of severity in this subgroup of SLE patients, driving therapeutical approach in order to prevent chronic damage accrual.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4963

## SAT0308 THROMBOCYTOPENIA IS A THROMBOTIC RISK FACTOR IN PATIENTS WITH POSITIVE ANTIPHOSPHOLIPID ANTIBODIES WITHOUT CLINICAL CRITERIA OF THE DISEASE?

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**Background:** Antiphospholipid Syndrome (APS) is an acquired immune disorder defined by the presence of thrombosis and/or pregnancy morbidity together with the presence of positive antiphospholipid antibodies (aPL) (anticardiolipin antibodies (aCL), anti -beta2 glycoprotein I (AB2GPI) and/or lupus anticoagulant (LA). There is a clear relationship between aPL and some events not included in the clinical criteria such us the hematologic manifestations. Among these, thrombocytopenia has been described in 20–50% of patients with APS. Although thrombocytopenia in APS is usually not serious, its impact on the clinical curse of the diseasesis unknown.
**Objectives:** a) To study the probability of developing clinical APS in patients with positive aPL and thrombocytopenia b) To identify potential risk factors for the development of APS. c) To study the association of thrombocytopenia with aPL autoantibodies.
**Methods:** Retrospective study of patients with positive aPL on at least 2 times, separated by a minimum of 12 weeks in medium or high titers without fulfilling clinical criteria for APS. The patients were selected from the database of the Department of Immunology of a tertiary hospital (1999–2004). Thrombocytopenia was defined as a platelet count $\leq$100000 platelets/L. We excluded patients with other causes of thrombocytopenia.
**Results:** 17 of 138 (12%) patients in the study had thrombocytopenia (mean platelet count 60,000/mm$^3$). Ten patients received oral glucocorticoids. Only 2 patients with <5.000 platelets/mm$^3$ were treated with intravenous gammaglobulins. Smoking was more common in patients with thrombocytopenia (47.1% vs 24%; p=0.044). The risk for thrombocytopenia was almost 3 times higher in smokers (OR 2.8; 95%CI 1.0–8.0; p=0.044).
We found no statistically significant relationship with the distribution of the different antibodies, except for AL (OR 13.5, 95%CI 3.8–47.6; p<0.001). Patients with 2 and 3 positive antibodies were more likely to develop thrombocytopenia than those with a single antibody (OR 12.4 and 50.8 respectively; p=0.002 and p<0.001).
After a mean follow-up of 146±60.3 months, 5 patients with thrombocytopenia (29.4%) developed thrombosis (4 arterial: 1 anterior ischemic optic neuropathy, 1 transient ischemic attack, 1 stroke and 1 acute myocardial infarction, and 1 deep venous thrombosis of the lower limbs with secondary pulmonary embolism), fulfilling clinical criteria for APS. The mean time from the confirmation of the presence of aPL to the diagnosis of APS was 73±61.5 months. Patients with thrombocytopenia had higher number of thrombosis compared with patients with normal platelet count (29.4% vs 6.6%, OR 5.9; 95%CI 1.7–20.9; p=0.003).
**Conclusions:** a) In our series, the incidence of thrombocytopenia in patients with positive antiphospholipid antibodies that do not meet clinical criteria for APS is 12%. APL-positive patients who develop thrombocytopenia have a potential risk of developing APS in the future. b) Tobacco use could be a risk factor for the development of thrombocytopenia in this population. c) Autoantibodies load is a risk factor for the development of thrombocytopenia.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5274

## SAT0309 PRIMARY SJÖGREN'S SYNDROME AND LYMPHOMA – A POPULATION-BASED STUDY FOCUSED ON LYMPHOMA AS EXCLUSION CRITERION FOR PRIMARY SJÖGREN'S SYNDROME DIAGNOSIS

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**Background:** In the widely used American-European Consensus Group (AECG) classification criteria for primary Sjögren's syndrome (pSS), pre-existing lymphoma is one of the exclusion criteria for pSS diagnosis (1). This is in contrast to the American College of Rheumatology (ACR)/Sjögren's International Collaborative Clinical Alliance (SICCA) 2012 classification criteria (2). The rationale and consequences of excluding or not excluding pSS in patients with pre-existing lymphoma have not specifically been described.
**Objectives:** To compare patients with pre-existing lymphoma and a later pSS diagnosis, and patients with pSS and a subsequent lymphoma, derived from a large-population-based cohort of individuals with pSS and lymphoma.
**Methods:** Patients with an International Classification of Diseases (ICD) diagnosis code for "Sjögren's syndrome/sicca syndrome" (SS) and prior or subsequent lymphoma diagnosis were identified by linking the Swedish Patient Register 1964–2007 with the Cancer Register 1990–2007 (n=205). Clinical data and lymphoma tissues were reviewed and the diagnoses evaluated. All 71 patients fulfilling the AECG and/or the proposed ACR-EULAR criteria for pSS (3) with a confirmed lymphoma were included in the study.
**Results:** We identified 11 patients with pre-existing lymphoma, defined as lymphoma diagnosed before (n=4, median time four years to pSS diagnosis) or within six months after pSS diagnosis (n=7, median time three months to lymphoma diagnosis), and 60 pSS patients with subsequent lymphoma.
The pSS characteristics were similar in patients with pre-existing lymphoma and pSS patients with subsequent lymphoma. There were no differences in reported duration of sicca symptoms (median time from sicca onset until pSS diagnosis 5 years in pre-existing lymphoma group vs. 4 years in pSS patients with subsequent lymphoma, p=0.1), sex distribution, median ages at sicca onset, pSS and lymphoma diagnoses, presence of autoantibodies, laboratory findings, overall survival after lymphoma diagnosis, and extraglandular pSS manifestations. However, lymphadenopathy at pSS diagnosis was more common in patients with pre-existing lymphoma (p<0.0001).
There were some differences in lymphoma characteristics. Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) (72% vs. 22%, p<0.002), and lymphoma involvement of the salivary glands (82% vs. 32%, p<0.005) were more common in patients with pre-existing lymphoma than in pSS patients with subsequent lymphoma.
**Conclusions:** This study suggests that pre-existing lymphoma should not be used as a general exclusion criterion for pSS, which may erroneously remain

undiagnosed. On the contrary, the combination of sicca symptoms and MALT lymphoma in the salivary glands could instead be a reason for adequate pSS investigation.

**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5308

## SAT0310 THE RELATIONSHIPS BETWEEN THE OCCURRENCE OF ANTIBODIES USED IN CLINICAL PRACTICE FOR DIAGNOSIS OF LUPUS AND CLINICAL CRITERIA USED IN THE SLICC CLASSIFICATION SYSTEM

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**Background:** The relationships between the occurrence of antibodies used in clinical practice for diagnosis and monitoring of the disease activity of systemic lupus erythematosus (SLE) and clinical criteria used in the SLICC classification system are a matter of discussion.
**Objectives:** The aim of the study was to investigate whether there are any relationships between the presence of clinical criteria used in the SLICC classification system and the presence of antibodies characteristic for SLE detected by multiparametric assay.
**Methods:** The study involved 81 (72-female and 9-male) consecutive SLE patients treated in the Department of Rheumatology and Connective Tissue Diseases. All patients fulfilled the SLICC classification criteria of SLE and 21 SLE pts - criteria of secondary Antiphospholipid Syndrome (SAPS). The mean age in the study group was: 37.6±11.1 years (from 19 to 71), the duration of the disease was 9.6±8.5 (from 0 to 33) years and mean SLE activity (SLEDAI scale) 4.1±4.9 (from 0 to 22).
The presence of antibodies (Ab) was determined by multiparametric enzyme-linked immunosorbent assay Polycheck Rheuma (Biocheck, GmbH, Münster, Germany). Statistical data analysis was performed using Statistica v10.0.
**Results:** In the studied group the following symptoms of SLE were found: malar rash – 46 pts, discoid rash -3 pts, photosensitivity – 34 pts, vasculitis – 21pts, oral ulcers – 22 pts, alopecia – 36 pts, musculoskeletal – 58 pts, arthritis – 36 pts, serositis – 14 pts, renal disorder – 7 pts, lupus nephritis – 33 pts, neurological disorders – 20 pts, hematologic disorders – 56 pts.
In the examined group of 81 patients the following antibodies were detected: anti-dsDNA – 10 pts (12.3%), anti-Sm-9 pts (11.1%), anti-Rib P – 4 pts (4.9%), anti-Histons – 15 pts (18.5%), anti-Ro/SS-A 52 – 2pts (2.5%), anti-Ro/SS-A 60 – 22 pts (27.2%), anti-La/SS-B – 7 pts (8.6%), anti-Scl-70 – 3 pts (3.7%), anti-CENP-B – 1 pts (6.2%), anti-PM/Scl-100 – 3 pts (3.7%), anty-U1-snRNP – 9pts (11.1%), anti Ku – 5 pts (6.2%), anty-Jo-1 and anty-Mi-2 – 0 pts.
In the data group of SLE patients, a statistically significant correlation was found only between vasculitis and presence of antibodies: anti-dsDNA (p=0.021, Φ Yule'a=0.27), anti-Ro SS-A 60 (p=0.027, Φ Yule'a=0.26), anti-Sm (p=0.028, Φ Yule'a=0.26).
**Conclusions:** In the SLE pts no significant association was found between the presence of clinical criteria used in the SLICC classification system and the antibodies used in clinical practice for diagnosis and monitoring of disease activity. Only vasculitis is significantly associated with the presence of anti-dsDNA, anti-Ro SS-A 60, and anti-Sm antibodies.

**Disclosure of Interest:** None declared
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## SAT0311 THE COMPARABILITY OF PATIENT AND PHYSICIAN GLOBAL ASSESSMENT IN EARLY AND NON-EARLY SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Objectives:** To compare patient and physician global assessment of disease activity in patients with systemic lupus erythematosus (SLE) depending on disease duration.
**Methods:** In performed case-control study were included patients that fulfilled SLICC classification criteria, 2012. The research included two groups: patients with early SLE – first group (disease duration less than 24 months) and non-early SLE – second group (disease duration more than 24 months). Patient and physician global assessments (PGA and PhGA) were rated by 0 -100 numeric scale. We evaluated the concordance of PGA and PhGA in each group and compared the results between groups.
**Results:** A total of 72 SLE patients were analyzed. First group included 36 patients with a mean age 37.2±13.2 (range 18–67) years, 83.3% female and mean disease duration was 12±9.4 months. Mean PGA value were lower compared to PhGA values in this group (47.5±22.0 versus 49.1±21.0), but the difference wasn't statistically significant (p>0,05). The second group included also 36 patients, mean age was 43±10.6 (range 24–73) years, 91.7% female and mean disease duration was 120±50 months. Mean PGA value was also lower than mean PhGA in this group, but with a smaller discrepancy (50.0±19.7 versus 50.2±20.9, p>0,01). The comparison of groups showed that in patients with early SLE the discordance between PGA and PhGA, is more important than in patients with longer disease duration.
**Conclusions:** The comparison of PGA and PhGA in patients with early SLE patients and ones with longer disease duration showed that patients early in disease duration tend to diminish PGA underestimating their general estate, but without statistically significant difference. In longer disease duration PGA and PhGA variables become similar, that suggest the patient's better understanding of their disease and general estate.

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## SAT0312 WORK DISABILITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN MOLDAVIAN LUPUS STUDY GROUP

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**Background:** As systemic lupus erythematosus (SLE) is a chronic disease, it can lead in time to important functional limitations that impair not only their quality of life but also their ability to work. Prior studies on work disability in patients with SLE have shown that about one third of the patients become disabled within 3–12 years of diagnosis [1,2].
**Objectives:** To assess the work disability in patients with systemic lupus erythematosus in Moldavian lupus study group.
**Methods:** Using a cross-sectional design, patients who fulfilled the SLICC (2012) classification criteria for SLE, were recruited from rheumatology departement. Data collection included demographics, disease duration, physician-rated indices of disease activity (SLAM) and damage index (SLICC DI). Work disability was defined by patients self-report.
**Results:** The study included 106 patients (97 females, 9 males) with a mean age (±SD) of 41,1±12,6 years, mean disease duration of 90,0±87,2 months. The disease activity by SLAM was 11±5,17 points and mean SLICC/ACR DI 1,9±2,4 points. The rate of self-reported work disability among the 106 patients studied was 35,8% (38 patients). Disability rate in the first year of disease was reported by 39,5% (15) patients; after 2 to 5 years of disease the estimated rate was of 47,4% (18 patients); after 6 to 10 years of disease the estimated rate was of 10,5% (4 patients) and after 10 years of disease the self-reported work disability was 2,6% (1 patient).
**Conclusions:** The rate of work disability was 35,8% with the highest rate in the first five years of disease, affecting younger persons, which make crucial to identify strategies aimed to reduce work disability is in those patients.

**References:**
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## SAT0313 DIFFERENT SEROLOGICAL PROFILES AND ACTIVITIES IN TWO ONSET CATEGORIES OF LUPUS NEPHRITIS

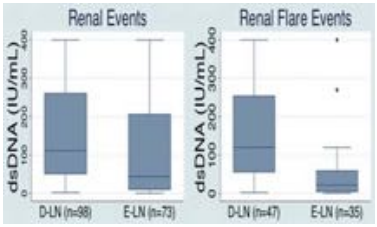
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**Background:** Previously, we reported a different renal prognosis between two onset categories of lupus nephritis (LN): LN that developed as a flare of systemic lupus erythematosus (SLE) after treating the prior non-renal SLE conditions successfully (delayed, D-LN) and LN manifesting at the time of SLE onset (early, E-LN).[1)] D-LN had a poorer renal prognosis than E-LN independent of the renal histology based on the chart review, but we had not analyzed the serological data in those LN patients.
**Objectives:** This study investigated possible differences in the serological profiles and activities between E-LN and D-LN. We focused on the serum levels of complement C3 and anti-ds DNA antibodies (Ab) as serological activities, and anti-Sm Ab as a serological profile.
**Methods:** Our hospital records for 1990–2015 were reviewed, and we identified 361 SLE patients diagnosed according to the American College of Rheumatology criteria for SLE. This study had two parts.
1. *Serological activity (C3 and anti-dsDNA Ab):* Of the 361 patients, 166 with LN (83 E-LN, 83 D-LN) had serum C3 and anti-dsDNA Ab levels measured on each admission to treat a total of 347 active SLE events (204 renal and 143 non-renal events). The serum data were compared between the E-LN and D-LN groups using the Mann–Whitney U-test and two-way analysis of variance (ANOVA).

2.*Prevalence of positive serum anti-Sm Ab:* From the 361 patients, we enrolled 129 patients diagnosed with SLE between Jan. 1996 and Oct. 2010 who were observed for more than 5 years. Patients diagnosed before 1996 were excluded because comprehensive anti-Sm Ab data were not available. Anti-Sm-Ab-positive patients were defined by at least once positive result before or at an LN manifestation. The frequency of anti-Sm-Ab-positive patients was compared among three patient-groups: E-LN, D-LN, and non-LN-SLE (the patients with no LN for more than 5 years).

**Results:** 1. The treated SLE conditions in the 83 E-LN patients included 91 renal events (35 flares) and 36 non-renal events, and those in the 83 D-LN patients comprised 113 renal events (52 flares) and 107 non-renal events. Serum anti-dsDNA Ab levels were higher in D-LN than in E-LN for the renal events (169 ± 139 IU/mL (EIA), n=98 *vs.* 120 ± 143 IU/mL, n=73, $p<0.01$) and renal flare events (169 ± 130 IU/mL, n=47 *vs.* 48.8 ± 79.7 IU/mL, n=35, $p<0.01$) (Fig). In both the D-LN and E-LN groups, the serum anti-dsDNA Ab levels were higher at renal events than non-renal events. The serum C3 levels were similar in the D-LN and E-LN groups during renal events.

2. The enrolled patients comprised 39 E-LN, 23 D-LN, and 67 non-LN-SLE. The frequency of anti-Sm-Ab-positive patients was higher in D-LN than non-LN-SLE (15/23, 65.2% *vs.* 16/67, 23.9%, $p$=0.001) and higher in D-LN than E-LN (15/23, 65.2% *vs.* 12/39, 30.8%, $p$=0.016).




**Conclusions:** High serum anti-dsDNA Ab titers were characteristic of LN that developed later in the course of an SLE flare (D-LN) compared with LN manifesting at the onset of SLE (E-LN). D-LN may reflect intractable SLE conditions. Positive serum anti-Sm antibodies were prevalent in D-LN patients in our study. Therefore, anti-Sm-Ab-positive SLE patients without LN may be at risk for the subsequent development of D-LN.

**References:**

[1] Takahashi Y, et al. Time of initial appearance of renal symptoms in the course of systemic lupus erythematosus as a prognostic factor for lupus nephritis. Mod Rheumatol 2009; 19: 293–301

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## SAT0314 CLINICAL AND IMMUNOLOGICAL FEATURES OF ANTI-CENTROMERE ANTIBODY POSITIVE SJÖGREN'S SYNDROME

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**Background:** Sjögren's syndrome (SjS) is a systemic autoimmune disease presenting dryness symptoms and various extraglandular manifestations. Anti-centromere antibody (ACA)-positive SjS is considered as a distinct clinical subgroup in SjS. [1–2] While ACA is often detected in sera from other autoimmune diseases, such as limited cutaneous systemic sclerosis (SSc) and primary biliary cirrhosis, the role of ACA in their pathogenesis still remains unclear. In addition, comprehensive and enough clinical information from the point of view of ACA positive cases have not been accumulated.

**Objectives:** To clarify clinical and immunological features of ACA-positive SjS and their association with autoantibodies.

**Methods:** Patients with discrete-speckled pattern in anti-nuclear antibody (ANA) test and/or positive ACA, who visited to our service between 2012 and 2015, were enrolled. Clinical information and immunological tests including serum autoantibodies and immunoglobulins (Ig) were collected and statistically analyzed.

**Results:** Discrete-speckled pattern in ANA test and/or positive ACA were identified in 198 patients. There were 190 female and 8 male and the average age was 59. 142 patients were classified into any autoimmune disease. In the 142 patients, 59 patients and 19 patients were diagnosed with SSc without SjS and SSc/SjS overlap cases, respectively. Another 33 patients were diagnosed with primary SjS and 17 patients were diagnosed with rheumatoid arthritis. Proportion of concomitant ANA patterns in 142 patients were speckled (15%), homogenous (11%), cytoplasmic (6%) and/or nucleolar (4%) pattern. Focusing on ACA positive two dominant diseases, SSc and SjS, no significant difference was not observed in age. All patients except one were female. Raynaud's phenomenon and sclerodactyly were less frequent in SjS patients (65% and 18%) than SSc patients and SSc/SjS overlap patients (100% and 100%, 76% and 84%) ($p<0.01$ and $p<0.01$, $p<0.01$ and $p<0.01$). Dryness symptoms were more frequent in SjS patients (96%) and SSc/SjS overlap patients (84%) than SSc patients (20%) ($p<0.01$ and $p<0.01$). Examining autoantibodies, serum anti-SS-A/Ro antibodies were positive in 39% of SjS patients and SSc/SjS overlap patients (30%), which were significantly higher than SSc patients (11%, $p<0.01$ and $p<0.01$). In laboratory parameters, peripheral leukocyte count in SjS patients was lower than in SSc patients (p=0.014). Other laboratory findings including platelets, hemoglobin, serum IgG, A, M, C3, C4 and CH50 did not significantly differ between SjS and SSc patients. Interestingly, leukocyte count and C4 in anti-SS-A/Ro antibody positive SjS patients were lower than the negative SjS and SSc patients (p=0.017). Anti-SS-A/Ro negative SjS patients and SSc/SjS overlap patients did not differ from SSc patietns without SjS in all laboratory parameters.

**Conclusions:** Our cross-sectional cohort study confirmed that ACA-positive cases were dominantly classified into SSc and/or SjS, presenting different clinical characteristics. Our data suggested that ACA-positive SjS was immunologically characterized by low peripheral leukocyte counts different from other ACA-positive diseases, and additional anti-SSA/Ro positivity critically determined serum level of C4 and leucocyte count in ACA-positive patients.

**References:**

[1] J Rheumatol 2001; 28: 2238
[2] Int J Rheum Dis 2015; 18: 776

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## SAT0315 DEMYELINATING SYNDROME SECONDARY TO SYSTEMIC LUPUS ERYTHEMATOSUS: SYSTEMATIC LITERATURE REVIEW AND ANALYSIS OF A MONOCENTRIC COHORT

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**Background:** Demyelinating syndrome (DS) secondary to Systemic Lupus Erythematosus (SLE) is rare (<1%) but represents a challenging condition for both patients and clinicians.

**Objectives:** To describe the features of DS secondary to SLE through a systematic review and the analysis of a monocentric cohort of patients.

**Methods:** Using PubMed a systematic review was carried out according to PRISMA guidelines including the following Mesh terms: " Lupus Erythematosus, Systemic", "Lupus Vasculitis, Central Nervous System", "Demyelinating Diseases", "Leukoencephalopathies", "Vasculitis, Central Nervous System", "Cranial Nerve Diseases", "Diplopia", "Brain Stem". Last Medline was performed on the 31/01/2015.

Moreover, a retrospective analysis of 334 SLE adult patients, followed-up in a third level center of Rheumatology between 1990 and 2015, was performed to identify those patients that developed DS.

Patients were classified as affected with DS defined as acute of relapsing demyelinating encephalomyelitis with evidence of discrete neurologic lesions distributed in space and time according to the 1999 ACR nomenclature and attributed to SLE according to the algorithm proposed by the Italian Society of Rheumatology (1).

Cases identified by systematic review and cohort analysis were classified as affected by 4 different syndromes: A) neuromyelitis optica (NMO), B) neuromyelitis optica spectrum disorders (NMOS), C) DS prevalently involving the brain (DSB), D) DS prevalently involving the brainstem (DSBS).

**Results:** The literature search identified 1612 articles, of which 50 were considered relevant for the present study for a total of 74 case reports. The retrospective cohort analysis retrieved 4 cases. Presented data have been pooled. The mean age at the time of DS onset was 33.3 years and only 6 patients were male. DS was the onset manifestation in 57 (73.1%) patients. Among the 78 patients identified 40 (51.3%) were classified as suffering with NMOS, 23 (29.5%) with NMO, 8 (10.2%) with DSBS and 7 with DSB (9.0%). The clinical spectrum of the identified syndromes was heterogeneous but longitudinal extensive transverse myelitis was the most frequent manifestation being present in 23 patients with NMO and 26 (65.0%) with NMOS. Cranial nerve palsies was the less frequent being present in 9 (11.5%) patients (4 NMOS, 3 NMO, 1 DSBS and 1DSB). The most prescribed treatment was methylprednisolone pulses (60, 76.9%) associated with cyclophosphamide (36, 46.1%), but plasma-exchange (15, 19.2%) and Rituximab (7, 9.0%) were also used. Worse functional prognosis was associated with NMO (8.7% complete and 34.8% partial resolution). Demise was reported in 6 NMO cases (26%), 3 (7.5%) NMOS and 1 (14.2) DSB as a results of DS or associated complications.

**Conclusions:** Although rare DS secondary to SLE may be life-threatening. If DS occurs in SLE patients it should be promptly treated with high dose of intravenous corticosteroids and Cyclophosphamide or Rituximab as steroid sparing agents.

**References:**

[1] Bortoluzzi A et al. Development and validation of a new algorithm for attribution of neuropsychiatric events in systemic lupus erythematosus. Rheumatology (Oxford). 2015 May;54(5):891–8.

**Disclosure of Interest:** None declared

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## SAT0316 NEUROLOGICAL INVOLVEMENT IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: A CASE SERIES WITH A LONG-TERM FOLLOW-UP

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**Background:** Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by autoantibody production and thrombosis or pregnancy morbidity. Central nervous system abnormalities are a common feature of APS that have been attributed to both vascular thrombosis as well as direct injury to neuronal tissue by antiphospholipid antibodies. Neurological manifestations in APS are diverse and may be confused with other neurologic syndromes.
**Objectives:** The aim of our study was to determine the prevalence and the type of neurological involvement in patients with APS.
**Methods:** A case series of patients with APS diagnosed and followed for a long period in a specific unit of Thrombosis and Vasculitis was conducted. Clinical and laboratory data were collected in a retrospective manner. Patients with neurological manifestations were compared with patients without nervous system involvement. Chi2 and t-student were used, using the statistical package SPSS22.0.
**Results:** 88 patients with APS were included, 63 (71,6%) female, mean age 56,5 ± 20 years [range 11–89], with a mean follow-up of 9,1 years (median 7 years). 23 patients (26,1%) had a secondary APS: 20 SLE, 2 systemic sclerosis and 1 Sjögren's syndrome. 4 (4,5%) were pure obstetric APS, 36 (40,9%) had an arterial thrombosis, 30 (34,1%) had a venous thrombosis and 18 (20,4%) had mixed events (arterial, venous and obstetric). 60 (68,2%) patients had a cardiovascular risk factor (hypertension, dyslipidemia, type 2 DM) and 15 (17%) had atrial fibrillation. 49 patients of 88 with APS (55,7%) had neurological involvement. 26 (53,1%) patients had ischemic stroke, 8 (16,3%) transient ischemic attack, 16 (32,6%) cognitive deficits, 14 (28,6%) epilepsy, 8 (16,3%) headache, 5 (10,2%) psychosis, 7 (14,3%) movement disorders and 3 (6,1%) had sensorineural hearing loss. 28 (31,8%) patients had ≥2 neurologic symptoms. 19 patients (38,8%) had white matter lesions on MRI but only 1 patient was diagnosed with multiple sclerosis. In 17 patients (34,7%) neurological involvement was diagnosed before APS (mean 7,2 ± 7,9 years). Only 3 patients had livedo reticularis: 2 SLE y 1 Sneddon syndrome. No significant differences in age, sex, classification, antiphospholipid antibodies, comorbidities and therapy were observed between patients with or without neurological manifestations. Hospitalization (93,9% vs 74,4%, p 0,01) and mortality (36,7% vs 7,7%, p 0,001) was higher in neurological APS.
**Conclusions:** More than half of patients with APS had neurological involvement. Cerebrovascular ischemic events and cognitive deficits were the most common manifestations. Neurological involvement was associated with higher mortality and hospitalization. Neurological symptoms may occur long before diagnosis of APS. We have not identified risk markers of central nervous system involvement.
**References:**
[1] Arnson Y et al. The antiphospholipid syndrome as a neurological disease. Semin Arthritis Rheum. 2010;40(2):97.
[2] Muscal E, Brey RL. Neurologic manifestations of the antiphospholipid syndrome: integrating molecular and clinical lessons. Curr Rheumatol Rep. 2008;10(1):67.
**Disclosure of Interest:** None declared
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## SAT0317 THE ASSOCIATION BETWEEN ABO BLOOD TYPES AND VENOUS THROMBOEMBOLISM IN INDIVIDUALS WITH A POSITIVE ANTIPHOSPHOLIPID PROFILE IS VARIED BY SEX

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**Background:** Persistently positive antiphospholipid antibodies (aPLs) are associated with an increased risk of arterial and venous thrombotic events (VTE). The pathogenesis of thrombosis is multifactorial and non-aPL thrombosis risk factors including hypertension (HTN), obesity, smoking, and diabetes (DM) influence the risk of thrombosis.[1] ABO blood group, a determinant of plasma levels of von Willebrand factor (vWF), is an established thrombosis risk factor in the general population; non-type O blood type is associated with a higher risk of VTE. It is not known whether non-O blood type is associated with VTE in patients with persistent aPLs.
**Objectives:** To investigate the association of ABO blood type with VTE in patients with persistent aPLs.
**Methods:** We included patients >18 years old followed at an urban tertiary care center between 2000 and 2015 with the serologic criteria for aPL positivity by the revised Sapporo Criteria (anticardiolipin IgG or IgM >40 IU, and/or anti-beta-2-glycoprotein1 IgG or IgM >40 IU or LAC+ measured twice at least 12 weeks apart) and a type and screen.[2] VTEs were verified through chart review by radiological criteria and historical records. Data including age, sex, race, body mass index, smoking status, blood type, HTN or DM diagnoses, and ever use of aspirin or warfarin were ascertained from chart review. Odds ratios of VTE were estimated with logistic regression models for O vs. non-O blood type.
**Results:** Of the 230 patients included in the study, 48 (21%) were men, 78 (19 men, 59 women) had a VTE. Patients with and without VTE were similar with respect to age, sex, race, HTN, DM, and other clinical risk factors for VTE. The prevalence of non-O blood type was 46% in non-VTE and 56% in VTE, unadjusted OR 1.5 (95% CI 0.88, 2.62), p=0.14. However, among men, the prevalence of non-O was significantly higher in VTE than in non-VTE, 68% and 34%, respectively, p=0.021. Men with non-O blood type had higher odds of developing VTE, OR 4.0 (95% CI 1.1, 14.0), p=0.04 after adjusting for age, race, and DM and HTN. The association between ABO and VTE was not significant among women. In the overall sample, women were slightly younger at the time of aPL measurement, and were less likely to smoke, but more likely to have low density lipoprotein levels ≥100 mg/dl (Table 1). aPL positive women who developed VTE were more likely to be Hispanic compared to men with VTE, 54% and 25%, respectively, p=0.03, and were less likely to smoke compared to men.

**Table 1. Baseline characteristics of aPL+ patient by sex.**

| Patient Characteristics | APL positive women n=182 | APL positive men n=48 | p-value |
|---|---|---|---|
| Age, at APL measurement, median (IQR), years | 43 (29, 53) | 47 (38, 63) | 0.02 |
| Black race, n (%) | 57 (36) | 16 (36) | 0.92 |
| Hispanic ethnicity | 61 (33) | 11 (43) | 0.22 |
| History of diabetes, n (%) | 63 (35) | 22 (46) | 0.15 |
| History of hypertension, n (%) | 112 (62) | 36 (75) | 0.08 |
| Ever Smoked, n (%)* | 45 (30) | 19 (51) | 0.01 |
| LDL>100 mg/dL, n (%)* | 60 (53) | 9 (27) | 0.01 |
| BMI, median (IQR), kg/m$^2$ | 28 (23, 34) | 28 (25, 36) | 0.55 |
| Aspirin use | 88 (48) | 26 (54) | 0.48 |
| Anticoagulation use | 72 (40) | 27 (56) | 0.04 |
| Prednisone use | 88 (48) | 26 (54) | 0.47 |
| SLE by ACR/SLICC criteria | 61 (36) | 9 (21) | 0.06 |
| Non-type O blood type | 91 (48) | 23 (50) | 0.80 |

*Data unavailable for >30% of patients
BMI: body mass index
LDL: low density lipoprotein

**Conclusions:** In this retrospective study, we have shown that the association between ABO and VTE varies by sex in aPL+ individuals. The non-O blood type is associated with a higher risk of VTE in men, but not women. The effects of ABO blood types on vWF in aPL+ individuals may be attenuated by genetic and environmental factors that differ by sex. Understanding the relationship between sex, ABO, and aPL may elucidate thrombosis mechanisms of VTE in aPL+ individuals.
**References:**
[1] Miyakis S, et al. J Thromb Haemost. 2006;4(2):295–306.
[2] Erkan D, et al. Rheumatology. 2002;41(8):924–9.
**Disclosure of Interest:** None declared
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## SAT0318 THE SIGNIFICANCE OF ANTIPHOSPHOLIPID TESTING IN MULTIPLE SCLEROSIS: SYSTEMATIC REVIEW AND META ANALYSIS

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**Background:** The association between antiphospholipid antibodies (aPL) and multiple sclerosis (MS) is controversial.
**Objectives:** To evaluate whether aPL relate to MS and its severity.
**Methods:** Systematic review of EMBASE and PubMed from inception to October 2015 according to PRISMA guidelines. Peto's meta-analysis for rare events.
**Results:** The relationship between aCL (anticardiolipin) antibody of either IgG/IgM isotype and MS was addressed in 10 case control studies totalling 801 controls and 614 MS patients; the pooled prevalence for IgG was 1.9% in controls and 6.8% in MS yielding an odds ratio (OR) of 3.602 (95% CI 2.005, 6.471); the pooled prevalence for IgM aCL was 2.49% in controls and 10.7% in MS patients yielding an OR of 4.720 (95% CI 2.828, 7.877). The relationship between anti-beta$_2$glycoprotein-I (a$\beta_2$GPI) of IgG isotype and MS was addressed in 5 case control studies totalling 405 controls and 401 MS patients; the pooled prevalence was 5.18% in controls and 1.24% in MS yielding an OR of 0.230 (95% CI 0.086, 0.618); the relationship between IgM a$\beta_2$GPI and MS was addressed in 5 case control studies totalling 379 controls and 367 MS patients; the pooled prevalence for the IgM isotype was 2.49% in controls and 10.7% in MS patients yielding an OR of 3.251 (95% CI 1.805, 5.855). The relationship between anti-prothrombin antibody (aPT) of IgG isotype and MS was addressed in 3 case control studies totalling 328 controls and 260 MS patients; the pooled prevalence was 9.75% in controls and 4.61% in MS yielding an OR of 0.447 (95% CI 0.225, 0.887).
Three studies addressed the relationship between aPL and MS employing as controls patients with ischaemic stroke (IS) totalling 599 IS and 505 MS patients. The pooled prevalence of IgG aCL in IS was 8.9% and in MS was 6.34% for an OR of 1.011 (95% CI non evaluable). The pooled prevalence of IgM aCL in IS was 6.84% and in MS was 9.72% for an OR of 0.995 (95% CI non evaluable). The relationship between aCL of either isotype and stable/active MS was evaluated in 4 case control studies totalling 200 stable/remission MS patients and 84

active/relapsing MS patients. The pooled prevalence of IgG aCL in the former was 19.5% and in the latter 22.6% for an OR of 1.206 (95% CI 0.649, 2.241) and likewise the pooled prevalence of IgM aCL was 21% and 36.9% respectively for an OR of 0.150 (95% CI 0.086, 0.264). The relationship between a$\beta_2$GPI of either isotype and different disease stages of MS was evaluated in 123 stable/remission MS patients and 69 active/relapsing MS. The pooled prevalence of IgG $\beta_2$GPI was 1.62% in stable/remission MS and 20.2% in active/relapsing MS for an OR of 15.4 (95% CI 3.383, 70.095). The pooled prevalence of IgM $\beta_2$GPI was 3.2% in stable/remission MS and 40.5% in active/relapsing MS for an OR of 20.3 (95% CI 6.721, 61.411).

**Conclusions:** The calculated OR suggest that IgG/IgM aCL and IgM a$\beta_2$GPI are weakly associated with MS and that IgG/IgM $\beta_2$GPI are associated with active/relapsing MS though with very wide CIs. Most of the studies reported the percentage of positive aPL per group but not the average PL titre per group, precluding better assumptions on the relationships found.

**Disclosure of Interest:** None declared

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## SAT0319 SEVERITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A LATENT TRAIT ANALYSIS

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**Background:** Systemic Lupus Erythematosus (SLE) is a complex disease which can potentially involve any organ and, therefore, has a wide range of clinical manifestations (i.e., subphenotypes) [1].

**Objectives:** To propose a novel methodology for building an index of severity in patients with SLE.

**Methods:** A cross-sectional analytical study was done on 319 SLE patients (1997 ACR). A structural model for the latent trait in the 2pl item response theory model was fitted following the Ogasawara's formulation [2] in order to characterize a severity construct of 17 variables. In addition, the model analyzed possible associations of the severity latent trait with other patient covariates including cardiovascular disease, age at onset of the disease, and expositional factors.

**Results:** Baseline characteristics of patients were as follows: female gender 91%, median age 37 (IQR 21) years, median duration of the disease 5 (IQR 10) years, lupus nephritis 37.3%, and central nervous system involvement in 16%. Several symptoms were excluded from the severity construct due to inconsistency according to Cronbach-Mesbah Curve including lupus nephritis, diffuse alveolar hemorrhage, and vasculitis. A total of 11 symptoms were included in the item response theory model showing three levels of disease severity (Figure 1). The only covariate registered that reaches an association with severity was coffee consumption.

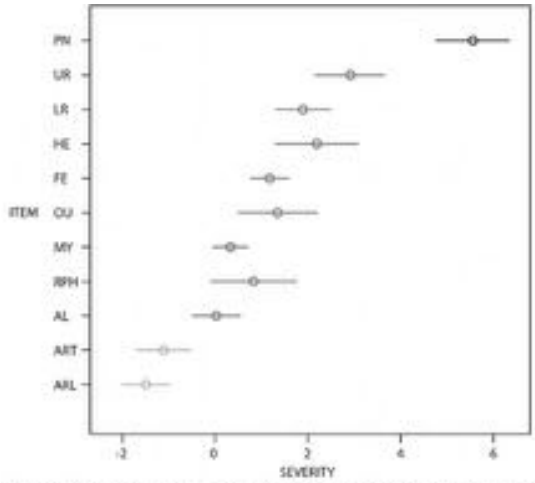



**Figure 1.** Graphic approximation to performance levels for the severity scale in the 2plScov model. *Low-severity*: Arthritis (ART), Arthralgia (ARL); *Moderate-severity*: Fever (FE), Myalgia (MY), Headache (HE), Raynaud phenomenon (RPH), Urticaria (UR), Livedo reticularis (LR), Oral ulcers (OU), Alopecia (AL); *High-severity*: Peripheral neuropathy (PN)

**Conclusions:** Symptoms excluded due to inconsistency share the same pathogenic mechanism in SLE, which corresponds to autoantibody-driven tissue damage, and are associated with high mortality risk. The remaining symptoms are related to inflammation and vasculopathy, and in most cases, require a less aggressive immunosuppressive treatment [3]. The order of symptoms on the present scale of severity coincides with clinical experience, and the three levels of performance can be associated with low, moderate, and high severity. The present index of severity is useful for SLE patients with less severe phenotype (i.e., without nephritis, diffuse alveolar hemorrhage, and vasculitis). A further replication study is necessary to validate these results.

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**Disclosure of Interest:** None declared

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## SAT0320 IGG3 AUTOANTIBODIES BINDING TO STATHMIN-4 AS MARKER OF POLYNEUROPATHY IN PRIMARY SJÖGREN SYNDROME

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**Background:** Primary Sjögren-syndrome (pSS) is considered as autoimmune phenomena affecting exocrine glands with various clinical phenotyps. PSS can appear with different extraglandular manifestations such as arthritis, myositis, vasculitis and peripheral or central neuropathies. 8.5–67% of patients with pSS complain about neurological symptoms. About 9% can be diagnosed having a destinct form of polyneuropathy (PNP).

**Objectives:** Here, we investigated autoantibodies binding to stathmin-4 (STMN-4) in pSS with PNP.

**Methods:** We screened 4 versus 4 having pSS with and without PNP for discriminating autoantibodies by using protein array technology. We identified autoantibodies binding to STMN-4 in patients with pSS and PNP. We evaluated our finding by establishing different ELISA detections for STMN-4 autoantibodies using sera of different underlying diseases (n=484).

**Results:** Using Anti-IgG3 STMN-4, we tested the following groups. In pSS with PNP 33% had anti-IgG3 STMN-4 antibodies and 6% without PNP had anti-IgG3 STMN-4 (likelihood 5.5).

| Groups | Frequency of anti-STMN |
|---|---|
| pSS | 8/62 13% |
| pSS without PNP | 3/47 6% |
| pSS with PNP | 5/15 33% |
| *pSS with sensomotoric/axonal PNP* | *5/11 45%* |
| Blood donors | 5/128 4% |
| RA | 11/62 18% |
| SLE | 3/36 8% |
| GPA | 2/21 10% |
| Plasmacytoma | 3/44 7% |
| Multiple Sclerosis | 0/37 0% |
| sSS | 3/20 15% |
| UCTD | 4/27 15% |
| PNP (metabolic, toxic origin) | 1/47 2% |

Anti-IgG3 STMN is associated with PNP in pSS patiens (Fisher exact two-tailed p-value=0.016). We could not see any significant association in other diseases with PNP and metabolic or toxic induced PNP.

**Conclusions:** Anti-IgG3 STMN is a new potential marker for PNP in patients with pSS.

**References:**
[1] none

**Disclosure of Interest:** S. Ross Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, T. Witte Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, M. Stangel Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, R. Schmidt Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, N. Baerlecken Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none

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## SAT0321 PREVALENCE AND MORTALITY FROM INFECTIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN A TERTIARY LEVEL HOSPITAL

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**Background:** Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease characterized by clinically heterogeneous manifestations. Infections can be the initial trigger to the development of autoimmunity. Initial presentation of SLE can mimic infections, and in turn infections can mimic disease flares in established SLE. Infections are an important cause of morbidity and mortality in SLE. Bacterial infections are most frequent, followed by viral and fungal infections. The impaired cellular and humoral immune functions seen in patients with SLE are predisposing conditions. Disease activity and high doses

of methylprednisolone or cyclophosphamide are well-recognized risk factors for infection.
**Objectives:** To determine the prevalence and mortality from infection in SLE patients as well as to identify etiology, associated factors to severity and site of infection.
**Methods:** We performed a retrospective study from 2010 to 2014 in a referral hospital. We analyzed risk factors (RF) on admission, involved organ, infectious type and etiology. Statistical analysis: We did descriptive statistical, $Chi^2$, multivariate analysis.
**Results:** There were 328 patients, 87% women and 13% men, mean age 32.4±9.9 years. Infections as cause of hospitalizations were 42.2%, prevalence of infections was 49%, and mortality from severe infections was 45%. The RF for severe infections were: renal involvement Odds Ratio (OR) 3.057, $P<0.019$; hematologic OR 1.9, $p<0.001$; increased dsAnti-DNA RM 5.1 $p<0001$, hypocomplementaemia: OR 2.673, $P<0.02$, leukolymphopenia OR 2.5, $p<0001$. Type of infecctions: bacterial 87%, viral: 3.4%, fungal: 8%, mycobacterial: 1.5%. Site of infection: lower respiratory tract 38%, urinary tract: 49% soft tissues: 6.1%, central nervous system: 1.2%, Others: 4.2%. Most frequent etiology agent were: bacterial: *S. aureus, E. coli, A. baumanii, E. faecalis. Virales: H. zoster, mycotic: candida albicans and M. tuberculosis.*
**Conclusions:** Infections are an important cause of morbidity, mortality and hospitalization in SLE patients. The lower respiratory tract infections of bacterial origen were most frequent. The renal and hematological involvement, increased dsAnti-DNA, hypocomplementaemia, and leukolymphopenia were the most important factors for severe infections. Infections in active SLE patients constitute a true challenge for the clinician
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5254

## SAT0322 PREVALENCE AND RISK FACTORS FOR COGNITIVE IMPAIRMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Neuropsychiatric disorders have a high morbidity being cognitive impairment (CI) one of the most frequent syndromes in systemic lupus erythematosus (SLE) which lead to a poor quality of life
**Objectives:** To determine the prevalence and risk factors of CI in patients with systemic lupus erythematosus
**Methods:** Twenty seven patients were selected from a total of 150 patients with SLE. CI was evaluated in all patients by the test of Barcelona (for qualitative evaluation of cognitive state: language, reading, writing, visual recognition, memory and abstraction) and the Montreal cognitive assessment (COCA). The following risk factors were evaluated: SLEDAI, obesity/overweight, systemic arterial hypertension, dyslipidemia, pulses of methylprednisolone, SLIC/ACR, use of benzodiazepine, cyclophosphamide and chloroquine. Statistical analysis: Fisher test, T-test Student and logistical regression.
**Results:** There were 27 SLE patients (25 women and 2 men), mean age 42±14 years) mean disease evolution (10±8.6 years), length of education (11.7±4.2 years). With the test of Barcelona we found that 100% of patients had involvement in at least one item, being the most affected areas: attention in 33%, memory in 52%, analysis synthesis and abstraction in 44.4%. With respect to the MOCA a prevalence of 55.6% (15 of 27) of CI was found. Of these patients 12 of 15 had mild CI and 3 of 15 dementia. We only found that the use of chloroquine conferred protection against cognitive impairment (OR 0.236, CI 0.120–0.692, $p<0.003$). The other risk factors were not significant: dyslipidemia (OR 8.5, CI 0.508–143, p= NS), SLIC/ACR (OR 6.3, CI 0.64–109.7), obesity/overweight (OR 0.407, CI 0.02–5-2, systemic arterial hypertension (OR 0.782, CI 0.031–754), pulses of methylprednisolone (1. 85, CI 0.64- 18.119), use of cyclophosphamide (OR 0. 327, CI 0.115–7.056), among others.
**Conclusions:** We found a high prevalence of cognitive impairment being the use of chloroquine a protective factor. It is important to recognize these patients in order to offer them a medical alternative with a psychological rehabilitation.
**Disclosure of Interest:** None declared
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## SAT0323 CLINICAL VARIANTS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN CHILDREN

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**Background:** In pediatric rheumatology, features of the initial period of systemic lupus erythematosus (SLE) and clinical types, depending on which principles and tactics of therapy should be based, remain undifferentiated.
**Objectives:** To study the variants of the clinical manifestations of SLE in children at an early stage of the disease
**Methods:** The basis of this work was aimed to survey results and data of archival materials of 153 SLE patients observed in the clinic of the Scientific Center of Pediatrics and Pediatric Surgery, the Republic of Kazakhstan.
**Results:** We noted lupus carditis most commonly in the debute of the disease – 129 children (84.3%), and generalized vasculitis – 128 (83.7%) cases, followed by nephritis – 78 (51.0%), polyserositis – 72 (48.4%) and cerebrovascular – 47 (31.0%) children. Less relatively marked was a detection of secondary antiphospholipid syndrome – 40 (26.1%) children. In distribution of SLE patients over the age, main group consisted of 12 years and older aged children (60.1%) and younger than 12 years children (39.9%). While in children under the age of 12 years, the first manifestations of the disease in almost half of the cases, along with fever, dermatitis and arthritis were cardio, polyserositis and cerebrovascular (42,1% ± 3,65, 48,6% ± 3,26 and 49,1% ± 3,11, respectively), lupus nephritis (LN), generalized vasculitis (GV) and secondary APS (61,5% ± 3,25, 66,7% ± 8,55 and 70% ± 8,24, respectively, $p<0.05$). Diagnosis of carditis (78.29% ± 2,18), polyserositis (94,44% ± 1,09) in patients older than 12 years were significantly more determined in the first year of the disease. While considering the remaining forms of the disease (SLE with APS, GV and VN), diagnosis from the first signs of the disease in the first year was 35.0 ± 3,35, 50% ± 8,42 and 56,41% ± 2,41, respectively, ($p<0.01$ - 0.05), which complicates the course and outcome of the disease.
Precede factors were - ARI (42.6%), hyperinsolation (28.7%), sore throat (11.6%), other factors of 3.9%, not connection was in 17 (13.1%) cases. In SLE mainly affecting the kidneys, one of the main trigger factors were acute respiratory infections (51.2%), followed by photosensitivity (23.0%), purulent tonsillitis as a prior factor was found in 10 children less frequently representing 12.8%, other factors were important in 2.7% of cases, and not established causes composed 10.3%. In polyserositis, a prior factor in the development of the disease in half of the cases was an acute viral infection (52.8%) and purulent infection and insolation was revealed equally often (21.1% and 20.8%, respectively). The prior factor in CNS in almost half of the patients (43.9%) was acute respiratory infection, and in third of the children - hyperinsolations (19.1%).
In patients with secondary APS and generalized vasculitis (GV), viral (62.5% (APS), 62.5% (GV)) and purulent infection (25.0% (APS), 33.3% (GV)) had fundamental importance. Hypothermia, physical and emotional overloads, vaccinations were noted among the other factors.
**Conclusions:** Clinical variants of the disease were established: with primary lesions of a heart and/or kidney, with generalized vasculitis and antiphospholipid syndrome. For carditis, polyserositis and nephritis main prior factors have been infection and hyperinsolation. For generalized vasculitis (95.8%) and a secondary APS (87.5%) infection was more important in triggering the disease.
**Disclosure of Interest:** None declared
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## SAT0324 HEADACHES IN PATIENTS WITH SLE – CLINICAL CHARACTERISTICS

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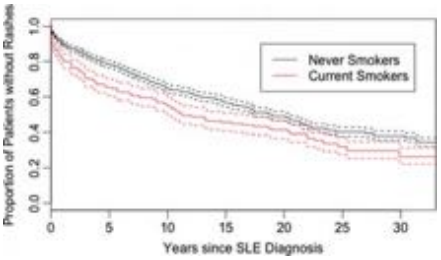
**Background:** According to different authors central nervous system involvement in SLE called neuropsychiatric SLE (NPSLE) varies widely. One of the manifestations of NPSLE is the headache. Although the latter is not included into the diagnostic criteria, its presence is a sign of disease activity. Lupus headache could presents as: migraine, tension, headache of intracranial hypertension, atypical and relapsing pattern.
**Objectives:** The objective of our study is to identify and characterize the lupus headache in SLE patients with different clinical characteristics.
**Methods:** 225 SLE patients were included in the study. They were divided in three groups: group I - 62,28% of the patients, with clinically manifested of neuropsychiatric symptoms, group II – 37,72%, with no clinical manifestations of NPSLE and group III – 25,78%, with incomplete SLE. The presence of lupus headache was diagnosed based on the 1999 ACR classification criteria and other possible causes for it have been excluded (untreated hypertension, infections, treatment regimen, etc.).
**Results:** Lupus headache was present in 52 (23,11%) of the studied patients. It was more common in the patients with clinically active NPSLE (group I) – in 41 (39,42%) of them. In 24 (58,54%) of them the headache had a tension characteristic and a duration from 10 minutes to 4 days. In 10 (24,39%) of them it had a characteristic of migraine. In the rest of the patients with lupus headache – 7 (17,07%), is was the only symptom in the absence of neurologic abnormalities, and in 2 of them (4,88%) retinal vasculitis has been diagnosed by direct ophthalmoscopy. The use of corticosteroids had good therapeutic effect in 87,80% of cases of lupus headache. In group II there were not patients with lupus headache. Lupus headache was demonstrated in 11 patients (18,97%) patients in group III. Lupus headache was more common in the patients with longer disease duration (p=0,047) or higher levels of matrix metalloproteinase 9 in the serum ($p<0,001$).
**Conclusions:** In the majority of the SLE patients the lupus headache has a tension characteristic. The use of corticosteroids has good effect in controlling this disease manifestation.

**Disclosure of Interest:** None declared
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## SAT0325 SMOKING IS ASSOCIATED WITH FUTURE LUPUS CUTANEOUS ACTIVITY IN PROSPECTIVE ANALYSES

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**Background:** Smoking is associated with increased disease activity in patients with systemic lupus erythematosus[1] (SLE) and cutaneous lupus erythematosus (CLE) in cross-sectional analyses.[2]
**Objectives:** We determined the associations between smoking status, cutaneous activity, and SLE disease activity among patients enrolled in a US-based SLE Cohort featuring a large African-American population.
**Methods:** The Hopkins Lupus Cohort was queried for demographic/clinical information and laboratory parameters between current smokers and never smokers among SLE patients. SLE patients that developed rash vs. those that did not (according to the SLEDAI criteria for rash) were compared with smoking status and the following co-variables: age, ethnicity, sex, ESR, urine protein/creatinine ratio, anti-Ro, anti-La, anti-DNA, Low C3, and Low C4.
**Results:** *Current smokers vs. never smokers.* Current smokers were significantly more likely than never smokers to have an active rash (49.58% vs. 36.31%, $p<0.0001$) and ESR $>20$ (63.25% vs. 52.75%, $p<0.0006$). Non-smokers were significantly more likely to have anti-Ro antibodies as compared to current smokers (32.62% vs. 26.44%) with no significant differences found in anti-La, urine protein/creatinine ratio, anti-dsDNA antibody, low C3 or low C4.
*SLE Patients who developed new rash during the course of follow-up vs. patients without rash.* SLE patients who developed a new rash were significantly more likely than SLE patients without a rash to have a younger age of SLE diagnosis (30.69 vs. 32.79, $p<0.0015$), higher SLEDAI continuous score (5.53 vs. 2.26, $p<0.0001$) and SLEDAI score $\geq 2$ (100% vs. 57.04%, $p<0.0001$), Urine protein creatinine ratio $>0.5$ (17.14% vs. 10.67%, p 0.0256), anti-dsDNA $\geq 10$ (36.12% vs. 23.78%, $p<0.0001$), low C3 $<79$ (28.1% vs. 20.08%, 0.0001) and low C4 $<12$ (20.49% vs. 12.86%).
*Association between smoking and new rash.* Smoking was significantly associated with new rash in SLE patients after adjusting for sex, ethnicity, and hydroxychloroquine use ($p<0.0001$). In addition, duration from SLE diagnosis to new rash were compared between current smokers and never smokers. Both non-parametric Kaplan-Meier curve and a parametric Weibull curve demonstrated current smokers developed rash significantly earlier than never smokers. Based on the Weibull distribution, the hazard of developing a rash is 40% higher among current smokers than never smokers, with the effect persisting after adjusting for sex and ethnicity.




**Conclusions:** Current smokers with SLE are significantly more likely than non-smokers to have an active rash. In addition, the hazard of developing a rash is 40% higher among current smokers than never smokers. SLE patients who developed rash as compared to patients that did not develop a rash had significantly increased SLE disease activity and several laboratory abnormalities including increased urine protein creatinine ratio $>0.5$ (17.14% vs. 10.67%, p 0.0256), anti-dsDNA $\geq 10$ (36.12% vs. 23.78%, $p<0.0001$), low C3 $<79$ (28.1% vs. 20.08%, 0.0001) and low C4.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5681

## SAT0326 EFFICACY AND SAFETY OF AUTOLOGOUS PLATELET LYSATE EYE DROPS IN SJÖGREN'S SYNDROME: A NEW APPROACH

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**Background:** Sjögren's Sydrome (SS) is a chronic multisystem autoimmune disease characterized by hypofunction of salivary and lacrimal glands. The result of the immune-mediate infiltration of the lacrimal gland is a severe dry eye disease. None of the commercially available artificial tear preparations and anti-inflammatory topical treatment has the properties of the human tears as Growth factors (GFs), that are necessary for maintenance of normal corneal epithelium. Platelet alfa granules are a major source of GFs and are rich in platelet derived growth factor (PDGF), which plays an important role in the maintenance of ocular surface and tear film stability (1).
**Objectives:** To determine the efficacy and safety of autologous platelet lysate (APL) eye drops in patients with primary SS dry eye, refractory to standard therapy, in comparison to patients treated with artificial tears. We focused on the effect of APL on cornea morphology with the in vivo confocal microscopy (IVCM).
**Methods:** We included patients with a diagnosis of SS according to the classification criteria of the American-European Consensus (2), a dry eye severity level $\geq 2$ (Dry Eye Severity Grading Scheme, Workshop 2007). Patients were assigned in two groups, according to the randomization criteria 1:1
– Group A used autologous platelet lysate (BiomedDevice) QID for 90 days.
– Group B used preservative-free artificial tears QID (Ialuronic Acid 0,2%) for 90 days.
Ophthalmological assessments included: ocular surface disease index (OSDI), Schirmer test, fluoresceine score and break up time (BUT). Both Group A and Group B underwent IVCM; corneal basal epithelium, sub basal nerves, Langherans cells, anterior stroma activated keratocytes were evaluated. The study was conducted in accordance with the Declaration of Helsinki (1964) and approved by our Ethics Committee.
**Results:** 43 patients (female:male =42:43) with mean age of 59,75 years (SD±13,10) affected by primary SS from 7,48 years (SD±5,56) were enrolled. The two groups (A=22 pts; B=21 pts) did not have significant differences at baseline in terms of disease (duration, autoantibodies) and treatment (steroids, DMARDs) characteristics. In group A, the mean of improvement of OSDI, fluorescein score and BUT values ($\Delta$38.82; $\Delta$1.0; $\Delta$1.5 respectively) were higher than group B ($\Delta$7.07; $\Delta$0.0; $\Delta$0.0 respectively) with statistical significance ($p<0.05$). The IVCM showed a significant increase in basal epithelium cells density, sub basal nerve plexus density and number and a decrease in Langerhans cells density ($p<0.05$) only in group A. No adverse events were observed in all patients treated.
**Conclusions:** APL has proved to be effective and safety in the treatment of SS dry eye and IVCM seems to be a useful tool to visualize cornea morphologic modifications. Further studies are required to evaluate the long-term effects and the timing of retreatment.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5217

## SAT0327 B CELL-BOUND COMPLEMENT ACTIVATION PRODUCTS IN THE DIAGNOSIS AND MONITORING OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by diverse pathogenic autoantibodies and clinical phenotype. Laboratory monitoring of complement activation products (CAP; C3a, C5a, C3d, C4d) is commonly used in diagnosis and follow up. CAP bound to cellular surfaces (CB-CAP) analysed by flow cytometry offer a relatively novel approach to study complement turnover in SLE.
**Objectives:** We evaluated the significance and usability of cell bound CAP in monitoring complement turnover in a whole blood staining approach, comparing cell bound CAPs on different leucocyte subpopulations with conventional complement and disease activity parameters.
**Methods:** CAP bound to lymphocyte subpopulations were analysed by flow cytometry, compared to serological complement and other SLE activity parameters determined by nephelometry, rocket electrophoresis and ELISA.
**Results:** We have analysed CB-CAPs bound to lymphocytes in 50 adult patients with SLE. B-cells and CD4+ T-cells of SLE patients showed significantly

higher levels of cell-surface-bound C4d compared to controls. C4d bound to B-lymphocytes was inversely correlated with serum levels of C4 (r = -0.309, p=0.013) and C3 (r= - 0.356, p=0.004) reflecting complement decay. In addition, B-cell C4d showed a significant positive correlation with anti-dsDNA antibody levels (r =0.574, p<0.001) and plasma C3d (r =0.319, p=0.009) thereby corresponding to disease activity. CB-CAPs were stable over 24 hours after blood drawing thus offering more flexibility in sample handling than conventional complement turnover assays.
**Conclusions:** Our data show that CB-CAP measurement correlates with established disease activity markers, and given its easier handling, is of possible utility in routine diagnostic and monitoring of patients with SLE. A multicentre study for evaluation of this method in a cohort of paediatric patients is planned.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5672

### SAT0328 BIG-FIVE PERSONALITY IN SJOGREN SYNDROME – ASSOCIATION WITH ESSPRI

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**Background:** The severity of symptoms of dryness, pain and fatigue may be determined by psychological features patients with Sjogren's syndrome (SS). The Big-Five framework is a widely examined model which represent personality at the broadest level of abstraction. The NEO Personality Inventory-Revisited (NEO-PI-R) is frequently used questionnaire to assess the Big-Five domains: Neuroticism (*N*), Extraversion (*E*), Openness to Experience (*O*), Agreeablenes (*A*) and Conscientiousness (*C*).
**Objectives:** To Big-Five analyse of personality of SS patients and association with the severity of dryness, pain and fatigue measured by ESSPRI (EULAR SS Patient Reported Index).
**Methods:** One hundred and five patients with confirmed SS by AECG criteria (mean age 51,34 years, mean disease duration 5,98 years) and fifty-four healthy controls (mean age 51,35 years) participated in study. All participants were females and provided written informed consent. The diseasy activity was measured by ESSDAI (EULAR SS disease activity index) and ESSPRI. All participants filled out the sociodemographic questionnaire (age, educational level, work and marital status, residence, social support and comorbidity). The Big-Five personality traits were measured using NEO-P-R. The 240 items are answered on a 5-point Likert scale ranging from strongly disagree to strongly agree. The analysis was performed using the SPSS program (version 16.0). Data were examined by independent *t*-test, Chi-square test and Mann-Whitney test. The association of the Big Five personality traits with the ESSPRI was examined using linear regression analyses. A p-value $<0.05$ was considered significant.
**Results:** Statistical significant differences between two groups were observed in educational level (p=0.001), work status (p=0.001), residence (p=0.001) and social support (p=0.05), but they did not different in age, marital status and comorbidity (p>0.05). In SS patients, the median of ESSDAI was 6 (range 4–11), the median ESSPRI was 5.33 (range 3.66–6.66). Compared to healthy controls, SS patients showed significatly higher scores in *N* (94.76 vs. 84.63, p=0.006) and lower *E* (94.79 vs.104.20, p=0.002) and *O* (101.86 vs. 111.17, p=0.05) domens. Scores *A* and *C* were similare in groups (120.48 vs 121.04 and 122.97 vs. 125.02, p>0.05). Futher, *E* and *O* domens were significantly associated with ESSPRI (p=0.008, p=0.000), while *N* was borderline (p=0.056). After adjustment for confounding variables, only *E* domen remained significantly associated with ESSPRI (p=0.01). The analyse showed that *E* domen was negatively associated with age (B= -0.341, p=0.013), unmarital status (B= -4.317, p=0.013) and positive associated with social support (B=7.952, p=0.013).
**Conclusions:** Patients with SS had a higher levels of Neuroticism and lower levels of Extraversion and Opennes to experiences compared to healthy persons. In SS patients, Extraversion and Openness were associated with severity of symptoms of dryness, pain and fatigue. The social support is significantly associated with higher level Extraversion, in contrast to older and single individuals.
**Disclosure of Interest:** None declared
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### SAT0329 LUPUS NEPHRITIS IS ASSOCIATED WITH MORE CORTICOSTEROID-ASSOCIATED ORGAN DAMAGE BUT LESS CORTICOSTEROID NON-ASSOCIATED ORGAN DAMAGE

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**Background:** Lupus nephritis (LN), one of the most serious manifestations of systemic lupus erythematosus (SLE), has been suggested to be a predictor of organ damage accrual. Also, LN is considered a strong determinant for survival. Since patients with LN are more exposed to immunosuppressive agents, such as cyclophosphamide and high-dose corticosteroid, and also have high inflammatory burdens, they might be more vulnerable to organ damage than patients without LN. Thus, proper adjustment for these potentially confounding variables needs to be performed to determine the precise effect of LN on organ damage. Also, it is important to identify the types of organ damage that are associated with LN. However, these aspects have not been previously investigated.
**Objectives:** We investigated the impact of LN on organ damage accrual and mortality after adjusting for potential confounders. In particular, we identified the types of organ damage that are more or less associated with LN.
**Methods:** Patients with SLE were propectively enrolled and followed from 198 to 2012 in the Hanyang BAE Lupus cohort. LN was defined as the disorder with the persistent proteinuria greater than 0.5 grams per day Organ damage was assessed using SLICC/ACR Damage Index (SDI). Damage presumed to be corticosteroid associated (cataract, avascular necrosis, diabetes and osteoporosis items) and non-associated (5 pulmonary, 5 gastrointestinal, erosive arthritis, 3 skin, premature gonadal failure and malignancy items) selected from 41 items were compared. Association of LN with organ damage was analyzed using multivariable logistic regression analysis, adjusting for potential confounders. Age- and sex adjusted standardized mortality ratio (SMR) was evaluated in patients with or without LN.
**Results:** Among the 1,112 SLE patients, 515 (46.3%) had LN. Patients with LN showed higher percentage of male (p=0.003), were younger at diagnosis (p<0.001), had longer disease duration (p<0.001), higher adjusted mean SLE Disease Activity Index (AMS) score (p<0.001), lower percentage of prescribed anti-malarial agents (p<0.001), and higher percentage of corticosteroids (p<0.001) and immunosuppressant use.
After mean follow-up of 7.6 years, patients with LN had higher percentage of overall organ damage than patients without LN (51.5% vs 35.7%, p<0.001) with OR of 1.40, after adjusting for age at diagnosis, gender, disease duration, anti-malarial agents, corticosteroids and immunosuppressant. However, LN was not associated with non-renal organ damage (p=0.883). In subgroup analysis, the odds of corticosteroid-associated damage was higher in patients with LN (2.06, 95% CI 1.43–2.96), but whereas odds of non-associated damage was lower in patients with LN (0.50, 95% CI 0.35–0.75), compared not having LN.
Age- and sex adjusted SMR of patients with LN was 5.17 (95% CI 3.49–7.38) and 2.32 (95% CI 1.47–3.48) in patients without LN.
**Conclusions:** LN was associated with more overall organ damage but not more non-renal organ damage. Patients with LN had more corticosteroid-associated damage, but less corticosteroid non-associated damage compared with patients without LN. Additionally, the SMR of patients with LN was significantly higher than the SMR of patients without LN
**Disclosure of Interest:** None declared
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## Vasculitis

### SAT0330 EFFECTIVE AND RAPID TREATMENT OF FLARES IN PATIENTS WITH BEHÇET'S DISEASE BY THE SINGLE CHAIN ANTI-TNF ANTIBODY DLX105

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**Background:** Behçet's Disease is a rare, chronic variable vessel vasculitis presenting with oral and genital aphthous lesions, a variety of skin symptoms, arthritis and depending on its severity with uveitis, CNS and GI symptoms. Most often used drugs are colchicine, corticosteroids, azathioprine and cyclosporine. TNF inhibitors are used off-label (only in Japan approved) in particular for patients with uveitis to prevent blindness. Usually given TNF inhibitors are infliximab and adalimumab. These monoclonal antibodies are large molecules and as such they do not penetrate well into tissues following systemic administration.
We explored the clinical effect of a single chain anti-TNF antibody fragment (DLX105) consisting of 246 amino acids (molecular weight: 26 kDa) for flaring mucocutaneous Behçet's Disease.
**Objectives:** The primary objective of this study was the describe the pharmacokinetics of DLX105 after a single fixed dose in patients with Behçet's Disease. The exploratory objective was to explore the preliminary efficacy of a single fixed dose of DLX105 on mucocutaneous lesions in patients with Behçet's Disease.
**Methods:** A total of 6 patients with flaring Behçet's Disease received a single dose of 10 mg/kg i.v. DLX105. The main inclusion criteria were: males and females aged 18 to 65, with flaring Behçet's Disease defined by the criteria of the "International Study Group for Behçet's Disease (ISBD)" with at least two oral ulcerations for at least 3 days prior to enrollment. Patients were allowed to be on colchicine or low dose corticosteroids (≤7,5 mg/d). After a dosing visit (Day1) all patients attended two follow-up visits (Day 5 and 8) and an end-of-study-visit (Day 15).
**Results:** Each patient had oral lesions at baseline (mean 3.7 ulcers, SD 2) which rapidly and almost completely disappeared within one week (mean 1 ulcer, SD 1.3) and stayed improved even after 2 weeks (mean 1.5 ulcers, SD 1). Genital lesions in one patient also resolved. Two patients with erythema nodosum showed a prompt and complete disappearance of skin nodules after one week of treatment. The number of papulo-pustular skin lesions in 5 patients also rapidly declined (mean 14.3 at baseline, after one week 7.2). Arthralgia present in 3

patients resolved within one week of treatment. The ISBD questionnaire score (range 0–12) dropped from 4.3 to 3.3 within one week and to 3.0 within two weeks indicating a sustained response. There were no SAEs and adverse events were mild and disappeared within 2 weeks.
**Conclusions:** These data suggest that DLX105 has a rapid and strong onset of action likely due to its unique property to penetrate effectively into inflamed tissues. The duration of the response is far longer than its serum pharmacokinetics with a half-life of roughly one day suggested. Thus, DLX105 is a strong development candidate to treat flaring mucocutaneous Behçet's Disease.
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## SAT0331 ITNFα AGENTS IN REFRACTORY NON-INFECTIOUS AORTITIS: STUDY ON 19 PATIENTS

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**Background:** Non-infectious aortitis is often refractory to standard immunosuppressive therapy. In these cases, the use of inhibitors of TNF-α (iTNF-α) had been reported.
**Objectives:** Our aim was to assess the efficacy of iTNF-α in a series of patients with refractory non-infectious aortitis.
**Methods:** Retrospective multicenter study of patients diagnosed with aortitis refractory to traditional immunosuppressive agents and who received iTNFα. The diagnosis of aortitis was based on imaging techniques (MRI-angiography, computed tomography, PET scan, ultrasonography and/or arteriography).
**Results:** We studied 19 patients (15 women/4 men) with a mean age of 42±13 years. The iTNFα used were: infliximab (IFX) (n=14), adalimumab (ADA) (n=3) and etanercept (ETN) (n=2). The underlying conditions were: Takayasu arteritis (TA) (n=11), giant cell arteritis (GCA) (n=2), relapsing polychondritis (RP) (n=1), ulcerative colitis (n=1), Crohn's disease (n=1), Behçet's disease (n=1), sarcoidosis (n=1) and psoriatic arthritis (n=1). Seventeen patients were previously treated with traditional immunosuppressive agents [methotrexate (MTX) (n=15), azathioprine (AZA) (n=7), cyclophosphamide (CPM) (n=5), mycophenolate mofetil (MM) (n=3), chlorambucil (n=1), cyclosporine A (n=1), tacrolimus (n=1)]. Two patients needed a switching between biologic agents (a female with TA who switched from IFX to ETN; and a male with psoriatic arthritis who switched from ETN to ADA; in both cases switching was due to inefficacy of the first biologic drug). After a median follow-up of 16 [12–36] months, most patients experienced clinical improvement, showing a reduction of erythrocyte sedimentation rate from 37.5 [30–56] mm/1st hour at baseline, to 20.5 [10–24] mm/1st hour at the last visit. Besides, C-reactive protein decreased from 1.5 [0.1- 2.6] mg/dL to 0.3 [0.1–0.8] mg/dL. After 3 months of treatment, 55% of patients had experienced clinical improvement ($p<0.01$); and at 12 months, clinical improvement was attained by 94% of the patients ($p<0.01$). A corticosteroid sparing effect was also achieved (from 25.7±22.0 mg/day of prednisone at iTNFα onset, to 6.6±5.4 mg/day at the last visit). Improvement on imaging techniques was also observed in 10 out of 13 patients (77%) who underwent a follow-up imaging procedure. Three patients had to discontinue the iTNFα agent (IFX in the 3 cases) due to inefficacy (n=1), recurrent pneumonia (n=1) and severe infusional reaction (n=1).

**TABLE**

| | At onset | At 3 months | At 6 months | At 12 months |
|---|---|---|---|---|
| CRP, median [IQR] | 1.5 [0.1-2.6] (15) | 0.1 [0.1-0.5] (12)* | 0.3 [0.1-0.9] (12)* | 0.2 [0.1-0.6] (11)* |
| ESR, median [IQR] | 37.5 [30-56] (14) | 17.5 [9-25] (14)* | 16 [9-20] (13)* | 16 [11-18] (13)* |
| Prednisone dose, median [IQR] | 20 [5-50] (17) | 12.5 [5-20] (15)* | 10 [5-10] (16)* | 7.5 [5-10] (16)* |

In brackets, the number of patients with available data.
*p≤0.05
"p" refers to the percentage of improvement at 3, 6 and 12 months compared to baseline

**Conclusions:** iTNFα therapy appears effective and relatively safe in patients with non-infectious aortitis refractory to traditional immunosuppressive drugs.
**Acknowledgement:** This study was supported by a grant from "Fondo de Investigaciones Sanitarias" PI12/00193 (Spain). This work was also partially supported by RETICS Programs, RD08/0075 (RIER) and RD12/0009/0013 from "Instituto de Salud Carlos III" (ISCIII) (Spain).
**Disclosure of Interest:** None declared
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## SAT0332 TAKAYASU ARTERITIS (TA): THE PATHOLOGICAL CHANGES IN THE CORONARY ARTERIES

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**Background:** There is controversy surrounding the prevalence of abnormalities of the coronary arteries (CA) in TA. A Japanese institute (1) reported 38.3% of CA involvement in TA. Sun T. et al. (2) estimated the prevalence of CA lesions at 7, 7% in 587 patients hospitalized with TA.
**Objectives:** To investigate the variants of pathological findings in the coronary arteries in autopsy cases of TA.
**Methods:** Microscopic examinations of the coronary arteries were performed in sixty fatal cases (52 men and 8 women aged 18 to 45 years) of TA over period of 11 years. The median age at disease onset was 25, 7 years.
**Results:** The second-leading cause of death from TA was acute heart failure due to myocardial infarction (25%). Pathological changes in the coronary arteries have been found in 46 cases (76, 7%) of TA. The predominant lesions were on the coronary orifices, or more rarely, in the proximal parts of CA. The most remarkable finding was intimal hyperplasia consists of areas of musculo-fibrous proliferation or multi-layer scleral hyaline plaques. This pillow-like thickening of the intima around of the coronary orifices leads to their luminal narrowing. No morphological abnormalities were observed in the distal parts of CA. In the studied material we found the features of granulomatous arteritis with diffuse or focal infiltration of lymphocytes, plasma cells, histiocytes. Infiltrate being preferentially located in the medio-adventitial junction and also around the vasa vasorum of the adventitia. Contrary to other studies giant cell granulomatous reaction has not been detected in any specimen. Complete obliteration of the arterial lumen with recanalization of organized thrombi has been presented in 13 cases of TA complicated by fatal acute myocardial infarction. Coronary atherosclerosis of varying severity was observed in 35 cases (58, 3%). The most common location of atherosclerotic deposits was regions of the pillow-like thickening of the intima around of the coronary orifices. In two patients, a 30-year-old man and a 35-year-old man, typical for TA changes accompanied by severe atherosclerotic narrowing of the coronary arteries resulted in a fatal myocardial infarction.
**Conclusions:** Our date show high frequency (76, 7%) of pathological changes of CA in TA. It can be assumed that intimal hyperplasia, granulomatous arteritis, and coronary atherosclerosis are typical lesions of CA in TA. The coronary orifices are the site most commonly affected by TA. Luminal narrowing of CA with coronary flow reduction led to subsequent fatal myocardial infarction in 15 cases (25%). High prevalence of coronary atherosclerosis in TA (58, 3%) may be regarded as accelerating the atherosclerotic process due to chronic autoimmune inflammation in CA. In addition, it should be noted that in our series of autopsy cases of TA, males (86, 7%) were most frequently affected compared with results other investigations.
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**Disclosure of Interest:** None declared
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## SAT0333 HEMOSTATIC MECHANISMS MAY PLAY A ROLE IN THE DEVELOPMENT OF THROMBOSIS IN MALE PATIENTS WITH BEHCET'S DISEASE: A THROMBOELASTOGRAPHIC ANALYSIS

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**Background:** In Behcet's disease (BD), vascular involvement is seen frequently in young male BD patients. However, its reason is not well known.
**Objectives:** Our aim was to compare thrombotic tendency according to gender by using the modified Rotational Thromboelastography parameters and platelet-leucocyte complex levels.
**Methods:** 126 BD patients (71 male, 55 female; mean age:41±9 yrs) who met ISSG criteria for Behcet's disease were included into study. This group was divided into 3 subgroups as non-thrombotic (n=73), acute thrombotic (n=25) and chronic thrombotic group (n=28). As disease control and healthy control group, 23 patients with vasculitis (16 female, 7 male; mean age 49±16 yrs), 8 patients with thrombosis (3 female, 5 male; mean age:55±11 yrs) and 25 healthy individuals (11 female, 14 male; mean age:37±10 yrs) were included to study.

By using the modified rotation thromboelastogram, clotting time (CT), clot formation time (CFT) and maximum clot formation (MCF) were determined by INTEM and EXTEM analysis. Thrombocyte-leucocyte complexes and thrombocyte activation marker (p62) were investigated by flow-cytometric method.
**Results:** In terms of thrombocyte-leucocyte complexes and P62 levels, no significant difference was found in female BD patients vs male BD pts, active BD pts vs inactive BD pts and thrombotic BD pts vs non-thrombotic BD pts. Thrombocyte-leucocyte complexes levels were higher in vasculitis group than BD group ($p<0.01$) and HC group ($p<0.04$). I-MCF was significantly prolonged in male BD patients than female BD patients. E-CFT was found to be shorter in male BD patients compared to female BD patients. E-MCF was statistically prolonged in male BD patients. In inactive male BD patients, while I-CFT was shorter than HC individuals, I-MCF and E-MCF were statistically prolonged than HC ($p<0.02$, $p<0.03$), respectively. However, No significant differences were found between inactive female BD patients and HC in terms of all ROTEM parameters. In active BD patients, E-CFT was shorter ($p<0.02$) and E-MCF was significantly prolonged than those of inactive BD patients ($p<0.005$).
**Conclusions:** These results support that male BD patients have a hypercoagulable state compared to female BD patients which may be an explanation why male patients are prone to thrombotic complications.
**Disclosure of Interest:** None declared
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## SAT0334 NATIONWIDE TRENDS IN HOSPITALIZATION AND IN-HOSPITAL MORTALITY ASSOCIATED WITH ANCA-ASSOCIATED VASCULITIS (AAV)

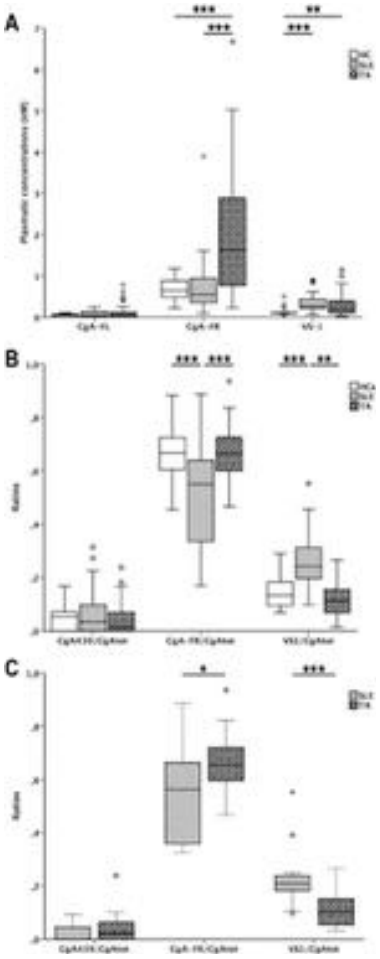
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**Background:** ANCA-associated vasculitis (AAV) is associated with severe end-organ damage (e.g., renal failure) and treatment-related complications (e.g., severe infection) which often lead to hospitalization. However, no data on recent hospitalization trends and associated mortality are available[1].
**Objectives:** We evaluated recent trends in nationwide hospitalization, cost, and in-hospital mortality among patients with AAV.
**Methods:** We used the National Inpatient Survey (NIS) which is the largest all-payer inpatient database in the US. We studied all hospitalizations with a discharge diagnosis of AAV (ICD 9: 446.4) between 1993 and 2011. We investigated trends in hospitalization, cost, and mortality by comparing AAV to overall inpatient hospitalization trends. Analyses were performed using hospital-level sampling weights provided by the NIS to obtain US national estimates.
**Results:** From 1993 to 2011, the rate of hospitalization for AAV increased from 1.9/100,000 persons to 4.5/100,000 persons (P-for-trend $<0.0001$). This was primarily driven by a rapid increase in the hospitalization rate among those with a secondary discharge diagnosis of AAV (1.4/100,000 persons to 3.9/100,000 persons, $P<0.0001$). Over the study period, there was a significant decline in in-hospital death from 9.9% (±1.2%) in 1993 to 3.5% (±0.4%) in 2011 (P-for-trend $<0.0001$). Overall, the annual relative change in AAV mortality was - 4.8% (95% CI: -5.6 to -4.0%). This was a significantly greater decline than overall US inpatient hospitalization mortality (-2.18%, 95% CI -2.19% to -2.17%). Infection was the most common principal diagnosis when AAV was a secondary diagnosis.
**Conclusions:** Between 1993 and 2011, there was a significant decline in in-hospital mortality among those admitted with a diagnosis of AAV. This decline was significantly greater than that of the overall US in-hospital mortality rate. The declining in-hospital mortality rate may be due to earlier recognition of GPA, shifts in treatment that emphasize less cyclophosphamide use and more tempered use of glucocorticoids, and secular trends in the management of infections and end-organ complications[2].
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5833

## SAT0335 DIFFERENTIAL MODULATION OF THE CHROMOGRANIN-A SYSTEM IN TAKAYASU ARTERITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Chromogranin-A (CgA) is a multi-source protein proteolitically processed into a family of peptides with various paracrine and endocrine functions. CgA-derived peptides influence vascular biology and neoangiogenesis: CgA1–439 (CgA439) and vasostatin-1 (VS1, CgA1–76) have anti-angiogenic properties, while fragments lacking the C-terminal domain (CgA-FRs) are pro-angiogenic. The mechanisms regulating vascular events and systemic inflammation in Takayasu Arteritis (TA) and Systemic Lupus Erythematosus (SLE) are poorly characterized.
**Objectives:** To evaluate how the CgA system is modulated in TA and SLE
**Methods:** 42 consecutive patients (pts) with TA were enrolled and matched with 20 age- and sex- matched SLE pts and 20 healthy subjects (HCs). Exclusion criteria were moderate/severe heart failure or contraindication to MR angiography (MRA). TA pts were longitudinally studied with 2 MRAs (12 months apart). Disease activity was assessed with NIH criteria and SLEDAI in the TA and SLE group, respectively. Arterial progression was defined as the appearance of new lesions or worsening of pre-existing lesions at MRA. CgA peptides and total CgA (CgAtot) were quantified with validated ELISAs. CgA processing was studied by ratios of CgA peptides to CgAtot. The antiangiogenic CgA potential was quantified in TA by summing the ranks of CgA439 and VS1.
**Results:** Median age of TA patients (39W, 3M) was 46 (IQR 34–54) years. Median disease duration was 10 (IQR 7–14) years for TA, and 13 (7–21) years for SLE. Twelve TA and 8 SLE pts had active disease. Thirty TA and 10 SLE pts received proton pump inhibitors (PPI), which are known to increase CgA levels. Nine TA pts (8 treated with PPIs) underwent arterial progression. Serum CgA-FR were significantly higher in TA pts than in SLE pts ($p<0.001$) and HCs ($p<0.001$); VS1 was higher in SLE and TA than HCs ($p<0.001$ and $p=0.020$, Fig 1A). CgA processing was similar in TA and HCs; a distinctive processing was evident in SLE, with higher VS1/CgAtot ($p<0.001$ Vs Ta and HCs) and lower CgA-FR/CgAtot ($p=0.001$ Vs TA and 0.009 Vs HCs, Fig 1B). PPI increased serum CgA-FR, with a greater effect in TA, and quenched of the distinctive SLE-associated processing (Fig 1C). CgA peptides did not correlate with disease activity in TA nor in SLE. However, in the homogeneous group of TA pts on PPI, arterial progression was associated with reduced a reduced antiangiogenic CgA potential ($p=0.010$).




**Conclusions:** A selective processing of CgA is evident in SLE, whose molecular bases are unknown. TA associates with a greater increase in CgA-FR levels than SLE during PPI therapy. CgA peptides do not correlate with disease activity. Antiangiogenic CgA potential is reduced in TA pts on PPI undergoing progression, underlining the importance of angiogenesis in arterial remodelling and suggesting an involvement of CgA peptides in TA pathogenesis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6062

## SAT0336 DAMAGE-ASSOCIATED MOLECULAR PATTERNS IL-33 AND HIGH-MOBILITY GROUP BOX 1 AMPLIFY INFLAMMATORY PROCESSES IN GRANULOMATOSIS WITH POLYANGIITIS

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**Background:** Granulomatosis with polyangiitis (GPA) is characterized by extravascular necrotizing granulomatous inflammation and systemic anti-neutrophil cytoplasmic autoantibody (ANCA) – associated vasculitis. The pathogenic mechanisms, especially of the granulomatous inflammation, are still not fully understood. Cell death and tissue damage could be a driving force for chronic inflammation in GPA.
**Objectives:** To investigate the role of the damage-associated molecular patterns (DAMPs) IL-33 and high-mobility group box 1 (HMGB1) in the granulomatous inflammation of GPA.
**Methods:** Tissue expression of HMGB1, IL-33 and their corresponding DAMP receptors "receptor for advanced glycation end products" (RAGE) and "suppression of tumorigenicity 2" (ST2), respectively, were analyzed in nasal GPA biopsies compared to chronic rhinosinusitis (CRS) by immunostaining. Circulating soluble RAGE (sRAGE) and soluble ST2 (sST2) were measured in GPA sera compared to CRS or healthy controls (HC) using ELISA. Expression of HMGB1 and the autoantigen proteinase 3 (PR3) in nasal GPA tissues and on isolated neutrophils was determined by immunofluorescence staining. Full-length IL-33 was cleaved *in vitro* by either activated, necrotic or NETotic neutrophils. The biological activity of these IL-33-cleavage fragments was tested by subsequent stimulation of human mast cells (HMC-1). The resulting activation of mitogen-activated protein kinases (MAPK) was determined by western blot.
**Results:** Increased tissue expression of extranuclear HMGB1 ($p<0.01$) and strong upregulation of RAGE was observed in the necrotizing granulomatous inflammation compared to CRS. In addition, substantial numbers of IL-33 and ST2 expressing cells were found in close proximity to necrotic areas and lymphoid structures in the granulomatous inflammation compared to CRS. However, neither sRAGE nor sST2 were elevated in GPA sera compared to controls. In GPA tissue co-localization of HMGB1 and PR3 was detected on neutrophils. This co-localization could be induced on isolated neutrophils by apoptosis *in vitro*. Full-length IL-33 was processed by activated, necrotic or NETotic neutrophils into different cleavage products. IL-33 fragments produced by necrotic GPA neutrophils induced a significantly stronger MAPK activity in HMC-1 compared to those from HC.
**Conclusions:** In this study, we demonstrate a direct link between dying neutrophils and necrosis-derived DAMPs HMGB1 and IL-33 in the granulomatous inflammation of GPA. Differential cleavage of IL-33 by dying neutrophils, IL-33-dependent MAPK activation and high tissue expression of RAGE and ST2 suggest a considerable role of these DAMPs in sustaining chronic inflammation in GPA. Moreover, HMGB1/PR3 co-localization on apoptotic neutrophils reveals a possible adjuvant function of HMGB1 for the autoimmune response against PR3.
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## SAT0337 HYPERTROPHIC PACHYMENINGITIS ASSOCIATED WITH ANCA VASCULITIS; A CASE SERIES OF 16 PATIENTS

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**Background:** Recent reports indicate that hypertrophic pachymeningitis (HPM) develops in association with myeloperoxidase (MPO) anti-neutrophil cytoplasmic antibody (ANCA)-positive vasculitis[1,2]. However, little is known about clinical features and outcomes of the disease.
**Objectives:** We aimed to describe clinical, laboratory and radiological features and treatment course of HPM occurred in patients with ANCA-associated vasculitis (AAV).
**Methods:** We retrospectively analyzed 16 Japanese adult patients (11 males and 5 females), who had been treated at our hospital in a study period from January 2006 through December 2015. Diagnosis of HPM was made with MRI T1 sequence with gadolinium by detecting thickening and enhancing of brain and/or spinal dura mater in patients manifesting neurological symptoms. Diagnosis and classification of AAV was performed according to a report by Watts, et.al.[3].
**Results:** The mean age at HPM onset was 60.1 years (range, 35–78 years). Out of 16 patients, HPM was detected at the onset of AAV in 9 (56.3%), at the relapsing AAV under treatment in 6 (37.5%), and before the diagnosis of AAV as idiopathic HPM in 1 (6.3%). Headache and cranial nerve palsy due to HPM were observed in 13 (81.3%) and 11 (68.8%) patients, respectively. Otitis media and sinusitis were found as complications of AAV in 7 (43.8%) and 6 (37.5%) patients. Twelve patients (75%) were classified as granulomatosis with polyangiitis (GPA). Microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis and unclassifiable vasculitis were applied to 2 (12.5%), 1 (6.3%) and 1 (6.3%) patients, respectively. Serum myeloperoxidase (MPO)-ANCA and proteinase 3 (PR3)-ANCA were positive in 9 (56.3%) and 5 (31.3%), respectively, and 2 (12.5%) patients had neither of them. The mean serum C-reactive protein levels were 4.87 mg/dL (range, 0.26–17.11 mg/dL). Spinal fluids were analyzed in 6 patients, and a mild increase in spinal cell counts and protein levels were identified in 3 patients each. With MRI, thickening of dura mater in cranial fossa and tentorium cerebelli were found in 11 (68.8%) and 9 (56.3%) patients, respectively. All patients were treated with corticosteroids and 10 (62.5%) patients were concomitantly administered with other agents including cyclophosphamide, methotrexate, azathioprine and mizoribine for remission induction. All patients achieved remission of the neurological symptoms and improvement of dura mater thickening. In a mean follow-up period of 41.8 months (range, 5–89 months) after diagnosis, 4 (25%) patients experienced a relapse of HPM and received re-induction therapy.
**Conclusions:** Our results indicate that occurrence of HPM is mostly associated with GPA having either type of ANCA serology. Dura mater in cranial fossa and tentorium cerebelli was commonly involved, which could lead to cranial nerve impairment. Immunosuppressive therapy is effective, but a relapse of HPM occasionally occurs.
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## SAT0338 CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WITH CHRONIC PERIAORTITIS

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**Background:** Chronic periaortitis (CP) is rare disease that involves the aorta which is characterized by a fibro-inflammatory periaortic cuff in imaging studies and adventitia-predominant inflammation and fibrosis in histopathology. Associations between aortitis and idiopathic retroperitoneal fibrosis, inflammatory abdominal aortic aneurysm had been reported, and this spectrum of disorders is now categorized as CP. CP has aroused controversy on the question of incorporating it into the spectrum of primary large vessel vasculitis. Recent investigations have documented significant overlap between CP and the newly recognized systemic inflammatory disorder known as IgG4-related disease (IgG4-RD), suggesting that at least a fraction of cases of CP might be IgG4-RD.
**Objectives:** The aim of this study is to investigate clinical characteristics and treatment outcomes of patients with CP.
**Methods:** A retrospective review was performed on 2,496 patients who visited Samsung Medical Center between January 2004 and December 2014. Patients compatible with CP based on characteristic imaging findings of fibrosclerosing encasing lesions around the aorta were enrolled. The clinical, radiological, histopathological features, treatments and outcomes of patients were analyzed. Additionally, patients were further classified into two subgroups: IgG4-related and non IgG4-related CP according to the comprehensive diagnostic criteria for IgG4-RD proposed by a Japanese study, and comparison of the subgroups was performed. Patients without an initial serum IgG4 level or with a history of prior treatment were excluded from this analysis.
**Results:** A total of 61 patients with CP were identified. Patients showed a male predominance with the median age of 61 at diagnosis. The abdominal aorta was the most commonly involved site (84%), and half of the patients had aortic lesion confined to the abdominal aorta without involvement of the thoracic aorta. The thoracic aorta was involved in 46% of patients. Only 2 (3%) patients had stenotic lesions of the aorta, while 19 (31%) patients had aneurysmal changes of the aorta. Ureteral obstruction was found in 30% of patients. 49 (80%) patients received glucocorticoids with a median initial dose of 50 mg per day as prednisolone. 19 (31%) patients received additional immunosuppressant including azathioprine, methotrexate and mycophenolate. Nine patients underwent vascular surgery including seven cases of surgical abdominal aorta aneurysm repair, two cases of aortic valve replacements and four patients underwent endovascular abdominal aneurysm repair during their disease course. Overall 60% of patients achieved remission without relapse during the course. When the Japanese criteria for IgG4-RD were applied to patients, ten were classified as IgG4-related and twenty-five as non IgG4-related. The overall male predominance did not differ and there were no significant differences in clinical features, treatments and outcomes between two groups, with the exception of older age (median 69 vs. 59 years, $p=0.021$), higher serum globulin, IgG and IgG4 levels and greater pancreas involvement in IgG4-related patients (30% vs. 0%, $p=0.018$).
**Conclusions:** We identified 61 patients with CP. Further integrated investigations into pathogenesis, practical diagnostic criteria and markers for disease activity and prognosis are warranted.
**Disclosure of Interest:** None declared
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## SAT0339 THE EFFICACY OF THE 2015 EULAR/ACR RECOMMENDATIONS FOR THE MANAGEMENT OF POLYMYALGIA RHEUMATICA IN JAPANESE PATIENTS

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**Background:** Glucocorticoids (GCs) are effective for polymyalgia rheumatica (PMR); however, some patients show inadequate responses to initial GC doses or relapses during GC tapering and develop side effects of GCs. The 2015 EULAR/ACR recommendations for the management of PMR has been proposed very recently, in which early introduction of methotrexate (MTX) in addition to GCs was recommended for such GC-resistance or -intolerance[1)]. Similarly, we have used MTX frequently for PMR patients with relapse, prolonged GC therapy and high risk of GC adverse effects.
**Objectives:** To examine the efficacy of this 2015 EULAR/ACR recommendation for managing Japanese patients with difficult-to-treat PMR.
**Methods:** Thirty-five patients were diagnosed with PMR according to the 2012 EULAR/ACR provisional classification criteria for PMR[2)], including 13 males and 22 females. The average (± SD) age was 69.2 ± 9.4 years; disease duration before therapy 1.9 ± 1.8 months; and the length of observation after starting treatment 23.8 ± 20.7 months.
**Results:** All patients had active PMR, as demonstrated by high serum CRP levels (6.43 ± 4.50 mg/dL), erythrocyte sedimentation rate (ESR; 85 ± 33 mm/hr) and matrix metalloproteinase-3 (MMP-3; 188 ± 132 ng/mL). All patients with newly-diagnosed PMR were treated first with GCs (starting with the mean dose of prednisolone (PSL) of 15 mg/day; rage 10 - 60 mg/day; 60 mg/day for giant cell arteritis). Twenty-two patients experienced disease relapses, when PSL dose was reduced to 7.1 ± 3.7 mg/day at 7.9 ± 5.8 months. MTX (8.8 ± 3.4 mg/wk) was added in 21 patients and PSL was increased in a patient. Seven patients relapsed after MTX introduction, followed by adding tocilizumab (TCZ) in 6 patients and azathioprine in a patient. One patient with tocilizumab was thereafter switched to adalimumab due to insufficient response to TCZ. At present, PMR became inactive and GC was successfully withdrawn in 8 patients after total 18.0 ± 4.7 month treatment. No significant differences in basal levels of CRP, ESR and MMP-3 was found between GC-response and –resistant patients. Adverse effects included cataract (n=2), diabetes (n=1), metabolic syndrome (n=1), and osteoporosis (n=1).
**Conclusions:** The results indicate that early addition of MTX for GC-resistance and –intolerance, as recommended by the EULAR/ACR recommendations, may be effective also for Japanese patients, but there are cases refractory to MTX addition, who will require further treatment options including TCZ.
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## SAT0340 DISTINCT DISTRIBUTION PATTERNS OF LARGE VESSEL VASCULITIS ASSESSED WITH 18F-FDG PET/CT: A CLUSTER AND PRINCIPAL COMPONENT ANALYSIS STUDY

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**Background:** The interpretation of data from 18F-FDG PET/CT studies on large vessel vasculitis (LVV) is difficult due to the scarcity of studies and to the heterogeneity of LVV populations examined. In the absence of gold standard parameters for the assessment of LVV arterial inflammation, there is a great need to develop analytical methodologies useful to properly exploit the information derived from such studies. Principal component analysis (PCA) and cluster analysis (CA) have not yet been applied to explore the LVV distribution patterns, assessed by 18F-FDG PET/CT.
**Objectives:** The aim of our study was to investigate whether PCA and CA are useful methods in identifying distinct distribution patterns of LVV, according to the specific diagnostic entity examined (giant cell arteritis, GCA; Takayasu's arteritis, TAK).
**Methods:** A total of 130 18F-FDG PET/CT studies have been retrospectively examined by a nuclear physician blinded to clinical data. Maximum standardized uptake values (SUVmax) in 14 vascular districts including aortic segments (ascending aorta, thoracic aorta, aortic arch, discending thoracic aorta and abdominal aorta) and the main tributaries (carotid, subclavian, axillary, iliac and femoral arteries) have been measured and transformed into Z-scores. Identification of distribution patterns of vascular involvement has been performed using PCA and agglomerative hierarchical CA (SPSS Statistics, version 22nd).
**Results:** Three groups of vascular districts with similar trends in terms of standardized SUVmax have been identified: epiaortic arteries; aortic arch and ascending aorta; descending and abdominal aorta, with iliac and femoral arteries. A component including the entire aortic district was identified in TAK group, but not in GCA group.
**Conclusions:** PCA and CA approach revealed a subtle skewing in terms of distribution patterns of arterial involvement between TAK and GCA, assessed by 18F-FDG PET/CT SUVmax values. The influence of atherosclerosis and immunosenescence on the different trends in the aorta districts of TAK and GCA needs to be further elucidated.
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## SAT0341 ASSESSMENT OF DAMAGE IN BEHCET'S DISEASE: DO WE NEED A SPECIFIC DAMAGE INDEX?

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**Background:** Behcet's Disease (BD) is a systemic inflammatory disease characterized by involvement of vessels of any size and type. In the course of systemic vasculitis, it is important to distinguish disease activity from disease damage to prevent unnecessary immunosuppression. Additionally damage is an important surrogate for long-term outcome in vasculitis. Although a well-established validated damage index, "vasculitis damage index" (VDI) is available for vasculitis, its performance in determining the damage in BD has never been assessed.
**Objectives:** To assess the damage in BD by using VDI, to determine whether VDI covers all BD-associated damage and lastly to develop a preliminary BD-specific damage index with the obtained data.
**Methods:** A total of 139 consecutive patients with BD (F/M: 58/81, mean age 38.9±10.9 yrs, disease duration 9.5±7.4 yrs) from a single center were evaluated for damage in a cross-sectional study using the VDI. Considering the patients data and items of VDI with further literature search for BD-specific damages, new items (detailed cardiovascular, ocular, and vascular involvement-, particularly venous disease-related damages) were added to VDI. This modified VDI (Behcet's Disease-VDI [B-VDI]) was also scored in all patients.
**Results:** Seventy seven patients (55.4%) had major organ involvement and 105 (75.5%) patients were on immunosupressive (IS) treatment (Table 1). The mean VDI score was 0.3±0.7 and the majority of the patients had score "0" ("0" in 107 [77%], "1" in 22 [15.8%], "2" in 7 [5%], "3" in 1 [0.7%], and "4" in 2 [1.4%] patients). The mean B-VDI score was 0.6±1.1 ("0" in 92 [66.2%], "1" in 25 [18%], "2" in 13 [9.4%], "3" in 4 [2.9%] and "4" in 3 [2.2%] patients, "5" in 1 [0.7%], and "6" in 1 [0.7%] patient) and was significantly higher than VDI ($p<0.001$). The main difference between VDI and B-VDI was in vascular (0.05±0.2 vs 0.3±0.6, $p<0.001$) damage items. Both VDI and B-VDI scores were significantly higher in patients with major organ involvement compared to mucocutaneous BD. Both scores also positively correlated with the age, disease duration and total duration of IS treatment. When individual organ items were evaluated, damage in patients with major organ involvement was observed to be predominantly associated with ocular and vascular involvements. Although VDI-eye and B-VDI-eye scores were not significantly different (both 0.3±0.6, p=0.32), B-VDI-vascular scores were significantly higher than VDI-vascular scores both in the entire cohort and in patients with major organ involvement (0.6±0.8 vs 0.1±0.3, $p<0.001$).

**Table 1.** Baseline demographic and clinical characteristics of patients with Behcet's Disease (n=139)*

| | |
|---|---|
| Age, years | 38.9±10.9 |
| Male, n (%) | 81 (58.3) |
| Disease duration, years | 9.5±7.4 |
| Oral ulcer, n (%) | 139 (100) |
| Genital ulcer, n (%) | 119 (85.6) |
| Erythema nodosum/folliculitis, n (%) | 110 (79.1) |
| Arthritis, n (%) | 84 (60.4) |
| Ocular involvement, n (%) | 55 (39.6) |
| Vascular involvement, n (%) | 41 (29.5) |
| Gastrointestinal involvement, n (%) | 4 (2.9) |
| Neurologic involvement,n (%) | 4 (2.9) |
| Glucocorticoid treatment, n (%) | 86 (61.9) |
| Immunosuppressives, n (%) | 105 (75.5) |
| Cyclophosphamide | 7 (5) |
| Azathioprine | 77 (55.4) |
| Others | 21 (15.1) |
| Anticoagulant treatment, n (%) | 27 (19.4) |

*The values are presented as mean±SD, unless indicated otherwise.

**Conclusions:** Both VDI and B-VDI capture reliable data on damage among patients with BD. However, VDI does not cover all vascular involvement-related damages of BD. Therefore addition of new items, especially about vascular damage, to VDI will provide more comprehensive assessment of damage in BD. Further prospective follow-up is required to determine the prognostic value of these damage indices in BD.
**Disclosure of Interest:** None declared
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## SAT0342 FEATURES OF ORBITAL INFLAMMATORY DISEASE AND RESPONSE TO IMMUNOSUPPRESSIVE THERAPY

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**Objectives:** To characterize a single centre retrospective case series of patients with infra-orbital inflammatory masses with autoimmune disease including granulomatosis with polyangiitis (GPA) (formerly Wegener's granulomatosis), eGPA (eosinophillic granulomatosis with polyangiitis) or Immunoglobulin G4 (IgG4) related disease (IgG4-RD).
**Methods:** We identified 30 patients with infra-orbital inflammation on MRI imaging. Clinical and laboratory data was collected from electronic clinical records. Comprehensive Diagnostic Criteria were used for IgG4-RD and Chapel Hill criteria for GPA and eGPA. Statistical analysis was performed by GraphPad software; continuous variables were compared between IgG4-RD and GPA groups using non-parametric Mann-Whitney test and categorical variables were compared by Fisher's exact test.
**Results:** The study included 21 Caucasian, 6 Asian and 3 patients of African descent. There were 19 female and 11 male patients. The median age of the patients was 44 years (range 29–76).
13 patients were diagnosed with GPA, 1 with eosinophillic granulomatosis with polyangitis 9eGPA), 11 patients had IgG-RD, 1 patient with lymphoma, 2 other vasculitis, 1 IgA dacryoadenitis, 1 non-specific granuloma.
7/12 patients with IgG4-RD had isolated infra-orbital masses whereas all 14 GPA patients suffered extra-ocular manifestations (p=0.01), usually sino-nasal or pulmonary.
11/14 GPA patients had positive ANCA vs 2/12 patients with Ig4-RD (p=0.04). IgG4 level was elevated pre-treatment in IgG4 RD patients (median 2.46 g/l (range 1.2–23.7)) and dropped to 1.25 g/l (range 0.37–10.4) after therapy; immunoglobulin subclasses were not checked routinely in GPA.
All 12 patients with IgG4-RD underwent diagnostic orbital biopsy vs 3/14 GPA (p=0.0001).
All 30 patients were treated with corticosteroids (used alone in 3/12 IgG4-RD patients). The median number of DMARDs ever used to treat GPA was 3 vs 1 DMARD for IgG4-RD (p=0.001). Rituximab was effectively administered to 10/14 GPA patients vs 3/12 IgG4-RD (p=0.04), is planned for 2 further IgG4-RD patients and approval was refused for 1 case. Surgical debulking was undertaken in 6/12 IgG4-RD vs 1/14 GPA (p=0.03). All 40 patients had subsequent MRI to assess response to therapy.

| Patient Group | GPA | IgG4-RD | P value |
|---|---|---|---|
| Number of patients | 14 | 11 | |
| Median age (years) | 46 | 58 | 0.16 |
| Gender distribution | 8 female / 6 male | 7 female / 4 male | 1.0 |
| Ethnic distribution | 10 Caucasian / 3 Asian / 1 African | 6 Caucasian / 3 Asian / 2 African | 0.4 |
| ANCA status | 11 ANCA+ / 3 ANCA- | 2 ANCA+ / 9 ANCA- | 0.04 |
| Bilateral orbital inflammation | 4/14 | 2/11 | 0.7 |
| Extra-ocular manifestations | 14/14 | 4/11 | 0.01 |
| Median number of DMARDs | 3 (range 1-5) | 1 (range 0-3) | 0.001 |
| Rituximab treatment | 10/14 | 3/11 | 0.04 |
| Surgical debulking | 1/14 | 6/11 | 0.02 |
| Chronic damage (visual loss, diplopia, orbital pain /swelling) | 8/14 | 5/11 | 0.7 |
| Improvement of orbital inflammation on MRI | 9/14 | 10/11 | 0.2 |

**Conclusions:** IgG4-RD is an important differential diagnosis of infra-orbital inflammation, especially if ANCA is negative. Unlike GPA that was associated with extra-ocular manifestations in all patients, IgG4-RD was more likely to present with isolated orbital inflammation and to require biopsy or surgical debulking as the diagnosis was initially uncertain. Treatment with corticosteroids +/– DMARDs was effective. Rituximab can specifically deplete the pool of autoreactive B lymphocytes producing IgG4 and future systematic studies are required to establish the optimum therapeutic strategy.
**Disclosure of Interest:** None declared
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## SAT0343 UTILITY OF VASCULAR FINDINGS BY PET/CT SCAN IN THE DIAGNOSIS AND ACTIVITY ASSESSMENT OF TAKAYASU ARTERITIS

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**Background:** Takayasu arteritis (TA) is a large-vessel vasculitis predominantly affecting the aorta and its main branches. Assessing disease activity is difficult and mainly based on the clinical findings, levels of acute phase reactants and angiography, but these items generally do not correlate well
**Objectives:** The aim of the this study was to investigate the role of PET/CT in the diagnosis of the disease and assessing disease activity in TA
**Methods:** Thirty TA patients fulfilling ACR criteria underwent FDG-PET/CT were retrospectively assessed. Disease activity was defined according to NIH criteria. A nuclear physician who was blinded to clinical and laboratory data examined all PET/CT scans. PET/CT scans were considered negative if vascular FDG uptake was lower than liver uptake, if there was moderate (equivalent to that of liver) or marked (more than liver) FDG uptake in at least one vessel area, the scan was considered positive for vasculitis. The levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were measured concomitantly. The correlation between CRP and ESR with $SUV_{max}$ values of vessels was investigated. Disease activity with the NIH cirteria, CRP levels and ESRs were compared in subjects with or without positive PET/CT scans. ROC curve analyses were performed to assess the sensitivity and specificity of CRP and ESR according to PET/CT positivity
**Results:** PET/CT was performed for diagnostic purposes early in the disease course in 9 subjects and to assess disease flare in 21 subjects on follow-up. The rate of a positive PET/CT examination tended to be higher in diagnostic/early use (88.9% positive) compared with use for flare-assessment (61.9% positive), although the difference was not significant (Fisher=0.2). Median CRP and ESR tended to be higher in PET/CT positive patients compared with PET/CT negative subjects (median CRP 19 vs. 14, p=0.16; mean ESR 59.8±36.5 vs. 35.2±19.7, p=0.07). ROC curve analysis showed an ESR of 38 mm/h or higher was 68.4% sensitivity and 66.7% specificity to predict a positive PET/CT examination (positive and negative predictive values 81.6% and 50%). A CRP of 14.5 mg/L or higher was 66.7% and 55.6% specific to predict a positive PET/CT examination (positive and negative predictive values 77.8% and 41.7%). While CRP was significantly correlated with mean $SUV_{max}$ value of aorta (r=0.41, p=0.02), ESR was weakly correlated with $SUV_{max}$ value of aorta (r=0.3, p=0.13). There was moderate agreement between PET-CT and NIH criteria (kappa 0.462, p=0.01, sensitivity 81%, spesificity 67%).
**Conclusions:** These results suggested that clinical benefit of PET/CT might be higher in diagnostic use (early in the disease course) compared with use for flare assessment (after treatment) in TA. There was a moderate association between NIH activity criteria and PET/CT activity. The predictive value of increased ESR and CRP was similar for a positive PET/CT scan with lower negative predictive values. CRP levels had a better correlation with $SUV_{max}$ levels of aorta compared to ESR. PET/CT is a promising tool in the diagnosis and activity assessment of TA but discrepancies with other activity parameters do exist.
**Disclosure of Interest:** None declared
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## SAT0344 TREATMENT OF NON-INFECTIOUS AORTITIS: STUDY OF 32 PATIENTS FROM A SINGLE CENTRE

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**Background:** Non-infectious aortitis is often an underrecognised condition. Early diagnosis and treatment is crucial to prevent serious complications.
Corticosteroids represent the first-line therapy of non-infectious aortitis. However, disease-modifying antirheumatic drugs (DMARDS) and/or biologic therapy are usually required.
**Objectives:** Our aim was to assess the treatment and outcome of patients diagnosed with non-infectious aortitis from a single centre.
**Methods:** Retrospective study of 32 patients (22 women/10 men) diagnosed with non-infectious aortitis based on imaging techniques. We have considered 3 groups: *group a)* patients who only received corticosteroids; *group b)* patients

treated with corticosteroids and DMARDs; and *group c)* those who required biologic therapy. Results were expressed as mean±standard deviation (SD) or as median and interquartile range (IQR) as appropriate. Wilcoxon test was used to compare the study parameters at baseline and at the last visit.
**Results:** The mean age±SD of the patients was 68±11 years and the mean±SD follow-up was 24.7±22.7 months. *Group a)* included 11 patients; *group b)* 12 patients treated with methotrexate (MTX) and 2 hydroxychloroquine (in one of them associated to MTX); and *group c)* 9 patients on biologic therapy: adalimumab (ADA) (n=3), tocilizumab (TCZ) (n=5) and rituximab (RTX) (n=1). In this group, 8 patients were previously treated with DMARDS: MTX (n=7) and azathioprine (n=1). The results are shown in the TABLE. Two patients receiving MTX had to withdraw it due to raised liver function test, and two patients who were on TCZ had to discontinue it because of neutropenia. Moreover, one of them had angina pectoris related to a hypertensive episode during the third TCZ infusion.

**TABLE**

| | Group a (n= 11) Only corticosteroids | Group b (n= 12) DMARDS | Group c (n= 9) Biologic therapy |
|---|---|---|---|
| Age, mean ±SD | 69.4±12.4 | 69.3±10.4 | 65.8±9.9 |
| Sex (W/M) | 5 (54.5%)/5 (45.4%) | 9 (75%)/3 (25%) | 7 (77.8%)/2 (22.2%) |
| Months until treatment onset | 0 | 2.5 [1-36] | 4 [0-14] |
| Underlying condition | GCA (n= 2), PmR (n= 7), idiopathic (n= 2) | GCA (n= 7), PmR (n= 3), BA (n= 1), SS (n= 1) | GCA (n= 4), PmR (n= 1), SS (n= 1), PsA (n= 1), UC (n= 1), sarcoidosis (n= 1) |
| Follow-up (months) | 14 [6-22] | 14 [2-36] | 22 [12-34] |
| Clinical improvement at last visit# | 11 (100%)* | 12 (100%)* | 8 (89%)* |
| CRP<br>- treatment onset<br>- last visit | 3.4 [1.5-9.1] (10)<br>0.3 [0.1-1.4] (10)* | 0.9 [0.1-3.3] (11)<br>0.1 [0.1-0.4] (10)* | 1 [0.1-2.4] (8)<br>0.1 [0.1-0.6] (9)* |
| ESR<br>-treatment onset<br>- last visit | 76 [43-92] (11)<br>16 [4-19] (10)* | 50.5 [25-70] (12)<br>14 [4-26] (11)* | 33 [12-46] (9)<br>2 [2-7] (9)* |
| Prednisone dosage<br>- treatment onset<br>- last visit | 20 [10-30] (10)<br>2.5 [0-6.25] (9)* | 26 [10-40] (12)<br>2.5 [0-5] (12)* | 15 [10-25] (9)<br>2.5 [0-5] (7)* |
| Improvement by PET | 3, 100% (3)* | 5, 83.3% (6)* | 5, 71.4% (7)* |

*p<0.05
# Improvement in at least one clinical manifestation.
In brackets, the number of patients with available data.

**Conclusions:** Corticosteroids are the cornerstone of treatment of noninfectious aortitis, although frequently DMARDS (usually MTX) and sometimes biologic therapy are required. The treatment seems effective and relatively safe.
**Acknowledgement:** This study was supported by a grant from "Fondo de Investigaciones Sanitarias" PI12/00193 (Spain). This work was also partially supported by RETICS Programs, RD08/0075 (RIER) and RD12/0009/0013 from "Instituto de Salud Carlos III" (ISCIII) (Spain).
**Disclosure of Interest:** None declared
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## SAT0345 HISTOPATHOLOGICAL DIFFERENCES BETWEEN SINGLE-ORGAN CUTANEOUS SMALL VESSEL VASCULITIS AND OTHER CUTANEOUS VASCULITIS ASSOCIATED WITH SYSTEMIC INVOLVEMENT

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**Background:** Cutaneous vasculitis (CV) encompasses a wide and heterogeneous group of disorders characterized by the presence of necrotizing inflammatory lesions in the cutaneous blood vessels. Single-organ cutaneous small vessel vasculitis (SoCSVV) is, according to 2012 Chapel-Hill criteria, a vasculitis confined to the skin.
**Objectives:** Our aim was to compare the histopathological findings of skin biopsies from patients with SoCSVV and those with systemic involvement.
**Methods:** From a series of patients with CV, we selected 3 groups: *group a)* SoCSVV; *group b)* CV with systemic involvement; *group c)* subgroup of patients of group b with involvement of 3 organs other than the skin. A comparative study between the group a) with the other two groups (b and c) was performed.
**Results:** *Group a)* was integrated by 9 patients (7 W/2 M; mean age, 64±16 years). In the *group b)* 43 patients were included (18 W/25M; mean age, 54±21 years). The underlying conditions were: severe bacterial infections (n=12), hypersensitivity vasculitis with involvement of other organs besides the skin (n=10), HSP (n=9), panarteritis nodosa (n=4), microscopic polyangiitis (n=2), cryoglobulinemia (n=2), malignancy (n=2), SLE (n=1) and Sjögren's syndrome (n=1). Finally, 7 patients (3 W/4 M; mean age, 50 ± 20 years) were included in *group c)*. The underlying conditions were: severe bacterial infections (n=3), HSP (n=3) and cryoglobulinemia (n=1). The results of histopathological comparison of *group a)* with the *groups b)* and *c)* are shown in the table. Although no parameter reached statistical significance, in our series we observed that the greater systemic involvement was more frequently associated with tissue neutrophilia, pustular dermatosis and deep involvement of arterioles. By contrast, SoCSVV tend to develop greater tissue eosinophilia and tissue lymphocytosis, whilst the intensity of the inflammatory infiltrate was lower. On the other hand, none of the samples of patients with SoCSVV showed involvement of deep arterioles.

| | SoCSVV (a) (n=9) | CV with systemic involvement (b) (n=43) | CV with involvement of 3 organs besides the skin (c) (n=7) |
|---|---|---|---|
| Hodge index#, mean±SD | 6±1 | 7±3 | 6±1 |
| Tissue eosinophilia | 3 (33.3%) | 5 (11.6%) | 0 (0%) |
| Tissue neutrophilia | 4 (44.4%) | 32 (74.4%) | 7 (100%) |
| Tissue lymphocytosis | 2 (22.2%) | 4 (9.3%) | 0 (0%) |
| Intensity of inflammatory infiltrate, mean±SD | 1±0 | 1.4±0.7 | 1.1±0.3 |
| Pustular dermatosis | 1 (11.1%) | 11 (25.6%) | 2 (28.6%) |
| Deep arterioles involvement | 0 (0%) | 5 (11.6%) | 1 (14.3%) |

#Hodge SJ, et al. J Cutan Pathol. 1987; 14: 279–84.

**Conclusions:** In this series we observed that qualitative and quantitative histological differences were correlated with the degree of systemic involvement. However, these results need to be tested in prospective studies with a larger number of patients.
**Acknowledgement:** "Fondo de Investigaciones Sanitarias" PI12/00193 (Spain) and RETICS Programs, RD08/0075 (RIER) and RD12/0009/0013 from "Instituto de Salud Carlos III" (ISCIII) (Spain).
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## SAT0346 CUTANEOUS VASCULITIS ASSOCIATED TO CONNECTIVE TISSUE DISEASES AND OTHER AUTOIMMUNE DISORDERS. STUDY OF 35 PATIENTS FROM A SINGLE CENTRE

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**Background:** Cutaneous vasculitis (CV) can be a clinical manifestation of a connective tissue or other autoimmune disease.
**Objectives:** Our aim was to assess the frequency and clinical features of CV associated to connective tissue diseases.
**Methods:** Study of a large series of 766 unselected patients with CV attended in the same tertiary-care hospital. CV was considered as secondary to connective tissue disease or other autoimmune disorder when occurred in the setting of any of these conditions.
**Results:** In 35 (10 men/25 women; mean age±SD, 48±15 years) of 766 patients (4.57%) CV was associated to the following connective tissue disease or autoimmune disorder: systemic lupus erythematosus (SLE) (n=15), rheumatoid arthritis (n=9), Sjögren's syndrome (n=5), ankylosing spondylitis (n=2), relapsing polychondritis (n=1), Behçet's disease (n=1), sarcoidosis (n=1) and autoimmune hepatitis (n=1). All patients developed vasculitic skin lesions: palpable purpura (n=31), maculopapular erythema (n=4) and urticarial lesions (n=2). The most common CV locations were: lower limbs (n=30), upper limbs (n=12) and trunk (n=10). The mean duration of skin lesions was 13.83±7.62 days. Other clinical features were nephropathy (n=9), joint involvement (n=6), constitutional symptoms (n=4) and gastrointestinal involvement (n=1). Regarding laboratory parameters, elevated ESR was observed in 25 patients, hematuria in 4, anemia in 7 and proteinuria in 5 patients. Immunologic findings were as follows: positive rheumatoid factor (10 of 13 patients tested), positive antinuclear antibodies (15 of 19 patients tested), and decreased serum complement levels (11 of 20 patients tested). Twenty-five patients required some drug for CV: corticosteroids (n=22), cyclophosphamide (n=6), methotrexate (n=5), NSAIDs (n=4), azathioprine (n=4), chloroquine (n=3), hidroxichloroquine (n=2), dapsone (n=1) and rituximab (n=2).
**Conclusions:** CV, although infrequent, is not exceptional in the setting of any connective tissue disease or autoimmune disorder.
**Acknowledgement:** This study was supported by a grant from "Fondo de Investigaciones Sanitarias" PI12/00193 (Spain). This work was also partially supported by RETICS Programs, RD08/0075 (RIER) and RD12/0009/0013 from "Instituto de Salud Carlos III" (ISCIII) (Spain).
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## SAT0347 VALUE OF THE DOPPLER-ULTRASONOGRAPHY FOR THE DIAGNOSIS OF TEMPORAL ARTERITIS

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**Background:** Temporal Arteritis (TA) is the most common systemic vasculitis in adults. Usually, the diagnosis is based on the American College of Rheumatology (ACR) classification criteria published in 1990 based on the clinical history,

physical examination, laboratory information and histological findings in the biopsy. However, according to the literature, the biopsy can be negative in up to 68% of patients with TA and without it the predictive value diminishes considerably.
**Objectives:** Assess the value of Doppler Ultrasonography for the diagnosis of TA, compared with ACR criteria and biopsy, using the definitive clinical diagnosis of the patient as gold standard.
**Methods:** A retrospective observational, descriptive and analytical study was made, reviewing the clinical history of the patients who had an ultrasound scan of the temporal artery performed in our hospital on suspicion of TA. The standard exploration consists of the bilateral examination of the temporal superficial artery, with its common trunks and the frontal and parietal branches. In the case of diagnostic doubt, the exploration is extended to the occipital arteries and/or axilares. The ultrasound scans were realized and reported by the same person to avoid bias. The variables registered were age and sex, the presence or absence of ACR criteria, VSG value, the final diagnosis and the results of the biopsy and the ultrasound examination as well as the number of affected branches. The statistical analysis was realized by means of the software program SPSS Statistics version 20.0.
**Results:** Of the 451 patients studied, 399 were women and 52 men (88.5% vs 11.5%), with a mean age of 81. Two hundred fifty six patients (58,8%) had a definite diagnosis of TA while 195 (43,2%) presented other diagnoses. Two hundred forty patients (55.79%) fulfilled ACR criteria and 211 did not (46,78%). Of the 166 biopsies, 54 (32,53%) were positive. The validity (sensitivity and specificity) and security (positive predictive value [PPV], negative predictive value [NPV], Likelihood Ratio [LR] + and LR -) of diagnostic tests used were as follows:

| | Sensitivity | Specificity | VPP | VPN | LR+ | LR– |
|---|---|---|---|---|---|---|
| ACR criteria | 65.37% | 62.89% | 70% | 57.82 | 1.7619 | 0.5506 |
| Biopsy | 42.86% | 100% | 100% | 35.71% | | 0.5714 |
| Doppler ultrasonography | 91.60% | 95.83% | 96.62% | 89.76% | 21.81 | 0.0876 |

**Conclusions:** Doppler Ultrasonography shows great validity and safety as a diagnostic test of TA, being in addition, a cheaper and less harsh technique than the biopsy.For this reason its use in clinical practice should be considered a diagnostic option of the first line in the diagnosis of this disease.
**Disclosure of Interest:** None declared
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## SAT0348 ASYMPTOMATIC DEEP VEIN THROMBOSIS IN ANCA-ASSOCIATED VASCULITIDES

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**Background:** Chronic inflammatory diseases, e.g. ANCA-associated vasculitides (AAV), are associated with increased incidence of venous thromboembolism (VTE) that can be asymptomatic in a proportion of patients.
**Objectives:** To evaluate a prevalence of asymptomatic deep vein thrombosis (DVT) in a cohort of AAV patients compared with healthy controls.
**Methods:** We used compression US to study the occurrence of asymptomatic DVT in 99 patients with AAV (67 females and 32 males, average age of 54.0 years, range of 18 to 77), including granulomatosis with polyangiitis (GPA; n=72), microscopic polyangiitis (MPA; n=13) and eosinophilic granulomatosis with polyangiitis (EGPA; n=14), and 514 healthy controls (339 females and 175 males; average age of 54.7 years, range of 17 to 89 years) without signs and symptoms of DVT. Signs of activity of AAV were present in 64 patients.
**Results:** Asymptomatic DVT was detected in 8 (8.1%) of 99 patients with AAV, including 3/72 (4.2%) GPA patients, 3/13 (23.1%) MPA patients and 2/14 (14.3%) EGPA patients. All 8 patients with DVT had active vasculitis. In 6 of 8 patients AAV was diagnosed within 6 months prior to US. A prevalence of traditional VTE risk factors was comparable in patients with and without DVT, but prednisolone dose at the time of US was higher in patients with DVT (38.8 vs 10.8 mg daily, $p<0.001$). One patient with asymptomatic DVT died within 3 months after US from acute myocardial infarction, and one patient developed postthrombotic syndrome. There were no cases of pulmonary embolism. AAV was associated with significantly increased risk of asymptomatic DVT compared with healthy controls (OR =22.5, CI 4.7 to 107.7). This risk was even higher in patients with active AAV (OR =36.6, CI 7.6 to 174.5).
**Conclusions:** Patients with AAV have a high risk of asymptomatic DVT within 6 months after diagnosis. These data may justify wider screening for DVT in AAV.
**Disclosure of Interest:** None declared
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## SAT0349 DURATION OF STEROID TREATMENT IN POLYMYALGIA RHEUMATICA

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**Background:** The duration of steroid treatment in polymyalgia rheumatic (PMR) is variable. Some patients do not have raised inflammatory markers and anecdotal evidence suggests they may need a shorter duration of treatment. In order to evaluate parameters that may predict the duration of steroid treatment we have undertaken a retrospective analysis of patients on our database with a diagnosis of PMR.
**Methods:** We evaluated patients who presented with new onset PMR to the Trafford Rheumatology Unit between 2005 and 2010. Following a 14 day therapeutic trial of prednisolone 20mg od and a diagnosis of PMR confirmed by a consultant rheumatologist, all patients received a standard reducing regime of prednisolone, reducing every 2 weeks to initial maintenance of alternate day 10mg/5mg after 2 months (if possible). Doses were increased for recurrence of symptoms. After 6 months the dose was reduced to 5mg od if they had not required a dose increase and tailed off once asymptomatic on 5mg od for 6 months. All patients were followed for 10 years or until drug free remission. The electronic records were reviewed for demographic data, blood count, inflammatory markers, liver enzymes, immunology, and duration of treatment prior to drug free remission.
**Results:** 96 patients were evaluated. 15 were excluded from analysis if they had incomplete documentation or because of a positive rheumatoid factor, other immunology or revised diagnosis. The mean age was 68yrs; range 53–90yrs. Female to male ratio was 2.8:1. The median duration of symptoms prior to presentation was 4.5 months (1–36 months). At diagnosis 14% of patients were anaemic, mean CRP was 35mg/l, mean ESR was 45mm/hr and 26% had normal inflammatory markers. Only 1% of patients had raised liver enzymes. 44% were able to reduce to 5mg prednisolone after 6 months and a further 6% after 9 months. The mean duration of steroid treatment for all patients was 30 months (13–108 months). For patients with a normal ESR and CRP at diagnosis, the mean duration of steroids was 22 months compared with 32 months with raised ESR and 35 months with raised CRP. 10% relapsed after steroid withdrawal. 2 patients remained on long term steroids.
**Conclusions:** Approximately 25% of patients with PMR do not have raised inflammatory markers at diagnosis and have shorter total duration of steroids (mean 22 months). Almost half can reduce prednisolone to 5mg after 6 months. The average duration of steroids prior to drug free remission is almost 3 yrs in patients with raised inflammatory markers at diagnosis. 10% relapse after gradual steroid withdrawal.
**Disclosure of Interest:** None declared
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## SAT0350 FUNCTIONAL CHARACTERISATION OF TAKAYASU ARTERITIS VASCULAR LESIONS BY MR AND FDG-PET/CT PROVIDES NON-REDUNDANT INFORMATION OVER CLINICAL ASSESSMENT

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**Background:** Disease activity (DA) assessment in Takayasu arteritis (TA) is an unresolved enigma as systemic inflammation and current activity measures poorly correlate with arterial progression. Morphological imaging, e.g. with morphological magnetic resonance (MR) sequencies, is the goal standard to evaluate arterial progression after its occurrence, and it is not clear whether functional characterisation of the lesions (e.g. contrast enhancement at MR or fluorodesoxyglucose [FDG] uptake at FDG-PET/CT [PET]) can predict arterial progression before its occlusion. We are prospectively following 60 TA patients with functional and morphological imaging to understand the predictors of arterial progression. Here we present the baseline assessment of the first 47 patients.
**Objectives:** to verify if activity measures, and functional lesion characterisation with PET or MR provide independent information.
**Methods:** Cross-sectional analysis of 47 TA patients according to ACR criteria followed at our Institution and undergoing closely related MR, PET and clinical evaluation. DA was evaluated with NIH criteria, indian Takayasu activity score (ITAS2010) and physician global assessment (PGA). At MR, arterial lesions were characterized by length, thickness and percentage of stenosis. Contrast to noise ratio (CNR) was calculated, when technically possible. Each vascular lesion uptake large enough to be evaluated by PET was evaluated with a quantitative ($SUV_{max}$) method. Per patients and per lesion analyses were performed.
**Results:** The median interval between MR and PET was 24 days. TA was active in 25, 17 and 35 patients according to NIH criteria, ITAS2010 and PGA (including active and grumbling disease). In total, MR identified 333 arterial lesions (median lesion N per patient 6, IQR 1–15). At the "per patient" analysis, median $CNR_{max}$ at MR was 12,43 (IQR 0,00–54,29). $CNR_{max}$ did not correlate with acute-phase markers nor activity measures, except for ITAS-CRP (rho 0.300, p=0,038). PET showed significant uptake in 18 patients. Meadian $SUV_{max}$ was 1,19 (IQR 0,00–9,00). SUVmax did not correlate with activity measures.
At the "per lesions" analysis, 56 lesions had positive uptake in PET. There was no correlation between the degree of enhancement at MR and of FDG uptake at PET (rho 0,094, p=0,529).
**Conclusions:** Current activity measures, mainly based on systemic inflammation, and functional characterisation of the arterial lesions by MR and FDG-PET provide independent information in TA. The prospective part of this study will clarify the

clinical relevance and the predictive values for progression of these different pieces of information.
**Disclosure of Interest:** None declared
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## SAT0351 TOCILIZUMAB IN GIANT CELL ARTERITIS: A MULTICENTRE OPEN-LABEL STUDY OF34 PATIENTS

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**Background:** Giant cell arteritis (GCA) is a vasculitis of large and medium sized arteries affecting people older than 50 years. Glucocorticosteroids (GC) are the mainstay of therapy but relapses are common, resulting in prolonged treatment course and adverse events. IL-6 correlates with disease activity of GCA and temporal artery biopsy samples show enhanced IL-6 production. Cases series and open label studies reported the efficacy of tocilizumab (TCZ) on symptoms and inflamamtory markers in GCA.
**Objectives:** To report the French experience on the efficacy and safety of TCZ in patients with GCA and the evolution after treatment withdrawal.
**Methods:** A retrospective multicenter study on patients treated with TCZ for their GCA was conducted. Treatment efficacy was evaluated at a clinical and biological level. Side effects and evolution after treatment withdrawal were also recorded.
**Results:** Thirty-four patients (27 women and 7 males) aged 70.5±8.2 (mean±SD) were included. Diagnosis of GCA was based on the ACR criteria (30 patients) and/or on imaging abnormalities suggestive of GCA (8 patients). Giant cell disease was treated by GC and another immunosuppressant was added before TCZ introduction in 20/34 patients. Tocilizumab (8 mg/kg monthly) was introduced after a mean disease evolution of 18 months (0–107). It was efficient in all but 6 patients who still had mild symptoms while CRP was reduced from 40.4 mg/L to 1.5 mg/L ($p<0,0001$) and GC were tapered from 26.3 to 10.3 mg/day ($p<0.0001$). One patient died from a septic shock and 3 patients had to stop TCZ for adverse events. Among the 23 patients who stopped treatment (planned medical decision in 20 cases and side effects in 3 cases) eight patients experienced relapses that occurred after a mean of 3.5±1.3 months.
**Conclusions:** TCZ therapy leads to rapid and maintained improvement in patients with refractory GCA. However, side effects should be kept in mind in this population. Questions remain regarding the suspensive nature of this treatment and this should be specifically studied in future studies.
**Disclosure of Interest:** None declared
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## SAT0352 ANALYSIS OF VARICELLA-ZOSTER VIRUS IN TEMPORAL ARTERY BIOPSIES POSITIVE AND NEGATIVE FOR GIANT CELL ARTERITIS

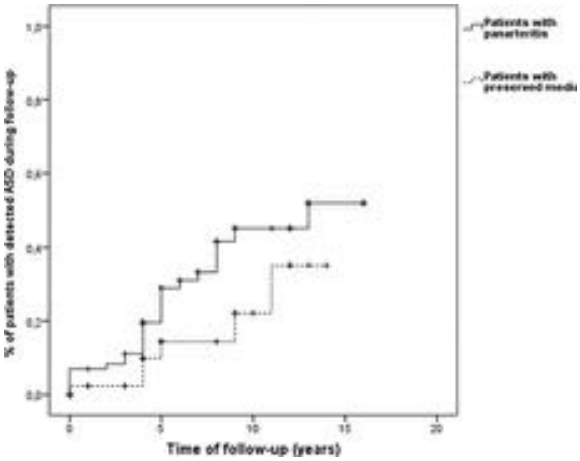
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**Background:** Recent studies found an high prevalence of varicella-zoster virus (VZV) infection in temporal arteries (TAs) from both temporal artery biopsy (TAB)-positive and TAB-negative giant cell arteritis (GCA) patients compared to controls, suggesting that VZV infection may trigger the inflammatory cascade that characterizes GCA (1,2).
**Objectives:** To analyze VZV infection in TAs from patients with TAB-positive GCA (biopsy-proven GCA), TAB-negative GCA (patients with negative TAB and a final diagnosis of GCA) and controls (patients with negative TAB and a final diagnosis different from GCA).
**Methods:** A total of 75 formalin-fixed, paraffin-embedded (FFPE) TABs performed between 2009 and 2012 at a single institution from 30 TAB-positive GCA patients, 15 TAB-negative GCA patients and 30 controls were retrieved. Six 5-$\mu$m sections of all FFPE TABs were cut. The first section was analyzed by immunohistochemistry using mouse monoclonal anti-VZVgE IgG1 antibody (Santa Cruz Biotechnology) and OptiView DAB Detection Kit (Ventana, Roche). DNA was extracted from the remaining 5 sections with the QIAamp DNA FFPE tissue kit (Qiagen) and analyzed by real-time polymerase chain reaction for the presence of VZV DNA (VZV ELITe MGB kit, ELITechGroup). In addition DNA was extracted with the RNA/DNA/Protein purification kit (Norgen Biotek) from 5 positive TABs of 2 mm length obtained from GCA patients and immediately stored frozen at -80°C. Beta globin (included in the VZV ELITe MGB kit) and a short intergenic region were amplified to verify the quality of DNA.
**Results:** 60/75 (80%) patients were female. Mean (± SD) age at TAB was 72.1 (± 8.3) years. There were no significant differences in sex and age distributions between TAB-positive GCA, TAB-negative GCA and controls.
Median (Q1, Q3) time from symptoms onset to TAB was 11 (5.5, 19.3) weeks for TAB-positive GCA, 15 (9, 20) weeks for TAB-negative GCA and 12 (6, 41.6) weeks for controls, p=0.414. 22/30 (73.3%) TAB-positive GCA, 8/15 (53.3%) TAB-negative GCA and 20/30 (66.7%) controls were receiving prednisone at the time TAB was performed, p=0.407.
Immunohistochemical analysis detected VZV antigen in 1/30 TAB-positive GCA, 0/15 TAB-negative GCA and 0/30 controls, p=0.467. DNA obtained from all TABs was amplifiable. DNA obtained from frozen TABs was more concentrated than that obtained from FFPE TABs which allowed to load a higher quantity of DNA per reaction increasing assay sensitivity.VZV DNA was not found in any of the FFPE TABs as well as in frozen TABs but was clearly detected in FFPE skin lesions from patients with active infection (threshold cycle for VZV DNA =26 when 0.5 ng of DNA were amplified).
**Conclusions:** Our data do not support a role for VZV infections in the etiopathogenesis of GCA.
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**Disclosure of Interest:** None declared
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## SAT0353 RELATIONSHIP BETWEEN DISRUPTION OF THE MUSCULAR LAYER IN TEMPORAL ARTERY BIOPSIES OF GCA PATIENTS AND THE DEVELOPMENT OF AORTIC DILATATION/ANEURYSM DURING FOLLOW-UP

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**Background:** Giant cell arteritis (GCA) may be complicated by aortic dilatation/aneurysm (aortic structural damage; ASD), which may lead to life-threatening events. In GCA patients, ASD occurs 17.3 times more frequently than in the general population, affecting up to 33.3% of patients after long term follow-up[1]. ASD is in most cases a delayed complication and its pathophysiology is unclear. Necropsy/surgery specimens from patients subjected to standard treatment and control may reveal persistent inflammatory infiltrates but these are usually mild or absent and extensive disruption of elastic fibers is the most striking finding[2]. We hypothesized that extensive loss of vascular smooth muscle cells during the initial injury may prevent regeneration of elastic fibers and contribute to aortic wall weakening and subsequent dilatation.
**Objectives:** To assess whether the extent of medial layer injury in temporal artery biopsies (TABs) predicts subsequent development of aortic dilatation.
**Methods:** We performed histopathological scoring of TABs from all biopsy-proven GCA patients that underwent thoracic CT examination during follow-up for any reason. Aortic diameters in the ascending aorta, aortic arch and descending aorta were measured and ASD was defined as described [1,2]. Histopahotlogical scoring was performed as reported[3]. Fisher exact test and Kaplan-Meier estimates and long-rank test were used for statistical analysis.
**Results:** Between 1995 and 2013, 144 patients with biopsy-proven GCA were



subjected to a chest CT. In 36 (25%) patients, this was part of a prospective screening protocol for large-vessel involvement in newly diagnosed patients[4], in 94 (65.3%) CT was part of a prospective detection of a ASD[2], and in 14 (9.7%) CT was performed for a variety of medical indications. ASD was detected in 34 (23.6%) patients after a median follow up of 55.5 months (range 0–156). In 43 (29.9%) of biopsies inflammatory infiltrates preserved the medial layer and in 101 (70.1%) inflammation was panarteritic severily disrupting the structure of the media which could be hardly identified. ASD was detected at some point in 28 (27.7%) of patients with panarteritic involvement and in 6 (14%) of patients with a preserved media. However, differences did not reach statistical significance (p=0.089). In patients with panarteritic involvement, ASD was detected after a mean follow-up of 53.9 months (SD±37.7) whereas in patients with a preserved media ASD was observed after a mean follow-up of 74.1 months (SD±35.2) (p=0.094).

**Conclusions:** Patients with severe disruption of the medial layer in their temporal arteries at diagnosis had a trend to develop more frequent and earlier ASD, although differences did not reach statistical significance. Further studies are necessary to clarify this point. Supported by Marató TV3 2014/201507

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## SAT0354 STUDY OF 13 AORTITIS CASES FROM A SINGLE UNIVERSITY HOSPITAL IN THE LAST 3 YEARS. DIAGNOSIS, TREATMENT AND EVOLUTION

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**Background:** Aortitis is a several and potentially lethal clinical condition. It is usually oligosymptomatic or may present with non-specific symptoms that complicate and delay the diagnosis. On the other hand, treatment of aortitis is not established.

**Objectives:** The objetive of this study is to describe clinical manifestations, laboratory studies and treatment of patients with aortitis in a single center.

**Methods:** We have reviewed the medical records of patients who had positive Positron Emission Tomography (PET) for aortitis fron January 2013 to December 2015 in the Rheumatology Department of a University Hospital. We included 13 cases and we recorded epidemiological, clinical data, laboratory results, treatment and evolution.

Quantitative variable results were expressed as mean±standard deviation (SD) or median (interquatile range-IQR). Qualitative variable results were expressed as percentage. The analysis was performed with the SAS System for Windows V 9.2.

**Results:** In the last 3 years 13 cases of aortitis were diagnosed (3 in 2013, 3 in 2014 and 7 in 2015). The male to female ratio was 3/10. Mean age±SD was 72.23±12.36 years [range, 51–83]. The underlying conditions were: giant cell arteritis (GCA) (n=7), polymyalgia rheumatica (PmR) (n=2), idiopathic (n=2), relapsing polychondritis (n=1) and Sjögren syndrome (n=1). The median interval between the diagnosis of the underline disease and the aortitis was 7 months [1–20]. The most common manifestations were constitutional syndrome (n=5), inflammatory back pain (n=4), pain irradiated to lower limbs (n=4), atypical polymyalgia (n=1) and fever (n=1).

All patients exhibited increased acute phase reactants except for the two patients

TABLE. AORTITIS. CLINICAL, LABORATORY AND TREATMENT FEATURES

| Case | Underlying disease | Months between the diagnosis of underlying disease to aortitis | Constitutional syndrome | Fever | Inflammatory back pain | Pain irradiated to lower limbs | Hb (g/dL) | CRP (mg/dL) | ESR (mm/1st hour) | Initial treatment for aortitis | Months during follow-up | CRP, last visit (mg/dL) | ESR last visit (mm/1st hour) | Last visit treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Relapsing polychondritis | 20 | no | no | no | no | 11.6 | 3.31 | 35 | Pred (30 mg)+MTX (20 mg)* | 5 | 0.10 | 1 | Pred (5 mg)+MTX (20 mg)+TCZ 800 mg IV |
| 2 | GCA | 1 | no | no | no | no | 9.3 | 4.11 | 110 | Pred (30 mg)+MTX (20 mg)* | 10 | 0.10 | 20 | Pred (5 mg)+MTX (20 mg) |
| 3 | GCA | 24 | yes | no | no | yes | 9.6 | 0.94 | 69 | Pred (30 mg)+MTX (15 mg) | 2 | NA | NA | Pred (20 mg)+MTX (15 mg) |
| 4 | GCA | 20 | no | no | no | no | 13.3 | 1.63 | 34 | MP bolus+Pred (60 mg)+MTX (15 mg) | 5 | 0.10 | 2 | Pred (20 mg)+MTX (15 mg) |
| 5 | GCA | 60 | yes | no | no | no | 11.6 | 3.63 | 69 | MP bolus+Pred (60 mg)+MTX (20 mg)* | 17 | 0.10 | 8 | Pred (2.5 mg)+MTX (20 mg)+TCZ 800 mg IV |
| 6 | GCA | 1 | no | no | no | no | 13.6 | 21.85 | 67 | Pred (50 mg) | 7 | 0.10 | 9 | Pred (15 mg) |
| 7 | GCA | 7 | yes | no | no | yes | 12.6 | 3.43 | 73 | Pred (20 mg)+MTX (15 mg) | 21 | 0.01 | 22 | None |
| 8 | PmR | 4 | yes | yes | no | no | 12.2 | 2.31 | 101 | Pred (60 mg)+MTX (15 mg)* | 5 | 0.10 | 24 | Pred (7.5 mg) |
| 9 | GCA | 0 | no | no | yes | no | 12.1 | 5.11 | 81 | MP bolus+Pred (20 mg)+MTX (7.5 mg) | 12 | 0.26 | 24 | Pred (10 mg)+MTX (7.5 mg) |
| 10 | Idiopathic | 0 | no | no | yes | yes | 12.1 | 5.72 | 7 | Pred (40 mg) | 5 | 0.20 | 7 | Pred (15 mg) |
| 11 | Idiopathic | 0 | no | no | yes | no | 14.6 | 0.55 | 6 | Abdominal angioplasty surgery | 27 | 0.72 | 4 | None |
| 12 | PmR | 7 | no | no | no | no | 13.6 | 10.38 | 64 | Pred (30 mg)+MTX (15 mg) | 3 | 0.27 | 10 | Pred (10 mg)+MTX (15 mg) |
| 13 | Sjögren syndrome | 5 | yes | no | yes | yes | 11.7 | 3.01 | 60 | Pred (30 mg) | 5 | 0.10 | 9 | Pred (10 mg) |

*were receiving MTX previously

Abbreviations: MP: methylprednisolone / Pred.: prednisone/MTX: methotrexate / TCZ: tocilizumab / GCA: giant cell arteritis / PmR: polymyalgia rheumatica / s.c.: orally / sc: subcutaneous / iv: intravenous /NA: not available

with idiopathic aortitis. Erythrocyte sedimentation rate (ESR) mean was 62±33.84 mm/1st hour and C Reactive Protein (CRP) median level mas 3.3 [2.91–5.13] mg/dl. Five patients presented anaemia.

At the time of diagnosis, 9 patients were receiving prednisone (mean dose, 18.89±19.3 mg/day), 4 were with methotrexate (MTX) (mean dose, 15±5.77 mg/week) and the remaining 3 were not receiving any drug.

Treatment of aortitis was based on the onset or increase in prednisone dose (mean dose, 34.17±9.73 mg/day) in all cases except for one patient who needed surgery for aortic aneurysm. MTX was initiated in 5 patients and its dose was increased in 4 more (mean maximum dose, 14.72±6.43 mg/week). Three patients were treated with methilprednisolone i.v. (0.5 g/day, 3 consecutive days). Tocilizumab (TCZ) was added to therapy in 2 cases due to refractory disease.

In the first visit, two to four months later, the ESR mean was 25.92±24.88mm/1st hour and CRP median was 0.32 [0.16–1.11] mg/dl. In successive clinical controls, after a mean follow-up of 10±4.32 months, clinical and laboratory improvement was maintained.

Four patients had a new PET-TAC control 6–16 months later, 3 of them presented complete remission and another one partial remission.

**Conclusions:** According to our data, clinical and laboratory data are often nonspecific in aortitis. The increase in the diagnosis cases in the last years is probably related to a higher index of suspicion. The presence of GCA or PmR refractory to standard treatment or unexplained raised ESR or CRP, may be red flags for suspecting an aortitis. Treatment with moderate doses of corticosteroids and MTX was effective in most of our patients. In 2 refractory cases, TCZ was useful.

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## SAT0355 INHIBITION OF HUMAN AORTIC ENDOTHELIAL IL-6 LEVELS BY CANDIDA ALBICANS WATER-SOLUBLE FRACTION (CAWS)

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**Background:** Serum interleukin-6 (IL-6) has been shown to closely follow disease activity in large vessel vasculitis[1]. Prior research by our group has demonstrated that mast cell degranulation downregulates lipopolysaccharide (LPS) induced aortic expression of IL-6 in vivo. This is accompanied by aortic upregulation of SOCS-1[2]. This effect is lost in histamine 1 receptor knockout mice suggesting that histamine is a primary mediator of aortic IL-6 inhibition. Prior studies have also demonstrated that mice injected with *Candida albicans* water-soluble fraction (CAWS) develop coronary and aortic arteritis[3]. The mechanism through which arteritis is induced by CAWS remains poorly understood.

**Objectives:** The objective of this study is to determine the effects of histamine and CAWS on IL-6 production by human aortic endothelial cells (HAEC) in vitro.

**Methods:** HAEC were cultured with histamine (10$\mu$M), LPS (100ng/mL), CAWS (10$\mu$g/mL), CAWS (1$\mu$g/mL) or a combination of these. After 22 hours, levels of IL-6 and 6-ketoprostaglandin-F1$\alpha$, a breakdown product of prostacyclin, were measured. Microculture tetrazolium (MTT) assays were used to determine cell viability.

**Results:** IL-6 levels were significantly lower in cells treated with CAWS 10$\mu$g/mL compared to controls (175.2±11.9 vs 270.0 pg/mL, p=0.006). Similarly, IL-6 levels were significantly lower with the addition 10$\mu$g/mL CAWS to LPS compared to LPS alone (359.8±37.74 vs 2906.5±318.02, p=0.0001). No significant differences were seen between the 10$\mu$g/mL and the 1$\mu$g/mL CAWS concentrations. Histamine synergistically enhanced IL-6 levels over LPS alone (3758.0±38.18 vs 2906.5±318.0, p=0.028). CAWS had no effect on prostacyclin levels compared to controls. MTT assays demonstrated no differences in cell viability in CAWS or histamine treated cells compared to controls.

**Conclusions:** Our experiments suggest that CAWS inhibits IL-6 production in HAEC. Since IL-6 is a key cytokine in the development of large vessel vasculitis we suspect that endothelial cells do not play a role in CAWS mediated arteritis. Similarly, the inhibitory effects of histamine do not appear to be mediated through endothelial cells. Future research will focus on the in vivo effects of histamine on the development of CAWS mediated vasculitis.

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## SAT0356 EXPERIENCE IN THE USE OF 18F-FDG PET/CT IN PATIENTS WITH POLYMYALGIA RHEUMATICA IN HUP LA FE

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**Background:** Polymyalgia rheumatica (PMR) is an inflammatory disease characterized by pain and stiffness that usually affects the upper body and the pelvis. PMR is related frequently to another inflammatory disorder called giant cell arteritis (GCA), where about 50% of patients present polymyalgia. PET/CT offers functional and molecular information about inflammatory diseases that leads to the vasculitis diagnosis in an early stage, so PET/CT is a useful diagnosis tool to identify CGA associated with PMR

**Objectives:** To evaluate the incidence of GCA in patients diagnosed of PMR.

**Methods:** Prospective study from January 2011 until December 2015 including patients with PMR from the Rheumatology Department of HUP La Fe. In all cases to confirm the diagnosis of vasculitides an 18-FDG PET/CT was made. Also blood analysis that includes CRP and ERS, US and biopsy and treatment with esteroids or another DMARD was done. Statistical analysis was performed using R software 3.2.3.

**Results:** 23 patients with PMR diagnosis according to established Bird/Wood criteria were included, with a mean age at the time of PET/CT of 69.3 years (38–85). 18 were treated with steroids before PET/CT and 11 had another DMAR during follow up.

In 47.8% of patients vasculitis was detected using PET/CT. Most frequent injury locations were aorta, iliac artery, and femoral artery. In these patients there is an increase in the CRP value (P=0.03) comparing to those without vasculitides. There were no significant differences in the ESR value or in the DMAR administration.

**Conclusions:** PET/CT is a useful diagnostic tool for the early diagnosis of vasculitides associated with PMR. This allows an early and adequate treatment in order to avoid structural damages within the blood vessel (aneurysms, stenosis, oclussions), reducing morbi-mortality and fatal outcomes.

**Disclosure of Interest:** None declared

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## SAT0357 COMMON AND UNCOMMON MANIFESTATIONS OF GRANULOMATOSIS WITH POLIANGIITIS (GPA) AT CHEST CT: A VASCULITIS CENTER EXPERIENCE

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**Background:** Lung involvement is not only a presenting finding but also might have widespread pathologic findings in Granulomatosis with Poliangitis (GPA). Even though chest computed tomography (CT) has superior sensitivity and specificity for evaluation of the airways, lung parenchyma and mediastinum, there are only a few studies regarding detailed analysis of Chest CT findings in GPA.

**Objectives:** To evaluate pulmonary pathologies in GPA at the time of diagnosis with CT.

**Methods:** Hacettepe University Vasculitis center is one of the main referral centers in the country. All patients starting from October 2014 have been included and defined according to the 2012 revised Chapel Hill nomenclature criteria. Our database was screened for patients with GPA. Totally 98 patients were evaluated and 43 patients were excluded since missing data. Fifty-five patients (Female: 31 (56.4%), were included in further analysis. Demographic and clinical findings were recorded. CT scans were read by two different radiologists who were aware of the diagnosis GPA, but unaware of the phase of disease. Final CT findings were reached in consensus. The following CT findings were evaluated: Parenchymal nodules or masses, ground-glass opacification or consolidation, tracheobronchial involvement, pleural irregularities, pleural effusions, hilar and mediastinal lymphadenopathy, cardiomegaly, pericardial effusions and vascular abnormality.

**Results:** The mean age was 51.5 (16.0) years and ANCA positivity (MPOANCA/PR3ANCA: 15/29) was in 80% of patients. 76.4% of patients (n=42) have any of CT findings. In 70.9% (n=39) of patients had parenchymal involvement and most commonly observed findings were nodules/masses in 24 (43.6%) patients, ground-glass opacification or consolidation in 22 (40.0%) patients. These parenchymal findings were bilateral in 87.2% (34/39) of patients. A combination of both patterns were also available in 17.9% (7/39) of patients. Of examinations with nodules; 70.8% (17/24) demonstrated more than five nodules, and 33.3% (8/24) had cavitary lesions. Pleural effusions were seen in 13 patients (23.6%) and 46.2% (6/13) of them were bilateral. Hilar or mediastinal lymph node enlargement was discovered in 6 (10.9%) patients and all also had parenchymal involvement. In only two patients had tracheobronchial involvement; one was subglottic stenosis, the other was thickening of bronchial wall. Pericardial effusion and/or cardiomegaly was detected in 9 (16.4%) patients and all these patients also had parenchymal involvement. In subgroup analysis according to ANCA positivity and sex, pulmonary nodules/masses were more frequent in ANCA positive patients (50%vs. 18.2%, p=0.057). And ground-glass opacification or consolidation were more often in males (54.2% vs. 29.0%, p=0.059).

**Conclusions:** Even though at disease onset, most of GPA patients had any of pulmonary pathologies observed by CT. Not only nodules/masses and consolidation/ground-glass opacification were seen but also pericardial effusion and/or cardiomegaly, tracheobronchial involvement and subglottic stenosis could be found. ANCA positivity and sex might contribute pulmonary pathologies. Further studies are required.

**Disclosure of Interest:** None declared

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## SAT0358 EFFICACY OF METHOTREXATE IN GIANT CELL ARTERITIS

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**Background:** Prospective trials evaluating methotrexate (MTX) as adjunct immunosuppression in Giant cell arteritis (GCA) have provided evidence of a modest benefit for reducing risk of relapse and decreasing glucocorticoid exposure. Limited information is available regarding the use of this medication in routine clinical practice.

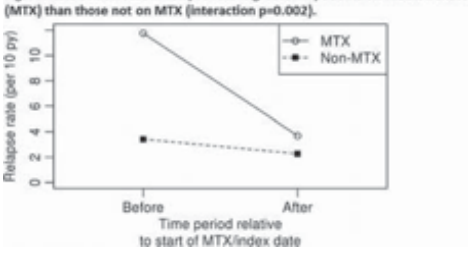
**Objectives:** To determine the effect of methotrexate on relapse risk and glucocorticoid use in a large single-institution cohort of patients with GCA.

**Methods:** A retrospective review of patients diagnosed with GCA from 1998–2013 was performed. Patients diagnosed with GCA were ≥50 years and had either a temporal artery biopsy (TAB) that was consistent with GCA or radiographic evidence of large vessel vasculitis. Each patient with GCA treated with adjunct MTX (case) was matched to a similar GCA patient without MTX (control). Cases and controls were matched on age, sex, disease duration at start of MTX and initial corticosteroid dose. Each control was assigned an index date to make the number of days from GCA diagnosis to index date in the control equivalent to the number of days from the GCA diagnosis to the start of MTX in cases. Baseline demographics, disease characteristics and relapse events were abstracted. Glucocorticoid requirements and relapse events before and after methotrexate initiation (or corresponding index date) were compared using rate ratios.

**Results:** A total of 84 patients with GCA receiving MTX were identified and compared to 84 patients with GCA receiving only prednisone. Mean age at diagnosis 69.5±7.0 years in cases and 70.3±6.9 in controls. No significant differences in demographics, laboratory parameters or baseline disease characteristics were observed between groups. Mean initial prednisone doses were similar (53.5±15.8 mg/day in cases, 55.0±13.5 mg/day in controls). The median (interquartile range [IQR]) time from GCA diagnosis to MTX initiation in cases was 0.7 (0.3, 1.6) years and the median (IQR) starting dose was 13.5 (10, 15) mg per week.

Prior to MTX initiation the observed relapse rate was 11.8 relapses per 10 person-years and decreased to 3.69 relapses per 10-person years following initiation. The rate ratio comparing relapse rates observed after MTX to the rate prior to initiation was significantly reduced; rate ratio (95% CI): 0.31 (0.24, 0.41). In the control group the relapse rate was 3.42 relapses per 10 person-years before the index date and 2.27 relapses per 10 person-years following the index date [rate ratio (95% CI); 0.66 (0.45, 0.99). Although both groups had a reduction in relapse rate ratios, the rate of decrease in relapse rate was significantly greater in patients on MTX than those not on MTX (p=0.002) [figure].The ratio of rates after MTX initiation/index date for achieving steroid doses <10 mg/day for >6 months or steroid discontinuation >6 months did not differ for cases and controls.

Figure: Rate of decrease in relapse rate is greater in patients on methotrexate (MTX) than those not on MTX (interaction p=0.002).




**Conclusions:** In this large single-institution cohort, the addition of methotrexate to glucocorticoid decreased the rate of subsequent relapse by 2-fold compared to patients on glucocorticoids alone. Methotrexate should be considered as adjunct therapy in patients with relapsing GCA to decrease the risk of further relapse events.

**Disclosure of Interest:** None declared

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## SAT0359 EVALUATION OF MEDICATION COMPLIANCE IN BEHÇET'S DISEASE

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**Background:** The management of Behcet's disease (BD) should be tailored to each patient by taking into account the existing symptoms, clinical manifestations and prognostic factors. Since there are effective treatment alternatives for each manifestation, the patient's adherence to treatment is one of the most important elements for a successful management of the disease. Adherence to treatment in patients with BD is not known well

**Objectives:** To investigate the compliance status to drug therapy in patients with BD.

**Methods:** This study was conducted at the rheumatology outpatient clinic of a tertiary hospital and 125 BD patients were included. Patient interview form, the Turkish Translation of the Compliance Questionnaire on Rheumatology (2015) (CQR-T; score 0–100), validated by Cinar et al, and Morisky Medication Adherence Scale, developed by Morisky (1986), were used to determine the sociodemographic and medical characteristics. In addition, disease activity was evaluated with Behcet's Syndrome Activity Score (BSAS, score =0–100) and Behcet's Disease Current Activity Form (BDCAF; score =0–12).

**Results:** The mean age of the patients was 31.42 ± 8.11 years and 91.2% were male. The mean disease duration, age at diagnosis, BDCAF score and BSAS score of patients were 9.34 ± 5.76 years, 25.02 ± 7.82 years, 4.79 ± 2.05 and 45.22 ± 23.56, respectively. 76.8% of the patients were using colchicine, 44.8% azathioprine, 16.0% corticosteroids, 4.8% cyclosporine, 4.0% cyclophosphamide, 4.0% infliximab, 3.2% non-steroidal anti-inflammatory drugs, 2.4% methotrexate, 1.6% sulfasalazine and 7.2% were using anticoagulants. 40 patients (32.0%) experienced drug-induced side effects. The total CQR-T score of patients was 66.48 ± 13.49 (min: 19.30-max: 94.74). According to the Morisky Medication Adherence Scale, medication compliance score of the patients was high in 25.6%, medium in 55.2%, and lower in 19.22% of patients. The total Morisky Medication Adherence Scale score was 1.43 ± 1.16 (min-max, 0–4). The demographic/medical characteristics of the patients (age, sex, marital status, education level, employment status, social support status, treatment, transportation, disease duration, symptom onset time, BSAS, BDCAF, ESR and CRP) had no association with total CQR-T scores. The total CQR-T score had a significant but weak correlation (r =0.197; p=0.027) with the age at diagnosis.

**Conclusions:** In our study, it was found that the majority of treated patients were at an intermediate level of compliance status. Adherence to treatment status of patients increases with increasing ages at diagnosis. This study emphasizes the necessity of developing new strategies for increasing the patients' adherence.

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**Disclosure of Interest:** None declared

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## SAT0360 HENOCH - SCHÖNLEIN PURPURA IN ADULTS: DATA FROM A REFERRAL CENTER IN SWEDEN

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**Background:** Henoch-Schönlein purpura or IgA vasculitis (IgAV) is a systemic vasculitis encountered both in children and adults. It may lead either to single-organ vasculitis as cutaneous IgAV or a systemic disease[1]. IgAV in adults is considered to have worse clinical features and outcome compared to that of children[2].

**Objectives:** Retrospective analysis of 43 consecutive adult IgAV patients referred to a secondary and tertiary referral centrum in a Swedish university hospital between 2008 and 2014.

**Methods:** Electronic records of patients were reviewed. EULAR/PRINTO/PRES and ACR criteria for diagnosis and EUVAS criteria for disease activity were applied[3]. MedCalc Statistical Software version 15.11.4 (MedCalc Software bvba, Ostend, Belgium) was used.

**Results:** Twenty-eight of the patients were male and 15 female. Mean age at disease onset was 43 (SD=21) years. Ten of 43 patients (23%) suffered an upper respiratory tract infection prior to disease onset. All 4 major organs were involved in 12/43 patients (28%). Skin vasculitis was present in 40 (93%), arthritis in 13 (30%), gastrointestinal involvement in 22 (51%) and renal manifestations in 29 patients (67%). Nine patients (21%) had positive findings from either endoscopy or computed tomography. Twenty of 34 patients examined (59%) had various cellular casts. Seventeen patients (40%) had albuminuria and 29 (67%) hematuria. Skin biopsy showed leucocytoclastic vasculitis in 63% of all 43 patients. IgA was shown in 9/11 renal (82%) and in 27/29 (93%) skin biopsies. Five skin biopsies had IgM deposition whereas 3 had both IgM and IgG. All 8 patients had renal involvement ($\chi^2$=4,12, p=0,04). Regarding treatment, 86% of the patients received prednisolone while 30/43 (70%) were given other immune therapy, namely mycophenolate mofetil in 6/43 (14%). Time to joint remission was shorter for women (p=0.04) but renal remission was shorter for men (p=0.001). Thirty out of 43 patients (70%) had just one incidence of IgAV while 9/43 (21%) had more than one episode, in some cases even 4 or 5 relapses.

**Conclusions:** These results confirm those from other centra[2] in an attempt to elucidate IgAV in adults. Time to remission is to our knowledge not previously studied. Unique in this study was the finding that joint response was statistically significant slower in men than women and the opposite was observed regarding renal response. IgM deposition in skin biopsy was associated to renal involvement. The outcomes may vary depending on period of follow-up and age of patients. In the lack of therapeutic consensus guidelines, treatment continues to be symptomatic and immunomodulation regimens are reserved for those with more severe disease. These results need to be confirmed in larger cohorts.

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**Disclosure of Interest:** None declared

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## SAT0361 KIDNEY INVOLVEMENT IN MICROSCOPIC POLIANGIITIS – RUSSIAN EXPERIENCE

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**Objectives:** Our aim was to assess frequency, clinical features and prognosis of renal involvement in microscopic poliangiitis (MPA) and used treatment modalities based on experience of Clinic of Nephrology, Internal and Occupational diseases in Moscow, Russia.

**Methods:** We performed a retrospective analysis of 61 patients with MPA, diagnosed according to Chapel-Hill Consensus Conference 2012, 23 male and 38 female, who were followed over a median of 29 (11;74) months. 58 patients (95.1% of 61) had a history of active renal vasculitis. Rapidly progressive glomerulonephritis (RPGN) was defined by the doubling of serum creatinine in $\leq$3 months. Acute kidney injury (AKI) and chronic kidney disease (CKD) stages were diagnosed according to KDIGO 2012 definition.

**Results:** In 43 patients (74.1%) renal involvement developed at the onset of the disease. Other 15 (25.9%) developed glomerulonephritis after a median of 7 (6;14) months. All patients had active urinary sediment; hematuria was present in 55 (94.8% of 58) patients; 8 patients (13.8%) developed nephrotic syndrome. Nephrogenic hypertension was present in 27 (46.5%) patients. RPGN developed in 35 patients (60.3% of 58), 6 of them (17.1%) also had nephrotic syndrome. During follow up 12 patients (20.7%) developed AKI, stage 2 was diagnosed in 5 patients, stage 3 in 7 patients. In 9 patients (15.5%) AKI developed during their first admission to the hospital. Renal involvement was confirmed by kidney biopsy in 9 cases (15.3% of 59).

By the end of the follow-up CKD stage 1 was diagnosed in 9 (15.5%), stage 2 in 13 (22.4%), stage 3A in 9 (15.5%), stage 3B in 12 (20.7%), stage 4 in 10 (17.3%) patients and only 5 (8.6%) developed end-stage renal disease (ESRD). Three more patients were likely to develop ESRD, but they died before it could be diagnosed according to KDIGO criteria. ESRD developed in 9 (8;13) months from the onset of the disease. A total of 4 patients (6.8%) died.

As the first line induction therapy all patients received corticosteroids (CS), 51 (87.9%) – cytotoxic agents, predominantly cyclophosphamide (90.3% of 51), and 4 (6.9% of 58) – rituximab (RTX). Plasmapheresis was used in 13 (22.4%) patients. Complete remission was achieved in 40 (69%) patients who received cytotoxic agents and/or CS, 14 (24.1%) developed partial remission, in 4 (6.9%) remission was not achieved. During follow up 18 patients received RTX for remission induction due to refractory disease in 12 (66.7%), severe relapses in 2 (11.1%) and/or CS and cytotoxic agents side effects or intolerance in 8 (44.4% of 18) patients. Thirteen (72.2% of 18) patients achieved complete remission on RTX, 3 (16.7% of 18) achieved partial remission, in 2 (11.1%) RTX was ineffective. 29 patients (50%) developed one or more severe relapses during follow-up; corresponding to a relapse rate of 0.186 per patient per year. Renal relapses developed in 21 (36.2%) patients, with a renal relapse rate of 0.105 per patient per year.

**Conclusions:** Our research revealed considerably lower prevalence of ESRD and fewer lethal outcomes in patients with MPA when compared with the published data. Nevertheless more than a half of patients develop RPGN during the course of the disease, and 46.6% have CKD stage 3B or worse by the end of the follow up. Despite effective induction therapy with high-dose CS, cytotoxic agents and/or RTX relapses, both renal and extrarenal, are frequent.

**Disclosure of Interest:** None declared

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## SAT0362 MYCOPHENOLATE MOFETIL VERSUS METHOTREXATE IN THE MANAGEMENT OF LARGE VESSEL GIANT CELL ARTERITIS

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**Background:** There is an unmet clinical need to identify an effective conventional adjuvant immunosuppressive agent in the treatment of large vessel giant cell arteritis. Traditionally the therapeutic approach has employed prolonged courses of high dose glucocorticosteroids (GC) with poor long-term outcomes. Methotrexate (MTX) is currently recommended as adjuvant GC sparing immunosuppression based on modest evidence[1,2]. Evidence for the use of Mycophenolate mofetil (MMF) in this setting is lacking.
**Objectives:** We investigated the outcome of MMF and MTX usage in an extended cohort of large vessel giant cell arteritis (LVV-GCA) patients from 2 large tertiary centres in the United Kingdom.
**Methods:** We retrospectively analysed laboratory and treatment outcomes for United Kingdom patients diagnosed with LVV-GCA between January 2008 and January 2015 who attended two geographically distinct specialist Vasculitis Clinics. The two centres use different first line GC sparing agents in LVV GCA, one generally uses MMF the other MTX.
Following retrospective record review, cases were selected based on radiologic evidence of large vessel vasculitis, fulfilment of the Chapel Hill Consensus Conference 2012 GCA definition and a first line prescription of GC with adjuvant MMF or MTX. Baseline and follow up characteristics were collated. Unpaired t-test was used to compare differences between the groups.
**Results:** Twenty patients (7 male) were identified in total: 11 patients (3 male) treated with MMF and 9 patients (4 male) treated with MTX. Mean age (SD) at diagnosis was 66.15 (7.1) years with the MMF group being older (68.9 (5.9) versus 62.7 (7.2) years). Positron emission tomography–computed tomography (PET CT) confirmed evidence of active large vessel vasculitis in all patients.
At diagnosis, there was no significant difference between the mean CRP value between the two groups (56.1 (46.9) versus 47.7 (34.3) mg/l, p=0.67). Following 6 weeks of treatment, there was a dramatic reduction in the mean CRP level in both groups (8.1 (8.7) versus 3.1 (2.2), p=0.14), a response which was maintained at one year (7.6 (5.8) versus 4.5 (3.1), p=0.16). Although at diagnosis Prednisolone dose was higher in the MMF group (54.5 (9.3) versus 41.1 (17.6) mg, p=0.042), no significant difference was found between the groups at 6 weeks (24.1 (5.4) versus 29.1 (12.8) mg, p=0.26) and throughout the year (8.4 (2.8) versus 5.8 (3.7) mg, p=0.1 at one year)
**Conclusions:** To our knowledge, we describe the first case-series of MMF use in LV-GCA.
Within the limitations of this study, MMF appears to be comparable to MTX as adjunctive therapy in patients with LV-GCA, allowing a rapid taper of GC. A randomized controlled trial is required to further evaluate the role of MMF in this challenging disease subset.
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**Disclosure of Interest:** None declared
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## SAT0363 A SYSTEMATIC LITERATURE REVIEW ON THE TREATMENT OF SKIN, MUCOSA AND JOINT INVOLVEMENT OF BEHÇET'S SYNDROME INFORMING THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF BEHÇET'S SYNDROME

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**Objectives:** The aim of this systematic literature review was to inform the task force for updating the European League Against Rheumatism recommendations for the management of Behçet's Syndrome (BS), about the evidence for treatment of skin, mucosa and joint involvement of BS.
**Methods:** A systematic literature search, data extraction and statistical analyses according to pre-specified and protocolised eligibility criteria were performed using the GRADE approach. The protocol for the review was registered and is available at PROSPERO (CRD42015027033). The Cochrane Library, including the Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessments (HTA), MEDLINE (from 1950), EMBASE (from 1980) and International Pharmaceutical Abstracts Database (IPAD) were systematically searched. Randomised controlled trials (RCT), non-randomised controlled clinical trials and open label trials (OLT) on BS comparing an active intervention (alone or in combination) with any control or placebo were eligible. If controlled trials were not available for answering a specific research question, uncontrolled evidence from cohort studies or case series involving $\geq$5 patients were considered. The quality of evidence was assessed by using the GRADE approach. Risk ratios were calculated for the binary outcomes whereas for the continuous outcomes we calculated the standardized mean difference (SMD).
**Results:** Among the 3927 references that we have screened, 22 studies satisfied the inclusion criteria for mucocutaneous involvement and 15 studies for joint involvement. Seventeen of these studies were RCTs assessing mucocutaneous and/or joint involvement. RCTs with colchicine, azathioprine, interferon-alpha, thalidomide, etanercept and apremilast showed different levels of beneficial results on different types of skin and mucosa lesions and arthritis. Differences in the outcome measures that were used across the included studies made it difficult to compare the results. These agents were generally well tolerated with few adverse events causing withdrawal from the study in BS patients.
**Conclusions:** It was gratifying to see that randomised trials formed the majority (17/22, 77%) of the sources forming the basis for the recommendations related to skin mucosa and joint involvement in the updated EULAR recommendations for the management of BS.
**Disclosure of Interest:** None declared
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## SAT0364 PENTRAXIN 3 AS BIOMARKER IN ASSESSMENT OF DISEASE ACTIVITY IN TAKAYASU ARTERITIS

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**Background:** In Takayasu arteritis (TA) Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are used to monitor disease activity. Thirty percent of patients with active inflammation have normal ESR while 40% without vascular inflammation have elevated ESR.[1] Pentraxin 3 (PTX3) produced in vascular wall during inflammation, may be a better biomarker of disease activity.
**Objectives:** To compare PTX3 levels in TA patients with healthy controls and to compare the accuracy of PTX3 levels with high sensitive CRP (hs CRP) and ESR in distinguishing active from inactive disease.
**Methods:** Cross sectional prospective study conducted from 2014 to 2015.Forty consecutive TA patients fulfilling 1990 American College of Rheumatology criteria for TA and 20 healthy controls were included. Disease activity was assessed by Physician Global Assessment (PGA), Indian Takayasu Arteritis Score (ITAS)[2] and ITAS-ESR. Serum PTX3 levels (pg/ml) was measured in TA patients and controls, hsCRP (ng/ml)and ESR (mm/hr)were measured in TA patients. Based on PGA patients were divided into active, grumbling and inactive disease.Serum PTX3, hs CRP and ESR were expressed as mean (SD). ROC were constructed for serum PTX3, hs CRP and ESR in differentiating active from inactive disease. p value $<$0.05 was considered significant. SPSS Software (version 21) was used.
**Results:** Mean age of TA patients and Healthy controls was 27 (7.9), 20 (3.4) years respectively.90% patients were female.Mean disease duration was 3.4 (3.1) years (range 1–12 yrs). Weight loss, fatigue, anorexia were the presenting symptoms followed by claudication. There were 14 patients with active disease, 8 with grumbling disease and 18 with inactive disease.Mean (SD) ITAS in patients with active disease 5.9 (3.5) was significantly higher than in patients with grumbling disease 0.9 (1.2) or inactive disease 0.6 (1). Mean ITAS-ESR in active disease was higher than in grumbling and inactive disease but not different between grumbling and inactive disease.

Laboratory markers in TA patients grouped by the PGA

| | Active | Grumbling | Inactive | p |
|---|---|---|---|---|
| ESR | 52 (22.1) | 45.6 (16.2) | 34.7 (14) | $<$0.026 |
| hsCRP | 13719 (8409) | 10583 (9961) | 6165 (6658) | $<$0.03 |
| PTX3 | 1431 (1013) | 1170 (1190.5) | 357 (244) | $<$0.002 |

Mean PTX3 levels were significantly higher in cases compared to healthy controls (895 (935.6), 317 (215.5)) ($p<0.026$).

ROC parameters of Biomarkers for detecting active TA patients

| | SE % | SP% | AUC | CI |
|---|---|---|---|---|
| ESR ($>$46 mm/hr) | 50 | 89 | 0.74 | 0.563–0.921 |
| HsCRP ($>$17090 ng/ml) | 57 | 89 | 0.79 | 0.626–0.953 |
| PTX3 ($>$631 pg/ml) | 71 | 95 | 0.86 | 0.720–0.994 |

Sensitivity (SE), specificity (SP) and area under the curve (AUC) with confidence intervals (CI).

**Conclusions:** PTX3 performed better than hs CRP and ESR in differentiating active from inactive disease. Grumbling disease could not be differentiated from inactive disease using ITAS/ITAS-ESR. Inflammatory markers did not perform well in differentiating grumbling disease from active or inactive disease in TA.
**References:**
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## SAT0365 RISK FACTORS FOR VISUAL LOSS IN GIANT CELL ARTERITIS (GCA)

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**Background:** visual loss is the most frequent ischemic complication and the main cause of permanent disability among patients with GCA. To identify factors related to this complication may help physicians to start an early treatment and assay new therapies

**Objectives:** To analyse clinical and histological findings related to visual loss in patients with GCA

**Methods:** demographic, clinical and histological features of patients with biopsy-proven GCA recruited at 10 Hospitals from Spain (REVAS Study) were analysed. Statistical analysis was performed using SPSS vs. 20

**Results:** 418 patients were included: 290 (69.4%) females (ratio F/M: 2.3/1). The mean age at diagnosis was 75.5 ± 7 (53–92), 55% patients being older than 75y. The median diagnosis delay was 7 weeks (IQR 4–12). Cardiovascular risk factors were present in 45% of patients (hypertension in 48.8%, hypercholesterolemia in 26.6%, diabetes mellitus in 19.4%). The most frequent symptoms at CGA diagnosis were recent onset headache (81%), constitutional symptoms (47%) and polymyalgia rheumatic (44.5%). Jaw claudication, cranial hyperesthesia and amaurosis fugax were reported by 44.5%, 31.8% and 16.5%2 of patients, respectively. A total of 84 patients suffered vision loss (in 4 cases involving both eyes), due to anterior optic ischemic neuropathy (AION) in 78 (92.8%), and to central retinal artery occlusion in 6 (7.1%). CVA was recorded in 6.5% of cases. Anemia was present in 76.3% of patients. Mean ESR was 98±23.4. Patients with visual loss presented more frequently jaw claudication (71.6% vs 39.2%), cranial hyperesthesia (52.6% vs 28.7%) and amaurosis fugax (52.6% vs 8.6%), and less frequently low-grade fever (16.7% vs 43.1%) and toxic syndrome (37.2% vs 53.4%). Regarding to histological findings: patients with visual loss presented on TAB more intimal hyperplasia (70.5% vs 57.7%) and lumen occlusion >50% (53.8 vs 19.4%). No other differences were found. Univariated analysis showed than AION was significantly related to the presence of amaurosis fugax (OR 12.8, 95% CI 7.0–23.3, $p<0.001$), jaw claudication (OR 4, 95%CI 2.3–7.1, $p<0.001$), cranial hyperesthesia (OR 2.4, 95%CI 1.5–4), and age at diagnosis ≥75 years old (OR 2.7, 95% CI 1.5–4.6, $p<0.001$). An inverse relationship between AION and the presence of low-grade fever and toxic syndrome was found. No significant relationship was found between visual loss development and cardiovascular risk factors or CVA

**Conclusions:** AION is the most frequent cause of vision loss in GCA. Jaw claudication, cranial hyperesthesia, amaurosis fugax, and age >75 older at diagnosis are significantly related to AION. A wider recognition of the disease would potentially reduce the prevalence of irreversible visual loss among GCA patients.

**Disclosure of Interest:** None declared

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## SAT0366 COMPARING THE CHARACTERISTICS OF ADULT AND PEDIATRIC PATIENTS WITH POLYARTERITIS NODOSA

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**Background:** Polyarteritis nodosa (PAN) as a necrotizing vasculitis of medium or small arteries without glomerulonephritis or vasculitis in arterioles, venules or capillaries and not associated with antineutrophil cytoplasmic antibodies. It is more common in middle-aged adults when compared with children.

**Objectives:** The aim of this study was to examine and compare the clinical characteristics of adult and pediatric patients with PAN.

**Methods:** Nine pediatric (<18 years of age) and 28 adult patients with a clinical diagnosis of PAN who were seen at the Departments of Rheumatology and Pediatric Rheumatology, Hacettepe University, Ankara, Turkey were included in the study group. The pediatric and adult patients were classified as PAN according to the Ankara 2008 and ACR 1990 criteria, respectively. The clinical features and response to therapy were evaluated retrospectively.

**Results:** The characteristics of PAN patients were summarized in Table 1. According to the results with a statistical significance, neurologic involvement was more common and the duration of induction treatment was longer in adults ($p=0.008$ and $p<0.001$, respectively). Renal involvement was more common in adults than children, however this difference did not reach statistical significance. 4/28 (14.2%) adult and 3/9 (33.3%) pediatric patients had accompanying familial Mediterranean fever. Of adult patients, 85% (n=23) had received cyclophosphamide plus corticosteroid for induction treatment while three pediatric patients received CYC and four received mycophenolate mofetil addition to corticosteroid treatment.

**Conclusions:** Although our study population is limited, neurologic and renal involvement were more common and the duration of induction treatment was longer in adults patients with PAN. There is no previous study comparing the characteristics of pediatric and adult patients with PAN Multicenter collaboration remains essential to determine the characteristic features of PAN in patients of different age groups.

Table 1. The characteristics of adult and pediatric patients with polyarteritis nodosa (PAN)

| | Pediatric patients (n=9) | Adult patients (n=28) | P value |
|---|---|---|---|
| Gender | 5F/4M | 9F/19M | 0.25 |
| Fever, n (%) | 6 (66.7) | 17 (60.7) | 1 |
| Myalgia, n (%) | 6 (66.7) | 14 (50) | 0.70 |
| Weight loss, n (%) | 2 (22.2) | 14 (50) | 0.11 |
| Fatigue, n (%) | 8 (88.9) | 25 (89.3) | 1 |
| Arthralgia/arthritis, n (%) | 8 (88.9) | 18 (64.3) | 0.39 |
| Cutaneous involvement, n (%) | 9 (100) | 21 (75) | 0.30 |
| Hypertension, n (%) | 4 (44.4) | 14 (50) | 1 |
| Renal involvement, n (%) | 1 (11.1) | 13 (46.4) | 0.056 |
| Neurologic involvement, n (%) | 1 (11.1) | 18 (64.3) | 0.008 |
| Testicular involvement, n (%) | 0 (0) | 2 (7.1) | 1 |
| Gastrointestinal system involvement, n (%) | 5 (55.6) | 9 (32.1) | 0.26 |
| Cardiovascular involvement, n (%) | 1 (11.1) | 1 (3.6) | 0.45 |
| Pulmonary involvement, n (%) | 1 (11.1) | 4 (14.3) | 1 |
| Time period between onset of symptoms and diagnosis (months, median) | 6 (0–48) | 6 (1–84) | 0.92 |
| Erythrocyte sedimentation rate at diagnosis (mm/h, median) | 73 (16–120) | 56 (6–120) | 0.53 |
| C-reactive protein at diagnosis (mg/dl, median) | 5.39 (0.2–17) | 5.4 (0.2–13.4) | 0.78 |
| Presence of biopsy at diagnosis, n (%) | 9 (100) | 19 (67.9) | 0.07 |
| Presence of angiography at diagnosis, n (%) | 3 (33.3) | 20 (71.4) | 0.057 |

**References:**

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**Disclosure of Interest:** None declared

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## SAT0367 CAN WE DIFFERENTIATE TAKAYASU ARTERITIS FROM ATHEROSCLEROSIS USING CAROTID AND FEMORAL ARTERY DOPPLER USG?

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**Background:** Clinicians can have difficulty in making differential diagnosis between Takayasu arteritis (TA) and atherosclerosis. This is especially true when laboratory evaluations and FDG PET are inconclusive. In addition to that atherosclerosis load is potentially increased in TA (1–2). About 1/3rd of the patients with TA had carotid artery plaques and almost half had diffuse aortic wall calcifications (1–2).

**Objectives:** We thought that TA might have unique vascular changes distinct from atherosclerosis when evaluated with Doppler ultrasonography (USG).

**Methods:** Consecutive patients with TA seen in the department of Rheumatology at Cerrahpasa Medical Faculty at Istanbul were studied along with healthy controls. TA patients and healthy controls were aged between 18 and 50 years. Patients with diabetes mellitus (DM) who were followed by the endocrinology outpatient clinic were also studied. For the purposes of this study, no age limit was set for patients with DM. Only females were studied. Traditional atherosclerotic risk factors were also assessed. The radiologist scanned the right and left common, internal and external carotids, carotid bulb as well as the right and left common femoral arteries using Doppler USG. Intima-media thickness (IMT) was measured and resistivity index was calculated. The presence of atherosclerotic plaques and diffuse IMT was assessed. Diffuse IMT was defined as diffuse homogenous intima-media thickening of at least 0.9 mm.

**Results:** We studied 58 patients with TA (mean age: 43 ±11), 42 patients with

Table 1. Mean age and vascular parameters observed on carotid and femoral artery USG

| | TA, n=58 | DM, n=42 | HC, n=24 |
|---|---|---|---|
| Mean age | 43±11 | 57±9* | 41±4 |
| Carotid artery | | | |
| Presence of diffuse IMT, n (%) | 45 (78)** | 1 (2) | 0 |
| Atherosclerotic plaques, n (%) | 21 (36) | 28 (67)§ | 2 (8) |
| Turbulence, n (%) | 8 (14)** | 0 | 0 |
| Intima-media thickness, mm | 0.90±0.36† | 0.96±0.25 | 0.40±0.12 |
| Resistivity index | 0.63±0.10** | 0.50±0.04 | 0.56±0.04 |
| Femoral artery | | | |
| Presence of diffuse IMT, n (%) | 5 (9)** | 0 (0) | 0 (0) |
| Atherosclerotic plaques, n (%) | 6 (10) | 15 (36)§ | 0 (0) |
| Intima-media thickness, mm | 0.71±0.26 | 1.0±0.29§ | 0.38±0.09 |

*TA vs DM. DM vs HC: $p<0.001$; **TA vs DM. TA vs HC: $p<0.05$; †TA vs HC. DM vs HC: $p<0.001$; §TA vs DM. DM vs HC. TA vs HC: $p<0.001$.

DM (mean age: 57 ± 9) and 24 healthy controls (mean age: 41 ± 4). Patients with DM were significantly older and had significantly more atherosclerotic risk factors. The mean carotid IMT was comparable between TA and DM, whereas the mean femoral IMT was significantly lower in TA. The frequency of atherosclerotic plaques in both carotid and femoral arteries was significantly higher among patients with DM (Table). Presence of diffuse wall thickenning of at least 0.9 mm and turbulence were observed almost only among patients with TA. Finally the mean resistivity index was only significantly increased in TA (Table).

**Conclusions:** Diffuse homogenous increase in IMT, presence of turbulence and higher resistivity index can be considered as suggestive of TA rather than atherosclerosis. This study showed that carotid and femoral artery USG may be helpful in differentiating TA from atherosclerosis.

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**Disclosure of Interest:** None declared

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## SAT0368 A SYSTEMATIC LITERATURE REVIEW ON THE TREATMENT OF MAJOR ORGAN INVOLVEMENT OF BEHÇET'S SYNDROME INFORMING THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF BEHÇET'S SYNDROME

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**Background:** The first EULAR recommendation for the management of Behçet's syndrome (BS) was published in 2008 and since then new data including biologic agents have appeared.

**Objectives:** To review the evidence for efficacy and safety of management strategies in BS patients with eye, vascular, gastrointestinal (GI) and neurologic involvement.

**Methods:** We used the GRADE methodology as framework for guidelines development. For the systematic literature review, we searched The Cochrane Library, Database of Abstracts of Reviews of Effects, Health Technology Assessments, MEDLINE, EMBASE and International Pharmaceutical Abstracts Database. Randomized controlled trials (RCT), controlled clinical trials, or open label trials comparing an active drug in patients with BS with other agents or placebo were included. If controlled trials were not available for answering a specific research question, uncontrolled evidence from prospective or retrospective studies or case series about a minimum of 5 patients were also included.

**Results:** We reviewed the titles and abstracts of 3927 references, followed by the full texts of 397. A total of 166 studies related with major organ involvement met our inclusion criteria. Three RCTs with cyclosporine-A (CycA) and 1 with azathioprine (AZA) showed beneficial results in BS patients with eye involvement. There were several observational studies with interferon-$\alpha$ and TNF-$\alpha$ antagonists in patients with eye involvement, including those among patients refractory to conventional treatment modalities. Decreases in the frequency of ocular attacks, remission and improvement in visual acuity were observed in the majority of patients treated with these agents. As for vascular involvement, retrospective studies showed that immunosuppressives (IS) significantly decreased the frequency of recurrences in BS patients with deep vein thrombosis (RR 95%CI: 5.8, 2.8–11.8). A similar effect was not observed with anticoagulants+IS compared with IS alone (RR 95%CI: 1.5, 0.8–2.6). Observational studies showed that cyclophosphamide and high dose glucocorticoids (GC) decreased mortality in patients with arterial aneurysms. Treatment with IS and GC decreased postoperative complications in patients who had surgery for arterial aneurysms. Observational studies showed beneficial results with 5-ASA derivatives and AZA in the initial management of BS patients with GI involvement. Remission could be obtained with thalidomide and/or TNF- $\alpha$ antagonists in the majority of patients with refractory GI involvement. Retrospective studies also showed IS decreased postoperative recurrences in patients operated for intestinal perforations or major bleeding (RR 95%CI: 0.56, 0.33–0.95). Observational studies in BS patients with neurologic involvement showed IS and GC improved the outcome. CycA should be avoided in such patients since retrospective studies showed that CycA had increased the risk of development of neurologic involvement (RR 95%CI: 12.6, 4.7–33.7).

**Conclusions:** It is sobering to note that the majority of the studies forming the basis for the recommendations related to major organ involvement in the updated EULAR recommendations for the management of BS come from observational studies.

**Disclosure of Interest:** None declared

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## SAT0369 WEIGHT GAIN IN ANCA-ASSOCIATED VASCULITIS IS INDEPENDENT OF GLUCOCORTICOID DOSING

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**Background:** The treatment of ANCA-associated vasculitis (AAV) includes high doses of glucocorticoids, the use of which has been associated with increased body-mass index (BMI)[1]. A previous study suggested that this change in BMI is independent of glucocorticoid exposure[2].

**Objectives:** We sought to evaluate whether increases in BMI are related more directly to improved disease control than to glucocorticoid use.

**Methods:** We analyzed AAV patients enrolled in the Rituximab in ANCA-Associated Vasculitis (RAVE) trial[3]. Details regarding glucocorticoid exposure before and during the trial were collected, as were regular measurements of BMI and disease activity. We used multivariate linear regression to adjust for important confounders of the relationship between glucocorticoid exposure and BMI changes. We used analysis of response profile to evaluate differences in BMI over time between subgroups and mixed effects models to determine the relationship between disease activity and change in BMI.

**Results:** Of the 197 patients enrolled in RAVE, 99 (50%) were male and the mean age was 52.8 (±15.5) years. The baseline BVAS/WG was 8.0 (±3.1). The majority (75%) had granulomatosis with polyangiitis, and PR3-ANCA+ was the most common (67%) ANCA specificity. The baseline BMI was 28.8 (±6.3) and the most significant change in BMI occurred during the first six months of the trial (+1.1 (±2.2), $P<0.0001$). In fully adjusted models, there was no association between glucocorticoid exposure and change in BMI over the course of the trial ($P>0.3$ for all analyses). Reduced disease activity (e.g., lower BVAS/WG, ESR, CRP) was independently associated with increased BMI ($P<0.0001$ for all analyses), as was randomization to rituximab ($P<0.02$ for all analyses). There was a significant association between disease status at enrollment (new diagnosis) and increasing BMI ($P\leq0.04$ for all analyses), but this association was lost in analyses adjusted for disease activity.

**Conclusions:** Following the initiation of AAV treatment, changes in BMI are related more closely to improvements in disease activity than to total glucocorticoid exposure. Additional studies are necessary to identify the respective impact of glucocorticoids and disease activity on temporal variations in BMI, including adiposity and skeletal muscle mass. The observed association between rituximab and increased BMI also deserves additional evaluation.

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**Disclosure of Interest:** None declared

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## SAT0370 ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) TYPE AND BODY MASS INDEX IN ANCA-ASSOCIATED VASCULITIS

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**Background:** Recent studies have highlighted important phenotypic, genetic, and treatment differences between PR3- and MPO-ANCA+ ANCA-associated vasculitis (AAV) patients[1,2]. No study has evaluated differences in body mass index (BMI) between the PR3- and MPO-ANCA+ AAV subtypes.

**Objectives:** We sought to evaluate whether differences in BMI exist between patients with active PR3-ANCA+ and MPO-ANCA+ AAV using data from the Rituximab in ANCA-Associated Vasculitis (RAVE) trial[3].

**Methods:** We analyzed AAV patients who were either anti-proteinase 3 (PR3)

antibody+ or anti-myeloperoxidase (MPO) antibody+ from the Rituximab in ANCA-Associated Vasculitis (RAVE) trial. In univariate analyses, we compared the BMI/weight of PR3- and MPO-ANCA+ AAV patients at enrollment, using linear regression to adjust for age, gender, glucocorticoids prior to enrollment, relapsing disease at baseline, and baseline disease activity. We used an analysis of response profile to evaluate trends in BMI and weight by ANCA type, adjusted for the above confounders as well as cumulative steroid dosing during the trial and flares during the trial.

**Results:** Three fourths of the patients were PR3+ (147, 75%). PR3-ANCA+ patients had a higher BMI at baseline compared to MPO-ANCA+ patients (29.6±6.6 vs. 27.2 ± 5.3; P=0.01); the same was true for weight differences (89.3 ±22kg vs. 77.2 ± 16.0kg, respectively, P<0.001). A significantly greater proportion of PR3-ANCA+ patients (42%) were obese compared to MPO-ANCA+ patients (24%, P=0.04). Among those with a new diagnosis of AAV at enrollment (N=96), PR3-ANCA+ patients had a significantly higher BMI (29.2 ± 6.2) compared to MPO-ANCA+ patients (26.8 ± 4.9, P=0.04). In multivariate linear regression analyses, these differences (PR3-ANCA + BMI 2.1 kg/m$^2$ (±1.1) higher than MPO-ANCA+ patients) remained significant (P=0.047 for BMI and 0.04 for weight, respectively) after accounting for confounders. The difference in weight between PR3-ANCA+ and MPO-ANCA+ patients remained stable during the study (P=0.3).

**Conclusions:** PR3-ANCA+ patients have a significantly higher BMI than MPO-ANCA+ patients, even after adjustment for important potential confounders. Our findings may have important implications for our understanding of AAV pathogenesis, its relationship to metabolic pathways, and the management of AAV.

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**Disclosure of Interest:** None declared

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## Spondyloarthritis - treatment

### SAT0371 HLA-B27 STATUS IS ASSOCIATED WITH TNFα INHIBITOR TREATMENT OUTCOMES IN ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS – OBSERVATIONAL COHORT STUDY FROM THE NATIONWIDE DANBIO REGISTRY

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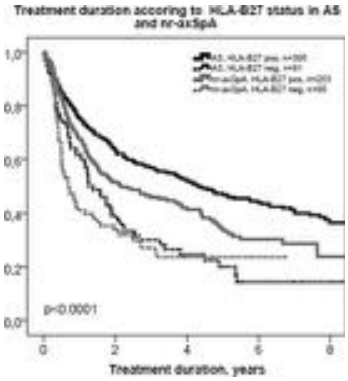
**Background:** Little is known about tumor-necrosis-factor-alpha-inhibitor (TNFi) treatment outcomes in Ankylosing Spondylitis (AS) vs. non-radiographic axial spondyloartrhitis (nr-axSpA).

**Objectives:** To compare baseline disease activity and treatment outcomes in biologic naïve patients with AS and nr-axSpA, who initiate TNFi treatment in clinical practice taking potential confounders into consideration.

**Methods:** We performed an observational cohort study based on prospectively registered data in the nationwide Danish quality registry, DANBIO, including baseline and 3–6 months' follow-up markers of disease activity (visual analogue score (VAS) global disease, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), BAS metrology index (BASMI) and serum C-reactive protein (CRP)). Treatment response was defined as either a 50% or a 20 mm reduction in BASDAI after 3–6 mths treatment. We used Kaplan-Meier plots, Cox and logistic regression analyses to study the impact of diagnosis (AS vs. nr-axSpA) and potential confounders (gender, age, start year, HLA-B27, disease duration, TNFi type, smoking, baseline disease activity) on TNFi adherence and response. Numbers are medians (IQR) unless otherwise stated.

Table 1. Characteristics and outcomes according to axSpA sub-diagnosis

| | Nr-axSpA (N=362) | AS (N=622) | P |
|---|---|---|---|
| Baseline demographics | | | |
| Age, years | 38 (30–46) | 42 (33–52) | <0.001 |
| Male sex, n (%) | 183 (50) | 455 (73) | <0.0001 |
| HLAB27 positive, n (%) | 253 (70) | 395 (83) | 0.005 |
| Disease duration, years | 1 (0–3) | 3 (1–12) | <0.0001 |
| Baseline disease activity | | | |
| CRP, mg/l | 7 (3–17) | 11 (5–22) | <0.0001 |
| BASDAI, mm | 64 (54–77) | 59 (46–71) | <0.0001 |
| BASFI, mm | 52 (33–69) | 49 (34–67) | 0.7 |
| BASMI | 20 (10–40) | 40 (20–50) | <0.0001 |
| VAS global, mm | 76 (62–88) | 68 (50–80) | <0.0001 |
| Crude outcomes | | | |
| BASDAI50%/20mm response, % | 46 | 48 | 0.9 |
| Adherence, median (95%CI), years | 1.59 (1.15–2.02) | 3.67 (2.86–4.49) | <0.0001 |




**Results:** We identified 1,250 TNFi naïve patients in DANBIO with axSpA according to the treating physician. Of these, 50% had AS, 28% nr-axSpA and 21% lacked X-rays of sacroiliac joints. Baseline demographics and disease activity differed in nr-axSpA vs. AS (Table). Response rates were similar, but treatment adherence was poorer in nr-axSpA than in AS (univariate, Table). In confounder adjusted analyses, axSpA sub-diagnosis was not associated with response rates or treatment adherence. However, HLA-B27 positivity was associated with better treatment adherence (HLA-B27 neg/pos, nr-axSpA: HR 1.74 (1.29–2.36), AS: HR 2.04 (1.53–2.71.), both p<0.0001) (Figure) and higher response rates (nr-axSpA: 30%/55%, AS: 29%/54%, univariate, both p<0.05). Similar results for HLA-B27 were found in confounder-adjusted analyses.

**Conclusions:** In this nationwide cohort, patients with nr-axSpA had higher subjective disease activity at the start of the first TNFi treatment but had similar confounder adjusted treatment adherences and response as AS pts. HLA-B27 positive pts had better outcomes irrespective of axSpA sub-diagnosis.

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### SAT0372 IMPACT OF DOSE TAPERING OF TUMOUR NECROSIS FACTOR-BLOCKERS ON RADIOGRAPHIC PROGRESSION IN THE ANKYLOSING SPONDYLITIS – A 4 YEAR PROSPECTIVE FOLLOW UP FROM SINGLE-CENTRE COHORT

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**Background:** Although dose tapering of tumour necrosis factor (TNF)-blockers in ankylosing spondylitis (AS) showed a comparable clinical efficacy with favourable safety and cost in some studies, there has been no investigation comparing the radiographic progression of patients with tapering regimen versus patients with standard-dose treatment.

**Objectives:** To investigate the impact of dose reduction of TNF-blockers on radiographic progression in the AS over 4 years

**Methods:** One hundred sixty five patients treated with etanercept or adalimumab were selected from single-centre, prospective observational cohort based on the availability of cervical and lumbar radiographs at baseline and after 2 and/or 4 years of the treatment. Radiographs were scored using modified Stokes AS spinal score (mSASSS) by two independent readers. Radiographic progression of patients treated with standard-dose (standard-dose group, n=49) was compared with that of patients who tapered the dosage during the TNF-blocker treatment (tapering group, n=116) using linear mixed models.

**Results:** Demographic and clinical factors at baseline between two groups were not significantly different except for higher initial BASDAI (7.1 vs. 6.3, p=0.003) in the standard-dose group. Baseline mSASSS (SD) of the standard-dose group and the tapering group were 17.3 (17.7) and 11.0 (16.0), respectively (p=0.059). At 2 years after the treatment, mean dose quotient (SD) of the tapering group was 0.59 (0.17) and time to first dose reduction (SD) was 36.6 (28.4) weeks. During the observation period, the rate of radiographic progression in the overall patients was 0.90 mSASSS unit/year. Rate of progression was significantly higher in patients with longer disease duration (≥10 years), elderly patients (≥40 years old), smokers, or patients with a hip involvement at baseline.

Radiographic progression over 4 years between two treatment strategies was similar after the adjustment for baseline status. However, in the subgroup of

patients who have syndesmophytes at baseline, it occurred significantly faster in the tapering group (1.30 mSASSS unit/year vs. 1.82 mSASSS unit/year, p=0.008) (figure). This result was concordant when radiographic progression was assessed by the development of new syndesmophytes (0.52/year vs. 0.73/year, p=0.047).

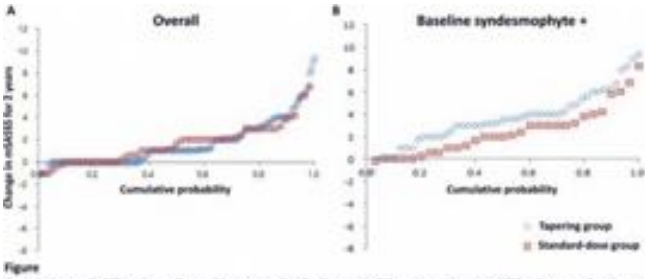



Figure
Cumulative probability plot radiographic progression for 2 years in (A) entire patients and (B) subgroup of patients who had syndesmophytes at baseline; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

**Conclusions:** Dose tapering strategy of TNF-blockers is associated with more rapid radiographic progression in AS patients who have syndesmophytes at baseline.

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**Disclosure of Interest:** None declared

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## SAT0373 EFFICACY AND SAFETY OF GOLIMUMAB IN PATIENTS WITH ACTIVE, VERY EARLY PERIPHERAL SPONDYLOARTHRITIS: FIRST RESULTS FROM THE CRESPA STUDY, A MONOCENTRIC, PLACEBO-CONTROLLED RANDOMIZED TRIAL

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**Objectives:** To evaluate the efficacy and safety of golimumab in patients with active peripheral Spondyloarthritis (pSpA) in a very early stage of the disease.

**Methods:** CRESPA (Clinical REmission in peripheral SPondyloArthritis) is an ongoing monocentric study of golimumab treatment in pSpA patients. Eligible patients were ≥18 years and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for pSpA. All patients had a symptom duration of less than 3 months. Patients were randomized 2:1 to receive golimumab 50 mg every 4 weeks or matching placebo for 24 weeks. The primary endpoint was the percentage of patients achieving clinical remission at week 24. Clinical remission was defined as the absence of arthritis, enthesitis and dactylitis on clinical examination. From week 12 onwards, there was an option to start rescue medication with golimumab 50 mg SC every 4 weeks. Adverse events were recorded throughout the study.

**Results:** In total 60 patients were randomized of whom 20 to the placebo group and 40 to the golimumab group. Baseline demographics and disease characteristics were generally similar between the 2 groups. At week 24 a significant higher percentage of patients receiving golimumab achieved clinical remission compared to patients receiving placebo (75% (30/40) versus 20% (4/20); P<0.001). At week 12 similar results were observed (70% (28/40) versus 15% (3/20); P<0.001). Overall, improvement in other outcomes was significantly greater in the golimumab group compared to the placebo group (table 1). In the placebo group 10 out of 20 patients (50%) entered the rescue arm, compared to only 4 of 40 (10%) patients in the golimumab arm. The rates of adverse events were very low and similar in both treatment groups.

**Conclusions:** In patients with active, very early peripheral spondyloarthritis, treatment with golimumab led to high percentages of clinical remission and significant improvement in all secondary efficacy outcomes, compared to placebo, with a safety profile consistent with that observed in anti-TNF trials with ankylosing spondylitis and psoriatic arthritis patients.

**Disclosure of Interest:** None declared

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## SAT0374 PREGNANCY OUTCOME IN COUPLES WITH MALES EXPOSED TO LONG TERM ANTI –TNF ALPHA BLOCKER THERAPIES

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**Background:** Biologic disease- modifying antirheumatic drugs (b DMARDs) are used often by patients with ankylosing spondylitis (AS) around the time of conception. Pregnancy outcomes in couples where men were exposed to TNF alpha blockers needs to be carefully examined, as information regarding paternal exposure may highly influence further couple counseling. Scarce information regarding the men fertility, pregnancy outcome and risk for congenital malformations associated with chronic TNF blockers treatment prior to conception is available.

**Objectives:** To examine pregnancy outcome and decision to conception time frame in the partners of AS male patients who were exposed to TNF alpha blockers before conception compared to the outcomes in age matched men from general population.

**Methods:** Outcomes of pregnancies in fathering men exposed to continuous long term (>12 months) anti TNF alpha blockers therapies were compared with outcomes in age matched reference subjects between 2008–2015.

**Results:** Out of 127 men diagnosed with AS, mean age (37.3 ± 10.3 years), disease onset (11.7 ± 10.5 years) treated with different bDMARDs in monotherapy, 13 patients were exposed to minimum 12 months preconception therapy. One patient received Infliximab 5 mg/ kg/ 8 weeks (72 months), 9 patients received Etanercept 50 mg/ week (34.6 ± 19.4 months), 3 patients received Adalimimab 40 mg/ 2 weeks (25.25 ± 10.11 months) monotherapy. One patient fathered 2 children after 42 months and 60 months of preconception Etanercept exposure. One patient had a recent switch from Adalimumab (24 months) to Etanercept introduced 2 months prior to conception. One patient with Etanercept therapy (60 months) has a partner with an ongoing 10 weeks pregnancy. Thirteen men fathered 14 healthy, on term delivered children. All newborns had normal weight and no signs of neonatal patology. No cases of abortion, preeclampsia, eclampsia, preterm delivery or neonatal death were reported in this group. Forty-five age matched healthy men (35.1 ± 1.2 years old) fathered 37 children: 35 healthy, one with cleft lip and one with Down syndrome. Eight pregnancies ended with abortion, 3 spontaneous and five by request. The time frame between mental decisions for reproduction to conception was 14.3 ± 3.3 months vs 7.7 ±1.2 months in the patients group vs reference group.

**Conclusions:** Long term preconception paternal exposure to TNF alpha blockers is not associated with an increase in adverse pregnancy outcomes. All born children were healthy. The interval between decision for reproduction and conception is longer in patients with AS treated with b DMARDs in comparison to general population.

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**Disclosure of Interest:** None declared

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**Abstract SAT0373** – Table 1

| | Baseline | | | Week 12 | | | Week 24 | | |
|---|---|---|---|---|---|---|---|---|---|
| | golimumab (n=40) | placebo (n=20) | p | golimumab (n=40) | placebo (n=20) | p | golimumab (n=40) | placebo (n=20) | p |
| TJC | 5.0 (3.0, 7.5) | 4.0 (2.0, 12.0) | 0.84 | 0 (0.0, 3.0) | 4.5 (1.0, 11.5) | 0.0011 | 0.0 (0.0, 2.0) | 5.0 (1.0, 7.5) | 0.0006 |
| SJC | 4.0 (2.5, 5.5) | 3.0 (2.0, 6.0) | 0.46 | 0.0 (0.0,1.0) | 2.5 (0.5, 7.0) | 0.0003 | 0.0 (0.0, 0.0) | 1.5 (0.0, 6.0) | 0.0004 |
| CRP | 1.06 (0.34, 3.38) | 1.68 (0.48, 4.87) | 0.43 | 0.12 (0.06, 0.24) | 0.72 (0.17, 2.03) | 0.0009 | 0.10 (0.06, 0.24) | 0.65 (0.15, 0.85) | 0.0043 |
| ESR | 21.5 (8.5, 41.5) | 28.0 (11.0, 60.0) | 0.45 | 3.0 (2.0, 6.0) | 17.5 (4.0, 31.0) | 0.0016 | 3.0 (2.0, 8.0) | 8.5 (4.0, 21.0) | 0.0244 |
| BASDAI | 5.25 (4.00, 6.30) | 6.05 (4.50, 6.80) | 0.27 | 2.20 ( 1.05, 3.50 ) | 6.30 (2.75, 6.75) | 0.0006 | 1.55 (0.20, 2.40) | 6.00 (2.00, 6.95) | 0.0002 |
| BASFI | 3.60 (2.35, 5.30) | 4.90 (3.35, 6.95) | 0.08 | 1.20 (0.40, 2.60) | 5.40 ( 1.95, 6.50) | 0.0006 | 0.80 (0.05, 1.85) | 5.05 (2.05, 6.35) | <.0001 |
| Response criteria | | | | | | | | | |
| pSpARC 40% | | | | 23 (57.5%) | 4 (20%) | 0.0069 | 20 (50%) | 3 (15%) | 0.0112 |
| pSpARC 50% | | | | 22 (55%) | 4 (20% | 0.0132 | 22 (55%) | 3 (15%) | 0.0048 |
| pSpARC 70% | | | | 20 (50%) | 3 (15%) | 0.0112 | 16 (40%) | 3 (15%) | 0.0768 |
| ASAS 20 respons | | | | 25 (62.5%) | 3 (15%) | 0.0008 | 27 (67.5%) | 6 (30%) | 0.0122 |
| ASAS 40 respons | | | | 19 (47.5%) | 3 (15%) | 0.0219 | 26 (65%) | 3 (15%) | 0.0003 |

SAT0375 **CERTOLIZUMAB PEGOL FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-AXSPA TRIAL**

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**Background:** The RAPID-axSpA trial (NCT01087762) investigated the efficacy and safety of certolizumab pegol (CZP) for the treatment of patients (pts) with axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS; also termed radiographic-axSpA) and non-radiographic (nr)-axSpA pts. Previous reports have shown CZP to be safe and efficacious over 96 weeks (wks) of treatment.[1]

**Objectives:** To report 4-year efficacy and safety data from the RAPID-axSpA trial.

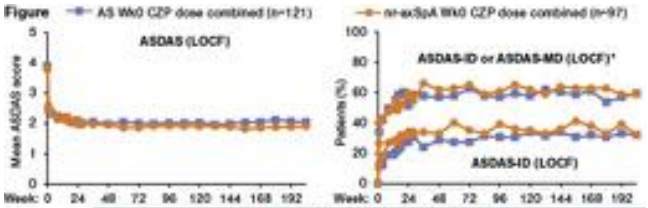
**Methods:** RAPID-axSpA was double-blind and placebo (PBO)-controlled to Wk24, dose-blind to Wk48 and open-label (OL) to Wk204. Pts fulfilled ASAS criteria and had active axSpA with positive sacroiliac joint MRI and/or raised CRP (>7.9mg/L). Pts originally randomized to CZP (200mg Q2W or 400mg Q4W) continued on their assigned dose in the OL period. Outcomes assessed included: ASAS responses, ASDAS, BASDAI, BASFI, BASMI-linear and enthesitis. Efficacy data are presented for pts originally randomized to CZP (combined doses) as observed case and with imputation: NRI for categorical and LOCF for continuous measures. The safety set consisted of all pts treated with ≥1 dose of CZP to Wk204.

**Results:** 325 pts were randomized, of whom 218 received CZP from Wk0. Of CZP-randomized pts, 93% completed to Wk24, 88% to Wk48 and 65% to Week 204 (AS: 67%; nr-axSpA: 63%). In the OL period, 9.2% of pts withdrew due to an adverse event (AE) and 1.4% due to lack of efficacy.

The proportion of pts achieving ASAS20/40 and partial remission (PR) responses at Wk24 was maintained over 4 years (to Wk204) in pts remaining in the study (Table). Efficacy, expressed as ASDAS ID rates (LOCF: Wk24: 30.3%; Wk204: 32.1%), mean ASDAS score (baseline: 3.84; LOCF: Wk24: 2.07; Wk204: 1.98), and all other outcomes reported, was maintained to Wk204. Similar improvements were seen in AS and nr-axSpA pts (Figure/Table) and in both CZP dose regimens (data not shown). Function (BASFI) was also improved in both subpopulations, with nr-axSpA pts having a particularly low mean score by Wk204 (Table).

Pts in the safety set (N=315) had a total CZP exposure of 981 patient-years (PY), with an AE rate (ER) per 100 PY of 292.9. No new safety signals were identified from Wk96 to Wk204, and no deaths were reported over 4 years.

Figure




Table

| | Combined CZP 200mg Q2W + 400mg Q4W | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | axSpA (n=218) | | | AS (n=121) | | | nr-axSpA (n=97) | | |
| | Wk24 (NRI) | Wk204 (NRI) | Wk204 [a] (OC) | Wk24 (NRI) | Wk204 (NRI) | Wk204 [c] (OC) | Wk24 (NRI) | Wk204 (NRI) | Wk204 [e] (OC) |
| ASAS20 (%) | 68.3 | 54.1 | 83.7 | 68.6 | 56.2 | 85.3 | 68.0 | 51.5 | 81.7 |
| ASAS40 (%) | 51.8 | 44.0 | 68.1 | 52.9 | 44.6 | 68.0 | 50.5 | 43.3 | 68.3 |
| ASAS PR (%) | 30.3 | 23.4 | 36.5 [b] | 28.1 | 21.5 | 32.5 [d] | 33.0 | 25.8 | 41.7 |
| Mean [f] | BL | Wk24 (LOCF) | Wk204 (LOCF) | BL | Wk24 (LOCF) | Wk204 (LOCF) | BL | Wk24 (LOCF) | Wk204 (LOCF) |
| ASDAS | 3.8 | 2.1 | 2.0 | 3.9 | 2.1 | 2.0 | 3.8 | 2.0 | 1.9 |
| ASDAS-ID (%) | - | 30.3 | 32.1 | - | 27.3 | 32.2 | - | 34.0 | 32.0 |
| ASDAS-ID or ASDAS-MD (%) | - | 55.1 | 59.2 | - | 51.3 | 59.5 | - | 59.8 | 58.8 |
| BASDAI | 6.4 | 3.3 | 3.0 | 6.4 | 3.4 | 3.0 | 6.6 | 3.3 | 2.9 |
| BASFI | 5.3 | 3.0 | 2.7 | 5.6 | 3.3 | 3.0 | 5.0 | 2.6 | 2.2 |
| BASMI-linear | 3.8 | 3.2 | 3.1 | 4.2 | 3.6 | 3.6 | 3.2 | 2.6 | 2.5 |
| MASES | 3.5 | 1.6 | 1.2 | 3.0 | 1.1 | 0.9 | 4.0 | 2.3 | 1.6 |

*Percentage of patients achieving either an ASDAS-ID or an ASDAS-MD response. [a] n=139; [b] n=137; [c] n=75; [d] n=77; [e] n=60; [f] Unless otherwise noted. ASAS PR: ASAS Partial Remission; ASDAS -ID: ASDAS Inactive Disease (<1.3); ASDAS-MD: ASDAS Moderate Disease activity (<2.1); BL: baseline; LOCF: last observation carried forward; MASES: Maastricht Ankylosing Spondylitis Enthesitis; NRI: non-responder imputation; OC: observed case.

**Conclusions:** CZP efficacy was maintained in axSpA pts over 4 years with no new safety signals. Treatment responses to CZP were similar in AS and nr-axSpA pts.

**References:**

[1] Sieper J. Arthritis Rheum 2015;67:668–77

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SAT0376 **SERUM CRP LEVELS DEMONSTRATE PREDICTIVE VALUE FOR RADIOGRAPHIC AND MRI OUTCOMES IN PATIENTS WITH ACTIVE AS TREATED WITH THE TNF-INHIBITOR GOLIMUMAB**

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**Background:** While the introduction of anti-tumor necrosis tumor (TNF) biologic agents can significantly improve signs/symptoms of ankylosing spondylitis (AS) and reduce magnetic resonance imaging (MRI)-detected spinal inflammation, the effect of such therapy on future radiographic progression is less clear. Serum C-reactive protein (CRP) associates with radiographic progression in AS patients untreated with TNF-antagonists.

**Objectives:** We assessed correlations between serum CRP after 2 years of anti-TNF therapy and radiographic progression/inflammation in the GO-RAISE trial.

**Methods:** Active AS patients receiving golimumab/placebo through week-16 (early-escape) or week-24 (crossover by design), followed by golimumab through 4 years, had sera/images obtained through week 208. Lateral spinal radiographs and spinal MRIs were scored using the modified Stoke AS spine score (mSASSS) and AS spinal MRI activity (ASspiMRI-a) score, respectively. Analyses of variance assessed differences based on CRP levels and mSASSS progression. The relationships between CRP levels and mSASSS/ASspiMRI-a score were assessed by Spearman correlation and logistic regression.

**Results:** 299/356 (84.0%) randomized GO-RAISE patients had spinal radiographs available at both timepoints. Larger proportions of patients with week-104 CRP ≥0.5mg/dL (n=47) vs. <0.5mg/dL (n=236) (40.4% vs. 22.9%; p=0.0121) had mSASSS changes ≥2 at week-104 (Figure). Across several visits, serum CRP demonstrated weak associations with mSASSS change ($r_s$ ≤0.21; p<0.05; n=262–293) and moderate associations with ASspiMRI-a change ($r_s$= -0.33–0.54; p<0.05; n=65–89). Higher baseline CRP was associated with increased risk for syndesmophytes at week-104/week-208, while large decreases in CRP from baseline to week-14/week-24 yielded decreased risk of new bone formation (Figure 1).

**Conclusions:** This is the first study to show that CRP level is not only a useful marker at baseline of the initiation of anti-TNF therapy but also at follow up examinations. Thus, elevated CRP after 2 years of anti-TNF treatment correlated with greater radiographic progression risk at 4 years. Intermittent measurements of serum CRP weakly predicted subsequent radiographic progression and

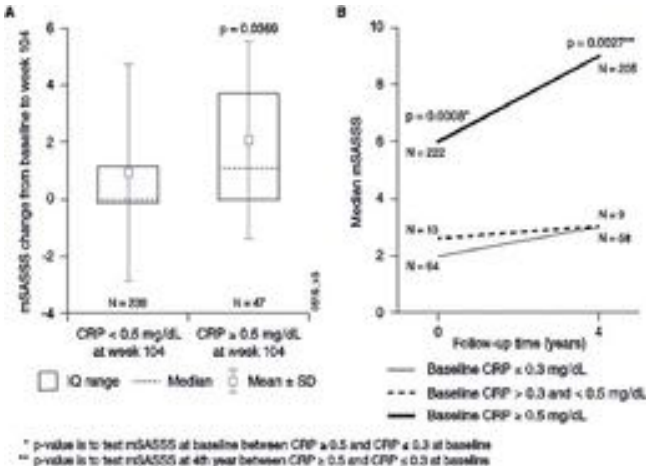



Figure 1

modestly predicted residual spinal inflammation in anti-TNF treated AS patients. Thus, incomplete suppression of inflammation in AS patients may be a relevant factor for new bone formation, and serum CRP appears to be a pertinent predictive biomarker for long-term AS progression among patients receiving TNF-antagonists. It is possible that higher doses of anti-TNF agents are necessary for patients with persistently elevated CRP values to prevent new bone formation more effectively.

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## SAT0377 DRUG SURVIVAL OF TUMOR NECROSIS FACTOR-α INHIBITORS IN PATIENTS WITH ANKYLOSING SPONDYLITIS IN KOREA

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**Background:** Studies about factors for drug survival for patients with AS have not sufficient as compared with RA patients and only a few studies are available for the Asian population.

**Objectives:** To evaluate drug survival of the tumor necrosis factor-α inhibitors (TNFi) and risk factors for the drug discontinuation in patients with ankylosing spondylitis (AS).

**Methods:** We retrospectively evaluated 487 AS patients at a single tertiary hospital. Among the TNFi users, drug survival and risk factors of TNFi discontinuation were investigated.

**Results:** Among 487 patients, 128 AS patients were treated with at least one TNFi. Patients who were treated with TNFi were younger at disease onset, had more peripheral manifestations, and had higher level of acute phase reactants and BMI than those of TNFi non-users at baseline. Of 128 patients, 28 (21.9%) patients discontinued first TNFi therapy during the follow-up period of 65.1 ± 27.9 months. In the multivariable analysis, female (HR 6.08, 95% CI 2.27–16.27, p=0.003), hip involvement (HR 2.52, 95% CI 1.08–5.87, p=0.033) and a high CRP (HR 1.10, 95% CI 1.00–1.21, p=0.044) were risk factors for drug discontinuation. Etanercept showed better survival rate than infliximab. The main reason for discontinuation of TNFi was inefficacy.

**Conclusions:** About one fifth of patients with AS discontinued their first TNFi. Female sex, hip involvement, CRP, and the type of TNFi were associated with TNFi discontinuation.

**Disclosure of Interest:** None declared

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## SAT0378 MODIFICATION OF STRUCTURAL LESIONS ON MAGNETIC RESONANCE IMAGING BY ETANERCEPT: A 12-WEEK RANDOMIZED PLACEBO-CONTROLLED TRIAL

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**Background:** Modification of structural lesions by anti-TNF therapy has not been demonstrated in a randomized placebo (PBO)-controlled trial. The Spondyloarthritis Research Consortium of Canada (SPARCC) sacroiliac joint (SIJ) score (SSS) assesses the degree of fat metaplasia (new tissue growth after resolution of inflammation), erosion, backfill (new tissue growth at erosion site), and ankylosis observed on MRI in the SIJ.

**Objectives:** To evaluate the impact on these lesions at 12 wks in patients with non-radiographic axial SpA receiving PBO or etanercept (ETN) in the EMBARK study (ClinicalTrials.gov: NCT01258738).

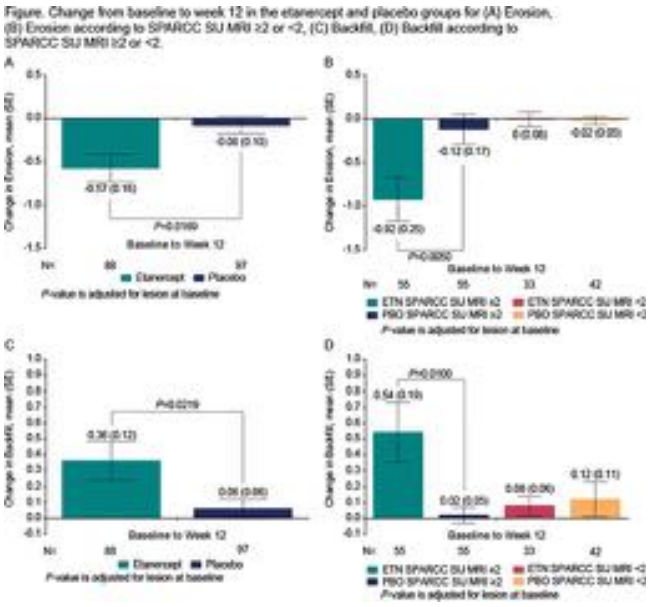
**Methods:** Patients had axial SpA per ASAS criteria without meeting modified NY radiographic criteria; BASDAI score ≥4; symptoms for >3 months and <5 yrs; and had failed ≥2 NSAIDs. Patients were randomized to double-blind ETN 50 mg/wk or PBO for 12 wks, then received open-label ETN. Structural lesions were scored using the SPARCC SSS method on T1-weighted spin echo (T1WSE) MRI. Two readers independently scored baseline (BL) and 12-wk T1WSE MRI scans, blinded to patients, time point, and inflammation scores assessed by short tau inversion recovery MRI scans. Readers' mean scores were used.

**Results:** Mean (SD) age was 32 (7.8) yrs, 60.5% were male, duration of disease symptoms was 2.4 (1.8) yrs, 71.6% were human leukocyte antigen B27+, and 80.9% had sacroiliitis on MRI (modified intent-to-treat [mITT] population, N=215). MRI scans from 185 patients (ETN, n=88; PBO, n=97) with BL and 12-wk scans were reviewed. At BL, there were no significant differences in mean SPARCC SSS scores between ETN and PBO (table). From BL to 12 wks, change in mean SPARCC SSS score was significantly greater for ETN than PBO for erosion (-0.57 vs -0.08, respectively, $p$=0.009) and backfill (0.36 vs 0.06, $p$=0.021), table. A treatment difference was also present for the subgroup of patients with MRI inflammation (figure).

Table 1. SPARCC SSS scores at baseline, week 12, and change from baseline to week 12

| | | ETN N=88 | PBO N=97 | *P*-value* ETN vs PBO ΔBL to week 12 |
|---|---|---|---|---|
| Erosion | Baseline | 2.25 (0.33) | 1.73 (0.32) | 0.009 |
| | Week 12 | 1.68 (0.25) | 1.65 (0.30) | |
| | ΔBL to week 12 | –0.57 (0.16) | –0.08 (0.10) | |
| Backfill | Baseline | 0.76 (0.22) | 0.64 (0.20) | 0.021 |
| | Week 12 | 1.13 (0.29) | 0.70 (0.23) | |
| | ΔBL to week 12 | 0.36 (0.12) | 0.06 (0.06) | |
| Fat Metaplasia | Baseline | 0.50 (0.19) | 0.27 (0.09) | ns |
| | Week 12 | 0.56 (0.22) | 0.32 (0.10) | |
| | ΔBL to week 12 | 0.06 (0.07) | 0.05 (0.05) | |
| Ankylosis | Baseline | 0.15 (0.10) | 0.13 (0.11) | ns |
| | Week 12 | 0.15 (0.11) | 0.13 (0.11) | |
| | ΔBL to week 12 | 0.01 (0.01) | 0.01 (0.01) | |

Values are mean (standard error). Observed case analysis, mITT population. *2-sample t-test. BL SPARCC SSS scores did not differ significantly between ETN and PBO. Treatment differences in ΔBL to wk 12 for erosion and backfill remained significant after adjusting for BL SPARCC SSS scores using analysis of covariance models. Δ, change; ns, non-significant.




**Conclusions:** Treatment with ETN was associated with significantly greater reduction in erosion and increase in backfill at 12 wks vs. PBO, consistent with a very early reparative response to anti-TNF therapy. The impact of this new data on disease progression in SpA should be studied further.

**Disclosure of Interest:** W. Maksymowych Grant/research support from: AbbVie, Consultant for: AbbVie, Amgen, Boehringer Ingelheim, Eli Lilly, Janssen Pharmaceutica, L.P, Pfizer, UCB, S. Wichuk: None declared, M. Dougados Grant/research support from: Pfizer, AbbVie, UCB, Merck, Eli Lilly, Sanofi, Consultant for: Pfizer, AbbVie, UCB, Merck, Eli Lilly, Sanofi, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, A. Szumski Employee of: InVentiv Health, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer, J. Bukowski Shareholder of: Pfizer, Employee of: Pfizer, R. Lambert Consultant for: Bioclinica

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## SAT0379 REDUCTION IN SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS PATIENTS RECEIVING PROLONGED TREATMENT WITH TNF INHIBITORS: RESULTS FROM THE GLAS COHORT

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**Background:** Previous studies showed no inhibition of spinal radiographic progression in patients with ankylosing spondylitis (AS) receiving TNF inhibitors for 2 years. There are few studies with more than 4 years of follow-up showing a possible reduction, but the results are under scientific debate.
**Objectives:** To evaluate the course of spinal radiographic progression up to 8 years of follow-up in a large cohort of AS patients treated with TNF inhibitors.
**Methods:** Consecutive patients from the Groningen Leeuwarden AS (GLAS) cohort who were treated with TNF inhibitors for 2 to 8 years were included. Baseline and biannual radiographs were randomized with radiographs of TNF naïve AS patients from a historical cohort and were scored in chronological time order by two independent readers according to the mSASSS. Longitudinal modeling of radiographic damage over time with generalized estimating equations (GEE) was used to investigate whether spinal radiographic progression followed a linear or non-linear course. The estimated progression rates per 2-year time interval were calculated based on the time model with the best fit for the data. Primary analysis was performed in patients with complete data over 4, 6, and 8 years of follow-up. Sensitivity analysis was performed after single linear imputation of radiographic data in case patients had missing data at one or more intermediate follow-up visits.
**Results:** Of 188 included GLAS patients, 70% were male, 78% HLA-B27+, mean age was 42±11 years, median symptom duration 14 (IQR: 7–23) years, mean BASDAI 6.1±1.6, mean ASDAS 3.7±0.8, and mean mSASSS 9.8±15.3. Patients were exposed to TNF inhibitors during 97% (IQR: 83–100%) of their follow-up time. All baseline characteristics including mSASSS were similar between included and excluded patient, except for age (42 vs. 46 years).
During the first 4 years of follow-up, spinal radiographic progression followed a linear course (Table 1). A deflection of a linear course was found in patients with complete and imputed data over 6 and 8 years of follow-up. The estimated progression rates based on the time model with the best fit showed a reduction in progression over time (Table 1). The non-linear time model remained statistically significant after adjustment for patient characteristics including baseline radiographic damage (mSASSS and presence of syndesmophytes), gender, HLA-B27 status, age, symptom duration, smoking duration, BMI, disease activity, and NSAID use over time in both patients with complete en imputed data.

**Table 1.** Estimated mSASSS status and progression scores of the GEE model with the best fit for the data in AS patients treated with TNF inhibitors with complete and imputed data over 4, 6, or 8 years of follow-up.

| | | 4 years (n=110) | 6 years (n=53) | 6 years with imputed data (n=80) | 8 years (n=19) | 8 years with imputed data (n=41) |
|---|---|---|---|---|---|---|
| Time model with best fit | | Linear | Non-linear | Non-linear | Non-linear | Non-linear |
| mSASSS status scores | 0yr | 11.5 (8.4-14.6) | 8.2 (4.2-12.1) | 8.7 (5.4-11.9) | 9.9 (2.9-17.0) | 13.4 (7.2-19.6) |
| | 2yr | 13.3 (9.8-16.8) | 9.9 (5.2-14.7) | 10.4 (6.5-14.2) | 12.3 (2.2-22.3) | 16.2 (7.9-24.5) |
| | 4yr | 15.0 (11.1-18.9) | 11.5 (5.8-17.2) | 11.9 (7.3-16.5) | 13.7 (1.4-25.9) | 18.3 (7.4-29.1) |
| | 6yr | - | 12.6 (5.4-19.7) | 12.9 (7.2-18.6) | 14.7 (0.7-28.7) | 19.7 (6.0-33.4) |
| | 8yr | - | - | - | 15.5 (0.0-31.1) | 20.5 (3.4-37.5) |
| mSASSS progression scores | 0-2yr | 1.7 (1.3-2.1) | 1.8 (1.0-2.6) | 1.7 (1.1-2.3) | 2.3 (-0.7-5.4) | 2.8 (0.6-4.9) |
| | 2-4yr | 1.7 (1.3-2.1) | 1.6 (0.6-2.5) | 1.5 (0.8-2.3) | 1.4 (-0.7-3.6) | 2.1 (-0.4-4.6) |
| | 4-6yr | - | 1.1 (-0.4-2.5) | 1.0 (-0.1-2.1) | 1.0 (-0.8-2.8) | 1.4 (-1.5-4.3) |
| | 6-8yr | - | - | - | 0.8 (-0.8-2.4) | 0.8 (-2.5-4.0) |

Values are presented as mean (95% confidence intervals); mSASSS: modified Stoke AS Spine Score.

**Conclusions:** This observational cohort study in AS patients receiving TNF inhibitors showed a reduction in spinal radiographic progression after more than 4 years follow-up.
**Acknowledgement:** The GLAS cohort was supported by an unrestricted grant from Pfizer. Pfizer had no role in the design, conduct, interpretation, or publication of this study.
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## SAT0380 NSAIDS MODIFY THE EFFECT OF TUMOR NECROSIS FACTOR INHIBITORS ON NEW BONE FORMATION IN ANKYLOSING SPONDYLITIS

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**Background:** Radiographic damage in Ankylosing Spondylitis (AS) is largely defined by new bone formation. The beneficial effects of pharmacologic therapy on osteoproliferation have been difficult to prove.
**Objectives:** The objective of this study was to examine the relationship of NSAIDs and Tumor Necrosis Factor inhibitors (TNFi) on New bone formation in AS.
**Methods:** 511 AS patients meeting the modified New York criteria with at least 2 years of radiographic follow-up were included in this prospective longitudinal study. Progression was defined as an increase at any vertebral corner from 0/1 to 2 or 0/1 to 3 at any interval between radiographs to reflect syndesmophyte development. We grouped patients according to the interval between baseline and the last visit, and used progression as a dichotomized outcome in a mixed effect logistic regression model. Patients taking NSAIDs for more than 50% of the time between visits were considered high NSAID users for that visit. TNFi use was assessed at each visit and adjusted for baseline use and total duration.
**Results:** In our multivariable models after adjusting for significant covariates, we found that TNFi use was associated with less new bone formation in AS with the strongest association in patients who had 2.1–3.5 years of follow-up (OR=0.27; 95% CI 0.08–0.94; p=0.04) [Table 1]. Though not statistically significant, in patients who were followed up for 3.6 years or longer, the odds of progression for the TNFi user group was 41% (3.6–5.9 year group) and 14% (6+ year group) lower than in non-users (OR=0.59, OR=0.86). We found a significant interaction (p=0.01) between NSAID use and TNFi in relation to radiographic progression. Those patients exposed to both TNFi and with high NSAID use had an OR for progression of 0.31, 95% CI 0.13–0.75, compared to those not on high dose NSAIDs (OR=1.23, 95% CI 0.41–3.66).

| Label | Odds Ratio | p-value |
|---|---|---|
| *TNFi* follow-up year group 0.33* | | |
| TNFi use vs. no | | |
| FU year 2 | 1.03 (0.29, 3.70) | 0.96 |
| FU year 2.1–3.5 | 0.27 (0.08, 0.94) | 0.04 |
| FU year 3.6–5.9 | 0.59 (0.19, 1.82) | 0.36 |
| FU year 6– | 0.87 (0.27, 2.82) | 0.82 |
| *TNFi* NSAID 0.01* | | |
| TNFi use vs. no | | |
| **NSAID use** | **0.31 (0.13, 0.75)** | **0.01** |
| No NSAID use | 1.23 (0.41, 3.66) | 0.71 |
| **Baseline mSASSS** | **1.01 (1.00, 1.03)** | **0.03** |
| **Disease duration >10 years** | **2.61 (1.56, 4.38)** | **<0.001** |
| **Male gender** | **2.57 (1.43, 4.65)** | **0.002** |
| Education > college | 0.81 (0.43, 1.52) | 0.51 |
| **Current smoking** | **2.47 (1.22, 4.97)** | **0.01** |
| # Comorbidity ≥1 | 1.28 (0.77, 2.14) | 0.34 |
| First available BASDAI ≥40 | 0.96 (0.56, 1.64) | 0.88 |
| First available BASFI ≥40 | 1.17 (0.63, 2.18) | 0.62 |
| Baseline CRP high | 1.30 (0.80, 2.11) | 0.29 |

Figure 1. Probability of New bone formation with TNFi use and/or NSAIDs




**Conclusions:** TNFi are associated with less new bone formation in AS, and this appears to be modified by the use of NSAIDs.
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## SAT0381 SAFETY AND EFFICACY OF SWITCHING FROM INNOVATOR TO BIOSIMILAR INFLIXIMAB IN PATIENTS AFFECTED BY SPONDYLOARTHRITIS. A 6-MONTH OBSERVATIONAL STUDY

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**Background:** Biosimilar infliximab (INX) was recently approved by the European Medicine Agency based on comparable pharmacokinetics, safety and efficacy profile to innovator INX for the treatment of Rheumatoid Arthritis, Ankylosing Spondylitis (AS), Crohn's disease, Ulcerative Colitis, Psoriatic Arthritis (PsA), and psoriasis. (1)
Switching from innovator to biosimilar INX offers cost savings but, up to now, limited evidence (from conference abstracts of open-label extension studies suggesting similar clinical efficacy) and no guidelines are available. (2)
**Objectives:** To investigate efficacy and safety of switching from innovator to biosimilar INX in patients affected by spondyloarthritis (SpA) in real life clinical practice.
**Methods:** Thirty-one patients (17 with diagnosis of AS, 4 with enteropathic arthritis, 7 with PsA and 3 with undifferentiated SpA), from three Italian Rheumatologic centers with a previous diagnosis of SpA, treated for more than 6 months with innovator infliximab (in according with the ASAS/EULAR guidelines) and clinically with an inactive or moderate disease activity (ASDAS-CRP $<$2.1), were switched to biosimilar infliximab for pharmacoeconomic reasons. All patients signed a consent form.
A six months evaluation of BASDAI, BASFI, ASDAS-CRP, DAS28-CRP (if peripheral disease), MASES, VAS pain, morning stiffness and collection of adverse events (AE) were performed.
**Results:** At switch, patients had a median age of 50,9 years (range 23–80), with a median disease duration of 124,5 months (range 14–372) and median ongoing treatment with innovator INX of 73,7 months (range 6–144). After 6 months of biosimilar INX therapy we cannot find any statistical difference in terms of median values of BASDAI (2.73 ± 1.5 Vs 2.6 ± 1.3 p=0.27), BASFI (2.34 ± 1.3 Vs 2.17 ± 1.2 p=0.051), ASDAS-CRP (1.35 ± 0.3 Vs 1.28 ± 0.2 p=0.24), DAS28-CRP (2.66 ± 0.67 Vs 2.67 ± 0.35 p=0.92), MASES (0.35 ± 0.7 Vs 0.17 ± 0.4 p=0.08), VAS pain (18 ± 14.7 Vs 16,7 ± 11.3 p=0.55). The median duration of morning stiffness was statistically lower 6 months after the switch (7.2 ± 6.9 Vs 5.8 ± 6 p=0.02). During the first six months of biosimilar INX a very low number of patients experienced an AE without a significance difference with the AE collected the six months before the switch (Fisher Test p=1.0). One patient (3%) stopped biosimilar INX therapy, after the first two administrations, for the appearance of a severe palmoplantar psoriasis.
**Conclusions:** No statistically significance differences in terms of BASDAI, BASFI, ASDAS-CRP, DAS28-CRP, MASES, VAS pain values and number of adverse events were found six months after the switch from innovator to biosimilar INX in an SpA multicentre Italian cohort.
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**Disclosure of Interest:** None declared
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## SAT0382 THERAPEUTIC RESPONSE IN PSORIATIC ARTHRITIS PATIENTS RECEIVING BIOLOGICAL OR CONVENTIONAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS. A 5-YEAR OBSERVATIONAL STUDY

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**Background:** Introduction of biological disease modifying antirheumatic drugs (DMARDs) in the treatment of Psoriatic arthritis (PsA) have altered the therapeutic approach of these patients showing a good outcome.
**Objectives:** The main purpose of the present observational study was to estimate treatment response in PsA patients receiving conventional DMARDs, biological DMARDs or combined therapy.
**Methods:** We studied 254 patients diagnosed with PsA. Patients with axial involvement fulfilled the Assessment of SpondyloArthritis international Society (ASAS) criteria and additionally the ClASsification criteria for Psoratic ARthritis (CASPAR) for patients with peripheral joint involvement. We compared the therapeutic response in patients receiving conventional DMARDs, biological DMARDs and combined therapy. Data were collected at predefined time points, baseline, 12 weeks (wks), 24 wks, 48 and 240 wks after initiation of therapy. The treatment response was assessed by using Bath Ankylosing Spondylitis Activity Index (BASDAI), Bath Ankylosing Spondylitis Functionality Index (BASFI), Disease Activity Score in 28 joints-CRP (DAS28-CRP), Disease Activity Score in 28 joints -TKE (DAS28-TKE) and Health Assessment Questionnaire (HAQ). Patients were categorized in three groups according to their treatment: patients mainly with axial disease who were treated with biological DMARDs (anti-TNFa agents) (group A), patients with peripheral arthritis with or without axial involvement treated with conventional DMARDs: methotrexate, leflunomide, cyclosporine (group B) and combined therapy: biological and conventional DMARDs (group C) according to their therapeutic response.
**Results:** Treatment with biological DMARDs showed a statistically significant difference in all disease activity scores early in the disease course ($p<0,05$) in comparison with those receiving conventional DMARDs. More specifically 12 wks after the initiation of the treatment patients receiving biological DMARDs had significant lower values for DAS28-TKE (2,04±0,69 – 3,35±0,94 p=0,0446), DAS28-CRP (2,44±0,83 – 3,73±1,22 p=0,015), BASDAI (0,85±0,59 – 2,73±1,60 p=0,0426), BASFI (1,2±1,08 – 3,29±2,07 p=0,0366) and HAQ (0,32±0,38 – 0,80±0,48 p=0,001). The patients receiving combined therapy showed better response rates at week 12 in comparison with the patients receiving conventional DMARDs but the differences were not statistically significant ($p>0,05$ in all cases). At the time points 24, 48 and 240 wks all disease activity scores were stable with no statistically significant differences within or between the three groups ($p>0,05$).
**Conclusions:** In the current study, treatment with biological DMARDs showed better response in PsA patients than those treated with conventional DMARDs early in the disease course. After the first 12 wks there were no significant differences in treatment response with respect to treatment choice.
**Disclosure of Interest:** None declared
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## SAT0383 EFFICACY OF TNF INHIBITORS IN AXIAL SPONDYLOARTHRITIS ACCORDING TO THE PRESENCE OF OBJECTIVE SIGNS OF INFLAMMATION: A MULTICENTRIC RETROSPECTIVE STUDY

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**Background:** TNF inhibitors (TNFi) are effective treatment in radiographic and non-radiographic axial spondyloarthritis (r-axSpA and nr-axSpA). Nr-axSpA have lower response rate in case of absence of sacroiliitis on magnetic resonance imaging (MRI) or elevated C-reactive protein (CRP) but TNFi efficacy in the absence of clinical, biological or radiological inflammatory signs is unknown due to the low number of patients included in previous studies.
**Objectives:** To compare TNFi response rate in axSpA depending on the presence or not of objective signs of inflammation.
**Methods:** Nx-axSpA patients fulfilling ASAS 2009 criteria, without objective signs of inflammation defined as the absence at the time of TNFi initiation of radiographic and MRI sacroiliitis, elevated CRP level, dactylitis, anterior uveitis and inflammatory bowel disease, treated for at least 3 months between January 2001 and September 2015 were included in this retrospective multicentric study. They were matched 1:1, by age, sex and type of TNFi, with axSpA patients with at least one objective signs of inflammation. Efficacy was defined as an achievement of 50% improvement of the initial Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at 3, 6 or 12 months and both groups were compared. Predictive factors of response were investigated in the two groups.
**Results:** We included 84 nx-axSpA patients without objective signs of inflammation and 84 ax-SpA patients with objective signs. Patients were mainly women (76.2%) with a mean ± standard deviation age of 42 ± 11 years. BASDAI 50 achievement rate, at 3, 6 or 12 months, was significantly higher in patients with objective signs than in patients without (61.9% versus 21.4% considering all time point for evaluation, $p<0,0001$). The BASDAI mean improvement was also significantly higher in patients with objective signs at 3 (-24.3 ± 19.8 versus -9.7 ± 15.9; $p<0.0001$), 6 (-27.7 ± 22.6 versus -8.8 ± 18.3; $p<0.0001$) and 12 months (-26.5 ± 22.5 versus -13.7 ± 24.3; p=0.01). The only significant predictive factor of non-response considering the two groups was a high mean body mass index (BMI) (26.2 ± 5.7 kg/m$^2$ in non-responders versus 24.2± 4.6 kg/m$^2$ in responders; p=0.04). This factor was especially predictive of non-response among nr-axSpA without objective signs (26.5 ± 5.6 kg/m$^2$ in non-responders versus 22.3 ± 3.0 kg/m$^2$; p=0.008).
**Conclusions:** TNFi are efficient only in 20% of axSpA patients when objective signs of inflammation are absent. A high BMI is a predictive factor of non-response in axSpA in the presence or not of objective signs of inflammation.
**Disclosure of Interest:** None declared
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## SAT0384 LONG-TERM SAFETY OF ANTI-TNF AGENTS IN PATIENTS WITH SPONDYLOARTHRITIS AND POTENTIAL OCCULT HBV: AN OBSERVATIONAL MULTICENTER STUDY ON 131 PATIENTS

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**Background:** drugs targeting tumor necrosis factor-α (TNF) biological activity deal with an increased risk of infections. Few papers address whether TNF blockers in rheumatic patients with potential HBV occult infection are safe (1–9).
**Objectives:** to evaluate the safety of anti-TNF agents in cases of spondyloarthritis with resolved hepatitis B (HBsAg negative, HBcAb±anti-HBs positive) through a close monitoring of a possible HBV reactivation and/or rise in the aminotransferase levels.
**Methods:** the medical records for 992 outpatients with rheumatic inflammatory diseases attending two Italian Rheumatology Units between 2007–2015 were retrospectively reviewed for diagnosis of spondyloarthritis, current treatment with anti-TNF agents and seropositivity for past HBV infection. 131 patients (70 men, 61 women; mean age:60,63±9,59 years) were included in the study: 55 with ankylosing spondylitis, 65 psoriatic arthritis, 9 inflammatory bowel disease-associated arthritis, 2 non-radiographic axial spondyloarthritis. Mean disease duration was 98,64±42,60 months. 64 patients were currently in treatment with Etanercept (29 in monotherapy, 31 with MTX, 3 with SSZ, 1 with CsA); 32 with Infliximab (18 as monotherapy, 10 with MTX, 3 with SSZ, 1 with CsA); 31 with Adalimumab (16 in monotherapy, 12 with MTX, 2 with LEF, 1 with CsA); 4 with Golimumab (3 with MTX, 1 as monotherapy). 101 patients received only 1 TNF inhibitor (54 Etanercept, 27 Infliximab, 20 Adalimumab); 23 patients switched to a second and 7 patients switched to a third anti-TNF agent. 51 patients had concomitant prednisone <12,5 mg/die. All 131 patients were anti-HBc+, of which 109 were anti-HBc and anti-HBs+. No patient was positive for HBV-DNA at baseline, none received antiviral therapy prior to or during anti-TNF treatment.
**Results:** at the end of the follow-up (mean of 75,50±33,37 months of anti-TNF therapy), no case of viral reactivation was observed in anti-HBc+ patients, no matter anti-HBs positivity. HBV-DNA remained undetectable, HBsAg negative, aminotransferases normal, nor it was necessary to stop biologic therapy because of viral infection.
**Conclusions:** our retrospective analysis supports the safety of TNF inhibitors for spondyloarthritis patients with a serological pattern of previous HBV infection during a follow-up >6 years. Pre-emptive antiviral prophylaxis is not necessary routinely, but strict monitoring for AST/ALT increase, as well as for changes in HBV serology and HBV-DNA, is necessary and seems a cost-effective approach to identify early viral reactivation, whose occurrence is low, but not negligible, and consequently start antiviral therapy.
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## SAT0385 IMMUNOGENICITY, TNF-INHIBITORS LEVELS AND DISEASE OUTCOMES IN ANKYLOSING SPONDYLITIS: RESULTS FROM AN OBSERVATIONAL COHORT STUDY

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**Background:** Up to one third of spondylarthritis (SpA) fail to respond to anti-TNF agents or experience drug toxicity leading to treatment withdrawal. Part of the treatment failure can be explained by the development of anti-drug antibodies (ADA).
**Objectives:** To evaluate the relation between immunogenicity, drug levels and clinical efficacy of TNF inhibitors (TNF-i) in ankylosing spondylitis (AS).
**Methods:** We performed a prospective observational study in a cohort of 47 consecutive AS patients receiving adalimumab (ADL) (13; 27.7%), infliximab (IFX) (13; 27.7%) or etanercept (ETN) (21; 44.7%). Disease
Disease activity (BASDAI, ASDAS), outcomes and adverse events were evaluated at baseline and study visit, while serum TNF-i and ADA levels collected as a single-point data in both bio-naïve (37, 78.7%) and bio-experimented patients. Serum drug levels were considered positive for IFX if >0.035 μg/mL, for ADL >0.024 μg/mL and for ETN >0.035 μg/mL, while the cut-off value for the ADA positivity to IFX was established at 5AU/ml, for ADL at 10AU/mL and ETN at 142 AU/mL (ELISA, Progenika).
Statistical analysis was performed using SSPS version 19.0, $p<0.05$
**Results:** At baseline mean BASDAI was 7.69 and mean ASDAS-CRP 3.50, with no difference in disease activity between patients who did or did not later develop ADA ($p<0.05$). 37 (78.7%) AS were BASDAI responders at study visit (BASDAI 1.16, ASDAS-CRP 1.73).
ADA were detected in 8/47 (17%) and were more frequent in patients treated with ADL (5 cases; 38.5%) *vs* IFX (3 cases; 23.1%); no with ETN. Both ADL and IFX levels were significantly higher for ADA negative than for ADA positive patients (ADL: 3.92μg/mL *vs* 0.02μg/mL, $p<0.01$; IFX: 1.82μg/mL *vs* 0.03 μg/mL, $p<0.01$).
A significant association between clinical activity (ASDAS) and immunogenicity (ADA status) was reported: patients who had developed ADA had higher disease activity (3.10 *vs* 1.73, $p<0.01$), and more patients were classified as being in a high or very high disease activity status.
Furthermore, a relation between clinical improvement (change in ASDAS) and immunogenicity was reported: ADA-positive AS achieved worse clinical response than ADA-negative cases, with a significant association between ADL respectively IFX levels and ASDAS ($p<0.05$).
**Conclusions:** ADL and IFX levels are commonly influenced by ADA-positivity, and related to clinical response in AS, suggesting that therapeutic drug monitoring should be investigated as a possible tool to optimise treatment such patients.
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## SAT0386 FREE DKK-1 SERUM LEVELS ARE UNCHANGED IN SPONDYLOARTHRITIS PATIENTS TREATED BY ANTI-TNF – DATA FROM THE SPARSE STUDY

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**Background:** DKK-1 and SOST are two inhibitory proteins of the Wnt signaling pathway which lead to decreased bone formation by osteoblasts and osteocytes, respectively. Due to the limited data assessing free DKK-1 and SOST in SpA patients under anti-TNF treatment, a post-hoc examination of the SPARSE study was designed in order to answer these question.
**Objectives:** To assess free DKK-1 and SOST serum levels at Baseline and 24 weeks after etanercept or placebo treatment in patients from the SPARSE study.
**Methods:** In the SPARSE study, patients were randomized to receive either etanercept (N=42) or placebo (n=48) in case of active AxSpA disease (defined by mini BASDAI >40) despite optimal NSAIDs intake. The 90 patients from the SPARSE study were quantified for free DKK-1 and SOST serum levels, at Baseline and at Week 8 (w8) corresponding to the end of the placebo controlled period. DKK-1 and SOST serum levels were assessed by the use of a classic sandwich ELISA test (Biomedica, Vienna) and results were provided in pmol/L. Changes in DKK-1 and SOST serum levels were adjusted for disease activity, CRP levels, NSAIDs intake, X-ray status and treatment groups.
**Results:** LS Mean (±SE) serum DKK-1 at Baseline was not significantly different between treatment groups (ETN: 36.2 ± 1.97; PBO: 37.1 ± 1.84; p=0.72). At Baseline, DKK-1 was not associated with any of the patients' or disease characteristics: ASDAS-CRP (r=0.096; 95% CI [-0.122, 0.305]); CRP (r=0.002; 95% CI [-0.210, 0.214]); X-ray status (LS Mean (SE): negative 37.4 (±2.38) versus positive 36.3 (± 1.77); p=0.71). There were no significant differences between treatment groups in the change from Baseline to w8 in the DKK-1 serum levels (p=0.97). We also considered patients with (N=67) or w/o NSAIDs intake (n=19) within the week preceding w8 serum level assessment and found no significant difference (p=0.99). We further assessed DKK-1 serum levels at Baseline according to their Baseline CRP (<6mg/L; ≥6mg/L), X-ray status (Positive; Negative), or NSAIDs intake (Yes; No) within the week preceding w8, and found no significant differences. These analyses were repeated for SOST serum levels at Baseline and with the exception of patients with Negative X-ray status at Baseline having significantly lower values than those patients with Positive X-ray status (p=0.047), no significant differences were observed in terms of the Baseline disease characteristics; Similarly there were no differences between treatment groups in the change from Baseline to w8 SOST serum levels.
**Conclusions:** This post-hoc examination of patients randomized in the SPARSE study suggest that etanercept does not significantly change DKK-1 or SOST serum levels within the 8 first weeks of treatment. Disease activity, CRP, NSAIDs intake and X-ray status were not significantly associated with DKK-1 serum levels. These results should be considered in the context of previous studies suggesting that DKK-1 was dysfunctional in SpA patients (1). Taken together, these results suggest that DKK-1 should not be considered as a valuable bone remodeling marker in SpA, unlike in rheumatoid arthritis.

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## SAT0387 ANTI TNF TREATMENT OF REACTIVE ARTHRITIS. A MONOCENTRIC EXPERIENCE

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**Background:** Reactive arthritis is still a matter of interest and a current problem, since its treatment is not standardized, with the possibility of a chronic evolution. Nevertheless, anti TNF agents may be of interest, as illustrated by small multicentric series.
**Objectives:** To evaluate efficacy and safety of anti TNF agents in the treatment of patients with reactive arthritis followed in a single center.
**Methods:** We analyzed retrospectively the data of patients with reactive arthritis, according to proposed criteria treated with TNF blockers, from July 2007 to December 2013 in an University Hospital in France.
**Results:** Over this period, 31 cases of Reactive arthritis were followed in our department, of whom 15 (48%) received at least one dose of anti TNF. They are in majority male (n=13), mean age 35 years, 66% HLA-B27 positive. Evidence of infection was found in 9/15 patients (4 Chlamydia). After failure of NSAIDs, steroids and conventional DMARDs, anti TNF agents were introduced with a median delay of 116 days after onset of rheumatic symptoms: etanercept (ETN) 9 cases, infliximab (IFX) and adalimumab (ADA) (3 cases each) (Table). The clinical improvement was rapid, all the patients developed a clinical response to anti TNF therapy which could be stopped in 5 cases: 3 IFX after a mean of 4.6 infusions, 2 ETN after 4 and 10 months. Eight patients developed chronic spondyloarthritis, and one psoriatic arthritis, with a mean follow-up of 4.8 years, and requiring anti TNF continuation. The last patient was lost in follow-up. The treatment was well tolerated, with a mean exposition duration of 34 months by patient, neither serious infection nor reactivation of the triggering infection was recorded. Compared to the patients with reactive arthritis not treated with anti TNF over the same period, we found no differences regarding clinical data (age, arthritis distribution, type of initial infection), biologic data (CRP, HLA-B27 positivity, evidence of infectious agent). Dactylitis were more frequent (although not significant) in patients treated with anti TNF agents (40% vs 20%). In the same way, there were no differences between the patients who could stop anti TNF after several months, due to remission, and those for whom continuation was necessary, except a shorter median delay of initiation of the TNF blocker: 44 days versus 173 days respectively.

Table 1

| Anti TNF | Delay of anti TNF introduction (days) | Duration of anti TNF if stop possible (months) | Duration of anti TNF (ongoing) (years) | Evolution | Duration of follow-up under anti TNF (months) |
|---|---|---|---|---|---|
| ADA | 3386 | | | Pso Ar | 51.6 |
| IFX | 193 | 3.5 | | remission | 1.6 |
| ETN | 70 | 4 | | remission | 3.9 |
| ETN | 59 | | 5.4 | SpA | 78.4 |
| ETN | 230 | | 5.0 | SpA | 56.6 |
| ETN | 1485 | 10 | | lost FU | 10.4 |
| ETN | 11 | | 4.8 | remission | 35.3 |
| ETN | 335 | | 3.8 | SpA | 56.3 |
| ETN | 116 | | 3.7 | SpA | 33.7 |
| ADA | 79 | | 3.4 | SpA | 46 |
| ETN | 464 | | 2.5 | SpA | 39.3 |
| IFX | 83 | 5 | | remission | 5.5 |
| IFX | 39 | 2 | | remission | 2.6 |
| ADA | 454 | | | SpA | 22.1 |
| ETN | 96 | 15 | 0.5 | SpA | 20.4 |

**Conclusions:** Anti TNF therapy for reactive arthritis seems to be associated with symptomatic efficacy and good tolerance with the possibility, in one third of the cases of short lasting treatment leading to remission, which seems associated to the precocity of anti TNF initiation, suggesting a kind of window of opportunity in this subset of spondyloarthritis. However, the impact of this treatment upon the outcome of the disease needs to be further evaluated.
**Disclosure of Interest:** None declared
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## SAT0388 LONG-TERM EFFICACY AND TOLERABILITY OF GOLIMUMAB IN ACTIVE NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS OF THE OPEN-LABEL EXTENSION OF A RANDOMIZED, DOUBLE-BLIND STUDY

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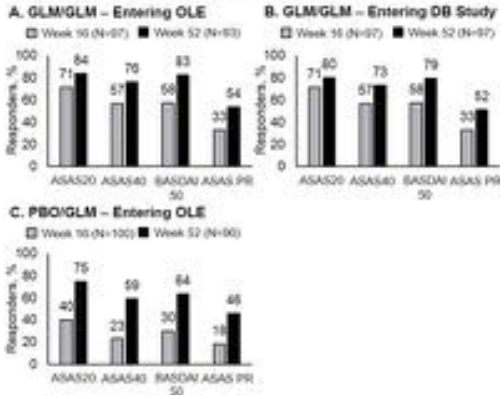
**Background:** The efficacy and tolerability of golimumab (GLM) for nonradiographic axial spondyloarthritis (nr-axSpA) have been demonstrated in a 16-week randomized, double-blind (DB), placebo (PBO)-controlled, phase 3 study (GO-AHEAD; NCT01453725).[1]
**Objectives:** We report the long-term results from an open-label extension (OLE) of GO-AHEAD.
**Methods:** Patients (pts) completing the 16-week DB study (GLM or PBO) received open-label GLM 50 mg every 4 weeks (36-week efficacy period; 8-week safety follow-up). Prespecified responder analyses for ASAS20, ASAS40, BASDAI50, and ASAS partial remission (PR) at weeks 16, 20, 24, 32, 40, and 52 used the OLE-treated population (GLM/GLM, n=93; PBO/GLM, n=96). In a post hoc analysis, the DB-treated population was used for GLM/GLM responder analyses (GLM/GLM, n=97). Non-responder imputation was used for missing ASAS20, ASAS40, and ASAS PR values; LOCF imputation was used for missing BASDAI data. The incidence/severity of adverse events (AEs) were recorded. Data were summarized descriptively.
**Results:** In total, 176/189 (93%) pts entering the OLE completed week 60 (GLM/GLM, 85/93 [91%]; PBO/GLM, 89/96 [93%]). In the prespecified analysis, the proportions of ASAS20, ASAS40, BASDAI50, and ASAS PR responders in the OLE were similar to those in the DB phase among pts who continued GLM (GLM/GLM group); consistent results were observed in the GLM/GLM group when using the DB-treated population (Figure A,B). Among pts who switched from PBO in the DB phase to GLM in the OLE (PBO/GLM group), there were higher proportions of responders to GLM in the OLE than responders to PBO in the DB phase (Figure C). There were no notable differences in the number/types of AEs between the GLM/GLM and PBO/GLM groups (Table).

Table 1. Summary of AEs in the GO-AHEAD OLE

| AEs[a], n (%) | GLM/GLM (N=93) | PBO/GLM (N=96) | Total (N=189) |
|---|---|---|---|
| Treatment-emergent AE | 39 (41.9) | 52 (54.2) | 91 (48.1) |
| Treatment-related AE[b] | 12 (12.9) | 16 (16.7) | 28 (14.8) |
| Nasopharyngitis | 2 (2.2) | 3 (3.1) | 5 (2.6) |
| Upper respiratory tract infection | 2 (2.2) | 2 (2.1) | 4 (2.1) |
| Headache | 2 (2.2) | 2 (2.1) | 4 (2.1) |
| Discontinuation due to AE[c] | 1 (1.1) | 2 (2.1) | 3 (1.6) |
| Serious AE[d] | 2 (2.2) | 3 (3.1) | 5 (2.6) |
| Fatal AE | 0 | 0 | 0 |

[a]Includes pts who received ≥1 dose of study drug. [b]The most common AEs considered treatment-related (occurring in ≥3 pts in total) are shown. [c]GLM/GLM: acute tonsillitis and treatment-related bacterial infection (n=1); PBO/GLM: hepatitis, treatment-related rhinitis (each n=1). [d]GLM/GLM: bacterial infection, duodenitis (each n=1); PBO/GLM: treatment-related migraine, uterine polyp, staphylococcal infection (each n=1).

**Figure. Proportions of Responders in the GO-AHEAD OLE**




**Conclusions:** In the GO-AHEAD OLE, improvements in disease activity were retained in pts who received GLM and in pts who switched from PBO to GLM. Consistent with results of the GO-AHEAD DB study, treatment with GLM in the OLE was generally well tolerated in pts with nr-axSpA.
**References:**
[1] Sieper J, et al. Arthritis Rheum. 2015;67(10),2702–2712.
**Disclosure of Interest:** D. van der Heijde Consultant for: AbbVie, Amgen, AstraZeneca, Augurex, BMS, Boehringer Ingelheim, Celgene, Centocor, Chugai, Covagen, Daiichi, Eli-Lilly, Galapagos, GSK, Janssen Biologics, Merck, Novartis, Novo-Nordisk, Otsuka, Pfizer, Roche, Sanofi-Aventis, UCB, Vertex, Employee of:

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## SAT0389 LONG-TERM IMPROVEMENTS IN WORKPLACE AND HOUSEHOLD PRODUCTIVITY AND SOCIAL PARTICIPATION OVER 4 YEARS OF CERTOLIZUMAB PEGOL TREATMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, INCLUDING ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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**Background:** Axial spondyloarthritis (axSpA), including patients (pts) with ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA), is associated with a significant burden of disease and typically affects pts of working age.[1] AS has a substantial impact on pt absenteeism, as well as impeding performance at work and home;[2] limited data are available for nr-axSpA. AxSpA can also present a significant burden to caregivers.[3] Effective long-term treatments should minimize work disability, allowing pts to maintain employment and independence in household work.

**Objectives:** To report the long-term effect of certolizumab pegol (CZP) treatment on workplace and household productivity and social participation in axSpA pts over 4 years (204 weeks [wks]).

**Methods:** The RAPID-axSpA trial (NCT01087762) was double-blind and placebo-controlled to Wk24, dose-blind to Wk48 and open-label (OL) to Wk204. Pts had active disease and fulfilled ASAS criteria. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W) continued on assigned dose in the OL period. The validated arthritis-specific Work Productivity Survey (WPS)[4] assessed the impact of disease on workplace and household productivity and social participation. Data are reported for pts originally randomized to CZP (randomized set) using LOCF imputation and as observed values for pts completing each study visit.

**Table:** Workplace and household productivity over 204 wks of the RAPID-axSpA trial

| | | Wk0 CZP dose-combined | | | | | |
|---|---|---|---|---|---|---|---|
| | | axSpA (n=218) | | AS (n=121) | | nr-axSpA (n=97) | |
| | | Imputed (LOCF) | Observed case | Imputed (LOCF) | Observed case | Imputed (LOCF) | Observed case |
| **Productivity at workplace (employed patients), mean (n) [a]** | | | | | | | |
| Work days missed [b] | BL | 1.8 (157) | 1.8 (156) | 1.7 (89) | 1.7 (88) | 2.0 (68) | 2.0 (68) |
| | Wk24 | 0.8 (161) | 0.8 (153) | 0.7 (89) | 0.7 (83) | 1.0 (72) | 1.0 (70) |
| | Wk204 | 0.2 (167) | 0.2 (115) | 0.3 (90) | 0.2 (64) | 0.2 (77) | 0.2 (51) |
| Days with work productivity reduced by ≥50% [b,c] | BL | 5.2 (157) | 5.2 (156) | 4.6 (89) | 4.6 (88) | 6.0 (68) | 6.0 (68) |
| | Wk24 | 2.6 (161) | 2.1 (153) | 2.5 (89) | 1.6 (83) | 2.7 (72) | 2.7 (70) |
| | Wk204 | 1.4 (167) | 1.0 (115) | 1.4 (90) | 0.5 (64) | 1.4 (77) | 1.5 (51) |
| Arthritis interference with work productivity (0–10 scale) [d] | BL | 4.5 (157) | 4.5 (156) | 4.5 (89) | 4.5 (88) | 4.5 (68) | 4.5 (68) |
| | Wk24 | 2.1 (161) | 2.0 (153) | 2.1 (89) | 1.9 (83) | 2.1 (72) | 2.2 (70) |
| | Wk204 | 1.2 (167) | 1.1 (115) | 1.1 (90) | 0.9 (64) | 1.3 (77) | 1.2 (51) |
| **Household productivity, mean (n)** | | | | | | | |
| Household work days missed [b] | BL | 5.3 (218) | 5.3 (217) | 4.8 (121) | 4.8 (121) | 5.8 (97) | 5.8 (96) |
| | Wk24 | 2.3 (218) | 2.1 (203) | 2.0 (121) | 1.6 (112) | 2.5 (97) | 2.4 (91) |
| | Wk204 | 1.5 (218) | 1.2 (141) | 1.3 (121) | 0.8 (80) | 1.7 (97) | 1.6 (61) |
| Household work days with productivity reduced by ≥50% [b,c] | BL | 7.5 (218) | 7.5 (217) | 7.0 (121) | 7.0 (121) | 8.1 (97) | 8.1 (96) |
| | Wk24 | 3.3 (218) | 3.2 (202) | 3.0 (121) | 2.7 (111) | 3.6 (97) | 3.8 (91) |
| | Wk204 | 1.8 (218) | 1.5 (141) | 1.9 (121) | 1.3 (80) | 1.8 (97) | 1.8 (61) |
| Arthritis interference with household productivity (0–10 scale) [d] | BL | 4.8 (218) | 4.8 (217) | 4.9 (121) | 4.9 (121) | 4.7 (97) | 4.7 (96) |
| | Wk24 | 2.3 (218) | 2.2 (203) | 2.4 (121) | 2.2 (112) | 2.2 (97) | 2.3 (91) |
| | Wk204 | 1.7 (218) | 1.3 (141) | 1.6 (121) | 1.0 (80) | 1.7 (97) | 1.7 (61) |

[a] Based only on employed patients at the specific visit; patients employed at baseline: axSpA (157), AS (89), nr-axSpA (68); [b] Due to arthritis per month; [c] Does not include work days missed counted in the previous question; [d] 0–10 scale: 0=no interference, 10=complete interference. BL: baseline; LOCF: last observation carried forward.

**Results:** 325 pts were randomized, of whom 218 received CZP from Wk0. Of the 218 pts, 203 (93%) completed Wk24 and 142 (65%) Wk204. 157/218 (72%) pts were employed outside the home at baseline (BL). Pts reported a high BL burden of arthritis, with a mean of 7.0 days of paid work (employed pts, n=157), 12.8 days of household work, and 4.0 days of social activities (all pts, n=218) affected in the previous month.

Initial improvements in workplace and household productivity to Wk24 of CZP treatment were further sustained to Wk204 in axSpA pts, as well as in both the AS and nr-axSpA subpopulations (Table). Improvements were seen in social participation, with the number of days of family/social/leisure activities missed in the previous month reduced from 4.0 (BL) to 1.5 at Wk24 and 0.7 at Wk204 (LOCF, n=218). Caregiver burden also improved over time with 40.8% of pts at BL needing regular assistance in usual activities from a relative or friend, decreasing to 26.6% at Wk24 and 12.4% at Wk204 (LOCF, n=218, data from socio-professional module collected at each study visit).

**Conclusions:** Initial improvements seen to Wk24 with CZP treatment in workplace and household productivity, increased social participation and reduced caregiver burden further continued over long-term (4-year) treatment of axSpA, AS and nr-axSpA pts, suggesting sustained benefits to pts' lives and society.

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## SAT0390 SECUKINUMAB FOR THE TREATMENT OF ANKYLOSING SPONDYLITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS CURRENTLY LICENSED BIOLOGICS FROM A NETWORK META-ANALYSIS

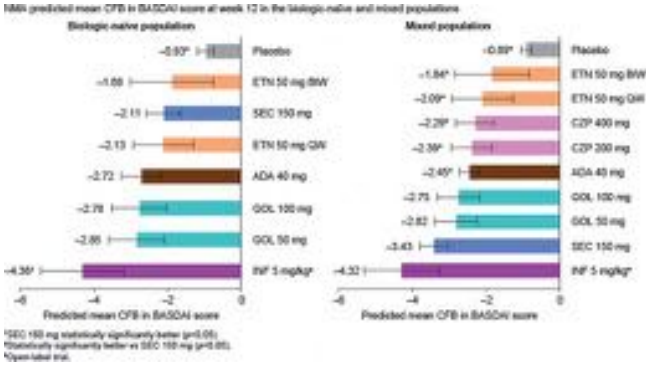
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**Background:** Secukinumab 150 mg (SEC) is approved for the treatment of active AS in adults who have responded inadequately to conventional therapy. The MEASURE 1 (M1) and MEASURE 2 (M2) RCTs, which included biologic-naïve and biologic-experienced patients, demonstrated superiority of SEC over placebo. In AS no direct trial comparisons of SEC with licensed biologics are currently available.

**Objectives:** To use network meta-analysis (NMA) to compare SEC vs licensed biologics in the short term.

**Methods:** A systematic literature review (January 2015) identified RCTs of licensed biologics in adults with active AS in whom conventional therapy had failed. NMAs were conducted in accordance with health technology assessment guidance using Bayesian fixed-effects models. To analyse ASAS and BASDAI50 response rates, a standard NMA model with logit link function was used. Analyses of changes from baseline (CFBs) in BASDAI and BASFI used a linear model with identity link and normal distribution. Pairwise comparisons were conducted using relative risks and mean differences. SEC results are presented as the probability of response (95% credible interval [CrI]) for ASAS and BASDAI50, and as CFB (95% CrI); CrIs can be interpreted similarly to CIs. Non-responder imputation data were used, if available; otherwise, LOCF data were used. For infliximab 5 mg/kg (INF) only data from an open label trial was available. Analyses were run at week 12 for biologic-naïve (M1, n=92; M2, n=44) and mixed (naïve or experienced; M1, n=125; M2, n=72) populations.

**Results:** In the biologic-naïve population, ASAS20 results for SEC were similar to those for adalimumab (ADA), etanercept (ETN) 50 mg BIW/QW, golimumab (GOL) 50/100 mg, and INF. The SEC response rates were 58% (46–68) for ASAS20, 42% (31–55) for ASAS40 and 39% for BASDAI50 (28–50); BASFI CFB was –1.99 (–2.39 to –1.60). For BASDAI CFB, SEC [–2.11 (–2.60 to –1.63)] was similar to all other biologics except INF, which had a statistically significantly greater CFB than SEC.
In the mixed population, SEC had similar efficacy to ADA, certolizumab pegol (CZP) 200/400 mg QW, ETN and GOL for ASAS20 [SEC response, 53% (43–63)]. SEC was also similar to ADA, CZP, ETN, GOL and INF for ASAS40 [39% (29–51)], BASDAI50 [35% (25–46)] and BASFI CFB [–1.89 (–2.24 to –1.53)]. SEC was statistically significantly superior to ADA, CZP and ETN for BASDAI CFB [–3.43 (–3.82 to –3.05)].




**Conclusions:** This NMA shows that SEC has similar efficacy to most licensed biologics at most endpoints investigated, with the exception of INF for BASDAI CFB in the biologic-naïve population and ASAS20 in the mixed population. SEC also demonstrated statistically significant superiority over ADA, ETN and CZP for BASDAI CFB in the mixed population. The short-term nature of this study is a limitation (long-term data [≥52 weeks] are available for SEC).
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## SAT0391 THE 8-YEAR RETENTION RATE OF THE FIRST TNF-INHIBITOR IN THE TREATMENT OF SPONDYLOARTHROPATHIES: REAL-LIFE DATA FROM A MULTICENTRIC LOCAL REGISTRIES

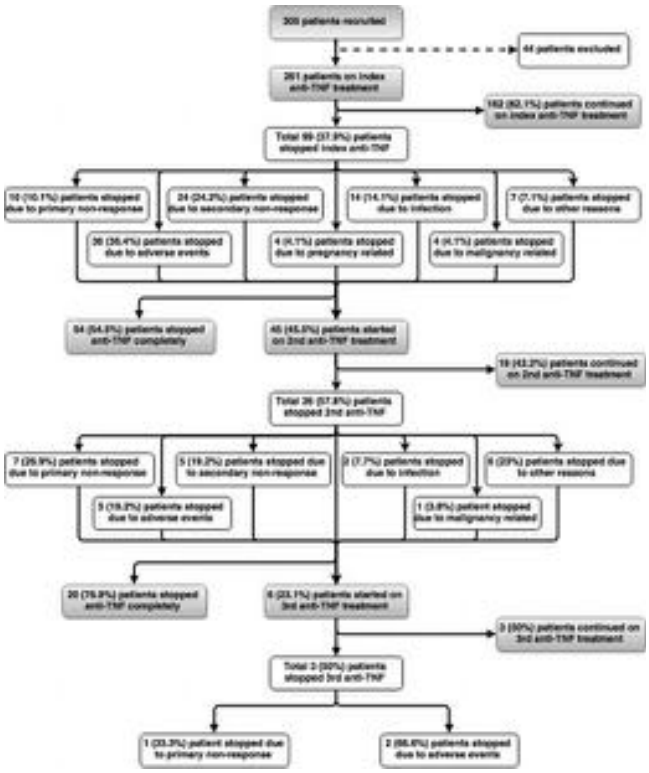
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**Background:** Long-term data on drug survival of TNF inhibitors (TNFi) in the treatment of spondyloarthropathies are still lacking.
**Objectives:** The aim of the study is to analyze in a setting of real-life the 8-year retention rate of the first TNFi for the treatment of psoriatic arthritis (PsA) and axial spondyloarthritis (ax-SpA) and to compare the between-group discontinuation rates for each TNFi (infliximab [IFX], etanercept [ETN], and adalimumab [ADA]).
**Methods:** Data were retrospectively extracted from four local registries including all patients affected by PsA and ax-SpA treated with a biologic drug between January 2005 and May 2015. The analysis was limited to patients treated with IFX, ETN, or ADA as first-line biologic agent, with at least 1-year follow-up period. The 8-year drug survival was evaluated by Kaplan-Meier method and the risk for discontinuation among the 3 treatment groups was compared by a stratified log-rank test.
**Results:** The study population (614 patients) included 316 ax-SpA (69.9% male, mean age [±SD] 42.8 [±12.1] years, mean disease duration 7.2 [±7.9] years), treated with ADA (n=95), ETN (n=42), or IFX (n=179); and 298 PsA (51.7% male, mean age 47.8 [±12.1] years, mean disease duration 8.8 [±7.7] years), treated with ADA (n=108), ETN (n=89), or IFX (n=101). The overall median survival on treatment of the whole study population was 117.17 months (102.84 and >117.17 months for axSpA and PsA, respectively; p=NS).
The overall retention rate was 66.2% (69.5% versus 62.8% in axSpA and PsA, respectively) at 5 years and 55.5% (57.2% versus 53.4% in axSpA and PsA, respectively) at 8 years. No significant differences emerged in the comparison among ADA, ETN, and IFX in both ax-SpA group (p=0.1065) and PsA group (p=0.06). IFX and ETN showed similar survival rates in PsA and axSpA (HR 1.252, 95% CI 0.600–2.608, and HR 1.224, 95% CI 0.8441–1.774, respectively), whereas ADA showed a significantly higher survival in axSpA compared to PsA (HR 1.775, 95% CI 1.045–3.013). Overall, 265 (43.1%) patients (129 [43.2%] PsA and 133 [42.1%] axSpA), stopped the first course TNFi. Inefficacy led to discontinuation in 115 (18.7%) patients (65 [21.8%] PsA and 50 [15.8%] axSpA), without significant differences between the two disease groups (p=0.1076). Adverse events led to discontinuation in 88 (14.3%) patients, (43 [14.4%] PsA and 45 [14.2%] axSpA), without significant differences between PsA and axSpA (p=0.9049).
**Conclusions:** In a real-life setting, the 8-year retention rate of the first TNFi in the treatment of spondyloarthropathies was about 50%, with no significant difference between ax-SpA and PsA. The risk of stopping IFX and ETN treatment was similar in both ax-SpA and PsA group, whereas ADA showed a higher survival in axSpA group.
**Disclosure of Interest:** None declared
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## SAT0392 THE DRUG SURVIVAL OF ANTI-TUMOUR NECROSIS FACTOR (TNF) TREATMENT IN A UK COHORT OF AXIAL SPONDYLOARTHRITIS PATIENTS

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**Background:** The use of anti-Tumour Necrosis Factor (TNF) therapy has made a huge impact in the treatment of axial spondyloarthritis (axSpA) patients which include ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA). Patients typically commence these drugs if they fulfil criteria set out by the National Institute for Health Care and Excellence (NICE) guidelines[1]. Continuation of anti-TNF therapy depends on their response, or the occurrence of adverse events (AEs). Current NICE guidelines allow switching to an alternative anti-TNF if side effects occur early in the treatment course. However, few studies have provided data regarding the patterns of drug survival and reasons for discontinuation of anti-TNF in a UK cohort of AxSpA patients[2].



**Objectives:** To analyse the long-term survival of anti-TNF in AS patients and the reasons for switching anti-TNF therapy in a UK cohort.
**Methods:** We conducted a retrospective analysis of patients who fulfilled AS or nr-axSpA ASAS Classification criteria[3], aged 18 years or above, who received at least one anti-TNF agent at the Royal National Hospital for Rheumatic Diseases (RNHRD) Bath. Data were collected from review of the patients' medical notes. Data included the types and duration of anti-TNF used, and the reasons anti-TNF therapy needed to be stopped or changed. The initial anti-TNF agent prescribed is described as the index treatment.
**Results:** 305 patients,with a mean age of 49.7 (SD12.81), were recruited from the RNHRD AxSpA Biologics database. 261 patients were included in the final data analysis with 90.8% fulfilling the modified New York criteria. Female n=63 (24.1%). The index anti-TNF treatment were Adalimumab n=123 (47.1%), Etanercept n=84 (32.2%), Golimumab n=27 (10.3%), Certolizumab pegol n=15 (5.7%), and Infliximab n=12 (4.6%). 110 (40.4%) patients had to discontinue their index treatment. The most frequent reasons for discontinuation of index anti-TNF included AEs n=36 (36.4%) and loss or lack of efficacy (LOE) n=34 (34.3%). In patients who proceeded to switch to a 2nd anti-TNF, the main reason for stopping the index anti-TNF was AEs n=18 (40%). 26 (57.8%) patients stopped their 2nd anti-TNF treatment with LOE n=12 (46.1%) as the main reason. 6 (23.1%) patients proceeded to have a 3rd anti-TNF with 3 (50%) patients had to stop this completely.
**Conclusions:** About half of the patients had to discontinue their anti-TNF treatment either as an index treatment or subsequent treatment. The most common reason for stopping anti-TNF treatment in our cohort was due to adverse events. 45.5% of patients switched to a second anti-TNF agent and 23.1% of the patients switched from a second to a third anti-TNF agent.
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## SAT0393 CLINICAL AND QUALITY OF LIFE IMPROVEMENTS OBSERVED WITH GOLIMUMAB AND INFLIXIMAB IN A LARGE REAL-LIFE ANKYLOSING SPONDYLITIS POPULATION: RESULTS FROM THE QUO-VADIS STUDY

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**Background:** Loss of health-related quality of life (HRQoL) is documented in Ankylosing Spondylitis (AS) patients and improvement has been observed upon therapy with anti-tumor necrosis factor (TNF) agents. Parameters such as higher ASDAS, elevated CRP and younger age have been described in literature to be associated with improved clinical outcomes.
**Objectives:** The relationship between baseline (BL, pre-anti-TNF treatment) disease-specific parameters and HRQoL improvement during anti-TNF therapy with golimumab (GLM) or infliximab (IFX) was evaluated in the QUality of Life as Outcomes and its VAriation with DIsease States (QUO-VADIS) study.
**Methods:** This prospective observational study included bio-naïve AS patients (modified New York criteria) newly treated with GLM or IFX (originator). Patients were followed-up for ~6 months (data collected at BL, 3, and 6 months). Demographic and clinical characteristics, disease activity and HRQoL were summarized accordingly. The Classification and Regression Trees (CART) analysis evaluated the association of BL parameters (demographic, clinical, disease severity) with change in HRQoL at 6 months, measured by an improvement of ≥5 points of the Short-Form 36 (SF-36) Physical Component Summary (PCS) score. Clinical parameters included Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), and AS Disease Activity Scores (ASDAS).
**Results:** 963 patients received ≥1 dose of medication; 78% received GLM and 22%received IFX. Mean age was 42.7 years, 61.4% were male, and 65.3% had ≥ one comorbidity. Mean symptom and diagnosis duration were 11.6 and 5.3 years, respectively, and 63.8%of patients were Human Leukocyte Antigen (HLA)-B27 positive. At BL, mean BASDAI, ASDAS-CRP and BASFI scores were 6.21, 3.59 and 5.34, respectively. High and very high ASDAS disease activity was observed in 41.4% and 49.3% of patients, respectively. Clinical and HRQoL improvements were shown in all collected measures following 6 months of treatment with GLM or IFX, as documented in the Table. PCS response at 6 months (improvement of ≥5 points from BL) was achieved in 52.3% (n=504) of patients. Using CART analysis, the baseline parameters, and their cutoff values, associated with HRQoL improvement as measured by SF-36 PCS response at 6 months were ASDAS (≥3.48), C-Reactive Protein (CRP) (≥8.55 mg/L), and age (≤35.5 years), and BASFI (≥1.15). This algorithm correctly identified 57.5% (sensitivity) of the patients who had improvement on PCS >5 points and 61.0% (specificity) of the patients who had improvement on PCS ≤5 points with ROC-AUC=0.61.

**Table: Improvement in Clinical and QoL Parameters Following 6 months of Treatment**

| | Overall population N=963 | Golimumab-only cohort N=751 |
|---|---|---|
| Mean (SD) BASDAI change from BL | -2.7 (2.3) | -2.6 (2.3) |
| Mean (SD) BASFI change from BL | -2.1 (2.3) | -2.2 (2.2) |
| BASDAI50 Response | 39.5% | 39.9% |
| ASAS20 Response | 50.6% | 52.6% |
| ASDAS Major Improvement | 26.6% | 26.0% |
| ASDAS Disease Activity Category | | |
| Inactive (<1.3) | 19.9% | 20.4% |
| Moderate (≥1.3 to ≤2.1) | 21.2% | 22.2% |
| High (>2.1 to ≤3.5) | 29.4% | 29.6% |
| Very High (>3.5) | 7.0% | 5.1% |
| Missing | 22.5% | 22.8% |
| SF36 PCS responders (improvement of ≥ 5 points from BL) | 52.3% | 53.3% |

**Conclusions:** This study demonstrated clinical and HRQoL improvements over 6 months in a large, real-world population of AS patients newly treated with GLM or IFX. The QUO-VADIS study also demonstrates, for the first time, the association of parameters such as higher ASDAS, elevated CRP and younger age with improvements in HRQoL and with a more robust response. The use of these predicting factors may aid clinicians in better evaluating which patients to start on antiTNF therapy with GLM or IFX.
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## SAT0394 IMPACT OF DISEASE DURATION ON PATIENT REPORTED AND CLINICAL OUTCOMES IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH ANTI-TNF: AN ANALYSIS FROM A PROSPECTIVE, OBSERVATIONAL REGISTRY

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**Background:** Previous studies have shown that treatment outcomes are affected by disease-related aspects and patient-related factors.
**Objectives:** The aim of this analysis was to compare ankylosing spondylitis (AS) patient profiles in terms of patient characteristics and disease parameters based on disease duration and to investigate the impact of disease duration on patient reported and clinical outcomes in patients treated with anti-TNF.
**Methods:** BioTRAC is an ongoing, prospective registry of pts initiating treatment for rheumatoid arthritis, AS, or psoriatic arthritis with infliximab (IFX) or golimumab (GLM). Eligible people for this analysis included AS patients treated with IFX and enrolled since 2005 or with GLM and enrolled since 2010. Patients were classified in three subgroups (≤1 yr, 2–10 yrs, >10 yrs) based on the tertile distribution of the time elapsed since their diagnosis. The impact of disease duration on outcomes upon adjusting for potential confounders was assessed with generalized linear models and logistic regression.
**Results:** A total of 580 AS patients were included in this analysis with a mean age of 45.8 yrs and disease duration of 8.3 yrs. The majority were male and 92.6% were biologic naïve. At baseline, mean BASFI was 5.6, BASDAI was 6.2, and ASDAS was 3.6. With the exception of age which was significantly higher among pts with longer disease duration (P<0.001) no significant between-group differences were observed in baseline demographics and disease parameters.
Upon 6 mos of treatment, clinically meaningful and statistically significant improvements were observed in BASFI, BASDAI and ASDAS which were further enhanced at 12 mos. Upon adjusting for baseline age and respective parameter levels, pts diagnosed within ≤1 yr experienced significantly lower improvements in BASFI (P=0.030), BASDAI (P<0.001), and ASDAS (P=0.030) at 12 mos as compared to pts with disease duration >10 ys. For ASDAS, concomitant DMARD use was also identified as a significant predictor of improved outcome (P=0.042). Gender and prior biologic experience did not have a significant impact on outcomes. Inactive or moderate disease activity, based on ASDAS, was achieved by 47.2% of pts while clinically important and major improvements were observed for 54.9% and 32.7% of pts, respectively. Similarly to the absolute improvements, pts diagnosed within ≤1 yr were significantly less likely to achieve these endpoints.
**Conclusions:** The results of this real-world analysis have identified prior disease duration at anti-TNF initiation as a significant independent predictor of treatment outcome. Concomitant use of a DMARD was associated with significantly higher

improvement in ASDAS. These results suggest that pts with early disease may be harder to treat and highlight the need for more aggressive treat-to-target approaches in this patient subgroup.
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## SAT0395 STATIN TREATMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Patients with ankylosing spondylitis (AS) have increased risk of cardiovascular disease (CVD). In the general population, CVD risk reduction can be achieved by lipid lowering therapy (LLT).
**Objectives:** We aimed to evaluate the effect of statins in AS patients and factors associated with the changes (Δ) in low-density lipoprotein cholesterol (LDL-c) and total cholesterol (TC).
**Methods:** In this longitudinal, observational study, 108 patients with AS underwent CVD risk evaluation. Of these, 48 patients had an indication for LLT and received statin treatment which was adjusted until lipid targets were achieved. Variables obtaining a p-value of $<0.25$ in a univariate analyses were entered in forward, stepwise, linear regression models with ΔLDL-c and ΔTC as the dependent variables and were adjusted for age and gender, as well as baseline LDL-c levels (for ΔLDL-c) and intensity of LLT (for ΔTC).
**Results:** At first visit, median (IQR) age was 61.5 (56.0, 66.8) years, 72.9% were male, median disease duration was 27 (17.8, 32.8) years, 12.5% smoked daily, 70.8% had hypertension (HT), mean (SD) body mass index (BMI) was 26.0 (3.50) kg/m$^2$, mean LDL-c and TC, were 3.82±1.02 and 6.04±1.16mmol/L and 70.8% had carotid plaque(s). Twenty patients were treated with low or moderate intensity LLT (simvastatin 20 mg or 40 mg, rosuvastatin $<40$ mg or atorvastatin $<40$ mg), while the remaining 28 received intensive LLT (rosuvastatin 40 mg or atorvastatin $>40$ mg). LDL-c goals (50% reduction in LDL-c and /or LDL-c $<2.5$ /$<1.8$ mmol/L, for primary (n=10) or secondary prevention (n=38), respectively) were achieved in 85.4% of patients (90.0% and 84.2% for primary and secondary prevention, respectively). Reductions in LDL-c and TC were 1.60+0.41 mmol/L and 2.42+1.15 mmol/L ($p<0.001$ for both). Predictive variables explaining 86.5% ($R^2$) of the ΔLDL-c included erythrocyte sedimentation rate (ESR), established CVD and HT. Only ESR ($p=0.03$) and baseline LDL-c ($p<0.001$) contributed significantly to the final model. ESR was inversely related to ΔLDL-c. In addition, higher baseline LDL-c levels were associated with larger LDL-c reduction. The final model for ΔTC, accounting for 33.0% ($R^2$) of the variation, included ESR, waist circumference, BMI, non-steroidal anti-inflammatory drugs, and use of biologic and synthetic disease modifying anti-rheumatic drugs. Intensive LLT and high waist circumference were predictive of greater TC reductions (p=0.002 and 0.04, respectively).

Table 1

| | ΔLDL-c, $R^2$=0.865 | | | ΔTC, $R^2$=0.330 | |
|---|---|---|---|---|---|
| | B (95% CI) | p-value | | B (95% CI) | p-value |
| Age | 0.004 (–0.01, 0.02) | 0.56 | Age | 0.02 (–0.02, 0.05) | 0.39 |
| Sex (gender) | –0.05 (–0.31, 0.21) | 0.70 | Sex (gender) | –0.03 (–0.88, 0.83) | 0.95 |
| LDL-c at baseline | –0.78 (–0.89, –0.66) | <0.01 | LLT (statin dose) | –1.09 (–1.74, –0.43) | <0.01 |
| ESR | 0.01 (0.00, 0.02) | 0.03 | ESR | 0.01 (–0.02, 0.03) | 0.61 |
| CVD | 0.20 (–0.12, 0.52) | 0.21 | Waist circumference | –0.06 (–0.12, –0.00) | 0.04 |
| Hypertension | –0.16 (–0.42, 0.11) | 0.25 | BMI | 0.14 (–0.06, 0.33) | 0.16 |
| | | | NSAIDs | –0.33 (–1.08, 0.42) | 0.37 |
| | | | Biologic DMARDs | –0.34 (–1.06, 0.39) | 0.35 |
| | | | Synthetic DMARDs | 0.18 (–0.87, 1.23) | 0.73 |

**Conclusions:** Lipid lowering with statins was highly effective in AS patients. Inflammation measured by ESR was inversely related to change in LDL-c, possibly due to the suppressive effect on lipid levels. Further studies are needed to elucidate if the anti-inflammatory effect of rheumatic medication influence the lipid lowering effect of statins in patients with AS.
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## SAT0396 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE ANKYLOSING SPONDYLITIS: 2-YEAR RESULTS FROM A PHASE 3 TRIAL WITH SUBCUTANEOUS LOADING AND MAINTENANCE DOSING (MEASURE 2)

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**Background:** Secukinumab, an anti–interleukin-17A monoclonal antibody, improved the signs and symptoms of ankylosing spondylitis (AS) over 52 weeks (wks) in the randomised, double-blind, placebo (PBO)-controlled, Phase 3 MEASURE 2 study (NCT01649375).[1]
**Objectives:** To evaluate the long-term (104 wks) efficacy and safety of secukinumab in MEASURE 2 study.
**Methods:** 219 subjects with active AS, classified by modified New York criteria, despite therapy with NSAIDs, were randomised to subcutaneous (s.c.) secukinumab 150 or 75 mg or PBO at baseline (BL), Wks 1, 2 and 3, and every 4 wks (q4w) from Wk 4. At Wk 16, PBO-treated subjects were re-randomised to secukinumab 150 or 75 mg s.c. q4w. At BL, 39% of subjects had an inadequate response/intolerance to prior anti-TNF therapy (anti–TNF-IR). Primary endpoint was ASAS20 response rates at Wk 16. Secondary endpoints included ASAS40, hsCRP, ASAS5/6, BASDAI, SF-36 PCS and ASAS partial remission. Endpoints were assessed through Wk 104, with multiple imputation for binary variables and a mixed-model repeated measures for continuous variables. Analyses stratified by anti-TNF history were pre-specified and are reported as observed.
**Results:** 60/72 (83.3%), 57/73 (78.1%) and 57/74 (77%) subjects completed 104 wks of treatment with secukinumab 150 mg, 75 mg and PBO, respectively. As reported previously, secukinumab 150 mg significantly improved all pre-specified endpoints at Wk 16 vs. PBO, except ASAS partial remission; the 75 mg dose did not reach statistical significance at Wk 16 based on hierarchical testing.[1] ASAS20/40 response rates at Wk 104 were 71.5/47.5% with both secukinumab doses. Clinical improvements with secukinumab were sustained through Wk 104 across all secondary endpoints (Table). In the subgroup of anti–TNF-naïve subjects, ASAS20/40 response rates at Wk 104 (observed data) were 76.9/56.4% and 80.0/60.0% with secukinumab 150 mg and 75 mg, respectively; corresponding rates in anti–TNF-IR subjects were 85.0/50.0% and 68.8/43.8%. Across the treatment period (mean secukinumab exposure: 735.6 days), exposure-adjusted incidence rates for serious infections/infestations, IBD, malignant/unspecified tumours and MACE with secukinumab were 1.2, 1.4, 0.5 and 0.7 per 100 subject-years, respectively. No cases of TB, opportunistic infections or suicidality-related AEs were reported.

**Table. Summary of 104 week Efficacy Results**

| | Secukinumab 150 mg s.c. N = 72 | Secukinumab 75 mg s.c. N = 73 |
|---|---|---|
| ASAS20 response, n (%) | 51 (71.5) | 52 (71.5) |
| ASAS40 response, n (%) | 34 (47.5) | 35 (47.5) |
| hsCRP, change from baseline score (Mean ± SE) | 0.50 ± 1.13 | 0.59 ± 1.13 |
| ASAS5/6, n (%) | 36 (50.2) | 30 (41.0) |
| BASDAI, mean change from baseline score (Mean ± SE) | –2.92 ± 0.27 | –2.85 ± 0.27 |
| SF-36 PCS, mean change from baseline score (Mean ± SE) | 7.29 ± 0.97 | 6.55 ± 1.01 |
| ASAS partial remission, n (%) | 14 (19.9) | 10 (13.7) |

ASAS, Assessment of Spondyloarthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high sensitivity C-reactive protein; n, number of subjects meeting criteria; N, total number of subjects in the analysis; s.c., subcutaneous; SE, standard error; SF-36 PCS, short form-36 health survey physical component summary

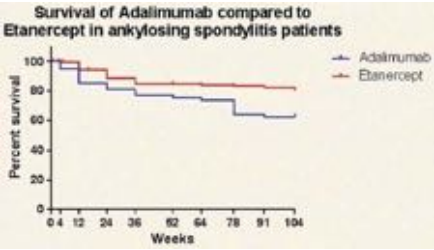
**Conclusions:** Secukinumab provided sustained improvement through 2 years in the signs and symptoms of AS with improved physical function, regardless of anti-TNF status. Safety was consistent with previous reports.
**References:**
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**Disclosure of Interest:** H. Marzo-Ortega Grant/research support from: Janssen and Pfizer, Consultant for: Abbvie, Celgene, Janssen, Novartis and UCB, Speakers bureau: Abbvie, Celgene, Janssen and UCB, C. Legerton Grant/research support from: AbbVie, Ablynx, Acerta, Amgen, AstraZeneca, Celgene, GSK, Janssen, E. Lilly, BMS, Pfizer, Novartis, Sandoz, UCB, Daiichi Sankyo, Chemo-Centryx, Boehringer Ingelheim, Speakers bureau: Celgene and Amgen, J. Sieper Grant/research support from: AbbVie, Pfizer and Merck, Consultant for: AbbVie, Pfizer, Merck, UCB and Novartis, Speakers bureau: AbbVie, Pfizer, Merck and UCB, A. Kivitz Consultant for: AbbVie, Pfizer, Genentech, UCB and Celgene, Speakers bureau: Celgene, Pfizer, and Genentech, R. Blanco: None declared, M. Cohen Consultant for: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche,

Sanofi and UCB, J. Zuazo Employee of: Novartis, A. Readie Shareholder of: Novartis, Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, H. Richards Employee of: Novartis
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## SAT0397 COMPARISON OF LONG-TERM DRUG SURVIVAL OUTCOME WITH ETANERCEPT TREATMENT AND ADALIMUMAB TREATMENT OF ANKYLOSING SPONDYLITIS

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**Background:** Treatment with Tumor Necrosis Factor inhibitors (TNFi) has improved the outcome of patients with ankylosing spondylitis (AS) but it is currently unknown, if response varies between different TNFi. One systemic review could not find a significant difference in clinical response and adverse events (AE) between adalimumab (ADL) and etanercept (ETN) in AS patients [1].
**Objectives:** To compare rates of drug survival and clinical response during 2-years of follow-up in patients with AS treated with ETN or ADL in routine care.
**Methods:** Two-hundred-forty-nine consecutive AS patients previously unexposed to TNFi were treated with ETN (164) or ADL (85). Treatment allocation was at the discretion of the treating rheumatologist. Clinical parameters were measured at each time point. Discontinuation was due to inefficacy on the drug, AE, lost to follow up, pregnancy wish and other reasons. Disease activity was assessed by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Response was defined as an improvement of BASDAI with 50% or as a 2 point drop compared to baseline. Data is corrected for baseline C-reactive protein, methotrexate use, BASDAI and body mass index. We imputed missing data by using last observation carried forward to assess mean BASDAI and BASDAIresponse at 2 years in patients who discontinued ETN or ADL prematurely.
**Results:** A total of 57 (22.9%) patients discontinued the drug, 28 (32.9%) patients discontinued ADL and 29 (17.7%) patients ETN. Cox-regression analysis demonstrated a significant difference in survival rate between discontinuation of the drug in the ADL patients compared to ETN patients; Hazard Ratio (HR) 2.09 (95% CI 1.25–4.50) p=0.005 (see figure) corrected for confounding; HR: 2.65 (95% CI 1.46–4.80) p=0.001. An independent t-test shows no difference at 2-years of follow-up between the ADL and the ETN patients in mean BASDAI; 3.5 (SD±2.5) respectively 4.1 (SD±2.1) p=0.336. Moreover, no difference between the ADL and the ETN patients was found in BASDAIresponse; 17 out of 30 (56.6%) reached BASDAI response at 2 year in patients treated with ADL compared to 73 out of 115 (63.5%) in patients treated with ETN; p=0.493.

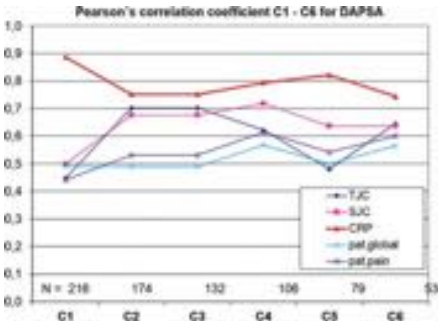



**Conclusions:** No difference was found in BASDAI or BASDAIresponse at a 2-year follow up. AS patients using ETN had a higher drug survival in the first 2 years of the treatment compared to AS patients using ADL. However, this study is not designed as a head-to-head trial, which has the risk of a selection bias.
**References:**
[1] Cochrane Database Syst Rev. 2015 Apr 18;4: CD005468
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## SAT0398 APPLICATION OF DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA) IN A COHORT OF PATIENTS FOLLOWED IN THE INSTITUTE OF RHEUMATOLOGY PRAGUE

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**Background:** At present new guidelines for the therapy and monitoring of psoriatic arthritis are in progress, inspired by the EULAR guidelines 2015. We propose the Minimal Disease Activity (MDA) as a target of therapy. Given the fact that the major problem of our patients is joint manifestation of psoriatic disease (PD) and only occassionally severe skin syndrome, which usually requires different therapeutic approach we have searched for an instrument which would assess the severity of joint involvement numerically, taking into account the patient's point of view. For this purpose we used the recently validated index DAPSA[1]
**Objectives:** (1) To ascertain the correlation of this index with its individual components (2) to take a look at the development of this index over time in a sample of patients from our database.
**Methods:** We picked 53 cases out of our database of 216 patients, who had at least 6 yearly controls with full set of data available. Subsequently we calculated DAPSA according to the formula: SJC+TJC+pat.pain VAS10,0cm+pat. Global VAS10,0cm+CRPmg/l[1]. Then we determined the correlation between DAPSA and individual components of the index using Pearson's correlation coefficient for each of 6 controls (C). We followed further the development of this index during the course of 6 years and calculated the percentage of patients who achieved remission (REM), low disease activity (LDA), moderate disease activity (MDA), or high disease activity (HDA) according to this index. The usual treatment algorythm was used, only the more tight control was employed.
**Results:** (1) The best correlation with DAPSA was found for CRP (0,74–0,93) and to a lesser degree for the number of swollen and tender joints (0,50–0,72 and 0,49–0,70 respectively) and for patient reported outcomes (pat. global-0,57–0,75 and pat. pain-0,44–0,61). (2) The proportion of patients in REM and LDA increased linearly during the 6-year follow up. (3) The average DAPSA score decreased during their follow-up (21,1–3,59).




**Conclusions:** The newly validated index of disease activity DAPSA seems to be a good indicator of disease activity and treatment response in patients with psoriatic arthritis. It could be a good component of local guidelines for treatment and monitoring of PsA.
**References:**
[1] Schoels M, Aletaha D, Alasti F, et al. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Ann Rheum Dis2015.
**Acknowledgement:** Supported by the Research program of the Ministry of health of Czech Republic: IGA MZ CR: No. 000 000 23728
**Disclosure of Interest:** None declared
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## SAT0399 EFFICACY OF GOLIMUMAB FOR NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: SUBGROUP ANALYSIS BY BASELINE MRI AND C-REACTIVE PROTEIN STATUS

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**Background:** The efficacy of golimumab (GLM) for nonradiographic axial spondyloarthritis (nr-axSpA) was demonstrated in a randomized, double-blind (DB), placebo (PBO)-controlled, phase 3 study (GO-AHEAD; NCT01453725).[1]
**Objectives:** We investigated the effect of GLM in patients (pts) with nr-axSpA based on presence or absence of objective inflammation (ASAS+ MRI sacroiliitis and/or C-reactive protein [CRP] $>$ upper limit of normal [ULN]) at baseline.
**Methods:** Pts with nr-axSpA (ASAS criteria, centrally read SI joint X-rays/MRIs, disease duration $\leq$5 years, chronic back pain $\geq$3 years, high disease activity, and inadequate response or intolerance to NSAIDs) were randomized (with

ASAS-defined MRI sacroiliitis by single central reader [yes, SI+; no, SI–] and CRP level [≤ULN or >ULN] as stratification factors) to GLM 50 mg SC or PBO Q4W for 16 wks. The primary endpoint was ASAS20 response at wk 16. Estimated between-group differences in ASAS20, ASAS40, BASDAI50, and ASAS partial remission (PR) response at wk 16 for four pt subgroups (MRI SI+ & CRP >ULN; MRI SI– & CRP >ULN; MRI SI+ & CRP ≤ULN; MRI SI– & CRP ≤ULN) were compared by Miettinen-Nurminen methods. No multiplicity control was used.

**Results:** In total, 197 pts were treated (GLM=97; PBO=100). Treatment group differences in ASAS20, ASAS40, BASDAI50, and ASAS PR response were greater in pts with baseline objective inflammation (Table). Results should be interpreted with caution, given the small subgroups and absence of multiplicity control.

Table 1. Subgroup analysis of response by MRI SI status and CRP level at baseline

| Endpoint | Subgroup | GLM n/N (%) | PBO n/N (%) | Difference vs PBO % Estimate (95% CI) | *P* value |
|---|---|---|---|---|---|
| ASAS20 | MRI SI+, CRP >ULN | 22/26 (84.6) | 10/27 (37.0) | 47.6 (21.9, 67.2) | 0.0005 |
| | MRI SI–, CRP >ULN | 12/13 (92.3) | 5/14 (35.7) | 56.6 (21.3, 79.2) | 0.0028 |
| | MRI SI+, CRP ≤ULN | 26/39 (66.7) | 15/39 (38.5) | 28.2 (5.9, 47.8) | 0.0132 |
| | MRI SI–, CRP ≤ULN | 9/19 (47.4) | 10/20 (50.0) | –2.6 (–32.7, 27.9) | 0.8711 |
| ASAS40 | MRI SI+, CRP >ULN | 18/26 (69.2) | 7/27 (25.9) | 43.3 (16.5, 64.2) | 0.0018 |
| | MRI SI –, CRP >ULN | 10/13 (76.9) | 3/14 (21.4) | 55.5 (17.6, 79.1) | 0.0047 |
| | MRI SI+, CRP ≤ULN | 19/39 (48.7) | 8/39 (20.5) | 28.2 (7.1, 47.1) | 0.0093 |
| | MRI SI–, CRP ≤ULN | 8/19 (42.1) | 5/20 (25.0) | 17.1 (–12.8, 44.6) | 0.2636 |
| BASDAI50 | MRI SI+, CRP >ULN | 18/26 (69.2) | 10/27 (37.0) | 32.2 (5.1, 54.9) | 0.0201 |
| | MRI SI –, CRP >ULN | 11/13 (84.6) | 4/14 (28.6) | 56.0 (18.7, 79.2) | 0.0041 |
| | MRI SI+, CRP ≤ULN | 17/39 (43.6) | 9/39 (23.1) | 20.5 (–0.6, 40.0) | 0.0562 |
| | MRI SI–, CRP ≤ULN | 10/19 (52.6) | 7/20 (35.0) | 17.6 (–13.6, 45.8) | 0.2733 |
| ASAS PR | MRI SI+, CRP >ULN | 8/26 (30.8) | 7/27 (25.9) | 4.8 (–19.6, 29.0) | 0.6983 |
| | MRI SI –, CRP >ULN | 9/13 (69.2) | 3/14 (21.4) | 47.8 (9.8, 73.8) | 0.0142 |
| | MRI SI+, CRP ≤ULN | 10/39 (25.6) | 5/39 (12.8) | 12.8 (–5.0, 30.6) | 0.1535 |
| | MRI SI–, CRP ≤ULN | 5/19 (26.3) | 3/20 (15.0) | 11.3 (–15.1, 37.3) | 0.3879 |

**Conclusions:** In the DB phase of GO-AHEAD, nr-axSpA pts with baseline objective inflammation (particularly with CRP >ULN) had greater responses to GLM. No GLM treatment benefit was observed in pts with MRI SI– & CRP ≤ULN.

**References:**

[1] Sieper J, et al. Arthritis Rheum. 2015;67(10),2702–2712.

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## SAT0400 CLINICAL FACTORS IMPACTING STATIN USAGE IN A LONGITUDINAL ANKYLOSING SPONDYLITIS COHORT

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**Background:** Patients with ankylosing spondylitis (AS) are at higher risk for developing cardiovascular comorbidities. While aortic valve and conduction defects are most common, increased levels of LDL cholesterol are also seen. Statin usage has been reported to lower CRP and ESR though the power of these studies are limited due to small sample size and short-term follow-up (1,2).

**Objectives:** This study examines associations of statin usage with socio-demographic and clinical factors, including disease activity, functional impairment, and radiographic severity in patients with two years of follow-up or more.

**Methods:** 655 AS patients meeting modified New York criteria followed at least 2 years (and up to 12 years) were included in the analysis. Demographic and clinical parameters (disease activity and functional impairment were collected every 6 months, as well as radiographic assessments (BASRI and mSASSS) every 2 years. Univariable and multivariable mixed effect models were developed to identify independent factors associated with statin usage over time.

**Results:** Mean disease duration was 18 years (SD=13). 10% (n=66) of the cohort were using statins. Univariable longitudinal regression models are shown below:

Factors associated with statin usage based on a univariable longitudinal analysis

| Variable | OR | 95% CI | P-value |
|---|---|---|---|
| Male gender | 2.7 | (1.4,5.4) | 0.004 |
| White | 3.8 | (1.7,8.6) | 0.001 |
| Marital status: married | 3.3 | (1.9, 6.0) | <0.001 |
| Disease duration >20 years | 15.8 | (8.6, 28.7) | <0.001 |
| Age >40 years | 5.5 | (2.3,13.3) | <0.001 |
| History of hip involvement | 0.4 | (0.3, 0.8) | 0.004 |
| History of cardiovascular comorbidity | 13.7 | (7.7,24.4) | <0.001 |
| History of diabetes | 4.7 | (1.4,15.4) | 0.01 |
| History of smoking | 2.2 | (1.2,3.8) | 0.01 |
| History of hypertension | 9.9 | (5.4,17.4) | <0.001 |
| Concomitant use of NSAID's | 0.4 | (0.2,0.8) | 0.01 |
| Concomitant use of TNF-blockers | 1.0 | (0.6,1.5) | 0.96 |
| Radiographic severity (mSASSS >4) | 3.8 | (2.1,6.7) | <0.001 |
| Radiographic severity (BASRI >6) | 2.6 | (1.6,4.4) | 0.001 |
| Impaired functionality (BASFI >4) | 1.6 | (1.1,2.5) | 0.03 |
| Disease activity (BASDAI >4) | 0.6 | (0.3,0.9) | 0.04 |
| Elevated CRP | 0.7 | (0.5,0.9) | 0.03 |
| Elevated ESR | 1.1 | (0.7,1.5) | 0.76 |

Multivariable longitudinal analyses controlling for confounders showed independent associations of age >40 years (p<0.001, OR=5.5 (2.3, 13.3)), the presence of cardiovascular disease (p<0.001, OR=7.6 (3.8, 15.5)), diabetes (p=0.01, OR=4.7 (1.4, 15.4)), opiate use (p=0.03, OR=2.0 (1.1, 3.7)), and CRP (p=0.03, OR=0.4 (0.2, 0.9)).

**Conclusions:** Statin usage was, as expected, more likely in those of older age with greater disease duration and greater radiographic severity. Even though statins are known to reduce CRP, the association with markers of lower disease activity, both subjective (BASDAI on univariable analysis) and objective (CRP on both univariable and multivariable analyses), raises the possibility of a role in suppressing inflammation in patients with AS.

**References:**

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## SAT0401 TWO-YEARS SURVIVAL OF GOLIMUMAB IN 400 PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND AXIAL SPONDYLOARTHRITIS IN REAL-LIFE WORLD

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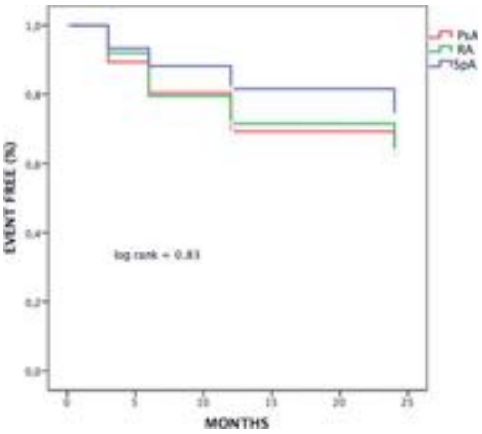
**Background:** It has previously been shown that the survival of anti-TNF drugs was lower in Rheumatoid arthritis (RA) than in other chronic arthritis.

**Objectives:** The objective of this study was to investigate the drug retention, as surrogate of effectiveness, of Golimumab (GOL) with axial Spondyloarthritis (AxSpA), Psoriatic arthritis (PsA) and RA. Furthermore, predictors of drug retention were evaluated.

**Methods:** This is a multicenter prospective observational study of unselected patients with AxSpA, PsA and RA starting GOL because of their active disease despite prior treatment with conventional disease modifying drugs (DMARDs) or biological DMARDs (bDMARDs) in the settings of standard care from 11 rheumatologic centres of Apulia (Southern Italy). The primary endpoint was GOL drug retention at 2 years. Time to discontinuation was defined as the time between drug initiation and last administration plus one dispensation interval. Kaplan-Meier curve analysis was used to assess drug retention, and a Cox proportional regression model, adjusting for potential confounders, including prior

bDMARD exposure, glucocorticoid or DMARD intake, patient demographics and disease characteristics, for the analysis of predictors. Clinical response was evaluated at 3,6,12 and 24 months.

**Results:** To date, 416 patients (PsA 180, RA 89, AxSpA 147) have been included in the study, 171 (41%) were biologic-naïve. Disease duration was 6.9 ±6 yrs for PsA, 8.1 ±8 for RA, and 7.4 ±7 for AxSpA, respectively. RF/ACPA were present in 72.5% of RA patients, and HLA-B27 in 43% of AxSpa. Within PsA 58 patients had also spinal involvement. At 2 years (Fig.1), the drug persistence rate was 74.5% (20.8±0.5 months) for AxSpa, 62.5% (19.5±0.8 months) for RA, and 63.9% (18.8±0.6) months for PsA, being the difference not statistically significant. For AxSpa patients, the chance of stopping GOL was associated with the female gender (hazard ratio (HR) 3.15 (95% CI 1.4–8.5), and the presence of extra-articular manifestation (HR 0.20 (95% CI 0.48–0.88). In RA the only predictor of GOL discontinuation was the achievement good EULAR response at 3 months (HR 0.36 ((95% CI 0.15–0.88), while no baseline factors correlating with drug persistence was detected for PsA. The percentage of AxSpa patients achieving BASDAI<4 was 63.4% at3 months, 69.3% at6 months, 77.5% at12 months, and 70.8% at24 months. In RA, DAS28 based remission was attained in 22.5% at3 months, 26.8% at6 months, 36.2% at12 months, and 43.9% at24 months. Finally for PsA DAS28 based remission was found in 27.5% at3 months, 33.2% at6 months, 42.1% at12 months, and 42.6% at24 months, while BASDAI<4 was 56.4% at 3 months, 73.1% at 6months, 76.2% at12 months, and 82.1% at24 months.




**Conclusions:** Unlike previous studies on TNF inhibitors, GOL seems to have similar drug survival in different chronic arthritides. Male sex and the presence of extra-articular manifestations were independently associated with GOL discontinuation in AxSpa. The achievement of good EULAR response at 3 months was the best predictor of continuing GOL in RA.

**Disclosure of Interest:** None declared

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## SAT0402 SAFETY OF ETANERCEPT THERAPY IN HBSAG CARRIERS WITH ANKYLOSING SPONDYLITIS: A PROSPECTIVE STUDY

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**Background:** The prevalence rate of hepatitis B virus (HBV) infection in China (13%) and many other developing countries are much higher than that in developed countries. When anti-TNF agents are more available and affordable in developing countries, the safety of anti-TNF therapy in terms of the reactivation of hepatitis B virus (HBV) infection need more concern. Rare data from a prospective study focus on the use of TNF antagonists in patients with concurrent ankylosing spondylitis (AS) and HBV infection are available by now.

**Objectives:** To evaluate the influence of Etanercept on the re-activation of HBV infection in HBsAg carriers with AS.

**Methods:** In this 48 weeks observation, HBsAg carriers with active AS (BASDAI ≥4) despite failed treatment with at least two NSAIDs and sulfasalazine (for patients with persistent peripheral arthritis) were studied. Patients must have normal liver function prior to Etanercept therapy. All patients received the treatment of Etanercept 50mg each week.

For patients who had positive HBV load (>100 copy/ml) at baseline, lamivudin were prescribed preventively. Pre-existing NSAIDs and sulfasalazine were allowed. During the study, serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and HBV load (polymerase chain reaction) were monitored every 6 weeks in the first 12 weeks and every 12 weeks after week 12. Increased AST/ALT and HBV load were managed and monitored according to expert opinion. After withdraw of Etanercept due to any reason, monitoring of ALT, AST and HBV load must be conducted until normal result was obtained in 2 consecutive tests.

**Results:** Fourteen patients (12 male, 2 female) were recruited. At baseline, ten patients (group 1, including 1 female) had normal viral load (<100 copy/ml), other 4 patients (group 2, with preventive lamivudin) had abnormal viral load (4.7e4, 5.3e7, 2.8e3, 9.8e4 copy/ml, respectively). Two patients from group 1 and one patient from group 2 discontinued Adalimumab at week 12 due to ineffectiveness. Reactivation of hepatitis B occurred in one patient from group 1, and another from group 2. The patient from group 1 had mild elevated ALT and AST (71 and 46 IU/L, respectively) and increased HBV load (7.6e3) at Week 12. After prescription of Entecavir, abnormal laboratory finding was monitored every 4 weeks, both liver enzyme and viral load decreased to normal range in 8 weeks and remained normal. The patient from group 2 (baseline viral load 4.7e4) had mild elevated ALT and AST (57 and 49 IU/L, respectively) and increased HBV load (5.2e8) at week 24. After prescription of Adefovir (combined with the pre-existing Lamivudin), both liver enzyme and viral load decreased to normal range in 8 weeks and remained normal. For the rest 12 patients, no significant elevated AST/ALT or increased viral load was seen during follow-up.

**Conclusions:** Etanercept therapy represent a safe and effective option for HBsAg carriers with AS refractory to traditional treatment. Prophylaxis strategy with more effective anti-viral drugs is recommended to reduce the risk of hepatitis B reactivation.

**Disclosure of Interest:** None declared

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## SAT0403 TREATMENT WITH GOLIMUMAB OR INFLIXIMAB REDUCES HEALTH RESOURCE UTILIZATION AND INCREASES WORK PRODUCTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS IN THE QUO-VADIS STUDY, A LARGE, PROSPECTIVE REAL-LIFE COHORT

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**Background:** The true cost of treating Ankylosing Spondylitis (AS) comprises several elements including not only medication, but also healthcare resource utilization (HCRU), reduced work productivity, and absenteeism.

**Objectives:** We report the results from the QUality of Life as Outcomes and its VAriation with DIsease States (QUO-VADIS) study on the effect of the anti-tumor necrosis factor (TNF) agents, golimumab (GLM) and infliximab (IFX), on HCRU for patients with AS as well as their ability to work.

**Methods:** This was a prospective observational study in bionaïve AS patients (modified New York criteria) newly treated with GLM or IFX (originator) in a clinical practice setting. Patients were followed-up for ~6 months of treatment with GLM or IFX and data was collected at baseline (BL), and at 3 and 6 months. The assessment of HCRU was done by evaluating data on the use of concomitant medications, hospitalizations (inpatient care or acute care) and visits in day care and outpatient settings; HCRU data reflected the prior 3 months for each timepoint. Work productivity and activity impairment (WPAI) was assessed by the number of work days missed as well as quantifying absenteeism, presenteeism, work impairment, and activity using the WPAI instrument adapted to Spondylarthritis (WPAI-SpA)(1); WPAI was based on the 7 days prior to the administration of the questionnaire.

**Results:** 963 patients received ≥1 dose of medication. The vast majority (78%, n=751) was treated with GLM, while the rest (22%, n=221) received IFX. Mean age of the patients was 42.7 years, 61.4% were male. Concomitant medication usage for AS treatment was reported by 84.3% of patients, the vast majority of whom received NSAIDs, followed by analgesics, DMARDs and corticosteroids. At BL, the percent of patients who reported hospitalizations (inpatient care) in the prior 3 months was 13.6%, which decreased to 3.1% at 6 months, while outpatient care in the 3 months prior to BL was reported by 39.4% of patients, which decreased to 19.0% at 6 months. The percent of patients receiving acute emergency care in the 3 months prior to BL reduced from 1.6%0.3% at 6 months. Further details on HCRU at BL and at 6 months are shown in the Table. The mean

**Table: Health Care Resources Utilization and WPAI-SpA Scores**

| Mean (SD) Health Care Resource Utilization Among All Patients | | |
|---|---|---|
| | Baseline | 6 months |
| Acute Care (duration of stay, hours) | 13.7 (32.5) | 3.3 (2.08) |
| Acute Care (number of admissions) | 1.1 (0.3) | 1.3 (0.6) |
| Hospitalization (duration of stay, days) | 7.3 (6.1) | 4.1 (4.5) |
| Outpatient/Day Care (number of visits) | 2.4 (1.8) | 2.1 (2.7) |
| **Mean (SD) Work Productivity and Impairment Among All Patients[a]** | | |
| | | |
| Absenteeism | 16.4 (32.3) | 6.3 (19.8) |
| Presenteeism | 51.9 (30.6) | 28.0 (26.0) |
| Work Impairment | 48.3 (34.0) | 25.1 (26.4) |
| Activity | 62.5 (24.7) | 36.1 (26.9) |

[a]Score interpretation: For all 4 outcomes, greater scores (range 0–100%) indicate greater impact of health.[15]

(SD) number of days at work, missed due to AS, was reduced from 6.3 (31.1) days at BL to 2.7 (12.3) days at 6 months. Results for WPAI-SpA assessment are presented in the Table.
**Conclusions:** In patients with AS newly treated with GLM (almost 80% of the study population) or IFX for 6 months, HCRU was reduced, as shown by the shorter mean duration of hospitalizations and the proportion of patients receiving acute, inpatient or outpatient care. Additionally, work productivity and activity increased, and patients reported fewer days of work missed due to AS after 6 months of treatment.
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**Disclosure of Interest:** P. Sarzi-Puttini: None declared, F. Van Den Bosch Consultant for: Merck & Co., Inc.; Abbvie; Novartis; Pfizer; UCB; Bristol Myers Squibb, Celgene, Janssen, P. Claudepierre: None declared, S. Sajjan Employee of: Merck Sharp & Dohme, N. Vastesaeger Employee of: Merck Sharp & Dohme, M. Govoni Employee of: Merck Sharp & Dohme, S. Kachroo Employee of: Merck Sharp & Dohme
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## SAT0404 EVALUATION OF THE CLINICAL USEFULNESS OF A STANDARDIZED DOSE REDUCTION PROTOCOL FOR MAINTENANCE OF REMISSION IN PATIENTS WITH AS UNDER ANTI-TNF TREATMENT

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**Objectives:** To assess if reduced dose of iTNF is not less effective than complete dose for response maintaining
**Methods:** Prospective, randomized, multicenter, real life open-label study of non-inferiority coordinated by Spanish Societies of Clinical Pharmacology and Rheumatology.
Patients included were randomized (1:1) in a complete dose arm (C) or in a reduced dose arm according to a previous standardized protocol (E).
The primary objective was the proportion of patients who after a year of following maintained the acceptable therapeutical goal (ATG) (BASDAI, physicianVAS, patientVAS, night axial pain all <4). Secondary endpoints were: proportion of patients with clinical remission) (BASDAI, physicianVAS, patientVAS, night axial pain all <2), disease activity assessed with ASAS, BASFI and quality of life.
The main analysis was made per protocol (PP), considering an ATG percentage in C group of 87% with a maximum settled difference between both treatments inferior than 17%
**Results:** 113 AS, 84% men, age of 45'6y and mean disease duration of 13'5y. 22 (40%) were treated with adalimumab, 19 (35%) with etanercept, 10 (27%) with infliximab and 4 (7%) with golimumab. Main results are shown in table1. At 12 months follow-up 48 (82.8%) in the full dose arm vs 47 (85.5%) in reduced dose arm maintained the ATG demonstrating the non inferiority hypothesis (p=ns, dif -2.5%, 95%CI -16.6 to 11.7%). We did not observe also any significant difference in any of the rest of variables analyzed including the proportion of patients in remission and safety issues. Although 30% of patients showed ≥1 flare, without differences between both treatment arms, less than 15% required treatment dropout.

Table 1

| | Control (n) | Experimental (n) | Difference |
|---|---|---|---|
| Per protocol efficacy analysis | 55 | 58 | |
| ATG 12 months (% [95%CI]) | 83.8% [64.8% to 102.7%] | 81.3% [62.8% to 99.8%] | –2.5% [–16.6% to 11.7%] |
| ITG 12 months (% [95%CI]) | 83.7% [64.7% to 102.7%] | 78.2% [59.7% to 96.8%] | –5.5% [–20.6% to 9.7%] |
| Intention to treat efficacy analysis | 60 | 60 | |
| ATG 12 months (% [95%CI]) | 84.8% [66.2% to 103.3%] | 80.1% [61.7% to 98.5%] | –4.7% –4.7% |
| ITG 12 months (% [95%CI]) | 84.7% [66.1% to 103.2%] | 77.3% [59.0% to 95.7%] | –7.33% [–22.2% to 7.5%] |
| Other variables of efficacy | | | |
| BASDAI (median (P25, P75)) | 1 (0.6, 1.7) | 1 (0.2, 1.4) | ns |
| VAS nocturnal axial pain (mean (SD)) | 0.84 (1.01) | 1.02 (1.15) | ns |
| Physician GA (median (P25, P75)) | 1 (0.0, 2.0) | 1 (0.0, 1.0) | ns |
| Patient GA (median (P25, P75)) | 1 (0.0, 2.0) | 1 (0.0, 1.0) | ns |
| ASDAS-CRP (median (P25, P75)) | 1.1 (0.8, 3.5) | 1.0 (0.7, 1.9) | ns |
| Withdrawal for inefficacy (physician crit.) | 3 (5%) | 9 (14%) | ns |
| Safety | | | |
| Adverse events | 40% | 30% | ns |
| Infections | 25% | 17% | ns |
| Severe adverse events | 7% | 3% | ns |

**Conclusions:** In patients with persistent clinical remission, dose reduction is not inferior to the standard dose. The presence of clinical flare is not uncommon, although less than half of cases lead to a change in the treatment.
**Disclosure of Interest:** None declared
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## SAT0405 NO RADIOLOGICAL SACROILIAC JOINT PROGRESSION AFTER 2 YEARS OF ETANERCEPT TREATMENT IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: DATA FROM THE EMBARK STUDY

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**Background:** Radiological structural changes in the sacroiliac joint (SIJ) over time in non-radiographic axial spondyloarthrits (nr-axSpA) can be evaluated by measuring the progression from non-radiographic to radiographic damage status according to modified New York (mNY) criteria but also with other more sensitive methods.[1,2] However, the question remains whether anti-tumor necrosis factor therapy can prevent this structural progression, particularly in patients with nr-axSpA.
**Objectives:** To evaluate radiographic progression in SIJ after 2 years of etanercept (ETN) treatment in nr-axSpA according to different outcome measures.
**Methods:** *Study design:* 104-week follow-up of patients enrolled in the EMBARK trial who received ETN either from baseline (active treatment arm) or week 12 (placebo [PBO] arm). *Patients:* Active nr-axSpA refractory to ≥2 NSAIDs. *Study drug:* ETN 50 mg once a week. *Outcome measures:* Pelvic X-rays were performed at both baseline and week 104. After anonymization, 3 trained readers evaluated the films blinded to chronology using the 0–4 grade scale of the mNY radiographic criteria for each (left and right) SIJ. *Statistical analysis:* X-rays from patients who completed the 104-week study were assessed. For continuous variables (e.g., total score from 0 to 8 for the left and right SIJ according to mNY grading), the mean score from the 3 readers was evaluated (bias was possible because readers knew that all patients were previously considered to have nr-axSpA); for binary variables (e.g., change from non-radiographic to radiographic axSpA, worsening of ≥1 grade in ≥1 SIJ and an absolute final value of ≥2 in the worsened joint), the score agreed upon by ≥2 readers was used for analysis.
**Results:** Of 215 randomized patients, 169 completed the open-label period at 104 weeks; 161 patients had X-rays available at both baseline and week 104. Only 1 patient was found to have satisfied mNY criteria for radiographic SIJ damage (ie, at least bilateral grade II or unilateral grade III) at baseline. Of 160 patients with mNY negative scores at baseline, none became mNY positive at week 104. The mean score (SD) for the total (left and right) SIJ (scale, 0–8) was 0.87 (0.83) at baseline and 0.88 (0.85) at week 104 (change, 0.01 [0.15]; *P*=0.386). No patients had *both* worsening of ≥1 grade in ≥1 SIJ *and* an absolute final value of ≥2 in the worsened joint.
**Conclusions:** This study suggests that, whatever the outcome measure, no structural radiological progression in the SIJ occurred after 2 years of etanercept treatment in patients with nr-axSpA. Given this study's limitations, eg, lack of controls and inclusion of completers only, it is unclear whether this is an effect of etanercept. Additional studies using X-rays and MRI of the SIJ should be conducted to further address this question.
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**Disclosure of Interest:** M. Dougados Grant/research support from: Pfizer, AbbVie, UCB, Merck, Eli-Lilly, Sanofi, Consultant for: Pfizer, AbbVie, UCB, Merck, Eli-Lilly, Sanofi, W. Maksymowych Grant/research support from: AbbVie, Consultant for: AbbVie, Amgen, Boehringer Ingelheim, Eli Lilly, Janssen Pharmaceutica, L.P, Pfizer, UCB, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Celgene, Daiichi, Eli-Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Employee of: Director of Imaging Rheumatology bv., R. Pedersen Shareholder of: Pfizer, Employee of: Pfizer, R. Bonin Shareholder of: Pfizer, Employee of: Pfizer, I. Logeart Shareholder of: Pfizer, Employee of: Pfizer, J. Bukowski Shareholder of: Pfizer, Employee of: Pfizer, H. Jones Shareholder of: Pfizer, Employee of: Pfizer
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## SAT0406 EFFICACY AND SAFETY OF LOXOPROFEN HYDROGEL PATCH VERSUS LOXOPROFEN TABLET IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Non-steroidal anti-inflammatory drugs (NSAIDs) are the cornerstone of medication for patients with ankylosing spondylitis (AS). However, oral NSAIDs are associated with adverse events such as gastrointestinal, cardiovascular and renal events.
**Objectives:** To assess the efficacy and safety of loxoprofen sodium hydrogel patch (LX-P) versus loxoprofen sodium tablet (LX-T) in the treatment of active AS.
**Methods:** The study population consisted of patients who met the modified New York radiographic criteria for AS and had to be active disease, defined by the Bath AS Disease Activity Index (BASDAI) ≥4 or the Ankylosing Spondylitis Disease Activity Score using the C-reactive protein level (ASDAS-CRP) ≥1.3. Patients were randomly assigned to either the LX-P group or the LX-T group

for 4 weeks. The primary efficacy endpoint was the proportions of patients reaching Assessment in Ankylosing Spondylitis 20% response (ASAS20) at week 4. Secondary efficacy outcomes included mean changes from baseline to week 4 for ASDAS-CRP, BASDAI and patient's global assessment of disease activity (PTGA). Adverse events were monitored throughout the study.
**Results:** Of 70 randomized patients, 35 patients were allocated to the LX-P group and 35 to the LX-T group. In the intent-to-treat population, no significant differences were found between the two groups in the proportion of patients achieving ASAS20 response at week 4 (19 of 35 [54.3%] for LX-P group versus 26 of 35 [74.3%] for LX-T group; P=0.081). And there were no significant differences for the mean change of ASDAS-CRP, BASDAI and PTGA from baseline to week 4 between LX-P and LX-T group. Post hoc analyses suggested that patients without peripheral arthritis in the LX-P group were more likely to achieve ASAS20 response than those with peripheral arthritis. A lower incidence of gastrointestinal disorders was observed in LX-P group. No serious adverse events were reported in the two groups.
**Conclusions:** LX-P is noninferior to LX-T for improvement of disease activity in patients with active AS, and has few gastrointestinal adverse events.
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## SAT0407 DERMOSCOPIC CHANGES IN MELANOCYTIC NEVI IN PATIENTS WITH ANKYLOSING SPONDYLITIS USING TUMOR NECROSIS FACTOR-ALPHA INHIBITORS: A PROSPECTIVE COHORT STUDY

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**Background:** Tumor necrosis factor-alpha (TNF-α) inhibitors have been proposed to increase the risk of malignancy. Skin tumors have been reported among the most common malignancies seen in the use of these drugs and melanoma has a much higher importance compared to other skin tumors.
**Objectives:** To investigate the dermoscopic changes in melanocytic nevi in ankylosing spondylitis (AS) patients, under TNF-α inhibitors or conventional therapy (CT-sulfasalazine, non-steroidal anti-inflammatory drugs).
**Methods:** The study included 94 consecutive ankylosing spondylitis patients with at least one melanocytic nevus. 56 patients (F/M=5/51) in the cohort were patients initiated TNF-α inhibitor treatment and 38 (F/M=1/37) were patients receiving CT. Treatment-related changes that occur in nevi were prospectively followed dermoscopically. All changes detected in the follow-up period were recorded, and evaluated in two groups as substantial and non-substantial changes in terms of melanoma development risk. Substantial changes included expansion of nevi, shape change, regression, discoloration and melanoma-specific structural changes; and non-substantial changes included opening/darkening of the global color of nevi, change in the number of brown globules, reduction/loss of blackheads, diffuse-brown pigmentation at the pigment network and the presence of inflammation.
**Results:** Mean age of the TNF-α inhibitor group was 39.7±7.7 years and disease duration was 11.3±6.0 years. The mean age of CT patients was 37.5±7.2 years and disease duration was 8.4±4.5 years. Among age groups, there was no difference in terms of gender and disease duration ($p>0.05$). In TNF-α inhibitor group 220 (3.9±4.6) nevi, and in CT group 129 (3.4±1.8) nevi were followed (p=0.823). The median follow-up periods of the TNF-α inhibitor and CT groups were 20.4±4.8 and 16.5±4.2 months, respectively (p=0.052). 5 nevi in TNF-α inhibitor group (5 shape changes) and 4 nevi in CT group (3 shape changes, 1 expansion) had substantial changes in terms of the risk of melanoma (p=0.468). 15 nevi in TNF-α inhibitor group (7 opening in color, 3 darkening in color, 1 change in the number of brown globules, 3 reduction/loss of blackheads, 1 inflammation) and 6 nevi in the CT group (2 opening in color, darkening in 2 colors, 1 change in the number of brown globules, 1 reduction/loss of blackheads) had non-substantial changes in terms of melanoma risk (p=0.590). 3 of 5 nevi having major changes in terms of the risk of melanoma were excised.Pathological examination did not reveal malignancy.
**Conclusions:** In the literature, an association between rheumatoid arthritis and risk of developing melanoma has been reported, but there is no similar data pointing to an increased risk in patients with AS. This study has shown that the TNF-α inhibitors did not cause the development of melanocytic nevi in about 2 years of follow-up in patients with AS. While a limitation of the study is the small number of patients, close monitoring of patients under the risk of melanoma development is an important long-term benefit of the study.
**Disclosure of Interest:** None declared
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## SAT0408 ANTI TNF-α THERAPY PROVIDES BENEFICIAL EFFECTS ON CHOROIDAL THICKNESS INCREASE IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: A POSSIBLE MECHANISM OF INFLIXIMAB EFFECTIVENESS IN SUPPRESSING UVEITIS ATTACKS

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**Background:** Patients with ankylosing spondylitis (AS) have higher choroidal thickness values (CT) compared to controls.
**Objectives:** To quantitatively asses the profile of CT in patients with AS using optical coherence tomography (OCT), and to examine whether the posterior eye segment abnormalities in active AS patients were reversible by infliximab therapy
**Methods:** Thirty-one patients with AS receiving infliximab therapy and 24 healthy controls were enrolled. Patient's clinical and demographic characteristics were recorded. Using OCT, we performed retinal imaging and choroidal *thickness measurements* in AS patients before and after 6 months of infliximab therapy, and in healthy controls who returned 6 months after the first visit. We compared patients before versus 6 months after infliximab therapy, as well as controls.
**Results:** Patients with AS had higher CT (mean± SD; 347.5±114.4 μm) compared to healthy controls (322.1±62.8 μm) (p=0.283), although this did not reach statistical significance. At 6 months after the first measurement, the mean CT was significantly decreased (after treatment with infliximab: 326.5±99.7μm vs. before: 347.5±114.4 μm, n=31, p=0.018) in AS group, but not in the control group ($p$=0.102). Retinal nerve fiber layer was significantly decreased at 6 months after treatment with infliximab in AS group (106.4±13.5 μm vs 105.0±13.0μm *p=0.008*).
**Conclusions:** This is the first study to evaluate the posterior eye segment in patients with AS using OCT. Our data indicate that CT abnormalities in active AS is reversible by therapy, and this CT decreasing effect of infliximab may be involved in its effective suppressing action of uveitis attacks in AS.
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## SAT0409 IMPROVED CLINICAL OUTCOMES AND WORKABILITY IN SPONDYLOARTHRITIDES DURING REAL-LIFE ADMINISTRATION OF ADALIMUMAB IN CENTRAL AND EASTERN EUROPE

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**Background:** There is a dearth of data on effectiveness and patient reported outcomes in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA) treated with adalimumab (ADA) in Central and Eastern Europe
**Objectives:** P12–768 study aimed at establishing the impact of ADA on disease activity, extra-articular manifestations (EAMs), functional capacity, work productivity and collecting ADA's safety data in patients with AS and PsA
**Methods:** A prospective, 12-month follow up, single-arm, multi-country observational study enrolling AS and PsA patients eligible for ADA therapy with 3-monthly follow up visits. Upon the presence of axial (ax) or peripheral (per) symptoms, disease activity was assessed by BASDAI and ASDAS or DAS28, whereas functional capacity was assessed by BASFI or HAQ-DI, respectively. Primary endpoint was the percentage of patients with BASDAI 50% decrease (ax) or DAS28 decrease by at least 1.2 (per). WPAI-questionnaire was used to assess productivity impairment. Frequencies of EAMs and serious adverse events (SAEs) were reported. Descriptive statistics and LOCF-analysis were used
**Results:** 566 subjects were enrolled, 555 had sufficient data for statistical analysis (72.6% AS; 27.2% PsA); 449 completed last visit. 64.9% were male; mean age was 45.6 (range 18–80) years, mean disease duration 12.2 ± 10.0 years. At baseline 76.1% and 26.1% of patients had axial and peripheral symptoms, respectively. 54.8% of patients previously received NSAIDs and

34.6% were biologic experienced. Primary endpoint was achieved in 76.1% with axial symptoms and in 83.5% with peripheral symptoms. BASFI decreased from 6.8±2.0 to 2.8±2.3 and HAQ-DI from 1.3±0.6 to 0.6±0.5. At baseline, enthesitis was the most frequent EAM in patients with AS (23.1%) followed by uveitis (12.7%). Most frequent EAM in patients with PsA were psoriasis (90.1%) and enthesitis (17.2%). Percentage of patients with EAMs decreased from 40.4% to 9.7% (AS) and from 90.1% to 46.4% (PsA), whereas proportion of patients free of EAMs increased from 46.1% to 79.5% by study end. Total activity impairment decreased from 64.3% to 28.0%. Among all employed patients (n=255; 45.9% at baseline) presenteeism decreased from 56.7% to 20.1%, absenteeism from 15.6% to 6.4% and total work productivity impairment from 59.9% to 22.1%. 52 episodes of SAEs occurred in 26 patients (4.7%)

**Conclusions:** Adalimumab was effective in improving clinical, functional and working status and reduced frequency of EAMs in patients with AS and PsA in routine clinical use. No new safety signals were observed.

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## SAT0410 SECUKINUMAB IMPROVES PHYSICAL FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 2-YEAR DATA FROM MEASURE 1, A PHASE 3 RANDOMISED TRIAL

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**Background:** Ankylosing spondylitis (AS) has significant adverse effects on an individual's health status.[1] Secukinumab, an interleukin (IL)-17A inhibitor, improved signs and symptoms and patient-reported outcomes (PROs) over 52 weeks (wks) in the randomised, double-blind, placebo (PBO)-controlled, Phase 3 MEASURE 1 study (NCT01358175).[2,3]

**Objectives:** To evaluate the effect of secukinumab on disease activity, pain, physical function, fatigue, and general and AS-specific quality of life (QoL) measures over 104 wks.

**Methods:** 371 adults with active AS were randomised to receive secukinumab 10 mg/kg i.v. at baseline (BL), Wks 2 and 4, and then s.c. 150 mg (IV→150 mg) or 75 mg (IV→75 mg) every 4 wks from Wk 8, or PBO. At Wk 16, PBO-treated patients (pts) were re-randomised to receive secukinumab 150 mg or 75 mg s.c. from Wk 16 (non-responders) or Wk 24 (responders). PROs assessed included: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Short Form-36 physical and mental component summaries (SF-36 PCS and SF-36 MCS, respectively); AS Quality of Life (ASQoL); patient's global assessment of disease activity; patient's assessment of total spinal pain; patient's assessment of nocturnal pain; Bath Ankylosing Spondylitis Functional Index (BASFI); Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue); and EuroQoL-5-dimension health status questionnaire (EQ-5D). BASDAI, SF-36 PCS and ASQoL were predefined secondary endpoints and are reported using a mixed-effect model repeated measures (MMRM) analysis. Other PROs and analyses by prior anti-tumor necrosis factor (anti-TNF) therapy use were exploratory endpoints and are reported as observed data (Wk 104).

**Results:** 97/125 (77.6%) and 103/124 (83.1%) pts randomised to IV→150 mg and IV→75 mg, respectively, completed 104 wks of treatment. The improvements in BASDAI, SF-36 PCS and MCS, ASQoL, BASFI, and FACIT-Fatigue achieved with secukinumab at Wk 52 were sustained at Wk 104, with mean changes from BL being greater than minimum clinically important differences (Table). Improvements were also observed in patient's global assessment of disease activity, total spinal pain, nocturnal pain, and EQ-5D. Sustained improvements were observed regardless of prior anti-TNF use. In anti–TNF-naïve pts, mean changes from baseline at Wk 104 with secukinumab IV→150 mg and IV→75 mg were: –3.5 and –3.1, respectively, for BASDAI; 8.4 and 7.4 for SF-36 PCS; and –5.0 and –4.4 for ASQoL. Corresponding changes in anti-TNF-IR pts, were: –3.2 and –2.9 (BASDAI); 6.9 and 7.6 (SF-36 PCS); and –4.1 and –5.1 (ASQoL).

**Conclusions:** In pts with active AS, secukinumab provided sustained improvements through 2 years in PROs including disease activity, pain, physical function, fatigue, as well as general and AS-specific measures of QoL.

**Table. Mean Change from Baseline in Patient-Reported Outcomes (PROs) for Patients Originally Randomised to Secukinumab**

| | Wks | Secukinumab IV→150 mg N = 125 | Secukinumab IV→75 mg N = 124 |
|---|---|---|---|
| BASDAI | 52[a] | −2.8 ± 0.2 | −2.7 ± 0.2 |
| | 104[b] | −2.9 ± 0.2 | −2.8 ± 0.2 |
| SF-36 PCS | 52[a] | 6.7 ± 0.6 | 6.6 ± 0.6 |
| | 104[b] | 6.9 ± 0.7 | 6.4 ± 0.7 |
| ASQoL | 52[a] | −4.4 ± 0.4 | −4.2 ± 0.4 |
| | 104[b] | −4.4 ± 0.4 | −4.3 ± 0.4 |
| BASFI | 52[a] | −2.2 ± 0.2 | −1.9 ± 0.2 |
| | 104[b] | −2.8 ± 2.3 | −2.3 ± 2.1 |
| SF-36 MCS | 52[a] | 4.5 ± 0.8 | 5.5 ± 0.8 |
| | 104[b] | 5.7 ± 9.0 | 5.2 ± 10.0 |
| FACIT-Fatigue | 52[a] | 9.1 ± 0.8 | 7.5 ± 0.8 |
| | 104[b] | 10.2 ± 10.0 | 8.8 ± 9.4 |

BASDAI MCID ≥1; SF-36 PCS MCID ≥2.5; SF-36 MCS MCID ≥2.5; ASQoL MCID ≥1.8; BASFI MCID ≥0.7; FACIT-Fatigue MCID ≥4

[a]Values are Least Squares Mean ± Standard Error from mixed-effect model repeated measures (MMRM)

[b]Values are Mean ± Standard Deviation from observed data

BASFI: n = 87 for secukinumab IV→150 mg; n = 86 for IV→75 mg; SF-36 MCS and FACIT-Fatigue: n = 87 for secukinumab IV→150 mg; n = 85 for IV→75 mg

MCID, Minimum Clinically Important Differences

**Results:** Of the 251 PsA patients meeting the inclusion criteria, 26% (n=65) discontinued/switched the index biologic and 74% (n=186) stayed on the index biologic by the 2nd follow-up visit. A significantly greater percent of females discontinued/switched the index biologic (56% vs 41%, $p<0.05$). However both cohorts were similar in age (mean: 55 yrs vs 53 yrs), and disease duration (12 vs 12 yrs.). Group 1 patients reported significantly higher scores for pain (mean: 42 vs 27) and fatigue (mean: 48 vs 33) compared to Group 2 ($p<.0001$). Almost one-third of patients in Group 1 reported greater overall work impairment (mean: 30% vs 15%, $p<0.01$) compared to Group 2. Patients in Group 1 were most likely to have higher disease activity (mean CDAI: 13 vs 9, $p<0.0001$) and enthesitis (26% vs 15%, $p<0.05$) vs. group 2. Overall a majority of patients had a history of prior biologic use (97%), with about 55% on current monotherapy. The major reason for discontinuing the index biologic was lack of efficacy (60%), followed by other reasons (16%) and side effects (12%).

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## SAT0411 BIOLOGIC DISCONTINUATIONS AMONG PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS REGISTRY

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**Background:** Over the past years, introduction of biologics for treatment of psoriatic arthritis (PsA) has improved the treatment responses in all clinical domains. However, little is known regarding the characteristics of patients who discontinue/switch biologics in non-clinical trial setting.

**Objectives:** To characterize PsA patients who discontinue/switch the index biologic and evaluate the reasons for discontinuation in the Corrona PsA/Spondyloarthritis (SpA) registry, a large US national cohort of patients with PsA/SpA.

**Methods:** PsA patients enrolled in the registry between 3/2013 and 7/2015, with a biologic at baseline (registry enrollment) and at least 2 follow-up visits were included. Two cohorts were identified: patients who discontinued/switched the index biologic (group 1) and those who stayed on the index biologic by the 2nd follow-up visit approximately 15 months after the enrollment (group 2). Descriptive analyses on patient demographics, clinical outcomes (eg. clinical disease activity index (CDAI), dactylitis, enthesitis), patient reported outcomes (eg. pain, fatigue, work productivity and activity impairment (WPAI)) and treatment at time of enrollment were examined. Chi-square tests and t-tests were used for continuous and categorical variables respectively to evaluate differences.

**Conclusions:** About a quarter of patients discontinued their index biologic over an average of 15 months follow up period. Those patients were more likely to have higher disease activity (CDAI) and poorer patient reported outcomes (pain, fatigue, WPAI) at enrollment. The most common reason for switching was lack of efficacy.

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## SAT0412 BIOLOGICAL THERAPY IN PSORIATIC ARTHRITIS (PSA): DIFFERENCES BETWEEN SWITCHERS AND NON-SWITCHERS

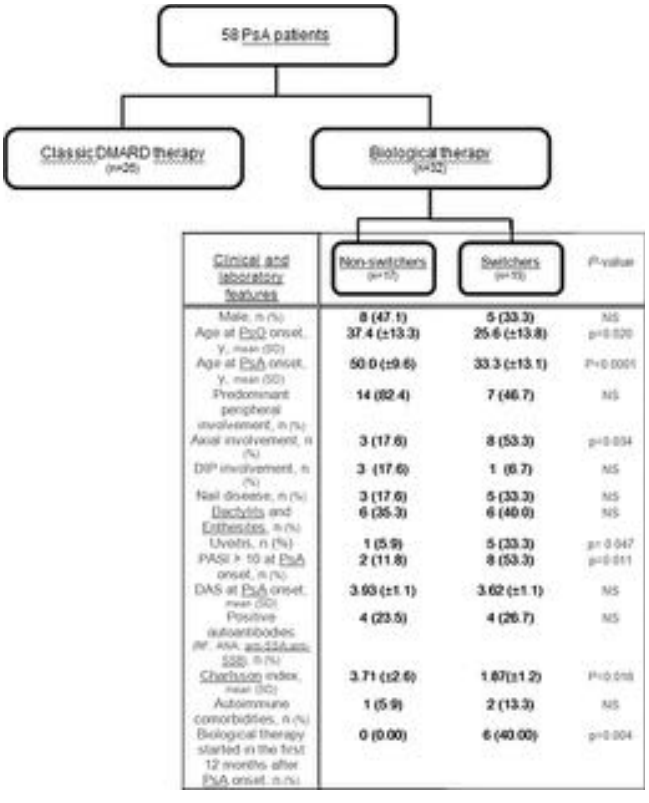
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**Background:** Switching biological therapies is becoming increasingly common in routine management of PsA patients. However, evidence in this topic is still scarce. Predictive markers for an optimal approach to the sequential prescription of biologics are lacking.

**Objectives:** In a population of PsA patients, we aimed to determine differences in baseline clinical and laboratory features between switchers and non-switchers.

**Methods:** We conducted a retrospective analysis of the PsA patients followed at our outpatient clinic in the last 24 months. Demographic, clinical and laboratory data were collected. Severity of skin manifestations and peripheral arthritis at PsA onset were recorded using PASI and DAS28 score. Patients who changed biological therapies due to therapeutic failure (primary or secondary) or toxicity were defined as switchers.

For comparison of clinical and laboratory features we used chi-square test for categorical variables and Mann-Whitney or T-Student test for continuous variables.




| Clinical and laboratory features | Non-switchers | Switchers | *P*-value |
|---|---|---|---|
| Male, n (%) | 8 (47.1) | 5 (33.3) | NS |
| Age at PsO onset, y, mean (SD) | 37.4 (±13.3) | 25.6 (±13.8) | |
| Age at PsA onset, y, mean (SD) | 50.0 (±9.6) | 33.3 (±13.1) | |
| Predominant peripheral involvement, n (%) | 14 (82.4) | 7 (46.7) | NS |
| Axial involvement, n (%) | 3 (17.6) | 8 (53.3) | |
| DIP involvement, n (%) | 3 (17.6) | 1 (6.7) | NS |
| Nail disease, n (%) | 3 (17.6) | 5 (33.3) | NS |
| Dactylitis and Enthesitis, n (%) | 6 (35.3) | 6 (40.0) | NS |
| Uveitis, n (%) | 1 (5.9) | 5 (33.3) | |
| PASI > 10 at PsA onset, n (%) | 2 (11.8) | 8 (53.3) | |
| DAS at PsA onset, mean (SD) | 3.93 (±1.1) | 3.62 (±1.1) | NS |
| Positive autoantibodies (RF, ANA, anti-CCP, anti-SSB), n (%) | 4 (23.5) | 4 (26.7) | NS |
| Charlsson index, mean (SD) | 3.71 (±2.6) | 1.67(±1.2) | |
| Autoimmune comorbidities, n (%) | 1 (5.9) | 2 (13.3) | NS |
| Biological therapy started in the first 12 months after PsA onset, n (%) | 0 (0.00) | 6 (40.00) | |

**Results:** 58 PsA patients were included, 60.3% were women; the mean age at PsA and psoriasis (PsO) onset was 46.4 (±15) and 34.8 (±15) years, respectively. At PsA onset, 24.1% of patients had a PASI score>10 and a mean DAS of 3.76 (±1.0). Laboratory features, arthritis and extra-articular manifestations were assessed (Image). 94.8% of patients were prescribed with non-biologic DMARD therapy and 55.2% with biological therapy, after failing to respond to a classic DMARD treatment alone. Median time from diagnosis until biological therapy prescription was 25.9 (±56,5) months.

Out of 32 patients prescribed with biologics, 15 (46.9%) switched to another biologic agent, mainly due to secondary failure (63.6%), primary failure (18.2%) and adverse events (13.6%). 15.65% and 3.1% of patients required 2 or 3 switches. Etarnacept was the first line agent prescribed in the majority (78.8%) of patients. Adalimumab (73.3%) and ustekinumab (50.0%) were the most used agents as second and third line biological therapies, respectively.

Switchers were significantly younger at psoriasis onset (25.6 (±13.8) vs 37.4 (±13.3) years, p=0.020) and also at PsA onset (33.3 (±9.6) vs 50.0 (±13.1) years, p<0.0001). They had higher PASI (p=0.011) levels comparing to non-switchers. Uveitis and axial involvement were significantly more common in switchers (p=0.047 and p=0.034, respectively). All patients starting biological therapy on the first 12 months after disease onset switched to another biological agent.

**Conclusions:** Age at PsO and PsA onset is a well-established clinical factor with significant impact in disease severity and in skin and arthritis manifestations. Our work suggests that it might also play a role in first biological treatment failure determining a need to switch. Higher PASI score at PsA onset, axial involvement and uveitis also seem to be associated with more likelihood of switching.

Our results should be considered exploratory. Larger studies are required to determine the role of these clinical features in predicting biological treatment switching.

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## SAT0413 GENETIC ASPECT OF INTER-INDIVIDUAL VARIABILITY IN THE RESPONSE TO NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN AXIAL SPONDYLOARTHRITIS

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**Background:** Non-steroidal anti-inflammatory drugs (NSAIDs) are first line therapies in patients with axial spondyloarthritis (axSpA). Patients with axSpA frequently response to NSAIDs and good response to NSAIDs is an important clinical feature. However, nearly 20–50% of patients with ankylosing spondylitis may have active disease despite NSAID treatment. NSAIDs acts through cyclooxygenase (COX) inhibition and inter-individual variability in response to NSAIDs may be related to genetic factors that regulate COX enzymes.

**Objectives:** We hypothesized that incomplete inhibition of COX enzymes as a consequence of genetic variability in the regulatory region of the COX genes may influence the response to NSAIDs. To examine this hypothesis, we investigated the association between selected polymorphism in COX-1 and COX-2 genes and NSAIDs response in axSpA.

**Methods:** Patients with axSpA who were followed by our outpatient clinic and met ASAS classification criteria for axSpA were enrolled. Healthy controls were recruited from hospital staff and visitors. Patients and controls were assessed for clinical and laboratory data. Inadequate response (IR) to NSAID therapy was defined either as persistence of symptoms despite maximal dosage of NSAIDs therapy or as persistent disease activity with a BASDAI>4 or an ASDAS >2 during NSAID therapy. Promoter variant of COX-2 -765G>C that is located in a putative binding site for the Sp1 transcription factors plays significant role as a positive activator of COX2 transcription. The Pro17Leu variant of COX-1–50C/T is associated with changed prostaglandin production and coxib selectivity. The DNA was isolated from blood samples the frequency of both COX-2- 765G/C (rs20417) and COX-1–50C/T (rs3842787) polymorphisms were analyzed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methods using the Faul restriction enzyme and appropriate primers.

**Results:** A total of 177 patients with axSpA (108M, 69F; mean age, 37.5±9.6 yrs) and 103 healthy controls (60M, 43F; mean age, 33.0±7.6 yrs) were included. Genotype distribution is given in the table. We did not found any significant differences in genotype of COX polymorphism regarding good/inadequate response to NSAIDs in patients with axSpA. Also there was no significant difference in the allele frequency distributions of COX-2–765G/C and COX-1–50C/T between patients and healthy controls.

| axSpA | NSAID responders (n=95) | NSAID IR (n=81) | *p* |
|---|---|---|---|
| Male, n (%) | 50 (52.6) | 58 (71.6) | **0.010** |
| nr-axSpA | 46 (48.4) | 21 (25.9) | **0.002** |
| COX-1–50C/T | | | |
| Heterozygote, n (%) | 6 (6.3) | 5 (6.2) | 0.969 |
| COX-2–765G/C | | | |
| Heterozygote, n (%) | 26 (27.4) | 33 (40.7) | 0.061 |
| Homozygote, n (%) | 6 (6.3) | 4 (4.9) | 0.755 |
| Current smoker | 33 (34.7) | 40 (49.4) | **0.049** |
| HLA-B27 +ve n=154 | 45 (50.0) | 44 (68.8) | 0.356 |

**Conclusions:** The current study is the first to investigate the possible role of genetic variation of COX genes in the NSAID response in axSpA. Our results suggest that genetic polymorphism of COX-1–50C/T and COX-2 -765 do not play a significant role in NSAID response in axSpA. Further studies are needed to confirm these finding in patients with axSpA from different ethnic population.
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## SAT0414 IN SPONDYLOARTHRITIS; DOES IMMUNOGENICITY INFLUENCE ON DRUG SURVIVAL OF ANTI-TNF?

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**Background:** The anti-TNF therapy has been demonstrated effective in patients with Spondylarthritis (SpA). The lack of efficacy and adverse events (1) have been reported as the most common reasons for the discontinuation of these drugs. In Rheumatoid Arthritis, the immunogenicity has been proved to be an influential factor in the survival of treatment, but this has not been proved in SpA.
**Objectives:** To assess the survival of 3 anti-TNF agents in a cohort of patients with SpA, and to determine if there are differences in the survival of the 3 anti-TNF between patients who develop anti-TNF antibodies and those who do not.
**Methods:** Patients with SpA who started Adalimumab (ADA), Infliximab (IFX) or Etanercept (ETN) as first anti-TNF treatment between 2001–2015 were included. Diagnoses were: Ankylosing Spondylitis (55.5%), Non Radiographic Axial SpA (20%), SpA associated with inflammatory bowel disease (5.9%) and Psoriatic SpA (18.6%). Patients with only peripheral involvement were excluded. Clinical and demographic data were collected, and in the case of ADA and IFX, the presence or absence of anti-drug antibodies were identified. No anti-ETN antibodies were identified. The reasons for drug discontinuation were classified as adverse event, administration reaction, primary inefficacy, secondary inefficacy, recovery and other (this included pregnancy, malignancies, etc). The event was defined as drug discontinuation due to only the first 4 reasons. Cumulative incidence through competitive risk was performed to compare drug survival.
**Results:** Of the 220 patiens studied, 58.6% were men, with a mean age of 43.5±12.4 years. Out of them, 38.6% (85) started treatment with IFX, 30% (66) with ADA, and 31.4% (69) with ETN. No statistically significant difference (p=0.3) was found in the survival of the 3 anti-TNF: IFX had a probability of drug discontinuation of 32.9% at 5 years, compared to 35.5% of ADA and versus 31.8% of ETN. The most common reasons for discontinuing treatment were: Primary inefficacy for IFX (22.4%), primary and secondary inefficacy for ADA (13.6% each), and others (pregnancy, etc) for ETN (26.1%).
30.6% of patients treated with IFX developed anti-IFX antibodies (AIA). Anti-ADA antibodies (AAA) were observed in 22.7% of 66 patients who received ADA. In both drugs, the drug survival was lower in patients who developed anti-TNF antibodies, but this difference was statistically significant only in the group of IFX:

Cumulative incidence through competitive risk (probability of drug discontinuation)

| | 1 year | 5 years | 10 years | p value |
|---|---|---|---|---|
| Infliximab | | | | |
| NO AIA | 13.5% | 25.4% | 34.3% | 0.003 |
| WITH AIA | 11.5% | 50.0% | 69.2% | |
| Adalimumab | | | | |
| NO AAA | 14.7% | 33.4% | | 0.5% |
| WITH AAA | 21.0% | 43.5% | | |

When survival was analyzed by subgroups of patients treated with IFX and ADA who had not developed antibodies compared with ETN, no statistically significant difference was found (p=0.5).
**Conclusions:** In our cohort, the three anti-TNF showed a similar survival. However, and particularly in the case of IFX, the development of anti-drug antibodies proved to be an influential factor in the survival of treatment.
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## SAT0415 DIASTOLIC LEFT VENTRICULAR DYSFUNCTION IN ANKYLOSING SPONDYLITIS IMPROVES DURING TUMOR NECROSIS FACTOR ALPHA BLOCKING THERAPY

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**Background:** Ankylosing spondylitis (AS) is associated with concomitant cardiac pathology, such as diastolic left ventricular (LV) dysfunction (1), valvular dysfunction, and aortic disease (2), all presumably caused by inflammation. The precise prevalence of diastolic left ventricular (LV) dysfunction and the effects of anti-inflammatory treatment thereon are currently unknown.
**Objectives:** To investigate the prevalence of diastolic LV dysfunction compared to controls and the effects of tumor necrosis factor (TNF) -α blocking therapy on ventricular function in AS patients.
**Methods:** Forty consecutive AS patients were included and treated for one year with TNF-α blocking therapy. Transthoracic echocardiography was performed at baseline and at one year. Forty age and gender matched asymptomatic random controls were included from an established echocardiographic cohort. Diastolic LV function (normal, dysfunction grade I, II, or III) and systolic LV function (ejection fraction, EF) were assessed. Valvular and aortic pathology was documented. Disease activity was measured with C-reactive protein (CRP), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score–CRP (ASDAS).
**Results:** At baseline, diastolic LV dysfunction (all grades) was present in nine patients (23%) vs one (3%) control (p=0.011). Systolic LV dysfunction was present in 0 (0%) patients vs one (3%) control (p=0.625). In total, 13 (33%) AS patients and six (15%) controls (p=0.066) had some form of cardiac pathology (i.e. one or more of the following: diastolic and/or systolic LV dysfunction, aortic valve dysfunction, aortic dilatation; one AS patient and one control had two disorders). Treatment with TNF-α blocking therapy had no effect on systolic LV function, but diastolic LV dysfunction (n=3 grade I, n=1 grade II) improved to normal in four patients (p=0.125), and neither worsened nor developed in the other patients. After the start of TNF-α blocking therapy CRP decreased from 4.0 (1.3–12.0) mg/l to 2.0 (1.9–3.2) mg/l ($p<0.001$), BASDAI decreased from 5.2±1.6 to 3.7±2.0 (p=0.001) and ASDAS decreased from 3.1±1.2 to 2.0±1.0 ($p<0.001$).
**Conclusions:** AS patients had a significantly increased prevalence of diastolic LV dysfunction compared to controls which improved during treatment with TNF-α blocking therapy. This appears to be related to the anti-inflammatory effects of TNF-blocking therapy.
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## SAT0416 SIGNIFICANTLY REDUCED RECURRENCE RATE OF ACUTE ANTERIOR UVEITIS IN ANKYLOSING SPONDYLITIS DURING TREATMENT WITH GOLIMUMAB

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**Background:** Acute anterior uveitis (AAU) is common in ankylosing spondylitis (AS) (1). Golimumab, a tumor necrosis factor alpha (TNF-α) blocker, has proven to be effective in the treatment of AS (2). We have shown earlier that treatment with adalimumab, another TNF-α blocker, leads to a significant decrease in the recurrence rate of AAU (3) in AS. At present, the effect of golimumab on the recurrence rate of AAU in AS is unknown.
**Objectives:** To investigate the effect of golimumab treatment on the recurrence rate of AAU attacks in AS patients.
**Methods:** Consecutive AS patients were enrolled who all fulfilled the 1984 Modified New York criteria, and fulfilled the criteria for initiating treatment with a TNF-α blocker in the Netherlands. All patients were treated with golimumab 50mg once a month for 12 months. During treatment, all occurring AAU attacks were assessed. The historic presence of AAU attacks was assessed from the year before baseline for non-biological treated patients, or the year before the first

treatment with a TNF-α blocker in case of a switch from another TNF-α blocker to golimumab. Disease activity was measured with the Ankylosing Spondylitis Disease Activity Score – C-reactive protein (ASDAS). Response to treatment was assessed with the ASAS-20.

**Results:** In total, 93 patients (65% male) were evaluable as per protocol, with a mean age of 44±13 years and a median disease duration of 7 (0–53) years. Fifty-one patients (55%) were TNF-α blocker naive. Median ASDAS score at baseline was 3.1 (0.7–5.5), which decreased to 1.9 (0.1–5.1) at 12 months. ASAS-20 response was achieved by 36% of patients at month three ($p<0.001$), and by 49% of patients at month twelve ($p<0.001$).

Six patients (7%) had a prior history of AAU with a total of nine attacks in the year prior to the first TNF-α blocker use (9.8/100 patient years). During golimumab treatment, the rate of recurring AAU attacks was reduced to two new attacks (2.2/100 patient years), a significant reduction of 78% ($p<0.001$). These two AAU attacks occurred in two separate patients, of whom one had no history of AAU.

**Conclusions:** Treatment of AS patients with golimumab leads to a significant decrease in disease activity. Simultaneously, the rate of recurring AAU attacks decreased significantly during golimumab treatment.

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## SAT0417 EVOLUTION OF MRI INFLAMMATION AND STRUCTURAL LESIONS ON SERIAL SCANS OVER 5 YEARS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TUMOR-NECROSIS-FACTOR-ALPHA INHIBITORS

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**Background:** Only few studies have investigated evolution of MRI inflammation (infl.) and structural lesions by serial MRI and radiography (CX) in patients with ankylosing spondylitis (AS).

**Objectives:** To investigate evolution of infl. and structural lesions over 5 years on MRI and CX during treatment with TNFα inhibitors (TNFα-I) with multiple serial examinations.

**Methods:** The study population comprised 34 patients with AS followed for 5 years after initiation of TNFα-I. MRIs of the sacroiliac joints (SIJs) and lower spine (Th9-S1) and spinal CXs were performed 7 and 4 times, respectively. UW and RSN evaluated the MRIs and CXs, respectively, in known time sequence. MRIs were evaluated according to the SPARCC sacroiliac (SIJ) and Spine Infl. Index and Structural Scores (SSS) (1). The Canada-Denmark MRI definitions of infl., fat (2), erosion and new bone formation (3,4) were transformed into scores. The CXs were scored according to the modified Stoke AS Spine Score (mSASSS).

**Results:** MRI infl., compared to baseline, decreased significantly in SIJ and spine from week 22 and onwards, while SIJ erosion decreased significantly from week 46 (see table). Conversely, the SIJ and spinal MRI fat and SIJ ankylosis scores increased significantly from week 22. Only minor changes for SIJ backfill and spine erosion score were observed. These findings indicate that reduction of infl. during TNF-I is followed by structural progression. During the 5 years of TNF-I, mSASSS and the structural MRI spine score SASSS had, compared to baseline, increased significantly from year 1 and 2, respectively, and onwards.

**Conclusions:** Shortly after initiation of TNF-I spine and SIJ MRI infl. decreased and structural scores changed indicating new bone formation. Thereafter the MRI scores remained unchanged. In constrast, mSASSS continuously increased.

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## SAT0418 THE EFFECT OF BISPHOSPHONATES ON BONE MINERAL DENSITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS IN DAILY CLINICAL PRACTICE

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**Background:** Ankylosing spondylitis (AS) is not only characterized by excessive bone formation, but also by excessive bone loss which may lead to low bone mineral density (BMD). So far, little is known about the effect of treatment with bisphosphonates on BMD in patients with AS.

**Objectives:** To evaluate the effect of bisphosphonates in combination with calcium/vitamin D supplements on BMD over 2 years in patients with AS stratified for the use of TNF-α inhibitors.

**Methods:** Patients from the Groningen Leeuwarden AS (GLAS) cohort, fulfilling the modified New York criteria for AS, who were treated with bisphosphonates and had 2-year follow-up BMD measurements available were included. All patients were treated with bisphosphonates in combination with calcium and/or vitamin D supplements. Alendronate (70 mg/week) and risedronate (35 mg/week) were used most frequently.

BMD of the lumbar spine (anterior-posterior projection at L1-L4) and hip (total proximal femur) were measured using DXA. Wilcoxon-signed rank test was used to compare BMD scores at first visit and after 2 years. Analyses were stratified for the use of TNF-α inhibitors.

**Results:** In total, 28 patients were included; 68% were male, 82% HLA-B27+, mean age was 53 ± 14 years, median symptom duration 20 years (range 1–60), and mean BASDAI 5.1±2.5. Fifteen patients (54%) started treatment with bisphosphonates before inclusion in the GLAS cohort (median 3.1 years). Most patients (86%) used bisphosphonates during the entire 2-year follow-up within GLAS.

Overall, lumbar spine BMD increased significantly from median Z-score of -0.8 at first visit to -0.3 after 2 years of treatment with bisphosphonates within the GLAS cohort. Hip BMD increased significantly from -1.1 at first visit to -0.9 after 2 years. In the 10 patients not using TNF-α inhibitors, only lumbar spine BMD increased significantly after 2 years of treatment. In the 14 patients starting TNF-α inhibitors,

**Abstract SAT0417** – Table 1. MRI and CX scores before TNFα-I initiation (week 0) and at follow-up

| | MRI and radiography scores | | | | | | |
|---|---|---|---|---|---|---|---|
| Follow-up | Week | | | Year | | | |
| | 0 | 22 | 46 | 2 | 3 | 4 | 5 |
| SPARCC SIJ MRI scores | | | | | | | |
| Infl. | 5.2 (9.8) | 0.7 (2.3)* | 0.6 (2.1)# | 1.0 (2.2)# | 0.9 (2.2)† | 1.2 (3.0)† | 2.5 (8.2)† |
| Fat | 19.7 (15.5) | 21.2 (15.6)# | 21.5 (15.1)# | 21.5 (14.6)* | 22.1 (14.2)# | 22.1 (14.5)# | 22.1 (14.8)# |
| Erosion | 5.6 (7.0) | 5.1 (6.7) | 4.7 (6.2)* | 4.4 (6.0)* | 3.7 (5.4)* | 3.9 (6.2)* | 3.7 (6.4)* |
| Backfill | 3.1 (5.2) | 3.2 (5.2) | 3.2 (5.1) | 3.2 (4.9) | 2.5 (4.3) | 2.1 (3.6)* | 2.2 (3.6) |
| Ankylosis | 6.0 (8.6) | 6.2 (8.5)* | 6.6 (8.4)# | 6.8 (8.4)# | 7.4 (8.5)# | 7.6 (8.5)# | 7.9 (8.4)# |
| Spine MRI scores | | | | | | | |
| SPARCC Infl. | 5.9 (9.1) | 2.3 (6.5)# | 0.9 (2.9)# | 0.6 (2.4)# | 0.4 (1.1)# | 0.7 (1.6)# | 0.5 (1.5) |
| CanDen Infl. | 3.8 (7.1) | 0.7 (2.2)# | 0.6 (2.0)# | 1.1 (2.7)# | 0.7 (1.6)# | 0.9 (2.3)# | 1.4 (4.5)* |
| FASSS | 6.1 (6.8) | 8.0 (8.2)# | 8.2 (8.3)# | 8.1 (8.5)* | 7.7 (8.3) | 7.4 (8.1) | 7.7 (8.3) |
| Erosions | 1.8 (3.1) | 1.9 (3.7) | 1.9 (3.7) | 1.9 (3.7) | 1.9 (3.5) | 1.9 (3.5) | 1.9 (3.5) |
| SASSS | 2.4 (4.3) | 2.5 (4.3) | 2.5 (4.3) | 2.6 (4.5)* | 2.6 (4.5)* | 2.6 (4.3)* | 2.6 (4.0) |
| Total mSASSS | 9.6 (12.5) | – | 11.7 (13.1)# | – | 12.7 (12.9)† | – | 14.6 (13.7)† |
| Lumbar mSASSS | 4.9 (7.9) | – | 6.1 (8.3)* | – | 6.7 (8.1)# | – | 8.0 (8.9)† |

Mean (SD). Wilcoxon Signed-Rank Test. Follow-up visit compared with week 0. *$p<0.05$; #$<0.01$; †$p<0.001$.

lumbar spine and hip BMD increased significantly after 2 years. The remaining 4 patients already used TNF-α inhibitors (Table 1). Comparable results were found for BMD T-scores.

Table 1. Lumbar spine and hip BMD Z-scores at first visit and after 2 years of follow-up in AS patients treated with bisphosphonates, stratified for the use of TNF-α inhibitors.

| | First visit | 2-year follow-up | P-value |
|---|---|---|---|
| *Total group (n=28)* | | | |
| BMD LS Z-score | -0.8 (-2.1 – 0.4) | -0.3 (-1.5 – 1.0) | <0.001 |
| BMD hip Z-score | -1.1 (-1.6 – -0.6) | -0.9 (-1.5 – 0.0) | 0.006 |
| *Patients not using TNF-α inhibitors (n=10)* | | | |
| BMD LS Z-score | -1.2 (-2.5 – -0.3) | -0.8 (-2.0 – 0.8) | 0.007 |
| BMD hip Z-score | -1.2 (-1.6 – -0.2) | -0.9 (-1.4 – -0.3) | 0.433 |
| *Patients starting TNF-α inhibitors (n=14)* | | | |
| BMD LS Z-score | -1.5 (-2.2 – 0.3) | 0.2 (-1.5 – 4.9) | 0.004 |
| BMD hip Z-score | -1.2 (-1.8 – -0.8) | -0.8 (-1.6 – 0.0) | 0.007 |
| *Patients using TNF-α inhibitors (n=4)* | | | |
| BMD LS Z-score | 0.2 (-0.8 – 2.6) | 0.6 (-0.7 – 3.1) | 0.066 |
| BMD hip Z-score | -0.8 (-1.4 – 2.3) | -0.7 (-1.6 – 2.8) | 0.593 |

Values are presented as median (interquartile range).

**Conclusions:** In our observational cohort study, lumbar spine BMD improved significantly after 2 years of follow-up in all AS patients treated with bisphosphonates. This improvement was most pronounced in patients starting TNF-α inhibitors. Hip BMD only improved significantly in patients also starting TNF-α inhibitors.
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## SAT0419 GENDER DIFFERENCES IN DISEASE ACTIVITY, PHYSICAL FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TNF-α INHIBITORS

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**Background:** The clinical presentation of ankylosing spondylitis (AS) can be different between genders.
**Objectives:** To investigate differences in clinical assessments of disease activity, physical function and quality of life between male and female AS patients before the start of TNF-α inhibitors and after 2 years of follow-up.
**Methods:** Patients from the Groningen Leeuwarden AS (GLAS) cohort who started TNF-α inhibitors because of active disease with baseline and 2-year follow-up visits were included. Disease activity was assessed using the BASDAI, ASDAS, CRP, and patient GDA. Physical function and quality of life were assessed using the BASFI and ASQoL, respectively.
**Results:** Of the 220 included AS patients with active disease, 69% were male, 78% HLA-B27 positive, mean age was 43±12 years, and median duration of symptoms 16 years (IQR 8–25). Patient characteristics were comparable between men and women.
At baseline, female patients with AS experienced significantly higher disease activity according to BASDAI, ASDAS, and patient GDA compared to male patients. Baseline CRP levels were comparable between genders. Furthermore, physical function (BASFI) and quality of life (ASQoL) were significantly worse in female patients (Table 1).
After staring TNF-α inhibitors, all clinical assessments improved significantly during 2 years of follow-up. The change over 2 years was comparable between male and female patients for all measures of disease activity, physical function, and quality of life (Table 1). After 2 years, significantly less women were still using their first TNF-α inhibitor (53% vs. 81%) and significantly more women had switched to a second TNF-α inhibitor (31% vs. 15%).

Table 1. Clinical assessments at baseline and change over 2 years in male and female AS patients who started treatment with TNF-α inhibitors

| | All (n=220) | Men (n=152) | Women (n=68) |
|---|---|---|---|
| *Baseline* | | | |
| BASDAI (0–10) | 6.0 ± 1.7 | 5.8 ± 1.7 | 6.6 ± 1.6* |
| $ASDAS_{CRP}$ | 3.75 ± 0.82 | 3.67 ± 0.85 | 3.92 ± 0.72* |
| CRP (mg/l) | 13 (5-24) | 13 (4-22) | 13 (6-27) |
| Patient GDA (0–10) | 6.6 ± 1.9 | 6.4 ± 1.9 | 7.0 ± 1.9* |
| BASFI (0–10) | 5.8 ± 2.1 | 5.5 ± 2.1 | 6.3 ± 2.1* |
| ASQoL (0–18) | 9.9 ± 4.1 | 9.3 ± 4.0 | 11.4 ± 4.0* |
| *2-year change* | | | |
| BASDAI (0–10) | -2.7 ± 2.1 | -2.7 ± 2.0 | -2.6 ± 2.2 |
| $ASDAS_{CRP}$ | -1.59 ± 1.10 | -1.67 ± 1.11 | -1.42 ± 1.07 |
| CRP (mg/l) | -8 (-17-0) | -8 (-16-0) | -8 (-20-0) |
| Patient GDA (0–10) | -3.1 ± 2.8 | -3.2 ± 2.6 | -2.8 ± 3.1 |
| BASFI (0–10) | -2.1 ± 2.2 | -2.1 ± 2.1 | -2.2 ± 2.4 |
| ASQoL (0–18) | -4.7 ± 4.1 | -4.5 ± 3.8 | -5.3 ± 4.8 |

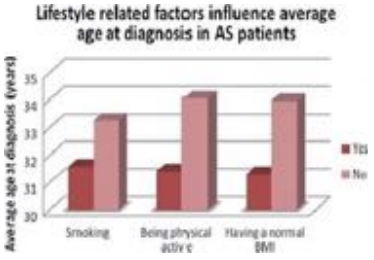
Values are presented as mean ± SD or median (interquartile range).
* P-value<0.05 compared to men.

**Conclusions:** In this large cohort of AS patients with active disease, cross-sectional analysis showed that women experience higher disease activity and worse physical function and quality of life on self-reported assessments than men. Longitudinal analysis after starting TNF-α inhibitors showed that the changes in clinical assessments over 2 years were comparable between genders.
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## SAT0420 SMOKING RELATED WITH DISEASE RESPONSE AND AGE AT DIAGNOSIS IN ANKYLOSING SPONDYLITIS

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**Background:** Lifestyle related factors, such as smoking and Body Mass Index (BMI) are known to increase the disease activity and progression in rheumatoid arthritis (1,2). In ankylosing spondylitis (AS), only a few studies are available regarding this topic (3–5). Smoking was associated with an earlier diagnosis of AS, higher disease activity (OR=2.5) and a doubled increased radiographic progression compared to non smokers. In addition, alcohol consumption and having a physical demanding occupation were associated with more axial radiographic lesions. A higher BMI was associated with a lower response rate to Tumor Necrosis Factor inhibitors (TNFi) compared to AS patients with a normal BMI (49% vs 78%, respectively). Most studies included only one lifestyle related factor in association with disease activity and early diagnosis in AS, while our study aimed to test for multiple related lifestyle factors on disease activity and early diagnosis.
**Objectives:** To determine whether factors related to lifestyle (smoking, alcohol consumption, BMI, physical activity and occupation) are associated with age at diagnosis of AS and response rate to TNFi.
**Methods:** Consecutive AS patients (fulfilling the modified New York criteria) who started or switched treatment with TNF inhibitors were included in a prospective, observational cohort. Data on disease activity (Ankylosing Spondylitis Disease Activity Score (ASDAS) and lifestyle factors (smoking, alcohol consumption, BMI, occupation and physical activity) were collected at baseline and 6, 12 and 24 months after the start of treatment. Lifestyle factors, with $p<0.05$ in relation to age at diagnosis and ASDAS were subsequently entered in the overall regression model.
**Results:** In total 312 AS patients were included with a mean follow-up of 18.9 months (6–24). The majority 172 (55%) improved on TNFi whereof, 86 patients (27.7%) showed a clinical important improvement (decrease in ASDAS >1.1) and 86 (27.7%) a major clinical improvement (decrease in ASDAS >2.2). In multivariate analysis, age at diagnosis was negatively influenced by a positive smoking status ((regression coefficient in years) B= -2.78, p=0.041, 95% CI= -5.60 – -0.01), being physical active (B=-2.98, p=0.026, 95% CI=-5.59 – -0.37) and having a normal BMI (B= -3.1, p=0.019, 95% CI=-5.73 – -0.52) (Figure 1). No risk factors were related with the change in ASDAS during treatment. No relation between alcohol consumption and disease onset or treatment response was found.



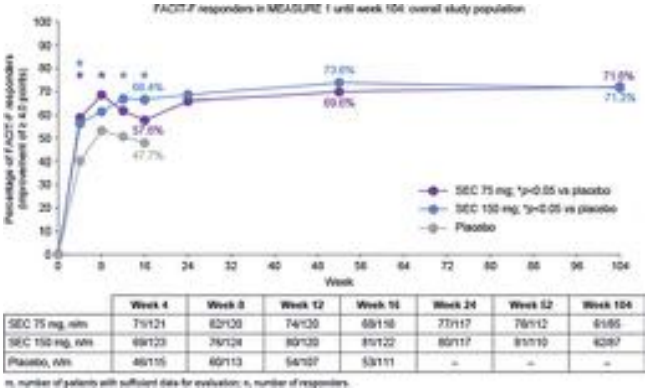

**Conclusions:** Smoking, moderate physical activity and normal BMI were associated with an earlier age at diagnosis. A significant improvement of the ASDAS at both 1 and 2 year follow-up under TNF treatment was found, confirming the efficacy of TNF inhibitors in a real life cohort. However, contrary to the expectations no relations were found between lifestyle factors and disease activity.

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## SAT0421 REDUCTION IN FATIGUE IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS OF TWO PHASE 3 STUDIES OF SECUKINUMAB

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**Background:** Patients with active ankylosing spondylitis (AS) experience fatigue which frequently leads to reduced health-related quality of life (HRQoL). Secukinumab (SEC) treatment results in rapid improvements in signs and symptoms, physical functioning and HRQoL in patients with active AS versus placebo (PBO) in the phase 3 studies MEASURE 1 (M1) and MEASURE 2 (M2).
**Objectives:** To assess the impact of SEC on fatigue in patients with AS, including biologic-naïve patients and those with an inadequate response to TNF therapy (TNF-IR) and to investigate correlations between fatigue and baseline characteristics or clinical endpoints.
**Methods:** The two phase 3 studies involved patients with active AS (M1, N=371; M2, N=219). Patients were randomized to receive subcutaneous SEC 150 mg or 75 mg or PBO administered every 4 weeks after initiating therapy. Patients randomized to PBO who did not meet predefined response criteria at week 16 were re-randomized at week 24 to SEC 150 mg or 75 mg. Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale. The FACIT-F response analyses were based on observed data with no imputation. A change in FACIT-F score of $\geq$4 from baseline was used to define fatigue response. Possible correlations between baseline characteristics or clinical response criteria and improvements in fatigue at weeks 16 and 52 were investigated using a logistical regression model.
**Results:** From week 4 onwards, greater improvements in fatigue response were observed for both SEC groups compared with PBO. At week 16, 66.4% (M1) and 77.6% (M2) of patients receiving SEC 150 mg achieved a fatigue response, compared with 47.7% (M1) and 50.0% (M2) for PBO ($p$ <0.05 for both comparisons; see figure). Response rates for SEC 150 mg at week 16 were numerically higher in biologic-naïve patients (M1, n=271; M2, n=134) than in TNF-IR patients (M1: 68.9% vs 59.4%; M2: 86.0% vs 62.5%, respectively). Responses were sustained at week 52 in both studies (M1, 73.6%; M2, 80.6%) and at week 104 in M1 (71.3%; see figure for M1 data) in the overall population, and in the two subgroups according to prior biologic therapy status. Correlation analyses based on pooled data from both studies did not identify any baseline factors that consistently predicted an improvement or worsening of FACIT-F score at week 16 or 52. Achieving a fatigue response was strongly positively correlated at weeks 16 and 52 with clinical response (ASAS20, 40, 5/6 responses, ASAS partial remission, ASDAS-CRP major improvement and BASDAI 50 response).




| | Week 4 | Week 8 | Week 12 | Week 16 | Week 24 | Week 52 | Week 104 |
|---|---|---|---|---|---|---|---|
| SEC 75 mg, n/m | 71/121 | 82/120 | 74/120 | 69/116 | 77/117 | 78/112 | 61/85 |
| SEC 150 mg, n/m | 69/123 | 76/124 | 80/120 | 81/122 | 80/117 | 81/110 | 62/87 |
| Placebo, n/m | 46/116 | 60/113 | 54/107 | 53/111 | – | – | – |

n, number of patients with sufficient data for evaluation; n, number of responders.

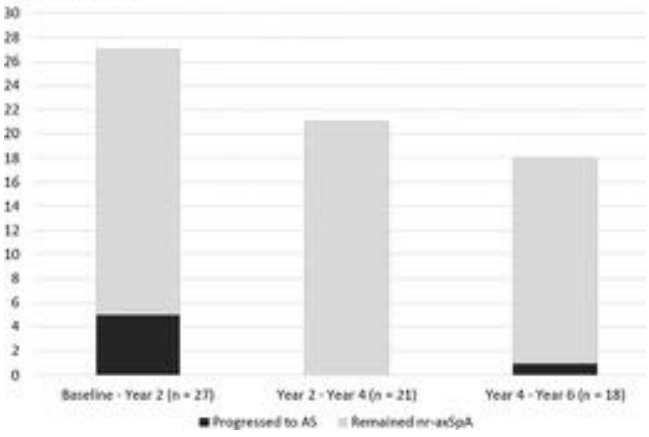
**Conclusions:** SEC 150 mg provided rapid improvement in fatigue, regardless of prior biologic therapy, and response was sustained up to 104 weeks. Fatigue response showed a strong correlation with improvement in clinical response criteria, indicating a relationship between fatigue and disease activity in AS and is an important treatment goal for patients with AS.
**Disclosure of Interest:** T. K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB, Consultant for: AbbVie, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Orion Pharma, Pfizer, Roche, Sandoz and UCB, P. Conaghan Speakers bureau: Abbvie, Janssen, Lilly, Novartis, Pfizer and Roche, A. Deodhar Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer and UCB, Consultant for: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer and UCB, L. Gossec Consultant for: Abbvie, Celgene, Janssen, Novartis, Pfizer, Roche and UCB, M. Østergaard Grant/research support from: Abbvie, BMS, Janssen, Merck, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth., J. Cañete Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Biogen, Janssen, Merck, Novartis, Pfizer and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Biogen, Janssen, Merck, Novartis, Pfizer and UCB, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, H. Richards Shareholder of: Novartis, Employee of: Novartis, N. Williams Consultant for: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
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## SAT0422 LONG-TERM ANTI-TNF TREATMENT IS ASSOCIATED WITH REDUCTION OF PROGRESSION OF RADIOGRAPHIC CHANGES IN THE SACROILIAC JOINTS IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPA: SIX-YEAR RESULTS OF THE ESTHER TRIAL

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**Background:** Data from observational studies suggests a 10–12% biannual rate of progression from non-radiographic axial SpA (nr-axSpA) to ankylosing spondylitis (AS) [1] in patients not treated with tumor necrosis factor $\alpha$ (TNF) blockers. It is not known, whether anti-TNF treatment might be able to prevent such a progression in patients with nr-axSpA.
**Objectives:** To assess the radiographic progression in the sacroiliac joints (SIJ) during long-term (up to 6 years) treatment with the TNF-blocker etanercept in patients with early axSpA.
**Methods:** In the ESTHER trial [2] a total of 76 patients with early ($\leq$5 years symptom duration) and active axSpA were randomized to be treated with either etanercept or sulfasalazine for one year. At year 1, all patients who were not in remission continued with etanercept directly; patients in remission discontinued their therapy and were followed-up until year 2, in case of disease flare the etanercept therapy was (re)-introduced and continued until the end of year 6. X-rays of SIJ were collected at baseline and every 2 years thereafter. Two trained readers (VRR and DP), who were blinded for all clinical data, scored independently the SIJ x-rays in a concealed and randomly selected order, according to the grading system of the modified New York (mNY) criteria for AS. Patients were classified as having AS if both readers recorded the presence of definite radiographic sacroiliitis according to the mNY criteria. Active inflammatory and fatty lesions on magnetic resonance imaging (MRI) of SIJ were assessed according to the Berlin MRI scoring system (KGH and CA).
**Results:** A total of 55 patients from the 76 patients of ESTHER trial were included in the current analysis due to the availability of X-rays of SIJ. 19 patients (34.5%) were classified at baseline as AS and 36 (65.5%) as nr-axSpA based on the independent reading results with a fair agreement between both readers (k =0.33, p=0.01). Radiographic progression from nr-axSpA to AS was observed mainly between baseline and year 2 – in 18.5% (5/27) of the patients classified as nr-axSpA at baseline with available SIJ X-rays at year 2. There were no patients who progressed to AS between year 2 and year 4 and only one patient (5.6%, 1/18) progressed to AS between year 4 and year 6 – figure.

**Figure.** Progression from nr-axSpA to AS in patients treated with etanercept for up to 6 years in the ESTHER trial.



Treatment arm in the first year (entanercept or sulfasalazine) had no significant impact on progression from nr-axSpA to AS. Elevated C-reactive protein – CRP (≥5 mg/l) at baseline was associated with a higher odds for progression: odds ratio =7.0 (95%CI 0.7–73.9). There was no difference in the baseline osteitis score on MRI of SIJ between progressors and non-progressors (since MRI inflammation was an entry criterion), however, progressors had higher fatty lesions score at baseline as compared to non-progressors: 10.3±7.1 vs. 4.9±5.8, respectively, p=0.064.

**Conclusions:** In the ESTHER trial, there was a substantial reduction of radiographic sacroiliitis progression between year 2 and year 6 of anti-TNF treatment. Higher baseline CRP and higher MRI fatty lesions score demonstrated a positive association with progression from nr-axSpA to AS.

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[1] Poddubnyy D, et al. Ann Rheum Dis 2011;70:1369–74.
[2] Song IH, et al. Ann Rheum Dis 2011;70:590–6.

**Disclosure of Interest:** V. Rios Rodriguez: None declared, J. Sieper Grant/research support from: Abbvie, BMS, Janssen, MSD, Pfizer, Consultant for: Abbvie, BMS, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbvie, Janssen, MSD, Novartis, Pfizer, Roche, UCB, K.-G. Hermann Speakers bureau: Abbvie, MSD, Pfizer, H. Haibel Consultant for: Abbvie, MSD, Speakers bureau: Abbvie, MSD, Pfizer, UCB, C. Althoff: None declared, B. Buß Consultant for: Abbvie, UCB, O. Behmer Employee of: Pfizer Pharma, D. Poddubnyy Consultant for: Abbvie, Boehringer, MSD, Pfizer, Novartis, Speakers bureau: Abbvie, BMS, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, UCB

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### SAT0423 PATIENT-REPORTED QUALITY OF LIFE IN PATIENTS WITH BASELINE OBJECTIVE SIGNS OF INFLAMMATION AND ACTIVE NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH GOLIMUMAB: RESULTS OF THE OPEN-LABEL EXTENSION OF A RANDOMIZED, DOUBLE-BLIND STUDY

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**Background:** In a randomized, double-blind (DB), placebo (PBO)-controlled, phase 3 study (GO-AHEAD; NCT01453725), patients (pts) with nonradiographic axial spondyloarthritis (nr-axSpA) had significantly greater improvement in quality of life (QoL) after 16 weeks of treatment with golimumab (GLM) compared with PBO.[1]

**Objectives:** To assess QoL during the open-label extension (OLE) of GO-AHEAD in pts who had objective signs of inflammation (MRI sacroiliitis+ and/or C-reactive protein >upper limit of normal) at baseline of the DB phase.

**Methods:** Pts completing the 16-week DB study (GLM or PBO) received GLM 50mg Q4W during the 44-week OLE (36-week efficacy period; 8-week safety follow-up). QoL evaluations in pts with objective inflammation included Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL), 36-item Short Form Health Survey (SF-36), and EuroQol Group 5 Dimensions Health Questionnaire (EQ-5D) Index and Health State (0–10cm VAS), and Work Productivity and Activity Impairment (WPAI) at weeks 16 and 52 and the Patient's Global Disease Assessment (PGDA; 0–10cm VAS) at weeks 16, 20, 24, 32, 40, and 52. Data were summarized descriptively.

**Results:** In total, 153 pts with objective inflammation at baseline of the DB study were treated in the OLE (GLM=76; PBO=77). Pts who received GLM during the DB phase and continued GLM in the OLE (the GLM/GLM group) had continued improvement in QoL at week 52 as measured by the EQ-5D, SF-36, ASQoL, and PGDA VAS scales (Figure). Pts who received PBO during the DB phase and switched to GLM during the OLE (the PBO/GLM group) had notable improvements in these QoL scales at week 52 (Figure). Likewise, pts in the GLM/GLM group had continued benefits in work productivity and impairment, and those in the PBO/GLM[1] group had notably improved benefits in work productivity and impairment (Table).

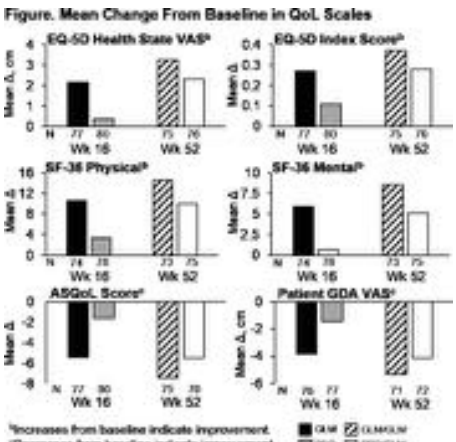



Table 1. Mean (SD) change from baseline in WPAI scores

| | n | GLM Week 16 | n | GLM/GLM Week 52 | n | PBO Week 16 | n | PBO/GLM Week 52 |
|---|---|---|---|---|---|---|---|---|
| Percent impairment while working* | 51 | –23.3 (26.5) | 47 | –30.4 (25.3) | 46 | –11.7 (29.8) | 46 | –26.7 (30.0) |
| Percent work time missed* | 47 | –6.0 (17.6) | 47 | –7.1 (24.0) | 46 | 2.1 (30.9) | 45 | –8.7 (19.7) |
| Percent overall work impairment* | 46 | –21.2 (24.7) | 45 | –31.1 (25.3) | 45 | –8.4 (28.5) | 45 | –26.5 (27.2) |
| Percent activity impairment | 76 | –25.5 (28.7) | 74 | –36.4 (26.2) | 80 | –7.0 (78.3) | 75 | –22.7 (32.1) |

*Questions completed only by patients who were working.

**Conclusions:** Among pts with objective inflammation before treatment in the DB phase of GO-AHEAD, those who continued GLM in the OLE had continued benefits in QoL and work productivity, and those who switched to GLM in the OLE from PBO in the DB phase had notable improvement in QoL and work productivity.

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[1] Sieper J, et al. Arthritis Rheum. 2015;67(10):2702–2712.

**Disclosure of Interest:** W. Maksymowych Grant/research support from: AbbVie, Janssen, Pfizer, Consultant for: AbbVie, Amgen, UCB, Pfizer, Merck, Janssen, Eli Lilly, Celgene, Synarc, Boehringer, M. Dougados Grant/research support from: AbbVie, Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, J. Sieper Consultant for: AbbVie, Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, J. Braun Grant/research support from: Abbvie (Abbott), Amgen, Biogen, Boehringer, BMS, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Epirus, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Consultant for: Abbvie (Abbott), Amgen, Biogen, Boehringer, BMS, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Epirus, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, G. Bergman Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck & Co., Inc., Kenilworth, NJ, USA, S. Curtis Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck & Co., Inc., Kenilworth, NJ, USA, A. Tzontcheva Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck & Co., Inc., Kenilworth, NJ, USA, G. Philip Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck & Co., Inc., Kenilworth, NJ, USA, S. Huyck Shareholder of: Merck & Co., Inc., Kenilworth, NJ, USA, Employee of: Merck & Co., Inc., Kenilworth, NJ, USA, D. van der Heijde Consultant for: AbbVie, Amgen, AstraZeneca, Augurex, BMS, Boehringer Ingelheim, Celgene, Centocor, Chugai, Covagen, Daiichi, Eli-Lilly, Galapagos, GSK, Janssen Biologics, Merck, Novartis, Novo-Nordisk, Otsuka, Pfizer, Roche, Sanofi-Aventis, UCB, Vertex, Employee of: Imaging Rheumatology BV

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## Osteoarthritis

### SAT0424 TRENDS IN OSTEOARTHRITIS INCIDENCE IN BRITISH COLUMBIA, CANADA, 2001-2012

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**Background:** Osteoarthritis is the most common joint disease and a massive public health problem worldwide. Incidence rates of OA reported in the literature vary widely. Several studies predicted that OA burden would increase due to population aging and increasing prevalence of obesity. However, population data on trends in OA incidence are extremely limited.

**Objectives:** The purpose of the study was to describe trends in crude, age-specific and age-adjusted incidence of physician-diagnosed OA for men and women in British Columbia, Canada, between 2001 and 2012.

**Methods:** A random sample of 742,070 records was obtained from Population Data BC, an administrative database which covers virtually all hospitalizations and visits to health professionals in the province of British Columbia, Canada since 1986. Similar to prior studies [1,2], we defined incident OA as a hospital discharge or two visits to a health professional (within 2 years and not on the same day) with a diagnostic code for OA (715 in ICD-9 or M15-M19 in ICD-10) in a person without OA within the previous 10 years. Person-years were obtained from individual data on registration with the provincial health plan. The 2006 BC population was used for standardization of rates. Confidence intervals were estimated as exact Poisson intervals and p-values for trend were obtained using a Poisson regression model with a linear year effect.

**Results:** Crude OA incidence rate in the population (men and women combined) rose from 7.1 (95% CI 6.9–7.4) per 1000 person-years in 2001 to 10.2 (9.9–10.4) per 1000 p-y in 2012. The rates were higher in women and increased in both men (5.9 to 8.7 per 1000 p-y) and women (8.4 to 11.5 per 1000 p-y). Age-specific

rates increased significantly ($p<0.05$) among those aged 40–49 and 50–59 in both sexes. Age-standardized rates for selected years are shown in Table 1. A significant upward linear trend between 2001 and 2012 was observed for men ($p<0.001$) and women ($p=0.008$).

Table 1. Age-standardized OA incidence rates per 1000 p-y in BC, Canada

| Year | Men | Women | Overall |
|---|---|---|---|
| 2001 | 6.7 | 9.5 | 8.1 |
| 2006 | 7.0 | 9.9 | 8.4 |
| 2012 | 7.4 | 9.7 | 8.5 |

**Conclusions:** The study confirms an upward trend in crude OA incidence rates in BC observed in prior studies [1,2]. Unlike prior studies, which covered a shorter period, current data show a significant trend in age-standardized incidence in both men and women. This could be due to an increase in obesity prevalence in BC [3]. Our data also show an increase in OA incidence in relatively young persons (40–59), which has not been previously reported. A limitation of the study is the definition of OA based on administrative data.

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**Disclosure of Interest:** None declared

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## SAT0425 DOES WEIGHT IN THE OFFSPRING OF PEOPLE WITH A TOTAL KNEE REPLACEMENT FOR SEVERE PRIMARY KNEE OSTEOARTHRITIS HAVE A MORE DETRIMENTAL EFFECT ON KNEE CARTILAGE AND PAIN? A 10-YEAR PROSPECTIVE STUDY

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**Background:** Although being overweight or obese is an important risk factor for the development of knee osteoarthritis (OA), the complex interplay between weight and genetic factors on the early-onset knee OA is still unclear.

**Objectives:** To determine the effects of weight on knee cartilage volume, defects and knee pain over 10 years in offspring having at least one parent with a total knee replacement for severe primary knee OA and in controls with no family history of knee OA.

**Methods:** 372 participants (186 offspring and 186 controls) aged from 26–61 years were recruited at baseline, and followed at 2.3 (Phase 2) and 10.2 (Phase 3) years later. T1-weighted magnetic resonance imaging (MRI) of the right knee was used to measure cartilage volume and defects at each time-point. Knee pain was only assessed at Phase 2 and Phase 3 using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Data were analysed using mixed-effects model with adjustment for potential confounders.

**Results:** Study participants were middle-age adults (mean age 45 years and mean weight of 77.5 kg) at baseline. In multivariable analysis, increasing body weight was negatively associated with medial tibiofemoral cartilage volume ($\beta$=-0.28 ml, per 1 SD increase, 95% CI -0.49 to -0.07) and the presence of medial tibiofemoral cartilage defects (OR=1.70, per 1 SD increase, 95% CI 1.20 to 2.33) in offspring over 10.2 years. Similar associations were observed for lateral tibiofemoral cartilage volume ($\beta$=-0.19 ml, P=0.059), and defects (OR=1.56, P=0.050). Over 7.9 years, body weight was positively associated with total knee pain ($\beta$=1.78, per 1 SD increase, 95% CI 0.49 to 3.06) and all pain subscales ($\beta$=0.36 to 0.58, all $P<0.05$) apart from sitting and standing in offspring while adjusting for potential confounders and knee structural factors. There were no statistically significant associations between weight, and cartilage volume or defects or pain in controls (all $P>0.05$).

**Conclusions:** Body weight is associated with knee cartilage volume, defects and pain in offspring of parent with primary knee OA but not in controls, suggesting an interplay between genetic factors and overweight/obesity in the pathogenesis of early knee OA.

**Disclosure of Interest:** None declared

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## SAT0426 FUNCTIONAL CONNECTIVITY ALTERATIONS IN KNEE OA PATIENTS: AN FMRI STUDY

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**Background:** Central sensitization (CS) is a common phenomenon among patients with knee osteoarthritis. In a previous study, our team showed that CS occurs gradually, and no dummy, and has an important role in the development of chronic pain. Neuroimaging is a procedure that allows us to objectify the pain assessment. The study of the resting state help us to detect alterations in brain function at rest.

**Objectives:** The aim of this study is to identify the subgroup of patients sensitized and to characterize their changes in functional connectivity with functional Magnetic Resonance Imaging (fMRI).

**Methods:** This is a cross-sectional, single blind (investigator) study of 60 patients with knee osteoarthritis. Presence of CS was assessed using extended version of the Arendt-Nielsen peripatellar map, following the evidence of regional spread of pain and, also, temporal summation which is increased pain response to repeated stimulation. FMRI included two resting sequences in which the subject had to remain lying down and stay as relaxed as possible and let flow the mind. These sequences were interspersed with another sequence in which painful stimulation of the medial interline was applied in order to observe changes in functional connectivity before and after a similar pain caused by the disease itself.

**Results:** A total of 33 patients showed some degree of CS of which 19 of them met all the established criteria. In the analysis of the resting state sequence before painful stimulation, no significant differences between sensitized and non sensitized patients were found. However, the results of resting state sequence after pain stimulation showed a significant heightened functional connectivity, especially in the posterior insula. When the somatosensory cortex (SII) was selected as a region of interest, we found enhanced functional connectivity, in resting state sequence before pain, with the anterior insula and also, a reduction of functional connectivity with the anterior cingulate cortex was identified. In the resting state sequence after pain stimulation, a similar pattern was revealed with increased intensity.

**Conclusions:** It is widely known that SII is associated to the information processing coming from the leg and insula, which is related to information integration and visceral sensation or interoception. The increased connectivity found between both SII and insula, after painful stimulation stopped, could show that sensitized patients experience pain even when the initial stimulation has disappeared, such a fingerprint.

These results, together with those previously obtained in the sequences of painful stimulation, help to get an overall picture of these patients. This study is a starting point to investigate new therapeutic approaches to expand the current management of these patients and improve their quality of life.

**Disclosure of Interest:** None declared

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## SAT0427 THE ABSENCE OF SYMPTOM IN SUBJECTS WITH ADVANCED KNEE OA

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**Background:** Although osteoarthritis (OA) is predominantly considered as a disease of cartilage, articular cartilage is an aneural tissue, and there is a consensus that the association between knee radiographic OA and knee pain is modest.

**Objectives:** To investigate the prevalence of asymptomatic subjects with advanced knee OA, we examined databases obtained from 2 Korean community residents.

**Methods:** Subjects included were from Hallym Aging Study (HAS) or from the Korean National Health and Nutrition Examination Survey (KNHANES, year 2010–2012). Participants in each study were asked knee-specific questions regarding the presence of knee pain. Radiographic evaluations consisted of weight-bearing anteroposterior, weight-bearing semi-flexed knee radiographs. For HAS cohort, MRI of the knee was available. Each knee was evaluated for the presence of osteophytes, joint space narrowing, subchondral sclerosis, and cysts, and was graded for overall evidence of radiographic OA using the K-L grade. Advanced knee OA was defined as K-L grade 4 (large osteophytes, severe joint space narrowing, and/or bony sclerosis). Clinical factors associated with the presence of knee pain were evaluated with multivariate logistic regression analysis.

**Results:** Included were 504 subjects from HAS and 8679 from KNHANES. Advanced knee OA was identified in 47 (9.3%) and 685 (7.8%) in HAS and KNHANES, respectively. The mean age of the study subjects were 72.5 years and 16.5% were male. Two hundred twenty five subjects (44.3%) did not report any pain despite having K-L grade 4 OA. Female, non-smoker, the presence of osteoporosis, and lower education were significantly associated with knee pain. After multivariate association, female and osteoporosis was significantly

associated with the presence of knee pain. Advanced OA subjects without knee pain did not differ from non-OA subjects in the general physical health measured with the short-form (SF-12), except for the physical functioning. Regardless of the presence of pain, MRI finding such as summary cartilage score, bone marrow lesion score, the presence of synovitis and effusion was similar in advanced OA subjects.

**Conclusions:** Our community study showed that a significant number of subjects with K-L grade 4 OA was asymptomatic. The guidance of therapeutic decision merely based on imaging study as well as treatment option focusing solely on cartilage engineering should be viewed with caution.

**Disclosure of Interest:** None declared

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## SAT0428 SAFETY, CLINICAL AND IMAGING OUTCOMES OF A NOVEL, INTRA-ARTICULAR, INJECTABLE, WNT INHIBITOR (SM04690) IN THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE: EXPLORATORY ANALYSIS OF RESULTS FROM A 24 WEEK, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 1 STUDY

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**Background:** Wnt signaling pathway plays a central role in joint tissue formation and altered Wnt signaling has been associated with cartilage loss in preclinical/clinical studies.[1] SM04690 is an IA small molecule inhibitor of the Wnt pathway.

**Objectives:** To report safety, clinical and imaging efficacy results from a 24 week phase 1 randomized, double-blind, placebo-controlled, dose-escalation clinical trial of a small molecule Wnt pathway inhibitor, SM04690, in knee OA.

**Methods:** Subjects with symptomatic, radiographic knee OA were randomized to receive a single IA injection in the target knee with either 0.03, 0.07, 0.23 mg SM04690 or vehicle (volume 2mLs) in a 4:1 SM04690 (N=16): vehicle (N=4) ratio. Safety, pharmacokinetics, WOMAC Total, Function, Pain subscales and strict OARSI responses[2], and radiographs were collected at baseline and during the 24 week trial. Analyses of efficacy outcomes were conducted using a modified Intention-To-Treat (mITT) baseline-adjusted analysis of covariance (ANCOVA) and logistic regression.

**Results:** A total of 61 subjects (female N=41, mean age 62.6 yrs, BMI 30.4 kg/m$^2$) were enrolled. Serum levels of SM04690 in all subjects were below limits of detection at all time points. Two dose limiting toxicities (DLTs), paroxysmal tachycardia, (also an SAE), and increased pain were reported in 0.07 mg cohort. A total of 72 AEs were reported in 28 (46%) subjects; 16 AEs in 8 subjects were considered possibly or probably related to study drug.

At Week 24, improved WOMAC Total Score was seen for both 0.03 mg and 0.07 mg cohorts (change from baseline, -27.4 and -26.6 respectively) compared to placebo (-21.7) (Figure 1). Odds of having an OMERACT-OARSI strict response in 0.07 mg cohort were higher than in the placebo cohort at week 12 (odds ratio=5.7, 95% CI: 1.1, 30.0, P=0.04); odds of an OMERACT-OARSI strict response in 0.03 mg cohort were higher than in the placebo cohort at week 24 (odds ratio=4.8, 95% CI: 0.9, 25.8, P=0.07) (Figure 2). Joint space width by radiographs showed no change from baseline to Week 24 in the 0.03 mg cohort (0.00 mm), an increase in the 0.07 mg cohort (0.49 mm), and a decrease in the 0.23 mg cohort (-0.15 mm), with the placebo cohort exhibiting a larger decrease (-0.33 mm). Compared to placebo, the change in joint space width seen in 0.07 mg cohort was statistically significant (P=0.02).

Figure 1. Change from Baseline in WOMAC Total over time by Cohort

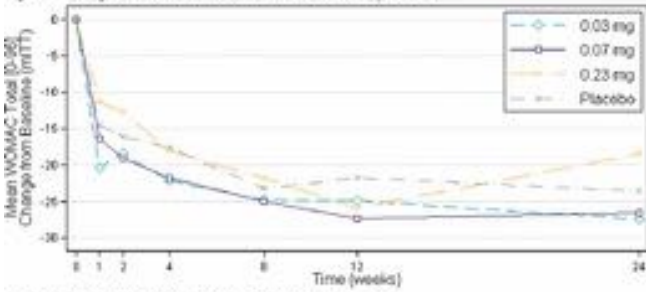
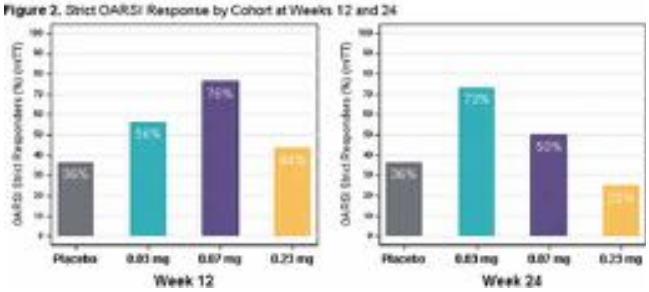



Figure 2. Strict OARSI Response by Cohort at Weeks 12 and 24




**Conclusions:** These phase 1 data suggested that an intra-articular injection with a novel Wnt inhibitor SM04690 into the knee of OA patients was safe and well-tolerated. SM04690 appeared to potentially improve function, pain and knee joint space width. Additional studies are underway to further evaluate safety, tolerability, efficacy and potential DMOAD properties.

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## SAT0429 EFFECT OF VITAMIN D SUPPLEMENTATION ON EFFUSION-SYNOVITIS IN KNEE OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Synovial inflammation is commonly observed in osteoarthritis (OA). Vitamin D has showed anti-inflammatory properties in joint disorders which have not been reported in OA.

**Objectives:** To examine the effect of vitamin D supplementation on synovial inflammation in patients with symptomatic knee osteoarthritis (OA) and low vitamin D levels over 24 months.

**Methods:** In a multi-center, randomized, placebo-controlled and double-blind trial, symptomatic knee OA patients with a low 25-(OH)D level (12.5–60 nmol/l) were recruited. 413 patients (age 63.2±7.0 years, 208 females) were allocated to either a 50,000IU monthly vitamin $D_3$ capsule (n=209) or placebo (n=204) for 24 months. In this post-hoc analysis, changes in knee effusion-synovitis volume and score (0–3) were assessed using MRI (fig 1). A least significant criterion (LSC) was used to define an increase of effusion-synovitis volume by correcting measurement errors.

**Results:** At baseline, total effusion-synovitis volume was 8.0 ml with a prevalence of 47.7% (score ≥2). Over 24 months, the total effusion-synovitis volume remained stable in vitamin D group (mean: 0.26 ml, 95% CI: -0.82, 1.34) but increased significantly in placebo group (mean: 2.20 ml, 95% CI: 1.01, 3.38) (difference between groups: -1.94 ml, 95% CI: -3.54, -0.33). This effect was evident in those with baseline effusion-synovitis (difference: -2.04 ml, 95%CI: -3.83, -0.25) and in suprapatellar pouch (difference: -2.49 ml, 95%CI: -4.74, -0.25). Increases in total (relative risk: 0.66, 95%CI: 0.49, 0.90) and suprapatellar (relative risk: 0.64, 95%CI: 0.44, 0.93) effusion-synovitis volume were less in vitamin D than placebo group.

**Conclusions:** Vitamin D supplementation over 24 months significantly reduced progression of effusion-synovitis in patients with knee OA and low 25-(OH)D level.

**Acknowledgement:** We specially thank the participants who made this study possible, and we gratefully acknowledge the role of Vitamin D Effect on Osteoarthritis Study staff and volunteers in collecting the data. We thank the research assistants Jodi Barling, Kay Nguo, Judy Hankin and Alice Noone who were involved in the coordination of this study. Special thank to Yuelong Cao who wrote the study protocol. We also thank Rob Warren measured knee cartilage volume.

**Disclosure of Interest:** None declared

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## SAT0430 NEITHER OBESITY, SMOKING AND ALCOHOL ARE ASSOCIATED WITH HAND OSTEOARTHRITIS (OA) - LONGITUDINAL DATA FROM OSTEOARTHRITIS INITIATIVE (OAI)

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**Background:** Obesity is a strong risk factor for knee OA. Despite few longitudinal studies, it is often stated that obesity also increases the risk of hand OA. Smoking has been suggested to decrease the risk of OA, but results have been inconsistent. Alcohol may also induce a pro-inflammatory state with negative impact on joints.
**Objectives:** To examine whether baseline obesity, smoking and alcohol intake are associated with more severe hand OA, and whether they are associated with hand OA development 4 years later.
**Methods:** We included 1232 persons (1598 hands) from OAI without *knee* OA. Longitudinal *hand* x-rays were available for 994 persons. We focused on the distal (DIP) and proximal interphalangeal (PIP) joints. 406 (41%) persons (502 hands) had no radiographic DIP/PIP OA at baseline and were included in analyses on incident radiographic hand OA.
In cross-sectional analyses, we explored whether obesity, smoking and alcohol use were associated with more severe hand OA (KL sum score in DIP/PIP joints) at baseline. In longitudinal analyses, we studied whether baseline obesity, smoking and alcohol were associated with incident DIP/PIP OA in persons who had *no* OA in these joints at baseline. We used linear and logistic regression, respectively, using Generalized Estimating Equations to account for two hands per person. Each risk factor was evaluated in a separate model adjusted for age, sex and education.
**Results:** Mean (SD) age was 58.4 (8.9) years, and 58% were women. Mean (SD) BMI was 26.8 (4.5) and 22.5 (2.9) kg/m$^2$ at baseline and age 25, respectively. Alcohol use was reported by 83%, and the majority had <1 drink/week (37%). Current and former smoking was reported by 9% and 41%, respectively, and mean (SD) pack-years in cigarette smokers were 20.0 (18.6).
In cross-sectional analyses, a statistically significant association was found between 1–3 alcoholic drinks/week and KL sum score (B=1.55, 95% CI 0.42–2.67), but no dose-response relationship was found. No associations were found for obesity (Table) or smoking (data not shown).
Incident hand OA was found in 82/502 (16%) hands. We found *higher* odds of incident hand OA in current smokers (OR=2.20, 95% CI 1.02–4.77), but no dose-response relationship was found for smoking pack-years. Obesity (Table) and alcohol use (data not shown) did not increase the odds of developing hand OA.

Table 1. Associations between overweight/obesity and hand OA

| | KL sum score (DIP/PIP) at baseline B (95% CI) | Incident DIP/PIP OA after 4 years OR (95% CI) |
|---|---|---|
| Current BMI | | |
| <25 | 0.00 (Ref.) | 1.00 (Ref.) |
| 25–30 | 0.56 (–0.19, 1.31) | 1.34 (0.76, 2.35) |
| 30+ | 0.58 (–0.30, 1.46) | 1.05 (0.53, 2.08) |
| BMI at age 25 | | |
| <25 | 0.00 (Ref.) | 0.00 (Ref.) |
| 25+ | 0.62 (–0.27, 1.52) | 1.29 (0.67, 2.47) |
| Waist circumference | 0.15 (–0.12, 0.43) | 0.97 (0.79, 1.18) |

**Conclusions:** In contrast to a common belief that obesity is associated with increased risk of hand OA, we did not find any statistically significant associations with hand OA for neither measures of overweight/obesity. Furthermore, alcohol use was not associated with increased risk of hand OA. An unexpected association was found between current smoking and the development of hand OA, but the lack of a dose-response relationship between smoking pack-years and incident hand OA and no associations in cross-sectional analyses suggest that this may be a chance finding.
**Disclosure of Interest:** None declared
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## SAT0431 THRESHOLD OF JOINT SPACE WIDTH FOR KNEE PAIN: THE ROAD STUDY

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**Background:** Knee pain is the principal clinical symptom of knee osteoarthritis (OA). Although much effort has been devoted toward defining knee pain, the correlation between knee pain and radiographic severity of knee OA by categorical methods, such as the Kellgren Lawrence grade, was not as strong as expected. In this categorical system, joint space narrowing and osteophytosis are not assessed separately, while accumulating lines of evidence indicate that joint space narrowing and osteophytosis may have distinct etiologic mechanisms, and their progression may be neither constant nor proportional. Although osteophytosis also has some effect on activities of daily living and quality of life, joint space narrowing is the primary outcome in studies of OA. Therefore, to examine the association between knee OA and pain, joint space narrowing should be assessed separately. Thus, an automatic system that can quantify the joint space width of the knee in OA on standard radiographs and allow for objective, accurate, and simple assessment of the structural severity of knee OA was developed.
**Objectives:** The objective of the present study was to clarify the association of joint space narrowing with knee pain in Japanese men and women using a large-scale, population-based cohort of the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study.
**Methods:** This study examined the association between minimum joint space width (mJSW) in the medial compartment and pain in the knee. mJSW was measured in the medial and lateral compartments of the knee using a knee OA computer-aided diagnosis system.
**Results:** From the 3,040 participants in the ROAD study, the present study analyzed the data from 2,733 participants who completed the radiographic examinations and questionnaires regarding knee pain (975 men and 1,758 women; mean age, 69.9 years). Subjects with lateral knee OA were excluded. mJSW in subjects with and without knee pain were 2.4 ± 1.2 mm and 3.3 ± 0.9 mm, respectively, in men ($p<0.05$) and 2.0 ± 1.1 mm and 2.8 ± 0.8 mm, respectively, in women ($p<0.05$). medial mJSW/lateral mJSW in subjects with and without knee pain were 57.2 ± 27.6% and 72.8 ± 20.8%, respectively, in men ($p<0.05$) and 52.2 ± 31.5% and 71.4 ± 33.0%, respectively, in women ($p<0.05$). After adjustment for age and BMI, medial mJSW and medial mJSW/lateral mJSW, were significantly associated with knee pain ($p<0.05$). The threshold of medial mJSW by ROC curve analysis was 2.87 mm (sensitivity 0.67, specificity 0.65, AUC 0.70) in men and 2.01 mm (sensitivity 0.43, specificity 0.689, AUC 0.69) in women, while that of medial mJSW/lateral mJSW was 55.2% (sensitivity 0.45, specificity 0.68, AUC 0.66) in men and 57.9% (sensitivity 0.57, specificity 0.75, AUC 0.69) in women.
**Conclusions:** The present cross-sectional study, using a large-scale population from the ROAD study, showed that joint space narrowing was significantly associated with knee pain. The thresholds of joint space width for knee pain were approximately 3 mm in men and 2 mm in women.
**Disclosure of Interest:** None declared
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## SAT0432 BLENDED PHYSICAL ACTIVITY INTERVENTION WITH REDUCED FACE-TO-FACE CONTACT AND USUAL PHYSICAL THERAPY SHOW SIMILAR EFFECTIVENESS IN PATIENTS WITH KNEE AND HIP OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Exercise therapy is an effective treatment in patients with knee and hip osteoarthritis. However, face-to-face therapy is an expensive regimen. Blended exercise therapy, in which face-to-face contact is combined with a web-based program, might be a cost-effective alternative. Moreover, a blended intervention supports home-exercises and self-management through technology which is available at any time and place. We developed the blended intervention e-Exercise, a 12-week program in which up to five usual physical therapy sessions are integrated with a web-based program.
**Objectives:** The objective of this study was to evaluate the short-term effectiveness of e-Exercise compared to usual physical therapy for patients with knee and/or knee osteoarthritis.
**Methods:** A multicentre cluster randomized controlled trial was conducted. A number of 247 physical therapists were randomly allocated to e-Exercise (intervention group) or usual physical therapy (control group). The web-based part of e-Exercise is based on graded activity principles. Individual assignments for a central activity, such as walking or cycling, are gradually increased and supported with strength/stability exercises and information modules. Program progress can be evaluated during the face-to-face sessions. Content of these sessions were in both groups based on the Dutch physiotherapy guideline Osteoarthritis Hip-Knee which recommend education, self-management promotion, exercise therapy and if necessary manual therapy. Primary patient-outcomes, measured at baseline and after 12 weeks, were physical functioning and physical activity. Secondary outcome measures were pain, tiredness, quality of life, self-efficacy and the number of physical therapy sessions. Data were analysed using a mixed linear model.
**Results:** Totally, 208 patients were included. There were no significant differences in baseline demographics between the intervention (N=108) and control group (N=100). 176 (85%) participants completed the follow-up questionnaire. After 12 weeks, none of the primary outcome measures were significant different between groups. Within group analyses, however, showed for both groups a significant

improvement in physical functioning (IG: +4.1 points/100, p<0.01; CG: +5.3 points/100, p<0.01). Participants in the intervention group reported an increase of 23.7 minutes (p=0.03) physical activity per day, the control group an increase of 13.1 minutes (p=0.21). However, no significant differences were found for physical activity measured with ActiGraph accelerometers. With respect to the other outcomes, tiredness reduced significant (p<0.02) more in the intervention group (-1.3 points/10) compared to the control group (-0.5 points/10). Within both groups there were significant improvements for pain, tiredness, quality of life and self-efficacy. The intervention group received 5 face-to face sessions (range 2–16), the control group 12 (range 2–29).

**Conclusions:** In this study we found that e-Exercise is an effective treatment option in patients with knee and hip osteoarthritis. Subgroup-analysis, long-term effectiveness and cost-effectiveness of e-Exercise compared to usual physical therapy are forthcoming.

**Disclosure of Interest:** None declared

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## SAT0433 ZOLEDRONIC ACID DOES NOT SLOW SPINAL RADIOGRAPHIC PROGRESSION IN THOSE WITH RADIOGRAPHIC OSTEOARTHRITIS

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**Background:** Post-hoc analyses of pivotal studies for osteoporosis therapies such as alendronate[1] and strontium ranelate[2] have demonstrated a reduction in the progression of spinal structural osteoarthritis (OA) measures. There is strong data demonstrating that subchondral bone alterations in osteoarthritis are involved in cartilage degradation. In knee osteoarthritis, zoledronic acid (ZA) improved pain and decreased bone marrow lesion size over 6 months[3]. ZA helps back pain and this benefit is independent of changes in bone mass and fracture[4] suggesting a possible effect on OA. However, there is no data at present on whether ZA influences radiographic OA. We analyzed data from the HORIZON PFT study, in which osteoporotic post-menopausal women were randomised to 36 months of yearly ZA or placebo for fracture reduction. Our aim in this post-hoc analysis was to explore the effect of ZA on spinal osteophytes and disc space narrowing.

**Objectives:** To assess whether administration of ZA delays the structural progression of spinal osteophytes or disc space narrowing in those with pre-exiting spinal radiographic osteoarthritis.

**Methods:** A post-hoc blinded analysis of the spinal radiographs HORIZON PFT study was undertaken on a subset of paired spinal radiographs. Post menopausal women that received at least one dose of study medication, and who had both baseline and 36 month spinal radiographs, with a non zero score for spinal osteophytes at baseline were included. Xray scoring of paired images was performed, using the current gold standard method for osteoarthritis[5]; separately for osteophytes and disc narrowing at all evaluable levels from T4–12 and L1–5.

**Results:** 505 sets of paired radiographs were included in the analysis; 245 in the ZA group and 260 in the placebo group. Overall, rates of change were low but were not different between groups (see table).

Table 1

| | Treatment arm | Baseline | 36 Months | Change, whole spine | Change, L spine |
|---|---|---|---|---|---|
| Osteophytes, mean score (SD) | Placebo | 19.2 (8.0) | 20.0 (8.1) | 0.8 (1.3) | 0.3 (0.7) |
| | ZA | 20.0 (8.8) | 20.9 (9.0) | 1.0 (1.6) | 0.3 (0.8) |
| | p value | | | 0.1 | 0.4 |
| Disc space narrowing, mean score (SD) | Placebo | 3.6 (4.2) | 3.9 (4.4) | 0.3 (0.7) | 0.3 (0.8) |
| | ZA | 3.8 (4.6) | 4.1 (4.8) | 0.3 (0.8) | 0.3 (1.) |
| | p value | | | 0.7 | 0.7 |

**Conclusions:** ZA was not associated with a slowing of progression of osteophytes or disc space narrowing in the thoraco-lumbar spine in this cohort.

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## SAT0434 OSTEOARTHRITIS RELATED EFFUSION: FOLLOW UP OF PAIN AND FLUID THICKNESS AFTER TREATMENT WITH SPIRONOLACTONE. A PROSPECTIVE STUDY

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**Background:** Osteoarthritis (OA) is a group of mechanical disorders leading to joint components degradation, including articular cartilage and subchondral bone. Incidence and prevalence of knee OA is rising by increasing average age of general population and increasing obesity (1). Treatment of knee effusion includes: rest, cold compresses, elevation, NSAIDS and aspiration (2). Spironolactone is a specific pharmacologic antagonist of aldosterone, acting primarily through competitive binding of receptors at the aldosterone-dependent sodium-potassium exchange site in the distal convoluted renal tubule. (3).

**Objectives:** Evaulation of low dose Spironolactone as a treatment for osteoarthritis related effusion using ultrasound and pain VAS.

**Methods:** This study was carried out on 200 patients who aged 40 years or above with unilateral knee effusion related to osteoarthritis based on clinical examination, musculoskeletal ultrasonography (US) and synovial fluid analysis. Group 1 consisted of 50 patients received spironolactone 25 mg daily for 2 weeks, in group 2; 50 Patients took Ibuprofen 1200 mg daily for two weeks, in group 3; 50 patients used cold compresses two times daily for two weeks, and in group 4; 50 patients received placebo for the same time duration. Visual analog scale (VAS) for pain was done to the study participant at time 0 (baseline), after 2 weeks and after 4 weeks.

**Results:** The mean age of the participants was 51.2±8.1 years. The mean duration of effusion was 16.5±3.6 days. In group 1, 66% had complete improvement, 20% partial improvement and 14% no response. In group 2, 24% had complete improvement, 12% partial improvement and 64% no response. In group 3, 28% had complete improvement, 14% partial improvement and 58% no response. In group 4, 6% had complete improvement, 10% partial improvement and 84% no response. VAS had a strong relation to fluid thickness as it decreased with the improvement of effusion and increased again among those patients who developed recurrence after 4 weeks.

**Conclusions:** Low dose spironolactone is a safe and effective medical treatment for OA related knee effusion, especially in mild and moderate knee effusion.

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**Disclosure of Interest:** None declared

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## SAT0435 TIBIAL SPINE MORPHOLOGY AND ASSOCIATION WITH ANTERIOR CRUCIATE LIGAMENT DEGENERATION – A COMBINED MRI, X-RAYS AND HISTOLOGY STUDY OF EARLY KNEE OSTEOARTHRITIS

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**Background:** Knee osteoarthritis (OA) may supervene on traumatic anterior cruciate ligament (ACL) injury/rupture. However, knee OA with advanced disease on MRI may have ACL deficiency without a history of injury. We hypothesised that the complex enthesis organ structure of the ACL with the adjacent tibial tuberosities might be predisposed to ACL degeneration, and hence the elaborate ACL enthesis organ might contribute to joint degeneration.

**Objectives:** To describe the histology of the ACL enthesis organ structure including the relationship with the adjacent tibial spines and to determine whether tibial spine morphology and height (as determined by X-ray) may be linked to knee damage in early OA (as determined by MRI).

**Methods:** 333 datasets from the progression cohort of the Osteoarthritis Initiative (OAI) with Kellgren and Lawrence (KL) scores ≤1 were analysed. The lateral and medial tibial spine heights (LH, MH) were measured perpendicular to the tibial plateau width (W) (figure). 252 datasets with available corresponding MRI at 48 months were analysed for ACL injury and degeneration. Microanatomy of tibial spine was described from histology of tibial plateaus obtained from total knee replacement surgery.

**Results:** 170 ACLs assessed at 48 months were scored as normal (67.5%). 73

(29%) had tibial side ACL degeneration; 1 (0.4%) had femoral side degeneration; 3 (1.2%) were completely degenerate, and 5 (2%) had a chronic ACL tear. A significant association was seen between the increasing mediolateral width of the tibial plateau and ACL degeneration ($p<0.001$). Significant associations were also observed between the medial tibial spine height and ACL degeneration (p=0.007); and between lateral tibial spine height and ACL degeneration; (p=0.009). No significant associations were observed when medial and lateral tibial spine heights were normalised to the tibial plateau width (i.e. MH/W, LH/W). Histology shows the ACL curves reciprocally around the spine and the adjacent surface is modified as a sesamoid fibrocartilage. The ligament shows evidence of degenerative changes (numerous small cysts and loss of normal fibrillar density). The cartilage covering the spine including the intercondylar notch area showed typical early OA changes (cell clustering, fissuring, fibrillation and loss of surface staining). Proliferation of the synovium on the surface of the ACL and areas of inflammatory cell infiltration was observed within the ACL.




**Conclusions:** We describe the complex enthesis organ of the region posterior to the ACL and show that the intercondylar notch and tibial spines are part of an enthesis organ lined by cartilage. ACL degeneration was observed with increasing tibial plateau width or bigger bones, and increasing height of tibial spines relative to the tibial plateau. Age-related degenerative changes at the ACL have been noted in the absence of cartilage loss, suggesting that microdamage at the ACL could predate cartilage loss in anatomically susceptible individuals.
**Disclosure of Interest:** None declared
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## SAT0436 PLATELET-RICH PLASMA VERSUS HYALURONIC ACID IN TREATMENT OF KNEE OSTEOARTHRITIS

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**Background:** Platelet rich plasma (PRP) therapy is a simple, low-cost and minimally invasive method that provides a natural concentrate of autologous blood growth factors (GFs) that can be used to enhance tissue regeneration (1). Recent evidences have shown that PRP can be helpful as an osteoarthritis (OA) therapeutic tool by intra-articular injection (2). Hyaluronic acid (HA)is widely used therapy for relief of OA pain and stiffness by intraarticular injection. In addition, there is a sufficient evidence for being significant disease-modifying effects (3,4).
**Objectives:** our aim was to compare the clinical efficacy of platelet-rich plasma with that of hyaluronic acid viscosupplementation.
**Methods:** This study included forty patients with knee osteoarthritis. These patients were selected from the outpatient clinic of Physical Medicine, Rheumatology and Rehabilitation Department, Faculty of Medicine, Tanta University. Patients were randomly divided into two groups. The first group consisted of 20 patients treated by using intraarticular injection of 2 ml autologous PRP (PRP group).The second group consisted of 20 patients they were treated by using intraarticular injections of low molecular weight (hyaluronic acid [HA]) (32mg/2mL) of HA (HA group). All patients received 3 injections with one week interval (3) *For Follow up:* The subjective clinical outcome were measured at baseline, 1, 3, 6 and 12 months after the last treatment dose using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the 11-point pain intensity Numeric Rating Scale (NRS) (5).
**Results:** At 1,3 months' follow-up, the PRP and LW HA groups showed an improvement, with non-significant difference between the two groups. However after 6 months follow up there was significant improvement in PRP group than HA group ($P<0.005$). The follow up after 12 months reveled subsided improvement than that was at 6 months. Nevertheless, this subsidence was less in PRP group.
**Conclusions:** Autologous PRP injections showed more and longer efficacy than HA injections in reducing pain and symptoms and recovering articular function. Further studies are needed to confirm these results and to investigate the persistence of the beneficial effects observed.
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## SAT0437 OSTEOARTHRITIS PAIN IS DIFFERENTIALLY ASSOCIATED WITH TISSUE DEGRADATION AND JOINT INFLAMMATION

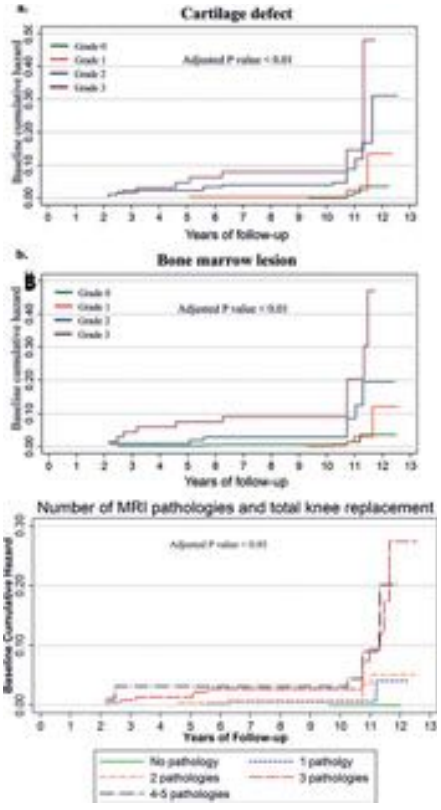
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**Background:** Osteoarthritis (OA) is heterogeneous disease characterized by pain and tissue destruction which is in some case concomitant with inflammation. However, the link between pain and tissue destruction is yet unknown, and there is a lack objective quantifiable parameters. Collagens are the main structural proteins of the joint extracellular matrix. The degradation type I (connective tissue), II (cartilage), III (synovium) and IV (basement membrane) collagens have been shown to be elevated in joint degenerative diseases.
**Objectives:** To investigate whether biomarkers reflecting collagen degradation were associated with symptomatic knee OA representing with different pain and inflammatory phenotypes.
**Methods:** 111 knee OA patients, 62% women, from NYUHJD progression cohort study with varying degree of OA were included: mean (SD) age, 32 (10); mean (SD) BMI, 27 (4); NSAID users, 23%; radiographic OA ($KL\geq2$) 68%; and bilateral knee OA; 87%. Pain was assessed by $VAS_{pain}$ and WOMAC at baseline (BL) at a 2-year follow-up (FU) visit. Median (IQR) were 39 (13–69) and 37 (13–52) for BL $VAS_{pain}$ and $WOMAC_{pain}$. 4 BL serum biomarkers of type I, II, III and IV collagen degradation (C1M, C2M, C3M, C4M), and the 2 inflammatory biomarkers CRPM and hsCRP, were assessed. Data were log2 transformed. Associations between BL biomarkers, BL pain and change (CHG) pain scores were assessed by multivariate linear model including gender, age, BMI, $KL_{signal\ knee}$, bilateral knee OA and NSAID use. Patients with cont. mild/moderate pain had a BL VASpain<54 and FU VASpain<30, cont. moderate/severe pain had VASpain>30 at baseline and FU, and transitional severe pain had either VASpain_BL<30 and VASpain_FU>54 or VASpain_BL>54 and VASpain_FU<30 (ref). Patients with; low biochemical disease activity index (bDAI) low in CRPM (<12nM) moderate bDAI were high in CRPM but low in hsCRP (<5), and high bDAI (flare) were high in CRPM and hsCRP.
**Results:** *BL association between pain and biomarkers.* C2M ($\beta$ -17.9, $p<0.0001$) and $KL_{signal\ knee}$ ($\beta$ -5.4, p=0.0031) were significantly associated with WOMAC pain. C2M ($\beta$ -12.4, p=0.0033), C3M ($\beta$ -19.9, p=0.059), age ($\beta$ -0.84, $p<0.0018$), $KL_{signal\ knee}$ ($\beta$ 8.9, p=0.0021) and bilateral knee OA ($\beta$ -12.2, p=0.087) were associated with $VAS_{pain}$. *Association between BL biomarkers and CHG pain.* C2M ($\beta$ 13.3, p=0.0016), age ($\beta$ 0.5, p=0.029) and bilateral OA ($\beta$ -12.0, p=0.043) were significantly associated with delta $WOMAC_{pain}$. Only age, BMI and NSAID use was associated with CHG $VAS_{pain}$. *Association between pain phenotypes and BL biomarkers.* Patients with cont. mild/moderate pain had significantly higher C2M compared patients with transitional severe pain (p=0.0014) and cont. moderate/severe pain (p=0.04). *Biomarker, BL pain and CHG pain in patients w. inflammatory OA.* Patient with low bDAI had lower $WOMAC_{pain}$ ($p<0.05$) and $VAS_{pain}$ ($p<0.1$). C1M was higher ($p<0.05$) in the flare group compared to the low and moderate bDAI groups. C3M was higher ($p<0.05$) in the moderate bDAI group than the low DAI group.
**Conclusions:** Different collagen degradation products are linked differentially to different phenotypes. Cartilage degradation (C2M) was consistently linked to pain CHG and phenotypes, whereas it was not associated with an inflammatory phenotype. In contrast, C1M and C3M were linked to inflammatory OA and flared OA.
**Disclosure of Interest:** A.-C. Bay-Jensen Shareholder of: Nordic Bioscience, Grant/research support from: DBOARD H2020, Employee of: Nordic Bioscienc, S. Abramson: None declared, J. Samuals: None declared, I. Byrjalsen Employee of: Nordic Bioscience, S. Krasnokutsky: None declared, T. Manon-Jensen Employee of: Nordic Bioscience, M. Karsdal Shareholder of: DBOARD H2020, Employee of: Nordic Bioscienc, M. Attur: None declared
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## SAT0438 MAGNETIC RESONANCE IMAGING MARKERS AS PREDICTORS FOR TOTAL KNEE REPLACEMENT OVER 10.7 YEARS IN OLDER ADULTS

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**Background:** Quantitative and semi-quantitative assessments of structural changes on magnetic resonance images (MRI) have been widely adopted in knee osteoarthritis (KOA) research. However, there are no long-term studies that describe the independent association of these structural factors and total knee replacement (TKR) in older adults.
**Objectives:** This study aimed to describe the predictability of MRI-based measures (cartilage defects, bone marrow lesions (BMLs), meniscal tears, meniscal extrusions, bone area increase and cartilage volume loss) for TKR over 10.7 years.
**Methods:** 983 participants (mean age 62.8 years, 50% female) were randomly recruited from the local community of southern Tasmania and followed up at 2.6 years (range 0.9–4.8) and 10.7 years (range 9.2–12.5) later. A 1.5T MRI scan of the right knee was acquired at baseline (n=930) and 2.6 years (n=399). Tibiofemoral and patellar cartilage volume and tibial bone area at baseline and 2.6 years were measured using a manual segmentation method on the T1-weighted fat saturated 3D GRE images. Cartilage defects were assessed on T1-weighted MRI using a modified Outerbridge scoring system (grade 0–4). BMLs were measured on T2-weigthed fat saturated FSE images using a modified Whole-Organ MRI scoring system (grade 0–3). Meniscal extrusion (grade 0–2) and meniscal tears (grade 0–3) were measured using the T1- and T2-weighted MRI. TKR data were recorded at baseline, 2.6 years, 5.1 years and 10.7 years later. Analyses were performed using cox proportional hazards models after adjustment for age, sex, body mass index (BMI), baseline WOMAC knee pain and radiographic KOA status. Other MRI structural pathologies were added to the model in order to explore the independent association of each of these predictors.
**Results:** 863 subjects (88%) responded for 2.6 years follow-up, 758 subjects (77%) for 5.1 years follow-up and 560 subjects (57%) for 10.7 years follow-up. After adjustment for age, sex, BMI, baseline WOMAC knee pain and radiographic KOA status, baseline MR imaging markers such as cartilage defects per grade (HR=2.28, $p<0.01$), BMLs per grade (HR=2.10, $p<0.01$), tibial bone area per $cm^2$ (HR=1.17, $p<0.01$), and percentage annual cartilage volume loss at medial tibiofemoral compartment (HR=1.19, $p<0.05$) were significantly associated with TKR over 10.7 years. These associations were independent of each other and there was a dose-response relationship between cartilage defects and BMLs at baseline and increased risk of TKR (Fig. a,b). Those who had TKR all had grade 3 meniscal tears at baseline, but meniscal extrusion was not associated with TKR. The risk of TKR increased significantly when more MRI pathologies were simultaneously present at baseline (HR=1.84/unit, $p<0.01$). There was also a number-response relationship between the number of MRI pathologies at baseline and the risk of TKR (Fig. c).




**Conclusions:** Baseline MRI structural pathologies such as cartilage defects, BMLs, meniscal tears, bone area increase and cartilage volume loss are independent predictors of TKR over 10.7 years. Presence of multiple pathologies increased the risk of TKR, suggesting that MRI structural markers are good predictors of rapid knee OA progression in the general population.
**Acknowledgement:** National Health and Medical Research Council of Australia funded this study
**Disclosure of Interest:** None declared
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## SAT0439 COMPREHENSIVE TRANSCRIPTOME ANALYSIS OF SYNOVIAL FIBROBLASTS FROM HEALTHY, RA AND OA KNEES

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**Background:** Synovial fibroblasts (SF) are recognized to play a vital role in the pathogenesis of rheumatoid arthritis (RA). However, their pathogenic role in osteoarthritis (OA), remains unclear despite the fact that OA SF are activated and affected during the course of the disease. To characterize the dysregulated pathways in both RA and OA several gene expression studies have been conducted mainly using microarrays and by comparing RASF to OASF. However these studies rarely include a healthy control group and do not take into account joint anatomical location.
**Objectives:** To measure changes in the expression of microRNA (miR) as well as mRNA and long non-coding RNA (lncRNA) in SF isolated from knees of RA and OA patients compared to healthy individuals.
**Methods:** SF were cultured from RA (n=3) and OA (n=3) patients undergoing total knee replacement. Healthy knee SF (n=3) were cultured from biopsies of individuals with arthralgia but no clinical or histological signs of synovitis. Total RNA was extracted after SF were grown for 5–7 passages and RNA sequencing was performed with the Illumina HiSeq 2000 sequencing system. Changes with a false discovery rate adjusted p-value below 0.05 were considered significantly changed. Functional annotation clustering of mRNAs was done using Database for Annotation, Visualization, and Integrated Discovery (DAVID).
**Results:** We found 31 mRNAs, 6 lncRNA and 3 miR (miR-7–5p; miR-181a-3p; miR-378a-3p) upregulated in OASF, but not RASF compared to healthy, and 14 mRNA, 3 lncRNA and 5 miR (miR-3118; miR-514a-3p; miR-585–5p; miR-615–3p; miR-615–5p) were downregulated in knee OASF specifically.15 mRNA, 11 lncRNA and 3 miR (miR-143–3p; miR-145–3p; miR-493–3p) were upregulated in knee RASF, but not OASF compared to healthy. In this RA group 7 mRNA, 4 lncRNA and 4 miR (miR-124–5p; miR-204–5p; miR-3065–5p; miR-4657) were specifically downregulated. 29 mRNA, 6 lncRNA and 8 miR were upregulated in RA as well as OASF and 9 mRNA, 2 lncRNA and 7 miR were downregulated. Pathway analysis in mRNAs that were upregulated specifically in OA included cell adhesion pathways mainly based on the regulation of protocadherins (PCDH1; PCDHAC2). Pathways that were restricted to RA were extracellular matrix related genes such as Fraser Extracellular Matrix Complex Subunit 1 (FRAS1). The Wnt signaling pathway was regulated in both diseases, e.g. by upregulation of R-Sponding 3 (RSPO3) which has previously found to be upregulated in RASF compared to healthy SF.
**Conclusions:** Using a next generation sequencing approach we have identified pathways and non-coding transcripts that are specifically dysregulated in OASF or RASF in the knees. These data corroborate and further elucidate the role of synovial fibroblasts in RA pathogenesis. Furthermore this study clearly demonstrates the involvement of SF in the pathogenesis of OA and identifies differences in the pathways activated in knee OA and knee RA, respectively.
**Disclosure of Interest:** None declared
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## SAT0440 RADIOLOGIC PROGRESSION OF DISTAL INTERPHALANGEAL JOINT OSTEOARTHRITIS IN RHEUMATOID ARTHRITIS

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**Background:** Distal interphalangeal (DIP) joint osteoarthritis (OA) is a disorder associated with female sex and age and is considered as unrelated to rheumatoid arthritis (RA). The long term radiologic course of DIP OA in patients with RA is unknown.
**Objectives:** To investigate the prevalence and demographic characteristics of DIP OA progression in RA patients.
**Methods:** RA patients of the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) cohort, who had at least two subsequent hand radiographies

taken between November 1983 and October 2014 were analysed. DIP joints (II-V) were scored for the radiologic presence and severity of osteophytes, subchondral sclerosis, joint space narrowing and erosions according to the modified Kellgren Lawrence Score (KLS).
**Results:** 2890 (35%) patients out of 8280 of the SCQM RA cohort fulfilled the inclusion criteria. Their mean age was 57.5 years (standard deviation (SD) 10.5), 76% were female, 78% were rheumatoid factor positive and 69% were ACPA positive. At baseline, the mean disease duration was 9.7 years (SD 8.5). The mean follow-up between the first and last radiography was 5.4 years (SD 3.2). Baseline radiographies showed osteophytes in 21% of 21,333 DIP joints, joint space narrowing in 13%, osteosclerosis in 9% and erosions in 1%. The KLS was 1 in 13% of DIP joints, 2 in 22%, 3 in 4% and 4 in 2% at baseline radiographies. The KLS increased in 12% of DIP joints during the radiologic follow-up, decreased in 2% and remained stable in 86% of DIP joints. Female sex ($p<0.001$), age>55 years (p=0.005) and a negative rheumatoid factor (p=0.049) were associated with OA progression.
**Conclusions:** Known risk factors for DIP OA were also associated with its radiologic progression in RA patients. Radiologic progression and erosions in DIP OA are low in this cohort, potentially due to RA treatment.
**Disclosure of Interest:** None declared
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## SAT0441 PREVALENCE OF SELF-REPORTED KNEE JOINT INSTABILITY AND ITS ASSOCIATION WITH RADIOGRAPHIC FEATURES IN SEVERE KNEE OSTEOARTHRITIS

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**Background:** Self-reported knee instability has been reported in 60–80% of all patients suffering from mild to moderate knee osteoarthritis (OA) [1], but the prevalence of self-reported knee joint instability in patients with end-stage OA is unknown. So far, a clear cause for this sense of instability has not been elucidated. Two opposing hypotheses have been described: (i) low knee joint instability is associated with osteophyte formation and (ii) high knee joint instability is associated with joint space narrowing.
**Objectives:** To describe the prevalence of self-reported knee joint instability in patients with end-stage OA and to explore the associations between self-reported knee joint instability and JSN and osteophyte formation.
**Methods:** In this cross-sectional study patients on the waiting list for primary Total Knee Arthroplasty (TKA) in one Dutch hospital were included. The primary outcome measures were preoperative self-reported knee joint instability and radiographic severity (assessed by conventional radiography (CR)). Self-reported knee instability was examined by means of a knee joint instability questionnaire. The item on the presence of knee joint instability was formulated as follows: "the sensation of buckling, shifting or giving way of the knee in the previous 3 months" with the following answering options: 1 never (0 episodes); 2 seldom (1–2 episodes); 3 regular (3–5 episodes); 4 very often (more than 5 episodes). These options were later dichotomized into no episodes of knee joint instability (option 1) or 1 or more episodes of knee instability (option 2–4). Radiographic severity consisted of the presence of osteophyte formation and joint space narrowing (JSN), which were both independently scored for the index knee on a 0–3 scale ranging from 0 no JSN/osteophytes, 1 minute JSN/osteophytes, 2 definite JSN/osteophytes and 3 ankylosis JSN/large osteophytes. These scores were dichotomized into present JSN/osteophyte formation (if JSN/osteophyte score >2) or absent JSN/osteophyte formation (if JSN/osteophyte score <2). Potential confounders included in the logistic regression analyses were patient characteristics (gender, age, body mass index) and joint characteristics (pain, physical function).
**Results:** 227 patients (mean age 68 years; SD 9.0 and 145 females (63%)) were included. Self-reported knee instability was present in 163 patients (72%). The distribution of JSN and osteophyte formation in the total group, the patients with knee joint instability and the patients without knee joint instability is shown in Table 1.

Table 1. Distribution of radiographic features in the total group, the patients reporting knee joint instability and the patients not reporting knee joint instability in the previous 3 months

| | Total group (n=227) | Knee joint instability, yes (n=163) | Knee joint instability, no (n=64) |
|---|---|---|---|
| JSN | | | |
| 0 | 26 (11%) | 19 (12%) | 6 (9%) |
| 1 | 45 (20%) | 31 (19%) | 13 (20%) |
| 2 | 108 (47%) | 80 (49%) | 28 (44%) |
| 3 | 50 (22%) | 33 (20%) | 17 (27%) |
| Osteophyte formation | 57 (25%) | 42 (26%) | 14 (22%) |
| 0 | 81 (35%) | 57 (35%) | 24 (38%) |
| 1 | 84 (37%) | 59 (36%) | 24 (38%) |
| 2 | 7 (3%) | 5 (3%) | 2 (3%) |
| 3 | | | |

In univariate regression analyses no associations were found between self-reported knee instability and JSN or osteophyte formation (p-values 0.537 and 0.829).
**Conclusions:** In conclusion, the majority (72%) of patients with severe OA reported knee joint instability. Knee joint instability was not associated with either JSN or osteophyte formation.
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**Disclosure of Interest:** None declared
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## SAT0442 WAIST CIRCUMFERENCE IS THE ANTHROPOMETRIC VARIABLE MORE RELATED TO CLINICAL SEVERITY IN WOMEN WITH KNEE OSTEOARTHRITIS WITH SYNOVIAL EFFUSSION

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**Background:** Different anthropometric variables such as obesity with its different ways of measure (body fat index, waist circumference, waist/hip ratio) as well as the metabolic syndrome and his individual components have been related to knee osteoarthritis (OA). However, no specific studies analyzing the influence of these factors on clinical severity have been carried out in patients with synovial effusion.
**Objectives:** To assess the relationship between different anthropometric measures, the metabolic syndrome and its individual components with clinical severity as measured by the Lequesne algofunctional questionnaire in women with knee OA and significant synovial effusion.
**Methods:** Transversal study including consecutively women aged 50 to 80 years with symptomatic knee OA, Kellgren-Lawrence I-IV with significant synovial effusion (>4mm at mid-patellar line on US examination). Demographic data and history of hypertension (HT), dyslipidemia, obesity or diabetes mellitus (DM) were collected. Blood samples were taken to determine basal glycemia, total, HDL- and LDL-cholesterol, insulinemia and glycated hemoglobin. Anthropometric variables assessed included weight, height, body mass index (BMI), waist circumference, hip circumference and percentage of body fat as measured by bioelectrical impedance analysis). Patients were evaluated for the presence of metabolic syndrome by strict NCEP-ATP-III criteria. All patients underwent joint aspiration to confirm non-inflammatory synovial fluid without microcrystals. To evaluate knee OA clinical severity patients completed the Lequesne algofunctional index. Univariant and multivariant analyses were performed to evaluate which variables had a greater influence on the Lequesne index.
**Results:** One hundred and fifteen women were analysed, average age 68.8 ±11.1 years, average knee OA symptoms duration 50 ±23 months. Percentage of HT was 54.58%, DM 10.4%, obesity 57.4% and dyslipidemia 47.8%, all above the expected by age and gender (40%, 10%, 40% and 30%, respectively). Metabolic syndrome was present in 40.9% of patients, also above 30% expected. In the univariant analysis all the anthropometric variables showed a significant association with the Lequesne index with weak to moderate correlation (body fat index p=0.008/r =0.243, BMI p=0.002/r =0.277, weight p=0.007/r =0.249, waist circumference $p<0.001$/r =0.404, waist circumference, p=0.006/r =0.252 and hip circumference and waist/hip ratio p=0.01/r =0.221). Neither the metabolic syndrome nor any of its individual components achieved statistical significance. After performing a forward stepwise multivariate analysis including OA symptom duration, age and Kellgren-Lawrence, waist circumference emerged as the only significant variable ($p<0.001$/r =0.338), observing a magnitude effect of a 0.9 increase in the Lequesne index for every increase of waist circumference of 5 cm (beta coefficient 0.180, 0.083–0.276). The relationship between BMI and Lequesne index was confirmed but when the waist circumference was included in the model only the waist circumference remained significant.
**Conclusions:** In this study waist circumference was the anthropometric variable more related to clinical severity measured by the Lequesne index in women with knee OA and synovial effusion.
**Disclosure of Interest:** None declared
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## SAT0443 COMPARISON OF THERAPEUTIC RESPONSE RATES, USING VARIOUS RESPONSE DEFINITIONS IN A PROSPECTIVE RANDOMIZED NON-INFERIORITY TRIAL COMPARING TWO INTRA-ARTICULAR HYALURONIC ACID PRÉPARATIONS (1-SHOT IAHA) IN SYMPTOMATIC KNEE OSTEOARTHRITIS (OA), AND PREDICTIVE FACTORS OF A BETTER RESPONSE

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**Background:** Selecting an appropriate primary efficacy criterion is of key importance in the design of a randomized controlled trial (RCT) evaluating

therapeutic interventions in knee OA. One may choose among various possible primary efficacy criteria which can be classified as 1/ continuous variables such as pain (on a visual analog scale (VAS)) or function by one of the OA-specific available instruments (providing a numeric variation on a scale indicating the amount of therapeutic effect, which clinical relevance has to be established), or 2/ binary global response criteria, such as the OMERACT-OARSI (1), or response criteria based on the Patient Acceptable Symptom State (PASS) or the Minimum Clinical Important Improvement (MCII) applied to pain, function, or patient global assessment (PGA) (2), which results are expressed in % of responders (yes/no). The sensitivity of these global response instruments has not been compared yet.
**Objectives:** The aim of this study was to compare responder's rates using various definitions of response in a knee OA trial of IAHA, and to identify factors associated with a better response.
**Methods:** Data obtained from a RCT comparing one single IA injection of 40 mg/2.0ml non-chemically modified HA with 48 mg/6.0ml hylan G-F20 were used for this post hoc analysis (3). As non-inferiority of the non-crosslinked HA was demonstrated over 6 months, data of both treatment groups were pooled (280 patients in the full analysis set, 266 completers). Uni- and multivariate stepwise regression analyses were performed to compare response criteria and identify potential factors associated with the best clinical response. OMERACT-OARSI responder criteria were compared to the PASS ($\leq$40 mm) and MCII ($\geq$15 mm improvement) responder criteria calculated for the following outcomes: pain using WOMAC A1 0–100mmVAS format, physical function using WOMAC C (VAS format) and the 0–100 normalized Lequesne index, and PGA on a 0–100 mmVAS.
**Results:** The three most sensitive response instruments were the MCII (relative) for pain, followed by the OMERACT-OARSI responder criteria and the MCII (absolute) for pain with around 80% responders (Fig1). Factors associated with a better response were: a higher pain at baseline (OR [95%CI]: 1.05 [1.02; 1.08]), a shorter delay since diagnosis of knee OA (0.93 [0.88; 0.99]), bilateral knee OA (2.51 [1.11; 5.68], and a better PGA (i.e. a lower score; 0.95 [0.92; 0.98]).

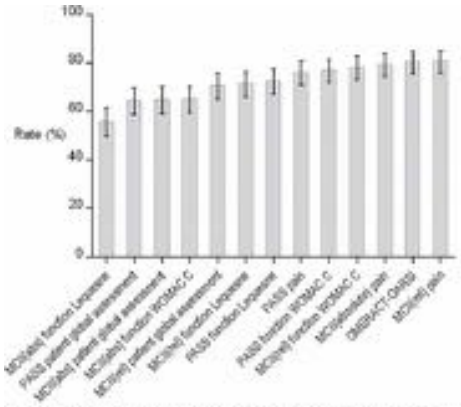


Fig. 1 Responder rates at 6 months using various response criteria (full analysis set, 280 patients)

**Conclusions:** In this post-hoc analysis, comparing for the first time several definitions of therapeutic response in a clinical trial of IAHA in knee OA, MCII for pain and OMERACT-OARSI criteria seemed to be the most responsive outcome criteria. Response rates were higher in patients presenting with more pain at baseline, a shorter duration since diagnosis, bilateral knee OA and a better PGA.
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[2] Tubach F et al. Arthritis Care Res 2012;64:1699–707
[3] Dreiser RL et al. Ann Rheum Dis 2015;74(Suppl 2):376. Abstract no THU0488.
**Acknowledgement:** We thank TRB Chemedica, for providing access to their trial Database.
**Disclosure of Interest:** E. MAHEU Grant/research support from: TRB Chemedica, L. DREISER Grant/research support from: TRB Chemedica, B. AVOUAC Grant/research support from: TRB Chemedica, T. BARDIN Grant/research support from: TRB Chemedica
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## SAT0444 COMPARASION OF EFFICACY OF INTRAARTICULER STEROID INJECTIONS IN THE PATIENTS WITH KNEE OSTEOARTHRITIS WITH OR WITHOUT SYNOVITIS

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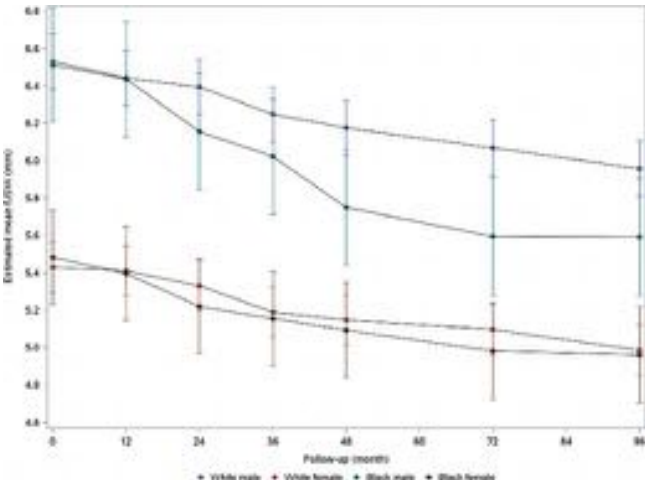
**Background:** Osteoarthritis is a common joint disorder. In the knee, injections of corticosteroids into the joint may relieve inflammation, and reduce pain and disability
**Objectives:** The present study aims to compare efficiency of intraarticular steroid injection administered on knee osteoarthritis (OA) patients between conditions whether synovitis exists, or not.
**Methods:** The study included totally 90 patients (76 women and 14 men) who applied to the knee pain symptom and were diagnosed with knee OA. Based on the existence of synovitis determined clinically, patients were subclassified in 3 groups each consisted of 30 patients. Whereas the 1st group was including the patients with clinicaly synovitis; the 2nd group was including without synovitis. The 3rd group was considered as the control group with no synovitis. Each group was administered quadriceps strengthening exercises in addition to the prescription including 5% ibuprofen topical twice a day, and 75 mg diclofenac sodium taken orally twice a day. Group 1 and 2 patients were administered intraarticular steroid injection (20 mg Triamcinolone hexasetonit). Before the treatment, patients were evaluated in terms of Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) pain score, joint involvement score, physical function score and visual analog scale. In the post-injection period, patients invited for control at the 2nd and 8th weeks were evaluated based on the same parameters.
**Results:** In all three treatment groups, a statistically significant recovery was observed in terms of pain, physical activity, and morning stiffness values at the end of both the 2nd and the 8th weeks compared to the initial period ($p<0.05$). The recovery in the injection groups was statistically more significant compared to the control group ($p<0.001$). There was no statistically significant all parameters difference between the synovitis OA and non-synovitis OA groups based on the controls at the 2nd and the 8th weeks ($p>0.05$)
**Conclusions:** It was observed that intraarticular steroid injection reduced pain and stiffness related scores whether patients diagnosed with knee OA have synovitis, or not; and developed the functionality. However, these effects were observed only for limited period. Thus, concerning the patients who do not respond to medical treatment, intraarticular steroid injection can be considered as an effective treatment only for a short term.
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[4] Jones A, Doherty M: Intra-articular corticosteroids are effective inosteoarthritis but there are no clinical predictors of response. Annals of the Rheumatic Diseases 1996; 55: 829–32.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2655

## SAT0445 RACE AND SEX DIFFERENCES IN RADIOGRAPHIC PROGRESSION OF KNEE OSTEOARTHRITIS

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**Background:** Knee osteoarthritis (KOA) is more common in African-Americans (AAs) than Whites (WHs) in the United States. The prevalence and severity of osteophytes, bone sclerosis and joint space narrowing (JSN) are also greater among AAs than among WHs. Radiographic KOA features between the two races may also vary according to sex.
**Objectives:** To determine if the pattern of radiographic progression in KOA varies by race and sex
**Methods:** Knees of AAs and WHs with minimal or no radiographic KOA (Kellgren-Lawrence [K-L] grades 0 or 1) at baseline in the Osteoarthritis Initiative (OAI) were selected for analysis. Serial fixed-flexion knee x-rays through the 96 month visit were scored for K-L grade and tibiofemoral JSN based on Osteoarthritis Research Society International grade. A subset, enriched for those that developed radiographic KOA, were assessed for joint space width (JSW) using digital imaging software. Mixed models for repeated measures were used to estimate race- and sex-specific mean JSW and 95% confidence interval at fixed locations in the medial (x=0.250mm) and lateral (x=0.725mm) compartments, as well as average annual loss in fixed JSW (fJSW). Generalized estimating equation logistic regression models were used to estimate the effect of race and sex on: summary radiographic grade progression (defined by any increase in K-L grade $\geq$1), and JSN progression (defined by any increase in OARSI grade $\geq$1) in the medial and lateral compartments. Models were adjusted for time to progression, baseline age, body mass index (BMI), family history of joint replacement, bony enlargements in the distal interphalangeal joints, frequent knee-bending, and history of knee injury or surgery.
**Results:** 3,776 knees were studied from 695 WH men, 932 WH women, 93 AA men, and 168 AA women, with mean age of 59 years and BMI of 28 kg/m$^2$. Mean baseline medial fJSW was as follows: 6.53 in WH men, 5.43 in WH women, 6.51 in AA men, and 5.48 in AA women. Figure 1 displays the race and sex-specific mean medial fJSW during the study period, after adjustment, with 95% CIs. Annual medial fJSW loss (mm/year) over 8 years was significantly greater in AA men (-0.13) than in all other subgroups (-0.07 WH men, -0.06 WH women, -0.07 AA women, $p<0.0001$). There was no evidence of difference in annual loss of JSW in the lateral compartment.
In the adjusted models, odds of radiographic K-L grade progression were significantly higher in AA men (adjusted odds ratio [aOR] 2.18, 95%CI [1.22–

3.91], p=0.009) and in WH men (aOR 1.53, 95% CI [1.18–1.98], p=0.002), in comparison to WH women. The odds did not significantly differ between AA and WH women (p=0.476). In fully adjusted models, the odds of having OARSI grade progression in medial JSN was slightly higher in AA women in comparison to WH women (aOR 1.38, 95% CI [0.91–3.46]), p=0.090), though this was not significant. Compared to WH women, WH men had greater odds of lateral JSN progression (aOR 2.25, 95% CI [1.29–3.92], p=0.004). There was no significant difference in lateral JSN progression among AA women (p=0.542) and AA men (p=0.509), in comparison to WH women.

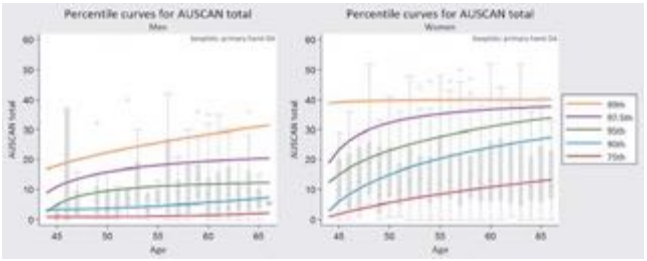


**Conclusions:** Compared to WHs and AA women, AA men were more likely to have radiographic knee OA progression over time. Loss of JSW and progression of JSN in specific compartments may vary based on race and sex. Further research to characterize and identify causes of differential KOA progression by race and sex is warranted.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2996

## SAT0446 REFERENCE CURVES FOR THE AUSTRALIAN/CANADIAN HAND OSTEOARTHRITIS INDEX (AUSCAN) IN THE GENERAL POPULATION

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**Background:** Patient-reported outcomes are important to evaluate treatment, but their interpretation depends on the availability of benchmarks. The AUSCAN is a widely used questionnaire evaluating hand pain, stiffness and function.
**Objectives:** To establish population-based reference curves for the AUSCAN, and to investigate factors associated with AUSCAN scores in the general population.
**Methods:** Analyses were performed in a population-based sample, the Netherlands Epidemiology of Obesity study (n=6671, aged 45–65 years). Participants completed questionnaires on demographic and clinical information, including the AUSCAN (range 0–60, higher is worse). Standardised physical examination of the hands was performed. Primary hand osteoarthritis (OA) was defined as fulfilment of the American College of Rheumatology criteria for hand OA without an inflammatory rheumatic disease. “Pre-hand OA” was defined as having hand pain and at least two bony swellings or deformities of distal interphalangeal joints (IPJs), proximal IPJs or first carpometacarpal joints and not having primary hand OA or an inflammatory rheumatic disease. Age- and sex-specific reference curves were developed using quantile regression in conjunction with fractional polynomials. Factors associated with AUSCAN scores were analysed with ordered logistic regression, since AUSCAN data were non-normally distributed and heavily zero-inflated, dividing AUSCAN into three categories (0 vs. 1–5 vs. >5). Analyses are reported as odds ratios (ORs) with 95% confidence intervals (CIs), representing the OR of being in the highest compared to the middle or lowest category for a unit change in the determinant. The final percentile curves were compared to observed AUSCAN scores of individuals with primary hand OA. All analyses were stratified by sex.
**Results:** Median age was 56 years (interquartile range (IQR) 50–61), 56% were women. Primary hand OA was present in 12% of participants. AUSCAN scores were low (median 1, IQR 0–4). Reference curves were higher for women, and moderately increased with age (figure). Other associated factors (adjusted for age) were not only primary hand OA (OR 13.8 (95% CI 9.3 to 20.5) and 8.4 (6.2 to 11.4) in men and women), but also self-reported inflammatory rheumatic diseases (OR 2.3 (1.4 to 3.6) and 4.5 (2.7 to 7.5)), fibromyalgia (OR 265 (32 to 2203) and 20.2 (9.6 to 42.5)), “pre-hand OA” (OR 9.8 (6.1 to 15.8) and 5.7 (3.8 to 8.5)), education (as proxy for socio-economic status, OR 0.8 (0.6 to 0.9) and 0.8 (0.7 to 1.0)), and BMI (OR 1.03 (1.00 to 1.06) and 1.03 (1.02 to 1.05)). Median AUSCAN scores of individuals with primary hand OA spread constantly between the 75th and 95th centiles of the general population (figure).




**Conclusions:** AUSCAN scores in a population-based sample were overall low, and higher in women than in men. These reference curves could serve as benchmark in both research and clinical practice settings in hand OA, although it should be kept in mind that the AUSCAN does not seem to measure hand complaints specific for hand OA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3729

## SAT0447 IDENTIFICATION OF PREDICTIVE BIOMARKERS OF THERAPEUTIC RESPONSE IN KNEE OA: THE MOVES STUDY

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**Background:** The high costs incurred when drugs fail during clinical trials has prompted interest in biomarkers as biological indicators for progress of disease, effect of therapeutic interventions, and/or drug-induced toxicity[1].
**Objectives:** The aim of this study is to identify predictive protein biomarkers useful to stratify osteoarthritis (OA) patients into responders and non-responders, either to Droglican® (Bioiberica S.A.,Barcelona,Spain) or Celecoxib, in order to optimize therapeutic outcomes in OA.
**Methods:** A shotgun proteomic analysis was performed on sera from patients enrolled in the Multicentre Osteoarthritis interVEntion trial with Sysadoa (MOVES)[2]. Sixteen serum pools from a representative group of the whole cohort (n=80) were analyzed to find a panel of proteins quantitatively different between responders and non-responders at baseline. The samples were classified between responders and non-responders, either to Droglican (glucosamine hydrochloride+chondroitin sulfate) or Celecoxib, according to the WOMAC pain score (<20 and <70) and the OMERACT-OARSI criteria recorded at the end of the trial (after 6 months of treatment). Two independent set of experiments were carried out. The pools from each condition to be compared were subjected to immunodepletion, protein digestion and labeled with the different 8-plex iTRAQ reagents as previously described[3]. The labeled peptide mixtures were mixed and resolved by reversed phase chromatography. The eluted fractions were collected onto a MALDI plate for the subsequent mass spectrometric analysis. The identification of proteins was performed with ProteinPilot v4.0 software (ABSciex). Furthermore, the results obtained were verified by ELISA assay.
**Results:** The proteomic screening led to the identification of 176 different proteins in the serum samples at baseline. The Protein Pilot software also provided data relative to the quantification between each of the samples (iTRAQ ratios). All ratios were obtained comparing the abundance of each protein identified in the responders to the abundance in the non-responders. Several proteins showed at baseline a statistically significant increase in the responder groups, such as beta-2-glycoprotein 1 (APOH) in the droglican responders and thrombospondin 1 (TSP1) in the celecoxib responders, among others. The putative biomarker usefulness of TSP1 was validated by ELISA assay on individual sera from the same cohort. The results for TSP1 (n=80) confirmed that the levels of this protein at baseline are lower in the group of non-responders to celecoxib in comparison to the responders one according to WOMAC criteria.
**Conclusions:** Protein biomarkers, such as APOH or TSP1, can predict patient response to a specific compound (droglican or celecoxib) by identifying certain OA patient populations that are more likely to respond to a specific drug therapy. This shift toward personalized medicine can help the clinicians to choose the best treatment option for each OA patient, thus enhancing the probability of success of the pharmacotherapy while reducing specific adverse events.
**References:**
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[3] Fernández-Puente et al., 2011
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3403

## SAT0448 A COMPARISON OF THE DIFFERENT QUANTITATIVE SENSORY TESTING MEASUREMENTS ADDRESSING PAIN MECHANISMS IN PEOPLE WITH OSTEOARTHRITIS

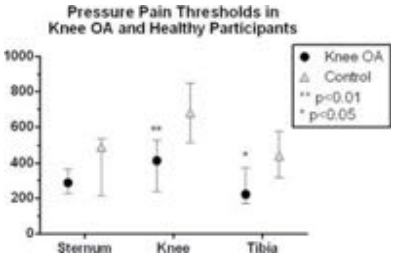
H. Hassan[1,2,3], D.F. McWilliams[1,2], D. Wilson[3], N. Frowd[1,2], D.A. Walsh[1,2,3]. *[1]Arthritis Research UK Pain Centre; [2]Division of Rheumatology, Orthopaedics and Dermatology, University of Nottingham, Nottingham; [3]Department of Rheumatology, Sherwood Forest Hospitals NHS Foundation Trust, Sutton in Ashfield, United Kingdom*

**Background:** People with osteoarthritis (OA) can experience both nociceptive pain, as a result of local joint damage, and pain that is indicative of abnormal central pain processing. Quantitative sensory testing (QST) is psychophysical testing of somatosensory function and can been used to investigate somatosensory abnormalities in people with OA.
**Objectives:** The aim of this study was to assess the reliability discriminant ability of two different mechanical stimuli for QST measurements, pressure and punctate, in people with knee OA and healthy participants.
**Methods:** Twenty six knee OA participants and 25 healthy participants were recruited. QST was performed in all participants at three sites on the body (sternum, index knee and anterior tibia). Two mechanical QST modalities (pressure and punctate) were performed. Pressure pain threshold (PPT) was assessed using digital algometry. Punctate QST measurements, {mechanical pain threshold (MPT), mechanical pain sensitivity (MPS) and wind-up ratio (WUR)}, were assessed using pinprick stimulators. The procedures were repeated during a second assessment four weeks later by the same examiner to determine repeatability. All participants completed the Intermittent and Constant Osteoarthritis Pain (ICOAP) questionnaire (Rasch transformed).
**Results:** The mean age for OA participants was 66 years (standard deviation (SD) (9), (50% female) and for the healthy participants was 58 years (SD 11), (48% female). People with knee OA demonstrated significantly higher values on ICOAP Rasch transformed; Intermittent {mean 7.13 (4.47) and Constant mean 4.40 (4.47)} than healthy participants; Intermittent {mean 1.12 (2.31) and Constant {mean 0.29 (1.03)} ($P<0.001$). The test-retest reliability of the QST measurements before and after 4 weeks interval expressed as intraclass correlation coefficients (ICCs) are given in Table 1.

Table 1. Test retest reliability of QST measurements

| QST | Site | ICC | 95% CI | P |
|---|---|---|---|---|
| PPT | Sternum | 0.90 | 0.79–0.95 | <0.0001 |
| | Knee | 0.90 | 0.80–0.95 | <0.0001 |
| | Tibia | 0.84 | 0.70–0.92 | <0.0001 |
| MPT | Sternum | 0.68 | 0.36–0.84 | 0.010 |
| | Knee | 0.14 | –0.96–0.51 | 0.483 |
| | Tibia | 0.75 | 0.49–0.87 | <0.0001 |
| MPS | Sternum | 0.70 | 0.40–0.85 | <0.0001 |
| | Knee | 0.74 | 0.48–0.87 | <0.0001 |
| | Tibia | 0.84 | 0.67–0.92 | <0.0001 |
| WUR | Sternum | 0.23 | –0.54–0.61 | 0.232 |

People with knee OA had significantly lower PPT at knee and tibia than normal controls (Graph). Differences between OA and control groups remained significant after adjustment for age and sex. Whereas there were no significant differences found in any punctate QST measurements between knee OA and healthy participants.




**Conclusions:** This study demonstrated that PPT is a reliable QST measurement with less variability compared to other mechanical QST measurements assessed. PPT at the tibia, a site distal to the affected joint, is believed to reflect augmented central pain processing. PPT may be a preferred QST modality to investigate altered central pain processing in people with OA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1269

## SAT0449 THE RELATIONSHIP BETWEEN THE ARTICULAR SURFACE PROJECTION AND RADIOLOGIC LAXITY OF THE TRAPEZIOMETACARPAL JOINT

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**Background:** The etiology of trapeziometacarpal joint (TMCJ) osteoarthritis is not yet clearly confirmed. Laxity of the TMCJ is considered as one of the causes of osteoarthritis. Previous studies evaluated the relationship between the bony morphology and TMCJ laxity mainly in osteoarthritic TMCJs. It is unclear, however, whether there is such relationship in non-arthritic TMCJ.
**Objectives:** We aimed to determine whether the articular surface projection was associated with laxity of the TMCJ.
**Methods:** We measured the trapezial tilt and the first metacarpal base articular slope in radiographs of 108 women without thumb TMCJ osteoarthritis. The mean age was 57 years (range, 32 to 79 years). The trapezial tilt (TT) was defined as the angle formed by the intersection of a tangent to the middle third of the distal trapezial articular surface and a line parallel to the longitudinal axis of the index metacarpal in the posteroanterior radiograph of the trapezium ($\alpha$ in Fig 1A). The metacarpal articular slope (MS) was defined as the angle between the dorsal cortex and the articular surface of the first metacarpal base in a true lateral view of the thumb metacarpal ($\beta$ in Fig 1B). We evaluated the radiologic laxity of the TMCJ using subluxation ratio (SR) in the TMCJ stress view radiograph (RS (radial subluxation)/AW (articular width) in Fig 1C). We divided the subjects into four subsets according to the TT and MS, and compared the mean SR between the upper and lower quartile groups.
**Results:** There was a statistically significant difference in the mean SR between those in the upper and lower quartiles of the MS (0.24 vs 0.32, P=0.013). However, there was no difference in the SR with regard to the TT (P=0.189).




**Conclusions:** This study suggests that a steeper articular slope of the first metacarpal base could be associated with radiologic laxity of the TMCJ. Further longitudinal studies are necessary to determine whether this anatomic difference represent a risk factor for later development of TMCJ osteoarthritis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2455

## SAT0450 IMPACT OF MYOFASCIAL PAIN SYNDROME ON PAIN AND FUNCTIONAL STATUS IN PATIENTS WITH HAND OSTEOARTHRITIS

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**Background:** Various upper extremity musculoskeletal diseases (MSDs) can affect pain and disability in patients with hand osteoarthritis (HOA). However, there was no previous study investigating the relationship between upper extremity MSDs and HOA.
**Objectives:** To explore the influence of major upper extremity MSDs on pain severity and functional status of patients with HOA.
**Methods:** In this study, we enrolled 1150 farmers who lived in Gyeongnam province in Korea from June 2013 to December 2015. Physical examinations were performed by rheumatologists, orthopedists, and rehabilitation specialists. Grip powers of both hands also were evaluated. Plain radiography, a nerve conduction velocity (NCV) examination, and magnetic resonance imaging (MRI) of shoulders were performed. The Australian/Canadian Osteoarthritis Hand Index (AUSCAN) was used to assess pain severity and functional status of hand joints. The diagnosis of HOA was made by the 1990 American College of Rheumatology classification criteria. Carpal tunnel syndrome (CTS) was confirmed by NCV findings, and rotator cuff tear (RCT) was diagnosed by MRI findings. Myofascial pain syndrome (MPS) was diagnosed by palpations of myofascial trigger points.
**Results:** Of 1150 participants, 307 were diagnosed with HOA. Among HOA patients, 151 (49.7%), 192 (62.5%), and 249 (80.1%) patients had CTS, RCTs, and MPS, respectively. HOA patients with MPS showed significantly higher AUSCAN scores (350.4±285.0 vs 200.4±201.8, $p<0.001$) and decreased grip power of a dominant hand (22.5±9.8 vs. 26.2±9.8, p=0.011) compared with HOA without MPS. Linear regression analysis also showed that MPS was associated with AUSCAN scores after adjustment for age and gender ($\beta$=0.21, p=0.001). The

existence of CTS or RCT did not influence on AUSCAN scores and grip power. Compared to participants with none of major upper extremity MSDs, participants with MPS only were also higher AUSCAN scores.
**Conclusions:** MPS has a significant impact on pain and functional status in patients with HOA. Therefore, management of coexisting MPS is the better way to improve pain and function of hand joints in patients with HOA.
**Acknowledgement:** This study was supported by a grant of the Center for Farmer's Safety and Health, Ministry of Agriculture, Food and Rural Affairs, Republic of Korea.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5114

## SAT0451 THE ASSOCIATION OF PATELLA ALTA WITH THE SEVERITY OF RADIOLOGICAL TIBIOFEMORAL KNEE OSTEOARTHRITIS

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**Background:** Patella alta is the malalignment of the patella in the vertical plane. There are a number of studies that confirmed the relation of patella alta and patellofemoral knee osteoarthritis (OA). Nevertheless, to our knowledge, none has studied the possible relationship between patella alta and tibiofemoral knee OA.
**Objectives:** The objectives of the current study were i) to determine the prevalence of patella alta among patients with radiographic tibiofemoral knee OA and ii) to evaluate whether the frequency of patella alta differs by the severity of knee OA.
**Methods:** Patients who had undergone X-ray examination of the knee with a diagnosis of knee OA between January 2013-February 2016 were included in the study. Following the application of the exclusion criteria, remaining patients' radiographs were graded according to the Kellgren Lawrence grading system. Knees were divided into mild OA (KL grade 1–2) and severe OA (KL grade 3–4) groups. Computerized measurement of the craniocaudal patellar distance (CPD) and the patellar tendon length (PTL) was performed on lateral knee radiographs. According to the Insall-Salvati method, the PTL/CPD ratio $>1.2$ was regarded as "patella alta". The overall prevalence of patella alta was determined. The rate of patella alta was compared between mild and severe OA groups.
**Results:** A total of 712 radiographs were assessed for eligibility. Measurements were performed on 416 lateral knee radiographs belonging to 253 patients with a mean age of 62.7±11.3 years. The prevalence of patella alta in the whole group was 9.1%. The frequency of patella alta was significantly higher in the severe OA group when compared with the mild OA group ($p<0.001$).
**Conclusions:** According to the results of the present study, patella alta appears to be associated with increased severity of radiographic tibiofemoral knee OA. "High riding" patella should be kept in mind as a determinant of disease severity in patients with knee OA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4046

## SAT0452 DO TRADITIONAL RISK FACTORS FOR KNEE OSTEOARTHRITIS PREDICT PAIN FLARES IN KNEE OSTEOARTHRITIS?

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**Background:** Knee pain is the main cause of disability and reduced function in knee osteoarthritis (KOA). Though knee pain in osteoarthritis was previously perceived as a chronic condition it is now established that KOA pain fluctuates.There is emerging evidence that time variant risk factors-such as knee injury, buckling and mood- are associated with knee pain flares. But, it is not known whether conventional risk factors associated with KOA – age, gender, body mass index-are associated with pain flares in KOA.
**Objectives:** This study examines whether conventional time invariant risk factors for KOA and baseline pain felt by the patient are associated with KOA pain flares.
**Methods:** Study participants were selected from a 3-month web-based longitudinal follow up study developed to identify risk factors for KOA pain flares. Participants were requested to complete online questionnaire at days 0, 30, 60 and 90 (control period assessment points) and at time points whenever they experienced knee pain flare (case period assessment points) during the follow up period. A KOA pain flare was defined as current pain with a greater than 2 point increase (on a 0–10 point numeric rating scale) from the mildest KOA pain intensity reported at day 0.
The association of pain flares with traditional risk factors for knee osteoarthritis -gender, weight, height, body mass index- was assessed by negative binomial regression. The duration of knee osteoarthritis, baseline pain intensity (lowest pain and highest pain scores at baseline) were similarly evaluated. The best explanatory variable was decided by forward selection.
**Results:** 345 persons (61.2% females) with multiple KOA pain flares were selected. Their mean age was 62.1years (SD ±8.2). The mean body mass index was 29.8kg/m$^2$ (SD ±6.5). The participants rated their baseline pain (on a numeric rating scale) as being 4.41 (SD± 2.02) and their worst pain as being 7.91 (SD ±1.74).
An average of 1.92 (SD 2.59) flares were documented during the 3-month period. The levels of baseline pain – usual and worst pain felt at baseline- were the only parameters significantly associated with KOA pain flares (Table 1).

Table 1. Association between time invariant risk factors of KOA and KOA pain flares

| | Incidence rate ratio (95% CI) | P value |
|---|---|---|
| Age | 0.99 (0.98–1.01) | 0.99 |
| Female gender | 0.87 (0.65–1.16) | 0.35 |
| Height | 0.99 (0.98–1.01) | 0.76 |
| Weight | 1.00 (0.99–1.01) | 0.16 |
| Body mass index | 1.02 (0.99–1.04) | 0.08 |
| Duration of knee osteoarthritis | 0.99 (0.98–1.00) | 0.49 |
| Baseline pain score – lowest level of pain intensity | 1.25 (1.17–1.34) | <0.001 |
| Baseline pain intensity – highest pain intensity felt at baseline | 1.29 (1.18–1.40) | <0.001 |

CI: Confidence Interval.

**Conclusions:** The baseline pain scores were the strongest predictors of pain flares of knee osteoarthritis. The traditional risk factors associated with knee osteoarthritis did not usefully predict pain flares. The traditional time invariant risk factors may not be associated with short term variability in pain though they are associated with long term outcomes of knee osteoarthritis. It is postulated that as knee pain is already present, time invariant risk factors that contributed to the original symptom causation are not associated with pain flare.
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**Disclosure of Interest:** None declared
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## SAT0453 DOES RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKADE INFLUENCE PAIN, FUNCTION AND RADIOGRAPHIC PROGRESSION IN KNEE OSTEOARTHRITIS? AN ANALYSIS OF OSTEOARTHRITIS INITIATIVE DATA

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**Background:** Renin-angiotensin-aldosterone system (RAAS) has been proposed as a potential target for the treatment of osteoarthritis (OA). In experimental studies, RAAS blockade led to the reduction of inflammation and modulated cartilage metabolism. Recently, a study showed chondroprotective effects of captopril in an animal model of OA [1]. The effects of RAAS blockade on knee OA have never been studied in humans.
**Objectives:** To investigate longitudinal effects of RAAS blockade on knee pain, function, and radiographic progression of knee OA.
**Methods:** For the current analysis we used data from the publically available Osteoarthritis Initiative (OAI) database. We assessed longitudinal data from OAI participants who did not use angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) on baseline (new user design) and who had radiographically suspected or confirmed knee OA. The evaluated clinical outcomes were WOMAC pain and WOMAC function subcategories. Radiographic progression was assessed using minimal joint space width (mJSW). The outcomes were measured annually from the baseline to year 4 of follow up. We used structural equation modeling to assess the correlations between the trajectories of ACEI/ARB use and WOMAC knee pain, WOMAC knee function, and mJSW. The models were adjusted for potential baseline confounders.
**Results:** A sample of 1796 OAI participants was analyzed. The proportion of ACEI/ARB users rose from 4.7% on year 1 to 15.14% on year 4 of follow up. No associations between ACEI/ARB use and knee pain, function, and knee OA radiographic progression trajectories were found in the analyses both adjusted or non-adjusted for baseline covariates.
**Conclusions:** RAAS system blockade has no influence on knee OA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2888

## SAT0454 IN A TWO-YEAR DOUBLE-BLIND RANDOMIZED CONTROLLED MULTICENTER STUDY, CHONDROITIN SULFATE WAS SIGNIFICANTLY SUPERIOR TO CELECOXIB AT REDUCING CARTILAGE LOSS WITH SIMILAR EFFICACY AT REDUCING DISEASE SYMPTOMS IN KNEE OSTEOARTHRITIS PATIENTS

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**Background:** In osteoarthritis (OA) treatment, although chondroitin sulfate (CS) was found in a number of studies using radiography to have a structure modifying effect, to date the question is still under debate. A clinical study using quantitative magnetic resonance imaging (qMRI) is therefore of the utmost importance.
**Objectives:** The present study has the objective to explore, as the first aim, in a two-year randomized, controlled double-blind clinical study using qMRI, the disease modifying effect of CS treatment versus celecoxib (CE) on cartilage volume loss (CVL) in knee OA. The second aim was to investigate and compare the effect of CS and CE on symptoms.
**Methods:** Symptomatic primary knee OA patients according to ACR criteria with Kellgren-Lawrence grades 2–3 and synovitis were included and treated with CS (1200 mg a day) or CE (200 mg once daily) for 24 months. Patients at high risk for cardiovascular and/or gastrointestinal disease were not included. MRI was performed at baseline, 12 and 24 months. CVL, bone marrow lesion (BML) size, and synovial membrane thickness were evaluated using qMRI, and presence of joint swelling and effusion clinically evaluated. Clinical symptoms were also assessed by validated questionnaires.
**Results:** In the intention-to-treat analysis (n=194), patients treated with CS had reduced CVL at 24 months in the medial compartment (p=0.026) and condyle (p=0.008) compared to celecoxib. In the completer analysis, CS reduced CVL in the medial compartment at 12 months (p=0.026) and medial compartment and condyle at 24 months (p=0.030, p=0.010). A trend toward a reduced (p=0.070) synovial thickness in the medial suprapatellar bursa was observed in CS patients. Both treatment groups experienced a marked reduction in incidence of patients with joint swelling/effusion and in symptoms (WOMAC total, pain, and function, and VAS pain) over time. Data showed similar good safety profiles for both drug treatments.
**Conclusions:** This trial demonstrated, for the first time, the superiority of CS over CE at reducing the long term progression of knee OA structural changes. Moreover, both drugs were found equally effective at reducing the symptoms of OA. These findings have important implications regarding the usefulness of CS for long term management of knee OA and its impact on disease outcome.
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## SAT0455 BASELINE AND PERSISTENT KNEE SYMPTOMS ARE INDEPENDENT PREDICTORS OF STRUCTURAL PROGRESSION OF KNEE OSTEOARTHRITIS

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**Background:** Although studies have predominantly focused on whether disease progression predicts symptoms in knee osteoarthritis (OA), there is very little data examining whether the presence of knee symptoms may be an independent predictor of the structural progression of knee OA.
**Objectives:** To complement and extend previous studies, we examined whether baseline and persistent knee symptoms predicted accelerated cartilage volume loss, incident and progressive radiographic OA (ROA) and total knee replacement (TKR).
**Methods:** Participants from the Osteoarthritis Initiative were grouped according to the absence (Kellgren-Lawrence [KL] grade $\leq$1, n=2120) or presence (KL $\geq$2, n=2249) of baseline ROA. Clinical symptoms (pain, stiffness and function) were assessed at baseline using Western Ontario and McMaster University Osteoarthritis Index (WOMAC). Cartilage volume in the medial and lateral compartments was assessed by magnetic resonance imaging (MRI) at baseline and 48 months. Associations with incident and progressive ROA were assessed at 48 months and TKR at 72 months.
**Results:** Higher levels of baseline and persistent knee symptoms predicted greater annual percentage of cartilage loss in the medial (all $p<0.05$) and lateral (all $p\leq0.03$) compartment in people both with and without ROA. Greater baseline and persistent knee symptoms were associated with incidence (OR range 1.02 to 1.29, all $p\leq0.005$) and progression (OR range 1.01 to 1.22, all $p\leq0.01$) of ROA, as well as TKR (OR range 1.03 to 1.35; all $p<0.001$).
**Conclusions:** Greater baseline and persistent knee symptoms predicted accelerated cartilage loss, incident and progressive ROA and TKR. Although a major focus in OA research has been the link between structural disease and symptom progression, data from this study demonstrate that symptoms are important independent predictors of disease progression. This suggests that targeting symptoms may be important for preserving joint structure.
**Disclosure of Interest:** J. Martel-Pelletier Shareholder of: ArthroLab Inc., A. Teichtahl: None declared, F. Cicuttini: None declared, Y. Wang: None declared, F. Abram Employee of: ArthroLab Inc., J.-P. Pelletier Shareholder of: ArthroLab Inc.
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## SAT0456 LONG-TERM EFFECTS OF TREATMENT ON THE PROGRESSION OF STRUCTURAL CHANGES IN KNEE OSTEOARTHRITIS: 6-YEAR FOLLOW-UP

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**Background:** The Osteoarthritis Initiative (OAI) is the largest knee osteoarthritis observational cohort. It provides the possibility to study the evolution of OA structural changes over time and the associated risk factors. It also allows the potential disease-modifying OA drug effects to be explored in patients over time.
**Objectives:** This study aimed to examine, for the first time, the long-term (6-year) protective effect of combined glucosamine (Glu) and chondroitin sulfate (CS) treatment on OA knee cartilage volume using the OAI cohort.
**Methods:** Participants from the OAI Progression and Incidence sub-cohorts who had MRI data on the target knee at baseline and at 6 years and with a JSW greater than 1 mm, and information on the Glu/CS consumption were included (n=1593). The participants were stratified into two main groups based on whether or not they had medial meniscal extrusion at baseline, and the former group (n=429) were further stratified into subgroups based on their exposure time: not exposed, 1 year, 2 to 3 years, and 4 to 6 years. MRI assessments were done using fully automated quantitative technologies[1,2]. Statistical analysis included the Jonckheere-Terpstra trend test as well as multivariate analysis test.
**Results:** Findings indicate that in participants with knee OA, treatment with the combined Glu/CS significantly reduced the loss of cartilage in the global knee associated with the lateral compartment. Moreover, the extent of the treatment's positive effect was also found to be related to the exposure time to treatment, the protective effect at 6 years being significant in participants who were exposed to 2 or more years of treatment.
**Conclusions:** The findings of this study are in line with previous data showing chondroprotective effects of glucosamine and chondroitin sulfate treatment with preferential effects, and provide future support for the long-term structure-modifying effects of such treatment in knee osteoarthritis subjects.
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**Disclosure of Interest:** J. Marte-Pelletier Shareholder of: Arthrolab Inc., Grant/research support from: Bioiberica, Consultant for: Bioiberica, J. P. Raynauld: None declared, F. Abram: None declared, P. Delorme: None declared, J. P. Pelletier Shareholder of: Arthrolab Inc., Grant/research support from: Bioiberica, Consultant for: Bioiberica, Speakers bureau: Bioiberica
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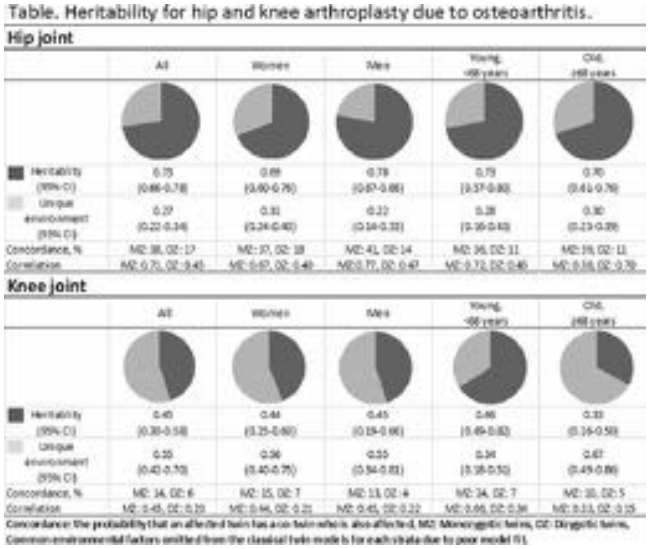
## SAT0457 A MARKEDLY HIGHER PROPORTION OF THE VARIANCE IN HIP ARTHROPLASTY THAN IN KNEE ARTHROPLASTY CAN BE EXPLAINED BY HERITABILITY

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**Background:** Osteoarthritis (OA) may lead to costly total joint replacements (TJR) of the knee and hip joints. To what extent TJR due to OA at the different joint sites is caused by hereditary or environmental factors is unknown. This information may aid in determining whether hip or knee arthroplasties are possible to prevent.

**Objectives:** To explore the genetic contribution to TJR due to hip and knee OA for women, men, young and elderly using a twin registry design.
**Methods:** The study is a prospective cohort study based on a linkage of the Norwegian Twin Registry and the Norwegian Arthroplasty Registry using the National ID number in 2014. The presence of a TJR due to hip and knee OA has been registered for >95% of the population from 1987 (hip) and 1994 (knee). We first calculated prevalence estimates across twin groups (same sex twin pairs born 1915–1960), and subsequently examined the relative contribution of genetic factors (heritability), shared and non-shared environmental factors, applying the classical twin model.
**Results:** The sample comprised 9029 complete pairs of which 3803 monozygotic (MZ) and 5226 dizygotic (DZ) pairs (54% females and mean (SD) age 71.5 (12.7) for both zygosity groups). The prevalence for having a TJR was similar across zygosity with 3.6% (n=614) for the hip and 1.8% (n=317) for the knee joint. In total 50 MZ/30 DZ and 10 MZ/5 DZ twin pairs were concordant for hip and knee arthroplasty, respectively. Concordances and polychoric correlations were higher for MZ twins than DZ twins both for hip and knee artrhoplasty in all age and sex strata (Table). A model including only genetic and environmental factors unique to each twin in a pair provided the best fit. The heritability for TJR largely depended on OA site. A markedly higher proportion of the variance in hip arthroplasty than in knee arthroplasty could be explained by heritable factors (Table). The variance in TJR due to knee OA was to a greater extent explained by environmental factors unique to each twin (Table). A significant gene-age interaction could be observed for the knee joint with a high observed heritability for twins below median age (68 years) changing to a low heritability after median age. Heritability estimates for TJR due to hip OA remained high and stable across age and sex groups, although a slightly higher heritability could be observed for men (Table).

Table. Heritability for hip and knee arthroplasty due to osteoarthritis.



Concordance: the probability that an affected twin has a co-twin who is also affected. MZ: Monozygotic twins, DZ: Dizygotic twins. Common environmental factors omitted from the classical twin model for each strata due to poor model fit.

**Conclusions:** The heritability of TJR due to OA depends on joint site. Preventive interventions may have a greater potential for knee arthroplasty than hip arthroplasty, particularly for knee arthroplasty at old age. The difference in heritability across age and sex groups for TJR due to knee OA should be further studied due to a low number of concordant pairs.
**Disclosure of Interest:** None declared
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## SAT0458 RISK FACTORS FOR LENGTH OF HOSPITAL STAY AFTER TOTAL KNEE ARTHROPLASTY: A FIVE-YEAR CONSECUTIVE CASE SERIES

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**Background:** The length of hospital stay (LOS) has become a valuable outcome measure of any operation, and it also directly impacts hospital cost.
**Objectives:** To identify risk factors for LOS after total knee arthroplasty (TKA) in rheumatoid arthritis (RA) and osteoarthritis (OA) patients.
**Methods:** A retrospective study involving 507 consecutive patients undergoing TKA was conducted during a five-year period from January 2010 to December 2014 (mean age 72 years, 433 females, 82 RA patients, and 58 bilateral TKA). The diagnosis of deep vein thrombosis (DVT) was based on ultrasonography.
Multiple linear regression analysis was performed to identify the variables predictive of prolonged LOS and operative time. Multiple logistic regression analysis was performed to analyze the risk factors for postoperative DVT (dependent variables: gender, age, BMI, RA, operative time, antiplatelet agents, cementless TKA, and bilateral TKA).
**Results:** Of the patients undergoing TKA, the mean LOS was 26 days, and the mean operative time was 73 minutes. The results of the multiple linear regression analysis indicated that female gender (P=0.006), age (P<0.001), higher BMI (P=0.03), operative time (P=0.001), and bilateral TKA (P=0.009) were risk factors for prolonged LOS. A subanalysis of operative time revealed that male gender (P=0.01) and BMI (P=0.03) were associated with longer operative time.
A total of 195 (38.5%) cases were DVT positive. Multivariate logistic regression analysis revealed that osteoarthritis (P=0.03) and cementless TKA (P=0.01) were risk factors for DVT after TKA.
**Conclusions:** Female gender, age, higher BMI, operative time, and bilateral TKA were risk factors for longer LOS. Male gender and higher BMI were risk factors for longer operative time. Osteoarthritis and cementless TKA were risk factors for DVT. Further research investigating the risk factors for longer LOS is needed to reduce total hospital costs.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3075

## SAT0459 ASSOCIATIONS BETWEEN BODY COMPOSITION MEASURES OF OBESITY AND RADIOGRAPHIC OSTEOARTHRITIS IN OLDER ADULTS: DATA FROM THE DONG-GU STUDY

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**Objectives:** We examined the effects of fat deposition on radiographic osteoarthritis (OA) to determine the role of obesity in the pathogenesis of radiographic OA.
**Methods:** Data were taken from the Dong-gu cohort, a cross-sectional study of 2,367 subjects. Baseline characteristics, waist circumference (WC), waist-to-hip ratio (WHR), fat mass, and fat percentage were collected, along with X-rays of the knees and hands. Total knee and hand radiographic OA scores were summed using a semi-quantitative grading system, and then stratified by gender using a multiple linear regression model.
**Results:** After adjusting for confounders, weight was the only factor significantly associated with knee radiographic OA, regardless of gender (all p<0.01). Regarding the hand, fat percentage had the largest effect on radiographic OA in males (p=0.008), while WHR was the most significant factor in females (p=0.001). For the knee, fat mass was the most important factor for radiographic OA in males (p=0.001), while in females, body mass index was the most important factor (p<0.001). Among the variables, only fat percentage was significantly related to both hand and knee radiographic OA in both genders (all p<0.01).
**Conclusions:** Regardless of gender, mechanical stress was significantly associated with knee radiographic OA. Otherwise, fat deposition correlated with hand and knee radiographic OA in both genders, while the distribution of fat tissue was significantly associated with hand and knee radiographic OA only in females, with the largest effect on hand and knee radiographic OA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1953

## SAT0460 THE EFFECT OF THERAPEUTIC ULTRASOUND ON PAIN AND PHYSICAL FUNCTION IN THE PATIENTS WITH KNEE OSTEOARTRITIS

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**Background:** Osteoartritis (OA) is one of the most frequent causes of pain, loss of function and disability in adults (1,2). The prevalence of OA is expected to increase substantially in the future (1). Knee osteoarthritis is the most common subset of OA (2). Therapeutic ultrasound (US) is one of several physical therapy modalities suggested for the management of pain and loss of function due to OA (3).
**Objectives:** The purpose of our study was to investigate the efficacy of US therapy in reducing pain and functional loss and improving the quality of life in patients with knee osteoarthritis in comparison to sham ultrasound therapy.
**Methods:** The study involved 62 patients. The patients were randomly divided into two groups. The patients in Group 1 (n=30) were administered 1 Watt/cm$^2$, 1 MHz continuous US, and the patients in Group 2 (n=32) were administered sham US. The ultrasound treatment was applied for 8 min to each knee, 16 min in total, 5 days a week, for a total of 10 sessions during two weeks. The patients were evaluated immediately after treatment and 1 month after therapy according to VAS, night pain, EHA, morning stiffness, WOMAC, Lequesne and SF-36 scales, and 6 min walking distance.
**Results:** Improvement in pain and joint functions was observed in both groups according to the evaluation immediately after treatment and at 1 month after the therapy. According to the evaluation results immediately after treatment; there was significant improvement in all pain scales (VAS, WOMAC, Lequesne, SF-36), morning stiffness and 6 min walking distance in patients receiving real US treatment (p<0.05) but only in some pain scales (VAS, WOMAC) and functions in the group receiving sham US (p<0.05). Significantly better improvement was observed in some pain scales (SF-36), functions (WOMAC, SF-36) and 6 min walking distance in the real US group. At 1 month after therapy, no significant difference was observed between groups except for improvement in night pain in real US group.

**Conclusions:** This study comfirms that US therapy is effective to improve physical function, in reducing pain and also it is a reliable method. Short term efficacy of US is superior to plasebo, on the other hand long term effect is not different from placebo. The results can provide guidance regarding the organization of the treatment of the patient with knee OA. Further systematic investigation is needed with larger group of patients.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.1320

## SAT0461 EFFICACY OF HYALURONIC ACID IN SMALL JOINTS OSTEOARTHRITIS (OA) – THE RESULTS OF MULTICENTER RANDOMIZED PLACEBO-CONTROLLED 48 WEEKS STUDY

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**Objectives:** Assessment of the efficacy, tolerability and aftereffect period on the single administration into Ist carpometacarpal and Ist metatarsophalangeal OA joints of 1.0ml (20mg) of hyaluronic acid (Durolane SJ) as compared with placebo.
**Methods:** The study included 120 pts with OA of small hand joints or feet, pain intensity >40mm by VAS and consisted of two phases: "blind" phase up to 24 weeks, period of open assessment of long term efficacy results – 48 weeks. The efficacy was assessed by 40% pain subsiding, index AUSCAN (for the hand), daily dose of NSAID, total effect assessment by VAS.
**Results:** Both groups were comparable by basic clinical criteria. 40% pain subsiding by VAS (mm) was noted in experimental group to 24th week in 79.7%, in the placebo group – 30% (chi-square: $p<10^{-5)}$ relation of chances (OR) equal to 9.1 (3.9–21.1). Dispersion analyses of pain, stiffness and function by AUSCAN index revealed reliable differences between Durolane SJ and placebo. Adverse effects related to the therapy were not found. Effect, achieved to 24th week of observation included pain, stiffness, functional status, general assessment of condition by the therapist and patient, was preserved without changes to 48th week.
**Conclusions:** High efficacy and 48 weeks considerable duration of aftereffect of single administration of Durolane SJ (small joints) as compared to placebo was demonstrated.

**Disclosure of Interest:** None declared

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## SAT0462 AUTOLOGOUS PLATELET-RICH PLASMA (PRP) IN OSTEOARTHRITIS TREATMENT

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**Background:** The results of the PRP use in knee OA treatment are discussed ib the article.
**Objectives:** To study the efficacy and safety of the PRP use in early stages of the knee OA.
**Methods:** The study was conducted at the Department of Family Medicine of the NMA of Postgraduate Education (Kyiv, Ukraine) and included 68 patients with diagnosed knee OA (I-II radiological stages).The patients with severe co-morbidities,trauma or after knee surgery were not included at the study.68 patients (27 men (39.7%) and 41 women (60.3%), mean age 41,3±1,2 years) were divided into 2 groups.Gr.1 included 34 patients who consented to receive standard OA treatment and 3 intra-articular injections of PRP (total volume 24–30ml,mean platelets number 869,24±32,$1x10^9/\mu l$)weekly;gr.2 consisted of 34 patients of comparable age with the same diagnosis who received only standard OA treatment.The CRP-level,WOMAC scale and Lequesne index was analyzed before treatment and in 1,3,6,12 months after course of treatment in both groups.
**Results:** CRP level was modestly abnormal in the 43,5% patients of group 1 and 38,7% patients of group 2; during the treatment period CRP got to normal in all patients, but during the follow-up period-after 6 and 12 months of treatment in the study group it was significantly lower (6,44±0,52) and (4,34±0,22) mg/L, than in the control group (7,96±0,60) and (6,72±0,51)mg/L ($p<0,005$). In addition in 5 patients of group 2 CRP level had increased again after 6 months which was the sign of OA exacerbation.WOMAC and Lequesne index had positive dynamic during treatment in both groups.At month 12 functional status of the patients in gr.1 improved by 33% in stiffness,pain during movement and after passing the distance decreased after treatment by 38.5% in gr.1,pain and discomfort when climbing and descending the stairs decreased by 38.9%. At the end of follow up period patients functional activity increased by 47.4% in gr.1 which was better then positive changes in gr.2 and was accompanied by a significant reduction of restrictions in daily activities.There were no adverse events due to use of PRP injections in gr.1.
**Conclusions:** The course of 3 intra-artricular injections added to the standard treatment of knee OA improves functional activity,reduces pain and probably can prolong remission in patients with the early stages of disease.The further long-term studies are needed with ultrasound/MRI monitoring of the articular cartilage to obtain more accurate information and determine the most effective methods of PRP use in OA treatment.

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**Disclosure of Interest:** None declared

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## SAT0463 THE PREVALENCE OF KNEE OSTEOARTHRITIS ESTIMATED BY VALIDATED SCREENING QUESTIONNAIRE IN THE GENERAL POPULATION OF SINGAPORE

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**Background:** Knee osteoarthritis (OA) is one of the leading causes of disability worldwide. The prevalence of knee OA is higher in Chinese than Caucasian subjects, despite the lower body mass index in Chinese populations.[1,2] Among other Asian ethnicities, the prevalence of knee OA may also be high, and the prevalence of knee OA in the multi-ethnic Singapore population is still unknown.
**Objectives:** Our study aimed to estimate the prevalence of knee OA in the general population of Singapore, using a validated questionnaire consisting of 3 knee OA symptoms or 1 symptom and a physician diagnosis (sensitivity of 54%, specificity of 87%).[3]
**Methods:** We recruited a subset of subjects from the National Health Surveillance Survey (NHSS) 2013 who provided telephone numbers. Consenting subjects were invited to complete a validated screening questionnaire by mail.[3] If no response was received after 4 weeks, the subjects were interviewed by telephone to complete the screening questionnaire. The national prevalence of knee OA was estimated by accounting for the proportion of subjects who provided telephone numbers; it was weighted to the gender, age, and ethnic distribution profiles of the final respondents.
**Results:** From the NHSS cohort of respondents (n=9,631 subjects), 4,633 (48.1%) subjects provided telephone numbers. A total of 3,364 sets of screening questionnaires were completed, out of 4,557 sent (response rate=73.8%). The demographic profile of the responders were not significantly different from the original NHSS cohort profile. The estimated national prevalence of knee OA was 11%. Women (13.1%) had a higher prevalence of knee OA than men (8.8%). The prevalence of knee OA increased with age and was 19.7% for age ≥60 years old, compared to 8.6% for age 18–59 years old. Across the different ethnic groups, knee OA was more prevalent among Indian (20.5%), followed by Malay (17.7%), and Chinese (9.3%).
**Conclusions:** Using a validated screening questionnaire, we estimated the national prevalence of knee OA in the multi-ethnic Singapore population. Indian and Malay had higher prevalence of knee OA, which could be attributed to the higher prevalence of obesity among these ethnic groups as compared to Chinese.[4]

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**Disclosure of Interest:** None declared

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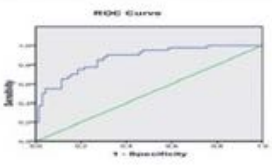
## SAT0464 RISK FACTORS FOR PROGRESSION OF KNEE JOINT OSTEOARTHROSIS IN PATIENTS WITH EARLY GONARTHROSIS IN THE 5-YEAR PROSPECTIVE STUDY

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**Background:** -
**Objectives:** To identify risk factors for progression of knee joint osteoarthrosis (OA) in the first 5 years of disease.
**Methods:** Prospective 5-year study included 110 female-patients with primary knee OA (CCR criteria), in 52 of them disease duration did not exceed 5 years, (mean age – 59,11±8,95 years). All relevant patients' data, including anthropometric parameters, case history, evaluation of pain intensity by VAS, knee joint status and therapeutic modalities used during the follow up period were recorded in individual patient's file. Instrumental diagnostic methods used in each patient included plain radiography of knee joints (gonarthrosis stage was classified by Kellgren J.- Lawrence J. scale), dual energy X-ray absorptiometry (DEXA) of the lumbar spine, femoral neck and of subchondral bone of the hip and tibia, ultrasound (US) and MRI examination of knee joints. First OA stage was documented in 22 (42,3%) out of 52 patients, 2-nd - in 24 (46,2%) patients, 3d stage - in 6 (11,5%) patients.
**Results:** During 5 year follow up radiographic progression of knee OA was documented in 14 patients (Group with progression), while in 38 patients radiographic stage remained unchanged. Patients from both groups were similar in terms of age (58,29 ± 7,68 vs 56,05 ± 8,74 years), and disease duration (3,43 ± 1,34 vs 3,47 ± 1,33 years). Although, patients with OA progression had more intense knee pain when walking: 60,36 ± 18,33 vs 48,71 ± 17,81, $p$=0,043 (mm); higher BMI: 34,45 ± 4,60 vs 28,92 ± 4,92, $p$=0,001 (kg/m$^2$); higher incidence of synovitis: 57,1% vs 18,4%, $p$=0,006 based on US findings, bone marrow edema in medial tibia aspect 64,3% vs 13,2%, $p$=0,001, based on MRI findings, and higher rate of serious medial condyle damage: 50,0% vs 7,8%, $p$=0,001 distinct from patients without OA progression. DEXA identified significantly higher absolute bone mineral density (BMD) values in the lumbar spine 0,91 ± 0,08 vs 0,82 ± 0,11, $p$=0,015 (g/cm$^2$) and femoral neck 0,85 ± 0,09 vs 0,76 ± 0,08, $p$=0,007 (g/cm$^2$), as well as higher BMD in the medial condyle of the tibia 0,95 (0,85–1,24) vs 0,75 (0,65–0,82), $p$=0,001 (g/cm$^2$) as compared to patients without OA progression. Patients' re-examination in 5 years revealed similar statistically significant differences between the groups. Multifactorial analysis identified the following major risk factors, responsible for gonarthrosis progression: synovitis, bone marrow edema, and high BMD values in the medial condyle of the tibia, while intake of chondroitin sulfate (ChS) and glucosamine (GA) combination for more than 6 months a year during 5 years was identified as risk reduction factor. Based on identified factors and their coefficients a predictive model was suggested (with area under the ROC curve equal to 0,93), allowing to prognosticate the future course of the disease in an individual patient with high accuracy, i.e. 85,7%, sensitivity and 84,2% specificity.

| Factors | Discriminant function coefficients |
|---|---|
| US: synovitis | 2,17 |
| MRI: bone marrow edema | 3,19 |
| Tibial medial condyle BMD | 5,19 |
| Intake of ChS and GA | −1,03 |
| Constant | 11,83 |

ROC-curve



**Conclusions:** synovitis, bone marrow edema, and high subchondral BMD in the medial condyle of the tibia are the major risk factors responsible for progression of knee OA in patients with disease duration up to 5 years. While intake of ChS and GA had a positive impact on radiological OA progression.
**Disclosure of Interest:** None declared
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## SAT0465 SENSORIMOTOR PERFORMANCE AND FUNCTION IN PEOPLE WITH OSTEOARTHRITIS OF THE HAND: A CASE-CONTROL COMPARISON

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**Background:** Hand osteoarthritis (OA) is a common cause of pain and disability, affecting 20% of adults over age 70 [1]. Classically this pathology has been attributed solely to impairments of peripheral structures (e.g. joint and surrounding tissues). However, recent evidence has shown that changes in the central nervous system may contribute to the maintenance of pain and disability [2]. To date no evidence has focused on brain related sensorimotor impairments in hand OA, highlighting the need for further studies on this topic. We hypothesised that patients with hand OA would present with evidence of sensorimotor impairments and that these changes would be correlated to hand function.
**Objectives:** To determine whether motor imagery (MI), tactile acuity, and body perception, are disrupted in people with hand OA. To verify if a correlation exists between these measures and hand function in people with hand OA.
**Methods:** Twenty patients with symptomatic hand OA and 19 healthy pain-free controls undertook MI (hand left/right judgments), a brain speed processing task (controls left/right judgments), two-point discrimination (TPD) threshold testing, a neglect-like symptoms questionnaire (assessing body perception) and hand performance tests.
**Results:** People with hand OA were slower and less accurate in the MI task ($P$ <0.05) when compared to healthy controls, with no brain processing differences between groups. No difference was found between groups for two-point discrimination measures. Patients with hand OA presented with higher ($P$ <0.05) scores on the neglect-like questionnaire. Interestingly, people with left hand pain demonstrated enhanced neglect-like symptoms ($P$ <0.05) compared to those with right-sided hand pain. A correlation between TPD thresholds and measures of hand performance was identified, however no relation was found between MI and hand function.
**Conclusions:** Patients with hand OA demonstrate brain related sensorimotor deficits. Additionally, the side of the pain appears to influence body perception, probably due to differences in right and left hemispheric functions. Sensorimotor measures partially correlate to function, specifically tactile acuity is moderately related to hand function.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2294

## SAT0466 PROGRESSION OF PAIN AND ULTRASOUND DETECTED SYNOVITIS IN PATIENTS WITH EROSIVE HAND OSTEOARTHRITIS OVER ONE YEAR

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**Background:** Hand osteoarthritis (HOA) is a common and frequent cause of pain. HOA is a heterogeneous group of disorders with two main subsets including non-erosive disease and erosive, sometimes referred to as inflammatory, HOA. Few studies demonstrated inflammatory ultrasound changes and more severe clinical symptoms in patients with erosive compared with non-erosive disease, however the results are inconclusive.
**Objectives:** The aim was to evaluate progression of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a one-year longitudinal study.
**Methods:** Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling were assessed. Patients reported joint pain on 100 mm visual analogue scale (VAS). Pain, joint stiffness and disability were assessed by the Australian/Canadian OA hand index (AUSCAN). Radiographs of both hands were examined and erosive disease was defined by at least one erosive interphalangeal joint. Synovial hypertrophy and power Doppler signal (PDS) were scored with ultrasound. Synovitis was graded on a scale of 0–3 and osteophytes were defined as cortical protrusions seen in two planes. Patients were examined at baseline and one-year follow-up.
**Results:** Altogether, 129 patients (12 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2015. Out of these patients, 72 had erosive disease. The disease duration ($p$<0.01) was significantly higher in patients with erosive compared with non-erosive disease at the study entry.
Patients took symptomatic slow-acting drugs (SYSADOA) twice a year, non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics on demand. Duration of morning stiffness ($p$<0.01) and number of clinically swollen joints ($p$<0.05) were significantly higher in patients with erosive compared with non-erosive disease at study entry. Duration of morning stiffness ($p$<0.05) become shorter in patients with erosive, but not in those with non-erosive disease, however the number of clinically swollen joints were not significantly changed at one year follow-up in both groups.
According to the AUSCAN, patients with erosive compared with non-erosive disease had more pain ($p$<0.05) and stiffness ($p$<0.01) at study entry. Pain, but not stiffness, got worse ($p$<0.05) in patients with erosive compared with non-erosive disease. US-detected pathologies such as gray-scale synovitis total score ($p$<0.001), intensity of PDS ($p$<0.01) and number of osteophytes ($p$<0.01) were significantly higher in patients with erosive compared with non-erosive disease at study entry and got worse in gray-scale synovitis total score ($p$<0.01), intensity of PDS ($p$<0.01) and numerically also in number of osteophytes ($p$<0.1) at one-year follow-up. There were no significant differences in consumption of NSAIDs and SYSADOA for OA between both groups during the study.
**Conclusions:** This study shows that pain associated with US-detected synovial hypertrophy, inflammatory signs and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease and is more likely to progress over one year.
**Acknowledgement:** This work was supported by the project (Ministry of Health, Czech Republic) for consensual development of research organization 023728.

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## SAT0467 NEUROPATHIC PAIN IN KNEE OSTEOARTHRITIS: IS ITS PREVALENCE RELATED TO A GREATER IMPACT?

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**Background:** Knee osteoarthritis (OA) is a common and progressive joint disease with an estimated incidence rate of 240 per 100000 person-years. Pain from Knee OA is generally classified as nociceptive; however, a neuropathic component is possible.
**Objectives:** The objective of this study was to determine the prevalence of neuropathic pain (NP) in patients with painful knee OA using the DN4 questionnaire and to evaluate the relationship between NP, pain intensity, WOMAC function and stage of OA.
**Methods:** We included in this study patients with knee osteoarthritis according to ACR criteria. Pain score using Visual Analogue Scales (VAS), Western Ontario and McMaster Universities Osteo-arthritis Index (WOMAC), DN4 score, duration of symptoms, severity of OA using the Kellgren-Lawrence (KL) system, were evaluated using a Pearson's correlation coefficient. $p<0.05$ was considered statistically significant.
**Results:** One hundred patients (96 females, 4 males) with a mean±SD age of 59.4±10.4 years were included in the study. Mean±SD duration of symptoms was 72±54 months. The mean ± SD VAS was 5.2±2 and the total WOMAC 50±19. The prevalence of neuropathic pain was 26%. DN4 score was significantly correlated with the VAS (r=0.6, p=0.0001) and the WOMAC (r=0.53, p=0.0001). However, there was no significant correlation between DN4 score and KL grade.
**Conclusions:** DN4 score classified 26% of pain from knee OA as NP. Patients with severe pain and disability may have a NP component in their knee OA pain. It is important to be aware of considering the existence of NP in the treatment of knee OA pain.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5042

## SAT0468 DIFFERENTIAL PROFILE OF ENDOGENOUS PEPTIDES DETECTED BY TARGETED PROTEOMICS IN CARTILAGE SECRETOME, SYNOVIAL FLUID AND SERUM FROM OSTEOARTHRITIS PATIENTS AND CONTROLS

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**Background:** Peptidomics is an emerging field branching from proteomics that targets endogenously produced protein fragments. A peptidomic analysis that we recently performed enabled the identification of endogenous peptides that were differentially released from wounded (WZ) and unwounded (UZ) zones of human articular osteoarthritic cartilage, compared to healthy tissue.
**Objectives:** In the present work, we aimed to develop a targeted method for the quantitative monitoring of this panel of peptides in synovial fluids and sera from osteoarthritis (OA) patients, in order to unravel the putative biomarker value of these molecules.
**Methods:** Synovial fluid and serum samples were obtained from OA patients at different stages of the disease. Proteins secreted from human articular cartilage (secretomes) were obtained by culture of tissue explants, according to optimized procedures [1]. The enrichment of endogenous peptides in these three types of samples was standardized, using ultrafiltration procedures and solid phase extraction (SPE) with reversed phase (C18) resins. A method for the targeted identification of endogenous peptides by Multiple Reaction Monitoring (MRM)-mass spectrometry was developed employing cartilage secretome samples, and then applied on synovial fluid and serum. The peptides were separated by nano-LC coupled to a 5500 QTRAP mass spectrometer. Data analysis was performed using the Skyline software. Peptide identifications were searched against a human database (human_fasta) using the ProteinPilot program.
**Results:** The peptidomic study led to the identification of a panel of 262 peptides corresponding to 36 different proteins that were differentially released from the WZ and UZ in OA cartilage. From these, we first performed independent data analyses (IDA) by mass spectrometry using cartilage secretomes and synovial fluids to detect those peptides that are better identified in these types of samples, which led to a list of 27 different peptides. Then, a final MRM method was designed for the detection of these peptides, belonging to unique proteins that were characteristic of human articular cartilage.
**Conclusions:** A multiplexed targeted method for the simultaneous identification of a panel of 17 endogenous peptide released from 7 proteins characteristic of articular cartilage has been developed. The proteins detected are Cartilage oligomeric matrix, Cartilage intermediate layer protein 1, Fibronectin, Prolargin, Dermcidin, Matrix gla protein, Clusterin and Glia-derived nexin. This method is based on liquid chromatography-multiple reaction monitoring (LC-MRM) mass spectrometry. By these means, endogenous peptides were simultaneously detected and relatively quantified in synovial fluids and sera from OA patients and controls. Further qualification studies will be necessary to establish their usefulness for OA diagnosis and progression studies.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4970

## SAT0469 OSTEOARTHRITIS IS THE MOST FREQUENT CAUSE OF RHEUMATHOID ARTHRITIS MISDIAGNOSIS IN A COLOMBIAN SPECIALIZED CENTER

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**Background:** There is a lack of expertise in rheumatoid arthritis (RA) diagnosis in primary level of Colombian medical centers, leading to misdiagnosis; many times osteoarthritis (OA) and another rheumatic diseases are misdiagnosed as RA which derives in wrong treatment for patients with clinical and health economics implications.
**Objectives:** The objective of this study was to describe demographic and clinical characteristics of a cohort of patients derived to a specialized RA center with presumptive RA diagnosis and finally diagnosed as osteoarthritis.
**Methods:** A descriptive cross sectional study was done. Patients referred to a specialized RA center in a 48 month period with presumptive diagnosis of rheumatoid arthritis were assessed. Each patient was evaluated to confirm or rule-out diagnosis of RA as follows: a rheumatologist fulfilled a complete medical record, including all previous clinical, laboratories and imaging data; it was assessed rheumatoid factor, anti-citrullinated antibodies and other laboratories depending on each case. Also were made x-rays of hands and feet, and in some cases of persistent doubt about the diagnosis was requested comparative MRI of hands or/and feet. Frequencies and percentages were calculated for the demographic and clinical characteristics of the cohort of patients in which the diagnosis of RA was ruled-out.
**Results:** A total of 5176 patients derived during the last four years to specialized in RA center with presumptive RA diagnosis, after medical, laboratory evaluation and imaging had a wrong RA diagnosis; of them patients 2930 (57%) had finally osteoarthritis diagnosis and of these patients 2594 (88%) were women and 336 (12%) men, with an average age of 59 ± 13 years old. Majority of these patients were followed by general physicians or internists and treated with non-biologic and some few cases with biologic disease modifying anti-rheumatic drugs (DMARDs) in the past years, for an average time of 4.5 years.
**Conclusions:** In this cohort of patients the most frequent diagnosis of patients misdiagnosed with RA was osteoarthritis, being more than two thirds of them, predominantly women. This shows the need for the implementation of specialized clinics in RA and educational strategies for primary care physicians in order to avoid the impact of this wrong diagnosis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5150

## SAT0470 VALIDITY AND RELIABILITY OF THE CHINESE VERSION OF THE PAINDETECT QUESTIONNAIRE IN SUBJECTS WITH KNEE OSTEOARTHRITIS

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**Background:** Patients with knee osteoarthritis (KOA) may have pain sensitization which is a potential risk factor for chronic pain after total knee replacement surgery (TKR). A neuropathic pain questionnaire may facilitate the identification of patients with KOA who has central sensitization.
**Objectives:** We aim to evaluate the validity and reliability of the Singapore Chinese version of the painDETECT questionnaire (PDQ-Chi).
**Methods:** The PDQ-Chi was cross-culturally adapted from the source English version with forward and backward translation according to standard guidelines, followed by cognitive debriefing in ten patients with KOA. The PDQ-Chi was administered to consecutive KOA patients enlisted for TKR in two weeks' time. The construct validities of the 7-items and 9-items PDQ-Chi were evaluated in comparison with the pressure pain threshold measured at medial knee joint line (the side that is going for TKR), and the volar area of right forearm. Test retest reliability was assessed by intraclass correlation coefficient (ICC) and classification consistency (proportion with no change in pain phenotype), in a subset of patients on day of TKR.

**Results:** 165 patients (82.4% women, mean age 67.5 ± 7.8 years) were recruited to the study. The patients generally had low scores for PDQ-Chi (mean 4.9 ± 3.9). Only one patient had neuropathic pain as classified by PDQ-Chi (score ≥19). The Cronbach's alpha of the 7-items and 9-items PDQ-Chi were 0.60 and 0.58 respectively. Factor analysis of the 7-items PDQ-Chi revealed a 2-factor structure that explained 48% of total variance. The 9-items total PDQ-Chi scores correlated with pain scores, but not pressure pain threshold of knee or forearm. The PDQ-Chi did not correlate with the hypothesized trait of measurement. 17 patients administered the PDQ-Chi a second time on the day of TKR. The ICC of the 7-items and 9-items PDQ-Chi was 0.59 and 0.50, respectively; while the classification consistency of the 9-items PDQ-Chi was 94%.
**Conclusions:** In this group of patients with KOA enlisted for TKR, both the 7-items and 9-items of PDQ-Chi were suboptimal in internal consistency and hypothesis testing. Using the 9-items PDQ-Chi with cut-offs as screening instrument for neuropathic pain, it had good classification consistency. Further studies with larger sample size are required for criterion validity.
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**Disclosure of Interest:** None declared
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## SAT0471 OSTEOARTHRITIS IS RELATED TO CARDIOVASCULAR DISEASE AND INCREASED ARTERIAL STIFFNESS. A CASE-CONTROL STUDY

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**Background:** Osteoarthritis (OA) is associated with an increased risk of CVD[1], but confounder bias has not been sufficiently explored in observational studies. Pulse wave velocity (PWV) and augmentation index (AIx) are predictors of future CVD events.
**Objectives:** To investigate the relationship between OA and CVD, PWV and AIx, accounting for confounders.
**Methods:** All residents of Ullensaker municipality, aged between 40 and 79 years were mailed a questionnaire concerning general health and musculoskeletal pain (Musculoskeletal pain in Ullensaker Study (MUST)). Respondents who reported having OA were invited to an extended clinical examination at Diakonhjemmet Hospital, Oslo, Norway. OA was diagnosed according to the ACR clinical classification criteria. Demographics and co-morbidities were recorded on questionnaires. AIx and PWV were measured (Sphygmocor apparatus, Atcor®). Participants in the Oslo control cohort were recruited by Statistics Norway, and underwent a similar data-collection (response rate 41%). Data from the Anglo-Cardiff Collaborative Trial (ACCT), a community based population study (response rate 85%) from the United Kingdom, formed a secondary control population. In separate logistical regression models, adjusted for age, sex, we compared the odds ratio (OR) for CVD and elevated AIx and PWV (dichotomized at median) between participants in MUST, ACCT controls and Oslo controls. Patients with hand OA were compared against patients with lower limb OA (hip and/or knee OA). AIx was adjusted for heart rate and height, whereas PWV was adjusted for heart rate. A confounder was defined as a variable which changed the estimate of the exposure effect by ≥20% when entered into the model.
**Results:** Out of 583 patients in MUST with self-reported OA, 153 (26.2%) had isolated hand OA according to the ACR criteria and 153 (26.2%) had lower limb OA. 134 persons consented to participate in the Oslo control cohort. 1111 patients without inflammatory joint disorders from the ACCT were randomly selected as controls. The age and sex adjusted logistical regression models are presented in the table. Analyses with additional adjustment for smoking, BMI, CRP, anti-hypertensive and statin treatment, respectively, gave similar results.

Table 1

| | MUST vs ACCT | MUST vs Oslo controls | Hand OA vs Lower limb OA | ACCT vs Oslo controls |
|---|---|---|---|---|
| CVD dependent variable, OR (95% CI) | 4.2 (2.7, 6.3)** | 2.0 (0.7, 5.4) | 0.5 (0.2, 1.0)* | 0.5 (0.2, 1.4) |
| AIx dependent variable, OR (95% CI) | 2.4 (1.8, 3.3)** | 1.6 (0.9, 2.8) | 1.0 (0.6, 1.7) | 0.9 (0.5, 1.5) |
| PWV dependent variable, OR (95% CI) | 1.4 (1.1, 1.8)* | 1.0 (0.6, 1.7) | 0.8 (0.4, 1.4) | 0.9 (0.6, 1.6) |

*p<0.05, **p<0.001.

**Conclusions:** Patients with OA have an increased frequency of CVD, and higher levels of AIx and PWV, compared to ACCT controls. Lower limb OA seems to be associated with CVD to a greater extent than hand OA. No confounder variables were identified in these analyses.
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**Disclosure of Interest:** None declared
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## SAT0472 IS ELECTROTHERAPY EFFECTIVE IN THE MANAGEMENT OF PAIN, RANGE OF MOTION, QUALITY OF LIFE, EDEMA FOLLOWING TOTAL KNEE ARTHROPLASTY SURGERY? RANDOMIZED CONTROLLED TRIAL

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**Background:** Knee osteoarthritis is a current problem that causes limitations in patients' activities of Daily living (1). There are many therapeutic options. Total knee arthroplasty is one of these treatment methods.Postoperative pain is one of the most commonly seen problems after this operation.The target of postoperative pain management is pain alleviation with minimum morbidity that is caused by analgesic modalities (2). Interferential current (IFC) therapy is a physical modality whose effects on postoperative pain, range of motion, edema and analgesic use has previously been shown (3).
**Objectives:** In this double-blind randomized controlled study, we aimed to investigate the effectiveness of interferential current (IFC) following total knee arthroplasty (TKA) surgery
**Methods:** 98 patients who had TKA surgery were included into the study. Patients were randomized into two groups: Group 1: IFC (n=49) and group 2: sham IFC group (n=49). After all patients received the same rehabilitation programme and cold pack, the patients in group 1 administered IFC 30 minutes 2 times a day for 5 days. Same treatment instructions were given in sham group blindly. Patients were assessed at days 0, 5 and 30th after surgery with following parameters: VAS pain (cm), edema (cm), range of motion (ROM), Short Form 36 (SF 36) and paracetamol intake (gr)
**Results:** All patients had significant improvements in all evaluation parameters ($p<0,05$) except the subscales of the physical role and mental health in the SF 36. In comparison of the groups, paracetamol intake was significantly lower in the IFC group at 5th day ($p<0.05$). There was no difference between groups for other evaluation parameters in all visits.
**Conclusions:** Although all patients showed significant improvement in all parameters during the study, paracetamol intake was significantly lower in the IFC group. This finding supports that IFC can decrease pain -even postoperative pain-. However, it is still uncertain which frequency is most suitable, how many times and how much minutes we need to use IFC in these patients in order to improve pain significantly.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2036

## SAT0473 POOR DIETARY CARBOHYDRATE QUALITY IS ASSOCIATED WITH SYMPTOMATIC KNEE OSTEOARTHRITIS IN WOMEN: A CROSS-SECTIONAL STUDY

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**Background:** Knee osteoarthritis (KOA) related to metabolic stress and its risk factors, so called metabolic KOA, is a well-known subtype. Recent epidemiologic studies showed that poor dietary carbohydrate quality, such as a high proportion of carbohydrate energy intake as sugar, is associated with a higher risk for metabolic complications and cardiovascular mortality.
**Objectives:** The purpose of this study was to analyze dietary nutritional factors

associated with KOA, focusing on the dietary glycemic index (DGI), a higher score of which means poor dietary carbohydrate quality.
**Methods:** This was a cross-sectional study including 9,203 participants aged ≥50 years from The Fifth Korean National Health and Nutrition Examination Survey, who were selected using two-step stratified clustered equal-probability systematic sampling. Radiographic KOA (RKOA) was defined as a Kellgren-Lawrence grade of ≥2. Dietary information was obtained using the 24-hour dietary recall method. The quality of dietary carbohydrate was calculated using glycemic index (GI) based on glucose (GI of glucose being 100). The amount of carbohydrate (g) from each food item participants recalled having had in the previous 24 hours was multiplied by the GI of each item, and the products were summed. The summation was divided by total carbohydrate intake (g) in the 24 hours, and the resulting average GI, the DGI was used as the measure of dietary carbohydrate quality. Sensitivity analysis was performed in a sub-population not undergoing diet modification for weight loss, and excluding participants having extremely high or low dietary energy intake (beyond 2 standard deviation of the distribution). All analyses were stratified by sex and weighted for the sampling design.
**Results:** The prevalence of each knee-state group was as follows: normal (NO) 72.0% (95% CI 70.2%–73.8%), radiographic KOA (RKOA) 16.8% (15.3%–18.3%), chronic knee pain without RKOA (CP) 6.8% (5.9%–7.8%) and symptomatic RKOA (SRKOA) 4.4% (3.8%–5.2%) in men, and NO 47.3% (45.4%–49.2%), RKOA 23.9% (22.4%–25.4%), CP 9.6% (8.7%–10.6%) and SRKOA 19.2% (17.8%–20.6%) in women. In women, DGI was significantly higher in CP (61.2 [SE 0.4]) and SRKOA group (63.1 [0.3]) than in NO group (59.3 [0.2]), and the estimates for age-adjusted mean difference were 1.3 (SE 0.4, P-value 0.007) for CP group and 1.2 (0.3, 0.001) for SRKOA group. In analysis adjusted for age, obesity and the day of week of the dietary recall, the association with SRKOA across quintiles of DGI was Q1 1.00 (reference), Q2 OR 1.20 (95% CI 0.81–1.76), Q3 1.54 (1.09–2.18), Q4 1.63 (1.14–2.32) and Q5 1.73 (1.22–2.44; P value 0.025). CP did not show a linear relationship across the quintiles of DGI. RKOA was not significantly associated with DGI. The association was consistent in the sub-population of no dietary modification and no extreme energy intake. In men, there was no significant association between DGI and any knee state.
**Conclusions:** There was a significant association between poor dietary carbohydrate quality and symptomatic KOA in women. This study provides the foundation for clinical research that addresses the causality of the relationship and the effect of dietary modification on KOA and its co-morbidities.
**Disclosure of Interest:** None declared
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## SAT0474 A PROTEOMIC PANEL PREDICTS DRUG RESPONSE TO THE COMBINATION OF GLUCOSAMINE AND CHONDROITIN SULFATE

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**Background:** Biomarkers can help identify patients that are more likely to respond favorably to a given therapy (a Predictive or patient stratification biomarker). Biomarkers can also be used to provide objective proof of a biological response to a drug (Efficacy of Intervention biomarker).
**Objectives:** The overall goal of this project was to identify protein biomarkers that predict likelihood of response to glucosamine hydrochloride and chondroitin sulfate (GH+CS), both predictive and efficacy of intervention biomarkers. We hypothesized that a subset of peptides in a mass spectrometry panel, developed to predict Osteoarthritis (OA) progression, would identify responders to GH+CS, knowing that CS is an NFkB activity and inflammation inhibitor.
**Methods:** This study analyzed a subset of 80 baseline serum samples from the MOVES (Multicentric Osteoarthritis Intervention Study with SYSADOA) trial[1]. The MOVES trial was an international multicentric, phase IV, double-blind, non-inferiority, randomized trial to compare the efficacy and safety of the combination of glucosamine hydrochloride (GH 1.500mg/day) and chondroitin sulfate (CS 1.200mg/day) known as Droglican® (Bioiberica), versus celecoxib Celebrex (200mg/day) in patients with Kellgren Lawrence grades 2–3 knee OA with severe pain. The sample selected for this study consisted of half drug responders and half non-responders by OARSI-OMERACT criteria. A total of 25 peptides from 23 proteins were analyzed by mass spectrometry. This panel was based on results of discovery proteomic studies in synovial fluid (n=23), urine (n=45) and serum (n=40) from knee OA subjects to identify biomarkers indicative of an OA diagnosis and OA progression.
Quantitative LC/MRM was performed on a 1 μg of protein digest spiked with 10 fmol of 25 stable isotope labeled peptides using a nanoAcquity UPLC system (Waters Corp) coupled to a Waters Xevo TQ-S triple quadrupole mass spectrometer via a nanoelectrospray ionization source. Technical variability (based on spiked in yeast alcohol dehydrogenase was 10.4%). Logistic regression was used to evaluate the association of demographics (age, gender and BMI) and the biomarkers with drug response (yes/no) after 180 days of treatment. P values <0.05 were considered significant.
**Results:** The sample was 90% female, mean age 64 (SD 7) years, 55% with BMI >30 kg/m$^2$. Higher age (p=0.004) but neither gender, nor KL grade were associated with likelihood of drug response. Age plus the marker panel significantly predicted drug response (overall model p=0.0007). In the multivariable logistic regression, adjusted for age, a total of 12 peptides, corresponding to 11 proteins, were significantly independently associated with drug response (p<0.0001 by Effect likelihood Ratio tests).
**Conclusions:** These biomarkers in theory could be used to stratify different patient groups in terms of likelihood of clinical response to GH+CS in efforts to develop personalized treatment algorithms for OA patients.
**References:**
[1] Hochberg et al. ARD 2015.
**Disclosure of Interest:** None declared
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## SAT0475 HEALTH SYSTEM FRUSTRATION EXPRESSED BY PATIENTS WITH KNEE OSTEOARTHRITIS

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**Objectives:** To explore the challenges experienced by patients with knee osteoarthritis.
**Methods:** A structured interview was conducted with patients that fulfilled the ACR classification criteria for knee osteoarthritis (OA) (1991). We collected data on demographic and socioeconomic characteristics, use of health and social services, and effect on occupation and living arrangements over the previous 12 months. The patients completed Knee Osteoarthritis Outcomes Score (KOOS) and Patient Satisfaction Questionnaire. This study was conducted according to the principles of the Declaration of Helsinki (1996) and Good Clinical Practice.
**Results:** There were 51 patients enrolled in the study including 39 females (76,5%), mean age 64,45 ±8,07 (range 50–82) and the disease duration was 9,9±6,97 (range 2–24) years. Knee pain was present in 49 (96%) of patients. The radiographic characteristics: KL I – 1 (1,9%), II – 29 (56,9%) patients, KLIII – 17 (33,3%) and the most severe form KLIV – 4 (7,9%) cases. The KOOS results showed that Pain was 59,6±20,6%, Symptoms 63,74±17,38%, Activity Daily Living – 45,35±21,1%, the possibility to practice sport was the worse score 25,69±25,2%, and the QoL-37,66±28,88% qualified as low. Patients notice health system frustration: poor communication (70,6%), uncoordinated health services (86,2%), lack of efficient and timely information (41,2%), that determine the difficulties in making decisions about their care. The patients in 50 (98,0%) cases manifested a high level of dissatisfaction with financial aspects (the out-pocket expenders representing 29,7% from incomes) and low level of social support.
**Conclusions:** Patients with knee osteoarthritis experience social-economic and organizational difficulties, their pointing could lead to the improvement of the quality of medical care and increased patient's satisfaction.
**Disclosure of Interest:** None declared
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## SAT0476 EFFICACY OF 14% PLAI VS. PLACEBO CREAMS FOR SYMPTOMATIC CONTROL OF PATIENTS WITH KNEE OSTEOARTHRITIS

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**Background:** Non-operative treatments for mild to moderate knee osteoarthritic (OA) is recommended. Plai (Zingibercassumunar Roxb.) belongs to the ginger family. It is a Thai herb used in Thai traditional medicine for relieving muscle and joint pain (1–2). Plai has anti-inflammatory activities due to compounds found in its extracts (1–4). These findings suggest that topical plai cream is a potentially useful drug for the treatment of painful OA of the joints. Since there have not been any studies on the efficacy of plai cream alone for relieving symptoms of OA knee joint, we aimed to test its value.
**Objectives:** To assess the efficacy of topical plai cream for the treatment of primary osteoarthritis (OA) knee.
**Methods:** This was a 9-week (4 weeks treatment + 1 week wash-out + 4 weeks placebo) phase III randomized, double-blind, controlled, cross-over, community trial of Plai vs. placebo, in adults with OA of the knee. This study aimed to determine whether Plai cream was more effective at reducing pain than a placebo cream, as measured using a visual analog scale (VAS) plus the Western Ontario McMaster (WOMAC) score.
**Results:** A total of 120 pairs of subjects were enrolled. The mean different VAS favoring Plai varied between 0.46 and 1.4 (p<0.05). The respective percentage of patients in the Plai group who reached MCII of VAS, WOMAC pain, stiffness and function was 37.9%, 40.10%, 26.45% and 54.58%. The respective percentage of patients in the Plai group who experienced 50% improvement of VAS, WOMAC pain, stiffness and function was 33.33%, 31.77%, 41.66% and 24.68%. The respective number of cases needed to treat to reduce pain of Plai based on MCII and 50% improvement of VAS was 2.63 (95% CI; 2.44, 2.84) and 3 (95% CI; 2.75, 3.29). Four cases in the Plai group had a mild skin reaction.
**Conclusions:** This cross-over, randomized, controlled, communit, trial demonstrated that Plai cream is an effective topical agent for relieving the symptoms of mild to moderate OA knee.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1132

## SAT0477 LYSOPHOSPHATIDYLCHOLINES TO PHOSPHATIDYLCHOLINES RATIO PREDICTS ADVANCED KNEE OSTEOARTHRITIS

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**Background:** Knee Osteoarthritis (OA) is a heterogeneous disease with variable clinical outcomes. Some patients do not have any symptoms or significant functional loss for many years after the onset of the disease whereas others can progress rapidly to advanced stage [1], making it highly clinical relevant to identify those who are at high risk of progressing rapidly so that targeted interventions at early stage of the disease can be implemented [2–4].
**Objectives:** To identify novel biomarker(s) for predicting advanced knee OA.
**Methods:** Study participants were derived from the NFOAS and the TASOAC studies. All knee OA cases were patients who underwent total knee replacement (TKR) due to primary OA. Metabolic profiling was performed on fasting plasma using a targeted metabolomics approach. 4,018 plasma metabolite ratios that were highly correlated with that in synovial fluid in our previous study [5] were generated as surrogates for joint metabolism.
**Results:** The discovery cohort included 64 TKR cases and 45 controls and the replication cohorts included a cross-sectional cohort of 72 TKR cases and 76 controls and a longitudinal cohort of 158 subjects, of whom 36 underwent TKR during the 10-year follow-up period. We confirmed the previous reported association of the branched chain amino acids to histidine ratio with advanced knee OA ($p=9.3\times10^{-7}$) and identified a novel metabolic marker - lysoPCs to PCs ratio - that was associated with advanced knee OA ($p=1.5\times10^{-7}$) after adjustment for age, sex, and BMI. When the subjects of the longitudinal cohort were categorized into two groups based on the optimal cutoff of 0.09 of the ratio, we found the subjects with the ratio $\geq$0.09 were 2.3 times more likely to undergo TKR than those with the ratio $<$0.09 during the 10-year follow-up (95% CI: 1.2–4.3, p=0.02).
**Conclusions:** We identified the ratio of lysoPCs to PCs as a novel metabolic marker for predicting advanced knee OA. Further studies are required to examine whether this ratio can predict early OA change.
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## SAT0478 COMORBIDITY IN HAND OSTEOARTHRITIS: ITS IMPACT ON HAND PAIN AND FUNCTION

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**Background:** Although hand pain and function are important complaints in patients with hand osteoarthritis (OA), their determinants are unclear. Comorbidity is shown to be associated with complaints in knee and hip OA.
**Objectives:** Therefore, we studied the association of comorbidities with hand pain and function in hand OA patients.
**Methods:** Cross-sectional data were used of the HOSTAS (Hand OSTeoArthritis in Secondary care) study, which included consecutive patients diagnosed by their treating rheumatologist with primary hand OA from 2009 to 2015. Self-reported comorbidity was assessed by a 17-item list (modified Charlson index). Additionally, presence of knee and/or hip OA (poly OA) was determined by fulfilling the ACR criteria and presence of obesity by body mass index (BMI) $\geq$30 kg/m$^2$. Number of comorbidities (max 19) and groups of comorbidities (figure) were studied. Self-reported hand pain (0–20) and hand function (0–36) were assessed by Australian/Canadian Hand OA Index (AUSCAN, Likert scale), where higher scores mean worse health. Multivariable linear regression analysis was used to associate comorbidities with hand pain and function, adjusting for age, sex and education (3 categories, as proxy for socioeconomic status). To assess clinical relevance, we compared mean differences between absence and presence of specific comorbidities, with the minimal clinically important improvement (MCII, published by Bellamy et al.), which was 1.6 (95%CI 1.0 to 2.0) for pain and 1.4 (0.1 to 2.2) for function.
**Results:** 538 patients were included with a mean (SD) age of 61 (9) years, mean BMI of 27 (5) kg/m$^2$, 86% women and 91% fulfilling the ACR hand OA criteria. 27% had a low education level. 38% of patients reported $\geq$1 comorbidity (of 17), 24% had poly OA (mainly knee) and 23% had obesity. Mean (SD) pain and function were 9.3 (4.3) and 15.6 (8.5), where women had worse scores than men. Presence of any comorbidity was associated with worse pain and function; mean difference (95%CI) pain 1.1 (0.3 to 1.9) and function 1.8 (0.2 to 3.3). Also the number of comorbidities resulted in worse complaints (regression coefficient (95%CI) pain 0.8 (0.4 to 1.1) and function 1.4 (0.8 to 2.1)). Presence of poly OA or lung disease was associated with both pain and function, while presence of cardiovascular disease was associated with pain only and osteoporosis with function only. Other comorbidities, like obesity, were not associated (figure). For pain, only the presence of cardiovascular disease was similar to the MCII, while all associations (i.e. presence of any comorbidity, poly OA, osteoporosis and lung disease) were clinically relevant for function. For example, presence of lung disease resulted in 3.4 points higher (worse) score for function (figure), while MCII was 1.4, so this difference could be considered clinically relevant.

**Figure:** Association between specific comorbidities and hand pain or function. Mean differences with 95% confidence intervals, adjusted for age, sex and education.

| Comorbidity | Present/absent, n of patients | Self-reported pain | Self-reported function |
|---|---|---|---|
| Poly OA (ACR knee/hip) | 161/366 | **0.8 (0.01 to 1.7)** | **1.9 (0.3 to 3.5)** |
| Osteoporosis | 42/477 | 1.2 (-0.3 to 2.6) | **3.7 (0.9 to 6.5)** |
| Obesity | 121/402 | 0.6 (-0.3 to 1.5) | 1.1 (-0.7 to 2.8) |
| Diabetes mellitus* | 40/479 | 1.1 (-0.4 to 2.5) | 1.5 (-1.3 to 4.3) |
| Lung disease (COPD) | 58/461 | **1.3 (0.1 to 2.5)** | **3.4 (1.0 to 5.7)** |
| Malignant disease* | 34/485 | 1.2 (-0.4 to 2.8) | -0.2 (-3.2 to 2.9) |
| Gastrointestinal disease* | 24/495 | 1.0 (-0.8 to 2.8) | 2.4 (-1.1 to 5.8) |
| Cardiovascular disease* | 59/460 | **1.6 (0.3 to 2.9)** | 2.0 (-0.5 to 4.4) |

*Diabetes mellitus: combination of diabetes with and without end organ damage. Malignant disease: combination of malignancy and metastatic solid tumor. Gastrointestinal disease: combination of ulcer disease and mild and moderate/severe liver disease. Cardiovascular disease: combination of myocardial infarction, cardiac failure, peripheral vascular disease and stroke.

**Conclusions:** Presence as well as number of comorbidities showed a clinically relevant association with self-reported hand pain and function in patients with hand OA. Remarkably, as in knee OA, not only musculoskeletal comorbidity was associated with hand symptoms, but also non-musculoskeletal comorbidities (lung and cardiovascular disease). Further studies should investigate the role of comorbidities in clinical burden in hand OA and how these can be modified.
**Disclosure of Interest:** None declared
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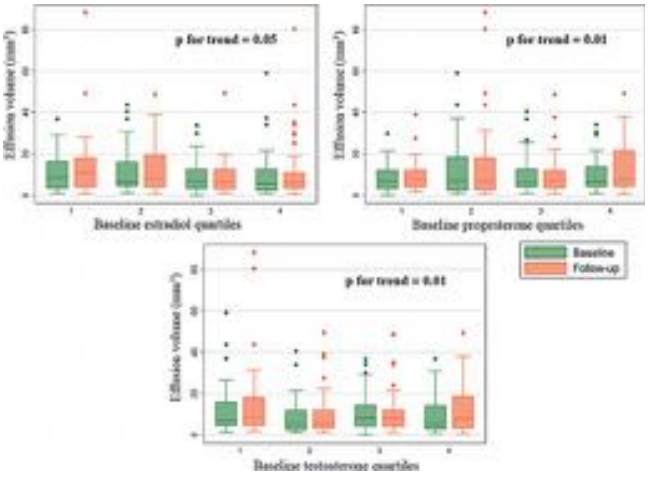
## SAT0479 ASSOCIATIONS BETWEEN ENDOGENOUS SEX HORMONES AND MRI STRUCTURAL CHANGES IN PATIENTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS

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**Background:** Increased prevalence of knee osteoarthritis (OA) among post-menopausal women suggests involvement of endogenous hormones in pathogenesis. However, the effects of endogenous sex hormones on knee OA structures remain uncertain.
**Objectives:** To describe the longitudinal associations between serum levels of estrogen, progesterone and testosterone and knee structural changes using magnetic resonance imaging (MRI) in both males and females with symptomatic knee OA.
**Methods:** We examined 200 participants (mean age 63.0 ± 7.3 years) from a

clinical trial of vitamin D supplement for symptomatic knee OA. Serum levels of estradiol, progesterone, testosterone and sex hormone binding globulin (SHBG) were analyzed at baseline and 24 months later. Magnetic resonance imaging (MRI) scans of the knees were obtained at both baseline and follow-up for the measurement of cartilage volume, cartilage defects, bone marrow lesions (BMLs) and effusion-synovitis volume. Knee pain was assessed using a 100mm visual analogue scale (VAS). Longitudinal data were analyzed using linear mixed-effects model.

**Results:** 107 males and 93 females were included in this study. For females, after adjustment for age, body mass index, and treatment allocation, progesterone was associated with cartilage volume (β =0.12 per quartile, p=0.01). Estradiol levels were associated with lower grades of BMLs (β = -0.45 per quartile, p=0.03), while estradiol (β = -1.26 per quartile, p=0.05), progesterone (β = -1.60 per quartile, p<0.01) and testosterone (β = -1.49 per quartile, p=0.02) were inversely associated with effusion-synovitis volume for females. No consistent associations were observed for males.




**Conclusions:** Endogenous estradiol, progesterone and testosterone may be protective for joint structural changes in women but not men. This may contribute to observed sex differences in knee OA.

**Acknowledgement:** Jodi Barling, Kay Nguo, Judy Hankin and Alice Noone have been involved in the coordination of this study. Rob Warren measured knee cartilage volume.

**Disclosure of Interest:** None declared

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### SAT0480 BONE MARROW LESION IN ADVANCED OSTEOARTHRITIS OF THE KNEES. CORRELATION STUDY BETWEEN HISTO-PATHOLOGICAL FINDINGS AND STRUCTURAL DAMAGE

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**Background:** Osteoarthritis, the most common form of arthritis, is the leading cause of mobility-related disability in elderly persons. With the aging of the population, the prevalence of osteoarthritis is increasing. Loss of hyaline articular cartilage is a central pathologic event in osteoarthritis, but the pathogenesis of cartilage loss is poorly understood. Specifically, there is a paucity of information about what factors identify joints at high risk for progression. Identification of such factors might permit better understanding of the disease process.

**Objectives:** To correlate histopathology of a bone marrow lesion (BML) pattern with severity and structural damage in osteoarthritic knees.

**Methods:** Twenty consecutive patients (age range, 59–66 years; mean, 65 years) referred for total knee replacements were examined with sagittal short inversion time inversion-recovery (STIR) and T1- and T2-weighted MRI one week prior to surgery before surgery. Different structural abnormalities on MRI were compared with those on histologic maps.

**Results:** The histopathology of BML in cases of OA revealed that 6 biopsies of cases showing bone marrow fibrosis (30%), 4 of them grade 1 (20%) and 2 of them grade 2 (10%). 18 biopsies showing cyst (90%), 9 biopsies showing abnormal trabeculae (45%), 2 of them with grade 1 (10%), 4 of them grade 2 (20%) and 3 of them grade 3 (15%). 5 biopsies showing lymphocyte (25%), 40% of them had ++CD3, while 60% of them had ++CD20. 5 biopsies showing fatty marrow (25%), 9 biopsies showing haemosidrotic marrow (45%), 6 biopsies showing blood vessels (30%), 5 of them with grade 2 (25%) and 1 with grade 3 (5%).

The MRI findings of OA patients had been revealed that there were 6 patients with BML of grade 1 (30%), 10 patients of grade 2 (50%) and 4 patients of grade 3 (20%).

**Conclusions:**

– BML has a strong correlation with radiographic everity measurements of osteoarthritis of the knee and pain.
– In patients with knee osteoarthritis, BML in bone underneath cartilage markedly increase risk for structural progression in the knee.
– Hyperemia and hematopoietic marrow were possible reasons for appearance of BML as high signal- intensity on STIR images.
– BMLs are a cornerstone in progression of osteoarthritis.

**Acknowledgement:** My deepest gratitude to prof. Dr. Hassan Bassiouni, for offering me the idea of the research. I would like to thank Prof. Dr. Ibrahim Hassan for his great effort in examination of slides which is the fundamental of our study. My deepest thanks to Ass. Prof. Dr. Sami Abd El-Hakem for his cooperation and continous guidence. My deepest thanks to Ass. Prof. Dr, Abdellah Nazeer who tought me the first steps in MRI which is a fundamental brick in my work. I would like to thank Dr. Ahmed Ali Abdel Aziz for his unlimited support in reviewing the manuscript.

**Disclosure of Interest:** None declared

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## Infection-related rheumatic diseases

### SAT0481 CLINICAL FEATURES ASSOCIATED WITH HIGHER MORTALITY IN ADULTS WITH SEPTIC ARTHRITIS - A 10-YEAR RETROSPECTIVE STUDY

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**Background:** Septic Arthritis (SA) is associated with considerable morbidity and mortality.

**Objectives:** We describe the clinical features and outcomes of SA in patients admitted to a tertiary hospital in Singapore over 10 years.

**Methods:** Adult patients admitted between 2005 and 2015 with diagnosis codes for SA were identified from electronic medical records. Detailed medical record review was performed to confirm the diagnosis of SA based on positive gram stain or cultures from the joint, or alternatively a clinical diagnosis of SA with positive cultures from blood or genital swabs. Patients with negative cultures, purely extra-articular infections and insufficient documentation were excluded. Data were collected by 2 independent researchers with standardization performed on 30 randomly selected patients.

**Results:** 1067 patients were identified from diagnosis codes, of which 249 (23.3%) were confirmed to have culture positive SA. The median (IQR) age at diagnosis was 58 (46, 71) years and 64% were male. Sixty percent were Chinese, 22% Malay and 11% were Indian.

*Clinical features:* The most commonly affected joints were the knee (56.2%), shoulder (12.8%) and ankle (11.6%); 13.6% of patients had involvement of more than one joint. Fever was present in 43% patients and elevated white count (WC) and C-reactive protein (CRP) were observed in 62.6% and 96.8% respectively. Only 2.7% had both a normal CRP and WC. The most common organism was *Staphylococcus aureus* (53%), 29.6% of which (15.6% of all patients) were methicillin resistant *Staphylococcus aureus* (MRSA). Gram negative bacteria and Group B streptococcus (19.7% and 18.1%, respectively) accounted for most of the remaining cases.

*Predisposing conditions:* Pre-existing joint disease was identified in 59 (23.9%) patients (30 gout, 25 osteoarthritis, 5 rheumatoid arthritis and 1 systemic lupus erythematosus). Prosthetic joint infections accounted for 18.9% of cases. 3.6% patients were current intra-venous drug abusers and 27.7% had diabetes. Ten patients had potential preceding joint inoculation, including two with recent intra-articular corticosteroid injection and three with recent acupuncture to the index joint. Data on use of complementary medications and alcohol were not readily available in this retrospective study.

*Treatment and prognosis:* Eighty-three percent patients underwent surgical joint washout. Of those with prosthetic joint infection, 49% required removal of the prosthesis. The median (IQR) duration of intravenous antibiotics was 33 (18, 42) days and median (IQR) length of hospital stay was 21 (11, 35) days. 7.6% patients

Table: Clinical factors and their association with mortality in patients with culture positive septic arthritis

| Variable | Odds ratio (95% Confidence Interval) | P value |
|---|---|---|
| **Age, years (≥ 70 vs. < 70)** | **3.55 (1.09, 11.58)** | **0.04** |
| Female gender (vs. male) | 1.27 (0.39, 4.12) | 0.69 |
| Diabetes mellitus (vs. no diabetes) | 1.9 (0.58, 6.19) | 0.29 |
| Pre-existing joint disease (vs. none) | 1.06 (0.28, 4.07) | 0.93 |
| **White count ($10^9$/L) (for every 1 x $10^9$ increase)** | **1.11 (1.04, 1.18)** | **0.002** |
| CRP, mg/L (top vs. bottom tertile) (top tertile median = 319mg/L, bottom tertile median = 58mg/L) | 4.11 (0.45, 37.7) | 0.21 |
| **Fever (vs. those without fever)** | **0.10 (0.01, 0.82)** | **0.03** |
| Surgical washout (vs. no surgical washout) | 2.04 (0.25, 16.39) | 0.5 |
| Infection with *Staphylococcus aureus* (vs. other organisms) | 1.82 (0.53, 6.22) | 0.34 |
| Infection with Methicillin sensitive *Staphylococcus aureus* (MSSA) (vs. other organisms) | 0.53 (0.14, 2.03) | 0.36 |
| **Infection with Methicillin resistant *Staphylococcus aureus* MRSA (vs. other organisms)** | **4.26 (1.28, 14.21)** | **0.02** |

experienced a recurrence of infection in the same joint within a year. There were inpatient 12 deaths. Using univariate logistic regression, age ≥70 years, high WC, absence of fever and infection with MRSA were associated with higher mortality (Table).

**Conclusions:** *Staphylococcus aureus* remains the most common cause of SA. Most patients in our dataset had at least one predisposing factor. There were more deaths in patients who were afebrile at presentation, possibly because the absence of fever led to a delay in diagnosing SA. Early aggressive treatment may be warranted in older patients, especially in those with higher WC or infection with MRSA.

**Disclosure of Interest:** None declared

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## SAT0482 RISK FACTORS FOR SEVERE INFECTION AND OUTCOME OF SECONDARY HYPOGAMMAGLOBULINAEMIA IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES TREATED WITH RITUXIMAB: PRELIMINARY RESULTS FROM 400 PATIENTS AT A SINGLE CENTRE

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**Background:** Rituximab (RTX) is used in various autoimmune rheumatic diseases (AIRDs) that are refractory to standard therapies. Attrition of long-lived plasma cells and hypogammaglobulinaemia may occur with repeat cycles of therapy leading to serious infection.

**Objectives:** To evaluate risk factors for severe infection and assess outcome of secondary hypogammaglobulinaemia during RTX treatment in AIRDs.

**Methods:** We conducted a retrospective observational study of all patients with AIRDs treated with RTX at a single centre.Each cycle of RTX consisted of 2x1000mg infusions repeated on clinical relapse. IgM, IgA and IgG levels were measured at baseline and 6 months after each cycle. Baseline factors for association with serious infection within 12 months of a RTX cycle were tested using univariate (UVA) and multivariate (MVA) logistic regression analyses.

**Results:** The first 400 consecutive patients from a total cohort of 800 were analysed. 254 (63%) had RA, 88 (22%) SLE, 47 (12%) AAV, 6 (1.5%) DM, 3 APS (1%) and 2 (0.5%) SSc. Total follow-up: 1650.3 patient-years. There were 166 serious infections recorded in 101 patients; 135 in 88 within 12 months of a cycle (8.1/100 patient years). Rates were lower in connective tissue disease (6.5) than RA (9.4). In MVA, previous severe infection, corticosteroids and low IgG were significantly associated with increased risk of serious infection.

Ig data were available in 375 (94%) patients. At RTX initiation, 23 (6%) patients had low IgG (normal range 6–16 g/L). Following RTX treatment, 18 remained low, 3 returned to normal and 15 had developed new low IgG. 6 patients required Ig replacement due to recurrent serious infections related to low IgG.

**Conclusions:** We have identified risk factors for serious infection at RTX initiation including previous serious infection, concomitant corticosteroids and low IgG. Most hypogammaglobulinaemia persisted with subsequent treatment thus highlighting the need for Ig monitoring. Further analysis of changes in Ig levels and infection in repeat cycles is in progress and can be used to develop guidelines for safety monitoring of rituximab.

**Acknowledgement:** Dr John Baptiste Candelier, Lt Kol Dr Hatem and Huma Cassamoali

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**Abstract SAT0482** – Table 1

| | No severe infection (n=312) | Severe infection (n=88) | UVA OR (95% CI) | MVA OR (95% CI), *P* |
|---|---|---|---|---|
| Age, mean (SD) | 53.5 (16.7) | 57.3 (17.3) | 1.2 (1.0–1.3) per 10 yrs | 1.0 (0.8–1.2), 0.892 |
| Female% | 75 | 76 | 1.0 (0.6–1.8) | – |
| Disease duration, median (IQR) years | 6.8 (2.9–13.9) | 7.4 (2.5–15.1) | 1.0 (1.0–1.0) | – |
| Follow-up, median (IQR) years | 3.4 (2.0,6.1) | 3.9 (2.0,6.9) | 1.0 (1.0–1.1) | – |
| Ever smoking% | 41 | 56 | 1.8 (1.1–3.0) | 1.4 (0.8–2.5), 0.244 |
| Previous cancer% | 7 | 9 | 1.4 (0.6–3.2) | – |
| Chronic lung disease% | 21 | 39 | 2.3 (1.4–3.8) | 1.2 (0.6–2.3), 0.670 |
| Heart failure% | 1 | 5 | 4.9 (1.1–22.3) | 3.9 (0.5–28.4), 0.177 |
| Diabetes% | 6 | 10 | 1.9 (0.8–4.3) | 1.8 (0.6–5.0), 0.284 |
| CTD% | 37 | 36 | 1.0 (0.6–1.6) | 1.0 (0.5–2.1), 0.992 |
| Previous severe infection% | 9 | 44 | 8.4 (4.7–15.0) | 5.9 (3.0–11.7), <0.001 |
| Previous DMARDS, median (IQR) | 2 (1–3) | 2 (1–3) | 1.0 (0.8–1.1) | – |
| Previous cyclophosphamide% | 27 | 29 | 1.1 (1.7–1.9) | – |
| Previous biologics, median (IQR) | 0 (0–1) | 0 (0–1) | 0.9 (0.7–1.2) | – |
| Corticosteroids% | 44 | 64 | 2.2 (1.4–3.6) | 1.8 (1.0–3.3), 0.040 |
| Corticosteroid dose, median (IQR) mg | 0 (0–10) | 5 (0–10) | 1.0 (1.0–1.1) | – |
| IGM Low% (<0.5) | 8 | 17 | 2.4 (1.2–4.8) | 1.7 (0.7–4.0), 0.262 |
| IGA Low% (<0.8) | 3 | 3 | 1.3 (0.3–4.8) | 0.6 (0.1–3.7), 0.586 |
| IGG Low% (<6.0) | 4 | 16 | 4.8 (2.1–11.1) | 3.1 (1.1–9.1), 0.035 |

## SAT0483 ULTRASONOGRAPHY CHANGES DURING THE COURSE OF SEPTIC ARTHRITIS ARE ASSOCIATED WITH FUNCTIONAL OUTCOME

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**Background:** Ultrasonography (US) is useful to study the joints and the synovial tissue. It allows the evaluation of the synovial membrane thickness and inflammation. It can depict effusions and help to assess the surrounding soft tissues. Therefore, US could be of interest in the monitoring of septic arthritis.

**Objectives:** The main goal of this study was to describe the US changes observed during the course of septic arthritis and their association with clinical and functional outcomes.

**Methods:** We included all patients seen for a native joint infection in 3 different hospitals between January 2014 and July 2015. We collected baseline demographic, clinical, biological and microbiological characteristics. Patients were followed up prospectively with clinical and US evaluation at Day 0, 4, 15 and at 3 months (M3). US exam included the study of synovial membrane thickness, Power Doppler and involvement of the periarticular tissue. Evolution of the synovial thickness was compared to baseline (% of change). X-Ray of the joint was made at baseline and M3. Functional outcome was assessed at M3 (range of motion; SF-36 score).

**Results:** Thirty four patients were included, mean age 63.7 (range 22–90) with 24 men (70.6%). Most of the time, septic arthritis occurred in patients with pre-existing joint disease (n=24; 70.6%) and the knee was mostly affected (n=19; 55.9%). Predominant causative organism was Staphylococcus Aureus (n=15; 44.1%). Twelve patients (35.3%) underwent joint lavage mean time 4.2 days (range 0–13) after the diagnosis with synovectomy in 2 cases (5.9%). US synovitis was present in 96.4% of the cases at D0, 100% at D15 but was less frequent at M3 (77.8%; p=0.051). The synovial thickness increased at D4 and D15 compared to baseline (respectively median +17.3%, +20%, p=0.015) and significantly decreased at M3 (median -31.5%; p=0.015). Doppler signal was frequent (64.3% (D0); 66.7% (D4); 61.3% (D15)) and decreased significantly at M3 (25.9%; p=0.04). The effusion was present at D0 (92.8%), D4 (88.9%), D15 (80.6%) and significantly less frequent at M3 (55.6%, p=0.001). Periarticular abscess or cellulitis was rare (10.7% and 3.7% at D0 respectively). At M3, one patient died (2.9%) and 5 (14.7%) patients were lost to follow-up. Twenty (58.8%) patients had a decreased joint range of motion. A high total Sharp score and a high joint space narrowing score at M3 was associated with a late start antibiotic treatment (respectively p=0.048, p=0.03). We found no correlation between US characteristics and any of the baseline clinical or biological parameters. In contrast, joint limitation at M3 was associated with an increase of the synovial thickness between D0 and M3 (p=0.024) and with the persistence of Doppler at D15 and at M3 ((p=0.033; p=0.002).

**Conclusions:** Septic arthritis have a poor functional outcome in more than half of the cases. US synovitis remains present at 3 months in most patients but with a significant decrease in synovial thickness compared to baseline. Doppler signal persists in a quarter of the cases at M3. Persistence of Doppler signal and a thickened synovial tissue at 3 months are associated with a poor clinical outcome.

**Disclosure of Interest:** None declared

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## SAT0484 LONG-TERM SAFETY OF NON-TNF INHIBITOR BIOLOGICS IN RHEUMATOID ARTHRITIS PATIENTS WITH CHRONIC OR PAST HEPATITIS B VIRUS INFECTION

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**Background:** Rheumatoid arthritis (RA) patients with chronic hepatitis B virus infection (HBV) are at risk for HBV reactivation during TNF inhibitor (TNFi) therapy.

Recent data in patients with hematologic diseases have shown an increased risk for HBV reactivation after rituximab (RTX)-based therapies, even in past HBV infection. Similar data are sparse in RA patients especially with the newer non-TNFi biologics (abatacept-ABA, tocilizumab-TCZ).

**Objectives:** To evaluate the long term safety of non-TNFi biologics in RA patients with chronic or past HBV infection and in HBV vaccinated patients.

**Methods:** A retrospective systematic chart review of the 346 RA patients treated with biologics in our Rheumatology Unit from 1/1/2003 to 31/12/2015 was performed. All patients were followed regularly with appropriate clinical and laboratory monitoring (ALT, HBV DNA levels). We identified 44 patients; 8 with chronic HBV infection (HBsAg+), 25 with past infection (anti-HBc+/anti-HBs+ n=12, anti-HBc+ only n=10, anti-HBs+ only n=3) and 11 HBV vaccinated patients (anti-HBs+) who were treated with IV non-TNFi biologics (ABA, RTX, TCZ). Patient's files were reviewed for biochemical or virological reactivation and anti-HBs titers (before and during therapy) were measured in stored patients' sera.

**Results:** 38/44 (86%) of patients were women with a mean age of 64 ± 16.8 years and a mean disease duration of 14.4 ± 11.3 years. 28/44 (65%) were seropositive (RF and/or anti-CCP) and 80% had been previously treated with TNFi (median: 14 months). Eight patients with chronic HBV infection (all HBV DNA negative at baseline) received 9 courses of non-TNFi (RTX: n=4, ABA: n=4, TCZ n=1) under appropriate antiviral prophylaxis (tenofovir: n=5, lamivudine: n=2, entecavir: n=2, median treatment period: 19 months). During follow-up, no evidence of biochemical or virological reactivation was observed. Similarly, there were no cases of HBV reactivation among 25 patients with past HBV infection treated with 33 courses of non-TNFi (RTX: n=21, TCZ n=7, ABA: n=5, median treatment period: 18 months). Anti-HBs titers were measured during non-TNFi treatment in 26 anti-HBs+ patients (past infection: n=15, vaccinated: n=11, median interval between testing: 28 months) who had received 32 treatment courses (RTX: n=15, TCZ: n=12, ABA: n=5). Although anti-HBs titers decreased with all non-TNFi, this was statistically significant only for TCZ (from 436 ± 388 iu/L to 323 ± 368 IU/L, p=0.021) and not for RTX (from 394 ± 396 iu/L to 381 ± 417 IU/L, p=0.213) or ABA (from 362 ± 413 IU/L to 279 ± 410 iu/L, p=0.144). Anti-HBs titers dropped $<$10 IU/L in only 3 patients (10%, 2 with past infection on RTX, 1 vaccinated on TCZ); all had low anti-HBs titers before treatment (26 ± 9 IU/L) and none exhibited HBV reactivation.

**Conclusions:** In this long term study, non-TNFi biologics proved to be safe for patients with chronic HBV infection on oral antivirals as well as in patients with resolved HBV infection. Despite a small decrease in anti-HBs titers during treatment, only 10% of anti-HBs+ patients exhibited levels below the protective cut-off and this was not associated with HBV reactivation.

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## SAT0485 PREVALENCE OF AUTOIMMUNE DISEASES IN HIV-INFECTED PATIENTS IN MEXICO

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**Background:** Autoimmune diseases (AD) in patients with HIV have been observed since the beginning of the HIV/AIDS pandemic. Epidemiologic studies have reported a prevalence of rheumatic and autoimmune manifestations ranging from 1–72%, including only systemic (SAD) and articular AD (AAD), and not organ-specific AD (OSAD)[1]. Prevalence of AD in patients with HIV infection in Mexico has not been fully addressed.

**Objectives:** The aim of this study was to assess the prevalence of AD in HIV-infected patients.

**Methods:** We performed a retrospective study in two tertiary referral centers in Mexico. All subjects seen from june 15th 2003 to june 15th 2014 with a confirmed diagnosis of HIV infection and a diagnosis of an AD were included. We extracted demographic data, HIV infection history, and AD history from the clinical record

**Results:** A total of 5876 HIV-infected patients were seen during the study period. Eighty one AD were found in 77 patients (prevalence: 1.31%). Eight (9.9%) were SAD, 12 (14.8%) AAD and 61 (75.3%) OSAD (Table 1). Four patients (5.2%) had 2 AD. Fifty eight were male (75.3%). Mean age at diagnosis of AD was 34.8 years. In twenty two (27.2%) AD preceded HIV infection, in 23 (28.4%) HIV infection was diagnosed simultaneously with the AD, in 36 (44.4%) AD developed after HIV infection. Mean CD4 T lymphocyte count in patients with a simultaneous diagnosis of HIV infection and AD was 287 cel/μl, only one with undetectable viral load; mean CD4 T lymphocyte count in patients who developed AD after HIV infection was 353 cel/μl, half with undetectable viral load. Sixteen patients were classified with AIDS at AD diagnosis. Five (6.2%) AD were a consequence of immune reconstitution inflammatory syndrome (IRIS); prevalence of autoimmune IRIS was 0.08%. Prevalence of HBV and HCV coinfection was 5.2% and 2.6% respectively. Immunosuppressive treatment was used in 87% of patients.

Table 1

| Autoimmune diseases | No. | Prevalence |
|---|---|---|
| Systemic: SLE (5), AFS (1), Sjögren syndrome (1), DILS (1) | 8 | 0.13% |
| Articular: rheumatoid arthritis (5), spondyloarthritis (7) | 12 | 0.20% |
| Neurological: Guillain-Barré syndrome (3), CIDP (2), ADEM (1) | 6 | 0.10% |
| Dermatologic: psoriasis (10), vitiligo (1), alopecia areata (1), cutaneous vasculitis (3) | 15 | 0.25% |
| Endocrinological: DM1 (5), autoimmune adrenal insufficiency (2), Graves' disease (3), Hashimoto's thyroiditis (1) | 11 | 0.18% |
| Gastroenterological/hepatic: ulcerative colitis (6), Crohn's disease (2), autoimmune hepatitis (2) | 10 | 0.17% |
| Hematologic: immune thrombocytopenia (18), autoimmune hemolytic anemia (1) | 19 | 0.32% |

**Conclusions:** This is the first study to address solely AD without combining non-autoimmune musculoskeletal entities and the largest cohort to date. Prevalence of AD in HIV-infected patients in Mexico was low (1.31%) and OSAD was the most frequent. AD were diagnosed in all stages of HIV infection. Prevalence of HBV and HCV coinfection and autoimmune IRIS was very low. Prospective studies are needed to identify risk factors for the development of autoimmune IRIS.

**References:**

[1] Patel N, Patel N, Espinoza LR. HIV infection and rheumatic diseases: the changing spectrum of clinical enigma. Rheum Dis Clin North Am. 2009; 35(1):139–161.

**Disclosure of Interest:** None declared

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## SAT0486 TNF INHIBITORS HAVE NO EFFECTS TO HUMAN T-LYMPHOTROPIC VIRUS TYPE-I (HTLV-I)-INFECTED CELL LINE

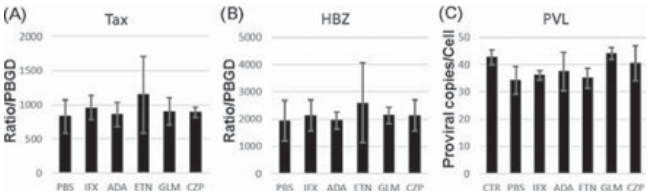
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**Background:** Biologics are very effective to autoimmune diseases including rheumatoid arthritis and ankylosing spondylitis, but could cause infectious diseases as adverse effects. Human T-lymphotropic virus type-I (HTLV-I) is a retrovirus that infects 10 to 20 million people worldwide (1). The virus is associated with severe diseases, such as adult T-cell leukemia/lymphoma and HTLV-I-associated myelopathy (HAM). It is unknown if HTLV-I proliferates when biologics including TNF inhibitors (TNFi) are used.

**Objectives:** We evaluated effects of TNFi to HTLV-I infected cells regarding cytokine profiles, TNF receptor (TNFR), mRNA of associated proteins, proviral load (PVL) and apoptosis.

**Methods:** We used an HTLV-I infected cell line named HCT-5, which is derived from cells in spinal fluid of a patient with HAM. Multiplex cytokine/chemokine bead assays, cytokine levels assessed by enzyme-linked immunosorbent assays (ELISA), fluorescence activated cell sorting (FACS) analysis of TNFR, immunofluorescence staining of GAG, which is a HTLV-1 structural protein, quantitative reverse transcription PCR for Tax (2) and HTLV-I bZIP factor (HBZ) (3), which are needed for immortalization and proliferation of HTLV-I infected cells respectively, HTLV-I PVL (4), and apoptotic ladder detection were performed. We also used Jurkat as a control cell line.

**Results:** Multiplex cytokine/chemokine bead assays showed supernatants of HCT-5 without any stimuli had time-dependent elevation of IL-6, TNF-alpha, RANTES and ICAM-1. Supernatants of HCT-5 treated with infliximab (IFX), adalimumab (ADA), etanercept (ETN), golimumab (GLM) and certolizumab pegol (CZP) assessed by ELISA showed no differences in levels of these molecules compared to that of HCT-5 with phosphate buffered saline (PBS). In FACS analysis, except for TNFR 2 with ETN, expressions of TNFR 1 and TNFR 2 with each TNFi did not differ from PBS. TNFR 2 declined and internalization of TNFR 2 was detected in HCT-5 with ETN. There was no differences in levels of mRNA of Tax (Figure A, PBGD: house keeping gene) and HBZ (Figure B) with TNFi compared to that with PBS. PVL were also not changed (Figure C, CTR: without any reagents). Immunofluorescence staining of GAG showed no differences between each TNFi and PBS. DNA ladder was not detected in any TNFi and PBS.




**Conclusions:** *In vitro*, TNFi did not affect the cytokine profiles, TNFR 1, mRNA of associated proteins, proviral load and apoptosis of HCT-5. Only ETN caused internalization of TNFR 2.

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**Disclosure of Interest:** None declared
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## SAT0487 SCREENING FOR PAST INFECTION WITH HEPATITIS B IN PATIENTS RECEIVING RITUXIMAB: AN AUDIT

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**Background:** Hepatitis B virus (HBV) causes an acute, often subclinical infection which can progresses to chronic disease with active viral replication. The risk of chronic infection is determined largely by the age at which the virus is contracted. Even in patients who clear the initial infection, the virus may lie dormant; one study found evidence of HBV DNA in 13 of 14 healthy liver donors with serological evidence of past but not current infection (HBV surface antigen (HBsAg) negative, core antibody (HBcAb) positive) [1]. There are case reports of viral reactivation in patients receiving immunosuppressive therapy including rituximab and as such Roche recommend screening all patients to include HBsAg and HBcAb prior to treatment [2]. In our experience not all rheumatology clinical staff are familiar with this guidance.
**Objectives:** Our primary objective was to establish what proportion of patients receiving rituximab through a rheumatology department were fully screened for HBV before and after an education programme. Our secondary objective was to establish what proportion of newly screened patients had evidence of past HBV infection.
**Methods:** We undertook an audit of patients receiving rituximab for all rheumatological indications between January and August 2015 in a unit with a catchment area of 450,000 patients. We recorded the proportion of patients who were tested for HBsAg and HBcAb prior to treatment and then undertook an education programme to clinical staff and updated an electronic blood requesting system before re-auditing patients between September 2015 and January 2016.
**Results:** 89 rheumatology patients received Rituximab between Jan 2015 and August 2015. 43 (48%) had a complete screen (HBsAg and HBcAb) prior to treatment; 37 (42%) had been tested for sAg only; 7 (8%) for HBcAb only and 2 (2%) had neither test. Following an education programme 60 of 68 patients (90%) were fully screened. 38 patients were newly tested for HBcAb and 1 patient was found to be HBcAb positive suggestive of past infection (HBsAg negative). Subsequent analysis for HBV DNA was negative. Following discussion with a hepatologist this patient was treated with lamivudine whilst continuing Rituximab therapy.
**Conclusions:** There is a risk of reactivation of HBV in patients who have evidence of past infection and are treated with rituximab. We found there was some uncertainty regarding the required serological screening blood tests amongst rheumatology staff, highlighted by incomplete testing in 52% of patients receiving Rituximab. Following an education programme, the proportion of patients completely screened rose to 90%. One patient with evidence of past infection was identified.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3221

## SAT0488 TUBERCULOSIS IN A REGISTRY OF RHEUMATIC PATIENTS TREATED WITH BIOLOGICAL DRUGS

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**Background:** Biologic therapies (bDMARDs) have improved the treatment of rheumatic diseases; however, the risk of tuberculosis (TB) infection or reactivation in patients treated with this drug class remains a concern.
**Objectives:** We investigated the clinical characteristics and prognostic factors of TB in an Argentine registry of rheumatic diseases patients treated with bDMARDS.
**Methods:** Database included demographics of patients, type and duration of treatments and clinical information of adverse events. A control group was included for comparison consisting of patients not treated with bDMARDs but similar demographics. Values are expressed as mean±standard deviation, median (ranges), and frequencies (percentages), as appropriate. Multivariate logistic regression analysis was used to identify variables associated with the occurrence of TB; OR and 95% CI were calculated by exponentiation of regression coefficients.
**Results:** As of January 2016, 3483 patients, 4762 treatments and 2580 adverse events were studied. Mean age 56.1±15,7 years; 2748 (78.9%) patients were women. Initial treatments were 1472 (42.3) bDMARD *vs.* 2011 (57.7) non-bDMARD. Main diagnosis: Rheumatoid arthritis (RA) 2706 (77.7), Psoriatic arthritis (PsA) 293 (8.4), juvenile idiopathic arthritis (JIA) and lupus with 117 (3.36) each. Of 4762 treatments, most frequent biological drugs were etanercept 119 (25,1), adalimumab 626 (13,2), and abatacept with 282 (5.9). Of 3483 patients, 18 (0.5) presented TB as an adverse event, their mean age was 52.9±2.8; 16 (88.9) had AR and 2 (11.1) had PsA; 16 (88.9) had initially received bDMARD vs. 2 (11.1) who had received non- bDMARD treatments. PPD test was performed in 2002/2883 (69.4) bDMARD treatments vs. 372/1879 (19.8%) non-bDMARD treatments, with 126 (6.3) vs 35 (9.4) positive tests, respectively. Median time from treatment commencement to TB was 15.1 (range 1.6–137.5) months. Treatments during which, TB was diagnosed were etanercept 5 (27.8), adalimumab 4 (22.2), non-bDMARD 3 (16.7), abatacept and infliximab with 2 (11.1) each and tocilizumab 1 (5.6), the distribution was not significantly different (Table 1). The risk of developing TB was higher in patients whose first treatment was bDMARDs (OR 5.6 95%CI 1.3–24.3).



**Conclusions:** A higher frequency of TB was seen in patients treated with bDMARDs; however, results should be interpreted cautiously because of registries inherent limitations.
**Disclosure of Interest:** None declared
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## SAT0489 BIOLOGIC THERAPIES AND INFECTIONS IN THE DAILY PRACTICE: A STUDY ON HISTORICAL COHORT FROM 3 ITALIAN RHEUMATOLOGIC UNITS

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**Background:** Since the introduction of biologics many concerns about the increased risk of infections, have been reported [1]Available data from randomized controlled trials, national registries and open label studies do not fully clarify the magnitude of this risk [2]. To date, the real impact of infections in the daily practice in the rheumatologic centers is still largely unknown.
**Objectives:** To evaluate the infection rates associated with the use of biologics in a large cohort of patients enrolled in 3 tertiary referral rheumatologic units in Italy. In addition, the risk of infections, including serious infections, was correlated with different clinical features.
**Methods:** A retrospective study, between January 2010 and December 2013, enrolled 731 rheumatic patients: 332 with rheumatoid arthritis (RA), 308 with psoriatic arthritis (PsA), 85 with ankylosing spondylitis (AS), 16 with primary Sjogren syndrome (pSS). Demographic and disease characteristics, therapies, comorbidities and infectious events were recorded and statistically analysed by multivariate analysis.
**Results:** All patients received at least 1 biologic, 82 patients 2 biologics, 30 patients 3 biologics, 6 patients 4 biologics and 4 patients 5 biologics. Two-hundred-thirty-five infectious episodes were observed in 208 (28.4%) patients. About total infections, bacteria were identified in 70.6% out of total cases, and viruses in 18.3%. The most common site of infection was the urinary tract (39.1%). Duration of disease (p=0.02), longer follow-up (p=0.0001), concomitant steroid therapy (p=0.001), comorbidities (p=0.015), treatment with infliximab (p=0.001), etanercept (p=0.029), golimumab, (p=0.004), abatacept (p=0.0001) and tocilizumab (p=0.0001) were significantly associated with any infection. In our cohort, 17 episodes fulfilled the criteria of serious infection, and occurred in 17

different patients (2.3%), the majority involving the lower respiratory tract (41.2%). Serious infections were associated with the beginning of biologics in older age (p=0.002), the use of i.v. therapy with infliximab (p=0.02), rituximab (p=0.05) and tocilizumab (p=0.01).

**Conclusions:** Surprisingly, our study shows that, in daily practice, a lower rate of infections was observed in our patients, when compared with previous reports. Duration of disease, concomitant steroid therapy and comorbidities may be considered risk factors for the occurrence of infections in treated patients. Of note, serious infections seem to be associated with older age of patients and i.v. treatments.

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## SAT0490 POOR LONG-TERM ADHERENCE TO SECONDARY PENICILLIN PROPHYLAXIS AMONG PEDIATRIC PATIENTS WITH RHEUMATIC FEVER

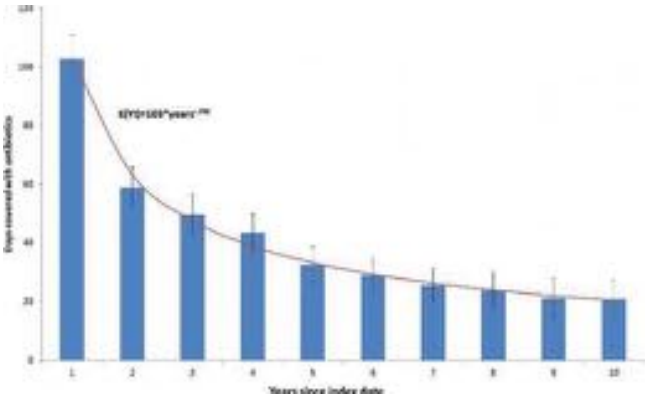
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**Background:** Recurrent episodes of acute rheumatic fever (RF) may contribute to the development or worsening of rheumatic heart disease (RHD) and was estimated to occur in 50–70% of RF patients prior to the introduction of penicillin. Meta-analyses from the United States showed that secondary penicillin prophylaxis (SPP) may reduce the incidence of RHD. Moreover, SPP using monthly Intra muscular (IM) Benzathine Penicillin was more effective in prevention of RF recurrences than daily oral SPP.

**Objectives:** We aimed to evaluate the long-term adherence to SPP in RF patients using real-life data.

**Methods:** The study population included children up to 18 years old in Maccabi Healthcare Services (MHS), a 2-million member health organization in Israel, who were diagnosed with acute RF between 1/1996 to 5/2015 and were dispensed at least one monthly pack of penicillin (either in oral or IM form). Treatment persistence was defined as continuation of drug use for the entire duration of therapy or until age 18, whichever occurred first. Adherence to treatment refers to the extent of drug use during the period of persistence, expressed as mean proportion of days covered (PDC). This was calculated by dividing the quantity of penicillin dispensed by the total time span between index date and age 18, leaving MHS, or 31 April 2015, whichever occurred first.

**Results:** A total of 842 RF patients were identified. Mean (SD) ages at diagnosis among patients on oral (n=734) and IM (n=108) initial therapy were 8.6y (3.7y) and 10.9y (3.2y), respectively. The median PDC for the treatment regimens were oral: 8% [interquartile range (IQR) 2–33%] and IM: 10% (IQR 3–28%). Overall, days covered with SPP (figure 1) decreased exponentially from 103 days in the first year of therapy to 20 days in the 10th year.



**Conclusions:** Adherence and persistence to secondary penicillin prophylaxis among Israeli children diagnosed with RF is poor. Although less effective, oral SPP was the preferred regimen. Intervention plans to increase adherence and persistence to SPP must be implemented in countries where RF still exists.

**Disclosure of Interest:** None declared

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## SAT0491 HIGHER LEVELS OF ANTI-BORRELIA IGG ASSOCIATE WITH ARTHRITIS IN LYME DISEASE AT PRESENTATION: A NORTHERN ITALY REFERRAL CENTER COHORT

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**Background:** Lyme disease (LD) is a multisystemic infection caused by Borrelia burgdorferi (*Bb*) *sensu lato* complex, involving skin, joints, nervous system and heart.

**Objectives:** To assess clinical and serological data of patients with LD at presentation in an endemic area of Northeast Italy (Trentino), with a special focus on rheumatic manifestation.

**Methods:** We retrospectively collected clinical data of *Bb* seropositive patients from 2014 to 2015, tested with ELISA (Enzyme-Linked Immunosorbent Assay) IgM/IgG and Western blot (WB; IgM/IgG immunoblots). Only patients with a LD' diagnosis confirmed by a trained physician of our center were selected. Other laboratory and instrumental tests (*Bb*-PCR on synovial fluid, anti-*Bb* antibodies research on cerebrospinal fluid, etc.) were performed if deemed necessary by clinical judgment.

**Results:** Seventynine patients resulted seropositive for *Bb*, but only 54 met the inclusion criteria. Among patients with confirmed LD, 27 (50%) were female, mean age at presentation was 48±21years; children were 12.9%. The main presenting symptom was erythema migrans in 72% of cases (39/54), arthritis in 17% (9/54), flu-like symptoms in 7% (4/54), chronic atrophic acrodermatitis and cognitive dysfunction in 2% of cases (1 patient each). Among arthritis, 89% (8/9) presented with acute knee monoarthritis and one patient with hand PIP arthritis. Other concomitant or further developed manifestations were CNS involvement (2/54), cranial neuropathy (1/54), pleuropericarditis (1/54), I°grade atrioventricular block (1/54), transitory leucopenia (2/54), flu-like symptoms (12/54). All patients received antibiotic treatment: 58% doxycycline, 25% amoxicillin, 5% ceftriaxone (12% not reported). Twentysix (48%) patients remember tickborne bite, with a mean latency of 10.4±16.9 weeks.

When compared to the rest of the cohort, patients presenting with arthritis were younger (48y±12 vs 56y±12; p=.04), remember tickborne bite in 22% of cases (2/9; p=ns), and had increased ESR (mm/h, 51.1±36.6 vs 24.3±20.3; p=.03) and CRP levels (mm/L, 19.6±23.3 vs 5.6±10.2; p=.01).

Arthritis-presenting LD-patients had higher serum IgG antibody levels if compared to overall non-arthritis presenting LD-patients (124.0 vs 25.5; $p<.0004$) and to the subset tested for anti-*Bb* antibodies presence after the 4th week from bite (124.0 vs 29.0, $p<.0003$; mean latency 7.8±5.9 weeks).

**Conclusions:** Arthritis is the second most frequent presenting symptoms of LD (17%). Knee monoarthritis is typical, patients affected are younger and only 20% recall a tick bite.

We first demonstrated higher levels of serum anti-*Bb* IgG antibodies in patients presenting with arthritis. This seems not directly related to a longer time from bite to disease development, since anti-*Bb* IgG levels of patients with arthritis remain significantly higher if selectively compared to patients without arthritis tested for antibodies after the decline of the primary immune response, after 4th week.

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**Disclosure of Interest:** None declared

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## SAT0492 WHIPPLE'S DISEASE MIMICKING RHEUMATOID ARTHRITIS LEADS TO MISDIAGNOSIS, TREATMENT FAILURE, AND PROLONGED DISEASE COURSE: A SINGLE-CENTER CASE SERIES OF SEVEN PATIENTS

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**Background:** Whipple's disease (WD) is a rare disease caused by a chronic infection with *Tropheryma whipplei* (TW). Joint involvement is common. The rarity, the broad spectrum of symptoms, and the similarity to rheumatoid arthritis (RA) may result in misdiagnosis. Without antibiotic treatment WD may be fatal, misleadingly induced immunosuppressive treatment may even accelerate disease progression.

**Objectives:** To describe the clinical presentation, the disease course with respect to immunosuppressive treatment and the response to antibiotic treatment in patients with WD presenting with inflammatory arthritis.

**Methods:** Retrospective single center observational study of seven patients. Medical charts were screened for articular and extra-articular symptoms. Diagnosis of WD was made by histological analysis using periodic acid-Schiff stain (PAS) and/or polymerase chain reaction (PCR).

**Results:** Median age at disease onset was 57 years (range 34- 64), six patients were male. The median time until diagnosis of WD was 5 years. All patients presented with polyarthritis with a predominantly symmetric pattern in

five and a chronic, intermittent disease course in six patients. Affected joints were: wrists (5/7), MCP (5/7), knees (5/7), PIP (3/7), hips (2/7), elbow (2/7), shoulder (2/7). All patients had increased C-reactive protein and/or ESR and were negative for RF and anti-CCP-antibodies. Three had erosive arthritis. Thus, initially all patients were classified as a seronegative RA following EULAR/ACR criteria with a median DAS28 of 4.34 (range 2.8–6.28). All but one patient received antirheumatic treatment consisting of prednisone (n=6), combined with methotrexate (n=5) or leflunomide (n=4). Three patients were treated with at least one biologic agent (anti-TNFα, abatacept, rituximab, tocilizumab). All patients showed insufficient treatment response, in one disease course was even worsened by the use of biologicals. Finally diagnosis of WD was made by a combination of positive PAS staining and a positive TW-PCR test in three patients. In five patients PCR was positive in at least two different sites. In all patients TW was detected in synovial fluid. Extra-articular manifestations of WD were frequent, but mainly mild and unspecific for WD, GI-symptoms were mild or absent even in patients with TW detected in small bowel biopsy. Five patients received long-term trimethoprin/sulfamethoxazole, two started with doxycycline plus hydroxychloroquine. Five patients had to change antibiotic regimen due to side effects or microbial resistance. All had a good treatment response with improvement of arthritis and extra-articular manifestations. Two are still on antibiotics while five patients could already stop treatment.

**Conclusions:** WD is rare and can mimic RA. Patients are therefore at risk of not only a delay of diagnosis but also of receiving insufficient or even worsening treatment. Hence, seronegative RA with a prolonged disease course and insufficient treatment response should be reevaluated for WD.

**Disclosure of Interest:** None declared

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## SAT0493 TUBERCULOSIS OF THE HAND: CLINICAL PRESENTATION AND TREATMENT

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**Background:** The tuberculosis remains one of the most world wide spread infectious diseases. The ostéoarticular localization is rare, affecting the hand remains exceptional. The incidious presentation, the poor symptomatic character of the tubercular dactylitis may explain the constant delay in the diagnosis. It is often delayed and confused essentially with bone tumors which imply histological confirmation.

**Objectives:** To study the epidemio-clinical features, stages, therapeutics and course of tuberculosis of the hand.

**Methods:** We made a retrospective study of 14 medical records of cases of tuberculosis involving the hands in an orthopedic department over the last ten years. We collected and analyzed the clinical, bacteriological, radiological and therapeutic data.

**Results:** The mean age was 45 years. There were 9 men and 5 women. A manual work was noted in 10 cases. Two patients had a diabetes mellitus and one breast cancer. The dominant side was achieved in 60% of cases. Mean symptoms duration was 3.6 months. Lesions are divided into 6 cases of pseudotumoral tuberculosis of soft tissue of the hand, arthritis and osteoarthritis in 5 cases and tenosynovitis in 3 cases. The ring and little fingers are the most affected fingers. Biopsy was done in all cases. Anti-tubercular chemotherapy was indicated for all patients: isoniazid, rifampicin, pyrazinamide and ethambutol for 2 months followed by isoniazid and rifampicin during 10 months. These antibiotics were combined with immobilization in all cases. Good outcome was seen in the 14 cases.

**Conclusions:** Tuberculosis should be suspected in cases of longstanding pain and swelling of a finger especially in an endemic area. Efficiency of anti-tubercular treatment remains undisputed. The surgical indications are limited to the biopsy, usually essential to the diagnosis.

**Disclosure of Interest:** None declared

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## SAT0494 BACTERIOLOGIC PROFILE OF SEPTIC ARTHRITIS: A RETROSPECTIVE STUDY OF 59 CASES

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**Background:** Septic arthritis (SA) is an infection of synovial tissue that can affect one or more joints in patients of any age. It is considered as a medical and therapeutic emergency. Diagnosis is based on the presence of a microorganism in joint aspiration or in withdrawal of a possible gateway or a secondary location.

**Objectives:** To describe the bacteriologic profile of SA among adult subjects in a rheumatologic department.

**Methods:** This is a descriptive retrospective study including records of cases of SA collected in a rheumatology department, over a period of 17 years [1998–2014]. The epidemio-clinical features and evolution were noted. Bacteriologic exams were collected and analyzed.

**Results:** Fifty nine records of 59 patients with SA were selected. The mean age was 54.6 ± 19 years [range 15 to 95]. There were 28 men and 31 women with a sex ratio M/F =0.9. Fifty 50 cases (84.7%) had a single joint involvement, 6 cases (10.2%) had oligoarticular arthritis and 3 cases had polyarticular arthritis (5.1%). The joint aspiration was performed in 53 patients (89.8%). The appearance of the liquid was clear in 6 cases (11.5%), hematic in 5 cases (9.6%), purulent in 18 cases (34, 6%) and trouble in 23 cases (44.2%). White blood cells varied between 4000 and 100,000/mm$^3$ with an average of 27.520 elements. Direct bacteriologic exam was positive in 16 cases (30.8%). Twenty seven subjects (46%) had a positive culture. The study of the synovial fluid identified staphylococcus as the most frequently isolated microorganism (5 cases), followed by Streptococcus (3 cases), Koch bacillus (2 cases) and E.Coli (2 cases). One patient had septic arthritis due to Neisseria gonorrhoeae.

**Conclusions:** The bacteriologic profile is this series is not different than known in literature but showed that less than a half of patients had an identified microorganism as defined the SA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.3257

## SAT0495 CHIKUNGUNYA VIRAL ARTHRITIS IN MEXICO: INFLAMMATORY BIOMARKERS, DISABILITY AND DISEASE ACTIVITY INDEX MAY BE PREDICTORS OF CHRONIC ARTHRITIS

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**Background:** Between 2013 to 2014 autochthonous cases ChikV virus were confirmed in the Americas and Mexico. The clinical and inflammatory profile and the prevalence of chronic disease were analyzed in Mexican patients.

**Objectives:** To describe clinical profile, self reported-disability, inflammatory biomarkers and chronic articular (CA) disease during 10 month follow-up in ChikV Mexican patients.

**Methods:** Ten patients with ChikV confirmed by real-time PCR were included. Clinical manifestations, Disease Activity Index (DAS-28), self-reported disability by 32 item WHODAS-2 score and inflammatory biomarkers (C-reactive protein (CRP), eritrosedimentation rate (ESR), Rheumatoid Factor (RF), high sensivity Interleukin-6 (hsIL-6) were measured at onset and every month until 10 months of follow-up.

**Results:** Ten patients (6 women and 4 men) with mean age 48.0 15.04 years-old were followed. Acute symptoms were: fever (100%), arthralgias (100%), myalgias (80%), rash (80%), synovitis (60%), nausea (50%), vomiting (20%) and back pain (20%); number of tender joints was 13.8 (SD 5.09) and number of articulations with synovitis was 7.1 (SD 3.78). At diagnosis biomarkers were: CRP 5.09 (SD 7.23) mg/dl, ESR: 32.6 (SD 17.5) mm/h, rF: 64 (SD 21.7) IU/ml and hsIL-6: 17 (SD 10.3) pg/ml. At diagnosis WHODAS-2 score was 74.5 (SD 7.59) % and DAS-28 was 4.37 (SD 0.78). Four cases resolved in acute phase, 5 developed subacute and CAand 1 patient died (with Systemic Lupus Erythematosus). During follow-up ESR, hsIL-6, DAS-28 index and WHODAS2 score were higher in patients with subacute or CA compared to solved cases ($p<0.05$). High levels of ESR and hs-IL6 at onset of ChikV infection were related with the development of CA ($p<0.05$). High DAS 28 index and WHODAS-II score were related to development of subacute or CA ($p<0.05$).

**Conclusions:** Fever, polyarthralgias, myalgias and rash were the main acute symptoms of ChikV fever and 50% of patients developed CA and a high disability. High levels of hsIL-6 and ESR could be used as a biomarkers to predict CA since acute phase. Inflammatory biomarkers, disability and DAS-28 remained high in subacute an CA compared to solved cases.

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**Disclosure of Interest:** None declared

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## SAT0496 BRUCELLOSIS SPONDYLODISCITIS: RETROSPECTIVE EVALUATION OF THE CLINICAL, LABORATORY AND EPIDEMIOLOGICAL FEATURES OF 21 CASES

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**Background:** Brucellosis is a common zoonosis which still remains a major health problem in our country. Osteoarticular involvement is the most frequent complication.
**Objectives:** The aim of this study was to retrospectively evaluate the clinical, radiological aspects, laboratory characteristics, complications and treatment oucomes of brucellar spondylodiscitis (BS) cases who were followed between 1997 and 2015.
**Methods:** this is a retrospective study of 21 cases of brucella spondylitis collected in our rheumatology department
**Results:** Among 118 cases of infectious spondylodiscitis diagnosed and treated, 21 (17, 8%) were due to brucellosis. It was 16 men and five women with a mean age of 48.9 years. Among our patients, 38% had a profession exposed and 76, 2% were consumers of unpasteurized milk and dairy product. The delay from onset to diagnosis was 4 months and a half. The clinical presentation was fever in 81% cases, sweating in 81% and spinal pain in 100% cases. Neurological signs were observed in 42, 8% cases. A muscular deficit was objectified in 14, 3% cases. Vésicosphinctériens disorders were observed in 9, 5% cases. A single case of spinal cord compression was noted. The localisation of the infection was thoracic, thoraco-lumbar, lumbar and lombo-sacral respectively in 14, 3%, 9, 5%, 62% and 14, 3%. One vertebrae level was affected in 71, 4%. In view of laboratory findings, increased erytrocyte sedimentation rate was detected in 76, 2%, C-reactive protein positivity in 62%, lymphomonocytosis in 19% and anemia in 28, 5% of them. All of the patients had > or =1/160 titers of brucella agglutination test and negative blood culture. MRI findings are as follows: Predilection for the lumbar spine (62%), moderate paraspinal abnormal soft tissue with abscess formation only in 14,3% cases, and diffuse but exclusively anterior involvement, intact vertebral architecture despite evidence of diffuse vertebral osteomyelitis, and disc space involvement. Additionally, epidural extension was detected in 28, 5% cases, and root compression in 9, 5% cases. Clinical and radiological improvements were observed with a combined antimicrobial therapy of doxycycline and rifampicin during 12 weeks.
**Conclusions:** In endemic areas and in our country, BS is still a public health problem and should be considered in the differential diagnosis of patients with spondylodiscitis. It is difficult to diagnose because its symptoms and signs are non-specific. Therefore, MRI, blood cultures, tissue biopsy and cultures are recommended in suspected cases.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1600

## SAT0497 EPIDEMIOLOGICAL STUDY OF INFECTIOUS SPONDYLITIS IN A TUNISIAN CENTER: ABOUT 118 CASES

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**Background:** Infectious spondylitis remains frequent in Tunisia and is a common reason for hospitalization in rheumatology. We report the experience of our rheumatology department in the diagnosis and management of infectious spondylitis.
**Methods:** This is a retrospective study of 118 cases of infectious spondylitis observed between 1997 and 2015. The diagnosis was based on clinical, biological, radiological and bacteriological data.
**Results:** Our population consisted of 76 men (64.4%) and 42 women (35.6%) with a mean age of 59.2 years [18–84]. A supporting ground was found in 27% of patients. This was diabetes in 17.8% of cases, extra-articular history of tuberculosis in 7.6% of cases, hemodialysis for renal failure in 2.5% of cases, recent spinal surgery in 3.4% of cases, visceral surgery in 2.5% of cases and a long-term corticosteroid in 1.2% of cases. Spinal pain was present in all cases and had an inflammatory rhythm in 89.8% of cases. Fever was observed in 48.3% of cases, night sweats in 27.1% of cases and impaired general condition in 50% of cases. Neurological signs, present in 55.9% of cases were: radiculalgia in 55.1% of cases, motor deficit in 20.3% of cases and spinal cord compression in 9.3% of cases. The inflammatory syndrome was absent in 10.2% of cases. Spinal MRI and CT performed respectively in 77% and 47.4% of cases showed an epidural in 52.5%, a soft tissue abscess in 34.7%, soft tissue infiltration in 27.9% and a root canal abscess in 14.4% of cases. The spondylitis was multifocal in 7.7% and multi-stage in 11% of cases. Affected levels were: lumbar spine in 66.6%, the thoracic level in 26.9% and the cervical level in 8.5% of cases. The germ was isolated in 53.5% of cases. The disco-vertebral biopsy (performed in 42.3% of cases) was contributory in 27.2% of cases. A puncture of a soft tissue abscess (formed in 14.1% of cases) was contributory in 85.9% of cases. Blood cultures were positive in 7.7% of cases. The urine culture had found the germ in 6.4% of cases and a skin sample in 1.2% of cases. Wright serology was positive in 20.5% of cases. These germs were: tuberculosis in 44.9% of cases, brucellosis in 20.5% and pyogenic germs in 29.5% of cases.
**Conclusions:** The clinical presentation of infectious spondylitis is polymorphic and determination of the causative organism can be difficult. In our series, in most cases it was a spondylodiscitis -specific germ. Support by appropriate antibiotic therapy leads overall to a good clinical outcome. Neurological complications can regress, more rarely from is fatal.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1637

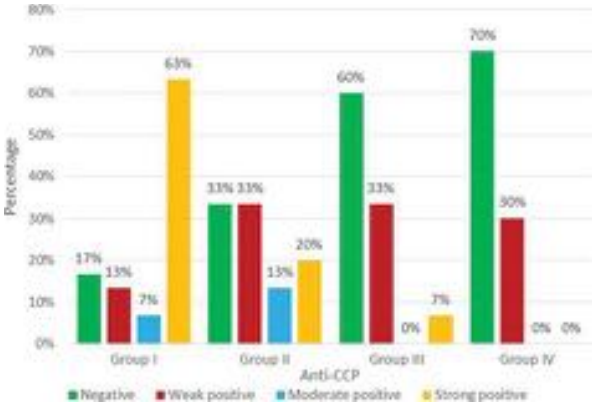
## SAT0498 IMPORTANCE OF ANTI- CYCLIC CITRULLINATED PEPTIDE AS A MARKER DIFFERENTIATING HEPATITIS C RELATED ARTHROPATHY FROM RHEUMATOID ARTHRITIS

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**Background:** Hepatitis C arthropathy is one of the most important extra-hepatic manifestations of HCV. Its clinical presentation is rheumatoid like in about 30% of the cases and the differentiation between both is very important and difficult at the same time as the treatment is completely different. Anti-cyclic citrullinated peptide (Anti- CCP) antibodies can be used as serological markers in differentiation between them but many studies have variable and non-conclusive results concerning its importance.
**Objectives:** The aim of this study is to determine whether anti- CCP antibody is helpful alone in discriminating patients with HCV-associated arthropathy from patients with rheumatoid arthritis.
**Methods:** In this cross sectional comparative study we included 70 subjects, from Tanta University Hospital, Egypt and divided them into four groups: 30 Rheumatoid arthritis patients not infected with HCV,15 HCV patients with typical polyarthritis like RA without erosions or rheumatoid nodules, 15 HCV patients without arthropathy and 10 Normal subjects as a control group. We measured the level of Anti-CCP and RF in all groups.
**Results:** By the end of the study we found that anti-CCP was positive in 83.3% of RA group, 66.7% of HCV with arthropathy group, 40% of HCV without arthropathy group and in 30% of normal control group and there was a significant difference between RA group and HCV without arthropathy and control group, but there was no significant difference between RA and HCV arthropathy However during the comparison between the four groups as regard the degree of positivity of anti-CCP level there was a big difference in the degree of positivity in RA group and HCV arthropathy where 19 (63.3%) were strong positive in RA groups while only (20%)were strong positive in HCV related arthropathy.

Table 1. Comparison between anti-CCP among the studied groups

| | Group I | Group II | Group III | Group IV | $\chi^2$ | P value |
|---|---|---|---|---|---|---|
| Negative | 5 (16.7%) | 5 (33.3%) | 9 (60%) | 7 (70%) | | |
| Weak positive | 4 (13.3%) | 5 (33.3%) | 5 (33.3%) | 3 (30%) | | |
| Moderate positive | 2 (6.7%) | 2 (13.3%) | 0 (0%) | 0 (0%) | 29.7 | 0.000* |
| Strong positive | 19 (63.3%) | 3 (20%) | 1 (6.7%) | 0 (0%) | | |




**Conclusions:** Anti CCP can be a used as an early step in differentiating RA from HCV related arthropathy. If its level is strong positive this can highly suggest early rheumatoid arthritis but if the level is moderately positive or weak positive or even negative it is not enough alone as a marker differentiating RA from HCV related arthropathy.
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**Disclosure of Interest:** None declared

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SAT0499 **SEPTIC ARTHRITIS IN RHEUMATOLOGY: MANAGEMENT AND EVOLUTION OVER THE PAST 50 YEARS. ABOUT 374 CASES**

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**Background:** Septic arthritis is a multidisciplinary emergency which poses diagnostic problems due to the lack of biological and clinical specificity, and variable treatment modalities in the absence of formal consensus.
**Objectives:** The objective of this study was to describe epidemiology, management and evolution of rheumatologic septic arthritis over the past 50 years.
**Methods:** This epidemiological, retrospective, observational, single-center study, included patients hospitalized between 1997 and 2014 in one Rheumatology Department of a University Hospital, for septic peripheral arthritis of native joint. The diagnosis was determined according to Newman's criteria. After a first descriptive part, we tried to determine associated factors for joint morbidity (define by the use of a non-sparing surgery or functional sequelae) and mortality after a follow-up of 1 year. Finally, we compared the results with a previous study, conducted in the same Department between 1966 and 1993 over 176 cases.
**Results:** On the 1997–2014 period, 198 patients were included corresponding to an annual incidence of 11 cases. The average age of patients was 56 years, with 57% men. Main comorbidities were arthropathy (37%), neoplasia (18%) and diabetes (17%). The most common presentation was monoarthritis (88%), of the knee (32%), caused by Staphylococcus aureus (56%). Nine percent of patients had received prior intra articular intervention. We noted 15% of arthritis with no identified pathogen. Endocarditis was found in 6% of patients. The support was multidisciplinary particularly between 2006 and 2014, with an increase of cooperation with bacteriologist (15% of cases between 1997–2005 versus 67% between 2006 and 2014, $p<0.0001$), and a decrease in antibiotic duration (97.1 days versus 75.5 days, p=0.002). The surgical treatment was required in 33% of cases. The death rate at 1 year was 6% and the joint morbidity rate was 20%. Mortality risk factors have been identified (endocarditis OR =12.6 [2.0 to 81.4], p=0.008); MRSA OR =13.8 [1.9 to 100.6], p=0.009). Patients receiving corticosteroids had an excess risk of joint morbidity (OR =3.0 [1.0 to 8.7], p=0.04). In comparison with the previous study, there were more comorbidities ($p<0.01$ for diabetes, neoplasia, rheumatoid arthritis), more bacterial identification and surgical care ($p<0.01$). Iatrogenic origin and mortality remain stable.
**Conclusions:** In the absence of formal recommendations, multidisciplinary cooperation could impact directly on the diagnostic and therapeutic management of septic arthritis. The management seems better than in the 60–90's period, with no change in mortality. Infective endocarditis appears to be an important risk factor for mortality and its research should be systematic.
**Disclosure of Interest:** None declared
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SAT0500 **A COMPARATIVE ANALYSIS OF RADIOLOGICAL FINDINGS BETWEEN TUBERCULOUS AND BRUCELLAR SPONDYLODISCITIS**

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**Background:** Tuberculous and brucella spondylodiscitis are endemic in tunisia. Both present in various pathological patterns, but there are significant radiological differences that permit a presumptive aetiological diagnosis and orient the initial empirical treatment.
**Objectives:** The aim of this study was to compare radiological features between these two diseases.
**Methods:** A retrospective monocentric study was performed. Patients diagnosed with tuberculous spondylodiscitis (TSD) or brucellar spondylodiscitis (BSD) between 2008 and 2016 were included. Clinical status and radiological results were assessed.
**Results:** A total of 33 patients were enrolled in the study including 17 men and 16 women. The mean age was 59 years (29–96 years). Twenty four had TSD (72,8%) and 9 BSD (27,2%). CT scan was performed in 9 cases and magnetic resonance imaging (MRI) in 24 cases. For both TSD ans BSD the most common region affected wad lumbar spine (respectively 58% and 77%). Preverebral, paravertebral, epidural and psoas abscess formations were significantly more frequent in TSD compared with BSD [p=0,01]. When considering neurological complications such as epiduritis and cord compression, TSD was not significantly different from BSD [p=0,17].
**Conclusions:** The results of this study show that TSD is a more suppurative disease with abscess formation.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6023

SAT0501 **HLA SYSTEM IN CHLAMYIDIA TRACHOMATIS-INDUCED REACTIVE ARTHRITIS**

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**Background:** It should be noted considerable incidence rate of reactive arthritis (ReA) in the last decades and the fact that the majority of them are due to Chlamydia trachomatis infection (CTI) [1,2]. In some patients with CTI ReA and chronic ReA will develop [3,4], therefore search for risk factors of possible ReA development in CTI patients is an essential problem.
**Objectives:** To perform the typing of ReA patients induced by CTI for HLA antigens in order to reveal possible genetic markers of susceptibility and resistance to ReA development.
**Methods:** 30 ReA patients observed in Byelorussian Republican Rheumatologic Center (17 women and 13 men from 19 to 56 years old, mean age 36.4±10.5 years) with urogenital CTI confirmed by culture and immunofluorescence serology were studied for frequency of I and II class HLA antigens (A, B, C, DR, DQ locus, total number of studied specificities - 71) by means of microdroplet lymphocyte cytotoxicity test. Data on frequency of I and II class HLA antigens in 308 and 106 unrelated Minsk (Belarus) inhabitants were used as a control.
**Results:** We revealed significant increase of antigen frequency in B locus for B27 ($\chi^2$=26.5; $p_{corr}$=0.00025; RR=5.7) and B60 ($\chi^2$=4.3; $p<0.05$; RR=2.7) antigens, in DR locus for DR1 (43.3% in ReA vs 16.6% in controls, $\chi^2$=10.1; RR=4.0) and DR13 (40.0% in ReA vs 21.7% in controls, $\chi^2$=4.1; RR=2.4) antigens as well as for phenotype DR1,DR13 frequency ($\chi^2$=5.3; $p<0.05$, RR=5.3) in ReA patients. In addition significant decrease of DR7 (10.0% vs 32.1% in controls, $\chi^2$=5.8; RR=-4.2), DR11 (13.3% vs 31.1%, $\chi^2$=3.7; RR=-2.9) and DR53 (23.3% vs 47.2% $\chi^2$=5.4; RR=-2.9) antigen frequency was revealed in ReA patients. We registered significant increase of antigen DQ5 frequency (56.7% vs 28.3%, $\chi^2$=8.3; RR=3.3) as well as phenotype DQ5,6 frequency ($\chi^2$=10.1; RR=16.2) and significant decrease of antigen DQ2 frequency (20.0% vs 37.7%, $\chi^2$=3.4; RR=-2.4) in ReA patients in comparison with controls.
**Conclusions:** The revealed genetic markers of susceptibility to ReA development in patients with urogenital CTI are: HLA B27, B60, DR1, DR13, DQ5 antigens, as well as DR1, DR13 and DQ5, DQ6 phenotypes. We consider DR7, DR11, DR53, DQ2 antigens as factors of resistance to ReA development.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6024

## Back pain, mechanical musculoskeletal problems, local soft tissue disorders

SAT0502 **TOLERANCE AND ACCEPTABILITY OF US GUIDED EPIDURAL INJECTIONS VIA THE SACRAL HIATUS**

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**Background:** Epidural injection with corticosteroids is a common treatment option for patients with lower back pain or sciatica. It can be performed via the interlaminar/interspinous routes or via the sacral hiatus. US has shown its interest to guide steroid injection via the sacral hiatus with a high rate of injection success. However, it is thought that this route might be less well tolerated and more painful for the patient than the interspinous one. It has also been demonstrated that the shape of the sacral hiatus could lead to more difficult injections.
**Objectives:** The goal of our study was to evaluate the pain during the injection, the acceptability of the procedure and to find clinical or anatomical factors associated with a painful procedure. We compared the pain during sacral hiatus epidural and interspinous injections.
**Methods:** We performed a cross-sectional study. Patients undergoing an epidural steroid injection for the treatment of radicular pain due to a disc herniation were included. Epidural injection was performed under US guidance via the sacral hiatus. After a local anesthesia with 5 mL lidocaine, 1.5 mL of cortivazol followed by 18.5 mL sterile serum were slowly injected. Pain during the procedure was evaluated using VAS pain scale. US characteristics of the sacral hiatus was recorded. Acceptability was assessed by the question "If needed, would you accept to have the procedure again". Association between pain and any clinical or anatomical characteristics of the hiatus were assessed by linear regression analysis. Pain during the procedure was compared to the pain during interspinous injection evaluated in one of our previous study (1).
**Results:** There were 52 patients, 28 male (53%), with a mean age 52.5 years

(±15). Mean BMI was 26.5 (±5). Radicular VAS pain before the procedure was 5.2 (±2.1). On US, sacral hiatus mean depth was 7.4 mm (±5.4). Intercornual distance was a mean 12.3 mm (±4) and the mean length of the sacrococcygien ligament was 22.8 mm (±7). Mean VAS pain during the procedure was 3 (±2.4) with no significant difference when compared to the interspinous route (mean VAS = 2.8±2.1; p=NS). No immediate complication was recorded. Forty-height patients (92%) would either be very likely or somewhat likely to a repeat procedure. Only one patient would be somewhat unlikely to have a new injection. Thirty-six (69%) patients would surely recommend this procedure to one of their friends. We found no significant association between the pain during the procedure and any of the clinical or anatomical parameters. Importantly, no association was found between the pain and the US shape of the sacral hiatus.

**Conclusions:** US guided epidural injections through the sacral hiatus is a simple and well tolerated procedure. We found no difference of pain between the interspinous or the sacral hiatus routes. Most of the patients would accept to have this procedure again. We did not find any clinical or anatomical characteristic associated with a painful procedure.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4828

## SAT0503 RELATIONSHIPS BETWEEN WEIGHT, PHYSICAL ACTIVITY AND BACK PAIN IN YOUNG ADULT WOMEN

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**Background:** Back pain is a major global health problem, causing greater disability worldwide than any other condition. It is associated with a significant economic burden and major disability, as therapeutic options have limited efficacy. Given limited treatment options, clarifying predictors of back pain is important in order to optimize preventive strategies. Furthermore, as previous episodes of back pain are predictive of future recurrence, understanding risk factors associated with back pain in early adulthood is particularly important.

**Objectives:** The study aims were to identify whether modifiable risk factors, weight and physical activity, are predictive of back pain in young adult women.

**Methods:** Community dwelling women born between 1973 and 1978 were randomly selected from the Australian national health insurance scheme database to participate in the Australian Longitudinal Study of Women's Health. Women were recruited nationally with intentional oversampling from rural and remote areas. Self-reported data on back pain in the last 12 months, age, weight, physical activity, depression and other socio-demographic factors were collected in 2000, 2003, 2006, 2009 and 2012. In 2000, 9,688 women completed the questionnaire and 83% completed follow up 12 years later.

**Results:** At baseline, median age was 24.6 years and 41% had self-reported back pain. For every 5kg higher weight at baseline, there was a 5% (95% CI 4% - 6%) increased risk of back pain over the next 12 years, after adjusting for age, height, education status, physical activity and depression. Higher weight also predicted back pain risk over each 3 year survey interval ($p<0.001$). The effects of weight on back pain were most significant in those with body mass index $\geq$25 kg/m$^2$ and were observed at all levels of physical activity. Inadequate physical activity and depression were independent predictors of back pain over the following 12 years (both $p<0.001$), after adjusting for above confounders.

**Conclusions:** Back pain is common in community-based young adult women. Higher weight, inadequate levels of physical activity and depression were all independent predictors of back pain over the following decade. Furthermore, the adverse effects of weight on back pain were not mitigated by physical activity. Our findings highlight the role of both higher weight and physical inactivity in back pain among young adult women and suggest potential opportunities for future prevention.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1498

## SAT0504 PREVALENCE AND CORRELATES OF HOUSEHOLD WORK RELATED MUSCULOSKELETAL DISORDERS IN LOW BACK REGION AMONG SRI LANKAN HOUSEWIVES

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**Background:** Household work is a significant cause of low back disorders particularly in the South Asian settings where work is manually performed and labour intensive. However, the prevalence household work related back pain in south Asian settings is unknown.

**Objectives:** To determine the prevalence of household work related musculoskeletal disorders (HWMSD) in low back region and its correlates among 20–50 year old housewives in an urban setting in Sri Lanka

**Methods:** A community based cross-sectional study was conducted on a sample of eligible housewives (n=1102) in an urban Sri Lankan setting using the multi-stage cluster sampling technique. Participants were women whose sole occupation was unpaid household work in their own homes for a minimum of 4 hours (continuously or intermittently) daily for at least 5 days a week, for a minimum of 2 years. Those with menopause, inflammatory arthritis, pregnant or in postpartum period, previous disability unrelated to household work were excluded. A novel validated tool- household work related musculoskeletal disorder questionnaire (HWMQ) with a sensitivity of 94.5% (91.7–97.3) and specificity of 99.3% (98.3–100) was used to identify HWMSD in low back. Correlates of HWMSD in low back region were conceptualized as physical exposures related to the housework, psychosocial factors and individual level factors. An analytical cross-sectional study using multivariate analyses comparing those with HWMSD of the low back region (n=397) and without HWMSD in any region of the body (n=405) determined the correlates of HWMSD in the low back region among housewives.

**Results:** The majority of housewives were performing multiple of household chores [cooking related activities (n=1031, 93.6%), hand washing clothes (n=811, 73.6%), ironing (n=972, 88.2%), sweeping indoor and outdoor (n=374, 33.9%), cleaning bathrooms/toilets (n=912, 82.8%), shopping (n=725, 65.8%) and carrying children (n=374, 33.9%)]. The prevalence of HWMSD in low back region among 20–50 year old housewives was 36% (95%CI: 33.1%>39%).

Correlates of HWMSD in low back region among 20–50 year old housewives identified as significant are shown in Table 1.

Table 1. Correlates of HWMSD in low back among 20–50 year old housewives

| Correlates of HWMSD in low back | Adjusted OR (95% CI) |
|---|---|
| Physical exposures | |
| Handling weight | 1.5 (1.1–2.2) |
| Working in awkward posture | 2.2 (1.5–3.1) |
| Working ≥8 hours per day | 2.3 (1.6–3.3) |
| Psychosocial factors | |
| Psychological distress | 1.8 (1.3–2.6) |
| Not having rest breaks | 1.8 (1.1–3.3) |
| Individual level factors | |
| Not being satisfied with family income | 1.8 (1.2–2.5) |
| Being employed more than two years prior to the study | 1.9 (1.3–2.7) |
| Having a child aged <5 years | 1.7 (1.1–2.6) |
| Married for ≥10 years | 2.0 (1.3–3.0) |
| Poor self-rated general health status | 3.7 (2.5–5.4) |
| Having long term illness | 1.8 (1.1–2.8) |
| Usual residence not being an owned house | 0.7 (0.5–0.9) |

**Conclusions:** Prevalence of HWMSD in low back was high among housewives in Sri Lanka. The study identified several modifiable and a few non-modifiable physical exposures, psychosocial factors and individual level factors as significant correlates of HWMSD in low back region.

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**Disclosure of Interest:** None declared
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## SAT0505 SEVERELY-DISABLING CHRONIC LOW BACK PAIN: COMBINATION TREATMENT WITH GLUCOSAMINE–CHONDROITIN SULFATE REDUCES DISABILITY, PAIN AND NSAID CONSUMPTION – RESULTS FROM A LARGE, COMMUNITY-BASED, PILOT, OPEN PROSPECTIVE INTERVENTIONAL STUDY

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**Background:** Low back pain (LBP) is the leading cause of Years Lived with Disability worldwide (1). The number of people suffering from LBP grew more than 50% from 1990 to 2013, to 651 million (1). Glucosamine-chondroitin sulfate (GCS) combination is widely used in the treatment of OA; however there are few prospective scientific investigations of its therapeutic merits in severe LBP.

**Objectives:** To study the efficacy of GCS in the decreasing disability in patients with severe disability due to chronic low back pain in a large open pilot prospective observational study.

**Methods:** We studied patients 40–65 years of age who had severe disability (Oswestry Score >40) due to LBP. The Oswestry scale contains ten sections on pain intensity, lifting, ability to care for oneself, walking, sitting, standing, sexual function, social life, sleep quality, and ability to travel. Each question is scored on a scale of 0–5 with the scores for all questions summed, then multiplied by two to obtain the index (range 0 to 100). Scores above 40 indicate severe disability. Major exclusion criteria were the presence of fibromyalgia, degenerative spondylolisthesis, and alcohol and/or drug abuse. All patients were treated with ARTRA (combination of glucosamine hydrochloride 500 mg and chondroitin

sulfate 500 mg in tablet form; Unipharm Inc.) at a dose of 1 tab bid for the first month and then 1 tab daily for the next two months. Oswestry index was measured at enrollment into the study and then after 1 month, 2 months and 3 months of starting therapy.

**Results:** The study population included a total of 4,588 patients with Oswestry index of 40 or more (mean age 52.9±7.4 years, 66% women, mean BMI 27.7±5.4, median of duration of LBP 6 months, LQ-4.0; UQ-20.0). Intent-to-Treat (ITT) analysis with worst observation carried forward (WOCF) showed an improvement in disability Oswestry Scale mean (95%CI) from 58.4 (57.9 -58.7) to 13.9 (13.5–14.3) ($p<0.0001$, ANOVA for repeated measures). Significant improvement was also observed in pain scores: pain at rest improved from mean (95%CI) of 5.93 (5.87–5.98) at study entry to 1.49 (1.45–1.55) at 3 months ($p<0.0001$). Pain at movement decreased from 7.53 (7.49–7.57) to 2.36 (2.31–2.42) ($p<0.0001$). NSAIDs were used by 74.9% of patients at study entry; at 3 months of treatment, only 9.9% of patients required NSAIDs for pain control ($p<0.0001$, McNemar's test).

An adverse event (AE) was reported by 311 (6.8%) patients (mostly GI in origin, such as nausea, abdominal pain and dry mouth) but only 134 (2.9%) patients deemed the AE to be severe enough to discontinue therapy.

**Conclusions:** Although open and uncontrolled, this pilot, community-based efficacy and safety study shows dramatic reductions in pain and disability in patients with severe disability as measured with Oswestry index. With its benign safety profile, GCS therapy deserves serious evaluation in the management of severe LBP in a prospective randomized double-blinded clinical trial.

**References:**

[1] Vos T et al. Lancet. 2015; 386(9995): 743–800.

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## SAT0506 TELEVISION VIEWING TIME, PHYSICAL ACTIVITY AND LOW BACK PAIN IN COMMUNITY-BASED ADULTS: RESULTS FROM A PROSPECTIVE COHORT STUDY

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**Background:** Low back pain (LBP) has an enormous negative economic impact on individuals, families, communities, industries and governments. As such, understanding the aetiology and risk factors for LBP is important in reducing the significant burden of this condition. In an effort to achieve this, epidemiological studies have examined a number of factors, including demographic (age and gender), obesity, and lifestyle factors (physical activity and sedentary lifestyle). The role of lifestyle factors on LBP has become a particular area of importance as they can be modified. Two systematic reviews concluded that there was limited evidence to support an association between physical activity and sedentary behaviour and developing (LBP).

**Objectives:** To examine the associations of physical activity and television viewing time with LBP intensity and disability in community-based adults.

**Methods:** 5,058 participants (44% men) of the Australian Diabetes, Obesity and Lifestyle Study had physical activity and television viewing time measured in 1999–2000, 2004–2005 and 2011–2012, and LBP intensity and disability assessed in 2013–2014 using the Chronic Pain Grade Questionnaire. Logistic regressions were used to estimate the odds ratio for LBP intensity and disability associated with physical activity and television viewing time. Analyses were adjusted for age, education, smoking, dietary guideline index score, body mass index, Mental component summary score. To test whether associations of physical activity or television viewing time with LBP intensity and disability were modified by sex, obesity, or age, interactions were tested using the likelihood ratio test.

**Results:** 81.7% men and 82.1% women suffered from LBP. Most of the men (63.6%) and women (60.2%) had low intensity LBP with a lower proportion having high intensity LBP (18.1% men, 21.5% women). Most of the participants had no LBP disability (74.5% men, 71.8% women) with the remainder reporting low (15.8% men, 15.3% women) or high (9.7% men, 12.9% women) disability due to LBP. Insufficient physical activity (<2.5 hours/week) was not associated with LBP intensity or disability in either men or women. High television viewing time (≥2 hours/day) was associated with greater prevalence of disability due to LBP in women (low disability OR 1.35, 95% CI 1.04–1.73; high disability OR 1.29, 95% CI 1.01–1.72). Women with insufficient physical activity and high television viewing had an increased risk of disability due to LBP (OR 1.42 95% CI 1.07–1.88) compared with women with sufficient physical activity and low television viewing.

**Conclusions:** Our findings indicate that high levels of television viewing, a marker of sedentary behaviour, is associated with an increased risk of LBP disability in women but not in men. Insufficient physical activity was not associated with LBP intensity or disability in either men or women. These findings suggest that targeting time spent watching television and possibly other prolonged sedentary behaviours such as occupational sitting may have the potential to reduce disability due to LBP in community-based adults, particularly in women.

**Disclosure of Interest:** None declared

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## SAT0507 COMPARISON OF ORAL SPLINTING AND KINESIOTAPING IN TEMPOROMANDIBULAR JOINT PAIN

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**Background:** Kinesiotaping is widely used in pain due to various musculoskeletal conditions. Especially sports injuries are the main area for kinesiotaping.

**Objectives:** In our study we aimed to use in different topic, temporomandibular joint (TMJ) pain and to show the efficacy on joint function and quality of life.

**Methods:** We assessed 86 patients aged 18 to 38 years who attended outpatient clinic with acute or chronic TMJ pain and discomfort while chewing. A board of one physiatrist and a dentist (oral and maxillofacial surgeon) evaluated the patients. Previous dental surgery/ jaw injury and other dental pathologies excluded and 69 patients with myofascial pain and the history of sleep disorders like clenching or grinding teeth while sleeping were randomly divided into the oral splint (bite guard) and the kinesiotaping group. Kinesio taping was applied to the skin over TMJ in reverse "V" shape extended to inferior border of jaw muscle and to the anterolateral aspect of neck. Taping was applied two times per week for two weeks. In splint group, bite guard were used all day long for two weeks except sleeping period. Presence of locking of the the joint, clicking or crepitation sound were noted and limitation of ROM in TMJ were measured by distance between upper and lower incisives, Speech, eating and sleeping behaviors were assessed for daily living activities. Pain intensity was measured by the visual analog scale (VAS). All the parameters were evaluated before and after intervention.

**Results:** Thirty four subjects were assigned to the kinesiotaping group, and thirty five subjects were assigned to the oral splint group. Both in the kinesiotaping and splint group, the level of pain intensity was decreased and the ROM was increased significantly ($p<0.01$), ($p<0.05$). Comparison between the groups did not reveal significant differences in VAS and ROM. Daily eating activity and sleeping quality were improved in both groups but not in other oral activities.

**Conclusions:** Although many etiological causes of TMJ pain, for the patients with myofascial pain and fibromyalgia, kinesiotaping is as effective as oral splints like bite guards. During daily practice, the myofascial pain syndrome and fibromyalgia background should be assessed for the ideal treatment. In contrast to splinting, kinesiotaping is non-invasive, easy-to-apply intervention method and do not interrupt daily oral activities.

**Disclosure of Interest:** None declared

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## SAT0508 MANUAL THERAPY AND EXERCISE FOR ROTATOR CUFF DISEASE: A COCHRANE REVIEW

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**Background:** Initial management of rotator cuff disease often includes manual therapy and exercise, usually delivered together as components of a physical therapy intervention. To best inform current practice, an up-to-date review which incorporates the most recently available evidence is needed.

**Objectives:** To systematically identify and synthesise the available evidence regarding the benefits and harms of manual therapy and exercise, alone or in combination, for the treatment of rotator cuff disease.

**Methods:** We included randomised controlled trials, including adults with rotator cuff disease, and comparing any manual therapy or exercise intervention with placebo, no intervention, a different type of manual therapy or exercise or any other intervention. Interventions included mobilisation, manipulation and supervised or home exercises, delivered alone or in combination. Trials investigating the primary or add-on effect of manual therapy plus exercise were the main comparisons of interest. Main outcomes of interest were overall pain, function, pain on motion, patient-reported global assessment of treatment success, quality of life and the number of participants experiencing adverse events.

We searched CENTRAL, MEDLINE, EMBASE, CINAHL Plus, ClinicalTrials.gov and the WHO ICTRP clinical trials registries up to March 2015, unrestricted by language. Two review authors independently selected trials for inclusion, extracted data, performed risk of bias assessment and assessed the quality of the body of evidence for the main outcomes using the GRADE approach.

**Results:** We included 60 trials (3620 participants). Only one trial compared manual therapy plus exercise with placebo (inactive ultrasound therapy) (120 participants; high quality evidence). At 22 weeks, there were no between-group differences in mean change in overall pain (placebo: 17.3 points on a 100-point scale; manual therapy plus exercise: 24.1 points; adjusted mean difference (MD) 6.8 points, 95% CI -0.7 to 14.3 points) and similar findings for function, pain on motion, treatment success and quality of life. More participants reported adverse events with manual therapy plus exercise (17/55, 31%) versus placebo (5/61, 8%):

RR 3.77 (95% CI 1.49 to 9.54)) but these were mild and short-lived (short-term pain following treatment).
Five trials (low quality evidence) found no important differences between manual therapy plus exercise compared with glucocorticoid injection and one trial (low quality evidence) showed no important differences between manual therapy plus exercise and arthroscopic subacromial decompression.
**Conclusions:** Despite identifying 60 eligible trials, only one trial has compared a combination of manual therapy and exercise reflective of common current practice to placebo. It was judged of high quality and found no clinically important differences between groups in any outcome. Effects of manual therapy plus exercise may be similar to those of other active interventions (e.g. glucocorticoid injecton, surgery), but this is based on low quality evidence.
**Disclosure of Interest:** None declared
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## SAT0509 FEASIBILITY OF ULTRASOUND-GUIDED FACET JOINT INJECTIONS THROUGH A LONGITUDINAL APPROACH

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**Background:** Facet joint-mediated pain has been identified as a common cause of lumbar pain. Steroid injections are currently made to treat them, they are usually performed under fluoroscopy or computed tomography guidance. Ultrasound (US) is also appropriate to study facet joints and some studies showed feasibility and efficacy of facet joint injections performed under US-guidance through a transversal approach. On a longitudinal view, facet joints are easy-to-identify as a series of lumps with the joint capsule appearing as a thin hypoechoic line that envelops the joint.
**Objectives:** Considering the good visibility of these joints and their capsule on the longitudinal view, we studied the feasibility of US-guided facet joint injections using a longitudinal inline approach.
**Methods:** Patients referred to our rheumatology department to receive facet joint injections under fluoroscopy were included. To realize the injection, we first located the accurate lumbar level on a longitudinal median view going through the spinous processes. Facet joints were identified as previously described placing the probe 2–3 cm away from the median line. Then, the needle was inserted to reach the hypoechoic line corresponding to the capsule or, if not visible, the top of the lump formed by the inferior articular process of the superior vertebra overlying the superior articular process of the vertebra below it. When we obtained the bone contact, we injected iodinated contrast medium followed by cortivazol. Finally, we made a lumbar X-ray to analyze the needle position and the quality of the arthrography.
The first objective was to assess the number of injections realized in front of the joint. For secondary objectives, we assessed the number of accurate arthrography, the duration of the procedure and the occurrence of adverse events. During US examination, the visibility of the capsule and the presence of osteophytes were collected.
**Results:** Thirty-eight patients have been included by two operators. We excluded four patients because of a poor visibility of the spinal structures. Mean age was 58,4 years (range, 30–82) and mean BMI was 25,2 kg/m$^2$ (range, 18–34). US showed osteophytes in 42% and the joint capsule was inconstantly visible (25%). One-hundred and forty-four injections were performed (72 at the L4-L5 level and 72 at the L5-S1 level) and 141 X-ray were analyzed. One-hundred and twenty-three injections (87%) were accurately realized in front of the joint, i.e. in front of the inferior articular process of the superior vertebra. However, a proper arthrogram was obtained in only 35 cases (25%). Mean procedure duration was 8.5 minutes for four injections. Six patients (18%) reported transient pain exacerbation and no severe complication occurred during the first month after the procedure.
**Conclusions:** With a longitudinal inline approach, US-guided facet joint injections were feasible and 87% injections were realized right in front of the joint. However, we obtained a correct arthrogram in only 25%. The depth of the target-point, the inconstant visualization of the capsule and the obliquity of the needle probably explain this result. Additional studies will be necessary to improve the accuracy of the technique.
**Disclosure of Interest:** None declared
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## SAT0510 PAINFUL SHOULDER: RELEVANCE OF CLINICAL AND SONOGRAPHIC DATA ON CORTICOSTEROID INJECTION OUTCOME

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**Background:** Painful shoulder (PS) is a common condition and a frequent cause of referral to a Rheumatology department, particularly in refractory patients.
**Objectives:** To study the association between clinical and sonographic data and corticosteroid injection (CI) outcome in PS patients.
**Methods:** Adult patients with PS, consecutively observed in a Rheumatology outpatient clinic were included. Demographic and clinical data (age, gender, time of symptoms, pain in contralateral shoulder, past CI of any shoulder, active abduction limitation and dominant side) were registered. The portuguese version of QuickDASH questionnaire (QD) and pain Visual Analogic Scale (VAS) were answered by the patient. If the patient fulfilled clinical criteria for CI (inflammatory or mixed pattern of pain, refractory to at least a 2 week NSAID treatment on full dose, or contra-indication to NSAID, and absence of contraindication to CI), a shoulder ultrasound (US) was performed before CI, and the sonographic findings were registered (presence of subacromial bursitis (SAB), long bicipital head tenosynovitis (LBHT), tendon calcification or supraspinatus (SS) tear). After 9 ± 2 weeks, patients were reassessed, repeating the QD and VAS questionnaires. Absolute and relative variation of QD score (a$\Delta$QD and r$\Delta$QD, respectively) and absolute and relative variation of pain VAS (a$\Delta$VAS and r$\Delta$VAS, respectively) were calculated. Patients with generalized pain syndromes, with suspected or confirmed chronic rheumatic inflammatory disease or secondary cause of the shoulder pain, with sonographic complete supraspinatus tear or glenoumeral effusion and those refusing CI treatment or proposed for calcification lavage, or those in whom reassessment was out of the defined interval were excluded. Statistical analysis was performed using SPSS 21.0 software.
**Results:** Sixty-eight patients were included, of whom 36 were excluded because of presenting at least one of the exclusion criteria. Thirty-two patients, 23 women, with a mean age of 58.9 ± 10.2 years, concluded the study. The mean time of symptoms was 8 ± 7.4 months; 11 (34.4%) patients had also pain in the contralateral shoulder, 8 (25%) had active abduction limitation, 5 (15.6%) had history of shoulder CI, and 24 (75%) had pain on the dominant side. Regarding US findings, 18 (56.3%) had SAB, 12 (37.5%) had LBHT, 16 (50%) had intratendinosis or transtendinosis SS tear and 11 (34.4%) had any tendon calcification.
Age or time of symptoms did not correlate with any of the improvement scores. Higher baseline QD score correlated with higher a$\Delta$QD ($r$=0.55, $p$<0.01) and r$\Delta$QD ($r$=0.37, $p$<0.05); higher baseline VAS score correlated with higher a$\Delta$VAS ($r$=0.38, $p$<0.05). SS tear was present in older patients ($p$<0.05), but it was not associated to improvement scores. Active abduction limitation was associated with greater a$\Delta$QD or r$\Delta$QD ($p$<0.01), and a$\Delta$VAS or r$\Delta$VAS ($p$<0.05). Patients with sonographic inflammatory signs (SAB or LBHT) had greater a$\Delta$VAS and r$\Delta$VAS scores ($p$<0.05); there was also a trend towards greater improvement on QD scores, although not statistically significant.
**Conclusions:** Patients with more severe symptoms or active abduction limitation have greater benefit from CI; having any of the inflammatory US findings described is also associated with greater pain relief after CI.
**Disclosure of Interest:** None declared
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## SAT0511 MANAGEMENT OF ADHESIVE CAPSULITIS WITH LANDMARK GUIDED HIGH VOLUME STEROID INJECTIONS IN THE COMMUNITY BASED MUSCULOSKELETAL CLINIC

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**Background:** Pathology of frozen shoulder (FS) includes inflammatory response with fibroblastic proliferation [1]. It results in global loss of motion due to rotator cuff interval and coraco-humeral ligament contracture as well as capsular thickening. Recently, image guided hydro-dilatation combined with steroid inj became popular FS management. Sometimes three injections with 2 week intervals are given [2]. This procedure is usually performed in outpatient radiology department and requires referral to secondary care. I present an audit of community based treatment of the frozen shoulder. All patients were treated during their 1st appointment at musculoskeletal clinic. I observed that patients respond well to landmark guided high volume steroid injection. It is quick to administer, does not require assistance or additional imaging.
**Objectives:** To assess whether landmark guided high volume steroid injections combined with home based unsupervised stretching exercises are effective in the treatment of frozen shoulder.
**Methods:** All patients diagnosed with Frozen shoulder during 1st appointment between September 2013 and August 2015 were included in the audit. They were followed up at 2–3 months. They were treated with high volume steroid injection: 1 ml 40 mg triamcinolone, 9 ml of 0.5% marcaine +/– normal saline. Standard posterior approach was used for glenohumeral joint injection. Four shoulder stretches were advised to patients for regular home unsupervised exercise. All patients had opportunity to access MSK service within 6 months from the 1st appointment. Their electronic record was reviewed again in January 2016 to establish whether they represented to our MSK service with the same problem. The primary end point of the study was the need for further secondary care orthopaedics referral.
**Results:** 90 patients were treated within the study period. 35.6% (32) of patients were male and 64.4% (58) were female. The mean age of the patients was 56.6 years. 54.4% of patient had duration of symptoms from 1–6 months, 37.8% of patient had duration of symptoms from 7–12 months, 6.7% had duration of symptoms from 13–18 months and 1.1% - 1 patient had symptoms for 24 months. 29 patients (32.2%) had ≥30ml of fluid injected in the glenohumeral joint (GHJ). 48 patients (53.3%) had 10 ml injected the GHJ. 10 patients (11.1%) had ≥20 ml injected in the GHJ. 3 patients (3.3%) had 15ml volume injection. 35 (38.8%) patients required more than 1 injection.

Overall, during study period 3 (3.3%) patients required further orthopaedic management. 96.7% of patients were satisfied with the management and declined further orthopaedic referral during follow up appointment.
**Conclusions:** Landmark guided high volume steroid injections combined with stretching exercises are effective at relieving symptoms of frozen shoulder. This treatment can be recommended before considering further secondary care orthopaedics interventions.
**References:**
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**Disclosure of Interest:** None declared
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## SAT0512 DOES SWITCHING FROM ONE NON-STEROIDAL ANTI-INFLAMMATORY DRUG (NSAID) TO ANOTHER IMPROVE PAIN CONTROL?

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**Background:** NSAIDs - the main medications for control of musculoskeletal pain in rheumatic diseases (RD). However, their use does not always lead to a significant reduction of pain and may be accompanied by side effects. There is a need to replace the first NSAID with another in many patients.
**Objectives:** To evaluate the results of the use of the selective COX-2 inhibitor etoricoxib in patients with acute/subacute pain related to background RD despite using other NSAIDs.
**Methods:** A group of patients of 1566 patients (63.5% women and 31.1% men, age 48.8 ± 13.9 years) with acute/subacute pain associated with RD (mainly osteoarthritis and back pain) was included in an open-label study. The criterion for selection of patients was dissatisfaction with the treatment (10 cm VAS pain >3 cm) by background NSAIDs. The patients mainly used diclofenac (24.5%), nimesulide (27.2%) and meloxicam (25.6%). After inclusion in the study all patients started etoricoxib instead of other NSAIDs. The dose and duration of treatment were determined by a physician: the majority of patients (59.6%) took etoricoxib 90 mg/day. The results of treatment were assessed after 2 weeks.
**Results:** After start of treatment with etoricoxib a significant improvement was observed in the majority of patients. Pain decreased from 6.21 ± 1.4 to 1.93 ± 1.3 cm VAS. The complete pain relief was achieved in 12.5% of patients, 58.3% achieved low intensity of pain (VAS <2 cm). Additional therapy for symptom control (muscle relaxants, other analgesics, local injections of glucocorticoids, and others) needed in 31.2% of patients. The best effect was observed when using a higher dose of etoricoxib: decrease of pain intensity on 120 mg, 90 mg and 60 mg per day was 4.77 ± 1.88, 4.69 ± 2.01 and 3.50 ± 1.48 cm VAS respectively (the difference between 120 and 60 mg/day, 90 and 60 mg/day was significant, $p<0.001$). Treatment tolerability was assessed as “good” in 62.7%, "satisfactory" in 36.7% and "bad" in 0.6% of patients. Adverse events were reported in 55 patients (3.5%), mainly dyspepsia – in 21 (1.3%) and arterial hypertension - in 27 patients (1.7%).
**Conclusions:** Switching from previous therapy with NSAIDs to etoricoxib provides an effective reduction of acute/subacute pain. High doses etoricoxib are more effective. Short-term use of etoricoxib rarely causes adverse events.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4726

## SAT0513 OSTEOID OSTEOMA OF THE ODONTOID PROCESS OF THE AXIS: A RARE CAUSE OF NECK PAIN

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**Background:** Osteoid osteoma is painful benign tumor that comprises approximately 3% of all bone tumors and approximately 10% of all benign bone tumors. Most of the cases occur in the first three decades and two to three times more frequently in men than in women. The tumor is very uncommon after the age of 40 years or during infancy. More than 50% of osteoid osteomas involve long tubular bones especially those of the lower extremities. Osteoid osteoma of the spine is relatively uncommon. Pain is the primary symptom of initial and recurrent disease, although reports of osteoid osteoma without the presence of pain exist. It is often difficult to diagnose, especially when the patient does not complain of pain.
**Objectives:** Here we report our patient who had an osteoid osteoma at the odontoid process of the second cervical vertebra (axis).
**Case presentation:** A 48-year-old woman was admitted to the of physical medicine and rehabilitation department with an 8-month history of neck pain. There was no history of previous injury. For the first 4 months, she had intermittent neck pain, but there after severe neck pain developed during the nighttime that sometimes kept her awake. Her neck pain was relieved transiently by non-steroidal anti-inflammatory drugs (NSAIDs). The pain was worsened 4 months prior to presentation and was associated with frequent occipital headaches. External immobilization with a soft neck collar could not control her symptoms.



Figure 1. CT of cervical spine: A.Axial B.Coronal C.Sagittal images showing the nidus and perifocal sclerosis.

Physical examination revealed limitation of rotation and extension with neck pain. Neurologic examination was normal. There was no spinal tenderness. Her laboratory data was within the normal ranges. Computed tomography showed an oval nidus and marked sclerosis around the lesion at the odontoid process of the axis (Figure 1A-C). Since the patient refused surgery and considering the benign nature of osteoid osteoma, we prescribed NSAID to the patient. With the treatment, the patient’s symptoms improved and the range of motion of the cervical spine was also recovered. At one-year follow-up, the patient is free of symptoms with the conservative treatment.
**Conclusions:** Osteoid osteoma most frequently involves the posterior vertebral elements. An osteoid osteoma of the odontoid process of C2 is rare. Previously, only three cases between the ages 14–18 were reported to have osteoid osteoma involving the odontoid process of the axis. To the best of our knowledge this is the first case of osteoid osteoma involving the odontoid process in an adult female patient. Our patient demonstrated the typical radiological appearance of osteoid osteoma on imaging modalities. Since surgery is risky regarding the damage of the spinal cord, and/or vertebral artery, conservative approach should be considered for the treatment of osteoid osteoma of the cervical spine, especially the odontoid process. Surgery may be suggested to the patients who do not respond to palliative treatment.
**Disclosure of Interest:** None declared
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## SAT0514 EFFECTIVENESS OF ABDOMINAL CORE STABILIZATION EXERCISES IN PATIENTS WITH LOW BACK PAIN. OVERVIEW OF SYSTEMATIC REVIEWS (PRELIMINARY RESULTS)

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**Background:** Low back pain is a large and frequent disorder, with a lifetime prevalence that ranges from 60 to 80%. It is also the main cause of work absence and permanent disability. Exercise therapies appear to be an effective treatment to reduce pain and improve axial performance in patients with chronic low back pain. Yet, abdominal CORE exercises have been incorporated for several years in different rehabilitation programmes. Core muscles, can be divided into two groups: 1- deep muscles or stabilizing muscles (connected to lumbar vertebral segment) and 2- shallow muscles, (not connected to lumbar spine (LS)) but enables additional spinal control. Physical activity focused on these groups of muscles could contribute to pain alleviation and spinal functional improvement.
**Objectives:** To perform a global review (overview) of systematic reviews (SR) to evaluate the beneficial effect of abdominal core stabilization exercises on: 1- pain, 2- LS performance, 3-evaluate adverse effects.
**Methods:** We conducted a global review of systematic reviews (SR), based on 3 online databases: CENTRAL, MEDLINE/Pubmed y PEDro, in English and Spanish. Critical appraisal of included studies was performed by 3 authors independently. AMSTAR system was used to rate the quality of SR.
**Results:** From 17 potential studies found, 9 were included and analysed. Quality of SR was good (AMSTAR 6–11). Metanalysis was performed in 55, 5% of references, Quality of references included in SR were rated on different scales: PeDro (3), Cochrane collaboration (5) and Jadad (1). Globally there were 59 articles included but two were not RCT. Interventions and comparisons assessed were deeply heterogeneous. In addition the study population was small. In general, pain and LS function experimented improvement with CORE stabilization exercises in the short and medium term follow-up, but not in the long term. The types of exercises performed on CORE muscles were drastically heterogeneous. The five papers were metanalysis was performed, showed a significant improvement of pain and LS function with Motor Control exercises (MCE) when compared to general exercises or minimal interventions or control. This was observed in the short and medium term, but not in the long term. No studies mentioned adverse effects.
**Conclusions:** 1. The reviews analysed showed methodological limitations 2. CORE stabilization exercises improve pain and LS function in the short and medium term, but not in the long term. 3. MCE appear to be better than general exercises, minimal interventions or control for pain and LS function. 4. There is no information about adverse effects. 5. Due to the different exercises programmes performed on CORE muscles, and different comparisons evaluated, the clinical efficacy remain uncertain.

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## SAT0515 LUMBAR CT-GUIDED STEROID INFILTRATION ON THE REFRACTORY LOW BACK PAIN. STUDY OF 258 PROCEDURES IN THE SAME CENTER

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**Background:** Low back pain of mechanical origin is a major cause of disability and surgical intervention. The lumbar computed tomography (CT)-guided steroid infiltration can accelerate the recovery process and sometimes avoid the surgery.
**Objectives:** Our aim was to review the indications, efficacy and complications of this technique in a wide series of unselected patients. In addition a comparative study of efficacy was performed according to the lumbar underlying pathology, type of steroid and approach of injection.
**Methods:** Study of lumbar CT-guided steroid injections performed in a University Hospital between January 2012 and June 2015. The minimum follow-up was 3 months.
The procedure was performed in patients with low back pain refractory to standard medical therapy and Lumbar Spine Rehabilitation.
Efficacy was assessed at 1 and 3 months according to a semiquantitative scale as the pain response as a) total response, b) partially c) no or d) worsening pain.
A comparative study of the efficacy and safety was performed, regarding: a) underlying pathology, b) approach of injection and c) the different types of steroids used.
Fisher's test and $\chi^2$ and the SAS System for Windows V program 9.2.were used for statistical analysis.
**Results:** During the study period 258 procedures were performed in 171 patients (132 men/126 women) with a mean age ± SD of 58.24±13.45 years (range, 18–88).
The indications for the injection were: a) disc herniation (44.57%), b) lumbar stenosis (34.11%), c) postoperative fibrosis and spondylolisthesis (20.15%) and d) facet joint synovial cysts syndrome (1.17%).
Approaches used were: a) posterior epidural (24.42%), b) lateral recess (58.91%), and c) foraminal (16.67%).
The chosen steroid was triamcinolone (74.81%), dexamethasone (23.64%) and methylprednisolone (1.55%).
In a significant proportion of the procedures improvement in the patient's sintomatology was reported at the first month, regardless of the indication, route of corticosteroid injection and steroid used (TABLE).
Regarding the overall outcome, at 3 months 72.48% of the patients experienced clinical improvement. And only 21.71% of patients required a subsequent surgery.
The clinical efficacy showed no statistically significant differences according to the indication of the procedure or the route used for the injection. However, the improvement of pain was significantly greater in patients treated with triamcinolone than those treated with dexamethasone (p=0.01).
Regarding safety there were 6 (2.3%) local complications (puncture of the thecal sac) and 3 (1.16%) systemic complications (allergic reaction). None of these complicationes were of clinical relevance and they were not associated with the corticosteroid used.

Table: Efficacy at 1 month according to Indication, Approach and Steroid

| | Total response n(%) | Parcial response n (%) | No response n (%) | Worsening n (%) | TOTAL n (%) |
|---|---|---|---|---|---|
| Indication | | | | | |
| -disc herniation | 7 (6.9%) | 83 (72.2%) | 23 (20.0%) | 2 (1.7%) | 115(44.6%) |
| -spinal stenosis | 4 (4.6%) | 60 (68.2%) | 22 (25.0%) | 2 (2.3%) | 88(34.1%) |
| -postsurgical pain syndrome | 1 (2.1%) | 36 (75.0%) | 11 (28.6%) | 0 (0.0%) | 48(18.6%) |
| -others | 0 (0.0%) | 5 (71.4%) | 2 (28.6%) | 0 (0.0%) | 7(2.7%) |
| Approach | | | | | |
| -posterior epidural | 2 (3.2%) | 43 (68.3%) | 18 (28.6%) | 0 (0.0%) | 63(24.4%) |
| -lateral recess | 9 (5.9%) | 107 (70.4%) | 33 (21.7%) | 3 (2.0%) | 152(58.9%) |
| -foraminal | 1 (2.3%) | 34 (79.07%) | 7 (16.3%) | 1 (2.3%) | 43(16.7%) |
| Steroid | | | | | |
| -Triamcinolone Acetonide | 12(6.2%) | 142 673.6%) | 36 (18.7%) | 3 (1.6%) | 193(74.8%) |
| -Dexamethasone | 0 (0.0%) | 39 (63.93 %) | 21(34.4%) | 1 (1.6%) | 61(23.6%) |
| -Methylprednisolone | 0 (0.0%) | 4 (100.0%) | 0 (0.0%) | 0 (0.0%) | 4(1.6%) |
| TOTAL n= 258 | 12 (4.7%) | 184 (71.3%) | 57 (22.5%) | 4 (1.6%) | 256(100%) |

**Conclusions:** CT-guided corticosteroid injection is an effective and safe treatment in low back pain refractory to standard medical therapy in patients with spinal stenosis, disc herniation and postoperative fibrosis.
Triamcinolone infiltration seems to be more effective than dexamethasone.
**Disclosure of Interest:** None declared
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## SAT0516 EPIDURAL ABSCESS PREDICTS THE PROGNOSIS OF PATIENTS WITH CONSERVATIVELY TREATED PYOGENIC SPONDYLITIS

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**Background:** Although initial treatments for pyogenic spondylitis include conservative approaches such as rest and antibiotics, some cases are refractory to conservative therapy.
**Objectives:** The objective of this study was to clarify the predictors for achievement of C-reactive protein (CRP) normalization in pyogenic spondylitis.
**Methods:** In the present study, we enrolled 83 patients (51 men and 32 women) with conservatively treated pyogenic spondylitis at Saitama Medical University from 2006 to 2015. We defined CRP normalization as a CRP level decrease to $<$0.25 mg/dl. A multiple logistic regression analysis was used to examine the association of achievement of CRP normalization with the number of infected vertebrae, bacterial strain, blood data, and the expansion of abscess to the epidural space by using functional magnetic resonance imaging. The blood data analysis included the following measurements: WBC, Hb, ALB, GOT, GPT, gamma GTP, BUN, Cr, UA, ALP, LDH, eGFR, TG, LDL, HDL, IP, and HbA1c levels.
**Results:** Among 83 patients, 39 patients (47.0%) achieved the normalization of CRP levels. The average period from the onset to admission was 56.3 days. The average number of infected vertebrae was 2.19. Of the 83 patients, 81% had the following complications: diabetes (25 patients), high blood pressure (22 patients), heart disease (16 patients), urinary tract disease (9 patients), collagen disease (7 patients), dialysis (5 patients), malignant tumor (5 patients), hepatic dysfunction (4 patients), high uric acid (hyperuricemia, 3 patients). The pathogenic bacteria were MSSA (14 patients), MRSA (23 patients), others (5 patients), and unknown (41 patients). We found significant differences in the subjects with and without achievement of CRP normalization with respect to age (68.6 vs. 62.5 years), the number of affected vertebrae (1.9 vs. 2.6), ratio of resistant pathogenic bacteria (10% vs. 43%), ratio of expansion of abscess to the epidural space (27% vs.71%), and blood data such as Hb (12.0 vs. 10.6), ALB (3.1 vs. 2.8), eGFR (91.2 vs.71.8), Cr (0.9 vs. 1.9), and ALP (369 vs. 290) levels. After adjustment for age and sex, the number of infected vertebral bodies ($\geq$3 vs. 2, odds ratio 1.03, 95% confidence interval: 1.00–1.07), resistant bacteria (7.7, 1.97–42.4), expansion of abscess to the epidural space (4.20, 1.63–11.5), and Hb level (1.31,1.04–1.69) showed significant associations with the normalization of CRP. In addition, to examine the variables independently associated with the normalization of CRP level, we used multiple logistic regression analysis with age, sex, number of infected vertebral bodies, resistant bacteria, expansion of abscess to the epidural space, and serum Hb level as explanatory variables, and found that expansion of the abscess to the epidural spaces was significantly associated with the normalization of CRP level (3.40, 1.11–10.7).
**Conclusions:** The number of infected vertebral bodies, resistant strains of pathogenic bacteria, expansion of abscess to the epidural space, and serum Hb level predicts the prognosis of patients with pyogenic spondylitis. Particularly, expansion of abscess to the epidural spaces was strongly associated with the achievement of CRP normalization.
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## SAT0517 MIZORIBINE IS AS EFFECTIVE STEROID-SPARING AGENT AS METHOTREXATE FOR POLYMYALGIA RHEUMATICA: A RETROSPECTIVE CASE SERIES ANALYSIS

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**Background:** Patients with polymyalgia rheumatica (PMR) often need long-term steroid treatment, which raises concern for chronic side effects of steroid. In the 2015 ACR/EULAR recommendations for the management of PMR, methotrexate (MTX) was recommended as a 1st line agent for steroid sparing. However, elderly patients often cannot tolerate MTX. Mizoribine (MZR), an inosine monophosphate dehydrogenase inhibitor, has been widely used in the field of organ transplantations in Japan. We have reported the efficacy and the excellent safety of MZR in the rheumatology field (1), and its steroid sparing effect as well (2). The role of MZR on PMR treatment has not been clarified.
**Objectives:** To evaluate efficacy and safety of MZR compared to MTX in terms of steroid-sparing effect in PMR.
**Methods:** The study design was a retrospective single-institution case series analysis. We searched for all PMR patients who were diagnosed as PMR at St. Luke's International Hospital from 1998 to 2014. The inclusion criteria were

fulfillment of the 1979 classification criteria of PMR, and receiving treatment with prednisone in combination with either MTX or MZR. The exclusion criteria were the diagnosis of giant cell arteritis or other connective tissue diseases, use of both MTX and MZR, and use of other immunosuppressants. The following data were collected; total prednisone dose that participants had received within 48 weeks after stating MTX or MZR, the dose of the steroid on 48 weeks after starting MTX or MZR, and side effects profile.

**Results:** A total of 24 participants (14 for MZR group; 10 for MTX group) were included. The cumulative prednisone dose in 0–48 weeks was 2154 (1181 to 3127) mg in MTX group and 1940 (1379 to 2502) mg in MZR group, and the difference between the arms was -214 mg (a one-sided 90% CI: -1019 to 591.7). The dose of the steroid on 48 weeks after starting steroid sparing agent was 4.17 mg (95%CI: 1.64 to 3.90) in MTX arm and 2.71 mg (95% CI: 1.78 to 6.55) in MZR arm, seeming in favor of MZR although statistically not significant (P=0.20). Side effect profile was as follows; in MTX group, 3 out of 10 patients experienced a transient elevation in liver enzymes and 1 patient developed gastrointestinal symptom which lead to MTX withdrawal. In MZR group, one patient experienced a transient elevation in liver enzymes, 1 patient developed gastrointestinal symptom which were tolerable, and one patient was hospitalized due to pneumonia requiring 1 week of iv antibiotics, which lead to MZR withdrawal.

**Conclusions:** MZR may be non-inferior or may be even superior to methotrexate in terms of steroid sparing effects on PMR patients, although statistically not significant due to small sample size. MZR generally has fewer side effects than MTX. Further investigation with a larger number of patients in RCT is needed for confirmation.

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## SAT0518 LOW BACK PAIN PREVALENCE IN ITALIAN ADOLESCENTS AND ITS ASSOCIATION WITH QUALITY OF LIFE

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**Background:** Low Back Pain (LBP) is a very common health problem that affects people of all ages. It has profound effects on well-being and is often the cause of significant physical and psychological disability. Until now, very few studies have investigated these aspects in adolescents[1].

**Objectives:** To define the prevalence and the characteristics of LBP in high school adolescents from the city of Venice (Veneto region, Italy) and to investigate its impact on disability, lifestyle and quality of life (QoL).

**Methods:** The cross-sectional study included 145 students (89 females and 56 males) with a mean age of 15.9 ± 0.72 years that completed the Short Form 36 Questionnaire (SF-36) for QoL assessment and a structured questionnaire concerning anthropometric data and participants' characteristics as well as the symptoms prevalence, duration and treatment, health provider consultation, and referral for diagnostic tests. For normally distributed variables the Student T test was used while, for categorical variables, the Pearson's Chi Square was performed.

**Results:** Among the 145 subjects included in the study, 82 (56.5%) referred having experienced LBP: 8.2% at the moment of survey, 27.6% in the past with complete resolution of the symptoms, and 20.7% in the past without symptoms resolution. Females experienced LBP significantly more frequently than males (52.2% versus 47.8%, $p<0.05$). There was no association between LBP and age or physical activity. 59.0% of the adolescents with LBP had sought medical evaluation and the 47.3% of this group had been referred for diagnostic tests.

Concerning pain resolution, 78.9% of positive resolved respondents did not take any actions while, out of the total number of subjects involved, 58.3% used drugs, 60.0% recurred to rehabilitation and 20.0% combined drugs and rehabilitation. This latter category was also more sceptical than the others (p=0.016) about the future possibility of solving LBP, confirmed by lower QoL scores, although it was the most interested in participating to a prevention program (p=0.04).

Furthermore, there was a strong correspondence between the QoL of the students that experimented LBP only in the past and the QoL of those who had never suffered of LBP in their lives.

**Conclusions:** Our study confirmed that LBP is frequent in Italian adolescents and that a large number of subjects consult a healthcare service[1]. The results highlighted the strong impact of LBP on QoL, leading to significant physical and psychological health issues. According to our data, SF 36 may be a reliable tool to describe the QoL modifications related to the presence of pain. Further investigations are necessary to understand the inverse association observed between therapy and pain resolution.

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## SAT0519 THE ASSOCIATION BETWEEN OBESITY AND LOW BACK PAIN AND DISABILITY IS AFFECTED BY MOOD DISORDERS – A POPULATION-BASED, CROSS-SECTIONAL STUDY OF MEN

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**Background:** Low back pain (LBP) and obesity are both major public health problems. Obesity has been linked with LBP, with recent studies reporting that increased fat but not lean tissue mass is associated with LBP, however previous studies predominantly examined women. The relationship between body composition and LBP in men is unknown.

**Objectives:** The aim of this study was to examine the relationship between body composition and LBP and disability in a population-based sample of men.

**Methods:** 978 male participants from the Geelong Osteoporosis Study (GOS), a population-based Australian study designed to investigate the epidemiology of osteoporosis among adults, were invited to participate in a follow up study in 2006. Participants completed questionnaires on sociodemographics and health status. LBP was determined using the validated Chronic Back Pain Grade Questionnaire and the presence of mood disorders was assessed using the Hospital Anxiety Depression Scale. Body composition was measured using dual energy x-ray absorptiometry. Independent samples t-tests and chi-square tests were used to compare the baseline characteristics of men with and without LBP and/or disability. Estimated marginal means were used to examine the relationships between obesity measures and body composition in participants with high intensity pain and disability compared to those with no or low pain and disability. Multivariate analyses included adjustments for age, mood disorder, education, mobility and body mass index (BMI). To examine the multivariate associations between body composition and back pain, adjustment was also made for the alternate body composition measure. Interactions between risk factors for LBP and measures of obesity, including measures of body composition were examined.

**Results:** Of the 820 respondents (84% response rate), 124 (15%) had high intensity LBP and/or disability. Participants with high intensity pain and/or disability were older, more likely to have a mood disorder, less likely to have completed secondary school and more likely to have poor mobility than those with no or LBP and disability ($p<0.002$ for all). LBP was associated with higher BMI (28.7±0.4 vs 27.3±0.2 kg/m$^2$, p=0.02) and waist-hip ratio (0.97±0.006 vs 0.96±0.006, p=0.04), with increased tendency towards having a higher fat mass index (8.0 vs 7.6 kg/m$^2$, p=0.08), but not fat-free mass index (p=0.68). The associations between LBP and measures of obesity were stronger in those with a mood disorder, particularly for waist-hip ratio (p=0.05 for interaction) and fat mass index (p=0.06 for interaction).

**Conclusions:** In a population-based sample of men, high intensity LBP and/or disability were associated with increased levels of obesity, particularly in those with mood disorders. This provides evidence to support a biopsychosocial interaction between mood disorders and obesity with LBP.

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## SAT0520 INDICATIONS AND CLINICAL IMPACTS OF MAGNETIC RESONANCE IMAGING OF THE KNEE IN OLDER PATIENTS: ARE WE CHOOSING WISELY?

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**Background:** The use of magnetic resonance imaging (MRI) seems to be increasing in patients with gonalgia. Findings such as osteoarthritis and meniscal damages are very prevalent in older patients, often simultaneously [1–3]. These findings are of undetermined significance, as invasive therapeutic procedures provide no additional benefit [4].

**Objectives:** The aim of this study is to analyze MRI indications and clinical impact in this population in our center.

**Methods:** We retrospectively analyzed 215 medical records of patients older than 50 yo having undergone a knee MRI in 2009. Medical charts were reviewed up

to 2014 for: patient characteristics, MRI indication, ordering physician specialty, radiography prior to MRI, MRI findings and clinical impacts of the MRI.
**Results:** Patient's average age was 60.6±7.5. Main MRI indications were meniscopathy: 148 (68.8%) and chronic pain: 92 (42.8%). Most MRIs were ordered by general practitioners (GP): 148 (68.8%) and orthopedic surgeons (OS): 55 (25.6%). Chronic pain investigation was significantly higher in GPs than in OS (48.0% vs 27.3%, p=0.008). Findings show that 185 (86%) patients had osteoarthritis (OA) and 170 (79.1%) had meniscal lesions. Overall, 87 (40.5%) patients were seen by an OS and 27 (31%) of them underwent an invasive intervention. Among the 81 patients with moderate-to-severe OA on MRI, 36 (46%) had evidence of moderate-to-severe OA on a previous plain radiography, 28 (34.6%) were seen by an OS, and 3 (3,7%) underwent a meniscectomy.
**Conclusions:** Our study reproduces the known association between OA and degenerative meniscal changes in older patients. About half of our cohort could have been appropriately diagnosed and treated based on available radiographic information, thus avoiding the MRI and subsequent OS evaluation. Meniscectomy - an MRI dependent procedure - was rare, particularly in patients with advanced OA. Educational and pragmatic measures must be emphasized to limit the inappropriate use of this costly imaging modality.
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## SAT0521 DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS: CAN WE IDENTIFY DIFFERENT CLINICORADIOLOGICAL PATTERNS?

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**Background:** Diffuse Idiopathic Skeletal Hyperostosis (DISH) was described based on vertebral radiological signs (Resnick-Niwayama 1976). Subsequently, Utsinger presented other criteria that add extraspinal involvement that allowed DISH diagnosis even without vertebral signs [2]. Mader et al have tried to develop a new set of criteria without a final consensus about the inclusion of multiple peripheral enthesopathies [3].
**Objectives:** To identify in our patients affected from DISH the existence of different clinicoradiological patterns based on the spinal and/or extraspinal involvement.
**Methods:** We conducted a descriptive analysis of our cohort of patients who met Resnick and/or Utsinger classification criteria for DISH. Demographic, clinical, radiographic and comorbidity data were collected. Radiographic scans and medical records were reviewed since 2004. Patients were divided into 3 clinicoradiological patterns: 1) Axial pattern 2) Peripheral pattern 3) Mixed pattern. We excluded patients with positivity of HLA27 and/or past o present psoriasis and/or inflammatory bowel disease although radiographic features met the criteria described.
**Results:** We included 93 patients, 57% were male. The average age at diagnosis was 65.5 y (47–84) but the age of onset of symptoms was 58.5 y (36–80). In women the age at onset and diagnosis was earlier, 62.8 and 55.7 y, respectively. The delay in diagnosis was 6.36 years (0–25). All patients met Utsinger criteria: 72% definite; 20.5% probable and 7.5% possible, 28% did not meet Resnick's definition. The symptoms that led to the diagnosis were: 46.2% pain and/or limitation of thoracic-lumbar spine, 15.4% pain and/or limitation cervical spine, 22% a peripheral enthesopathy, 5.4% hip pain and 11% was a radiological finding. We identified: a) predominantly axial pattern (69.5%); b) predominantly peripheral pattern (19.6%); and a mixed pattern (10.9%). We also observed that women predominated in peripheral pattern (66%) and men in axial (65%). We didn't find any sex differences in the mixed pattern. Moreover, patients with peripheral pattern were diagnosed at earlier ages. We found hyperostotic signs in: 63.4% cervical spine, 93% thoracic spine and 55.4% lumbar spine, 51.9% had bony excrescencies of acetabulum, 80% enthesopathies of pelvic girdle and/or trochanter, 65% in knees, 68.4% elbows, 82% in Achilles tendon and 62% in fascia plantaris. Although the value of retrospective data is limited, the clinical history of enthesopathy was collected in a 46.2%.
**Conclusions:** We propose three patterns in DISH based on clinical symptoms and characteristic radiological signs. We need prospective studies to elucidate if they correspond to different stages of the disease or if they are different patterns related to sex or age.Because our evidence we consider the importance to investigate the extraspinal involvement when we establish the diagnosis of DISH.
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## SAT0522 EFFICACY AND SAFETY OF ULTRASONOGRAPHIC GUIDED PERCUTANEOUS NEEDLE PLANTER FASCIOTOMY AS A TREATMENT FOR CHRONIC PLANTER FASCIITIS

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**Background:** Plantar fasciitis (PF) is the most common cause of heel pain. Approximately 10% of the cases develop recalcitrant symptoms and are offered various forms of surgical intervention. Ultrasound guided needle planter fasciotomy is a minimal invasive method that may help this group of patients (1).
**Objectives:** To assess the efficacy and safety of ultrasonographic guided percutaneous needle planter fasciotomy as a treatment for chronic planter fasciitis.
**Methods:** ultrasound guided planter fasciotomy (1) was carried out in one hundred and seven patients who had chronic planter fasciitis that did not respond to conservative treatment including medical treatment, physiotherapy and local corticosteroid injection. Following induction of local anesthesia, a 14-gauge needle was guided toward and into the plantar fascia by real-time sonography.Visual analogue scale (VAS) for heel pain and ultrasonographic character of planter fascia (thickness and echogenicity) were assessed on the initial (W0), 2 weeks later (W2) and 6 months after treatment (W24).
**Results:** A highly significant difference was found between VAS and sonographic findings before and after fasciotomy. Patients improved significantly at 2 weeks compared to baseline and also at 6 months compared to baseline and 2 weeks (table 1). Nighty seven (90.7%) of patients stated that "the procedure had been worthwhile". There were no complications during or following needle fasciotomy.

Table 1. Comparison between VAS and sonographic findings at Baseline, 2 weeks and 6 months post-injection

| | Baseline | Two weeks | Six months | P |
|---|---|---|---|---|
| VAS | 80 (60–100) | 20 (10–60) | 10 (0–80) | 0.000** |
| Sonography | | | | |
| Fascia thickness | 6.9 (4.8–8.3) | 6.1 (5.1–7.9) | 5.3 (4.6–7.3) | 0.000** |
| Echogenecity | 2.5 (1–3) | 2 (1–3) | 1 (0–3) | 0.000** |

VAS visual analogue scale. **Highly significant difference $p<0.001$. Analysis was done by Kruskal Wallis tests. Post-Hoc tests were done also and revealed highly significant difference between baseline & 2 weeks (P=0.000), between baseline & 6 months (P=0.000), and between 2 weeks & 6 months (P=0.000) regarding VAS and sonographic findings.

**Conclusions:** Ultrasonographic guided percutaneous needle planter fasciotomy is a safe and an effective method in patients with chronic planter fasciitis who did not respond to conservative treatments including local corticosteroid injections.
**References:**
[1] Folman et al, Foot and Ankle Surgery 11 (2005) 211–214
**Disclosure of Interest:** None declared
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## SAT0523 EFFICACY OF LOCAL AUTOLOGOUS PLATELET RICH PLASMA INJECTION COMPARED TO LOCAL CORTICOSTEROID IN TREATMENT OF PLANTAR FASCIITIS; AN ULTRASONOGRAPHIC EVALUATION

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**Background:** Plantar fasciitis (PF) is the most common cause of heel pain. Corticosteroid injections are used for cases of PF refractory to conservative treatment. Platelet-rich plasma (PRP) has been gaining popularity as a treatment for PF pain.
**Objectives:** The aim of this study was to compare between local autologous PRP injections and local steroid injections both clinically and sonographically within 3-months regarding its effect on pain, function, thickness, and echogenecity of the plantar fascia and also regarding its safety.
**Methods:** This study was carried out on 50 patients with chronic PF, attending the Rheumatology and Rehabilitation outpatient clinic in Zagazig University Hospitals. Patients were divided into two groups: Steroid group (n=25) and PRP group (n=25). Pre-injection all patients of our study were subjected to full history taking, thorough physical examination, visual analogue scale (VAS: 0–100), Foot Health Status Questionnaire (FHSQ) which included Short Form 36 (SF36), complete blood count (CBC) to exclude anemia and thrombocytopenia, plain x- ray to

detect calcaneal spur, and ultrasonography. Patients were reassessed by VAS, FHSQ, and ultrasonography at 1.5 months & 3 months postinjection. The clinical evaluator and sonographer were blinded to the type of injection.
**Results:** We found that at 1.5 months post injection, there was more improvement in the PRP group than the steroid group both clinically and ultrasonographically ($p=0.008$, $p<0.01$). Also, although at 3 months no great difference was found between the two groups ($p>0.05$), PRP patients continued to improve from 1.5 months to 3 months ($p=0.000$, $p<0.01$). None of our patients of either groups experienced any complications from injection at the end of the follow-up period. No post-injection foot deformities nor infection were noted ($P>0.05$).
**Conclusions:** We suggest that the PRP injection is a new, readily available and safe choice of therapy for PF and is not inferior to steroid injection in short term follow up. To our best knowledge this is the first study to compare steroids and PRP by ultrasonography.
**Disclosure of Interest:** None declared
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## SAT0524 COMPARISON OF ULTRASONOGRAPHY-GUIDED INJECTION WITH BLIND INJECTION IN FACET SYNDROME; A 6-WEEK RANDOMIZED CONTROLLED TRIAL

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**Background:** Local injection is a good alternative medical treatment in soft tissue disorders. Ultrasonography (US) is a good guide for local applications which increases the efficacy of the treatment.
**Objectives:** To compare the local injection performed by US-guided with blind injection in facet syndrome
**Methods:** Forty seven patients with the diagnosis of facet syndrome were included in the study.Patients were randomized into two groups. The patient's history, physical examination and routine laboratory parameters were used to diagnosis of facet syndrome.
Inclusion criteria for the study were as follows: pain for at least 6 weeks, pain extending to gluteal region and thigh, presence of pain with lumbar hyperextension and lateral flexion, paravertebral tenderness at the facet joint localization, negative straight leg raising test and normal neurological examination findings.
Approximately 5 cc of injection solution which was a mixture of 1–2% lidocaine hydrochloride and triamcinolone was applied twice within 15 days to maximum 2 points most tender with palpation (bilateral; L4–5 or L5-S1, unilateral; L4–5 and L5-S1). Assessment was made within 0, 2 and 6 weeks with Visual analog scale (VAS), Modified Oswestry scale and State-Trait Anxiety Inventory.
**Results:** The patients' initial VAS and Oswestry scale scores were similar. When the two groups were compared at the 6th week in terms of VAS scores, improvement was more pronounced in US-guided injection group (US-guided group before 7.6±2.2, after 3.0±1.7, $p=0.000$ vs blind group before 7.2±1.3, after 5.2±2.0, $p=0.000$). According to Oswestry scale scores at the 6th week there was no statistically significant difference between the two groups. The improvement in initial and 6th week Oswestry scale scores was statistically significant in the US-guided injection group ($p=0.006$). The improvement in trait anxiety scale scores was significant in both groups.
**Conclusions:** The US-guided local injections used in the treatment of facet syndrome have positive impact on both pain and functions.
**Disclosure of Interest:** None declared
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## SAT0525 THE USE OF ANALGESIC AND OTHER PAIN RELIEF DRUGS TO MANAGE CHRONIC LOW BACK PAIN – RESULTS FROM A NATIONAL SURVEY

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**Background:** Managing chronic pain is challenging due to the long-term safety profile of most drugs. The treatment of chronic Low Back Pain (CLBP) represents a significant medical and financial burden and aims at relieving pain, improving functional ability, and preventing recurrence and chronicity. It is therefore important to gain insight into how CLBP is managed in the population.
**Objectives:** To characterize the intake profile of analgesic and other pain relief drugs in the Portuguese adult population with CLBP, taking the World Health Organization (WHO) analgesic ladder and pain intensity into account. To assess the relationship between having CLBP and the intake of analgesic and other pain relief drugs.
**Methods:** EpiReumaPt was a cross-sectional Portuguese population-based study (10,661 subjects). Self-reported active CLBP (ACLBP) was considered: LBP on the day of enrollment and for ≥90 days. Prevalence and profile of analgesic intake was characterized among those self-reporting ACLBP, taking into account the intensity of pain and the WHO analgesic ladder. To understand whether the presence of ACLBP was a factor associated with drug intake, multivariable logistic regressions were conducted for each of the analgesic/pain relief therapeutic groups (in separate models), adjusted for confounders.
**Results:** Among 1,487 subjects with ACLBP, 18.7% were using analgesic/pain relief drugs. Estimated prevalences were: anxiolytics, 14.1%; NSAIDs, 12.3%; antidepressants, 10.1%; analgesic antipyretic, 6.6%; anticonvulsants, 3,4%; central muscle relaxants, 2.6%; opioids, 1.6%. Most subjects with severe pain were in the 1st step of the WHO analgesic ladder: NSAIDs plus anxiolytics, sedatives & hypnotics (4.6%); NSAIDs plus antidepressants (3.2%); NSAIDs plus central muscle relaxants (2.5%). The presence of ACLBP was significantly associated with the intake of all therapeutic groups (table):

Table 1. Association of the presence of ACLBP with the intake of each class of analgesic/pain relief drugs (separate multivariable models)

| Dependent variables* | Active CLBP (yes/no) | |
|---|---|---|
| | OR (95% CI) | p-value |
| Anxiolytics, sedatives & hypnotics§ | 8.86 (6.08–12.90) | <0.001† |
| NSAIDs± | 8.56 (5.84–12.53) | <0.001† |
| Antidepressants§ | 12.56 (7.96–19.81) | <0.001† |
| Analgesics, Antipyretics¶ | 7.68 (3.38–17.48) | <0.001† |
| Anticonvulsants | 9.27 (4.16–20.69) | <0.001† |
| Analgesic Opioids | 8.13 (2.78–23.77) | <0.001† |
| Central Muscle Relaxants | 12.01 (5.88–24.51) | <0.001† |

*All the analyses were adjusted for: age, gender, geographic area, education level, number of self-reported comorbidities, and self-report of rheumatic and musculoskeletal diseases. §Additionally adjusted for: anxiety and depressive symptoms; ¶Additionally adjusted for: heart disease and gastrointestinal diseases.

**Conclusions:** ACLPB was associated with the intake of drugs belonging to all analgesic drug classes. Nevertheless, this drug intake was very low, even for those with severe pain. The WHO analgesic ladder was carefully followed with an extremely conservative use of analgesic opioids even for those with severe pain. There is clearly an unmet need in what concerns pain management in patients with ACLBP, particularly taking into account the well-know burden of LBP.
**Disclosure of Interest:** None declared
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## SAT0526 SELF-MANAGEMENT IN CHRONIC NECK PAIN CAUSED BY CONGENITAL CERVICAL VERTEBRA BLOCK: A RANDOMIZED CLINICAL TRIAL

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**Background:** Single congenital fusions are common anomalies, found most often at the C2–3 and C5–6 levels had moderate or severe degenerative changes in their cervical spines, or displayed signs of cervical instability. There is no motion at the level of congenital block vertebrae, as noted in flexion and extension radiographic analysis, resulting in excessive mobility and early degenerative changes at the adjacent unfused motion segments.
**Objectives:** The aim of our single blind, randomized controlled study was to assess the efficacy of comprehensive home exercise program on neck pain and physical performance in patients with block vertebrae in lower cervical segments (C5-C6 and C6-C7).
**Methods:** 36 patients with chronic neck pain and cervical block vertebrae were randomly assigned into exercise home group (G1, 19 patients) and second group (G2, 17 patients - noncompliant to exercise program). All patients were complete assessed (clinical, imagistic, functional). Kinetic program (first light positive exercise, next gradually strengthening exercises for the all cervical muscle exercise, one set of 10 repetitions each direction, twice a day and neck school exercises) was initiated in rehabilitation clinic. Duration of follow-up was 16 weeks after start of the intervention. At 4 and 16 weeks an independent physiotherapist unaware of the treatment allocation performed outcome assessments - pain (VAS) and Neck Disability Index (NDI) for functional status.
**Results:** Comparing week 16 with baseline, pain improved significantly ($p<0.05$). Significant improvement in NDI scores for pain and functional status were found at week 4 and week 16 in the G1 compared to baseline. At 16 weeks, 16 (84.2%) patients mentioned their functional status as improved and only 3 (15.8%) as similar at baseline.
**Conclusions:** The exercise program performed daily led to improvements in pain and physical measures. Optimal neck care in congenital cervical vertebra block includes pain-relieving exercises that also help restore neck posture, limitation of the neck movement and the muscular weakness. These techniques can help recover and provide good control against future symptoms (atrophy and neurological sensory loss, myelopathy).
**Disclosure of Interest:** None declared
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SAT0527 **PREDICTORS OF BACK PAIN IN MIDDLE AGED WOMEN: DATA FROM THE AUSTRALIAN LONGITUDINAL STUDY ON WOMEN'S HEALTH**

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**Background:** Back pain is a major public health issue, causing greater disability worldwide than any other condition. Given the limited treatment options available, an understanding of the predictors of back pain is vital to optimize preventive strategies. Women are not only more likely to suffer from back pain, they are also more likely to utilise health care services to a greater extent than men. However, few studies to date have examined modifiable predictors of back pain in middle-aged women, with exposure and outcome measures assessed at multiple time points and major inconsistency and knowledge gaps persist in this area.
**Objectives:** Our aim was to identify modifiable risk factors for back pain in middle-aged women.
**Methods:** Women born between 1946 and 1951 were randomly selected from the Australian national health insurance scheme database to participate in The Australian Longitudinal Study of Women's Health. Self-reported data on back pain in the last 12 months, weight, height, age, physical activity, depression, menopause status and other socio-demographic factors were collected in 1998, 2001, 2004, 2007, 2010 and 2013. In 1998, 12,338 women completed the survey and 10,011 (74%) completed the 2013 survey 15 years later.
**Results:** At baseline, median (range) age was 49.5 (44.6 – 53.5) years and 54% reported back pain. In longitudinal multivariate analysis, baseline weight (per 5kg increments) and depression were independent predictors of back pain over each 3 year survey interval and over the following 15 year period, whereas participation in vigorous physical activity was protective. Mean weight gain over the first three years of 1.4kg was associated with an increased risk of back pain over the following 12 years (multivariate OR 1.01, 95% CI 1.01–1.02). The effects of weight on back pain were not affected by participation in vigorous physical activity, being menopausal, or depression status, but the association between weight and back pain tended to be more consistent in those who were overweight or obese.
**Conclusions:** Back pain is common in middle-aged women. Increased weight, weight gain and depression were independent predictors of back pain over 15 years, whereas participation in vigorous physical activity was protective. Targeting these lifestyle factors is an important area for future research on reducing the burden of back pain in middle-aged women.
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## Diagnostics and imaging procedures

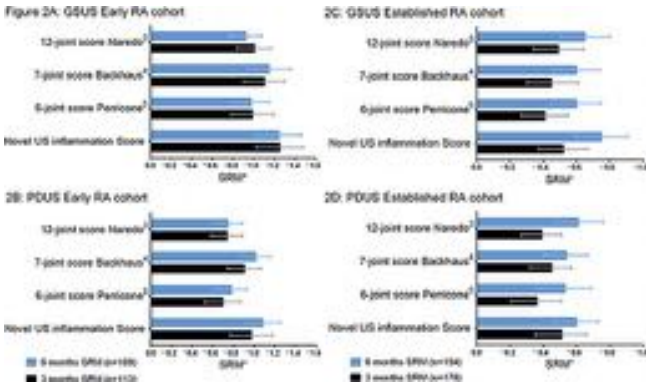
SAT0528 **DEVELOPMENT AND VALIDATION OF A RESPONSIVE ULTRASOUND JOINT INFLAMMATION SCORE FOR RHEUMATOID ARTHRITIS THROUGH A DATA-DRIVEN APPROACH**

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**Background:** No consensus exists on which joints and tendons should be systematically examined by ultrasound (US) to assess inflammation in rheumatoid arthritis (RA). Validity and responsiveness must be balanced against feasibility. Our group has previously developed and validated an US joint inflammation score[1].
**Objectives:** To optimize the US joint inflammation score in terms of sensitivity to change and feasibility, and to validate the score in a separate cohort.
**Methods:** Between Jan 2010 and June 2013 patients (pts) were included in two cohorts: Early RA (DMARD-naïve pts with RA of <2 yrs symptom duration fulfilling 2010 ACR/EULAR classification criteria), and established RA (pts starting or switching biologic DMARDs). An extensive US examination was performed by experienced sonographers using a validated grey-scale (GSUS) and power Doppler (PDUS) semi-quantitative scoring system with scores 0–3 for GSUS and PDUS in each of the following 36 joints and 4 tendons bilaterally: MCP 1–5, PIP 2–3, radiocarpal, distal radioulnar (DRUJ), intercarpal, elbow, knee, talocrural, MTP 1–5, extensor carpi ulnaris (ECU) and tibialis posterior (TP) tendons. An US atlas was used as reference[2]. We performed principal component factor analyses (PCA) of GSUS and PDUS changes from baseline to 3 months (ΔGSUS and ΔPDUS) to identify joint groups with high internal correlation, and selected a candidate joint/tendon set based on these analyses. 3- and 6-month standardised response means (SRMs) with 95% CIs (bootstrapping) were estimated for the candidate set and 3 formerly developed scores in both the early RA cohort and the validation cohort of established RA. Finally, as part of the validation, we assessed the loss of information in the novel score compared to the full score by $R^2$ from linear regression analyses in both cohorts.
**Results:** A total of 330 pts were included, 118 with early and 212 with established RA; 71% vs. 81% anti-CCP pos, mean (SD) age 51 (13) vs. 52 (13) yrs, DAS28 4.7 (1.2) vs. 4.7 (1.4), median (25–75 perc) 28-SJC 6 (3–11) vs. 5 (2–10), disease duration 0.5 (0.2–0.8) vs. 8 (3–15) yrs. We identified 12 joint/tendon groups based on PCA in the early RA data, and 8 joints* and 1 tendon* were included in the final score based on these results (Table). SRMs at 3 and 6 months were higher for the novel score than formerly developed scores in the early RA cohort, with similar results in the validation cohort of established RA (Fig). Based on baseline data from the early RA cohort, the final score retained 87% (GSUS) and 90% (PDUS) of the information in the full score. The corresponding numbers in the validation cohort were 90% (GSUS) and 92% (PDUS).

Table 1

| Group 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Radiocarpal* | MCP3* | MTP2* | Elbow | MCP2* | MCP1* | MTP3* | TP-t | ECU-t* | PIP2* | PIP3* | MTP1 |
| Intercarpal | MCP4 | | | | | MTP4 | | | | | |
| DRUJ | MCP5 | | | | | MTP5 | | | | | |




**Conclusions:** We used a data-driven approach to further develop an ultrasound inflammation score in RA. We propose a score of 8 joints and 1 tendon assessed bilaterally, with improved sensitivity to change compared to formerly developed scores. Our results show that assessment of inflammation by US is feasible and may be a valuable addition to RA disease assessment.
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[2] Hammer et al ARD 2011,
[3] Naredo et al Arthritis Rheum 2008,
[4] Backhaus et al Arthritis Rheum 2009,
[5] Perricone et al Rheumatology 2012.
**Disclosure of Interest:** A.-B. Aga: None declared, E. Lie: None declared, I. Olsen: None declared, H. Hammer Grant/research support from: AbbVie, BMS, Pfizer, Roche, UCB, T. Uhlig: None declared, S. Lillegraven: None declared, D. van der Heijde: None declared, T. Kvien: None declared, E. Haavardsholm Grant/research support from: AbbVie, MSD, Pfizer, Roche, USB
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SAT0529 **HYDROXYCHLOROQUINE RETINOPATHY: UPDATE ON APPLICATION OF THE 2011 SCREENING GUIDELINES IN AN ACADEMIC PRACTICE**

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**Background:** The risk of end-stage retinopathy (bull's eye maculopathy) from hydroxychloroquine is reported as 0.65%. With recent advances in retinal structure and function testing, American Academy of Ophthalmology (AAO) issued revised guidelines to detect early signs of hydroxychloroquine retinopathy with the use of ancillary testing including Optical Coherence Tomography (OCT), Fundus Autoflourescence (FAF) and multifocal Electroretinography (mfERG) in addition to clinical exam and visual fields. Risk of retinopathy as defined by combination of these tests ranges from 7.5–12% in those on HCQ for at least 5 years or longer. This is an expanded cohort of patients previously presented at the 2015 American College of Rheumatology (ACR) meeting in San Francisco, CA.
**Objectives:** To determine the application of AAO guidelines in an academic practice and the prevalence of HCQ retinopathy based on advanced ancillary tests recommended by AAO.
**Methods:** Microperimetry (MP) was used as a substitute for Humphrey Visual Fields (HVF). Ophthalmic exam, MP, OCT, FAF, mfERG were performed on SLE patients meeting SLICC criteria on hydroxychloroquine. Ophthalmic examinations and testing were interpreted by experienced retina specialists.
**Results:** The mean duration of treatment with HCQ was 11.8 years in 125 (246 eyes) consecutive patients with SLE on whom all 4 tests done. Overall, HCQ-related abnormalities were noted in 12 (5%) eyes on OCT, 14 (6%) on FAF, 26 (11%) on mfERG and 24 (10%) on MP. A total of 45 eyes (18%) had abnormal findings on OCT and 12 (27%) of these were related to HCQ. A total of 36 eyes (15%) had abnormal findings on FAF and 14 (39%) of these were related to HCQ. For mfERG, we found a total of 99 (40%) abnormal tests with 26 (26%) eyes with

changes consistent with HCQ retinopathy. A total of 72 (29%) of all MP tests were abnormal and 24 (33%) of these were related to HCQ. Only 3 patients (2.4%) showed changes in all 4 tests suggestive of HCQ retinopathy.
**Conclusions:** Our updated series reaffirms our previous findings presented at the ACR conference and demonstrates that in absence of pre-HCQ data for the AAO recommended ancillary tests it may be difficult to interpret changes seen on these tests since most of the screenings are done by regular ophthalmologists who lack the equipment and experience with specialized testing such as mfERG, FAF and OCT. Nonspecific abnormalities are common with these tests, which need careful interpretation by retina specialists. We recommend repeat testing in those with abnormal tests and additional testing in patients in which all four modalities were not used to determine early toxicity. In our expanded cohort, we found substantial number of cases with abnormalities unrelated to HCQ. A discussion needs to take place between the patient care team including the ophthalmologist and rheumatologist to decide about the continuation or stopping HCQ based on these nonspecific abnormalities in individual tests that are not supported by the respective other modalities.
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[1] Scholl HP, Shah SM. We need to be better prepared for hydroxychloroquine retinopathy. JAMA Ophthalmol. 2014 Dec;132(12):1460–1.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6147

## SAT0530 DEEP CLINICAL REMISSION - AN OPTIMIZED TARGET IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS? EXPERIENCE FROM AN ULTRASONOGRAPHY STUDY

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**Background:** Treat-to-target strategy, aiming at clinical remission, has greatly improved the prognosis of RA. However, the ultrasonographic subclinical synovitis was correlated with bone erosion and disease flare.
**Objectives:** The aim of this study was to evaluate whether deeper clinical remission (DAS28(ESR) $\leq$1.98) reflects the better control of subclinical synovitis.
**Methods:** 126 RA patients in clinical remission were enrolled in the study. Disease activity and ultrasongraphy were evaluated at baseline, and every 3 months during a 12-month follow-up. The relationship between the extent of clinical remission, flare and ultrasonographic features was analyzed.
**Results:** In 126 RA patients, 76 achieved deep clinical remission and 50 achieved mild clinical remission. In all, 54 (42.9%) patients relapsed at average of 6.8±3.3 months during follow-up. Patients in deep remission possessed not only lower risk to relapse (30.3% vs. 62.0%, $P<0.01$), but also longer duration of remission before relapse (8.1±3.3 vs. 5.9±3.1 months, $P<0.05$). Besides, applying DAS28(ESR) $<$1.895 to predict ultrasonographic remission defined as negativity of both PD and SH was highly accurate ($P<0.001$). Subclinical PD synovitis at baseline was an independent risk factor for predicting relapse in RA patients achieved clinical remission (OR 8.8 [95% CI 2.7–28.4]).
**Conclusions:** Subclinical synovitis was common in RA patients even in deep clinical remission. The deeper the clinical remission, the milder the subclinical synovitis, and the lower risk to relapse. Therefore, achieving deeper clinical remission, which reflected better control of subclinical synovitis and less tendency to flare, could be an optimized treatment target of RA.
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**Disclosure of Interest:** None declared
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## SAT0531 CAN HISTOLOGICALLY DEFINED PERI-ARTICULAR VASCULAR CHANNELS BE IDENTIFIED ON HIGH-RESOLUTION COMPUTED TOMOGRAPHY? A STUDY IN CADAVERIC FINGER JOINTS

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**Background:** Several studies have indicated that High Resolution peripheral CT (HR-pQCT) scanning is more sensitive than radiography in detecting cortical breaks in destructive joint diseases like rheumatoid arthritis (RA)[1–3]. Cortical breaks are also seen in healthy controls, but the exact nature of these breaks is not known, and might represent vascular channels (VCs). No previous study has compared histology to HR-pQCT images in finger joints. We hypothesized that VCs seen on histology can also be detected by HR-pQCT imaging.
**Objectives:** To identify histologically defined VCs in cadaveric hand joints on HR-pQCT imaging.
**Methods:** Based on HR-pQCT, three regions in metacarpophalangeal joints from female cadavers with an unknown medical history (mean age 84.7, SD 5.5 years) were selected. These regions were extracted, embedded undecalcified in methylmetacrylate and histologically sectioned (thickness 15$\mu$m) parallel to the axial plane. Every second section (n=450) was stained with Goldner Trichrome. VCs were identified as a cortical break in one histological section which contained one or more vessels. HR-pQCT images (thickness 82$\mu$m) were independently scored by two trained readers for the presence of cortical breaks and if applicable categorized as VC. A break on HR-pQCT was defined as an interruption of the cortex seen on 2 consecutive slices in at least 2 orthogonal planes. A VC was defined as a break that is linear in shape with parallel lining. Finally, the histological sections were matched visually to corresponding axial HR-pQCT images.
**Results:** A total of 56 VCs were identified on histology. On HR-pQCT 20 breaks were identified, of which 7 were categorized as VC. Only 3 VCs matched with VCs on histology. Of the remaining 53 histologically identified VCs, 34 could be detected on HR-pQCT, but the interruption of the cortex was not seen on 2 consecutive slices therefore they were not classified as a break. Eight histologically VCs fulfilled the definition of a break on HR-pQCT, but were not categorized as a VC. Eleven histologically VCs could not be identified on HR-pQCT. Figure 1 demonstrates histology and HR-pQCT images.

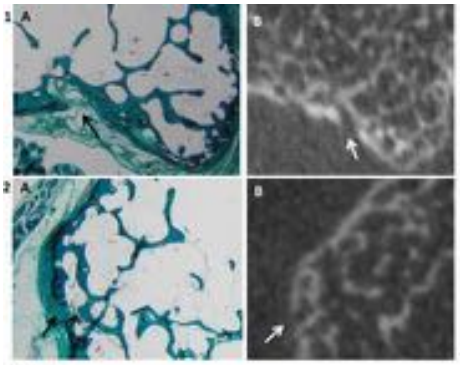


Figure 1.
Panel 1: A vascular channel on histology (A) (arrow) and HR pQCT imaging (B) (arrow)
Panel 2: A vascular channel on histology (A) (arrow) and a cortical break not defined as vascular channel on HR pQCT (B) (arrow)

**Conclusions:** VCs were frequently seen on histology. Only a minority of histologically defined VCs is interpreted as VC using a pre-specified definition on HR-pQCT images. Small histological VCs were often identified as an interruption but rarely considered a break according to the current definition of a VC on HR-pQCT. Therefore, additional criteria in order to diagnose the presence of VCs on HR-pQCT are warranted.
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**Disclosure of Interest:** A. Scharmga: None declared, K. Keller: None declared, M. Peters: None declared, A. van Tubergen: None declared, J. van den Bergh: None declared, B. van Rietbergen Consultant for: Scanco Medical AG, R. Weijers: None declared, D. Loeffen: None declared, E. M. Hauge: None declared, P. Geusens: None declared
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## SAT0532 TIBIAL CORTICAL THICKNESS MEASURED BY HIGH–RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY DISCRIMINATES VERTEBRAL FRACTURES IN PATIENTS ON LONG-TERM GLUCOCORTICOIDS INDEPENDENT OF AREAL BONE MINERAL DENSITY

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**Background:** Glucocorticoid-induced osteoporosis is the commonest cause of secondary osteoporosis and related fracture. The current gold-standard for the diagnosis of osteoporosis is dual x-ray absorptiometry (DXA) that measures areal bone mineral density (aBMD). However, aBMD has a low predictive value for vertebral fracture. High–resolution peripheral quantitative computed tomography (HR-pQCT) allows assessment of volumetric BMD (vBMD) and bone macro/microstructure. Whether HR-pQCT can better predict vertebral fractures in patients on long-term glucocorticoids (GC) compared to DXA remained uncertain.
**Objectives:** To determine if peripheral bone parameters evaluated by HR-pQCT can discriminate patients on long-term GC with and without vertebral fracture independent of aBMD.
**Methods:** This is an ongoing, cross-sectional study of 1100 rheumatic disease patients on long-term GC to access prevalent vertebral fracture radiographically (Genant semi-quantitative assessment). 110 patients with fracture (fracture group) and 110 patients without fracture (control group) underwent assessment with 1) aBMD using DXA; and 2) vBMD/structural assessment of the non-dominant distal radius and tibia using HR-pQCT. We hereby report the interim results of the first 78 and 77 patients in the fracture and control groups respectively.
**Results:** Both groups were matched in gender [female: 63 (81%) vs 59 (77%); $p$=0.528], disease type [SLE/RA/others: 28 (36%)/27 (35%)/23 (29%) vs 36 (47%)/16 (21%)/25 (32%); $p$=0.143], and cumulative GC dose (17.3±13.6 vs 20.2±18.1g, $p$=0.447). Patients in the fracture group were older (62±14 vs 57±11 years, p=0.009), more postmenopausal [50 (79%) vs 37 (63%), $p$=0.048], of lower body mass index (BMI) (22.7±3.5 vs 24.2±3.4 kg/m$^2$, $p$=0.010), and more likely to be on vitamin D [53 (68%) vs 35 (45%), $p$=0.005] and bisphosphonates [19 (24%) vs 6 (8%), $p$=0.005]. Only 26 (35%) of the vertebral fracture patients were classified as osteoporotic (femoral neck T-score$\leq$2.5). Fracture patients had a lower vBMD and impaired bone architecture compared with controls (Table). In multivariate logistic regression analysis, after adjusting for age, gender, BMI, vitamin D and bisphosphonate use, and aBMD, lower cortical thickness in the distal tibia (odds ratio: 1.38 for per 0.1mm decrease, 95%CI 1.13–1.67; $p$=0.001) and current use of vitamin D (3.78, 1.47–9.71; $p$=0.006) were independently associated with vertebral fracture.

Table 1. HR-pQCT parameters in patients with and without vertebral fracture

| | Fracture | Control | Difference (%) | $p$ |
|---|---|---|---|---|
| Radius | | | | |
| Total vBMD, mg/cm$^3$ | 268±77 | 339±72 | –21.0 | <0.001 |
| Ct. vBMD, mg/cm$^3$ | 843±90 | 899±61 | –6.2 | <0.001 |
| Ct. thickness, mm | 0.69±0.23 | 0.87±0.20 | –20.8 | <0.001 |
| Tb. vBMD, mg/cm$^3$ | 101±43 | 132±43 | –23.5 | <0.001 |
| Tb. number, mm$^{-1}$ | 1.27±0.42 | 1.47±0.30 | –13.6 | 0.002 |
| Tibia | | | | |
| Total vBMD, mg/cm$^3$ | 218±64 | 273±62 | –20.1 | <0.001 |
| Ct. vBMD, mg/cm$^3$ | 798±78 | 856±62 | –6.7 | <0.001 |
| Ct. thickness, mm | 0.82±0.27 | 1.09±0.28 | –24.9 | <0.001 |
| Tb. vBMD, mg/cm$^3$ | 116±38 | 140±36 | –17.1 | <0.001 |
| Tb. number, mm$^{-1}$ | 1.36±0.32 | 1.52±0.27 | –10.5 | 0.002 |

Ct, Cortical; Tb, Trabecular.

**Conclusions:** Our results suggest that skeletal abnormalities in patients with vertebral fracture are much more pronounced than those indicated by DXA. In particular, reduction in cortical thickness may be an important mechanism of vertebral fracture in rheumatic patients on long-term GC.
**Disclosure of Interest:** None declared
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## SAT0533 KNEE SYNOVITIS: ULTRASONOGRAPHIC FINDINGS STRONGLY CORRELATE WITH SYNOVIAL MEMBRANE HISTOLOGY

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**Background:** Arthroscopy, by allowing direct visualization of the synovial membrane, is the gold standard for the assessment of knee synovitis. Given the fact that it is an invasive procedure, other reliable ways to assess synovitis has developed over the past few years. Ultrasonography (US) is a fast, available and low cost imaging tool and has been validated for detecting knee synovitis (1). Ultrasonographic and arthroscopic findings have been shown to correlate (2). However, few studies have yet assessed the correlation between ultrasonographic and histological findings.
**Objectives:** The aim of this study was to assess the correlation between ultrasonographic scores, arthroscopic scores and histological scores for inflammation and vascularity in knee joint synovitis.
**Methods:** Patients with knee pain and/or effusion were prospectively included. Knee was divided in three compartments (medial, lateral and superior). 1 operator (AN) performed a knee ultrasonography (B mode and Doppler mode) prior to the arthroscopy with a semi-quantitative assessment for degree of synovitis. 1 operator then performed a knee arthroscopy (CO, DJV) and scored macroscopic aspects with a 100-mm visual analogic scale (VAS) blindly from US findings and retrieved biopsies from each compartment. Biopsies were analyzed by 1 operator (UF) blindly from both US and arthroscopic findings and scored for: lining layer hyperplasia, inflammation and vascularity. Statistical analysis was made with non parametric Spearman correlation test.
**Results:** 23 patients were included. 16 had rheumatoid arthritis (RA) (ACR/EULAR 2010 criteria). 3 patients had psoriatic arthritis (PsA) (CASPAR criteria), 3 had osteoarthritis (OA) and 1 had gout. Mean ultrasonographic, arthroscopic and histological scores for both synovitis and vascularity were calculated for each patient. A strong correlation was observed between: US synovitis grade and histological inflammation score (r=0.71; p=0.001), US Doppler grade and histological score for vascularity (r=0.6; p=0,0003); US measured synovial thickness and lining layer hyperplasia (r=0.61; p=0,002). Moreover, high positive correlations were observed for both histological lining layer hyperplasia and inflammation between lateral and medial compartments (r=0,90; p=0,00005 and r=0,66; p=0,014 respectively), lateral and superior compartments (r=0,75; p=0,001 and r=0,51; p=0,048, respectively) and medial et superior compartments (r=0,61; p=0,012 and r=0,62; p=0,010, respectively).
**Conclusions:** B mode and Power Doppler US findings strongly correlate with histological inflammation and vascularity scores in actively inflamed knee joints. Ultrasound is therefore a reliable tool for knee joint assessment of the four most common rheumatological diagnoses - RA, PsA, OA and gout -. Moreover, the histological inflammation and hyperplasia scores highly correlate between the superior, medial and lateral compartments of the knee, highlighting the homogeneity of synovial membrane features within the same joint.
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## SAT0534 HOW TO DEFINE SONOGRAPHIC SIGNS OF AXILLARY VASCULITIS IN GIANT CELL ARTERITIS?

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**Background:** Extracranial large vessel vasculitis (LVV) diagnosis is delayed compared to classical temporal arteritis. There is a need for simple and reliable tests for the diagnosis of extracranial large vessel giant cell arteritis (GCA). Identifying extracranial giant cell arteritis increases diagnostic specificity and adds prognostic value, as extensive vascular involvement may be associated with a poorer treatment response. Color duplex sonography (CDS) is most promising tool for the assessment of not only temporal but also large vessel arteritis. However, the proper interpretation of the vasculitis findings remain an important concern, as for an inexperienced ultrasonographer it remains elusive. There is still a need to define ultrasound findings, unify the diagnostic cut-offs and implement such standards by educating ultrasonographists.[1,2]
**Objectives:** We present a novel idea to define a simple, sonographic sign of axillary arteritis.
**Methods:** 214 consecutive patients suspected for GCA were included in the study between 2011 and 2015 and followed up for at least 0,5 year. Axillary arteries were scanned from axillary approach by continuing distally in a longitudinal plane down to brachial arteries. All examinations, together with categorization into arteritis and non-arteritis findings, were performed by a single physician with at least 5 years long experience in LVV ultrasound, that was blinded to diagnosis but aware of clinical presentation. Esaote MyLab25Gold Machine with 10 and 18 MHz linear probes was used.
Slide sign was considered positive (Figure 1) if there was an increased axillary artery wall thickening, (hypoechoic, homogenous, with distorted wall structure resulting in no clear intima-media structure, usually circumferential, over long distance but not limited only to the place of arterial bifurcation), that was followed by a brachial artery without wall thickening and with normal IM structure (clear double line).
The diagnosis was based on ACR criteria (for cranial GCA), or presence of typical manifestations together with large vessel arteritis confirmed by whole aorta CT or ultrasound (for extracranial GCA). Non-GCA patients served as controls.
**Results:** GCA was diagnosed in 81 patients. Extracranial LVV was diagnosed in 28 patients. Axillary vasculitis was diagnosed in 23 patients and was not found in controls. Positive slide sign was found in 23 patients. They've matched the patients with ultrasnographic signs of axillary vasculitis, so congruency between both methods was 100%.



Figure 1

**Conclusions:** Slide sign compared with large vessel halo sign serves at least non inferior diagnostic performance. Although qualitatively accessed slide sign does not bring additional diagnostic value over signs of axillary vasculitis it is easier to define and to observe.
This proposed definition of slide sign contains description of pathological findings in axillary artery, normal findings in brachial artery - which is typically not involved in vasculitis or involved only per continuum in a proximal part, and some features to help to exclude arteriosclerosis.

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## SAT0535 CAROTID ULTRASOUND IN THE CARDIOVASCULAR RISK STRATIFICATION OF PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS OF A POPULATION-BASED STUDY

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**Objectives:** To determine if the use of carotid ultrasonography (US) may improve the cardiovascular (CV) risk stratification in patients with ankylosing spondylitis (AS).
**Methods:** A set of 127 consecutive patients without history of CV events, diabetes mellitus or chronic kidney disease that fulfilled definitions for AS according to the 1984 modified New York criteria were recruited to assess carotid intima-media thickness and presence of plaques. CV risk was calculated according to the systematic coronary risk evaluation (SCORE), the Framingham Risk Score (FRS) and the Reynolds Risk Score (RRS).
**Results:** Men outnumbered women (61.4%). The mean±SD age at the time of the study was 44.5±11.6 years. The median (interquartile range) delay to the diagnosis was 5 (1–12) years. HLA-B-27 was positive in 77.2%, and syndesmophytes were present in 38.9%. Carotid plaques were found in 43 (33.9%). Regardless of the algorithm used for CV risk stratification, more than 50% of the patients classified as having moderate CV risk had carotid plaques. Moreover, 20.8%, 24.6% and 53.3% of AS that fulfilled the category of low CV risk according to the total cholesterol (TC)-SCORE, FRS and RRS, respectively had carotid plaques. A model that included patients with a chart TC-SCORE $\geq$5% or SCORE-TC $\geq$1% $<$5% plus carotid plaques or TC-SCORE $<$1% and CRP $>$3 mg/L at diagnosis plus syndesmophites and carotid plaques or TC-SCORE $<$1% and CRP $>$3 mg/L at diagnosis plus extraarticular manifestations plus carotid plaques yielded the highest sensitivity (93.0%) for high/very high CV risk in these patients. The presence of syndesmophytes was associated with increased risk of carotid plaques in AS that fulfilled definitions for low CV risk according to the TC-SCORE (OR 8.75 [95% CI 2.11 - 36.40]; p=0.002).
**Conclusions:** Our results support the use of carotid US in the assessment of CV risk in patients with AS.

**Disclosure of Interest:** None declared
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## SAT0536 UTILITY OF 18F-FLUORO-DEXOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY FOR THE DIAGNOSIS OF POLYMYALGIA RHEUMATICA: A CONTROLLED STUDY

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**Objectives:** To compare[18]f-Fluoro-Dexoxyglucose Positron Emission Tomography (FDG-PET/CT) findings in patients with polymyalgia rheumatica (PMR) and controls without rheumatologic disease.
**Methods:** We have retrospectively included 50 patients with a diagnosis of PMR (EULAR/ACR criteria), who have had a FDG-PET/CT. For comparison, 53 patients who have had a FDG-PET/CT for initial staging or follow-up of neoplasm have been included as controls. 17 sites have been analyzed (2 shoulders, 2 acromio-clavicular and 2 sterno-clavicular joints, 2 greater trochanters, 2 hips, 2 ischial tuberosities, 2 iliopectinal bursitis, 2 pubic symphysis enthesis and only the interspinous space with the most FDG uptake). An FDG uptake score has been used (semi-quantitative scoring system, by Goerres and al. to evaluate visually FDG uptake (0 to 3 compared to liver uptake) into these sites. We calculated the FDG uptake score corresponding to the mean of intensity over all sites, and the number of sites with significant uptake (FDG uptake 2 or 3) for each patient. The cut offs for number of sites with high activity and for FDG uptake score were assessed using ROC curves and Odds Ratios.
**Results:** The two groups were comparable for the median patient age (69.3 years for PMR vs. 68.1 for controls). Significant differences between the two groups were found for FDG uptake score (1.12 vs 0.34, p$<$0.00001) and for number of sites with significant uptake: 6.36 sites vs 1.49 sites, p$<$0.00001.
The presence of 3 or more sites with significant uptake was correlated with the diagnosis of PMR with 74% sensitivity, 79% specificity [OR =10.8]. For the FDG uptake score the cut off is 0.53 [Se 80%, Sp 77%; OR 13.6].
We found significant differences in all sites for FDG uptake score, and number of sites with significant uptake, particularly marked for shoulders, ischial tuberosities and interspinous bursitis (p$<$0.00001 for FDG uptake score).

| | FDG uptake score (0–3) | Number of sites with significant uptake (0–17) |
|---|---|---|
| PMR group (N=50) | 1.12 [%CI 0.90–1.33] | 6.13 [%CI 4.99–7.26] |
| Control group (N=53) | 0.34 [%CI 0.26–0.41] | 1.49 [%CI 1.38–1.59] |
| p | p$<$0.00001 | p$<$0.00001 |

**Conclusions:** We found significant uptake in all sites studied in PMR compared to controls. We propose the number of 3 sites with significant uptake and a FDG uptake score superior at 0.53 for the diagnosis of PMR.

**Disclosure of Interest:** None declared
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## SAT0537 SENSITIVITY AND SPECIFICITY OF ULTRASOUND SCORE FOR THE DIAGNOSIS OF GOUT

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**Objectives:** To determine sensitivity and specificity of ultrasound score (US-score) for the diagnosis of gout, by ultrasound (US) examination, of the first metatarsophalangeal (MTP1) joint.
**Methods:** A groups of 60 patients (pts) with primary gout of the MTP1 joints were examined. Diagnosis was established by EULAR criteria for diagnosis of gout. In the group of gouty patients, only symptomatic MTP1 joints (n=83 joints) were examined by US. US findings of 60 pts (83 joints) were compared with US findings of 35 healthy controls (n=70 joints). Both groups were comparable according to age, sex and BMI. US examination was done by 18 MHz probe. The existence of: “double contour”, tophi, “starry sky” and/or “snowstorm” signs, hyperechoic cloudy areas (HCA), joint effusion, bone erosions, power Doppler signal and synovial hypertrophy were assessed. After determining the sensitivity and specificity of all these US signs individually, they were qualitative scored as 0 (absent) or 1 (present) and scored as follows: US8-US0-score “0–8”, whereby “0” means that none of the characteristics are present, and “8” means that all listed US findigns are present.
**Results:** The area under the ROC curve for total US8-score was 0.901 ± 0.025. The diagnostic sensitivity and specificity of US8-score in the MTP1 joint was 79,5% and 85,7% respectively, if value 1,50 was determined as cut-off (table 1). The synovial hypertrophy was excluded from the equation and US7- score was calculated. According to our findings US7-score in the MTP1 joint had the best sensitivity and high specificity for diagnosis gout, because the area under the ROC curve was 0.924 ± 0.021. The sensitivity of the US7-score was 82.9% and specificity 91.7%, if value 1.50 was determined as cut-off (table 1).

Table 1. The area under the ROC curve, sensitivity and specificity of US8-score and US7-score

| Test result variable(s) | The area under the ROC curve | Positive if greater than or equal to[a] | Sensitivity | Specificity |
|---|---|---|---|---|
| US8-score | 0.902 | 1.50 | 0.795 | 0.857 |
| US7-score | 0.924 | 1.50 | 0.829 | 0.917 |

**Conclusions:** US7 score (“double contour”, tophi, “starry sky” and/or “snowstorm”

signs, HCA, joint effusion, bone erosions and power Doppler signal) had highest area under the ROC curve (0,924), and highest sensitivity (82,9%) and specificity (91,7%) for the diagnosis of gout.

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## SAT0538 KNEE ULTRASOUND EXAMINATION – DO WE KNOW ENOUGH? A SYSTEMATIC LITERATURE REVIEW OF ADULT KNEE ULTRASOUND ASSESSMENT FEASIBILITY STUDIES

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**Background:** Musculoskeletal ultrasound (MSUS) has an increasingly important role in the evaluation and monitoring of knee arthritis, mainly because it is definitely more sensitive than clinical examination for detecting synovitis [1]. Although the method has been dramatically improved and refined in the last two decades, it can't occupy the right place in patient's medical management without a feasibility assessment.
**Objectives:** To identify and analyse existing data regarding the feasibility of knee ultrasound (US) exam in clinical practice.
**Methods:** A systematic literature search of PubMed and Web of Knowledge (Thomson Reuters), along with hand search of any available work or references not yet indexed, was performed using the terms: ("knee") AND ("ultrasound" OR "ultrasonography") AND ("feasibility" OR "pilot" OR "proof of concept"). The inclusion criteria consisted of feasibility studies regarding knee US or MSUS aided maneuver involving knee joint (unless including a surgical intervention) published during 2005–2015; non-adult based studies and those focused only on accuracy, reliability or validity, without considering the entire feasibility aspects, have been excluded. The selected papers were evaluated against a complex framework constructed around key areas mandatory for feasibility studies: acceptability, demand, implementation, practicality, adaptation, integration and expansion [2]. Aspects that might influence feasibility, such as machine characteristics, assessor's level of training and use of standardized scoring systems, were also considered.
**Results:** One hundred fifty-two papers have been identified, of which 11 were finally selected for the review; 8 papers evaluated novel US scores, while the rest (3 articles) focused on evaluating US measurement of articular cartilage thickness by comparison with magnetic resonance imaging, US-guided intra-articular injections and incorporating MSUS in clinical practice, respectively. The total number of patients involved was 1172 – most of them (81.5%) suffering from rheumatoid arthritis (RA). Nine out of eleven studies quantified feasibility by the amount of time spent for the evaluation, without assessing any other aspects related to it; two discussed few more aspects: acceptability, implementation and practicality, but none of them practiced a systematic assessment of all feasibility areas.
**Conclusions:** Although the knee is one of the most accessible joints with MSUS, the feasibility of this technique is poorly addressed. Almost all of the identified papers focus on a very limited aspect of feasibility (namely the amount of time needed to perform US) and on a very narrow pathology (patients with RA have been studied ten times more than those with osteoarthritis, despite the prevalence of these two diseases). This information gap should be properly addressed in next future works, in order to ensure the right place for MSUS technique.

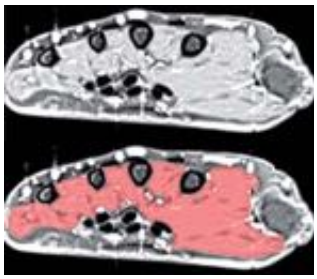
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## SAT0539 A NEW METHOD FOR THE QUANTITATIVE ANALYSIS OF HAND MUSCLE VOLUME FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is characterized by bone, cartilage and muscle loss in context of chronic inflammation. While bone and cartilage damage have been extensively studied in the past, the effects of RA on the muscles of the hand have not been studied. This situation is surprising, since visible hand muscle atrophy is a hallmark of RA and hand muscle composition determines the functional state of the patients function.
**Objectives:** Development of a method to quantitatively assess hand muscles in patients with RA, using magnetic resonance imaging (MRI) and 3D segmentation of the hand muscles.
**Methods:** T1 weighted MRI scans of healthy subjects and RA patients were used to develop a new segmentation method for hand muscles. Three groups (20 subjects each) were studied: (1) healthy subjects, (2) untreated RA patients and (3) DMARD-treated RA patients. The new approach uses a graph cuts based segmentation, which is initialized by fuzzy clustering. In a second step the segmented muscle volume of interest (VOI) is further refined and limited to the interosseal muscles and the *thenar* and *hypothenar* eminence. This segmentation procedure is fully automated. Nevertheless an extensive set of 3D editing tools such as hole filling, morphological operators and 3D surface manipulation is available to the operator, should the automatic approach not be satisfactory. Typically this happens in elderly diseased subjects with pathologic muscle and bone changes.
The results of the automatic hand muscle segmentation were checked and confirmed by two experienced MRI readers.
**Results:** The automatic segmentation procedure took about 3 min per patient. In about 70% of the cases the automatic procedure resulted in an accurate muscle segmentation, as judged by the experts. In 30% of the cases additional operator interaction was necessary, primarily to correct for over segmentation. On average, the user interaction could be completed within 2 min. Final segmentation results were confirmed again by the experts. The figure shows a slice of a T1 weighted fat suppressed MRI image in the metacarpal region. Top without and bottom with overlaid muscle VOI (red). The quantitative analysis of muscle volume and the determination of among group differences is currently being performed.



**Conclusions:** We successfully developed a new accurate 3D-segmentation for hand muscles, which allows quantitative analysis of hand muscles in RA patients.

**Disclosure of Interest:** None declared
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## SAT0540 POWER DOPPLER ULTRASOUND IMAGING OF THE JOINT-DRAINING LYMPH NODE COMPLEX IN RHEUMATOID ARTHRITIS

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**Background:** The afferent lymphatic network and the draining lymph node (LN) are fixed environments acting as remote complementary check-points through progressive phases of the inflammatory response. LN Power Doppler ultrasonography (PDUS) is a non-invasive and sensitive imaging technique commonly adopted in the preoperative diagnostic work-up of cancers. Whether the draining LN undergoes PDUS-sensitive dynamic modifications during chronic inflammation in humans and whether these modifications can be tracked to improve disease assessment is currently unclear.
**Objectives:** To investigate axillary LN sono-morphology and Doppler activity in established RA, defining the existence of alterations compared to healthy individuals and dissecting their relationship with synovitis in peripheral joints.
**Methods:** 40 RA patients refractory to conventional synthetic DMARDs (DAS28$\geq$3.2) were evaluated through complete clinical and PDUS examination in hands/wrists and axillary LN. 20 healthy individuals served as controls. 31 patients starting anti-TNF treatment were followed-up prospectively with further assessments at weeks 4 and 24. Axillary LN PDUS characteristics were assessed according to 0–3 semi-quantitative scores for global LN volume, structure of the lymphocyte-rich cortex and local perfusion. Patient-related indices for each parameter were constructed for comparative, correlative, response-to-treatment and outcome analyses. Synovitis degree (PD and gray scale) was quantified according to 0–3 semi-quantitative scales and 12-joint cumulative indices.
**Results:** Baseline assessment of perfusion and sono-morphologic characteristics showed the existence of quantitative changes in a subset of RA axillary LN, collectively leading to a distinct sonotype differentiating patients and controls. Combining data derived from morpho-structural and vascularity indices, evidence for parameters exceeding the threshold of controls was restricted to 17 out of 40

patients (42.5%), indicating variable levels of LN response despite established active disease. No relationships were observed between LN parameters and ACPA-RF status, DAS28, acute phase reactants, tender-swollen joint counts. Significant correlations (at systemic and ipsilateral level) were instead consistently detected when sensitive PDUS imaging of the synovium was applied (LN-joint PD index correlation: r=0.35, p=0.03). Plasticity of the observed LN alterations was confirmed by responsiveness analyses showing clear-cut reduction at week 24 of both structural and perfusion scores in patients with LN alterations at baseline (LN PD index: $p<0.002$, LN cortical index: $p<0.02$, LN volume index: $p<0.03$). Patient stratification according to EULAR response at 6 months demonstrated the existence of specific differences in baseline LN scores (but not in clinical features and joint US parameters) with significant decrease in the moderate/non responder group (LN PD index median [IQR] 0 [0–1] vs 2 [1–4.25], p=0.01). At its lowest detectable threshold, the LN perfusion index was the only negative predictor of achievement of good response (OR=0.08, p=0.005).

**Conclusions:** PDUS assessment of axillary LN allows detection of inflammatory-related changes in a subset of patients with active established RA. Lack of signs of LN challenge appears a negative predictor of clinical response.

**Disclosure of Interest:** None declared
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## SAT0541 MORE THAN HALF OF DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS PATIENTS MAY FULFILL THE ASAS DEFINITION OF A POSITIVE MRI OF THE SPINE: A RETROSPECTIVE ANALYSIS OF 53 CASES

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**Background:** Clinical and radiological presentation of diffuse idiopathic skeletal hyperostosis (DISH) and axial radiographic spondyloarthritis (axSpA) may overlap in the elderly. To date, it is not known whether MRI may help to discriminate between those two diseases.

**Objectives:** 1) To describe the MRI findings in DISH patients and 2) to assess the proportion of DISH patients whose MRI findings would fulfill the Assessment of SpondyloArthritis international Society (ASAS) criteria for a positive MRI of axSpA [1] and the factors associated with such fulfillment.

**Methods:** This retrospective study involved all DISH patients (diagnosed with DISH according to the rheumatologist) who had a spine or sacroiliac joints (SIJ) MRI performed between January 2009 and December 2014. Demographics, and disease characteristics were collected by review of the medical files. Available X-rays and MRI were analyzed and blindly scored by an experimented reader (modified Stoke AS Spine Score (mSASSS) and modified New York (mNY) grades for spine and SIJ Xrays and the Spondyloarthritis Research Consortium of Canada (SPARCC) score for both spine and SIJ MRI).

**Results:** Fifty-three DISH patients (mean age ± SD 65.6 ± 13.0 years, 71.7% male patients) were included in the analysis, with 31 SIJ MRI, 52 spine MRI and 37 spine or SIJ Xrays. On SIJ Xrays, 8 (19.5%) patients presented with sacroiliitis according to the mNY criteria. On spine Xrays, mean mSASSS score was 6.48 (± 8.86) and 40 (97.6%) patients had osteophytes with an angle of $\geq$45°, and up to 14 (34.15%) with an angle <45°. Mean SPARCC score of the spine was 18.3 ± 23.5. Thirty five (67.3%) patients had at least one fatty corner, and 41 (78.9%) patients had osteophytes $\geq$45° while only 2 (3.88%) with <45°. Thirty (57.7%) patients met the ASAS definition of a spine MRI suggestive of axSpA, but only 6 (19.4%) patients with an available SIJ MRI had a sacroiliitis according to ASAS criteria, and none of them had $\geq$3 erosions on the SIJ. Severe intervertebral disc lesions (Pfirmann score $\geq$4/5) were found in 38 (73.1%) patients. No factor was found to be significantly associated with fulfilment of ASAS criteria for a positive MRI of the Spine for axSpA.

**Conclusions:** Inflammatory lesions of the spine are also present on the MRI of patients with DISH and more than a half of DISH patients presented with inflammatory lesions of the spine that would meet the ASAS criteria for a spine MRI suggestive of axSpA. However only few patients would meet the ASAS definition of a positive MRI for SIJ, suggesting that MRI of the SIJ but not of the spine might allow the differential diagnosis of DISH vs. axSpA in the eldery.

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## SAT0542 THE PREVALENCE OF CALCIUM PYROPHOSPHATE DEPOSITS AT ULTRASOUND EXAMINATION: RETROSPECTIVE ANALYSIS IN A COHORT OF PATIENTS

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**Background:** The Calcium Pyrophosphate Deposition Disease (CPPD) is a disease frequently observed in the clinical practice but currently its exact prevalence is unknown. In fact, the data available in the literature vary depending on method used, generally x-ray or synovial fluid analysis, while no studies evaluated the ultrasound (US) prevalence of Calcium Pyrophosphate (CPP)deposits.

**Objectives:** The evaluation of the prevalence of CPP deposits in a cohort of patients (pt) that undergo US examination of wrists and knees.

**Methods:** We extracted from our database all reports of pt undergoing US exam of wrists and knees, referred to our outpatient clinic from October 2005 to January 2015. All US exams were performed by rheumatologists expert in muscoloskeletal ultrasound (MSUS) using an Esaote MyLab70 equipped with a 4–13 MHz linear probe. We recorded the presence of CPP deposits at the medial meniscus (MM), the lateral meniscus (LM) and the hyaline cartilage (HC) in the knees and at the triangular fibrocartilage (TF) of the wrists. Statistical analysis was performed with SPSS.

**Results:** US reports of 984 pt (81,9% female, mean age 50,28 SD±17,22) were included in this study. The overall prevalence of CPP deposits was 6,6% (65/984pt). In this group, the CPP deposits were observed in the 32,3% (21/65pt) of the wrists (bilaterally 61,9%) and in the 93,8% (61/65pt)of the knees (bilaterally 67,21%). The involvement of both joints were observed in the 26,15% (17/65pt).
Analysing the prevalence by ages, it was 2,1% (14/664pt) in pt under 60 years old (yo), while it increased to 16,7% (51/306pt) in pt over 60. The prevalence was 8,7% (16/184pt) between 60 and 70 yo, 26,7% (24/90pt) between 70 and 80 yo, and increased to 34,4% (11/32pt) in pt over 80.
Regarding the different joint structures, the prevalence was 89,2% (58/65pt) in menisci, (83,1% MM, 78,5% LM) and 32,3% (21/65pt) in the HC. The TF was involved in 32,3% of cases (21/65pt). Thus, according to previous studies[1], our results showed that menisci, particularly MM, are the most involved by CPPD, appearing as the favorite site for US identification of CPP deposits. Moreover, this study confirmed the correlation between the aging and the increased prevalence of CPP deposits. However, our analysis showed a higher prevalence respect to the values obtained in previous studies that considered the x-ray as the reference method[2]. However, this trend should be further confirmed with a prospective assessment conducted in a larger sample of patients.

**Conclusions:** To our knowledge this is the first attempt to define the CPPD prevalence with US, that recently entered in EULAR recommendations as a promising diagnostic tool for CPPD[3]. Considering its accuracy, non-invasiveness and low cost, the US could be widely used for CPPD diagnosis also for large scale evaluation, planned in order to define the prevalence of this disease.

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## SAT0543 ACCURATE DETERMINATION OF PERIARTICULAR BONE COMPOSITION IN HEALTHY INDIVIDUALS AND COMPARISON TO ACPA-POSITIVE RHEUMATOID ARTHRITIS PATIENTS

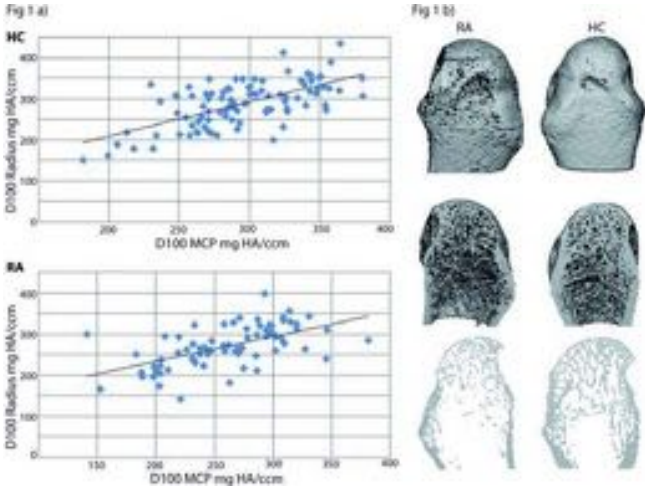
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**Background:** Periarticular bone loss is a typical finding in rheumatoid arthritis (RA) patients. However, this structural bone change is yet insufficiently characterized. Larger studies assessing periarticular bone composition in healthy controls (HC) and RA patients by high-resolution imaging have not been undertaken and have not been validated against standard measurement at the distal radius.

**Objectives:** To assess periarticular bone by high-resolution peripheral quantitative computed tomography (HR-pQCT) in the metacarpal heads and compare it with standard measurement in the distal radius in HC and anti-citrullinated peptide antibodies-positive (ACPA+) RA patients.

**Methods:** HR-pQCT (XtremeCT, Scanco, Switzerland) scans of the distal radius and of the metacarpal head 2 joints of HC and RA patients were performed. In contrast to previous studies the entire metacarpal head was assessed. After motion grading of the images by two independent readers, images with a motion grade more than 3 were excluded. A graphical objet (GOBJ) was generated and evaluated using the standard evaluation protocol for the radius provided by the manufacturer for both, the metacarpal head and the distal radius. In the last step, bone density values such as average bone density (D100 [mg HA/cm$^3$]), bone volume/total volume (BV/TV), number of trabeculae (Tb N [1/mm])) were

determined and compared between (i) the metacarpal head and the radius and (ii) between HC and RA patients.
**Results:** 222 subjects (110 HC and 112 RA) were analyzed. Sex and age distribution were balanced between HC (f/m: 58/52; 50.1±16.1 years) and RA patients (f/m: 53/59; 53.2±12.4 years; disease duration 9.2±8.7 years). Bone density in HC was 288.3±54.7 mg HA/cm$^3$ in the distal radius and 294.4±43.3 mg HA/cm$^3$ in the metacarpal head with significant correlation ($\rho$=0.583 ($p<0.001$)) (Fig1a, top row). Respective bone densities in RA patients were 269.8±49.6 mg HA/cm$^3$ and 263.3±46.0 mg HA/cm$^3$ with significant correlation ($\rho$=0.632 ($p<0.001$)) (Fig. 1a, bottom row). Similar correlations were found for BV/TV (HC: $\rho$=0.590, $p<0.001$, RA: $\rho$=0.687, $p<0.001$) and Tb N (HC: $\rho$=0.576, $p<0.001$, RA: $\rho$=0.705, $p<0.001$). Comparing bone densities between HC and RA patients we found significant bone loss in both the metacarpal head ($p<0.001$, U=3834.5, Z=-4.860) and the distal radius (p=0.018, U=2700.5, Z=-2.357) in RA patients. Examples of measurements in the metacarpal heads of HC and RA patients are shown in Figure 1b.




**Conclusions:** In this large study, we show that the assessment of periarticular bone structure in metacarpal heads is feasible and correlates well with standard measurement in the distal radius. Furthermore, we show significant bone loss in RA patients as compared to HC in both anatomical sites.
**Disclosure of Interest:** None declared
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## SAT0544 ENTHESEAL INVOLVEMENT IN ASYMPTOMATIC HIV PATIENTS: AN ULTRASONOGRAPHIC STUDY

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**Background:** A complex variety of musculoskeletal manifestations have been described in HIV patients, including conditions belonging to the wide spectrum of spondyloarthropathies (SpA). Enthesitis is a distinctive feature of SpA. Peripheral enthesitis is usually revealed by clinical findings but it may also be asymptomatic and detected only by imaging, such as conventional radiography, magnetic resonance or ultrasonography (US).
**Objectives:** The aim of the present study was to evaluate by US examination the prevalence of enthesitis in patients with HIV infection without rheumatic clinical symptoms in comparison with control healthy subjects.
**Methods:** 28 patients with aymptomatic HIV infection (22 M and 6 F; mean age:43 ± 8.6) were consecutively examined with US (Toshiba- Aplio XG- 12–18 MHz linear array transducer). All patients were recently diagnosed as HIV infected, didn't take any HIV treatment and had no clinical signs or symptoms of joint or enthesis involvement. 25 healthy subjects, matched for sex, age and BMI were studied as controls. The following sites were examined bilaterally by US: common extensor tendon insertion on the lateral epicondyle of the humerus; quadriceps tendon insertion on the superior pole of the patella; patellar tendon insertion (patellar ligament origin and the patellar ligament insertion at the tibial tuberosity); Achilles tendon insertions on the calcaneus. The following abnormal findings were recorded: thickness, bony erosions, enthesophytes and bursitis. Local blood flow was examined using Power Doppler (PD) mode. US and PDUS were performed by an experienced operator and blinded to the clinical examination.
**Results:** 20/28 HIV patients (71.4%) presented almost one enthesis abnormality in comparison with 3/25 (12%) healthy controls ($p<0.05$). In 17/28 (60.7%) HIV patents was evidenced thickness; in 15/28 (53.5%) bursitis; in 13/28 (46.4%) enthesophytes and in 4/28 (14.2%) erosions. PD was positive in 11/28 (39.2%) HIV patients. In healthy controls, US showed thickness in 2/25 (8%), enthesophytes in 1/25 (4%) and altered PD in 1/25 (4%). The intra and inter-reader agreements were high (>0.8 intra-class correlation variability).
**Conclusions:** US revealed a high frequency of subclinical enthesis abnormalities in asymptomatic HIV patients without rheumatic clinical signs and symptoms, highlighting the important role of US investigation and the strong association of HIV infection with rheumatic manifestations typical of SpA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4622

## SAT0545 THE EFFECT OF ANTI-TNF ALPHA TREATMENT ON EROSION PROGRESSION IN RHEUMATOID ARTHRITIS BY HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY: THREE-MONTH DATA

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**Objectives:** High-resolution peripheral quantitative computed tomography (HR-pQCT) is an emerging imaging technology for early detection of erosion in rheumatoid arthritis (RA). In this study, we use HR-pQCT to investigate the effects of anti-tumor necrosis factor alpha (anti-TNFa) treatment on erosion progression for three months follow-up period.
**Methods:** Fourteen patients with clinically diagnosed RA (Group I, n=4, on methotrexate (MTX) treatment only, and Group II, n=10, on combined anti-TNFa and MTX treatment) underwent clinical evaluation using disease activity score (DAS) score and HR-pQCT scan. Scans were performed on metacarpophalangeal (MCP) joint at baseline (prior to anti-TNF initiation for Group II) in all patients and in twelve patients (4 in group I, 8 in group II) after three months. The maximum width and depth of erosions at the second, third MCP and proximal phalangeal bases (PB) were measured manually in accordance with SPECTRA definition. Erosion volume was calculated as width depth. Mann-Whitney U, Chi-square and paired T-test were done to compare measurements between and within groups from baseline to 3-month.
**Results:** The mean of ages was 71.8±3.8 in group I vs. 49.4±13.6 years in groups II (p=0.019), and of disease duration was 9.0±6.3 vs. 4.0± 4.5 years (p=0.076). The mean of total erosion volume at baseline was 8.0±10.4 mm$^3$ in group I vs. 24.5±42.1 mm$^3$ in group II (p=0.733). In group I, erosions were on PB2 (n=1), MCP2 (n=2), PB3 (n=0), and MCP3 (n=2); in group II, it was 2, 6, 2, and 5 respectively. There was a significant decrease of disease activity in group II (DAS28-CRP, p=0.001 and DAS28–ESR, p=0.002) from baseline to 3-month. Although there was no statistically significance between or within the groups, the mean changes of erosion volume by HR-pQCT tended to increase in group II (0.0±2.5 in group I vs. 4.0±6.8 in group II).
**Conclusions:** At 3 months follow-up, we observed a dissociation between clinical response and erosion volume measured by HR-pQCT in patients on anti-TNFa treatment. The significant decrease in DAS28-CRP, DAS28-ESR and tendency of increase in erosion volumes suggest that although anti-TNFa treatment suppresses inflammation within a 3-month treatment period, the structural joint damage may require more time to be hold. HR-pQCT is a sensitive tool for evaluating erosion volume changes even within a time window of 3-month. Now we are waiting one-year data of our cohort.
**Disclosure of Interest:** None declared
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## SAT0546 ULTRASOUND-DETECTED SYNOVITIS AND TENOSYNOVITIS PREDICT RA IN EARLY DISEASE

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**Background:** Ultrasound-detected synovitis improves the prediction of RA in early disease. Although ultrasound-detected tenosynovitis in common in early RA, its relative utility in the prediction of RA alongside ultrasound-detected synovitis and conventional serological and clinical variables is unclear.
**Objectives:** To identify a minimal core set of ultrasound, clinical and serological variables predicting RA in a cohort of patients with early arthritis using a data-driven approach.

**Methods:** 107 patients [female n=60, median age 51] with ≥1 joint with clinically apparent synovitis and a symptom duration ≤3 months underwent clinical, laboratory and ultrasound assessments. Final diagnoses were determined at 18 month follow-up. Ultrasound assessment determined the presence of synovitis at 28 joints (bilateral MCPs 1–5, PIPs 1–5, wrists, and MTPs 2–5) and tenosynovitis at four tendon sites (bilateral finger flexor and extensor carpi ulnaris tendon). First, principal component analysis (PCA) was performed on 1) clinical and serological variables (age, gender, symptom duration, ESR, CRP, RF, ACPA, duration of early morning stiffness, tender joint and swollen joint count), and 2) joint and tendon ultrasound variables. Then the variable with the highest loading factor from each component was extracted and made available in a forward step-wise multivariate logistic regression analysis.
**Results:** 46 patients developed RA, 17 developed non-RA persistent inflammatory arthritis and 44 patients had resolving disease. Seven components were identified on clinical and serological PCA and four components were identified within ultrasound synovitis and tenosynovitis variables (Table 1). The final multivariate logistic regression model included ACPA positivity (OR=12.61, CI: 3.50–45.52, p<0.001), digit flexor ultrasound tenosynovitis (OR=4.58, CI: 1.67–12.56, p=0.003) and MCP 1 ultrasound synovitis positivity (OR=4.75, CI: 1.78–12.64, p=0.002).

Table 1. PCA analysis of clinical, serological, joint and tendon ultrasound variables

| Component | Clinical and serological variables |
|---|---|
| 1 | Swollen joints >6* , tender joints >6 |
| 2 | Age ≥60* |
| 3 | Early morning stiffness ≥60 min* |
| 4 | Swollen joint = 1*, Tender joint = 1 |
| 5 | ACPA positivity* |
| 6 | Abnormal CRP*, abnormal ESR |
| 7 | Gender* |
| **Component** | **Joint and tendon ultrasound variables** |
| 1 | MCP 1*, MCP 4, MCP 5, PIP 1, PIP 4 |
| 2 | Digit flexor tendon*, MCP 2, MCP 3, extensor carpi ulnaris tendon, wrist joint |
| 3 | PIP 2*, PIP 3, PIP 5 |
| 4 | MTP 2*, MTP 3, MTP 4 |

*Variables with the highest loading factor within each component.

**Conclusions:** Both ultrasound-detected synovitis and tenosynovitis provide independent data in addition to clinical and serological variables in the prediction of RA in early disease. MCP 1 and digit flexor scanning provide the optimal predictive data in this cohort.
**Disclosure of Interest:** None declared
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## SAT0547 ULTRASOUND ASSESSMENT OF CARTILAGE DAMAGE AT METACARPAL HEAD LEVEL IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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**Background:** Ultrasound (US) with very high frequency probe (up to 22 MHz) has a resolution power of 0.1 mm and allows for the direct visualization of the hyaline cartilage of the metacarpal head.
**Objectives:** To determine the prevalence and distribution of US-detected cartilage damage at metacarpal heads of patients with rheumatoid arthritis (RA) and osteoarthritis (OA) and to investigate if cartilage damage evaluated by US method is associated with radiographic scores (Sharp van der Heijde score and Simple Erosion Narrowing Score (SENS) in RA and Kallman score in OA).
**Methods:** 50 patients with RA and 19 patients with OA were enrolled in this study. The US examination of the metacarpal head cartilage from II to V finger of both hands was performed. 400 metacarpophalangeal (MCP) joints in RA and 152 MCP joints in OA were scanned with a very high-frequency linear probe (i.e. 10–22 MHz), using a previously described scoring system for cartilage damage[1]. In a subgroup of 27 patients with RA and 7 with OA the radiographic scores were calculated. Pearson's correlation coefficient and Cohen κ were used to investigate associations between US and radiographic scores.
**Results:** The US examination of the metacarpal head cartilage from II to V finger of both hands lasted a mean of 6 minutes. The metacarpal head cartilage was found positive for cartilage damage by US in 139 out of 400 (34.8%) MCP joints in RA and in 65 out of 152 (42.8%) MCP joints in OA. In RA, the hyaline cartilage of the II right metacarpal head was the most frequently affected followed by the II left and the III right metacarpal head. The less affected was the V metacarpal head bilaterally. In OA, cartilage damage was homogeneously distributed in all MCP joints. Symmetric damage of cartilage was observed in 97/400 (24.3%) RA joints and in 44/152 (28.9%) OA joints. Conversely, asymmetric damage of the cartilage was observed in 42/400 (10.5%) RA joints (only in patients with disease duration more than 2 years) and in 21/152 (13.8%) joints in OA. A significant positive correlation was found between US total score and either Sharp van der Heijde score or SENS score (r=0.584, p<0.001; r=0.510, p<0.001, respectively) in RA and between US total score and Kallman score (r=0.687, p<0.001) in OA. Agreement between two imaging methods was high, 78% in RA (κ=0.570, p<0.001) and in 91% in OA (κ=0.750, p<0.001).
**Conclusions:** The present study provides evidence supporting the feasibility of the US assessment of the metacarpal head cartilage. A positive significant correlation was found between the US findings, obtained with a very high frequency probe by an experienced sonographer and the radiographic scores assigned by an expert radiologist.
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**Acknowledgement:** Supported by EULAR, IGA grant No. NT12437 and GAUK grant No. 1010213.
**Disclosure of Interest:** None declared
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## SAT0548 POSITRON EMISSION TOMOGRAPHY WITH 18F-FLORBETAPIR (FBP) AS A MARKER OF BURDEN OF DISEASE IN AMYLOIDOSIS

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**Background:** Amyloidosis comprises a group of diseases characterized by a deposition of amyloid fibrils which have an antiparallel B-sheet secondary structure. Active research in seeking evolution of deposits must be done regularly with several tests. FBP is a radiotracer with tropism to proteins with β-sheet conformation that is used in Alzheimer's disease[1].
**Objectives:** The purpose of this study was to evaluate the utility of FBP in studying the extension of the amyloidosis.
**Methods:** We performed an observational descriptive study with 14 subjects controlled at our Amyloidosis Unit: twelve patients with a biopsy-proven disease, one patient with senile amyloidosis and one woman with a familiar TTR mutation without evidence of diposits. Study was conducted from February 2015 until August 2015. A PET/CT was performed with injection of 370MBq FBP. Images were acquired after 40–50 minutes of injection and a qualitative description was done. Evaluation also included traditional techniques like echocardiogram, cardiac MRI, blood and urine tests, and electromyography. If other organs were involved, they were registered. The correlation between traditional techniques and PET/CT was studied.
**Results:** The median age at diagnosis was 69 years (IQR: 60 – 75) and the median follow up 22.2 months (IQR 2 – 32). Two patients had hereditary amyloidosis by transthyrretin (TTR), 1 patient a senile amyloidosis, 8 patients a primary amyloidosis and 2 a secondary amyloidosis. Traditional evaluation detected heart involvement in 9 patients (69.23%), kidney involvement in 6 (46.15%) and soft tissue was involved in 4 patients (30.76%): 2 of them had macroglossia, 1 patient had thyroid gland amyloidosis and the remaining one had amyloid deposits in the stomach.
PET/CT showed cardiac involvement in 8 patients (61.53%), kidney in 3 patients (23.07%) and soft tissue in 6 (46.15%) patients: tongue in 2 patients, thyroid gland in 2, spleen in 1, lungs in 2. Multiple organs were involved in 4 patients (30.76%).
Correlation between traditional techniques and PET/CT showed that 6 patients had both positive tests for heart involvement. Two patients identified as having cardiac amyloidosis by echocardiogram and cardiac MRI had a negative PET. Two patients with a positive PET had a negative cardiac MRI but echocardiogram showed left ventricular hypertrofia. Kidney involvement was present in 3 patients with a previously known renal disease (50% of patients). Soft tissue involvement showed an increased uptake in the tongue in the two patients with macroglossia, thyroid involvement in the patient with goiter but didn't show gastric involvement in the remaining patient. Two subjects had bilateral lung involvement which was not previously suspected and another patient had thyroid and spleen involvement. The healthy subject (affected by the familial TTR mutation) had a normal PET/CT.
**Conclusions:** FBP PET/CT is a promising technique to evaluate the number of organs affected in patients with amyloidosis. Prospective studies with bigger cohorts are required to validate its use during our clinical practice.
**References:**
[1] Lin KJ, Hsu WC, Hsiao IT et al. Whole-body biodistribution and brain PET imaging with [18F]AV-45, a novel amyloid imaging agent–a pilot study. Nucl Med Biol. 2010;37:497–508.
**Disclosure of Interest:** None declared
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## SAT0549 VALIDATION OF 3 NOVEL AUTOANTIGENS FOR SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a systemic autoimmune disease that manifests as progressive fibrosis of the skin and internal organs. SSc is associated with the presence of several autoantibodies (aab) to intracellular targets, with the three most important SSc-specific being anti-centromere antibodies, anti-Scl70 antibodies and anti-RNA polymerase III antibodies, which occur in over 50% of SSc patients. Autoantibody specificities are strongly associated with pattern of organ involvement and disease outcome, making autoantibodies an essential tool in the clinical management of SSc. This highlights the need for additional specific and sensitive diagnostic and prognostic biomarkers in SSc. We have recently conducted high-content autoantibody profiling studies of SSc, systemic autoimmune diseases (AID), and healthy controls and found novel SSc associated autoantibodies.
**Objectives:** These novel SSc-associated autoantibody biomarker candidates and their diagnostic value were evaluated by testing samples derived from different SSc cohorts from the University Hospital Düsseldorf and the University Hospital Zurich.
**Methods:** Three novel identified biomarker candidates, namely Lysine (K)-specific demethylase 6B (*KDM6B*), Protein Phosphatase Inhibitor 2 (PPP1R2) and Bicaudal Drosophila Homolog 2 (BICD2) were developed into ELISA Kits using highly purified recombinant antigen and evaluated. Autoantibody specificities were analyzed using an independent and well characterized cohort consisting with sera of patients suffering from SSc (n=198), myositis (n=20), RA (n=20), SLE (n=40) and healthy blood donors (n=132). Assay threshold levels were calculated using a receiver operation characteristic analysis and set for specificities of >95%.
**Results:** Using the respective cut-off for the ELISA tests we were able to find autoantibody reactivity against BICD2 in 29.2% of SSc patients and 4.8% of control samples, against PPP1R2 in 15% SSc and 3.2% of controls and against KDM6B in 20% of SSc patients and 2.6% of control samples, respectively. Positive results of anti-BICD2 and anti-PPP1R2 aab co-migrated with anti-Centromere aab, but were also found in anti-Centromere and anti-Scl-70 negative samples. Interestingly, both anti- BICD2 and anti-PPP1R2 aab were found in SSc samples tested negative for anti-RNA Polymerase III auto-reactivity.
**Conclusions:** In this study we were able to confirm the diagnostic value and high specificity of the newly discovered autoantigens using ELISA. Anti-BICD2 aab showed significant inverse correlation with pulmonary fibrosis. Thus, anti-BICD2 aab may be associated with a decreased incidence of severe lung disease.
**Disclosure of Interest:** J. Schulte-Pelkum Employee of: Protagen AG, P. Budde Employee of: Protagen AG, H. Zucht Employee of: Protagen AG, D. Wirtz Employee of: Protagen AG, P. Schulz-Knappe Employee of: Protagen AG, O. Distler Grant/research support from: Bayer, Sanofi, Ergonex, Boehringer Ingelheim, Actelion, Pfizer, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, EpiPharm, Ergonex, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Pharmacyclics, Pfizer, Serodapharm, Sinoxa, S. Jordan: None declared, N. Hunzelmann: None declared, M. Schneider: None declared, B. Maurer: None declared
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## SAT0550 PREDICTIVE VALUE OF POWER DOPPLER ULTRASONOGRAPHY (PDUS) FOR THE DIAGNOSIS OF RHEUMATOID ARTHRITIS IN PATIENTS WITH BASAL NEGATIVE ACUTE PHASE REACTANTS

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**Background:** The presence of acute phase reactants high can assist in the diagnosis and classification of patients with rheumatoid arthritis, although on occasions in early arthritis may be within the range of normality.
**Objectives:** The objective was to establish whether the presence of basal Doppler signal in patients with negative reactants may be helpful in order to establish the risk of final diagnosis of rheumatoid arthritis a year, following ACR criteria 1987
**Methods:** We studied the presence of Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, knees) and 44 joints (28 joints and in addition hips, Tarsus, ankles and MTPs), with a mid-range equipment GE L5, in patients with suspected early arthritis in which the ESR was normal according to two different criteria or the CRP was negative. The patients had at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes (*Criteria SERAP Study), with <12 months of evolution of the symptoms. None of the patients had a previous diagnosis of rheumatoid arthritis or other inflammatory joint disease nor had received prior treatment with steroids or DMARDs. It was considered normal CRP ≤5mg/L (normal range 0–5). It was considered normal ESR (mm/h) according to two criteria: a) ESR +1: ≤20 in all patients or (b) ESR +2 (criterion depending on the age and sex): Age ≥50 years is normal ≤20 in males and ≤30 in women; minors of 50 years is normal ≤15 mm/h in males and ≤20 in women (1). At one year follow-up was established whether patients met criteria for RA 1987 ACR.
**Results:** In 35 patients with normal basal ESR, by criteria 2 (criterion by ESR age and sex), the presence of basal power doppler signal in ≥1 joints of 44 (PD44) in baseline visit shows statistically significant association with the RA diagnosis at 12 months by ACR 1987 classification criteria, with p=0.032, OR=6 (1,33–27,05). In 32 patients with normal basal ESR by criteria ESR 1 (<20 mm/h), the presence of basal power doppler signal in at least one joint of 44 (PD44 basal) shows statistically significant association with the diagnosis at year of AR, with p=0.030, OR=6 (1,25–28,84), not so PD28 (p=0.150). In 25 patients with basal negative CRP, the presence of at least one joint with power doppler signal (PD28 and PD44) are not associated in a statistically significant way with final diagnosis of RA at 12 months following ACR 1987 criteria (p=0.428 and p=0.226, respectively).

| | | | RA YES | Chi-square Fisher exact test (p) | OR | 95 % CI |
|---|---|---|---|---|---|---|
| CRP | PD44 | YES | 9/15 (60%) | 0.226 | - | - |
| NEGATIVE | | NO | 3/10 (30%) | | | |
| ESR+1 | PD44 | YES | 15/20 (75%) | 0.030 | 6 | (1,25-28,84) |
| NEGATIVE | | NO | 4/12 (33,3%) | | | |
| ESR+2 | PD44 | YES | 16/22 (72,7%) | 0.032 | 6 | (1,33-27,05) |
| NEGATIVE | | NO | 4/13 (30,8%) | | | |

**Conclusions:** The presence of at least one joint with power doppler signal of 44 joints (PD44) on baseline visit may help to predict the RA diagnosis at 12 months of follow up according to criteria ACR 1987, in patients with normal basal ESR. In patients with normal basal CRP, PD44 could not establish statistically significant differences for the diagnosis of AR a year according to criteria ACR 1987. In our study PD28 could not predict the RA diagnosis at 12 months by ACR 1987 criteria.
**References:**
[1] Bottiger LE, Svedberg CA. Normal erythrocyte sedimentation rate and age. Br Med J 1967; 2:85–7.
**Disclosure of Interest:** None declared
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## SAT0551 PREDICTIVE VALUE OF ULTRASONOGRAPHY FOR RADIOGRAPHIC PROGRESION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** There is a short window of opportunity for early diagnosis and treatment of rheumatoid arthritis, that may be crucial for reaching remission and a low rate of radiographic progression. High resolution power doppler ultrasonography (PDUS) is helpful in early detection of synovitis and may help to select patients at higher risk of developing structural radiographic progression of joint damage.
**Objectives:** To establish whether the presence of basal power doppler signal in patients with early arthritis may be helpful in order to establish the risk of radiographic progression at 12 months of follow-up.
**Methods:** We studied the presence of ultrasonographic Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, knees) and 44 joints (28 joints and in addition hips, Tarsus, ankles and MTPs), with a mid-range equipment GE L5, in 70 patients with suspected early arthritis. The patients were included with at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes with <12 months duration of the symptoms. Presence or not of basal high acute phase reactants (CPR>5 mg/dl; ESR >20 mmHg) and DAS28>5.1 for each patient were registered. In 62 patients completed hands and feet radiology were available both in basal and 12 months visits. Scores according Sharp/van der Heijde method (Sharp modified method) (1) were recorded for each patient. Clinical relevant Radiographic progression was defined for each patient as a stadistical significant difference between Sharp/van der Heijde method scores in basal and 12 months visits that exceeded the SDD (smallest detectable difference) obtained from the intraobserver variability study for radiographic assessment (SDD: Erosions 2,5; narrowing 2,71; Total 2,25). Statistical study: Chi-square, Fisher exact test, p univariant and Odds Ratio calculation, SDD.
**Results:** The presence of basal power doppler signal in ≥1 joints of 44 (PD44) at baseline shows statistically significant association with radiographic progression of erosions and total progression (erosions plus narrowing) at 12 months p<0.005, OR 5,57 (1,56–19,79) and p=0.048, OR=3,42 (1,02–11,49) respectively, whereas the presence of at least one joint with power doppler signal of 28 joints (PD28) was only associated to total progression p=0.017, OR 4,23 (1,23–14.49). High acute phase basal reactants (CRP and ESR) were as well associated to progression of erosions, p=0.005 OR 4,80 (1,53–15,16) and p=0.025, OR 3,25 (1.14–9,28)

respectively. A DAS28>5,1 at baseline was associated to radiographic progression of erosions (p=0.021), narrowing (p=0.005) and both (p=0.001).

| | | PROG EROSIONES | PROG PINZAMIENTO | PROG TOTAL (E+P) |
|---|---|---|---|---|
| PD28 | SI<br>NO | NS | NS | 37/44(84,1%)<br>10/18 (55,5%)<br>p=0.017<br>OR=4,23(1,21-14,69) |
| PD44 | SI<br>NO | 28/46 (60,8%)<br>5/16 (31,2%)<br>p=0.048<br>OR=3,42 (1,02-11,49) | NS | 39/46 (84,8%)<br>8/16 (50%)<br>p=0.005<br>OR=5,37 (1,56-19,79 |
| DAS>5,1 | SI<br>NO | 22/32 (68,7%)<br>11/30 (36,6%)<br>p=0,021<br>OR=3,80(1,32-10,89) | 23/32 (71,8%)<br>11/30 (36,6%)<br>p=0.005<br>OR=4,41 (1,51-12,87) | 30/32(93,7%)<br>17/30 (56,6%)<br>p=0.001<br>OR=11,47 (2,30-56,99) |
| VSG1 | SI<br>NO | 23/35 (65,7%)<br>10/27 (37%)<br>p=0.025<br>OR=3,25(1,14-9,28) | NS | NS |
| PCR | SI<br>NO | 27/43(63,8%)<br>6/21(28,5%)<br>p=0.005<br>OR=4,8(1,53-15,16) | NS | NS |

**Conclusions:** The presence of at least one joint with power doppler signal of 44 joints (PD44) at baseline may help to predict the progression of erosions at 12 months of follow up in patients with early RA. The presence of positive acute phase reactants (CRP,ESR) and DAS28 high activity (>5,1) in our study increased the risk of radiographic progression of erosions as well.

**References:**

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## SAT0552 MUSCULOSKELETAL ULTRASOUND (MSUS) SHOWING ENTHESEAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): SOMETHING UNEXPECTED

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**Background:** Musculoskeletal involvement is one of the most common manifestations of SLE and, recently, different studies have demonstrated the role of MSUS in the evaluation of tendons and joints involvement in SLE patients (1). The enthesis is traditionally not included as a potential target of the inflammatory process of the disease, remaining a yet unexplored anatomical area in this cohort of patients.

**Objectives:** To investigate the prevalence and distribution of entheseal abnormalities in SLE patients using MSUS.

**Methods:** 30 consecutive SLE patients were enrolled in the present study. The scanned entheses were those included in the Glasgow Ultrasound Enthesitis Scoring System: the patellar insertion of the quadriceps tendon (QT), the patellar and distal insertion of the patellar tendon (PT), the calcaneal insertion of the Achilles tendon (AT) and the calcaneal insertion of the plantar fascia (PF). All patients underwent both clinical and ultrasound examination aimed at assessing the entheseal involvement. MSUS entheseal pathology was evaluated by detecting the presence of grey scale changes and power Doppler (PD) signal, as defined by the OMERACT Ultrasound Task Force (2). All the factors that may affect the MSUS findings at entheseal level (lipid profile, body mass index, history of trauma, sport activity and corticosteroid therapy) were carefully evaluated.

**Results:** MSUS entheseal abnormalities were found in 20 out of the 30 patients (66.6%) and in 59 of the 300 entheses examined (19.6%). Patients were clinically asymptomatic in 71.4% of the cases. Among the entheses affected, the distal insertion of the PT was the most commonly involved area (37.2%), followed by the calcaneal insertion of the AT (22%) and the proximal insertion of the PT (16.9%). The patellar insertion of the QT and the calcaneal insertion of the PF were involved in the 13.5% and 10.4% of the cases respectively. With regard to the pathological changes PD signal, hypoechoic areas and entheseal thickening were the most frequently detected abnormalities (29.3%, 26.7% and 24.1%, respectively). Calcifications and bone erosions were found in 11.3% and 8.6% of the cases respectively.

**Conclusions:** Although the inflammatory process in SLE patients is traditionally considered to be localized at synovial tissue level, this study shows that entheseal changes are not uncommon in SLE, especially at PT insertions, occurring frequently in asymptomatic patients. These preliminary results should lead to further investigations aimed at identifying the factors associated with entheseal involvement in SLE patients.

**References:**

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[2] Terslev L et al. Defining enthesitis in spondyloarthritis by ultrasound: result of a Delphi process and of a reliability reading exercise; Outcome Measures in Rheumatology Ultrasound Task Force. Arthritis Care Res 2014; 66:741–8.

**Disclosure of Interest:** None declared

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## SAT0553 DIAGNOSTIC VALUE OF QUANTITATIVE SIALOSCINTIGRAPHY COMPARED TO LABIAL SALIVARY GLAND BIOPSY IN PATIENTS WITH SUSPECTED SJÖGREN' SYNDROME

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**Background:** Salivary gland dysfunction is one of the most common features of Sjögren' syndrome (SS). Sialoscintigraphy (sSC) is the only technique nowadays available to objectify salivary gland dysfunction that provides simultaneous information about type of functional defect, distribution and severity. In recent years its interpretation based mainly on qualitative indices and the appearance of the American College of Rheumatology (ACR) criteria have shifted in favor of the biopsy (Bp). Some studies have analyzed the role of quantitative scintigraphic indices, mainly excretion fraction (EF%), in the diagnosis of SS, with mixed results.

**Objectives:** 1) To describe glandular involvement patterns and EF% values useful in SS diagnosis. 2) To compare diagnostic accuracy of scintigraphic indices and Bp.

**Methods:** Patients with suspected SS and with sSC and Bp performed between 2006–2012 were included. sSC were performed in a 30 minutes protocol with 99mTc sodium pertechnetate and lemon juice stimulation. Patients already diagnosed of SS and/or with sSC or Bp requested by specialists other than rheumatologists were excluded. Correlations between glandular involvement patterns and EF% and diagnosis of SS were analyzed with Fisher exact test and Kruskal Wallis respectively. Sensitivity, specificity and receiver operating characteristic curve analysis of scintigraphic indices and Bp were performed.

**Results:** Among 272 patients with sSC performed in that period, 71 fulfilled inclusion criteria. 68 (96%) were women with a mean age of 52 ± 14 in the timing of sSC. 57 (80%) reported xerostomia, the majority (39%) with onset in recent months. Qualitative sSC were reported as abnormal in 51 cases (71%); data on age, xerostomia duration, xerostomia related drugs and presence of thyroid disease showed similar frequencies among normal and abnormal sSC groups. Sufficient data to apply American-European Consensus Group and ACR criteria were available in 69 and 48 patients respectively, with diagnosis of SS in 38 (54%). Uptake dysfunction (96 vs 77% p 0.134) and submandibular involvement (59 vs 30% p 0.236) were observed most frecuently in SS patients. All glands showed lower EF% medians in this group, with significant differences for submandibulary ones: right gland 29 (7–37) vs 49 (41–57) p 0.004; left gland 30 (10–45) vs 52 (29–64) p 0.007. Submandibular EF% (right gland AUC 0.793 ± 0.091 p 0.004 IC 95% [0.61–0.97]; left gland AUC 0.764 ± 0.083 p 0.007 IC 95% [0.60–0.93]) showed better diagnostic accuracy than qualitative sSC (AUC 0.601 ± 0.070 p 0.149 IC 95% [0.47–0.74]) and similar to Bp (AUC 0.789 ± 0.055 p 0.000 IC 95% [0.68–0.90]). Submandibulary EF% cuttoff values of 39.5 (right gland) and 47.5 (left gland) showed a sensitivity of 95–82% and specificity of 71–67%, compared to 82% and 39% for qualitative sSC, and 58% and 100% for Bp.

**Conclusions:** 1) Patients fulfilling SS criteria show lower submandibular EF% compared to those who do not. 2) Diagnostic accuracy of submandibular EF% is better than qualitative sSC and similar to Bp. 3) Cutoff values of submandibular EF% of 39.5 (right gland) and 47.5 (left gland) show a sensitivity comparable to qualitative sSC but a significantly higher specificity.

**Disclosure of Interest:** None declared

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## SAT0554 TIME-INTENSITY CURVES OF CONTRAST-ENHANCED ULTRASONOGRAPHY: PARAMETERS VARIATION AND JOINT DIFFERENCES IN EARLY ARTHRITIS PATIENTS WITH WRIST INVOLVEMENT

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**Background:** Contrast enhanced ultrasonography (CEUS) may be superior to power Doppler US in detecting synovial inflammation by visualizing and quantifying low velocity blood flow at the microvascular level, thus making possible the differentiation of active synovitis from inactive intra-articular thickening. Time-intensity curve (TIC) parameters are descriptive and offer an objective quantification of vascularization in a specific anatomical area. Currently, the role of CEUS in daily rheumatological clinical practice is not well defined. [1,2] It is still not clear which CEUS abnormalities are of special interest for rheumatologists.

**Objectives:** The main objective of our study was to compare TIC parameters of CEUS at four joint levels in early arthritis (EA) patients having wrist involvement, with the purpose of characterizing CEUS parameters uniformity. As a secondary objective, we aimed to identify which TIC parameters vary most in the examined joints.

**Methods:** Patients diagnosed with active early rheumatoid or undifferentiated arthritis on the basis of the 2010 ACR/EULAR classification criteria, having bilateral wrist arthritis and both radiocarpal (RC) and intercarpal (IC) synovial hypertrophy identified by grey scale US, were consecutively enrolled. CEUS was performed using a second-generation contrast agent and quantified using dedicated software. The examinations started with the dominant hand. After 30 minutes, the other hand was examined, using the same protocol. The region of interest (ROI) was selected as the area corresponding to the synovial hypertrophy of the RC and IC joints. TIC parameters were calculated for the first minute of contrast enhancement and were analyzed in each of the four examined joints.
**Results:** Nineteen patients were included in the study. Right hand dominance was present in 94.7% of patients. Dominant hand expressed higher peak, AUC and slope values, compared to the other hand. The percentage difference of the parameters measured at right IC and the other joints varied between 12–32% for Peak (p=0.007), 22–38% for AUC (p=0.015) and 9–30% for slope (p=0.514). No differences for any of the TIC parameters between the other assessed joints were found.
**Conclusions:** CEUS behaviour was not uniform in the wrists joints of EA patients, TIC parameters revealing the highest degree of inflammation at IC joint of the dominant hand. Peak and AUC in CEUS, measured at this joint level, demonstrated the highest variation when compared to the other examined joints, suggesting their potential value for quantification of synovial inflammation.
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## SAT0555 PROOF OF CONCEPT – STUDY FOR THE EVALUATION OF HEALTHY JOINTS AND PERIARTICULAR STRUCTURES IN CHILDREN

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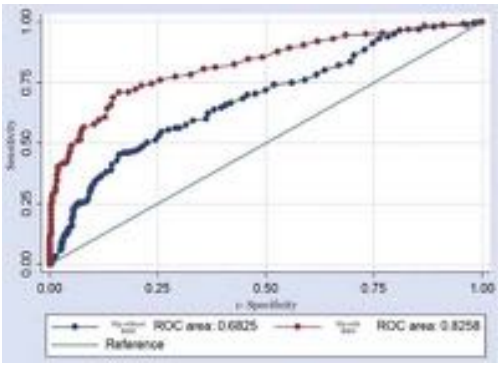
**Background:** Musculoskeletal ultrasonography (US) has become an important diagnostic tool for the diagnosis and follow-up of inflammatory joint diseases in pediatric rheumatology. However, there is lack of clinical studies in pediatric joint ultrasonography concerning normal findings of healthy joints and periarticular structures in children.
**Objectives:** The aim of the study was to evaluate normal values for the thickness of healthy joint cartilage, capsule and tendons of the hand (finger/wrist), elbow, hip, knee, ankle and forefoot in children by musculoskeletal ultrasound (US). Furthermore, power Doppler activity was measured.
**Methods:** The joints were assessed by four physicians experienced in musculoskeletal US with equally preset Esaote Mylab Twice with high frequency (13 to 18 MHz) probes. N=75 healthy children (41 boys, 34 girls) between 4.9–11.1 years (girls) and 4.3–13.1 years (boys) were included in the study.
**Results:** If there was no significant difference between girls and boys, common reference intervals were calculated (see attached Table 1). Otherwise, 95% separate reference intervals were defined for boys and girls each (not presented in abstract). Power Doppler US (PDUS) signals were measured in all joints. PDUS signals were found regularly, notably in the wrist and finger joints.
**Conclusions:** The reference intervals for healthy children are helpful for the interpretation of pathological findings in juvenile idiopathic arthritis (JIA). The intervals show a wide range; therefore pathology should be examined carefully. Especially in younger children, joint measurements might have different values due to the growing structures, which need further evaluation. Furthermore, PDUS signals in children can be quite common, depending on the joint region and the selected standard scan.

Table 1:

| Examined joint and periarticular structure | gm (mm) | 95% RI (mm) | N |
|---|---|---|---|
| **Elbow:** Capsule in the humero-radial joint (anterior longitudinal view) | 1.19 | 0.43-3.28 | 21 |
| **Wrist:** Capsule above the radio-scaphoid joint (dorsoradial longitudinal view) | 0.95 | 0.41-2.21 | 26 |
| **Wrist:** Cartilage above the radio-scaphoid joint (dorsoradial longitudinal view) | 0.80 | 0.36-1.80 | 26 |
| **Finger joints:** Cartilage of the MCP II (dorsal longitudinal view) | 0.61 | 0.26-1.43 | 25 |
| **Finger joints:** Capsule of the MCP III (dorsal longitudinal view) | 0.67 | 0.33-1.40 | 25 |
| **Finger joints:** Capsule of the MCP V (dorsal longitudinal view) | 0.67 | 0.31-1.46 | 25 |
| **Finger joints:** Cartilage of the MCP V (dorsal longitudinal view) | 0.64 | 0.23-1.31 | 25 |
| **Finger joints:** Capsule of the MCP V (volar longitudinal view) | 1.18 | 0.54-2.56 | 23 |
| **Finger joints:** Cartilage of the MCP V (volar longitudinal view) | 1.13 | 0.47-2.71 | 22 |
| **Hip:** Capsule in the middle of femoral head perpendicular to the head (anterior transverse view) | 3,40 | 1.94-5.96 | 36 |
| **Knee:** diameter of the quadriceps tendon (anterior longitudinal subpatellar view) | 4.59 | 2.94-7.15 | 42 |
| **Forefoot:** Cartilage of the MTP III (dorsal longitudinal view) | 1.17 | 0.64-2.54 | 32 |
| **Forefoot:** capsule of the MTP IV (dorsal longitudinal view) | 1.28 | 0.76-2.05 | 29 |

**gm:** geometrical mean; **95% RI:** 95% reference interval based on T-distribution; **N:** Number of subjects

**Objectives:** To compare the indication for pharmacological treatment in a Brazilian elderly population considering the results of FRAX® with bone mineral density (FRAX®/BMD), FRAX® without BMD (FRAX®) and of BMD classification according to the WHO.
**Methods:** The study population consisted of patients over 60 years of age from primary care units who had clinical indication for BMD assessment. BMD was undertaken at lumbar spine and femur by dual-energy X-ray absorptiometry (DXA) Hologic Discovery W system (Madison USA, software version 3.3.01) and BMD results were classified according to the WHO criteria. Clinical data was obtained from patient records (secondary osteoporosis, smoking, alcohol consumption, use of glucocorticoids, rheumatoid arthritis, family history (father or mother) with hip fracture, and previous history of fracture) and the 10-year probability of hip and major fractures was calculated using FRAX® tool. Receiving operator curve (ROC) analysis, model calibration and decision curve analysis were used to compare fracture prediction in FRAX® and FRAX®/BMD groups.
**Results:** 1,000 subjects were included, mean age 76.4 years, 755 (75.5%) women. Osteoporosis, osteopenia and normal BMD were found in 439 (43.9%), 426 (42.6%) e 135 (13.5%) patients, respectively. One hundred and nine (10.9%) patients have already suffered a fragility fracture and 40 of those individuals presented with normal BMD or osteopenia. In 366 (36.6%) patients it was not possible to calculate FRAX® score due to inability of recollection. The application of FRAX® tool would lead to the indication of treatment for 40% of the osteopenic patients and for 62.4% of the osteoporotic patients. Correlations between FRAX and FRAX/BMD were positive and statistically significant for both the 10-year probability of hip fracture and major fracture (0.704 and 0.594, respectively, $p<0.001$). ROC curve analysis showed that the FRAX/BMD was superior in identifying patients at risk of hip (Figure 1) and major fractures.




**Conclusions:** Despite the easy access and simplicity of FRAX® it is not possible to disregard the DXA, especially for patients with risk factor for fragility fractures.

## SAT0556 UTILITY AND PITFALLS OF THE FRAX® TOOL RESULTS IN BRAZILIAN ELDERLY POPULATION

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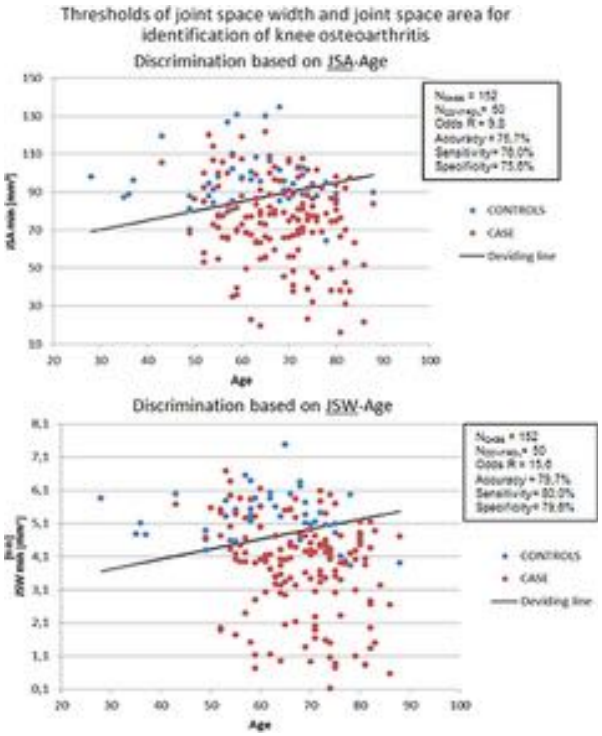
**Background:** The Fracture Risk Assessment Tool (FRAX®) was introduced by the World Health Organization (WHO) to estimate the 10-year probability of osteoporotic fractures in untreated patients with osteopenia[1]. This tool is validated for Brazilian population since 2013 but the applicability in this developing country has not been confirmed.

**References:**
[1] WHO Scientific group on the assessment of osteoporosis at primary health care level, 2004. www.who.int/chp/topics/Osteoporosis.pdf
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## SAT0557 A CLINICAL STUDY TO EXAMINE THRESHOLDS OF JOINT SPACE WIDTH AND JOINT SPACE AREA FOR IDENTIFICATION OF KNEE OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) is a degenerative, slowly developing joint disease and characterized by pain and functional disability. Although clinical indications of OA can vary among different definitions there is a general agreement that the disease is associated with cartilage narrowing and the development of osteophytes and sclerosis within the subchondral bone. However, there is no general consensus about the threshold below which the joint space width (JSW) and the respective joint space area (JSA) can be certain indicators for the state of OA.
**Objectives:** Therefore this study evaluates these limits to reveal quantitative information about indicators of OA.
**Methods:** The study included 226 standardized knee radiographs from 101 female patients with OA, and 125 controls. All images were acquired in PA direction and standardized positions. The minimum JSW and JSA were calculated by using the i3a software. 3 physicians assessed the 2D radiographs by using the Kellgren & Lawrence Score and assigned the images to either a Case or Control group. A knee was assigned to the Case group, if at least two physicians assessed it as being affected by OA. The JSW was defined as the vertical distance from the inferior femur condyle to the superior tibia condyle on both the medial and lateral compartment, obtained from 4 distinct points from each side. By building a spline curve between the points of each condyle, the upper and lower boundaries of the JSA are defined for each side, whereas the outer points define the horizontal boundaries. For the JSW and JSA, only the minimum value of each variable was taken into account.
**Results:** Considering the minimum JSW, an odds ratio of 5.63 (CI: 3.17–9.99) with an accuracy of 70.35% and a sensitivity of 70.30% can be obtained. Every subject that has a minimum JSW below 3.4mm belongs to the Case group. With respect to the minimum JSA, the odds ratio is 3.60 with an accuracy of 65.49% and a sensitivity of 65.35%. Results also show that every subject with a minimum JSA below 50mm$^2$ is being considered to have OA.




**Conclusions:** Based on this study it can be concluded that a JSW below 3.4mm and a JSA below 50mm$^2$ at the knee joint are strong indicators for OA. Thus, for clinical assessments it is suggested to consider these threshold values for diagnostic purposes. In further studies, symptomatic knee OA should be incorporated to verify whether minimum JSWs and JSAs can also be linked to symptomatic knee pain.
**Disclosure of Interest:** R. Ljuhar Employee of: Braincon Technologies, S. Nehrer: None declared, B. Norman Employee of: Braincon Technologies, D. Ljuhar Employee of: Braincon Technologies, T. Haftner Employee of: Braincon Technologies, J. Hladuvka: None declared, M. Bui Thi Mai: None declared, H. Canhão: None declared, J. Branco: None declared, A.-M. Rodrigues: None declared, N. Gouveia: None declared, A. Fahrleitner-Pammer: None declared, H.-P. Dimai: None declared
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## SAT0558 NEW GENERATION TRANSLOCATOR PROTEIN PET TRACERS TO IMAGE ARTHRITIS BY MACROPHAGE TARGETING IN RHEUMATOID ARTHRITIS PATIENTS: A PROOF OF CONCEPT STUDY

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**Background:** Previously, PET and macrophage targeting by translocator protein (TSPO) tracer [$^{11}$C]-(R)-PK11195 has shown promising value to predict development of RA in the very early arthralgia phase, and flares in clinical remission. Nevertheless, the tracer [$^{11}$C]-(R)-PK11195 showed rather high peri-articular background uptake which may limit detection of more subtle arthritis activity. In preclinical setting, our group recently showed more favorable imaging characteristics of two new candidate high affinity translocator protein (TSPO) tracers, [$^{11}$C]DPA-713 and [$^{18}$F]DPA-714, to visualize arthritis.
**Objectives:** To investigate the imaging potential of [$^{11}$C]DPA-713 and [$^{18}$F]DPA-714 as compared to [$^{11}$C]-(R)-PK11195 for visualization of inflamed joints of RA patients using PET-CT.
**Methods:** RA patients with at least two clinically inflamed hand joints were included. PET-CT scans of their hands were obtained after intravenous injection of [$^{18}$F]DPA-714, [$^{11}$C]DPA-713 or [$^{11}$C]PK11195. Two different tracers were compared per patient, respectively [$^{11}$C]PK11195 vs. [$^{18}$F]DPA-714 or [$^{18}$F]DPA-714 vs. [$^{11}$C]DPA-713. Quantitative analysis was done by drawing volumes of interest (VOI) over joints with visually elevated tracer uptake and background VOIs were drawn on metacarpal bone. Standardized Uptake Values (SUVs) and target-to-background (T/B) ratios were determined. Data of the tracer [$^{18}$F]DPA-714 were pooled for analysis. Furthermore, blood was drawn to investigate TSPO receptor polymorphism because a TSPO rs6971 polymorphism is believed to show lower binding affinity (1).
**Results:** Nine RA patients (female3/9; age 54±18; RF+ 7/9; aCCP+ 6/9) were included with a DAS28 of 4.7±1.4 at inclusion. Clear visualization of arthritic joints was obtained with all three tracers. The absolute uptake (SUV) in arthritic joints was comparable for all 3 tracers with a trend of slightly higher uptake of [$^{11}$C]DPA-713 (Table). However, T/B ratios of both [$^{18}$F]DPA-714 and [$^{11}$C]DPA-713 were higher than of [$^{11}$C]PK11195 respectively almost 2-fold higher of [$^{18}$F]DPA-714 and 2,5-fold of [$^{11}$C]DPA713 (Table). Although the “low binding” TSPO polymorphism rs6971 was present in 3/9 patients, PET outcome was not different from patients without the polymorphism.

| | [$^{11}$C]PK11195 | [$^{18}$F]DPA714 | [$^{11}$C]DPA713 |
|---|---|---|---|
| SUV (mean ± SD) | 1.5±0.1 | 1.5±0.2 | 1.7±0.1 |
| T/B ratios (mean ± SD) | 2.4±0.2 | 4.2±0.7 | 5.6±3.4 |

**Conclusions:** This is the first study that shows excellent arthritis imaging with both new generation TSPO tracers, [11C]DPA-713 and [18F]DPA-714, in active RA patients. Although imaging outcome was slightly more favorable of [11C]DPA-713, both tracers performed well with higher target-to-background as compared to the previously investigated macrophage tracer [$^{11}$C]PK11195. The tracers provide opportunities for potential clinical applications of both early diagnosis and therapy monitoring of RA disease activity.
**References:**
[1] Zanotti-Fregonara et al., ACS Chem. Neurosci. 2014, 5, 963–971,dx.doi.org/10.1021/cn500138n
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4215

## SAT0559 THE ANATOMICAL DISTRIBUTION OF INFLAMMATION, FAT, EROSION AND NEW BONE FORMATION IN THE SPINE ASSESSED ACCORDING TO THE CANADA-DENMARK MRI DEFINITIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** On MRI, patients with axial spondyloarthritis (axSpA) demonstrate lesions at several anatomical locations. These locations include the vertebral bodies, e.g. anterior and posterior corners and lesions without relation to the corners, and also the posterior segments of the vertebrae, e.g. the costo-transversal joints, costo-vertebral joints, facet joints, spinous/transverse processes, and surrounding soft tissue. The Canada-Denmark (CanDen) definitions of MRI lesions in the spine allows a detailed evaluation of all these anatomical locations for inflammation, fat, erosions and new bone formation.(1–3)
**Objectives:** To assess the anatomical location of positive scores by the CanDen MRI scoring system of the spine.
**Methods:** 49 patients with axial SpA (ASAS criteria) and clinical indication for tumor necrosis factor alpha (TNF$\alpha$) inhibitor, including BASDAI $>$40 mm, had MRI of the spine performed at baseline. 51% were male. Median symptom duration (range) was 12 (0–45) years. Images were scored using the CANDEN MRI scoring system by a reader blinded to clinical data.
**Results:**

Table 1. Percentage of patients with a score $\geq$1 according to the CANDEN MRI scoring system by anatomical location and category (inflammation, fat, erosion, bone spurs/ankylosis). No soft tissue inflammation was found

| | | Cervical spine (C2/C3 to (C7/T1) | Thoracic spine (T1/T2 to (T12/L1) | Lumbar spine (L1/L2 to (L5/S1) |
|---|---|---|---|---|
| Anterior corner lesions | Inflammation | 16% | 41% | 51% |
| | Fat/Erosion | 16%/0% | 45%/2% | 33%/0% |
| | Bone spurs/Ankylosis | 6%/2% | 0%/2% | 4%/6% |
| Posterior corner lesions | Inflammation | 4% | 29% | 18% |
| | Fat/Erosion | 8%/0% | 16%/2% | 22%/0% |
| | Bone spurs/Ankylosis | 2%/0% | 0%/6% | 0%/2% |
| Non-corner lesions | Inflammation | 4% | 14% | 10% |
| | Fat/Erosion | 2%/2% | 4%/8% | 12%/4% |
| | Bone spurs/Ankylosis | 0%/0% | 0%/6% | 0%/2% |
| Antero-lateral corner lesions | Inflammation | NA | 22% | 29% |
| | Fat/Erosion | NA | 16%/0% | 18%/0% |
| Postero-lateral corner lesions | Inflammation | NA | 33% | 8% |
| | Fat/Erosion | NA | 18%/0% | 6%/0% |
| Costo-transversal joint transverse process | Inflammation | NA | 4% | 2% |
| Facet joint | Inflammation | 6% | 8% | 6% |
| | Fat/Erosion | 0%/0% | 2%/0% | 2%/0% |
| | Bone spurs/Ankylosis | 10%/0% | 8%/0% | 8%/0% |
| Spinous process | Inflammation | 0% | 2% | 0% |

In total, 10 of 49 patients (20%) had involvement of the costo-transversal joints, facet joints, spinous/transverse processes or soft tissue.
**Conclusions:** The most frequent lesion in patients with axSpA were inflammation and fat lesions in the rim of the vertebral bodies (the anterior, posterior, antero-lateral and postero-lateral corner lesions) in the thoracic and lumbar spine. 1/5 of the patients had involvement of the posterior segments.
**References:**
[1] Østergaard et al. J Rheumatol 2009;36-S84:18–34
[2] Lambert et al. J Rheumatol 2009;36-S84:3–17
[3] Pedersen et al. J Rheumatol 2009;36-S84:35–38
[4] Chiowchanwisawakit et al. J Rheumatol 2009;36-S84:39–47
**Disclosure of Interest:** None declared
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## SAT0560 AUTOMATED IFA METHODS COMPARE WELL WITH ESTABLISHED MANUAL IFA SCREENING AND TITRATION FOR ANA HEP-2

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**Background:** Often, only basic nuclear patterns, like homogenous, speckled, nucleolar, centromere or cytoplasmic, are reported by laboratories. The detection of other patterns requires well trained readers. As a result, different systems have been developed which automate part of or the complete IFA method and reading process.
**Objectives:** This study compares 2 commercially available HEp-2 antinuclear antibody (ANA) indirect fluorescent antibody (IFA) assays using a sensitivity panel (120 clinically determined patients) and a specificity panel consisting of 80 clinically confirmed negative patients.
**Methods:** We compared two different automated systems (A and B) to assess their capability for screening and titration of these samples. The automated method was directly compared to manual reading of the same processed slides on respective microscopes and also compared with the known clinical information.
**Results:** The results of the two automated methods were in good agreement. System A detected 188 samples correctly from negative and positive samples, versus 187 samples detected by the system B. The falsely detected positive samples were all of low titer (1:80). System A found 157 and System B 156 patterns in agreement to the target pattern. From 80 negative samples system A detected 73 and system B 71 samples correctly.
**Conclusions:** Both systems resulted in an overall sensitivity $>$95% and a specificity of 91.25% and 88.75%. The pattern recognition also showed only minor aberrant findings resulting in a slightly better detection of cytoplasmic and nuclear membrane patterns by system A while system B detected slightly better the centromeric pattern.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3958

## SAT0561 FINGER JOINT CARTILAGE EVALUATED BY ULTRASOUND AND X-RAY IN RHEUMATOID ARTHRITIS AND CONTROL JOINTS

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**Background:** Joint destruction in RA includes both bone and cartilage lesions. By X-ray examination, cartilage destruction is evaluated as a joint space narrowing (JSN). However, joint space narrowing is not a direct evaluation of cartilage.
**Objectives:** The aim of the study was to examine the finger joint cartilage by ultrasound (US) imaging and to compare it with JSN score in relation to clinical relevance.
**Methods:** We enrolled 27 RA patients in low disease activity or clinical remission (DAS28-CRP $<$2.7) and 21 healthy controls in this study. The cartilage thickness (CT) of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of 2nd to 5th fingers was bilaterally visualized and measured from a dorsal view, with approximately 90 degrees flexion. In addition, JSN of finger were scored by van der Heijde- modified Sharp method.
**Results:** In patients with RA, CT in MCP joints ranged from 0.0 to 0.8 mm (median 0.4 mm), and CT in PIP ranged from 0.0 to 0.4mm (median 0.2mm), respectively. The sum of total CT from 8 fingers ranged from 2.7 to 6.8 mm (median 4.7 mm), and there was a significant difference in CT, but not in JSN score, between male and female patients (5.6 versus 4.6, respectively, p=0.005). Healthy controls had the sum of total CT significantly thicker as compared with RA ($p \leq 0.001$). Importantly, CT was well correlated with JSN ($r=-0.696$, $p<0.001$). Although CT was not correlated with age, disease duration, DAS28-CRP, functional disability score, positivity of rheumatoid factor and anti-CCP-antibody, CT was reduced in RA patients with elevated serum matrix metalloproteinase-3 (MMP-3) values compared with those with normal MMP-3 (3.9 versus 5.0, p=0.015).
**Conclusions:** The US method of direct visualization and quantification of cartilage in MCP and PIP joints can be valid and useful in RA, and our results may support the importance of MMP-3 in the pathophysiology of cartilage destruction.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5541

## SAT0562 COMPARISON OF MRI AND RADIOGRAPHY IN DETECTING STRUCTURAL DAMAGE OF THE SACROILIAC JOINTS IN PATIENTS WITH CHRONIC LOW BACK PAIN USING LOW-DOSE CT AS STANDARD OF REFERENCE – RESULTS FROM THE SIMACT STUDY

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**Background:** The ability of magnetic resonance imaging (MRI) to detect structural changes of the sacroiliac joint (SIJ) is subject to discussion, whereas radiography as established method provides poor reliability.
**Objectives:** The aim of this study was to compare the ability of MRI and radiography in detecting erosions, sclerosis, pseudowidening and ankylosis of the SIJ using low dose computed tomography (ldCT) as standard of reference.
**Methods:** We prospectively included 110 patients in the study. All patients underwent a ldCT (Somatom Definition Flash, Siemens, Germany) and an MRI (3.0T Magnetom Skyra, Siemens, Germany) including a paracoronal T1 sequence of the SI-joints. Imaging data were compared with X-ray of the pelvis. Two readers independently scored the datasets for the presence of erosions, sclerosis and changes of the joint space in a blinded fashion using a comprehensive scoring system. Contingency table analysis was performed using ldCT as standard of reference. Inter-rater reliability was calculated using Cohen's kappa. The agreement of all modalities with the expert rheumatologists diagnosis was calculated for three diagnostic categories (axSpA, mechanical back pain, normal).
**Results:** We found following sensitivity and specificity for the detection of structural lesions on patient's level: erosions (0.42/0.86 for radiography, 0.79/0.93

for MRI), sclerosis (0.7/0.9 radiography, 0.3/0.96 MRI) and joint space alterations (0.41/0.95 radiography, 0.76/0.99 MRI), respectively. Inter-rater reliability was fair for radiography (0.32 to 0.4) and substantial for MRI (0.35 to 0.62) and ldCT (0.5 to 0.7) with the poorest reliability for sclerosis each. Diagnostic accuracy ranged from 0.41 to 0.52 for radiography, 0.62 to 0.72 for MRI and 0.63 to 0.75 for ldCT.
**Conclusions:** MRI is superior to radiography in detecting erosions and alterations of the joint space, however, inferior in detecting sclerosis. Most reliable diagnostic parameters amongst all imaging modalities were erosions and joint space alterations. Cross-sectional imaging modalities, including MRI, provide a superior diagnostic accuracy compared to conventional radiography.
**Acknowledgement:** The authors thank the Assessment of Spondyloarthritis international Society (ASAS) for supporting the study with a research grant.
**Disclosure of Interest:** None declared
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## SAT0563 OPTIMIZED DOPPLER SETTING INCREASE SCORES OF SYNOVITIS AND COLOUR FRACTION IN RHEUMATOID ARTHRITIS WRIST JOINTS - EXPERIENCE FROM A TARGETED ULTRASOUND INITIATIVE WORKSHOP

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**Background:** Blood flow in small vessels of synovial membrane in inflamed joints is characterized by slow-flow. The ability to detect this flow with Doppler ultrasound (US) is influenced by the quality of the US unit, Doppler modality and the Doppler settings. The standard Doppler settings provided by manufacturers of US units have previously been shown not to be optimal for the detection of this slow flow. However, significant improvement of Doppler sensitivity is possible.[1]
**Objectives:** The purpose of the study was to investigate how factory Doppler settings (FS) on a high-end US unit could be improved with respect to Doppler sensitivity by ultrasonographers who had just received lectures on optimizing Doppler settings. Secondly, how scoring and quantification of Doppler activity were affected by more sensitive Doppler settings.
**Methods:** During an US course arranged as part of targeted ultrasound initiative (TUI) in Helsinki, participants were taught on Doppler settings and how to optimize these. The Doppler settings were adjusted by participants for increased Doppler sensitivity as suggested by Torp-Pedersen et al.[2] A General Electric LOGIQ-E9 ultrasound unit with a 6–15 MHz linear array transducer was used. Four rheumatoid arthritis (RA) patients with a clinically active wrist joint were examined with US by four groups of course participants. US was done using both the FS for superficial musculoskeletal US and the optimized setting (OS). Findings of each joint was scored semi-quantitatively (0–3) and for the maximum colour fraction (CF) using four seconds video clip. CF was calculated using the US unit's software for quantitative analysis based on a drawn region of interest (ROI).
**Results:** All groups were capable of adjusting FS to a more sensitive Doppler setting as suggested in the preceding lectures. The median Doppler score for the four wrist joints were 1 (range: 0–2) on FS and 2 (1–2) on OS. In 12/16 evaluations the Doppler score increased by at least one point on OS compared to FS, and were unchanged in the remaining. In 5/16 evaluations (three patients) the score changed from 0 (normal) to a score of 1 or 2 using OS. The mean CF was 0.021 (range: 0–0.093) on FS and 0.082 (0.008–0.20) on OS (p=0.001; Wilcoxon signed rank test). No significant difference was observed in the area of the ROI (mean: 45 and 44 $mm^2$ on FS and OS, respectively).
**Conclusions:** Optimization of Doppler settings for increased sensitivity for slow flow in synovial tissue of RA wrist joints is possible after proper instruction. An optimized Doppler setting led to significantly higher scores and CF in the examined wrist joints and in some patients synovial Doppler activity was observed only with an optimized setting. Consequently, using FS could result in active joint inflammation being missed or underestimated by the examiner. This small study demonstrates that knowledge on optimizing Doppler settings can be learned in workshops and highlights the importance of knowledge on how to improve Doppler sensitivity wherever US is used in clinical practice.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4730

## SAT0564 ARTICULAR INVOLVEMENT IN BEHÇET DISEASE: AN ULTRASONOGRAPHIC STUDY

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**Background:** An articular involvement is reported in Behçet disease up to 70% of patients, varying from referred arthralgia to arthrtitis, generally non-erosive, poly- or oligoarticular. Some authors compared this joint involvement to Seronegative Spondyloarthritis, reporting prevalent involvement of entheses and sacroiliitis. Few US studies has been conducted in Behçet, focusing on tendon and enthesal evaluation
**Objectives:** To evaluate the presence of US pathological findings of joints, tendons and entheses of patients affected by Behçet disease
**Methods:** We enrolled consecutive patients with Behçet disease reaching the Rheumatologic Unit of our hospital between Feb 2014 and Jan 2016, irrespective of disease activity status and therapy. US exams was performed by a single operator with 8–18 MHz linear transducers (Esaote MyLab70). 42 joints (shoulders, elbows, wrists, MCPs, PIPs, hips, knees, ankles, MTPs), 12 entheses (triceps tendons,common extensor tendons, knee entheses, Achilles tendons) and 20 tendon sheats (flexor digitorum tendons, wrist's flexor and extensor tendons, anterior and posterior tibialis and peroneal tendons) were evaluated for each patient, using a stardardized technique. Grey scale (GS) and power Doppler (PD) US exam was performed to detect joint effusion, synovial hypertrophy and PD, classified with dicotomic and semiquantitative score (grade 0–3); effusion and synovial hypertrophy were combined in a single score and defined as synovitis. The presence/absence of tenosynovitis was evaluated for each site. At the entheseal level, we evaluated the presence of GS abnormalities of tendon structure (hypoechogenicity/thickness), enthesophytes and Doppler signal within the tendon or at the entheseal site, all classified as present/absent
**Results:** We evaluated a total amount of 1596 joints, 760 tendons and 456 entheses from 38 patients (20 women). A grade 1 synovitis was observed in 158 joints (9,9%): 87 MTPs, 21 knees, 19 MCPs, 14 wrists, 11 ankles, 4 PIPs and 2 elbows; in 72 patients the finding was monolateral while in 43 patients it was observed bilaterally, notably at I and II MTPs and knees joints. A grade 2 synovitis was observed in 18 joints (1,12%): 16 MTPs, 1 knee and 1 MCP; no grade 3 synovitis was observed. A grade 1 PD was detected in 2 wrists, 2 MCPs and 7 MTPs joints and a grade 3 PD was observed in a single MCP joint. We observed the presence of tenosynovitis in 36 cases, all involving hand or wrist tendon structures. 12 entheses presented altered fibrillar pattern with hypoecogenicity (8 common extensor tendons and 4 knee entheses), while the presence of enthesophytes was observed at the common extensor in 4 cases, at triceps in 8, at quadriceps in 6, at proximal patellar insertion in 2, at Achilles tendon in 21; the presence of at least 1 grey scale abnormality was observed in 63 entheseal sites (13,81%). An intratendineous PD signal was observed in 27 cases (5,9%): 16 common extensor tendons, 4 quadriceps, 3 proximal patellar insertion, 4 Achilles tendons
**Conclusions:** In a population of patients with Behçet disease we observed the presence of joint effusion in 11% and PD signal in 0,7% of examined joints, notably involving hands and feet joints. GS alteration of tendon structure was detected in 13,81% and an intratendineous PD signal in 5,9% of entheseal sites.A mild tenosynovitis was observed in 4,7% of examined tendons
**Disclosure of Interest:** None declared
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## SAT0565 RELIABILITY OF THE QUANTITATIVE ASSESSMENT OF PERIPHERAL BLOOD PERFUSION BY LASER SPECKLE CONTRAST ANALYSIS IN A SYSTEMIC SCLEROSIS COHORT

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**Background:** In systemic sclerosis (SSc) there is increasing interest to evaluate blood perfusion in a dynamic way, to evaluate evolution of disease and response to therapy. Laser speckle contrast analysis (LASCA) is an emerging technique that measures peripheral blood perfusion (PBP) in real time over a large area and is convenient in use (1,2). In order to be used as an outcome measure, first reliability of LASCA needs to be attested.
**Objectives:** To investigate the reliability of the quantitative assessment of PBP by LASCA between two raters in a SSc cohort.
**Methods:** Two independent raters evaluated PBP in 40 consecutive patients with SSc (according to the 2013 ACR/EULAR classification criteria) using LASCA. After acclimatization for 20 minutes in a temperature controlled room, PBP was measured at the level of the fingertips, dorsal and volar bilaterally, for 30 sec each. Measurements were performed under standardized environmental, patient and instrumental conditions. PBP values were reported as perfusion units (PU) by creating regions of interest with fixed 1 cm diameter at central area of the fingertips. Mean PU per finger, left and right, dorsal and volar, per rater was calculated. Inter rater reliability was assessed by calculation of intraclass correlation coefficients (ICC). Patients with flexion contractures (n=6) were excluded because they could not meet the standardization requirements.
**Results:** ICC (95% confidence interval) values for PBP measurements varied from 0.82 (0.67 to 0.91) to 0.91 (0.83 to 0.96) for the dorsal fingertips, and from 0.74 (0.55 to 0.86) to 0.86 (0.74 to 0.93) for the volar fingertips (Table 1).

Table 1. ICC (95% CI) for PBP measured by LASCA by two independent raters

| | ICC | 95% CI |
|---|---|---|
| Dorsal left | | |
| F2 | 0.85 | 0.71; 0.92 |
| F3 | 0.89 | 0.79; 0.94 |
| F4 | 0.89 | 0.80; 0.95 |
| F5 | 0.83 | 0.68; 0.91 |
| Dorsal right | | |
| F2 | 0.91 | 0.83; 0.96 |
| F3 | 0.90 | 0.81; 0.95 |
| F4 | 0.88 | 0.77; 0.94 |
| F5 | 0.82 | 0.67; 0.91 |
| Volar left | | |
| F2 | 0.86 | 0.74; 0.93 |
| F3 | 0.85 | 0.72; 0.92 |
| F4 | 0.84 | 0.70; 0.92 |
| F5 | 0.80 | 0.63; 0.89 |
| Volar right | | |
| F2 | 0.84 | 0.70; 0.91 |
| F3 | 0.76 | 0.58; 0.87 |
| F4 | 0.74 | 0.55; 0.86 |
| F5 | 0.81 | 0.66; 0.90 |

ICC, intraclass correlation coefficient; CI, confidence interval; PBP, peripheral blood perfusion; LASCA, laser speckle contrast analysis; F, fingertip.

**Conclusions:** This is the first study to demonstrate reliability of the quantitative assessment of peripheral blood flow by LASCA in a SSc cohort between two raters, performed under standardized patient, instrumental and environmental conditions. With this study, we took the first step in the validation of LASCA, though further studies are needed to confirm these results.

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**Disclosure of Interest:** None declared

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## SAT0566 SALIVARY GLAND ULTRASONOGRAPHY AND ITS APPLICATIONS IN PATIENTS WITH SJÖGREN'S SYNDROME AND SICCA SYMPTOMS

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**Background:** Sjögren's syndrome is an autoimmune disease that involves the exocrine glands. In the criteria declared in 2002 and 2012, salivary gland biopsy remains crucial in diagnosing the disease, and the aggregation of lymphocytes correlates with the disease activity. However, salivary gland biopsy is invasive and is not recommended for monitoring the disease activity. Ultrasonography provides easy access, low cost and real-time image. Recent systemic review indicated ultrasonography revealing abnormalities of salivary glands, which may be helpful for rheumatologist in diagnosing Sjögren's syndrome, but the reliabilities need to be confirmed among different scoring systems.

**Objectives:** To investigate the usefulness of salivary gland ultrasonography in Sjögren's syndrome and its correlations with EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) questionnaires (Seror R, 2011).

**Methods:** 50 patients, including primary and secondary Sjögren's syndrome, as well as some patients with sicca symptoms were enrolled. Ultrasonography by a 13MHz linear probe was performed at parotid and submandibular glands. Each gland was scored from 0 to 4 according to the criteria proposed by previous study (Takagi Y, 2010), with a total maximum score with 16. ESSPRI questionnaires and blood samplings were also performed within 1 week after ultrasonography.

**Results:** Total 31 primary Sjögren's Syndrome, 8 secondary Sjögren's Syndrome, and 13 patients with sicca symptoms were enrolled. The average score of salivary gland ultrasonography was 8, 8, 5 respectively in each group. A significant correlations between salivary gland ultrasonography summation score with serum anti-La (SSB) ($p=0.006$) and ESSPRI score ($p<0.001$) were noted. The score also correlated with the fatigue score ($p<0.001$) and dry score ($p=0.001$) in the ESSPRI questionnaire, but not with the pain score ($p=0.135$). The correlations with serum anti-Ro antibody was not significant ($p=0.902$).

**Conclusions:** Summation score of salivary gland ultrasonography correlated well with serum anti-La titers and ESSPRI score. Ultrasonography provided real-time, easily accessible information on patients' salivary gland conditions, as well as good correlations with patients' subjective discomfort. The relationship between the ultrasonography images and disease activity deserves further investigations.

**References:**

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.5981

# Epidemiology, health services and outcome research

## SAT0567 DEMOGRAPHIC, CLINIC AND LABORATORY FEATURES OF 755 PATIENTS WITH NEONATAL LUPUS ERYTHEMATOSUS: SYSTEMATIC REVIEW

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**Background:** Neonatal lupus erythematosus (NLE) which is caused by trans placental transmission of maternal anti SS-A/Ro and anti SS-B/La antibodies. Cutaneous, cardiac, hepatic and hematologic manifestations can be seen.

**Objectives:** The objective of this systematic review was to analyze demographic data, clinical manifestations, autoantibodies, treatment modalities and mortality status of NLE patients.

**Methods:** Systematic review has been done at August 2015 on Pubmed Medline. Publications are determined by using MeSH term: ("neonatal lupus, congenital hearth block" (MeSH)) and restricted to "in humans" and "in English". Out of study design, abstracts of all publications has been assessed. 1377 article has been assessed in abstract format, after that; 277 original article/case report has been evaluated in full-text format. Finally, 199 article/ case report has been included to study after full-text evaluation. Totally, 755 patients enrolled. Demographic, clinical, laboratory features were assessed both maternal and infant level.

**Results:** *Maternal features:* Mean maternal age was 29.7 (4.8) years. Median gestational week was 23 (21–40) weeks. Accompanying diseases were known in 547 patients (SLE 176 (32.2%), Sjogren syndrome 99 (18.1%), undifferentiated connective tissue disease 31 (5.7%), rheumatoid arthritis 7, other autoimmune disease 53 (9.6%), no disease 179 (32.7%)). ANA results were known in 349 mothers with 287 (82.2%) positivity. ENA were known in 601 mothers (SS-A 506 (84.2%), SS-B 313 (52.1%), anti-RNP 31 (5.2%), negative 57 (9.1%)). In 327 mothers, diagnosis time of collagen tissue disease was known (212 (64.8%) mothers before pregnancy, 18 (5.5%) during pregnancy and 97 (29.7%) postpartum period). Maternal treatments before pregnancy were known in 137 of mothers (glucocorticoid 38 (27.7%), hydroxychloroquine 13 (9.5%), azathioprine 4 (2.9%), IVIG 2 (1.4%), and no treatment 94 (68.6%)).
*Infants' features:* Totally, 272/477 (57.0%) was female. Mean birth weight was 2680 (364–4370) gram, median delivery week was 37 (19–42) and 126 of 295 (42.7%) NLE was premature. Autoantibodies were known in 272 infants (225 (82.7%) SS-A, 126 SS-B (46.3%), 25 (9.2%) anti-RNP, all negative 20 (7.4%)). Mortality data were available for 485 infants with 412 (84.9%) were alive (85 with pacemaker), 37 (7.6%) were intrauterine exitus, and 36 (7.4%) were post-partum exitus.
*NLE features:* Most common manifestations of NLE was; cardiac 467 (61.8%), cutaneous 249 (33.1%), hematologic 117 (15.5%), and hepatic 78 (10.5%). Cardiac involvement types were known in 284 infants (AV complete block 219 (77.1%), 2. block 27 (9.5%), 1. block 19 (6.7%), and sinus bradycardia 19 (6.7%). Totally, 62 of 195 (31.2%) AV complete block detected post-partum period.

**Conclusions:** NLE was cause of premature (almost 43%) delivery and had high mortality ratio (almost 15% of infants). SLE and Sjogren's syndrome were leading maternal diagnosis. Although ANA and SS-A are main maternal autoantibodies, SS-B may also be found half of the cases. Congenital heart block, particularly AV block, is life-treating involvement, and unfortunately one of three infants have diagnosed at post-partum period.

**Disclosure of Interest:** None declared

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## SAT0568 INITIATION OF BIOLOGIC TREATMENT OVER THE PAST 15 YEARS REFLECTS CHANGES IN TREATMENT STRATEGIES: RESULTS FROM THE PROSPECTIVE COHORT OF THE GERMAN BIOLOGICS REGISTER RABBIT

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**Background:** Since approval of the first biologic (b) DMARDs for the treatment of rheumatoid arthritis (RA) in 2001, bDMARDs have been utilized to treat patients with severe disease. However, characteristics of patients treated with bDMARDs in the first years after approval differ substantially from those receiving bDMARDs nowadays.

**Objectives:** To investigate which clinical parameters influence the decision of rheumatologists to start the 1st bDMARD treatment in patients with RA over the past 15 years.

**Methods:** We used data of a prospectively observed cohort of RA patients from the German biologics register RABBIT. Since 2001, patients have been enrolled at start of a conventional synthetic (cs)DMARD or bDMARD after $\geq$1 csDMARD failure. 13,568 RA patients were included until April 2015. After exclusion of patients with prior biologic treatment (n=2558), insufficient information on prior treatment (n=579) or inclusion in 2007/2008 (n=918), where no patients with

csDMARD start were recruited, 9.513 patients remained for the analyses. They were stratified according to their year of inclusion in RABBIT (2001–2003, 2004–2006, and 2009–2015). We applied a machine learning method of model-based boosting to select clinical parameters which have a relevant impact on treatment decisions in each of the three episodes and compared the results with multiple logistic regression models.

**Results:** N=1781 biologic-naive patients were included during 2001–3, n=2781 in 2004–6 and n=4951 after 2008. The proportion of patients included with the start of a bDMARD was consistently between 60–62%. Patient characteristics at start of the first bDMARD changed over time. Mean disease duration decreased from 11.9 to 9.1 years, mean number of DMARD failures declined from 3.6 to 2.2 and mean disease activity (DAS28) fell from 6.0 to 5.0. The proportion of patients with osteoporosis declined from 24.5% to 11.9%.

High disease activity (DAS28), prior DMARD failures and high doses of glucocorticoids (GC) were associated with starting a biologic treatment independent from the enrollment year. Over time, more patients with only moderate disease activity, lower doses of GC and positive rheumatoid factor as well as those with more severe comorbidities like heart failure and chronic renal disease were included in the bDMARD cohort. Male sex was associated with the start of bDMARD in 2001–2003 but the effect receded in recent years of enrollment.

| | Enrollment period | | | |
|---|---|---|---|---|
| | 2001-2003 | | 2009-2015 | |
| | OR LogReg (95%CI) | Boosting approach | OR LogReg (95%CI) | Boosting approach |
| Intercept | 0.70 (0.19-2.60) | * | 0.19 (0.10-0.37) | * |
| Sex (males vs. females) | 2.04 (1.52-2.74) | * | 1.17 (1.00-1.37) | |
| Age (by 10 years increase) | 0.66 (0.59-0.74) | * | 0.78 (0.73-0.82) | * |
| Rheumatoid factor (neg. vs. pos.) | 1.15 (0.86-1.54) | | 1.55 (1.34-1.78) | * |
| # previous csDMARDs | 2.61 (2.34-2.90) | * | 4.20 (3.79-4.66) | * |
| Renal disease (yes vs. no) | 2.78 (1.26-6.17) | | 2.14 (1.43-3.19) | * |
| Heart failure (yes vs. no) | 1.68 (0.75-3.77) | | 4.56 (2.16-9.59) | * |
| Glucocorticoids (<5mg/d Reference) | | | | |
| GC 5-7.5 mg/d | 1.13 (0.83-1.53) | * | 1.42 (1.21-1.65) | * |
| GC >7.5 mg/d | 2.08 (1.55-2.78) | * | 2.60 (2.16-3.12) | * |
| DAS28 (<3.2 Reference) | | | | |
| DAS28 3.2-5.1 | 1.35 (0.57-3.15) | | 1.95 (1.55-2.46) | * |
| DAS28 >5.1 | 2.32 (0.99-5.44) | * | 3.22 (2.51-4.13) | * |
| Fatigue | 1.03 (0.98-1.09) | * | 0.99 (0.96-1.03) | |
| Pain | 0.97 (0.90-1.04) | * | 0.98 (0.95-1.02) | |
| Improved physical function (by 10%) | 0.87 (0.81-0.93) | * | 0.96 (0.92-1.00) | * |

* Covariates marked with an asterisk were selected in the boosting approach with comparable ORs, the remaining covariates were excluded from the model.

**Conclusions:** The increasing use of biologics in patients with moderate disease activity and GC treatment shows that new treatment guidelines recommending earlier use during disease course to prevent further damage are realized in daily care practice. Growing knowledge and experience with biologics increasingly allows rheumatologists to treat also patients with serious comorbidities like heart failure.

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**Disclosure of Interest:** None declared

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## SAT0569 THE IMPACT OF PAIN AND PHYSICAL FUNCTION UPON QUALITY OF LIFE IN OSTEOARTHRITIS

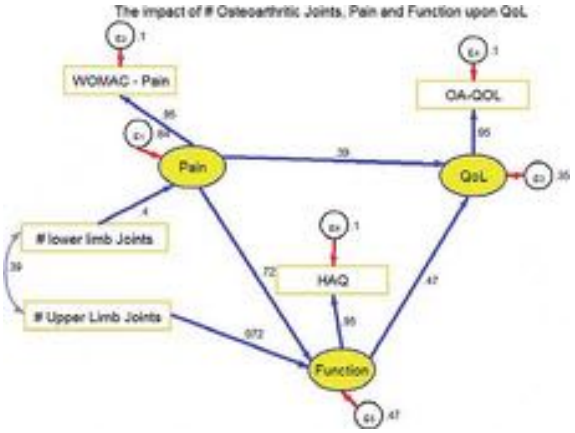
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**Background:** Pain, physical function (PF) and quality of life (QoL) are important aspects of the lived experience of those with chronic disease[1].

**Objectives:** A EULAR funded study to adapt the Osteoarthritis Quality of Life Scale (OAQoL) into five languages (German, Hungarian, Italian, Spanish, Turkish) gave the opportunity to explore the relationships between these key attributes in osteoarthritis (OA).

**Methods:** A Path Model was employed, within a Structural Equation Framework, utilising Rasch-transformed latent estimates as single indicator latent variables. Measures included lower & upper limb joint count (Manikin), pain on function (WOMAC), PF (HAQ) and QoL (OAQoL). The hypothesis was that the impact of pain upon QoL would be partially mediated by PF and this relationship will be invariant by age, gender and country.

**Results:** 677 patients with OA were recruited across 5 countries, approximately 20% from each. 76% were female, 33% aged 60 and under. 65% were married, 22% in work. Duration differed significantly across countries, with 10.1% of those in Turkey with duration of 15 years or more, compared with 32.5% of those in Spain. Joint count also varied significantly, e.g. 33.8% of those recruited in Spain reported no lower limb involvement compared with just 1.5% in Hungary. Path model fit was acceptable ($\chi^2$ 7.52 (df 4) p=0.111; RMSEA 0.036; TLI 0.992, CFI 0.997) (Figure). All path weights were consistent with the basic hypothesis and 43% of the impact of pain upon QoL was mediated through PF (Sobel-Goodman Z 10.93; $p<0.001$). The number of upper & lower joints influenced PF and pain respectively. Thus an increase in pain, and greater limitation in PF gave a worse QoL. The total effect of pain (direct & indirect) was the strongest influence upon QoL. The Wald Test for group invariance showed no significant difference of regression weights ($p>0.01$) by age, gender, duration and, to a large extent, by country. In the latter there were slight variations in the magnitude of paths weights between pain and PF. The effect appeared much stronger in Italy and Turkey than elsewhere. Overall, the model appeared robust across countries (Model fit $\chi^2$ 26.85 (df 20) p=0.14; RMSEA 0.05; TLI 0.985, CFI 0.993). Country-specific adjusted $R^2$ for explained variance in QoL ranged between 0.59–0.71.




**Conclusions:** Pain, PF and the consequent reduction in perceived QoL are at the centre of the lived experience of those with OA. The relationship between these three variables, including the mediating role of PF, was found to be consistent across age, gender and, with slight variations, country. This "standard model" for OA opens up the opportunity to further explore potential psychological mediating factors which may improve QoL as well as moderating factors such as different types of intervention.

**References:**

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**Disclosure of Interest:** None declared

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## SAT0570 BIOLOGICS AND BIOSIMILARS: DO PHYSICIANS UNDERSTAND THE DIFFERENCES?

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**Background:** Physicians across many medical specialties, including Rheumatology, Dermatology, and Neurology, commonly prescribe biologic therapies, such as TNF inhibitors, botulinum toxins, growth factors, and vaccines. A biosimilar is not identical to the innovator biologic. Because biosimilars are structurally distinct from innovator biologics, biosimilars may produce significantly different side effects and safety profiles compared to innovator biologics. Therefore, it is critically important that physicians are aware of the differences between biologic therapies. It is unknown whether physicians' understanding of biologic and biosimilar medicines differs across geographic regions.

**Objectives:** To determine whether differences exist in physicians' understanding of biologic and biosimilar medicines in the U.S., Latin America, and Europe.

**Methods:** An internet-based survey was completed by physicians in the U.S., Latin America (Colombia, Argentina, Brazil, and Mexico), and Western Europe (Spain, UK, France, Italy, and Germany). Survey respondents practiced in multiple settings and represented the following medical specialties: Rheumatology, Neurology, Dermatology, Nephrology, Endocrinology, and Oncology.

**Results:** The survey was completed by 376 U.S. physicians, 399 Latin American physicians, and 470 European physicians. The majority of survey respondents in the U.S., Latin America, and Europe (91%, 88%, 92%, respectively) indicated that they prescribed biologic medicines to patients. U.S. physicians were 41% more likely than Latin American physicians and 43% more likely than European physicians to believe that biologic medicines with the same non-proprietary name have identical chemical structures. In addition, U.S. physicians were 34% more likely than Latin American physicians and 43% more likely than European physicians to believe that biologics sharing the same non-proprietary name produce the same therapeutic results. Eighty-two percent of U.S. physicians, 85% of Latin American physicians, and 74% of European physicians indicated that the

authority to write "dispense as written" when prescribing a biologic is critical or very important.
**Conclusions:** Across all geographic areas, physicians consistently believe that it is critically important that physicians retain the authority to choose which biologics their patients will receive. However, significant differences exist in the proportion of physicians who believe that biologics sharing the same non-proprietary name have the same chemical structure and produce identical results. These differences suggest that European physicians have a more accurate and complete understanding of the differences between biologics and biosimilar medicines compared to U.S. and Latin American physicians. Additional research is needed to determine the reasons for these differences.
**Acknowledgement:** Data for this study was obtained with permission from surveys conducted by the Alliance for Safe Biologic Medicines.
**Disclosure of Interest:** A. Molinari: None declared, H. Gewanter: None declared, M. Reilly: None declared, B. Kennedy: None declared, D. Charles Consultant for: Dr. Charles receives income from Allergan, Ipsen, Medtronic, and the Alliance for Patient Access for consulting services.
**DOI:** 10.1136/annrheumdis-2016-eular.5829

## SAT0571 TRENDS IN STRONG OPIOID ANALGESIC PRESCRIPTIONS BY FRENCH RHEUMATOLOGISTS: A NATIONWIDE SURVEY

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**Background:** Opioid analgesic prescription represents a growing problem in many countries with increased opioid-related overdoses and deaths being reported. In rheumatology setting, strong opioids are considered poorly effective and not recommended as first line treatment in pain management.
**Objectives:** The aim of this study was to investigate rheumatologists' opioid prescribing patterns, demographic and practice characteristics, in relation with beliefs about prescription appropriateness and risks of opioids use.
**Methods:** We conducted a nationwide survey with a 47-item questionnaire. The questions were developed by the French Study Group on Rheumatic Pain (CEDR), focusing on opioid prescription and pain training Questionnaires were mailed and e-mailed to every registered rheumatologist in France, with the help of French Rheumatology Society. Answers were anonymous.
**Results:** 2490 questionnaires were sent, response rate was 33.7% (n=839), mean age 50,4 years, 49,2% were men, 33,6% had exclusive hospital practice, 65,4% reported having no special education on pain. Of these 58 (6.9%) self-reported never prescribing opioids in non-cancer pain.
Specific pain assessment was performed by 66,1% of rheumatologists to initiate, modify or maintain opioid prescription. It was significantly more frequent in young rheumatologists (<40 years), in women, in hospital practice and after special education on pain.
Main indications for opioids were: acute radicular pain (93,1%), vertebral fracture (91,4%) and acute back pain (67,1%). Only 1% would consider prescribing opioid in fibromyalgia.
Morphine and/or oxycodone were first line treatments for 613 prescribers (78,5%), fentanyl, hydromorphone and buprenorphine only for 168 prescribers (21,5%). The average starting daily dose was 45mg morphine equivalent, 80% (n=625) described a mean of 1.2 months testing period for opioid efficacy. 42% (n=328) reported a ceiling daily dose of 100mg/day morphine equivalent above which they stop increasing prescription. 70,3% reported screening for opioid misuse risk before initiating treatment.
Specific training on pain was significantly associated with opioid testing period (p=0,006); screening for risk of misuse at initiation (p<0,0001) and at continuation (p<0,0001).
Opioid side effects were prevented in 69,8% with a laxative and in 62,1% with anti-vomiting treatment. Prescribers with pain training prescribed more frequently laxative (p=0,015) and anti-vomiting treatment (p=0,0003).
**Conclusions:** To our knowledge, this is the first national survey on trends in strong opioid prescriptions concerning rheumatologists. French rheumatologists are more likely to prescribe opioids in acute pain conditions at low dose, without exceeding the recommended 200mg daily dose for non-cancer pain, together with side effects prevention. Morphine sulfate is the first drug choice. Impact of pain education in rheumatologists' opioid uses is important, and emphasizes the need to include systematically pain training in rheumatology core curricula.
French rheumatologists have mostly a safe and careful prescribing pattern of opioid in non-cancer pain. Mostly they abide by national and international recommendations.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5594

## SAT0572 LIVER FAT INDICES RELATE WITH INFLAMMATORY PROFILE IN INFLAMMATORY ARTHRITIS PATIENTS

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**Background:** Rheumatic diseases associate with metabolic and cardiovascular disorders [1]. These complications might be a side effect of drugs exposure (i.e. corticosteroids) but also a direct consequence of the widespread systemic inflammation. While the association between inflammatory markers and metabolic disturbance has been extensively explored, few data are available about liver involvement in inflammatory arthritis [2].
**Objectives:** To explore possible association between inflammatory markers and serum indicators of non-alcoholic fatty liver disease (NAFLD) in a sample of unselected inflammatory arthritis subjects. The liver fat score (LFS) and the hepatic steatosis index (HSI) were employed as serum NAFLD markers [3].
**Methods:** Subjects who met ACR/EULAR criteria for rheumatoid arthiritis (RA), CASPAR criteria for psoriatic arthritis (PsA) and ESSG criteria for undifferentiated spondiloarthritis (uSPA) were consecutively recruited for the present investigation. After overnight fasting, the following serum analytes were determined: blood glucose, lipids, insulin, complete blood count, erythrocyte sedimentation rate (ESR), high sensitivity C-Reactive Protein (hsCRP). *LFS* was calculated with the formula: -2.79 + 1.18 * Metabolic Syndrome (yes=1/no=0) + 0.45 * Type 2 Diabetes (yes=2/no=0) + 0.15 * Insulin + 0.04 * AST - 0.94 * AST/ALT. *HIS* was calculated with the formula: 8 * ALT/AST + BMI +2, if DM2; +2, if females. Metabolic syndrome was defined according to the criteria of the International Diabetes Federation. Pearson's or Spearman's correlation analyses were used as appropriate to test the associations between continuous variables. Not normally distributed variables were log-transformed before analysis.
**Results:** Overall, a total of 55 subjects (27 AR, 18 PsA and 10 uSPA) were recruited. The prevalence of female gender was 60%. The mean age was 53.5±9.8. Twenty-four patients were under stable treatment with methotrexate (MTX). In simple correlation analyses, LFS significantly correlated with ESR (r=0.37, p<0.01), LnCRP (r=0.46, p<0.001), complement C3 (r=0.46, p<0.001), BMI (r=0.55, p<0.001), Waist (r=0.52, p<0.001); HSI significantly correlated with ESR (r=0.40, p<0.01), LnCRP (r=0.28, p=0.05), complement C3 (r=0.38, p<0.01). After correction for MTX therapy, waist and BMI only ESR and complement C3 correlated with LFS and HSI.
**Conclusions:** The results of the present study, although conducted in a limited sample, demonstrated an interesting association between liver fat indices and inflammatory markers. Our data, if confirmed in other population, might add important information about the relationship linking metabolic complications and rheumatic diseases.
**References:**
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[2] Selmi C, De Santis M, Gershwin ME. Liver involvement in subjects with rheumatic disease. Arthritis Res Ther. 2011;13:226.
[3] Kahl S, Straßburger K, Nowotny B, et al. Comparison of liver fat indices for the diagnosis of hepatic steatosis and insulin resistance. PLoS One. 2014;9:e94059.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4870

## SAT0573 VALIDITY OF THE SHORT FORM 6D UTILITY MEASURE IN EARLY AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE DESIR COHORT

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**Background:** The quantification of health improvements is essential, notably in the current context of increasingly expensive therapies and more and more limited resources. Preference-based measures of health have become important for estimating health states in calculating quality-adjusted life years (QALYs), an essential component of cost-utility analysis. The SF-6D is an indirect preference-based health-related quality of life instruments increasingly being used for economic evaluation of clinical interventions and health programs. Data on economic as well as QoL outcomes among early axial Spondyloarthtritis (axSpA) patients remain scarce.
**Objectives:** To evaluate the validity of an utility measure, the SF-6D, in early axSpA especially concerning the ability of this measure to reflect the change in patients' condition over time.
**Methods:** DESIR (Devenir des Spondyloarthropathies Indifférenciées Récentes) is a French, multicentre, longitudinal cohort of 708 patients with early inflammatory back pain suggestive of axSpA.
SF-6D utility measures were assessed in 607 patients over 1 year. To investigate whether the change in SF-6D is a valid measure of change in axSpA health status, we used Spearman's product-moment correlation to compare change scores for SF6D with those for external measures of health, the HAQ, SF36 physical component, SF36 mental component and AS-QOL from baseline to 6

and 12 months. Responsiveness was tested by the effect size (ES) at 6 and 12 months for the entire sample and subgroups by disease evolution (increase or decrease-stabilization in BASDAI). Bootstrap methods were used to estimate 95% confidence intervals [95% CI]. Sensitivity to change of the HAQ was calculated as a benchmark.

**Results:** At baseline, mean value of SF-6D was 0.69±0.12 (range 0.30 to 0.95). The distribution was near normal. Few missing values were observed: 2.4%. No floor or ceiling effects were evidenced. Correlations of the SF6D change with change in HAQ and physical component of SF-36 scores were moderate at 6 months (r=-0.42 and 0.44, respectively). Correlations with change in mental component of SF-36 and AS-QOL scores were good (r=0.60 and -0.60, respectively). Correlations were stable over 1 year.

For the entire sample at 6 months, the SF-6D was more sensitive to change than the HAQ: ES 0.36 [95% CI 0.28;0.44] versus -0.22 [-0.28;-0.17]. The SF-6D was more responsive than the HAQ for improved condition: ES 0.45 [0.37;0.54] vs -0.32 [-0.38;-0.26] without difference for patients with deteriorated condition: ES SF-6D -0.23 [-0.41;-0.04] vs 0.33 [0.18;0.50] for HAQ. Results were similar at 12 months.

**Conclusions:** The SF-6D is valid and able to reflect the change in patients' condition over time, especially improvement, in patients with early inflammatory back pain suggestive of axSpA.

**Disclosure of Interest:** None declared

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## SAT0574 IMPROVING TIMELY FOLLOW-UP AFTER HIGH BLOOD PRESSURES IN RHEUMATOLOGY CLINICS USING STAFF PROTOCOLS

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**Background:** Hypertension (HTN) is the most prevalent cardiovascular disease (CVD) risk factor among adults with rheumatic conditions. However, we found that blood pressures were addressed in <1/3 of rheumatology visits, even when severely elevated (≥160/100 mmHg). At this range, only 11 patients need to be treated for HTN to prevent one CVD event. In primary care, HTN protocols executed by nurses (RNs) or medical assistants (MAs) during vital sign assessment have improved control of high blood pressure (BP). Yet, such protocols have not been tested in rheumatology clinics.

**Objectives:** Our objective was to study the feasibility and impact of an intervention using a staff HTN protocol to facilitate timely (<4 wks per Medicare quality measure) primary care follow-up for patients with high blood pressures at rheumatology visits.

**Methods:** We conducted a pre-post study in three academic rheumatology clinics. All eligible adult (≥18 years-old) rheumatology visits with BP ≥140/90 mmHg (12/2014–5/2015) were compared to pre-intervention visits (2012–9/2014). Our multi-dimensional intervention included: (1) educating staff on HTN, rheumatologic diseases, and CVD risk, (2) electronic health record (EHR) alerts for staff to re-measure BPs if ≥140/90 and 3) cuing brief patient education and scheduling primary care follow-up if 2nd BP ≥140/90, and (4) monthly audit and feedback with staff about performance. We assessed timely primary care follow-up of high BPs among patients who received primary care in our system using EHR data.

We performed multivariable logistic regression and compared the odds (OR, 95%CI) of timely primary care follow-up before and during intervention, while controlling for baseline socio-demographics, comorbidities, utilization, and clinic.

**Results:** We compared 689 intervention period visits to 4,683 pre-intervention visits with BPs ≥140/90. Patient groups were comparable before and during intervention. Staff initiated BP re-measurement in 80% of eligible visits during intervention months 4–6, compared to <1% pre-intervention; overall improvement 60%, p<0.001. More patients received timely primary care follow-up for HTN during the intervention, (44%, vs 29% before, p=0.0003). Multivariable analysis showed that eligible visits during the intervention had two-fold higher odds of timely follow-up compared to pre-intervention, OR 2.1, 1.4–3.0 (p<0.0001). We observed positive associations between timely follow-up and race (black vs. white OR 1.7, 1.1–2.5) and diabetes (vs. no diabetes OR 1.3, 1.01–1.6) post intervention.

**Conclusions:** Our intervention was feasible for usual rheumatology clinic staff and it doubled rates of timely BP follow-up. Future studies should examine this intervention in other rheumatology clinics, and its impact on HTN control to reduce CVD risk in rheumatology patients.

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## SAT0575 FIRST AND SECOND LINE TREATMENT PERSISTENCE AMONG PATIENTS WITH IMMUNE-MEDIATED RHEUMATOID DISEASE TREATED WITH SUBCUTANEOUS TNF-ALPHA INHIBITORS

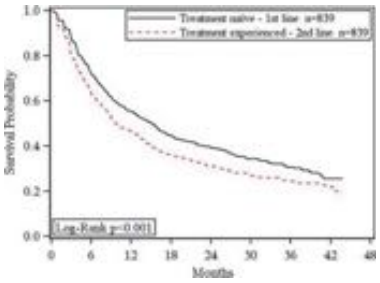
J. Dalen[1], A. Svedbom[2], C.M. Black[3], S. Kachroo[3]. *[1]Mapi; [2]Department of Medicine, Karolinska Institutet, Stockholm, Sweden; [3]Merck & Co., Inc., Kenilworth, United States*

**Background:** The treatment of ankylosing spondylitis (AS), psoriatic arthritis (PsA), and rheumatoid arthritis (RA), collectively referred to as Immune-Mediated Rheumatoid Disease (IMRD), has evolved in recent years with the introduction of subcutaneous TNF-alpha inhibitors (SC-TNFi).

**Objectives:** The aims of this study were: i) To assess real-world persistence in SC-TNFi naïve and experienced patients treated with SC-TNFi for IMRD in Sweden; and ii) to estimate and compare health care resource utilization (HCRU) costs in these two patients populations.

**Methods:** This study was a retrospective, observational register analysis of treatment patterns and costs based on anonymized patient-level data extracted from Swedish national health data registers. Patients (≥18 years old) were identified through filled prescriptions for adalimumab, etanercept, certolizumab pegol, and golimumab between 5/6/2010 and 12/31/2012 from the Swedish Prescribed Drug Register. Information on prescriber specialty and department was used to exclude patients initiating treatment with SC-TNFi for diseases other than IMRD. Patients were excluded if they filled at least one prescription from a department other than rheumatology, orthopedics or rehabilitation and if the prescription was issued by a non-rheumatologist. The included patients were classified by diagnosis as AS, PsA, RA, "other arthritis", or "unknown". To enhance comparability, propensity score matching (PSM) was implemented. Patients were matched based on age, gender, index year, diagnosis, therapy, Charlson Comorbidity Index, and non-biologic DMARD use. Persistence was estimated using non-parametric survival analysis. Health care resource utilization (HCRU) was captured 12 months after treatment initiation and comprised specialized outpatient care, inpatient care, and non-DMARD medication.

**Results:** A total of 5,748 patients were identified (treatment naïve – 1st line: 4,903, treatment experienced – 2nd line: 845). A successfully balanced PSM cohort was generated with 839 matched pairs. Comparisons over the study period showed that patients initiating their first line of treatment had significantly higher persistence than patients initiating their second line of treatment with SC-TNFis (p<0.001). HCRU was evaluated for a subset of 393 matched pairs, where both patients were persistent for at least six months. In the twelve months post treatment initiation, patients on first line therapy incurred lower mean total costs than patients on second line therapy (USD 3,206 vs. 4,540, p<0.001).




**Conclusions:** SC-TNFi-naïve IMRD patients initiating treatment had significantly higher persistence rates than patients initiating a second line of treatment with SC-TNFis in Sweden. In addition these patients also incurred significantly lower mean total HCRU costs twelve months post treatment initiation. These results indicate that it may be advisable to prescribe the SC-TNFi which has demonstrated best long-term persistence as first line SC-TNFi. It appears especially important for indications which have fewer choices of approved biologics.

**Disclosure of Interest:** J. Dalen Consultant for: Merck, A. Svedbom Consultant for: Merck, C. Black Employee of: Merck, S. Kachroo Employee of: Merck

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## SAT0576 ASSOCIATIONS BETWEEN FIVE IMPORTANT DOMAINS OF HEALTH AND THE PATIENT ACCEPTABLE SYMPTOM STATE IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS: A CROSS SECTIONAL STUDY OF 977 PATIENTS

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**Background:** The objectives of treatments in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) include acceptable quality of life from the patient's perspective. One simple question can be used to evaluate the level of acceptability of the disease status by a patient: the patient acceptable symptom state (PASS) which corresponds to the concept of "feeling well".

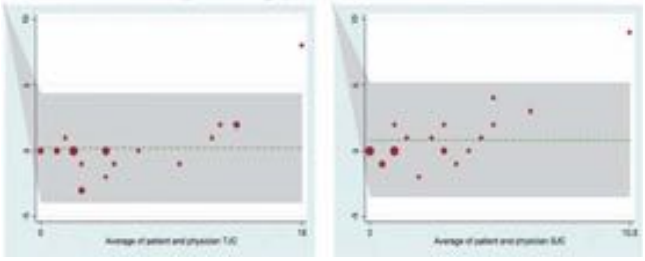
**Objectives:** The objective was to explore the link between a patient acceptable symptom state (PASS) and patient-perceived impact in rheumatoid arthritis (RA) and psoriatic arthritis (PsA).
**Methods:** Cross-sectional study of unselected patients with definite RA or PsA. Five domains of health were analysed: Pain, functional capacity, fatigue, coping and sleep disturbance. They were assessed by a numeric rating scale (0–10) and were compared between patients in PASS or not (Cohen's effect sizes). The domains of health associated with PASS status were assessed by multivariate logistic regression, and PASS thresholds were determined using the 75th percentile method and ROC analyses.
**Results:** Among 977 patients (531 RA, 446 PsA) mean age was 53.4±13.2 yrs; mean disease duration was 11.2±10.0 yrs; 637 (65.8%) were females. In all, 595 patients (60.9%) were in PASS: they had lower symptom levels, and all domains of health except sleep disturbance discriminated clearly between patients in PASS or not (effect sizes, 0.73 to 1.45 in RA and 0.82 to 1.41 in PsA). In multivariate analyses, pain and coping were predictive of not being in PASS: odds ratio [95% confidence interval] 0.81 [0.67–0.96] and 0.63 [0.52–0.75] for pain and 0.84 [0.74–0.96] and 0.83 [0.71–0.97] for coping, in RA and PsA respectively. The cut-offs of symptom intensity (range 0–10) corresponding to PASS for the five domains of health and the two diseases with a score were similar, i.e. around 4–5.
**Conclusions:** Two thirds of 977 unselected tertiary care patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) were in PASS. In RA and PsA, PASS was associated with the five domains of health analysed, and in particular with less pain and better coping. PASS levels in the two diseases for the five domains of health, as well as the RAID and PsAID scores were similar with cut-offs around 4–5 points (0–10 scale).
**References:**
[1] Gossec L. et al, Ann Rheum Dis, 2014.
[2] Gossec L. et al, Ann Rheum Dis 2009.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2772

## SAT0577 PATIENT-REPORTED DAS28 IN RHEUMATOID ARTHRITIS: ITS RELIABILITY IN A LONGITUDINAL STUDY

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**Background:** There have been increasing studies focusing on patient derived joint counts in RA. Patient self-reported DAS28 with training has not been observed longitudinally in the UK.
**Objectives:** The aims of the study were to (1) evaluate the reliability of patient self-assessment of DAS28 compared to physician DAS28; (2) determine whether the agreement between patient-reported and physician-reported DAS28 improves over time with training.
**Methods:** This was a longitudinal study with a total of 3 study visits 6 weeks apart carried out at two hospitals sites in the United Kingdom. All 42 patients had training on joint count self-assessment. A single physician performed joints assessment on patients independently blinded to the patients' data. Correlations between patient and physician measurements were analysed using Spearman correlation coefficient whereas agreement between patient and physician was analysed with Bland-Altman plots.

**Figure 1.** Bland Altman plot of the difference between patient TJC, SJC and physician TJC, SJC versus mean of patient and physician TJC, SJC



**Results:** There was very strong correlation between patient and physician DAS28-CRP, DAS28-ESR, TJC and SJC ($r > 0.80$). The limits of agreement of DAS28 were consistent (range -0.65 to 0.69) but exceeded the set difference of 0.6, although with very small mean difference.
**Conclusions:** Overall, it is reasonable to conclude that there were good agreement of tender and swollen joint assessments between patient and physician. Patient training has positive effects in increasing the reliability of patient self-assessment of joint counts. Our study showed patient-reported DAS28 was not exactly same as physician-reported DAS28, although DAS28, TJC and SJC from both patient and physician were all very strongly correlated. Patient-reported joint counts were shown to have a strong predictive value and therefore could be incorporated in clinical practice. Patient DAS28 and physician DAS28 could act synergistically to reach a consensus evaluation of RA in order to achieve treatment optimisation.

Table 1. Agreement between patient and physician of disease activity, tender joint count and swollen joint count over three study visits

| | First visit | Second visit | Third visit |
|---|---|---|---|
| Number of patients | 42 | 34 | 24 |
| DAS28-CRP | | | |
| Range | 1.56–6.09 | 1.35–6.51 | 2.48–5.69 |
| Mean difference | 0.0007 | –0.023 | 0.022 |
| Limits of agreement | –0.66–0.66 | –0.69–0.64 | –0.65–0.69 |
| DAS28-ESR | | | |
| Range | 1.46–6.33 | 1.33–6.96 | 1.41– 6.15 |
| Mean difference | –0.0002 | –0.023 | 0.022 |
| Limits of agreement | –0.66–0.66 | –0.74–0.69 | –0.65–0.69 |
| TJC | | | |
| Range | 0–18 | 0–24 | 0–16 |
| Mean difference | 0.07 | –0.03 | 0.21 |
| Limits of agreement | –4.3–4.4 | –3.7–3.7 | –3.9–4.3 |
| SJC | | | |
| Range | 0–22 | 0–18 | 0–11 |
| Mean difference | 0.76 | 0.88 | 0.83 |
| Limits of agreement | –4.7–6.2 | –3.9–5.7 | –3.5–5.1 |

DAS28: disease activity score in 28 joints; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; TJC: tender joint count; SJC: swollen joint count.

**Acknowledgement:** Dr Jamie Sergeant, a Lecturer in Statistics, Centre for Musculoskeletal Research, Institute of Inflammation and Repair, the University of Manchester.
**Disclosure of Interest:** None declared
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## SAT0578 THE ASSOCIATION OF ARTHRITIS AND LUNG DISEASE: A POPULATION-BASED STUDY

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**Background:** Rheumatoid arthritis (RA) is known from clinical studies to be associated with a number of different lung conditions, but the relationship with arthritis in the population, where overwhelmingly the most frequent type of arthritis is osteoarthritis, has been less well studied.
**Objectives:** To examine whether arthritis is associated with an increased likelihood of reporting asthma and/or COPD.
**Methods:** Data from the 2011- 2012 Canadian Community Health Survey, a representative survey of the household population were used, restricting analyses to the population age ≥35 years (n=88,734). Participants were asked whether they had specific long term health conditions diagnosed by a health professional: conditions asked about included arthritis (excluding fibromyalgia), asthma, and COPD (specifically chronic bronchitis, emphysema or chronic obstructive pulmonary disease). Multinominal logistic regression was used to examine associations between lung conditions (none, asthma only, COPD only, both asthma and COPD) and arthritis, controlling for covariates: age, sex, education, household income, smoking status (never, former, current), body mass index (BMI: underweight, normal, overweight, obese), and mean number of other chronic conditions (out of 9). As metabolic and inflammatory pathways have been postulated given the strong association of obesity and arthritis, sensitivity analyses were undertaken stratified by BMI category.
**Results:** People with arthritis (23% of the population) more frequently reported lung conditions than those without, respectively asthma 8.2% vs 5.5%, COPD 5.4% vs 2.0%, and asthma+COPD 3.4% vs 0.8%. There was no difference in the proportion of current smokers between those with and without arthritis (20.5%), although those with arthritis were more likely to be former smokers (49.8% vs 36.5%). They were also more likely to be obese (26.8% vs 16.7%) and have more other chronic conditions (mean 1.5 vs 0.5). In regression analyses controlling for covariates, arthritis was significantly associated with reporting of all lung conditions: OR (95%CI): asthma only 1.48 (1.26, 1.73); COPD only 1.60 (1.34, 1.91); asthma+COPD 1.98 (1.65, 2.37). In addition, the odds of all lung conditions were significantly higher for females. Obesity was also a significant risk factor for reporting all lung conditions, as was the number of other chronic conditions. The sensitivity analyses showed the associations between arthritis and the lung conditions were significant and similar for normal, overweight and obese BMI categories. Being a current or former smoking was significantly associated with COPD, but not with asthma only.
**Conclusions:** This study confirms a relationship between arthritis and lung disease, and the multivariate analyses adds to the scant previous population-based literature which was mainly descriptive. That those with arthritis had increased odds of reporting lung disease, asthma, COPD, and asthma+COPD compared to those without arthritis, controlling for a range of other factors, including smoking, raises questions as to the mechanism. The consistency of the association over levels of BMI suggests other pathways in addition to those mediated by obesity/metabolic factors. The findings also suggest that recommendations for the management of arthritis should consider the potential implications of having lung disease, for example, for physical activity.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4957

## SAT0579 TRENDS IN USE OF PHYSIOTHERAPISTS, CHIROPRACTORS AND COMPLEMENTARY AND ALTERNATIVE MEDICINE PRACTITIONERS FOR ARTHRITIS OVER TIME AND ACROSS GENERATIONS

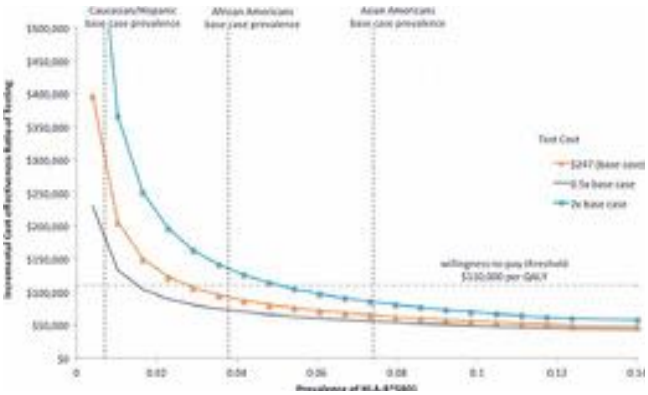
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**Background:** Non-pharmacologic strategies contribute to the management of arthritis in the community, but little is known about the use of these therapies and how this varies by age and over time. Rehabilitation therapies, such as physiotherapy (PT), and chiropractic, have been shown to improve the management of arthritis, and there is also evidence for the benefit of acupuncture and massage therapy.
**Objectives:** a) to compare the age-trajectories of use, by people with arthritis, of physiotherapy, chiropractic, and complementary and alternative medicine (CAM) over 18 years by birth cohort and b) to determine how these trajectories are affected by socio-economic status (SES), lifestyle factors, and reported pain.
**Methods:** We used data from the Canadian Longitudinal National Population Health Survey (1994–2010). We examined 10,330 participants in five birth cohorts: pre-World War II (born 1935–1934), World War II (born 1935–1944), Older Baby Boomer (born 1945–1954), Younger Baby Boomer (born 1955–1964), and Generation X (born 1965–1974). Data on visits to physiotherapists, chiropractors, and CAM practitioners, arthritis, SES (education, income), and lifestyle factors (BMI, physical activity, sedentary behavior, and smoking), and pain that prevents activities were collected biannually. For each type of practitioner our outcome was whether participants reported 1+ visits in the past year. We used multilevel logistic growth models to examine cohort effects and predictors of each outcome, among arthritis patients.
**Results:** At baseline (in 1994), 14.5% reported visiting physiotherapists, 14.2% chiropractors, and 6.0% CAM practitioners (most frequently for massage therapy or acupuncture). We found an increase in use of all types of practitioner with age in all cohorts. Comparing the age-trajectories of PT, chiropractic, and CAM use over time, we found significant cohort differences ($p<0.0001$) such that when compared at the same age, each succeeding younger cohort had higher odds of consulting with these practitioners than their older counterparts. Cohort differences were largest for CAM, where recent cohorts were more likely to use these services. Women had higher odds of using all types of practitioner than men in all cohorts. Pain and high SES were the main predictors of PT and chiropractic use. The predictors of CAM were similar with the addition of having a normal BMI as a significant predictor.
**Conclusions:** The use of PT, chiropractic, and CAM is significantly higher in younger cohorts of people with arthritis. While pain was a major predictor, notably use of these practitioners was greater in those with higher SES, implying potential educational and income access barriers to this type of care. Healthcare providers for people with arthritis need to be aware that younger generations may have different patterns of use of other services such PT, chiropractic, and CAM.
**Disclosure of Interest:** None declared
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## SAT0580 THE COST-EFFECTIVENESS OF HLA-B*5801 GENETIC SCREENING TO GUIDE INITIAL URATE-LOWERING THERAPY FOR GOUT

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**Background:** Allopurinol is the most commonly used first-line urate-lowering therapy for the management of gout. Although allopurinol is generally safe, it is associated with severe allopurinol-hypersensitivity syndrome (AHS) (i.e., Steven Johnson Syndrome and Toxic Epidermal Necrolysis). AHS is fatal in up to 30% of cases. Patients with the human leukocyte antigen *HLA-B*5801* are at higher risk of developing AHS. The prevalence of *HLA-B*5801* and risk of AHS varies by race and is highest in Asians. The 2012 ACR gout guideline recommends testing for *HLA-B*5801* in Asians prior to the allopurinol initiation, but the guideline did not take into account its cost-effectiveness.
**Objectives:** We evaluate the cost-effectiveness of testing for *HLA-B*5801* prior to initiation of allopurinol according to race.
**Methods:** We modified a previously developed Markov decision model to evaluate the cost-effectiveness of testing for *HLA-B*5801* prior to the initiation of allopurinol (300mg) – febuxostat (80mg) sequential therapy compared to treating with allopurinol (300mg) –febuxostat (80mg) sequential therapy without testing. Hypothetical patients in the testing strategy received a polymerase chain reaction test for *HLA-B*5801* prior to the initiation of therapy. Patients that tested positive for *HLA-B*5801* were assumed to be treated with febuxostat. Patients that tested negative for *HLA-B*5801* and those in the no testing strategy were assumed to initially receive allopurinol. We took account of the variation in risk of hypersensitivity by race (Caucasians 0.0003; African Americans 0.0015; Asian Americans 0.0034) and prevalence of *HLA-B*5801* by race (Caucasians 0.007; African Americans 0.038; Asian Americans 0.074). Patients on allopurinol could experience a minor (e.g., erythema multiforme minor) or major (e.g., Stevens-Johnson Syndrome) AHS event. Cost and quality-adjusted life years (QALYs) were evaluated over the lifetime of a hypothetical gout cohort. Finally, we conducted a sensitivity analysis to evaluate the effect variation in cost of testing, the prevalence of *HLA-B*5801,* and background AHS risk on the cost-effectiveness of testing.
**Results:** Given a willingness-to-pay threshold of $110,000 per QALY, *HLA-B*5801* testing is not cost-effective for Caucasians (incremental cost-effectiveness ratio $268,020), but it is cost-effective for African Americans (incremental cost-effectiveness ratio $91,870) and Asian Americans (incremental cost-effectiveness ratio $64,140). As the prevalence of HLA-B*5801 increases the incremental cost-effectiveness ratio of testing decreases (Figure 1). When the prevalence of *HLA-B*5801* is greater than 0.029 testing is cost-effective.



**Conclusions:** Testing for the presence of *HLA-B*5801* is cost effective in African American and Asian Americans compared with accepted willingness-to-pay thresholds.
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## SAT0581 COST SAVINGS WITH BIOSIMILARS IN RHEUMATOLOGY: A SYSTEMATIC LITERATURE SEARCH OF BUDGET IMPACT ANALYSIS

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**Background:** The growing use of biological therapies in immune-mediated rheumatic diseases represents a significant burden to healthcare systems struggling with tighter budgets.
**Objectives:** Our aim was to assess potential cost savings associated with the use of biosimilar anti-rheumatic therapies.
**Methods:** We performed a systematic literature search in the Medline database as well as EULAR, ACR and ISPOR meeting abstracts to identify budget impact analysis on biosimilars of infliximab (IFX), etanercept (ETA) and adalimumab (ADA) used in the treatment of rheumatic diseases. We included articles and abstracts published from 2013 onwards.
**Results:** We screened 195 articles by title and abstract and 2 publications fulfilled our inclusion criteria, both concerning IFX. Five abstracts were also included (2 on ETA, 2 on IFX and 1 on IFX+ETA+ADA). Five studies performed the analysis on rheumatoid arthritis and the other 2 also in spondyloarthritis, psoriasis and inflammatory bowel disease. The heterogeneity of budget impact models didn't allow for direct comparisons but all studies pointed out significant cost savings, from dozens to thousands of millions of euros, depending on the countries analysed, time horizon, discount scenarios and biosimilar uptake shares. The reinvestment of biosimilar-related savings would also allow for the treatment of thousands of additional rheumatic patients. The authors of these models stress, however, that some of the assumptions made may not reflect real-world scenarios. Table 1 summarizes the main findings in the included studies.
**Conclusions:** The use of biosimilar anti-rheumatic therapies may represent a strategy to reduce drug-related expenditure and contribute to financial sustainability of healthcare systems worldwide.

**Abstract SAT0581** – Table 1

| | Biosimilar; Population | Time horizon (years) | Projected cost savings (millions) | Additional treated patients |
|---|---|---|---|---|
| Ruff L, et al (2015) | ETA; RA | 5 | UK €62–162; France €19–46; Germany €42–105; Italy €26–62; Spain €16–37 | 1530 UK, 8430 Germany |
| Ruff L, et al (2015) | ETA; RA/PsA/PsO/AS | 5 | UK €111–284; France €35–81; Germany €76–187; Italy €46–111; Spain €28–65 | 3100 UK, 17130 Germany |
| Jha A, et al (2015) | IFX; RA/PsA/PsO/AS/IBD | 1 | 10%, 20% and 30% discount scenarios: €2.3, €4.6 and €6.9 in RA; €2.2, €4.3 and €6.4 in AS; €2.7, €5.3 and €8 in PsA | 10%, 20% and 30% discount scenarios: 300, 676 and 1158 in RA; 139, 313 and 538 in AS; 186, 419 and 718 in PsA |
| Brodszky V, et al (2014) | IFX; RA | 1 | €15.3 if only biologic-naive; €20.8 if also interchanging | 1205 if only biologic-naive; 1790 if also interchanging |
| Hong J, et al (2014) | IFX; RA | 5 | 10%, 20% and 30% discount scenarios: €95.9, €233 and €433.5 | NA |
| McCarthy G, et al (2013) | IFX; RA | 5 | €5.3 | 337 |
| Whitehouse J, et al (2013) | IFX; RA | 1 | €26 in France; €351 in Germany; €98 in the UK | 39% in France, 36% in Germany and 40% in the UK |

ADA: adalimumab, AS: ankylosing spondylitis, ETA: etanercept, IBD: inflammatory bowel disease, IFX: infliximab, NA: not assessed, PsA: psoriatic arthritis, PsO: psoriasis, RA: rheumatoid arthritis, UK: United Kingdom.

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## SAT0582 INCIDENCE OF MALIGNANCIES IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES AND BIOLOGICAL DRUGS: EXPERIENCE FROM ONE CENTER IN ITALY

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**Background:** Over the past decade, it has been frequently suggested that the risk of cancer may be increased in patients with inflammatory rheumatic diseases treated with biologics. These drug have been considered as reducing immune surveillance. However, data from registries from different continents reported that treatment with TNF inhibitors did not increase the risk of malignancies, except for skin cancer (1).
**Objectives:** To evaluate the incidence of malignancies in a cohort of our patients with inflammatory rheumatic diseases treated with biological drugs.
**Methods:** The charts of 1468 patients with Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis treated with Adalimumab, Etanercept, Infliximab, Certolizumab, Golimumab, Tocilizumab and Abatacept followed up from 2005 to 2015 at the Department of Rheumatology, University of Florence, were reviewed. Patients who developed a cancer (excluding basal cell skin cancer) during biological therapy were identified. The incidence of malignancies in our patients was compared to the incidence of cancer in the general population in the same period, same geographic area and with same age.
**Results:** Out of 1468 patients, 828 (56,4%) were affected by Rheumatoid Arthritis, 290 (19.7%) by Ankylosing Spondylitis and 350 (23.9%) by Psoriatic Arthritis. Twenty-five out of 1468 patients (1.7%) (mean age 65±9 years), developed cancer: in details, we found 5 (20%) lung cancer, 5 (20%) melanoma, 2 (8%) breast cancer, 1 (4%) liposarcoma, 1 (4%) tongue cancer, 1 (4%) colo-rectal cancer, 1 (4%) liver cancer, 1 (4%) squamous cell skin cancer, 1 (4%) intestinal lymphoma, 1 (4%) myeloid leukemia, 1 (4%) endometrial cancer, 1 (4%) cervical intraepithelial neoplasia (CIN III), 1 (4%) gastric cancer, 1 (4%) bladder cancer, 1 (4%) laryngeal carcinoma and 1 (4%) follicular NHL of parotid gland. Incidence among patients resulted as follows: 2,05% Rheumatoid Arthritis, 1,37% Ankylosing Spondylitis and 1,14% Psoriatic Arthritis. The percentage of cancer in patients was respectively: Etanercept 2,31%, Adalimumab 1,46%, Infliximab 1,18%, Golimumab 1%, Abatacept 1%, Tocilizumab 3,92% and Certolizumab 2,43%. From 2005 to 2010, the incidence of malignancies (excluding basal cell skin cancer), in general population between the age of 60 and 70 years in the Florence area was 0.39%.
**Conclusions:** Our data suggest that in patients with inflammatory rheumatic diseases treated with biological drugs, cancer is increased of 289% compared to the general population. In these patients, the risk of malignancy still remains to be verified in larger cohorts in our area with a long-term controlled registry.
**References:**
[1] Codreanu C, Damjanov N. Safety of biologics in rheumatoid arthritis: data from randomized controlled trials and registries. Biologics. 2015 Jan 27;9:1–6. doi:10.2147/BTT.S68949. eCollection 2015. Review.
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## SAT0583 A SYSTEMATIC REVIEW OF SYSTEMIC SCLEROSIS INSTRUMENTS FOR THE EULAR OUTCOME MEASURES LIBRARY: AN EVOLUTIONARY DATABASE OF VALIDATED PATIENT-REPORTED INSTRUMENTS

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**Background:** Over time, a patient-centered evaluation of health status has become more important for systemic sclerosis (SSc), both in research and

**Abstract SAT0583** – Table 1

| SSc-specific PROs | Domains | No. of items and range | Measurement properties | | | |
|---|---|---|---|---|---|---|
| | | | Reliability IC/TR/ME | Validity | Responsiveness | Interpretability |
| SAQ | Functional status (vascular, respiratory, GIT and musculoskeletal apparatus) | Items: 23<br>Range: 0–3 | ICC 0.79–0.95 | Total score higher in pts with systemic involvement | Vascular z=0.92–2.97; Respiratory z=1.34–2.52; GIT z=–3.14–4.03; Musculoskeletal status z=0.68–3.16 | – |
| FS | Functional ability (upper limbs & muscle weakness) | Items: 11<br>Range: 0–33 | Intra-observ $k_w$ 0.19–0.6<br>inter-observ $k_w$ 0.69–0.94 | HAQ-DI r=0.90<br>Skin score r=0.11 | FS correlates with HAQ-DI 0.59, & Hand HAQ-DI 0.58 | – |
| RCS | Severity and impact of Raynaud's phenomenon | Item: 1<br>Range 0–10 | ICC 0.70 | Disease activity, Rp measures, digital ulcers, mood/tension 67% variance | ES 0.6<br>SRM 0.64 | MID 14–15 points (0–100 VAS)<br>PASS 34 points |
| MHISS | Disability involving the mouth | Items: 12<br>Range: 0–48 | ICC 0.96 | HAQ r=0.33, CHFS r=0.37, mouth opening r=–0.34, MACTAR r=0.11, HADd r=0.26, HADa r=0.17 | – | – |
| UCLA SCTC GIT 2.0 | GIT symptoms severity | Items: 34<br>Range: 0–3 | Cronbach's $\alpha>0.70$, constipation ($\alpha=0.67$)<br>ICC 0.71 | Total GIT score r=0.60; Upper GIT r=0.52; Lower GIT r=0.60 | rho 0.05–0.48 | MID/improvement: 0.07–0.36;<br>MID/worsening: 0.06 –0.21;<br>Floor: none<br>Ceiling: 4% |
| Skin self-assessment | Skin thickening | Items: 17<br>Range: 0–51 | ICC 0.5–0.61 | Skin score r=0.435 | No changes 1 yr follow-up | – dcSSc<br>Floor <15%<br>Ceiling <15%<br>– lcSSc<br>Floor >15%<br>Ceiling n.a. |

clinical setting. Patient-reported outcomes (PROs) are being increasingly used to measure various domains of disease status relevant to patients and physicians. The EULAR Outcome Measures Library (OML) is a freely available website with structured access to a growing database of validated PROs [1], but currently there are no PROs available on SSc at the EULAR OML.
**Objectives:** To provide a comprehensive review of validated SSc-specific PROs and to critically appraise their validity.
**Methods:** A sensitive search was developed in Medline and Embase (08/2015) to identify all validation studies, cohort studies, reviews or metaanalyses in which the objective were the development or validation of PROs evaluating organ involvement, disease activity or damage in SSc. A reviewer screened title and abstracts, selected the studies, and collected data concerning validation using ad hoc forms based on the COSMIN checklist.
**Results:** From 13,140 articles captured, 74 met the predefined criteria. After excluding an instrument for the unavailability of an English version, the selected studies provided information on 6 SSc-specific PROs: the Scleroderma Assessment Questionnaire (SAQ), the scleroderma functional score (FS), the Raynaud's condition score (RCS), the Mouth Handicap in SSc (MHISS), the University of California Los Angeles-Scleroderma Clinical Trial Consortium Gastro-Intestinal tract (UCLA-SCTC-GIT 2.0), and the Skin Self-Assessment. The table summarizes the instruments and their measurement properties:
**Conclusions:** Six SSc-specific PROs have a minimum validation and will be included in the EULAR OML. In general, the level of validation attained could be improved. Further development in the area of disease-specific PROs in SSc is warranted.
**References:**
[1] Castrejón I, Gossec L, Carmona L. Ann Rheum Dis. 2015;74(2):475–6
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## SAT0584 THE INCIDENCE AND PREVALENCE OF THROMBOANGIITIS OBLITERANS IN TAIWAN: A NATIONWIDE, POPULATION-BASED ANALYSIS OF DATA DURING 2002–2011

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**Background:** Thromboangiitis obliterans (TAO) is a nonatherosclerotic segmental inflammatory disease that most commonly affects the small and medium-sized arteries, veins, and nerves of the arms and legs. Most epidemiologic studies were conducted using hospital-based data, and only few population-based epidemiologic studies of TAO have been published.
**Objectives:** To estimate the incidence and prevalence of thromboangiitis obliterans (TAO) in Taiwan during 2002 to 2011.
**Methods:** We identified all patients with a diagnosis of TAO (International Classification of Diseases, Ninth Revision code 443.1) in Taiwan's National Health Insurance Research Database from January 2002 to December 2011. We calculated the age- and sex-specific incidence and prevalence rates of TAO during the study period.
**Results:** During 2002–2011, 158 patients were diagnosed with TAO; of these, 76% were men. Most (63%) patients were <50 years of age when they were first diagnosed. After attaining 20 years of age, the incidence rate increased with age and peaked among those aged ≥60 years. The average incidence rate of TAO during 2002–2011 was 0.068 per $10^5$ years. The incidence of TAO decreased with time: from 0.10 per $10^5$ years in 2002 to 0.04 per $10^5$ years in 2011. The prevalence increased from $0.26\times10^{-5}$ in 2002 to $0.65\times10^{-5}$ in 2011.

| Age group | Case number | | | Person-years | | | Incidence rate† | | |
|---|---|---|---|---|---|---|---|---|---|
| | F | M | T | F | M | T | F | M | T |
| 0–9 | 1 | 2 | 3 | 19050837 | 20763899 | 39814736 | 0.01 | 0.01 | 0.01 |
| 10–19 | 1 | 0 | 1 | 16112069 | 17223717 | 33335786 | 0.01 | 0.00 | 0.00 |
| 20–29 | 7 | 20 | 27 | 20335969 | 19005493 | 39341462 | 0.03 | 0.11 | 0.07 |
| 30–39 | 1 | 30 | 31 | 19137215 | 19243068 | 38380283 | 0.01 | 0.16 | 0.08 |
| 40–49 | 8 | 29 | 37 | 17444626 | 17434089 | 34878714 | 0.05 | 0.17 | 0.11 |
| 50–59 | 5 | 17 | 22 | 10321223 | 10007057 | 20328281 | 0.05 | 0.17 | 0.11 |
| ≥60 | 15 | 22 | 37 | 12027557 | 11781867 | 23809424 | 0.12 | 0.19 | 0.16 |

†per $10^5$ years.

**Conclusions:** This is the first epidemiologic study of TAO in Taiwan using a nationwide, population-based analysis of data from 2002 to 2011. This study showed a trend of decreasing incidence of TAO with time. It is warranted to conduct future clinical studies to further investigate whether or not such findings are associated with a decreasing smoking rate or periodontal disease prevalence in Taiwan.
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[1] Olin JW. Thromboangiitis obliterans (Buerger's disease). N Engl J Med. 2000;343: 864–869.
[2] Sasaki S, Sakuma M, Kunihara T, Yasuda K. Current trends in thromboangiitis obliterans (Buerger's disease) in women. Am J Surg. 1999;177: 316–320.
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## SAT0585 BARRIERS TO T2T IMPLEMENTATION: RA PATIENT'S PERSPECTIVES ABOUT COMORBIDITIES AND STRUCTURAL DAMAGE IN THERAPEUTIC DECISIONS

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**Background:** T2T strategies have been largely recognized and incorporated in national guidelines. Structural changes, functional impairment and comorbidities should be considered along with RA disease activity state when making therapeutic decisions.
**Objectives:** To evaluate patient's perspectives on the interference of comorbidities and structural changes/functional impairment in treatment decisions.
**Methods:** RA patients (1987 criteria) in regular follow-up were recruited from community (private practice) and academic public medical centers by 11 investigators in different urban and rural areas of the country. Structured questionnaires were applied and socio-demographics, disease activity and treatment data were collected. The focus of this study was two main questions: a) In your opinion, other diseases that you have can change the arthritis treatment? b) Do you think that having deformities modify your treatment? Affirmative answers would be followed by more specific questions. Statistical analysis: ANOVA or Kruskal-Wallis; Fisher or Fisher-Freeman-Halton (FFH) as needed; $p<0.05$. Data expressed as % [95%CI} or mean (SD).
**Results:** 485 RA patients were included, 89.7% females, mean age 52.3 (13.8) years, 8.0 (5.2) years of education; 32.4% in use of biologics and 28.3% in private practice. Less than 40% of the patients considered that any of these conditions influenced the treatment.
Deformities, surrogate for structural damage, were considered to imply in more severe disease or more pain and medications by respectively 54.8% and 34% of the positive responders (n=177); these patients were more frequently living in the northwest area (60.2vs 31.7%; =0.0001; [16.2–40]), were from higher socio-economic level (43.2vs30.2%; p=0.0001; [4,1–21.7]), younger (49.4 (12.3) vs 54.3 (12,7); p<0,001) and with shorter disease duration (median 8.0 (range4.0–15) vs 12 (6.0–19); $p<0.001$).
Regarding comorbidities, there were 39.4% (n=191) positive answers, predominantly from younger patients [51.3 (13.1) vs 54.5 (11.6); $p<0.003$]. The patients from private system (80.3 vs 56.3%;p=0.0004; [9.3–36.7]) and higher socio-economic level (71.8 vs55%; p=0.01;[2.9–30.1]), as well as patients with more schooling years ($p<0.001$) and shorter disease duration ($p<0.041$) worried that comorbidities could hinder the choice of arthritis medication, while some patients from public service (25.5vs9.8%;p=0,01;[3.2–25.8]) and low socio-economic levels (14 vs 1.99%;p=0,001;[4.1–20.6]) had concerns about too many pills.
**Conclusions:** patient's skepticism about comorbidities or structural changes interfering with their therapeutic decisions is prevalent and needs to be addressed.
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## SAT0586 HERPES ZOSTER IN THE BRAZILIAN REGISTER -BIOBADABRASIL

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**Background:** Herpes Zoster has been reported with increased frequency in association with rheumatic diseases and biologic therapy.
**Objectives:** To study herpes zoster (HZ) in patients with rheumatic diseases included in the Brazilian Register for monitoring of biologic therapies in rheumatic diseases - BiobadaBrasil,
**Methods:** BiobadaBrasi is a prospective observational cohort study, part of an international initiative (biobadaAmerica) in collaboration with BiobadaSer. Patients with rheumatic diseases are enrolled at the moment of introduction of their first biologic therapy; a comparison cohort of patients with active RA receiving traditional disease-modifying antirheumatic drugs (DMARDs) was recruited in parallel in each center. This register was established in 2009 and is an ongoing study ran by the Brazilian Society of Rheumatology comprising 32 centers (30 public, located at academic centres, 2 private) in almost all states of the country. Data quality is under constant monitoring (online, by phone and "in situ"). In this report all biologic administered to more than a hundred patients were included: abatacept, adalimumab, etanercept, infliximab, rituximab and tocilizumab. Data

was expressed as mean (SD); crude incidence rates (IR) were calculated as number of HZ episodes per 1000 patient-years- IR (1000 patient-years).
**Results:** Up to January 2016, 2715 patients were included in the register, 70% female, mean age 51 (14.3) yrs, submitted to 3770 treatments; 1721 patients with diagnosis of RA; \$54 with AS and APs=181.
61 HZ episodes were related including only one relapse reported in a 44years-old female patient with AR and in use of rituximab. The crude IR (95% CI) of HZ in the study population (biologic agentes) was 8.3 (1000 patient-years) vs 4.45 (1000 patient-years) in the control population (traditional DMARds), (p=0,7 95%CI-3,7–4,7). Only 6 cases were considered severe by the investigators, two of them were HZ ophthalmicus, one periorbital and all lead to some impairment. These patients were taking different biologic agents (etanercept, adalimumab, infliximab – 2 patients) and one was using traditional DMARDS.
Treatment with steroids (HR 1.99; 95%CI 1.092–3.6) was the only factor associated with zoster development. There was no difference in age, sex, specific disease or biologic agent associated with HZ episodes.
**Conclusions:** In our database, the risk of HZ was significantly increased in association with corticosteroid treatment but neither with biologic agents nor with inflammatory rheumatic diseases.
**Acknowledgement:** for monitor P Cabral, for contribution to the BiobadaBrasil registry, L.Barbosa, W.Chahade, A.Hayata, A.Kakehasi, M.Pinheiro, A.Ranzolin, M.Scheinberg, F.Sztajnbok, I.Silveira
**Disclosure of Interest:** None declared
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## SAT0587 RHEUMATOLOGISTS' ESTIMATES OF PROGNOSIS WITHOUT AND WITH TREATMENT IN ROUTINE CARE OF PATIENTS WITH RA, SLE, OA, FM

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**Background:** Physician estimates of prognosis affect management of patients with chronic rheumatic diseases. Different rheumatic diseases may be associated with varying estimates of the value of therapy in affecting prognosis in individual patients. Therefore, two simple quantitative scales for prognosis without and with therapy, may be useful as a form of "triage," to support and document the basis for clinical decisions in patient care.
**Objectives:** To analyze physician estimates of prognosis without and with treatment in 4 rheumatic diseases: rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), osteoarthritis (OA), and fibromyalgia (FM), seen in routine care at an academic rheumatology center.
**Methods:** All patients complete a multi-dimensional health assessment questionnaire (MDHAQ) at each visit, and doctors complete a RheuMetric, which includes prognosis estimated without and with therapy as excellent=1, very good=2, good=3, fair=4, and poor=5. Patients seen over a six-month period in 2015 were classified according to diagnosis into four categories: RA, SLE, OA, and FM. Mean levels of prognosis without and with therapies, and the differences between estimates with and without therapies, were compared for each diagnosis according to ANOVA.
**Results:** The study included 791 patients, 231 with RA, 146 with SLE, 263 with OA, and 151 with FM. Mean estimate for prognosis without therapy in all patients was 2.67 (between "fair" and "good" - closer to "fair"); estimates were in a relatively narrow range from 2.55 in OA to 2.60 in SLE, 2.75 in RA, and 2.81 in FM (Table). Estimates of prognosis with therapy in all patients was 1.76 (between "good" and "very good" – closer to good), a difference of 0.91 units from the prognosis without therapy (34%, $p<0.001$). These estimates differed over a wider range, from 1.44 in SLE, to 1.49 in RA, 1.91 in OA, and 2.21 in FM. The rheumatic disease rated most likely to improve with therapy was RA (1.26 units), followed by SLE (1.16 units), OA (0.65 units) and FM (0.60 units) ($p<0.001$). The proportion of patients rated to have a poor or fair prognosis without therapy ranged from 57% for OA, to 63% for SLE, 64% for RA and 74% for FM, versus very good or excellent in 10% or fewer. The proportions rated as likely to have a good to excellent prognosis with therapy were 12% for FM, 21% for OA, 34% for SLE, and 49% in RA with therapy ($p<0.001$), with an increase of 43% in RA, 24% in SLE, 18% in OA, and 8% in FM (Table).

| | RA (N=231) | SLE (N=146) | OA (N=263) | FM (N=151) |
|---|---|---|---|---|
| Prognosis scales, mean value | | | | |
| Prognosis without | 2.75 | 2.60 | 2.55 | 2.81 |
| Prognosis with | 1.49 | 1.44 | 1.91 | 2.21 |
| Difference | 1.26 | 1.16 | 0.65 | 0.60 |
| Prognosis without treatment | | | | |
| Excellent or very good | 14 (6%) | 22 (10%) | 8 (3%) | 6 (4%) |
| Good | 69 (30%) | 42 (18%) | 104 (40%) | 33 (22%) |
| Poor or fair | 148 (64%) | 82 (63%) | 151 (57%) | 112 (74%) |
| Prognosis with treatment | | | | |
| Excellent or very good | 113 (49%) | 79 (34%) | 55 (21%) | 18 (12%) |
| Good | 106 (46%) | 59 (26%) | 175 (67%) | 82 (54%) |
| Poor or fair | 12 (5%) | 8 (3%) | 33 (13%) | 51 (34%) |

**Conclusions:** Rheumatologists estimated improvement with therapy to be greatest for patients with RA, followed by SLE, OA, and FM. While these findings have face validity, they demonstrate the practicality of assigning quantitative estimates of prognosis in routine care. Quantitative estimates of prognosis rather than narrative descriptions may influence clinical decisions and help document a rationale for treatment choices.
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## SAT0588 MDHAQ AS A USEFUL SCREENING TOOL FOR FIBROMYALGIA IN BUSY CLINICAL SETTINGS

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**Background:** Fibromyalgia (FM) is more prevalent than most rheumatic diseases in the general population, and is seen as a secondary phenomenon in 20–40% of people who have inflammatory rheumatic diseases. Formal ACR criteria to identify FM using self-report questionnaire data have been established (1), but generally not applied in busy clinical settings, in which it is not feasible to use multiple different patient questionnaires. A multidimensional health assessment questionnaire (MDHAQ) is feasible for completion by patients in the waiting area, and informative in rheumatoid arthritis (RA) as well as many other rheumatic diseases, and may be useful in FM. (2)
**Objectives:** To develop a cumulative index based on specific cutpoints of individual MDHAQ measures to screen for patients with primary or secondary fibromyalgia in busy clinical settings.
**Methods:** In two rheumatology settings, patients complete an MDHAQ at each visit. Nine MDHAQ scales were analyzed: 0–10 scores for physical function, pain, patient global estimate, and fatigue; 0–3 sores for sleep quality, anxiety, and depression; a RA disease activity index (RADAI) 0–48 self-report painful joint count and symptom checklist of 60 items. Scores on all MDHAQ scales were compared in Setting A in patients with a clinical diagnosis of primary FM vs RA with no secondary FM, and in Setting B in patients who had secondary FM according to ACR FM criteria vs other patients who did not meet ACR FM criteria. Only patients with complete data for all 9 MDHAQ scales and the ACR FM scales in Setting B were included in the study. Comparisons included frequencies, t tests, cross-tabulations with various cut-points, and receiver-operator curves, as well as a kappa statistic comparing clinician diagnosis of secondary FM vs FM by ACR criteria in setting B. A possible cumulative index based on specific cutpoints of individual measures, analogous to RA classification criteria (3), was explored with several cutpoints of different numbers of MDHAQ measures.
**Results:** In Setting A, 286 patients with RA were compared to 195 with FM. In setting B, 22 patients who had other diagnoses but secondary FM by ACR criteria were compared to 68 patients who had no FM by ACR criteria. All 9 MDHAQ scales were significantly higher in patients with FM compared to patients with RA or other diagnoses in both settings according to t tests and receiver-operator curves (data not shown). In Setting B, the kappa statistic was 0.68, indicating >80% agreement between the clinician diagnosis and ACR FM criteria. The highest levels of significance were seen for symptom checklist, RADAI self-report joint count scores, and pain scores. For example, an index provided a clue to primary or secondary FM at either site, with 2 of the following 3 measures: Pain ≥5, RADAI ≥16, symptom checklist ≥16.

Table 1

| Setting A | | | Setting B | | |
|---|---|---|---|---|---|
| 1° Fibro – Clin (n=195) | RA Clin (n=286) | p | 2° Fibro ACR (n=22) | No 2° Fibro (n=68) | p |
| 156 (80%) | 94 (33%) | p<0.0001 | 18 (81%) | 12 (18%) | p<0.0001 |

**Conclusions:** MDHAQ scales can provide clues to identify primary and secondary FM. Of course, a diagnosis requires a physician history and physical examination, but a screening tool may save time and increase recognition of FM in busy clinical settings.
**Disclosure of Interest:** None declared
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## SAT0589 MEDICATION ADHERENCE IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: A REGISTER STUDY

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**Background:** Previous studies have reported medication adherence ranging from 49.5% to 98.5% in patients with rheumatoid arthritis (RA) [1]. Adherence to TNFi has been estimated to be 59%[2]. Non-adherence has been associated with poorer health outcomes, such as physical disability and increased need for health services.
**Objectives:** The aim of the study was to analyse adherence to self-injectable biologic disease-modifying antirheumatic drugs (bDMARDs), conventional syn-

thetic disease-modifying antirheumatic drugs (csDMARDs) and glucocorticoids in Finnish RA patients using their first bDMARDs.
**Methods:** RA patients starting their first bDMARD in 2007–2011 were identified from the National Register for Biologic Treatment in Finland (ROB-FIN). Restriction to the patients with available baseline data and at least 360 days follow-up with their first bDMARD was made. Data on prescribed medication was recorded in ROB-FIN while medication claims were retrieved from the register of the Social Insurance Institution of Finland. The proportion of days covered (PDC) during a 360-day period was calculated to define adherence. Patient was considered adherent if PDC was ≥80%.
**Results:** Fifty-two percent (n=424) of the 823 patients remained on the first bDMARD and were followed for at least 360 days. Forty-three percent of them (205) were adherent to all prescribed anti-rheumatic medication. CsDMARDs were prescribed to 372 patients of which 53% (196) were adherent while 5% (20) claimed no cdDMARD at all. Methotrexate was the most common csDMARD and was prescribed to 281 patients. The proportions of patients adherent to methotrexate and patients who claimed no methotrexate at all were 60% (170) and 9% (26), respectively. Self-injectable bDMARDs were prescribed to 319 of which 59% (187) were adherent and 8% (25) did not claim any of the prescribed bDMARD. Mean PDC for csDMARDs, methotrexate and self-injectable bDMARDs were 73%, 74% and 74%, respectively.
**Conclusions:** Less than half of the RA patients using bDMARDs were adherent to their antirheumatic medication. However, the current data measures only the medication claims instead of actual use. Moreover, the high proportion of patients lost to follow-up may cause bias to the results.
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## SAT0590 PNEUMOCOCCAL VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS – RESULTS OF A CLAIMS DATA ANALYSIS

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**Background:** Due to autoinflammation and immunosuppressive therapy, patients with rheumatoid arthritis (RA) are at increased risk of developing pneumonia. The German Standing Vaccination Committee recommends standard vaccination against pneumococcal infections from age 60 onwards and for all persons with an increased health risk [1]. In patients with immunosuppression, booster vaccination is recommended every 5 years.
**Objectives:** To assess the vaccination status for pneumonia and the prevalence of hospitalised pneumonia in patients with RA and unaffected population controls in Germany using claims data.
**Methods:** This cross sectional study based on data of a large German statutory health insurance fund (Barmer GEK). The members had to be continuously insured between 2009 and 2013 and had to be between 18 and 99 years old. Insurants who had a diagnosis of RA (ICD-10 codes M05 or M06) in at least two quarters of the year 2013 were matched by age and sex in a ratio of 1: 5 to members without RA. Pneumococcal vaccination (once between 2009 and 2013) was evaluated with regard to age, sex, comorbidities, biologic treatment, primary or rheumatologic care and region of residence. Prevalences of inpatient pneumonia were compared to regional vaccination rates.
**Results:** The data of 111,482 RA patients and 557,410 matched controls were available for analysis. The mean age was 66.2 years and 79.7% were female. Compared to controls, RA patients were vaccinated more frequently (15.0% vs. 10.0%). Vaccination rates were comparable between male and female insurants and increased with older age. In proportion, RA patients <60 years were vaccinated 4–11 times and patients >60 years 1.2–1.5 times more frequently than controls. In East Germany, pneumonia vaccination rates were highest, the lowest rates were found in Southern Germany. Inpatient pneumonia prevalence was 2–3 times higher in RA patients compared to controls and tended to be higher in regions with low vaccination rates.
**Conclusions:** The increased pneumonia prevalence in RA patients confirms their status as a risk group. In consequence, they are vaccinated more frequently than controls, especially if they do not meet the generally recommended age criterion or if other additional risk factors are present. Overall, vaccination rates are still low. Historically, vaccination was performed more frequently in East Germany due to stricter regulations, and the lower pneumonia prevalences in these areas indicate that consequent vaccination may help to reduce pneumonia in RA.

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**Acknowledgement:** This study was funded by the German Federal Ministry of Education and Research (01EC1405).
**Disclosure of Interest:** None declared
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## SAT0591 CONSENSUS STATEMENT FOR THE EVALUATION AND MANAGEMENT OF PATIENTS WITH AUTOIMMUNE AND INFLAMMATORY DISEASES DURING FERTILITY, PREGNANCY, POST-PARTUM AND BREASTFEEDING

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**Background:** Nowadays there is a great variability in evaluation and management of patients with autoimmune and inflammatory diseases during fertility, pregnancy, post-partum and breastfeeding, in part due to lack of knowledge.
**Objectives:** To develop recommendations on the evaluation and management of patients with autoimmune and inflammatory diseases during fertility, pregnancy, post-partum and breastfeeding based on the best evidence and experience.
**Methods:** Recommendations were generated following nominal group methodology and Delphi technique. A panel of experts was established (12 rheumatologists). A systematic literature review and a narrative review (websites, clinical guidelines and other relevant documentation) were performed and presented to the panel in the 1st panel meeting to be discussed and to help define recommendations. A first draft of recommendations was generated and circulated for comments and wording refinements. A national survey analyzing different aspects of this topic was undertaken separately. Then, a Delphi process (2 rounds) was carried out. Recommendations were voted from 1 (total disagreement) to 10 (total agreement). We defined agreement if at least 70% voted ≥7. The level of evidence and grade or recommendation was assessed using the Oxford Centre for Evidence-based Medicine Levels of Evidence.
**Results:** A total of 14 recommendations (see figure) were generated on the preconception period (oral and hormonal anticonception, reproductive techniques), pregnancy (planning, treatment and follow-up), and breastfeeding (treatment and follow-up). High risk situations were included as lupus or antiphospholipid syndrome. A consensus >90% was reached in all but one recommendation.




**Conclusions:** These recommendations are intended to provide rheumatologists, patients, families and other stakeholders a consensus on the evaluation and management of patients with autoimmune and inflammatory diseases during fertility, pregnancy, post-partum and breastfeeding.

**Disclosure of Interest:** None declared
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## SAT0592 PEAK-INCIDENCE AGE IN RHEUMATOID ARTHRITIS HAS NOT SHIFTED IN FINLAND SINCE THE TURN OF MILLENNIUM

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**Background:** Over the recent decades several studies have observed a shift towards higher age at disease onset in the incidence of rheumatoid arthritis (RA). The cause of this phenomenon is unknown.
**Objectives:** To find out whether the peak-incidence age has still been increasing during this millennium.
**Methods:** From the nationwide drug reimbursement register maintained by the Finnish Social Insurance Institution we collected data on all patients with incident inflammatory rheumatic diseases from January 1st 2000 to December 31st 2014. Patients with incident RA were identified by the ICD-10 codes of M05 and M06. The peak-incidence age of this cohort was modelled using the Poisson regression with restricted cubic splines (5 knots).
**Results:** During the observation time altogether 27 764 patients (mean age 61.3 at disease onset, 67.5% female) with a new diagnosis of RA were identified. Table shows the peak-incidence ages as well as mean ages at disease onset during the whole observation time and by 3-year periods. The peak-incidence age remained stable over the 15 years since the turn of millennium. The mean age at disease onset increased slightly in male.

| Period | All | Female | | Male | |
|---|---|---|---|---|---|
| | Peak-incidence age | Peak-incidence age | Mean age at RA onset (SD)* | Peak-incidence age | Mean age at RA onset (SD)** |
| 2000–14 | 69 | 67 | | 70 | |
| 2000–02 | 69 | 68 | 56.6 (15.3) | 70 | 57.7 (13.2) |
| 2003–05 | 68 | 66 | 56.8 (14.9) | 70 | 58.5 (12.7) |
| 2006–08 | 68 | 67 | 56.5 (15.8) | 68 | 59.1 (12.7) |
| 2009–11 | 68 | 66 | 56.8 (15.2) | 70 | 58.8 (13.4.) |
| 2012–14 | 70 | 69 | 57.1 (15.8) | 71 | 59.9 (13.5) |

*p=0.71; **p=0.001 for linearity of the trend in mean age at RA onset.

**Conclusions:** These results suggest that the unknown factors in the population and environment behind the earlier observed shift towards higher age in the incidence of RA have no longer been gaining power during the 21th century.
**Disclosure of Interest:** None declared
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## SAT0593 DISCREPANCY BETWEEN PATIENTS AND PHYSICIANS ON GLOBAL DISEASE ASSESSMENT OF RA AND ITS DETERMINANTS: AN ANALYSIS FROM THE TRAV COHORT

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**Background:** Patient-reported assessments have a considerable weight both in disease activity assessment in practice and response criteria in clinical trials of rheumatoid arthritis (RA). Discrepancies and disagreement on global disease activity between patients and physicians may result in disagreement in treatment decisions in routine care and impact assessment of treatment response in clinical trials as well.
**Objectives:** We aimed to illustrate the amount of discrepancy between patient and doctor global assessments (PGA and DGA) in routine care and asses the determinants thereof.
**Methods:** We used data from RA patients registered in the Turkish Rheumatoid Arthritis Registry (TRAV), a prospective registry established in 2010 in order to record clinical data at each visit of all RA patients seen at three academic rheumatology centers in a routine care setting. Currently 1923 RA patients are registered in TRAV. We used the initial visits of these patients to define a global assessment discrepancy (GAD) variable, GAD=PGA-DGA. We calculated the average GAD, overall correlation of PGA with DGA and constructed linear regression models to determine the predictors of PGA, DGA and GAD. Age, gender, physical function (MD-HAQ score), pain score (numeric rating scale; NRS), fatigue score (NRS), patient's joint assessment (PJA), physician reported tender (TJC) and swollen joint counts (SJC), erythrocyte sedimentation rate (ESR) and center of follow-up were included in these models as potential predictors.
**Results:** The mean age (standard deviation) of the registered patients was 52.0 (12.8) and 1561 (81%) were females. The average PGA was 3.59 (2.99) and the average DGA was 2.85 (2.63) Overall correlation of PGA and DGA was low (0.18) and average GAD was 0.70 (95% CI: 0.53–0.87). Confidence intervals around GAD indicated that on average patients rated their current disease activity as significantly worse than that of physicians. In the regression analyses; MD-HAQ, pain scores and center were common predictors of both PGA and DGA. Additional predictors of PGA were age, fatigue scores and PJA whereas additional predictors of DGA were ESR, PJA, TJC and SJC. Predictors of GAD were pain, fatigue, TJC, SJC, ESR and treatment center (see table).

| | Patient Global | | | Doctor Global | | | Difference | | |
|---|---|---|---|---|---|---|---|---|---|
| | *B* | *CI* | *p* | *B* | *CI* | *p* | *B* | *CI* | *p* |
| (Intercept) | 1.04 | 0.47–1.62 | <0.001 | 1.48 | 0.75–2.16 | <0.001 | -0.41 | -1.33–0.52 | 0.387 |
| Gender (male) | -0.17 | -0.48–0.12 | 0.245 | 0.09 | -0.32–0.39 | 0.833 | -0.19 | -0.68–0.27 | 0.419 |
| Age | -0.01 | -0.02–0.00 | 0.054 | -0.01 | -0.02–0.01 | 0.331 | -0.00 | -0.02–0.01 | 0.586 |
| Pain (NRS) | 0.36 | 0.31–0.40 | <0.001 | 0.12 | 0.06–0.18 | <0.001 | 0.24 | 0.16–0.31 | <0.001 |
| Fatigue (NRS) | 0.28 | 0.24–0.33 | <0.001 | 0.04 | -0.00–0.02 | 0.160 | 0.32 | 0.25–0.39 | <0.001 |
| TJC | -0.00 | -0.01–0.01 | 0.828 | 0.05 | 0.04–0.07 | <0.001 | -0.05 | -0.07–-0.03 | <0.001 |
| SJC | 0.00 | -0.02–0.03 | 0.692 | 0.08 | 0.05–0.10 | <0.001 | -0.08 | -0.11–-0.04 | <0.001 |
| PJA | 0.04 | 0.02–0.05 | <0.001 | 0.02 | 0.00–0.04 | 0.013 | 0.02 | -0.00–0.04 | 0.107 |
| MD-HAQ | 0.39 | 0.12–0.66 | 0.004 | 0.38 | 0.05–0.71 | 0.022 | 0.00 | -0.42–0.43 | 0.984 |
| ESR (log transformed) | -0.07 | -0.20–0.06 | 0.283 | 0.28 | 0.12–0.43 | <0.001 | -0.34 | -0.55–-0.14 | 0.001 |
| *Site-2 | 0.34 | 0.02–0.65 | 0.035 | -0.72 | -1.12–-0.31 | 0.001 | 0.98 | 0.45–1.51 | <0.001 |
| *Site-3 | 0.62 | 0.36–0.89 | <0.001 | -0.61 | -0.93–-0.29 | <0.001 | 1.23 | 0.81–1.65 | <0.001 |
| Observations | | 1321 | | | 1289 | | | 1281 | |
| $R^2$ / adj. $R^2$ | | .373 / .369 | | | .187 / .180 | | | .262 / .255 | |

NRS, numeric rating scale; TJC, tender joint count; SJC, swollen joint count; PJA, patient's joint assessment; MD-HAQ, multidimensional health assessment questionnaire; ESR, erythrocyte sedimentation rate
*Compared to Site-1

**Conclusions:** We found a weak correlation between patient and doctor global assessments of overall disease activity in RA patients under routine care. Higher pain and fatigue scores and different treatment centers were associated with a PGA higher than DGA whereas increasing TJC, SJC and ESR were associated with a DGA higher than PGA suggesting that patients and physicians prioritized different aspects of RA in their global assessments. Variation of the discrepancy by centers warrants further research with respect to a possible impact in multi-center treatment trials.
**Disclosure of Interest:** None declared
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## SAT0594 CHOICE OF BIOLOGICAL AGENTS IN THE PUBLIC HEALTH SECTOR OF TUCUMAN, ARGENTINA

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**Background:** The province of Tucuman is located northwest of Argentina and has a population of 1,448,716 inhabitants, according to the last census. Within the public health sector, access to high-cost medication in patients with rheumatic diseases depends on the provincial government. Since 2012 it carries a registration and monitoring of patients with autoimmune diseases treated with biological drugs in this province
**Objectives:** To determine the preference of biological agents prescribing for patients with Rheumatoid Arthritis (RA), Spondyloarthritis (SpA), Juvenile Idiopathic Arthritis (JIA), Systemic Lupus Erythematosus (SLE) and other connective tissue diseases and describe the reason for change of therapy
**Methods:** A descriptive cross-sectional study was conducted. Registration of children and adult patients, assisted in public hospitals, with drug treatment with high-cost was done in PRIS (Integrated Health Programs) belonging to the Provincial Health System TUCUMAN, from January 2012 to June 2015. In Tucuman, biological drugs are indicated only by rheumatologists, monthly record and approval is based on local recommendations of the Argentine Society of Rheumatology. Demographics data, pathology, drug start, drug switch (2nd, 3rd or 4th choice), kind of switch, continuation or discontinuation of treatment were analyzed.
**Results:** Of 445 registered patients with high-cost drugs, we excluded those with no rheumatic disease (example Vogt-Koyanagi-Harada), primary osteoporosis, and 1 patient with Graft vs Host Disease (sclerodermiform syndrome treated with etanercept). Treatments were then analyzed in 393 patients, 84% women, mean age 47.7 ± 13.7 years, whose diagnoses were: 321 RA (81.7%), 38 SpA (9.6%), 13 JIA (3.3%), 12 SLE (3.1%) and the rest consisting of other connective tissue diseases (vasculitis, MTDC, ITCD).
In RA the first biological drug applied was: etanercept (36%), adalimumab (25%) and tocilizumab (10%). The average treatment time with the first biological agent was 18 ± 14.6 months; 63% received treatment continuously. Required switch to another drug 68 patients (21.2%) being the most frequent cause secondary failure and the most frequently prescribed drug rituximab or tocilizumab. The same trend is maintained then the 2nd switch. Only one patient received in 3 years 5 biological agents (4 switch).
In patients with SLE, rituximab and belimumab were treatments in equal

proportion (50%). In patients with SpA, etanercept was the first drug prescribed and adalimumab in 2nd place.
**Conclusions:** In this register of patients treated with biological drugs in Tucuman, the drug of start choice was etanercept; 21.2% needed to change therapy and the most frequent cause was secondary failure.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6173

## SAT0595 SPONDYLOARTHRITIS PREVALENCE IN EUROPE, A EULAR-ENDORSED SURVEY

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**Background:** The spondyloarthritis (SpA) prevalence has shown a trend to increase in the last two decades, in line with better recognition of the disease as well as the use of new classification criteria (1). The need to estimate and compare the SpA prevalence accross Europe was recognized.
**Objectives:** to estimate the SpA prevalence in several European countries: France, Turkey, Lithuania and Serbia using identical methodology and sampling; to standardize the results with reference to the European Standard Population by using direct method.
**Methods:** A two-step approach was taken. First, a unique detection Questionnaire, covering self-reported diagnosis, SpA classification criteria (ESSG 1991), personal and family history for SpA (2), previously translated and validated for each of the participating countries, was administered to a population sample. A two-stage sampling was carried out on seven areas covering 20 counties in France, seven geographical regions covering 25 administrative provinces in Turkey, two largest cities- Vilnius and Kaunas in Lithuania and two geographical regions covering four counties in Serbia. Second, diagnoses were confirmed by rheumatologists. Results were standardized by age and sex using the European Standard Population, defined as EU-27+EFTA, 2010 estimates.
**Results:** Detection Questionnaire was administered by telephone on 15219 persons in France (3), 6558 in Lithuania (4) and 6213 in Serbia (1), with 64.7%, 64.7% and 63.3% response rate, respectively. In Turkey, Questionnaire was administered face-to face on 4012 persons. Diagnoses were confirmed for 29 cases in France (37.9% male), 18 in Turkey (16.7% male), 27 in Lithuania (55.6% male) and 16 in Serbia (37.5% male). Estimates of the SpA prevalence standardized for age and sex are given in Table 1.

Table 1. Age- and sex- standardized SpA prevalence, % (95% CI) for France, Lithuania, Turkey and Serbia, ≥18 years

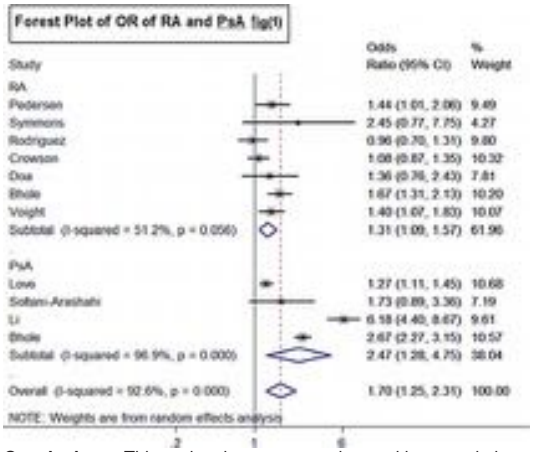
| | Men | Women | Total |
|---|---|---|---|
| France | 0.29 (0.12–0.47) | 0.31 (0.16–0.45) | 0.30 (0.19–0.41) |
| Lithuania | 1.38 (0.68–2.09) | 0.39 (0.16–0.63) | 0.89 (0.78–1.00) |
| Turkey | 0.17 (0.00–0.36) | 0.57 (0.28–0.87) | 0.37 (0.18–0.56) |
| Serbia | 0.38 (0.06–0.71) | 0.32 (0.10–0.54) | 0.35 (0.17–0.54) |

**Conclusions:** Age- and sex-standardized SpA prevalence estimates in France, Turkey and Serbia were in line, but were as twice as high in Lithuania, confirming a north-south decreasing gradient using homogenous sampling and case ascertainment method. Standardized SpA prevalence estimates in men and women were similar in France and Serbia, but not in Turkey and Lithuania. This study adds to previous observation on similarity of RA and SpA prevalence estimates.
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**Acknowledgement:** Study supported by a EULAR grant
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5982

## SAT0596 OBESITY AND INFLAMMATORY ARTHRITIS (RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS)

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**Background:** RA is the commonest autoimmune joint disease & the incidence is 0.5 – 2%. PsA is another common inflammatory condition, which affects women and men equally, with an incidence of 6 per 100,000 per year and a prevalence of about 1–2 per 1000. Metabolic syndrome increases the risk of inflammatory arthrides. This is also known as syndrome X and insulin resistance syndrome. Patients with chronic inflammatory arthritis such as RA and PsA are prone to accelerated atherosclerosis and its complications. We took this systematic review to establish the relationship between obesity & inflammatory arthritis
**Objectives:** The primary aim of the study was to establish whether the obesity has any relationship with the development of inflammatory arthritis. We also looked for the relationship between obesity & serology of RA as well. Smoking & ACPA status also plays role in development of RA
**Methods:** We searched Medline/EMBASE (1946 to July 2013) using the terms Arthritis, Psoriatic, Psoriatic arthritis, Rheumatoid, Rheumatoid Arthritis, seronegative arthritis.mp OR ankylosing spondylitis/ OR ankylosing spondylitis.mp OR spondyloarthritis.mp OR spondyloarthritis/ OR inflammatory arthritis.mp &Obesity/ OR Obesity.mp OR Body Mass Index/ OR Body Mass Index.mp OR BMI.mp. Observational studies were included in the review, which included case control, cohort & cross sectional for both RA and PsA, and the risk of inflammatory arthritis was reported. The data were used for the calculation of effect size ORs/RR with 95% CIs] in obese vs non obese. A Forest plot was created using the OR/RR for both RA & PsA.
**Results:** Ten studies (from 113793 articles) met our inclusion criteria, comprising three case control (954 RA cases; 3273 individuals) & two cohort studies (1372 RA cases; 6419 individuals) & one Cross sectional studies (105 RA cases; 210 individuals) for RA and two cohort (1122 PsA cases and 164103 individuals), ultivariate logistic regression analysis (116137 individual and 350 RA and 644 PsA patients)Hierarchical Cox Regression mode design (250 PsA cases and 1193 individuals) for PSA were found. A significant correlation was found between obesity & the development of inflammatory arthritis.The summary OR for RA was 1.31 (1.09, 1.57) and for PsA was 1.70 (1.28, 4.75) in obese vs non obese patients. The data to establish any relationship between serology and obesity was not completely given in all studies included so it was not possible to conclude on that relationship. On sub group analysis the positive correlation between obesity& inflammatory arthritis was seen in case control studies of RA but for PsA, the relationship has been noted in all the studies included except one with somewhat less effect.




**Conclusions:** This review has suggested a positive correlation with the development of inflammatory arthritis and obesity. These results are demonstrated in case control studies for RA and all studies for PsA. There were mixed results associated with presence and absence of ACPA and development of inflammatory arthritis in patients with high BMI. Further research is indicated using more cohort studies to show the correlation and also the more studies using ACPA/RF to determine the correlation with obesity.
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**Acknowledgement:** DR Amit Saha, Dr Ian Scott
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5078

## SAT0597 FACTORS ASSOCIATED WITH NON-ADHERENCE TO METHOTREXATE AMONG SERBIAN PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

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**Background:** Methotrexate (MTX) is a cornerstone therapy and common first-line drug for patients with rheumatoid arthritis (RA), worldwide. However, there is significant variability in patients' response to MTX, both in efficacy and toxicity. It has been hypothesized that this finding may be partially explained by non-adherence to MTX.
**Objectives:** The aims of this study were to assess patients' self-reported adherence to MTX and to identify factors associated with non-adherence.
**Methods:** In the period between November 1 and December 15, 2015, 315 consecutive RA patients who were treated in one of three randomly chosen Serbian clinics were enrolled in cross-sectional study. The inclusion criteria were: age $\geq$18 years, diagnosis of RA of at least 6 months, current MTX use for at least 1 month (with or without concomitant usage of another RA drugs), and written informed consent. The associations between investigated demographic and clinical characteristics of the patients and non-adherence to MTX were assessed applying univariate logistic regression analysis. Furthermore, baseline variables with a significant association with non-adherence in univariate logistic regression analysis (defined as $p<0.05$) were entered into a multivariate logistic regression equation to identify independent predictors of non-adherence to MTX.
**Results:** Study population was predominantly female (74.0%), and the average current age was 56.0±12.5 years. The median duration of RA was 8 years, while the median duration of MTX treatment was 5 years. The majority of the patients (82.2%) reported using the oral formulation of MTX. The median maximum dose of MTX which responders received was 15 mg per week. Most of the participants in our survey stated that MTX was well tolerated, while 20% of RA patients reported poor tolerance. The overall prevalence of non-adherence to MTX was 24.8%. Forgetting to take medication (43.7%) was the most commonly-reported reason for MTX non-adherence. According to the results of univariate regression analysis the following factors are significantly associated with non-adherence to MTX: younger age (OR=0.963; $p<0.001$), employment (OR=1.859; p=0.029), poor self-reported MTX tolerance (OR=1.289; p=0.041), laboratory blood analyses performed less than once in three months (OR=2.170; p=0.043) and concomitant use of biological therapy (OR=2.312; p=0.002). Finally, in the multivariate regression model the following variables remained statistically significant and were identified as independent predictors of non-adherence to MTX: younger age (OR=0.969; p=0.006), laboratory blood analyses performed less than once in three months (OR=2.735; p=0.015) and concomitant use of biological therapy (OR=2.067; p=0.017).
**Conclusions:** The results of our study have shown that about one forth of RA patients met the criteria for non-adherence to MTX. Identification of vulnerable groups who are likely to be non-adherent to MTX has practical implications in identifying the patients who would benefit from alternative RA treatments and, would present an opportunity for timely intervention and optimization of treatment response.
**Disclosure of Interest:** N. Damjanov: None declared, J. Nedovic: None declared, M. Lazarevic: None declared, S. Mamula Masic Grant/research support from: provided by Roche d.o.o., Employee of: Roche d.o.o.
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## SAT0598 OUTCOMES, RATES, AND RISK FACTORS OF TRANSITION OF RAYNAUD'S PHENOMENON TO A CONNECTIVE TISSUE DISEASE: SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** A number of observational studies were carried out in patients with isolated Raynaud's phenomenon (RP) to investigate the predictors of transition to RP secondary to connective tissue diseases (CTDs). Data from a meta-analysis, including studies until June 1996, highlighted the potential role of nailfold capillaroscopy and/or antinuclear antibodies (ANAs) in predicting such transition [1].
**Objectives:** To provide an updated comprehensive review and meta-analysis on the rates and the role of predictors of transition to CTDs and systemic sclerosis (SSc) in patients with RP.
**Methods:** A systematic search of observational studies was undertaken using Medline and Embase (07/1996 to 08/2014). From the list of records retrieved, studies were screened by titles/abstracts and the full papers were sought where abstracts were felt to be relevant. Cohort studies reporting incidence and risk factors of transition from primary RP (pRP) or suspected secondary RP (ssRP) to CTDs were selected and data collected in ad hoc forms. pRP was defined according to Leroy and Medsger criteria (no history or physical findings suggestive of a secondary cause, normal capillaroscopy, negative serologic findings); ssRP was defined in presence of positive ANAs and/or abnormal capillaroscopy (even in association with symptoms or physical findings suggestive of a secondary cause without fulfilling criteria for a definite CTD). Relative risk (RR) and 95% confidence interval (CI) were extracted or calculated to present the association between risk factors and transition to CTDs. Random effects model was used to pool the results.
**Results:** From 2.221 articles captured, 36 met the predefined criteria, 29 were excluded on full text, and 7 selected studies provided information on transition from pRP and/or ssRP to secondary RP: 5 prospective and 2 retrospective cohort studies. Six studies included a total of 4051 patients with pRP with a cumulative mean follow-up of 20241 person-years (mean follow-up 4.9±2 years); a total of 1220 transitions to overt CTDs were recorded (pooled incidence rate 2.5/100 person-years of observation, range 0–7.7); among these, 321 transitions were to SSc (pooled incidence rate 1.58/100 person-years, range 0–2.8). Five studies included 657 patients with ssRP with a cumulative mean follow-up of 2377 person-years (mean follow-up 3.6±1.1 years); a total of 188 transitions to CTDs were recorded (pooled incidence rate 7.9/100 person-years, range 3.3–26) and 135 to SSc (pooled incidence rate 5.7/100 person-years, range 2.1–13). With respect to the patients with pRP, having ANA without capillary abnormalities provided a modest risk to develop SSc (pooled RR 2.8, CI 2.1–3.8), even weaker resulted the association between capillary abnormalities without ANA and the risk of SSc transition (RR 1.3, CI 0.7–2.4). On the other hand, the coexistence of ANA and abnormal capillaroscopy significantly increased the risk of transition to SSc (RR 8.1, CI 6.9–9.7).
**Conclusions:** A low incidence rate of transition from pRP to overt CTDs was confirmed. In patients with ssRP, whilst accepting the influence of selection bias of different studies, there appears to be a strong risk of transition toward a CTD regarding the concomitant presence of ANAs and abnormal capillaroscopy.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5250

## SAT0599 AUTOIMMNUNE DISEASE IN ACUTE CORONARY SYNDROMES. CLINICAL IMPLICATIONS

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**Background:** Patients with autoimmune diseases (AID) have a high burden of cardiovascular disease leading to premature morbidity and mortality[1]. But it is unclear if it is due to a higher prevalence of cardiovascular disease, to a worse case fatality or to a different management after an index event.
**Objectives:** The aim of the study is to assess the prevalence of AID in patients with acute coronary syndrome (ACS), the management and prognostic implications.
**Methods:** The study included consecutive patients admitted after ACS from January 2011 to May 2014. For AID patients, in-hospital management and ACS presentation was compared to non-AID patients. We also compared in-hospital and 1-year major adverse events (MACE): death, recurrent myocardial infarction, stroke and major bleeding, between groups. The percentage lost to follow-up was $<$1%.
**Results:** Of 964 patients, 53 had AID (5.5%): 11 rheumatoid arthritis, 9 inflammatory bowel disease, 7 ankylosing spondylitis, 7 psoriatic arthritis, 5 polymyalgia rheumatica, 4 systemic lupuserythematosus and 10 miscellanea. Mean evolution of the disease was 14±3 years. No significant differences were found in clinical and demographics characteristics between groups except for a higher percentage of previous stable coronary heart disease in non-AID patients. Compared to non-AID patients, AID patients had similar clinical ACS presentation and no differences were found with respect to revascularization strategies or medical treatment at discharge. Overall there were 207 MACE (69% during hospitalization): 108 deaths, 52 recurrent myocardial infarctions, 19 ischemic strokes and 28 major bleedings. The two groups had comparable rates of MACE both during hospitalization (9.6% vs 12.2%, p=0.58) and at 1 year (26.4% vs 19.1%, p=0.19), AID vs non-AID respectively. The presence of AID was not associated with increased in-hospital mortality (OR 1.1, 95% CI 0.4 to 3.3) but it was a risk factor for higher 1-year crude mortality (OR 2.2, 95% CI 1.1 to 4.4), with a trend to higher 1-year mortality after multivariable adjusting (OR 1.7, 95%CI 0.8 to 3.9).
**Conclusions:** The presence of AID did not change ACS presentation and clinical management. Moreover it is not independently associated with worse outcomes during hospitalization although there is a trend to higher 1-year mortality.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5690

## SAT0600 THE APPROACH OF RHEUMATIC AND MUSCULOSKELETAL DISEASES COMBINING VIRTUAL AND FACE-TO-FACE CONSULTATIONS IS A RESOURCE-SAVING STRATEGY

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**Background:** The high prevalence of rheumatic and musculoskeletal diseases (Ref 1) along with the limited resources allocated to the specialty of rheumatology, has made us think about new models of care. A mixed virtual and face-to-face rheumatology consultation, working together Lo Morant's Health Center (HC) and the Rheumatology Section of Alicante Hospital, began to work in May-2014. (Ref 2).
**Objectives:** To analyse the causes of consultation from primary care to rheumatology, the distribution of the pathologies and the way they were resolved.
**Methods:** The primary care physician (PCP) made a virtual consultation (VC) to the rheumatologist within the electronic record system "Abucasis". Once a month, the rheumatologist and one of the PCP attended a face-to-face consultation (F2F) in the HC. The same day, a formative-informative session took place in the HC with rheumatologist and PCPs attendance. Variables recorded: Number of patients, VC, F2F, technics performed, diagnosis and attitude. STATISTICAL ANALYSIS: Descriptive variables.
**Results:** The period between May-2014 to December-2015 was analysed. 806 consultations (607 VC, 199 F2F, 537 patients), were performed. After VC, 75 patients (13,9%) were referred to specialised rheumatology consultation (SRC), but 280 were resolved (52,1%, 132 mechanical problems (47,1%), 51 osteoporosis (18,2%), 40 tendinitis (14,2%), 12 fibromyalgia (4,3%), 8 microcrystal diseases (2,8%), 5 inflammatory/autoimmune (1,7%), 5 no disease (1,7%), 21 were referred to other speciality (7,5%)). In F2F, 181 patients were attended (33,7%), 21 joint aspiration with microscopic synovial fluid exam, and 104 local injections were performed, 13 patients were referred to other speciality, and 31 were referred to SRC. The final diagnostics of the 106 patients referred to SRC were: 24 mechanical and tendinosus problems (22,8%), 22 chronic arthritis (20,9%), 21 microcrystal diseases (20%), 12 autoimmune diseases (11,4%), 9 severe osteoporosis (8,5%), 2 cancers, 2 no disease, 1 Sudeck atrophy, 1 neuropathy.
Comments:VC avoided displacement of 301 patients (280 resolved, 21 referred to appropriate speciality), reducing the lost of working days and displacement costs, and diminishing SRC load. Minor problems (soft tissue and mechanic problems) were usually resolved in F2F of HC, while severe and inflammatory pathologies were mainly referred to SRC, where chronic patients are managed.
**Conclusions:** Mixed rheumatology consultation is very effective, avoids unnecessary patients displacements, and makes easier the appropriate level of attendance of pathology. Continuing education in primary care and tight relationship with rheumatologist allowed a better referral of patients, reserving SRC for more severe and complicated situations that required it.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4950

## SAT0601 INCIDENCE OF SERIOUS INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS EXPOSED TO A-TNF THERAPY. RESULTS FROM BIOBADABRASIL REGISTRY

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**Background:** The safety profile of biologic drugs might have substantial regional differences. Since 2009, the Brazilian Society of Rheumatology runs BiobadaBrasil, a registry for monitoring of biologic therapies in rheumatic diseases, in collaboration with other Latin America countries (BiobadaAmerica) and with Biobadaser
**Objectives:** To report the incidence of serious infectious adverse events (SIAE) in Rheumatoid Arthritis (RA) and Spondyloarthritis (SpA) patients exposed to biologic a-TNF drugs in Brazil
**Methods:** BiobadaBrasil counts on thirty two centers, from almost all Brazilian states, that prospectively include patients with active rheumatic diseases who started a biologic drug or a synthetic DMARD as a parallel control group. A constant three level monitory of data quality is maintained (online, by phone and "in situ"). This study focuses on SIAE (for definition: Protocolo 1.1 at https://biobadaser.ser.es/biobadamerica/Brasil/cgi-_bin/upload/documentacion.aspx) in RA and SpA (Ankylosing Spondylitis+Psoriatic Arthritis) patients exposed to a-TNFs from January 2009 to June 2015. Time of exposure was set from start of the drug to the date of last administration or censorship. Continuous variables were expressed as mean with standard deviation (SD). SAE incidence rate was calculated per 1000 patient/years with 95%CI
**Results:** 1601 subjects with RA (1024) and SpA (577) exposed to a-TNF drugs were included in BiobadaBrasil, 6298 p/y, follow-up 2.9 (2.3) yrs, 65% females, at baseline: age 52 (12.5) yrs, disease duration 8.6 (8) yrs. Controls were 572 (RA 528, SpA 44), 2093 p/y, follow-up 3.6 (2.2) yrs, 90% females, at baseline: age 55 (13) yrs, disease duration 5.3 (7.3) yrs. The incidence rates of SIAE were: a-TNF RA & SpA 35 [30,40] vs controls 15 [10,21], ratio 2.34 [1.6,3.5] $p<0.001$, a-TNF RA 43 [37,50] vs a-TNF SpA 21 [16,28], ratio 0.5 [0.36,0.69] $p<0.001$. Subsequent a-TNF was associated with a higher incidence of SIAE when compared with first (ratio 1.6 [1.17,2.17], p=0.0013). When only RA patients were considered, incidence ratio between a-TNFs and controls raised to 3.11 [2.06,4.86] $p<0.001$ and Adalimumab comes out as the a-TNF with a lower incidence of SIAE, 29 [22,39] vs Infliximab 55 [43,70], ratio 0.53 [0.35,0.79] p=0.0006, with no statistical difference between Etanercept 48 [37,62] and Infliximab, ratio 0.87 [0.6,1.26] p=0.22. In both groups, a-TNF and controls, respiratory and urinary tracts serious infections accounted for 2/3 of all events, followed by skin/soft tissues and osteo articular and SIAE were not statistically associated with age, disease duration or corticosteroid use
**Conclusions:** In BiobadaBrasil registry, patients exposed to a-TNF drugs had an incidence rate of serious infections 2-fold that of the control group, significantly lower in SpA than in RA.
**Acknowledgement:** for data monitoring P Cabral, for contributing to BiobadaBrasil registry, L.Barbosa, W.Chahade, A.Hayata, A.Kakehasi, M.Pinheiro, A.Ranzolin, M.Scheinberg, F.Sztajnbok, I.Silveira
**Disclosure of Interest:** None declared
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## SAT0602 IS A BRIEF EDUCATION INTERVENTION EFFECTIVE TO MOTIVATE PATIENTS TO STOP SMOKING?

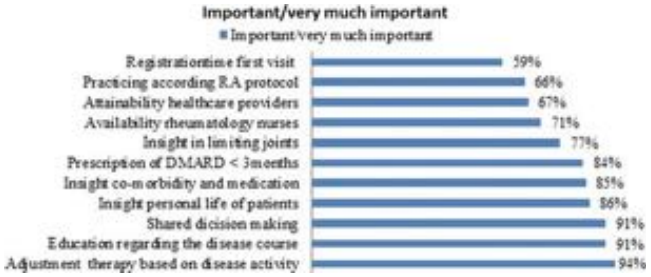
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**Background:** Smoking has been associated with an increased risk of developing rheumatoid arthritis (RA), more severe disease and poor response to disease modifying drugs (DMARD). Motivation is the most important aspect of giving up smoking and also awareness of its ill-effects, self-confidence and support.
**Objectives:** We have looked at the immediate effect on patient motivation to stop smoking by creating awareness of its ill-effects.
**Methods:** We surveyed Rheumatology outpatients with an anonymous questionnaire including demographics, smoking status, education status, employment status and awareness of the ill-effects of smoking. Motivation to stop smoking was assessed by 10cm Visual analogue scale (VAS) before and after receiving information on adverse effects of smoking on RA. The information provided was about increased risk of RA, severe disease and poor response to DMARD.
**Results:** 100 unselected patients completed the questionnaire: 74% female; 46% RA; 22% current smokers; 37% never smokers; 41% ex-smokers. 68% of patients in all categories had attended secondary school. A higher proportion of never smokers had attended University compared with current smokers [20% (8/37) vs. 5% (1/22)]. A higher proportion of current smokers were unemployed as compared with never smokers [32% (7/22) vs. 8% (3/37)]. 50% of patients stated that they had never asked about smoking during consultations. When asked how important smoking is in arthritis, 55% of all patients scored >8/10 on a VAS (0=not bad /10=very bad). There was no significant difference in understanding the importance of smoking on arthritis between current smokers (VAS mean; SD 7.06; 2.35) and never smokers (VAS mean; SD 7.37; 2.15) (p=0.115) and between current smokers and ex-smokers (Mean; SD 7.74; 1.87) (p=0.23).
73% (16/22) of current smokers motivation to give up smoking score increased after they were given information on adverse effects of smoking on RA (mean VAS 4.43 before; 5.79 after) (p=0.03). 27% (6/22) did not change, none decreased.
50% (11/22) of patients felt lack of support and help prevented them stopping smoking. Preferred methods for smoking cessation help were: leaflets 41%; verbal advice 9%; GP review 18%. 54% (22/41) of ex-smokers were happy to speak to the current smokers to provide tips on stopping smoking.
**Conclusions:** This small study suggests that brief educational intervention may help motivate patients to give up smoking. Lack of support is a common difficulty patients perceive when they try to give up smoking. As RA outcomes are worsened by smoking, clinicians need to be more proactive about promoting smoking cessation. Outpatient appointments provide a good opportunity for this.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5084

## SAT0603 EVALUATING QUALITY OF CARE IN RHEUMATOID ARTHRITIS: PATIENTS PERSPECTIVE

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**Background:** Standardized measurement of outcomes allows for quality improvement of health care delivery. While a total of seven sets of RA quality indicators are available in the international literature, none of them reports extensively on the patients' representation (1).
**Objectives:** As patients and healthcare providers have a different perspective regarding health care outcomes, we studied the patients' perspective on quality of care and incorporated this in the Dutch national Quality Registry for Rheumatoid Arthritis (DQRA).
**Methods:** A group of patients (n=6) connected through the Dutch Arthritis Foundation, was consulted by focus group methodology and inquired about their positive and negative experiences and thoughts with rheumatology-care. During the meeting, all patients were required to form a "top-three" of most important domains; resulting domains were ranked in order of importance by the group. A set of nine domains (physician domains), defined by Dutch rheumatologists in a separate process were then introduced. These domains were compared with the domains as formed by the patients, resulting in the preliminary set of domains. The preliminary set of domains was sent to all RA members of the Dutch Arthritis Foundation panel (n=1132) through an online survey. Patients were asked to score all items on a seven-point Likert scale from "not important" to "extremely important", and to rank the items into a top five of important domains for the evaluation of quality of care.
**Results:** The focus group discussion resulted in 7 domains: 1) education regarding the disease course; 2) attainability of healthcare providers; 3)availability of rheumatology nurses; 4) shared decision making; 5) insight in personal life of patient 6) insight in co-morbidities and co-medication 7) insight in limiting joints (for example after arthrodesis). The physician domains that were added to this set were; 8) adjustment of therapy based on disease activity; 9) prescription of a DMARD <3 months of diagnosis; 10) practicing according to a RA protocol and 11) registration time to first visit to rheumatologist.
A total of 640 RA patients completed the online survey. Domains considered as "important or extremely important" for rheumatology care are displayed in figure 1. The 5 domains that were ranked highest through the online survey included: 1) adjusting therapy based on the disease activity; 2) insight in personal life of patient; 3) shared decision making; 4) education regarding the disease course; 5) insight in co-morbidity and co-medication.

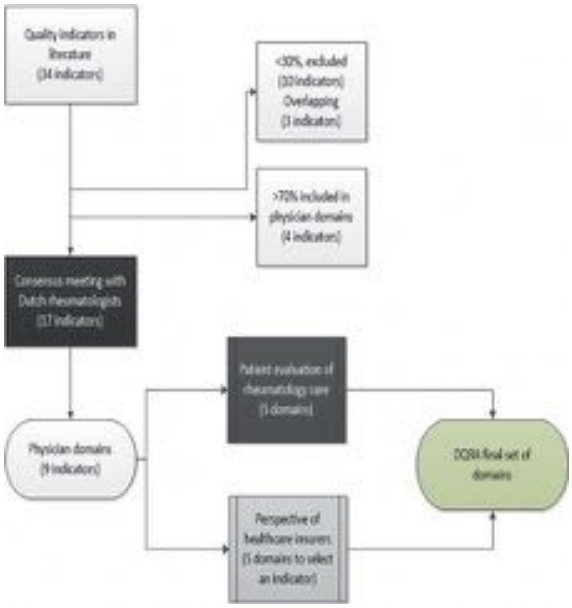



**Conclusions:** This is the first study that has incorporated the patients' perspective on quality of RA care in the development of a national quality indicator set. Five domains were identified by patients, reflecting their perspective on quality of RA care.
**References:**
[1] S. mahmood et al. 2015. Best Pract Res Clin Rheumatol
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5349

## SAT0604 DUTCH QUALITY REGISTRY RHEUMATOID ARTHRITIS: DEVELOPMENT OF QUALITY INDICATORS

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**Background:** While innovation and research has provided high quality care, we are largely unable to quantify this increase in quality in clinical practice, while costs are rising to unacceptable levels. As health care facilities are unable to measure their performance (use of different measures), no information is available about quality of care between facilities.
**Objectives:** In order to standardize care processes and to give more insight in the provided care in The Netherlands, the Dutch Quality registry Rheumatoid Arthritis (DQRA) is developed. The rise of the DQRA and selection of quality indicators is described in this abstract.
**Methods:** Stakeholders involved in the development of the DQRA were; rheumatologists, patients and healthcare insurers. All were approached in separate ways:
Rheumatologists: Expert group meetings were held to evaluate the current practice in the represented hospitals and regions. Available quality indicators for rheumatoid arthritis (RA) from the literature were presented and merged into an online survey. Indicators were selected based on their validity, feasibility and importance regarding the quality of rheumatology care. Indicators selected by <30% of rheumatologist were excluded; indicators selected by >70% of rheumatologists were directly included in the set of physician domains (domains are needed to form the actual indicator, e.g. disease activity). Remaining indicators were discussed further during a consensus meeting and were included to the physicians domains.
Patients perspective was assessed by means of a focus group discussion (n=6), combined with an online survey (n=1132). This approach resulted in the patients' perspective regarding quality of rheumatology care.
Healthcare insurers were also approached by means of a focus group discussion (n=6). The physicians' domains and the domains as formed by the patients were presented to representatives of healthcare insurers. This discussion resulted in domains that can be used to select an indicator.
During a final expert group meeting in which all three stakeholders were represented, the final set of domains was discussed and established after final adjustments.
**Results:** The physician domains consist of; tender and swollen joint count (28); acute phase reactant; patient and physician VAS (together forming the disease activity) and drug-treatment. Patient-evaluation of rheumatology care is measured by the following domains; 1) adjusting therapy based on disease activity; 2) insight in the patient's personal life; 3) shared decision making; 4) education about the disease (course); 5) insight into co-morbidities and co-medication).
These domains form the foundations for the development of quality indicators. Indicators will be selected based on the characteristics formed by healthcare insurers; 1) ability to detect quality differences; 2) ability to detect the expediency; 3) clearness; 4) can be standardized and 5) ability to detect the added value of a certain therapy.




**Conclusions:** The DQRA is the first Dutch quality registry with the ambition to comprise all RA patients in the Netherlands. A minimal set of quality domains is formed from the perspectives of three stakeholders. Prospective data from the registry will be used to develop valid and reliable quality indicators ("norms") that help clinicians to continuously improve their practices.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5580

## SAT0605 TOWARDS A TAXONOMY THAT IS SCIENCE-BASED AND CLINICALLY USEFUL: THE NEW WHO - ICD11 CLASSIFICATION OF MUSCULOSKELETAL PAIN DISORDERS

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**Background:** The current ICD 10 classification of musculoskeletal pain disorders is not relevant, combining anatomical, pathophysiological and clinical approaches. In 2015, the WHO started a new program for ICD11 classification, to be delivered in 2017. In this new program, physicians and researchers from rheumatology and pain clinics have been involved for the musculoskeletal pain chapter that will be developed in collaboration with the IASP/ International Association for the Study of Pain.

**Objectives:** To develop a taxonomy for musculoskeletal (MSK) pain conditions that merge insights from both pain pathophysiology and rheumatological clinical classification for both clinical and scientific uses.
**Methods:** As members of the IASP-WHO Task Force for the Classification of Chronic Pain in ICD-11, the authors have reviewed the taxonomy of musculoskeletal conditions in ICD-10 and earlier iterations and conventional taxonomy in rheumatology, all of which are disease-based and commonly do not reflect the problems encountered in the practice of pain medicine. The authors have pragmatically integrated recent advances in musculoskeletal pain pathophysiology into diagnostic labelling in this diverse field as a prelude to a multiaxial approach.
**Results:** Two sets of taxonomic reforms will be presented. The first conforms to the format required by ICD which remains anatomically or disease based. This comprises four main categories: chronic musculoskeletal pain from persistent inflammation; chronic musculoskeletal pain associated with structural changes; chronic musculoskeletal pain due to disease of the nervous system; and chronic primary musculoskeletal pain (to include spinal pain and widespread pain).
The second prefers classification by pain mechanisms and identifies conditions characterized by nociceptive pain and primary hyperalgesia and those characterized by nociplastic* pain and secondary hyperalgesia.
**Conclusions:** The authors contend that the somatic dimension of musculoskeletal pain conditions is better conceptualized by incorporating underlying pain pathophysiology in conventional disease labels rather than by describing MSK pain as different disease entities or as "pain syndromes". These proposed new taxonomic sets are not mutually exclusive and can probably be integrated for clinical purposes, not only in pain clinics but also in rheumatology settings. Although they refer to the somatic or biomedical dimension of the complex experience of musculoskeletal pain, they can be readily integrated with the psychological and social axes of evolving taxonomy.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5492

## SAT0606 THE COMORBIDITY BETWEEN SYSTEMIC LUPUS ERYTHEMATOSUS AND MALIGNANCIES: A CROSS-SECTIONAL POPULATION BASED STUDY

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**Background:** Autoimmune conditions often reflect dysregulation of the immune system, which appears to be of great significance in the development of malignancies [1]. Previous studies support an association between systemic lupus erythematosus (SLE) and malignancies; however, their findings on specific malignancies are inconsistent, and their design might not represent the population of SLE patients, due to selection bias [2–4].
**Objectives:** Our goal was to investigate the association between the presence of SLE and various malignancies, in a large-scale population-based study.
**Methods:** Data for this study was collected from the database of "Clalit Health services", the largest state-mandated health service organization in Israel. All adult members diagnosed with SLE were included (n=5,018) and their age and sex-matched controls (n=25,090), creating a cross-sectional population-based study. Medical records of all subjects were analyzed for documentation of malignancies. Logistic regression was preformed to control for age, gender, BMI, smoking and socioeconomic status.
**Results:** Diagnosis of malignancy (of any type) was more prevalent in the SLE population in comparison to controls (odds ratio [OR] 3.35, 95% confidence interval [CI] 3.02–3.72). Also, SLE diagnosis was found to be independently associated with higher proportions of non-Hodgkin lymphoma (OR 3.02, 95% CI 2.72–3.33), Hodgkin lymphoma (OR 2.43 95% CI 1.88–2.99), multiple myeloma (OR 2.57, 95% CI 1.85–3.28), cervix uteri malignancies (OR 1.65, 95% CI 1.10–2.20) and genital organ malignancies (OR 2.32 95% CI 1.42–3.22), after adjustment for confounding variables.

| | Non-Hodgkin lymphoma (OR, 95% CI) | Hodgkin lymphoma (OR, 95% CI) | Multiple myeloma (OR, 95% CI) | Cervix uteri malignancies (OR, 95% CI) | Genital organ malignancies (OR, 95% CI) |
|---|---|---|---|---|---|
| Age | 1.04 (1.03-1.05) | 1.01 (0.99-1.03) | 1.06 (1.04-1.09) | 1.02 (1.01-1.04) | 1.06 (1.03-1.09) |
| Sex - male | 1.28 (0.91-1.66) | 1.49 (0.84-2.15) | 2.52 (1.78-3.27) | - | 0.53 (-0.96-2.02) |
| Smoking | 1.06 (0.74-1.39) | 0.75 (0.14-1.36) | 1.78 (1.04-2.52) | 1.26 (0.73-1.78) | 0.81 (-0.23-1.84) |
| BMI | 1.0 (0.98-1.03) | 0.97 (0.92-1.03) | 0.92 (0.84-0.99) | 0.99 (0.95-1.04) | 0.95 (0.86-1.03) |
| SLE | **3.02 (2.72-3.33)** | **2.43 (1.88-2.99)** | **2.57 (1.85-3.28)** | **1.65 (1.10-2.20)** | **2.32 (1.42-3.22)** |

**Conclusions:** SLE diagnosis was found to be independently associated with higher proportions of malignancies, specifically hematologic malignancies. These findings should be considered when treating SLE patients, and possibly influence their screening routine.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2734

## SAT0607 PATTERNS OF ADOPTION OF TREAT-TO-TARGET APPROACHES IN RHEUMATOID ARTHRITIS AND THEIR IMPACT ON PATIENT BURDEN IN EUROPE

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**Background:** Heterogeneity in treatment strategies exist to varying degrees in the management of rheumatoid arthritis (RA). Assessment of impact of treat-to-target (T2T) approaches implemented in clinical practices may help identify best practices and to alleviate patient (pt) burden.
**Objectives:** To assess the patterns of adoption of T2T approaches in RA and their impact on patient burden in Europe (EU5: UK/France/Germany/Italy/Spain).
**Methods:** A multi-center medical chart-review study of RA pts was conducted among physicians (rheumatologists) in hospitals/private practices in EU5 to collect de-identified data on pts who were currently on (or recently discontinued $\leq$3mo) a biologic. Physicians were screened for practice-duration and patient-volume and recruited from a large panel to be geographically representative of respective countries. Patient charts of ~5 successive pts visiting each center/practice during study period were selected. Physicians abstracted patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease status (incl. assessment of "disease remission" per physician clinical judgment (both objective & subjective)). The adoption of the following T2T approaches was investigated: T2T-1: disease remission, with normalization of function; T2T-2: alleviate symptoms of disease or improve patient reported outcomes; T2T-3: Normalization of function or lower severity scores or inhibits disease progression; T2T-4: use validated composite measures of disease severity involving DAS28, tender joint count (TJC) or swollen JC (SJC) frequently; T2T-5: consider comorbidities (e.g., diabetes, obesity, heart disease), patient factors and drug-related risks; T2T-6: measure disease severity every month for moderate/severe disease pts and within 1–6 month frequency for mild/remission pts; T2T-7: Consider structural changes, functional impairment and comorbidity in addition to T2T-4; T2T-8: adjust drug therapy every 3mo until treatment target is reached; T2T-9: maintain desired treatment target for remaining course of disease; T2T-10: involve patient in treatment decisions. Pts for whom $\geq$7 T2T approaches applied (High-T2T) were compared to the rest (Low-T2T).
**Results:** In 2Q2015, 1331 RA patient charts were abstracted across EU5; adoption of T2T approaches were:T2T-1:36%, T2T-2:38%, T2T-3:70%, T2T-4:87%, T2T-5:31%, T2T-6: 63%, T2T-7: 60%, T2T-8: 86%, T2T-9: 52%, T2T-10: 64%; High-T2T: 39% (range: 29% (Italy)-44% (UK/Spain)), Low-T2T: 61% (range: 56% (UK/Spain)- 71% (Italy)). Age, gender, time since RA diagnosis, duration of current/recent biologic and frequency of physician visits were similar between High-T2T & Low-T2T, whereas, time from diagnosis to first biologic initiation (40.7/46.6mo), % positive rheumatoid factor (89%/83%; $p<.01$), % positive anti-CCP (76% /71%; $p<.05$), mean TJC (3.5/4.3; $p<.01$), mean SJC (2.4/2.9; $p<.05$), school/work lost because of disease in last 3mo (3.0/4.6 days), % in remission (78%/47%; $p<.01$) differed between High-T2T/Low-T2T respectively.
**Conclusions:** A significantly higher proportion of pts in High-T2T group were in remission and exhibited relatively lower disease burden. These observed patterns warrant further scrutiny to determine the best practices and profile pts still in need for improvement to alleviate burden.
**Disclosure of Interest:** S. Narayanan Employee of: Ipsos Healthcare, Y. Lu Employee of: Ipsos Healthcare, R. Hutchings Employee of: Ipsos Healthcare, S. Mentzer Employee of: Ipsos Healthcare
**DOI:** 10.1136/annrheumdis-2016-eular.5189

## SAT0608 PERCEPTION OF ANTI-TNF BIOSIMILARS AMONG PAYERS IN EUROPE

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**Background:** Tumour necrosis factor inhibitor class (anti-TNFs) represent the most widely prescribed biologic medications globally to manage chronic immunologic conditions. Biosimilars in this arena may provide an effective alternative

to curtail looming economic burden associated with managing these conditions while alleviating patient burden. A survey of rheumatologists revealed moderate barriers to uptake of biosimilars, with 60% in key European countries (EU5: UK/France (FR)/German (DE)/Italy (IT)/Spain (ES)) reporting definitely or highly likely to prescribe a biosimilar when available. (Narayanan & Nag, 2015) Regional and national payer perceptions concerning biosimilar adoption is evolving.

**Objectives:** To assess the perception of anti-TNF biosimilars among national, regional and hospital payers in the EU5.

**Methods:** A cross-sectional survey was conducted in the EU5 among individuals meeting the following inclusion criteria: have a clinical background in immunology and play a role in influencing the approval of new drugs in that area, must have participated in a review of autoimmune diseases for reimbursement, funding, and/or formulary placement decisions within the last 24 months at national or regional level, and must be in a role that influences hospital formulary decisions for autoimmune diseases (within hospital payer category). A forty-minute online survey assessed the overall perception of anti-TNF biosimilars, specific barriers to prescribing them and factors (besides price) influencing the endorsement of biosimilars.

**Results:** Eighty four payer stakeholders across EU5 (UK:15, FR:20, DE:15, IT:15, ES:19) participated; 61% (range: 20% (FR)–100% (UK)) reported highly or very favorable perception/opinion of biosimilars. Factors influencing their overall perception were: cost-benefit opportunities (23%), comfortability with biosimilar efficacy (23%), healthy market competition (13%) and saving opportunity and long-term sustainability (12%); 12% reported efficacy and safety concerns. On a scale of 1–7 (1: not at all important; 7: very important), rating of importance of place of manufacturing of anti-TNF biosimilars to be the same as the originator drug was 4.3 (range: 3.0 (DE)–5.6 (IT)); rating of level of comfort with extrapolation of clinical data permitting approval of a biosimilar for a therapeutic indication in which it has not been clinically evaluated, but for which an originator is approved was 4.8 (range: 4.3 (FR)–5.4 (ES)). 29% (range: 20% (UK/FR)–42% (ES)) reported the quality of clinical and economic data they have access to or would require to evaluate biosimilars to be very or extremely high. Top-5 factors influencing endorsement of biosimilar were availability of robust safety and efficacy data, comparable long-term clinical response, product quality and reliability of product supply. Majority (94%) expected biologically naïve patients to benefit the most from biosimilars.

**Conclusions:** Payer stakeholders reported positive perceptions towards biosimilars, while expressing some concerns towards product attributes. Evidence generation and communication efforts addressing these payer perceptions may facilitate optimal access to biosimilars.

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**Disclosure of Interest:** S. Narayanan Employee of: Ipsos Healthcare, Y. Lu Employee of: Ipsos Healthcare, R. Hutchings Employee of: Ipsos Healthcare, S. Mentzer Employee of: Ipsos Healthcare

**DOI:** 10.1136/annrheumdis-2016-eular.5223

## SAT0609 VITAMIN D BENEFICIAL EFFECT ON ARTERIAL HYPERTENSION

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**Background:** Both vitamin D deficiency and hypertension are increasingly prevalent public health concerns in developing countries.

**Objectives:** This study aims to assess 25-hydroxyvitamin D (25(OH)D) status in postmenopausal women and to analyze its relationships with arterial hypertension.

**Methods:** A total of 200 tunisian postmenopausal women aged from 50 to 89 years were recruited from the rheumatology departement in CHU Hedi Chaker, Sfax, Tunisia.

Clinical characteristics and patient medical history were collected using a validated questionnaire. Blood samples were taken for measurements of vitamin D, intact parathyroid hormone (PTH), and routine chemical analysis.

Serum 25(OH)D and PTH were measured by electrochemiluminescence.

SPSS 20 was used for the statistical analysis.

**Results:** The mean age was 63,74 ± 7,8 years. Mean PTH was 61,80 ± 25,6 ng/L.

Serum 25(OH)D levels were below 10, 20, and 30 ng/ml in 55, 30.5 and 14.5% of participants, respectively. Systolic blood pressure (SBP) was above 140mmHg in 60,5% of the patients while 26.5% had a diastolic blood pressure (DBP) higher than 90mmHg. PTH was highly correlated to 25(OH)D (r=-0,305, p<0,001) but not to the blood pressure levels. Serum 25(OH)D levels were negatively correlated to SBP (r=-0,121, p=0,045) and to HBP(r=-0,163, p=0,021).

After multivariate adjustment for a range of potential covariates (Age, Body mass index, waist size and glomerular filtration rate) in a binary logistic regression model, a significant inverse association was found between serum 25(OH)D concentration and systolic hypertension risk: In fact Risk of systolic hypertension seems to be lowered in the group with high 25(OH)D levels (≥15 ng/mL) compared with those with low levels (<15 ng/mL) (adjusted OR=0,512, CI 0.270–0.972), p=0,03). However, we have not noted a significant association between vitamin D levels and the risk of systolic hypertension (adjusted OR=1.01, 95% CI=0.495–2.064, p=0,97).

**Conclusions:** This study is timely, because a discrepancy exists between findings from observational studies and results of randomized intervention trials.

Reverse causation, inherent weakness of observational studies, is a possible explanation as individuals with hypertension might have more chronic diseases and therefore spend less time outdoors with sun exposure, important for endogenous vitamin D production.

In fact, randomized intervention trials will be needed to determine whether vitamin D supplementation can be used to prevent or treat hypertension.

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**Disclosure of Interest:** None declared

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## SAT0610 THE PROSPECTIVE RISK FOR LONG TERM SICKNESS ABSENCE, UNEMPLOYMENT, AND DISABILITY PENSION, AND THE PROBABILITY FOR RETURN TO WORK IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Long term sickness absence (LTSA), unemployment and early retirement are some of the most important outcomes of rheumatoid arthritis (RA), both for patient and society. Historically, RA patients have increased risk of LTSA and early disability pension. Modern treatment strategies have improved disease control in the last decades, and a decreased risk of LTSA and disability pension during later years have been reported. It is not known whether this represents a disease-specific decline or if the reduction of disability pension merely reflects a reduction in disability pension in general, due to political, demographic, and socioeconomic changes.

**Objectives:** To study in a multi-state model 1) the risks of LTSA, unemployment, and disability pension, and the chance of return to work in RA compared to a matched control population and 2) the changes in risks between1994–2011.

**Methods:** A cohort study of 6,677 RA patients at working age identified in the nationwide DANBIO registry, a register on adult patients with inflammatory joint diseases, and 56,955 matched (age, gender, area of residence) controls from the general population. By linkage with the DREAM registry (a national registry on employment status and sick-leave) and other registries, we analyzed in a multi-state model all shifts between the work-related states simultaneously and calculated hazard rates (HR), stratified by disease duration (early RA (<1yr) and established RA (≥1yr)), controlled for socio-demographic factors, physical job exposure, somatic and psychiatric comorbidities.

**Results:** The RA patients had increased risk of LTSA (e.g. early RA: HR=4.00) and disability pension (e.g. established RA: HR=2.75) relative to controls, see table. The relative risks of LTSA and disability pension decreased from 1994–99 to 2006–11 (e.g. in established RA: from work to LTSA HR 2.25 to 1.63, and from LTSA to disability pension HR 3.49 to 2.40). Compared to controls, RA patients had a lower chance of returning to work from LTSA (early RA: HR=0.60) or unemployment (early RA: HR=0.77), and this did not change over time.

RA patients compared to matched general population controls during follow up

| Shifts | | Dis. duration <1 yr | | Dis. duration ≥1 yr | |
|---|---|---|---|---|---|
| From | To | HR | 95% CI | HR | 95% CI |
| Work | LTSA | **4.00** | 3.64–4.30 | **1.84** | 1.75–1.94 |
| Unemployment | LTSA | **2.46** | 1.99–3.04 | **1.62** | 1.45–1.81 |
| Work | Unemployment | 0.92 | 0.83–1.03 | **0.82** | 0.77–0.87 |
| LTSA | Unemployment | **0.42** | 0.35–0.51 | **0.62** | 0.56–0.69 |
| LTSA | Work | **0.60** | 0.55–0.66 | **0.78** | 0.75–0.82 |
| Unemployment | Work | **0.77** | 0.70–0.85 | **0.80** | 0.76–0.83 |
| Work | Disability pension | **8.60** | 6.34–11.67 | **12.20** | 10.96–13.58 |
| LTSA | Disability pension | **1.52** | 1.26–1.84 | **2.75** | 2.54–2.98 |
| Unemployment | Disability pension | **2.36** | 1.57–3.54 | **3.41** | 2.92–3.98 |

Values in bold: P<0.001.

**Conclusions:** RA patients remain at high risk for LTSA and disability pension, but a positive trend is seen from 1996–1999 to 2006–2011. Returning to work from unemployment or LTSA remains a challenge for RA patients.

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## SAT0611 THE IMPACT OF ADHERENCE TO BIOLOGIC AGENTS ON HEALTH CARE RESOURCE UTILIZATION FOR PATIENTS WITH RHEUMATOID ARTHRITIS

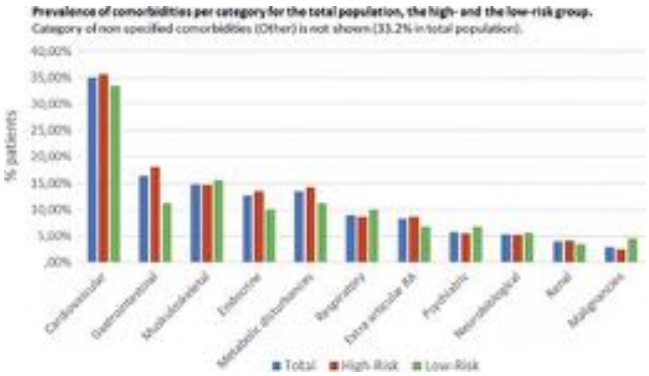
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**Background:** Poor adherence to therapy increases the burden and complexity of chronic diseases such as rheumatoid arthritis (RA). In the past 15 years, biologics have revolutionized the treatment of RA. However, little data is available on impact of adherence to biologics on health-care resources.
**Methods:** As part of a pilot project at the Institute for Clinical Evaluative Sciences (ICES), analyses were performed by ICES scientists on ICES administrative data to study the research question provided by Janssen Inc. Note, the approach and methodological details were determined by Janssen researchers. Patients were identified from the Ontario RA Database which contains all Ontario RA patients identified since 1991. Study population included RA patients, age 65+, with a prescription for a biologic drug between January 1, 2003 and December 31, 2013. Exclusion criteria are diagnosis of inflammatory bowel disease, psoriatic arthritis or psoriasis in the 5 years prior to the index event and discontinuation of biologic drug during the 12 months after the index event. Adherence was defined as a Medication Possession Ratio (MPR) of $\geq$0.8 measured as the proportion of days for which a patient had biologic treatment(s) over a defined follow-up period. Adherent were matched to non-adherent patients on a propensity score calculated using seventeen variables capturing patient demographics and heathcare resource use in the year prior to index event.
**Results:** A total of 4,667 RA patients were identified. Patients had a mean age (SD) of 69.9 (5.46) years and 75% were female. Of the total study cohort 1,877 matched pairs were identified (adherent to non-adherent patients). Relative rates for resource use (GP and cardiologist visits, ED visits, hospitalization, home care and rehabilitation) for the matched cohort were significantly lower ($p<0.0001$) in adherent patients. Additionaly the median (IQR) length of stay of hospitilizations was shorter for adherent patients - 10 days (4–23) vs. 14 days (5–38). 67% of non-adherent patients used oral prednisone which is significantly higher ($p<0.001$) than 54% in the adherent cohort.
**Conclusions:** The results of this large population based study have shown that RA patients who are adherent to biologic therapy have lower heathcare resource use and lower steroid use compared to non-adherent patients. Despite the inherent limitations of administrative database studies, the findings of the study have implications for physicians, patients and healthcare payers demonstarting the importance of adherence in the management of RA.
**Disclosure of Interest:** None declared
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## SAT0612 PREVALENCE OF COMORBIDITIES IN CARERA PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AT DISEASE ONSET

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**Background:** Comorbidities are highly prevalent in patients with Rheumatoid Arthritis (RA) and have been demonstrated to influence disease outcome. A better awareness of the number and type of comorbidities at disease onset and their influence on the disease course, could allow more timely intervention to prevent long term morbidity and mortality.
**Objectives:** To investigate the presence of comorbidities in patients with recently diagnosed RA, its association with clinical features and impact on disease outcome.
**Methods:** The presence of comorbidities was recorded on screening, before initiation of DMARDS or glucocorticoids in 379 patients with recently diagnosed RA (<1 year) participating in the Care in early RA (CareRA) trial, an RCT comparing different intensive remission induction strategies in a treat to target setting after stratification in a high- or low-risk arm based on classical prognostic markers (RF/ACPA, DAS28, erosion). Patients were grouped as having no comorbidities or having a comorbidity in at least one predefined category (cardiovascular, respiratory, endocrine, musculoskeletal, renal, neurobiological, psychiatric conditions, malignancies, metabolic disturbances, extra-articular RA manifestations and other). Disease activity (DAS28-ESR/CRP) was measured at baseline and after 1 year. Demographics including gender, age, smoking status, BMI and vital signs were registered on screening.
**Results:** Out of 379 patients (289 high- and 90 low-risk), 262 (69.1%) had a comorbidity in at least one of the predefined categories. In the group with comorbidities, the mean age was significantly higher (54.7 vs 45.7, $p<0.001$), as was the systolic blood pressure (134.9 vs 129.3 mmHg, $p=0.008$), compared to the group without comorbidities. Moreover, DAS28-ESR (5.3 vs 4.8 $p<0.001$) and DAS28-CRP (4.9 vs 4.5 $p=0.001$) were significantly higher in patients with compared to without comorbidities. DAS28 scores also tended to increase depending on the number of comorbidities per individual. After 1 year of intensive treatment to target, no more statistically significant difference was seen between the group with or without baseline comorbidities in terms of DAS28-CRP scores, but DAS28-ESR remained higher in patients with comorbidities ($p=0.031$). Overall, the most frequently reported comorbidities were cardiovascular (35.1%), gastrointestinal (16.4%) and musculoskeletal (14.8%). No significant differences in prevalence were found between risk groups.

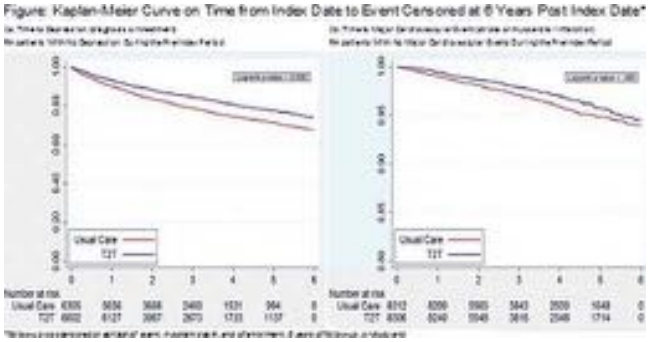



**Conclusions:** At the onset of RA, nearly three-quarters of patients had a comorbidity in at least one category. Patients with comorbidities were significantly older and had a significantly higher disease activity at baseline, disappearing after one year of treatment. No significant difference in the number or type of comorbidities was found between so-called High- and Low-Risk patients.
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**Disclosure of Interest:** None declared
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## SAT0613 DEPRESSION AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) USING A TREAT-TO-TARGET (T2T) APPROACH TO THERAPY VERSUS USUAL CARE

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**Background:** RA is an inflammatory autoimmune disease associated with increased prevalence of depression and cardiovascular comorbidities[1,2]. A T2T approach to therapy has been shown to significantly improve RA patient outcomes over usual care.
**Objectives:** To compare incidence rates of depression and major cardiovascular events in RA patients with a T2T approach to therapy to a matched group of RA patients with usual care.
**Methods:** This retrospective cohort study used MarketScan administrative claims databases to select adults with at least 1 inpatient or 2 outpatient diagnoses of RA (ICD-9-CM 714.0x) at least 30 days apart and within a year during 1/1/2005 to 1/31/2014. The index event was the first biologic or non-biologic disease-modifying antirheumatic drug at least 6 months following diagnosis. Patients had 6 months of pre-index continuous enrollment and follow-up was variable in length with a 1 year minimum imposed (baseline year). Patients were categorized as having T2T approach if they had at 3 or more visits to a rheumatologist where the initial visit was within the first 90 days of follow-up and were determined to have low disease activity through implementation of a validated claims-based algorithm[3] during the baseline year. Patients that did not meet both criteria were identified as having usual care. Incidence rates of depression (diagnosis or treatment) and major cardiovascular events (stroke or myocardial infarction) were calculated for the T2T cohort and the matched usual care cohort. Kaplan Meier (KM) method was used to examine the probability of time to event between groups.
**Results:** Of the 80,509 RA patients, 10.4% (N=8,333) were identified as having



T2T based management strategy and matched 1:1 to 8,333 of the 72,174 (89.6%) patients with usual care. After matching both cohorts had similar demographic characteristics (e.g., mean age 57.5 years, 73% female).Compared to the usual care cohort, a significantly ($p<0.001$) lower proportion of patients in the T2T cohort were newly diagnosed with a major cardiovascular event (2.5% vs. 3.2%) or newly treated for or diagnosed with depression (12.9% vs. 16.3%). Patients in the T2T cohort had a lower depression rate (1.56 vs. 2.14) per 10,000 person-years (PY) and major cardiovascular event rate (0.22 vs. 0.28) compared to patients with usual care. KM analysis also suggested that patients in the T2T cohort (versus usual care) had a significantly higher probability of not experiencing depression or a major cardiovascular event during follow-up (log rank tests all $p<0.001$) (Figure).

**Conclusions:** A T2T approach to RA management was associated with lower incidence of major cardiovascular events and depression and should be considered when prescribing care. Future studies in different populations are needed to confirm these findings.

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**Disclosure of Interest:** N. Princic Employee of: Employee of Truven Health Analytics which was funded by AbbVie to conduct this research, D. Fugh Employee of: Employee of Truven Health Analytics which was funded by AbbVie to conduct this research, B. C. Chu Employee of: Employee of Truven Health Analytics which was funded by AbbVie to conduct this research, V. Garg Employee of: Employee and AbbVie and may hold stocks in AbbVie

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## SAT0614 JOINT HYPERMOBILITY AND ANKLE OSTEOARTHRITIS IN A COMMUNITY-BASED COHORT

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**Background:** Clinical impressions suggest that joint hypermobility, a condition in which range of motion is greater than normal at most joints, is associated with osteoarthritis (OA), but results vary across the few published cohort studies on this subject. To our knowledge, no prior cohort study has examined the association of hypermobility and ankle radiographic features and symptoms of OA.

**Objectives:** This cross-sectional analysis examined the association of joint hypermobility and ankle OA outcomes in a large community-based cohort in the United States.

**Methods:** Of the 863 participants with complete tibiotalar radiograph data collected during 2012–2015, 848 had Beighton (joint hypermobility) data available for analyses. The Beighton criteria determined the ability to complete nine maneuvers: passive dorsiflexion right/left fifth finger $\geq$90 degrees, passive apposition right/left thumbs to forearm, right/left elbow hyperextension $\geq$10 degrees, right/left knee hyperextension $\geq$10 degrees, and palms on floor during forward trunk flexion with knees extended. One point was assigned for each completed maneuver (total score: 0 [unable to perform any maneuver] to 9 [performed all maneuvers]). Joint hypermobility was defined as a Beighton score $\geq$4; we also focused on the knee maneuver since the knee and ankle are closely linked along the kinetic chain. Radiographs were read for tibiotalar osteophytes (OST) and joint space narrowing (JSN). Presence of ankle symptoms consistent with OA was based on an affirmative response to the question: "On most days of any one month in the last 12 months did you have pain, aching or stiffness in your left/right ankle?" Separate logistic regression models were used to estimate associations of ankle OST, JSN, and symptoms with hypermobility, adjusting for covariates of gender, race, age, body mass index (BMI), and history of ankle injury. Statistical interactions between hypermobility and covariates were examined at the 0.10 significance level.

**Results:** The sample was 68% women and 33% African American with a mean age of 71 years and mean BMI of 31 kg/m$^2$. Hypermobiltiy was present in 59 participants (7.0%), which was most common among those <55 years (12.1%); 643 (75.5%) participants had OST, 65 (7.5%) had JSN, and 146 (17.2%) had ankle symptoms. Although not statistically significant, the adjusted odds of OST and ankle symptoms were 87% and 55% higher, respectively, among participants with vs. without hypermobility (Table). The adjusted odds of ankle symptoms was over 4 times as high among participants able vs. unable to perform the knee maneuver. There were no statistically significant interactions of hypermobility by covariates, but the estimates of the hypermobility-OST association generally increased with age (<55 years: adjusted odds ratio [aOR] = 1.02; 55–<65 years: aOR = 2.20, 65+years: aOR=2.88), while the hypermobility-ankle symptoms estimates declined (<55 years: aOR = 2.02; 55–<65 years: aOR = 1.68, 65+ years: aOR = 0.82).

Table. Unadjusted and adjusted* odds ratios (OR) and 95% confidence intervals (CI) for association of ankle outcomes and Beighton Criteria.

| | Beighton Score | | OR (95% CI) | |
|---|---|---|---|---|
| Ankle Outcome | ≥4 (n=59) | <4 (n=789) | Unadjusted | Adjusted* |
| Radiographic OST‖≥1 | 46 (81.4%) | 584 (74.0%) | 1.53 (0.78, 3.00) | 1.87 (0.92, 3.80) |
| Radiographic JSN‖≥1 | 2 (3.4%) | 63 (8.0%) | 0.40 (0.10, 1.70) | 0.47 (0.11, 2.03) |
| Ankle symptoms | 14 (23.7%) | 132 (16.7%) | 1.55 (0.83, 2.90) | 1.55 (0.80, 3.01) |
| | Knee Maneuver | | OR (95% CI) | |
| Ankle Outcome | Able (n=34) | Unable (n=811) | Unadjusted | Adjusted* |
| Radiographic OST‖≥1 | 27 (79.4%) | 602 (74.2%) | 1.34 (0.58, 3.12) | 1.50 (0.62 3.66) |
| Radiographic JSN‖≥1 | 3 (8.8%) | 61 (7.5%) | 1.19 (0.35, 4.00) | 1.32 (0.38, 4.56) |
| Ankle symptoms | 15 (44.1%) | 131 (16.2%) | 4.10 (2.03, 8.27) | 4.41 (2.06, 9.44) |

*Adjusted for age, gender, race, ankle injury and body mass index
‖ OST=osteophytes; JSN=joint space narrowing

**Conclusions:** Joint hypermobility may be associated with OST and symptoms of the ankle. Longitudinal studies are needed to determine the contribution of hypermobility to the incidence and progression of ankle OA outcomes.

**Disclosure of Interest:** None declared

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# Rehabilitation

## SAT0615 INFLUENCE OF FUNCTIONAL CAPACITY ON SELF-REPORTED PHYSICAL FUNCTION, AND ASSOCIATIONS WITH MECHANICAL MUSCLE FUNCTION IN SPORADIC INCLUSION BODY MYOSITIS PATIENTS

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**Background:** Sporadic inclusion body myositis (sIBM) represents a progressive inflammatory muscle disorder associated with severe loss of skeletal muscle tissue and impaired muscle function, which eventually results in drastically lowered physical function, reduced quality of life, and loss of independency[1–4]. No previous study has investigated the potential linkage between functional capacity and health-related quality of life and the relations to mechanical muscle function in sIBM patients.

**Objectives:** To investigate the associations between self-reported physical function, functional capacity and mechanical muscle function in patients with sIBM.

**Methods:** Twenty-two patients with sIBM volunteered to participate in the study. All participants filled out the short form (36) health survey, and performed a 2-min walk test (2MWT), a Timed up & go test (TUG) and a 30-sec chair stand test (CS), followed by evaluations of unilateral leg extension maximal muscle power (POW; Nottingham Power Rig) and maximal isometric knee extension muscle strength (MVC; KinCom dynamometer). Multiple linear regression analyses were applied to analyze associations between the investigated variables.

**Results:** All functional capacity tests revealed positive relationships with self-reported physical function (SF-36, physical function domain). TUG performance was the strongest predictor of self-reported physical function among the functional capacity tests (TUG: $r^2$=0.56; CS: $r^2$=0.43; 2MWT: $r^2$=0.42; $p<0.05$). MVC and MVC asymmetry (%inter-limb deficit) combined were the strongest indicators of TUG performance ($r^2$=0.50; $p<0.05$), with MVC exerting a positive effect and asymmetry a negative effect on TUG score. MVC asymmetry alone showed the strongest association (negative) with 2MWT performance ($r^2$=0.49; $p<0.05$). CS performance, was not correlated to MVC, but was predicted by POW and POW asymmetry combined ($r^2$=0.33, $p<0.05$) with a positive coherence for POW and a negative coherence for POW asymmetry.

**Conclusions:** The Timed up & go test appears to be the functional capacity test that best predicts self-perceived physical function in sIBM patients. Notably, it was found that between-limb asymmetry in maximal knee extensor strength had a clear negative impact on motor tasks involving gait function. This finding underlines that increasing attention should be directed to evaluate inter-limb strength asymmetry in sIBM patients in order to prevent function loss and achieve more effective rehabilitation in this patient group.

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**Disclosure of Interest:** None declared

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## SAT0616 KNEE ISOMETRIC AND ISOKINETIC STRENGTH IN FALLERS AND NON-FALLERS WITH RHEUMATOID ARTHRITIS

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**Background:** Muscular weakness is a cause of instability that has been reported to contribute to falling. Isokinetic and isometric dynamometry is a method of muscle assessment useful to measure the muscular strength and gives a quantification of the weakness and a comparison of strength across limbs and in reciprocal muscles.
**Objectives:** To compare isokinetic and isometric knee flexion and extension strength between fallers and non-fallers with Rheumatoid Arthritis (RA).
**Methods:** Sixty people with RA who gave informed consent were divided into two groups based on having a fall or not in the period of one year before evaluation, fallers (n=30, age 72.4years 15 males) and non-fallers (n=30, age 72.5 years, 16 males). Knee flexor and extensor strength was assessed using isokinetic and isometric dynamometry. Participants both limbs were tested at three fixed angular velocities isokinetically: 120°/s, 90°/s, and 60°/s and at three fixed positions isometrically, 90°, 60° and 30°. Bilateral comparison was determined by the percent deficit between left and right limbs for each participant. The ipsilateral comparison was determined between reciprocal muscles by the flexion/extension ratio. Independent t-test was used to identify significant differences between the fallers and non-fallers. The significance level was set at $p<0.05$
**Results:** 25 fallers and 30 non-fallers completed the isometric tests and 23 fallers and 28 non-fallers completed the isokinetic tests. In the bilateral comparison of the weaker and stronger limb in the fallers and non-fallers groups showed a large percentage deficit (range 22–43%) of isokinetic muscle strength between limbs in flexion and extension. Fallers had a significantly larger percentage deficit than non-fallers of isometric muscle strength between limbs in extension at 90° ($p=0.02$) and 60° ($p=0.01$).
The ipsilateral comparison shows that the fallers had a significantly ($p<0.05$) smaller flexion/extension ratio indicating a reduced hamstring strength at all isokinetic speeds (120°/sec F:0.73, NF:0.97, 90°/sec F:0.75, NF:0.94, 60°/sec F:0.74, NF:0.90). The fallers also had a significantly ($p<0.05$) smaller flexion/extension ratio isometrically at 60° and 30°.
**Conclusions:** These results demonstrate both RA fallers and RA non-fallers showed a large deficit in muscle strength between limbs. RA fallers had a significantly larger limb deficit in isometric extensor strength at 90° and 60°. The RA fallers had a significantly reduced flexion/extension ratio compared to the RA non-fallers indicating an imbalance between quadriceps and hamstring strength. Addressing the weakness in one limb and the imbalance between quadriceps and hamstrings may reduce the number of falls in this population.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4060

## SAT0617 12-MONTH COMPLEX REHABILITATION PROGRAM FOR RHEUMATOID ARTHRITIS PATIENTS RECEIVING BIOLOGIC DMARDS

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**Background:** Rehabilitation techniques, including physical exercises, physiotherapy, occupational therapy, patient education, give the patients with rheumatoid arthritis (RA) the strategies necessary to manage their disease in addition to drug treatment [1–4].
**Objectives:** To evaluate the efficacy of 12-month complex rehabilitation program in patients with RA receiving biologic DMARDs.
**Methods:** 64 patients with RA (87,5% females, age of 19 to 62 years, disease duration of 9 months to 10 years) were included and randomized into 2 groups. All patients received biologic DMARDs (adalimumab subcutaneously 40 mg once every 2 weeks or etanercept subcutaneously 50 mg per week or abatacept intravenously 750 mg once every 4 weeks) with methotrexate 20–25 mg per week. 34 study group patients underwent 12-month complex rehabilitation program: 15-min local air cryotherapy (–60°C, Criojet Air C600) for joints, 2 courses for 10 sessions with a mean interval of 6,4 months; 45-min therapeutic exercises 3 times a week, at first under the supervision of a trainer, further own at home; 45-min occupational therapy (joint protection strategies, use of assistive devices and adaptive equipment), 10 sessions; wrist and knee orthoses, orthopedic insoles; education program (4 daily 90-min studies). 30 patients received only drug therapy (control). Tender and swollen joint count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), joint pain on 100-mm VAS, DAS28, HAQ, RAPID3, hand grip strength, the average powers of knee extension and ankle flexion by EN-TreeM movement analysis were evaluated at baseline and at 12 months.
**Results:** 27 patients finished 12-month rehabilitation program. 7 patients did not complete the study, because they had a low compliance to home-based exercises. After 12 months in the study group tender joint count decreased by 83,7% ($p<0,01$), swollen joint count – by 81,6% ($p<0,01$), ESR – by 72,3% ($p<0,01$), CRP – by 68,3% ($p<0,01$), pain on VAS – by 80,4% ($p<0,01$), DAS28 – by 44,7% ($\Delta$DAS28=2,25±0,79, $p<0,05$), HAQ – by 73,8% ($\Delta$HAQ=1,39±0,56, $p<0,01$), RAPID3 – by 65,1% ($\Delta$RAPID3=6,23±1,73, $p<0,01$). The grip strength of a more affected hand enhanced by 48,6% ($p<0,01$), of a less affected – by 36,5% ($p<0,05$). The average extension power of a weaker knee increased by 87,3% ($p<0,01$), of a stronger – by 70,5% ($p<0,01$). The average flexion power of a more affected ankle joint elevated by 79,3% ($p<0,01$), of a less affected – by 74,7% ($p<0,01$). In the study group there were statistically significant differences from the control group in the most parameters ($p<0,05$), excluding CRP and DAS28 ($p>0,05$). After 12 months in the study group there was significantly more frequently a good response to treatment according to the EULAR criteria (DAS28) (92,6% vs 70,0% in the control group, $p<0,05$).
**Conclusions:** 12-month complex rehabilitation improves functional ability, motion activity and quality of life, relieves pain and helps to control disease activity in biologic DMARD-treated RA patients.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5365

## SAT0618 EFFICACY OF TWO LONG-TERM EXERCISE PROGRAMS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RESULTS OF 12-MONTH RANDOMIZED CONTROLLED TRIAL

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**Background:** International recommendations and results of randomized controlled trials consider physical exercises, aiming to improve range of motion, aerobic capacity and muscle strength, as an important part of treating rheumatoid arthritis (RA) [1–3].
**Objectives:** To compare the efficacy of two 12-month exercise programs in patients with early RA.
**Methods:** 51 patients with early RA (92,2% females, age of 18 to 53 years, disease duration of 2 to 17 months) were randomized into 3 groups. All patients received methotrexate or leflunomide. At hospital stage 15 patients underwent 10 high-intensity dynamic exercises using gym apparatus Enraf-Nonius with biofeedback for 45–60 min, including aerobic part (En-Cardio) and 18–20 muscle-strengthening exercises (En-Dynamic Track), 18 patients – 10 therapeutic exercises for joints for 45 min under the supervision of a trainer. At outpatient stage the exercises lasted for 12 months 3 times a week. 18 patients received only drug therapy (control). Tender and swollen joint count, pain on 100-mm VAS, erythrocyte sedimentation rate (ESR), DAS28, HAQ, RAPID3, the average powers of knee extension and ankle flexion by EN-TreeM movement analysis were evaluated at baseline and at 12 months.
**Results:** After 12 months in the both exercise groups there were statistically significant differences from the control group in most parameters ($p<0,05$), excluding ESR and DAS28 ($p>0,05$). Efficacy of the gym exercises was higher

**Abstract SAT0618** – Table 1

| Parameters | Baseline | | | 12 months | | |
|---|---|---|---|---|---|---|
| | Gym | Therapeutic exercises | Control | Gym | Therapeutic exercises | Control |
| Tender joint count | 7.9±3.1 | 7.6±2.5 | 7.8±2.4 | 1.3±0.6*#§ | 2.1±1.2*# | 3.3±1.5* |
| Swollen joint count | 4.8±2.8 | 4.5±1.9 | 4.9±2.5 | 0.9±0.3*# | 1.3±0.7*# | 2.4±1.5* |
| ESR, mm/h | 21.9±14.2 | 23.4±17.6 | 22.3±14.9 | 8.4±2.6* | 7.7±2.1* | 9.1±4.7* |
| Pain on VAS, mm | 60.5±21.3 | 62.4±18.3 | 59.7±14.6 | 10.5±8.3*#§ | 18.1±11.5*# | 27.2±16.1* |
| DAS28 | 4.13±1.28 | 4.32±1.53 | 4.49±1.42 | 2.64±1.16* | 2.79±1.62* | 3.18±1.31* |
| HAQ | 1.35±0.63 | 1.38±0.34 | 1.30±0.83 | 0.37±0.15*# | 0.45±0.21*# | 0.98±0.54* |
| RAPID3 | 9.84±3.17 | 10.34±4.25 | 10.11±6.52 | 2.47±1.26*#§ | 4.12±2.45*# | 5.84±2.16* |
| Extension power of a weaker knee joint, W | 4.54±2.58 | 3.99±3.11 | 4.27±1.13 | 9.97±4.34*#§ | 7.74±3.56*# | 5.72±2.17* |
| Flexion power of a weaker ankle joint, W | 0.39±0.15 | 0.44±0.21 | 0.41±0.22 | 0.79±0.26*# | 0.70±0.35*# | 0.56±0.24* |

*significance of differences from baseline, #significance of differences from control, §significance of differences between two exercise groups, $p<0.05$.

than the therapeutic exercises by tender joint count, pain on VAS, RAPID3 and extension power of a weaker knee joint ($p<0,05$).
Adherence to the regular therapeutic exercises for 12 months was better (72,2%) then to the gym exercises (53,3%). Predictors of the regular gym exercises were the young age (under 40 years) and the very early stage of RA at the onset of the study. Patients of the both exercise groups, who regularly did exercises during 12 months, had DAS28 low disease activity or remission.
**Conclusions:** The both long-term exercise programs reduce pain, increase functional status, quality of life and power of motion in early RA patients without negative effect on disease activity.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5447

## SAT0619 RELATIONSHIP BETWEEN HAQ DISABILITY SCORES AND MEASURES OF OBSERVED FUNCTIONAL ABILITY IN PATENTS WITH RHEUMATOID ARTHRITIS, OSTEARTHRITIS AND FIBROMYALGIA AND THE ASSOCIATION TO PAIN AND FATIGUE

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**Background:** Functional ability, which includes the ability to perform activities of daily living (ADL), is considered a core outcome domain in rheumatology. Recommendations for assessing ADL ability include the use of generic and diseases-specific questionnaires based on self-report and one of the most frequently used instruments is the Health Assessment Questionnaire Disability Index (HAQ-DI). Self-report reflects the person's perception of extent of disability, which may be influenced by pain and other psychosocial factors. A poor agreement between self-reported and observed ADL ability has previously been demonstrated in rheumatic populations based on other self-report instruments.
**Objectives:** to evaluate relationships between HAQ-DI scores and measures of observed ADL ability in patients with inflammatory and non-inflammatory rheumatic diseases and the association between pain and fatigue and these disability measures.
**Methods:** patients with rheumatoid arthritis (RA), knee osteoarthritis (OA) and fibromyalgia (FM) were assessed with the HAQ-DI. The Assessment of Motor and Process Skills (AMPS) was used to obtain measures of observed ADL ability. Two domains of observed ADL ability were evaluated: ADL motor skills (moving self and objects) and ADL process skills (organizing and adapting actions). Pain and fatigue were assessed by 100mm visual analogue scales (VAS). The project was approved by the local ethical committee (H-B-2007–084).
**Results:** 143 women (50 with RA, 27 with knee OA, 66 with FM), mean age 51.2 (11.8) participated. Baseline characteristics and correlations are presented in table 1. Patients with FM had the highest pain, fatigue, and HAQ disability scores and the poorest performance on the AMPS. The relationships between self-reported and observed ADL motor ability were weak to moderate across all diagnostic groups; strongest in patients with knee OA. Relationships with the AMPS ADL process ability measure were weak to insignificant. Level of pain, and not fatigue, showed the strongest relationship with self-reported functional ability across all diagnostic groups. A weak to moderate relationship between pain and AMPS ADL motor ability measures were also present in patients with RA and OA, but insignificant in patients with FM (r= -0.16, p=0.195).

Table 1

| Demographics | All (n = 143) | RA (n=50) | OA (n= 27) | FM (n=66) |
|---|---|---|---|---|
| Age (y) | 51.2 (11.8) | 54.1 (12.3) | 58.6 (7.5) | 48.2 (10.6) |
| HAQ-DI | 1.08 (0.60) | 1.02 (0.62) | 0.86 (0.61) | 1.22 (0.55) |
| VAS Pain (mm) | 52.6 (27.57) | 56.65 (25.55) | 45.00 (22.76) | 67.45 (22.74) |
| VAS Fatigue (mm) | 63.74 (29.26) | 51.45 (28.10) | 49.58 (25.51) | 78.45 (18.94) |
| AMPS ADL motor | 1.26 (0.46) | 1.40 (0.40) | 1.43 (0.49) | 1.08 (0.48) |
| AMPS ADL process | 1.11 (0.26) | 1.20 (0.17) | 1.05 (0.24) | 1.08 (0.24) |

| Correlations | | AMPS ADL Motor | | AMPS ADL Process | | HAQ-DI | |
|---|---|---|---|---|---|---|---|
| | Groups | r | p | r | p | r | P |
| HAQ-DI | All (n = 143) | -0.49 | 0.000 | -0.20 | 0.020 | | |
| | RA (n = 50) | -0.47 | 0.001 | -0.22 | 0.133 | | |
| | OA (n = 27) | -0.54 | 0.004 | -0.35 | 0.076 | | |
| | FM (n = 66) | -0.44 | 0.000 | -0.25 | 0.232 | | |
| VAS Pain | All (n = 143) | -0.42 | 0.000 | -0.24 | 0.004 | 0.55 | 0.000 |
| | RA (n = 49) | -0.31 | 0.033 | -0.24 | 0.091 | 0.60 | 0.000 |
| | OA (n = 27) | -0.53 | 0.006 | -0.31 | 0.119 | 0.62 | 0.001 |
| | FM (n = 66) | -0.16 | 0.195 | -0.20 | 0.103 | 0.40 | 0.001 |
| VAS Fatigue | All (n = 143) | -0.28 | 0.001 | -0.20 | 0.016 | 0.38 | 0.000 |
| | RA (n = 48) | -0.11 | 0.459 | -0.21 | 0.148 | 0.26 | 0.076 |
| | OA (n = 27) | -0.37 | 0.065 | -0.37 | 0.100 | 0.48 | 0.014 |
| | FM (n = 66) | -0.04 | 0.760 | -0.25 | 0.046 | 0.31 | 0.013 |

**Conclusions:** the relation between self-reported and observed functional ability is low across a spectrum of musculoskeletal diagnoses, even when using instruments recommended for these populations including the HAQ-DI. This has major implications on how to interpret and measure functional ability in the future as both methods should probably accompany each other. Interestingly pain was not associated with observed motor ADL ability in FM as opposed to RA and OA.
**Disclosure of Interest:** None declared
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## SAT0620 VALIDATION OF THE DUTCH-FLEMISH PROMIS FATIGUE ITEM BANK IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** In the assessment of patients with rheumatoid arthritis (RA) it is important to measure fatigue. The National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) initiative developed an item bank for measuring fatigue. This item bank was translated into Dutch-Flemish language according to the FACIT methodology.
**Objectives:** The aim of current study was to validate the Dutch-Flemish translation of the PROMIS Fatigue item bank (DF-PROMIS-Fatigue) in Dutch and Flemish RA patients. This is the first validation study of the PROMIS Fatigue item bank in RA patients.
**Methods:** 2030 RA patients (1370 Dutch and 660 Flemish RA patients) completed a paper-and-pencil or web-based survey, including the full DF-PROMIS-Fatigue (95 items, 5-point Likert scale). One-factor confirmatory factor analysis assessed unidimensionality. Item response theory (IRT) models evaluated the item characteristics of the item bank, to facilitate future development of a computer adaptive test (CAT). A graded item response model (GRM) was fitted and construct validity was studied. Ordinal regression models evaluated Differential Item Functioning (DIF) for e.g. language (Dutch-Flemish vs. English and Dutch vs. Flemish), to analyse cross-cultural validity.
**Results:** The analyses support unidimensionality of the DF-PROMIS-Fatigue (CFI=0.996 and TLI=0.996). Only 45 out of 4465 (1%) item pairs were marked as possibly locally dependent. The data of the item bank fit the GRM, and showed good coverage across the fatigue continuum (threshold-parameters ranged from -3.8 to 5.8). The item bank showed good cross-cultural validity: none of the DF-PROMIS-Fatigue items showed DIF between Dutch and Flemish language. Furthermore, the item bank showed good reliability (Cronbach's alpha=0.993). Analyses of construct validity are in progress and will be presented at the conference.
**Conclusions:** The results indicate that the items of the DF-PROMIS-Fatigue fit a GRM. The DF-PROMIS-Fatigue can be used to develop a CAT for measuring fatigue in Dutch and Flemish RA patients.
**Disclosure of Interest:** None declared
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## SAT0621 EFFECT OF AN EXERCISE THERAPY ON SYSTEMIC BIOMARKERS FOR CARTILAGE METABOLISM

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**Background:** The number of osteoarthritis (OA) patients is increasing year by year because of the aging society. Especially, knee OA is reported to reduce the health life expectancy. The majority of patients are at the early stage of knee OA and are adapted to conservative treatments such as exercise therapy. A lot of biomarkers for cartilage metabolism were previously reported. However, there are few reports that exercise therapy has an effect on the biomarkers related for cartilage metabolism.
**Objectives:** To investigate the effect of an exercise therapy on cartilage metabolism using biomarkers.
**Methods:** Thirty-eight females (mean age: 59 years) participated in this study. All participants started a weekly exercise and continued it for twelve weeks. Before and after the exercise program, we measured their physical activities; Timed Up and Go test (TUG) and Three Minutes Walking test (3MW). Since the program started, we have collected serum and urine samples from the participants at the start of the program (0 week), at the end of it (12 weeks) and 12 weeks after it (24 weeks). For the collected samples, we measured the following two anabolic and

one catabolic biomarkers; serum cartilage type II procollagen carboxy propeptide (sPIICP), serum cartilage oligomeric matrix protein (sCOMP), urine C-terminal telopeptide of collagen type II (uCTX-II). These biomarkers were measured with the enzyme-linked immunosorbent assay method.
**Results:** After the twelve weeks exercise program, both TUG and 3MW were significantly improved ($P < 0.01$ each, respectively) (Fig. A, B). sCOMP concentrations at 12 weeks were relatively greater than those at 0 week. However, sCOMP concentrations at 24 weeks were significantly greater than those at 12 weeks ($P < 0.01$) (Fig. C). In contrast, uCTX-II concentrations at 24 weeks were significantly less than those at 0 week ($P < 0.01$) (Fig. D). There was no significant difference between pre- and post-excise sPIICP concentrations.

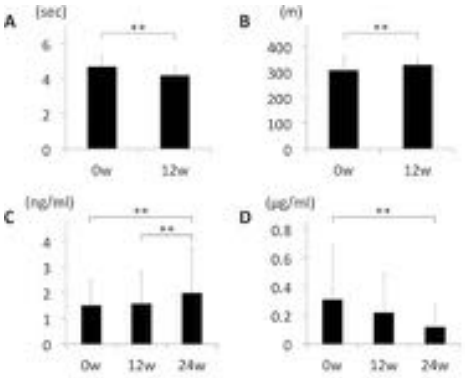



**Fig. A.** Timed Up and Go test. **B.** Three Minutes Walking test. **C.** Changes of serum cartilage oligomeric matrix protein concentrations. **D.** Changes of urine C-terminal telopeptide of collagen type II concentrations.
**: $P < 0.01$

**Conclusions:** These results suggest that an exercise therapy will improve physical activities and that this therapy could influence both cartilage anabolic and catabolic biomarkers.
**Disclosure of Interest:** None declared
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## SAT0622 CO-CREATING AN ONLINE REHABILITATION PROGRAMME FOR PEOPLE WITH CHRONIC KNEE/HIP PAIN

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**Background:** Chronic knee and hip pain is very prevalent, causes disability and reduces mobility. Evidence-based guidelines recommend exercise and self-management. *Enabling Self-management and Coping of Arthritic Pain through Exercise, ESCAPE-pain* (www.escape-pain.org), is a rehabilitation programme that integrates self-management advice with exercise that reduces pain, improves physical and psychosocial function and well-being[1]. It is usually delivered as face-to-face programmes in clinical departments. Unfortunately this limits its "reach" so few people benefit. An online version could reach many more people. However, online programmes developed without input from potential users often produce unwanted, unusable, "high tech, low impact" and ineffective programmes with poor uptake.
**Objectives:** We asked potential users what they considered were the important features of the content and design of an online *ESCAPE-pain* programme to maximise its uptake and effectiveness.
**Methods:** The opinions and preferences 24 people with chronic knee/hip pain as potential users of an online *ESCAPE-pain* programme were gathered to co-design a prototype website. From those 24 participants a further of 8 people were purposively selected to participate in semi-structured "think aloud" evaluations of the prototype website, commenting on its content, aesthetics, quality, verbalising their thoughts, difficulties, (dis)likes and suggestions.
Their opinions and preferences were thematically analysed, then aligned to the behavioural change techniques taxonomy (BCTT)[2] to see how the *ESCAPE-pain* online programme supported people to change their behaviour.
**Results:** PParticipants had many different opinions and preferences, often mutually exclusive, about the content and format of the online programme. They wanted a simple, easy to navigate, engaging online resource, which was succinct, unambiguous, jargon free, and tailored to each person's needs (BCTT 4.Shaping knowledge; 5.Natural consequences). Descriptive videos of older people exercising were enthusiastically welcomed (BCTT 4.Shaping knowledge; 5.Natural consequences; 7.1Associations – cues and prompts). Entering pertinent information about exercise (number of repetitions, time) to enable people to chart and monitor progress was important (BCTT 2.Feedback/monitoring). Some people wanted to share this information with others and receive feedback to get a comparative overview of their situation and progression (BCTT 2.Feedback/monitoring; 3.Social support; 6.Comparison of behaviour). Support from peers and healthcare professionals (BCTT 3. Social support) via blogs/forums was popular with some, but not all participants. Endorsement by trusted, non-commercial organisations or healthcare professionals was strongly advocated (BCTT 9.Comparisons of outcomes - credible sources). Commercially-backed websites were treated with suspicion.
**Conclusions:** People with chronic knee and hip pain helped us co-create an online version of the *ESCAPE-pain* programme which incorporates well recognised behavioural change techniques. It will be available as a mobile website and smartphone app from March 2016, enabling many more people to access and benefit from the *ESCAPE-pain* programme.
**References:**
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[2] Michie et al. Ann Behav Med (2013) 46:81–95
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**Disclosure of Interest:** None declared
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## SAT0623 THE ROLE OF REHABILITATION IN AVASCULAR NECROSIS OF THE HUMERAL HEAD – RANDOMIZED STUDY

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**Background:** Avascular necrosis of the humeral head (AVNHH), a pathologic process with multifactorial etiology that results from interruption of blood supply to the bone, leading to the collapse of humeral head that requires shoulder hemiarthroplasty, is the second most common site of this disorder behind the femoral head. Trauma is a common cause, but atraumatic necrosis has developed for patient with risk factors. The successful treatment is related directly to the stage of disease at diagnosis. Early detection and conservative treatment with physical therapy, modification of activity, kinetic program and analgesics is the key to best management.
**Objectives:** The objectives of our study (a single blind, randomized controlled trial) were: to establish the risk factors associated with disease and to evaluate the effect of rehabilitation program on clinical and functional parameters and to assess the short-term effects of this program on quality of life of patients with AVNHH.
**Methods:** 12 patients aged between 35 - 45 years with AVNHH stage I and II (precollapse stages), were randomized into two groups: Group 1 – 7 patients (G1) was treated by complex therapy (medication, stretching and strengthening exercises, ultrasound and interferential current), and group 2 – 5 patients (G2) control receiving only medication. The duration of rehabilitation program was 4 weeks. All patients were evaluated initial and finally. The outcome assessments at the beginning and at the end of the rehabilitation were pain intensity (with dolorimeter), active range of shoulder movements and HAQ score.
**Results:** The AVNHH is associated with shoulder traumatic conditions (5 patients) and the mentioned risk factors were corticosteroid administration (10 patients), heavy alcohol intake (4 patients), rheumatoid arthritis (3 patients).
In both groups, improvements were found in pain intensity (65% in G1 and 35% in G 2, respectively) and this reduction was significantly higher in G1. The mean value of range of shoulder movements (flexion, abduction, rotations) and HAQ score showed significant improvements in G1 group.
**Conclusions:** Our study confirms the literature data that rehabilitation program can be very effective in treating AVNHH if it is detected early. Maintaining range of motion and muscle strength are crucial to avoid further humeral head collapse and improvement in pain scores and upper limb function.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2965

## SAT0624 EFFICACY OF A 4-WEEK TEAM-REHABILITATION PROGRAM IN WARM CLIMATE ON DISABILITY, HEALTH AND BODY FUNCTION FOR UP TO ONE YEAR: A PROSPECTIVE STUDY IN SWEDISH PATIENTS WITH INFLAMMATORY JOINT DISEASES

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**Background:** The need of team-rehabilitation for patients with chronic arthritis in the era of biologics has been questioned.
**Objectives:** We evaluated the short and long-term patient-oriented effects of rehabilitation program in warm climate in patients with inflammatory joint diseases who had inadequate response to physiotherapy in Sweden. We further questioned if patient-reported responses were influenced by demographic, disease factors and level of physical activity.
**Methods:** In all, 161 patients with peripheral arthritis and spondyloarthritis, mean age 53 years (range 21 to 77), 73% women, 51% with comorbid condition, 49% treated with synthetic DMARDs and 63% with biologics, who experienced activity limitations and reduced quality of life despite physiotherapy in Sweden, received structured team-rehabilitation during 4 weeks in warm climate. The change in outcomes (variables of the International Classification of Functioning, Disability and Health) pre- and post-rehabilitation and after 3 and 12 months was assessed: HAQ (in patients with peripheral arthritis), BASFI (in patients with spondyloarthritis), EQ-5D, VAS of patient reported general health (VAS-GH) and

pain (VAS-pain). The International Physical Activity Questionnaire (IPAQ) was used to assess the level of physical activity.
**Results:** At inclusion patients reported activity limitations, HAQ mean (SD) 1.13 (0.55), and reduced quality of life, EQ-5D median (IQR) 0.66 (0.52–0.73). HAQ, VAS-GH and VAS-pain improved significantly from pre-rehabilitation to all follow-up time-points, and BASFI and EQ-5D from pre-rehabilitation up to 3 months. At the 3 and 12 months the proportion of patients reporting improvement from baseline above minimal clinically important difference (MCID) was for HAQ 62% and 35%, BASFI 73% and 61%, EQ-5D 47% and 39%, VAS-GH 68% and 52%, for VAS-pain 68% and 51%, respectively. The improvement in HAQ and VAS scores was not dependent on demographic or disease-related variables, while improvement in BASFI was hampered in older patients and improvement EQ-5D was lower in patients with comorbidity. The gained effect was not affected by changes in treatments as confirmatory analyses on patients without changed medication or unexpected clinical events yielded stable results across all outcomes.
Physical activity increased significantly from pre-rehabilitation to 12 months, $p<0.001$. Increased IPAQ correlated with improvement in EQ-5D ($r=0.20$, $p=0.040$) and trendwise with reduction in VAS-pain and HAQ ($r=0.18$, $p=0.059$; $r=0.19$, $p=0.086$).
**Conclusions:** Comprehensive team-rehabilitation in warm climate is still important for the patients treated up-to-date, benefits functional ability and quality of life. The benefit of the intervention was evident post-rehabilitation and in many patients sustained for up to one year. The improvements in HAQ, VAS general health and VAS pain 3-month post-rehabilitation were comparable with improvements reported in recent randomized clinical trials of biologicals in RA. The health advantages of the rehabilitation program were combined with increased health-enhancing physical activity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2997

## SAT0625 CHALLENGES OF DISEASE-RELATED COMMUNICATION IN THE DAILY LIVES OF PERSONS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES. RESULTS OF A PARTICIPATORY RESEARCH PROJECT

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**Background:** At least every ninth person with rheumatic and musculoskeletal diseases (RMDs) reports severe limitations of social participation due to multiple health problems and reduced resources [1]. Reduced participation is frequently associated with social interactions and communication around the subject of disease-related problems [2]. These conversations may be necessary for the patients in order to follow their interests or reach certain goals. If the patients experience difficulties in these situations, low communication skills may be significant barriers to social participation.
**Objectives:** To identify significant factors of disease-related everyday communication of persons with RMDs in a nationwide project funded by the Deutsche Rheumaliga Bundesverband e.V. (DRL). Based on the results, a training to enhance the communication skills of persons with RMDs in various situations significant for social participation will be developed.
**Methods:** An online questionnaire addressing context, content, difficulties, and burden of the disease-related everyday communication was answered by 1.015 persons with RMDs (87% females, mean age 55 (SD 12) years, mean disease duration 16 (SD 12) years). Communication skills were recorded by the short version of the Insecurity Questionnaire [3]. In this participatory research project four persons with RMDs are involved throughout the project.
**Results:** More than half of the participants report difficulties in disease-related conversations across various situations. The majority of these persons suffer from this experience as a burden particularly in conversations at the work place or in civil services. Compared to men, women report difficulties more frequently in the private environment and with representatives of public authorities and they feel a higher burden due to difficult conversations in all situations. In comparison with population samples the communication skills of persons with RMDs are lower with higher scores of the scales “fear-of-failure/criticism”, “fear-of-contact”, and “inability-to-say no” of the Insecurity Questionnaire.
**Conclusions:** The project offers new insight into the disease-related communication of persons with RMDs. The subsequent training (“KOKOS-Rheuma”) will include difficult and strenuous conversations especially at the work place or in civil services. Persons with RMDs will be given exercises for typical situations that require saying no, adequate arguing, and giving feedback in order to reduce fear of failure and criticism.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2825

## SAT0626 LOCAL CRYOTHERAPY (PULSED CO2 OR ICE) DECREASES IL-6, IL-1β AND VEGF SYNOVIAL LEVELS IN KNEE ARTHRITIS

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**Background:** Cryotherapy is widely and empirically used in an adjuvant and symptomatic setting in inflammatory rheumatic diseases, with a low level of evidence.
**Objectives:** The aim of this work was to evaluate the effects of two local cryotherapy (LC) techniques (ice or hyperbaric cold CO2) applied twice on pain and pro-inflammatory cytokine levels in arthritic knees.
**Methods:** Thirty-five patients suffering from non-septic knee arthritis were included (16 gouts, 8 calcium pyrophosphate dehydrate crystal deposition diseases, 5 spondyloarthritides, 6 rheumatoid arthritides). Patients didn’t receive any concurrent anti-inflammatory drug (corticosteroids, NSAIDs, colchicine, DMARDs, biologics) throughout the study period (24 hours). They were randomized to receive local ice (for 30 minutes) or cold pulsed CO2 (for 2 minutes - Cryo+® Cryonic) at 9 A.M and 5 P.M. Synovial fluid was collected just before the first cold application then 24 hours later (also at 9 A.M). Synovial fluid cell count and cytokine levels (IL-6, IL-1β, TNF-α, IL-17A, VEGF by Multiplex flow cytometry – CBA® BD biosciences) were measured and compared before and after the two LC applications. Paired Wilcoxon tests were performed. The factors associated with cytokine level evolution were assessed (uni- then multivariate analysis by logistic regression).
**Results:** Pain VAS significantly decreased after 24 hours in both treatment groups (Ice: 5.3±1.3 versus 2.7±1; n=20;p=0.0003 – CO2: 5.6±1.4 versus 3.1±1.2; n=15;p=0.002). Synovial fluid leukocyte count non-significantly decreased (23580±10015 versus 19120±8981; p=0.49). IL-6 levels significantly decreased after 2 LC applications 456100±163570pg/mL versus 281500±142006pg/mL; n=35; p=0.0001). This decrease was also significant in ice-treated subgroup (n=20; p=0.0002) but not in CO2-treated patients (n=15; p=0.07). In multivariate analysis, IL-6 decrease was associated with a higher CRP rate at baseline (r=0.35; p=0.004) and a greater skin temperature drop during LC (r=0.33; p=0.03). IL-1β levels also decreased after treatment (26.75±8.95pg/mL versus 23.10±10.11pg/mL; n=35; p=0.02) but the difference didn’t reach significance in treatment subgroups (Ice: n=19; p=0.07 – CO2: n=15; p=0.15). In multivariate analysis, IL-1β decrease was associated with “ice” modality (r=3.25; p=0.03) and negatively associated with BMI (r=-4.02; p=0.04). VEGF levels also decreased globally (1391±295pg/mL versus 1263±281pg/mL; n=34; p=0.03) but not significantly in subgroups (Ice: n=19; p=0.2 – CO2: n=15; p=0.07). IL-17A rates also tended to decrease (16.3±15.75pg/mL versus 14.95±15.2pg/mL; n=35; p=0.065). TNF-α levels tended to decrease in CO2 group (n=15; p=0.08).
**Conclusions:** LC (ice or pulsed CO2) applied twice during one day showed anti-inflammatory effects by reducing synovial IL-6, IL-1β and VEGF levels in arthritic knees. Both techniques equally reduced pain but sample sizes were still insufficient to show any difference in terms of local cytokine level reduction.
**Disclosure of Interest:** None declared
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# Abstracts Accepted for Publication

## Genomics, genetic basis of disease and HLA/T cell recognition

### AB0001 GENETIC VARIANTS IN IL-12B AND IL-27 IN THE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Type-1 immunity plays a fundamental pathogenic role in various diseases including systemic lupus erythematosus (SLE), which is a multisystem autoimmune disorder with heterogeneity in clinical manifestations and disease course. Although the etiology and pathogenic mechanisms of SLE remains elusive, the actual state of knowledge allow diagnose that genetic information is important for understanding the mechanisms of the disorder. In this respect several studies support that gene encoding cytokines, which regulate CD4+T cells differentiation, are attractive genetic factors that may predispose to susceptibility and severity of SLE
**Objectives:** To investigate the potential association between *IL-12B* and *IL-27* gene polymorphisms and SLE, we performed a case-control study based on Polish population.
**Methods:** SLE patients and healthy individuals, were examined for -6415 CTCTAA/GC (rs17860508) and +1188A/C (rs3212227) in *IL-12B* and -924A/G (rs153109) and 4730T/C (rs181206) in *IL-27* gene polymorphisms using the HRM method, PCR–RFLP method and TaqMan SNP genotyping assay, respectively.
**Results:** An increased frequency of GC/GC genotype as well as GC allele of the IL-12B rs17860508 was found in patients with SLE, as compared with healthy subjects ($p<0.001$). We did not find differences in genotype and allele frequencies of the *IL-12B* rs3212227 and IL-27 rs153109 and rs181206 variants between SLE patients and controls. *IL-27* haplotype CG indicated higher risk for SLE (P=0.002), whereas haplotype TG indicated reduced risk for SLE (p=0.005). The *IL-12B* rs3212227 A/C polymorphism was associated with the mean value of the platelets, urea and complement C3 level. Furthermore *IL-12B* rs17860508 genetic variant showed correlation with platelets, prothrombin time, international normalized ratio and alkaline phosphatase.
**Conclusions:** Our results revealed that *IL-12B* rs17860508 as well as *IL-27* haplotype CG are genetic risk factors for SLE and that both *IL-12B* rs17860508 and rs3212227 predict disease phenotype.
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### AB0002 GENETIC VARIANTS IN IL-17F, IL-23 AND IL-23R IN THE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a severe multi-system autoimmune disease characterized by uncontrolled autoantibody formation, excessive proinflammatory cytokine production, tissue inflammation and damage to multiple organ systems. The IL-23-IL-17 axis, rather than the loop of IL-12 and IFN-c, have a central role in the autoimmune inflammation, and interaction between IL-23 and IL-17 is not only essential for the onset phase, but also for the destruction phase of SLE characterized by the T cell-mediated activation of osteoclastogenesis.
**Objectives:** To investigate the potential association between IL-17F, IL-23 and IL-23R gene polymorphisms and SLE, we performed a case-control study based on Polish population.
**Methods:** SLE patients and healthy individuals, were examined for *IL-23A* 703 G/A (rs11171806) and *IL-23R* (rs1884444 G/T, rs10489629 G/A) by TaqMan SNP genotyping assay, and for *IL-17F* 7488A/ G (rs763780) and 7383A /G (rs2397084) gene polymorphisms using the PCR– RFLP method.
**Results:** An increased frequency of AG genotype as well as G allele of the IL-17F 7488 A/G (rs763780) was found in patients with SLE, as compared with healthy subjects (p=0.0007 and p=0.0012, respectively). Frequencies of the rs1884444 TT genotype and the rs1884444 T allele were also higher in SLE patients (both $p<0.0001$). Overall, very weak LD was observed between the *IL-17F* 7488A/ G (rs763780) and 7383A /G (rs2397084) polymorphisms (D'-0.003, r2 – 0.000). From four possible haplotypes, frequencies of one (AG) showed significant differences between both examined groups ($p<0.0001$). Moreover, we also observed a weak LD between the *IL-23R* rs10489629G/A and rs1884444 G/T (D'-0.199, r2 – 0.026). The genotype-phenotype analysis showed significant association between the IL-17F 7383 A/G (rs2397084) and mean value of the hemoglobin (p=0.01), between the IL-17F 7488 A/G (rs763780) and age (p=0.008) and lupus anticoagulant (p=0.09), between the IL-23 703 G/A (rs11171806) and urea (p=0.08) and C3 complement (p=0.03), and between the IL-23R rs1884444 G/T and activated partial thromboplastin time (p=0.06).
**Conclusions:** Present findings indicated that IL-17F 7488 A/G (rs763780) and IL-23R rs1884444 G/T polymorphisms may be involved in susceptibility to SLE in the Polish population.
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**Acknowledgement:** Supported by grant No 502–01–01124182–07474, Poznań University of Medical Sciences. The technical assistance of Mr. Agnieszka Hertel, Wieslawa Frankowska and Teresa Golaszewska is gratefully acknowledged. We are also grateful to all of the SLE patients whose cooperation made this study possible.
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### AB0003 IL-23R AND IL-17A POLYMORPHISMS CORRELATE WITH SUSCEPTIBILITY OF ANKYLOSING SPONDYLITIS IN CHINESE HAN POPULATION

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**Background:** The association between the IL-23R and IL-17A polymorphisms and ankylosing spondylitis (AS) in a Chinese Han population is still unclear.
**Objectives:** The purpose of this study is to detect the association between IL-23R and IL-17A polymorphisms and AS.
**Methods:** A case–control study consisting of 486 AS patients and 480 healthy controls was performed. We used the high-resolution melting methods (HRM) to

genotype the selected five single nucleotide polymorphisms (SNPs), four of them (rs6693831, rs7517847, rs1884444, rs10889677) on the IL-23R gene and one (rs2275913) on the IL-17A gene. Meanwhile the laboratory indexes (RBC, WBC, PLT, MONO%, LYMPH%, NEUT%, ALB, ALP, ALT, AST, BUN, CHOL, CK, CREA, Cys-C, DBIL, GGT, GLB, GLU, HBDH, HDL-C, IBIL, LDH, LDL-C, TBIL, CRP, C3 and C4) were recorded.

**Results:** In this study, patients with genotype CC (p=8.574E-8) and allele C (p=3.206E-31) on SNP rs6693831 (IL-23R) showed decreased risk of AS. The genotype TT (p=4.551E-6) and allele T (p=0.02) on SNP rs1884444 (IL-23R) showed significant lower risk of AS. Individuals carrying the allele A on SNP rs2275913 (IL-17A) showed higher risk of AS [p=0.04, OR (95%CI) = 0.825 (0.690–0.987)]. Significant higher level of CRP was found among AS patients with genotype CT on rs6693831 ($\chi^2$=7.633, P=0.030).

**Conclusions:** We first demonstrated that rs6693831 and rs1884444 on IL-23R gene and rs2275913 on IL-17A gene are genetic susceptibility factor for AS. We also noticed that patients with CT genotype on rs6693831 have higher CRP level.

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## AB0004 POLYMORPHISMS IN GENES IN THE IL-17 PATHWAY AND B CELL MEDIATED IMMUNE RESPONSE MODULATE THE DEVELOPMENT OF SPECIFIC AUTOIMMUNE MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease in which a complex interaction between genetic, environmental and immunological factors determines the susceptibility and the phenotype. Dysregulations in IL-17 pathway as well as in B-cell mediated immune response have been observed in SLE. We have recently demonstrated that polymorphisms in TRAF3IP2 gene are associated with susceptibility for SLE and can predispose for the development of pericarditis (1). TRAF3IP2 encodes for Act1, a molecule that acts as a negative regulator of B cell by inhibiting CD40-mediated signaling and as a positive signaling adapter in IL-17-mediated cellular responses. TRAF6 is essential for the IL-17/Act1-mediated activation of NF-kB, while CD40 is the target for the Act1 mediated inhibition of B cell response.

**Objectives:** The primary goal of our study was to evaluate the association of polymorphisms in CD40, TRAF6 and TNFSF4 (OX40) genes with susceptibility to SLE. Secondary objectives were to assess the possible association of these polymorphisms with the clinical and laboratory features.

**Methods:** We recruited 315 Italian SLE patients and 278 healthy controls. Genotyping of rs4810485 in CD40, rs4755453 and rs5030437 in TRAF6, and rs2205960 and rs10489265 in TNFSF4 (OX40) SNPs was performed by allelic discrimination assay. A case/control association study and a genotype/phenotype correlation analysis were performed.

**Results:** Deviations from Hardy–Weinberg equilibrium for the three SNPs were not observed. None of the studies polymorphisms was associated with susceptibility for SLE. Only CD40 rs4810485 was associated at genotypic (P=0.034) but not at the allelic level. Nonetheless, these polymorphisms seem to contribute to define disease phenotype. TRAF6 was associated with the presence of anemia (P=0.019, OR=1.96), rs2205960 of TNFSF4 was associated with the pericarditis (P=0.013, OR=2.14), and rs4810485 of CD40 with the presence of anti-SSB/La (P=0.014, OR=2.26) and lupus nephritis (P=0.024, OR=1.8).

**Conclusions:** We were not able to confirm previous association of TRAF6 and CD40 polymorphisms with susceptibility for SLE. However, such SNPs seem to influence the disease phenotype. In particular, it is of interest the association of rs4810485 in CD40 with lupus nephritis and the presence of anti-SSB/La. Indeed, the modulation of CD40-mediated T cell-dependent antibody response has already been associated with the development of anti-SSB/La in association with SLE-like nephritis in a mouse model (2), probably due to an uncontrolled B cell activation signal.

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## AB0005 WEIGHTED GENE CO-EXPRESSION NETWORK ANALYSIS REVEALS LINK BETWEEN PROTEIN KINASE SIGNALLING AND RESPONSE TO METHOTREXATE IN NEW-ONSET RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) is recommended as the first-line therapy in rheumatoid arthritis (RA). However, only 55% of patients remain on this inexpensive drug beyond 2 years after initiation of treatment. A stratified medicine approach therefore necessitates identification of reliable biomarkers of MTX response which are currently lacking.

**Objectives:** To identify gene co-expression networks in pre-treatment blood of new-onset RA patients that correlate with response to MTX at 6-months.

**Methods:** Patients with RA participating in the Rheumatoid Arthritis Medication Study (RAMS), a multi-centre one-year longitudinal observational study investigating predictors of response to MTX in the UK, who were EULAR good or poor responders at 6-months were included in this analysis. Total RNA was extracted from Tempus™ tubes using the Tempus Spin RNA isolation kit according to the manufacturer's protocol. Following extraction, quantification and assessment of RNA integrity, RNA samples were labelled with biotin and amplified (Illumina TotalPrep RNA Amplification Kit) prior to being loaded onto an Illumina HumanHT-12 v4 BeadChip, which targets over 47,000 probes. Highly correlated genes were identified from the expression data and summarised with a modular eigengene using the weighted gene co-expression network analysis (WGCNA) bioconductor package. Pearson's correlation was used to assess the significance of the correlation between eigengene and improvement in disease activity, defined using EULAR response and change in CRP.

**Results:** Thirty-two good and 43 poor responders were included in this study [76% female; mean age 60 (SD 14) years, median symptom duration 6-months (IQR 3.7, 19) at MTX start]. Seventeen co-expression modules were identified. None of the modules were correlated with EULAR response at 6 months. However, one module including 1,840 genes was correlated with change in CRP between baseline and 6-months (corr 0.37, p=0.001). Furthermore, the genes most central to the module were also the most correlated with CRP difference (cor 0.5, p=5.6e-117). The most significant gene ontology (GO) molecular function term for this module was protein kinase (61 genes, 1.50 fold enrichment, p=4.2e-04, Benjamini p=0.04). Within this GO the expression of TYK2 was found to be correlated with CRP change (p=0.005). Patients with higher TYK2 expression at baseline experienced more improvement in CRP following MTX treatment.

**Conclusions:** These results suggest gene co-expression network analysis has the potential to reveal important insight into the biological effects of MTX therapy in RA. The assumption behind this analysis is that networks of genes are co-regulated e.g. by an environmental exposure, transcription factor of genetic variants. The next step will be to incorporate genome-wide single nucleotide polymorphism data to identify eigengene and gene expression quantitative trait loci.

**Disclosure of Interest:** None declared

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## AB0006 ASSESSMENT OF RHEUMATOID AND PSORIATIC ARTHRITIS SUSCEPTIBILITY LOCI IN A GENETIC HOMOGENEOUS POPULATION OF GREECE

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**Background:** Genome wide association studies (GWAS) have detected a considerable number of rheumatoid arthritis (RA) susceptibility loci [1]. Some RA loci have also been found to be associated with psoriatic arthritis (PsA) [2], demonstrating that there is a degree of genetic overlap between various autoimmune diseases.
**Objectives:** We sought to investigate whether single nucleotide polymorphisms (SNPs) mapping to previously reported RA and/or PsA susceptibility loci, including *PLCL2* (rs4535211), *CCL21* (rs2812378), *REL* (rs13017599), *STAT4* (rs10181656), *CD226* (rs763361), *PTPN22* (rs2476601) and *TYK2* (rs34536443), are associated with risk for the two diseases in a genetically homogeneous Greek population.
**Methods:** A total of 392 RA patients, 126 PsA patients and 521 healthy age and sex matched controls from Greece were included. Genotyping of the SNPs was performed with Taqman primer-probe sets, using a Real-Time PCR platform (Applied Biosystems, ViiA™ 7 Real-Time PCR System). Odds ratios (OR) and 95% confidence intervals (CI) were calculated and the statistical difference in allele distribution was assessed by means of $x^2$ test or Fisher's exact test. Bioinformatic analysis was performed using BlastP, Pymol and Maestro and Desmond (Schrodinger Inc.).
**Results:** A significant association was detected between the GC genotype of rs34536443 (*TYK2*) in both the PsA (p=0.019, OR=0.099, 95% CI 0.005–1.65) and RA cohorts (p=0.033, OR=0.33, 95% CI 0.123–0.90). The C allele of this SNP was associated with PsA only (p=0.02, OR=0.10, 95% CI 0.006–1.681). This polymorphism, located on exon 3, causes a Pro1104Ala mutation which is located at the beginning of an alpha-helical structure. Significant evidence for association with PsA was also found for the GG genotype and G allele of the rs10181656 SNP of *STAT4* (p=0.04, OR=4.3, 95% CI 1.01–18.39 and p=0.03, OR=1.46, 95% CI 1.03–2.08, respectively). Bioinformatics analysis revealed that the C but not G allele of this SNP is located within a putative binding site for transcription factors Pax-4, PPAR/RXR and ZNF99. The TC genotype of the rs763361 SNP of *CD226* was associated with PsA (OR=0.61, p=0.04) but no association was found with RA. This SNP, results in a Gly307Ser substitution, and is thought to be associated with the generation of a protein phosphorylation site. No association was found with the remaining four loci examined.
**Conclusions:** Genetic overlap between PsA and RA was detected for the rs34536443 SNP of *TYK2* gene within a Greek population. The Pro1104Gly mutation of TYK2 may influence its functionality by affecting structural and dynamical elements of the molecule. An association of *STAT4* (rs10181656) with PsA was confirmed while *CD226* (rs763361) was associated with PsA but not RA, in contrast to previous reports. The different findings of this study compared to previous ones highlights the importance of comparative studies that include various ethnic or racial populations.
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## AB0007 GENOME-WIDE ASSOCIATION STUDY OF CLINICAL PHENOTYPES IN PSORIATIC ARTHRITIS

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**Background:** Genome-wide association studies (GWAS) in Psoriatic Arthritis (PsA)patients and controls have allowed the identification of multiple variants associated with disease risk. To date, however, no GWAS for PsA phenotypes has been reported.
**Objectives:** The main objective of this study was to identify new genetic variation associated with clinical phenotypes in PsA.
**Methods:** A total of n=835 patients diagnosed with PsA using CASPAR criteria were recruited in the discovery stage and genotyped for >600,000 single nucleotide polymorphisms. GWAS were performed for clinical and biological phenotypes associated with joint and skin disease. After allelic association analysis, those SNPs with highest level of significance were analyzed in an independent cohort of n=414 PsA patients.
**Results:** In the GWAS stage, several genomic regions showing high evidence of association with different PsA phenotypes (P<5e-6) were identified, including axial disease, peripheral disease, bone proliferation, degree of radiological sacroileitis and the presence of syndesmophytes. Also, GWAS on cutaneous phenotypes identified two regions associated with nail disease and skin disease severity. Using the replication cohort, the association between one locus and peripheral pattern, and two loci with axial pattern were validated.
**Conclusions:** Usign a GWAS approach, new loci associated with axial and peripheral disease in PsA have been identified.
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## AB0008 LACK OF ASSOCIATION BETWEEN POLYMORPHISMS IN INTERLUKIN (IL)-12, IL-12R, IL-23, IL-23R GENES AND TAKAYASU ARTERITIS IN A CHINESE POPULATION

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**Background:** Takayasu arteritis (TA) is a chronic inflammatory arteritis with unknown cause. Genetic components may play an important role in the pathogenesis of TA. It is indicated that HLA-B*52 allele contributes to TA development worldwide. *IL12B* is identified as a susceptibility gene for TA in two recent genome-wide association studies. To date, several loci in the genes coding for members of the IL-12/IL-23 pathway have been found to be involved in the pathogenesis of various immune-mediated diseases.
**Objectives:** The goal of this study was to investigate the relationship between polymorphisms in interleukin (IL)-12, IL-12R, IL-23, and IL-23R genes and TA in a Chinese population.
**Methods:** A case-control study was performed to investigate the associations of nineteen single nucleotide polymorphisms (SNPs) mapping to *IL12A*, *IL12B*, *IL12RB1*, *IL12RB2* and *IL23R* with susceptibility to TA in 145 Chinese TA patients and 300 healthy controls. Genotype identification was performed with the MassARRAY system from Sequenom. In addition, HLA-B*52 genotypes were detected by the polymerase chain reaction using the sequence-specific primers (PCR-SSP).The statistical analysis was conducted by chi-square test and unconditional Logistic regression with plink.
**Results:** No significant differences were found for the distribution of allele and genotype frequencies of these SNPs between TA patients and healthy controls. However, a trend for *IL12A* rs582054 and *IL23R* rs1004819 in association with the TA phenotype was detected. TA patients carrying the rs582054/ rs568408 haplotype ($P_c$=0.019) appeared less likely to progress to a more severe form of disease. And the C allele ($P_c$=0.082) of *IL23R* rs1004819 appeared to be a protective factor to refractory disease. The association of TA with HLA-B*52 was confirmed in this cohort of Chinese patients. Whereas, there was no interaction between HLA-B*52 and polymorphisms in IL-12/IL-23 axis genes.
**Conclusions:** These findings suggest that the polymorphisms of *IL12A*, *IL12B*, *IL12RB1*, *IL12RB2* and *IL23R* might make no contribution to the susceptibility of TA in the Chinese population.
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## AB0009 PADI4 GENE POLYMORPHISM AS A PREDICTOR OF RESPONSE TO METHOTREXATE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Methotrexate (MTX) is the most widely used disease-modifying anti-rheumatic drug in the treatment of juvenile idiopathic arthritis (JIA); however, there is a variation in the clinical response to MTX among the patients [1]. Previous studies have shown conflicting results regarding predictors of the response to MTX. No unequivocal predictive SNP has been found yet, because many were assessed in only one study, or were predictive in one study and showed no effect in others [2].
**Objectives:** The aim of the study was to assess whether the *PADI4* rs2240336 gene polymorphism is a predictor of the disease severity and the response to MTX in patients with JIA from Bashkortostan, Russia.
**Methods:** 283 patients with JIA were genotyped for the *PADI4* rs2240336 gene polymorphism using real-time PCR. The statistical analysis was performed using two-tailed Fisher's exact test, odds ratio, 95% confidence interval and logistic regression in Microsoft Excel, WinPepi v.11.44, R v.3.2.0, SNPStats programs. The disease course was assessed as more severe if the MTX therapy was required. The response to MTX was considered as good if clinical remission on medication (Wallace) was achieved, otherwise – as insufficient. An addition of a biological agent to the MTX therapy was also assessed as a marker of an insufficient response.
**Results:** The requirement of the MTX treatment and its absence was noted at 261 (92.3%) and 22 (7.8%) children with JIA respectively, and the distribution of the genotypes and alleles of the *PADI4* rs2240336 gene polymorphism were similar in both groups (p=0.982). At the same time the frequency of the genotype AG was significantly higher (59.8% vs. 35.5%, p=0.0029, OR=2.71, 95% CI 1.41–4.94), and the frequency of the genotype GG was significantly lower (23.8% vs. 45.2%, p=0.0041, OR=0.38, 95% CI 0.20–0.73) in patients, who received MTX and not achieved clinical remission on medication (n=122) than in those who achieved (n=62). The best model of inheritance was overdominant, where the genotype AG marked an insufficient response to MTX (AG vs. GG + AA, p=0.0017, OR=2.71, 95% CI 1.44–5.11). The association with an insufficient response to MTX was also observed under the dominant (AG + AA vs. GG, p=0.0034, OR=2.64, 95% CI 1.38–5.06) and codominant (AG vs. GG, p=0.0041, OR=3.20, 95% CI 1.58–6.48) models of inheritance. Moreover, the genotype AG frequency was significantly elevated in patients who required an addition of a biological agent to the MTX therapy (n=73) (p=0.012, OR=2.097, 95% CI 1.20–3.66) and the overdominant model of inheritance also proved the best (p=0.0088, OR=2.10, 95% CI 1.20–3.68).
**Conclusions:** Thus, in this study we revealed that the genotype AG of the *PADI4* rs2240336 gene polymorphism was a marker of increased risk of an insufficient response to MTX in children with JIA from Bashkortostan, Russia. If this finding will be confirmed in other studies, it can be potentially used for the early prediction of the response to MTX in patients with JIA.
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## AB0010 ASSOCIATION OF GENE POLYMORPHISMS IN ETS-1 WITH RANKL IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a complicated autoimmune disease characterized by progressive destruction of cartilage and bone. Recently, receptor activator of nuclear factor κB ligand (RANKL) have been found to be involved in the differentiation of osteoclasts [1]. Also, the association between the RANKL expression and the pathogenesis of bone-destructive rheumatoid arthritis (RA) has been described in several joints [2]. It indicated that RANKL play a crucial rule in RA. Meanwhile, E26 transformation specific sequence 1 (ETS-1), belonging to the ETS family of transcription factors that regulate the expression of various immune-related genes, was reported to confer susceptibility and development to RA [3]. Moreover, ETS-1 was found to be overexpressed in RA synovial membrane and to be involved in the destructive pathway of RA [4], but it was not clearly defined.
**Objectives:** We aimed to identify how RANKL changes in RA and whether polymorphisms in ETS-1 play a role in that changes by describing in Chinese Han population.
**Methods:** 170 RA patients and 136 healthy controls were included for this analysis. Clinical information was gathered and disease activity was determined according to the disease activity score for 28 painful/swollen joints (DAS28). The serum level of RANKL were detected by magnetic luminex assays. Four single nucleotide polymorphisms (SNPs) in ETS-1 were genotyped by high resolution melting (HRM) curve method.
**Results:** Compared with healthy controls, Level of RANKL in serum of patients was elevated (28.69 (17.24–44.90) versus 14.24 (17.00–20.00), $P<0.01$). The RA patients with rs73013527 TT genotype had higher RANKL levels (P=0.019 in a dominant model). Furthermore, we found that T allele of rs73013527 was overrepresented in RA group as well (25.7% versus 42.6%, $P<0.001$). Besides, an association was found between rs73013527 TT genotype and DAS28 (P=0.001). No statistically significant difference was observed in the distribution of other three SNPs (rs10893872, rs4937333 and rs11221332) alleles or genotypes in this study (all $P>0.05$).
**Conclusions:** This study suggests that RANKL increased in RA and the polymorphisms in the ETS-1 region may be associated with the changes of RANKL in RA. The patients with rs73013527 TT genotype may be not prone to RA but have higher RANKL which could lead a sever condiction. However, larger studies, most likely through multicenter collaboration will be needed to fully validate the significance of these findings.
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## AB0011 HLA-DP POLYMORPHISMS PLAY PROTECTIVE ROLE IN SYSTEMIC LUPUS ERYTHEMATOSUS IN CHINESE HAN POPULATION

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**Background:** With the application of Genome-Wide Association studies (GWAS), the SLE risk gene loci in HLA-DR and HLA-DQ are gradually revealed [1]. However, the association of HLA-DP polymorphisms with SLE is pretty few reported. Considering the variants in rs3077 and rs9277535 in HLA-DP region were estimated influenced the immune response by affecting antigen presentation of HLA class II molecules to CD4+ T cells [2], it is worthy to explore the role of HLA-DP polymorphisms in SLE.
**Objectives:** Exploring the effects of presently hot HLA-DP SNPs, rs3077 and rs9277525 on SLE.
**Methods:** 335 SLE patients and 635 healthy controls were recruited in present study. Genotyping was performed with polymerase chain reaction-high resolution melting (PCR-HRM) assay and the data was analyzed using SPSS19.0.
**Results:** A significantly positive correlation was observed between the SNP rs3077 and rs9277535 of HLA-DP and SLE susceptibility (rs3077, OR=0.74, 95%CI=0.60–0.91, P=0.004; rs9277535, OR=0.72, 95%CI=0.60–0.91, P=0.001). Moreover, in cytokines, there was significant positive association between rs3077 and IL-17 and INF-γ(P=0.037 and P=0.020 respectively; recessive model, P=0.011 and P=0.008, respectively) and the AA genotype predisposed to lower IL-17 and INF-γcompared with other two genotypes. However, none positive connection was found between rs3077 and IL-1 alpha, IL-4, IL-6, IL-10, and IL-23 (P=0.739, 0.624, 0.685, 0.887, and 0.937 correspondingly). None significant positive correlation could be observed between rs9277535 and any cytokines.
**Conclusions:** HLA-DP polymorphisms (rs3077 and rs9277535) play a protective role in SLE susceptibility. And rs3077 play the role by affecting antigen presentation of HLA class II molecules for CD4+T cells and down-regulating the Th17 signal pathway.
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AB0012 **GENETIC SIGNATURES IN RHEUMATOID ARTHRITIS: CHANGES UPON ANTI-TNF THERAPY AND ASSOCIATION WITH RESPONSE TO BIOLOGICAL TREATMENT**

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**Background:** Genetic signatures may be involved in the pathogenesis of rheumatoid arthritis (RA) and ankylosing spondylitis (AS). In addition, such genetic patterns may change overtime upon treatment with anti-TNF biologics. With respect to pharmacogenomics, pre-treatment genomics may predict response or non-response to biological therapy.
**Objectives:** In the present study, we wished to determine gene expression changes due to anti-TNF therapy. Furthermore, we wished to study associations between baseline genetic signature and response to TNF blockade.
**Methods:** Altogether 23 RA and 17 AS patients were recruited for the study. Among RA patients, 10 received certolizumab pegol (CZP), and 13 etanercept (ETN). All AS patients were treated with ETN. Gene expression analysis using Affymetrix microarray and PrimeView array was performed at baseline and after 2 weeks of treatment. EULAR response criteria were used to differentiate responders (R) from non-responders (NR) after 12 weeks of treatment using GeneSpring software. Principal Component Analysis (PCA) was also performed. Changes in gene expression patterns were also determined between baseline and 2 weeks.
**Results:** In the CZP-treated RA group, 4 patients were R and 6 were NR. Altogether 453 genes showed significantly differential expression between N and NR. In the RA-ETN group, 10 patients were R, and 3 were NR. Here, 836 genes exerted differential expression. When a CZP- and ETN-treated patients, were pooled, 165 genes separated R from NR. In the AS population, 14 patients were R and 3 were NR. 177 genes differentiated between R and NR. When changes in gene expression patterns from baseline to week 2 were determined, in the RA-CZP, RA-ETN, RA-all and AS groups 370, 79, 24 and 76 genes showed significant changes in expression.
**Conclusions:** Using microarray, genetic signatures may differentiate RA patients responding or not responding to anti-TNF therapy. Furthermore, a large set of genes show differential expression before versus 2 weeks after biologic treatment.
**Disclosure of Interest:** None declared
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## Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0013 **GLOMERULAR IL-4 SIGNALING MEDIATES FOOT PROCESS EFFACEMENT AND PROTEINURIA IN NEPHROTIC SYNDROMES**

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**Background:** Podocyte foot process effacement is a feature of proteinuria, thought to be a stereotyped response of the podocyte to injury. The stimulus for podocyte injury and foot process effacement is unknown, although changes in the actin cytoskeleton has been implicated. B cell depletion therapies have demonstrated efficacy in some patients with proteinuria including those with minimal change disease. Since pathogenic antibodies are not causative, we hypothesized that a B cell derived cytokine might be capable of directly inducing podocyte injury and foot process effacement.
**Objectives:** Develop a B cell model of proteinuria in mice, and identify glomerulopathic cytokines derived from B cells.
**Methods:** B cell model antigen model hen egg lysozyme (HEL) was biotinylated, complexed to avidin and injected into mice. HEL-specific B cells were adoptively transferred and proteinuria assessed. Two-photon microscopy was performed in vibrotomed kidneys following transfer of CFSE-labeled HEL-specific B cells with or without HEL antigen injection. Cultured podocyte membrane ruffling was assessed with DIC videomicroscopy. IL-4 expression in mice was achieved by hydrodynamically injecting murine IL-4 in the piggyBac vector system. Human kidney biopsies were assessed for phospho-STAT6 by immunohistochemistry.
**Results:** We identified IL-4 as a B cell derived cytokine capable of stimulating podocyte actin rearrangement. Using a novel model of B cell induced proteinuria, B cells polarized to secrete IL-4 upon activation with HEL induced proteinuria without antibody or complement deposition. Using two-photon microscopy, we observed an accumulation of HEL-specific B cells within glomeruli containing HEL antigen.
To confirm the glomerulopathic properties of IL-4, we overexpressed IL-4 in mice and found this was sufficient to induce foot process effacement and proteinuria. Inhibition of IL-4 signaling with a JAK1/3 inhibitor markedly reduced proteinuria in these IL-4 overexpressing mice. Finally, a subset of patients (31%) with steroid-sensitive nephrotic syndrome possessed glomerular STAT6 activation.
**Conclusions:** These findings suggest a potential explanation for the utility of immunosuppression and more targeted anti-B cell therapy with rituximab in the treatment of steroid-sensitive nephrotic syndromes. These results support the role of IL-4 in human nephrotic syndromes and represents a novel therapeutic target.
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AB0014 **NANOPARTICLES AS MRI CONTRAST AGENT FOR EARLY DIAGNOSIS OF RA: EFFECTS OF AMINO-PVA-COATED SPIONS ON CD4+ T CELL ACTIVITY**

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**Background:** In medical applications nanotechnology provides new opportunities for diagnostic and therapeutic interventions in a variety of human diseases. Superparamagnetic iron oxide nanoparticles (SPION) are used as high-sensitive enhancer for magnetic resonance imaging, where they represent a promising tool for early diagnosis of destructive diseases such as rheumatoid arthritis (RA) and osteoarthritis (OA).
However, safety aspects still represent crucial problems for the further development of nanotechnology based products. Therefore, the focus of our work here was to identify more in detail putative unwanted effects of amino-polyvinyl alcohol-coated (a-PVA) SPION on human immune cell functions.
**Objectives:** Since we could demonstrate in former studies that professional phagocytes are activated by a-PVA-SPION, we here focused on the influence of these nanoparticles on human T helper cell activity.
**Methods:** PBMCs were isolated from blood samples obtained from healthy donors (HD, $n \geq 9$) or patients suffering from RA ($n \geq 11$). Primary human CD4 positive T cells were separated via MACS-Sort and incubated with the mitogen PHA-L (5$\mu$g/ml) and/or varying doses of a-PVA-SPION (1 $\mu$g/ml, 10 $\mu$g/ml, and 100 $\mu$g/ml) or left untreated for 20 h (analysis of caspase-3/7-activity, intracellular ATP content and CD25 expression) or 72 h (analysis of proliferation and CD25 expression). Cells were incubated under either normoxia (app. 18%O2) or hypoxia (1%O2) in order to mimic conditions found in the circulation and in the inflamed joint, respectively.
**Results:** We observed for PHA-L/a-PVA-SPION co-stimulated T cells from HD a decrease in cell count (all $p<0.05$) whereas the caspase-3/7-activity is increased (all $p<0.05$) in these samples, as expected. Although, we observed that T cells from RA patients are more susceptible to low-dose a-PVA-SPION-induced apoptosis than T cells from HD ($p<0.05$), in both groups a-PVA-SPION do not activate CD4+ T cells *per se* and do not influence mitogen-mediated T cells activation with regard to CD25 expression and cell proliferation. Nevertheless, we were able to demonstrate that CD4+ T cells obtained from RA patients and healthy subjects differ in their response to mitogen stimulation and oxygen availability.
**Conclusions:** PVA-SPION at concentrations up to 100$\mu$g/ml do neither activate nor significantly influence mitogen-stimulated CD4+ T cells activation and have negligible influence on T cells apoptosis.
**Disclosure of Interest:** None declared
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AB0015 **EVALUATING THE EFFECT OF ANTI-TNF, ANTI-IL6R AND ANTI-CTLA4 ON ACPA ISOTYPES IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** B-cell depletion therapy decreases autoantibodies formation as rheumatoid factor and anti–citrullinated protein antibodies (ACPA). Other therapeutic targets (TT) such as anti-TNF (tumor necrosis factor), anti-IL-6R (interleukin-6 receptor) and anti-CTL4A (cytotoxic T-lymphocyte antigen-4) modulate the B-cells proliferation/maturation and indirectly the production of autoantibodies. ACPA titers provide us information about disease activity and may be critical for inducing clinical remission in rheumatoid arthritis (RA) patients.
**Objectives:** To evaluate the impact of the therapeutic targets: anti-TNF; anti-IL6R and anti-CTLA4 on ACPA titers in RA patients.
**Methods:** In this longitudinal study we selected ACPA positive patients naïve to

BT (N=27). All patients were assessed at baseline and after 4, 8, 12, 24 and 36 months (m) of treatment initiation. Disease activity was assessed by the 28 joint count-disease activity score (DAS28) according to C-Reactive Protein (CRP). ACPA isotypes (IgG, IgA and IgM) were determined by ELISA (CCP2-plates, Eurodiagnostica,SE). Anti-human antibodies isotype specific were used (Binding Site, UK). Statistical analysis was performed according to TT (anti-TNF, anti-IL6R and anti-CTLA4) and anti-TNF therapies (IFX, ADA, ETN).

**Results:** We found a significant DAS28-CRP decrease in: anti-IL6R (p=0.017, p=0.018, p=0.018, p=0.028, p=0.028) and anti-TNF (p=0.002, p=0.002, p=0.003, p=0.004, p=0.007) groups at 4, 8, 12, 24 and 36m. Evaluating the anti-TNF treatments, we found a significant decrease on DAS28 in ADL at 4 (p=0.046) and ETN groups at 4, 8, 12 and 24m of treatment (p=0.043, p=0.043, p=0.043, p=0.043). Comparing TT, the most outstanding reduction of DAS28 was found in anti-IL6R group compared to anti-CTLA4 group (p=0.017) at 8m, probably due to a greater reduction of CRP in anti-IL6R group (p=0.018). Regarding ACPA isotypes, we only found a significant decrease in IgA-ACPA titers in anti-IL6R group at 4, 8 and 12m of treatment (p=0.012, p=0.036, p=0.046). No changes were found neither in other TT nor in anti-TNF therapies. Comparing TT, we found lower IgG-ACPA titers in anti-CTLA4 group compared to anti-IL6-R group (50.25,98.2U/ml) at 4m. The highest IgG-ACPA titers were found in anti-IL6R (228.7 U/ml) than anti-TNF (53.7U/ml) and anti-CTLA4 groups (71.7U/ml) (p=0.048, p=0.024) at 24m. For IgM-ACPA, the lowest titers were found in anti-IL6R than anti-CTLA4 at 4 and 12m (4m: 2.988 y 3.093OD;12m: 3.004 y 3.116OD) (p=0.012, p=0.017, p=0.017).

**Conclusions:** Patients treated with anti-IL6R and anti-TNF had the most outstanding reduction of DAS28 at the first 8m of treatment. Regarding ACPA isotypes, IgM-ACPA levels were higher in anti-CTLA4 than anti-IL6R probably due to inhibition of B cells class-switching by anti-IL6R therapy. Those patients treated with anti-IL6R presented a progressive decrease of IgA-ACPA and total IgA, as well as, a higher IgG-ACPA titer at 24m. These results showed that both therapies modulate the B cell maturation/differentiation and ACPA production by different immune-regulation pathways, as well as, the cell-cell interaction process. Our data suggests that B-cells and ACPA isotypes monitoring may be useful to further understand their role in the RA pathogenesis and its association with clinical response to BT.

**Disclosure of Interest:** None declared

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## AB0016 B7 COSTIMULATION AND INTRACELLULAR INDOLEAMINE 2,3-DIOXYGENASE (IDO) EXPRESSION IN SYSTEMIC SCLEROSIS AND PRIMARY SJÖGREN'S SYNDROME

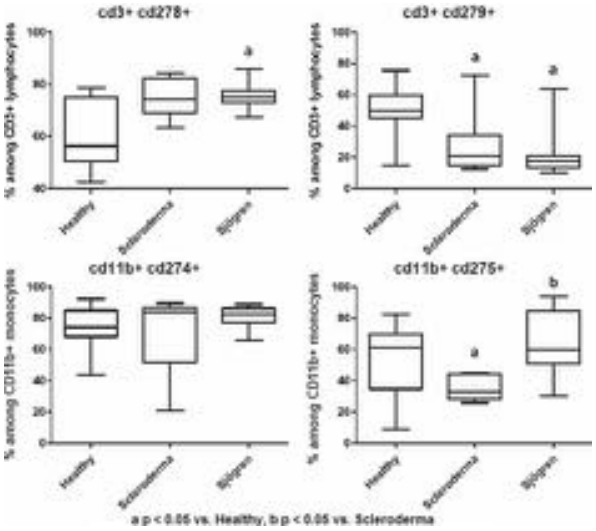
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**Background:** Antigen presentation and costimulation are the initial steps of adequate T cell function and play an important role in the coordination of pro- and anti-inflammatory events. B7 costimulatory molecules are expressed on antigen presenting cells (APCs) and influence intracellular expression of indoleamine 2,3-dioxygenase (IDO), another molecule with important immune regulatory functions. Alterations in the expression of B7 costimulatory molecules and receptors may play a role in the autoimmune response in two clinically and pathogenetically distinct disorders, systemic sclerosis (SSc) and primary Sjögren's syndrome (pSS).

**Objectives:** In this study, we aimed to describe the expression of B7 costimulatory molecules on monocytes and their corresponding receptors on T lymphocytes in SSc and pSS peripheral blood samples compared to healthy controls, as well as the intracellular expression of IDO.

**Methods:** We determined the frequency of activated (CD11b+) monocytes expressing B7-1 (CD80), B7-2 (CD86), B7-H1 (CD274), and B7-H2 (CD275) molecules, and that of CD3+ T cells and CD4+ T helper cells expressing the corresponding CD28, CTLA-4 (CD152), PD-1 (CD279), and ICOS (CD278) receptors in peripheral blood samples of 20 healthy adults, 9 SSc and 15 pSS patients using flow cytometry. We also examined the intracellular expression of IDO by staining with fluorescent antibodies.

**Results:** The expression of B7-1 and B7-2 costimulatory molecules was comparable in all three study groups. The expression of CD28 was lower in both SSc and pSS patients. Furthermore, the frequency of CTLA-4 was increased in pSS. The level of negative feedback in this pathway is more pronounced in pSS compared to SSc. The expression of ICOS, a stimulator of T cell activation was elevated in pSS, but not in SSc, while that of its corresponding costimulatory molecule, B7-H2 was strongly decreased in SSc compared to controls (Figure). Therefore, this pathway appears to play a more dominant role in pSS. The frequency of PD-1 expressing T lymphocytes was decreased both in pSS and SSc. At the same time, there was no difference in the expression of the corresponding CD274 molecule on APCs between the investigated study groups (Figure). The T cell inhibitory effect of this receptor appears to be diminished both in pSS and in SSc, which may be related to a common autoimmune pathogenesis. While no difference was observed in IDO expression between controls and SSc patients, the frequency of IDO expressing APCs, as well as intracellular IDO content (mean fluorescence intensity) in T cells was higher in pSS than in controls.




**Conclusions:** Our investigation identified a number off differences in B7 costimulation between SSc and pSS patients which may play a role in the distinct pathogenesis and clinical features of these autoimmune disorders. B7 costimulatory molecules and their receptors may be potential therapeutic targets in the future.

**Disclosure of Interest:** None declared

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## AB0017 PILOT STUDY ON THE PATTERNS OF B LYMPHOCYTS INFILTRATION IN KIDNEY FROM PATIENTS WITH LUPUS NEPHRITIS

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**Background:** B lymphocytes infiltration associated ectopic lymphoid tissue (ELT) formation in situ kidney tissue had been showed to play an important role in the pathogenesis of *MRL/lpr* lupus nephritis mice model, until now there are few studies to identify the significance of them in the pathogenesis, diagnosis and treatment of human lupus nephritis (LN).

**Objectives:** To know the significance of B lymphocytes infiltration and associated ectopic lymphoid tissue (ELT) formation in the pathogenesis, diagnosis and treatment of human LN

**Methods:** The renal specimen were analyzed by light microscopy examination of routine pathology and immunohistochemistry detection of CD3+,CD20+ and CD21+ cells expression. The enrolled patients were grouped based on the WHO classification of pathology or ELT patterns. Clinical datawere collected and evaluated.

**Results:** 89 LN patients were experienced with GC and IS combination therapy and WHO III 21, WHO IV 53 and WHO V 15. 69 cases of CD20+ cells group and 20 of CD20-cells group could be divided. comparing to CD20-group, no difference could be founded in age, sex, blood leucocytes, urine protein, C3 level, C4 level, ESR, CRP, antiDNA, acute injury index and chronic injury index of renal tissue and total remission rate (all $P>0.05$), but significant difference can be found in mean disease duration (CD20+group: 21.8±9.9 months VS CD20-group: 9.8±6.2 months) (P=0.045) and complete disease remission rate (CD20+group: 63.8% VS CD20-group: 90%) (P=0.047) at 6 month of treatment. With respect to B lymphocytes infiltration associated ELT formation, there was focal distribution of CD3+ T cells and CD20+B cells (type 2) in 51 cases (57.3%), scattering distribution of CD3+ T cells and CD20+B cells (type 1) in 18 cases (20.2%) and no CD20+B cells infiltration in 20 cases (22.5%) but no expression of CD21+ dendritic cells expression in all. There was longer disease duration in type 2 patients than in type 1 or type 0 patients. compared to WHO V-LN patients, there was different ELT distribution patterns in WHO III and WHO IV-LN patients, but there were no difference in ELT distribution patterns between WHO III and WHO IV-LN patients.

**Conclusions:** Focal distribution of CD3+ T cells and CD20+B cells (type 2 ELT)was main pattern in the renal interstitial tissue of LN patients. B cells infiltration-associated ELT formation is a predictor of longer disease duration and poor response to conventional combination therapy of high-dose GC and IS.

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**Disclosure of Interest:** None declared

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## AB0018 DISEASE SPECIFIC EFFECTS OF LIPID ANTIGENS ON VDELTA1+ AND VGAMMA9+ T CELLS IN SYSTEMIC SCLEROSIS

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**Background:** T cells (TC) expressing Vδ1+ TC receptors recognize lipids presented by CD1d (1). Oligoclonal Vδ1+ TC infiltrate skin and internal organs and are activated in the peripheral blood (PB) in systemic sclerosis (SSc) suggesting lipids as pathogenic immunogens (2,3).
**Objectives:** To determine effects and molecular pathways of the auto antigenic lipid – cardiolipin- in SSc and healthy controls (HC).
**Methods:** Mononuclear cells (MC) were isolated from PB of 12 SSc patients and 8 HC by density centrifugation and cultured in IL2C (RPMI-1640 with 10% fetal bovine serum + 100 international units of interleukin-2), CARDC or OCHC [IL2C+cardiolipin 2.5μg/ml or OCH 50ng/ml (analogue of α-galactosyl ceramide) respectively]. Zoledronate (zol, 2μM), a Vγ9+ γδTC stimulant that induces their CD1d expression, was added to parallel cultures (labeled ILCzol etc.) (4,5). Flow-cytometry (FC) of 4–5 day cultures after staining with monoclonal antibodies (mAb) or CD1d tetramers to detect %CD25+ cells (%CD25+) or tetramer+ cells, was performed.Means were compared by two tailed student t-test; $p<0.05$ was considered significant.
**Results:** Vδ1+ and Vγ9+TC consisted 11.85±2.0% and 14.7±3.5% vs 10.42±2.4% and 7.08±1.2% of the CD3+ TC in SSc and HC IL-2C respectively (values not significantly different). In HC cultures, %CD25+ was non significantly different in IL2C, OCHC and CARDC for all TC subsets.Furthermore, IL2Czol increased %CD25+ on all TC subsets relative to IL2C, which was further amplified on Vδ1+ TC in CARDCzol (33.16±7.0% to 56.93±6.3% $p<0.007$). In SSc, in contrast OCHC and CARDC enhanced %CD25+Vδ1+TC whereas CARDC %CD25+Vγ9+TC was suppressed (76.06±8.7% vs 66.9±10.9%, $p<0.036$) relative to IL2C. In IL2Czol, however, %CD25+Vγ9+TC increased to 73.93±8.12%. In contrast, IL2Czol decreased SSc %CD25+Vδ1+TC (69.58±8.29% to 55.02±10.54%, $p<0.028$), but this decrease was partially abrogated in CARDCzol. Both SSc and HC IL2C Vδ1+TC were highly reactive with native and OCH-bound CD1d tetramers (25–70%, n=5 and 50–54% n=2 respectively), but binding was suppressed in SSc samples by zol. In addition, blocking mAb against CD1d abolished the increased expression of CD25 in SSc CARDCzol Vδ1+ TC (from +27±3% to -8.9±2.3%, n=5 $p<0.0251$) but not in HC (n=2).
**Conclusions:** Cardiolipin induced suppression of CD25 expression on Vγ9+ TC in SSc, which could be reversed by zol. On the other hand cardiolipin reversed SSc- specific zol induced suppression of CD25 expression on Vδ1+TC in a CD1d dependent-manner. These results suggest that cardiolipin may suppress Vγ9+ TC while augmenting Vδ1+TC activation in SSc, at least in part via CD1d mediated interactions.
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## AB0019 IL-10-PRODUCING BREGS ARE DECREASED IN PSORIATIC ARTHRITIS AND INVERSELY CORRELATE WITH TH17 CELLS

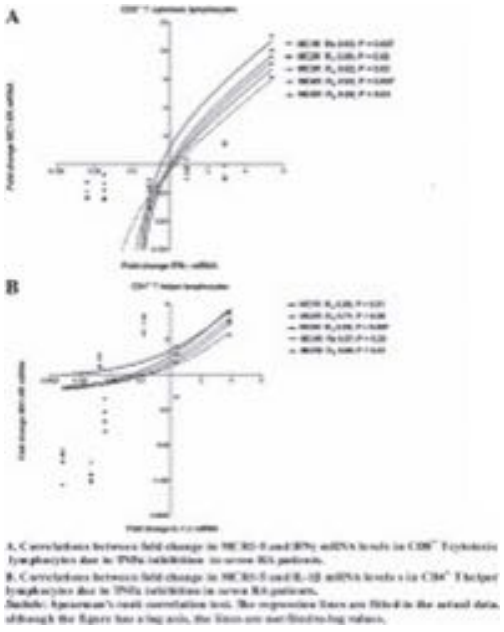
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**Background:** B cells may form ectopic lymphoid-like structures in the synovium of patients with psoriatic arthritis (PsA) but the significance of this finding is not clear. A recent study found high frequency of autoantibodies in PsA[1]. Whether regulatory B cells (Bregs) are decreased or not in PsA is not clear.
**Objectives:** To assess the phenotypic and functional characteristics of Breg subsets, CD19(pos)CD27(pos)CD24(high) memory and CD19(pos)CD24(high) CD38(high) transitional Bregs in patients with PsA.
**Methods:** Peripheral blood mononuclear cells, isolated from 61 PsA patients, 21 patients with psoriasis (Ps) and 15 normal controls (NCs), were assessed. The expression of surface CD19, CD24, CD27 and CD38 and cytoplasmic IL-10 by Bregs was examined by flow cytometry following 24 hour bacterial CpG (ODN2006) stimulation using fluorochrome-conjugated monoclonal antibodies. We also measured IL-17 expression from T cells (Th17 cells) stimulated with PMA plus Ionomycin for 5 hours followed by intracellular staining (BD Biosciences).
**Results:** Transitional Bregs were significantly decreased in PsA patients compared to NCs (0.72±0.54 *vs*1.56±0.58, $p$=0.000) and in Ps compared to NCs (1.08±0.38 *vs* 1.56±0.58, $p$=0.016, as well as in PsA compared to Ps patients ($p$=0.002). Memory Bregs were significantly decreased in PsA patients compared to NCs (2.93±2.31*vs* 6.94±2.03, $p$=0.000) and in Ps patients (2.97±1.83) compared to NCs ($p$=0.000) but did not differ between PsA and Ps patients. The impairment of Bregs in PsA was not associated with number of swollen or tender joints, CRP, ESR, or treatment with biologics. IL-10-producing Bregs inversely correlated with Th17 cells in PsA and in Ps.
**Conclusions:** PsA exhibits numerical decrease and functional impairment of Bregs, especially of transitional Bregs. IL-10-producing Bregs inversely correlate with Th17 cells. The impairment of IL-10-producing Bregs may contribute to the pathogenesis of psoriatic disease.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3427

## AB0020 THE MELANOCORTIN SYSTEM IS RESPONSIVE IN DISEASE DRIVING IMMUNE CELLS IN RHEUMATOID ARTHRITIS AND MAY OFFER A PATHWAY TO CURATIVE TREATMENT

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**Background:** Although biological agents may manage rheumatoid arthritis (RA), curative treatment is still the "holy grail". Induction of auto-antigen specific immune tolerance might offer a solution and obviate the need for life-long immunosuppression. Melanocortins are small peptides with considerable immune tolerance inducing, inflammation resolving and tissue preserving qualities (1). In animal experimental, autoimmune conditions, melanocortins have been demonstrated to bind differentially to melanocortin receptor (MCR) 1–5 on immune cells and to transform auto-reactive $CD4^+$ T helper (Th) lymphocytes (ly) as well as sensitized $CD8^+$ T cytotoxic (Tc) ly into regulatory T (Treg) ly and thus clear cell-mediated auto-immunity and delayed type hypersensitivity. In contrast to the situation in organ transplantation, clinical application of Treg therapy in human autoimmune disease is still non-existing, primarily because of a lack of in depth understanding.
**Objectives:** To explore if the pro-resolving melanocortin system may offer a pathway to immune tolerance induction, we examined whether the melanocortin system is present and responsive in pathogenic immune cell subsets in RA. To this end, we related changes due to TNFα inhibition (I) in MCR1–5 mRNA levels to changes in Th1 signature-, inflammatory and regulatory cytokine mRNA levels.
**Methods:** $CD4^+$ Th, $CD8^+$ Tc ly, $CD19^+$ B-ly and $CD14^+$ monocytes from seven patients with definite RA were isolated by Dynabeads before and three months after the start of TNFαI. Total RNA was extracted and mRNAs for MCR1–5 and a panel of disease driving Th1, inflammatory and regulatory cytokines were measured by real-time qRT-PCR. Fold changes in MCR1–5 gene levels were correlated to changes in cytokine gene levels.
**Results:** MCR1–5 gene expressions were reduced in al examined cell types, significantly so in $CD8^+$ Tc ly and $CD19^+$ B ly in RA patients responding to TNFαI. In addition, Th1 and inflammatory cytokine mRNA levels were reduced in all cell types in responders. In a non-responding patient MCR1–5 gene expressions as well as Th1 and inflammatory cytokine gene levels increased substantially. The changes in MCR1–5 gene expressions in $CD8^+$ Tc cells correlated significantly to changes in the Th1 cytokine IFNγ gene level in this cell type. Furthermore, we



found significant correlations between changes in MCR 1, 3, 5- and change in IL-1β gene levels in CD4+ Th ly.

**Conclusions:** Our results point at a responsive melanocortin system in immune cells in RA. Moreover, its regulation seems intimately connected to the disease driving Th1 response, that is IFNγ production by CD8+ Tc ly. Our results are underlined by the recently reported importance of IFNγ producing CD8+ Tc ly in early RA. Thus our findings indicate that the melanocortin pathway lies open to treatment of auto-reactive effector T ly from RA patients with MCR type specific synthetic ligands in vivo or in vitro to induce Treg transformation. Future curative induction of auto-antigen specific immune tolerance in RA may therefore involve the melanocortin system.

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**Disclosure of Interest:** None declared

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## AB0021 RESISTIN GENE TRANSCRIPTION IS REGULATED IN ADAPTIVE AND INNATE IMMUNITY IN RHEUMATOID ARTHRITIS

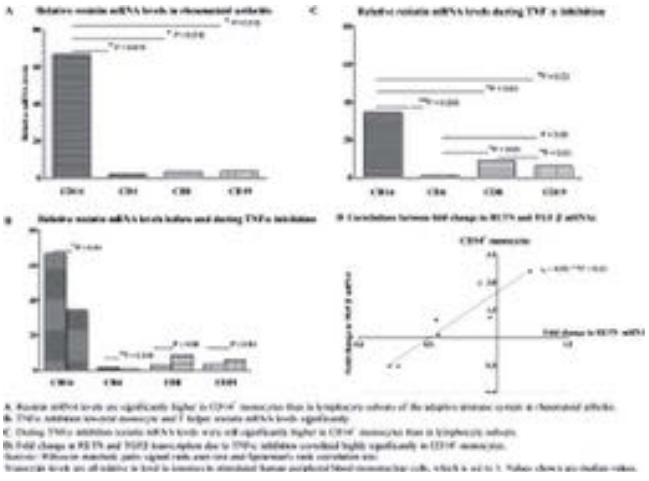
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**Background:** Resistin (RETN) was described in 2001 as an adipokine secreted by murine adipocytes resulting in insulin resistance. However, in man, adipocyte synthesis of RETN is controversial, while monocyte RETN production is well established (1). Curiously, RETN synthesis and its regulation in pathogenic immune cell subsets have not been examined in rheumatoid arthritis (RA), although blood RETN levels correlate to disease activity. In RA, -a risk factor for coronary artery disease (CAD), RETN might contribute to atherosclerosis. E.g. macrophage secreted RETN in atheromas, facilitates cholesterol uptake and plaque instability. Considering this, an in depth understanding of the regulation and effects of RETN synthesis in pathogenic immune cell subsets may provide clues to the aetiology of CAD, known to be associated with factors (high CRP, RF and ACPA), characterizing active RA.

**Objectives:** The aim of our investigation was to explore whether RETN gene transcription in pathogenic cell subsets of innate and adaptive immunity is detectable and if present, amenable to TNFα inhibition (I) and correlated to important cytokines in RA.

**Methods:** We examined the reaction of RETN gene transcription to TNFαI in CD14+ monocytes, CD4+ T helper (Th) lymphocytes (ly), CD8+ T cytotoxic (Tc) ly, and CD19+ B ly in RA patients, responding to adalimumab. Leukocyte subsets from 7 RA patients were isolated by Dynabeads before and 3 months after start of TNFαI. Total RNA was extracted and mRNAs for RETN and a panel of disease driving Th1, inflammatory and regulatory cytokines were measured by real-time qRT-PCR.

**Results:** RETN gene transcription was present in al cell subsets and in CD14+ monocytes and CD4+ Th ly responded to TNFαI with a significant decrease. In CD14+ monocytes the RETN gene was transcribed to a significantly higher degree than in lymphocyte subsets of the adaptive immune system both before and during TNFαI. In active RA, prior to TNFαI, RETN and TGFβ mRNA levels correlated significantly in CD4+ Th ly (P=0.03), while in CD14+ monocytes fold change in TGFβ and RETN mRNAs due to TNFαI correlated highly significantly (P=0.01). Furthermore, RETN and IL-8 mRNA levels tended to correlate (P=0.06) in CD14+ monocytes prior to TNFαI.



**Conclusions:** We here report regulated RETN gene transcription in human CD4+ Th ly as well as in CD14+ monocytes. Our results point at wider functions for RETN. Thus we found TNFαI regulated RETN gene transcription in CD4+Th ly in RA, indicating a possible immune response directing role. In this aspect, our results are in concert with increased RETN mRNA correlating to CD4+Th17 ly number in human cecum. The idea of RETN pleiotropic actions is further supported by the correlation to TGFβ transcription. RETN and TGFβ share a pathway for their synthesis and fibrogenic ability (2), on top TGFβ also has a prominent role in immune tolerance. The relation to IL-8 indicates influence on neutrophil trafficking (1).

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## AB0022 MODULATION OF TREG STABILITY AND FUNCTION BY INHIBITION OF IL-1BETA

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**Background:** High plasticity was described for Th1 and Th17 cells depending on the local cytokine milieu and regulation by Tregs. Pathogen-induced human Th17 cells and Tregs are strongly regulated by IL-1beta. So far, the influence of IL-1beta on FoxP3 methylation and stability of the Treg lineage has not been investigated. Further, whether inhibition of IL-1beta and its receptor is able to promote FoxP3 demethylation and to conserve Treg functions, such as suppression of Th17 and Th1 functions, has not been assessed in healthy humans, as well as in patients with autoimmune arthritis.

**Objectives:** Thus, the present study aimed to investigate *in vitro* nTreg and iTreg functions in lymphocytes obtained from stored routine blood samples of patients with juvenile idiopathic arthritis (JIA) or rheumatoid arthritis (RA) in different disease activity states.

**Methods:** Proportions of peripheral nTregs and cultured iTregs from stored routine blood samples taken from JIA, RA patients and healthy, age-matched controls (HC) and intracellular cytokine production were analyzed by flow cytometry. Suppressive function of iTregs under *in vitro* inhibition of IL-1beta was studied by suppression assays. *FOXP3* expression and methylation were analyzed by quantitative PCR and bisulfite pyrosequencing.

**Results:** Lower proportions of nTregs were found in samples of JIA patients with acute disease flare (mean 2.3% of CD4+ T cells) compared to HC (4.1%) ($p<0.001$). Using IL-1beta and other Th17-stimulating cytokines, proportions of induced iTregs were similar between JIA samples with acute disease flare (mean 34.6% of CD4+ T cells) and healthy children (38.1%), but lower in remission (13.2%) ($p<0.001$). Proportions of iTregs were markedly induced by blockade of IL-1beta in both JIA (mean 78.1% of CD4+ T cells) and HC (84.0%) compared to cells without blockade ($p<0.01$). IL-1beta blockade reduced proliferation of effector T cells by induction of suppressive function of iTregs in both JIA (suppression from 55.1% to 34.2% proliferating effectors) and HC (from 48.2% to 31.8%) ($p<0.001$). Intracellular IL-10 production was not influenced by blockade of IL-1beta.

**Conclusions:** Induction of Tregs seems to be different depending on disease activity status in autoimmune arthritis. DNA methylation at the *FOXP3* promoter and enhancer regions may influence expression of FoxP3 in Tregs and, thus, modify their phenotype. Although IL-10 was not markedly influenced by IL-1beta-dependent mechanisms, our findings indicate that suppressive iTreg functions may be restored by selective blockade of IL-1beta.

**Disclosure of Interest:** None declared

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## AB0023 THE REGULATION OF HUMAN IN VITRO TH17 CELL DIFFERENTIATION BY CYTOKINES

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**Background:** Th17 cells have a central role in inflammation via their pro-inflammatory cytokine production, such as interleukin (IL)-17A, -17F, -21, -22, tumor necrosis factor-α and the expression of master regulator transcription factor RORc. The Th17 cells have essential role in many autoimmune diseases via induction of the development of inflammation.

**Objectives:** We studied the *in vitro* Th17 cell differentiation of healthy donors and patients with rheumatoid arthritis (RA).

**Methods:** CD45RO- and CD45RO+ cells were isolated from peripheral blood mononuclear cells with a two-step negative magnetic separation. The cells were activated with anti-CD3 and anti-CD28 antibodies and treated with TGFβ (2.5

ng/ml), IL-6 (25 ng/ml), IL-1β (10 ng/ml) and IL-23 (10 ng/ml) cytokines and with an anti-IL-4 (10 μg/ml) blocking antibody. After 5 and 10 days IL-17 and IL-22 productions were measured by ELISPOT and ELISA; the RORc and Tbet expression were measured by quantitative real-time PCR methods. Cell viability was monitored by impendance-based cell analyzer (CASY-TT).
**Results:** Although anti-CD3/CD28 activation increased the IL-17 and IL-22 productions, it did not alter the RORc expression of the CD45RO- cells of healthy donors. The IL-22 production and the Tbet expression of the RORc producing cells were inhibited by TGFβ and stimulated by IL-23 treatment. The CD45RO+ cells of healthy donors expressed higher level of RORc, T-bet and IL17 without stimulation or cytokine treatment compared to the CD45RO- cells. However, there was no difference between the RORc and Tbet expression of the freshly separated CD45RO+ and CD45RO- cells of RA patients. IL-23 treatment increased both of IL-17 and IL-22 cytokine production of the differentiated CD45RO- cells.
**Conclusions:** IL-17 and IL-22 production are differently regulated during human Th17 differentiation. Our data suggest that the increased baseline RORc expression of CD45RO- cells may contribute to the accelerated Th17 differentiation in RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4265

## AB0024 B-CELL MARKERS EXPRESSION IS AFFECTED BY TNF-INHIBITORS AND TOCILIZUMAB TREATMENT IN RHEUMATOID ARTHRITIS

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**Background:** The use of TNF-inhibitors and/or the IL-6 receptor antagonist, tocilizumab, in rheumatoid arthritis (RA) have pleiotropic effects that also involve circulating B-cells.
**Objectives:** The main goal of this study was to assess the effect of TNF-inhibitors and tocilizumab on B-cell phenotype and gene expression in RA.
**Methods:** Blood samples were collected from untreated early RA (ERA) patients, established RA patients under methotrexate (MTX) treatment, established RA patients before and after treatment with TNF-inhibitors and tocilizumab, and healthy donors. B-cell subpopulations were characterized by flow cytometry and B-cell gene expression was analyzed by real-time PCR on isolated B-cells. Serum levels of BAFF, CXCL13 and sCD23 were determined by ELISA.
**Results:** The frequency of total CD19+ B cells in circulation was similar between controls and all RA groups, irrespective of treatment. However, established RA patients under MTX treatment had significantly increased frequencies of double negative (IgD-CD27-) B cells in comparison with controls. Treatment with TNF-inhibitors and tocilizumab did not affect the circulating levels of B-cell subpopulations. CD86 and CD95 had, respectively, a significantly lower and higher expression on B-cells after anti-TNF treatment. HLA-DR MFI values were also significantly increased in RA patients after treatment with TNF antagonists and tocilizumab. BAFF-R, TACI, BCMA, CD69, CXCR5, TLR9, IgM and CD5 expression on B cells were not significantly affected by TNF-inhibitors and tocilizumab. In addition, alterations in B cell gene expression of BAFF-R, TACI, TLR9, FcγRIIB, BCL-2, BLIMP-1 and β2M were found in ERA and established RA patients under MTX treatment when compared to controls, but no significant differences were observed after anti-TNF and tocilizumab treatments when comparing baseline and follow-ups. Moreover, CXCL13 and sCD23, but not BAFF serum levels were significantly increased since early RA, but no effect of TNF-inhibitors and tocilizumab treatment was observed.
**Conclusions:** In RA patients, the use of TNF-inhibitors and/or tocilizumab treatment affects B-cell phenotype in circulation, but not B-cell frequencies or B-cell gene expression. Our results suggest that TNF-inhibitors and tocilizumab help to reduce B-cell infiltration in inflammatory sites, allowing these activated B-cells to recirculate through blood and lymphatic systems.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5045

## AB0025 EVOLUTION OF REGULATORY B CELLS UNDER TREATMENT BY BIOLOGICS IN RHEUMATOID ARTHRITIS

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**Background:** In clinical daily practice, the response to biologics is unpredictable in patients with rheumatoid arthritis (RA) and there is a crucial need for biomarkers of response.
**Objectives:** The main objective of our study is to describe the evolution of regulatory B cells (Bregs) in patients with RA treated with biologics and to investigate whether there is a correlation between the rate of Bregs and the clinical response.
**Methods:** This was a propective single-center pilot study, descriptive and not randomized. Patients were included with RA fulfilling the ACR/EULAR 2010 criteria, with an active disease according to the DAS28 score despite treatment, and in whom initiation or switch of a biologic except rituximab was required. Acontrol group of patients without any autoimmune disease or immune dysfunction was also assessed. B and T lymphocytes whole blood phenotyping, as well as an analysis of the production of IL-10 were performed by multicolor flow cytometry (FCM) in both patients and controls at baseline (M0) and in patients after 1 (M1), 3 (M3) and 6 (M6) months of treatment. CD24hiCD38hi CD24hiCD27+ subpopulations were selected for the phenotypic study of Bregs (24–38 and 24–27 Breg). The primary endpoint was the rate and absolute value of Bregs as a percentage and absolute value measured at each time of the study and compared with disease activity.
**Results:** Thirty patients and 15 controls were included in this study. Nowadays, phenotypic analysis was performed at baseline in all patients, but only in 15 patients at M1 and 13 patients at M3. The complete data will be available for the EULAR congress. There was an increase in circulating 24–38 Bregs between M1 and M3 (p=0.06) whatever the biologic prescribed. At baseline, the 24–38 Bregs were significantly lowered in patients compared to controls in percentage and absolute value (p=0.001 and p=0.013 respectively). The DAS28 remission and EULAR response at M3 were associated with a quantitative increase of 24–38 and 24–27 Breg at baseline compared to the values of the non-responders patients. Thus, a high initial rate of 24–27 and 24–38 Breg seemed associated with a good clinical response and an EULAR remission at 3 months. The rate of CD19 + B producing IL-10 obtained by PBMC culturing seemed lower in controls as compared to the patients.
**Conclusions:** We observed an increase of Bregs under treatment by biologics and a quantitative decrease in Bregs in patients with active RA compared to healthy subjects and patients with inactive disease. Thus, Bregs could be a marker of activity of the disease and their level may represent a potential predictor of the therapeutic response. Full data are required to confirmed these preliminary results.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3118

## AB0026 A SIMPLE METHOD OF REMOVING LOW DENSITY GRANULOCYTES FROM PERIPHERAL BLOOD MONONUCLEAR CELLS IN AUTOIMMUNE DISEASES

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**Background:** Low density granulocytes (LDGs) can form neutrophil extracellular traps (NETs) spontaneously and excessively. When peripheral blood mononuclear cells (PBMCs) were used for studying T lymphocytes, PBMCs-contained LDGs may decrease the threshold of activating T lymphocytes by forming NETs.
**Objectives:** This study focused on profiles of LDGs in common autoimmune diseases and method of removing LDGs from PBMCs.
**Methods:** LDGs percentages in PBMCs from 55 dermatomyositis (DM) patients, fifteen polymyositis (PM) patients, forty-two rheumatoid arthritis (RA) patients, twenty-five SLE patients and 19 healthy controls were tested by flow cytometer. Increasing relative centrifugal force (RCF) method, PBMCs adherence method and whole blood sedimentation method were used to remove LDGs from PBMCs. PBMCs from six patients with positive T-SPOT.*TB* were adhered one hour and then tested for T-SPOT.*TB* again.
**Results:** Compared with controls (1.28±0.73%), patients with DM (8.41±10.87%, $P<0.0001$), PM (8.41±10.39%, $P<0.0001$), RA (4.05±6.97%, $P=0.0249$) and SLE (7.53±11.52%, $P=0.0006$) showed significantly higher LDGs percentage in PBMCs. Increasing RCF in a limited range can decrease LDGs percentage for cases with high LDGs percentages, but not remarkably increase LDGs clearance rate. PBMCs adherence method can significantly remove LDGs and scarcely influence the T lymphocyte percentage in PBMCs compared to whole blood sediment method. T-SPOT.*TB* value significantly decreased after LDGs were removed from PBMCs by using the PBMCs adherence method.
**Conclusions:** Similar to SLE, LDG percentages in PBMCs were significantly increased in patients with DM, PM and RA. LDGs' influences on T lymphocytes cannot be ignored in PBMCs culture. PBMCs adherence method was a simple and easy-to-use method of removing LDGs from PBMCs.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1496

## Innate immunity in rheumatic diseases

### AB0027 A NOVEL TRANSCRIPTION FACTOR NFAT5 PLAYS AN IMPORTANT ROLE AS CRITICAL REGULATOR IN THE INFLAMMATORY RESPONSE OF RHEUMATOID ARTHRITIS FIBROBLASTS MEDIATED VIA TOLL-LIKE RECEPTOR 4 SIGNALING PATHWAYS

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**Background:** Damage-associated molecular patterns (DAMPs) are proposed to drive aberrant stimulation of Toll-like receptors (TLRs) in the rheumatoid arthritis (RA) joints resulting in increased expression of proinflammatory cytokines and chemokines. In the recent study we demonstrated that the neutrophil-derived lactoferrin (LTF) induces inflammatory response in RA synovial fibroblasts (RASF) via TLR-4 (Ref.). However, the molecular mechanisms of TLR-4 signaling in activated RASF are still unclear.
**Objectives:** To clarify the molecular mechanisms of TLR-4 signaling pathways in activated RASF.
**Methods:** Recombinant human neutrophil-derived LTF was used as one of the TLR-4 ligands. RASF were treated with LTF and/or TNF-α, and the expression of proinflammatory cytokines and chemokines, such as IL-6, IL-8 and CCL20 in RASF was measured by RT-qPCR and ELISA. To repress the TLR-4 signaling pathways, a small molecular inhibitor of TLR-4 (TAK-242), TAK1 inhibitor (5Z-7-Oxozeaenol), nuclear factor kappa B (NF-kB) inhibitor (BMS345541), and p38 mitogen activated protein kinase (MAPK) inhibitor (SB202190) were used. The role of nuclear factor of activated T cells 5 (NFAT5) in the TLR-4 signaling in RASF was investigated using a small interfering RNA targeting NFAT5.
**Results:** Stimulation of RASF with LTF significantly increased the expression of IL-6, IL-8 and CCL20 mRNA and proteins (p=0.01). LTF enhanced the expression of these cytokine and chemokine mRNA in RASF stimulated by TNFα. TAK-242 completely repressed the expression of these cytokines and chemokines in RASF stimulated by LTF, while the TAK-1 inhibitor did not suppress the expression of these cytokines and chemokines in RASF. The NF-kB inhibitor, but not the p38MAPK inhibitor, partially repressed the expression of IL-6 and IL-8 mRNA induced by LTF. However, neither the NF-kB inhibitor nor p38MAPK inhibitor repressed the expression of CCL20 mRNA. Interestingly, silencing of NFAT5 significantly decreased the basal expression of IL-6, IL-8 and CCL20 mRNA in RASF. Additionally, silencing of NFAT5 significantly repressed the expression of not only IL-6, IL-8, but also of CCL20 mRNA in RASF treated by LTF.
**Conclusions:** These findings suggest that NFAT5 plays an important role as a critical regulator in the proinflammatory response of RASF mediated by the TLR-4 signaling pathway.
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**Acknowledgement:** We thank Ms. Yuki Kaseda, Ms. Ayaka Miyamoto and Dr. Yatsuki Aratake for their excellent technical assistance.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1676

### AB0028 INNATE LYMPHOID CELLS ARE PRESENT AT NORMAL HUMAN ENTHESIS PROVIDING A POTENTIAL MECHANISM FOR SPONDYLOARTHROPATHY PATHOGENESIS

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**Background:** The pathogenesis of murine spondyloarthropathy (SpA) has been intimately linked to the presence of IL-23 responsive, innate like lymphocytes at peripheral and spinal enthesis (1). Human SpAs are associated with SNPs in genes related to the IL-23 pathway and drugs that block IL-12/23 have shown efficacy (2).
**Objectives:** We hypothesised that the normal human enthesis has a population of resident innate lymphoid cells (ILCs) that could be key in governing entheseal immune homeostasis partly via interaction with resident mesenchymal stromal cells (MSCs). Therefore we examined the lymphocytic content of human entheseal tissue with particular emphasis on ILCs.
**Methods:** Normal spinal enthesis were harvested from patients undergoing spinal decompression surgery and enzymatically digested prior to sorting or flow cytometry. Immunophenotyping and cell sorting was performed on enthesis samples harvested from 6 patients and unmatched peripheral blood. The expression of RORγt and key immunomodulatory transcripts was tested in sorted populations by RTqPCR. Anterior cruciate ligament and Achilles enthesis were obtained from patients with knee OA and Achilles tendon rupture and analysed by immunohistochemistry (IHC). Adherent cells from entheseal digest were cultured under standard MSC culture conditions and expression of known MSC markers was assessed by flow cytometry.
**Results:** All sorted samples contained ILC3s, median proportion 0.09% (range 0.015–0.63). Transcript analysis confirmed elevated expression of RORγt transcript in sorted ILC3 compared to all other ILCs and 51-fold greater relative expression in comparison to unsorted mononuclear cells (p=0.043). 5 of 6 sorted samples contained ILC2s, median proportion 0.20% (range 0–0.49). RORγt expression was detected in knee OA and there was widespread expression of RORγt in inflammatory infiltrates in injured enthesis as shown by IHC. Culture expanded adherent cells grew in characteristic fibroblastoid colonies and expressed phenotypic markers consistent with bone marrow derived MSCs.
**Conclusions:** Our findings show that both ILCs and MSCs are present in the normal human spinal enthesis. ILCs may also be greatly increased in frequency following injury. The co-localisation of ILC and MSC populations at the enthesis suggests a potential link between cellular dysregulation of the IL-23/17 axis and human SpA pathology.
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**Acknowledgement:** Thanks to Mark Coles at the University of York for his generous contribution of control tissue for assay optimisation. Thanks also to Adam Davison and Elizabeth Straszynski for their expertise in cell sorting. Lastly thank you to all the staff at the Leeds General Infirmary spinal surgery unit for their help in collection of donor tissue.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2270

## Cytokines and inflammatory mediators

### AB0029 RELATIONSHIP SCD36 LEVELS AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The main cause of death in RA patients is cardiovascular disease [1]. CD36 is a scavenger receptor has been postulated as a molecule involved in the atherogenic process [2,3]. A soluble fraction, sCD36 has been reported and has been proposed as a marker of atherosclerosis and other metabolic diseases [4,5], however, little is known of the pathways involved in these processes in RA.
**Objectives:** The objective of this study was to evaluate the levels of sCD36 and examine the association between clinical characteristics, disease activity and inflammatory markers in patients with RA.
**Methods:** The study groups were composed of 59 patients with RA (ACR/EULAR 2010) vs. 79 controls. sCD36, PCR, FR, Anti-CCP, insulin, TC, TG, HDL-C, VLDL-C, LDL-c were measured by ELISA. Index Disease Activity 28 (DAS-28) C-reactive protein (CRP) was calculated. VSG by Wintrobe method. cIMT using a Class B ultrasonography. Data were analyzed using descriptive statistics, Student t test, chi-square and ANOVA, as appropriate, with SPSS V.23 software.
**Results:** We found high levels of sCD36 in the control group (1861.10 ±6491.42±29.87 vs. 76.71, $P<0.01$) as well as ESR (21.26±12.79 vs. 13.29±8.85, $P<0.01$), CRP (8.97±7.32 vs. 7.27±4.11, $P<0.01$), and VLDL-c (33.36±17.26 vs. 52.21±21.70, $P<0.01$). sCD36 was positively correlated with the levels of DAS28pCr, PCR, FR, TG, insulin and IMT; negatively with HDL-c. Finally, we note a proportional direct relationship between sCD36 levels and Index Disease Activity 28 by pCr (Fig. 1).

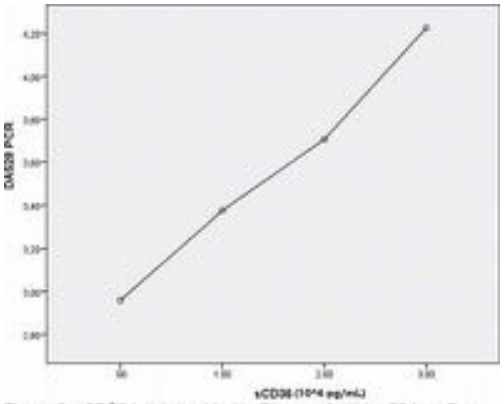


Figure 1. sCD36 levels and Index Disease Activity 28 by pCr

**Conclusions:** High levels of sCD36 were observed in serum from RA patients compared to a control group, as well as a relationship between sCD36 levels and Index Disease Activity 28 by pCr. It could be proposed to sCD36 as a marker of clinical activity of RA, however, more studies are needed to validate our findings and clarify the regulation and the role of sCD36 in RA.

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**Disclosure of Interest:** None declared

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## AB0030 CYTOKINE PROFILES IN SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

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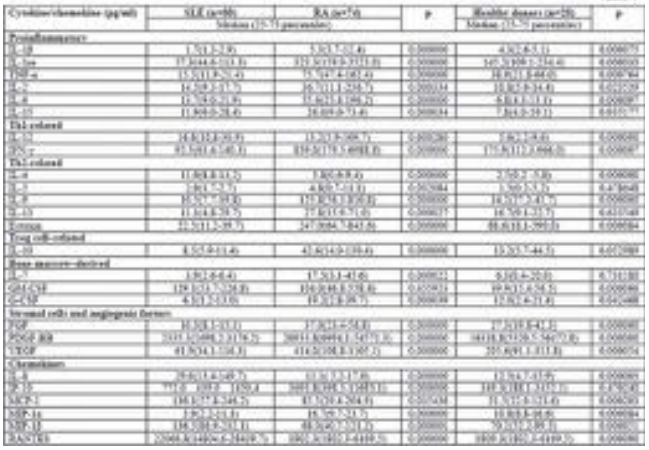
**Background:** Our aim was to compare serum levels of cytokines in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

**Objectives:** Comparative data on cytokine profile in SLE and rheumatoid arthritis RA patients are scarce.

**Methods:** We examined serum samples from 80 pts with SLE, median and interquartile range (25th–75th percentile) of disease duration 48 (2–432) months; age 31,5 (16–65) years; 72 female; 74 pts with RA, disease duration 90,0 (30,00–192,0) months; age 54,0 (44,0–62,0) years; 59 female, and 28 healthy donors. Cytokine analyses were performed with Bio-Plex® technology (Human Grp I Cytokine 27-plex panel).

**Results:** Pts with SLE had significantly lower levels of IL-1β, -1ra, -2, -9, eotaxin, G-CSF, IFN-γ, MIP-1β, TNF-α, VEGF and higher levels of IL-4, -6, -8, -12, GM-CSF, MCP-1, PDGF-BB, RANTES than healthy donors. Compared to RA, cytokine/chemokine levels from SLE were significantly different. The concentrations of IL-1β, -1ra, -2, -5, -6, -7, -9, -10, -13, 15, eotaxin, FGF, G-CSF, IFN-γ, IP-10, MIP-1α, TNF-α, VEGF in SLE were significantly lower than RA. The concentrations of IL-4, -8, MCP-1, MIP-1β, PDGF-BB, RANTES was higher in the SLE cohort (Table 1).

Table 1



**Conclusions:** Serum concentration of most proinflammatory, Th-2 related, bone marrow–derived cytokines, stromal cells and angiogenic factors in SLE pts is substantially lower than in healthy donors and pts witch RA. These data demonstrate significantly higher chemokine levels in SLE versus RA.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.3130

## AB0031 EVALUATION OF SERUM FETUIN-A AND APELIN LEVELS IN FAMILIAL MEDITERRANEAN FEVER (FMF) PATIENTS AND HEALTHY SUBJECTS

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**Background:** Apelin is an adipokine that its level is increased by some proinflammatory cytokine such as TNF-alpha in metabolic, autoimmune and inflammatory conditions (1). Fetuin-A is protein secreted by liver, kidney, bone, brain, lungs and cardiovascular system (2). The levels of fetuin-a are decreased in some rheumatic diseases (ie. Rheumatoid arthritis, osteoarthritis). It has been suggested that fetuin-a can be a novel inflammatory biomarker in familial Mediterranean fever (FMF) (3).

**Objectives:** To evaluate of the serum Apelin, Fetuin-A levels in patients with FMF during attack-free period (AFP) and to compare with healthy subjects.

**Methods:** Thirty-FMF patients with AFP and thirty healthy subjects were included this study. The erythrocyte sedimentation rate (ESR), CRP, fibrinogen, hemogram, Mediterranean fever (MEFV) gene profiles, BMI, insulin, HOMA-IR, lipid profiles, serum apelin, fetuin-a levels were investigated.

**Results:** Of the FMF patients and control, 20 (66.7%) was female and 10 (33.3%) was male. The distribution of MEFV gene mutation frequencies in the FMF patients was no mutation in 4 (13.3%) patients, M694V heterozygous in 7 (23.3%), M694V homozygous in 3 (10%), E148Q heterozygous in 5 (16.7%), M680I heterozygous in 2 (6.7%), M680I homozygous in 1 (3.3%), V726A in 2 (6.7%) and compound heterozygous mutation in 6 (20%). The median levels of apelin were 307.82±52.76 ng/mL in healthy subjects and 113,07±15,9 ng/mL in FMF (p=0.002) (Figure 1). The median levels of fetuin-a were 843,82±137.66 ng/mL in control group and 1352.2±127.61 ng/mL in FMF group (p=0.009) (Figure 1).

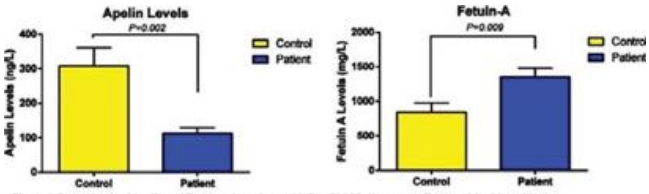



**Figure 1. Serum levels of Apelin and Fetuin-A in patients with Familial Mediterranean Fever and healthy subjects.**

**Conclusions:** The lower serum apelin and higher fetuin-a levels in FMF patients with AFP than in healthy subjects were observed. It may be suggested that subclinical vascular inflammation is continued during attack-free period in patients with FMF.

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**Acknowledgement:** We would like to thank to Ahmet Altun, M.D. for his statistical analysis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.5079

## AB0032 THE ADENOSINE DEAMINASE ISOFORMS ACTIVITY IN SYNOVIAL FLUID IN PATIENTS WITH DIFFERENT ARTHRITIS

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**Background:** Arthritis is one of the most common causes of people's disability in the world. Recent years investigations were done to find biomarkers which can help in differentiating the type of arthritis, to evaluate the correlation between marker and disease severity. A purine nucleoside adenosine possesses anti-inflammatory activity via decreasing the level of pro-inflammatory cytokines, increasing the level of anti-inflammatory cytokines and represents one of the potent regulators of the inflammatory response. Adenosine deaminase (ADA) metabolizes adenosine

to inosine, decreasing its anti-inflammatory activity. The significant elevation of ADA activity in rheumatoid arthritis (RA) and other inflammatory joint disorders has been observed. In our earlier study we have shown that the ADA activity can be used as a biomarker suitable for RA and osteoarthritis differentiation (1). The cutoff value of the enzyme activity in synovial fluid (SF) for differentiating these diseases in Armenian population has been evaluated. We observed the increasing of small-molecular (SADA, catalytic unit) to large-molecular (LADA, a complex of the catalytic unit with ADA-binding protein) isoforms ratio in RA SFs at increasing of the total activity of enzyme. The linear correlation between the initial activity and the SM/LM ratio of ADA isoforms has been shown (correlation coefficient r =0.97, P=0.0017).

**Objectives:** The aim of the present investigation was to analyze the levels of ADA activity in SFs of patients with different arthritis and their probable correlation with the SADA/LADA ratios in various cases.

**Methods:** The SFs of RA, reactive arthritis, ankylosing spondylitis and gout patients were studied. The activity of ADA was assayed, evaluating the amount of ammonia, liberated in the reaction of adenosine deamination. To compare the levels of SADA and LADA isoforms, the SFs were subjected to gel-filtration on the column with G-200 Sephadex. The elution diagrams regarding the ADA activity in the obtained fractions were constructed.

**Results:** The values of ADA activity in SFs of different arthritis mainly scatter in the higher region of the enzyme activities in SFs of RA. The elution diagrams after G-200 Sephadex gel-filtration of SFs of various arthritis manifested the absence or very low levels of SADA isoform even at high total initial activity of the enzyme. That excluded any correlation between the total activities of the enzyme and the ratios of its isoforms.

**Conclusions:** The earlier observed and proved in this study significant correlation between total activity of ADA and its isoforms ratio at RA might be in account of the SADA release from the damaged synoviocytes. This phenomenon appeared specific for RA and was not observed in the other arthritis types. We can conclude that the mechanism of joint inflammation at RA has some peculiarities, which may be a subject of special future study.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.3162

## AB0033 HIGH MOBILITY GROUP BOX 1 PROTEIN IS NOT ELEVATED IN ACTIVE PHASES OF GIANT CELL ARTERITIS

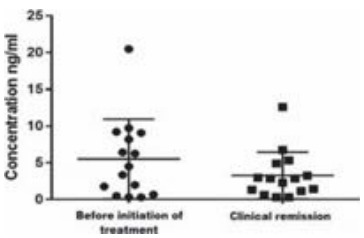
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**Background:** High mobility group box 1 (HMGB1) is a non-histone DNA-binding protein. It exists in all types of cells and has complex functions. When secreted extracellularly HMGB1 acts as an alarmin and induces and potentiates *NF-κB* activity. HMGB1 is raised in patients with active granulomatous vasculitis (1). However, a recent study did not find any association of HMGB1 protein concentration and disease activity in Giant cell arteritis (GCA) (2). Our aim was to investigate whether HMGB1 protein rises during the active phase of giant cell arteritis (GCA) and falls after initiation of treatment.

**Objectives:** Our aim was to investigate whether HMGB1 protein rises during the active phase of giant cell arteritis (GCA) and falls after initiation of treatment.

**Methods:** GCA patients were recruited at the Department of Rheumatology at the Hospital of Southern Norway in Kristiansand between January 2012 and January 2014. The diagnosis was based on positive ultrasonography of temporal arteries and /or large vessels and typical clinical manifestations. All patients fulfilled the ACR classification criteria. Blood samples were drawn at time of diagnosis and before treatment and after clinical remission. HMGB1 levels in serum were measured by ELISA (IBL International GMBH, Hamburg, Germany), using a high sensitive protocol (range 0,313–10 ng/ml).

**Results:** Fifteen GCA patients (mean age 68 years (SD 9.2), 3 males and 12 females), were included during the study period. The median time until remission was 6 months (range 1–6). Eight patients had isolated cranial arteritis while seven patients had in addition large vessel vasculitis (LVV). Mean HMGB1 concentration at diagnosis and in clinical remission were 5.5 ng/ml (SD 5.4) and 3.3 ng/ml (SD 3.0) respectively. The difference was not significant (mean difference 2.2 ng/ml (CI 95% -1.2–5.7, p=0.182), Figure 1. No differences were observed for HMGB1 concentrations at diagnosis nor at remission for cranial (p=0.2) or LVV (p=0.7).




**Conclusions:** In GCA patients, no differences in HMGB1 protein levels were observed at diagnosis compared with remission. In addition, no differences were seen between pure cranial and LVV. Thus, HMGB1 protein seems not to be a useful biomarker for disease activity in GCA.

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**Disclosure of Interest:** None declared

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## AB0034 PHARMACOKINETICS AND SAFETY OF BCD-057, ADALIMUMAB BIOSIMILAR CANDIDATE, COMPARED TO HUMIRA IN HEALTHY VOLUNTEERS (RESULTS OF PHASE I CLINICAL STUDY)

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**Background:** BCD-057 is an adalimumab biosimilar candidate manufactured by BIOCAD, Russia. Full spectrum of physicochemical and preclinical studies showed equivalence of BCD-057 to innovator drug Humira (reference adalimumab, rADA).

**Objectives:** To establish the equivalence of pharmacokinetics and absence of differences in safety of BCD-057 and rADA after the single subcutaneous injection in healthy volunteers.

**Methods:** 94 healthy volunteers were enrolled into the study. 10 of them withdrew consent before drug administration and were not included in analysis. All patients were randomly assigned into 2 groups in a ratio of 1:1 to receive a single subcutaneous injection of BCD-057 or rADA at a dose of 40 mg. The primary endpoints were $C_{max}$ and $AUC_{0-\infty}$ after the single adalimumab injection. The secondary PK endpoints included $AUC_{0-1680\,h}$, $T_{max}$, $T_{1/2}$, $V_d$, $K_{el}$, CL. Adalimumab serum concentrations were evaluated immediately before the injection and after 6, 24, 48, 72, 96, 120, 144, 168, 192, 336, 672, 1008, 1440 and 1680 hours after it. Safety and immunogenicity were also assessed during the study.

**Results:** Pharmacokinetic (PK) analysis demonstrated that 90% CI for the ratio of geometric means of $C_{max}$ of adalimumab after single injection of BCD-057 or rADA was 87.48–111.84%. 90% CI for the ratio of geometric means of $AUC_{0-\infty}$ lied within 87.90–117.22%. Both of these facts confirm the bioequivalence of BCD-057 and rADA. There were no statistically significant differences between the groups for all other secondary PK parameters. BCD-057 and rADA were well tolerated. No SAEs were observed during the study. AEs were observed in 9 (22.5%) healthy volunteers in BCD-057 group and in 14 (31.8%) volunteers in rADA group (p=0.463, Fisher's exact test [two-tailed]). They were presented by laboratory abnormalities including leucopenia, neutropenia, monocytosis, monocytopenia, increase in total bilirubin, ALT and AST. All AEs were mild (Grade 1 [CTCAE 4.03]), transient and were not associated with any clinical symptoms. 27 (67.5%) subjects in BCD-057 group and 33 (75.0%) subjects in rADA group (p=0.478, Fisher's exact test [two-tailed]) developed anti-adalimumab antibodies. Neutralizing antibodies to adalimumab were found in 2 (5.0%) volunteers in BCD-057 group and in 5 (11.4%) volunteers in rADA group (p=0.437, Fisher's exact test [two-tailed]).

**Conclusions:** PK, safety and immunogenicity of BCD-057 and rADA after a single subcutaneous administration in healthy volunteers are considered to be equivalent. These data allow to proceed to the subsequent BCD-057 study aimed to assess efficacy and safety in patients with moderate-to-severe plaque psoriasis.

**References:**

[1] final study report on phase 1 clinical study of BCD-057 in healthy volunteers. Clinical trial information: NCT02395055.

**Disclosure of Interest:** A. Eremeeva Employee of: CJSC BIOCAD, S. Fogt Employee of: CJSC BIOCAD, E. Chernyaeva Employee of: CJSC BIOCAD, A. Kushakova Employee of: CJSC BIOCAD, T. Ostroukhova Employee of: CJSC BIOCAD, R. Ivanov Employee of: CJSC BIOCAD

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## AB0035 BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN LEVELS IN HUMAN SYNOVIAL FLUID AND ITS EFFECTS IN EXPERIMENTAL CRYSTAL-INDUCED INFLAMMATION

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**Background:** Bactericidal/Permeability-Increasing Protein (BPI) is an antibacterial and antiinflammatory protein stored in polymorphonuclear cells (PMN). BPI has been detected in synovial fluid (SF) of patients with reactive arthritis, rheumatoid arthritis (RA), psoriatic arthritis (PsA) and osteoarthritis (OA).

**Objectives:** The aims of this study were to evaluate the presence of BPI in SF of patients with crystal-induced arthritis and to compare its levels with those of

other arthropathies. Furthermore, we tested whether BPI exerts antiinflammatory effects in *in vitro* models of sterile inflammation.
**Methods:** SF was collected from the knees of 50 untreated patients: 9 with gout, 9 with calcium pyrophosphate (CPP) crystal-induced arthritis (CPP-IA), 8 with OA, 8 with OA and CPP crystals in SF (OA+CPP), 8 with RA and 8 with PsA. SF was examined under optical light microscopy. White cell count (WBC) and the PMN percentage were determined in SF according to standard procedures. SF BPI levels were assayed by ELISA.
As regard the study in vitro, the THP-1 cell line was primed for 3h with phorbole myristate acetate (300 ng/ml), reincubated overnight, and treated with sterile synthetic monosodium urate (MSU) (0.5 mg/ml) or CPP (0.1 mg/ml) crystals for 24h in presence or absence of BPI (1 or 5 μg/ml). Cell supernatants were tested by ELISA for IL-1β and IL-8 production.
**Results:** The results of SF analysis and BPI levels are reported in the table.

| | No. cases | WBC, $\times 10^3/mm^3$ | PMN, % | BPI, ng/ml |
|---|---|---|---|---|
| Total group | 50 | 12.40±12.68 | 59.03±36.62 | 43.78±53.17 |
| Gout | 9 | 25.32±10.13 | 87.75±15.28 | 31.07±7.31 |
| CPP-IA | 9 | 25.32±10.13 | 87.75±15.28 | 23.53±9.47 |
| OA | 8 | 0.3±0.54 | 0.33±0.52 | 12.21±8.40 |
| OA+CPP | 8 | 0.82±0.70 | 28.80±25.16 | 15.87±14.73 |
| RA | 8 | 21.35±8.98 | 68.00±22.63 | 146.02±32.10 |
| PsA | 8 | 9.16±3.56 | 63.00±24.17 | 63.79±31.87 |

BPI levels were similar and the lowest in SFs from OA and OA+CPP. Although the BPI concentrations in gout and CPP-IA SFs were higher than in OA and OA+CPP, the differences did not reach statistical significance. RA SF showed the highest BPI levels ($p<0.001$ vs gout, CPP-IA, OA, OA+CPP, PsA). In the total group of patients, we found a correlation between BPI and WBC count ($r=0.474$; $p=0.004$) and PMN ($r=0.354$; $p=0.037$).
Exposure of THP-1 cells to MSU or CPP crystals increased the production of IL-1β (MSU: 655.5±28.28 pg/ml; CPP: 496.5±9.19 pg/ml) and IL-8 (MSU: 4538.5±37.48 pg/ml; CPP: 4424.7±9.55 pg/ml). The treatment with BPI decreased the release of both cytokines induced by crystals in a dose dependent manner. Indeed, in the presence of BPI 1 or 5 μg/ml, the IL-1β secretion was reduced by 19% and 40%, respectively. IL-8 crystal-induced production was inhibited in the presence of BPI 1 μg/ml (MSU: 20%; CPP: 27%), and abolished when THP-1 cells were treated with BPI 5 μg/ml.
**Conclusions:** This study is the first to define the presence of BPI in SF of crystal-induced arthritis. Our results demonstrate that although SFs from gout and CPP-IA contained the WBC and PMN highest levels, BPI was present at significantly lower concentrations than in RA and PsA. This could be explained by the lack of PMN activators able to induce the release of BPI in crystal-induced arthritis.
The use of BPI in our *in vitro* models of crystal-induced inflammation leads to a significant inhibition of the proinflammatory cytokine release, suggesting an antiinflammatory activity of this protein also in sterile inflammation.
**Disclosure of Interest:** None declared
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## AB0036 SOLUBLE CD83 PLASMA LEVELS ARE ASSOCIATED WITH DISEASE ACTIVITY AND COURSE OF DISEASE IN EARLY RHEUMATOID ARTHRITIS

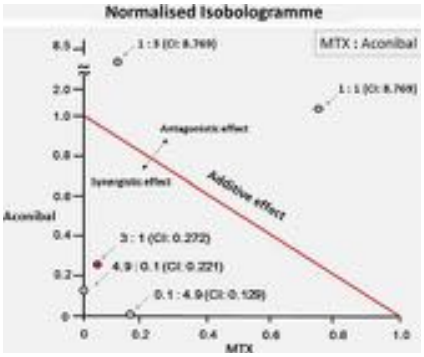
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**Background:** The immune modulatory dendritic cell (DC) marker CD83 has previously been associated with autoimmune diseases.[1,2] Levels of soluble CD83 (sCD83) are elevated in RA synovial fluid[3], however the relation to clinical outcome of RA remains unknown. We hypothesize that CD83 plays a central role in the inflammatory process and disease development in RA.
**Objectives:** To investigate the potential association of sCD83 with disease activity measures, treatment response and auto-antibody status in patients with early RA (eRA).
**Methods:** Plasma samples from eRA (n=88) randomized to conventional DMARD treatment with or without 12 months of additional adalimumab therapy (MTX+ADA and MTX+PLA, respectively) were randomly selected from the OPERA cohort.[4] A commercial sandwich ELISA was used to quantify plasma levels of sCD83 in patients and in age- and gender-matched healthy volunteers (HV, n=43). Spearman's rank correlation coefficient between soluble CD83 plasma levels and measures of disease activity (tender joint count (TJC28,40), swollen joint count (SJC28,40), DAS28 and CRP), treatment response (ACR20,50,70,90) and auto-antibody status (IgM-RF and ACPA) was calculated. All results are expressed as median with interquartile range and compared by non-parametric statistics.
**Results:** At baseline, sCD83 in eRA was significantly higher than in HV plasma (168.5pg/ml (136.1pg/ml-203.5pg/ml) and 136.1pg/ml (116.9pg/ml-149.4pg/ml), respectively), $p<0.0001$. At 12 months follow-up sCD83 had decreased by approximately 10% (167.2 vs 151.2pg/ml, p=0006) in the MTX+PLA group while it remained unchanged in the MTX+ADA arm, (p=0.3).
In MTX+ADA (n=43) group baseline sCD83 levels correlated with ACR50 at 6 and 24 months ($\rho$= -0.33, p=0.04 and $\rho$= -0.34, p=0.03, respectively) and ACR90 at 24 months ($\rho$= -0.37, p=0.02). In the MTX+PLA (n=45) group baseline sCD83 levels were found to correlate with TJC28 at 12 and 24 months ($\rho$= -0.30, p=0.05 and $\rho$= -0.43, p=0.003, respectively) and TJC40 at 24 months ($\rho$= -0.32, p=0.04). sCD83 showed no association with IgM-RF and ACPA positivity.
**Conclusions:** This study demonstrated that sCD83 levels were significantly elevated in eRA compared with HV. With additional adalimumab treatment, high sCD83 levels at baseline were sustained over time. A high sCD83 level at baseline was associated with changes in prospective disease activity parameters in both treatment groups, which points to a possible predictive value of sCD83 in eRA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3850

## AB0037 CHARACTERISING MULTIPLE MOLECULE-MODULATING RESPONSE OF TNF-ALPHA AND INTERLEUKIN-6 BY COMBINATION OF METHOTREXATE AND ACONITE IN INTERFERON GAMMA-INDUCED TOXICITY SETTING

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**Background:** TNF-alpha (TNF-α) and interleukin-6 (IL-6) are one of the molecules which have been the targets of interest in rheumatoid arthritis (RA). Among the therapeutic strategies, simultaneous modulation of the two is regarded as providing the stability on the networks of the relevant molecules and sufficient profile for multi-therapeutic targets.
**Objectives:** To characterise multiple molecule-modulating profile of TNF-α and IL-6, we experimented the anti-inflammatory phenotypes of the two by adopting well-known therapeutic, methotrexate (MTX) and newly recognised herbal, aconite (*Aconitum carmichaelii*) in the setting of interferon-gamma-induced inflammatory toxicity in macrophage.
**Methods:** Mouse macrophage Raw264.7 cells were treated with MTX (0.01–1 mM) and processed aconite (Aconibal®, 0.01–1 mg/mL). The levels of TNF-α and IL-6 were measured by spectrophotometre (VersaMax ELISA, Molecular devices, USA), then, as a parametric approach, median and dose effect were analysed to calculate the combination index (CI) and standard isobologramme were presented using CalcuSyn software (CalcuSyn 2.0, Biosoft, UK).
**Results:** Anti-inflammatory phenotypes of TNF-α and IL-6 level were shown in aconite dose-dependent manner. The doses of 0.75 mg/mL of aconite and 0.25 mM of MTX indicated the lowest CI as 0.272 for TNF-α and 7916 for IL-6, which was sparing effect compared with single treat by 3.9 mM and 0.6 mM of MTX, respectively. Reflecting the response, TNF-α was modulated with the synergistic profiles in normalised isobologramme.




**Conclusions:** Stable modulation of TNF-α and IL-6 and synergistic response on TNF-α were characterised. Further approaches on network stability of the relevant molecules are needed.
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acetaminophen-induced hepatotoxicity via B-cell lymphoma-2 protein-mediated inhibition of mitochondrial dysfunction. Environ Toxicol Pharmacol in press doi:10.1016/j.etap.2016.01.012
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**Disclosure of Interest:** None declared
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## AB0038 SERUM AND SYNOVIAL GRANULOCYTE COLONY STIMULATING FACTOR (G-CSF) LEVELS AS MARKERS OF DISEASE ACTIVITY AND SEVERITY IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic polyarticular disease manifesting as painful inflammation of the synovial tissue with progressive joints destruction. The colony-stimulating factors (CSFs) are a family of four cytokine growth factors originally identified by their ability to support the proliferation and differentiation of hemopoietic progenitor stem cells into mature monocytes/macrophages and granulocytes. The CSF family comprises the lineage-specific members, macrophage CSF (M-CSF or CSF-1) and granulocyte CSF (G-CSF), and the nonlineage-specific members, granulocyte-macrophage CSF (GM-CSF) and multi-CSF [also called interleukin (IL)-3
**Objectives:** to determine serum and synovial levels of the granulocyte colony stimulating factor (G-CSF) in order to evaluate their utility as biomarkers of disease activity and/or severity in rheumatoid arthritis (RA) patients.
**Methods:** Thirty patients with established RA as well as a control group of 20 apparently healthy individuals matched for age and sex to our patients were included and thoroughly examined. RA disease activity was assessed using the modified disease activity score of 28 joint count (DAS28)while, disease severity was evaluated using the clinical spread severity Index (SSI).Plain radiography was done for both knees as well as affected joints with evaluation according to Laresn scores. *Serum and synovial* levels of (G-CSF) were measured by the ELISA technique
**Results:** Both serum and synovial G-CSF levels of RA patients were higher than their levels in the controls (mean±SD 1.36± 0.69pg), (0.875±0.531pg)versus (mean±SD 0.47±0.07 pg), (0.47±0.04 pg) with a significant difference between both groups ($p<0.05$). The serum and synovial G-CSF levels were also higher in patients with a positive rheumatoid factor ($p<0.05$) and those with subcutaneous nodules ($p<0.01$) compared to other RA patients and the difference were statistically significant. Investigating the correlations of serum and synovial G-CSF levels with different clinical and laboratory parameters of RA showed that both levels of G-CSF significantly correlated positivey with morning stiffness durations ($p<0.01$),VAS values ($p<0.05$), spread severity index scores ($p<0.01$), DAS scores ($p<0.01$), ESR values ($p<0.01$), inversely with HB concentrations ($p<0.01$) but they were not correlated with either disease durations or radiographic larsen scores
**Conclusions:** Our results reveal that G-CSF has a potential role in driving joint inflammation and also underscore that G-CSF would likely be a therapeutic target in RA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4627

## AB0039 INTERLEUKIN-17 IN SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS PATIENTS: CORRELATION WITH CLINICAL PRESENTATION, LABORATORY PARAMETERS AND ACTIVITY INDICES

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**Background:** Serum interleukin (IL)-17 concentrations have been reported to be increased in systemic lupus erythematosus (SLE), but associations with clinical characteristics are not well understood. Autoimmune diseases such as RA, classically believed to be Th1-mediated, are predominantly driven by a Th17 immune response.
**Objectives:** this study aimed to compare the serum levels of IL-17 in patients with SLE and RA, it is correlation with clinical presentations, laboratory findings and disease activity in both diseases.
**Methods:** The study was carried out on 3 groups. Group I: 20 patients with SLE. Group II: 20 patients with RA. Group III: 10 of age and sex matched healthy subjects as control group.
**Results:** In this study, the mean of age were 43.1±8.98, 46.8±8.17 and 41.98±8.25 for group I (SLE), II (RA) and III (control) respectively, with no statistical significant differences between the studied groups. Also, there were no statistical significant differences between the three studied groups regarding sex, disease duration, disease activity, laboratory investigations (except HB, WBC and platelet count). The mean of IL-17 were 173.2±52.11, 82.6±48.17 and 73.07±41.05 for group I (SLE), II (RA) and III (Control) respectively, group I have values statistically higher than other groups, and group II have values statistically higher than group III. Serum IL-17 levels were significantly higher in SLE patients compared to healthy group.
**Conclusions:** Serum IL-17 concentration correlates with SLE and RA diseases activity but is significantly elevated in patients with SLE disease. The association of other cytokines with serum IL-17 suggests that IL-17 may drive activation of diverse immune pathways in SLE and RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1558

## AB0040 ANTIOXIDANT POTENTIAL AND FREE RADICAL POTENTIAL OF SYNOVIAL FLUID (SF) IN RHEUMATOID ARTHRITIS (RA) AND OSTEOARTHRITIS (OA)

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**Background:** Intra-articular dynamics of free radical processes in RA and OA reflects the degree of cellular destruction and the depth of the membrane pathological changes. Multi-component antioxidant system hinders the development of these negative phenomena.
**Objectives:** We studied the dynamics of free radical processes (the rate of lipid peroxidation (LPO - the level of malondialdehyde - MDA), activity of phospholipase (PHL-A2) and phospholipids - PHL) and the antioxidant defense system (activity superoxiddismutase (SOD), catalase (CAT), glutathione-S-transferase (G-S-T), tocopherols (TF) and ceruloplasmin (CP) in SF of patients with RA and OA. The data were compared with the levels of inflammation cytokines.
**Methods:** Investigated the SG of the knee in 15 patients with RA and 15 patients with OA, female, age 50±12 years. Besides the well-known methods of biochemistry and enzymology, for determining the activity of PHL-A2 used immunoassay method and reagent kits of company "Cayman chemical", analysis of cytokines was performed enzymelinked immunosorbent method.
**Results:** In OA, and especially in RA in SF, with the intensification of free radical processes (intensified the breakdown of phospholipids, increases the level MDA – secondary product of LPO and marker of degradation of membrane structures). Against this background, the observed inhibition of the antioxidant defense system (decreased activity of SOD, CAT, G-ST – enzyme conjugates with glutathione toxic products LPO and promotes their excretion; reduced level TF, designed to stabilize the lipid composition of membranes and protect them from degradation caused PHL-A2, and also block the damaging effect of singlet oxygen; also dramatically reduced the level of CP, which neutralizes free radicals). These changes are consistent with activation in SF with RA and OA proinflammatory cytokines and TNF-$\alpha$. Table 1.Free radicals, antioxidant defense system and cytokine status of SF with RA and OA

| The analyzed parameters | Normal level | RA | OA |
|---|---|---|---|
| PHL (mg/l) | 215.9±24 | 97.8±9.2* | 110.5±7.4* |
| PHL-A2 (ng/ml) | 0.64±0.10 | 1.47±0.04* | 0.98±0.09* |
| MDA (mmol/l) | 1.54±0.27 | 4.47±0.31* | 3.74±0.25* |
| SOD (unit/ml) | 1370.2±30. | 4 670.±25.9* | 820.7±45.9* |
| CAT (mmol/ml/min) | 10.4±0.7 | 5.9±0.9* | 8.9±0.8** |
| G-S-T (mmol/ ml/min) | 44.6±6.4 | 18.2±0.5* | 27.3±0.9* |
| TF ($\mu$/ml) | 41.5±7.2 | 22.4±8.3* | 38.2±2.7** |
| CP (mg/ml) | 259.7±37.5 | 137.9±12.7* | 154.8±13.9* |
| TNF-$\alpha$ (pg/ml) | 6.4±0.2 | 69.7±8.4* | 29.8±1.3* |
| IL-1$\beta$ (pg/ml) | 5.9±0.2 | 65.4±2.1* | 20.2±2.1* |
| IL-6 (pg/ml) | 5.1±0.2 | 120.3±9.7* | 29.4±1.3* |

The difference with a normal level *$p<0.05$. **$p>0.05$.

**Conclusions:** Intensification of free radical processes, generation of reactive oxygen species as a result of suppression of antioxidant protection is a cause of metabolic disorders of proteins and lipids in LF with RA and OA, the cause of the inflammatory process that causes apoptosis and cell destruction. The current strategy for the treatment of RA and OA is focused on reducing pain and preventing progressive degeneration of articular cartilage and subchondral bone, based on identified pathogenetic mechanisms, such as the development of inflammation and tissue destruction caused by the activation of free radical processes, suppression of antioxidant protection, dynamics of proinflammatory cytokines and TNF-$\alpha$.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5832

## AB0041 SERUM AMYLOID A STIMULATES THE INDUCTION OF INFLAMMATORY MEDIATORS IN MONOCYTES FROM BEHÇET'S DISEASE PATIENTS: A PROOF OF CONCEPT STUDY

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**Background:** Behcet's disease (BD) is a complex inflammatory disorder characterised by an abnormal innate and adaptive immune response leading to hyper-activation of pro-inflammatory mediators. Recurrent oral aphthous, genital ulcers and chronic relapsing bilateral uveitis are the hallmarks of the disease. Serum amyloid-A (SAA) is a biomarker of inflammation recently associated to BD, and pro-inflammatory stimuli including IL-6, IL-1 and TNF are known to be involved in the SAA production. Moreover, several innate immune cells such as neutrophils, monocytes and macrophages have been reported to produce pro-inflammatory cytokines also through inflammasome activation after SAA stimulation.
**Objectives:** The purpose of this study was to investigate the involvement of SAA in the pathogenesis of Behçet's disease
**Methods:** Monocytes obtained from heparinised venous blood of Behçet's disease patients (BD, n=14) and healthy controls (HC, n=7) were stimulated or not with SAA, and serum cytokine levels of IL-1β, IL-18, IL-6 and TNF-α were analysed in the medium using a multiplex bead analysis. Statistical approaches included two-tailed Mann-Whitney test (for two non-parametric groups) and Student's t-test (for two parametric groups) were used for statistical comparisons between groups. Correlations were calculated using Spearman's correlation (two-tailed p-value) analysis.
**Results:** BD monocytes showed an increased IL-1β (p=0.0017), TNF-α (p=0.0003) and IL-6 (p=0.0003) secretion after SAA stimulation. No differences were observed in the amounts of pro-inflammatory cytokines production between HC and BD. We also found that IL-1β levels positively correlated with IL-6 (r=0.842, p<0.001), and TNF-α (r=0.889, p<0.001), whilst TNF-α levels positively correlated with IL-6 (r=0.894, p<0.001) levels. Moreover, also IL-18 showed a positive trend with no significant differences between the two groups

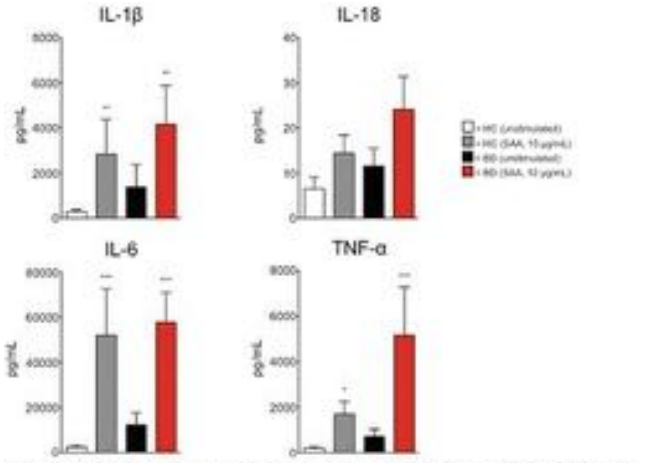



**Fig.1. SAA induction of cytokines in monocytes from Healthy Controls (HC) and Behçet's Disease (BD) patients.** Monocytes from BD patients (n=14) and HC (n=7) were stimulated or not with SAA (10 μg/mL) in serum-free RPMI for 24 h and cytokines concentrations in supernatants were measured by multiplex bead analysis. Data are expressed as mean + SEM. Mann-Whitney U-test and Student's t-test were carried out to check for statistical significance between groups (*p<0.05, **p<0.01, ***p<0.01).

**Conclusions:** These findings suggest that SAA can promote inflammatory mediators production thereby contributing to the inflammatory manifestations typically observed in BD.
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## AB0042 IDENTIFICATION OF SULFIDO-CONJUGATED MEDIATORS THAT PROMOTE RESOLUTION OF INFECTION AND ORGAN PROTECTION

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**Background:** When inflammation is self-limited it is host protective and leads to the repair and regeneration of damaged tissues. Chronic conditions, such as inflammatory arthritis, are though to arise from a failure of the host response to engage resolution mechanisms. The pro-resolving mechanisms engaged by the host response to promote tissue regeneration remain of interest.
**Objectives:** In the present stud we aim to identify mediators produced during the resolution phase of acute inflammation, that promote the termination of the inflammatory response, tissue repair and regeneration.
**Methods:** We employed LC-MS-MS and RP-UV-HPLC based lipid mediator metabololipodomics to investigate novel bioactive molecules in isolates from mouse and human tissues and cells. Bioactions for identification and characterization of the novel molecules were determined using planaria, mice and human primary leukocytes.
**Results:** Here we identified potent molecules present in infectious murine exudates, regenerating planaria, human milk as well as macrophages that stimulated tissue regeneration in planaria and are pro-resolving. Characterization of their physical properties and isotope tracking indicated that the bioactive structures contained sulfido-conjugated (SC) triene double bonds that proved to be 13-glutathionyl,14-hydroxy-docosahexaenoic acid (SCI) and 13-cysteinylglycinyl, 14-hydroxy-docosahexaenoic acid (SCII). These molecules rescued *E. coli* infection-mediated delay in tissue regeneration in planaria, improving regeneration intervals from ~4.2 to ~3.7 days. Administration of SC protected mice from second organ injury and promoted repair via limiting neutrophil infiltration, upregulating Ki67 and Roof plate-specific spondin 3 in lung tissues. At nanomolar potencies these conjugates also resolved *E. coli* infections by limiting neutrophil infiltration, stimulating bacteria phagocytosis and clearance as well as efferocytosis of apoptotic cells.
**Conclusions:** Together, these findings identify previously undescribed, conserved chemical signals and pathways in planaria, mice and human tissues that stimulate resolution of inflammation and promote the restoration of function.
**Acknowledgement:** This work was supported in part by the National Institutes of Health (Grant P01GM095467).
**Disclosure of Interest:** None declared
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## AB0043 SERUM CYTOKINE CONCENTRATIONS IN INFLAMMATORY BOWEL DISEASE (IBD) AND IBD-RELATED SPONDYLOARTHRITIS (SPA)

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**Background:** Inflammatory bowel disease (IBD) is a group of recurrent gastrointestinal disorders, involving Crohn disease (CD) and ulcerative colitis (UC), that is characterized by chronic mucosal inflammation and extraintestinal symptoms. Rheumatic abnormalities of a broad spectrum of symptoms, from arthralgia to spondyloarthritis (SpA), are the most common extraintestinal manifestations of IBD. The pathogenesis of IBD-related arthritis is unclear.
**Objectives:** In this study, we analyzed the serum cytokine concentrations (interleukins: IL-10, IL-18, IL-21, IL-23, interferon γ) in patients with IBD-associated spondyloarthritis and patients with IBD not complicated with SpA symptoms.
**Methods:** The study group consisted of 75 patients (44 female/29 male, age 43,7±12,3 year) suffering from IBD alone (n=35) or with IBD accompanied by arthritis (n=39), i.e. spondyloarthritis (IBD-SpA, n=16) or ankylosing spondylitis (IBD-AS, n=23). The control group included age and sex matched healthy volunteers (n=42). Serum cytokine concentrations were measured using commercially available kits from eBioscience, San Diego, CA, USA (Platinum ELISA for IL-18, ReadySetGo ELISAs for IL-10, IL-21, IL-23, interferon γ).
**Results:** The concentrations of IL-23 (the mean ± SEM =156 ±14 vs 115±49 pg/ml) and IL-21 (232±79 vs 20.6 ±8 pg/ml) were significantly higher (p<0.0001) in the total group of patients than control sera. Similar significant elevation of IL-21 and IL-23 was found in IBD (146±35 and 133±40 pg/ml, respectively), IBD-SpA (124±48 and 151±37 pg/ml, respectively) and IBD-AS (194±62 and 417±228 pg/ml, respectively) groups comparing with control sera (p≤0.001). There was no significant difference between control and patients groups in the serum concentrations of other tested cytokines, except IL-18. The levels of IL-18 were significantly lower in the sera of IBD-AS group than in healthy volunteers (59±19 vs 180±36 pg/ml, p=0.02). Although we failed to show significant difference in serum cytokine concentrations between IBD and IBD-SpA or IBD-AS patients, in the IBD-AS group there was again tendency to downregulation of serum IL-18

in comparison with patients suffering from IBD alone (59±19 vs 121 ±27 pg/ml, p=0.08).
**Conclusions:** Significant elevation of serum IL-21 and IL-23 found in IBD patients irrespectively of complication with SpA suggests implication of these cytokines in the underlying disease pathology. On the other hand, diminution of serum IL-18 in IBD-AS may point to protective action of this cytokine in AS development.
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**Disclosure of Interest:** None declared
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## AB0044 NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE IN THE PATHOGENESIS OF INFLAMMATION IN OSTEOARTHRITIS

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**Background:** Nicotinamide phosphoribosyltransferase (Nampt) is involved in various biological processes such as metabolism, stress response and the aging process.There are some data that TNF-α and other proinflammatory molecules may influence on exchange of NAD.
Currently, there is no common understanding of the Nampt's role in the pathogenesis of joint diseases. The recent recearches of its participation in the processes of metabolism and inflammation support the hypothesis of involvement of this protein in the induction and maintenance of inflammation in osteoarthritis (OA). The presence of pseudogenes complicates Nampt investigation and enhance research bias.
**Objectives:** To clarify the OA pathogenesis by examining serum concentrations of Nampt.
**Methods:** We observed 87 patients with various forms of OA aged 36 to 78 years, comparable with the group of healthy subjects ($t = 1,87$ $p > 0.05$).We used Althman R. D. criteria to diagnose OA (199). X-ray stages were evaluated using the Kellgren-Lawrence scale. Serum Nampt level was determined by ELISA with commercial test kits (RaiBiotech, cat No. EIA-VIS-1).
**Results:** We assessed the level of Nampt in the serum of healthy individuals. The Median of Nampt normal values was 2,29 [Confidence interval (CI) =2,02 - 2,8] ng/ml. The Median Nampt level OA patients was 3,98 [CI =2,00 - 9,04] ng/ml, which was significantly higher than in normal subjects ($p < 0.001$).
Elevated levels of Nampt were revealed more often in patients with constant pain than in ones who had pain only on movement.
The correlation coefficient between Nampt level and Lequesne functional index was equal to 0,4917 (p=0,041), with total index WOMAC - 0,589 (p=0,049).
We notedsignificant statistical link between the Nampt's serum level and laboratory markers of inflammation in OA. Higher C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)concentrations were detected in patients with elevated Nampt level. Those facts indirectly confirm the anti-inflammatory properties of Nampt. These studies may support the hypotheses of Nampt's properties to influence on cytokines production, which are responsible for the maintenance of the inflammatory process in the synovium and the destruction of the cartilage.
There are some data that Nampt inhibitors lead to downstream NF-kBinhibition, resulting in decreasing of intracellular level of nicotinamide adenine dinucleotide (NAD). So Nampt inhibitors may be used to suppress inflammation, for the treatment of diseases in which angiogenesis is involved, for the prevention and treatment of ischemia and other pathological states.
Significant advances in molecular biology allow us to hope for the development of highly effective drugs that can delay the progression of OA and change his clinical course.
**Conclusions:** Thus, in our study the increased Nampt level was detected in 29% of OA patients. It's increasing is associated with secondary synovitis, elevated of ESR, CRP, with most severity of articular syndrome.
The findings suggest the likely role Nampt in the pathogenesis of OA.
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## AB0045 LOW MOLECULAR WEIGHT-BAFF RECEPTOR ANTAGONISTS SUPPRESS IGG PRODUCTION BY B CELLS CO-CULTURED WITH MONOCYTES

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**Background:** We have previously reported that soluble BAFF (sBAFF) robustly increases IL-6 production in vitro by peripheral monocytes of patients with primary Sjogren's syndrome (pSS) and that the expression level of a BAFF receptor (BR3) is abnormally enhanced in pSS monocytes. Additionally, the proportion of BR3-positive monocytes to total monocytes was positively and significantly correlated with the sBAFF-induced IL-6 production by peripheral monocytes and the serum IgG level of pSS patients. These data collectively suggest that the elevated expression of BR3 in monocytes is involved in the pathogenesis of pSS which is often accompanied with hypergammaglobulinemia (HgG). Our findings also suggest that BR3 is a therapeutic target to treat pSS. However, no therapeutics has been available except antibodies against BAFF signaling so far. In this study, we show some of our latest data on low molecular weight compounds that inhibit a BAFF signaling pathway.
**Objectives:** The purpose of our study is to discover low molecular weight BAFF receptor antagonists as drug candidates for pSS.
**Methods:** High-throughput screening (HTS) of a chemical library was carried out to search for compounds that block binding of sBAFF to BR3. In brief, human BR3-expressing CHO-K1 cells were cultured in the presence of FMAT Blue-labeled sBAFF and each compound in 384-well plates, and the binding of sBAFF to BR3 was monitored by an Applied Biosystems 8200 Cellular Detection System. Hit compounds were further screened to eliminate false positives as follows: First, IFN-γ-stimulated THP-1, a human acute monocytic leukemia cell line, was cultured in vitro with sBAFF and primary hits, and the cumulative production of IL-6 was measured by ELISA. Second, sBAFF-stimulated pSS monocytes were cultured in vitro with or without pSS B cells in the presence of hit compounds, and IL-6 production by monocytes and IgG production by B cells were measured by ELISA.
**Results:** A total of 18,562 compounds were examined for inhibitory activities of sBAFF binding to BR3. Finally, two hit compounds, both of which were pyrrolopyrimidine derivatives (BIK12 and BIK13), were discovered and further investigated for biological activities. IL-6 production by sBAFF-stimulated peripheral pSS monocytes was significantly suppressed by BIK12 and BIK13 in a dose dependent manner. Similarly, IgG production by B cells cultured with sBAFF-stimulated peripheral pSS monocytes was also significantly suppressed by these compounds. Because sBAFF itself had no effects on IgG production by B cells, these data suggest that inhibition of BAFF binding to BR3 on monocytes caused suppression of IgG production by B cells in the co-culture probably through suppression of IL-6 production by monocytes.
**Conclusions:** We have successfully discovered low molecular weight BR3 antagonists, pyrrolopyrimidine derivatives, by HTS and found that these compounds suppressed IgG production by B cells in a co-culture with monocytes. These compounds may provide not only lead compounds in drug development for pSS which often accompany HgG, but also novel tools to explore pathological mechanisms of pSS.
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## AB0046 ENDOCANNABINOID SYSTEM AND SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Endocannabinoid (eCB) system comprises endogenous lipid mediators (eCBs) like *N*-arachidonoylethanolamine (anandamide, AEA) and 2-arachidonoylglycerol (2-AG), along with their specific G protein-coupled type-1 ($CB_1$) and type-2 ($CB_2$) cannabinoid receptors, and the proteins responsible for eCB biosynthesis, inactivation, transport, and accumulation. In recent years, many studies have evaluated the role of eCBs in the homeostasis of the immune system. Notably, AEA and the eCB-like molecule *N*-palmitoylethanolamine (PEA) seem to be anti-inflammatory mediators, while 2-AG is implicated in both pro-inflammatory and anti-inflammatory functions. Moreover, the effects of eCBs on immune system seem to be mostly mediated by $CB_2$, more expressed in immune cells than by $CB_1$. The latter receptor, instead, is more implicated in neurotransmission. Several studies have already investigated the role of eCB system in different immune-mediated diseases, such as multiple sclerosis and type-1 diabetes.
**Objectives:** To investigate the role of eCB system in patients with systemic lupus erythematosus (SLE) and age and sex matched healthy subjects.
**Methods:** 10 female patients with SLE and 10 healthy subjects were enrolled from outpatient clinic of Campus Bio-Medico University of Rome. Every SLE patient was positive for anti-dsDNA antibodies and/or exhibited hypocomplementemia with or without hypergammaglobulinemia, ENA or aPL positivity. None of them was treated with biological therapy at the time of enrolment, nor with steroid bolus in the previous six months, while treatment with conventional immunosuppressants was allowed. SELENA-SLEDAI and BILAG were used to assess disease activity and SDI as damage index. AEA, 2-AG and PEA levels were quantified in plasma of SLE patients and healthy controls by using liquid chromatography-tandem mass spectrometry (LC-MS).

**Results:** No significant difference among ages was found in the two groups (SLE patients 37.9±5.9 years, healthy subjects 37.8±6.2, p=ns). In SLE patients, 80% of the subjects exhibited low C3, 50% low C4, 90% anti-dsDNA positivity; 30% of them were not taking glucocorticoids, 20% $\leq$5 mg of daily prednisone and 50% $>$5 mg of daily prednisone; 70% were taking conventional immunosuppressive treatment and 80% were taking hydroxychloroquine. Value of the disease activity score evaluated by SELENA-SLEDAI was assessed as 6±4.7; 10% of the patients exhibited at least 1 BILAG A and 60% at least 1 BILAG B; value of the damage index evaluated by SDI was assessed as 0.6±0.8. eCBs was significantly altered in SLE patients. In particular, plasma levels of 2-AG were significantly increased in SLE patients compared to healthy controls (p=0.005), while no differences were found in AEA and PEA concentrations between the two groups.
**Conclusions:** Our results demonstrate, for the first time, an alteration of eCB system in SLE patients; these data may help to better understand the role of lipid mediators in SLE pathogenesis.
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## AB0047 HIGH SOLUBLE IL-7 RECEPTOR EXPRESSION IN SJÖGREN'S SYNDROME IDENTIFIES PATIENTS WITH INCREASED IMMUNOPATHOLOGY AND DRYNESS

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**Background:** Increased expression of interleukin (IL)-7 and its receptor plays a critical role in immunopathology of primary Sjögren's syndrome (pSS). The IL-7/IL-7R axis is involved in formation of (ectopic) lymphoid structures, which is a predictor for lymphoma development in pSS. IL-7 activity is potentiated by the soluble form of its receptor (sIL-7R), which is produced in inflamed tissues by activated stromal cells. Thus, sIL-7R may serve as a biomarker for IL-7-driven activation and lymphoid neogenesis.
**Objectives:** We studied the expression of sIL-7R in pSS in relation to markers of inflammation and saliva production.
**Methods:** 95 pSS patients were diagnosed according to the 2002 criteria. sIL-7R concentration was measured in serum of 68 pSS patients using ELISA and compared to 51 healthy individuals (HC). Labial salivary gland (LSG) biopsy tissues were taken from 27 patients and were incubated in sterile saline for 1 hour at room temperature. sIL-7R was measured using multi-cytokine analysis by Luminex and compared to 24 non-Sjögren's sicca (nSS) patients.
**Results:** Serum levels of sIL-7R were significantly higher in pSS patients compared to healthy controls (median [range]: 610 [52–2201] vs. 294 [58–821] pMol/mL, p=0.0001). pSS patients with sIL-7R levels above those of HC, defined as sIL-7Rhigh, showed markedly increased ESR, serum IgG and lymphocytic focus scores compared to the other pSS patients. Furthermore, sIL-7Rhigh patients had significantly decreased salivary output, as measured by stimulated whole saliva and unstimulated whole saliva (median [range]: 0.2 [0.0–0.9] vs. 1.2 [0.0–4.6] mL/min, p=0.01). In addition, we observed increased sIL-7R production in LSG supernatants from pSS patients compared to nSS. Similar to serum, a sIL-7Rhigh group could be discerned, with higher levels of serum IgG and increased prevalence of ANA, anti-SSA, and anti-SSB autoantibodies (all at least $p<0.05$).
**Conclusions:** Thus, sIL-7R is increased in serum and LSG supernatant of pSS patients, in which high sIL-7R levels identifies patients with increased markers of inflammation and decreased salivary output. The sIL-7R increase in pSS LSG supernatants indicates that the increased systemic sIL-7R levels are at least partially mediated by local production. High local production of sIL-7R was related to increased B-cell activity and autoimmunity, in line with the described role of IL-7 in lymphoid neogenesis.
**Disclosure of Interest:** None declared
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## AB0048 DEVELOPMENT OF THE NEW RHEUMATOID ARTHRITIS DISEASE ACTIVITY MARKER USING GLYCOSYLATION CHANGE OF MMP-3

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**Background:** It is known that almost all secreted proteins are glycosylated, that glycosylation patterns are influenced by cellular differentiation, and that serum glycoproteins exhibiting disease-associated glycosylation changes have potential to be biomarkers [1]. In rheumatoid arthritis (RA), C-reactive protein (CRP) and matrix metalloproteinase-3 (MMP-3) are widely used as serologic disease activity markers, but they lack sufficient specificity or precision. Thus, development of a RA-specific fine disease activity marker is needed.
**Objectives:** We focused on an existing marker, MMP-3, and examined the association between its glycosylation pattern and RA disease activity.
**Methods:** Serum was taken from RA patients (n=24) whose disease activity was scored using composite measures, and MMP-3 immunoprecipitated and subjected to recently developed antibody-overlay lectin microarray analysis. A disease activity index was developed based on lectin signal, and validated using another cohort, which included 60 serum samples from 30 RA patients, before and after treatment. Synovial fluid MMP-3 in RA and osteoarthritis (OA) patients was also analysed.
**Results:** Intense signals were observed on the O-glycan binding lectins (ABA, ACA, and Jacalin) and a sialic acid binding lectin (ACG) by applying sub-nanogram levels of serum MMP-3. Jacalin and ABA, ACA, and ACG revealed differences in MMP-3 quality and quantity, respectively. The resultant index, ACG/Jacalin, correlated with disease activity. This correlation was validated using second cohort ($r^2$=0.341, $p<0.0001$), and the correlation was greater than those of MMP-3 and CRP. In addition, the change in ACG/Jacalin and disease activity before and after treatment also correlated. Furthermore, we confirmed that MMP-3, which generated a high ACG/Jacalin score, accumulated in RA but not OA patient synovial fluid.
**Conclusions:** We succeeded in development a new RA specific and sensitive disease activity marker using glycosylation change of MMP-3. The difference in quality but not quantity of MMP-3 may be a useful index for estimating RA disease activity.
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## AB0049 OXIDATED LIPIDS IN EARLY ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** There is increasing evidence that oxidatively modified form of low-density lipoprotein cholesterol (LDL) is more important than native LDL in atherogenesis and vascular damage. The accelerated development of atherosclerosis has been recognized in patients with autoimmune rheumatic diseases, such as rheumatoid arthritis and systemic lupus erythematosus. Recent studies reported about the oxidation ratio of LDL that can be more significant in the premature development of coronary artery disease.
**Objectives:** To estimate the oxidated forms of LDL and their involvement in atherosclerotic lesions of the vessel wall in female-patients with autoimmune rheumatic diseases (ARD).
**Methods:** The study included 77 female-patients with ARD (RA (n=37), mean age 45,0 (33,0; 51,0) years old, disease duration 9,0 (3,0; 14,0) years, disease activity (DAS28=5,37 (4,69; 5,86) points) and SLE (n=40), mean age 33,5 (27,5; 44,5) years old, disease duration 8,0 (5,0; 14,5) years, disease activity SLEDAI-2K 7,0 (4,0; 11,5) points). Twenty-two women with the history of myocardial infarction (MI) (i.e. clinical manifestation of atherosclerosis) formed the control group.
The levels of OxLDL, high sensitive C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor - $\alpha$ (TNF-$\alpha$) were determined with ELISA according to the instruction of manufacturer. The oxidation ratio of LDL (Ox-LDL/TC, Ox-LDL/HDL-C, Ox-LDL/LDL-C) was calculated. The presence of carotid atherosclerotic alterations (intima-media thickness and the presence of atherosclerotic plaques) was revealed ultrasonographically according to the described ESH/ESC Guidelines for the management of arterial hypertension.
**Results:** The levels of OxLDL, hs-CRP, IL-6, TNF-$\alpha$, Ox-LDL/HDL-C were significantly higher in ARD patients than in the control group, what may indicate the disease activity. The presence of subclinical atherosclerosis was observed in 54,55% patients with ARD. When we compared the values of investigated parameters in patients with subclinical and clinical atherosclerosis, we revealed that only inflammatory markers (hs-CRP, IL-6, TNF-$\alpha$) were significantly higher in ARD patients with atherosclerosis. However those without atherosclerosis had significantly higher values of OxLDL, hs-CRP, IL-6, Ox-LDL/TC, Ox-LDL/HDL-C,

Ox-LDL/LDL-C than the control group. The positive association between hs-CRP, IL-6 and oxidation ratio Ox-LDL/TC was found in patients with subclinical atherosclerosis (p=0,0003 and p=0,007, respectively), between TNF-α and Ox-LDL/LDL-C in patients without atherosclerosis (p=0,002). The negative association between TNF-α and Ox-LDL/TC was found in patients with MI that can explain because of the lower levels of OxLDL in this group of patient considering that statins can inhibit oxidative stress.

**Conclusions:** More than half of patients with ARD had subclinical atherosclerosis. We demonstrated the elevated levels of OxLDL and inflammatory markers (hs-CRP, IL-6, TNF-α) in patients with ARD. The presence of OxLDL, especially when used in combination with TC, is better than only OxLDL for estimation of association with inflammation in patients with clinical and subclinical atherosclerosis. Thus we suggest that inflammation can influence to oxidative modification of LDL in patients with RA and SLE and during this process induce endothelial dysfunction and early development of atherosclerosis as its result.

**Disclosure of Interest:** None declared

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## AB0050 DETECTION OF INTERLEUKIN-22 AND TUMOR NECROSIS FACTOR RECEPTOR ASSOCIATED FACTOR 1 (TRAF1) IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS: CORRELATION WITH DISEASE ACTIVITY

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**Background:** In autoimmune diseases including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), cytokines play a central role in initiating and maintaining diverse immune and inflammatory responses.In addition to IL-17A and F, Th17 cells also secrete IL-21, IL-22, and granulocyte macrophage colony-stimulating factor (GM-CSF). IL-22, member of IL-10 cytokine family, has been believed as an important player in regulating inflammatory responses associated with many inflammatory diseases. There is apparently a strong functional synergism of TNF-α and IL-22; the interaction of IL-22 & TNF-α is mediated through TNFR I and IL-22R heterodimer and intracellularly by MAP kinases. The combination of IL-22 & TNF-α strongly induced the phosphorylation and translocation of MAP kinases to the nucleus whereas the single cytokine only weakly contributed to MAP kinase activation. The discovery of the IL-22/TNF-α axis gives a first insight that could lead to new therapeutic approaches of RA.

**Objectives:** to evaluate the role of IL-22 and TRAF1 in patients (pts) with RA & SLE, and their association to the disease activity.

**Methods:** 70 RA pts, 64 SLE pts aged & 45 healthy matched controls were enrolled. DAS28 & SLEDAI were used to assess activity.

**Results:** IL-22 was significantly higher in RA&SLE pts than healthy controls. significant positive correlation was found between IL-22 levels and tender joints count, CRP and ESR. However, In SLE pts CRP only showed a positive correlation with IL-22 levels

Comparison between TRAF1 genotyping, clinical and laboratory data

| | Genotype | | | P |
|---|---|---|---|---|
| | A/A | A/G | G/G | |
| ESR mm/hr | 76.40±9.63 | 49.76±26.81 | 51.83±37.93 | 0.006* |
| CRP (mg/L) | 14.8 (14.8–71.0) | 15.0 (2.9–67.0) | 21.0 (3.0–48.0) | 0.152 |
| RF (IU/mL) | 24.0 (15.1–24.0) | 24.0 (6.9–359.0) | 10.1 (7.3–15.0) | <0.001* |
| Anti-CCP (U/mL) | 29.7 (29.7–30.1) | 33.6 (12.1–178.0) | 21.9 (18.0–175.4) | 0.690 |
| DAS28 | 5.43±0.74 | 4.48±0.91 | 4.34±0.99 | 0.001* |
| Tender joints count | 4.0 (4.0–26.0) | 8.0 (2.0–16.0) | 6.0 (2.0–14.0) | 0.004* |
| Swollen joints count | 2.0 (2.0–2.0) | 2.0 (0.0–12.0) | 2.0 (0.0–3.0) | 0.238 |
| Disease duration (yrs) | 1.0 (1.0–4.0) | 3.0 (0.33–20.0) | 2.0 (1.0–6.0) | 0.004* |
| MHAQ | 0.60 (0.50–2.25) | 0.60 (0.12–0.80) | 0.60 (0.13–1.50) | 0.354 |

*Statistical significance at p<0.05.RF +ve>20 IU/ml. Anti-CCP +ve >30 IU/ml.

Analysis of TRAF1 polymorphism: in RA pts; the magnitude of association was increased in those patients who were autoantibody positive either RF+ or anti-CCP+. TRAF1 A allele was significantly associated with RF+ and anti-CCP+ RA patients when compared withcontrol. (OR =3.344 CI: 1.79–6.24, P<0.001, OR =1.881 CI: 1.03–3.41 P<0.034)respectively,in SLE pts, TRAF1 rs10818488 was not significantly different in pts and control

**Conclusions:** Theses results indicate that IL-22 is associated with inflammatory process and it has a role in RA and SLE pathogenesis and prognosis.Although there are inconsistent findings which need to be resolved, there are a synergism between TNF-α, IL 17 & IL-22,mso,targeting IL-22 cytokine may be an effective therapeutic approach for chronic inflammation in the future.Also TRAF1 was significantly associated with RF positive, anti-CCP positive pts, ESR and tender joints count and this confirm importance of TRAF1 in progression of RA

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.5913

## AB0051 ANGIOGENIC AND ANTI-ANGIOGENIC FACTORS: BIOMARKERS FOR LARGE VESSEL VASCULITIS?

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**Background:** Large vessel vasculitides (LVV) – Takayasu Arteritis (TA) and Giant Cell Arteritis (GCA) are inflammatory diseases of the aorta and its main branches. A cytokine cluster involving the IL-6 – IL-17 axis as well as another one centring on the IL-12-IFN-γ axis are involved in LVV pathogenesis. (1) Disease activity could be evaluated by measuring ESR and CRP as well as by using imaging techniques (Doppler Ultrasound, Computed Tomography scan, Magnetic Resonance Imaging or Positron Emission Tomography scan – CT/PET) and specific scoring systems (Indian*Takayasu's* Arteritis Activity *Score* - ITAS and Kerr/National Institutes of Health index - *Kerr*/*NIH)*. To date, angiogenic factors have been evaluated but specific biomarkers for disease activity are still lacking (2)

**Objectives:** The aim of our study was to evaluate angiogenic and anti-angiogenic factor expression in LVV, in order to evaluate their role as biomarkers.

**Methods:** We enrolled 67 patients with LVV [TA (40, 59.7%) or GCA (27, 40.3%)] and 50 Normal Controls (NC). Angiogenic (angiopoietin-1, angiopoietin-2, Fibroblast Growth Factor2 – FGF-2, Vascular Cell Adesion Molecule1 – VCAM-1, Vascular Endothelial Growth Factor – VEGF) and anti-angiogenic (angiostatin, Endostatin-1, Pentraxin 3 – PTX3) factors were analysed using enzyme-linked immuno-sorbent assay (ELISA). Disease activity was evaluated according to Kerr (≥2) and ITAS (≥1) scores, only 47 (70.1%) patients underwent CT/PET. Serum levels of angiogenic and anti-angiogenic factors were compared among active LVV, inactive LVV and NCs. When evaluating disease activity according to CT/PET, it was considered active if SUV >2. Statistical analysis was performed utilizing Mann Whitney, Kruskal Wallis for multiple comparison and Dunn's post hoc test, using Graph Pad Prism software.

**Results:** No significant differences were found between LVV and NCs in angiogenic factors. Conversely, anti-angiogenic factors were all significantly increased in LVV (both GCA and TA) in comparison with NCs (angiostatin: TA vs NC, p<0.0001; GCA vs NC, p=0.0008; endostatin: TA vs NC, p=0.0002; GCA vs NC, p=0.001; PTX-3: TA vs NC, p<0.0002; GCA vs NC, p=0.001). Stratifying patients according to disease activity (with Kerr and Itas scoring systems, as well as taking into account CT/PET), no significant differences were found in angiogenic factors. Anti-angiogenic factors were significantly higher both in active LVV and inactive LVV compared with NCs (p<0.05).

**Conclusions:** Our data show an imbalance between angiogenic and anti-angiogenic factor levels in serum. No disease activity related changes were observed for these factors.

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## AB0052 INVESTIGATING THE NEUTROPHIL-MACROPHAGE INTERPLAY IN JUVENILE LUPUS NEPHRITIS PATHOGENESIS

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**Background:** Juvenile systemic lupus erythematosus (JSLE) is a multifactorial systemic autoimmune disease that can cause severe kidney damage and lead to end-stage renal failure. In JSLE increased neutrophil apoptosis and NETosis combined with impaired phagocytosis[1,2] result in prolonged autoantigen exposure and enhanced autoimmunity. We hypothesized that in lupus nephritis (LN) apoptotic and/or NETotic neutrophils infiltrate the kidneys in response to pro-inflammatory stimuli. Monocytes are then recruited to the kidney where they induce native kidney cell damage leading to proteinuria and potentiated inflammation. Studies have shown that monocytes isolated from SLE patients produce high levels of IL-1Ra, and IL-1β has been detected in the glomerular biopsies from LN patients[3]. Macrophages may significantly contribute to LN development by regulating the local IL-1β/IL-1Ra balance in the kidney.

**Objectives:** To investigate the mechanisms and outcomes of macrophage activation by viable and apoptotic neutrophils and determine how this affects the secretion of pro-inflammatory IL-1β and anti-inflammatory IL-1Ra.

**Methods:** Paired monocytes and neutrophils were isolated from healthy adult donors (n=7), neutrophil culture medium was collected at 2h and 24h after incubation at 37℃. Monocytes were cultured for 6 days in RPMI (+10% FCS +50ng/mL M-CSF) and their differentiation into macrophages was determined by light microscopy. Macrophages were then treated for 6h with culture media

from the 2h viable (mean apoptosis - 9.5%) and 24h apoptotic neutrophils (mean apoptosis - 70%), with LPS as a positive control. Following 6h the macrophage culture media were collected and IL-1β/IL-1Ra levels were assessed via ELISA.
**Results:** IL-1β levels did not significantly differ within treatment groups with levels being below the lower limit of detection for most samples. IL-1Ra expression however was significantly increased in LPS-treated macrophages (4374pg/ml ±910.3, P=0.0012) compared to control (845.6pg/ml ±240) while no significant difference was seen with 2h (1379pg/ml ±344.4) or 24h (1696pg/ml ±371.1) neutrophil culture medium.
**Conclusions:** Macrophages treated with culture medium from both apoptotic and viable neutrophils produce high levels of IL-1Ra, however this does not differ from levels seen in control macrophages. IL-1β levels are below the level of detection under all conditions. This suggests that secreted factors from apoptotic neutrophils do not induce an IL-1 response in macrophages but does not exclude a role for direct cell-cell contact. Other immune cells may also be playing a role in promoting renal cell damage through IL-1β secretion.
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## AB0053 A USEFUL MARKER IN ASSESSMENT OF REMISSION AND ACTIVATION OF DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS: SERUM HUMAN NEUTROPHIL PEPTIDES 1-3

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**Background:** Rheumatoid arthritis (RA) is a chronic disease of unknown etiology that is characterized by articular inflammation and deformities and may also present with extra-articular findings. Various cellular and molecular immunological factors are involved in the pathophysiology of RA. Recent studies suggest that neutrophils and alpha-defensins released from the neutrophils assume significant roles in the pathogenesis of RA.
**Objectives:** The purpose of this study was to investigate the potential association between serum alpha-defensin levels especially human neutrophil peptides (HNP) 1–3 and disease activity, functional status and radiologic damage as well as some other laboratory parameters such as erythrocyte sedimentation rate (ESH) and C-reactive protein (CRP) in patients with RA.
**Methods:** A total of 42 patients with established RA who presented to the Outpatient Clinic of Physical Medicine and Rehabilitation of Dicle University Hospital and 38 healthy control subjects were included in this study. All the subjects underwent a through physical examination. Swollen and tender joints were noted for each patient. Disease activity was assessed by Disease Activity Scale 28 (DAS28). Quality of life was assessed by Rheumatoid Arthritis Quality of Life (RAQoL) Questionnaire and Nottingham Health Profile (NHP). Functional status was assessed by Stanford Health Assessment Questionnaire (HAQ). Laboratory examinations included complete blood count, ESH, CRP, and human neutrophil peptides (HNP) 1–3 tests.
**Results:** The patients with an active disease exhibited higher HNP 1–3 levels compared to the patients in remission. At cut off 708 pg/ml, the sensitivity and the specificity of the test for HNP 1–3 were 72% and 70.6%, respectively. Moreover, HNP 1–3 levels correlated significantly with WBC counts as well as with HAQ, NHP total, NHP pain, NHP physical activity and NHP sleep scores. There were no significant differences between the patients and the control subjects in serum HNP 1–3 levels.
**Conclusions:** In the present study, serum HNP 1–3 levels correlated significantly with WBC counts as well as with HAQ, NHP total, NHP pain, NHP physical activity, and NHP sleep scores. In addition, the patients with an active disease had significantly higher serum HNP 1–3 levels compared to the patients in remission. In this respect, serum HNP 1–3 can be a useful marker in assessment of disease activity and remission in patients with RA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2671

## AB0054 FORMULATION OF IBUPROFEN IN LIPID-CRYSTAL NANO-PARTICLES ENHANCES EFFICACY AND REDUCES GASTRIC MUCOSAL EROSIONS IN A RAT CARRAGEENAN-INDUCED PAW INFLAMMATION MODEL

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**Background:** Non-steroidal anti-inflammatory drugs (NSAIDs) are some of the most commonly prescribed drugs in the world for their analgesic and anti-inflammatory properties. However, NSAID use is limited by gastrointestinal (GI) toxicity. NSAIDs injure the gut by causing topical injury to the mucosa and by systemic effects associated with mucosal prostaglandin depletion derived from COX inhibition. New formulations that prevent exposure of the NSAID to the GI mucosa may help reduce the GI toxicity associated with NSAIDs and maintain their anti-inflammatory effects.
**Objectives:** To demonstrate that ibuprofen formulated in two types of cochleates (lipid-crystal, nano-particles) provide enhanced anti-inflammatory effects while reducing the associated mucosal GI toxicity.
**Methods:** Male Sprague Dawley rats treated orally (one hour prior to right hind footpad injection of carrageenan) with vehicle or 50, 10, 2, 0.4, or 0.1 mg/kg of Ibuprofen, Ibuprofen Geodates or Ibuprofen Lipid-Crystal Cochleates (LCC) were evaluated for effects of treatment on inflammatory edema. Animals were terminated five hours after dosing with test articles (four hours after carrageenan injection). Efficacy evaluation was based on weight difference due to inflammation-induced swelling in injected (right) vs. uninjected (left) paws. In addition, gastric mucosa were evaluated for differences in incidence and severity of mucosal congestion and erosions.
**Results:** Treatment of rats with 50 mg/kg of all test articles or with 10 or 2 mg/kg Ibuprofen Geodates or 10 mg/kg Ibuprofen LCCs resulted in significant inhibition of paw weight difference when compared to the vehicle control group. The Ibuprofen LCC formulation was most effective ($ED_{50}$=6 mg/kg) followed by Ibuprofen Geodates ($ED_{50}$=7 mg/kg) and Ibuprofen ($ED_{50}$=30 mg/kg). Rats treated with 50 mg/kg Ibuprofen had significantly increased numbers of gastric lesions and increased total stomach lesion length. Some rats treated with 10 mg/kg Ibuprofen also had gastric lesions. Rats given 50 mg/kg Ibuprofen LCC had increased length and number of stomach lesions as compared to vehicle treated rats, but both parameters were significantly smaller when compared to Ibuprofen treatment alone. Rats treated with 50, 10 or 2 mg/kg Ibuprofen Geodates ($ED_{50}$=7 mg/kg) had significant inhibition of carrageenan-induced paw edema without evidence of gastric irritation. Treatment with LCCs at 10 mg/kg resulted in the greatest inhibition of paw edema for any formulation at this dose and there was no evidence of gastric irritation. There were no gastric lesions in rats given 2, 0.4 or 0.1 mg/kg of any formulation.
**Conclusions:** Results of this study demonstrated that Ibuprofen LCC ($ED_{50}$=6 mg/kg) had greater beneficial effects on carrageenan paw edema than did either Ibuprofen ($ED_{50}$=30 mg/kg) or Ibuprofen Geodates ($ED_{50}$=7 mg/kg). Gastric lesions occurred in some rats treated with single-dose 50 mg/kg (9 of 10) or 10 mg/kg (1 of 10) Ibuprofen whereas none were observed in rats given Geodates. Only 6 of 10 rats given 50 mg/kg LCC and none treated with 10 mg/kg had gastric lesions. Therefore both efficacy as well as incidence and severity of gastric irritation were significantly improved by cochleate formulations of Ibuprofen.
**Disclosure of Interest:** R. Lu Shareholder of: Matinas BioPharma, Inc., Employee of: Matinas BioPharma, Inc., R. Mannino Shareholder of: Matinas BioPharma, Inc., Employee of: Matinas BioPharma, Inc.
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## AB0055 CYTOKINE PROFILES OF KOREAN PATIENTS WITH ADULT ONSET STILL'S DISEASE TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS

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**Background:** Adult onset Still's disease (AOSD) is a rare inflammatory disorder of unknown etiology. Several studies have reported that pro-inflammatory cytokines including interleukin (IL)-1, IL-6, IL-18, tumor necrosis factor (TNF)-α, and interferon (INF)-γ, are involved in the pathogenesis of AOSD. Refractory AOSD patients have been treated successfully with anti-cytokine biologics.
**Objectives:** Herein, to investigate predictors for therapeutic response of biologic drugs in refractory AOSD, we analyzed cytokines profiles in Korean patients with AOSD who were treated with anti-TNFα inhibitors.
**Methods:** Twenty two AOSD patients treated with anti-TNFα agents were recruited from a university hospital for rheumatic diseases in Korea. The dosages

of anti-TNFα (infliximab in 18 patients, etanercept in 4, and adalimumab in 3) were same as rheumatoid arthritis. White blood cells, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, ferritin levels, liver enzymes, and serum cytokines (TNFα, IL-1β, IL-6, IL-8, IL-17α, and INF-γ) and IL-2 receptor α in sera were analyzed by multiplex flowcytometry. A good response to anti-TNFα inhibitors was defined as decreased modified Pouchot score more than 2 score compared to initial treatment of anti-TNFα inhibitors. A no response to anti-TNFα inhibitors was defined as no decrease of modified Pouchot score. We used the Mann-Whitney test or Wilcoxon signed rank test for continuous variable and Fisher's exact test for categorical variables.

**Results:** Six (27.3%) patients showed good response to anti-TNFα inhibitors and 3 (13.6%) patients showed partial response. Thirteen (59.1%) patients did not respond to anti-TNFα inhibitors. At starting time point of anti-TNFα inhibitors, levels of ferritin, TNFα, IL-1β, IL-6, and IFNγ in no responders (mean±SD 4,142.0±7,128.6 ng/mL (range 27–18,331), 6.9±10.5 pg/mL (0.0–27.9), 2.6±2.9 pg/mL (0.0–7.4), 16.9±18.7 pg/mL (1.2–221.6), and 13.2±9.1 pg/mL (4.9–30.9), respectively) seemed to be higher compared to those with good response (566.4±633.0 ng/mL (18–1,901), 13.8±24.3 pg/mL (0.0–67.0), 8.7±16.9 pg/mL (0.0–50.8), 77.1±157.8 (2.0–485.4), and 69.3±146 pg/mL (0.0–453.3), respectively), but without statistically significant differences between the 2 groups. We didn't raise the dosage of infliximab in no responders, in whom tocilizumab was used as second biologic therapy. Of those, seven (63.6%) patients showed improvement in clinical and laboratory findings.

**Conclusions:** This study showed that AOSD patients who were refractory to anti-TNFα inhibitors might have distinct cytokine profiles. Therefore, dosage of anti-TNF agents in AOSD patients might be individualized according to pre-treatment cytokine profiles.

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**Disclosure of Interest:** None declared
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## AB0056 DOWNREGULATION OF TUMOR NECROSIS FACTOR AND INTERLEUKIN-1 BY ELLAGIC ACID

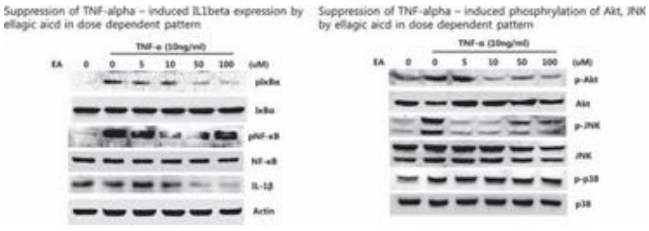
S.-H. Park, H. Lee, J.-Y. Choe, S.-K. Kim, C.W. Lee, J.-W. Kim, J. Kim. *Catholic University of Daegu School of Medicine, Daegu, Korea, Republic Of*

**Background:** Ellagic acid (EA) is a phenolic constituent in fruits and nuts, such as raspberries, strawberries, walnuts, mango kernel and pomegranate. It was documented that EA shows anti-fibrotic, anti-inflammatory activity in vivo model of bowel inflammation and lung fibrosis, however the precise mechanism of signal inhibition was not extensively investigated.

**Objectives:** The objectives of this study are first, to elucidate the anti-inflammatory effect of EA in RAW 264.7 murine macrophage cell line by NF-kB pathway in vitro, and second, to compare it with effect of other immuno-modulating agent, tacrolimus and colchicine.

**Methods:** We determined the cytotoxic effect of EA using MTT assay. The effects of EA on tumor necrosis facor (TNF)-alpha induced mRNA and protein expression were investigated using quantitative real-time PCR and western blot. In addition, we examined the effects of pharmaceutical drugs with anti-inflammatory properties on expression of TNF-alpha.

**Results:** EA significantly suppressed the expression of interleukin-1 beta and TNF-alpha in a dose dependent manner. EA suppressed TNF-alpha induced inflammatory genes expression by inhibiting the phosphorylation of JNK and Akt, whereas had no significant effect on p38 activation. In addition, the inhibitory effect of EA on TNF-alpha induced inflammatory genes expression was regulated by suppression of IkB-alpha phosphorylation and NF-kB translocation. The expression of TNF-alpha mRNA level was reduced comparably treated with EA and other anti-inflammatory agents (ascorbic acid, dexamethasone and colchicine).




**Conclusions:** These findings suggest that EA suppresses inflammatory genes expression through phosphorylation of JNK/Akt and regulation of NF-kB signal pathway in TNF-alpha induced inflammation. Further investigation regarding effects of EA on autoimmune, inflammatory is scheduled.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2594

## AB0057 SWIMMING EXERCISE CAN ALTER THE PATTERN OF PLASMA CYTOKINES IN HEMARTHROSIS: AN EXPERIMENTAL STUDY

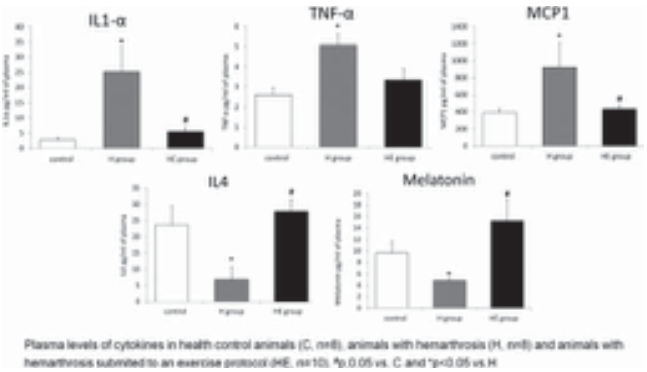
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**Background:** Arthropathy is one of the major complications in hemophilia, leading to functional limitations and poor quality of life. Exercise is recommended as being beneficial for people with hemophilia to counteract the consequences of repetitive hemarthrosis, yet a lack of exercise-related evidence using exercise and control groups exists in this population.

**Objectives:** To evaluate in an experimental model of blood-induced joint damage the effects of swimming exercise on systemic inflammatory parameters and pain behavior.

**Methods:** The arthropathy was induced in Wistar rats by eight weekly intra-articular injections of 0.1 mL of autologous blood in their right knees, contra lateral knees were injected with the same amount of saline. Animals were divided into Control Group (C; n=8), Hemarthrosis (H; n=8), Hemarthrosis + Exercise (HE; n=10). HE group performed during 8 weeks a swimming protocol during 60 min/day (5 x week) with 5% body weight attached on their tails. Joint diameters were measured with a digital microcaliper and the difference (Δ) between both side were calculated post-study. Pain status was also assessed with a static weight-bearing incapacitance test (SWIT). Blood samples were collected before sacrifice and the serum levels of interleukins (IL-10, IL-1α, IL-6, IL-4, IL-17), tumor necrosis factor (TNF)-α, vascular endothelial grown factor (VEGF) and monocyte chemoattractant protein-1 (MCP-1) were analyzed by Multiplex assay. Plasmatic Corticosteroid, ACTH and Melatonin hormones were also assessed.

**Results:** When compared with H group, HE group presented reduced joint swelling (Δ=2.39cm vs. 0.66cm; p=0.0001) and pain (39.54 vs. 8.58% decrease weight-bearing in hemarthrosis side; p=0.002). As show in the figure below, hemarthrosis promoted an increase in the plasmatic level of IL1-α (H=10.9 pg/ml ±0.13 vs. HE=5.51 pg/ml ±0.46; p=0.039), TNF-α (H=5.08 pg/ml ±2 vs. HE=3.35 pg/ml ±1.78; p=0.031) and MCP-1 (H=639.86 pg/ml ±45.9 vs. HE 433.1 pg/ml ±10.7; p=0.033) and were reduced by swimming exercise protocol. The level of these plasmatic pro-inflammatory cytokines were also positively correlated with pain (IL1-α: p=0.039; TNF-α: p=0.013; MCP-1: p=0.014). A contrary effect was observed in the anti-inflammatory cytokine IL-4 (p=0,001) where it was reduced in hemarthrosis group (H=6,81pg/ml ±0.81) and was increased by the exercise protocol (HE=27.77 pg/ml ±4.8). Interestingly the pattern of Melatonin levels (H: 4.75 pg/ml ±1.4 vs. HE: 15.26 pg/ml ±5.4; p=0,049) was similar to IL-4.




Plasma levels of cytokines in health control animals (C, n=8), animals with hemarthrosis (H, n=8) and animals with hemarthrosis submitted to an exercise protocol (HE, n=10). *p 0.05 vs. C and *p<0.05 vs. H

**Conclusions:** This is the first study showing the beneficial effects of swimming exercise inflammatory parameters of the blood-induced hemarthrosis in rats. Our data also showed the effectiveness of the exercise in controlling at the same time systemic cytokines and pain in the arthropathy. The most surprising finding of this study was swimming promoting melatonin liberation, which possibly act as an anti-inflammatory agent.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2174

### AB0058 EOSINOPHIL CATION PROTEIN (ECP) – THE TOPPING ATTRACTOR OF THE DISEASE ACTIVITY IN RHEUMATIC ARTRITIS (RA)

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**Background:** RA is systemic autoimmune disease characterized by the production of auto-reactive antibodies, formation of immune complexes causing tissue and organ damage, that reflects the degree of cellular destruction and the depth of the membrane pathological changes. ECP hinder the development of these negative phenomena.
**Objectives:** To assess serum levels of ECP, interleukins (IL-5, IL-10, IL-18) levels and immunoglobulins (IGA, IGE) levels in a population of patients with RA.
**Methods:** 15 patients with RA and 20 healthy controls were investigated in this study. Their ages changed from 35 to 60 years (female/male=3:1). The serum ECP, IL-5, IL-10, IL-18 and IGA, IGE levels were determined using (ELISA), and their correlations with the disease activity were measured using the DAS 28 and laboratory parameters including RF, antiCCP, erythrocyte sedimentation rate, complement (C3, C4), anti-double stranded – DNA antibody levels were analyzed. The clinically relevant correlation reported in the study parameter.
**Results:** The serum ECP, IG and IL levels were significantly higher (mean values ECP: 2500±134,7 ng/ml; IGA: 6970,5±357,9 mg/ml; IGE: 4350,9±210,7 ng/ml; IL-5: 632,5±19,9 pg/ml; IL-10: 956,4±14,7 pg/ml; IL-18: 2307,8±325,4 pg/ml) in RA patients compared to the control (mean values ECP: 21,7±0,9 ng/ml; IGA: 516,7±39,4 mg/ml; IGE: 37,0±9,4 ng/ml; IL-5: 53,7±12,6 pg/ml;IL-10: 93,4±17,8 pg/ml; IL-18: 187,3±25,4 pg/ml), ($p<0,001$). Furthermore, such in increase in the levels of these analyzed parameters showed a highly significant positive correlation with the disease activity and laboratory parameters.
**Conclusions:** The production of pro-and anti-inflammation mediators and ECP in blood from patients with active RA shows a high degree of correlation with clinical disease activity measures. The level of ECP reflects the intensity of RA-inflammatory processes. It is proved expediency of application of the ECP-test in dynamics, status and forecast of the RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6066

## Cartilage, synovium and osteoimmunology

### AB0059 TNF PRODUCED BY INFLAMMATORY BLOOD MONONUCLEAR CELLS DIRECTLY CONTRIBUTES TO ARTICULAR CARTILAGE DAMAGE

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**Background:** TNF is one of the major cytokines involved in the pathogenesis of rheumatoid arthritis (RA) and anti-TNF therapies are effective at preventing inflammation and structural damage in this disease. However, it is not clear whether TNF destroys cartilage directly or via induction of other cytokines including IL-1β. Furthermore, the cellular sources for TNF within the inflamed joints remain controversial.
**Objectives:** Here, we studied effects of TNF on cartilage and compared TNF production by different cell types to gain deeper insights into the mechanism of action for anti-TNF biologics in RA.
**Methods:** *In vitro* studies were performed using primary human synovial fibroblasts (SF), chondrocytes or cartilage explants, and human peripheral blood mononuclear cells (PBMC) from individuals without history of joint disease. Cells and tissues were stimulated with recombinant human TNF, IL-1β, LPS, or members of alarmin family (S100A8 and S100A9). Adalimumab, etanercept, or certolizumab pegol were used to block TNF. Levels of cytokines and matrix metalloproteinases (MMPs) were detected using mesoscale discovery (MSD) assay, and gene expression was measured by real-time PCR. For *in vitro* cartilage destruction studies, bovine explants were co-cultured with activated human PBMC followed with proteoglycan quantification. *In vivo* effects of adalimumab on cartilage were evaluated in human TNF transgenic (hTNF-Tg) mouse model of arthritis.
**Results:** We first examined whether TNF blockade provide cartilage protection *in vivo* and found that adalimumab treatment significantly decreased proteoglycan depletion from the articular cartilage of hTNF-Tg mice. *In vitro*, TNF induced strong up-regulation of IL-6, MMP1, and MMP3 in isolated human chondrocytes and cartilage explants. Additionally, TNF treatment resulted in significant proteoglycan depletion from bovine cartilage explants confirming previous findings; showing that bovine cartilage can respond to human cytokines. In an effort to identify cellular sources of TNF, we challenged chondrocytes, PBMC and SF with inflammatory stimuli, including alarmins, known to be involved in joint pathology and found that PBMC produced significantly higher levels of TNF. In sharp contrast with SF and chondrocytes, TNF failed to induce high amounts of IL-6, MMP1, and MMP3 in PBMC; suggesting that different cell populations play a distinct role in triggering and propagating joint inflammation. Furthermore, blocking both endogenous and exogenous TNF with anti- TNF biologics protected cartilage from proteoglycan depletion *in vitro*.
**Conclusions:** This work demonstrates that TNF directly triggers the catabolic program in human chondrocytes leading to cartilage damage. Our findings also suggest that neutralization of TNF, produced by PBMC infiltrating inflamed joint, decreases catabolic activity of chondrocytes and fibroblasts, which contributes to cartilage protective effects of anti-TNF biologics in RA.
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**Disclosure of Interest:** A. Yarilina Shareholder of: Abbvie, Employee of: Abbvie, T. Melim Shareholder of: Abbvie, Employee of: Abbvie, Z. Kaymakcalan Shareholder of: Abbvie, Employee of: Abbvie
**DOI:** 10.1136/annrheumdis-2016-eular.2278

### AB0060 HISTOPATHOLOGICAL CHANGE CAUSED BY BIOLOGICAL TREATMENT IN RHEUMATOID ARTHRITIS SYNOVIAL TISSUE

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**Background:** Multiple studies addressing the effects of biologics on the synovial tissue in rheumatoid arthritis (RA) patients have been reported. There are, however, few studies comparing histopathological changes in the synovial tissue in the same RA patients between before and after biologics treatment.
**Objectives:** We examined biologics impacts on RA synovial tissues based on pathological findings in them collected during surgeries for the same patient before and after biological drug usage.
**Methods:** Synovial tissues were collected from 22 RA joints before and after biologics. The average age and disease duration of the study subjects were 63.3 and 21.8, respectively. Histopathological changes in the synovial tissues were compared based on Rooney's score, and presence or absence of fibrinoid degeneration and plasma cell infiltration in the subsynovial tissue. We examined correlation between pathological findings in RA synovium and disease activity under biologics. Disease activity was assessed by CDAI. Etanercept, Infliximab, Tocilizumab, Adalimumab and Abatacept was used as biological drug for 11, 5, 2, 2 and 2 joints respectively.
**Results:** Rooney score between before and after biological drug usage improved from 30.6 to 12.6 showing significant difference. Significant improvement in Rooney score was observed in all items. Fibrinoid degeneration was observed in 18 cases (81.8%) and 4 cases (18.2%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. After biologics treatment, Rooney's scores in the remission and low disease activity, and moderate disease activity were 7.1 and 15.9, respectively, showing a statistically significant difference. In addition, the moderate disease activity had significantly higher scores in perivascular lymphocytic infiltration, lymphoid follicle and lymphocyte infiltration compared to the remission and low disease activity. Plasma cells after biologics treatment were observed at 0%, 22.2% and 63.3% in the remission, low disease activity and moderate disease activity respectively, indicating the greater disease activities were associated with the more plasma cells in the subsynovial tissue.
**Conclusions:** The study results demonstrated that biologics treatment significantly ameliorated inflammatory changes in the synovial lining cells and subsynovial tissue. In addition, the results suggested that histopathological findings in the subsynovial tissue reflected disease activity.
**Disclosure of Interest:** None declared
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### AB0061 EFFECTS OF LONG TERM ADMINISTRATION OF RANITIDINE, AN ANTAGONIST OF H2 - RECEPTOR, ON BONE METABOLISM IN MALE GROWING RATS

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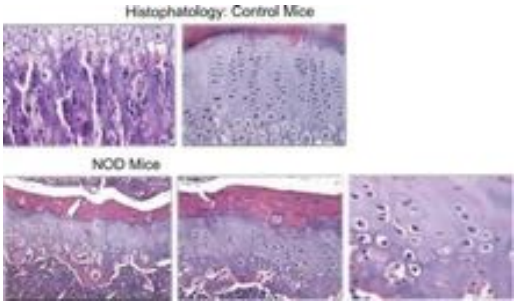
**Background:** $H_2$ - antagonists belong to wildly used drugs. Results of epidemiological studies assessing the influence of long-term therapy with $H_2$-antagonists on bone mineral density (BMD) and fractures risk are ambiguous [1,2].
**Objectives:** The aim of the study was top evaluate influence of ranitidine, a $H_2$ antagonist, on bone turnover and bone mineral density (BMD) in growing rats.
**Methods:** The experiment was carried out on 24 young (8-week-old) male Wistar rats. Rats were randomly assigned to one of two groups (12 animals in each group): group R – rats receiving ranitidine (10 mg /kg) in saline solution (4ml/kg), and group C (control group) – rats receiving saline solution (4ml/kg). Saline solution and ranitidine were given intraperitoneally once daily for 84 days. On day 85 blood samples for serum isolation were collected. After animal scarification right femurs were obtained from each animal and femur index defined as ratio of femur weight and body weight (15 femur mass [g] body mass [g] x 100%'>) was calculated. Serum calcium and phosphate levels were assessed in certified laboratory. Markers of bone turnover were assessed with commercial ELISA kits according to producers' instruction. Bone mineral density (BMD) of right femur was measured by dual-energy X-ray absorptiometry (DXA) with Hologic

DXA equipment (Hologic Dicovery W 81507) using a small animal software. The experiment was performed with the approval of the First Local Ethics Committee for Experiments on Animals in Wroclaw.
**Results:** Femur index and BMD were significantly decreased in rats receiving ranitidine comparing co control group (0.36% ±0.03% vs. 0.03% ±0.02%, p=0.02 and 0.263±0.008 g/cm$^2$ vs. 0.272±0.007 g/cm$^2$, p=0.01, respectively). Serum phosphate level was significantly increased in rats receiving ranitidine comparing to control group (5.06±1.21 mg/dl vs. 4.14±0.39 mg/dl, p=0.02). No significant difference in serum calcium levels between analyzed groups was detected (10.15±0.38 mg/dl in group R vs. 10.34± 0.21 mg/dl in group C, p>0.05). C-terminated telopeptide of type I collagen (CTX) level was increased in group R comparing to group C (140.5± 35.1vs. 102.2±50.0 pg/mL, p=0.04). No significant differences between analyzed groups in serum osteocalcin (OC), osteoprotegerin (OPG) and receptor activator of nuclear factor kappa B ligand (RANKL) levels were detected (342.5±123.3 pg/ml vs. 269.3±76.6 pg/ml, p>0.05; 0.42±0.25 ng/ml vs. 0.30±0.18 ng/ml, p>0.05 and 227.4±57.3 pg/ml vs. 214.7±50.5 pg/ml, p>0.05, respectively).
**Conclusions:** In young growing rats receiving ranitidine we observed decreased BMD and femur index. It seems to be the consequence of increased bone resorption in rats receiving ranitidine.
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**Disclosure of Interest:** None declared
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## AB0062 ALTERATION OF TIBIAL METAPHYSIS AREA IN NOD MICE WHIT SJÖGREN'S SYNDROME

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**Background:** Previously our group described in X-ray studies bone alterations in NOD mice affected with Sjögren's syndrome (SS), characterized by the radiopacity decrease of the tibia cortical layers, compared to controls. These results would suggested that NOD mice with SS could developed disorders in tibial histological architecture. In the current literature, have not been described accurately bone disorders related to the SS.
**Objectives:** To assess histologically the tibial metaphysis area of non-obese diabetic mice with SS, compared to controls NOD without SS.
**Methods:** We used 10 NOD female mice with SS (group SS) and 10 controls NOD without SS (group C, control). They were cared in the animal facilities of the Faculty of chemistry of the UNC. At 4 months of age (weight 80 g ± 10) mice were anesthetized with ketamine-xylazine, both tibias were extracted, and then they were taken to euthanasia. The bones were fixed in formalin buffer, decalcified with EDTA and processed for its inclusion in paraffin; cuts were oriented to the longitudinal axis of the tibia. The samples obtained were stained with hematoxilin and eosin and was assessed qualitatively the tibial metaphysis area histology of both groups.
**Results:** In the SS group an histological architecture alteration was demonstrated in the cartilage and bone trabeculae, which less trabeculae, with less length, as well as sealing trabeculae, when they were compared to the C group.




**Conclusions:** The radiographic findings of the previous study in which it was observed a decrease in the tibial cortical bone density and the alterations in the histological architecture detected in the tibial metaphysis area in this qualitative preliminary study, we would suggest that NOD with SS mice generate changes in bone tissue. It's necessary to carry out histomorphometric studies in 2D and immunostaining techniques of quality and activity of bone tissue, with the purpose of objectify the response in NOD mice with SS.
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**Disclosure of Interest:** None declared
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## AB0063 COMPLEX OF ADALIMUMAB AND TNF INDUCES A DIVERGENT PROTEOMIC PROFILE IN TNF-STIMULATED HUMAN OSTEOCLAST PRECURSORS TO THAT RESEMBLING A MONOCYTIC CELL

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**Background:** TNF has been shown to contribute to osteoclastogenesis independently and in conjunction with M-CSF or RANKL, two key cytokines involved in osteoclast (OC) development. We have previously demonstrated that TNF enhances the kinetics of RANKL-induced human osteoclastogenesis and that its effects are mitigated more effectively by the anti-TNF biologic adalimumab (ADA) as compared to etanercept (ETN).
**Objectives:** To determine the mechanism responsible for the difference in effectiveness between the two biologics, a label-free quantitative proteomics study was conducted on TNF-activated human OC upon biologic treatment using an EASY Nano LC1000/ QExactive Plus LC/MS system.
**Methods:** Human OC precursors (OCP) were exposed for 5 days to M-CSF, M-CSF+RANKL (RANKL) alone or in combination with 100 ng/mL TNF +/– 5 ug/mL ADA, ETN or human IgG1 (IGG) as a pre-formed complex. OC differentiation was confirmed by measuring tartrate-resistant acid phosphatase 5b (TRAP 5b) activity. Peptides from cell lysates were generated using modified Filter Aid Sample Preparation (FASP). Quality control sample pooling (sham) strategy was used to minimize false discovery by applying a cut off value (ratio >150% or <66.7%) based on reproducibility between sham samples. Data was analyzed with a 3 database search algorithm through Proteome Discoverer (PD) 2.0 and a 4th algorithm using MaxQuant. Protein IDs were aggregated in Scaffold software using the Local FDR data (LFDR) scoring system. Relative quantification was achieved using precursor ion area extraction function within PD and summarized as top 3 precursor ion intensity in Scaffold. Data is expressed as percentage based on ratio of ion counts of each condition to that of RANKL with differences considered significant if ≥150% only for proteins whose percentage between TNF and IGG conditions are similar.
**Results:** Ten OC-related proteins were identified (CA2, ITGAV, ITGB3, OSTF1, NFATC1, *ACP5*, *CTSK*, *MMP9*, *TCIRG1*, *ATP6V0D2*), 5 of which (underlined) were induced by TNF (≥161%), decreased by ADA (≤77%), but unaffected by ETN. Overall, TNF upregulated the levels of 110 proteins as compared to that of RANKL. A greater proportion of these proteins had levels reduced following ADA treatment as compared to ETN (69% and 20%, respectively) concordant with a greater reduction in OC maturation in the presence of ADA as to that of ETN (similar to IGG) (TRAP 5b levels of 11, 40, and 38 U/L, respectively). In addition to lowering the levels of TNF-induced proteins concordant with neutralization by adalimumab, we observed indications for OCP development toward an alternative myeloid lineage based on its ≥1.5-fold induction of 25 proteins that are typically expressed at high levels in monocytic cells (e.g., PSMB9, DPP7, IFI30 & BAG3) including 2 proteins reportedly shown to negatively regulate OC development (LGMN & ZFAND5).
**Conclusions:** Our findings demonstrate that ADA treatment, unlike exposure to ETN, dramatically reduces the TNF-induced protein levels in human OC and moreover, that the TNF:ADA complex may potentially alter their proteome to a profile resembling that of a monocytic cell through an increase in negative regulators of OC development.
**Acknowledgement:** Authors thank Drs. Jochen Salfeld, Anna Yarilina and Nathan Brown for their critical review.
**Disclosure of Interest:** B. Harvey Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., C. Hu Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., D. Wang Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Y. Tian Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Z. Kaymakcalan Shareholder of: AbbVie Inc., Employee of: AbbVie Inc.
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## AB0064 ADALIMUMAB IS MORE EFFECTIVE THAN ETANERCEPT IN REDUCING CHEMOTAXIS OF HUMAN MONOCYTES IN RESPONSE TO TNF-INDUCED CHEMOKINE SECRETION FROM HUMAN OSTEOCLAST PRECURSORS

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**Background:** Tumor necrosis factor-alpha (TNF) contributes to the pathological osteolysis observed in rheumatoid arthritis either directly by stimulating the development of osteoclasts, or indirectly through the induction of the pro-osteoclastogenic cytokine RANKL. However, the role of TNF in promoting human

osteoclast differentiation and/or recruitment of osteoclast precursors (OCP) through the secretion of chemokines in the presence of RANKL is poorly understood.
**Objectives:** To determine the impact of TNF on RANKL-induced human osteoclast development and then assess the contribution of TNF-induced chemokines to promote the chemotaxis of monocytes, potential precursors of osteolasts, to inflammatory sites, both in the absence or presence of various anti-TNF biologics.
**Methods:** Human OCP were cultured for up to 6 days with M-CSF and RANKL +/– 100 ng/mL TNF pre-treated for 30 min with increasing concentrations of hIgG, adalimumab (Ada) or etanercept (Etn). Osteoclast maturation was determined by measuring tartrate-resistant acid phosphatase (TRAP5b) activity. Collagen degradation was assessed by measuring release of plate-bound Europium-labeled collagen (Eu-col). Chemokines were identified by 9-plex MSD. Chemotaxis was assessed in 5 mm pore size plate with human monocytic THP-1 cells in upper chamber, and culture supernatant harvested on day 5 from OCP in lower chamber +/– pre-treatment for 30 min with anti-chemokine antibodies. Cell migration was detected with CellTiter Fluor.
**Results:** TNF promoted greater maturation (3-fold increased TRAP5b) and enhanced collagen degradation (3-fold increased Eu-col levels) of osteoclasts as compared to RANKL alone. Ada restored osteoclast differentiation (at a 10-fold lower concentration than Etn, 0.74 μg/mL and 20 μg/mL, respectively) as well as collagen degradation to levels comparable to RANKL alone. Chemokines including MDC, IL-8, MCP-1 and MIP-1b were detected at higher levels in TNF-exposed OCP cultures as compared to RANKL alone, with a 2-fold reduction in each only in the presence of Ada except for MDC, which was equally inhibited by both Ada and Etn. Culture supernatants from OCP treated only with combination of TNF and RANKL significantly induced chemotaxis of THP-1 ($p<0.0001$) in an MCP-1 dependent manner as demonstrated by a 3-fold reduction in presence of anti-MCP-1 neutralizing antibody. Addition of Ada, but not Etn, to TNF-exposed OCP cultures led to a significant reduction ($p<0.001$) in THP-1 chemotaxis in response to TNF-induced chemokines secreted from the OCP.
**Conclusions:** Overall, the results of our investigation demonstrate that TNF can enhance RANKL-induced osteoclast development and promote secretion of chemokines such as IL-8, MIP-1b and MCP-1. In addition, TNF stimulation of OCP led to the chemotaxis of human monocytic cells, suggesting that additional precursors, such as monocytes, may be recruited to the erosion site through the increased chemokine expression. Interestingly, Ada was more effective than Etn to inhibit all three TNF-mediated events, suggesting that Ada may be more effective in preventing TNF-induced OCP population development and expansion in areas of osteolysis.
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**Disclosure of Interest:** B. Harvey Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Z. Kaymakcalan Shareholder of: AbbVie Inc., Employee of: AbbVie Inc.
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## AB0065 GALECTIN-3 IS A MAJOR DETERMINANT OF FEMORAL NECK BONE MINERAL DENSITY IN A PARTIAL REGRESSION MODEL: A PRELIMINARY STUDY

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**Background:** Low bone mass is an essential extra-articular feature of rheumatoid arthritis (RA). Patients with RA might present an increased risk of low bone mass as a result of systemic inflammation by alteration of the RANK/RANKL/osteoprotegerin and Wnt/ catenin pathways. In RA, serum galectin-3 correlated with C-reactive protein levels and was considered as biomarker of inflammation. However, recent studies showed abundant galectin-3 observed in the area of severe bone destruction may act as a negative regulator for the upregulated osteoclastogenesis. The role of Galectin-3 is unclear in the regulation of bone resorption in RA.
**Objectives:** The objectives of our study were to evaluate bone mineral density (BMD) and the levels of Galactin-3 and Dkk-1 in RA patients and to study the relation between these parameters.
**Methods:** Patients with active RA were checked with galactin-3, Dkk-1 and followed up with BMD assessment and inflammatory evaluation by ultrasonography (US). Serum galectin-3, Dkk-1 concentrations were assayed with ELISA assay. BMD was measured at hip neck by a Dual-energy X-ray absorptiometry (DXA) (Explorer; Hologic Inc., USA). Grey scale and Power doppler US were graded using a 4-grade semiquantitative scoring system, on a scale of 0–3 at wrist. Each wrist was scanned from lateral to medial aspects in longitudinal planes Radius-Lunate-capitate (volar and dorsal), dorsal Radius-scaphoid-trapezoid, and dorsal Ulna-triquetral. Demographic and clinical data, DAS-28, and erythrocyte sedimentation rate (ESR) were recorded for each patient. Correlations between variables and multilinear regression analysis were performed to check serum galectin-3 expression levels and BMD parameters.
**Results:** (1) Six RA patients 50% were female, age was 57.3±4.4 years, disease duration was 6.9±3.8 years and disease activity DAS 28 was 6.33±0.31. (2) The galectin-3, Sonography inflammatory score and serum iPTH levels showed a significant negative association with BMD at the hip.(Table.1) (3) The multilinear regression analysis showed iPTH, Galactin3 and US score were found to explain 99% of the variance in BMD in hip neck.(4) However, the galectin-3 in multilinear regression analysis showed a positive association with BMD at the hip. (correlation coefficient=0.126, *p* value=0.014) (Table.2)

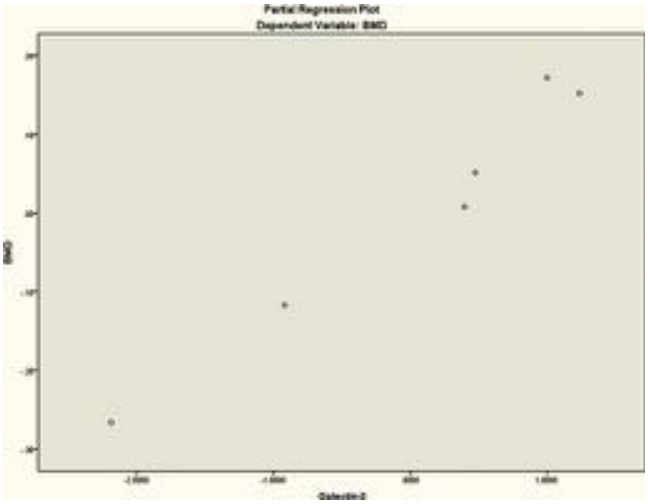
Table 1. Characteristics of patient and Variables that correlated with hip neck bone mineral density (BMD)

| | Mean ± standard deviation (N=6) | Correlation (BMD) |
|---|---|---|
| Age | 57.3±4.4 | –0.164 |
| Rheumatoid factor | 282±178.1 | –0.337 |
| Erythrocyte sediment rate (1hour) | 24.3±10.2 | –0.317 |
| Sonography inflammatory score | 12±5.4 | –0.865* |
| Dkk-1 | 2450.4±712.7 | –0.657 |
| Galactin-3 | 6.02±3.18 | –0.828* |
| iPTH | 40.1±12.5 | –0.921** |
| Alkyine phosphatase | 87.8±18.3 | –0.460 |

*Correlation is significant at the 0.05 level. **Correlation is significant at the 0.01 level.

Table 2. Final step in multilinear regression analysis with backward elimination

| | Unstandardised coefficients | | 95% CI for B | |
|---|---|---|---|---|
| (Constant) | B | P Value | Lower bound | Upper bound |
| Galactin3 | 0.126 | 0.014 | 0.060 | 0.192 |
| iPTH | –0.116 | 0.002 | –0.139 | –0.093 |
| Sonography | –0.081 | 0.002 | –0.096 | –0.065 |




**Conclusions:** Galectin-3 is a major determinant of femoral neck BMD in this partial regression model, after controlling iPTH and sonography inflammatory score, in our preliminary study.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2627

## AB0066 MRI-DETECTED OSTEITIS IS NOT ASSOCIATED WITH THE PRESENCE OR LEVEL OF ACPA ALONE, BUT WITH THE COMBINED PRESENCE OF ACPA AND RF

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**Background:** In patients with rheumatoid arthritis (RA) bone marrow edema (BME) as observed by magnetic resonance imaging (MRI) represents osteitis with infiltration of leucocytes and an increased number of osteoclasts. Both BME and anti-citrullinated protein antibodies (ACPAs) are predictors of radiographic progression in RA and recent data indicate that ACPA can directly activate osteoclasts. These findings together lead to the hypothesis that ACPA is associated with BME; indeed, two small studies observed an association between BME and ACPA. Thus far the association of ACPA with other forms of MRI-detected inflammation (synovitis and tenosynovitis) has not been thoroughly explored. Furthermore, it is unknown if the association with MRI-detected inflammation is only present for ACPA or also for other RA-related auto-antibodies.
**Objectives:** This study aimed to investigate the associations of ACPA, RF and antiCarP with BME, synovitis and tenosynovitis.
**Methods:** A total of 589 early arthritis patients, included in the Leiden Early Arthritis Clinic cohort, underwent contrast-enhanced 1.5T MRI of the unilateral wrist, metacarpophalangeal and metatarsophalangeal joints at baseline. BME, synovitis and tenosynovitis were scored according to the RAMRIS-method. ACPA, rheumatoid factor (RF) and anti-carbamylated protein (antiCarP) antibodies were determined at baseline.

**Results:** BME, synovitis and tenosynovitis were concomitantly present on MRI. In univariable analyses, ACPA-positive patients had higher BME-scores than ACPA-negative patients (median scores 4.5 vs. 2.0, $p<0.001$), but not more synovitis and tenosynovitis. Besides ACPA, also RF (median scores 3.75 vs 2.0, $p<0.001$) and antiCarP antibodies (median scores 3.5 vs 2.5, $p=0.012$) were associated with higher BME-scores in univariable analyses. To explore the association of the different antibodies with BME the BME-scores of patients with different auto-antibody combinations were compared. ACPA+RF-antiCarP- patients did not have higher BME-scores than ACPA-RF-antiCarP- patients, however ACPA+RF+antiCarP- and ACPA+RF+antiCarP+ patients had higher BME-scores (median 5.0 and 4.5 versus 2.0 respectively, $p<0.001$ and $p<0.001$). ACPA and RF levels were not associated with BME-scores.
**Conclusions:** The presence and the level of ACPA alone were not associated with BME-scores. However, the combined presence of ACPA and RF did associate with more BME. This suggests an additive role of RF to ACPA in mediating osteitis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2628

## AB0067 AUTOTAXIN INVOLVEMENT IN OSTEOCLAST DIFFERENTIATION AND FUNCTION

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**Background:** Autotaxin (ATX) is a secreted protein produced by various tissues in the body including the liver, adipose tissue and bone. Autotaxin (ATX) is an enzyme with a phospholipase D activity responsible for cleavage of lysophosphatidylcholine (LPC) in lysophosphatidic acid (LPA). LPA is a bio phospholipid, which acts as a growth factor, affecting proliferation, differentiation, and migration. It has been shown that the biological effect of LPA could be the direct consequence of local production of Autotaxin (ATX) in a given tissue or cell type (1). Recently, we have shown that LPA controls two steps of osteoclastogenesis: the fusion and bone resorption capacity of osteoclasts (2).
**Objectives:** The aim of this study is to test if ATX produced by osteoclasts could play a direct role in osteoclastogenesis and in bone mass control.
**Results:** First we observed that Enpp2 (ATX gene) was a target gene of RANK-L and as a consequence was up regulated during the course of osteoclastogenesis from bone marrow (BM) wild type (WT) cells. Next we generated Ctsk-Cre+;ATXfl/fl mice and use of these animals as a source of osteoclasts-ATX deficient progenitors. In vitro experiments showed a major impact of ATX on osteoclastogenesis and osteoclast mediated bone resorption. Because LPA is massively present in sera, to explore either LPA or ATX putative effect in culture, the use of delipidated serum was mandatory. Using such conditions, we observed a drastic reduction in the number of mature osteoclasts after 5 days of differentiation from BM-WT progenitors, but osteoclasts number were restored by the use of LPA, recombinant ATX plus LPC, or LPC. These results were confirmed by the use of LPA and ATX specific inhibitors (KI16425 and PF8380). Osteocorning bone resorption assays showed that ATX is required for osteoclasts activity, that decreased of 50% when delipidated sera is used in the assays and that was fully restored by the addition of either LPC or recombinant ATX plus LPC.
**Conclusions:** All together, and more specifically the results obtained in presence of LPC alone suggest that (i) ATX is secreted by osteoclasts and (ii) is functionally involved in osteoclast differentiation and function in vitro. Current studies are conducted on Ctsk-Cre+;ATXfl/fl mice to fully characterize the role of ATX in the bone mass control in physiological and pathological conditions due to ageing (osteoporosis) and inflammation (rheumatoid arthritis).
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## AB0068 STRUCTURAL CHARACTERISTICS OF POLYSACCHARIDES INFLUENCE VISCOSUPPLEMENTATION EFFICACY IN OSTEOARTHRITIS

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**Background:** Intra-articular (i.a) injection of a purified Guar gum (GG) solution or hydrogel provided analgesia similar to that of Hylan G-F20 in experimental osteoarthritis (eOA) suggesting that rheology is not crucial to viscosupplements.
**Objectives:** Evaluate the effect of purified GG (DGG), sulfated (DGGSU) of oxidized (DGGOX) GG on pain and cartilage damage in eOA
**Methods:** GG was oxidated with a n-oxil-2, 2, 6, 6-tetra metilpiperidina (TEMPO) reagent or subjected to sulfation to produce carboxylated and sulphate groups. Rats subjected to anterior cruciate ligament transection (ACLT) of the knee received 100 μg GG, sulfated or oxidized GG or vehicle (NT) i.a. at day 4 to 7 after ACLT. Joint pain was recorded using the articular incapacitation test. A group received GG weekly or vehicle from day 7 to 70 and joint damage assessed by histology and biochemically, measuring hondroitin-sulfate (CS) cartilage content (μg/mg) and Mw of CS through PAGE.
**Results:** FT-InfraRed spectra of DDGSU and DDGOX were different from protein free DGG. DGGSU has a new intense band at 1262 $cm^{-1}$, due to S=O. Spectral difference occurs in DGGOX but not DGG and a C=O stretching is present in DGGOX spectrum (COOH group). $^{13}C$ NMR spectrum of DGGOX and DGG revealed absence of the signal at 63.7 ppm present in DGG and two new signals at 177.5 and 177.8 ppm. Absence of the signal from C-6 of free mannose indicates it was substituted in the oxidation. The new signals are from C=O group from COOH. $^{1}H$-$^{13}C$ HSQC spectra exhibited a shift to a lower d value of the proton H-1 from mannose residue in DGGOX, indicating substitution at C-6 from mannose. New signals at 70.3, 75.6, and 100.5 ppm were observed in $^{13}C$ NMR spectrum of sulfated gum due to the insertion of sulfate group in the primary carbon (C-6). All derivatives show lower molar mass than the original guar gum. DGG $M_w$ =3.9 x $10^6$ g/mol, DGGOX and DGGSU, 2.6 x $10^6$ and 2.8 x $10^6$ g/mol, respectively. DGGOX has the lowest intrinsic (2.2 dL/g) and apparent viscosity (9.0 mPa s).DGG exhibits the highest values ([h] =6.2 dL/g and $h_{app}$ =58 mPa s). Intermediate values are obtained for DGGSU ([h] =4.9 dL/g and $h_{app}$ =39 mPa s). GG significantly reduced joint pain, as compared to vehicle whereas oxidat ion or sulfation of GG abrogated GG analgesia. GG also prevented the increase in both CS content (43.8±4.7 μg/mg) and Mw (mobility: 1.18 ±0.03), as compared to NT ($p<0.001$). GG also significantly prevented joint damage at histopathology (median =7; range 2.5 - 18), as compared to NT ($p<0.05$).
**Conclusions:** The structural integrity of GG is crucial to its analgesia. Intra-articular polysaccharides can be analgesic and chondroprotective regardless of being water-soluble.
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## AB0069 FOLLISTATIN-LIKE 1 PROMOTES OSTEOCLAST DIFFERENTIATION VIA RANKL-MEDIATED ACTIVATION OF NF-κB AND MAPK SIGNALING PATHWAYS

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**Background:** Follistatin-like 1 (FSTL1) functions as a pivotal modulator of inflammation and is implicated in many inflammatory diseases such as rheumatoid arthritis, yet its role in osteoclast development is currently unknown.
**Objectives:** The aim of this study was to investigate the role of FSTL1 in osteoclast development mediated by M-CSF and RANKL.
**Methods:** Osteoclastogenesis was assessed using mouse primary bone marrow-derived macrophages. The mRNA expression was analyzed by real-time or RT-PCR. RANKL or M-CSF signaling was assessed by immunoblotting and NF-κB transcriptional activity by luciferase reporter assay. Apoptosis assay was performed by cell death ELISA and cell proliferation using BrdU ELISA system.
**Results:** We show that FSTL1 expression is strongly upregulated during osteoclast differentiation of bone marrow-derived macrophages (BMMs) and FSTL1 positively regulates receptor activator of NF-κB ligand (RANKL)-induced osteoclastogenesis. The overexpression of FSTL1 or the treatment of recombinant FSTL1 (rFSTL1) in BMMs enhances the formation of multinuclear osteoclasts and the induction of c-Fos and nuclear factor of activated T cells c1 (NFATc1), transcription factors important for osteoclastogenesis. Conversely, knockdown of FSTL1 using a small hairpin RNA suppresses RANKL-mediated osteoclast formation and the expression of these transcription factors. While FSTL1 does not affect the RANKL-stimulated activation of p38 MAPK, the phosphorylation of IκBa, JNK, and ERK was increased by overexpression or addition of rFSTL1. Furthermore, rFSTL1 accelerated RANKL-induced NF-κB transcriptional activity in a dose-dependent manner.
**Conclusions:** Our study demonstrates that FSTL1 promotes osteoclast differentiation by stimulating NF-κB and MAPK activation in response to RANKL. Thus, we identify FSTL1 as a pro-osteoclastogenic factor that plays an important role in RANKL-induced osteoclast differentiation.
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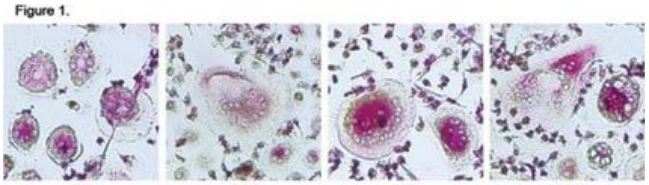
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## AB0070 A ROLE OF SYNOVIAL EXOSOMES IN OSTEOCLAST DIFFERENTIATION OF INFLAMMATORY ARTHRITIS

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**Background:** Exosomes are small membrane vesicles (40–150 nm) of endocytic origin secreted by many types of cells and engage in cell-to-cell communication by transferring proteins, microRNAs, mRNA, and lipid to recipient cells. Exosomes are also identified in various biological fluids including blood, urine, amniotic fluid, saliva, malignant ascites, and synovial fluid. Until now, the role of exosomes from synovial fluid (SF) on human osteoclastogenesis is unknown.
**Objectives:** We aimed to identify the characteristics of synovial exosomes and evaluate the effects on human osteoclastogenesis.
**Methods:** Synovial exosomes were isolated from SF of rheumatoid arthritis (RA), osteoarthritis (OA), ankylosing spondylitis (AS), and gout patients using ExoQuick (System Biosciences, USA). Monocytes were isolated from human peripheral blood mononuclear cell and were differentiated into macrophages by treatment of 20 ng/ml recombinant human macrophage colony-stimulating factor (M-CSF) for 3–4 days. Then, macrophages were incubated with synovial exosomes in alpha-MEM supplemented with 10% FBS and 1% penicillin/streptomycin for 9–10 days. Osteoclast differentiation was evaluated by tartrate resistant acid phosphatase stain. Exosomes from RA (n=11), OA (n=5), AS (n=6), and gout (n=6) patients were quantified by measuring acetylcholinesterase activity in colorimetric assay.
**Results:** The number of synovial exosomes isolated from same volume of SF from RA, OA, AS, and gout patients was assessed. We found that exosomes are abundant in SF of RA, AS, and gout patients compared to OA patients. (mean ± SEM $7.36\times10^7\pm1.35\times10^7$, $9.91\times10^7\pm2.50\times10^7$, $7.50\times10^7\pm2.17\times10^7$ vs. $2.66\times10^7\pm0.42\times10^7$). Interestingly, the number of exosomes from AS SF was significantly higher (by 3.72 fold, p=0.0476) than exosomes from OA SF. Exosomes from RA, OA, AS, and gout patients induced proliferation and osteoclast formation without M-CSF and receptor activator of nuclear factor kappa-B ligand (RANKL) (Figure 1), which is essential to proliferation and differentiation of osteoclast. Noticeably, exosomes from RA SF had higher potential on osteoclast differentiation than other three diseases. (20.28±14.28 fold vs. 2.38±0.42 fold).

Figure 1.




**Conclusions:** Our results suggest that exosomes from SF of various inflammatory diseases might have differential functional roles in osteoclast differentiation and the number of exosomes may be associated with inflammatory conditions.
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## AB0071 ALPHA-ENOLASE EXPRESSION ON THE CELL SURFACE OF OSTEOCLAST PRECURSORS PLAYS A POSITIVE ROLE IN OSTEOCLASTOGENESIS OF MONOCYTE/MACROPHAGE IN RHEUMATOID ARTHRITIS

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**Background:** The local bone loss around the inflamed joints is found from the early stage of rheumatoid arthritis. We previously reported that cell-surface expression of alpha-enolase (ENO1), multifunctional glycolytic protein, is increased in monocytes and macrophages isolated from RA patients and related to production of proinflammatory cytokines (1).
**Objectives:** This study was performed to examine the role of surface ENO1 on osteoclastogenesis in rheumatoid arthritis.
**Methods:** Monocytes isolated from RA patients and healthy control were used to examine the surface level of ENO1 by flow cytometry and confocal microscopy. U937, human monocytic cell line, was treated with ENO1-targeting siRNA (siENO1) to down-regulate ENO1 expression, then osteoclast differentiation were induced by RANKL and the level of ENO1 and NFATc1 was measured. Also, monocytes from RA patients were differentiated into macrophages and transfected with siENO1 to assess the effect on osteoclast differentiation.
**Results:** We found the surface expression level of ENO1 was higher in monocytes isolated from RA patients than healthy control and gradually decreased during osteoclastogenesis in both cells, while the total level of ENO1 remained unchanged. ENO1-specific siRNA significantly decreased the surface ENO1 level in U937, but did not affect the viability and proliferation of the cells. When osteoclast formation was induced by RANKL, osteoclast-specific transcription factor, nuclear factor of activated T-cells, cytoplasmic 1 (NFATc1) expression was markedly inhibited in ENO1 down-regulated cells compared to control cells. We also examined the effect of down regulation of ENO1 in osteoclast precursor cells isolated from RA patients (N=10). The surface ENO1 level was significantly decreased and RANKL-induced osteoclast differentiation was markedly inhibited in ENO1 down-regulated cells compared to control cells.
**Conclusions:** These results suggest that increased expression level of ENO1 on the surface of monocytes/macrophages have positive effect on osteoclast formation in RA.
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## AB0072 RECRUITMENT OF RNA TARGETS BY CONNEXIN 43 RNA-BINDING MOTIFS: NOVEL MECHANISMS OF CELLULAR COMMUNICATION

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**Background:** Connexins (Cxs) are integral membrane proteins that form plasma membrane channels, allowing cell-matrix and cell to cell communication. Initially described in joining excitable cells (nerve and muscle), gap junctions (GJs) are found joining virtually all cells in solid tissues and are essential for the functional co-ordination of organs by enabling direct transfer of small signalling molecules, metabolites, ions, and electrical signals. Several studies have revealed diverse channel-independent functions of Cxs, including control of cell growth and tumorigenicity. Chondrocytes from osteoarthritic cartilage have increased expression of connexin 43 (Cx43). The myriad roles of Cx43 and its implication in the development of diseases such as cancer, osteoarthritis or alzheimer have rise to many novel questions.
**Objectives:** The aim of this study was to investigate possible RNA binding domains in the Cx43 and Cx26 sequences in order to study if cells are able to exchange molecules of RNA anchored to Cx43/Cx26 sequences present in exosomes or vesicles.
**Methods:** Amino acids sequences from Cx43 and Connexin 26 (Cx26) were obtained from the Protein Database (NCBI) and the Cx26 structure from the Protein Data Bank (RCSB) [1]. Protein sequences from both Cxs were aligned and compared with Protein Blast and Lalign servers. Analysis of RNA-binding propensity of Cx43 and Cx26 sequences was evaluated with three computational methods with the high predicting accuracy [2] aaRNA, Bind+ and Pprint.
**Results:** Protein sequences were highly conserved between Cx43 and Cx26 with the exception of the the C-terminal end (CTD). The combination of the scores obtained from the three predictors showed four domains that potentially interact with RNA sequences. Two of these domains include the intracellular loop (ICL) and the CTD.
**Conclusions:** Our results suggest that Cx43 and Cx26 are able to interact with RNA targets including siRNA and mRNA. These interactions would have a range of potential implications for cellular communication and control of signalling pathways.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1665

## AB0073 A VALUE OF PULSE THERAPY IN THE TREATMENT OF RELAPSING POLYCHONDRITIS

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**Background:** Relapsing polychondritis (RP) - is a rare systemic disease with undulating course, presumably autoimmune origin characterized by recurring exacerbations of inflammation in the cartilage tissue, leading to their destruction. Clinical manifestations of RP are divided according to location, severity and duration. In the pathological process may involve all types of cartilage and other

structures, rich proteoglycans: eyes, internal ear and vessels. So far, a unified approach to the treatment of RP in terms of evidence-based medicine does not exist. Due to the rarity of the disease clinical studies for comparative evaluation of different drugs have been conducted. For relief of attacks polychondritis most commonly used nonsteroidal antiinflammatory drugs (NSAIDs) and glucocorticoid therapy (corticosteroids), but there is no evidence of their impact on the progression of the process and to prevent relapse.
**Objectives:** to study the efficiency of pulse therapy in patients with RP.
**Methods:** 4 patients with RP were hospitalized in the clinic of I cardiorheumatological department of Tashkent Medical Academy (TMA). The diagnosis was made on the basis of diagnostic criteria developed by Macadam. All patients underwent clinical, immunological, biochemical studies, chest X-ray, ECG.
**Results:** Patients were performed following treatment, Prednisolone 30 mg/day per os, NSAIDs and combination pulse therapy course (1st and 3rd - days solumedrol 1.0 g intravenously, the second day solumedrol 1.0 g in combination with cyclophosphamide 800 mg). The therapy was showed improvement of general condition of patients, decreased pain in the cartilage of nose and swelling of ears, back pain, general weakness. Patients were discharged under the supervision of district therapeutist and rheumatologist with recommendations to continue receiving NSAIDs, corticosteroids and program of the pulse therapy for 6 months.
**Conclusions:** Thus, the use in the treatment of RP pulse therapy had a positive effect on the clinical condition of patients and prevent progression of disease.
**Disclosure of Interest:** None declared
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## AB0074 THE EFFECT OF EXTRACELLULAR VESICLES ON HUMAN IN VITRO OSTEOCLASTOGENESIS IN HEALTH AND IN ARTHRITIS

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**Background:** Extracellular vesicles (EVs) like microvesicles (MVs) and exosomes (EXOs) are released in an evolutionary conserved manner by cells. EVs mediate intercellular communication with the transmission of molecules from their parent cell to their targets.
**Objectives:** Our objective was to investigate the effect of EVs on human *in vitro* osteoclastogenesis in healthy donors, rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients.
**Methods:** Blood samples of healthy volunteers, RA patients and PsA patients with peripheral arthritis were collected. EVs were isolated by filtration and differential centrifugation. CD14+ cells were isolated from PBMCs by using positive selection, and the cells were stimulated with 50 ng/ml recombinant human M-CSF for 24 hrs. Then the samples were treated with 50 ng/ml recombinant human RANKL and blood-derived microvesicles or exosomes. After 7 days, the cells were fixed and stained for tartarate resistant acid phosphatase (TRAP). TRAP-positive cells with at least 3 nuclei were considered as osteoclasts and counted by using the ImageJ software.
**Results:** Healthy and RA-derived exosomes significantly ($p<0.01$) inhibited osteoclast differentiation of the CD14+ cells from the same donors, while PsA-derived exosomes had a stimulatory effect ($p<0.05$) on osteoclastogenesis. In cross-induction experiments where EXOs and cells were interchanged between the 3 groups healthy (n=5) and RA (n=5) derived EXOs inhibited ($p<0.01$) the generation of osteoclasts in both groups but PsA (n=7) derived EXOs did not have an inhibitory effect. Microvesicles did not alter the number of mature osteoclasts in any groups.
**Conclusions:** Our data suggest that EXOs profoundly regulate human osteoclastogenesis. PsA-derived EXOs stimulate, while healthy and RA-derived EXOs inhibit the osteoclast differentiation.
**Disclosure of Interest:** None declared
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## AB0075 AICAR INDUCED MITOCHONDRIAL APOPTOSIS AND INHIBITED CELL PROLIFERATION AND MMP-3/RANKL SECRETION VIA ENHANCEMENT OF MITOCHONDRIAL BIOGENESIS IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIAL CELLS

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**Background:** Joint destruction in rheumatoid arthritis (RA) progresses via the hyperproliferation of the synovium and secretion of MMP-3/RANKL from fibroblast-like synoviocytes (FLS). [1] In tumors, we previously reported that the expression of mitochondrial biogenesis-related genes is low and increased numbers of mitochondria enhance cell apoptosis. [2] However, the relationship between mitochondrial biogenesis and cell apoptosis in RA-FLS remains unclear.
**Objectives:** This research was investigated the relationship between mitochondrial biogenesis and cell apoptosis in RA-FLS.
**Methods:** RA and Osteoarthritis (OA)-FLS were obtained during total knee replacement surgery from patients with RA. All experiments were conducted using cells from passages 3–7. Quantitative PCR was used to assess the expression of mitochondria-related mRNA (PGC-1α, NRF-1, and TFAM) and number of mitochondrial DNA (mtDNA) in RA- and OA-FLS with/without 5-aminoimidazole-4-carboxamide riboside (AICAR) (2 mM). Apoptosis was evaluated immunoblot analysis for cleaved caspase-3, -8, -9, and PARP 48 hours after an AICAR treatment in RA-FLS. Cell viability was assessed using WST-8 assay, and MMP-3/RANKL secretion was measured using an immunoassay (immunoblot and ELISA) with/without IL-1β or TNFα stimulation in RA-FLS. Inhibitory experiments were used AMPK inhibitor (20 μM Compound C) and mitochondrial biogenesis-inhibitor (10 μM TFAM-siRNA) by Lipofectamine® RNAiMAX Reagent in RA-FLS.
**Results:** The expression of NRF-1 and TFAM and the levels of mtDNA were lower in RA-FLS than in OA-FLS. In RA-FLS, the levels of mtDNA and mRNA expression of mitochondria-related genes were enhanced by AICAR. Additionally, AICAR enhanced mitochondrial apoptosis (Increased the protein of cleaved caspase-3, -9, and PARP), and Treatment with an AMPK inhibitor (compound C) and a mitochondrial biogenesis- inhibitor (TFAM-siRNA) suppressed the inhibitory effect of AICAR on apoptosis. Moreover, AICAR inhibited cell viability and IL-1β- or TNFα-induced MMP-3/RANKL secretion in inflammation-induced RA-FLS.
**Conclusions:** Mitochondrial biogenesis in RA-FLS was down-regulation. Enhancement of mitochondrial biogenesis resulted in the suppression of disease activities of RA, such as increasing mitochondrial apoptosis and reducing RA-FLS viability and secretion of MMP-3/RANKL from RA-FLS. A novel therapeutic approach by changing mitochondrial biogenesis is proposed.
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## AB0076 ANALYSIS FOR THE GENE EXPRESSION PROFILES IN RHEUMATOID SYNOVIAL FIBROBLASTS REGULATED BY LIGHT

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**Background:** Rheumatoid Arthritis (RA) is an autoimmune disease characterized by over-proliferation of synovial tissues and subsequent joint destruction [1]. Lymphotoxin-like, exhibits inducible expression, and competes with herpes simplex virus glycoprotein D for herpes virus entry mediator, a receptor expressed on T lymphocytes (LIGHT) is a member of tumor necrosis factor (TNF) receptor superfamily and is expressed on antigen-presenting cells through the activation of T cells. LIGHT modulates T-cell activation and promotes inflammation through the activation of nuclear factor (NF)κB by binding to its specific receptors herpes virus entry mediator (HVEM) and lymphotoxin (LT)-βR [2]. Furthermore, decoy receptor 3 (DcR3) competitively binds soluble LIGHT and inhibits LIGHT signaling via HVEM [3,4]. Studies have suggested that LIGHT is overexpressed in RA fibroblast-like synoviocytes (RA-FLS) and production of TNFα is induced by stimulation with LIGHT, and that LIGHT may be related to autoimmune diseases such as inflammatory bowel disease or multiple sclerosis [5].
**Objectives:** In this study, we investigated the genes regulated by LIGHT in RA-FLS by comprehensive genetic analysis using microarrays to elucidate the involvement of LIGHT in RA pathogenesis.
**Methods:** *Microarray assay.* Four individual lines of primary cultured RA-FLS were incubated with either 1.0 μg/ml recombinant human LIGHT protein or phosphate buffered saline (PBS) diluted with serum-free Opti-MEM medium as non-stimulated control for 12 hours at 37℃ with 5% CO2. Gene expression was detected using cDNA microarray assay (Human Genome U133 Plus 2.0, GeneChip® 3' Expression Array, Affymetrix), and the gene expression profiles of LIGHT-stimulated cells and controls were compared.
*Real-time polymerase chain reaction (real-time PCR).* The four most highly up- and down-regulated genes were discovered by comprehensive genetic analysis using the microarray. The relative mRNA expression levels of those genes were compared using TaqMan® real-time PCR on a StepOne™ real-time PCR system.
**Results:** *Microarray assay.* The microarray analysis revealed that 1042 genes were up-regulated and 801 genes were down-regulated more than twofold by stimulation with LIGHT in RA-FLS.
*Expression of LIGHT-related genes in RA-FLS.* The real-time PCR analysis

confirmed that mRNA expression of the top-four genes up-regulated and those down-regulated was actually regulated by LIGHT.
**Conclusions:** To our knowledge, this is the first report on the expression profiles of genes regulated by LIGHT in RA-FLS, which suggested the involvement of LIGHT-HVEM/DcR3 signaling in the pathogenesis of RA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2241

## AB0077 TARGETING SYNOVIAL FIBROBLASTS WITH MELANOCORTIN DRUGS

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**Background:** The adrenocorticotropin hormone (ACTH) is a melanocortin (MC) peptide approved for the treatment of inflammatory conditions including gout and rheumatoid arthritis (RA) but undesired effects associated with continued elevated glucocorticoid production limit its clinical use[1]. Research in the last few years has focused on new strategies to develop melanocortin drugs without those side effects. The anti-inflammatory and protective effects of melanocortins on immune and joint cells - such as chondrocytes and osteoclasts – are well characterized. However melanocortin role and therapeutic potential on synovial fibroblasts (SF) are unknown. SF are key effector cells in RA, involved in leukocyte recruitment, cartilage destruction and RA progression and hence proposed as therapeutic targets for RA.
**Objectives:** To characterize expression and function of the MC system in SF and explore its potential therapeutic application in synovial inflammation.
**Methods:** Expression of the MC system in SF from RA patients was studied by PCR (receptors expression $MC_1$-$MC_5$) and ELISA (endogenous peptides $\alpha$-,$\gamma$-MSH and ACTH). MC-induced signalling was assessed by measuring cAMP production, $Ca^{2+}$ flux and ERK1/2 phosphorylation. Cytokine release was measured in supernatants by ELISA. The MC compounds studied include $\alpha$-MSH (endogenous peptide, non-selective), DTrp (synthetic peptide, non-selective) and BMS-470539 (synthetic small molecule, $MC_1$ selective).
**Results:** SF expressed the receptors $MC_{1,3,4,5}$ and produced endogenous ACTH. MC targeting in these cells did not induce $G\alpha_s$ mediated cAMP production – of interest, as cAMP is the canonical MC pathway- but evoked increases in intracellular $Ca^{2+}$ and ERK1/2 phosphorylation suggesting a cell-specific differential signalling, not previously observed in other cell type. The consequences and molecular mechanism of this unusual signalling bias are not known. Treatment of SF with these drugs reduced cytokine release (IL-6, CXCL-5, CCL-2) as well as cell proliferation. Interestingly, the BMS-470539 compound induced cell senescence associated with $p16^{INK4a}$ expression, measured by SA-$\beta$-galactosidase staining and immunofluorescence. This effect was only observed with BMS-470539 – and not by the peptide agonists – suggesting a prominent role of $MC_1$ in MC-induced senescence in SF. On-going studies include the characterization of the BMS-470539-induced senescence associated secretory phenotype.
**Conclusions:** We show herein that the MC system is functional in SF from RA patients and may be targeted pharmacologically for innovative anti-inflammatory approaches. SF are aberrantly activated in the inflamed synovium and MC treatment can reduce activation state (reduced cytokines) and proliferation. Detailed analyses of senescence-associated secretory phenotype induced by the BMS-470539 drug will help to understand the benefits of this approach on SF-associated synovial inflammation.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3231

## AB0078 ROLE OF IL-8 AND ITS RECEPTOR IN ANTI-CITRULLINATED PROTEIN ANTIBODY MEDIATED OSTEOCLASTOGENESIS IN RA

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**Background:** Circulating levels of IL-8 is related to the bone loss associated with breast cancer metastasis. Recently, we have shown that anti-citrullinated protein antibodies (ACPA) can induce osteoclastogenesis.
**Objectives:** We aimed to investigate the role of IL-8 and its receptors in mediating osteoclastogenesis in presence or absence of ACPAs
**Methods:** IL-8 levels was measured by ELISA in serum of risk RA patients and synovial fluid samples of RA patients. CD14 positive monocytes were used to generate osteoclasts with M-CSF and RANKL. Inhibition of IL-8 and its receptor were tested with IL-8 neutralizing antibody or small molecule CXCR1/2 anta-agonist (Reparixin and SCH-527123) on osteoclasts (OC) in the presence or absence of ACPA. The number of the OC's were counted in light microscope after TRAP staining. Cell counting kit 8 (CCK8) assay was performed to detect cytotoxicity. CXCR1 and CXCR2 expression was analyzed using flow cytometry and immunohistochemistry during different days of osteoclasts maturation.
**Results:** Increased IL-8 levels were observed in the serum of ACPA positive at risk RA healthy individuals and in synovial fluid of established ACPA positive RA patients. Exogenous IL-8 dose dependently increased OC numbers in presence of RANKL. IL-8 neutralizing antibody inhibited the OC numbers even in the presence of ACPA. Reparixin and SCH-527123 significantly inhibited RANKL mediated osteoclastogenesis at 100 $\mu$M concentration. No cytotoxicity of the drugs were detected with CCK8 assay. Immunohistochemistry staining confirmed the CXCR1/2 expression on OC precursors. We found high expression of IL-8 using immunohistochemistry on the inflammed RA synovium.We observed CXCR1 and CXCR2 expression with flow cytometry in the OC precursors at day 0 and in presence of RANKL the expression was completely lost at day 1 and it reappeared at day 4.
**Conclusions:** Our data provides insights in to the importance of IL-8 autocrine loop in RANKL and ACPA mediated OC development. IL-8 receptor blockade might be a novel way of targeting bone loss in RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5380

# Rheumatoid arthritis - etiology, pathogenesis and animal models

## AB0079 DEMONSTRATION OF PARVOVIRUS B19 INFECTION IN RHEUMATOID ARTHRITIS

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**Background:** The exact cause of the rheumatoid arthritis (RA) is not known. Parvovirus B19 (B19) is one of the most perspective candidates in capacity of etiological agent of RA. Evidence implicating B19 in RA causation is conflicting, but several reports have clearly confirmed its role in the pathogenesis of RA.
**Objectives:** In this study we detect the presence of B19 infection markers and the spectra of synovial and supporting tissue damage in RA patients.
**Methods:** 52 RA patients and 25 age and gender matched healthy individuals were enrolled in this study and peripheral blood samples collected. RecomLine test was used to detect of B19-specific antibodies, nPCR – to detect virus-specific sequences and proliferation test – to detect PBMC response to B19 antigens. Patients' synovial, cartilaginous and osseous samples from 7 RA patients were obtained and conventionally processed for histopathology. B19 capsid proteins VP1/VP2 expression was assessed by immunohistochemistry.
**Results:** The markers of active B19 infection were found in 26.9% (14/52) RA patients in comparison with 8.0% (2/25) control group's individuals. Anti-B19 IgG class antibodies were detected in 76% of healthy persons and in 92.3% of RA patients. In control subjects the antibodies to no more than four B19 antigens were found. 38.5% (20/52) RA patients had also antibodies to B19 non-structural protein NS1 (p=0.001 in comparison with control group's individuals). The presence of viral genomic sequence in DNA from cell-free blood plasma was detected in 25% (13/52) of RA patients and 4% (1/25) of healthy individuals. On the 3rd day of cultivation in the presence of B19 antigens PBMC proliferation was observed in 48.0% (25/52) of RA patients and only in 8.0% (2/25) of healthy persons (p=0.00068). On the 6th day of cultivation PBMC of 63.5% (33/52) of RA patients and 32.0% (8/25) of control individuals responded to B19 antigens (p=0.01436). The PBMC of both control group persons with active B19 infection and 74.1% (10/14) of RA patients with the active virus infection had reacted to B19 antigens by proliferation on the 3rd day. Proliferative response to B19 antigens on the 3rd day was detected also in 44.8% (13/29) remotely infected RA patients while in control group no response was found in remotely infected persons (p=0.00071), but on the 6th day PBMC proliferative response to B19 antigens among remotely infected persons was detected in 68.9% (20/29) RA patients and 41.1% (6/17) control group's patients, respectively (p=0.0347). B19 capsid proteins' VP1/VP2 expression was confirmed as nuclear staining demonstrated in the sublining infiltrating cells and fibroblast-like synoviocytes in the intimal lining.
**Conclusions:** The high frequency of active B19 infection markers, increased PBMC proliferative response to B19 antigens and B19 antigen expression detected in RA patients' synovial, cartilaginous and osseous tissues suggest that B19 infection is involved in the RA development and course. Affection of

fibroblast-like synoviocytes may promote further behaviour changes contribute to disease mechanisms.
**Disclosure of Interest:** None declared
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AB0080

WITHDRAWN

## AB0081 OCCUPATION AND RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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**Background:** Due to the proposed etiologic involvement of the lung in the development of rheumatoid arthritis (RA), there is reason to study whether other airborne exposures than smoking and silica dust increase the risk of RA. By finding occupations that are related to RA, we can get a hint of which hazardous agents that may be involved in the disease development.
**Objectives:** The aim of this study was to estimate the association between occupation and the risk of anti-citrullinated protein antibody positive (ACPA+) or ACPA- RA in men and women.
**Methods:** The study was based on the Swedish population-based case-control study Epidemiological Investigation of Rheumatoid Arthritis (EIRA), including men and women aged 18–70 years. Controls were matched to cases on sex, age group and residential area. Participants were enrolled between 1996 and 2014. Self-reported data on occupational history, environmental- and lifestyle factors were collected by a questionnaire. Blood samples were taken at clinics to assess the ACPA status of the cases.
We used unconditional logistic regression to assess the odds ratios (ORs) and 95% confidence intervals (CIs) of RA due to last occupation before study inclusion among 3,557 cases and 5,665 controls. Occupations were divided into 70 occupational groups and occupations within the professional, technical, administrative, managerial and administrative fields served as the reference group. Crude ORs were adjusted for age group and geographical area, and for the adjusted model we added pack-years of smoking, alcohol use, university degree and BMI.
**Results:** After adjusting for confounding from pack-years of smoking, alcohol use, university degree and BMI, only assistant nurses and attendants in psychiatric care were associated with a significantly increased risk of ACPA+ RA (OR: 1.3, 95% CI: 1.1–1.5). No occupations among women were significantly related to ACPA- RA after adjustment for the confounders. Among men, electrical and electronics workers (OR: 2.1, 95% CI: 1.1–3.7), bricklayers and concrete workers (OR: 2.9, 95% CI: 1.4–5.7) and material handling operators (OR: 2.1, 95% CI: 1.2–3.9) had an increased risk of ACPA+ RA. Electrical and electronics workers (OR: 2.6, 95% CI: 1.3–5.0) as well as bricklayers and concrete workers (OR: 2.6, 95% CI: 1.1–5.9) also had an increased risk of ACPA- RA.
**Conclusions:** Several occupations were related to ACPA+ or ACPA- RA. Mainly occupations within the manufacturing field were related to RA, and fewer women than men were working in this field. Adjustment for pack-years of smoking, alcohol use, university degree and BMI could not explain why certain occupations were related to an increased risk of ACPA+ or ACPA- RA, supporting the theory that there is an involvement from other harmful, occupational agents.
**Disclosure of Interest:** None declared
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## AB0082 ANTI-INFLAMMATORY ACTIVITY OF A HUMAN ENDOGENOUS RETROVIRAL GENETIC ELEMENT IN EXPERIMENTAL ARTHRITIS

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**Background:** Human Endogenous Retroviruses (HERVs) are ancient retroviral integrations fixed in the genome of humans. As for all retroviruses, HERVs contain three protein coding genes: *gag*, *pol* and *env*. The retroviral envelope proteins can influence human biology through their inherent immune suppressive activity (1) localized to a secondary protein structure (the ISU domain) in the envelope protein.
Our previous research has shown that the env-59-protein of HERV-H is negatively correlated to the inflammatory marker IL-6 in SLE patients, and has an inhibitory effect on stimulated PBMC's from both RA and SLE patients. We aimed to investigate, if this effect could be translated from *in vitro* to *in vivo* experiments.
**Objectives:** To examine the anti-inflammatory potential of a peptide based on the ISU domain of HERV-H ENV-59 in the SKG mouse model (2).
**Methods:** At 7–11 weeks of age, female SKG mice were randomized to treatment groups. Arthritis was induced with mannan. After disease induction, the animals were treated daily with subcutaneous injections of a synthetically developed peptide (Env59-ISU), a scrambled peptide or saline. Two 4-week studies were performed. In study one, we wished to demonstrate an anti-inflammatory effect of Env59 ISU. Three groups of 5 mice were tested (group #1: 4 μg peptide/day, group #2:40 μg peptide/day, group #3: saline).
Study two aimed to confirm the results of study one. Forty mice were randomized to 5 treatment groups (group 1: saline, group 2: 1μg/peptide/day, group 3: 4μg/peptide/day, group 4: 20 μg/peptide/day and group 5: 4 μg/scrambled-peptide/day). SKG arthritis was assessed and scoring was performed independently by two persons and blinded to treatment group.
Hind paws from two mice were fixated in 70% ethanol, and subsequently embedded undecalcified in methylmethacrylate. Tissue sections were stained with Masson-Golden trichrome.
**Results:** In study one, we found significantly lower arthritis score in Env59-treated mice compared to those treated with saline. Group #3 receiving 4μg peptide had the lowest average arthritis score throughout the trial (Fig.1), which was confirmed by study two showing, that the 4μg peptide- treated group (group 3) had significantly lower arthritis score compared to saline and the scrambled peptide. The pattern observed in the arthritis score was confirmed using serum amyloid A3 (SAA3) as a biomarker for inflammation and using histology in mice treated with saline compared to peptide-treated mice.

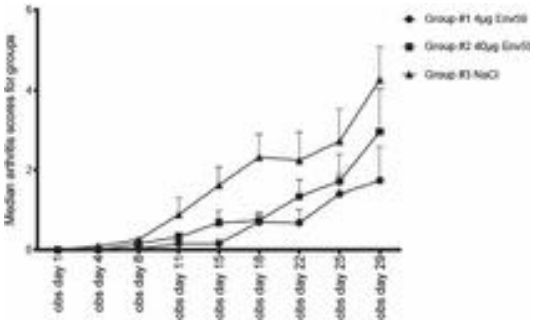


Figure 1

**Conclusions:** We demonstrate that a synthetic peptide corresponding to the sequence of Env59-ISU has anti-inflammatory effect in a chronic inflammatory mouse model of RA and propose the peptide as a potential new treatment for inflammatory diseases.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4267

## AB0083 ARTHRITIS INDUCES EARLY BONE STRUCTURAL DEGRADATION AND MECHANICAL WEAKNESS

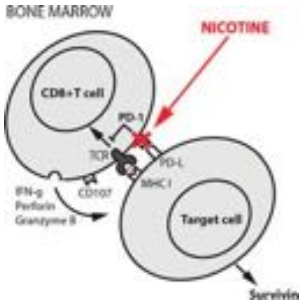
B. Vidal[1], R. Cascão[1], I. Lopes[1], M. Finnila[2,3], S. Saarakkala[2,4,5], H. Canhão[1,6], J.E. Fonseca[1,6]. *[1]Rheumatology Research Unit, Instituto de Medicina Molecular, Lisboa, Portugal; [2]Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, Oulu; [3]Department of Applied Physics, University of Eastern Finland, Kuopio; [4]Medical Research Center, University of Oulu; [5]Oulu University Hospital, Oulu, Finland; [6]Rheumatology Department, Lisbon Academic Medical Centre, Lisboa, Portugal*

**Background:** We have previously found in the chronic SKG mouse model of arthritis that long standing (5 and 8 months) inflammation directly leads to high collagen bone turnover, disorganization of the collagen network, disturbed bone microstructure and ultimately declining of bone biomechanical properties [1].
**Objectives:** Our main goal was to study the effects of the inflammatory process on the microarchitecture and mechanical properties of bone in the early stages of arthritis development.
**Methods:** Fifty Wistar adjuvant-induced arthritis (AIA) rats were monitored throughout arthritis development and sacrificed after 4, 11 and 22 days of disease induction. Thirty healthy non-arthritic rats, age and sex-matched, were sacrificed at the end of the experiment and used as controls for comparison. The inflammatory score, ankle perimeter and body weight were measured over the experimental period. At the time of sacrifice, bone and serum samples were collected for micro-CT and 3-point bending analysis as well as bone turnover markers (CTX-I and P1NP), respectively. All experiments were approved by the Animal User and Ethical Committees at the Instituto de Medicina Molecular (Lisbon University), according to the Portuguese law and the European recommendations.
**Results:** We have observed that bone turnover markers, CTX-I and P1NP, increased soon after arthritis onset ($p<0.0001$ and $p=0.0034$, respectively, when compared to healthy controls). Moreover, micro-CT analyses showed both in trabecular and cortical parameters, that the effects of inflammation on bone microstructure were evident since the 4th day of arthritis development. Of particular interest, trabecular bone volume fraction decreased and cortical porosity increased at day 22 post disease induction when comparing to healthy controls ($p=0.0001$ and $p<0.0001$, respectively). Biomechanical tests revealed that arthritic bone have altered biomechanical properties, such as maximal bending force (arthritic group lower than healthy control, $p<0.0001$).
**Conclusions:** The inflammatory process induced bone loss, and reduces bone strength since the very early phase of arthritis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4905

## AB0084 NICOTINE CAUSES ENRICHMENT OF SURVIVIN IN SERUM BY ACTIVATING CYTOTOXIC CD8+ T CELLS IN EXPERIMENTAL ARTHRITIS AND PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Smoking is the most extensively studied environmental risk factor of rheumatoid arthritis (RA). We have recently shown that smoking is associated with high serum levels of survivin (Svensson, Hafström et al. 2014). Survivin is a novel biomarker for RA that can predict severe joint destruction as well as treatment outcome for RA patients (Levitski et al, 2015). We hypothesized cytotoxic activity to be the reason for the increased serum levels of survivin observed in RA patients and we wished to further investigate possible molecular mechanisms behind cytotoxicity in RA.
**Objectives:** We have studied the effect of nicotine on cytotoxic activity of T lymphocytes during RA paying special attention to the expression of PD-1, a receptor that inhibits activation of T cells.
**Methods:** We used female Balb/c mice that received 0.03% nicotine in drinking water or regular tap water as controls, after 18 days mice were immunized with collagen and subsequently developed arthritis (CIA). At the end of experiment bone marrow, lymph nodes and serum were collected and analyzed using flow cytometry (FACS), qPCR and ELISA. To confirm nicotine-dependent nature of experimental findings, we analyzed blood samples of female RA patients and healthy women with known smoking status.
**Results:** The proportion of CD8+ cells was 1.9 times larger in nicotine treated mice compared to control ($p=0.00020$). Meanwhile, the nicotine treated mice had a 2.3 times less PD-1 expressing CD8+ cells in the bone marrow ($p=0.032$), but PD-1 expression in the lymph nodes was not affected by nicotine. This resulted in an accumulation of the CD8+PD-1- population in the bone marrow of the nicotine treated mice ($p=0.0074$). The nicotine treated mice had higher levels of serum survivin (0.0 vs 0.29 ng/ml, $p=0.017$) which also correlated to the size of CD8+PD-1- population in the bone marrow ($r=0.52$, $p=0.024$). The decrease in PD-1 expression of CD8+ T cells caused by nicotine was confirmed in smoking women. Smokers had a 1.7 times less PD-1 positive CD8+ T cells compared to non-smokers ($p=0.041$). In patients, the serum levels of survivin correlated to the expression of the cytotoxic marker CD107 on CD8+ T cells ($r=0.52$, $p=0.047$).




**Conclusions:** Nicotine exposure supports cytotoxic phenotype of CD8+ T cells characterized by high CD107 and low PD-1 expression in experimental arthritis and RA patients. Increased cytotoxic activity of CD8+ T cells is a plausible mechanism for the enrichment of survivin in serum in RA patients. See graphical abstract.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4149

## AB0085 OSTEOCLAST PROGENITORS ARE ATTRACTED BY CCL2/CCR2 AND CCL5/CCR5 CHEMOTACTIC SIGNALS TO THE SITES OF OSTEITIS ASSOCIATED WITH COLLAGEN INDUCED ARTHRITIS

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**Background:** Osteitis, replacement of bone marrow adipocytes with inflammatory cells, is an early sign of inflammation in rheumatoid arthritis (RA), seen as bone marrow edema by magnetic resonance imaging. Osteoclast progenitors (OCPs), normally present within circulating monocytes, are presumed to be increasingly attracted to inflamed joints in RA, where their enhanced activation and differentiation leads to excessive osteoresorption.
**Objectives:** Our goal was to identify attraction signals important for homing of OCPs to the sites of osteitis. Therefore, we analyzed changes in immune cell populations as well as OCP chemokine receptor profile and migration potential in circulation, affected joints and periarticular bone in collagen induced arthritis (CIA) as a mouse model of RA.
**Methods:** After obtaining Ethical approval, C57BL/6 mice were immunized with chicken type II collagen in complete Freund's adjuvant and evaluated for CIA development by clinical and histological scoring and anti-collagen antibody detection. Subchondral bone loss and osteitis were assessed by histology and histomorphometry. Distal tibial bone marrow, peripheral blood (PBL) and collagenase-digested tarsometatarseal joints were analyzed by flow-cytometry for the expression of hematopoietic markers and chemokine receptors (CD3, B220, NK1.1, CD11b, CD115, Gr1, CCR2, CCR5, CCR9). Transwell system was used to assess migration potential of M-CSF/RANKL stimulated PBL cells toward CCL2 or CCL5 gradient *in vitro*. For migration tracking, labeled PBL cells were transferred to recipient CIA mice and assessed by *in vivo* fluorescence imaging.
**Results:** Immunized mice developed CIA with the maximum incidence of 60%. Arthritic areas showed histological presence of osteitis and significant subchondral bone loss (BV/TV 46.8±13.4% in control vs 32.1±8.6% in CIA) with increased number of mature osteoclasts (1.4±1.1 in control vs 5.4±4.7 in CIA). Flow-cytometry analysis revealed significant expansion of several populations in CIA, including lymphoid-negative CD11b+/Gr-1+ OCP subset within affected joints (24±4.1% in control vs 49±12.7% in CIA); lymphoid-negative CD11b+CD115+ OCP subset in PBL (4.6±0.7% in control vs 8.8±3.3% in CIA) and periarticular bone marrow (9.6±1.1% in control vs 21.9±3.4% in CIA). PBL OCP populations expressing chemokine receptors were reduced in arthritis (CCR2+ 32.1±4.3% in control vs 24.7±5.1% in CIA; CCR5+ 23.3±4.5% in control vs 18.1±3.7% in CIA; CCR9+ 5.9±3.7% in control vs 0.4±0.1% in CIA). *In vitro* migration of PBL

cells toward chemotactic gradients was significantly enhanced in CIA (11.5 (IQR 11–13.25) in control vs 20.5 (IQR 20–25) in CIA for CCL2; 12.5 (IQR 9–18.5) in control vs 33.5 (IQR 23–35.75) in CIA for CCL5). Fluorescently-labeled PBL cells were efficiently attracted to tarsometatarseal joints 48 hours after *in vivo* transfer in mice with CIA.

**Conclusions:** In fully developed CIA OCP populations are highly induced, with the reduction of circulating OCP subpopulations expressing chemokine receptors, possibly indicating their increased migration and homing to bone surfaces of the inflamed joints. Therapeutic blocking of chemokine signals may therefore be a promising approach to reduce osteoresorption in RA.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.5635

## AB0086 ANTI-CITRULLINATED PROTEIN ANTIBODIES IN PATIENTS WITH CARDIOVASCULAR DISEASE WITHOUT RA

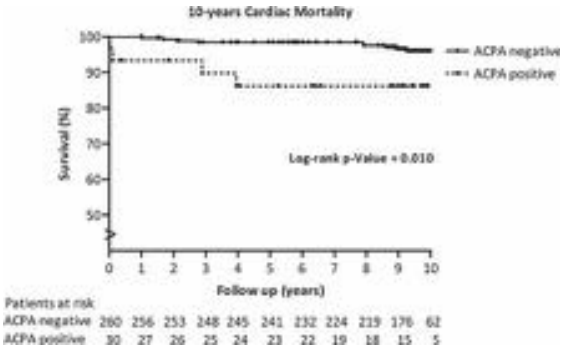
D. Van Der Woude[1], M.P. Hermans[2], D. van der Velden[1], L.A. Trouw[1], T.W. Huizinga[1], J. Kuiper[3], M.J. Schalij[2], W.J. Jukema[2], R.E. Toes[1]. *[1]Rheumatology; [2]Cardiology, Leiden University Medical Center; [3]Leiden Academic Center for Drug Research, Leiden, Netherlands*

**Background:** Anti-citrullinated protein antibodies (ACPA) are thought to be highly specific for RA. ACPA are associated with risk factors for RA and with joint destruction, and are therefore presumed to be involved in RA pathogenesis. ACPA-positive RA patients also have increased cardiovascular mortality (1). In cardiovascular disease, inflammatory changes occur in vessel walls, raising the question whether ACPA (presumed to be pro-inflammatory) may contribute to this process.

**Objectives:** To investigate the prevalence and prognostic implications of ACPA in patients with cardiovascular disease without RA.

**Methods:** ACPA were determined by anti-CCP3 commercial assay in baseline sera from 290 patients with ST-elevation myocardial infarction participating in the MISSION intervention study (2). Patients with RA were excluded. The association between ACPA and long-term mortality was investigated.

**Results:** 30/290 (10.3%) of the non-RA patients with cardiovascular disease were ACPA-positive. ACPA-positive non-RA patients had a significantly increased long-term cardiac mortality compared to ACPA-negative non-RA patients (Figure). Corrected for age, ACPA positivity was independently associated with long-term mortality [HR 2.4 (CI 1.1–5.4) p-Value=0.026].




**Conclusions:** ACPA can be detected in a considerable proportion of non-RA patients with cardiovascular disease. This challenges the presumed specificity of ACPA for RA. In both RA and cardiovascular disease, ACPA are associated with a worse disease outcome possibly by an ACPA-specific enhancement of inflammation. Future studies into ACPA in patients with cardiovascular disease offer the opportunity to dissect which risk factors are associated with ACPA in RA versus non-RA patients. This may supply crucial insights into the development of this autoimmune reaction.

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**Disclosure of Interest:** None declared

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## AB0087 CYTOTOXICITY AND GENOTOXICITY IN RHEUMATOID ARTHRITIS: A DUAL EFFECT OF DISEASE AND DRUGS

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**Background:** Studies about cytotoxicity and genotoxicity in rheumatoid arthritis (RA) are limited and the toxicity of Disease Modifying Anti-Rheumatic Drugs (DMARDs) commonly used in treatment is still a concern.

**Objectives:** to assess cytotoxicity and genotoxicity in RA and the possible cyto and genotoxic effects of some DMARDs used in treatment.

**Methods:** The study included 30 female RA patients divided according to treatment into three groups and ten healthy controls. Two groups received DMARDs for at least 3 months period: methotrexate (MTX) only group (n=12 patients), MTX with SSZ (sulphasalazine) group (n=8) and ten DMARDs naieve RA who received only Non Steroidal Anti-Inflammatory Drugs (NSAIDs). The MTX dose was 15–20 mg/wk, SSZ dose was 1.5–2 gm daily. All RA on DMARDs received concomitant daily folic acid dose of 0.5 mg.Peripheral blood samples were taken to assess the cytotoxicity by chromosomal analysis (karyotyping) using solid Giemsa stain and GTG-banding according to the International System for Human Chromosome Nomenclature. Genotoxicity and DNA damage was assessed by the miconucleustest usin g cytochalasin –B.

**Results:** Compared to controls, RA patients had significantly higher chromosomal aberrations (CAs) in the form of breaks, satellite association, endoreduplication, aneuploidy, double minute, and other aberrations. There was also a statistically significant increase in the markers of genotoxicity in RA patients compared to controls: micronuclei (MN), nucleoplasmic bridges (NPB) and necrotic and/or apoptotic cells (Table1). CAs were found in all RA groups, those receiving DMARDs as well as the DMARD naieve group. CAs were significantly higher in MTX and in MTX-SSZ group when compared to RA on NSAIDs only. Meanwhile, there was no significant difference between the CAs in the MTX and the MTX-SSZ groups. In addition, the number of binucleated (BN) cells with MN, NPB, and the necrotic and/or apoptotic cells was statistically higher in MTX-RA and MTX-SSZ-RA compared to the NSAIDs group. Whereas, no statistical difference was found between the two DMARDs groups.RA patients who were on DMARDs for a longer duration (>5 years) showed a statistically significant increase in all cytotoxicity and genotoxicity markers than those for shorter duration (<5 years).

| Markers of cyto/genotoxicity | Control (n=10) Mean ± SD | Total RA (n=30) Mean ± SD | P |
|---|---|---|---|
| Breaks | 0.6±1.07 | 14.77±11.58 | <0.001* |
| Satellite association | 6.2±6.49 | 38.16 ±14.77 | <0.05* |
| Double minute | 0.0±0.0 | 2.03±4.77 | <0.05* |
| Endo- reduplication | 0.0±0.0 | 9.7±8.31 | <0.05* |
| Aneuploidy | 0.0±0.0 | 5.3±4.5 | <0.05* |
| Other aberrations | 0.0±0.0 | 0.70±0.51 | <0.05* |
| BN cells with MN | 1.5±1.2 | 21.73±12.38 | <0.01* |
| BN cells with NPB | 0.8±1.0 | 13.27±9.96 | <0.01* |
| Necrotic and/or apoptotic cells | 2.3±1.8 | 29.93±12.10 | <0.001* |

*P is significant at values ≤0.05.

**Conclusions:** RA patients show significantly increased markers of cytotoxicity and genotoxicity, regardless the type of medications received, sugggesting them to represent underestimated disease features which could provide new insights into its pathogenesis. MTX further aggrevates the cyto- and genotoxicity, whereas SSZ combination does not seem to play additional role and concomitant folic acid supplementation does not provide the sufficient protection.

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## AB0088 TRANSGENIC ZAP-70+ B CELLS MICE SHOW A MORE SEVERE COLLAGEN ANTIBODY INDUCED ARTHRITIS (CAIA) THAN WILD TYPE

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**Background:** Zeta-chain-associated protein kinase 70 (ZAP-70), a tyrosine kinase constitutively expressed in T cells, can be found in B cells and is used as a prognostic marker in identifying different forms of chronic lymphocytic leukemia. We previously provided evidence that a subset of B cells in patients with rheumatoid arthritis (RA) expresses ZAP-70, that marks the memory B cell subsets (IgD+CD27+ and IgD-CD27+), thus suggesting that the ZAP-70+ B cells represent a memory activated subset likely involved in the maintenance of an activated B cell pool [1–3].

**Objectives:** The aim of the present study was to clarify whether B cells, especially ZAP-70 expressing B cells, represent indeed a risk for a severe expression of arthritis in a transgenic ZAP-70+B murine model.

**Methods:** Male transgenic ZAP-70+B mice, that has already been shown to present an high ZAP-70 expression in the B cell lineage [4], aged 8–12 weeks old were used for experiments. All the animals were injected with a cocktail of 5 monoclonal antibodies recognizing the conserved epitopes on various species of type II collagen. Three days later the mice were injected with LPS from *E. coli* 0111:B4 to trigger arthritis development. Animals were evaluated every 3 days after the infusion of the antibody cocktail for arthritis incidence and each paw was evaluated and scored individually on a scale of 0–4. An arthritis index (AI) that expressed a cumulative score for all paws was calculated for each animal.

**Results:** We found that the transgenic ZAP-70+B cells mice presented a more severe form of arthritis, compared to wild type age-matched mice ($p<0.001$) (Figure). Histological and immunohistochemical analyses confirmed the presence

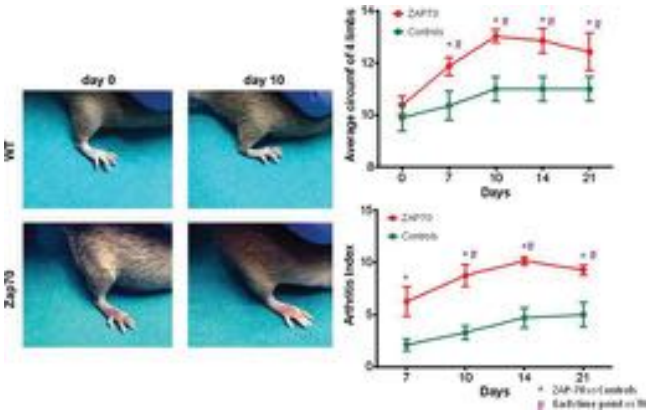



Figure 1

of joint erosions and inflammatory infiltrate at the level of the synovium of ZAP-70+B cells mice.
**Conclusions:** These data suggest that B cells amplify the degree of CAIA, that ZAP-70 is involved in the pathogenesis of arthritis in an RA-like model, and that this tyrosine kinase likely represents a possible target of therapy.
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## AB0089 NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND ENDOTHELIAL FUNCTION IN RA: HARMFUL OR BENEFICIAL? A STUDY IN RAT ADJUVANT-INDUCED ARTHRITIS

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**Background:** Rheumatoid Arthritis (RA) is associated with increased cardiovascular risk (CVR) explained in part by accelerated atherosclerosis as a consequence of endothelial dysfunction. Non-steroidal anti-inflammatory drugs (NSAIDs) are widely prescribed in RA patients in case of acute pain. Surprisingly, despite the commonly-held belief that NSAIDs worsen CVR, data regarding their effect on endothelial function in RA are lacking.
**Objectives:** The present study investigated the effect of naproxen (a non-selective COX inhibitor), diclofenac (a preferential COX-2 inhibitor) and celecoxib (a selective COX-2 inhibitor) on vascular function in arthritic rats and identified the underlying mechanisms.
**Methods:** Adjuvant-induced arthritis (AIA) was induced in 6 weeks-old male Lewis rats by injection of *Mycobacterium butyricum* in adjuvant at the basis of the tail. At the onset of arthritis, rats were daily treated (i.p.) with naproxen (10 mg/kg/d), diclofenac (5mg/kg twice a day), celecoxib (3 mg/kg/d) or saline (Vehicle) for 21 days. Arthritis scores were daily monitored. At the end of treatment, thoracic aortas were harvested to measure the relaxation to acetylcholine (Ach) on pre-constricted aortic rings in the presence or not of inhibitor of nitric oxide (NO) synthase (L-NAME), arginase (nor-NOHA), EDHF (Apamin/Charybdotoxin), or a superoxide dismutase analog (Tempol). The effects of a NO donor (sodium nitroprussiate, SNP) and norepinephrine (NE) were studied on endothelium-denuded aortic rings.
**Results:** All NSAIDs significantly reduced to the same extent arthritis score in AIA ($p<0.05$). By contrast, differences exist between NSAIDs regarding endothelial function. Both naproxen and diclofenac significantly ($p<0.05$) improved Ach-induced relaxation whereas celecoxib did not change the response to Ach. These differences on endothelial function were not explained by differences in the response of vascular smooth muscle to NE or SNP which remained unchanged after the 3 treatments. Of interest, the positive effects of naproxen and diclofenac likely relied on different mechanisms. Whilst naproxen tends to improve NOS activity and decrease superoxide anion production, diclofenac decreased arginase activity, superoxide anion production and improved EDHF production.
**Conclusions:** Our study demonstrates for the first time that naproxen and diclofenac have positive effects on endothelial function in case of arthritis whereas celecoxib had no effect, despite a similar reduction of inflammatory symptoms. From a clinical perspective, these data highlight the heterogeneity of effects of NSAIDs as regards CVR in RA and encourage designing clinical trials to confirm our experimental data and help guiding the better choice of NSAIDs for the global management of RA patients.

**Disclosure of Interest:** None declared
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## AB0090 REACTIVITY TO CITRULLINATED PEPTIDE OF 14-3-3ETA PROTEIN IS ASSOCIATED WITH WORSE RADIOGRAPHIC OUTCOMES IN PATIENTS WITH RECENT-ONSET INFLAMMATORY ARTHRITIS

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**Background:** 14–3-3η protein is citrullinated in the serum of Rheumatoid Arthritis (RA) patients. RA-associated HLA-DRB1 alleles preferentially bind citrullinated (cit) peptides but may bind both cit and arginylated (arg) peptides[1]. Autoreactivity to both cit and arg peptides may thus coexist in patients.
**Objectives:** To examine serum reactivity to 8 peptides representing the arg and cit versions of 4 putative citrullination sites on the 14–3-3η protein and their association with RA serology and radiographic outcomes.
**Methods:** Baseline serum reactivity to 4 pairs of cit and arg peptides was evaluated in a cohort of 331 patients (median age 60 years; 62% women) with recent onset polyarthritis (EPA). Receiver Operating Characteristic (ROC) curves were used to establish the optimal threshold of the ratios of reactivity to the 4 pairs of cit to arg peptides (Cit/Arg) for prediction of definite radiographic progression according to the Sharp/van der Heijde (SvH) score ($\Delta$SvH $\geq$5) from baseline to 3 to 5 years. Spearman correlations were used to determine the relationships between the Cit/Arg ratios with anti-CCP2 and 14–3-3η. Generalized estimating equations (GEE) with repeated measures were used to predict risk of developing $\Delta$SvH $\geq$5 over 5 years expressed as relative risk (RR) and 95% confidence intervals (95% CI).
**Results:** At baseline, comparable reactivity was found against all 4 sets of cit peptides (2 linear: CIT4 and CIT7; 2 cyclic: CYC-CIT1 and CYC-CIT2) and their corresponding arg peptides (ARG4; ARG7; CYC-ARG1; CYC-ARG2). Linear peptides appeared better recognized in their arg form, and the reverse was true for the cyclic ones (Table).
Only the anti-CYC-CIT2/CYC-ARG2 ratio was significantly associated with $\Delta$SvH $\geq$5 at 5 years (mean AUC=0.588, p=0.008); the best ROC cut-off for this ratio was 1.64. The anti-CYC-CIT2/CYC-ARG2 ratio was weakly correlated with anti-CCP2 (r=0.32, $p<0.001$) and with 14–3-3η (r=0.33, $p<0.001$), while anti-CCP2 and 14–3-3η protein were moderately correlated (r=0.53, $p<0.001$).
Anti-CCP2 positivity, 14–3-3η $\geq$0.50 ng/ml, and anti-CYC-CIT2/CYC-ARG2 $\geq$1.64 were respectively present in 133 (40.2%), 119 (36%) and 80 (24.2%) patients and were associated with higher risk for $\Delta$SvH $\geq$5 over time (RR 1.44 (1.14–1.80), p=0.002; 1.60 (1.28–2.00), $p<0.001$; RR 1.68 (1.35–2.09), $p<0.001$).
Patients with both 14–3-3η $\geq$0.50 and anti-CYC-CIT2/CYC-ARG2 $\geq$1.64 had an increased risk for $\Delta$SvH $\geq$5 compared to patients without either of the two (RR: 2.18 (1.68–2.83), $p<0.001$). The presence of only one marker also increased the risk (RR: 1.55 (1.20–2.01), $p<0.001$).
In a multivariate GEE model with 14–3-3η $\geq$0.50, positive anti-CCP2, positive Rheumatoid Factor, positive anti-Sa/citrullinated vimentin, CRP >8.0 mg/L and anti-CYC-CIT2/CYC-ARG2 $\geq$1.64, only CRP and anti-CYC-CIT2/CYC-ARG2 were significant to predict $\Delta$SvH $\geq$5 over 5 years (RR: 1.43 (1.11–1.84), p=0.006 and 1.45 (1.14–1.83), p=0.002; respectively).

| | Serum reactivity (Units/ml) Median (25th-75th percentile) | Ratio of serum reactivity cit/arg Median (25th-75th percentile) |
|---|---|---|
| CIT 4 | 274 (208-353) | |
| ARG 4 | 307 (230-409) | |
| CIT 7 | 316 (235-481) | |
| ARG 7 | 446 (333-584) | |
| CYC CIT 1 | 373 (279-502) | |
| CYC ARG 1 | 278 (215-372) | |
| CYC CIT 2 | 411 (299-565) | |
| CYC ARG 2 | 299 (233-403) | |
| Ratio CIT-4/ARG 4 | | 0.90 (0.76-1.10) |
| Ratio CIT-7/ARG 7 | | 0.73 (0.60-0.92) |
| Ratio CYC CIT-1/CYC-ARG 1 | | 1.28 (1.05-1.58) |
| Ratio CYC CIT-2/CYC-ARG 2 | | 1.32 (1.13-1.63) |

**Conclusions:** Many patients react against 14–3-3η arg peptides as well as against cit peptides. Citrullination at only one of 4 sites appeared linked to outcomes. An anti-CYC-CIT2/CYC-ARG2 $\geq$1.64 and elevated CRP protein both contributed independently to predict worse radiographic outcomes in patients with EPA.
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**Disclosure of Interest:** N. Carrier: None declared, A. Marotta Employee of: Augurex Life Sciences Corp. The 14–3-3η measurements were performed free

of charge by Augurex, Augurex remaining totally blinded to clinical data. All the analyses were performed by investigators from Université de Sherbrooke and personnel of Centre hospitalier universitaire de Sherbrooke, without sharing of clinical and laboratory data of individual patients with Augurex personnel., W. Maksymowych Consultant for: Augurex Life Sciences Corp, co-inventor of the 14–3-3 biomarker platform, and has received honoraria from Quest Diagnostics for consulting services and royalty payments from the University of British Columbia., G. Boire Grant/research support from: The Sherbrooke EUPA cohort was supported by The Arthritis Society Grants 00/201 and RG06/108 and the Canadian Institutes for Health Research MOP-110959 (G Boire). AJF, PL, AMas and GB are part of the Centre de Recherche Clinique du Centre Hospitalier Universitaire de Sherbrooke, which received a team grant from the Fonds de la Recherche en Santé du Québec. Since 2007, the Sherbrooke EUPA cohort has also received financial support from the Canadian ArTritis CoHort (CATCH), a study designed and implemented by investigators and financially supported initially by Amgen Canada Inc. and Pfizer Canada Inc. via an unrestricted research grant. As of 2011, further support was provided by Hoffmann-La Roche Ltd, United Chemicals of Belgium (UCB) Canada Inc., Bristol-Myers Squibb Canada Co., Abbott Laboratories Ltd, and Janssen Biotech Inc. (a wholly owned subsidiary of Johnson and Johnson Inc.)

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## AB0091 HYPOXIA INDUCE SLUG EXPRESSION VIA JAK/STAT3 PATHWAY IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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**Background:** Accumulating evidence implicates hypoxia in the pathogenesis of rheumatoid arthritis (RA). The effect of hypoxia on the expression of Slug, a transcriptional repressor that impairs apoptosis of RA fibroblast-like synoviocytes (FLS), remains unknown.
**Objectives:** The aim of this study is to investigate the role of hypoxia in the expression of Slug in RA FLS and to delineate the signaling pathway involved in the process.
**Methods:** After RA FLS were exposed to hypoxia, expression of HIF1-a and phosphorylation of ERK, JNK, and STAT3 were analyzed by Western blot. The experiment was repeated with RA FLS pretreated with WP1066, an inhibitor of the JAK/STAT pathway. RT-PCR was performed to measure HIF-1a mRNA and Slug mRNA expressions in RA FLS under hypoxia. RA FLS was transfected with HIF-1a cDNA to investigate the effect of overexpression of HIF-a on Slug expression. Immunohistochemistry was used to assess the presence HIF-1a and Slug in RA synovial tissue. Microarray analysis was performed to investigate the change in Slug gene expression when FLS were exposed to hypoxia. Finally, the effect of TNF-$\alpha$ on Slug and HIF-1$\alpha$ expressions under normoxic conditions was assessed in RA FLS by Western blot.
**Results:** Hypoxia induced the expression of HIF-1a and phosphorylation of STAT3, but not JNK and ERK was increased in RA FLS. Pre-treatment of RA FLS with WP1066 before exposure to hypoxia inhibited the expression of p-STAT and HIF-1a. Hypoxic conditions induced Slug mRNA expression from RA FLS, and similarly, overexpression of HIF-1a in RA FLS reproduced enhanced Slug expression. Microarray analysis revealed a significantly up-regulated Slug expression. Immunohistochemical staining showed that HIF-1a and Slug were co-localized in the lining area of RA synovium. Stimulation of FLS with TNF-$\alpha$ alone without hypoxia resulted in increased expression of Slug HIF-1a and Slug.
**Conclusions:** Our study demonstrates that HIF-1a expression from RA FLS induced by hypoxia or TNF-a alone is mediated through JAK/STAT3 signaling pathway, which ultimately leads to the expression of Slug. Hypoxia-driven pathway of Slug expression may become a novel treatment target in RA.
**Disclosure of Interest:** None declared

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## AB0092 ABLATION OF FC GAMMA RECEPTORS LEADS TO A DECREASED BONE EROSION IN EXPERIMENTAL ARTHRITIS BY INHIBITING SYNOVIAL INFLAMMATION AND OSTEOCLAST ACTIVATION

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**Background:** Rheumatoid Arthritis (RA) is characterized by bone destruction in joints caused by enhanced activity of osteoclasts. Ig-G containing immune complexes (ICs) correlate with disease severity and bone erosion and are recognized by Fc gamma receptors (Fc$\gamma$Rs) on myeloid cells. In this study we investigated the role of Fc$\gamma$Rs in osteoclast-mediated bone erosion comparing development of immune complex mediated antigen induced arthritis (AIA) between mice lacking all Fc$\gamma$Rs (Fc$\gamma$RI, II, III, IV$^{-/-}$) and their wild type controls.
**Objectives:** To investigate the role of Fc$\gamma$Rs in bone erosion in experimental arthritis
**Methods:** AIA was induced by injection of 60 $\mu$g mBSA into the knee joint of Fc$\gamma$RI, II, III, IV$^{-/-}$ and wild type (WT) control mice previously immunized with mBSA/CFA. Joint inflammation and bone destruction was determined in total knee joints sections. mBSA antibody titers were measured using ELISA and T cell response monitored with a lymphocyte stimulation test. The percentage of osteoclast precursors in the bone marrow was defined through FACS analysis. Gene expression was measured using RT-PCR. Number of mature osteoclasts within the inflamed joints was defined through TRAP staining. Protein expression was measured with bead-based multiplex immunoassay luminex in the synovial wash-out or through immunohistochemistry on knee joint section.
**Results:** In Fc$\gamma$RI, II, III, IV$^{-/-}$ mice the development of bone erosion in knee joints was significantly reduced both at days 7 and 21 after induction of AIA (30% and 25% lower) when compared to WT controls. The immune response against mBSA (serum level of specific anti mBSA (total IgG, IgG1, IgG2a, IgG2b) and mBSA specific T-cell response) was comparable between the two strains. The percentage of osteoclast precursors within the bone marrow (CD11b $^{low\text{-}neg}$/ Ly6C $^{high}$, described to be upregulated during arthritis) was comparable between Fc$\gamma$RI, II, III, IV$^{-/-}$ and WT controls. At day 7 after AIA induction, the decrease in bone erosion in Fc$\gamma$RI, II, III, IV$^{-/-}$ was associated with a significantly decrease in the number of inflammatory cells present within the joint (infiltrate and exudate 29% and 27% lower respectively compared to WT control). Although less macrophages were detected within the synovium, no differences were found in the number of mature osteoclasts present at locations of bone erosion (32±13 osteoclasts/section in Fc$\gamma$RI, II, II, IV$^{-/-}$ versus 28±9 osteoclasts/section in WT), suggesting that mainly the activity of osteoclasts was affected in the KO animals. In line with this observation levels of macrophage derived factors like IL-1$\beta$ and S100A8, known to strongly induce osteoclast activity, were reduced both at gene expression level and protein level in the synovium of Fc$\gamma$RI, II, III, IV$^{-/-}$ mice.
**Conclusions:** Fc$\gamma$Rs promote bone erosion in AIA by enhancing influx of macrophages within the synovium and release of factors such as IL-1$\beta$ and S100A8 able to stimulate osteoclast activity.
**Disclosure of Interest:** None declared

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## AB0093 REGULATION OF AUTOPHAGIC FLUX ALTERS INTERLEUKIN-17A-INDUCED MIGRATION AND PROLIFERATION OF FIBROBLAST-LIKE SYNOVIOCYTES FROM THE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Interleukin-17A (IL-17A) plays a critical role in the pathogenesis of rheumatoid arthritis (RA), which is characterized by exaggerated synovial proliferation. Autophagy is required to prevent accumulation of cellular damage and to ensure cellular homeostasis. Dysregulated autophagy has been reported to be involved in the pathogenesis of several diseases such as cancer and infections. Here, we hypothesized that IL-17A, a key cytokine in the development of RA, might have an impact on autophagic flux and that aberrant autophagy might be involved in expansion of synovial fibroblasts in the patients with RA, which is stimulated by pro-inflammatory cytokines.
**Objectives:** The aims of this study were (1) to evaluate whether IL-17A influences on autophagic flux in the synovium of the patients with RA and (2) to investigate whether the modulation of autophagy can regulate migration and proliferation of fibroblast-like synoviocytes (FLS) from the patients with RA (RA-FLS) under inflammatory milieu.
**Methods:** Synovial tissue was obtained from the patients with RA or osteoarthritis (OA) during total knee replacement surgery. FLS was cultured with IL-17A, autophagy inducer or inhibitor. The expression of marker proteins for autophagic flux (LC3B, Beclin1, Atg5, p62) and the formation of autophagolysosome (LAMP1) were analyzed by western blot. A migration scratch assay was used to assess FLS migration in response to stimulation with IL-17A. Proliferation of FLS was determined by the viable cell count using trypan blue. Bafilomycin was used for inhibiting autophagic flux.
**Results:** The expression of autophagy markers (LC3B, Beclin1, Atg5) was increased in the synovium of the patients with RA than in that of the patients with OA. Autophagy was also enhanced in RA-FLS compared with OA-FLS. IL-17A upregulated the expression of LC3B, Atg5, Beclin1, LAMP1 in RA-FLS. In particular, IL-17A-induced accumulation of p62 was prominent in RA-FLS. Migration and proliferation of FLS stimulated by IL-17A was suppressed by the inhibition of autophagy.
**Conclusions:** This study reveals that IL-17A stimulates autophagic flux and that intervention of autophagy can control IL-17A-induced migration and proliferation of FLS. Our results also provide additional evidence for a significant role of

autophagy in the pathogenesis of RA. Thus, we suggest that autophagy might be a potential therapeutic target for the management of RA.

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**Disclosure of Interest:** None declared
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## AB0094 A DUAL PATHOMECHNISM OF LOCAL TNF PRODUCEING IGA B CELLS IN RA SYNOVIAL TISSUE

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**Background:** So far no mechanism for non response to biologicals targeting TNFα has been described despite one third of rheumatoid arthritis patients treated are non-responders.
**Objectives:** We investigated the differences in seroreactivity of patients responding and not responding to TNF therapies prior and after therapy and identified diagnostically applicable IgA autoantigenicity set to identify non response.
**Methods:** Screening with patient sera were conducted with 5 different roteins candidates which were identified by protein maroarray screening (Anal Biochem. 1999 May 15;270(1):103–11.9) expressed recombinantly in *E. coli*, purified and further stratified with a large well defined patient cohort by ELISA. Baseline sera form PREDICT trial treated with Enbrel) and patients treated with Humira in the HIT HARD (Ann Rheum Dis. 2013 Jun;72(6):844–509 trial and 66 baseline sera from Charite in addition treated with (Cimzia, Infiximab) were ivestigated by Pre. mark TNF ELISA from DRDx GmbH.
**Results:** Pretreatment sera from patients with diagnosis of RA based on the ACR classification criteria who were initiated on therapy with TNFalpha inhibitors were analyzed with five markers from the biomarker set of highest priority (RAB11B, PPP2R1A, KPNB1,Cog 4, FTFT1) using an ELISAs assay. In total, analyses of 203 patients were carried out, of which 162 were clearly defined as Responder and 41 were clearly defined as non-Responder after 6 month treatment. 81% of Non-responder could be clearly identified with the pre.markTNF Test. The assay has currently a specificity 94%. Moreover, 80 baseline serum samples from the PREDICT study with Enbrel and 57 baseline sera from an early intervention trial Hit Hard (Ann Rheum Dis. 2013 Jun;72(6):844–509) with Humira were analysed. In early subset, all 3 non-responder were identified and the specificity of the assay was 98%. In the PREDICT study Enbrel non responders were identified with 68.8% sensitivity and a specificity of 92.5%. Moreover 60 patients treated with TNFalpha inhibitors TNF from Stockholm and Vienna have been tested with >90% specificity to predict non response. The amount of IgA produceing B cell in the synovia differs significantly between the patients which is not seen with IgG produceing B cells. Moreover the potent IgA autoantibodies induce high amount of TNF alpha in marophage assay were IgG do not. A dual pathomechnism of local TNF produceing IgA B cells in RA synovial tissue and TNF produceing macrophages is proposed.
**Conclusions:** These data suggest that non-response to anti-TNFα biologicals might be predicted based on frequency and magnitude of autoantibodies to specific IgA autoantigens. SFB can stimulate multiple intestinal homeostatic IgA and TNF induceing B cells might be important for disease persistence in TNFα non responders.

**Disclosure of Interest:** None declared
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## AB0095 INVESTIGATING THE ROLE OF TRANSIENT RECEPTOR POTENTIAL CANONICAL 5 (TRPC5) IN COMPLETE FREUND'S ADJUVANT (CFA)-INDUCED ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by inflammation of diarthrodial joints. Sensory neurons expressing transient receptor potential (TRP) channels, a wide family of non-selective cation channels, have been shown to play a role in the pathogenesis of RA[1]. Transient receptor potential 5 (TRPC5) is a member of the canonical family of TRPC channels and is abundantly expressed in the central nervous system and periphery[2], including $CD55^+$ fibroblast-like synoviocytes[3], but the role of TRPC5 in arthritis is unknown.
**Objectives:** To evaluate the for the first time, the contribution of TRPC5 in an *in vivo* model of arthritis and investigate the role of TRPC5 in the modulation of hyperalgesia and joint inflammation.
**Methods:** All experiments were conducted under the guidelines of the United Kingdom Home Office Animals (Scientific Procedures) Act 1986. Age-matched, male 129S1/SvImJ wildtype (WT) and TRPC5 knockout (KO) mice littermates bred from heterozygotic mice provided by Prof. D.E. Clapham, USA[2]. Induction of arthritis using CFA was performed as previously described[1]; inflammation was allowed to progress to 14 days. Nociceptive tests were carried out weekly. Synovial blood flow was assessed in anaesthetised WT and TRPC5 KO mice using a full-field laser perfusion imager (FLPI)[4] on day 14. *Ex vivo* analysis included assessment of cellular infiltration in the knee joint, and determination of cytokine concentrations. In separate studies, WT and TRPC5 KO mice received the TRPC4/5 antagonist, ML204[5](2mg/kg, *i.p.*, n=6) or vehicle (2% DMSO in saline, n=4) daily following *i.art.* injection of CFA. Results are presented as mean ± s.e.m. and analysed by 2-way ANOVA and Bonferonni *post hoc* test.
**Results:** WT mice developed primary hyperalgesia with a significant reduction in withdrawal threshold compared to baseline responses (334.7±25.7 vs 452.2±8.2 gram force (gf); $p<0.01$]). Primary hyperalgesia was exacerbated in TRPC5 KO mice compared to WT mice on day 14 (267.4±34.2 vs 334.7±25.4gf; $p<0.05$]). This was associated with similar deficits in weight-bearing on the ipsilateral hind-limb which was significantly reduced compared to WT mice. Ipsilateral synovial blood flow was significantly increased in TRPC5 KO mice compared to the contralateral synovium (291.3±50.2 vs 198.2±21.4 flux units (AU); $p<0.01$), and WT ipsilateral synovium ($p<0.001$). Pharmacological antagonism of TRPC5 in WT mice corroborated the results observed in TRPC5 KO mice, where hyperalgesia and joint inflammation was significantly exacerbated compared to vehicle treated WT mice.
**Conclusions:** Our results reveal a protective ability of TRPC5 in inflammatory joint conditions *in vivo*. Genetic deletion or pharmacological antagonism of TRPC5 resulted in an exacerbated inflammatory response highlighted by heightened nociceptive responses, increased cellular infiltration and cytokine concentrations in the knee joint.

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## AB0096 PRESENCE OF ACPA AND RF AUTOANTIBODIES IN ULCERATIVE COLITIS AND CROHN'S DISEASE

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**Background:** Presence of arthritis autoantibodies is specific for rheumatoid arthritis (RA). Anti-citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF) can be detected several years before the onset of arthritis and are thought to have a pathogenic role. However, where and when autoantibody production starts is unclear. A potential trigger could be chronic mucosal inflammation as in inflammatory bowel disease (IBD) since the gut microbiome is thought to be involved in induction of (auto) immunity. This assumption is supported by the demonstration of citrullinated proteins in intestinal tissue of IBD patients.
**Objectives:** To assess the prevalence of ACPA and RF in IBD patients as well as to assess the prevalence of joint complaints in autoantibody positive versus autoantibody negative IBD patients.
**Methods:** Serum was collected from 227 patients with ulcerative colitis (UC) and 164 with Crohn's disease (CD) participating in the Dutch IBD pearl chain institute biobank initiative. Baseline disease characteristics including enthesitis, arthralgia, arthritis and comorbid conditions like spondylarthropathy were obtained from medical electronic records. IgG and IgA ACPA levels were measured by anti-CCP2 ELISA from EuroDiagnostica (ED) and IgM and IgA-RF levels were measured by in-house ELISA. The cut-off value for IgG ACPA positivity was 2 U/mL and for IgA ACPA 1.04 aU/ml based on the mean +2SD of a group of healthy reference samples. Seropositivity for IgM and IgA-RF was defined at ≥10 IU/ml and ≥25 IU/ml, respectively.
**Results:** Thirty-two (14.1%) UC and 33 (20.1%) CD patients had an IgG ACPA level >2 U/ml. However, all IgG ACPA levels were below the diagnostic cut off level for RA which is set at ≥25 U/ml. IgA ACPA levels were increased in 83 (36.5%) UC and 48 (29.3%) CD patients. IgM-RF seropositivity was observed in 11 (4.8%) UC and 6 (3.7%) CD patients. IgA-RF seropositivity was observed in 6 (2.6%) UC and 8 (4.9%) CD patients. A total of 101 (44.5%) UC and 76 (46.3%) CD were seropositive for at least 1 arthritis autoantibody. Arthralgias were reported in 19.1% of UC and 33.3% of CD, respectively. Among patients with arthralgias, the percentage of individuals being seropositive for 1 or more autoantibodies was comparable to patients without arthralgias.
**Conclusions:** The results of our study support the hypothesis that inflammation of intestinal mucosa induces low systemic levels of ACPA, which eventually may play a role in induction of RA. However, the development of arthralgias in IBD patients is independent on the presence of low systemic presence of arthritis autoantibodies.

**Disclosure of Interest:** None declared
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## AB0097 THE PRESENCE OF STAPHYLOCOCCAL TOXINS IN THE URINE OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a disease of unknown etiology; with a pathogenesis that is due to a mixture of genetic, immunological and environmental factors. A T-cell immune response to the presence of pyrogenic toxin superantigens (PTSAgs) in the joints of RA patients has previously been described.
A link has been proposed between pathogenic micro-organisms and the development of chronic, autoimmune conditions. Potential pathogenic mechanisms include the hygiene hypothesis and molecular mimicry. Due to the widespread prevalence of RA, it has been hypothesised that the pathogenesis could involve a common bacterium. Previously, *Porphyromonas gingivalis*, a periodontal pathogen, has been suggested due to its ability to citrullinate proteins. In RA one potential bacterial candidate that has been suggested is *Staphylococcus aureus*. Current published data averages the presence of *S.aureus* at 30% in the general population from nasopharyngeal swabs[1]. Furthermore, our unpublished data suggests immune complexes containing *S.aureus* antigens are detectable in urine.
**Objectives:** To investigate the presence of staphylococcal enterotoxins B and C (SEB/SEC), toxic shock syndrome toxin 1 (TSST-1) and alpha haemolysin (AH) in the urine of patients with RA to support the hypothesis that they may play a role in RA.
**Methods:** Following ethical approval, mid-stream urine samples were obtained from patients with RA and a control group (patients with closed fractures). Both populations had no active infection(s) and were recruited from British Rheumatology and Orthopaedic departments in the same hospital. Samples were collected and processed aseptically, then analysed by western blot using commercially available primary (sheep) antibodies to SEB, SEC, TSST-1 and AH; and a rabbit anti-sheep HRP conjugated secondary antibody.
**Results:** The RA population comprises 110 females and 38 males aged 25–90 (median =65–74). The control population comprises 18 females and 9 males (median age =55–64) to date.
Western blot analysis demonstrated the presence of AH/SEB/SEC in 81 of 148 (54.7%) RA patient urine samples and 9 of 27 (33.3%) control samples.
**Conclusions:** Our work demonstrates the presence of bacterial toxins in urine from RA patients, with 54.7% demonstrating the presence of at least one staphylococcal toxin. This study is the first to demonstrate the presence of common staphylococcal enterotoxins in RA patient urine, raising the question of what role they may have in the disease pathogenesis, given that these patients have no active infections.
We also show that *S.aureus* toxins are present in urine of nearly 2 times more of the RA population than the general population. This raises questions of whether the bacteria and their toxins are involved in an individual's likelihood of getting RA; are those people with RA more likely to have *S.aureus* infections due to their immunological state? The presence of *S.aureus* in RA patient tissues warrants further investigation to determine if it is causative of, or a result of RA diagnosis.
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## AB0098 SHIFT WORK MAY BE ASSOCIATED WITH AN INCREASED RISK OF RHEUMATOID ARTHRITIS IN WOMEN, BUT NOT IN MEN

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**Background:** Rheumatoid Arthritis (RA) is a chronic inflammatory disease, with symptoms varying with the circadian rhythm (i.e. stiffness and pain are increased in the mornings, and associated with increased inflammatory cytokine production). Shift work, defined here as working outside regular day shifts, can cause circadian dysfunction, and is considered to be a potential contributory factor to a range of clinical and pathological conditions, including inflammation. There is limited data on the relation between shift work and RA, but one previous cohort study (1) reported an association between shift work and RA development in women.
**Objectives:** To further investigate the relation between shift work and the risk of subsequent development of RA in women and men separately.
**Methods:** Among participants in a population-based health survey (N=30447), incident cases of RA were identified by linking the cohort to local and national RA registers, followed by a structured review of the medical records. For each validated case, four controls, matched for sex, year of birth and year of screening, who were alive and free of RA when the index person was diagnosed with RA, were selected. Life style related factors and other exposures had been assessed in the survey using a questionnaire. Individuals who responded yes to the question "Does your work mean inconvenient working hours or shift work?" were classified as shift workers. The impact of shift work on the risk of RA was examined in conditional logistic regression models, stratified by sex.
**Results:** A total of 172 patients (136 women/36 men, mean age at RA diagnosis 63 years) were diagnosed with RA after inclusion in the health survey. The median time from inclusion to RA diagnosis was 5 years (range 1–13). Among pre-RA cases, 55 individuals, 47 women (38%) and 8 men (27%), were classified as shift workers. The corresponding figures for the controls were 28% among women and 25% among men. Shift work was associated with an increased risk of subsequent development of RA in women (odds ratio (OR) 1.60; 95% confidence interval (CI) 1.01–2.57). There was no significant association between shift work and RA in men (OR 1.04; 95% CI 0.35–3.05). The estimated impact of shift work on the risk of RA in women was similar in separate models adjusted for level of formal education (OR 1.56; 95% CI 0.97–2.50) and smoking (OR 1.53; 95% CI 0.95–2.45).
**Conclusions:** In this nested case-control study, women with inconvenient working hours or shift work had an increased risk of a future diagnosis of RA compared to those with regular working hours. This association did not appear to be explained by potential confounders, i.e. level of formal education or smoking. This suggests that exposures associated with shift work in women, possibly including circadian dysfunction, may contribute to the development of RA.
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## AB0099 OVEREXPRESSION OF UPAR IN FIBROBLAST-LIKE SYNOVIOCYTES PROMOTES ANGIOGENESIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Urokinase-type plasminogen activator receptor (uPAR), is a multifunctional receptor on cell surface, widely present in endothelial cells, fibroblasts, and a variety of malignant cells. Our previous studies have suggested that expression of uPAR is higher in patients with rheumatoid arthritis (RA) compared to osteoarthritis (OA) and the traumatic patients.
**Objectives:** Our objective was to investigate the promoting-angiogenesis effects of uPAR in fibroblast-like synoviocytes from patients with rheumatoid arthritis (RA-FLSs).
**Methods:** Chemically synthesized small interference RNA (siRNA) specifically targeting the uPAR gene was transfected into RA-FLSs by cationic liposome and the cell supernatants from uPAR gene-silenced RA-FLSs were extracted to cultivate the EA.hy926 (a human endothelial cell line). Transwell and tubule formation assays were used to explore the influence of RA-FLSs uPAR on EA.hy926 angiogenesis.
**Results:** EA.hy926 cells treated with conditioned medium of uPAR-siRNA RA-FLSs had a worse migrating ability and tubule formation effects, for they had only about 38% transmembrane cells and the average number of complete tubular structures decreased to 38.2%,relative to the transfection reagent control group (*P<0.05).

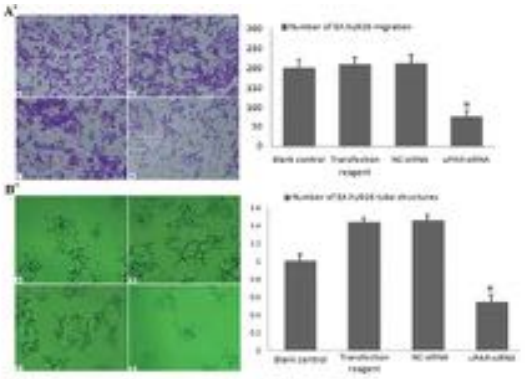


Figure • Interference of uPAR in RA-FLSs could suppress endothelicyte angiogenesis by reducing cell migration and tubule formation. A*. The EA.hy926 cell migration ability in different conditioned medium described below were evaluted by a transwell chamber assay. B*. The EA.hy926 cells with different conditioned medium described below were added into Matrigel coated 96-well for 24h to form tubule. A, Blank control group, serum-free DMEM; B, Transfection reagent group, conditioned medium of RA-FLSs transfected only with transfection reagent; C, NC-siRNA group,conditioned medium of RA-FLSs transfected with a negative control (NC, 40 nM) ; D, uPAR-siRNA group, conditioned medium of RA-FLSs transfected with uPAR-siRNA (40 nM). In both A* and B*, left panel showed representative images; right panel presented quantification (means ± SEM) of 4 independent experiments.*P < 0.05, compared with blank control.

**Conclusions:** uPAR in RA-FLSs affects neoangiogenesis of synovial tissues in patients with RA, which imply that targeting uPAR and its downstream signal pathway may provide beneficial therapeutic effects on RA.

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## AB0100 IL-22-MEDIATED BCL-2 EXPRESSION IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES THROUGH STAT3 ACTIVATION

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**Background:** Interleukin-22 (IL-22) is a novel cytokine that is mostly produced by T cells and innate lymphoid cells but selectively stimulates non- immune cells, which immediately caught the attention of many fields such as tumor, chronic inflammatory disease and infectious disease. Considering the persistent biological abnormalities in rheumatoid arthritis fibroblast-like synoviocytes (RA-FLSs) and transient effects of current best treatment such as anti-TNF biologics, other cytokines might be involved and we focus here on the role of IL-22.
**Objectives:** To test the effect of IL-22 on the survival of RA-FLSs and to investigate whether signal transducer and activator of transcription 3 (STAT3) is implicated in this process.
**Methods:** Bcl-2 mRNA and Bcl-xL mRNA expression in the RA-FLSs, osteoarthritis-FLSs and trauma-FLSs were determined using the Real-time quantitative polymerase chain reaction (RT-qPCR), Bcl-2 protein expression in FLSs were detected by the Western Blotting analysis. The effects of recombinant human interleukin-22 (rhIL-22) at concentrations of 0, 1, 10, 100 ng/mL and STA-21 (a STAT3 inhibitor at concentrations of 0, 25μM, 50μM) on the protein levels of Bcl-2 and p-STAT3 in the RA-FLSs were determined by Western blotting analysis. RA-FLSs were co-cultured with rhIL-22 in the presence or absence of STA21 for 24 h, and the protein levels of Bcl-2 and p-STST3 were evaluated by Western blotting analysis.
**Results:** The anti-apoptotic Bcl-2 ($P<0.05$) and Bcl-xL ($P<0.01$) are increased in RA-FLSs compared with osteoarthritis-FLSs and trauma-FLSs, and so is Bcl-2 protein ($P<0.01$). IL-22 increased, and STA-21 decreased the protein levels of Bcl-2 and p-STAT3 (IL-22: $F_{Bcl\text{-}2}=48.63$, $P_{Bcl\text{-}2}<0.01$; $F_{P\text{-}STAT3}=25.7$, $P_{P\text{-}STAT3}<0.01$ STA-21: $F_{Bcl\text{-}2}=49.74$, $P_{Bcl\text{-}2}<0.01$l; $F_{P\text{-}STAT3}=109.97$, $P_{P\text{-}STAT3}<0.01$) in the RA-FLSs obviously. Additionally, treatment with STAT3 inhibitor STA-21 reversed the effect of IL-22-induced Bcl-2 upregulation in the RA-FLSs ($F_{Bcl\text{-}2}=84.67$, $P_{Bcl\text{-}2}<0.01$; $F_{P\text{-}STAT3}=82.46$, $P_{P\text{-}STAT3}<0.01$).
**Conclusions:** STAT3 is critical in the process which IL-22-induced Bcl-2 upregulation in the RA-FLSs. The effects of IL-22/STAT3 confer on them the potential to be used for therapeutic applications in RA.
**Disclosure of Interest:** None declared
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## AB0101 IMPACT ON BONE DESTRUCTION BY LILRA3: A HIGH RISK SUSCEPTIBLE GENE IN RHEUMATOID ARTHRITIS

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**Background:** Leukocyte immunoglobulin-like receptor A3 (LILRA3) is a putatively secreted protein belongs to the leukocyte immunoglobulin-like receptor (LILR) family. Our previous study provided the first evidence that the functional LILRA3 was a novel genetic risk for rheumatoid arthritis (RA) in Chinese Han population.
**Objectives:** we undertake this study to investigate the role of LILRA3 on bone destruction in RA patients.
**Methods:** i) The expression of LILRA3 in serum and synovial fluid from patients with RA, OA, and health controls were measured by using ELISA. Bone destruction was scored using modified Sharp-vander Heijde score (SHS) on hands. ii) RAW264.7 cells and peripheral blood mononuclear cells (PBMCs) from RA,OA patients and health controls were cultured in the medium containing different concentration of recombinant LILRA3 protein in the presence or absence of Receptor Activator for Nuclear Factor-κ B Ligand (RANKL) and macrophage colony-stimulating factor (M-CSF). Osteoclasts were identified by tartrate-resistant acid phosphatase (TRAP) staining. Bone resorption activity of osteoclasts was determined by bone slices stained with toluidine blue, iii) PBMCs from patients with RA, OA and health controls were transfected with LILRA3 plasmid or control vector. The expression of osteoclasts related genes, including TRAP, CTSK, MMP-9 was measured by q-PCR array and Western Blotting method. MAPK and NF–κB signaling pathway activation levels were detected by Western Blotting method. One-way analysis of variance was used to detect the differences between the group means.
**Results:** Compared with health controls, the expression of LILRA3 in RA and OA serum was high and LILRA3 was specifically express in synovial fluid with RA patients. The serum level of LILRA3 in RA patients was positively correlated with bone damage. We demonstrated that LILRA3 can promote bone damage independently or synergy with RANKL in RAW264.7 cells through MAPK and NF–κB signaling pathway. Furthermore, we proved that LILRA3 can induce the differentiation of osteoclasts in the presence of RANKL and M-CSF both in vitro and in a transfect system in PBMCs with RA,OA patients and health controls.
**Conclusions:** Our data indicate that LILRA3 can promote done destruction through MAPK and NF–κB signaling pathway. These findings may give us some clues for the study on the pathogenesis of RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1897

## AB0102 IGURATIMOD (T-614) SUPPRESSES RANKL-INDUCED OSTEOCLAST DIFFERENTIATION AND MIGRATION IN RAW264.7 CELLS VIA NF-κB AND MAPK PATHWAYS

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**Background:** Iguratimod (T-614) has been confirmed as a highly efficacious and safe novel disease-modifying anti-rheumatic drug (DMARDs) for rheumatoid arthritis therapy in China and Japan due to its potent anti-inflammation effect.
**Objectives:** Here, we investigate the effects of Iguratimod on osteoclast differentiation, migration and function.
**Methods:** The effect of Iguratimod on osteoclastogenesis, migration and bone resorption were assessed by TRAP staining, transwell migration assay and osteologic discs, respectively. Relative expressions of osteoclastic related genes, chemokines and transcription factors were assessed by reverse transcription polymerase chain reaction (RT-PCR) and signaling pathways were analyzed by western blotting.
**Results:** Iguratimod significantly inhibits osteoclast differentiation, migration and bone resorption in RANKL-induced RAW264.7 cell in a dose-dependent manner. The expressions of osteoclastic related genes including TRAP, CTSK and CTR were increased in RAW264.7 cell upon RANKL stimulation but were obviously suppressed in the presence of Iguratimod. RANKL induced the expression of chemokines including CCL7, CCL4 and CCL12 and osteoclastic related transcription factors of c-Fos, c-JUN and NFATc1 could be significantly inhibited by Iguratimod in a dose dependent manner. Western blotting indicated Iguratimod could suppress the activation of MAPKs and NF-κB pathway in RANKL induced osteoclastogenesis in RAW264.7.
**Conclusions:** These findings revealed a directly inhibitory role of Iguratimod on osteoclast formation and function, which is distinct from previous report, suggesting Iguratimod provide a unique therapeutic strategy for RA and especially in light of preventing bone destruction.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5679

## AB0103 HUMORAL IMMUNITY TO FOOD ANTIGENS IN PATIENTS WITH EARLY STEROID AND DMARD NAÏVE RHEUMATOID ARTHRITIS

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**Background:** The presence of different antibodies in the serum of patients with rheumatoid arthritis (RA) before detectable joint inflammation points to a source of RA autoimmunity different then synovium. Recent data [1] support that RA-related autoimmunity may originate at a mucosal site: oral, lung and gastrointestinal mucosa. Special emphasis is on the antibodies of IgG class and their effector function of binding to Fc gamma receptors (FcRγ) on many different immune cells.
**Objectives:** The aim of this study was to investigate the presence and possible association between humoral immunity to food antigens and disease activity in patients with early treatment naive RA (eRA). Also, we examined the expression of FcRγ (CD16) on lymphocytes, NK cells and granulocytes in peripheral blood of these patients and its possible relation with humoral food immunity.
**Methods:** Study included 50 patients newly diagnosed with RA, who had not received any corticosteroid or DMARD therapy and whose conventional radiographs of hands and feet showed no structural damage. Control group consisted of 106 healthy volunteers. The presence and intensity of serum IgG, IgA and IgM antibodies to cow's milk proteins (CMP) and gliadin were determined by ELISA assays. The expression of CD16 and CD56 on immunocompetent cells of peripheral blood was performed by flow cytometry.
**Results:** Significantly enhanced levels of IgG antibodies to gliadin were detected in patients with eRA in comparison with healthy controls (p=0.028). Levels of IgA and IgM antibodies to CMP were significantly higher in sera of eRA patients compared to healthy controls (p=0.0009, p<0.0001, respectively). The percentage of CD16+ lymphocytes and CD16+CD56+ cells in peripheral blood were significantly decreased in patients with eRA compared to healthy controls

($p<0.0001$, $p<0.0001$, respectively). No significant difference in the percentage of CD16+ granulocytes in peripheral blood between the examined groups was detected, however significantly higher mean fluorescence intensity (MFI) of CD16 on granulocytes was detected in patients with eRA ($p<0.0001$). MFI of CD16 expression on lymphocytes was significantly increased in patients with eRA in comparison with healthy individuals ($p=0.004$). The significant decrease in the percentage of lymphocytes in patients with eRA ($p=0.002$) was detected. Positive correlation was found between IgG anti-gliadin antibodies and CD16 expression on lymphocytes ($r=0.360$, $p=0.025$). Furthermore, these antibodies inversely correlated with the percentage of CD16+ granulocytes ($r=-0.326$, $p=0.045$).

**Conclusions:** Significantly higher levels of antibodies to food antigens like gliadin and CMP are present in sera of patients with eRA and could have possible role in the early stages of this disease through activating IgG receptors on immunocompetent cells.

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## AB0104 ROLE OF CD14+ AND CD16+ MONOCYTE SUBTYPES IN THE ATHEROTHROMBOSIS ASSOCIATED WITH RHEUMATOID ARTHRITIS: EPIGENETIC MECHANISMS INVOLVED

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**Background:** Monocytes play a key role in the pathogenesis of the cardiovascular disease (CVD). Three monocyte subsets have been described based on their CD14 and CD16 profile, with different actions in the vascular pathology. The distribution of these monocytes subsets and their epigenetic profile associated with CVD in rheumatoid arthritis (RA) remain unravelled

**Objectives:** To functionally characterize the monocytes subsets in RA patients and analyze their role in the endothelial dysfunction, altered oxidative status and proinflammatory/prothrombotic profile associated to RA.

**Methods:** Fifty RA patients and 30 healthy donors were included. Endothelial function was measured through post occlusive hyperaemia using Laser-Doppler. Carotid intima media thickness (CIMT) was used as atherosclerosis marker. The monocyte subsets were characterized by flow cytometry and isolated by immunomagnetic selection. Proinflammatory cytokines, peroxides levels and cellular activation markers were analyzed. NanoString nCounter miRNA Expression Array was used to profile 800 microRNAs in isolated CD14+ and CD16+ monocytes. PCR array gene expression was used to analyze the expression of 84 genes related to atherosclerosis. Target genes of the differentially expressed miRNAs were identified by using the Ingenuity Pathway Analysis Software (IPA). The predicted microRNA-mRNA interactions were characterized by the microRNA Target Filter tool of IPA. The resulting identified interactions were revalidated by RT-PCR on the whole cohort of RA patients

**Results:** CD16+ monocytes were significantly extended in RA patients. These subsets had increased protein and gene expression of proinflammatory cytokines, markers of atherosclerosis and peroxide levels. miRNA expression profiling showed that 38 miRNAs were significantly altered ($\geq$2 fold) in CD14+ RA monocytes compared to CD16+ RA monocytes. Functional classification of those miRNAs showed a preponderance of targets mRNAs involved in the pathological process of RA such as inflammatory state, immune response and CVD. RA patients had impaired endothelial function, with a reduced perfusion value after ischemia. Increased CD16+ monocytes and reduced CD14+ cells percentage were associated with a pathologic CIMT. Clinical parameters strongly correlated with endothelial dysfunction, decreased percentage of CD14+ monocytes and increased number of CD16+ subsets.

**Conclusions:** 1) RA patients exhibit an increased number of CD16+ monocytes, which display a specific atherogenic and inflammatory pattern directly associated to the autoimmune profile, the progression of the disease and the altered microvascular function. This atherogenic profile might be associated with an altered epigenetic pattern. That data suggest that CD16+ subpopulation might play a key role in the CVD pathogenesis associated with RA.

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## AB0105 INHIBITION OF A STREPTOCOCCAL CELL WALL MODEL OF ARTHRITIS FLARE BY REPOSITORY CORTICOTROPIN INJECTION

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**Background:** Repository corticotropin injection (RCI), a melanocortin peptide preparation, is FDA approved as adjunctive therapy for short term administration to tide patients over acute episodes or exacerbations of rheumatoid arthritis (RA), but has not been studied in an animal model of arthritis flare.

**Objectives:** To test the efficacy of RCI in a *Streptococcal* cell wall-induced model of arthritis flare in rats [1].

**Methods:** Dark Agouti rats were primed on day 0 by an intra-articular injection of a proteoglycan/polysaccharide (PGPS) preparation from *Streptococcal* cell wall into the right ankle and vehicle (phosphate buffered saline) into the left. On days 14 and 28, transient arthritic flares were induced in the ankle by intravenous injection of PGPS. Caliper measurements of the right and left paw diameters were made daily beginning on the day of induction of the first flare. RCI was administered subcutaneously at doses of 40, 160, and 400 U/kg beginning day 1 after induction of the first flare and dosed every other day until animals were sacrificed on day 35, after recovery from the second flare. Arthritis was assessed by measuring the diameter difference between the right (PGPS injected) and left ankles. Histologic analysis was performed on the paws obtained at sacrifice (day 35).

**Results:** RCI dose-dependently inhibited paw swelling in rats after induction of both the first and second arthritic flares. Doses of 160 U/kg and 400 U/kg inhibited physical signs of the first flare by 69% ($p<0.01$) and 86% ($p<0.001$) and inhibited the second flare by 87% ($p<0.0001$) and 90% ($p<0.0001$), respectively. Histologic analysis showed that inflammatory cell infiltration into joints was significantly decreased by 53% ($p<0.01$) and 77% ($p<0.0001$) at the 160 and 400 U/kg doses of RCI, respectively, and that total histopathologic damage scores, which included measures of pannus, cartilage damage, bone resorption and periosteal bone formation were significantly reduced by 78% and 91% at 160 and 400 U/kg, respectively.

**Conclusions:** These preclinical results demonstrate the efficacy of RCI in an animal model of RA flare and support the potential clinical benefit of the drug for the treatment of inflammatory arthritis exacerbations.

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**Disclosure of Interest:** P. Higgins Employee of: Mallinckrodt, D. Decker Employee of: Mallinckrodt, P. Becker Employee of: Mallinckrodt

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## AB0106 CELECOXIB INDUCES BOTH APOPTOTIC AND AUTOPHAGIC CELL DEATH IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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**Background:** An aggressive proliferation of synovium is the hallmark of rheumatoid arthritis (RA). Previous studies suggested that resistance of fibroblast-like synoviocytes (FLS) to apoptosis is involved in synovial hyperplasia in the patients with RA. Recently, the possibilities that autophagy regulates apoptosis resistance and hyperplasia of FLS were also presented. Selective cyclooxygenase-2 (COX-2) inhibitor, celecoxib, has been reported to affect apoptosis or autophagy in various cancer cells.

**Objectives:** The aim of this study is to investigate the influence of celecoxib on viability of RAFLS and to reveal how celecoxib affects the viability of RAFLS.

**Methods:** RA synovial tissue was obtained from patients during total knee replacement surgery or arthroscopy. FLS was cultured with celecoxib, caspase inhibitor (z-VAD-fmk) or autophagy inhibitor (3-methyladenine; 3-MA, bafilomycin A1; bafi A1, chloquine; CQ). Cell viability was measured by MTS assay and by cell count using trypan blue staining. The expression of autophagy flux (LC3, p62) and apoptosis related protein (caspase3 and poly (ADP-ribose) polymerases (PARP)) was analyzed by western blot.

**Results:** Celecoxib dose-dependently decreased cell viability (mean IC50 of 120 $\mu$M) of RAFLS. Activation of Caspase 3 and PARP cleavage were observed in RAFLS after the treatment with celecoxib. Combination treatment with caspase inhibitor and celecoxib increased cell viability than a single treatment with celecoxib. Celecoxib also increased the expression of LC3II and p62 in RAFLS. Treatment with autophagy inhibitor (3-MA, bafi A1, CQ) restored viability of RAFLS which was decreased by celecoxib.

**Conclusions:** This study demonstrates that both apoptosis and autophagy contribute to celecoxib-induced cell death in RAFLS. Further studies to identify the effects of celecoxib on chronological sequence of autophagy and apoptosis in RAFLS are need.

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## AB0107 ASSOCIATION HETEROGENEITY MAPPING IDENTIFIES AN ASIAN-SPECIFIC ASSOCIATION OF THE GTF2I LOCUS WITH RHEUMATOID ARTHRITIS

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**Background:** Genetic association studies using multiple ancestral cohorts have revealed a large overlap of rheumatoid arthritis (RA)-risk alleles among different ancestries, but there are some exceptional loci showing heterogenic association among populations.
**Objectives:** Here we investigated genetic variants with distinct effects on the development of RA in Asian and European populations.
**Methods:** Ancestry-related association heterogeneity was examined using the association data from large Korean (n=9,299) and European (n=45,790) rheumatoid arthritis cohorts with Immunochip and genome-wide SNP array data. Novel disease associations detected in Koreans were validated using two independent Asian cohorts (n=5,166) and a meta-analysis.
**Results:** We identified significant heterogeneity between the two ancestries for the common variants in the *GTF2I* locus and showed that this heterogeneity is due to an Asian-specific association effect ($P_{Heterogeneity}$ =9.6×10$^{-9}$ at rs73366469 [$OR_{Meta}$ =1.37 and $P_{Meta}$ =4.2×10$^{-13}$ in Asians; $OR_{Meta}$ =1.00 and $P_{Meta}$ =1.00 in Europeans]) in RA. Trans-ancestral comparison and bioinfomatics analysis revealed a plausibly causal SNP (rs117026326; linked to rs73366469), whose minor allele is common in Asians but rare in Europeans.
**Conclusions:** We identified the largest effect on Asian RA across human non-HLA regions at *GTF2I* by heterogeneity mapping followed by replication studies, and pinpointed a possible causal variant.
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*Drs. Kwangwoo Kim and So-Young Bang contributed equally to this work.
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## AB0108 RESVERATROL INHIBITS CANONICAL WNT SIGNALING AND AMELIORATES EXPERIMENTAL ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an inflammatory joint disorder, the progression of which leads to the destruction of cartilage and bone. Wnt signaling pathway act several important biological functions, such as cell differentiation, embryonic development, limb development and joint formation. Accumulated evidence has suggested that this signaling pathway plays a key role in the FLS activation, bone resorption and joint destruction in RA.
**Objectives:** The purpose of this study was to investigate the activity of Wnt/β-catenin pathway in collagen-induced arthritis (CIA) in rats, and to research the therapeutic effect of resveratrol in this arthritis model.
**Methods:** Thirty Wistar albino female rats were randomized to 3 groups (n=10 in each group): Group-I as the control group, Group-II as the arthritis (sham) group, and Group-III as the Resveratrol group. Arthritis was induced by intradermal injection of chicken type II collagen combined with incomplete Freund's adjuvant. One day after the onset of arthritis, resveratrol (20 mg/kg/day) was given via oral gavage, until they were killed on day 29. Animals were sacrificed at the 15th day after the onset of arthritis. The paws of the rats were obtained for further analysis. Perisynovial inflammation and cartilage-bone destruction were determined histopathologically in the paws. Tissue Wnt-5a, axin-2, DKK1, mitogen-activated protein kinase (MAPK), Src tyrosine kinase and signal transducer and activator of transcription-3 (STAT3) mRNA expressions were determined by real-time polymerase chain reaction (RT-PCR).
**Results:** Arthritis was clinically developed at 12 to 13 days after the injection of collagen (Fig. 1a). The 29th day scores were decreased in the paricalcitol and pyrvinium groups compared to the own 13th day score ($p<0.05$ for both), while it was increased in the sham group ($p<0.05$). Histopathological analysis demonstrated the extensive perisynovial inflammation and marked cartilage-bone destruction in sham group rats. Resveratrol treatment decreased the perisynovial inflammation and cartilage-bone destruction in the paws. Moreover, the tissue mRNA expressions of Wnt5a (11 folds), axin-2 (22 folds) and DKK1 (3 folds) were increased in the sham group compared to the control group (Fig. 1b-d). However, resveratrol treatment decreased their expressions.

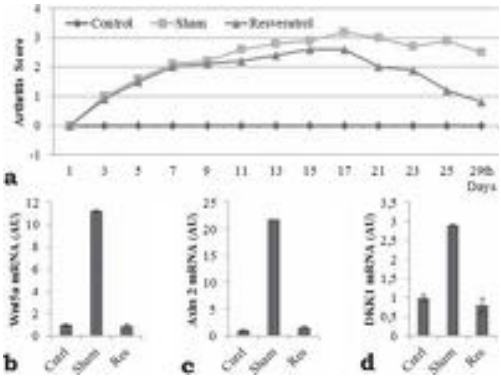


Figure 1. Assessments of daily arthritis score (a) and the tissue mRNA expressions of Wnt5 (b), axin 2 (c) and DKK1 (d) in the all study groups.

**Conclusions:** The present study shows that Wnt signaling pathway is active in CIA model. Resveratrol inhibits Wnt pathway and ameliorates CIA.
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## AB0109 THE LUNG MICROBIOME IN RHEUMATOID ARTHRITIS AND ASSOCIATED LOCAL/SYSTEMIC AUTOIMMUNITY

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**Background:** Airway abnormalities and increased lung tissue citrullination is found in both RA patients and individuals at at-risk for the development of disease. Recent data suggest that the gut (*Prevotella copri*) and oral (*Porphyromonas gingivalis*) microbiome might potentially contribute to the priming of an aberrant systemic immune response characteristic of RA.
**Objectives:** Our objective was to study whether RA lung microbiome contains distinct taxonomic features associated with local and/or systemic autoimmunity.
**Methods:** Bronchoalveolar lavage (BAL) samples from 20 subjects with RA, 10 with sarcoidosis and 28 healthy controls were obtained by research bronchoscopy. 16S rRNA sequencing was performed to define microbiota composition. Autoantibodies, including anti-CCP, RF and ACPAs were also measured in sera of RA subjects.
**Results:** The 16s sequencing data showed similar alpha/beta diversity between RA and sarcoid groups, but significantly different from healthy (ANOSIM test; p=0.002 and 0.021 for healthy vs RA and healthy vs sarcoid, respectively). Taxonomic comparison between groups was performed using LEfSe, which revealed several significant differences. RA BALF samples had a decrease in the families *Actinomycetaceae (*$P<0.0001$*) and Spirochaetaceae (*$P=0.0009$*)* compared to healthy. *Burkholderia* was significantly decreased in both RA and sarcoidosis compared to controls. The genus *Treponema* (also highly associated

with periodontitis) was exclusively found in healthy subjects' BALF ($P<0.01$ vs RA). RA disease activity was positively correlated with *Micrococcus* and *Renibaterium* at the genus level, and with various OTUs belonging to *Pseudonocardia* and *Xanthomonadaceae* whereas, the genus *Veillonella* and unclassified *Oxalobacteraceae* had a negative correlation. Levels of local autoantibodies i.e., anti-CCP2 correlated positively with the genus *Corynebacterium*, *Megasphera* and *unclassified Comamonadaceae*. Circulating anti-CCP (IgA isotype), had a positive significant correlation with relative abundance of BALF *Enhydrobacter* and unclassified *Bradyrhizobiaceae* (P=0.015 and 0.004, respectively). A modest association with erosive disease was observed with the presence and abundance of *Pseudonocardia* in the RA BALF (85% of erosive RA patients vs. 23% of non-erosive RA; P=0.019).
**Conclusions:** Despite the relatively small number of samples analyzed, several taxonomic differences were noted between groups. Correlations between relative abundance of specific taxa in RA BAL with serum autoantibodies (i.e., anti-CCP) support an association between the lung microbiome and the host immune phenotype in RA. Further evaluation of the functional aspects of this microbiome may provide insights into its possible contribution to RA.
**Disclosure of Interest:** None declared
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## AB0110 THE PROTEASOME IS RELATED TO MUSCLE WASTING IN EXPERIMENTAL ARTHRITIS AND IS ALTERED BY ETANERCEPT TREATMENT

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**Background:** Rheumatoid arthritis is an autoimmune inflammatory disease associated with systemic complications like fatigue and muscle wasting. Muscle wasting could be related to the activation of the ubiquitin-proteasome system.
**Objectives:** To evaluate muscle loss and involvement of the proteasome in collagen-induced arthritis (CIA), with or without treatment with methotrexate or a TNF inhibitor (etanercept).
**Methods:** Male DBA1/J mice were divided into 4 groups (n=8 each): CIA (saline); ETN (etanercept, 5.5 mg/kg) and MTX (methotrexate, 35 mg/kg), treated twice a week for 6 weeks, and a healthy control group (CO). Treatments started one week after booster injection. Clinical score, hind paw oedema, and body weight were analysed during the experimental period. Gastrocnemius muscles (GA) were weighted after death and used to quantify proteasome activity, protein levels and mRNA expression of its subunits by Western blot and rtPCR. Significance was considered when $p\leq0.05$.
**Results:** Treatments slowed disease development, observed through smaller clinical score and hindpaw edema in ETN and MTX. ETN presented higher body weight (21±1.0g) compared to MTX (19±1.3) at weeks 5 and 7. GA weight was heavier in ETN (105±12g) than CIA and MTX (80±10 and 79±10g, respectively), a result also observed after normalization of muscle with body weight. Of note, the catalytic properties of 26S proteasome showed an increase of caspase-like activity in CIA and MTX groups (150 and 200% of activity, respectively). Furthermore, muscles of MTX treated animals showed higher protein levels for proteasomal subunits PSMB8 and PSMB9 and increased gene expression for Psmb5, Psmb8 and Psmb9. In contrast, expression of Psmb6 was decreased and of Psmb9 was enhanced in CIA.
**Conclusions:** Although both drugs improved the disease score, ETN presented a stronger anti-arthritic effect and was the only treatment able to partially prevent muscle wasting. In contrast to ETN, MTX treatment did not prevent muscle loss due to CIA accompanied by persistent up-regulation of proteasome expression and activity.
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**Disclosure of Interest:** None declared
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## AB0111 THE UNDERLYING PATHOGENIC EFFECT OF IMPARED DNASE I ACTIVITY ON RHEUMATOID ARTHRITIS

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**Background:** Aberrant formation of neutrophil extracellular traps (NETs) play important role in the pathogenesis of rheumatoid arthritis (RA) and Deoxyribonuclease I (DNase I) can remove NETs in vivo.
**Objectives:** We aimed to investigate the underlying pathogenic effect of DNase I on RA.
**Methods:** Serum DNase I activity was measured by radial enzyme diffusion method in 83 RA patients and 60 healthy volunteers, synovial fluid (SF) from 27 RA patients and 38 other inflammatory arthritis patients was measured by the same way. The SF cfDNA level was measured by Pico Green Kit. Correlation analysis were performed between DNase I activity, cfDNA level and clinical parameters of RA patients.
**Results:** Serum DNase I activity was significantly lower in RA group than in healthy control group [0.2913 (0.2029, 0.4064)U/ml vs 0.3980 (0.2864, 0.5484)U/ml, $P<0.001$] and negatively correlated with ESR (r=-0.2862, P=0.0122), CRP (r=-0.2790, P=0.0184) and neutrophil cell counts (r=-0.287, P=0.011). SF DNase I activity in RA group, ankylosing spondylitis (AS) group and gouty arthritis (GA) group were almost negative. SF cfDNA level in RA group was significantly higher than that in OA group [40.00 (12.47, 163.22) ug/ml vs 9.27 (4.62, 17.58) ug/ml, P=0.002], but there were no significant difference when compared to AS group [36.80 (4.84, 84.82) ug/ml, P=0.428] and GA group [156.72 (89.81, 257.11) ug/ml,P=0.132]. In inflammatory arthritis patients, SF cfDNA level was positively correlated to ESR (r=0.4106, P=0.0116)and CRP (r=0.5747, P=0.0002).
**Conclusions:** Impairment of DNase I activity may be responsible for the enhanced NETs generation and involve in the pathogenesis of RA.
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**Disclosure of Interest:** None declared
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## AB0112 CSD-125, A SOFT CORAL-DERIVED ANTI-INFLAMMATORY COMPOUND, ATTENUATES JOINT DESTRUCTION VIA OSTEOCLASTOGENESIS IN A TYPE II COLLAGEN-INDUCED ARTHRITIS RAT MODEL

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**Background:** Rheumatoid arthritis (RA) is a common rheumatic disease that is characterized by synovial inflammation of the synovial tissue that lines the joints [1]. Osteoclasts become active and mature by stimulation of inflammatory cytokines such as macrophage colony-stimulating factor (M-CSF), interleukin-1b (IL-1b), interleukin-17A (IL-17A), and tumor necrosis factor-a (TNF-a), and also play a critical role in the bone destruction in RA [2]. Soft corals have been considered an important resource of anti-inflammatory agents that may be beneficial for treating inflammatory diseases [3–5].
**Objectives:** In this present study, we investigated the therapeutic effects of CSD-125, a soft coral-derived compound in type II collagen-induced arthritis (CIA), via its role in the anti-osteoclastic pathway.
**Methods:** A rat model of CIA was established, and knee joint tissue destruction was evaluated in rats treated with and without CSD-125 by the RA index, histopathology, immunohistochemistry, and western blotting. We also analyzed the level of pro-inflammatory cytokines such as M-CSF and IL-17A in the blood serum.
**Results:** The results demonstrated that CSD-125 significantly attenuated CIA-induced RA progression in rats. CSD-125 also decreased the expression of osteoclast-related proteins, including cathepsin K, matrix metalloproteinases-9, matrix metalloproteinases-2, cluster of differentiation molecule 11B, nuclear factor of activated T cells, cytoplasmic 1 (NFATC 1), and triggering receptor on myeloid cells 2 (TREM 2), in multinucleated cells. Moreover, CSD-125 reduced the number of cells showing positive expression of IL-17A, IL-1b, and TNF-a, phospho-extracellular signal-regulated kinases (p-ERK), phospho-c-Jun N-terminal kinase (p-JNK), and phospho-p38 (p-P38) in the synovial tissue of CIA-rats. The levels of M-CSF and IL-17A also decreased following administration of CSD-125 to CIA-rats.
**Conclusions:** These results provide strong support that CSD-125 could attenuate the joint destruction in type II CIA, likely through inhibition of osteoclast activation.
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## AB0113 THE SERUM AND SYNOVIAL FLUID LEVELS OF COLD-INDUCIBLE RNA-BINDING PROTEIN (CIRP) IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The cold-inducible RNA-binding protein (CIRP) is 18 kDa protein of the glycine-rich RNA binding protein (GRP) family, and these proteins function as RNA chaperones to facilitate translation. Extracellular CIRP is a recently identified endogenous proinflammatory mediator and damage-associated molecular pattern molecules (DAMP) that triggers inflammatory responses in sepsis and inflammatory bowel disease.
**Objectives:** This study was planned to investigate the relationship between CIRP and rheumatoid arthritis.
**Methods:** Peripheral blood and synovial fluid were collected from 15 patients with rheumatoid arthritis (RA) and 16 patients with osteoarthritis (OA). The concentration of CIRP was measured by sandwich Enzyme-Linked Immunosorbent Assay (ELISA).
**Results:** The concentration of serum CIRP was significantly elevated in RA patients group (RA patients=26.39±10.48 pg/ml, OA patients=17.14±7.24 pg/ml, p=0.009). Furthermore, the RA patients group showed significantly higher CIRP concentration than the OA patients group in synovial fluid (153.56±108.93 pg/ml vs. 23.63±16.18 pg/ml, p<0.001) (Fig.1).
The mean concentration of synovial fluid CIRP was significantly higher than that of serum in RA patients group (Serum concentration=26.39±10.48 pg/ml, Synovial fluid=153.56±108.93 pg/ml, p<0.001). Also, we found the tendency that the CIRP concentration of synovial fluid was significantly higher than that of serum in same patient (P=0.025) (Fig.2).
DAS28-ESR and DAS28-CRP were positively correlated with synovial fluid concentration of CIRP (DAS28-ESR: r=0.582, p=0.023, DAS28-CRP: r=0.541, p=0.037, by correlation analysis).

**Fig.1. The concentration of CIRP was increased in RA patients. a: The serum concentration of CIRP was higher in RA patients than in OA patients. b: The synovial fluid concentration of CIRP was significantly higher in RA patients than in OA patients. (Mean ± Standard Error of the Mean; SEM) * p<0.05, ** p<0.001**

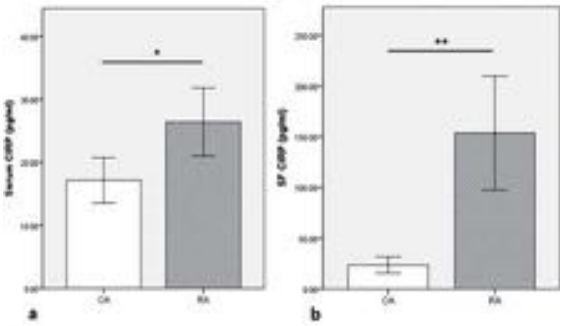
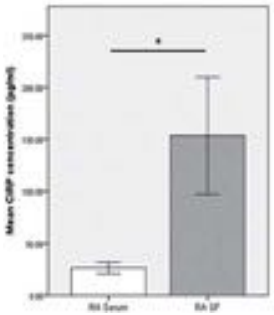



**Fig.2. The synovial fluid concentration of CIRP was elevated in RA patients. The concentration of CIRP was significantly increased in the synovial fluid of RA patients (RA SF). Data are shown as the Mean ± SEM. * p<0.05**




**Conclusions:** The serum and synovial concentration of CIRP in RA patients was increased compared to OA patients. Also synovial concentration of CIRP in RA patients correlated well with the disease activity, i.e. the DAS28-ESR/CRP. Based on these results, the CIRP mediates the inflammation and is potential marker for synovial inflammation.
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## AB0114 PTEN EXPRESSION IN FIBROBLAST-LIKE SYNOVIOCYTES OF RHEUMATOID ARTHRITIS

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**Background:** Fibroblast-like synoviocytes (FLS), with some tumor-like characters, play a key role in the pathogenesis of rheumatoid arthritis (RA) [1]. Phosphatase and tensin homolog (*PTEN*) is a tumor suppressor gene, and its mRNA expression has been reported to be absent in the lining layer of RA synovium, which is supposed to contribute to the invasive behavior of RA-FLSs [2,3]. It has been demonstrated in various kinds of tumor cells that the PTEN protein is a negative regulator of the PI3K/Akt signal pathway [4]. However, data of the PTEN protein level in RA-FLSs and its effect on the phosphorylation status of Akt (Thr308) is limited.
**Objectives:** To investigate the expression of *PTEN* gene in cultured human RA-FLSs and its effect on Akt (Thr308) phosphorylation status.
**Methods:** FLSs were isolated from synovial tissues obtained from patients with RA, osteoarthritis (OA) or joint trauma during joint replacement surgery or arthroscopy, and each group contains 3 patients. The mRNA expression of *PTEN* was detected by RT-qPCR. The protein levels of PTEN, pAkt (Thr308) and total Akt, were measured by western blotting. The phosphorylation status of Akt was determined by protein expression ratio of pAkt (Thr308)/total Akt.
**Results:** The expression of PTEN mRNA was significantly lower in RA-FLSs compared with OA-FLSs and joint trauma-FLSs ($P<0.01$), while no statistically significant difference was observed between those of OA-FLSs and joint trauma-FLSs ($P>0.05$). Similarly, the PTEN protein level in RA-FLS was much lower than OA-FLSs and joint trauma-FLSs ($P<0.05$), and there was no difference between the latter two ($P>0.05$). Moreover, the phosphorylation level of Akt (Thr308) in RA-FLSs was significantly higher than those in the other two control groups ($P<0.01$), and that in OA-FLSs was much lower than joint trauma-FLSs ($P<0.01$).
**Conclusions:** The mRNA and protein expression of *PTEN* are both decreased in cultured RA-FLSs, suggesting that low expression level of *PTEN* is conserved in RA-FLSs out of the inflammatory environment *in vitro* throughout passages. And it may contribute to the increased phosphorylation level of Akt (Thr308).
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## Spondyloarthritis - etiology, pathogenesis and animal models

### AB0115 DIFFERENTLY ASSOCIATED FREQUENCY OF B LYMPHOCYTE SUBPOPULATIONS WITH DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS COMPARED TO RHEUMATOID ARTHRITIS

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**Background:** Both rheumatoid arthritis (RA) and ankylosing spondylitis (AS) belong to the group of chronic rheumatic diseases with the important role of autoimmune pathogenic mechanisms. However, these forms differ in the major target tissues as well as the intensity of bone and cartilage destruction, with RA being the prototype of "destructive" arthritis affecting peripheral joints and AS being the prototype of "remodeling" arthritis predominantly of the axial skeleton.
**Objectives:** Both forms of arthritis are associated with abnormal immune cell functions, including B lymphocytes. Although several recent studies stressed the role of B lymphocyte subpopulations and autoantibodies in AS, these mechanisms in the AS pathogenesis are significantly less understood compared to RA and other rheumatic autoimmune diseases.The aim of our study was to compare the frequency of B lymphocyte subpopulations between RA and AS patients, and to correlate them with the disease activity.
**Methods:** Mononuclear cells were isolated from peripheral blood of healthy controls (n=30), RA (n=33) and AS (n=18) patients, after obtaining Ethical approval and informed consent from patients. The B lymphocyte phenotype of peripheral-blood mononuclear cells was determined using flow cytometry for the following surface markers: CD19, CD27, IgD, CD32 and CD38. In addition, statistical correlation was assessed to test the association between the frequency of selected B lymphocyte subpopulations and the disease-activity score, DAS28 (Disease Activity Score 28) for RA and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) for AS.
**Results:** Gating strategy applied for flow-cytometry data was set to discriminate between naïve B lymphocytes (CD19+ IgD+ CD27-), unswitched memory B lymphocytes (CD19+ IgD+ CD27+), class-switched memory B lymphocytes (CD19+ IgD- CD27-) and plasmablasts (CD19+ IgD+ CD27hi CD38+). In addition, expression of CD32 (FcgRII receptor) and CD86 (B7-2 co-stimulator), associated with the maturation and activation of B lymphocytes, within these B lymphocyte subsets were assessed. Data analysis showed expanded CD32+ subset among naïve and memory B lymphocytes in RA (16.4±11.6% and 9.8±8.2%) compared to control (4.3±2.7% and 7.6±3.5%) and AS (5.6±2.6% and 5.8±1.9%). Similarly, there were more CD86+ cells among naïve and unswitched memory B lymphocytes in RA (9.0±8.2% and 18.2±8.0%) compared to control (2.8±1.3% and 11.7±5.5%) and AS (4.9±5.9% and 11.6±6.2%). Class-switched memory B lymphocytes were negatively associated with disease activity score in RA ($\rho$=-0.45) but positively in AS ($\rho$=+0.39), whereas the associations were reversed for the population of naïve B lymphocytes ($\rho$=+0.32 for RA and $\rho$=-0.38 for AS).
**Conclusions:** Our results indicate that B lymphocyte-mediated immune response may be important for both RA and AS, but with distinct effector mechanisms. Therefore it is reasonable to suggest that B lymphocyte subpopulations may represent promising cellular targets for the therapeutic interventions in different forms of arthritis.
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### AB0116 INDUCTION OF NETOSIS-MEDIATED CELL DEATH IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease, of unknown aetiology, that mainly affects sacroiliac joints and spine, and is associated with the development of several comorbidities such as atherosclerosis. Recently, a cellular death mechanism, NETosis, has been described in neutrophils that involves the extracellular release of a meshwork of DNA nuclear and granule proteins upon activation by microorganisms and other activating molecules. Excessive generation of these meshworks, as a result of non-infectious inflammatory processes, is associated with the pathogenesis of inflammatory and autoimmune diseases, as well as with the development of atherosclerosis, thrombosis and other cardiovascular complications. Nevertheless, this process has not been described yet in AS patients.
**Objectives:** 1) To analyze the induction of NETosis in AS patients. 2) To evaluate the relationship among NETosis markers and their correlation with disease activity, oxidative stress and endothelial function.
**Methods:** Thirty four patients with AS and 34 healthy donors were included in the study. Disease activity was determined by BASDAI index and, CRP and ERS levels. To evaluate NETosis, purified neutrophils were stained with Sytox and visualized by fluorescence microscopy. In parallel, markers of oxidative stress, inflammation and NETosis were determined in neutrophils by flow cytometry and RT-PCR. Plasma DNA was quantified by fluorimetry. Antioxidant enzyme activities in neutrophils, as well as nitric oxide (NO) and total antioxidant capacity (TAC) of plasma were measured by specific kits. Endothelial function was determined by the post occlusive hyperaemia test using Laser-Doppler.
**Results:** Neutrophils from AS patients displayed a significant increase in NETosis percentage compared to healthy donors that was associated with an increase in plasma DNA in these patients. In parallel, AS patients showed endothelial dysfunction, along with an increase of inflammatory markers (STAT3, TNF-$\alpha$ and IL-1$\beta$ mRNA) in neutrophils. It was also observed an alteration of oxidative status, with an increase of catalase and glutathione peroxidase (GPx) activities, and a reduction of mitochondrial superoxide dismutase (mSOD) activity in neutrophils, as well as an increase in TAC and NO at plasma level.
Correlation and association studies showed that plasma DNA levels positively correlated with CRP, oxidative damage (catalase activity and TAC) and endothelial dysfunction in AS patients.
**Conclusions:** 1) NETosis is a cellular death mechanism occurring in AS patients. 2) NETosis induction is associated with an inflammatory and oxidative profile in neutrophils from AS patients. Thus, NETosis may act as a key mediator in disease progression and endothelial dysfunction in AS patients.
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**Disclosure of Interest:** None declared
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### AB0117 NEW IDENTIFIED IL-23 RECEPTOR GENE MUTATIONS IN ANKYLOSING SPONDYLITIS

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**Background:** The pathogenesis of ankylosing spondylitis (AS) has strongly been associated with the gene *HLA-B27*; however, AS occur only in 1%–5% of HLA-B27-positive individuals and increasing evidence suggests involvement of also non-HLA genes. Previous work has confirmed association with single nucleotide polymorphisms in interleukin-23 receptor (IL-23R).
**Objectives:** The aim of the study is to confirm the association of IL-23R gene polymorphisms with ankylosing spondylitis in Turkish population and to find out possible mutations responsible from this association.
**Methods:** We included 48 AS patients and 48 healthy unrelated individuals. Extracted DNA from patient specimens was amplified with polymerase chain reaction and sequenced.
**Results:** We identified 6 new point mutations at IL-23R gene in patients with AS (Table). 2824DelC mutation (1/41 - 2,4%) was found to be in the intronic region that probably does not have an effect on the protein. 34521GT mutation (1/36 - 3,8%) was located at the exon-intron boundary and changes the exon recognition site. This should be the reason for exon skipping. The mutation probably changes the protein structure and function of IL-23R protein. Ala228Ala (2/42 - 4,8% - p.0,0306) was a silent mutation that does not change the protein structure of the IL23R protein. Ala364Gly mutation (6/43–17% - p.0,074) missense mutation was found at 6 patients as a heterozygote. Ala364Gly mutation looks associated with AS. Leu371Phe mutation (1/43 - 2,3%) was also missense mutation and caused change on the aminoacid. As the last point, Tyr436Stop is a silent mutation that is an early stop truncating the protein 194 aminoacid earlier than the usual process.

**Abstract AB0117** – Table 1. Characteristics of IL-23R mutations determined in patients with ankylosing spondylitis

| Mutation | Function | Position | Homozygote major genotype | No. of homozygote major genotype | Heterozygote genotype | No. of heterozygote major genotype | Homozygote minor minor genotype | No. of homozygote minor genotype | p (genotype) | p (allelic) |
|---|---|---|---|---|---|---|---|---|---|---|
| 2824DelC | Intronic | – | –/– | 40 (97.6%) | –/DelC | 1 (2.4%) | DelC/DelC | 0 | 0.276 | 0.277 |
| 34251 GT | Exon skipping | – | GG | 35 (97.2%) | GT | 1 (2.8%) | TT | 0 | 0.245 | 0.246 |
| ALA(GCA)228ALA (GCC) | Aminoacid change ALA-ALA | 228 aa | GG | 40 (95.2%) | GC | 0 | CC | 2 (4.8%) | 0.126 | 0.0306 |
| ALA(GCT)364 GLY(GGT) | Aminoacid change ALA-GLY | 364 aa | CC | 37 (86%) | CG | 6 (14%) | GG | 0 | 0.074 | 0.085 |
| LEU(TTG)371PHE (TTC) | Aminoacid change LEU-PHE | 371 aa | GG | 42 (97.7%) | GC | 1 (2.3%) | CC | 0 | 0.288 | 0.284 |
| Tyr (TAT) 436 STOP (TAA) | Tyr-Stop | 436 aa | Tyr/Tyr | 43 (97.7%) | Tyr/STOP | 1 (2.3%) | STOP/STOP | 0 | 0.293 | 0.295 |

None of the mutation exist in control group.

**Conclusions:** We have determined 6 new point mutations in 11 patients included. Although two of the mutations probably do not have an effect on the protein, other four mutations cause changes in the protein structure of IL-23R protein. We consider that these mutations probably contribute to the pathogenesis of AS by effecting the functions of the protein.

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**Disclosure of Interest:** None declared

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## AB0118 MIR-29A AND MESSENGER RNA EXPRESSION OF BONE TURNOVER MARKERS IN CANONICAL WNT PATHWAY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Recent studies showed that canonical Wnt pathway and miR-29a play important roles in the pathogenesis of bone formation.
**Objectives:** We studied the levels of miR-29a and bone turnover markers in canonical Wnt pathway in ankylosing spondylitis (AS).
**Methods:** The levels of miR-29a and mRNA of bone turnover markers in canonical Wnt pathway from peripheral blood mononuclear cells were determined by real-time quantitative polymerase chain reaction in 43 patients with AS and 42 healthy controls. Correlation analysis was conducted between the levels of miR-29a and mRNA and clinical measurements using Spearman's correlation test. Serum levels of components of canonical Wnt pathway including Dickkopf-1 (DKK-1), GSK-3β, β-catenin, alkaline phosphatase (ALP) and osteocalcin (OC) were detected using ELISA method.
**Results:** Compared to healthy controls, the levels of miR-29a, Dickkopf (DKK)-1, β-catenin and Runx2 mRNA were significantly higher in AS patients ($p<0.05$). In contrast, the levels of Gsk-3βmRNA was significantly lower in AS patients than that in healthy controls ($p<0.05$). Gsk-3βmRNA was positively correlated withβ-catenin mRNA expression ($p<0.05$). Only DKK-1 mRNA expression was negatively correlated with disease course ($p<0.05$). No significant difference was observed between AS patients and healthy controls for the levels of GSK-3β, β-catenin, ALP and OC, respectively ($p>0.05$).The levels of DKK-1 was significantly higher in AS patients (1914.46±407.82 pg/ml) than that in healthy controls (1729.07±352.86 pg/ml) ($p<0.05$). There was no correlation between high DKK-1 level and any of the clinical parameters contributing to inflammation or bone formation. However, the correlation between OC and disease duration was significant in AS patients ($r=0.323$, $p=0.034$).
**Conclusions:** The osteoblastic marker miR-29a and downstream mRNA of canonical Wnt signaling was upregulated in AS, suggesting their possible role in the new bone formation in AS. Alteration of bone turnover markers in canonical Wnt pathway was observed in AS. This might partially explain the complicated mechanism of bone formation in the disease.

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**Disclosure of Interest:** None declared

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## AB0119 DEREGULATED EXPRESSION OF MIRNAS IN PURIFIED DISEASE RELEVANT BLOOD CELL POPULATIONS IN PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** MiRNAs have been shown to play a critical role in the regulation of both the innate and the adaptive components of the immune system. Deregulated miRNA expression has been found in different inflammatory and autoimmune diseases and may have anti- or pro-inflammatory activities based on their specific target mRNAs. Altered miRNA expression has been detected in several inflammatory diseases such as inflammatory bowel disease (IBD) and psoriasis. Although a few studies concerning correlation between Spondyloarthritis (SpA) and miRNA have been published, no systematic studies in specific cell populations have been reported so far. Moreover, a recently published computational analysis (1) showed a large overlap of active gene regulatory regions with genetic variation associated with SpA for CD4 T cells and CD14 monocytes.
**Objectives:** This study aimed to analyze the miRNA expression pattern in these two disease relevant cell populations of purified CD4 T cells and CD14 monocytes from SpA patients and controls.
**Methods:** SpA patients were monocentrically recruited between October 2014 and May 2015 in the department of rheumatology (Cochin hospital). These patients had an active disease despite NSAIDs intake and were eligible for a TNF-blocker treatment. The mean BASDAI (± SD) was 53.2±23.7; ASDAS 3.2±1.1 and CRP 13±16.6 mg/L. Among these patients, 23 fulfilled the ASAS classification criteria (imaging arm) with sacro-iliitis on X-rays (n=16) or objective signs of inflammation on MRI (n=21). Only one patient fulfilled the clinical arm. We first analyzed the expression of 360 MiRNAs in cell-sorted (MACS) monocytes and CD4 T-lymphocyte populations from these SpA patients and 16 age and sex-matched controls by qPCR using the Exiqon MicroRNA Ready-to-Use Human Panel I on the miRNA-enriched fraction from both CD4+ and CD14+ cell populations.
**Results:** In CD4 cells 6 miRNAs were found to be differentially expressed including miR-491-3p, recently reported to be downregulated in ulcerative colitis, and miRNA-26a, a well know inflammation associated miRNA implicated in both allergic inflammation and autoimmune diseases. In monocytes, 25 miRNAs were found to be differentially expressed including the paradigmatic anti-inflammatory miRNA miR-146a and as the most significantly expressed miRNA, a miRNA involved in the degradation of TNFα.
**Conclusions:** The study is the first to analyze miRNA expression in purified disease-relevant blood cell populations in SpA bringing into evidence a number of interesting miRNAs whose deregulation might contribute to the pathogenesis of the disease. Integration with RNA expression data will allow the functional impact of the miRNA expression changes patterns in the blood cell populations allowing to better understand the molecular changes in SpA and potentially identify novel targets for therapeutic intervention. The validation of 10 differentially expressed miRNAs by qPCR-based assays in additional samples of monocytes and CD4 lymphocytes from independent 12 patients and 12 controls is ongoing.

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## AB0120 CYTOKINE GENE EXPRESSION MRNA PROFILE OF PERIPHERAL BLOOD CELLS IN ANKYLOSING SPONDYLITIS

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**Objectives:** The aim of the present study was to investigate cytokine gene-expression profile into peripheral blood cells from Bulgarian patients with ankylosing spondylitis (AS).
**Methods:** Total RNA from peripheral blood was isolated from 12 healthy controls and 20 patients with AS with a mean disease duration of 13.2 years (range 2.9 - 26). Nine of the patients were only on first-line therapy, a non-steroidal anti-inflammatory drug (NSAID) and 11 were being treated with TNF-blocking agents. cDNAs were used for TaqMan gene expression assays of IL10, TGFB1, IL23A, IL12B, TNFA, IL18, Foxp3 and GAPDH. Relative quantitative evaluation of mRNAs was performed by the comparative ΔΔCt method and results are presented as relative quantity (RQ).
**Results:** From all examined cytokine genes in AS, we found up-regulated most

of them in the following order according to RQ values: IL12B>IL23A>TGFB>IL10>IL18. The gene expression of IL23A and IL12B was significantly higher (p=0.016; RQ=2.04; RQ=2.64, respectively) into peripheral blood cells from AS patients compared to controls, whereas TGFB, IL10 and IL18 were slightly but not significant overexpressed (RQ vary from 1.2 to 1.4.) In contrast, a significant down regulation of TNFA (RQ=0.716; p=0.02) was observed among investigated patients compared to controls. In addition, mRNA expression of FoxP3, a transcription factor driving regulatory FoxP3+ T cells was also down regulated in AS patients (RQ=0.455; p=0.0014). In terms of drug usage, the cytokine gene expression profile between AS patients treated with TNF inhibitors and those without TNF-blocking agents was comparable. A positive correlation was found between gene expression of IL23A with TNFA and IL18 in AS (r=0.67, p=0.001; r=0.456, p=0.038, respectively) and negative correlation between IL23A and TGFB1 (r=-0.58, p=0.006).

**Conclusions:** Our results demonstrated differences in the expression of mRNA encoded regulatory and effector cytokines in peripheral blood cells of AS patients pointed on IL-23 and cytokine related transcription factor FoxP3.

**Disclosure of Interest:** None declared

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## AB0121 DIFFERENTIALLY EXPRESSED MICRORNAS AS CANDIDATE BIOMARKERS FOR DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS

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**Background:** Research on miRNAs as regulators of immune system has fast emerged. miRNA expression profile is believed to be reflective of specific physiologic and pathologic processes and can serve as potential biomarkers of disease activity.

**Objectives:** In the present study, we proposed to test the hypothesis that, "patients with ankylosing spondylitis (AS) have an altered miRNA expression profile compared to control subjects." We also proposed to test whether the expression profile of selected miRNAs identified in the study correlates with disease activity as measured by BASDAI and ASDAS and markers of inflammation:ESR and CRP.

**Methods:** Fifty-one patients ≥18 years of age with AS based on modified New York classification criteria and 23 healthy controls were prospectively recruited. Subjects with malignancy in last 5 years, RA, SLE, evidence of HIV or chronic hepatitis B or C infection were excluded. Patients and controls were screened, consented and peripheral blood samples (5 ml) were obtained. ESR and CRP were measured using routine laboratory methods. Validated Questionnaires to assess disease, and functional activity in AS were administered to patients. Sixty-eight circulating miRNAs in the plasma of all the study subjects were profiled by Firefly Multiplex Circulating miRNA Assay (Abcam, Cambridge, MA) using the Immunology Panel. Forty microliters of plasma samples were first digested using supplied enzyme mix and then the assay was performed following the instructions provided by manufacturer. The assay beads were scanned on BD Accuri C6 flow cytometer. Data were analyzed using Firefly Analyis Workbench (Abcam). Descriptive analyses included continuous variables (the mean ± SD) and the categorical variables percentage. Linear regression analysis was performed to assess the association between BASDAI, BASMI, ASDAS, Rapid 3, ESR, CRP and differentially dysregulated miRNAs in AS patients.

**Results:** There were 34 males/51 with mean age of 49.8± 12.2; 30.6% African-Americans, 47.0% were HLA-B27 positive, 29.4% were negative and 23% indeterminate, and 45% on anti-TNF alpha inhibitors. Mean (±SD) values were: BASDAI score 5.23 (±2.5); BASFI score 4.7 (±2.8); PGA, 5.1 (±2.4); ASDAS-CRP score 3.4 (±1.13); RAPID 3 score 13.76 (±7.21); ESR, 22.4 mm/hr (±22.0) and CRP levels, 1.3 mg/dl (±1.9). Six microRNAs (miR-181b-5p, miR-181a-5p, let-7i-5p, miR-34a-5p, miR-30b-5p and miR-146a-5p) were found to be differentially expressed in AS patients compared to healthy controls ($p<0.05$). miR-181b-5p also showed a significant linear relationship with BASDAI score (p=0.0083) and ASDAS (p=0.0547). Some of the predicted targets of miR-181b-5p according to miRTarBase have been shown to inhibit TIMP-3 which is a tissue inhibitor of matrix metalloproteinase and TMED 7 which is involved in TLR-4 signaling. MicroRNA-181b has also been shown to serve as a potent regulator of downstream NF-κB signaling

**Conclusions:** Patients with AS as compared to controls, have dysregulated expression of selected miRNAs in the plasma; and levels of miR-181b-5p were significantly higher in patients with active disease and showed significant correlation with BASDAI and ASDAS scores. miR-181b-5p is predicted to target genes regulating inflammatory processes and may be proposed as a potential biomarker for disease activity in AS.

**Acknowledgement:** The study is funded by National Institute of Allergy and Musculoskeletal diseases

**Disclosure of Interest:** None declared

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## AB0122 CORRELATION STUDIES BETWEEN ANOCTAMIN 6 GENE POLYMORPHISM AND EXPRESSION AND ANKYLOSING SPONDYLITIS

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**Objectives:** To explore the gene polymorphism of a new susceptibility gene Anoctamin 6 (ANO6) related to disease risk of Ankylosing Spondylitis (AS), and the abnormal expression of ANO6 in AS patients. And provide theoretical basis for ANO6 involved in the pathogenesis of AS.

**Methods:** Direct sequencing was performed to explore disease-related SNP in exon and transcription regulatory region of ANO6 between 417AS patients and 541 healthy controls (HCs), and linkage disequilibrium and haplotype analysis was used with candidate SNP. RT-PCR was performed to test the difference of the expression of mRNA in peripheral blood mononuclear cells (PBMCs) between 40 AS patients and 32 HCs. Immunohistochemistry was employed to discover the difference of protein expression in tendon tissues between 9 AS patients and 5 control subjects.

**Results:** Age and sex were not significantly different between AS cases and controls. Our study found that risk alleles of 5 SNP loci (rs79662606, rs76186361, rs17095830, rs80224086 and rs75712006)had a significant correlation with the susceptibility of AS, and strong linkage disequilibrium among each two of SNP loci. Haplotype analysis dicovered a higher proportion of GTGCG, CATGTA and ACGTA in cases ($p<0.001$). The expression of mRNA of peripheral blood mononuclear cells is 0.49±0.21 in AS cases and 0.86±0.38 in HCs, and the difference is significant ($p<0.001$). The expression of ANO6 protein went up in tendon tissues (p=0.001), and average Histoscore of IHC in 9 AS patients (182.22±30.732) was significantly higher than in 5 controls (62.00±35.637)(P=0.001).

**Conclusions:** ANO6 is the new susceptibility gene of AS and risky haplotype is GTGCG, ATGTA and ACGTA. The risky haplotype have no relationship with phenotype of AS. The expression of mRNA of PBMCs decreased while the expression of ANO6 protein went up in tendon tissues, which suggested that ANO6 might participant in the generation and development of AS.

**Disclosure of Interest:** None declared

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## AB0123 IMMUNOPHENOTYPING OF LYMPHOCYTE POPULATIONS BY HYPERSPECTRAL CYTROMETRY ON PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** The etiology of spondyloarthritis (SpA) is unknown but seems to indicate a link between genetic and environmental factors. Many GWAS studies demonstrated a strong association between IL23R gene and the disease. Moreover, several IL-17 producing lymphocyte populations characterized by the expression of CCR6 (TD4+, TCD8, Tγδ and ILC) are involved in pathophysiolgy of SpA.

**Objectives:** The aim of the study was to identify cells population involved in the disease development:

- By comparing simultaneously cells population TCD4+, TCD8+, Tγδ et ILC (and sub-population ILC3) in patients and healthy controls.

By analysing simultaneously the expression of IL23R and CCR6 by TCD4+, TCD8+, Tγδ and ILC in patients

**Methods:** *Patients:* 10 patients aged from 18 to 50, fulfilling the ASAS criteria and presenting a BASDAI>40 were recruited from diagnosis (between February to may 2015), and compared to 7 healthy subjects paired according to their age.

Methods: The cell analysis was realized by hyperspectrale cytrometry (Sony SP6800®) after cell staining of the mononuclear cells. This emerging technology combines optical spectroscopy and flow cytrometry. The panel used included 13 colours (BV421 conjugated to anti-CD127, V450 conjugated to anti-CD3, V500 conjugated to anti-CD4, BV570 conjugated to anti-CD8, BV605 conjugated to anti-CD62L, BV650 conjugated to anti-CD117, BV711 conjugated to anti-CCR6, BV786 conjugated to anti-NKp46, Percp Cy5.5 conjugated to anti-CD161, PE conjugated to anti IL23R, PE-CF594 conjugated to anti-CRTH2, PE-Cy7 conjugated to anti-TCRgd).

**Results:** The quantitative analysis of cell populations did not show any significant difference between patients and controls: TCD4+ (p=0.2), TCD8+ (p=0.93), Tγδ (p=0.52), ILC (p=0.46) et ILC3 (p=0.71). These results suggested that the functional properties of immune cells (rather than their frequencies) were involved in the disease process. We have demonstrated TCD4+, TCD8+, Tγδ and ILC, all expressed IL23R as well as CCR6. However, we did not notice any difference in expression of these two markers between patients and controls. Then, we showed that in SpA, the level of CCR6 expression was higher in TCD4+ lymphocyte populations (p=0.0031). Similarly, the level of expression of IL23R was higher in TCD8+ lymphocyte ($p<0.0001$).

**Conclusions:** These preliminary results suggest SpA development does not result from the increase of specific cell populations but rather from the modification of

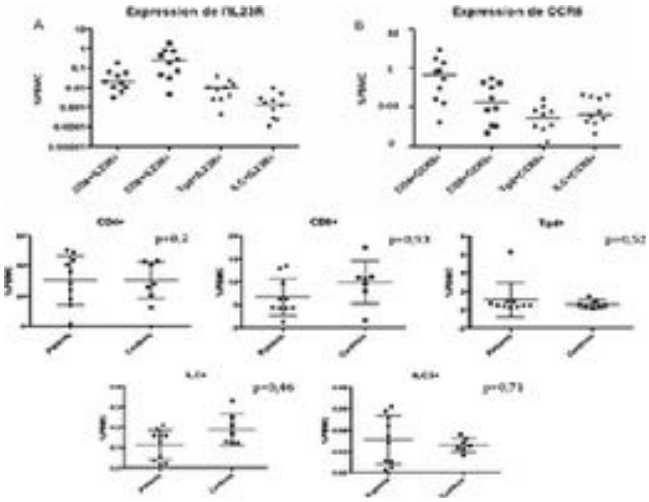


Figure 1. A: IL23R level of expression by TCD4+, TCD8+, Tγδ and ILC on patients. B: CCR6 level of expression by TCD4+, TCD8+, Tγδ and ILC on patients. Fig C: Comparison of TCD4+, TCD8+, Tγδ et ILC and ILC3+ cell populations between patients and controls.

the functional properties of immune cells. The increase of CCR6 expression in TCD4+ and IL23R in TCD8+ shows that these two cell populations take a major part in the disease. In spite of recent datas concerning Tγδ and ILC3, our results did not highlight a major participation of these cells. These prelimanry data need to be confirmed in a larger cohort of patient.

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### AB0124 PERIPHERAL BLOOD MONONUCLEAR CELLS FROM ANKYLOSING SPONDYLITIS PATIENTS DISPLAY AN ATHEROGENIC PROFILE ASSOCIATED WITH DISEASE ACTIVITY AND ENDOTHELIAL DYSFUNCTION

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**Background:** Several studies have demonstrated that Ankylosing Spondylitis (AS), a chronic inflammatory disease of unknown aetiology, is associated with several comorbidities such as cardiac pathology, accelerated atherosclerosis and cardiovascular disease. Yet, the relevance of peripheral blood mononuclear cells (PBMCs) in the development of atherosclerosis in AS patients is not fully known.
**Objectives:** 1) To analyze the gene expression profile associated with the development of atherosclerosis in PBMCs from AS patients. 2) To evaluate the role of PBMCs in the endothelial dysfunction present in AS patients.
**Methods:** Twenty five patients with AS and 25 healthy donors were included in the study. Disease function and activity status were analyzed using the BASFI and BASDAI indexes, respectively. The expression of 84 genes related to atherosclerosis was analyzed in purified PBMCs by PCR array, using total ARN pools of patients and healthy donors. Next, validation of several differentially expressed genes in PBMCs, selected on the basis of their expression levels and relevance in AS pathology, was carried out in our patient and healthy donor cohort. Endothelial function was determined by the post occlusive hyperaemia test using Laser-Doppler. To analyze the role of PBMCs in endothelial function, *in vitro* co-cultures of endothelial cells (HUVEC) and PBMCS from AS patients with different inflammatory status were performed.
**Results:** The endothelial function analysis demonstrated a significant reduction of post occlusive hyperaemia area in AS patients in relation to healthy donors, thus pointing at the presence of a prominent endothelial dysfunction in these patients.
The analysis of the genetic profile in PBMCs showed a significant alteration in the expression of genes related to inflammatory (CCL2, CCL5, CCR1, CCR2, IL1R2, IL1A, IL2, IL5, NOS3, SPP1), and oxidative stress response (APOE, SOD1). An altered expression of genes linked to cellular adhesion (CDH5, ICAM-1, SELL, SPP1, CTGF, FN1, THBS4, TNC), lipid metabolism and transport (ABCA1, APOA1, APOE, FABP3, LPL, LPA, MSR1), cell growth and proliferation (CSF2, SSP1, BCL2, FABP3, FGF2, LIF, CRGF), as well as transcription and apoptosis regulators (PPARA, PPARD, EGR1, BCL2, BCL2A1, BCL2L1) was further demonstrated.
*In vitro* treatment of HUVECs with PBMCs from AS patients with a high pro-inflammatory profile promoted a significant activation of the endothelial cells, which displayed increased expression of adhesion molecules, oxidative stress markers, cytokines and chemokines, all of them associated to the pro-atherogenic profile of these patients.
**Conclusions:** 1) Peripheral blood mononuclear cells from AS patients display an altered expression profile of key genes involved in the development of atherosclerosis. 2) That highly inflammatory PBMCs are responsible, at least partially, for the endothelial dysfunction displayed by AS patients.

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## SLE, Sjögren's and APS - etiology, pathogenesis and animal models

### AB0125 DENDRITIC CELLS DISPLAY ABERRANT TOLL-LIKE RECEPTOR RESPONSES DURING THE ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic, multifactorial autoimmune disease causing multi-organ damages (eg. kidney, heart and skin) and predominantly affects young female. The dysregulation of multiple immune cell populations leads to the development of SLE and the role of dendritic cells (DCs) in the disease pathogenesis has drawn great attention. Plasmacytoid DCs (pDCs) are potent type I interferon (IFN) producers and myeloid DCs (mDCs) are professional antigen-presenting cells. Clinically, the level of serum interferon alpha (IFNa) correlates with the severity of disease with pDC infiltration in nephritic kidney suggested that pDCs may contribute to SLE pathogenesis [1, 2]. Moreover, monocyte-derived mDCs from SLE patients also display activated phenotypes [3]. These findings suggested that different DC subtypes may contribute to the disease development but the exact mechanism is not fully understood.
**Objectives:** This study aimed to investigate whether different DCs subtypes display any abnormalities during the onset of SLE and thus, contribute to SLE pathogenesis.
**Methods:** Using the New Zealand Black /White F1 (BWF1) murine lupus model, the phenotypic and functional properties of different DCs subsets were compared before and after disease onset using flow cytometry, ELISA and qPCR.
**Results:** Symptomatic mice had a lower frequency but similar number of splenic pDCs when compared with its pre-symptomatic counterparts. In terms of activation markers and co-stimulatory molecules, splenic pDCs from symptomatic and pre-symptomatic mice expressed similar levels of CD40, CD80 and MHC II upon Toll-like receptor (TLR) 7 or TLR9 stimulation. The levels of IFNa produced upon TLR9 stimulation were also comparable. For splenic mDCs, both the frequency and number were higher in symptomatic mice. Surprisingly, *ex-vivo* mDCs from symptomatic mice expressed lower levels of CD80 and MHC II but their ability in inducing allogenic T cell proliferation was comparable to mDCs from pre-symptomatic mice. On the other hand, the basal mRNA expressions of TLR7 and TLR9 on mDCs from symptomatic mice were higher. Upon TLR7 or TLR9 stimulation, the induction of IL-10 and CXCL13 mRNA in mDCs from symptomatic mice were also greater than its pre-symptomatic counterparts
**Conclusions:** Results showed that mDCs displayed abnormality upon SLE onset and may contribute to SLE pathogenesis via aberrant TLR signalling. More work should be done to further investigate the exact role of mDCs in SLE pathogenesis.
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**Disclosure of Interest:** None declared
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### AB0126 COMPARISON OF SERUM APELIN, FETUIN-A LEVELS AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH SJÖGREN'S SYNDROME AND HEALTHY SUBJECTS

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**Background:** Apelin is a glycoprotein, adipocytokine that plays an important role in decreasing the vascular inflammation on cardiovascular and metabolic disorders (1). Fetuin-A is also another glycoprotein that can be an acute phase

protein negatively correlates with inflammation (2). Carotid intima-media thickness (C-IMT) may indicate vascular inflammation in primary Sjögren's syndrome (3). However, we do not know the relationship between serum apelin, fetuin-a levels and C-IMT in patients with Sjögren's syndrome.

**Objectives:** To compare of the serum Apelin, Fetuin-A levels and C-IMT in patients with Sjögren's syndrome (SjS) and healthy controls.

**Methods:** Sixty-SjS patients and sixty healthy subjects were enrolled to this study. Serum apelin, fetuin-a levels were measured by ELISA. Concomitant C-IMT evaluations of the participants were performed. The BMI, insulin, HOMA-IR, lipid profiles were studied. Other laboratory parameters, autoantibody profiles, minor salivary gland biopsy scores (Chisholm) were obtained from patient's record files. The study was approved by the local ethics committee.

**Results:** The median levels of apelin were 178.02±55.23 ng/mL in healthy subjects and 98.66±37.25 ng/mL in SjS ($p<0.05$) (Figure 1). The median levels of fetuin-a were 1370.3±81.74 ng/mL in control group and 1613±64.49 ng/mL in SjS group (p=0.021) (Figure 1). The C-IMT was negatively correlated with apelin levels in SjS patients (r= - 0.209, p=0.02). There was no significant correlation between fetuin-a levels and C-IMT in SjS (p=0.08). However, there were significant correletions between C-IMT and hemoglobin-A1c (r=0.353, p=0.005), C3 (r=0.36, p=0.004), C4 (r=0.351, p=0.005).

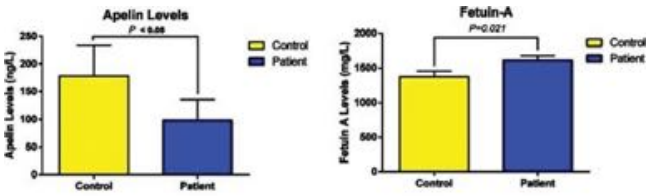



Figure 1. Comparison of serum Apelin and Fetuin-A levels of the patients with Sjögren's syndrome and healthy controls.

**Conclusions:** We found lower serum apelin and higher fetuin-a levels in SjS patients than in healthy subjects. Apelin and fetuin-a may be a new possible surrogate biomarker of inflammation in Sjögren's syndrome.

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**Disclosure of Interest:** None declared

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## AB0127 THE FREQUENCY OF NUEROLOGICAL INVOLVEMENT IN SJÖGREN'S SYNDROME: A SINGLE CENTER EXPERIENCE

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**Background:** Sjögren's syndrome is an autoimmune rheumatic disease that affects many glandular and extra-glandular tissues (1). Autoantibodies (mainly anti-Ro-SS-A and anti-La-SS-B) contribute to playing roles in its clinical pictures (2). Central and peripheral nervous system involvement may be seen as different sign, symptoms and varying its frequencies (2).

**Objectives:** The aim of this study is to investigate the frequency of neurological and other involvement patterns of the Sjögren's syndrome (SjS).

**Methods:** Between June 2015 and December 2015, fifty-eight-SjS patients that following-up at Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department were evaluated in the study. The clinical complaints, glandular and extra-glandular findings, age, sex, other epidemiological data, ANA, RF, anti-Ro/La, C3, C4, IgG, IgA, IgM levels were recorded.

**Results:** The mean age of the patients was 47.8±1.3 years, and the mean age at diagnosis was 46.8±1.2 years. Of the SjS patients, fifty-four (93.1%) were female and four (6.9%) were male. The frequencies of the clinical symptoms were as follows arthralgia in 81%, arthritis in 48.3%, skin dryness in 50%, rashes (including palpable purpuric lesions) in 17.2%, biopsy proven vasculitic lesions in 5.2%. The frequencies of the neurological symptoms were as follows headaches in 32.8%, localized numbness in 5.2%, seizure in 1.7%, paresthesia in 3.4%, diffuse nonfocal symptoms in 1.7% (Figure 1). The total frequency of neurological involvement was 24.1% in SjS patients. Peripheral nervous system involvement in 8.6%. The findings of the magnetic resonans imaging of the patient with neurological involvement were as non-spesific gliotic lesions in 21.4%, periventricular lesions in 28.6%, paranchymal vasculitic lesions in 35.7%, multiple sclerosis-like plaques in 14.3%. There was found that anti-Ro positivity in 58.6%, anti-La in 19.2%, RF in 51.7%, ANA in 48.3%, low complement levels in 15.5%. However, anti-Ro positivity was lower in patient with neurological involvement than in patient without neurological involvement (p=0.025).

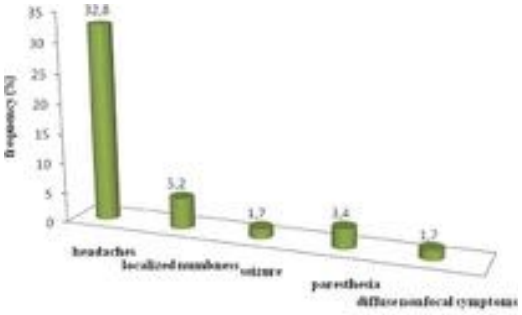



Figure 1. The frequency of clinical symptoms of the patients with Sjögren's syndrome.

**Conclusions:** The neurological involvement should be kept in mind when the patient has been diagnosed as SjS. It can be seen than it is expected. In addition, further studies need to be done to evaluate the role of anti-Ro autoantibody in SjS patients with neurological involvement.

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**Disclosure of Interest:** None declared

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## AB0128 P-SELECTIN ABSENCE TRIGGERS A LUPUS-LIKE SYNDROME IN MICE

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**Background:** Selectins regulate the tethering and rolling of leukocytes before their extravasation. P-Selectin/PSGL-1 interaction is involved in the generation of regulatory T cells[1] and *Psgl-1*$^{-/-}$ mice have altered the colonic lamina propria tolerance/immunity balance[2] and spontaneously develop an autoimmune syndrome similar to human scleroderma[3]. Systemic lupus erythematosus is an autoimmune disease characterized by the production of autoantibodies, immune complexes deposition, complement activation and polyclonal expansion of autorreactive lymphocytes[4,5].

**Objectives:** To characterize the development and progression of a lupus-like syndrome in P-Selectin KO (*P-sel*$^{-/-}$) mice and to analyze P-Selectin expression in skin biopsies of lupus patients.

**Methods:** Mice skin and internal organs were analyzed histologically. Deposition of Immune complexes was determined by immunohistochemistry (IHQ). Levels of serum autoantibodies were quantified by ELISA. Peripheral blood leukocytes and splenocytes were analyzed by flow cytometry. UVB radiation (0.306 J/cm$^2$) was performed to 3 month-old WT and *P-Sel*$^{-/-}$ mice every other day for a week. The expression of P-Selectin in skin biopsies from healthy controls and lupus patients was assessed by IHQ.

**Results:** *P-Sel*$^{-/-}$ mice showed skin alterations characteristic of lupus prone mice. Lupus-like pathogenesis was characterized by deposition of immune complexes in the dermoepidermal junction and renal glomeruli and the presence of anti-dsDNA and anti-Sm autoantibodies in the serum. The histological analysis revealed immune infiltration of the skin, kidney and lung, and tissue structural alterations such as renal infarcts and nonspecific interstitial pneumonia. We found a reduction in the IL-10 producing PBLs, and splenic T cells showed a more effector phenotype. More important, skin biopsies of lupus patients did not show increased expression of P-Selectin, as described for other inflammatory diseases, and the number of vessels expressing P-Selectin was reduced.

**Conclusions:** P-Selectin deficiency leads to a lupus-like syndrome similar to established lupus mouse models. Additionally, we found imbalanced regulatory/proinflammatory leukocytes ratio in peripheral blood and spleen. These results reaffirm the notion that the PSGL-1/P-Selectin axis is crucial for maintaining immune system homeostasis and preventing autoimmunity.

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**Disclosure of Interest:** None declared
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## AB0129 INVESTIGATING THE PHAGOCYTIC POTENTIAL OF NEUTROPHILS FROM JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (JSLE) PATIENTS

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**Background:** Reduced phagocytic clearance of apoptotic cells in Juvenile-onset Systemic Lupus Erythematosus (JSLE) may lead to prolonged exposure of nuclear autoantigen to the immune system. The generation of autoantibodies against nuclear antigens can cause damage in various organs and a diversity of symptoms.
Impaired phagocytosis is also thought to increase the formation of neutrophil extracellular traps (NETs) in a process called NETosis, which may be a potential source of nuclear autoantigens in SLE.
Understanding the phagocytic potential of JSLE neutrophils is therefore important. However only very limited data is published on this subject for neutrophils, especially in juvenile-onset disease.
Transcriptomic analysis of JSLE and control neutrophils by our group found genes for phagocytosis to be differentially expressed between the two groups. These genes included receptors for pathogen recognition (TLR-2), apoptotic material (AnxA3), for microbial size (Dectin-1), for opsonized material (CR3, FcγRIIIb), and adherence to and digesting of the target (CamK1D) as well as genes thought to promote phagocytosis (S100A9).
By investigating the expression of these genes as well as the phagocytic function of JSLE neutrophils, this study aims to provide important insight into the phagocytic potential of JSLE neutrophils.
**Objectives:** To compare the mRNA expression of phagocytosis genes in neutrophils from JSLE and paediatric healthy control patients and the ability of JSLE and control neutrophils to phagocytose different pathogens in the presence of JSLE and control serum.
**Methods:** Neutrophil RNA was extracted from children (diagnosed <17 years) with JSLE (n=9) and paediatric healthy controls (n=8). The mRNA expression of TLR-2, Dectin-1, AnxA3, CamK1D, FcγRIIIb, CR3 and S100A9 were measured using qPCR. The expression of b-actin was analysed as an internal standard. For functional assays the neutrophils were incubated in JSLE or control serum with *E.coli*, *S.aureus* and zymosan fluorescent particles and analysed using flow cytometry and confocal microscopy.
**Results:** Expression (fold change relative to housekeeping gene ± SEM) of TLR-2 (Control 0.013±0.001, JSLE=0.029±0.003, p=0.001) and S100A9 (Control 1.59±0.22, JSLE=2.73±0.33, p=0.02) were both significantly higher in JSLE patients compared to paediatric healthy controls. No difference was observed in CamK1D expression (p=0.94). Increased expression was also observed in the JSLE group of Dectin-1 (p=0.28), AnxA3 (p=0.18), FcγRIIIb (p=0.11) and CR3 (p=0.23), although was not statistically significant.
Early preliminary data of the functional assay indicate a general reduction of phagocytosis in JSLE compared to control neutrophils and decreased phagocytosis of each pathogen in the presence of JSLE serum.
**Conclusions:** Here, we show increased expression of key genes involved in phagocytosis in JSLE neutrophils compared to controls. This may be reflective of the response of the cells to the apoptotic burden observed in these patients. Further assays are currently being carried out to confirm the preliminary observations noted in this study.
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## AB0130 EXPRESSION OF REGULATORY B CELLS IN PERIPHERAL BLOOD OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** It is generally considered that B cells regulate immune response mainly through producing specific antibodies or a variety of cytokines., but recent studies have found that the lack of B cells and CDl9 –/– mice in experimental autoimmune encephalomyelitis (EAE) mouse model is more serious, and in T cell mediated inflammation experiment, CDl9–/– mice show a more serious contact hypersensitivity (CHS). Therefore, it indicated that B cells also play an important role in the negative immune regulation.
**Objectives:** To investigate the expression of regulatory B cells (Bregs) in peripheral blood of patients with systemic lupus erythematosus (SLE) and the function of Bregs in the pathogenesis of SLE.
**Methods:** Thirty-eight active SLE patients, twenty-two inactive SLE patients and twenty healthy controls were enrolled in this study. The expression of IL-10$^+$CD19$^+$Breg and CD19$^+$CD24$^{hi}$CD38$^{hi}$Breg in peripheral blood mononuclear cells (PBMC) was evaluated by flow cytometric analysis. IL-10 was measured in the culture supermatants by ELISA.
**Results:** The expression of IL-10$^+$CD19$^+$Breg in PBMCs of active SLE patients was 1.54±0.64%, lower than those in inactive SLE patients (2.42±0.75)% ($P$<0.001) and healthy controls (4.35±1.00)% ($P$<0.001). And the expression of CD19$^+$CD24$^{hi}$CD38$^{hi}$Breg was 1.26±0.45%, also lower than those in inactive SLE patients (2.01±0.61)% ($P$<0.001) and healthy controls (3.14±0.87)% ($P$<0.001). The level of IL-10 in the culture supermatants of active SLE patients significantly decreased, which was lower than those in inactive SLE patients ($P$<0.05) and healthy controls ($P$<0.001). The percentage of IL-10$^+$CD19$^+$Breg and CD19$^+$CD24$^{hi}$CD38$^{hi}$Breg in peripheral blood of SLE patients was positively correlated with the level of IL-10 in the culture supermatants (r=0.652, $P$<0.001 and r=0.574,$P$<0.001).
**Conclusions:** Expression of IL-10 related Bregs was significantly decreased in peripheral blood of active SLE patients. Bregs may play a critical role in the pathogenesis of SLE.
**Disclosure of Interest:** None declared
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## AB0131 TISSUE BETA 2 GLYCOPROTEIN I IN BRAIN ISCHEMIC INJURY

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**Background:** Thrombosis of arteries in the central nervous system (CNS) represents the most frequent CNS manifestation and the most frequent arterial event in antiphospholipid syndrome (APS). Previous in vivo studies demonstrated that beta2 glycoprotein I (β2GPI) - the main antigenic target for anti-phospholipid antibodies (aPL) - does not localize in brain in resting conditions. However, β2GPI is detectable on the brain vascular endothelium in association with IgG and complement elements in immunized mice treated with lipopolysaccharide. These data suggest that after an appropriate second hit, β2GPI can play a critical role of in APS CNS damage, likely interacting with the complement system. To date, the pathophysiological functions of β2GPI in brain ischemic injury have not been investigated.
**Objectives:** To investigate the presence and the distribution of the activated form of β2GPI in the ischemic brain at different time points.
**Methods:** Eleven-week old male mice underwent focal cerebral ischemia induced by 60' transient middlecerebral artery occlusion (tMCAo), or sham-operation. Mice were sacrified at 90', 6h, 24h, 48h, 4d or 7d after tMCAo to obtain brains and plasma. The presence and time course of β2GPI deposition within the ischemic territory and its spatial distribution relative to blood vessels and brain cells were defined the by *post mortem* immunofluorescence and confocal microscopy. The activated β2GPI was detected by anti-beta2 glycoprotein I minibody (MBB2) – a human monoclonal IgG antibody targeting β2GPI domain I.
**Results:** β2GPI was present in the ischemic brain tissue starting from 90' after ischemic onset and was still detectable at 7d. β2GPI localized within blood vessels and in brain parenchyma at all times. Notably, at 24h β2GPI was mainly extravascular and colocalized with neurons (NeuN positive cells). Sham-operated mice showed only a faint signal for β2GPI.
**Conclusions:** β2GPI is present in its activated conformation in the brain vessels and tissue after experimental cerebral ischemia. It localizes on neurons in brain ischemic areas. These data suggest that an ischemic/inflammatory hit may up-regulate β2GPI tissue presence and may expose the N-terminal domain I of the molecule which is thougth to be the main target for pathogenic aPL.
**Disclosure of Interest:** None declared
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## AB0132 INCREASED CD4+CD69+ T CELLS AND REDUCED CD4+CD25+ TREG CELLS IN MURINE LUPUS-LIKE MODEL

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**Background:** Proliferation of auto reactive T cells and loss of immunological tolerance are features of SLE. In human lupus, enhanced expression of CD69 in peripheral CD4 T cells indicates incremented activation and lower numbers of CD4$^+$CD25$^+$FoxP3$^+$Treg cells contributes to autoimmunity. Pristane-induced lupus murine model has clinical similarities to human disease, nonetheless whether cellular characteristics of this model resemble those of lupus patients remains unknown.

**Objectives:** To analyse the expressions of CD69 activation receptor on CD4 Tcells and of $CD4^+CD25^+FoxP3^+$Treg cells in peripheral blood and spleen of pristane-induced SLE balb/c mice.
**Methods:** Tweenty one female Balb/c mice were analyzed: 13 received a single intraperitoneal 0,5 ml dose of pristane and 8 the same dose of saline. Euthanized mice samples of blood and spleen were collected 120 (T120) days after inoculation of pristane or saline. Mononuclear cells from peripheral blood (PBMC) and splenocytes were obtained by lysis of erythrocytes followed by washings with RPMI medium 1640 and centrifugation, subsequently criopreserved until evaluation by flow cytometry using the appliance GuavaEasyCyteTM HT (Millipore). For this step, cells were unfrozen, washed with RPMI medium 1640 and incubated with monoclonal antibodies against CD3, CD4, CD25, CD28, CD69 and FoxP3 (BD PharmingenTM). The results are expressed as mean ± SD and Mann-Whitney test was used for statistical analysis, being considered significant $p<0,05$.
**Results:** Compared to control, SLE pristane-induced animals presented increase of CD4+CD69+ T cells in blood and in spleen ($p=0.008$ and $p=0.049$, respectively), while the porcentage of Treg CD4+CD25+FoxP3+ was lower in blood and in spleen ($p=0.012$ and $p=0.018$, respectively).
**Conclusions:** Increase of CD4+CD69+ T cell and reduction of CD4+CD25+ FoxP3+ Treg expression suggests activated T CD4 cells and loss of peripheral autotolerance in pristane-induced SLE mice. These alterations are similar to observations in human lupus, in indicating that this model may be useful in evaluating mechanisms of cellular activation, peripheral tolerance and homeostatic immune imbalance involved in LES.
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## AB0133 INCREASED EXPRESSION OF ACTIVATED LY6G+CD11B+CD62L- NEUTROPHILS IN BALB/C MICE WITH PRISTANE INDUCED LUPUS-LIKE DISEASE

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**Background:** Neutrophils are important cells of innate immunity's first line of defense and IL-8 cytokine contributes to its activation. In patients with lupus there is an increase of activated neutrophils in plasma, however data about the contribution of IL-8 on disease development are conflicting.
**Objectives:** To analyze and quantify activated Ly6G+CD11b+CD62L- neutrophils in peripheral blood (PB) and spleen as well to evaluate the production of IL-8 in Balb/c mice with pristane induced lupus-like disease.
**Methods:** We studied 37 mice (13 healthy controls; 24 pristane-induced mice). Pristane-induced mice (PIM) received a single intraperitoneal 0.5ml dose of pristane, while healthy controls received the same dose of saline. Samples of blood and spleen were collected after euthanasia 90 and 120 days after injections; red blood cells were lysed and remaining cells stained with monoclonal antibodies: anti-Ly6G (total neutrophils), anti-CD11b (activated neutrophils) and anti-CD62L (anergic neutrophils) (BDPharmingen™). All cell samples were evaluated by flow cytometry (Guava EasyCyte™ HT, Millipore). Plasmatic IL-8 levels were assessed by ELISA (MyBioSource™). Mann-Whitney's non-parametric test was used for statistical analysis, and $P<0.05$ considered significant.
**Results:** Compared to control, PIM had higher percentage of total neutrophils 90 and 120 days after injection in PB (26.9±2.46 vs. 46.75±5.41%, P=0.002 and 26.9±2.46 vs. 38.52±4.03%, P=0.004) and spleen (15.94±1.86 vs. 33.7±6.48%, P=0.01 and 15.94±1.86 vs. 35.98±3%, $P<0.0001$) respectively. In PB, the percentage of activated neutrophils was similar in PIM compared to controls ($P>0.05$), while in the spleen, PIM had increased activated neutrophils 120 days after induction (41.83±3.63 vs. 58.73±3.94%, P=0.004). PIM and controls expressed similar percentages of anergic neutrophils in both PB and spleen ($P>0.05$). Controls and PIM produced similar plasmatic IL-8 levels 90 and 120 days after injection (0.65±0.18 vs. 0.2±0.05pg/ml, $P\geq0.05$ and 0.65±0.18 vs. 1.2±0.51pg/ml, $P>0.05$), respectively though PIM had higher plasmatic IL8 levels

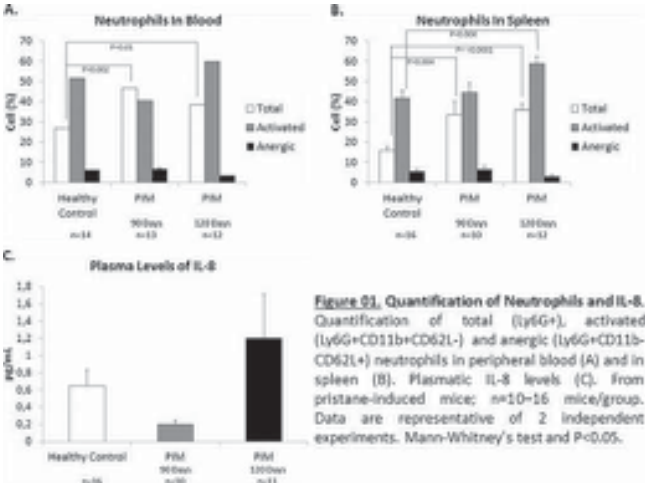


Figure 01. Quantification of Neutrophils and IL-8. Quantification of total (Ly6G+), activated (Ly6G+CD11b+CD62L-) and anergic (Ly6G+CD11b-CD62L+) neutrophils in peripheral blood (A) and in spleen (B). Plasmatic IL-8 levels (C). From pristane-induced mice; n=10-16 mice/group. Data are representative of 2 independent experiments. Mann-Whitney's test and P<0.05.

120 days compared to 90 days after induction (1.2±0.51 vs 0.2±0.05pg/ml, P=0.01).
**Conclusions:** Increased percentage of activated neutrophils in PIM indicates innate immunity involvement. Delayed IL8 levels increments over time might suggests that this cytokine may be involved in neutrophil activation in this animal model. Therefore, additional studies are needed in order to clarify IL8 role and further pathways involved in neutrophil activation and disease development in PIM.
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## AB0134 OXIDATIVE STRESS LEVELS ARE INCREASED IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH A HIGHER ACCUMULATIVE DAMAGE SCORE

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**Background:** Oxidative stress is increased in Systemic Lupus Erythematosus (SLE) patients, and contributes to the immune system imbalance, abnormal activation of apoptotic processes, autoantibodies production and the development of serious complications, such as cardiovascular comorbidities.
**Objectives:** To evaluate the influence of oxidative stress as an additional factor to the classical cardiovascular risk ones, in SLE patients.
**Methods:** Cross-sectional prospective study of SLE patients according to the SLICC-2012 criteria, coming from the Rheumatology Service of Arnau de Vilanova Hospital and La Fe Hospital. In all patients we analyzed the serum concentration of GS-Nem (GSH) and GSSG by UPLC-MS/MS (Acquity UPLC System). We have also taken healthy individuals as negative controls, who had the same blood-test. In patients was also made a complete blood-test, and clinical, treatment and biometric data were collected by personal interview. Biostatistical analysis was performed by the *R* software version 3.2.3., using a simple, binominal and logistic lineal regression.
**Results:** A total of 140 patients were evaluated; (95% women) with 33.39±13.63 year-old average at the diagnosis time with a 10.05± 11.42 year-evolution of SLE. We used GSH/GSSG ratio to assess the oxidative stress rate, being this value higher in patients than in healthy controls (P=0.005).
We observed a statistically significant relationship between the presence of oxidative stress and accumulated damage assessed by SLICC-ACR ($P<0.0001$). No differences according to the disease activity, specific autoimmune profile or by organ or systems affected. However, we found a slight difference in the GSH/GSSG ratio among patients who have had a CVD (1±0.39) and those who have not suffered CVD (1.19±0.55). No differences in the levels of oxidative stress are observed according to treatment with folic acid or the administration of biological therapies.
**Conclusions:** We observed increased levels of oxidative stress in our SLE patients compared to healthy controls. Data suggest a rise of oxidative stress in

patients with a greater cumulative damage, which is consistent with the presence of severe comorbidities in these patients. It seems to be a slight tendency to increased oxidative stress levels measured with GSH/GSSG ratio in patients with SLE and cardiovascular involvement, but more independent studies are needed to confirm it.
**Disclosure of Interest:** None declared
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## AB0135 DECREASED LUPUS MANIFESTATIONS IN PRISTANE-INDUCED MICRORNA 155-DEFICIENT MICE

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**Background:** Deregulation of endogenous miR155 was observed in many autoimmune conditions, including systemic lupus erythematosus (SLE).
**Objectives:** We herein examined the role of miR155 in the development of systemic manifestations in mice with pristane-induced lupus (PIL).
**Methods:** MiR155-deficient and C57/Bl6 mice were injected with pristane or PBS as control and analyzed after 8 months. Glomerulonephritis and pneumonitis were quantified by using the composite kidney biopsy score (KBS) and by analyzing the numbers of affected lung-vessels and the area of the inflammatory lung-infiltrate, respectively. Specimens were stained with B220 (B), CD3 (T), Neu7/4 (neutrophils) and F4/80 (macrophages) and analyzed by cell-identification algorithms for nuclear segmentation (HistoQuest). Serum levels of anti-dsDNA, anti-histone and anti-chromatin antibodies were measured by ELISA. Frequencies of B cells, activated and regulatory CD4+ T cells as well as Th1, Th2, Th17 cells were measured by flow cytometry. Quantitative real-time polymerase chain reaction was used to measure expression levels of interferon-signature and T-cell subset related as well as miR155-associated genes.
**Results:** All pristane-injected mice showed signs of pneumonitis, while controls did not. Compared to wild types treated with pristane, similarly treated knockouts showed significantly decreased perivascular inflammatory area with B cells being the most prominent inflammatory cell. Wildtypes had a more severe renal involvement in the KBS than knockouts. Corresponding with reduced organ involvement, miR155 deficient mice had significantly lower serum levels of anti-dsDNA antibodies, anti-chromatin and anti-histone antibodies and decreased frequencies of activated $CD4^+CD25^+(Foxp3^-)$ cells. Interestingly, also frequencies of $CD4^+CD25^+Foxp3^+$ regulatory T cells were lower in these mice. Upon restimulation, $CD4^+$ cells showed a more pronounced Th2 response in wild types, but no significant differences in Th1 and Th17 phenotype. Regarding INF-signature and T-cell subset activation, pristane-treated wild types showed significantly up-regulated gene-expression patterns whereas equivalently treated mutants showed the same levels as PBS-treated controls.
**Conclusions:** MiR155 deficiency in PIL mice did not prevent disease, but was associated with less severe organ involvement, lower serum auto-abs levels, lower frequencies of Th2 cells, whereas lower expressions of genes jointly responsible for disease development may be one key mechanism. Thus, antagonisation of miR155 might be a future approach in treating SLE.
**Disclosure of Interest:** None declared
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## AB0136 IN VITRO INDUCED REGULATORY T-CELLS CAN REDUCE SEVERITY OF LUPUS ARTHRITIS

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**Background:** Even though joint involvement is a major burden in patients suffering from systemic lupus erythematosus (SLE), it is not focus of scientific research and treatment strategies continue to be limited. Studying lupus arthritis and possible treatment options can be done with the murine model of Pristane-induced lupus (PIL).
**Objectives:** We herein investigate if *in vitro* induced regulatory T-cells (*i*Treg) are capable of ameliorating PIL arthritis and help us evaluate possible new treatment options.
**Methods:** BALB/c mice were injected i.p. with either 0.5ml of pristane (PIL-group) or PBS (controls). Naive $CD4^+$ thymocytes were sorted and cultured and cell suspensions with >80% of $CD4^+FoxP3^+$ cells (*i*Treg) were injected intravenously (i) once when PIL was induced ($5x10^6$ *i*Treg, *i*Treg-boost), or (ii) every 4 weeks ($1x10^6$ *i*Treg, *i*Treg-rep). Animals were monitored for paw swelling and grip strength. After 8 months histological analysis evaluated for cartilage degradation, number of osteoclasts and the extent of inflammation and bone erosion. In addition, the cellular composition of the inflammatory tissue was determined by a cell-identification algorithm for nuclear segmentation (HistoQuest). Serum levels of anti-dsDNA, anti-histone and anti-chromatin antibodies were measured by ELISA.
**Results:** Monthly injections of $1x10^6$ *i*Treg reduced the clinical as well as the histological severity of PIL-arthritis, seen by a higher mean grip strength (2.964±0.024 vs. 2.732± 0.063, $p<0.01$), less mean paw swelling (0.044±0.020 vs. 0.360 ±0.069) and retardation of the symptom onset. 62% of PIL-mice and 33% of *i*Treg-rep mice had erosive arthritis. There was a significant reduction of arthritis severity in all histological parameters (inflammatory area 0.188±0.0574 vs. 0.688±0.113; erosive area 0.011 ±0.009 vs. 0.069±0.017; number of osteoclasts 2.000± 1.125 vs. 9.143±1.999; cartilage degradation 0.059±0.004 vs. 0.187±0.033). The single boost of $5x10^6$ *i*Treg could not prevent joint manifestation. However, a slight retardation in "loss of grip strength" and a significantly less erosive area was seen. In regards to the cellular composition of the inflammatory tissue, a significantly increased relative amount of Foxp3 cells was seen in the *i*Treg-rep group compared to the PIL group (5.2±2.3 vs. 0.6±0.2). Corresponding to the reduced severity in joint involvement, the *i*Treg-group had significantly lower serum levels of antibodies.
**Conclusions:** Repeated injections of *i*Treg ameliorate the clinical and histological severity of PIL- arthritis. A single boost of *i*Treg at the time of disease induction does not prevent joint manifestation, but retards the onset of symptoms and progression of erosive bone degradation. Thus, *i*Treg have significant positive effects on PIL arthritis, which may have consequence for future therapeutic considerations.
**Disclosure of Interest:** None declared
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## AB0137 CD40-PATHWAY ACTIVATION IN ECTOPIC LYMPHOID STRUCTURE (ELS)-RESIDENT B CELLS CONTRIBUTES TO DISEASE PATHOLOGY IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** T cell-dependent activation of B lymphocytes is a key effector arm of the adaptive immune system, resulting in protective antibody responses and long-lived humoral immunity. Such B cell responses often occur in germinal centres (GCs); specialized anatomical locations within secondary lymphoid organs. Similar GC-like structures can also be found in involved tissue in various autoimmune diseases, including the salivary glands of primary Sjögren's syndrome (pSS) patients.
**Objectives:** Previous work has implicated CD40-CD154 pathway-dependent processes in regulating B cell survival and function in GCs, and we were wanted to investigate whether this costimulatory pathway might be linked to ELS formation and function in pSS.
**Methods:** Histological analysis of minor salivary gland biopsies from pSS patients revealed evidence of CD40 and CD154 expression on ELS-resident B and T cells respectively, co-locating receptor and ligand positive cells in affected tissue. These results suggested that there might be ongoing T-B cell collaboration in these ELS and we therefore wanted to examine whether there was evidence of CD40 pathway activation *in situ*. To do this we first generated a CD40-pathway gene signature in primary human B cells following recombinant CD154 stimulation *in vitro*.
**Results:** Using a published microarray dataset generated using parotid gland biopsies we could demonstrate upregulation of a portion of the B cell CD40 gene signature in biopsies from pSS patients but not from healthy donors or individuals with Sicca symptoms, suggesting that CD40 pathway activation was occurring within disease-relevant tissue in lymphocytes implicated in disease pathology. To better understand the role of CD40-CD154 interactions in ELS, we examined salivary glands in CD40 knockout NOD mice. Wild-type NOD mice develop sialadenitis, anti-SSA/SSB autoantibodies, and display evidence of ELS in salivary glands. In contrast, there was no evidence of ELS, sialadenitis or autoantibodies in CD40 deficient NOD mice up to one year of age. Further, anti-CD154 treatment resulted in disaggregation in splenic GCs as well as established ELS in NOD mice and resulted in decreased levels of IgG secreting cells in salivary glands.
**Conclusions:** Collectively our data indicate that CD40 pathway signalling is essential for formation and maintenance of salivary gland ELS and suggest that CD40 pathway signalling is active in established ELS from pSS patients, supporting the notion that blockade of CD40-CD154 interactions may provide therapeutic benefit in patients suffering from this autoimmune exocrinopathy.
**Disclosure of Interest:** G. Wieczorek Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, M. Bigaud Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, S. Pfister Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, S. Hoersch Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, K. McMichael Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, C. Afatsawo Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, M. Hamburger Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, C. Texier Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, C. Cojean Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland, M. Henry Employee of: Ex employee of Novartis Institutes for Biomedical Research, Basel, Switzerland, J. Rush Employee of: Novartis Institutes for Biomedical Research, Basel, Switzerland
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AB0138

WITHDRAWN

AB0139 **INTERLEUKIN-21 IS OVEREXPRESSED IN KIDNEY TISSUE FROM LUPUS NEPHRITIS PATIENTS AND ITS SERUM LEVELS ARE CORRELATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY**

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**Background:** Interleukin-21 (IL-21) has various effects on a number of immune cells including B cells, T cells, natural killer (NK) and NKT cells. One of the essential roles of IL-21 is to contribute to autoantibody production as a result of promoting hyperactivity of B cells. Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease characterized by pathogenic autoantibody production and systemic organ damage. A few studies have been conducted for investigating the contribution of IL-21 to the pathogenesis of murine SLE. However, only limited studies have been performed concerning the role of IL-21 in human SLE and the results are still controversial.
**Objectives:** The aim of this study was to evaluate whether IL-21 participates in the pathogenesis of human SLE.
**Methods:** Serum IL-21 levels were measured in SLE, osteoarthritis (OA) patients and healthy controls (HC). Serum IL-21 levels were analyzed for revealing the correlation with laboratory data or a disease activity index for SLE. Kidney tissues from patients with lupus nephritis and controls were used for evaluating the expression of IL-21 and IL-21R. Normal portions of human kidneys removed for renal carcinoma were used as normal controls.
**Results:** Serum levels of IL-21 were increased in the patients with SLE as compared to the patients with OA or HC. Serum IL-21 levels of the patients with SLE were positively correlated with serum levels of IgG, the titers of anti–double-stranded DNA antibodies and the scores of SLE Disease Activity Index. SLE patients with low C4 concentrations had higher serum IL-21 levels than those with normal C4 concentrations. The expression of IL-21 was higher in renal tubular epithelial cells of the patients with lupus nephritis than in those of controls.
**Conclusions:** This study reveals the association between IL-21 and disease activity in the patients with SLE. We also first demonstrate IL-21 expression in renal tissue of the patients with lupus nephritis. These findings suggest that IL-21 is critically implicated in the pathogenesis of SLE.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4506

AB0140 **ALTERED LIPOPROTEINS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS INDUCE AUGMENTED OXIDATIVE STRESS IN VITRO AND IN VIVO**

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**Background:** Patients with systemic lupus erythematosus (SLE) are at an increased risk of developing a cardiovascular disease which are not solely explained by the traditional cardiovascular (CV) risk factors. This higher CV risk might be associated with chemical and functional alteration of lipoproteins in SLE patients.
**Objectives:** This study aimed to investigate the lipoprotein modification from SLE patients and its effects on oxidative stress *in vivo* and *in vitro*.
**Methods:** A total of 35 SLE patients and 15 age and sex matched heathy controls (HC) were compared in regard to lipid profile including low density lipoprotein (LDL). Oxidation and susceptibility to oxidation as well as structure of LDL were measured by quantifying malondialdehyde (MDA), *de novo* formation of conjugated dienes in the presence of 5 uM CuSO4 and gel electrophoresis, respectively. The uptake of LDL by THP-1 cells was examined. In *vivo* radial oxygen species (ROS) formation and toxicity of LDL were examined in zebra fish embryos.
**Results:** LDL levels did not differ between SLE and HC (134.7±54.5 mg/dL vs. 118.3±29.9 mg/dL, P=0.277). LDL from SLE showed an increased fragmentation pattern during mobility through electrophoresis gel. As compared to HC-LDL, SLE-LDL were more oxidized (MDA level: 56.1±10 vs. 25.4±2.3 nM/mg, $p<0.001$) and were also more susceptible to cupric-ion-mediated oxidation *in vitro* (3.5±0.5% vs. 1.9±1.9%, $p<0.001$). In addition, more SLE-LDL were engulfed by THP-1 cells than HC-LDL (2501±401.2 AU vs. 524.1±59.8 AU, $p<0.001$). Finally, the zebra fish embryos that were injected with SLE-LDL generated higher levels of ROS (1592±58.7 vs. 459.6±66.4, $p<0.001$) and survived less (survival 49.1±2.8% vs. 87.8±1.2%, $p<0.001$) as compared to those treated with HC-LDL.

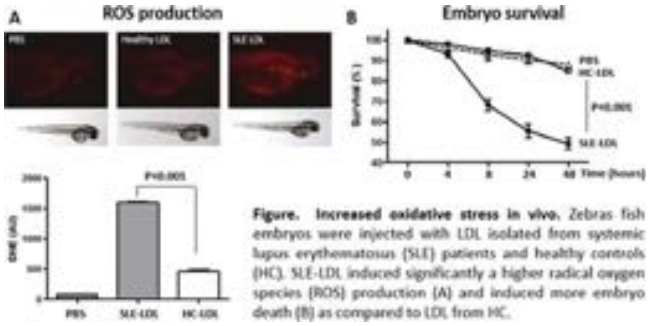



**Figure. Increased oxidative stress in vivo.** Zebras fish embryos were injected with LDL isolated from systemic lupus erythematosus (SLE) patients and healthy controls (HC). SLE-LDL induced significantly a higher radical oxygen species (ROS) production (A) and induced more embryo death (B) as compared to LDL from HC.

**Conclusions:** LDL from SLE patients is altered with increased oxidation, structural instability and an augmented oxidative potential. Treatment with anti-oxidants might normalize the altered LDL property and so decrease the CV risk in SLE patients.
**Disclosure of Interest:** None declared
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## AB0141 DEPLETION OF LYMPHOID-LIKE STROMAL CELLS IMPAIRS TERTIARY LYMPHOID ORGAN FORMATION IN AN ANIMAL MODEL OF SJÖGREN'S SYNDROME

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**Background:** Tertiary lymphoid organs (TLO) characterised by germinal centre formation and B cell proliferation represent the histological hallmark of primary Sjögren's syndrome (pSS). TLO persistence in the salivary glands is associated with systemic disease manifestations and lymphoma development in pSS patients (1).
We previously demonstrated that gp38+ stromal cells are instrumental for TLO development and provide chemokines, such as CXCL13, CCL19 and CCL21 necessary for lymphocyte recruitment and organization (2). Similarly, in the lymph node, FAP+gp38+ lymphoid stromal cells regulate lymphocyte homing and homeostasis. Accordingly, deletion of FAP+gp38+ cells results in aberrant expression of lymphoid survival factors, disrupted lymph node organization and decreased ability to mount efficient immune responses (3, 4).
**Objectives:** To dissect the effects of FAP+gp38+ cell deletion in TLO dynamic and function in an animal model of pSS.
**Methods:** We used a model of conditional depletion of FAP-expressing cells, in which FAP-DTR mice were treated prophylactically with Diphtheria Toxin (DTx). Following depletion, submandibular salivary glands of FAP-DTR mice and littermate controls were intra-ductally cannulated with luciferase-encoding replication-deficient adenovirus to induce TLO formation and pSS-like disease as previously described (5). A combination of immunofluorescence, quantitative RT-PCR and flow cytometry on digested salivary glands was used to address the consequences of stromal cell deletion in the TLOs.
**Results:** We confirmed that in cannulated, inflamed wild-type salivary glands, FAP is upregulated on a population of activated stromal cells that expresses gp38 and produces lymphoid chemokines. As anticipated, analysis of DTx-treated FAP-DTR salivary glands reveals significantly decreased numbers of gp38+ stromal cells and deletion of FAP+ stromal cells leads to a significant defect in lymphoid chemokine production, decreased number of infiltrating lymphocytes and severely compromises TLO formation.
**Conclusions:** These data demonstrate that salivary glands gp38+ activated stromal cells express FAP and are required for TLO organization and maintenance in the tissue. Deletion of activated lymphoid stroma affects lymphocyte recruitment and organization, thus providing the rational for stromal cell targeting in TLO associated autoimmune diseases.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4864

## AB0142 SJÖGREN'S SYNDROME-ASSOCIATED TRANSCRIPTS SHOW CORRELATION WITH OBJECTIVE MEASURES OF DRYNESS

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**Background:** Sjögren's syndrome (SS) is a chronic autoimmune disorder in which exocrine dysfunction can lead to chronic, debilitating dryness. Expression studies in SS have identified the dysregulated expression of coding and non-coding transcripts enriched in innate and adaptive immune response pathways.
**Objectives:** In our recent SS RNA-seq study, we identified 3748 transcripts showing differential expression (DE; FC>2 or <0.5, q<0.05) in SS patients compared to healthy controls. Of these SS-associated transcripts,[CL1] we sought to identify transcripts whose expression is significantly correlated with objective measures of dryness employed by the 2002 American-European Consensus Group (AECG) classification criteria of SS, including whole unstimulated salivary flow (WUSF), lissamine green (LG) staining, and Schirmer's (Sch) tear migration.
**Methods:** Normalized expression data from a whole blood SS RNA-seq study was obtained for 57 cases and 11 healthy controls who underwent multidisciplinary clinical evaluation for the 2002 AECG classification criteria. Objective dryness measures (WUSF, LG, & Sch) were normalized by $\log_2$ transformation and correlation analysis (Spearman for WUSF and LG; Pearson for Sch) was performed for each clinical measure against all of 3748 DE transcripts. Both $r$ or $\sigma$ and a FDR-corrected $p$-value, or $q$-value, were calculated. Significantly correlated transcripts were defined by $q<0.05$.
**Results:** For WUSF, the significant positive correlation between WUSF rate and the expression of 2 non-coding transcripts was observed: the small Cajal body-specific RNA 5 (*SCARNA5*; $\sigma$=0.50, $q$=0.018) and the uncharacterized antisense lncRNA RP11–137H2.4 ($\sigma$=0.50, $q$=0.018). For LG, positive correlation was observed for 31 transcripts ($0.42<\sigma<0.51$, $0.017<q<0.05$) mostly represented by interferon-inducible (IFI) protein-coding genes (e.g. *IFIT3*, *OAS3*, and *IRF7)*, although for the pseudogene, *ZDHHC4P1*, and its neighboring IFI gene *EPSTI1* both showed significant positive correlation. For LG, the only negatively correlated transcript was the sodium bicarbonate transporter *SCL4A10* ($\sigma$= -0.43, $q$=0.045). For Sch, 3 transcripts (*CARD16*, *HMGB2*, and *BLC2A1*) were negatively correlated ($-0.51<\sigma<-0.49$, $0.018<q<0.019$), while the transcript *IQCH* was positively correlated ($\sigma$=0.49, $q$=0.019).
**Conclusions:** We identified SS-associated transcripts whose expression correlates with clinical measures of dryness. For WUSF, the ncRNA *SCARNA5* is situated within an intron of the Crohn's disease-associated gene autophagy-related 16-like 1 (*ATG16L1*). Although IFI genes have previously shown correlation with WUSF, the ZDHHC4P1 pseudogene could regulate neighboring SS-associated IFI gene *EPSTI1*. For Sch, *CARD16* is a caspase inhibitor that influences apoptotic responses that induces NF-kB activation in inflammation, while *BLC2A1* has been shown to slow apoptoic responses. Further transcript characterization will allow us to assess their potentialas biomarkers or surrogates of objective clinical measures for SS.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6108

## AB0143 UMBILICAL CORD MESENCHYMAL STEM CELLS INCREASE TREG CELLS VIA SHLA-G IN SLE PATIENTS

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**Background:** Human leukocyte antigen-G (HLA-G) is a non-classical HLA class I molecule, exhibiting strong immunosuppressive properties by inducing the differentiation of regulatory T cells (Treg). Previous studies showed that umbilical cord mesenchymal stem cells (UCMSCs) transplantation could alleviate disease progression in SLE patients. However, the underlying mechanisms are largely unknown.
**Objectives:** To explore whether sHLA-G was involved in upregulation effects of MSCs on Treg, which contribute to the immune torlerance during SLE.
**Methods:** The level of sHLA-G was detected by ELISA in SLE patients and healthy controls. The correlations between the levels of sHLA-G and clinical features, percentages of HLA-G receptor ILT2 and Treg cells were analyzed by Sparman's correlation test respectively. The percentage of ILT2 on T and B lymphocytes was examined by flow cytometry. PBMC were isolated from SLE patients and co-cultured with UC-MSCs for 3 days at different ratios (50:1, 10:1, 2:1) with or without HLA-G antibodies, and then the frequencies of CD4+CD25+Foxp3+T cells were determined by flow cytometry.
**Results:** The concentration of sHLA-G was increased in SLE patients compared with healthy control subjects (21.76 ng/mL ±1.206 VS 16.84 ng/mL ±1.656, $p<0.05$). However, there was a negative correlation between sHLA-G levels and SLEDAI scores in active SLE patients (SLEDAI >4). We found that sHLA-G levels were negative correlated with urea nitrogen, serum creatinine and 24-hour urine protein but positively correlated with platelet in SLE patients. What's more, the sHLA-G levels were significantly lower in SLE patients with renal involvement compared with those without renal involvement. The expression of ILT2 in CD4+ T cells from SLE patients decreased significantly compared to controls. A positive relationship between the frequency of Treg cells and $CD4^+ILT2^+$ T cells in SLE patients was found. The levels of sHLA-G increased 24 hours post MSCs transplantation. *In vitro* studies showed MSCs increased the frequency of Treg cells in SLE patients in a dose-dependent manner, which was partly abrogated by anti-HLA-G antibody.
**Conclusions:** Our results suggested that UCMSCs could alleviate SLE through upregulating Treg cells partly dependent on sHLA-G.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2823

## AB0144 INTERLEUKIN-17 IMPAIRS SALIVARY TIGHT JUNCTIONS IN NON-OBESE DIABETIC MICE

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**Background:** Sjögren's syndrome (SS) is an inflammatory autoimmune disease that causes secretory dysfunction of the salivary glands. It has been reported that pro-inflammatory cytokine interleukin-17 (IL-17) was elevated and tight junction (TJ) integrity was disrupted in minor salivary gland from SS patients. The aim of the research was to observe the alteration of TJs in salivary glands of non-obese diabetic (NOD) mice and explore the impact of IL-17 on TJs.
**Objectives:** The aim of the research was to observe the alteration of TJs in

salivary glands of non-obese diabetic (NOD) mice and explore the effect of IL-17 on TJs.

**Methods:** 12-week-old female NOD mice and BALB/c mice were used. Stimulated salivary flow rate and histopathological changes were evaluated. The expression of TJ molecules and IL-17 in SMG and PG were detected by real-time PCR and western blot analysis. Immunohistochemistry was used to observe the distribution of TJ molecules and IL-17 in SMGs and PGs. In addition, the alternation of TJs under the stimulation of IL-17 (50 ng/ml) were evaluated in cultured SMG and PG tissues.

**Results:** Lymphocyte infiltration was mainly observed in submandibular glands (SMGs), but not in parotid glands (PGs) of NOD mice (Fig. A). Likewise, IL-17 was significantly increased and mainly located in lymphocytic infiltrating regions in SMGs, but not detectable in PGs of NOD mice (Fig. B-D). Claudin-1 and -3 were elevated whereas claudin-4, occludin and zonula occludens-1 (ZO-1) were reduced in SMGs of NOD mice. However, no change in the expression of TJ proteins was found in PGs. *In vitro*, IL-17 significantly decreased the protein levels of claudin-4 and ZO-1 in the cultured SMG tissues, as well as claudin-1, occludin and ZO-1 in PG tissues.

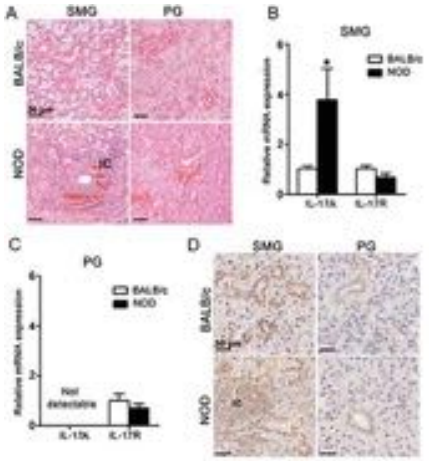



Figure (A) Histological evaluation of SMGs and PGs in BALB/c and NOD mice (B, C) The mRNA expression of IL-17A and IL-17R in SMGs and PGs of BALB/c and NOD mice (D) Immunohistochemical staining of IL-17A in SMGs and PGs of BALB/c and NOD mice.

**Conclusions:** IL-17 derived from infiltrating lymphocyte impairs the integrity of TJ, and thus might contribute to salivary gland dysfunction in SS.

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## AB0145 PUTATIVE ROLE OF A GENE ENCODING AN ENDOGENOUS RETROVIRAL ENVELOPE PROTEIN IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** Human Endogenous Retroviruses (HERVs) are remnants of past retroviral infections in the human genome. Most of HERV elements have accumulated mutations and deletions and thus have become inactivated with time. At the same time the presence of open reading frames (ORFs) in only a few HERV genes, suggest an evolutionary selective pressure to maintain the protein coding capacity of some HERV envelope ORFs (1).

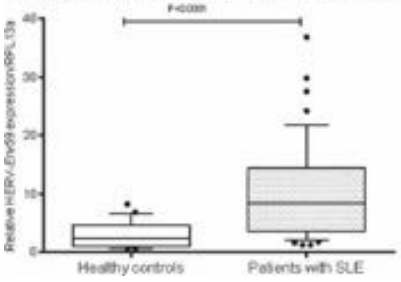
HERVs have been implicated both in diseases such as cancers and autoimmune disorders but interesting also shown to have been adapted to play a role in important aspects of human biology such as development of the placenta.

**Objectives:** We aimed to identify HERVs which affect development of Systemic Lupus Erythematosus (SLE) and to describe what role such putative HERV elements might play in autoimmunity.

**Methods:** The study subjects compromised 45 female patients with SLE and 50 geographically and age matched healthy female controls, recruited consecutively from Aarhus University Hospital, Denmark. Using real-time RT-PCR strategy we analyzed transcriptome of 11 genes with coding capacity for complete envelope protein in Peripheral Blood Mononuclear Cells (PBMCs) isolated from SLE patients or healthy controls. The Mann-Whitney *U* test analyzes showed that the expression of HERV-H *Env59* gene in SLE patients was significantly higher than in healthy controls. Subsequently we cloned the *Env59* envelope gene and using psuedotyped lentiviral particles, examined whether it retains its activity as a retroviral fusion protein. A sequence analysis of the protein identified an immune suppressive domain (ISD). A peptide corresponding to this ISD was synthesized and examined *in vitro* for immune suppressive activity on stimulated human PBMCs and the monocytic THP-1 cells line.

**Results:** We found that a specific HERV-H derived *Env* gene (Env59) is overexpressed in SLE patients ($P<0.0001$). Interestingly, we found that the expression of this gene is negatively correlated with etiological factors of autoimmune rheumatic diseases such as IL-6 ($P=0.0065$) and TLR-7 ($P=0.02$) in patients. This gene is capable of encoding a fully functional envelope glycoprotein and contains a domain which shows strong anti-inflammatory activity including the ability to lower IL-6 levels *in vitro*.

Figure 1 Expression of HERV-Env59 mRNA in patients with SLE and healthy controls




**Conclusions:** We interpret these results to show that the *Env59* gene has been adapted by the immune system as a control mechanism in autoimmunity. More precisely the activity of the immune suppressive domain of this retroviral envelope protein seems to be directly responsible for lower IL-6 levels in some SLE-patients. The ISD peptide derived from this retroviral gene shows anti-inflammatory activity *in vitro* and represents a potentially new strategy for treatment of autoimmune diseases.

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**Disclosure of Interest:** None declared

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## AB0146 SELF-REACTIVE IGE EXACERBATES INTERFERON RESPONSES ASSOCIATED WITH AUTOIMMUNITY

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**Background:** The discovery of Immunoglobulin E (IgE) nearly 40 years ago was a breakthrough in the field of allergy research. IgE directed against parasitic worms and allergens binds mast cells and basophils, triggering an inflammatory response that is characterized by the release of histamine and Th2 cytokines.

Here we report that double-stranded DNA (dsDNA)-specific IgE autoantibodies complexed to DNA activate plasmacytoid dendritic cells (pDC), an immune cell type linked to viral defense, leading to the secretion of substantial amounts of IFN-a. Although typical IgE mediated responses are not a hallmark of systemic lupus erythematosus (SLE), IFN-a producing pDCs are a key driver for loss of immune tolerance to host DNA in SLE. We, therefore, investigated this apparent paradox and found that even the small concentrations of circulating dsDNA-specific IgE found in SLE patients greatly potentiated pDC secretion of IFN-a by triggering phagocytosis via the Fc-epsilon receptor I (FceRI) and TLR9-mediated DNA sensing in the phagolysosome. Consequently, this potent pDC signaling mechanism reduces the threshold of pDC activation, which has the potential to expand anti-DNA responses and greatly exacerbate self-inflicted damage. These findings expand the known pathogenic mechanisms of IgE mediated inflammation beyond those found in allergies and demonstrate that, in addition to recognizing exogenous allergens, IgE can also bind to autoantigens and drive an aberrant and self-destructive anti-viral response. This previously unrecognized link between IgE and the interferon pathway provides additional insights into the pathological mechanisms underlying autoimmunity and may be useful in the rational design of therapies for the treatment of diseases such as SLE.

**Disclosure of Interest:** M. Sanjuan Employee of: Medimmune, J. Henault Employee of: Medimmune, J. Riggs Employee of: Medimmune, J. Karnell Employee of: Medimmune, V. Liarski: None declared, L. Shirinian Employee of: Medimmune, L. Xu Employee of: Medimmune, K. Casey Employee of: Medimmune, M. Smith Employee of: Medimmune, D. Khatry Employee of: Medimmune, L. Clarke Employee of: Medimmune, R. Herbst Employee of: Medimmune, R. Ettinger Employee of: Medimmune, M. Petri: None declared, M. Clark: None declared, T. Mustelin Employee of: Medimmune, R. Kolbeck Employee of: Medimmune

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## AB0147 STUDY THE SYNCHRONOUS EFFECT OF INTENSIVE CARE TO CONDITION OF CARDIOVASCULAR SYSTEM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** To date, little is known about the pathogenesis, course and efficacy of cardiac complications of systemic lupus erythematosus (SLE), which requires the development of new therapies that allow to increase the life expectancy of patients.

**Objectives:** To study the effect of simultaneous intensive therapy on cardiovascular system in SLE.

**Methods:** The study involved 92 patients with SLE at the age of 18–55 years, with disease duration from 2 to 23 years. We analyzed the traditional cardiovascular risk factors, disease activity (SLEDAIK2, EKLAM).

**Results:** The vast majority of patients - 72 (78.6%) - revealed a subacute variant of the disease, and the average level of activity (80.2%). The classic cardiovascular risk factors were observed in 85 (92.3%) patients. Depending on the treatment options for the patients were divided into the following groups: I group - 32 patients received the classic three-day pulse therapy - metipred or Solu-Medrol 1000 mg/day and the second day of cyclophosphamide 1000 mg/day, against the background of glucocorticosteroids (GCS) according to the degree activity. Group II - 24 patients underwent synchronous intensive therapy: 2–3 sessions of plasmapheresis followed by 1000mg metipred (solumedrol), against GCS disease activity, respectively, III group - 36 patients received conventional therapy with oral administration in dose of Valium 20–40mg/day.

Patients of group II marked a complete stabilization of clinical symptoms, decrease in activity, the positive dynamics of cardiovascular manifestations.

**Conclusions:** Thus, the ineffectiveness of the standard basic therapy in SLE patients should include the feasibility of timely implementation of synchronous pulse therapy, which helps to reduce cardiovascular complications and improves the quality of life of patients.

**Disclosure of Interest:** None declared

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## AB0148 DIFFERENTIAL PERIPHERAL B-CELL PHENOTYPE IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME (PSS) COMPARED TO SECONDARY SJÖGREN'S SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE/SS)

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**Background:** Peripheral B-cell abnormalities are a feature of both lupus (SLE) and primary Sjogren's syndrome (pSS). However, whereas patients with pSS have increased frequencies of Bm1/Bm2 (naïve), Bm2' (germinal centre founders) and Bm3–4 (centroblasts/centrocytes), but decreased Bm5 (memory) compared with healthy controls (HC), patients with SLE have increased Bm5 levels, which correlated with disease activity. No previous studies investigating the peripheral B-cell phenotype in patients with SLE and secondary SS (SLE/SS) are available.

**Objectives:** We questioned whether the defective B-cell phenotype in pSS patients was also present in patients with SS/SLE, and whether differences in B-cell phenotype could be related to changes in B-cell lipid-raft expression and BAFF-receptor function in pSS and SLE/SS patients.

**Methods:** Blood samples and clinical and laboratory parameters from 32 patients with pSS and SS/SLE and 13 age/sex matched HC were obtained. We used flow-cytometry to perform B-cell immunophenotyping and analysis of lipid-raft expression (marker of B-cell activation). *In vitro* cultures assessed lipid-raft expression in response to BAFF.

**Results:** Patients with SLE/SS had a district B-cell phenotype, characterised by decreased Bm1 and Bm5 and increased Bm2 populations compared to HC ($p=0.031$, $p=0.035$ and $p=0.01$, respectively), and increased Bm2 compared to pSS ($p=0.027$). Bm1-cells were decreased in both pSS and SLE/SS patients compared to HC ($p=0.028$ and $p=0.031$, respectively). Both age and disease duration correlated strongly with Bm2' cells in SLE/SS patients ($r=0.9572$, $p=0.0428$), and the immunosuppressive treatment correlated negatively with the number of circulating Bm2 and Bm2' cell in pSS ($r = -0.54$, $p=0.01$ and $r = -0.56$, $p=0.008$, respectively). B-cells from patients with pSS had a significant increase in lipid-raft expression compared to HC ($p=0.01$) and patients with SS/SLE ($p<0.05$). Furthermore, lipid-raft levels correlated with BAFF-receptor expression in HC and SLE/SS B-cells ($p=0.17$, $r=0.694$) but not in pSS patients. Both disease activity score (ESSDAI) and IgG level correlated positively with lipid rafts expression in B cells from patients with pSS ($r =0.79$, $p=0.004$ and $r =0.53$, $p=0.04$, respectively).

**Conclusions:** We showed that patients with SLE/SS had more significant B-cell abnormalities compared to HC and pSS, detectable even in a small number of patients. Also the relationship between lipid-raft and BAFF-receptor expression was altered between pSS and SLE/SS patients, and correlated with the disease activity and Ig G levels in pSS group. Further studies will validate our findings and investigate whether B-cell lipid-rafts mediate differential BAFF-receptor signalling.

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## AB0149 ASSOCIATIONS OF ANTI NUCLEOSOME ANTIBODY IN SYSTEMIC LUPUS ERYTHEMATOSUS IN INDIA

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**Background:** Nucleosomes are basic elements of chromatin and are considered to be the major antigens in the pathophysiology of systemic lupus erythematosus (SLE).

**Objectives:** This study aimed to look for associations between anti nucleosome antibodies and clinical and laboratory parameters in SLE

**Methods:** This retrospective study was done in department of Clinical immunology & Rheumatology in Christian Medical College, Vellore, India. Patients with SLE by SLICC 2012 criteria between March 2013 and September 2015 subjected to anti nucleosome antibody test formed the study cohort. A cut off of $\geq$20 U/ml by ELISA was defined as per manufacturer's (Euroimmune, Germany) instructions. Associations of anti nucleosome antibody with clinical and laboratory parameters in SLE was studied.

**Results:** Anti nucleosome antibody was available for 238 patients with SLE. Mean age of the patients was 28.98±9.01 years with male to female ratio of 17: 221. Median disease duration was 8 (5–12) months prior to doing this test. Positive titers of anti nucleosome antibody ($\geq$20 U/ml) were noted in 107 patients (46.5%). Renal involvement was seen in 134 (56.3%) patients. Univariate analysis reflected raised anti-c1q antibody, ESR, urinary protein creatinine ratio (UPC), anti dsDNA antibody, SLE disease activity index (SLEDAI), renal SLEDAI, low C3 and C4 as significant association of elevated anti nucleosome antibody levels. No significant association with arthritis, serositis, major infections, serositis, anti-phospholipid antibodies, autoimmune hematological cutaneous, neuropsychiatric, cardiovascular, respiratory, vasculitic and gastrointestinal manifestation was present.

Multivariate regression analysis showed that raised anti-c1q antibodies and DsDna were associated with raised anti nucleosome antibody with odds ratio of 17.46 (95 CI: 1.46–213.86, $p=0.02$) and 82.94 (95 CI: 3.62–189.93, $p=0.006$) respectively.

**Conclusions:** As per literature search, this is the largest single centre study of anti nucleosome antibody in SLE. In this study, raised anti-c1q antibodies and DsDna were independently associated with raised anti nucleosome antibody in SLE.

**Disclosure of Interest:** None declared

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## AB0150 UNDERSTANDING THE ROLE OF THE IL12/IL35 BALANCE IN SJÖGREN SYNDROME

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**Background:** Primary Sjögren Syndrome (pSS) is an autoimmune disease mediated by B-cells as evidenced by the occurrence of non-Hodgkin lymphoma mainly involving salivary glands and increased B-cell activation markers in the serum of pSS patients. A type I interferon response is also observed among some patients. However, some mice models and large genetic studies suggest an alternative/coexisting involvement of the Th1 pathway in the pathophysiology of the disease. In fact, polymorphisms of *IL-12A*, which encodes for IL-12p35, have been associated with pSS[1]. IL-12p35 subunit is shared by 2 heterodimers, IL-12 and IL-35.
**Objectives:** To confirm the genetic association of *IL-12A* polymorphism with pSS and to elucidate the involvement of the IL-12/IL-35 balance in pSS through functional studies.
**Methods:** The genetic studies were performed on French pSS from 2 cohorts. Functional studies were performed on sorted monocytes and stimulated *ex vivo* under inflammatory conditions. Interleukin-12A mRNA, IL-12 and IL-35 proteins were quantified by qRT-PCR for mRNA and by ELISA and multiplex kit respectively for IL-35 and IL-12.
**Results:** We confirmed the association between rs485497 and pSS and found an increased level of IL-12 in sera of pSS patients carrying the risk allele (p=0.016). IL-12 was increased in pSS compared to healthy controls (p=0.0001), especially in patients with a more active disease contrary to IL-35 which was decreased in pSS (p=0.0001). We observed that 99% of patients with high serum levels of IL-35 did not developed lymphoma *versus* 93% in the group with low IL-35 (p=0.03).
**Conclusions:** Our findings emphasize the involvement of the balance IL-12/IL-35 in the pathogenesis of pSS. Further studies especially on regulatory B-cells and plasma cells as well as in animal models of autoimmune diseases assessing the effect of recombinant IL-35, would help to decipher whether this regulatory cytokine could be of interest for future therapeutic approaches.
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## AB0151 ANTI-MAJOR VAULT PROTEIN: A NEW AUTOANTIBODY PREVALENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a complex, multifactorial autoimmune disease that affects multiple organ systems, including the kidney, skin, heart, lung, and hematopoietic and nervous systems. A hallmark of SLE is the production of high titers of autoantibodies against a broad spectrum of antigens. Given the broad spectrum of immune defects in SLE, it may be possible that autoantigens are generated by different pathogenic processes.
**Objectives:** Broad autoantibody profiling in SLE may yield novel autoantibody targets for and may shed light on pathogenic pathways leading to the generation of autoantigens.
**Methods:** In the discovery phase the autoantibody reactivity of serum samples from 130 SLE patients, 794 AID patients (systemic sclerosis, rheumatoid arthritis/RA, early RA, ankylosing spondylitis) and 343 healthy controls was tested against 6,912 recombinant human proteins. Following validation in independent SLE samples (n=101), consistent autoantibody reactivity against 46 antigens was found (p-value $<0.05$ and Cohen's d effect size $<0.3$).
**Results:** A data base search of 46 known and novel SLE-associated antigens revealed that the expression of ten proteins is upregulated by type I interferon (INF) (http://www.interferome.org). Beyond known antigens (TRIM21/Ro52, SSB), we identified a novel autoantibody target MVP with a frequency of 20 -38% in SLE. Interestingly, MVP is the major constituent of the vault particle, the largest known ribonuclear protein complex. Literature data suggest that vaults are involved in a diversity of cellular processes, including multidrug resistance, transport mechanisms, signal transmission, autophagy, immune and radiation response [1].
**Conclusions:** MVP is a virus- and INF$\gamma$-induced and host factor, which up-regulates type I INF production [2]. Although more studies are needed, our findings suggest a previously undescribed linkage of INF pathways and the generation of autoantigens.
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**Disclosure of Interest:** P. Budde Employee of: Protagen AG, S. Vordenbäumen: None declared, H.-D. Zucht Employee of: Protagen AG, P. Schulz-Knappe Employee of: Protagen AG, M. Schneider: None declared
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## AB0152 CLUSTERED AUTOANTIBODY REACTIVITY PROFILES AND DEFINITION OF HOMOGENEOUS SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENT GROUPS

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**Background:** In SLE, early diagnosis, differentiation to other autoimmune diseases and prognostic stratification are still great challenges. Hence, SLE represents an enormous challenge for the clinical development of effective therapies. Detecting a broad set of SLE-associated autoantibodies might help to utilize overall reactivities, co-prevalence and similarities of autoantibody reactivities in SLE patients. Such measures are expected to generate homogeneous SLE-subgroups which may represent common underlying pathophysiologies with different response to medicines and hence orffer improved medical care options.
**Objectives:** Here, we describe the development of a multiplexed autoantibody assay incorporating over 40 known SLE-antigens plus novel human protein antigens derived from large scale autoantibody screening in SLE and other autoimmune diseases such as rheumatoid arthritis, systemic sclerosis and healthy controls, The resulting assay is intendedto comprehensively analyse 87 autoantibodies in SLE patients for disease subgroupd formation.
**Methods:** A Luminex bead-based autoantibody assay was designed by combining traditional with novel biomarkers. Antigens were selected to be used for a) the diagnosis and b) differential diagnosis of SLE, have previously been linked to c) disease activity, and d) specific organ involvement, are encoded by e) interferon type I response genes, and f) may have utility for patient subgrouping. Autoantibody reactivity against these antigens was tested in over 700 SLE, healthy controls (n=1000), and autoimmune disease samples (n=500).
**Results:** Based on the individual marker pattern, we defined an autoantibody reactivity score and four SLE patient clusters (C1-C4) including patients: C1: with a higher disease activity score, broad and homogeneous autoantibody reactivity; C2: with broad, but heterogeneous autoantibody reactivity; C3) who have few autoantibodies and C4) with unusual autoantibody pattern.
**Conclusions:** High content autoantibody profiling of SLE patients reveals relevant differences in autoantibody reactivities both in amount of total reactivity as well as towards autoantibody clusters indicating specific pathophysiologies. Although more studies are needed, our findings suggest that SLE patients can be stratified into distinct, homogenous subgroups. This might be useful in clinical studies to increase the probability of successful drug development.
**Disclosure of Interest:** P. Schulz-Knappe Employee of: Protagen AG, P. Budde Employee of: Protagen AG, H. Goehler Employee of: Protagen AG, H.-D. Zucht Employee of: Protagen AG, M. Schneider: None declared, S. Vordenbäumen: None declared
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## AB0153 REDUCED REGENERATIVE POTENTIAL OF SALIVARY GLAND STEM CELLS IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** The involvement of the epithelium in the pathology of primary Sjögren's syndrome (pSS) has long been proposed. Epithelial cells have potential to transmit immune initiation signals and to serve as autoimmune targets, in addition to their function as saliva channeling/modulating agents in the salivary gland. Recently, we have demonstrated isolation of stem cells from the human salivary gland [1–2]. Salivary gland stem cells (SGSCs) are cultured as clusters of cells, termed salispheres. SGSCs, like all stem cells, possess the ability to self-renew (reproduce themselves) and to differentiate into all salivary gland lineages. Our ability to isolate and characterize the epithelium-derived SGSCs provides a tool to study the involvement of epithelial cells in pSS pathology.
**Objectives:** We aim to isolate SGSCs from biopsies of pSS parotid salivary glands, and characterize their regenerative potential in comparison to healthy controls. This will be a first step towards to assessment of complicity of SGSC/epithelial malfunction in pSS, and in identifying any innate properties specific to pSS-SGSCs.
**Methods:** Salivary gland stem cells were isolated using enzymatic and mechanical digestion, in a protocol adapted from Pringle et al, 2016. The self-renewal capability of pSS-SGSCs was assessed using our published self-renewal assay. The potential immunomodulatory nature of pSS-SGSCs was assessed using

qPCR for expression of matrix metalloprotease (MMP) enzymes, and mass spectrometry for identification of immune-related proteins in the medium.
**Results:** Yield of SGSCs from pSS biopsies was markedly lower than from healthy control tissues (Figure 1 A-C). When exposed to a self-renewal assay, SGSCs from pSS biopsies generated significantly fewer SGSCs (Figure 1 D-F). Expression of MMP2 and MMP9 was notably higher in SGSCs isolated from pSS biopsies. In addition, proteins involved in both pro-inflammatory (polymeric immunoglobulin receptor, immunoglobulin kappa constant) and anti-inflammatory (annexin A1) immunereactions and in rheumatoid arthritis (rheumatoid arthritis antigen A-47) were detected in conditioned medium from pSS SGSCs at greater levels than controls. These data suggest the transcriptome and secretome of SGSCs from pSS biopsies differs significantly from that of healthy controls.

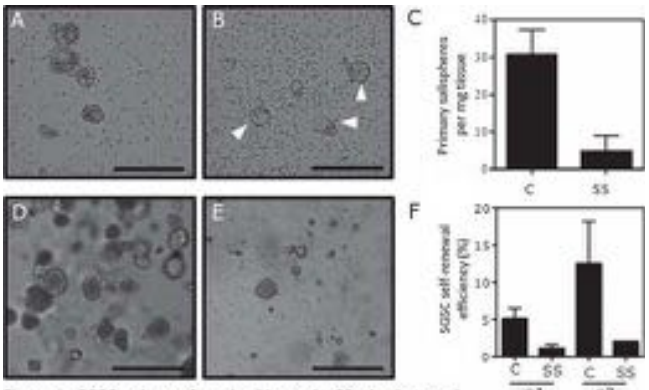


Figure 1. SGSC cultures from healthy and pSS glands reveal regenerative disadvantage in pSS samples. Bar = 50 µM. Arrowheads = salispheres with fewer cells.

**Conclusions:** Our preliminary data demonstrates that the established SGSC isolation technique can be applied to the study of primary Sjögren's Syndrome. Furthermore our data suggest there is an an innate difference in the regenerative potential and immune-reactive nature of SGSCs from pSS biopsies, compared to healthy controls. We anticipate that full characterization of SGSC from pSS biopsies will at least shed light on the mechanisms underpinning epithelial cell involvement in pSS, and permit development of new therapeutic and/or biological agents for the treatment of primary Sjögren's' Syndrome.
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## AB0154 ROLE OF PRO-INFLAMMATORY CYTOKINES IN THE ENDOPLASMIC RETICULUM ASSOCIATED-PROTEIN DEGRADATION IN SJÖGREN'S SYNDROME PATIENTS

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**Background:** Due to its high secretory activity and the complexity of synthesized secretory products, salivary gland (SG) acinar cells are susceptible to endoplasmic reticulum (ER) stress under physiological conditions. ER stress triggers a mechanism known as the "Unfolded Protein Response" (UPR) aiming to restore ER homeostasis. Various ER stress-related disorders have been described in SG of Sjögren's syndrome (SS) patients, including intracellular accumulation of mucins (1) and dilated ER cisternae (2). Also, high levels of pro-inflammatory cytokines present in SG of SS-patients may act as local ER stressors and may play an important role in ER stress induction and perpetuation (chronicity). Previous results from our laboratory indicate a decreased activation of the IRE1α/XBP-1s pathway of the UPR (unpublished data) indicating a chronic ER stress condition. Despite this, the SG acinar cells from SS-patients have low levels of apoptosis (3), suggesting that alternative UPR pathways such as ATF6α could be activated. ATF6α pathway promotes survival mechanisms such as ER-associated protein degradation (ERAD), which has been found hyper-activated in arthritis rheumatoid (4).
**Objectives:** To determine the expression and localization of ATF6α pathway components and molecules participating in ERAD in labial SG (LSG) of SS-patients. The effect of pro-inflammatory cytokines on both ERAD and cell survival was also studied using LSG extracts of SS patients and a three-dimensional (3D) acini model.
**Methods:** Expression of ATF6α, ERAD-components, pro-inflammatory cytokines, cIAP2 and cleaved-caspase-3 were determined in SG of SS-patients and controls by Western-blot and qPCR. Localization of selected molecules was evaluated by immunofluorescence. Correlation between cytokines and ERAD-components was analyzed with the Pearson's test. ATF6α and ERAD activation, pro- and anti-apoptotic markers and cell viability were determined in a 3D HSG cell culture system treated with cytokines.
**Results:** LSG of SS-patients showed high cytokines levels and high activities of ATF6α and ERAD pathways. No significant differences in cleaved-caspase-3 and cIAP2 levels between both groups were observed. Significant positive correlations were observed between pro-inflammatory cytokines and ERAD-components expression levels. These correlations were demonstrated in *in vitro* 3D cell cultures treated with TNF-α and/or IFN-γ for prolonged times, without increased apoptosis.
**Conclusions:** In SS-patients, the permanent action of pro-inflammatory cytokines establishes a chronic ER stress condition with ATF6α pathway activation and increased ERAD mechanism. Higher ATF6α pathway levels would increase ERAD activity, which may help to control chronic ER stress and prevent death by apoptosis.
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**Disclosure of Interest:** None declared
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## AB0155 MICRORNA-155 MEDIATES AUGMENTED CD40 EXPRESSION IN LUPUS PLASMACYTOID DENDRITIC CELLS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic multi-organ autoimmune disease characterized by hyperactivated immune responses to self and persistent systemic inflammation. In addition to autoreactive T and B cells, dendritic cells also play an important role in inducing inflammation. Previously, we have reported abnormalities in circulating and bone marrow (BM)-derived plasmacytoid dendritic cells (pDCs) from SLE patients which suggested that pDCs may play a role in mediating SLE pathogenesis[1–3].
**Objectives:** In this investigation, we aim to seek for potential regulators that mediate functional aberrations of pDCs in SLE.
**Methods:** Bone marrow-derived pDCs from NZB/W F1 mice before and after the disease onset were compared for costimulatory molecule expressions and toll-like receptor (TLR) 7 stimulated responses. TLR7-induced microRNA (miRNA) profile changes in pDCs were examined to identify specific miRNA regulator. Functional validation of specific miRNA was further studied by transfection of miRNA mimics.
**Results:** *In vitro* derivation of pDCs from BM of pre-symptomatic and symptomatic NZB/W F1 mice showed similar basal expression of co-stimulatory molecules and TLRs -7 and -9. Functionally, symptomatic pDCs exhibited hypersensitivity to TLR7 but not TLR9 stimulation, as represented by the elevated upregulation of CD40, CD86 and MHC class II molecules upon R837 stimulation. In miRNA profiling, a significantly higher induction of miR-155 in symptomatic pDCs following TLR7 stimulation was observed. The transfection of miR-155 mimics in pre-symptomatic pDCs induced an augmented expression of *Cd40* which is consistent with the increased CD40 expression in symptomatic pDCs. *Cd40* expression was also found to negatively correlate with the miR-155 target *Ship1* in pDCs.
**Conclusions:** Overall, results from the current study provide evidence for miR-155-mediated regulation in pDC functional abnormalities in SLE. Findings from this study contribute to a better understanding of SLE pathogenesis and ignite future interests in evaluating the molecular regulation in autoimmunity.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3092

## AB0156 QUANTITATIVE PROTEOMIC APPROACHES FOR IDENTIFYING URINARY BIOMARKERS IN LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) is a severe clinical manifestation of systemic lupus erythematosus (SLE) associated with significant morbidity and mortality. Assessment of severity and activity of renal involvement in SLE requires a kidney biopsy, an invasive procedure with limited prognostic value. Despite years of research, a need remains for proximal, non-invasive biomarkers to help inform treatment decisions and to monitor disease activity and progression. Recent retrospective studies have revealed that baseline urine protein-creatinine ratio (UPCR) and reduction in UPCR during induction therapy are significantly associated with renal outcome[1]. Although proteinuria is highly correlated with disease progression in LN, the composition of the urinary proteome of LN patients remains poorly characterized.
**Objectives:** To better characterize the urinary LN proteome, we performed a preliminary proteomics study comprised of three complimentary discovery proteomic methods to identify urinary biomarkers of LN.
**Methods:** Urine samples from three female patients with biopsy confirmed LN, high proteinuria (>3 mg/mmol, and low serum complement C3 (<80 mg/dL) were compared to age- and gender- matched healthy controls. These samples were profiled using three mass spectrometry-based methods: 2D SDS-PAGE fractionation, a chemical labeling approach using tandem mass tags, and a label free data-independent acquisition (DIA) method.
**Results:** Using these combined approaches >2600 proteins were identified, 290 of which are up-regulated >2-fold in LN samples compared to healthy controls. While the chemical labeling approach enabled identification of more total proteins (2,598 with chemical labeling vs. 919 with DIA, 1% False Discovery Rate), the DIA approach outperformed the chemical labeling approach in identification of proteins significantly up-regulated in LN samples (52 with chemical labeling vs. 173 with DIA).
**Conclusions:** These results suggest that DIA-based approaches are less biased towards high abundance analytes and therefore potentially more suitable for proteomic profiling of biological matrices with a broad dynamic range like urine. Furthermore, candidate biomarkers identified using the DIA method are easily adapted into a targeted, multiplexed mass spectrometry assay suitable for absolute quantitation of candidate biomarkers in a clinical trial. Results from this study will be used to inform longitudinal and interventional studies focused on understanding the biological implications of these candidate biomarkers and to direct development of novel tools to evaluate disease progression and treatment efficacy of current and future LN therapeutics.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4468

## AB0157 FC GAMMA RECEPTOR EXPRESSION PROFILE IN PEDIATRIC-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Polymorphisms in the Fcγ receptor (FcγRI, FcγRIIa, and FcγRIIb and FcγRIIIa genes) have been associated with an increased susceptibility to autoimmune diseases including SLE and up-regulation of these may vary with disease activity and infection. There is a paucity of data on FcγR expression pattern in pediatric subjects with SLE.
**Objectives:** To assess the expression of CD 64 (FcγRI), CD32b (FcγRIIb) and CD16 (FcγRIII) on B lymphocytes, neutrophils and monocytes in children with pediatric-onset SLE (pSLE) and their correlation with disease activity as estimated by the SLEDAI score.
**Methods:** A cross - sectional descriptive study was conducted at PGIMER, Chandigarh, India. Children aged between 0 and 15 years fulfilling American College of Rheumatology classification criteria (1997) for SLE were enrolled. The study population was divided into active and inactive group using SLEDAI score. Controls were age and sex matched.
Blood samples of cases and controls were assessed for CD 64, CD32b, and CD16 expression on B lymphocytes, neutrophils and monocytes by flow cytometry using standard techniques. Median fluorescence intensity (MFI) and percentage of cells expression were calculated using the FACS DIVA software and Kaluza software.
**Results:** Thirty one children with SLE (14 in active group) and 13 controls were analyzed. The median values of percentage expression of CD 64 on lymphocyte and monocytes and MFI of CD16 on neutrophils in cases and control are tabulated.
Statistically significant difference ($p<0.05$) in expression of CD64 on lymphocytes, MFI of CD16 on neutrophils was noted in cases as compared to controls, while there was no difference between active and inactive cases. No difference was noted in expression of CD64 on monocytes between cases and controls.CD20 was reduced in cases probably secondary to therapy.
**Conclusions:** The percentage expression of CD 64 expression in lymphocytes and MFI of CD 16 expression in neutrophils were increased in patients of pSLE but no significant association was obtained with disease activity. There is paucity of data in pSLE and thus further studies are warranted to substantiate our finding. No correlation of CD16 and CD32b expression with disease activity was noted in our cohort, probably due to the small sample size.
**Disclosure of Interest:** None declared
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## AB0158 THE EXPRESSION OF BLIMP-1 IN B CELLS IN PERIPHERAL BLOOD FROM PATIENTS WITH SLE AND ITS CLINICAL SIGNIFICANCE

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**Objectives:** To detect the mRNA expression of B lymphocyte induced maturation protein-1 (Blimp-1) in $CD19^+$ B cells in peripheral blood of patients with systemic lupus erythromatosus (SLE) and healthy controls, and explore its clinical significance.
**Methods:** Expression level of Blimp-1 mRNA in $CD19^+$B cells in peripheral blood was determined by real-time PCR in 40 SLE patients and 20 healthy controls. The ratio of $CD19^-CD138^+$ plasma cells to $CD19^+$ B cells and the ratio of $CD19^+CD27^+$ memory B cells to $CD19^+$ B cells were studied by flow cytometry in peripheral blood of two groups.
**Results:** 1. The expression level of Blimp-1 mRNA in $CD19^+$ B cells in peripheral blood od SLE patients was higher than that in healthy controls ($P<0.05$), and the expression level of Blimp-1 in active SLE patients was higher than that in inactive SLE patients ($P<0.05$). 2. The $CD19^-CD138^+$ plasma cells/$CD19^+$ B cells ratio was increased in SLE patients compared to healthy controls ($P<0.01$), and the $CD19^-CD138^+$ plasma cells/$CD19^+$ B cells ratio in active SLE patients group was higher than that in inactive SLE patients ($P<0.05$). However, the $CD19^+CD27^+$ memory B cells/$CD19^+$ B cells ratio showed no significantly different between SLE patients and healthy controls ($P>0.05$). 3. The expression level of Blimp-1 was positive correlated with the $CD19^-CD138^+$ plasma cells/$CD19^+$ B cells ratio ($r_s=0.336$, $P=0.034$), positive correlated with anti-dsDNA antibody and immunoglobulin G ($r_s=0.493$, $P=0.006$; $r_s=0.527$, $P=0.004$), positive correlated with anti-nucleosome antibody and anti-C1q antibody ($r_s=0.452$, $P=0.040$; $r_s=0.522$, $P=0.015$), negative related with white blood cell count and platelet count ($r_s= -0.367$, $P=0.046$; $r_s= -0.386$, $P=0.035$).
**Conclusions:** The expression of Blimp-1 was up-regulated in SLE patients and significantly correlated with plasma cells, which suggests that Blimp-1 may be involved in the pathogenesis of SLE by promoting plasma cells differentiation.
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**Disclosure of Interest:** None declared
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## AB0159 PROLACTIN INDUCES INTERFERON REGULATORY FACTOR 1 ACTIVATION AND HISTONE H4 HYPERACETYLATION IN PRIMARY MONOCYTES COMPARABLE TO CHANGES SEEN IN MONOCYTES FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Epigenetic changes in systemic lupus erythematosus (SLE) offer a potential explanation for the chronicity of disease. We previously found a global increase in histone H4 acetylation (H4ac) in SLE monocytes and 63% of genes with increased H4ac had potential interferon regulatory factor (IRF) 1 binding sites within the 5kb upstream region. We identified specific H4 lysine acetyl groups with significant hyperacetylation in SLE monocytes, as well as an imbalance in specific histone acetyltransferases (HATs) and histone deacetylases (HDACs) in favor of hyperacetylation. IRF1-overexpression drove H4 hyperacetylation and

**Abstract AB0157** – Table 1

| Parameter | Total cases Median (IQR)* | Active cases Median (IQR) | Inactive cases Median (IQR) | Controls Median (IQR) |
|---|---|---|---|---|
| Percentage of CD 64 on lymphocyte | 1.57 (0.86, 3.13) | 1.60 (1.14, 3.39) | 1.50 (0.66, 2.91) | 0.74 (0.44, 1.67) |
| Percentage of CD 64 on monocytes | 55.00 (30.31,73.50) | 55.75 (40.81, 77.85) | 40.92 (27.82, 69.78) | 44.08 (37.52,72.90) |
| MFI of CD16 on neutrophils | 3.47 (1.4, 21.40) | 2.70 (1.37, 6.65) | 6.25 (1.41, 47.85) | 11.40 (5.36, 37.91) |

*IQR- interquartile range.

IRF1 recruitment of HAT p300 to target genes increased IRF1 binding to genes with pathological expression in SLE monocytes.
IRF1 is highly inducible by prolactin, a hormone implicated in the pathogenesis of SLE: hyperprolactinemia has been reported in 15–33% of SLE patients as compared to 0.4–3% of controls. Prolactin upregulation of IRF1 can lead to H4ac in Nb2 T cells, representing a potential pathological pathway in SLE.
**Objectives:** Prolactin-induced IRF1 activation in primary monocytes and THP1 cells was examined, with the aim to identify IRF1 interactions with histone acetyltransferases (HATs) and histone deacetylases (HDAC) leading to pathological H4ac in SLE.
**Methods:** Flow cytometry for acetylated H4 lysines: K5, K8, K12, K16 were run on the Accuri C6 with isotype controls. H4ac was defined in primary monocytes from 12 normal males under both unstimulated and prolactin-stimulated conditions. Real-time quantitative reverse transcription polymerase chain reaction (qRT-PCR) evaluated HAT/HDAC expression in monocytes. IRF1 activation by prolactin in primary monocytes was studied by immunofluorescence microscopy. Interactions of IRF1 and HATs/HDACs were studied in THP1 cells by ChIP analysis.
**Results:** Flow cytometry found significantly increased total H4ac, H4K5, H4K8, H4K12, and H4K16 acetylation ($p$=0.01, 0.01, 0.01, 0.002, 0.04) in monocytes stimulated at prolactinoma levels (2000 ng/mL); acetylation at total H4ac, H4K5, H4K8, H4K12, and H4K16 was also increased at pregnancy levels (200 ng/mL).These results were similar to the increase in H4ac seen in SLE monocytes. Immunofluorescence showed translocation of IRF1 from the cytoplasm to the nucleus in prolactin-stimulated primary monocytes at both 200 ng/mL and 2000 ng/mL cells by 1 hr, demonstrating IRF1 activation.
qRT-PCR studies of HAT/HDAC expression patterns found increases in PCAF, P300, CBP, GCN5 and ATF2 expression monocytes stimulated by prolactin that was time dependent. Additionally, ChIP assays in THP1 cells suggested that prolactin-stimulation can recruit IRF1 and acetylated H4 to prolactin target genes.
**Conclusions:** These data demonstrate that prolactin stimulation of monocytes induces IRF1 activation and a pattern of acetylated H4 that corresponds to the changes seen in SLE. This helps to explain the known association of prolactinomas with SLE. The identification of candidate HATs that associate with IRF1 in the context of prolactin stimulation may provide for potential therapeutic targets in SLE.
**Disclosure of Interest:** None declared
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### AB0160 MIR-155 FACILITATE THE DIFFERENTIATION OF TH17 CELL BY INHIBITING THE GENE EXPRESSION OF ETS-1 IN VITRO/IN VIVO EXPERIMENTS

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**Background:** MicroRNA (miR) as a class of regulatory elements are plays important role in various autoimmune diseases, including rheumatoid arthritis.MiR-155 has been demonstrated as a central regulator of the autoimmune system, but its function during autoimmune arthritis is still poorly understood.
**Objectives:** To clarify the function of miR-155 in CD4$^+$regulatory Th17 cell differentiation, as well as the mechanism involved in autoimmune arthritiTo clarify the function of miR-155 in CD4$^+$regulatory Th17 cell differentiation, as well as the mechanism involved in autoimmune arthritis.
**Methods:** In vitro, CD4$^+$ cell was isolated from DAB1 mice' spleen. We performed gain-and-loss-of-function analysis by transfection miR-155 mimics and miR-155 inhibitors into purified CD4+T cells. Also, we used RNA interference to silence Ets-1 gene expression. In addition, in vivo, up regulation of miR-155 expression by lent virus miR-155 (LV-miR-155) infection and silencing of miR-155 expression by lent virus-anti-miR-155 (LV-anti-miR-155) was researched in the experimental mice with type II collagen (CII)-induced arthritis (CIA). The ratio of IL-17 was analyzed using flow cyctometry (FCM).The related gene expression such as Foxp3, RORgt, IFN-g, Ets-1and stat3 was detected by Quantitative Real-time PCR (qPCR) and western blotting.
**Results:** The result showed that miR-155 promoted Th17 cell differentiation. It also induced related gene expression, such as Foxp3, RORgt, IFN-g and stat3; it inhibited Ets-1 gene expression. This may because miR-155 modulates Th-17 cell differentiation by targeting Ets-1.Here we identify miR-155 was highly correlated with disease in mice with experimental CIA. In vivo over expression of miR-155 led to more Th-17cells and severe CIA, and the related genes were higher express, but Ets-1 was lower expression. In contrast, the down regulation of miR-155 expression resulted in fewer Th17 cells and Normal mice. The related genes were lower express, but Ets-1 was higher expression.
**Conclusions:** Our data show a critical role for miR-155 in Th17 differentiation and the pathogenesis of autoimmune arthritis, and it might be involved in the occurrence and development of autoimmune diseases in rheumatoid arthritis.
**Disclosure of Interest:** None declared
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## Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

### AB0161 INVESTIGATION OF OXIDATIVE STRESS, OXYGENATION AND ERYTHEMA IN PATIENTS WITH SYSTEMIC SCLEROSIS, PRIMARY RAYNAUD'S PHENOMENON AND UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE AND IN HEALTHY CONTROLS

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**Background:** Systemic sclerosis (SSc) is a rare connective tissue disease characterised by skin fibrosis and microvascular dysfunction. Oxidative stress, hypoxia and ischaemia have previously been implicated in SSc pathogenesis.
**Objectives:** The aim of this study was to further elucidate the pathophysiology of different subtypes of Raynaud's phenomenon (RP) by measuring oxidative stress, oxygenation and perfusion in patients with primary RP (PRP), undifferentiated connective tissue disease (UCTD), and SSc, comparing between groups and with healthy controls. Patients with UCTD were included to understand more about their early structural and functional changes as they are potentially an interim group between PRP and SSc. Our hypothesis was that oxidative stress would be increased in the UCTD and SSc groups and the oxygenation and perfusion would be decreased.
**Methods:** Measurements of oxidative stress, oxygenation and erythema (skin redness, an approximate, indirect measure of perfusion) were taken at a single point, at 9 sites, over the body using spectroscopy. Oxidative stress was measured as an increase in fluorescence induced by UV light. Oxygenation and erythema were calculated from white light reflection spectra.
**Results:** Measurements were taken from 53 healthy controls (HC), 36 female (f), median age 45, IQR [38–54] years; 20 patients with PRP, 17 f, 46 [39–52] years, duration of RP 8 [3–25] years; 37 patients with UCTD, 26 f, 43 [31–54] years, duration of RP 7 [5–16] years; 100 patients with SSc, 83 f, 59 [52–66] years, duration of RP 16 [8–24] years, duration of SSc 11 [4–18] years. A subset of data over the 9 sites is shown in Table 1. Oxidative stress was increased at all sites (statistically significant differences between groups [$p<0.05$] at 7/9 sites) in patients with SSc as compared to HC. Oxygenation showed no trend. Erythema showed a trend of lower values at all sites for patients with SSc vs. HC (statistically significant at 7/9 sites).
**Conclusions:** Patients with SSc showed a trend towards increased oxidative stress and decreased erythema compared to HC as hypothesised, providing further evidence that both oxidative stress and ischaemia are associated with SSc. Oxygenation showed no trend, suggesting that oxygenation measurements may not be sensitive enough to detect differences or that oxygenation is not affected at baseline (i.e. it is functional rather than structural). Further studies may clarify whether incorporating a dynamic challenge (e.g. temperature change) would aid differentiation between groups.
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### AB0162 ABNORMAL B-CELL DISTRIBUTIONS IMPROVED BY TOCILIZUMAB MONOTHERAPY IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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**Background:** Abnormalities in B-cell population distribution were recently reported in polymyalgia rheumatica (PMR), which improved with glucocorticoïds. Data about cytokine involvement in PMR pathophysiology are scarce and contradictory.
**Objectives:** Our objective was to analyze the subsets of lymphocytes and level

**Abstract AB0161** – Table 1. Subset of measurements taken at 9 sites (arbitrary units)

| | | HC | PRP | UCTD | SSC | p value |
|---|---|---|---|---|---|---|
| Oxidative stress | Dorsum hand | 4.05 [3.69–4.74] | 4.26 [3.47–4.62] | 4.25 [3.57–4.68] | 4.89 [4.28–5.74] | 0.0001* |
| | Forearm | 4.32 [3.81–4.82] | 4.46 [4.12–4.98] | 4.60 [3.94–5.66] | 5.06 [4.42–5.84] | 0.0022* |
| Oxygenation | Dorsum hand | 8.74 [0.83–14.29] | 11.10 [–0.37–21.11] | 7.45 [1.80–18.01] | 11.33 [5.94–16.97] | 0.598 |
| | Forearm | 4.23 [0.11–8.43] | 2.79 [0.43–8.33] | 6.26 [2.45–9.90] | 7.16 [2.08–11.92] | 0.123 |
| Erythema | Dorsum hand | 2.14 [2.08–2.19] | 2.08 [2.03–2.16] | 2.07 [1.98–2.19] | 2.06 [1.97–2.12] | 0.0004* |
| | Forearm | 2.14 [2.05–2.20] | 2.11 [2.05–2.18] | 2.07 [2.01–2.20] | 2.03 [1.90–2.12] | <0.0001* |

p value, ANOVA. *Statistically significant ($p<0.05$).

of cytokines in patients with PMR and to follow their evolution after tocilizumab treatment.
**Methods:** The TENOR study [Clinicaltrials.gov (NCT01713842)] was an open labeled prospective trial including patients with recent PMR fulfilling the Chuang criteria. Patients had active disease and were glucocorticoïds (GCs) free. Patients with suspected giant cell arteritis were excluded. Patients were treated with tocilizumab infusions (week 0, 4 and 8) without GCs (period 1) and then by low-dose GCs from week 12 to week 24 (period 2). Peripheral blood lymphocyte profiling was performed by multicolor flow cytometry in 18 patients at week (W) 0 (before first tocilizumab infusion), W2, W12 and W24. Cytokine levels were estimated using membrane cytokine array enabling detection of 34 different cytokines. Interleukine (IL) 6 and 10 levels were evaluated by ELISA at W0 and W12. They were compared to 16 sex and age-matched healthy controls (HC).
**Results:** At baseline, total lymphocyte (p=0.31), T cell (p=0.46), B cell (p=0.08) and NK cell (p=0.905) levels were similar between PMR patients and HC. Transitional B cells ($CD24^{high}$, $CD38^{high}$) and mature-naïve B cells ($CD24^{low}$, $CD38^{low}$) were lower in patients with PMR than in HC, 3±6 vs 6±6 per $mm^3$ (p=0.01) and 46±41 vs 92±53 per $mm^3$ (p=0.01), respectively. After tocilizumab, total lymphocyte count slightly increased (1739±539/$mm^3$ at W0, 2030±591/$mm^3$ at W2, 2068±775/$mm^3$ at W12, and 2031±584/$mm^3$ at W24, $p<0.01$). The absolute number and proportion of $CD4^+$ T cells and NK cells were unaffected by the treatment. In contrast, both absolute number and proportion of B cells increased between W0 and W12, respectively from 176±105/$mm^3$ to 260±192/$mm^3$ (p=0.004) and from 10.1% to 13.0% ($p<0.001$). Among B-cell subsets, these modifications were mainly attributable to the variations of the memory compartment. Unswitched (IgD+CD27+) and switched (IgD-CD27+) memory B-cell absolute number and proportions significantly increased after tocilizumab ($p<0.001$). After cytokines detection using membrane cytokine array only IL-6 level was significantly different between patients and HC. IL-6 and IL-10 levels were measured in ELISA. IL-6 level was higher in patients (112±78 pg/ml) than in HC (13±13) ($p<0.0001$) and was found associated with disease activity measured by PMR-AS (r=0.628; p=0.006). IL-6 decrease in patients treated with tocilizumab infusion was not significant.
**Conclusions:** The drastic clinical improvement following tocilizumab monotherapy in PMR patients is paralleled by an increase in peripheral blood memory B cells. These observations suggest that B cells are involved in disease pathophysiology, and that IL-6 blockade could restore B-cell homeostasis.
**Disclosure of Interest:** None declared
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### AB0163 NO ASSOCIATION BETWEEN THE PERCENTAGE OF MEMORY OR TRANSITIONAL B REGS AND DISEASE-RELATED AUTOANTIBODIES IN SYSTEMIC SCLEROSIS

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**Background:** Recently, we found that Breg cells are numerically decreased and functionally impaired in patients with systemic sclerosis (SSc)[1] A subsequent study confirmed these data and reported a negative correlation between Breg levels and the titres of anti-topo I and anti-centromere antibodies (ab) in patients with SSc[2].
**Objectives:** To assess the relation between memory or transitional Bregs with SSc-specific anti-topo I, anti-centromere (CEN) and anti-RNA pol I abs in our cohort of SSc patients.
**Methods:** Fifty patients with Ssc were tested for disease-specific abs (Topo I, CENP, RNA pol I) using line blot analysis (EUROIMMUN), and for memory [CD19(pos)CD27(pos)CD24(high)] and transitional [CD19(pos)CD24(high) CD38(high)] Bregs using flow cytometry.
**Results:** Anti-CEN, anti-Scl-70 and RNA pol I abs were present in 12 (24%), 23 (46%) and 7 (14%) patients with SSc, respectively. The % of memory and transitional B regs was comparable between anti-CEN ab-positive and -negative patients (1.56±1.40 vs 1.74±1.01 and 0.78 ±0.73 vs 0.65±0.68 respectively, $p>0.05$), and also beween anti-RNA ab-positive and -negative patients with SSc (1.96±1.26 vs 1.65±1.09 and 0.54±0.53 vs 0.7±0.72 respectively). While the % of memory Bregs did not differ between anti-topo I-positive and -negative patients (1.96±1.26 vs 1.65±1.09 and 0.54 ±0.53 vs 0.7±0.72 respectively), the % of transitional Bregs tended to be decreased in patients with anti-topo I-positive compared to anti-topo I ab-negative patients (0.49±0.46 vs 0.84±0.61 p=0.066). Levels of B regs (memory or transitional) did not negatively correlate with autoantibody titres by line blot analysis.
**Conclusions:** We failed to find an association between percentages of memory and transitional B regs with SSc-specific autoantibodies.
**References:**
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[2] Matsushita T et al Rheumatology 2016;55:263–7
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### AB0164 DISEASE PROGRESSION IN 282 PATIENTS WITH UNDIFFERENTIATED SSC – DATA FROM THE GERMAN NETWORK FOR SYSTEMIC SCLERODERMA

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**Background:** Systemic sclerosis (SSc) is a heterogeneous multisystem connective tissue disease, usually subdivided into the main SSc subsets, e.g. limited (lcSSc), diffuse SSc (dcSSc) and SSc overlap syndromes. However, some patients present with symptoms suggestive of, but not conclusive for a diagnosis of definite SSc. This subset has been referred to as undifferentiated or very early SSc. It was defined as positive RP together with at least one further feature of SSc and/or detectable SSc-specific autoantibodies.
**Objectives:**
**Methods:** Up to date, more than 3400 patients have been registered within the German network for systemic scleroderma. Disease progress after initial patient registration and further follow-up visits was analysed to determine, whether clinical features in patients with undifferentiated SSc change over time into definite SSc.
**Results:** Among 3473 registered patients, 8.1% (282/3473) were diagnosed with undifferentiated SSc. Of these, 87.5% were female with a mean age at onset of 59.9±1.5years. A significant difference was detectable comparing patients with undifferentiated SSc and lcSSc (54.8±0.5years; $p<0.001$) as well as dcSSc (49.8±0.6years; $p<0.001$). Positive antinuclear antibodies (ANA) were detectable in 219 (77.7%) patients; of these 40.2% were anti-centromer (ACA) positive and 12.8% anti-topoisomerase antibody (ATA) positive. No substantial difference regarding organ manifestations between patients with or without existing ANAs was found.
34.0% of undifferentiated SSc patients suffered from sicca symptoms, followed by 31.2% with gastrointestinal (GI) involvement, 30.5% with musculoskeletal involvement, 14.5% with lung fibrosis, 6.0% with heart involvement, 5.0% with pulmonary arterial hypertension (PAH) and 0.4% with renal crisis. Musculoskeletal involvement, sicca symptoms and heart involvement were found in a similar percentage in patients with undifferentiated and lcSSc. Lung fibrosis, PAH and GI involvement occurred significantly less in patients with undifferentiated SSc compared to lcSSc. Within a mean follow-up time of 3.6years, the majority of the patients classified initially as undifferentiated SSc, remained within this subset (76.6%), while only 16.3% converted into lcSSc. 4.6% were classified as dcSSc and 3.2% as SSc overlap syndromes.
**Conclusions:** Patients classified as undifferentiated SSc, develop clinical features suggestive of SSc at a significantly older age than other subsets (i.e. 5–10 years). During follow up progression into a limited, diffuse or SSc overlap syndrome subset was observed, however, the majority of undifferentiated SSc patients remained stable and did not develop definite SSc.
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## Basic science in paediatric rheumatology

### AB0165 IN DEPTH IMMUNOPHENOTYPIC ANALYSIS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): A CROSSECTIONAL STUDY

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**Background:** The potential of expanded flow cytometric analysis of PBLs has not been yet been fully exploited to study JIA heterogeneity neither to monitor JIA patients' on biological treatments
**Objectives:** To analyze in depth lymphocyte subpopulations in treated JIA patients stratified by age and gender.
**Methods:** One hundred one patients, 69 children and 32 adult fulfilling JIA (ILAR) criteria attending HUVH rheumatology clinic were included. All patients were treated with either MTX, anti-TNFα, or a combination of both. Controls were sex/age matched volunteers either healthy or attending the clinics of HUVH for

non inflammatory conditions (59 controls, 29 paediatric and 30 adult). Extended immunophenotype following FITMaN protocol that discerns 57 peripheral blood lymphocyte (PBL) subpopulations was applied. Bonferrroni's correction indicated that the cut off for significance was $p<0.00041667$.

**Results:** Changes common to each group of patients irrespective of treatment are as follows: paediatric patients showed lower percentage of CD8 effector cells (CD45RA+CCR7-) when compared to controls (10.53±5.71 *vs* 16.92±5.71). Percentage of total CD4 cells was higher on JIA children than in controls (42.21±7.40 *vs* 36.04±5.22). No differences were found on percentages nor in absolute number of Th1 (CXCR3+CCR6-), Th2 (CXCR3-CCR6-), or Th17 (CXCR3-CCR6-) CD4 cells. Interestingly all Th subpopulations showed decreased expression of HLA-DR in JIA children when compared with controls (6.06±3.08 *vs* 10.49±5.02; 0.81±0.51 *vs* 1.48±0.64; 8.57±3.81 *vs* 12.6±4.95; respectively). JIA adults presented no significant differences in T cells subpopulations compared to adult controls, but showed higher percentage of CD21- switch-memory B cells (IgD-IgM-CD27-) than controls (10.82±5.33 *vs* 4.29±4.33).

In a second analysis of the JIA patients few differences were observed according to the administered therapy. Paediatric patients treated with MTX (n=27) showed a lower proportion of the effector memory (CD45RA-CCR7-) cells both CD4+ and CD8+, when compared to controls, anti-TNF, and anti-TNF plus MTX groups (20.01±7.76 *vs* 27.64±9.27; 20.01±7.76 *vs* 27.84±4.27; 20.01±7.76 *vs* 27.07±10.05; for CD4s and 26.42±7.23 *vs* 37.10±12.38; 26.42±7.23 *vs* 42.08±11.59; 26.42±7.23 *vs* 37.27±12.54 for CD8s, respectively). Percentage of CD25+ lymphocytes was higher in the anti-TNF plus MTX group. The Th1–17 (CCR6+CXCR3+) CD4 cell subpopulation was significantly increased in anti-TNF and anti-TNFα plus MTX groups compared with controls and MTX (10.45±3.14 *vs* 6.38±3.89; 10.45±3.14 *vs* 4.78±2.56 and 9.43±4.63 *vs* 6.38±3.89; 9.43±4.63 *vs* 4.78±2.56, respectively). Adult patients treated with anti-TNFα+MTX and MTX presented higher levels of CD21- naïve B cells compared to HC and to anti-TNF groups (4.86±3.24 *vs* 2.32±1.69; 4.86±3.24 *vs* 2.95±1.94 and 5.38±1.54 *vs* 2.32±1.69; 5.38±1.54 *vs* 2.95±1.94).

**Conclusions:** In depth phenotypic analysis of PBL in JIA showed alterations in cell subpopulations that seem dependent on age group. Our data also suggests that detailed in depth phenotypic analysis can be a valuable tool for monitoring and comparing JIA treatments.

**Disclosure of Interest:** None declared

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### AB0166 SEX-SPECIFIC GENE EXPRESSION DIFFERENCES IN OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Juvenile idiopathic arthritis (JIA) is a paediatric autoimmune disease (AD) with a female preponderance, though this differs by subtype. Whether this sex bias is reflective of differing disease pathogenesis between the sexes is unknown. Gene expression signatures can be biologically and clinically informative, but few expression studies have been performed in JIA. Though gene expression is recognised as sexually dimorphic in many states, its role in JIA sex bias has not been considered. In response to infection females produce more antibodies than males, which could increase natural autoantibody production and the risk of developing AD. Gene expression differences between the sexes may reflect this. The reduced heterogeneity afforded by sex-stratified transcriptome-wide analysis may provide insight into how sex influences disease pathogenesis in JIA.

**Objectives:** We aimed to identify sex-specific differences in patients with oligoarticular JIA versus healthy controls through RNA-seq analysis on CD4+ T cells.

**Methods:** Six male and six female oligoarticular JIA cases, with no prior exposure to disease-modifying anti-rheumatic drugs, were age and sex-matched to healthy controls. CD4+ T cells were selected as existing data links T cell gene networks to JIA. RNA was extracted from CD4+ T cells using the Qiagen miRNeasy extraction kit. Sequencing library preparation was performed using the Illumina TruSeq Stranded Total RNA LT kit. One female sample did not pass quality control and was not sequenced. Sequencing was performed using 75bp paired-end reads to a depth of ~20 million reads on the Illumina NextSeq. Quality trimmed reads were mapped to the genome using the STAR aligner. Read counts across exons and genes were summarised using featureCounts. Normalised read counts were used for differential gene expression analysis with edgeR. GOseq was used for gene ontology analysis. Males and females were analysed separately.

**Results:** No sex-specific differentially expressed (DE) genes reached FDR adjusted $p<0.05$. At unadjusted $p<0.05$ there were far more male (1480) than female (118) specific DE genes, with 24 overlapping. Pathway analysis of male-specific DE genes highlighted antigen processing and presentation, immune response, and IFNϒ production, among other disease-relevant gene networks. Corresponding female-specific analysis did not reveal obvious disease-relevant networks. For many genes DE between male cases and controls, male case gene expression appeared more similar to all females (Figure 1).

**Conclusions:** We have identified sex-specific differences in CD4+ T cell gene expression between healthy controls and oligoarticular JIA cases predominantly in males, despite the female preponderance. Our data may reflect that some of the pathogenesis for JIA differs between the sexes, and that gene expression differences play a particularly important role in male JIA, perhaps by a more "female" immune response occurring in male cases. Given the small sample size, replication is necessary and is underway.

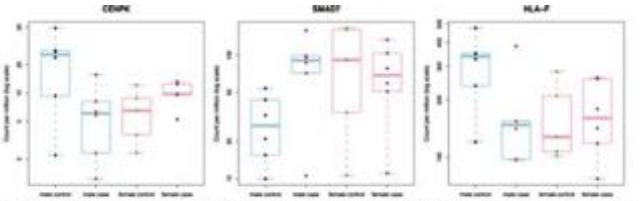



**Figure 1:** Distribution of normalised gene transcript counts by RNA-seq in male and female JIA cases and age-matched controls at top-ranked male-specific differentially expressed genes. *CENPK*, 2nd ranked gene, $p=1.1x10^{-5}$; *SMAD7* 4th ranked gene, $p=1.7x10^{-5}$; HLA-F, 5th ranked gene, $p=2.3x10^{-5}$. Note the similarity of the male cases to the female cases and female controls (columns 2,3,4).

**Disclosure of Interest:** None declared

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## Rheumatoid arthritis - prognosis, predictors and outcome

### AB0167 ACR/EULAR REMISSION IN EARLY RHEUMATOID ARTHRITIS ASSOCIATES WITH A SHORTER TIME TO FULFILMENT THE CLASSIFICATION CRITERIA AND A LOWER BMI

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**Background:** A prolonged disease duration is associated to a lower chance to achieve disease remission in rheumatoid arthritis. Onset of the disease can be defined in a number of ways and, when possible, the following data should be recorded: 1) first musculoskeletal (MSK) symptoms relevant to the current compliant 2) first persistent patient-reported joint swelling 3) initial fulfilment of criteria for RA based on data obtained retrospectively[1].

**Objectives:** The aim of this study was to identify the variables associated with ACR/EULAR remission[2] in a cohort of early rheumatoid arthritis (ERA). In particular, the different types of disease onset, as defined[1], were investigated.

**Methods:** All the patients, referred to the Early Arthritis Clinic of the University Rheumatology Clinic of Udine between October 2013 and October 2015, with a diagnosis of RA and fulfilling ACR/EULAR 2010 criteria, were included. The EULAR recommendations for treat to target were followed. At the first visit, 13 clinical and laboratory variables associated with RA, including the different type of onset[1], were recorded. The variables associated with remission at the 12th month (+12) of therapy by univariate analyses were included in a multivariate logistic regression model. Receiver operator characteristic (ROC) curves were used to evaluate the discriminative capability of the different types of onset.

**Results:** Ninety-two patients with ERA were assessed and 65 completed 12-month evaluation. 15/65 (23,1%) reached ACR/EULAR remission at +12. Two variables were selected in the logistic regression analysis (i.e. BMI and time to fulfilment of ACR/EULAR classification criteria). A low BMI (OR 0,54; CI 95% 0,33 to 0,86; p=0,01) predicted remission and 23,5 being the optimal BMI cut-off value. Time to fulfilment of ACR/EULAR classification criteria for RA was also significantly associated with remission at +12 (OR 0,21; CI 95% 0,05–0,92; p=0,039) and 2,5 months was the cut-off value showing the best discriminative power for remission achievement. By contrast, a shorter time from the onset of MSK symptoms (5.5 months showing the best discriminative power) was selected only by univariate analysis.

**Conclusions:** From a clinical perspective the present preliminary data may be reassuring if confirmed by larger analyses: a shorter time from the fulfilment of ACR/EULAR classification criteria of RA, when treatment has been frequently started (thus, not necessarily the time from the onset of MSK symptoms) is associated with disease remission at +12 in ERA. From a biologic point of view, starting the treatment as soon as disease begins (i.e. onset of MSK symptoms) may be more effective, but the currently available prognostic, diagnostic and treatment tools do not allow this recommendation yet. Furthermore remission is related to BMI, since patients with BMI >24 showed a lower chance to achieve remission

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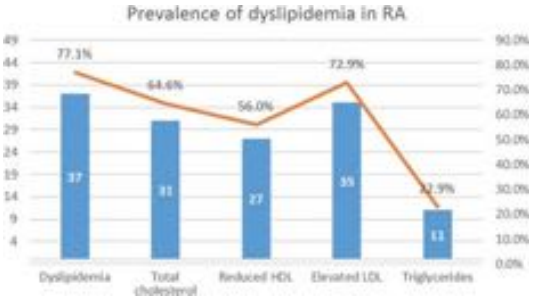
**Disclosure of Interest:** None declared

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## AB0168 DYNAMICS OF LIPID PROFILE IN PATIENTS WITH A HIGH ACTIVITY OF RHEUMATOID ARTHRITIS

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**Background:** The main cause of high mortality of RA patients is early formation and progression of atherosclerotic lesion in vessels, leading to an increased risk of myocardial infarction, congestive heart failure, stroke, and sudden death. A similar profile of the immune response is the activation of T-cells and mast cells, the production of proinflammatory cytokines, increased levels of α-metalloproteinase; the identity of cellular composition of an atherosclerotic plaque and the inflammatory infiltrate in synovium with RA; correlation between the level of C-reactive protein (CRP), ESR, cytokines (especially Interleukin-6 (IL-6)), cell adhesion molecules and blood lipid spectrum (HDL-C, apoA1) – all these indexes help to explain the high frequency of atherosclerosis manifestations in RA patients.
**Objectives:** Identify blood lipid profile disturbances in patients with a high activity of rheumatoid arthritis.
**Methods:** The study is based on the follow-up results of 48 RA patients under treatment at the Republican Centre of Rheumatology attached to Tashkent Medical Academy. Criteria for inclusion of patients in the study were – RA diagnosis, verified in accordance with the ACR/EULAR (2010) criteria, active RA, the informed consent to participate in the study. All patients had a high disease activity defined by DAS28. Activity indexes ranged from 5.11 to 8.29 and averaged 6.44. Analysis of the blood lipid profile was based on optimum values: total cholesterol (TC) – less than 5 mmol/l (193.4 mg/dl), low-density cholesterol (LDL) – less than 3 mmol/l (116.0 mg/dl), high-density cholesterol (HDL) – greater than 1.2 mmol/l (46.4 mg/dl) for women and more than 1 mmol/l (38.7 mg/dl) for men, triglycerides (TG) – less than 1.77 mmol/l (68.4 mg/dl).
**Results:** The average age of RA patients was 49.7 years (ranged from 36 to 72), the average RA duration was 8.2 years (ranged from 1 to 22 years). The dyslipidemia was revealed in 37 patients of the study group, amounting to 77.1%. TC level increase have been reported in 31 out of 48 (64.6%) cases and was associated with an imbalance of other components of the lipid profile. The average TC value was 5.8 mmol/l (224.28 mg/dl). Increased TG levels have been reported in 11 of 48 cases (22.9%), reduced HDL - in 27 out of 48 (56%) cases. The average TG level – 1.8 mmol/l (69.6 mg/dl), HDL – 1.1 mmol/l (42.5 mg/dl). The most significant was increase in LDL – revealed in 35 patients (72.9%). Mean LDL – 3.9 mmol/l (150.8 mg/dl). Most of the patients had type II hyperlipidemia (highly atherogenic): IIa – 23 (47.9%), IIb - 7 (14.6%).




**Conclusions:** Results of our investigation showed the presence of a coarse lipid imbalance in patients with highly active RA. The most expressed imbalance was the increase in TC and LDL. Similar violations observed in the majority of patients are associated with a highly atherogenicity in RA and a high risk of cardiovascular events.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5694

## AB0169 NEUTROPHIL TO LYMPHOCYTE RATIO AND CORRELATION TO RHEUMATOID ARTHRITIS ACTIVITY

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by joint pain and swelling, as well as destruction of synovial joints leading to significant morbidity and mortality[1]. Patients are classified as having RA with a combination of a history of prolonged symptom duration, a swelling of joints on physical examination, serological markers including rheumatoid factor (RF), anti-cyclic citrullinated peptide (CCP) antibodies, and acute-phase response measures including the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)[2]. The blood neutrophil-to-lymphocyte ratio (NLR) has been identified as a potentially useful marker of disease activity in disease states with an inflammatory component such as malignancies, cardiovascular disease, and rheumatologic diseases[3–5].
**Objectives:** To investigate whether NLR can be used as a marker of inflammation and disease activity in RA patients with varying disease activity levels as assessed by the RAPID 3 (routine assessment of patient index data 3) at their most recent visit in the rheumatology clinic.
**Methods:** We conducted a retrospective chart review of 229 consecutive patients with a diagnosis of RA as determined using the 2010 ACR criteria for diagnosis of RA seen at the outpatient Rheumatology clinic of Einstein Medical Center in Philadelphia, PA, a tertiary urban hospital. At the time of each visit, each patient completes the RAPID3 questionnaire and the data are recorded in the electronic medical record. NLR was calculated using data from the complete blood count drawn at the time of the visit. Pearson's correlation coefficient (r) between NLR and well accepted disease activity markers (RAPID 3, ESR, CRP) was calculated. Multivariate linear regression was also performed to assess the association of the above variables.
**Results:** Two hundred seven patients (85% women) with a mean age of 59.6 years were included in the analysis. At the time of the random visit, mean NLR was 2.97, RAPID 3 score 13.8, ESR 36.5 mm/hr and CRP 2.3 mg/L. The NLR significantly correlated with RAPID 3 score ($r=0.24$, $p<0.01$), but not ESR ($r=0.1$, $p=0.13$) or CRP ($r=0.12$, $p=0.07$). Multivariate linear regression analysis showed that NLR was independently associated with RAPID 3 score ($b=0.75$, $p<0.01$).
**Conclusions:** NLR is an inexpensive and readily available inflammatory marker which may be useful as an indicator of disease activity in patients with RA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4783

## AB0170 VITAMIN D DEFICIENCY IS ASSOCIATED WITH HIGHER DISEASE ACTIVITY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:**
Vitamin D deficiency is common in rheumatoid arthritis (RA) and may be related to disease activity.
**Objectives:** 1. To study the relationship between vitamin D deficiency and disease activity at RA onset. 2. To investigate possible influence of vitamin D supplementation on disease activity in early RA patients.
**Methods:** We studied 81 consecutive patients with new RA onset (71,6% women, mean age 60±14 years) admitted to the Department of Internal Medicine and Rheumatology, Military Institute of Medicine in Warsaw. Demographic, clinical, laboratory, and treatment variables were collected. The patients were treated with methotrexate, low dose of glucocorticoids and supplemented with vitamin D. Disease activity was assessed every month during the first year of therapy using DAS28-ESR, DAS28-CRP, CDAI, SDAI indices. Serum 25-hydroxy- vitamin D (25(OH)D3) was measured at baseline, after 6 and 12 months. Ultrasound assessment of hand joints was performed by the same assesssor at baseline and after 12 months. We defined vitamin D serum concentration <20ng/mL as vitamin D insufficiency and serum concentration <10ng/mL as vitamin D deficiency. New erosions found at ultrasound examination after 12 months were considered disease progression.
**Results:** At baseline mean 25(OH)D3 serum concentration was 14,6±7,7ng/mL. Sufficient vitamin D serum concentration was found in 22% patients, 49% of patients had vitamin D insufficiency and 29% were vitamin D deficient. The patients with vitamin D deficiency at baseline had significantly higher number of tender and swollen joints, higher physician global assessment and higher number of joint effusion detected by ultrasound examination than other patients. There were no significant differences in ESR and CRP values according to vitamin D concentration. After 12 months (the data available for 65 patients) 20,3% of the patients had still insufficient vitamin D concentration and 4,7% were vitamin D deficient. Taking into account the mean vitamin D concentration during

observation period only 52,4% of patients were vitamin D sufficient. New erosions in ultrasound examination were found in 14 (21,5%) patients. We have found no significant difference between vitamin D sufficient and insufficient patients according to the average indices of disease activity, disease activity improvement, time to achieve remission, duration of the remission and disease progression during the first year of therapy.

**Conclusions:** Higher disease activity at RA onset is associated with lower serum vitamin D concentration. Vitamin D supplementation does not improve disease outcome during the first year of therapy.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2634

## AB0171 AGGRECAN DEGRADATION IS NOT JUST AGGRECAN DEGRADATION – A STUDY OF NEO-EPITOPES (NITEGE AND ARGS) OF AGGRECANASE DEGRADATION

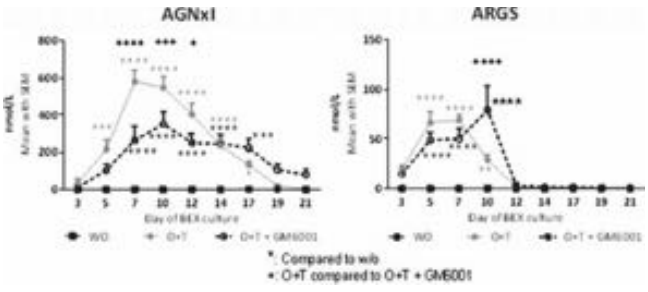
A.S. Siebuhr, Y. He, S. Hoielt, Y.R. Luo, M.A. Karsdal, A.-C. Bay-Jensen.
*Biomarkers and Research, Nordic Bioscience, Herlev, Denmark*

**Background:** Cartilage degradation is a hallmark of arthritic disease. The main constituents of cartilage is aggrecan and type II collagen. Previous studies have shown that aggrecan degradation is prior to type II collagen degradation and that only aggrecanase degradation but not matrix metalloproteinases (MMP) degradation of aggrecan was reversible[1]. It is therefore essential to have biomarkers that can detect reversible and irreversible aggrecan degradation to identify the condition of the cartilage. Of the well-known aggrecanase degradation site at NITEGE$^{373_374}$ARGS, ARGS is released by only aggrecanse, but NITEGE is retained in the aggrecan molecule and in theory needs additional aggrecan degradation to be released. The numbers indicate the aggrecanase cleavage site.

**Objectives:** Investigate the profile of two neo-epitope biomarkers of aggrecanase degraded aggrecan at NITEGE373–374ARGS in a bovine cartilage explants model.

**Methods:** Catabolic stimulated (oncostatin M and TNF-a; O+T) bovine cartilage explants were treated with or without the generic MMP inhibitor, GM6001. Explants without catabolic stimulation was used as negative control. In the culture supernatant two biomarkers investigating aggrecanase degraded aggrecan was measured. The AGNxI competitive ELISA detects the NITEGE$^{373}$ neo-epitope and the ARGS sandwich ELISA detects the $^{374}$ARGSVI neo-epitope. Statistical differences between groups were tested by two-way ANOVA.

**Results:** The AGNxI level was significantly increased compared to w/o from day 5 to day 17. GM6001 significantly lowered the release of AGNxI compared to O+T alone at day 7 ($p<0.0001$), day 10 ($p=0.0007$) and 12 ($p=0.01$). In addition, GM6001 shifted the release to 2days later in the culture period, as the AGNxI level was first significantly increased compared to w/o at day 7 to day 17, where the level was higher than O+T, but non-significant. The ARGS level was significantly increased at day 5, 10 and 12 for both O+T and O+T + GM6001 compared to w/o. At day 10 the ARGS level was higher in O+T + GM6001 than O+T ($p<0.0001$).




**Conclusions:** The prolonged release of AGNxI and the significantly lowered level of AGNxI with the MMP-inhibitor, suggest that the AGNxI release is somewhat dependent of MMP activity. In contrast, the ARGS release seems not to be MMP-dependent as there was a significant increase in O+T with the MMP-inhibitor compared to w/o and the peak was pronounced. In summary, aggrecan degradation is not just aggrecan degradation and different neo-epitopes have different importance in cartilage degradation.

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**Disclosure of Interest:** A. S. Siebuhr Employee of: NORDIC BIOSCIENCE A/S, Y. He Employee of: NORDIC BIOSCIENCE A/S, S. Hoielt: None declared, Y. Luo: None declared, M. Karsdal Shareholder of: NORDIC BIOSCIENCE A/S, Employee of: NORDIC BIOSCIENCE A/S, A.-C. Bay-Jensen Employee of: NORDIC BIOSCIENCE A/S

**DOI:** 10.1136/annrheumdis-2016-eular.3832

## AB0172 USEFULNESS OF THE JAPANESE VERSION OF THE PATIENT-RATED ELBOW EVALUATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Patient self-administered questionnaires remove the possibility of observer bias, and are important instruments for the assessment of clinical outcome. The patient-rated elbow evaluation (PREE) is a joint-specific, self-administered questionnaires.

**Objectives:** We aimed to investigate the correlation between the Japanese version of PREE (PREE-J) and other clinical parameters in rheumatoid arthritis (RA) patients before and after total elbow arthroplasty (TEA).

**Methods:** Thirty-five elbows in 32 RA patients (M/F: 3/29) were replaced by TEA. The mean age was 62.1 (range 41–79) years at the time of surgery, the mean follow-up period was 21.5 (range 12–36) months. All patients were assessed pre- and post-operatively by PREE-J, elbow and forearm range of motion (ROM), Disease Activity Score with 28 joint using CRP (DAS28-CRP), Mayo Elbow Performance Score (MEPS), Japanese version of the Disabilities of the Arm, Shoulder and HAND (DASH-JSSH) and Health Assessment Questionnaire Disability Index (HAQ-DI). The changes of parameters after surgery were examined by Wilcoxon signed-rank test, and the correlation between PREE-J and other parameters was examined using Spearman's correlation coefficients.

**Results:** Both pre- and post-operative PREE-J significantly correlated with DAS28-CRP, DASH-JSSH, and HAQ-DI. Significant improvement was observed after surgery in all parameters except for HAQ-DI. The mean postoperative MEPS improved from 50.3±16.4 points to 98.1±3.2 points, the average postoperative PREE-J improved from 54.7±19.3 points to 27.1±24.4 points. The correlation between PREE-J and MEPS was significant preoperatively ($p<0.01$), but the correlation disappeared postoperatively. The correlation between PREE-J and ROM was not significant pre- and post-operatively.

**Conclusions:** The current study indicated that elbow evaluation by patients who underwent TEA showed significant correlation with disease activity, upper limb function and disability in daily life. It was revealed preoperative PREE-J also well correlated with MEPS, which is widely accepted evaluation system by elbow surgeons. Interestingly, PREE-J did not correlate with MEPS and ROM postoperatively. As PREE-J contains many questions about complex motions required the multiple joint function of upper extremity, it is possible PREE-J might be influenced by other joints affected by RA. MEPS (up to 100 points) evaluates pain (45), ROM (20), function (25) and instability (10) of the elbow, and reached almost perfect score by TEA. PREE-J evaluates pain and function with more detailed questionnaires than MEPS, some of them cannot be solved by a single joint surgery. Our results suggested PREE-J might be useful and wide range evaluation instrument for functional improvement of upper extremity after TEA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2637

## AB0173 ROLE OF ANTI CITRULLINATED PROTEIN ANTIBODIES IN FOLLOW-UP AND RADIOGRAPHIC DAMAGE IN A GROUP OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Autoantibodies in early rheumatoid arthritis (RA) have important diagnostic value. Anti citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) are believed to be associated with more severe clinical outcomes, but the utility of both autoantibodies in the clinical follow-up of disease is controversial. It has recently been described that bone damage in early and even recent-onset RA is attributed to ACPAs, which form years before clinical symptoms start to emerge[1].

**Objectives:** To investigate the longitudinal course of immunological markers, ACPA and RF, during the first year after diagnosis of RA, to see their utility for the clinical follow-up. In addition, to assess if the baseline values of ACPA are associated with the severity of initial radiographic involvement.

**Methods:** The study population was 52 patients diagnosed with early RA according to ACR-EULAR 2010 classification criteria, with ACPA positive. Serum samples at baseline, 3, 6 and 12 months were analyzed, and levels of ACPA, RF, C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were determined. Values of DAS 28, SDAI and HAQ were employed as clinical activity markers.To analyse the variations of the measured parameters, we expressed the values of each analytic and clinical parameter as "Variation Index" on the baseline value for each patient (VI (x month)=Value (x month)/Value (baseline)). The statistical study was made through canonical correlation analysis and linear regression. Radiographic damage was evaluated using Sharp scores modified

by Van der Heijde. Comparisons between this score and ACPA levels and other serological markers were evaluated by Spearman correlation coefficient.
**Results:** A high correlation between clinical markers and analytical variables is observed with a first canonical correlation of 0,96 ($p<0,001$) at 3 months and 0,89 ($p<0,001$) at 12 months. The correlation is mainly determined by the relation between DAS 28 and HAQ with CRP and ESR. A correlation between autoantibodies and clinical markers is not found. We show no significant radiological damage in our patients, despite all being ACPA positive. The Sharp score modified by Van der Heijde was measured in 47 patients, with values between 0 and 101 (mean: 24,76±24,54). We find no correlation between Sharp score and ACPA, RF, ESR and clinical activity markers, and a weak correlation between Sharp Score and CRP (Spearman Rho: 0,459; p=0,005)
**Conclusions:** In our group of patients with early RA, repeated measurement of ACPA or RF during the first year after onset of RA does not offer major additional information. Their quantification would not be indicated for follow-up disease, which means a cost reduction in the Autoimmunity Laboratory. We find no correlation between radiographic damage and ACPA titers at diagnosis. So, although ACPA are associated with bone wound, this is independent of the levels of antibodies.
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**Disclosure of Interest:** None declared
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## AB0174 CHANGES IN TYPE VI COLLAGEN DEGRADATION REFLECT RESPONSE TO TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

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**Background:** Rheumatoid arthritis is a chronic autoimmune disease characterized by progressive inflammation and joint deterioration. Inflammation is driven largely by up-regulation of proteolytic enzymes such as MMPs and results in a greatly increased tissue turnover. Treatment with the αIL-6 receptor agent Tocilizumab (TCZ) results in decreased extracellular matrix (ECM) remodeling. Type VI collagen (Col VI) is found at the interface between the interstitial- and the basement membrane where it binds with both matrix proteins and support cell-cell interactions. The MMP mediated degradation of Col VI can be measured in serum by the protein fingerprint biomarker C6M.
**Objectives:** The aim of the study was to investigate the predictive value of C6M in response to tocilizumab (TCZ) treatment on a methotrexate (MTX) background for 52 weeks in patients with rheumatoid arthritis in the LITHE study.
**Methods:** C6M was measured in the LITHE study (n=740), a one year double blind, placebo controlled phase III parallel group study in patients receiving placebo, 4mg/kg or 8 mg/kg TCZ in combination with MTX. Col VI degradation was measured by the protein fingerprint biomarker C6M in serum at baseline, week 4, 16, 24 and 52. C6M's capacity to predict response to treatment was analyzed by calculating the odds ratio (OR) of ACR20, 50 and 70 criteria at 16 or 52 weeks, given a 20 or 50% reduction in C6M at 4 weeks, independent of treatment type and dose. Results were adjusted for age, sex, BMI, duration of disease and CRP.
**Results:** Treatment with TCZ resulted in an early dose dependent reduction of C6M serum levels in both 4 and 8 mg/kg doses compared to placebo and the reduction persisted throughout the study. In patients responding to treatment after 52 weeks, C6M was significantly decreased in patients with ACR70 ($p<0.01$) response, throughout the treatment period, while C6M reduction in ACR20 and 50 responders was only significant at week 52 ($p<0.05$ and $p<0.01$, respectively). C6M was also significantly reduced in patient with DAS remission (score $<2.6$ at week 52) and DAS score reduction ($>1.2$).
To assess the short term predictive value of C6M we calculated the OR for a 20% or 50% reduction in C6M resulting in an ACR response already after 16 weeks. The OR of an ACR response given a 20% reduction in C6M was ACR20) 1.56 (CI 1.14 to 2.13), ACR50) 2.20 (CI 1.49 to 3.24) and ACR70) 2.69 (1.48 to 4.90) respectively, while a 50% reduction gave the OR 1.88 (1.30 to 2.71), 2.49 (1.66 to 3.72) and 1.37 (0.75 to 2.50). Similar findings were seen for week 52 responders.
**Conclusions:** C6M was dose dependently and significantly decreased from week and throughout study in patients receiving either 4 or 8 mg/kg TCZ compared to placebo. Furthermore, C6M was significantly decreased in patients having ACR20, 50 and 70 response as well as DAS28-ESR reduction and remission compared to non-responders. Importantly, changes in C6M after 4 weeks were able to predict response to treatment by ACR score independent of treatment group. The data suggest that and early decrease in ECM turnover following TCZ treatment, measured by the protein fingerprint marker C6M, increases the odds of a positive patient outcome.
**Disclosure of Interest:** C. Thudium Employee of: Nordic Bioscience A/S, N. Gudmann Employee of: Nordic Bioscience A/S, K. Musa Employee of: Nordic Bioscience A/S, M. Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, A.-C. Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S
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## AB0175 PREVALENCE AND SIGNIFICANCE OF RHEUMATOID FACTOR AND ANTI-CCP IN PATIENTS WITH INTERSTITIAL LUNG DISEASE AND RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid Arthritis (RA) is an autoimmune disease that can cause systemic manifestations such as interstitial lung disease (ILD). In these patients serum autoantibodies may appear, such as Rheumatoid Factor (RF) and Anti-Citrullinated Peptide antibody (anti-CCP), important for its relationship with structural damage and extra-articular manifestations.
**Objectives:** To determine the presence of anti-CCP and RF, clinical-radiological characteristics and evaluate the degree of association between the titles of anti-CCP and RF and the time course of disease in patients with RA and diagnosis of ILD.
**Methods:** We performed a descriptive study, including 45 patients, treated at a specialized consultation Interstitial lung diseases, during the first half of 2015. Patients were subdivided into groups based on RF level: $<24$ U/ml Negative, 24–72 U/ml Low Titer and $>72$ U/ml High Titer. Anti-CCP level: 0–10 U/ml Negative, 10–150 U/ml Low Titer, 151–299 U/ml Moderate Titer and$>300$ U/ml High Titer.
Furthermore, ILD has been divided into different subtypes (the diagnostic includes a clinical exam, pulmonary function tests and high resolution CT): Usual Interstitial Pneumonia (UIP), nonspecific Interstitial Pneumonia (NSIP), Lymphocytic Interstitial Pneumonia (LIN), bronchiolitis obliterans (BO).
Evolution time (ET) of the disease was defined as the difference in months between the date of diagnosis of RA and the date of diagnosis of pulmonary involvement. The association between ET and Anti-CCP level and RF level was studied by two analyzes of variance of a ranking factor.
The association between the categories of titer and subtype ILD was studied by two tests Chi-square.
**Results:** Baseline characteristics were: 32 women and 13 men with a mean age of 66±9.6 years (mean ± SD), 36 RA and 9 with secondary Sjogren's syndrome. The most common extraarticular manifestation was ocular 37%. Erosive disease was present in 80% patients.
82% were RF positive (High Titer 78% and Low Titer 22%) and 8% seronegative. Anti-CCP were tested in 32 (71%) and present in 29 (27% High Titer, 42% Moderate Titer and 31% Low Titer).
The mean time from RA diagnosis to ILD diagnosis was 6.87 years, with a standard deviation of 6.90 years.
The time course of the disease is not significantly ($p<0.05$) affected by the titer of anti-CCP or the RF. On the one hand, the enormous variability in the time course of the disease and on the other the lack of information about the time of the determination of autoantibody titers, could explain the lack of statistical association found.
Among the different subtypes nor have we found: NSIP 42%, 35% UIP, LIN 7%, 15% BO. No significant association ($p<0.05$) between the titer of RF and anti-CCP with radiological clinical pattern in our series did not appreciate.
**Conclusions:** In our study, the high titers of RF and anti-CCP were not associated with prematurity on lung involvement in patients with RA, considering the enormous variability in the time evolution has been observed in the sample. Moreover RF levels and anti-CCP also not associated with subtype ILD.
Further prospective studies are needed to fully assess the implications of a positive RF and anti-CCP in patients with RA and ILD.
**Disclosure of Interest:** None declared
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## AB0176 PULMONARY ASSESSMENT IN ACPA POSITIVE SUBJECTS WITHOUT INFLAMMATORY ARTHRITIS AND IN PATIENTS WITH EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS: THE ROLE OF FUNCTIONAL AND INFLAMMATORY BIOMARKERS

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**Background:** It is known that citrullinated proteins (ACPA) may be present years before the onset of clinical manifestations of Rheumatoid Arthritis (RA). Recent findings suggest that the lung may represent an early site of autoimmune-related injury in ACPA-positive patients without signs of arthritis (1, 2).
**Objectives:** The purpose of the present study was to evaluate the presence of subclinical pulmonary abnormalities in ACPA-positive subjects without arthritis and in RA-patients through functional and inflammatory biomarkers.
**Methods:** Thirty consecutive patients: 11 ACPA-positive without arthritis, 10 naïve to therapy with early ACPA-positive RA ($<24$ weeks) and 9 with established

ACPA-positive RA (<36 months duration) were enrolled. After obtaining informed consent, all subjects underwent baseline pulmonary function tests (PFTs), DLCO measurement and cardiopulmonary exercise testing (CPET). A blood sample for the ELISA evaluation of Surfactant protein D (SP-D) serum levels was collected. Serum levels of SP-D were also measured in 9 healthy control age and sex-matched. Exclusion criteria were: cardiovascular disease, lung disease already known, diabetes, other autoimmune diseases

**Results:** The cohort consisted of 7 men and 23 women, mean age 48,93 (DS ±12.1). PFTs resulted abnormal only in 2 patients. A DLCO reduction was observed in 54.5% of ACPA-positive subjects without RA, in 60% and in 55.6% of patients with early and established RA, respectively. In RA patients, an inverse correlation between disease duration and ratio of the diffusing capacity to the alveolar volume (DLCO/Va) (r=-0.50; p=0.03) was observed. The exercise tolerance (V'O2 peak) at CPET was reduced in 54.5% of ACPA-positive subjects without RA, in 20% of patients with early RA and in 55.6% of those with established RA. Serum levels SP-D were higher in established RA (p=0.079) and in ACPA-positive subjects and early RA than in healthy control. Interestingly enough, ACPA levels positively correlated (r=0.45; p=0.01) with CPET parameters of ventilatory inefficiency (ratio of the increase in ventilation (V'E) to the increase in CO2 output (V'CO2) at lactic threshold (LT)-V'E/V'CO2@LT), suggesting a ventilation/perfusion mismatch. A negative correlation between ACPA and SP-D levels and CPET metabolic parameters (oxygen uptake (V'O2)) was also observed (SP-D-V'O2@LT/kg r=-0.38 p=0.03 – V'O2@LT/kg-ACPA r=-0.36 p=0.05).

**Conclusions:** The lung involvement in RA, particularly in the early phases of disease, is often subclinical and baseline PFTs are scarcely informative. Although preliminary, these findings suggest that DLCO, CPET parameters and SP-D can represent early markers of the subclinical lung injury. Additional studies are however needed to clarify lung abnormalities in RA.

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**Disclosure of Interest:** None declared

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## AB0177 PATIENT-REPORTED OUTCOME OF UPPER EXTREMITY SURGERY FOR RHEUMATOID ARTHRITIS

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**Background:** The goal of treat to target (T2T) is the clinical remission in patients with early disease, but it is difficult to achieve the functional remission. Although patient's subjective evaluation is important for the assessment of postoperative functions of rheumatoid arthritis (RA) patients, there are few reports examined the patients-reported functions after upper extremity surgery for RA.

**Objectives:** Between 2011 and 2014, 158 RA patients underwent the surgical treatment on upper extremities, and all patients were available for detailed clinical review over a 1-year follow-up period. There were 144 females and 14 males with a mean age at surgery of 59.7 (range, 18–85) years. The average disease duration at the surgery was 19.6 (range, 1–59) years.

**Methods:** The clinical outcome of the surgery was assessed by the disease activity (DAS28-CRP), Health Assessment Questionnaire Disability Index (HAQ-DI), Disability of Arm Shoulder and Hand (DASH), Hand20 questionnaire (Hand20). The patients were divided by surgical site into 3 groups (elbow, wrist and finger groups) and by the use of biological disease-modifying anti-rheumatic drugs (bDMARDs) into 2 groups (bDMARDs and non-bDMARDs groups) to compare and evaluate the outcomes.

**Results:** The mean of preoperative/postoperative DAS28-CRP, HAQ-DI, DASH and Hand20 were 2.9/2.3, 0.88/0.94, 46.4/39.1 and 59.1/47.6, respectively. All outcomes except for HAQ-DI significantly improved after the surgery. All outcomes improved significantly in the elbow group, but could not reach significant improvement in the finger group. We further examined the postoperative change in each items of DASH and Hand20, and found the significant improvements in items about pain and weakness in elbow group, pain and rotation of forearm in wrist group, and delicate movement and cosmetic factor in finger group. Postoperative DASH and Hand20 scores were tend to improve in the both bDMARDs and non-bDMARDs group.

**Conclusions:** Our results confirmed the surgery on upper extremity of RA improved the patient's reported function, as well as the disease activity. There were surgical site-specific pattern of improvement of DASH and Hand20, such as that gross movement and pain significantly improved in larger joints, and dexterity movement and cosmetic factor in smaller joints. Postoperative upper extremity function was tend to improve, but more significantly in non-bDMARDs group, probably because the patients might had relatively better baseline function in the bDMARDs group. Understanding of site-specific patterns of improvement after surgery might be useful to achieve the functional remission, and may contribute to decision making of surgical indication, priority of surgical site on upper extremity, and prospection of surgical outcome.

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**Disclosure of Interest:** None declared

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## AB0178 MENOPAUSE IS A PREDICTOR FOR THE DEVELOPMENT OF ANTI-CITRULLINATED PROTEIN ANTIBODIES IN WOMEN AT RISK FOR RHEUMATOID ARTHRITIS

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**Background:** Many controversies exist about the role of sex hormones and reproductive factors in the development of rheumatoid arthritis (RA). Post-menopause is a period of important hormonal and immunologic changes and has been associated with increased risk of seronegative-RA (1). Earlier age at menopause has been associated with increased risk of RA (2), therefore factors related to menopause may be relevant for the development of preclinical phases of RA.

**Objectives:** To study the association between reproductive and menopausal factors and the risk of development systemic autoimmunity associated with RA, in particular of anti-citrullinated protein antibodies (ACPA), in women at increased risk for RA.

**Methods:** This is a nested cohort study within an ongoing prospective study of individuals genetically at risk of developing RA, namely first degree relatives of patients with RA (FDRs). Individuals without clinical evidence of RA were enrolled, and followed-up yearly with clinical and laboratory assessments. We included all women with available ACPA status (anti-CCP 2, 3.1 or 3.0). Reproductive and menopausal factors were self-reported. We operationally defined perimenopausal women as those with recent menopause (<3 years) or aged between 47 to 53 years with menopause-related symptoms. Total ovulatory years were estimated by substracting the age at menarche from the age at menopause minus one year for every childbirth and the total years of oral contraceptive use as previously

*Pre- and Post- operative disease activity and clinical scores*

| | All | | Elbow | | Wrist | | Finger | |
|---|---|---|---|---|---|---|---|---|
| | Pre- | Post- | Pre- | Post- | Pre- | Post- | Pre- | Post- |
| DAS28-CRP | 2.9 | 2.3 p<0.01 | 3.2 | 2.3 p<0.01 | 3.0 | 2.4 p<0.05 | 2.7 | 2.2 p<0.01 |
| HAQ-DI | 0.88 | 0.94 p<0.05 | 1.01 | 0.91 n.s. | 0.86 | 0.75 n.s. | 0.78 | 1.01 p<0.01 |
| DASH | 46.4 | 39.1 p<0.01 | 54.3 | 37.5 p<0.01 | 42.6 | 38.9 p<0.05 | 44.1 | 39.9 P<0.05 |
| Hand 20 | 59.1 | 47.6 p<0.01 | 63.9 | 43.5 p<0.01 | 54.7 | 45.4 p<0.05 | 58.5 | 50.6 p<0.05 |

| | Bio | | non-Bio | |
|---|---|---|---|---|
| | Pre- | Post- | Pre- | Post- |
| DAS28-CRP | 2.7 | 2.2 p<0.01 | 2.9 | 2.3 p<0.01 |
| HAQ-DI | 0.91 | 1.00 n.s. | 0.86 | 0.91 n.s. |
| DASH | 43.6 | 37.4 p<0.01 | 47.4 | 39.6 p<0.01 |
| Hand 20 | 57.7 | 44.1 p<0.05 | 59.5 | 49.2 p<0.01 |

Wilcoxon signed-rank sum test

Table 1. Characteristics of analysed FDR women

| Factors | ACPA negative (n=759) | ACPA positive (n=50) | Univariable OR (95% CI)[a] | Multivariable OR (95% CI)[b] |
|---|---|---|---|---|
| Age, years, median (IQR) | 45 (36-56) | 54 (48-60) | 1.0 (1.0-1.1)[c] | - |
| Age, years, groups, n(%) | | | | - |
| <34 | 183 (24) | 5 (10) | 1 | - |
| 34-46 | 203 (27) | 4 (8) | 0.7 (0.2-2.7) | - |
| 46-56 | 183 (24) | 21 (42) | 4.2 (1.6-11.1)[c] | - |
| >56 | 192 (25) | 20 (40) | 3.8 (1.6-10.4)[c] | - |
| Tobacco smoking ever, n(%) | 357 (47) | 28 (56) | 1.4 (0.8-2.5) | 1.3 (0.7-2.4) |
| Obesity, n(%) | 67 (9) | 2 (4) | 0.4 (0.1-1.8) | 0.3 (0.1-1.5) |
| One or more tender joints on examination, n (%) | 195 (26) | 21 (42) | 2.1 (1.2-3.8)[c] | 1.9 (1.0-3.4)[c] |
| Total ovulatory years, median (IQR) | 18 (8-28) | 24 (15-34) | 1.0 (1.0-1.1)[c] | - |
| Perimenopausal women, n(%) | 157 (21) | 16 (32) | 1.8 (0.9-3.4) | - |
| Post-menopausal women, n (%) | 308 (41) | 34 (68) | 3.1 (1.7-5.7)[c] | 2.8 (1.5-5.3)[c] |
| Age at menopause, years, median (IQR) | 50 (48-53) | 52 (49-54) | 1.1 (0.9-1.1) | - |
| Earlier age at menopause (<45 years), n(%) | 36 (12) | 3 (9) | 0.7 (0.2-2.5) | - |
| Hysterectomy, n(%) | 72 (23) | 7 (21) | 0.8 (0.4-2.0) | - |

(a) Univariable logistic regression analysis (c) P<0.05
(b) Multivariable logistic regression analysis

described (3). We used logistic regression to analyze univariable and multivariable associations between ACPA-positivity and menopause factors.
**Results:** Of the 809 FDR women analyzed, 50 (6%) were ACPA-positive and had a median age of 46 (interquartile range (IQR): 34–56) years. Characteristics of FDR women are shown in Table 1. In univariable analysis, older age, ≥1 tender joint on examination, post-menopausal status and total ovulatory years were significantly associated with ACPA positivity. Perimenopausal status tended to be associated with ACPA status (OR:1.8, 95%CI:0.9–3.4), but did not reach significance. Other menopausal factors, such as age at menopause, earlier menopause or surgical menopause were not associated with ACPA positivity. Due to high correlation between age and menopausal status (r=0.73), we included tobacco smoking, post-menopausal status and having ≥1 tender joint on examination in the multivariable adjusted analyses, post-menopausal status and ≥1 tender joint on examination remained independently associated with ACPA positivity.
**Conclusions:** Post-menopausal FDR women have an increased risk of ACPA positivity, suggesting menopausal hormonal changes are associated with the development of ACPAs, which may be linked to previously described increase of pro-inflammatory cytokines during menopause (4).
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**Disclosure of Interest:** None declared
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## AB0179 REVISION OF EUROPEAN MEDICINE AGENCY'S (EMA) GUIDELINE ON CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS OTHER THAN NSAIDS FOR TREATMENT OF RHEUMATOID ARTHRITIS, 2016

E. Rook on behalf of Rheumatology/Immunology Working Party (RIWP), European Medicine Agency (EMA). *Medicine Evaluation Board, Utrecht, Netherlands*

**Background:** The EMA's Committee for Medicinal Products for Human Use (CHMP) prepares scientific guidelines in consultation with regulatory authorities in the EU Member States, to help applicants prepare marketing-authorisation applications for human medicines, including rheumatology. These guidelines are developed by the RIWP, which is composed of European experts selected from or associated with national agencies.
**Objectives:** The current EMA Guideline on rheumatoid arthritis (RA) dates from 2003. Ever since, there has been a major change in treatment paradigm of RA, with treatment to target in an earlier disease phase. These advancements require modified recommendations regarding the development of RA therapies.
**Methods:** Development and release for consultation of the concept paper by RIWP.
All external comments received are currently reviewed and the draft guideline will be amended as required before release of the final guideline by the CHMP.
**Results:** New primary endpoints were defined, reflecting treatment targets of low-disease activity (LDA) or even remission, in place of the previous primary endpoint of ACR20 scores. Furthermore, a distinction is made in the design and endpoints for DMARD naïve patients, where a DAS28-ESR score <2.6 is considered as a realistic target, or patients irresponsive to MTX or a biological DMARD, where a DAS28 score <3.2 is considered as an acceptable endpoint. For patients with long-standing disease irresponsive to multiple DMARDs, ACR20 is still considered a suitable primary endpoint. For the main study, a three-arm trial including placebo and an active comparator is required. For ethical reasons, placebo may be as short as 6–12 weeks, using rescue medication. Alternatively, superiority of the new product may be shown to an active comparator in a two-arm study.
The ultimate goal of RA treatment is the prevention of structural joint damage. However, showing an effect on structural damage has become increasingly challenging, since the placebo control should be kept short, and milder or more controlled patients may be eligible for studies of new DMARDs. According to this updated guideline, maintenance of remission and LDA could serve indirectly as an indicator for the prevention of structural damage, provided that routine monitoring by X-ray do not indicate a deviating trend as compared to an established comparator treatment. Considering the challenges of demonstrating structural damage regarding power, non-inferiority does not need to be demonstrated formally.
**Conclusions:** The EMA guideline on the development of products in the treatment of RA, has undergone some major revisions regarding endpoints and study design, in accordance to current European clinical practice.
**References:**
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## AB0180 SMOKING AND PERSISTENT DISEASE ACTIVITY ARE ASSOCIATED WITH AN INCREASED RISK OF RAPID JOINT DESTRUCTION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Joint destruction is a major cause of disability in patients with rheumatoid arthritis (RA). Early predictors of rapid joint destruction would be helpful in clinical decision-making, with the potential to yield better patient outcomes. There are conflicting data on the impact of smoking on radiographic progression, and limited information on the importance of disease activity over time in this context.
**Objectives:** To study the relation between patient characteristics at RA diagnosis (baseline) and after 1 year and subsequent rapid radiographic progression (RRP) of joint damage over 5 years.
**Methods:** An inception cohort of patients with early RA (symptom duration <12 months), recruited in 1995–2005 from a defined area, was investigated. Patients were followed according to a structured program, with follow-up visits at 12 and 60 months after inclusion. The same rheumatologist performed the clinical examinations. Those included in the study were managed according to usual care, with no pre-specified protocol for anti-rheumatic treatment. Radiographs of hands and feet were scored in chronological order by a trained reader according to the modified Sharp-van der Heijde score (SHS). RRP was defined as an increase of ≥5 points in SHS per year. Logistic regression models were used to assess potential predictors of RRP.
**Results:** Two hundred and thirty three patients with early RA (70% women, mean age 62 years, 62% RF- and 58% anti-CCP positive) were included. Radiographs were available from 232 patients at baseline, 211 at 1 year and 164 at 5 years. Thirty-six patients were classified as RRP from baseline to 5 years, and the same number from year 1 to 5 years. As expected, RF (odds ratio (OR) 5.70; 95% confidence interval (CI) 1.90–17.10) and anti-CCP (OR 6.04; 95% CI 1.98–18.47) were predictive of RRP over 5 years. A history of ever smoking was associated with a significantly increased risk of RRP up to 5 years (OR 2.69; 95% CI 1.01–7.18, adjusted for RF and baseline presence of erosions). High CRP and ESR at inclusion were predictive of RRP, whereas there were no significant associations for baseline DAS28, swollen joint count, tender joint count or patient's global assessment (Table 1). At the 1-year follow-up, in addition DAS28 and swollen joint count were also significantly associated with RRP up to 5 years (Table 1). Elevated CRP (>9 mg/l) at 1 year was a robust predictor of subsequent RRP (adjusted OR 6.98; 95% CI 2.85–17.14).

**Table 1. Impact of disease activity at inclusion and at the 1-year follow up on rapid radiographic progression up to 5-years**

| | 0-5 years | | | | 1-5 years | | | |
|---|---|---|---|---|---|---|---|---|
| | Crude | | Adjusted[1] | | Crude | | Adjusted[1] | |
| Variables | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| DAS28[2] | 1.47 | (0.99-2.18) | 1.41 | (0.94-2.11) | 2.89 | (1.81-4.61) | 2.54 | (1.54-4.19) |
| Swollen[2] joint count | 1.26 | (0.87-1.84) | 1.26 | (0.86-1.86) | 1.97 | (1.35-2.87) | 1.79 | (1.18-2.70) |
| Tender[2] joint count | 0.85 | (0.55-1.32) | 0.94 | (0.60-1.48) | 1.49 | (1.01-2.19) | 1.46 | (0.94-2.29) |
| Patient's[2] global assessment | 1.36 | (0.92-2.00) | 1.29 | (0.85-1.94) | 1.59 | (1.08-2.34) | 1.71 | (1.10-2.66) |
| ESR[2] | 1.89 | (1.33-2.69) | 1.70 | (1.17-2.46) | 2.82 | (1.77-4.50) | 2.10 | (1.30-3.37) |
| CRP > 9 mg/l | 2.89 | (1.31-6.39) | 2.36 | (1.04-5.38) | 10.32 | (4.44-24.00) | 6.98 | (2.85-17.14) |

OR=Odds ratio; CI=Confidence interval.
[1]Adjusted for RF and baseline erosions.
[2]Per standard deviation.

**Conclusions:** Early RA patients with a history of smoking were more likely to have rapidly progressive joint damage. High disease activity measures at 1 year were strongly associated with rapid radiographic progression. These results underline the importance of early successful anti-rheumatic treatment and suppression of disease activity, to lower the risk of rapid joint destruction in early RA.
**Disclosure of Interest:** None declared
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## AB0181 SONOGRAPHIC PERSISTENCE OF SUBCLINICAL JOINT AND TENDON INFLAMMATION IN RHEUMATOID ARTHRITIS PATIENTS ACHIEVING SUSTAINED CLINICAL REMISSION ON SYNTHETIC OR BIOLOGIC DRUG THERAPY: PRELIMINARY DATA OF A CROSS-SECTIONAL STUDY

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**Background:** Based on more recent recommendations, remission or low-disease activity are pivotal targets to be achieved in the treatment of rheumatoid arthritis (RA). However, despite a clinical remission, subclinical joint and tendon inflammation potentially leading to structural and functional worsening can be detected in a large number of patients.
**Objectives:** To determine the prevalence of joint and tendon inflammation by ultrasound (US) gray scale (GS) and power Doppler (PD) in RA patients treated with biological (bDMARDs) or synthetic disease modified anti-rheumatic drugs (sDMARDs) achieving a sustained clinical remission.
**Methods:** RA patients treated with sDMARDs or bDMARDs achieving a sustained clinical remission (defined as DAS28$<$2.6 since at least 6 months and no swollen joints) were prospectively selected from two Rheumatology Departments. All subjects underwent US examination of hands and wrists bilaterally. The US evaluation was performed on 22 joints (bilateral proximal interphalangeal, metacarpophalangeal and wrists) and 26 tendons/tendon compartments with synovial sheath (first through sixth wrist extensor compartments, first through fifth finger flexor digitorum superficialis and profundus tendons, flexor radialis carpi, and flexors digitorum at the carpal tunnel). The presence of synovial/tenosynovial effusion or hypertrophy in GS and pathological hypervascularization at PD were reported and graded based on a semi-quantitative scoring system: none, mild, moderate and severe (0 to 3). The two treatment groups were compared by Fisher exact test.
**Results:** Forty-eight RA patients were enrolled (20 on bDMARDs and 28 on sDMARDs). A total of 1056 joints and 1248 tendons/tendon compartments with synovial sheath were examined. Twenty-seven (56.2%) patients presented at least one joint with GS synovial effusion or hypertrophy (9/20 in bDMARD and 16/28 in sDMARD group, respectively; p=0.559). In 15 (31.2%) patients we found at least one joint with active PD signal (7/20 in bDMARD and 8/28 in sDMARDs group, p=0.755). In 8 (16.7%) patients at least one tendon sheath with GS synovial effusion or hypertrophy (2/20 treated with bDMARDs and 6/28 with sDMARDs, respectively; p=0.440) was reported. No patients presented at least one tendon sheath with active PD signal in bDMARD group and 3/28 in sDMARD group (p=0.255). Finally, GS alterations were significantly more frequent in the dominant hand compared to the contralateral (22 [45.8%] vs 10 [20.8%], p=0.017).
**Conclusions:** Our data confirmed the high prevalence of US-detected subclinical active synovitis/tenosynovitis in RA patients achieving a sustained DAS28 remission. Joints resulted more frequently involved than tendons in subclinical detected inflammatory process. No differences were found according with bDMARD or sDMARD treatment. GS synovitis was more frequently demonstrated in the dominant hand.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3890

## AB0182 BASELINE FINDINGS FROM A PATIENT-CENTERED, TREAT-TO-TARGET APPROACH IN RHEUMATOID ARTHRITIS

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**Background:** The Patient Reported Outcomes Measurement Information System (PROMIS) is an NIH initiative to develop patient-reported outcome measures for use across chronic conditions. PROMIS instruments assess outcomes relevant in Rheumatoid Arthritis (RA) including pain interference, physical function social function, fatigue, and depression. We aimed to learn whether the use of PROMIS instruments could inform the treat-to-target (T2T) approach to RA management, and to understand whether patient reports of disease impact correlate with objective clinical measures.
**Objectives:** For this study, patients are treated for 1 year using a T2T approach. Using PROMIS item banks, we developed patient-centered targets in five domains: pain, fatigue, depression, physical function, and social function. We report on the baseline status of the full sample of patients enrolled in the study (n=119) stratified by disease activity (remission or low disease activity, CDAI $\leq$10 vs. moderate or high disease activity, CDAI $>$10). We also report on patient satisfaction with the individualized T2T approach, in addition to clinician feedback on the feasibility and usefulness of this approach.
**Methods:** Patients with RA diagnosed by 2010 ACR/EULAR criteria were recruited from our academic clinical practice. At baseline data collection, standard RA assessments included joint counts, RAPID3, and CDAI scores. The research assessment battery included clinical questionnaires, PROMIS CAT's (computer adaptive tests), prioritization of PROMIS domains, and selection of five items that patients felt were most important within their most highly prioritized domain.
**Results:** The baseline sample consists of 119 RA patients with a median age of 57 years (range: 21–77). The sample was 91% female, 71% White, and 12% Hispanic. Approximately 54% (n=57) exhibited moderate or high disease activity (CDAI m=13.4; SD=11.0). When selecting prioritization areas for treatment targets, 39% of patients selected physical function, followed by 37% of participants selecting pain, 16% fatigue, 5% depression, and 3% social function. Those with high active disease were more likely to select pain (44% vs. 22%). Compared to the U.S. general population reference values for PROMIS (m=50; SD=10), patients reported worse fatigue (m=56.4), pain interference (m=57.6), and physical function (m=42.3). Baseline scores on depression and social functioning were closer to average in the general U.S. population. Patient feedback about the study has been positive. An overwhelming majority of patients reported that they would be "somewhat" (33%) to "very likely" (56%) to participate in similar treatment programs. Response from health care providers has been positive as well, with limited reports of negative impacts of data collection on clinic flow.
**Conclusions:** Most patients selected physical function, pain, and fatigue as the most important domains for their personal treatment goal setting. Consistent with these selections, patients' health ratings in these domains were worse compared to the general population. We will continue to explore correlations between PROMIS scores and standard disease activity measures, as well as clinician impressions of the impact of these data on their treatment decisions.
**Disclosure of Interest:** None declared
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## AB0183 LONG TERM OUTCOME OF EARLY ARTHRITIS: FROM REMISSION THROUGH RHEUMATOID ARTHRITIS

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**Background:** Real life experience of early arthritis; remission or evolving to rheumatoid arthritis
**Objectives:** To assess long term outcome, drug free remission rates of patients with early arthritis and classification based on 1987 ACR[1] or 2010 ACR/EULAR[2] rheumatoid arthritis (RA) criteria.
**Methods:** Patients with arthritis with symptom duration within the first 3 months at first visit were assessed after disease age of at least 6 months. Patients with unclassified arthritis (UA) and classified as RA were included. Patients using drugs other than non-steroidal anti-inflammatory drugs (NSAID) at first visit were excluded. Glucocorticoids were given if NSAIDs failed to induce remission. Patients were interviewed with telephone and those accepted were admitted to the outpatient clinic. Patients were telephoned for 3 times if first 2 call were missed. There were 135 patients. Among 92 patients interviewed only one refused to participate. 37 (27%) were admitted to outpatient clinics, 54 (40%) were interviewed with telephone. Patients were classified as RA according to either 1987 ACR or 2010 ACR/EULAR criteria.
**Results:** Demographic features were as follows: 66 (73%) were woman, mean age was 50 (19–85) (first admission). Mean swollen and tender joint count was 5 (1–22) and 8 (1–36) respectively. Most frequently affected joints were MCP (50%), wrist (48%), and PIP (32%). Morning stiffness was longer than 30 minutes in 67%. RF and anti-CCP were positive 20%, 17%, respectively. Mean age of disease at the last assessment was 4 years (6 months- 8 years). Patients were classified as RA according to 1987 ACR (8%) and 2010 ACR/EULAR (20%) criteria. Glucocorticoids were given 75%. Mean glucocorticoid dosage was 10 mg (5–50) and 8% patients were given 50 mg equivalent of prednisolon for 3 days in order to induce remission. Drug free remission was induced with NSAIDs and glucocorticoids in 18% and 20% patients respectively. DMARDS were given in 44 (48%) patients (HQ, 45%; MTX, 44%; SSZ 17%; LEF 11%; only 1 patient TNF inhibitors). 13 patients (14%) voiced that although they were given DMARD, they stopped to take DMARDs and they were symptom free for approximately 3 years.
**Conclusions:** Early arthritis patients with the diagnosis of unclassified arthritis or RA were assessed. Drug free remission was achieved in approximately 40% of the patients. These patients were still symptom free after about four years. Nearly half of the patients were given DMARD although only 20% of the patients fulfilled either 1987 or 2010 criteria. About 10% of the patients stopped taking DMARDs although given and they were symptom free. There are contradictory results about efficacy of MTX in probable RA and UA in disease progression. Along with these results, we are still in the need of criteria that would indicate the early arthritis patients to start with DMARDs so that we would neither be late nor avoid any unnecessary prescription.
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## AB0184 DISEASE-DRUG INTERACTION OF SARILUMAB AND SIMVASTATIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Elevated IL-6 levels occur in rheumatoid arthritis (RA) and can lead to modulation of cytochrome P450 (CYP) enzyme activity and changes in drug levels (CYP substrates) compared with individuals without RA. Conversely, blockade of IL-6 signaling by IL-6 receptor (IL-6R) antagonists may reverse this effect of IL-6 and restore CYP activity. Hence, IL-6 is expected to inhibit CYP3A4 activity, while IL-6 inhibitors, such as sarilumab, are expected to restore elevated simvastatin (a CYP3A4 substrate) concentrations in patients with RA back to those observed in healthy individuals.
**Objectives:** This study (NCT02017639) evaluated the pharmacokinetic profile of simvastatin, a CYP3A4 substrate, before and after a single dose of sarilumab, an investigational anti–IL-6R monoclonal antibody, in patients with active RA to assess disease-drug interaction of sarilumab on simvastatin.
**Methods:** Nineteen adult patients with moderate-to-severe RA with CRP >6.0 mg/L at baseline received simvastatin 40 mg 1 day before and 7 days after subcutaneous injection of sarilumab 200 mg. A series of plasma samples were collected over 24 hours and analyzed for concentrations of simvastatin and its major metabolite, β-hydroxy-simvastatin acid, using a validated LC-MS/MS method. Pharmacokinetic parameters of plasma simvastatin and β-hydroxy-simvastatin acid were calculated using noncompartmental analysis. The geometric mean ratios (with vs without sarilumab) and 90% CIs for peak plasma concentration ($C_{max}$) and area under the plasma concentration-time curve extrapolated to infinity ($AUC_{0-\infty}$) were calculated. C-reactive protein was also analyzed.
**Results:** The majority of patients were female (78.9%) and Caucasian (63.2%). All patients had moderate-to-severe disease activity per study inclusion criteria with a mean CRP (± SD) of 22.1±24.4 mg/L. Administration of a single dose of sarilumab along with simvastatin to patients with RA resulted in reduced exposure to simvastatin by 45% and to β-hydroxy-simvastatin acid by 36% compared with simvastatin alone. Mean effect ratios (90% CI) for simvastatin $C_{max}$ and $AUC_{0-\infty}$ were 54.1% (42.2%>69.4%) and 54.7% (47.2%>63.3%), respectively (Table). There were no changes in time to $C_{max}$ ($t_{max}$) or half-life ($t_{1/2}$) for either simvastatin or β-hydroxy-simvastatin acid following sarilumab exposure (Table). Levels of CRP decreased from 22.1±24.4 mg/L at baseline to reach a nadir of 1.9±0.9 mg/L at 1 wk after sarilumab administration and remained low thereafter. Consistent with the anticipated effects of IL-6 inhibition and the known safety profile of sarilumab, the most frequently reported TEAE across all study treatments was neutropenia, followed by increased alanine aminotransferase level.

**Table.** Geometric Mean (± SD) Pharmacokinetic Parameters for Simvastatin and β-Hydroxy-Simvastatin Acid With Treatment Ratio Estimates and Associated 90% CIs

| | Simvastatin | | | β-Hydroxy-simvastatin acid | | |
|---|---|---|---|---|---|---|
| Parameter | Simvastatin (n=17[a]) | Simvastatin after sarilumab (n=17[a]) | Point estimate ratio (90% CI) | Simvastatin (n=17[a]) | Simvastatin after sarilumab (n=17[a]) | Point estimate ratio (90% CI) |
| $C_{max}$, ng/mL | 21.3 (12.8) | 11.0 (5.8) | 0.541 (0.422-0.694) | 4.2 (3.4) | 3.0 (2.8) | 0.641 (0.555-0.741) |
| $t_{max}$, h[b] | 2.0 (1.0-4.0) | 2.0 (0.5-4.0) | | 4.0 (2.0-6.0) | 4.0 (4.0-6.0) | |
| $AUC_{last}$, ng*h/mL | 82.7 (52.8) | 46.6 (32.7) | 0.540 (0.465-0.628) | 29.6 (22.9) | 20.5 (18.3) | 0.628 (0.536-0.737) |
| $AUC_{0-\infty}$, ng*h/mL | 84.3 (53.6) | 47.9 (33.4) | 0.547 (0.472-0.633) | 31.5 (23.3) | 22.2 (19.0) | 0.641 (0.541-0.758) |
| $t_{1/2}$, h | 3.7 (1.2) | 3.8 (1.4) | | 3.8 (1.2) | 3.5 (1.3) | |

$AUC_{0-\infty}$, area under the plasma concentration-time curve extrapolated to infinity; $AUC_{last}$, AUC from time zero to last quantifiable concentration; CI, confidence interval; $C_{max}$, peak plasma concentration; SD, standard deviation; $t_{1/2}$, terminal half-life associated with the terminal slope; $t_{max}$, time to simvastatin $C_{max}$.
[a]Pharmacokinetic parameters could not be calculated for 2 patients because of sample stability issues during bioanalysis.
[b]Median (min – max).

**Conclusions:** Sarilumab reverses IL-6–mediated suppression of CYP3A4 activity in patients with active RA. The observed reduction of simvastatin exposure is consistent with similar studies conducted with tocilizumab and sirukumab, in agreement with IL-6–mediated disease-drug interaction effect.
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**Disclosure of Interest:** E. Lee Consultant for: Pfizer, N. Daskalakis Shareholder of: Sanofi, Employee of: Sanofi, C. Xu Shareholder of: Sanofi, Employee of: Sanofi, A. Paccaly Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, B. Miller Shareholder of: Sanofi, Employee of: Sanofi, R. Fleischmann Grant/research support from: has received research grants from AbbVie, Amgen, Ardea, AstraZeneca, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Eli Lilly, Merck, Pfizer, Roche, Sanofi, and UCB, Consultant for: has received consulting fees from AbbVie, Akros, Amgen, AstraZeneca, Bristol-Myers Squibb, Janssen, Eli Lilly, Pfizer, Roche, and UCB, I. Bodrug: None declared, A. Kivitz Shareholder of: has received research grants from and holds stock in Sanofi and Regeneron Pharmaceuticals, Inc., Grant/research support from: has received research grants from and holds stock in Sanofi and Regeneron Pharmaceuticals, Inc.
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## AB0185 UNDERCARBOXYLATED OSTEOCALCIN AS A MARKER FOR METABOLIC DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Osteocalcin (OC) has been known as one of bone-forming markers and the serum level in rheumatoid arthritis (RA) patients was usually lower than that in healthy control. Serum OC, secreted from osteoblasts, exists in either carboxylated OC (cOC, major form) or undercarboxylated OC (ucOC, minor form). Different to the osteogenic role of cOC, ucOC has been suggested to be involved in energy metabolism. Recent studies have shown that significantly lower concentration of ucOC in the blood was associated with metabolic derangement including insulin resistance. Therefore, we would like to investigate whether level of ucOC in RA patients decreased and it was accompanied by metabolic dysregulation, which has never been studied before.
**Objectives:** To determine the association between ucOC and metabolic alteration including insulin resistance in patients with RA
**Methods:** Clinical information of patients and healthy volunteers was collected from electronic data base of single center registry. The concentrations of cOC and ucOC were measured in the sera from established RA patients (n=30) and healthy subjects (n=13) by enzyme-linked immunosorbent assay (ELISA). Various metabolic parameters, including insulin concentration, homeostasis model assessment of insulin resistance (HOMA-IR) and body mass index (BMI), were measured and analyzed.
**Results:** The concentration of cOC in blood was not significantly different between RA patients (13.49±2.97 ng/mL) and healthy controls (14.45±2.48 ng/mL). However, the concentration of ucOC was significantly lower in the sera of patients with RA (3.29±2.36 ng/mL) than in those of healthy individuals (5.94±2.75 ng/mL, $p$=0.003). Intriguingly, ucOC levels have been found to be positively associated with parameters of metabolic derangement including insulin levels, HOMA-IR and BMI (Figure 1). These associations were not found in healthy controls.

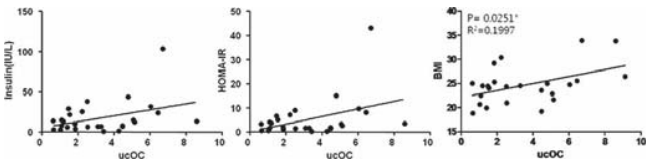



Figure 1. Positive correlation between the levels of ucOC and the values of insulin (left), HOMA-IR (middle), and BMI (right) in the sera of RA patients.

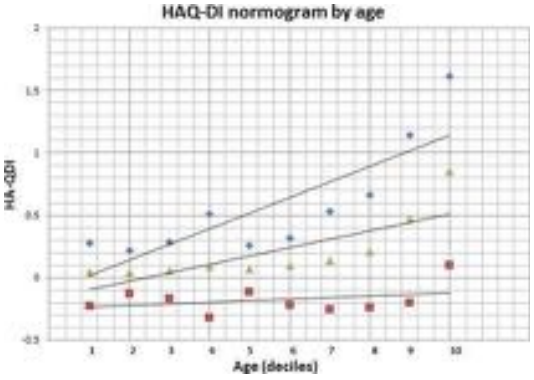
**Conclusions:** The present study show that the concentration of ucOC, but not cOC was significantly lower in patients with RA, and its value was positively correlated with insulin resistance. Therefore, ucOC can be supposed to have a unique role in metabolic dysregulation in RA.
**Disclosure of Interest:** None declared
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## AB0186 BENCHMARKING DISABILITY WITH THE HAQ-DI. A NEW NORMOGRAM IN A LATIN AMERICAN NON-RHEUMATIC POPULATION

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**Background:** The HAQ-Di is broadly used to measure functional disability in RA, and other rheumatic diseases. It can not differentiate disability caused by arthritis or that caused by other illnesses. Whether non-modifiable constitutional factors (e.g. age), personal behaviors, or common comorbidities exert influence over disability measurement, has only been assessed in quite few trials.
**Objectives:** We aimed to determine disability values in a population without previous musculoskeletal conditions, and recognize its main determinants.
**Methods:** Our Hospital ambulatory area offer primary care attention over thirty thousand people. HAQ-Di was ask to be filled by 1,000 patients of a an annual check-up program, and other primary care areas. Were evaluated those older than 18 years and younger than 95 who signed informed consent; participants with any previous rheumatic disease, and chronic pain condition were excluded. Demographic variables, as well as formal education, health behaviors (smoking and exercise), and comorbidities (Charlson index) were recorded. Bivariate correlations by Spearman, and Kruskall Wallis or t-tests were performed as appropriate. We considered $p<0.05$ as statistically significant value.
**Results:** Nine hundred and seventy eight patients were enrolled (22 rejected), their mean age was 56.5±14.6 years, 38% were female, mean BMI was 27.5±4.7

kg/m$^2$, and a Charlson's score of 1.15±1.9. HAQ-Di population mean was 0.21±0.51 with 29% of the respondents had some kind of disability (HAQ-Di value >0.0). Accordingly to the normogram, disability increased with age (figure 1) (r =0.4; p<0.000). Higher HAQ-Di scores were also related with female gender (women 0.307±0.596 vs. men 0.137±0.385; p<0.001); higher Charlson score (r=0.435; p<0.001); lower formal education (rs=0.41, p<0.001; from 0.723±0.847 in group with only 6 years of instruction to 0.078±0.230 in postgraduate group); and no or mild physical activities (rs=-0.320, p<0.001; from HAQ-Di of 0.489±0.724 in the lowest fitness group to 0.118±0.370 in higher exercise group). We could not find influence in disability by smoking status or BMI. Moreover, those with diabetes mellitus (DM) or high blood pressure (HBP) disclosed higher disability (with DM 0.434±0.7 vs. without DM 0.113±0.329, p=0.005, and with HBP 0.445±0.703 vs. without HBP 0.092±0.278; p=0.001)




**Conclusions:** Almost one third of our non-rheumatic population has some kind of functional disability. Although It seems to appear as an aging phenomenon in the general population, might be influenced by comorbidities, healthy behaviours, and sociocultural factors. Thus, these variations must be taken into account when HAQ-Di is used in patients with rheumatic conditions, particularly RA, where HAQ-Di is frequently used in the making decision process.

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**Disclosure of Interest:** None declared

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## AB0187 INFLUENCE OF EDUCATIONAL LEVEL ON THE OUTCOMES OF RHEUMATOID ARTHRITIS

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**Background:** Formal educational background has been associated with a worse health outcome and greater disease activity among patients with Rheumatoid Arthritis (RA).

**Objectives:** The aim of this study was to evaluate the influence of educational level on the outcomes of RA, in terms of disease activity and functional impairment.

**Methods:** This is a cross-sectional study, including patients with RA (1987 ACR criteria). Disease activity was evaluated by erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and Disease Activity Score (DAS28) ESR. Functional disability was assessed by Health Assessment Questionnaire (HAQ). Patients were classified according to their educational level into 4 categories: illiterate, primary, secondary or university levels. Statistical analysis was done using one-way analysis of variance (ANOVA) and linear regression models. The significance level was set at p<0.05.

**Results:** A total of 67 patients with RA were evaluated, 5 men and 62 women. The mean age was 53 years [28–75] and the mean disease duration was 9.19 years [1–30]. Eighty eight percent of patients were treated with synthetic DMARDs (Disease modifying antirheumatic drugs) and 20% were treated with biologic DMARDs.

With regard to the educational level, 34.3% were illiterate, 20.89% had primary level, 34.3% secondary level and 10.44% had university level

There were no statistically significant differences for ESR, CRP, DAS28 and HAQ when comparing the four educational levels (p=0.176, p=0.252, p=0.528, p=0.410, respectively). However, in the multivariate analysis, after adjusting for age and biologic DMARDs, DAS28 and HAQ were significantly associated to the educational level (p=0.024, p=0.014, respectively).

**Conclusions:** This study shows that educational levels may have an influence on the disease activity and functional impairment in patients with RA.

**Disclosure of Interest:** None declared

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## AB0188 EFFECT OF SMOKING ON JOINT DAMAGE AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** It is known that smoking is a poor prognostic factor for the development of rheumatoid arthritis (RA) and other inflammatory rheumatic diseases. According to our knowledge in Turkish population there are no studies about effects of smoking on joint damage and disease activity of RA patients.

**Objectives:** In this study, we investigated the relationship between smoking with disease activity and radiological damage in Turkish patients with RA.

**Methods:** The study included 165 patients with RA. Patients' demographics, disease duration, age at onset, drugs, rheumatoid factor (RF) levels, anti- Cyclic Citrullinated Peptide (a- CCP) levels and smoking habits recorded. Morning stiffness duration, tender and swollen joint count (TJC, SCJ), pain with using visual analog scale (VAS pain), patient and physician global assessment (PGA, PhGA), Health assessment questionnaire (HAQ) evaluated. Disease activity score 28 (DAS 28) calculated. All patients in the study examined for lung involvement and 127 patients standard hand radiographs evaluated using modified Sharp method.

**Results:** Mean disease duration was 139.4±96.4 months. Patients were divided into 3 groups according to smoking habits. Ninety nine (60%) patients were never smoker, 45 (27.3%) patients were long-term smoker (more than 2 years), and 21 (12.7%) patients were new smoker (2 or less years). While the groups were similar in terms of age and disease duration, male gender was more in long-term smokers. Three groups compared for disease activity. DAS 28 scores were 3.2±1.2; 3.2±1.3; 3.2±1.4 respectively (p>0.05). The erosion score (2.6±5.8; 7.1±10.9; 11.1±19.2 respectively) and joint space narrowing score (9.9±7.3; 18.6±14.9; 17.3±12.3 respectively) according to modified Sharp method were significantly lower in never smokers group than other groups (p<0.05). RF titrations were 55.2±58.9; 84.9±71.5; 60.5±63.1; and long- term smokers group was significantly higher than the other groups (p<0.05). Likewise RF titration was higher in ≥20 pack-years smokers than the other patients (never smokers and <20 pack-years smokers). There was no relationship between a-CPP levels with smoking and joint damage (p>0.05).

**Conclusions:** Although smoking known as a poor prognostic factor in RA, there was no correlation between disease activity and smoking in our population. On the other hand, less radiographic damage has been found in never smoker group. Although cigarette smoking does not appear to correlate with disease activity may be effective in the long-term joint damage.

**Disclosure of Interest:** None declared

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## AB0189 ANTI-MODIFIED PROTEIN ANTIBODY RESPONSE PATTERN INFLUENCES THE RISK FOR DISEASE RELAPSE IN RHEUMATOID ARTHRITIS PATIENTS TAPERING DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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**Background:** Autoimmunity is still present in rheumatoid arthritis patients in sustained disease remission. In the absence of inflammation the pattern of autoimmunity against post-translationally modified proteins could potentially impact the course of disease of rheumatoid arthritis patients, espepcially their risk to experience relapse of disease when disease modifying anti-rheumatic drugs (DMARDs) are tapered or stopped

**Objectives:** To perform a detailed analysis of the autoantibody response against post-translationally modified proteins in rheumatoid arthritis (RA) patients in sustained remission and to test whether its composition influences the risk for disease relapse when tapering DMARD therapy.

**Methods:** Immune responses against 10 citrullinated, homocitrullinated/carbamylated and acetylated peptides, as well as unmodified vimentin (control) and cyclic citrullinated peptide 2 (CCP2) were tested in baseline serum samples from 94 patients of the RETRO study. Patients were classified according to the number of autoantibody reactivities (0–1/10, 2–5/10 and >5/10) or specificity groups (citrullination, carbamylation and acetylation; 0 to 3) and tested for their risk to develop relapses after DMARD tapering. Demographic and disease-specific parameters were included in multivariate logistic regression analysis for defining the role of autoantibodies in predicting relapse.
**Results:** Patient varied in their anti-modified protein antibody response with the extremes from recognition of no (0/10) to all antigens (10/10). Antibodies against citrullinated vimentin (51%), acetylated ornithine (46%) and acetylated lysine (37%) were the most frequently observed sub-specificities. Relapse risk significantly (p=0.011) increased from 18% (0–1/10 reactivities) to 34% (2–5/10) and 55% (>5/10). With respect to specificity groups (0 to 3), relapse risk significantly (p=0.021) increased from 18% (no reactivity) to 28%, 36% and finally to 52% with one, two or three antibody specificity groups, respectively.
**Conclusions:** The data suggest that the pattern of anti-modified protein antibody response determines the risk of disease relapse in RA patients tapering DMARD therapy.
**Disclosure of Interest:** C. Figueiredo: None declared, H. Bang Employee of: Organtec Diagnostica, J. Cobra: None declared, M. Englbrecht: None declared, A. Hueber: None declared, J. Haschka: None declared, B. Manger: None declared, A. Kleyer: None declared, M. Reiser: None declared, S. Finzel: None declared, H.-P. Tony: None declared, S. Kleinert: None declared, J. Wendler: None declared, F. Schuch: None declared, M. Ronneberger: None declared, M. Feuchtenberger: None declared, M. Fleck: None declared, K. Manger: None declared, W. Ochs: None declared, M. Schmitt-Haendle: None declared, H.-M. Lorenz: None declared, H. Nuesslein: None declared, R. Alten: None declared, J. Henes: None declared, K. Krueger: None declared, J. Rech: None declared, G. Schett: None declared
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## AB0190 TREAT TO TARGET STRATEGY VERSUS ROUTINE CARE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** The treat to target (T2T) strategy has provided good results in clinical trials and is part of current management recommendations, but real life data are still needed to support the implementation of T2T in clinical practice.
**Objectives:** To investigate 2-year outcomes (DAS28 and EQ-5D) in early RA before and after implementation of the T2T monitoring and treatment strategy.
**Methods:** Pts in the Norwegian Very Early Arthritis Cohort (NOR-VEAC) were included from 2010 through 2015 and treated according to T2T with visits at baseline, 3, 6, 9, 12 months and then every 6 months *plus* monthly visits until DAS28<2.6. We compared this group of pts to pts included in the NOR-DMARD register during 2006–2009 who were treated according to routine care at the time and followed up at 3,6,12 months and then yearly after start of each new DMARD regime. Both groups had a clinical diagnosis of RA (<1 year), were DMARD naive and started DMARD treatment at baseline. We studied DMARD use, DAS28 and EQ-5D during 2-yr follow-up.
**Results:** The current analyses included 252 pts from NOR-VEAC (mean (SD) age 54 (14) yrs, 65% females, 73% seropos, duration of joint swelling median (25,75 perc) 97 (57,168) days) and 586 pts from NOR-DMARD (mean (SD) age 55 (13) yrs, 67% females, 74% seropos, median (25,75 perc) 4 (0,67) days since diagnosis). 2-yr follow-up data were available in 56%/67% of pts in NOR-VEAC/NOR-DMARD. Methotrexate monotherapy was the dominant initial DMARD treatment in both groups (93% in NOR-VEAC vs 87% in NOR-DMARD). Proportions of pts achieving remission (DAS28<2.6) at 1 and 2 yrs were higher in NOR-VEAC than in NOR-DMARD (64% vs 42% and 69% vs 50%, respectively, both p<0.001).Table 1 shows DAS28 and EQ-5D values at BL, 1 and 2 yrs in the NOR-VEAC-and NOR-DMARD cohorts as well as DMARD use during follow-up. 25% vs. 17% of those with 2-yr follow-up data used biologic DMARDs over 2 yrs, p=0.06.
**Conclusions:** Pts treated according to the T2T strategy achieved lower DAS28 scores and higher (better) EQ-5D scores during follow-up despite similar baseline values. The differences in DMARD use between cohorts were relatively small, however there is a trend towards more use of biologic DMARD in the T2T cohort.
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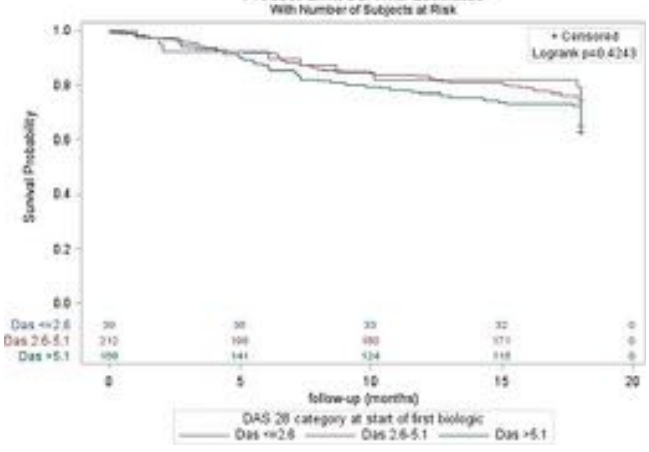
Comparison of disease outcomes after 1 and 2 years and DMARD use during follow-up in the NOR-VEAC- and NOR-DMARD cohorts

| | NOR-VEAC | NOR-DMARD | P-value |
|---|---|---|---|
| Total number of pts for current analyses | 252 | 586 | |
| DAS28: | | | |
| Baseline, mean (SD) | 4.73 (1.35) | 4.77 (1.39) | 0.72 |
| 1 year, mean (SD) | 2.40 (1.07) | 3.06 (1.40) | <0.001 |
| 2 years, mean (SD) | 2.37 (1.15) | 2.88 (1.40) | <0.001 |
| EQ-5D: | | | |
| Baseline, median (25,75 perc.) | 0.62 (0.15,0.73) | 0.59 (0.15,0.73) | 0.25 |
| 1 year, median (25,75 perc.) | 0.80 (0.69,0.81) | 0.69 (0.59,0.80) | <0.001 |
| 2 years, median (25,75 perc.) | 0.80 (0.69,0.82) | 0.73 (0.59,0.80) | <0.001 |
| Number of DMARDs used during follow-up (all pts/pts with 2-yr follow-up): | | | |
| 1 | 71.8%/66.9% | 75.8%/71.9% | |
| 2 | 19.4%/23.3% | 19.1% /21.2% | |
| ≥3 | 8.3%/9.2% | 5.1%/6.9% | |
| Number of switches from initial DMARD treatment (all pts/pts with 2-yr follow-up): | | | |
| 0 | 73.0%/66.9% | 78.2%/74.7% | |
| 1 | 19.4%/16.9% | 10.4%/10.7% | |
| 2 | 6.7%/9.2% | 6.5%/8.2% | |
| ≥3 | 1.6%/6.3% | 4.9%/6.4% | |

## AB0191 DURABILITY OF FIRST BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG IS NOT INFLUENCED BY INITIAL/EARLY DAS28

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**Background:** The Ontario Best Practices Research Initiative (OBRI) collects data on RA treatment in a real-world setting. Patients are enrolled and prospectively followed to assess among other things, response to biologic Disease-Modifyng Antirheumatic Drugs (bDMARDs) and conventional synthetic Disease-Modifying Antirheumatic Drug (csDMARD) therapy.
**Objectives:** The objective of this study was to look at a real-world population and determine if initial disease activity influences the durability of the first used biologic in RA treatment.
**Methods:** bDMARD-naïve RA patients were included if they started a biologic at baseline or at any time after entry into OBRI. For initial DAS, we used the DAS28 value between 6 months before and 3 months after the start of the first biologic, whichever was closer to the date of biologic use. Patients were censored at date of first biologic, or at date of last follow-up after initiation, whichever occurred first. Analysis was performed for all years of follow up, and also censored at 1.5 years (for investigating initial DAS impact). Persistence was defined as the length of time the patients continued to receive the drug, irrespective of change in dose, route, or addition of any other csDMARD or steroids. If the drug was stopped for <60 days after which the patient restarted the same medication, it was considered a continuation and the duration was calculated accordingly. Patients were divided into three groups for analysis based on initial DAS28 score: remission (≤2.60), medium to high DAS28 (2.61–5.10) and severe (>5.10). Survival was compared using KM curves.
**Results:** 563 patients were included. At 1 year, the survival probability was 0.78. The median survival of biologic was 57.8 (95% Confidence Interval: 42.2) months and with a mean survival of 44.5 (SE: 1.5) months. Patients who were on biologic monotherapy, with no concomitant csDMARD use, has worse persistence of their initial biologic. Figure 1 shows the KM Plot of survival on biologic stratified by

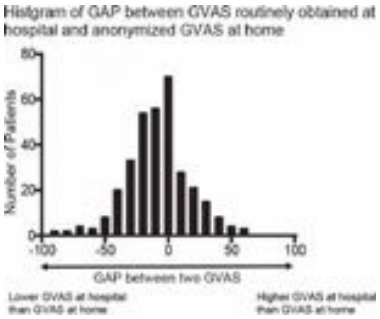


DAS28. Despite the initial trend towards better survival associated with lower initial DAS, this was not statistically significant. Similarly, type of insurance (public/private) did not impact biologic survival. As seen in other studies, the only factor to impact longer persistence on initial biologic was use of a csDMARD with the bDMARD.
**Conclusions:** Early/initial DAS28 score did not impact patients' persistence on their initial bDMARD, nor did insurance type. This suggests that initial DAS28 score does not influence the durability of the first bDMARD in active RA. Combination of csDMARD and bDMArD was more durable than bDMARD monotherapy.
**Disclosure of Interest:** None declared
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## AB0192 SOME OF THE PAINFUL RA PATIENTS UNDERRATE GLOBAL HEALTH VAS AT HOSPITALS

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**Background:** Evaluating patient global VAS is one of the most essential process in RA practice. Despite reliability of patient global VAS being highly important in clinical practice, there has been no study comparing global VAS scores obtained at hospitals and those obtained at home where patients answer anonymously.
**Objectives:** To compare the patient global VAS obtained before clinical examination in hospital with those answered anonymously at home.
**Methods:** We asked RA patients to answer and mail the EQ5D data set anonymously. EQ5D consisted of 5 component questions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and patient assessment global health VAS. EQ5D global VAS is anonymized patient global VAS evaluated at home. We compared the patient global VAS which is routinely surveyed at hospital before clinical examination with those surveyed anonymously at home.
**Results:** The anonymized VAS score was higher than those routinely evaluated at hospital ($p<0.0001$). Global VAS scores obtained at hospital poorly correlated with those obtained anonymously at home ($r=0.426$). We compared patients who had higher patient global VAS at hospital than anonymized VAS at home with patients who had lower patient global VAS at hospital than anonymized VAS at home. Pain VAS scores remained to be risk factor to be higher anonymized VAS at home than those routinely evaluated at hospital after multivariate analysis.




**Conclusions:** Discrepancy exists between patient global VAS evaluated in the hospital before clinical examination and those evaluated anonymously at home. There is a possibility that patients rating high pain VAS are underrating their global VAS scores at hospital.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1312

## AB0193 THE UTILITY OF USING ADMINISTRATIVE DATA TO STRATIFY US VETERANS WITH RHEUMATOID ARTHRITIS ON THE BASIS OF DISEASE ACTIVITY

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**Background:** The ability to assess rheumatoid arthritis (RA) disease activity using administrative data could provide a potential mechanism to identify patients with high disease activity who may be candidates for enhanced RA treatment. The Veterans Affairs rheumatoid arthritis (VARA) registry is a prospective observational cohort that collects RA disease activity measurements including the 28 joint count disease activity score (DAS28) at twelve US Veterans Affairs (VA) Medical Centers.
**Objectives:** This study used VA administrative data to develop a model to predict DAS28 in US Veterans.
**Results:** We identified 1,582 US Veterans with RA who fulfilled enrollment criteria. The average age was 62.7±11.0 years, 91% male, with a disease duration 13.7±12.1 years with 78% and 74% seropositive for rheumatoid factor and anti-CCP antibodies respectively. Of the 1,275 variables evaluated, 175 had prevalence of 1% or more for consideration in the model. Of these 175 candidate variables, 32 remained in the final model. The key variables associated with disease activity were related to number of clinic visits (rheumatology, primary care, and ancillary services), numbers of laboratory tests, medication changes, imaging episodes, and surgery. The association of the predicted and observed DAS28 was relatively limited with unadjusted and adjusted R-square as 0.24 and 0.22 respectively. The model was very sensitive for detection of high/moderate disease (sensitivity =91.3%) but the specificity was only 25.3%.US Veterans with RA enrolled in the VARA registry with administrative data available for the year prior to DAS28 measurement and were evaluated. Patients were excluded if they had cancer, organ transplantation, or other autoimmune diseases. We identified 1,275 administrative data elements with suspected association with disease activity to investigate for association with DAS28 score. Least absolute shrinkage and selection operator (LASSO) was used to develop a model for the prediction of DAS28 as a continuous variable. The sensitivity, specificity, positive and negative predictive values were calculated. For these calculations, we defined high/moderate disease as DAS28>3.2 and low disease as DAS28≤3.2 in a categorical manner.

| | | Measured DAS28 | | |
|---|---|---|---|---|
| | | High/Moderate | Low | Total |
| Predicted DAS28 | High/Moderate | 874 | 467 | 1341 |
| | Low | 83 | 158 | 241 |
| | Total | 957 | 625 | 1582 |
| | | Sensitivity | | 91.3% |
| | | Specificity | | 25.3% |
| | | Positive predictive value | | 65.2% |
| | | Negative predictive value | | 65.6% |

**Conclusions:** While there were multiple administrative elements that correlated with disease activity measured by DAS28, it was not possible to develop a strong predictive model using available administrative data. These observations suggest that the continued direct observation of disease activity remains the most effective measure to identify RA patients with high disease activity. However the transient nature of RA disease activity may predicate the need to refine our model to account for disease duration. Additionally a single point-in-time measurement may not be indicative of patient disease activity over a long period of time. The development of other methods that can extract information from provider assessment of disease from electronic medical records has the potential to meet this critical need.
**Disclosure of Interest:** G. Cannon Grant/research support from: Amgen, C.-C. Teng Grant/research support from: Amgen, N. Accortt Shareholder of: Amgen, Employee of: Amgen, D. Collier Shareholder of: Amgen, Employee of: Amgen, M. Trivedi Shareholder of: Amgen, Employee of: Amgen, B. Sauer Grant/research support from: Amgen
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## AB0194 ANTI-CYCLIC CITRULLINATED PEPTIDES ANTIBODIES (ANTI-CCP) IN CUTANEO-ARTHRITIC BUT NON-PULMONIC CASE OF SARCOIDOSIS

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**Background:** Anti-CCP antibodies have a high predictive value in RA patients and associated with disease severity. They have also been detected in few conditions such as Palindromic rheumatism, Psoriatic arthritis, Sjogren's syndrome and other rheumatic disorders. Sarcoidosis on the other hand is a chronic inflammatory and potentially multi-systemic disease which is classically forming non-caseating granuloma, is not characteristically associated with positive anti-CCP Abs. There is only one report in the previous English literature that has described 2 patients with pulmonic sarcoidosis who were tested positive for anti-CCP Abs.
**Case report:** For more than a year, this 52 year old smoker lady has been noticing the development of a rather painless papular rash into a nodular one over the extensor surface of the hands, mainly in the knuckles (figure 1). No specific diagnosis was offered to here in due course however, in the last few months she begun to experience polyarthralgia in the joints of the hands and mild stiffness. The initial impression by the dermatologist colleague was that of erythema elevatum diutinum Routine blood and biochemistry workups was runemarkable apart from an ESR of 29mm/HR and hypovitaminosis D but with normal serum total calcium of 10.1mg/dL (N 8.4–10.5). Tests for RF, ANF, ds DNA, ENAs, CPK and LDH were negative yet the ELISA test for anti- CCP was positive repeatedly but in rather low titre of 36.73 and 37.62 U/mL (N<17).The CXR showed no enlarged hilar lymphadenopathy or interstitial lung changes (Figure 2), the hands X-ray showed osteopenia and narrowing of the PIP Joint of the left ring finger (figure3).The MRI of the left hand showed erosion in the head of the 5th metacarpal bone and minimal effusion in the first MPJ (Figure 4, a and b). The biopsy of one skin nodule revealed many loose well circumscribed islands of granulomas but without caseous necrosis consistent with cutaneous sarcoidosis. Both tuberculin skin test and Quantiferon TB Gold test were negative. Serum angiotensin converting enzyme was within normal



values of 49 U/L (N 16–72).She was managed with hydroxychloroquine and pentoxifylline.
**Conclusions:** Sarcoidosis is capable of mimicking several rheumatic diseases. However, this case is unusual in the sense of being presented with cutaneo-arthritic sarcoidosis without any pulmonic disease. The presence of positive anti-CCP makes it the third reported case in the literature of such association and may also be reflecting an overlap syndrome of sarcoidosis-RA.
**Disclosure of Interest:** None declared
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## AB0195 BONE EROSION AND BONE LOSS PROFILE IN RHEUMATOID ARTHRITIS: ABOUT 93 MOROCCAN PATIENTS

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**Background:** Rheumatoid arthritis (RA) is a known cause of joint destruction and systemic bone loss. It is now clear that the management of inflammation in RA is the key to a better control of articular damage and osteoporosis. However, systemic inflammation is not the only determinant of bone damage.
**Objectives:** The aim of the present work is to evaluate the bone erosion and bone loss profile in RA patients.
**Methods:** Ninety-three patients have been identified meeting the ACR EULAR criteria of RA. We have collected data about age, smoking, alcoholism, steroid prescription, body mass index (BMI), disease duration and activity (DAS28), functional disability (HAQ) and bone mineral density (BMD) measured with DXA. Bone erosion was calculated by the Sharp Van Der Heijde score. Data analysis was carried out using the SPSS 20 Software. $p<0.05$ was considered statistically significant.
**Results:** The mean±SD age was 51.59±12.38 years and the mean±SD disease duration 12.07±9.19 years. The mean±SD sharp score was 70.33±48.93 and 36.6% of patients had osteoporosis. The median RA diagnosis lag time was 24 months [12–72] after onset of symptoms. Bone mineral density in the femoral neck was significantly associated with Sharp score (p=0.000) and age (p=0.004), HAQ (p=0.003), disease duration (p=0.000), steroid intake (p=0.035), spine BMD (p=0.000) and BMI (p=0.044). Adjusted to age, spine BMD and BMI, femoral neck BMD (p=0.04) was an associated factor of bone damage (OR: - 0.442, 95% CI -240.24 to -19.51).
**Conclusions:** Delayed diagnosis has led to greater bone damage in our RA population. Consequently, more efforts should be done to shorten this period in order to improve the disease control and the patients' quality of life.
**Disclosure of Interest:** None declared
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## AB0196 THE RELATION BETWEEN BASELINE ACR/EULAR 2010 CLASSIFICATION CRITERIA AND STRUCTURAL JOINT DAMAGE MEASURED WITH RAAD SCORE IN RHEUMATOID ARTHRITIS

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**Background:** In 2010 the ACR/EULAR classification criteria for rheumatoid arthritis (RA) were proposed. They focus on features at earlier stages of disease that are associated with persistent and/or erosive disease, which may help to adapt treatment regimens on the basis of individual prognosis. The criteria have been applied in a large number of studies, but information on the relation with long-term outcome is scarce (1). Early intervention with DMARDs aims to reduce current disease activity and prevent structural damage. Based on clinical assessment, the Rheumatoid Arthritis Articular Damage (RAAD) scores 1 or 2 points for structural damage in 35 joints, resulting in a range from 0 to 70 (2). The RAAD score correlates strongly with radiographic damage in hands and feet, but is more comprehensive, including all joints that may be damaged by RA. It has been applied in various small studies.
**Objectives:** To evaluate structural joint damage according to the RAAD score in RA patients with a disease duration of 5 years or longer and its relation to the ACR/EULAR 2010 classification criteria at baseline.
**Methods:** In a large regional teaching hospital, the RAAD score is recorded annually by rheumatologists and nurses since 2014 as part of routine clinical assessment of disease activity in order to evaluate disease progression and quality of care. ACR/EULAR 2010 classification criteria and the presence of radiological erosion were obtained retrospectively from the patients' medical records. Statistical analyses were performed on the total group of patients, and stratified by disease duration (5–9 years versus 10 years or longer). Data were analysed using Spearman correlation and Mann-Whitney U tests.
**Results:** The database consists of 1966 patients with a clinical diagnosis of RA. All patients were treated with s- and/or b-DMARDs. In January 2016, the RAAD-score had been performed at least once in 425 patients with a disease duration of at least 5 years. 68.5% of patients were female. At baseline, mean (SD) age was 64.1 (13.1) years, 78.4% were RF and/or anti-CCP positive and 73.2% scored 6 or higher on the ACR/EULAR 2010 classification criteria for RA. The median (IQR) disease duration at the time of assessing the RAAD score was 12.3 (7.8–19.6) years. The highest RAAD score was 55 and the median (IQR) in the total group was 2.0 (0.0–7.0). The correlation of the sum of the ACR/EULAR 2010 classification criteria at baseline and the RAAD score at follow-up was very weak (r=0.11, p=0.033). Table 1 presents the RAAD scores for individual ACR/EULAR 2010 classification criteria. Acute-phase reactants, higher number of affected joints and erosions at baseline resulted in higher RAAD scores.

*Table Median (IQR) RAAD scores presented for the total group, disease duration 5-9 years and disease duration 10+ years, stratified by clinical characteristics at baseline.*

| | Total | | | Disease duration 5-9 years | | | Disease duration 10+ years | | |
|---|---|---|---|---|---|---|---|---|---|
| *RAAD score* | Median (IQR) | n | p | Median (IQR) | n | p | Median (IQR) | n | p |
| All patients | 2.0 (0.0-7.0) | 425 | | 0.0 (0.0-2.0) | 167 | | 4.0 (1.0-11.0) | 258 | |
| ACR/EULAR 2010 score ≤5 | 1.0 (0.0-5.3) | 110 | 0.056 | 0.0 (0.0-2.0) | 49 | 0.25 | 4.0 (0.0-10.0) | 61 | 0.24 |
| ACR/EULAR 2010 score >5 | 2.0 (0.0-7.0) | 301 | | 0.0 (0.0-2.0) | 116 | | 5.0 (1.0-12.0) | 185 | |
| RF and anti-CCP negative | 2.0 (0.0-7.0) | 90 | 0.384 | 0.0 (0.0-2.0) | 39 | 0.721 | 4.0 (0.0-11.0) | 51 | 0.658 |
| RF and/or anti-CCP positive | 2.0 (0.0-7.0) | 327 | | 0.0 (0.0-2.0) | 126 | | 4.0 (1.0-11.0) | 201 | |
| CRP and ESR normal | 1.0 (0.0-5.0) | 140 | 0.032 | 0.0 (0.0-1.8) | 60 | 0.028 | 3.5 (1.0-12.0) | 80 | 0.866 |
| CRP and ESR not normal | 2.0 (0.0-7.0) | 271 | | 1.0 (0.0-2.0) | 106 | | 4.0 (1.0-11.0) | 165 | |
| ACR/EULAR 2010 affected joints subscore ≤3 | 1.0 (0.0-4.0) | 145 | <0.001 | 0.0 (0.0-2.0) | 68 | 0.33 | 3.0 (0.0-7.5) | 77 | 0.015 |
| ACR/EULAR 2010 affected joints subscore >3 | 2.0 (0.0-8.8) | 272 | | 0.0 (0.0-2.0) | 98 | | 5.0 (1.0-13.0) | 174 | |
| No erosions | 1.0 (0.0-5.0) | 290 | <0.001 | 0.0 (0.0-2.0) | 137 | 0.005 | 3.0 (0.0-9.0) | 153 | 0.01 |
| Erosions | 4.0 (1.0-9.0) | 108 | | 2.0 (0.0-3.0) | 28 | | 5.5 (2.0-13.0) | 80 | |

**Conclusions:** In a cohort of RA patients, the sum score of the ACR/EULAR 2010 classification criteria at baseline correlated weakly with long-term structural joint damage. The presence of erosions at baseline, not included in the criteria set, was the best predictor of a higher RAAD score.
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## AB0197 EVALUATION OF SERUM IL-10 AND IP-10 LEVELS IS USEFUL AS PROGNOSTIC BIOMARKERS FOR SELECTION OF IL-6R ANTIBODY (TCZ) PRIOR TO TUMOR NECROSIS FACTOR (TNF) INHIBITOR IN RHEUMATOID ARTHRITIS TREATMENT

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**Background:** Biomarkers of response to treatment in rheumatoid arthritis (RA) are sorely needed given the large inter-individual variability in efficacy of the available drugs. However, there is few reported to distinguish between responses to the different biologics (Bio) [1)]. Some authors think it will be difficult to obtain good predictive biomarkers for the efficacy of Bio before administration. Consequently, it is important that we identify the novel biomarker to predict the efficacy of these agents before the administration of Bio.
**Objectives:** To identify a serum biomarker for prediction of the response to Bio in patients with RA, we investigated whether serum cytokine level before treatment with Bio may represent useful prognostic biomarkers for TNF inhibitor (GLM) or IL-6R antibody (TCZ) treatment in bio-naïve RA.
**Methods:** To identify a serum biomarker for prediction of the response to Bio in patients with RA, we performed serum cytokines analysis in RA patients before and after Bio treatment with TCZ and GLM. At the first, we enrolled 10 responder and 10 poor-responder RA patients treated with Bio. 29 cytokines levels before treatment were measured using MILLIPLEX MAP Human Cytokine/Chemokine®. According to analysis of these 29 cytokines, IL-17, IL-6, IL-10 and IP-10 were eliminated as candidates for novel biomarker to predict the effectiveness of RA treatment. Then we enrolled 41 bio-naïve RA patients before administration of TCZ (n=27) or GLM (n=14). We measured these four serum cytokines before

and after treatment with each Bio using ELISA. At baseline and 24 weeks after Bio-therapy with TCZ or GLM, we assessed DAS28 and measured serum levels of IL-17, IL-6, IL-10 and IP-10 using commercial ELISA kits. Responders and non-responders were defined as patients who had clinical remission (CR; DAS28 $<2.6$) and non-CR (DAS28 $>2.6$) at 24 week after administration of Bio. Wilcoxon two samples test was performed to compare cytokine levels.

**Results:** Mean age was 57.6±15.9, 70.6±14.7 years old and mean disease duration was 77.1±86.2, 114.0±142.6 months in TCZ and GLM patients, respectively. Disease activity of RA was 4.78±0.98 and 4.23±0.76 with DAS28 in TCZ and GLM patients, respectively. In CR group of TCZ (n=19), the serum IP-10 and IL-10 levels decreased compared with non-CR group by ELISA, significantly ($P<0.05$). As for RA patients treated with TCZ, IP-10 levels were significantly higher in responders. As for RA patients treated with GLM, responders showed a trend toward higher levels of baseline IL-10 compared to non- responders, while IP-10, IL-17 and IL-6 differences did not reach statistical significance.

**Conclusions:** In our study, the serum levels of IP-10 and IL-10 before Bio administration appeared to be associated with favorable responses to TCZ. Furthermore, these cytokines including IP-10 were not associated to response of GLM treatment. It is suggested that bio-naïve RA with low serum IP-10 levels might be treated with TCZ better than TNFi (GLM).

**References:**

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**Disclosure of Interest:** None declared

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## AB0198 CLINICAL ANALYSIS OF PREOPERATIVE DEEP VEIN THROMBOSIS RISK FACTORS IN PATIENTS UNDERGOING PRIMARY TOTAL KNEE ARTHROPLASTY

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**Background:** Venous thromboembolism (VTE) [i.e., pulmonary embolism (PE) and deep vein thrombosis (DVT)] is a common complication during and after a hospital admission. Further, VTE is a leading cause of major complications and death after major orthopedic surgery. To avoid the development of VTE after orthopedic surgery, it is essential to reduce the onset of deep vein thrombosis (DVT) and to diagnose DVT early. It leads to early diagnosis to find a risk factor of DVT from medical history of the patient. Total knee arthroplasty (TKA) reliably relieves pain and improves function in patients with end-stage arthropathy of the knee such as osteoarthritis (OA) and rheumatoid arthritis (RA). The most common complication after knee arthroplasty is DVT. However, the risk for preoperative DVT in patients for knee joint orthopedic surgery remains unclear. Therefore, we investigated the patient's background and medical history in patients admitted to hospital for primary TKA, and identified the risk factors for DVT development before TKA.

**Objectives:** The objectives are investigated the risk factors of DVT in patients admitted for primary TKA.

**Methods:** *Patients.* From 2003 to 2013, 303 patients admitted for primary TKA at Mie University Hospital were eligible for the present retrospective study. The patients' sex, weight, body mass index (BMI, weight in kilograms divided by the square of the height in meters), and data from the medical history and medical condition were recorded.

*Diagnosis of DVT.* B-mode ultrasonography with compression and color Doppler imaging were performed for bilateral common femoral veins, the superficial veins, the popliteal veins, and the calf veins.

*Statistical analysis.* The patients' preoperative characteristics were compared between the DVT-positive and DVT-negative patients using the Mann-Whitney U test and Fisher's exact test. Multiple linear regression analysis was performed to identify independent risk factors for preoperative DVT. P values $<0.05$ were considered statistically significant.

**Results:** The preoperative diagnosis was OA in 261 patients (86.1%) and RA in 42 patients. The most frequent preoperative medical history or medical condition was hypertension (52.1%). The second most frequent preoperative medical history or medical condition was major surgery (47.5%).

Preoperative DVT was diagnosed in 48 of 303 (15.8%) patients overall. Significantly elevated risks of DVT were found in patients who had RA ($p<0.05$) using Fisher's exact test. Multiple linear regression analysis was performed to test the association of DVT with putative risk factors. The analysis showed that admission for RA ($p<0.05$) were significant independent risk factors for preoperative DVT.

**Conclusions:** A high prevalence (15.8%) of preoperative asymptomatic DVT was found in patients admitted for primary TKA. In this study, RA was risk factors for preoperative DVT among those admitted to the hospital for primary TKA.

**Disclosure of Interest:** None declared

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## AB0199 ULTRASOUND EXAMINATION IN RA PATIENTS ACHIEVING COMPREHENSIVE DISEASE CONTROL (CDC) OR CLINICAL REMISSION AFTER 1 YEAR FOLLOW-UP AND T2T STRATEGY: REAL LIFE EXPERIENCE FROM A SINGLE CENTER, EARLY ARTHRITIS CLINIC

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**Background:** According to international task force recommendations, primary goal of rheumatoid arthritis (RA) treatment is to achieve control of symptoms, prevent structural damage and normalize functional status.Simultaneous achievement of DAS28 PCR remission $<2.6$, HAQ DI $<0.5$ and change from baseline in modified Total Sharp Score (SHS)$<0.5$, has recently defined as comprehensive disease control (CDC). Residual sub-clinical synovitis on ultrasonography/power doppler (US-PD) examination is one of the major driver of radiographic progression, but US-PD evaluation has not been yet included in definition of CDC.

**Objectives:** To analyze the achievement of CDC in an Early Rheumatoid Arthritis (ERA) Cohort after 1 year from diagnosis and to evaluate if this status was also associated to absence of US subclinical active synovitis. Compared US status in patients who achieved CDC with those achieving DAS 28 PCR-REM but not CDC.

**Methods:** ERA patients fulfilling 2010 ACR/EULAR who consecutively attended our Early Arthritis Clinic between 2009–2014 were retrospectively analyzed. Patients with available follow-up of 1 year were included. Standardized therapeutic approach has been performed according to EULAR T2T guidelines. Disease activity and functional disability has been evaluated using DAS28 PCR and HAQ DI every 3 months and after 12 months (T12) from diagnosis. Being more easily applicable in daily practice activity, radiographic progression has been assessed using Simple Erosion Narrowing Score (SENS). Therefore we considered as radiographic non progressors those patients who showed no change in SENS score at 12 months, from baseline (assimilated to $<0.5$ point change in mHSS). Patients were stratified in CDC-achievers and CDC non-achievers. Among those patients who reached DAS28-REM alone were identified. All patients were evaluated by US-PD of both wrists and II and III metacarpophalangeal. US-PD assessment was drawn at T12, considering as active subclinical synovitis a PD signal $\geq 1$ in more than 1 Joint.

**Results:** 125 patients out of 323 met the inclusion criteria. After 12 month from diagnosis, 30% were CDC-achievers (n=38) and 70% CDC non-achievers (n=87); of this last group, 38,4% (n=48) achieved REM. 81,2% (39/48) of patients in REM didn't achieved CDC because of radiographic progression. When comparing US-PD findings in both CDC-achievers and REM 6/38 (15.7%) and 12/48 (25%) respectively showed residual US-PD synovitis. In REM 10/12 (83%) of those with residual synovitis didn't achieve CDC because of radiographic progression.

**Conclusions:** In our Cohort a significant proportion of patients achieved CDC one year after diagnosis and a T2T therapeutic strategy. As already known our findings confirm that clinical remission is not fully protective against radiographic progression in ERA since 83% of those with residual US-PD synovitis did radiographically progress.However, the meaning of residual synovitis observed also in our CDC-achievers patients, although to a lesser amount (15.7%), is still unknown and has to be ascertained in a properly designed prospective study with longer follow-up.

**References:**

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**Disclosure of Interest:** None declared

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## AB0200 CYP2C9 ACTIVITY IN TURKISH PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** *Rheumatoid arthritis* (RA) is a chronic, autoimmune, multisystemic, inflammatory and common disease with unknown etiology. *Cytochrome* P450 2C9 (CYP2C9) is responsible for up to 40 drugs metabolism in the liver such as oral anticoagulants (warfarin), oral antidiabetics (tolbutamide, glyburide), angiotensin II receptor antagonists (losartan, irbesartan), phenytoin (1). Most of the drugs convert to active or inactive metabolites by CYP2C9. In a recent study Goktas MT *et al.* showed that CYP2C9 activity reduced in Behçet's disease that an autoimmune disease (2).

**Objectives:** This study aimed to investigate activity of CYP2C9 in patients with RA.

**Methods:** Losartan and its metabolite (E-3174) concentrations were analysed in healthy subjects (n=38) and RA patients (n=32) urine by high-performance liquid chromatography (HPLC). A acetonitrile and 66/34 mixture of phosphate tamponate (NaH2PO4, 15 mM, pH=2.8) were used as mobile phase. Urine samples in mobile phase and isopropanol (2/1/1 in volume, respectively) were injected into Agilent Eclipse XDB-C18 (5 μm, 4.6x150 mm) column via Agilent Technologies 1200 HPLC system (Agilent Technologies, Waldbron, Germany).

Losartan and its metabolite E-3174 were detected via a UV detector at 245 nm. The inter- and intra-day coefficient of variation (CV) was less than %4 for losartan and its metabolite. The ratio of losartan to its metabolite (E-3174) was calculated (metabolic ratio, MR) and used as a marker of the activity of the CYP2C9 enzyme.
**Results:** MR (losartan/its metabolite ratio) was increased in RA patients from 1.34±0.22 to 1.75±0.31. This result shows that CYP2C9 activity decreased in RA patients compared with healthy subjects.
**Conclusions:** CYP2C9 activity decreased in RA patients so we must be carefully when using the drugs that metabolized with CYP2C9. The efficacy of some treatments would be compromised in RA patients because they were given drugs in dosages that might be ineffective or cause adverse drug reaction and toxicity. This study is continued at other centers.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2259

## AB0201 A NEW PERSPECTIVE OF IMMUNOLOGICAL DETECTION OF NEUROLOGICAL INJURIES IN RHEUMATOID ARTHRITIS

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**Background:** The neurological injury in rheumatoid arthritis (RA) is one of the most common organ lesions, but its clinical statement is quite complicated because of absence of reliable signs, as well as frequent coexistence with other neurological conditions. Therefore, the new improved approaches for diagnosing of nervous system involvement are rather necessary, and immunological methods of detection are appeared more promising and more specific for RA than imaging. The most obvious candidate antigens for this purpose are the constituents of nervous tissue, such as myelin and its principal component, myelin basic protein (MBP).
**Objectives:** Improvement of immunological detection of neurological involvement in RA by means of polyacrylamide magnetic beads with immobilized MBP.
**Methods:** The research was carried out in agreement with the principles of the World Medical Association Declaration of Helsinki. The informed consent had been signed by all involved persons, another obligate requirement was age 18 years or more. The patients were from the rheumatologic wards in Volgograd Municipal Hospital No. 25 and Volzhsky Municipal Hospital No. 1. Diagnosis of RA was established by ACR-EULAR criteria (2010), RA activity was evaluated using DAS28. Serum anti-MBP antibodies were measured by ELISA, with MBP immobilized on polyacrylamide magnetic beads as an antigen. The antibody concentrations were expressed as optical density units (ODU) and were considered positive if the cutoff value (M+2$\sigma$ of the reference group, 0.050 ODU) was exceeded. The results were expressed as mean±$\sigma$, differences were considered significant when $p<0.05$. Pearson correlation coefficient (r) was also used.
**Results:** 40 healthy persons (29 mans and 11 women), and 95 female patients with RA and the neurological signs, appeared during active phase of the disease, were recruited for this study. Mean age of the healthy controls was 36±7 years, and for the RA group it was equal to 55±11 years. Mean RA duration was 4.2±2.9 years. 13 patients had low, 52 – moderate, and 8 – high disease activity. The most common types of neurological involvement were mononeuropathy (n=29), polyneuropathy (n=65), radiculopathy (n=80); cervicocranialgias (n=51), and trigeminal neuralgias (n=14). The symptoms of central nervous system damage (TIA, seizures, cerebellar ataxia, dysarthria) were found in 21 patients. In RA group, anti-MBP antibodies were detected in 37 (38.9%) cases, with mean concentration 0.141±0.027 ODU. The patients with different neurological signs had mean anti-MBP antibody concentration 0.198±0.050 ODU, the subgroup without any neurological signs had 0.120±0.024 ODU (p=0.022). There was positive correlation between anti-MBP concentration and DAS28 score (r=0.67, p=0.039).
**Conclusions:** We found an association between neurological involvement in RA and elevation of anti-MBP antibody concentrations, as well as correlation between the latters and DAS28 score. These findings give us an opportunity to improve the diagnosis of minor neurological damage in RA and thus to make more precise adjustment of the treatment.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2375

## AB0202 HANDS MAGNETIC RESONANCE IMAGING (MRI) IN PATIENTS WITH SERONEGATIVE ARTHRITIS

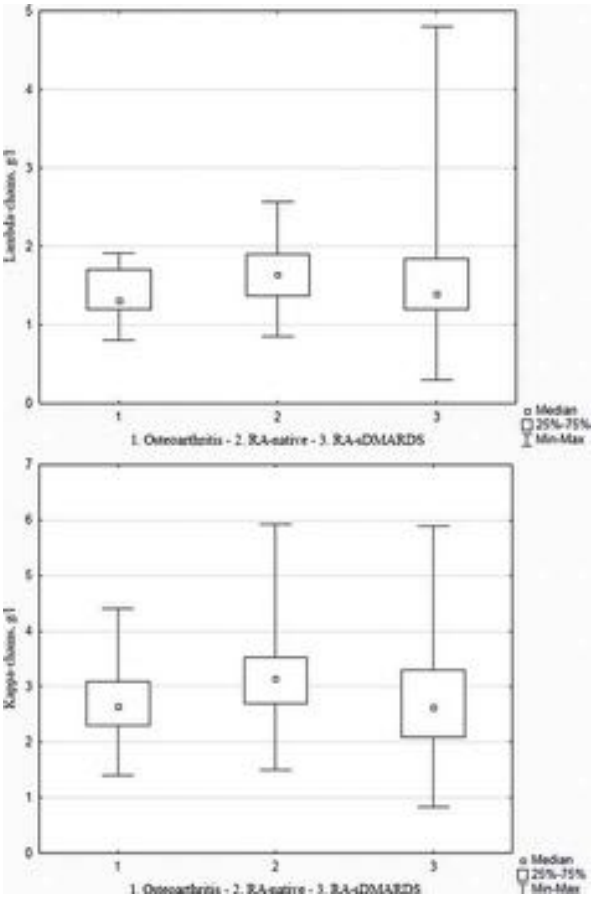
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**Background:** It is proved that early treatment can modify the further course of rheumatoid arthritis (RA), so early diagnosis is very important for better results of treatment. at present the most sensitive method for the detection of significant changes in the joints in the early stages of RA is magnetic resonance imaging (MRI).
**Objectives:** We have used this method to detect early RA in patients with seronegative (anticitrullinated peptide antibody (ACPA)/RF –negative) arthritis.[2]
**Methods:** 52 ACPA/RF-negative patients aged between 18 to 65 years with undifferentiated arthritis lasted for no more than 6 months and no clinical signs of hands and wrists joints involvement underwent MRI of hands and wrists; level of CRP and ESR was determined as well. Synovitis and bone marrow oedema (BME) were scored according to the OMERACT rheumatoid arthritis magnetic resonance imaging scoring system.
**Results:** In 22 of 52 patients (42.31%) MRI had detected significant signs of inflammation and BME in small hands joint and/or wrists which was used to establish diagnosis of early RA. The hither synovitis scores were correlated with CRP levels (P=0.007) and ESR (P=0.022).
**Conclusions:** MRI signs of synovitis in the small joints of the hands and wrists are observed in a significant amount of patients (42.31%) with seronegative arthritis without clinical signs of hands joints or wrists involvement, which can be used for early RA detection in patients without enough RA diagnostic criteria.[1]
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1551

## AB0203 POLYCLONAL IMMUNOGLOBULIN LIGHT CHAINS LEVELS IN ELDERLY PEOPLE WITH RHEUMATOID ARTHRITIS: REAL CLINICAL PRACTICE – THE INFLUENCE OF SDMARDS

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**Background:** Polyclonal immunoglobulin light chains (PLC) represent biomarkers of B cell activity in rheumatoid arthritis (RA) and are associated with increased mortality in general population. PLC levels appear to be elevated during preclinical and active periods of RA. Serum k and l light chains are important inflammatory indexes and may be used as indicators of disease activity in RA.
**Objectives:** To explore association between serum PLC in cohorts of patients with RA depending on treatment and to determine whether PLC can be used as markers of treatment effectiveness.
**Methods:** 150 patients with RA untreated and treated with sDMARDs were included in the study (n=52, n=98, respectively), and 31 patient with osteoarthritis. Approximately 75% of patients in all groups were elderly people. Serum levels of PLC were measured by immune nephelometry.
**Results:** Median [lower and upper quartiles] polyclonal k and $\lambda$ light chains serum concentrations in cohort of untreated RA patients were significantly higher in comparison with osteoarthritis and treated RA patients ($\kappa$: 3.1 [2.7; 3.6] vs 2.6 [2.1; 3.3] and 2.6 [2.3; 3.1] g/l, H=12.1, $p<0,01$; $\lambda$: 1.7 [1.3; 1.9] vs 1.4 [1.2; 1.8] and 1.3 [1.2; 1.7] g/l, p=0.014). Comparing groups treated with methotrexate, sulfasalazine and leflunomide (n=48, 15 and 16, respectively) showed no statistically significant difference of PLC levels. It appeared that treatment with methotrexate during at least 6 months reduced serum concentrations of PLC in patients with RA ($\kappa$ untreated 3.0 [2.6; 3.4] vs $\kappa$ methotrexate 2.6 [2.0; 2.8], $p<0.01$; $\lambda$ untreated 1.8 [1.6; 2,05] vs $\lambda$ methotrexate 1,4 [1.0; 1,7], $p<0.01$).
**Conclusions:** PLC can be used as markers of treatment with sDMARDs effectiveness among elderly patients with multimorbidity.
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## AB0204 GLUCOCORTICOID-SPARING EFFECTS OF ABATACEPT IN RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH BOTH ABATACEPT EFFECTIVENESS AND SEROPOSITIVITY

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**Background:** We recently reported a glucocorticoid (GC)-sparing effect of Abatacept (ABA) in patients with RA in real life practice (reference 1).
**Objectives:** To analyze the association between ABA GC-sparing effect and both disease characteristics, such as seropositivity, and abatacept effectiveness in RA patients.
**Methods:** This is a pooled analysis of nine European RA registries (ARTIS, ATTRA, BIOBADASER, DANBIO, GISEA, NOR-DMARD, ORA, SCQM, Reuma.pt) and one North-American (RHEUMDATA). Inclusion criteria were a diagnosis of RA, initiation of ABA treatment, and at least one subsequent follow-up visit with data on GC use. The basal dosage of GC was categorized as none (dose =0 mg/d), low (>0 and ≤5 mg/d), moderate (>5 and ≤10.0 mg/d) or high dose (>10.0 mg/d). We assessed the predictors of reaching both a EULAR good/moderate responder status and stopping/tapering GC in a multivariable model including age, sex, disease duration, number of previous biologics, DAS28 at baseline (BL), RF/ACPA positivity, and concomitant treatment with methotrexate.
**Results:** Of the 1719 patients with information on GC dose, 634 (36.9%) patients were on a low, 745 (43.3%) were on moderate, and 340 (19.8%) patients were on high dose GCs at BL. Patients with moderate/high dose of GCs had significantly higher BL disease activity (mean DAS28 5.3 vs 4.9, $p<0.001$) and were more frequently RF or ACPA-positive (73.6% vs 65.4%, p=0.02). Among the 373 patients who stopped or reduced GC, 276 (74.0%) were EULAR good/moderate responders at 12 months, compared to only 63.4% of those who did not reduce GC ($p<0.001$). 78.4% of the patients who could stop or reduce GC within 12 months were RF positive, compared to 70.8% among those who did not reduce GC. Similarly, 74.3% of patients stopping or reducing GC were ACPA-positive, compared to 62.2% ACPA-positive patients among those who did not reduce GC. In the multivariable model, shorter disease duration (OR 0.95, 95%CI: [0.91; 0.99], p=0.01), lower number of previous biologics (OR 0.76, 95%CI: [0.59; 0.99], p=0.04), lower initial DAS28 (OR 0.56, 95%CI: [0.41; 0.77], p=0.0003), and seropositivity (OR 1.86, 95%CI: [1.09; 3.29], p=0.03) were significantly associated with stopping and reducing GC and being a EULAR good or moderate responder.
**Conclusions:** These results add further evidence to the association between seropositivity and ABA effectiveness by demonstrating that a higher proportion of patients with seropositive RA on ABA therapy are able to reduce or stop concomitant GC compared to seronegative patients, despite having higher doses of GC at baseline.

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## AB0205 IL-22 SERUM LEVELS AS A BIOMARKER FOR EROSIVE DISEASE IN RHEUMATOID ARTHRITIS

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**Background:** Consistent with models of experimental arthritis implicating IL-22 in the development of joint destruction we could previously demonstrate that elevated IL-22 serum levels were associated with the development of erosive disease in patients with early RA.
**Objectives:** To study value of IL-22 as a marker for erosive disease in established RA, to assess whether IL-22 is increased in other joint destructive rheumatic diseases, and to evaluate the influence of comorbidities on IL-22 serum levels.
**Methods:** We measured serum IL-22 levels by Enzyme-Linked Immunosorbant Assay (ELISA) and analyzed their correlation to erosive disease (assessed by radiographs of hand and feet) and clinical parameters in patients with established RA (n=142), psoriatic arthritis (n=15), gout (n=15), age-matched patients with hypertension (n=10), diabetes (n=10), coronary heart disease (n=10), and healthy individuals as controls.
**Results:** 81 of 142 patients with established RA demonstrated elevated IL-22 levels compared with the range of healthy controls. A significant greater percentage of these "IL-22 high" patients (59%) demonstrated erosive disease compared the "IL-22 normal" patients (37%, $p<0.05$). In the "IL-22 high" compared to "IL-22 normal" group the fractions of patients positive for RF (70% vs 83%) and ACPA (74% vs 64%) were slightly higher, however not statistically significant different. Similar, measures of disease activity including DAS28 (2.3 vs 2.8) and CRP (0.5 vs 0.3 mg/dl) only tended to be higher in the "IL-22 high" than the "IL-22 low" group. Irrespective of erosive joint disease, patients with psoriatic arthritis and gout demonstrated lower IL-22 levels compared to established RA and only slightly higher than healthy individuals. Patients with hypertension, diabetes and coronary heart disease had IL-22 serum levels comparable to healthy controls.
**Conclusions:** High IL-22 levels are associated with erosive disease also in established RA, potentially in parts independent of serology, and might serve as a marker for joint destruction also in this cohort.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5902

## AB0206 TREATMENT PATTERNS IN RHEUMATOID ARTHRITIS AFTER METHOTREXATE: DATA FROM THE ONTARIO BEST PRACTICE RESEARCH INITIATIVES COHORT

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**Background:** Guidelines support the use of combination conventional synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs), switching csDMARDs and/or use of biologic DMARDs (bDMARDs) treatment in active rheumatoid arthritis (RA) after use of methotrexate (MTX).
**Objectives:** The purpose of this study was to determine treatment practices after use of MTX in patients with RA who were on either monotherapy or combination csDMARDs in a large observational cohort (OBRI) in order to determine contemporary practice where use of bDMARDs from government coverage is restricted to active RA (+RF and/or +ACPA) or erosions, SJC≥5 with MTX failure, combination failure (triple csDMARDs: MTX + hydroxychloroquine + sulfasalazine) or use of leflunomide.

**Methods:** Patients enrolled in OBRI with documented MTX failure defined as discontinuation due to side effect, primary/secondary failure, or patient/physician decision. Demographics and disease parameters at MTX failure were compared between monotherapy failures, double therapy (Rx) failures, and triple Rx failures.
**Results:** A total of 313 patients with MTX failure were included with a mean (SD) age of 58.8 (13.2) years and disease duration of 6.7 (8.2) years. Of these, 102 (32.6%) were on MTX monotherapy, 156 (49.8%) were double (MTX +1 csDMARD) Rx, and 55 (17.6%) were on triple or more (MTX + multiple csDMARDs)Rx, respectively, at the time of MTX failure. At the time of MTX failure disease duration was numerically higher in patients failing monotherapy and double Rx as compared to triple Rx (7.5 vs. 6.8 vs. 4.5 years, respectively; P=0.276) while patients failing triple Rx were more likely to have an erosion (43.1% vs. 37.2% vs. 61.8%; P=0.009) and had significantly higher patient global (3.5 vs. 3.9 vs. 4.8; P=0.046). When looking at patient transition to csDMARDs monotherapy, csDMARDs combination Rx or bDMARDs treatment, patients receiving monotherapy were more apt to have switches to other monotherapy (87% of patients), whereas those on combination Rx received more combination csDMARDs (78% and 74% of patients on MTX + 1 csDMARDs or MTX + multiple csDMARDs, respectively) and bDMARDs combination Rx (21% and 26%, respectively)(Figure 1).

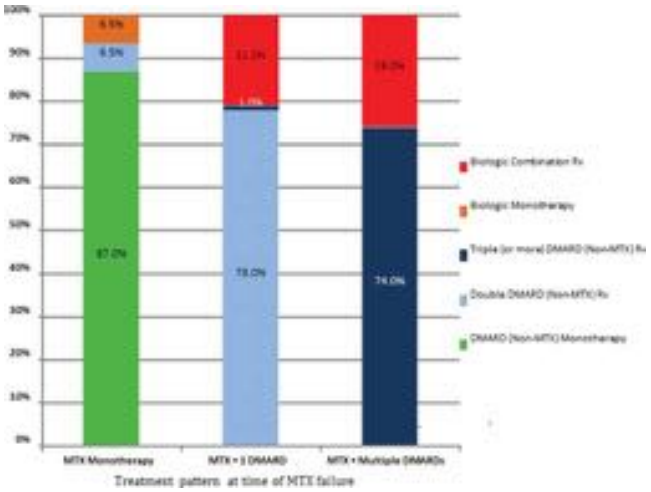


Figure 1. Treatment profile after MTX failure by type of MTX failure

**Conclusions:** There are inherent differences in the selection of subsequent treatment regimen between patients failing MTX monotherapy vs. MTX combination therapy. Overall, the results of the current analysis suggest the use of a sequential treatment intensification strategy in routine clinical practice in Ontario.
**Disclosure of Interest:** None declared
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## AB0207 DIAGNOSTIC EVALUATION OF A COHORT OF PATIENTS WITH UNDIFFERENTIATED ARTHRITIS

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**Background:** One of the most important knowledge of rheumatoid arthritis (RA) landmarks has been evidence that an early and vigorous treatment interferes with the progression and its physical consequences. That is why the early diagnosis has become essential. Today it is considered that the diagnosis must be made within the first 3 months of the onset of the disease, the period in which aggressive treatment should be started before the anatomical damage appears ("The Window oportunity"). The term of "indefinite arthritis" includes patients with different clinical ways of expression, shaped self-limiten arthralgia or arthritis of such low activity forms that when evaluated by the rheumatologis no notes about, so it is raeallity difficult the early manegement of this patients. There are a second group of patients with arthritis observable when assessed do not meet the classification criteria for RA, terming these forms as "undifferentiated arthritis" (UA). A third group of patients to be evaluated who meet the diagnostic criteria for RA are defined as "recent onset rheumatoid arthritis" RRA". Finally, there are a group of patient who are referred with positive laboratory tests without clinical disease criteria.
**Objectives:** 1) To evaluate UA prognostics factors in patients with UA that allow us to predict evolve to defined RA. 2) Analysis of other clinical characteristics predictive of progression to RA.
**Methods:** Descriptive observational study of a cohort of patients who, after a first clinical evaluation are diagnosed with UA, from 2005 to 2015, presenting arthritis in one or more joints lasting less than one year of evolution and not meet 87 ACR diagnostic criteria for RA. Of the patients evaluated at that time, 200 were diagnosed with UA and subsequently followed for more than 3 years. Were analyzed baseline and diagnosis characteristics for each patient
**Results:** Of the 200 patients diagnosed with (UA), 72 were women (52.2%) with a mean age of 48.44 (17–87) years. During the 12-month follow-up, 40 (20%) evolved AR, 52 (26%) a palindromic rheumatism, 53 (26.5%) and 52 to other rheumatic disease (26%) remained as undifferentiated. Of the group of patients who evolved RRA, 53.6% were women, with an average age of 51.7 (18–82) years. Introducing a form of polyarticular onset in 27 (67.5%), small and medium joints affected 22 (55%), symmetrical involvement 36 (90%) and morning stiffness>1 hour 20 (50%). 75% were FR+, OR =2.49 (95% CI =2.11 to 8.13) and 78,5% were ACPCC +, while it was negative in patients with UA remained as an OR =9.77 (95% CI 4.18 to 22.8). At 3 years of follow-up only 5.1% remained as undifferenciated forms, 24.8% as palindromic forms.
**Conclusions:** For early diagnosis, it is essential to identify patients with UA to develop an AR. A quarter of the patients analyzed in our study diagnosed with UA, evolved AR. Patients evolved AR debuted in more than half of the cases with a predominance of polyarticular involvement and medium and small joints affected. The presence of RF and ACPA are predictors of evolution AR, being the latter the most relevant.
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## AB0208 PREDICTION OF FLARE IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS WITH LOW DISEASE ACTIVITY RECEIVING TNF INHIBITORS: ROLE OF CALPROTECTIN AND DRUG TROUGH SERUM LEVELS. A ONE-YEAR PROSPECTIVE COHORT STUDY

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**Background:** Calprotectin and TNF antagonist (TNFa) trough serum levels are associated with disease activity.
**Objectives:** To determine if calprotectin serum levels or drug trough serum levels predict relapse in RA and PsA patients with low levels of disease activity during TNFa therapy.
**Methods:** Prospective 1-year follow-up, single center study (INMUNOREMAR cohort). RA (ACR 1987) and PsA (CASPAR) patients in clinical remission (CR) (DAS28-ESR <2.6) or low disease activity (LDA) (DAS28-ESR <3.2) in ≥2 consecutive visits treated with adalimumab (ADA), etanercept (ETN) or infliximab (IFX) for ≥3 months were included. Demographic data, disease duration, time to initiate csDMARD and bDMARD, time to achieve remission, remission duration, autoantibody status, radiological data, concomitant csDMARD therapy, dose and duration of biological therapy were collected. Clinical and laboratory assessment was made every 4 months and at the time of flare. Calprotectin serum levels (ELISA Kit Calpro AS®) and TNFa trough serum levels (ELISA Kit Promonitor®, Progenika) were determined. Disease flare was defined as DAS28-ESR>3.2 and increase in ΔDAS28-ESR >0.6. Univariate and multivariate regression models were used to identify predictors of disease flare.
**Results:** 103 patients (47RA, 56PsA) were included. Mean Age 57 (30–81) years. 78 (75.8%) had CR and 25 (24.2%) LDA. Mean CR/LDA duration was 58 (4–163) months. 36 patients had received treatment with ADA, 50ETN, and 17IFX. Mean biologic treatment duration 61 (7–166) months. 47.4% patients were on monotherapy, 47% on reduced dose, and 17.9% received steroids. 84 patients (91%) remained in CR/LDA for 12 months, and 12 patients (13%; 8 RA, 4 PsA) experienced flares. Patients with flares had a longer time to achieve CR/LDA [CR/LDA (n=81) 3.1 (1–6) months vs. Flare (n=12) 20 (5–31) months, p<0.001], a shorter CR/LDA duration [CR/LDA (n=81) 59 (5–163) months vs. Flare (n=12) 25 (3–134) months, p=0.031], higher calprotectin levels [CR/LDA (n=81) 1.4 (0.6–3.7) μg/mL vs. Flare (n=12) 6 (4.5–7.9) μg/mL, p<0.001], and lower drug trough serum levels [CR/LDA (n=83) 2.6 (0.6–12) μg/mL vs. Flare (n=12) 0.6 (1–1.2) μg/mL; p<0.001], even when analyzed by biologic [ADA CR/LDA (n=30) 7 (0.2–12) μg/mL vs. Flare (n=4) 0.5 (0.4–1) μg/mL; p=0.003; ETN CR/LDA (n=44) 1.5 (0.7–4.7) μg/mL vs. Flare (n=5) 0.8 (0.9–1.2)μg/mL; p=0.039; IFX CR/LDA (n=14) 3.1 (0.5–7.7) μg/mL vs. Flare (n=3) 0.1 (0–1) μg/mL; p=0.021] at baseline. According to the cut-off developed by our group [1], patients with flares had sub-therapeutic baseline drug serum trough levels [CR/LDA (n=22) 26% vs. Flare (n=12) 100%, p<0.001]. Baseline TNFi trough serum levels [hazard ratio (HR) = 0.47], steroid treatment (HR=3.21), time to CR/LDA (HR=1.17), and baseline calprotectin levels (HR=2.38) significantly predicted flare in the univariate analysis but only baseline calprotectin levels significantly predicted flare in the multivariate analysis [HR=2.74 (1.74–4.31); p<0.0001].
**Conclusions:** Calprotectin and TNF trough serum levels are promising biomarkers to predict flare in RA and PsA patients with low disease activity during anti-TNF treatment.

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## AB0209 FEMALE SEX INCREASES THE RISK OF FOREFOOT DEFORMITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Forefoot involvement in patients with rheumatoid arthritis (RA) is common, and reported to be present in 50–90% of patients without any clear gender predisposition. However, patients with RA that undergo surgical treatment for their forefoot deformities are mostly female, which seems much higher rate than the prevalence of forefoot involvement by arthritis condition.
**Objectives:** In this study we evaluate the factors that contribute to forefoot deformity in RA, and investigate the significance of gender differences in forefoot deformity.
**Methods:** In this cross sectional study, 265 patients (530 feet) with RA (165 females) were enrolled. On AP and lateral standing radiographs of the foot, the angle formed by the first and second (M1/M2) and first and fifth metatarsal bones (M1/M5), the angle formed by the first metatarsal bone and the first proximal phalanx (HV), and the calcaneal pitch angle (CPA) were measured. Patient characteristics and laboratory tests were also analyzed for their potential association with forefoot deformity. As the indications for the surgical treatment of rheumatoid forefoot deformities are strongly influenced by the severity of the hallux valgus deformity, we therefore analyzed patient factors in relation to the measured HV angle.
**Results:** The HV angle was statistically greater in female RA patients than males. Patient age, sex, body mass index, disease duration, Steinbrocker staging, M1/M2 angle, M1/M5 angle, CPA, erythrocyte sedimentation rate, c-reactive protein, matrix metalloproteinase-3, and anti-citrullinated protein antibody measurements were correlated with the HV angle using a single regression analysis. Patient age, BMI, Steinbrocker stage, M1/M2 angle, M1/M5 angle, and the female gender were correlated independently with the HV angle.

| | Regression coefficient (β) | Standard error | P value | Variance inflation factor |
|---|---|---|---|---|
| Gender | –3.175 | 1.295 | <0.0001 | 1.12 |
| M1/M2 | 1.538 | 0.171 | <0.0001 | 1.48 |
| M1/M5 | 0.458 | 0.118 | 0.0001 | 1.53 |
| Stage | 2.942 | 0.437 | <0.0001 | 1.56 |

**Conclusions:** The hallux valgus deformity observed in patients with RA was more severe in females, which was independent of other patient factors. This finding emphasizes that the female gender is a risk factor for the progression of the rheumatoid forefoot deformity.
**Disclosure of Interest:** None declared
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## AB0210 QUALITY OF LIFE INDEXES IN PATIENTS WITH VERY EARLY RHEUMATOID ARTHRITIS (VERA): A TWO CENTER SUBGROUP ANALYSIS FROM THE ADAPTHERA COHORT

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**Background:** The significance of early diagnosis and early therapy initiation in patients with RA is tremendous. ADAPTHERA is a state wide rheumatology network based in Rhineland-Palatinate, Germany. ADAPTHERA aims to improve RA prognosis and quality of patients' life by reducing the time-to-RA-diagnosis. While there have been a lot of studies regarding quality of life in patients with established RA[1,2], adequate data concerning very early rheumatoid arthritis (VERA) (disease duration <3 months) are lacking.
**Objectives:** To study quality of life in VERA patients and to investigate its associations with various RA associated clinical and laboratory parameters.
**Methods:** In a two center subgroup analysis from the ADAPTHERA cohort, we studied quality of life indexes such as Hannover Functional Ability Questionnaire (HFAQ), Health Assessment Questionnaire (HAQ), EuroQol-5D-3L (EQ-5D-3L), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) and World Health Organisation-5 Well Being Index (WHO-5) in patients with VERA. Moreover, we examined the statistical relationship of these indexes with various clinical and laboratory RA associated parameters such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), rheumatoid factor (RF)-/ cyclic citrullinated peptide antibodies (anti-CCP)-status and Disease Activity Score 28 (DAS28) as well as its components [counts of tender and swollen joints, Visual Analogue Scale (VAS)].
**Results:** 74 Patients (50 females, 24 males) with a median age of 62 years (IQR 49, 71) were identified as VERA patients. 36 of them were anti-CCP positive and 34 RF positive. Median scores for HFAQ, HAQ, EQ-5D-3L, FACIT-Fatigue, and WHO-5 were 75.5 (IQR 61, 92.5), 0.75 (IQR 0.26, 1.25), 0.89 (IQR 0.79, 0.89), 40 (IQR 32, 46) and 60 (IQR 32, 76) accordingly. The results of the statistical associations between these scores and RA associated parameters are seen in Table 1.

Table 1. Associations between quality of life indexes and RA associated clinical and laboratory parameters

| Significance (P) | HFAQ | HAQ | EQ-5D-3L | WHO-5 | FACIT |
|---|---|---|---|---|---|
| ESR¶ | 0.001** | 0.006** | 0.379 | 0.046* | 0,243 |
| CRP¶ | 0.001** | 0.008** | 0.392 | 0.020* | 0,424 |
| RF§ | 0.020** | 0.095 | 0.831 | 0.722 | 0.580 |
| anti-CCP§ | 0.003** | 0.003** | 0.597 | 0.460 | 0.922 |
| Tender joint count¶ | 0.001** | 0.003** | 0.021* | 0.066 | 0,342 |
| Swollen joint count¶ | 0.008** | 0.042* | 0.562 | 0.686 | 0,177 |
| DAS28 (ESR)¶ | 0.001** | 0.001** | 0.041* | 0.046* | 0.393 |
| DAS28 (CRP)¶ | 0.001** | 0.001** | 0.039* | 0.094 | 0.558 |
| Morning stiffness¶ | 0.017* | 0.002** | 0.130 | 0.143 | 0.584 |
| Disease Activity patient (VAS)¶ | 0.200 | 0.010** | 0.039* | 0.254 | 0.493 |
| Current pain¶ | 0.085 | 0.001** | 0.001** | 0.003** | 0.001** |

¶Spearman test was used; §Mann Witney test was used; * P<0.05; **P<0.005.

**Conclusions:** The quality of life indexes HFAQ, HAQ, EQ-5D-3L and WHO-5 are associated with two or more markers of disease activity in patients with VERA. Therefore, improvement of patients' quality of life is linked to the achievement of disease remission. In contrast, the FACIT-fatigue index seems to be solely associated with arthritis pain intensity. Thus, improvement of fatigue requires an effective pain management strategy.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5938

## AB0211 WHICH DISEASE ACTIVITY SCORE 28 (DAS28) BASED FLARE CRITERIA IMPACT ON FUNCTIONAL DISABILITY IN PATIENTS WITH RA IN DAS28 REMISSION STATE USING THE IORRA COHORT

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**Background:** The therapeutic goal for patients with rheumatoid arthritis (RA) is achieving remission state or at least low disease activity state. We demonstrated that sustaining remission leads to good functional disability at[1)]. However, not a few patients flared after achieving remission state in daily practice. Several published Disease Activity Score 28 (DAS28) based flare criteria are reported[2–5)]. It is useful to investigate which DAS28 based flare criteria lead to functional disability.
**Objectives:** To investigate associations between DAS28 based flare criteria and functional disability in RA patients after achieving DAS28 remission in daily practice using the large, observational, Institute Of Rheumatology, Rheumatoid Arthritis (IORRA) cohort.
**Methods:** The IORRA survey has been conducted biannually. RA patients with DAS28 remission in April 2012 (baseline) and participated in both subsequent surveys in October 2012 and October 2013 were extracted from the IORRA cohort. Flare in each patient was evaluated according to four previously published DAS28 based flare criteria [(1) increase in DAS28 >1.2 (2) increase in DAS28 >0.6 or if a DAS28 ≧3.2 (3) reaching DAS28>3.2 (4) reaching DAS28>2.6][2–5)] in October 2012. Functional disability was assessed by validated Japanese version of the Health Assessment Questionnaire (J-HAQ)[6)] in April 2012 and October 2013. Change in J-HAQ (ΔJ-HAQ) score was defined as follows: ΔJ-HAQ = J-HAQ score in April 2012 - J-HAQ score in April 2012. Average ΔJ-HAQ score in patients achieving each flare criteria was calculated. The association between ΔJ-HAQ as outcome and achieving each flare criteria as explanatory variable was analyzed using multiple regression analysis adjusting for gender, age, disease duration, pain (Visual Analogue Scale) VAS, general VAS and J-HAQ score at baseline.
**Results:** A total of 1,874 patients were analyzed. Females comprised 80.6% of the study population. The mean (SD) age and disease duration were 58.2 (12.7) years and 11.9 (8.9) years, respectively. The mean (SD) DAS28 and J-HAQ score were 2.0 (0.5) and 0.3 (0.5), respectively. Proportions of the patients met each flare criteria in October 2012 were (1) 9.7% (2) 24.4% (3) 11.3% and (4) 28.1%, respectively. Average ΔJ-HAQ score in patients met each flare criteria was (1) 0.13, (2) 0.06, (3) 0.10, and (4) 0.05, respectively. Multiple regression analysis demonstrated that achieving each flare criteria significantly associated with increase in J-HAQ score; (1) 0.11 (p<0.001), (2) 0.05 (p=0.0003), (3) 0.10 ((p≤0.001), and (4) 0.04 (p=0.0012), respectively.

**Conclusions:** Regardless of flare criteria, flares resulted in progressed functional disability in patients with RA. Aachieving flare criteria using (1) increase in DAS28 >1.2 and (3) reaching DAS28>3.2 led to worse physical functional outcome, suggesting that usage of these flare criteria might predict functional disability.

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## AB0212 CONTRIBUTION OF THE SUBJECTIVE COMPONENTS OF THE DISEASE ACTIVITY SCORE TO THE RESPONSE TO TREATMENT IN RHEUMATOID ARTHRITIS

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**Background:** In recently, with development of biologic agents, RA patients increased the change of reaching remission. But some patients with normalization of inflammatory sign didn't reach to clinical remission state after optimization of treatment.

**Objectives:** This study was performed to investigate the contribution of the more subjective versus the objective component of the DAS28 to response to treatment in RA patient. The secondary aim was to examine the factors associated with 6 month change in pain and EULAR response.

**Methods:** The DAS28-P was calculated (Subjective components of DAS28 relative to the total DAS28: DAS28-P=0.56*sqrt(TJC28) + 0.014*(VAS-GH)/0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.78 ln(ESR) + 0.014*(VAS-GH)). From September 2011 to 2013, 462 new patients were included in this study. EULAR response was assessed after 6month of treatment.

**Results:** The mean age of the included patient was 54 years, and 79% were female. The mean DAS28 at baseline was 4.91±1.07 (range 3.21–8.56) and that at after 6 months of treatment was 3.29±1.28 (range 0.49–8.47). Good responders according to the EULAR criteria were 180 (38.9%), moderate responders 150 (32.4%) and none responders 96 (22.5%). The change of DAS28-P score at baseline and 6 month was significant only for good responders (0.43±0.11 versus 0.3±0.25, p<0.001) and for moderate responders (0.45±0.09 versus 0.41±0.15, p=0.003) but not significant for none responders (0.44±0.13 versus 0.44±0.12, p=0.727). Among those were failed have good response, those who had objective measures (ESR, CRP, and swollen joint) normalized were defined as failure due to subjective measure. Subjects with failure due to subjective measure were less likely to be RF positive and had lower DAS28 after 6month but higher DAS28-P after 6 month.Higher baseline DAS28 score was associated with better pain response while DAS28, DAS28-P and baseline characteristics of patients (sex, age, RF) were not related to EULAR response

**Conclusions:** Our study showed that there are distinct RA patients with high DAS28-P, an index derived from subjective measures, who fails to respond adequately to treatment despite normalization of objective measures.

**Disclosure of Interest:** None declared

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## AB0213 IS DISEASE DURATION AN INDEPENDENT PREDICTOR OF LOW DISEASE ACTIVITY/REMISSION AMONG BIOLOGIC-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT?

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**Background:** Patients with long-standing RA may have more treatment-resistant disease than those with shorter disease duration.

**Objectives:** To examine whether disease duration is an independent predictor of treatment response among biologic-naïve patients with RA initiating abatacept in a US national, observational cohort.

**Methods:** Using the Corrona RA registry, we identified new initiators of abatacept between Feb 2006 and Jan 2014 who were biologic naïve with a follow-up visit at 1 year (±3 months) and assessment of disease activity (CDAI) at initiation and 1-year follow-up. The primary outcome was mean change from baseline in CDAI; the secondary outcomes were: 1) achievement of low disease activity (LDA; CDAI ≤10) among those who initiated abatacept in moderate or high disease activity, and 2) achievement of remission (CDAI ≤2.8) in those who initiated abatacept in low, moderate or high disease activity. Patients were stratified by disease duration (0–2, 3–5, 6–10, >10 years). For patients who switched agents before 1 year, the last observation before the switch was used to calculate mean change in CDAI. Switchers were imputed as non-responders for calculation of LDA and remission. Linear and logistic regression models were fit, as appropriate.

**Results:** In total, 281 biologic-naïve patients with RA initiating abatacept met inclusion criteria (disease duration 0–2 years: n=107; 3–5 years: n=45; 6–10 years: n=50; >10 years: n=79). Baseline characteristics were similar across disease duration groups for sex (76–89% female) and disease activity (mean CDAI: 15.3–19.1). Increasing disease duration was associated with older patient age (p=0.047) and a higher number of prior conventional (c)DMARDs (p<0.001). Mean change in CDAI ranged from –10.22 to –4.63 in patients with 0–2 and >10 years disease duration (Table). In analyses adjusted for age, sex, baseline CDAI and prior number of cDMARDs (Table), increasing disease duration was significantly associated with smaller mean change in CDAI (p=0.015) and lower likelihood of achieving LDA (p=0.048); association with decreasing likelihood of remission reached borderline significance (p=0.055).

Table 1

| | 0–2 years (n=107) | 3–5 years (n=45) | 6–10 years (n=50) | >10 years (n=79) | p |
|---|---|---|---|---|---|
| Unadjusted outcomes | | | | | |
| Mean (SE) Δ in CDAI | –10.22 (1.19) | –7.82 (1.83) | –6.16 (1.74) | –4.63 (1.38) | 0.017 |
| LDA, n (%)* | 53/91 (58.2) | 17/32 (53.1) | 15/33 (45.5) | 23/56 (41.1) | 0.21 |
| Remission, n (%)† | 29/103 (28.2) | 11/40 (27.5) | 12/48 (25.0) | 11/72 (15.3) | 0.23 |
| Adjusted outcomes‡ | | | | | |
| Mean (SE) Δ in CDAI | –9.65 (1.02) | –8.60 (1.53) | –6.77 (1.45) | –4.58 (1.19) | 0.015 |
| LDA, OR (95% CI)* | Reference | 0.89 (0.37, 2.10) | 0.49 (0.21, 1.18) | 0.36 (0.17, 0.78) | 0.048 |
| Remission, OR (95% CI)† | Reference | 0.85 (0.35, 2.05) | 0.57 (0.24, 1.35) | 0.32 (0.13, 0.77) | 0.055 |

*CDAI ≤10 among those with moderate or high disease activity. †CDAI ≤2.8 among those with low, moderate or high disease activity. ‡Adjusted by age, sex, baseline CDAI and prior number of cDMARDs. OR = odds ratio.

**Conclusions:** In biologic-naïve patients initiating abatacept, change in CDAI was significantly greater for shorter versus longer disease duration (unadjusted and adjusted models). After adjusting for covariates, shorter disease duration was associated with a greater likelihood of patients achieving LDA.

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## AB0214 ADIPONECTIN DETERMINATION IN RHEUMATOID ARTHRITIS PATIENTS COMPLICATED BY OSTEOPOROSIS

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**Background:** Bone mineral density and proteins/peptides determination in blood and urine as markers of bone resorption and formation are currently used to diagnose osteoporosis (OP) and metabolic bone diseases. However, these methods have some disadvantages for bone turnover evaluation. Recent evidence suggests that in RA changes in the secretion of hormones of white adipose tissue can be revealed [1,2]. One of them is Adiponectin possessing anti-inflammatory, anti-diabetic and anti-atherogenic properties. Changes in Adiponectin levels may reflect influence of immune inflammation on bone turnover.

**Objectives:** To study the clinical and diagnostic value of serum Adiponectin determination in RA patients complicated by OP.

**Methods:** We examined 88 women with documented diagnosis of RA and mean disease duration of 6.56±0.88 years. We used EULAR/ARA 2010 criteria to diagnose the patients. Female patients with II degree of disease activity (DAS28), Steinbrocker stage II (erosive), rheumatoid factor- and anti-cyclic-citrullinated peptide antibody-positive were prevalent. We excluded patients who had surgery or developed an infection within the last 8 weeks, pregnant and breast-feeding

women, those with severe heart, liver or kidney disease, immune deficiency, leukopenia or chronic infection.
A control group of 45 healthy females aged of 25 and 59 years were included in the study. There were no reported findings of joint pain and RA symptoms in the group. The groups were adjusted for age ($p>0.05$) and showed no statistically significant differences.
We measured serum Adiponectin levels (μg/ml) using Human Adiponectin ELISA commercial test systems (BioVendor, Czech Republic, cat No. RD195023100). We used spectrophotometer with wavelength of 450 nm to detect the test results ("Multiskan" immunoenzyme analyzer, Finland). We plotted a curve using computer software. We diagnosed OP using dual-energy X-ray absorptiometry with LUNAR DPX PRO (GE, USA).
**Results:** Serum adiponectin levels in the control group were 12.5±0.9 μg/ml (M±m). Adiponectin levels in healthy subjects measured as M ±2d, ranged between 0.44 and 24.56 μg/ml. Patients with OP and RA had significantly higher levels of serum Adiponectin ($p<0.001$). Mean serum Adiponectin levels in RA patients who had normal bone density and had no OP were 35.21±0.6 μg/ml. Mean serum Adiponectin levels in RA/OP patients with low bone mineral density were 52.42±0.69 μg/ml. Adiponectin levels of 44 μg/ml and higher were associated with osteoporosis. Adiponectin levels of 43.9 μg/ml and lower were associated with normal bone density.
**Conclusions:** Thus, we revealed that Adiponectin levels depend on osteoporosis presence in RA patients. We suppose that Adiponectin determination may be useful laboratory marker for OP diagnosis. The test may be used to reduce the risk of low-energy fractures and to improve the quality of life in RA.
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## AB0215 THE COMBINATION OF METHOTREXATE WITH HYDROXYCHLOROQUINE IS MORE EFFECTIVE THAN MONOTHERAPY IN EARLY RHEUMATOID ARTHRITIS: A QUASI-EXPERIMENT

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**Background:** A tight-control strategy starting with a combination of methotrexate (MTX) and hydroxy-chloroquine (HCQ) was implemented between 2010–2015 in our clinic; without evidence from RCTs for the combination of MTX with HCQ in early RA (1). Some physicians chose not to adhere to this combination, which post-hoc gave the opportunity for a quasi-experiment.
**Objectives:** To investigate the effect of starting with MTX + HCQ combination therapy, versus MTX or HCQ mono therapy, on the DAS28 at 6 and 12 months in patients with early RA, while treating to the target of remission (DAS28 $<2.6$).
**Methods:** All patients with early RA (ACR-EULAR criteria) between April 2010 and October 2015 were eligible. Two sub cohorts were formed according to whether the treatment was started with MTX+HCQ as intended, or with MTX or HCQ. There were n=50 patients in the adherent-group and n=38 patients in the non-adherent group who were initially treated with MTX or HCQ mono therapy (sometimes with addition of the other drug after more than four weeks). The primary outcome was the ΔDAS28 at 6 months.
**Results:** In the study period 176 RA patients were treated and 88 could not be included due to lack of follow-up data. At baseline, there were no large or significant ($p<0.05$) differences between MTX+HCQ and mono therapy groups regarding age (mean 57 years), gender (73% female), disease duration (median 21 weeks). Also, rheumatoid factor positivity (48% and 34%), mean baseline DAS28 (4.3 (1.3) and 4.2 (1.1)) were not different ($p>0.05$) between MTX+HCQ and mono therapy groups. In the mono therapy group, 30 patients started with MTX and 8 started with HCQ. After 6 months, the DAS28 decreased – 1.4 in the MTX+HCQ group and – 0.8 in the non-adherent group (p=0.044). After 12 months, the DAS28 decreased – 1.7 in the MTX+HCQ group and – 0.8 in the non-adherent group (p=0.007). After 12 months, 48% of adherent patients were in DAS28 remission compared to 26% of non-adherent patients (p=0.039). There were no baseline confounders operational.

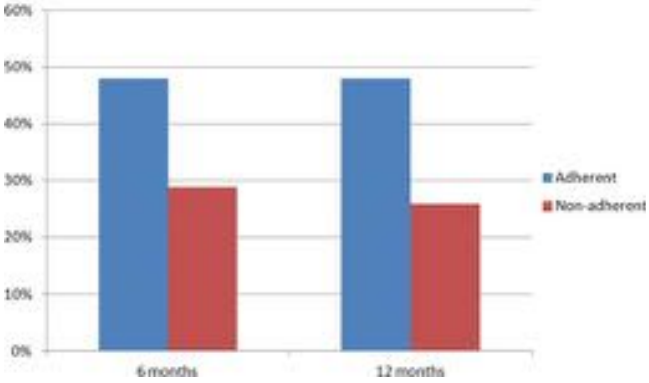
Table 1. (Decrease in) disease activity at 0, 6 and 12 months

| | Adherent (n=50) | Non-adherent (n=38) | p value* |
|---|---|---|---|
| DAS28 0 months (mean (SD)) | 4.3 (1.3) | 4.2 (1.1) | 0.755 |
| ΔDAS28 0–6 months (mean (SD)) | –1.4 (1.5) | –0.8 (1.3) | 0.044 |
| ΔDAS28 0–12 months (mean (SD)) | –1.7 (1.9) | –0.8 (1.3) | 0.007 |

*p value for between group comparisons.

**Conclusions:** In early RA starting with MTX and HCQ combination therapy leads to a larger decrease in DAS28 after 6 and 12 months and higher percentages of remission after 12 months in comparison with mono therapy with MTX or HCQ.

**Figure 1** Percentages of patients in remission (DAS28 < 2.6) at 6 and 12 months




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[1] Ma MH, Kingsley GH, Scott DL. A systematic comparison of combination DMARD therapy and tumour necrosis inhibitor therapy with methotrexate in patients with early rheumatoid arthritis. Rheumatology (Oxford, England). 2010;49(1):91–8.
**Disclosure of Interest:** None declared
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## AB0216 OVEREXPRESSION OF SYNOVIAL LINING PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA COACTIVATOR-1β INVOLVED IN JOINT DESTRUCTION THROUGH UPREGULATING MMP-3 IN RHEUMATOID ARTHRITIS

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**Background:** Our previous study showed that suppression of peroxisome proliferator-activated receptor-gamma coactivator-1β (PGC-1β) alleviated the secretion of matrix metalloproteinase (MMP)-3 from fibroblast-like synoviocytes and inhibited osteoclastogenesis in vitro. However, little was known about PGC-1β with joint destruction in RA patients.
**Objectives:** To investigate the expression and correlation of synovial PGC-1β with joint destruction in RA patients.
**Methods:** Eighty-one patients with active RA were recruited and followed up for one year. Serum MMP3 was detected by ELISA. Synovial tissue was obtained by closed-needle biopsy for H&E and immunohistochemistry staining for PGC-1β, MMP-3, CD3, CD20, CD38, CD68 and CD15. X-ray assessment of hand/wrist was repeated at baseline and one year and radiographic progression was defined as TSS≥0.5 unit.

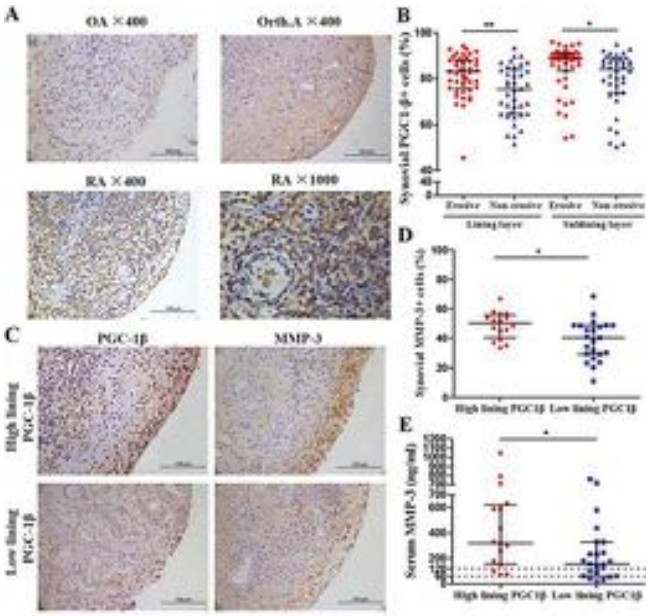



Fig. 1 A: Immunohistochemical staining of PGC-1β in OA, Orth.A and RA synovium; B: Percentage of synovial PGC-1β+ cells in patients with or without erosive disease (*$P<0.05$, **$P<0.01$); C: Immunohistochemical staining of PGC-1β and MMP-3 in patients with high or low synovial lining PGC-1β; D: Percentage of synovial MMP-3+ cells in patients with high or low synovial lining PGC-1β (*$P<0.05$); E: Serum MMP-3 in patients with high or low synovial lining PGC-1β (*$P<0.05$).

**Results:** (1) PGC-1β expression in RA was observed with intense nuclear staining in lining cells and sublining inflammatory cells (including macrophages, lymphocytes and plasma cells) which were significantly higher than osteoarthritis (OA) or orthopedic arthropathies (Orth.A, Fig. 1A).
(2) The percentage of lining PGC-1β+ cells significantly correlated with serum and synovial MMP-3 ($r$=0.394 and 0.376, both $P$<0.01), as well as CRP, ESR, CD15+ neutrophils and CD68+ macrophages in sublining area of RA synovium ($r$=0.266–0.356, all $P$<0.05), and the percentage of sublining PGC-1β+ cells significantly correlated with CRP, ESR, total synovitis score, CD3+ T cells, CD20+ B cells and CD38+ plasma cells, CD68+ macrophages in sublining area of RA synovium ($r$=0.225-0.428, all $P$<0.05).
(3) Forty-three (53%) RA patients had erosive disease (2013 EULAR definition) at baseline and their percentage of lining and sublining PGC-1β+ cells was significantly higher than non-erosive patients (both $P$<0.05, Fig. 1B). Both percentages of lining and sublining PGC-1β+ cells were significantly correlated with mTSS, joint space narrowing and erosion subscore ($r$=0.228-0.261, all $P$<0.05).
(4) Thirty-nine patients had finished one year follow-up and 23% of them had radiographic progression. The percentage of lining PGC-1β+ cells was significantly higher in progressive patients than non-progressive patients [83% (79%–91%) vs 75% (65%–82%), $P$=0.002]. ROC curve analysis showed that the tradeoff value of lining PGC-1β+ cells for predicting 1-year radiographic progression was 78% with sensitivity 89% and specificity 70% (AUC=0.833, 95% CI: 0.689–0.978, $P$=0.003).
(5) Serum and synovial MMP-3 were significantly higher in patients with high synovial lining PGC-1β than that in patients with low synovial lining PGC-1β (both $P$<0.05, Fig. 1C–E). Multivariate logistic regression analysis showed that high lining PGC-1β+ cells was a significant predictor of 1-year radiographic progression after adjustment for synovial and serum MMP-3 (OR: 15.002, 95% CI: 1.43–156.698, $P$=0.024, Fig. 1C).
**Conclusions:** Overexpression of synovial lining PGC-1β might play important roles in aggravating joint destruction through upregulating MMP-3 in RA.
**Acknowledgement:** This work was supported by National Natural Science Foundation of China (81471597), Specialized Research Fund for the Doctoral Program of Higher Education (20130171110075) and Guangdong Natural Science Foundation (2014A030313074).
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## AB0217 VALIDITY OF TREAT TO TARGET STRATEGY FOR COMPREHENSIVE DISEASE CONTROL IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS: A REAL-WORLD, PROSPECTIVE COHORT STUDY

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**Background:** The ultimate goal for rheumatoid arthritis (RA) management is comprehensive disease control (CDC) including clinical remission, normal physical function and non-radiographic progression. However, current recommendations suggest that decision and adjustment of RA therapy mainly bases on disease activity and adheres to the treat-to-target (T2T) strategy which target is remission or low disease activity (LDA). Little was known about the validity of T2T strategy in achieving CDC in real world practice.
**Objectives:** To evaluate the validity and impact factors of T2T strategy in achieving CDC in Chinese RA patients.
**Methods:** Patients with moderately to severely active RA (DAS28-ESR≥3.2) were recruited and treated according to T2T strategy and followed up at the 1st, 3rd, 6th, and 12th months. Clinical data was collected simultaneously at baseline and each visit. X-ray assessment of hand/wrist was repeated and scored according to modified total Sharp score (mTSS). Therapeutic target was remission (DAS28-ESR<2.6) or LDA (2.6≤DAS28-ESR<3.2). One-year CDC was defined as DAS28-ESR<2.6, HAQ score<0.5 and mTSS≤0.5.
**Results:** (1) One hundred and three patients fulfilled 1-year follow-up. There were 33%, 48%, 57% and 56% patients achieved therapeutic target at the 1st, 3rd, 6th, 12th months respectively and 32% patients achieved CDC at the 12th month (Table 1). (2) Comparing with CDC-achieving group, the disease duration, baseline bony erosion and mTSS were significantly greater in CDC non-achieving group, while bDMARDs therapy was significantly less (all $P$<0.05). Further multivariate logistic regression analysis showed that bDMARDs therapy was a significant predictor of CDC-achieving (OR: 3.089, 95% CI: 1.255–7.600, $P$=0.008), while bony erosion at baseline was a significant predictor of CDC-non-achieving (OR: 4.392, 95%CI: 1.484–12.998, $P$=0.008). (3) The percentages of patients achieved clinical remission and normal physical function in CDC-achieving group were significantly higher than those in CDC-non-achieving group at the 1st, 3rd, 6th, 12th months respectively (all $P$<0.05). Univariate logistic regression analysis showed that remission and normal physical function at the 1st, 3rd, 6th were significant predictors of 1-year CDC (all $P$<0.05). Adjusted for bony erosion at baseline and bDMARDs therapy, multivariate logistic regression analysis showed that remission at the 3rd month (OR: 4.159, 95% CI: 1.647–10.506, $P$=0.003) and normal physical function at the 1st month (OR: 8.199, 95% CI: 2.078–32.340, $P$=0.003) predicted 1-year CDC.
**Conclusions:** Our results implies only 32% patients achieved 1-year CDC under DAS28-based T2T strategy and the patients with baseline bony non-erosion, bDMARDs therapy and having rapid clinical and functional improvement within 3 months might be more likely to achieve 1-year CDC.

**Table 1. Baseline demographic, clinical features and outcome of RA patients**

| Characteristics | All patients (n=103) | CDC-achieving group (n=33) | CDC-non-achieving group (n=70) | *P* |
|---|---|---|---|---|
| **Baseline demographic** | | | | |
| Age, years, median (IQR) | 49 (38–58) | 48 (37–58) | 49 (38–58) | 0.904 |
| Female, n (%) | 78 (76) | 27 (82) | 51 (73) | 0.322 |
| Disease duration, mo, median (IQR) | 24 (12–72) | 12 (6–36) | 36 (12–75) | **0.004** |
| DAS28-ESR, median (IQR) | 5.9 (4.8–6.7) | 5.4 (4.6–6.4) | 6.1 (4.9–6.9) | 0.170 |
| HAQ score, median (IQR) | 0.15 (0–0.75) | 0.63 (0.23–1.44) | 0.87 (0.25–1.65) | 0.348 |
| RF positive, n (%) | 84 (82) | 25 (76) | 59 (84) | 0.298 |
| Anti-CCP positive, n (%) | 83 (81) | 25 (76) | 58 (83) | 0.395 |
| Bony erosions, n (%) | 64 (62) | 22 (67) | 42 (60) | **0.007** |
| mTSS, median (IQR) | 9.0 (3.0–21.0) | 4.5 (2.0–12.0) | 11.5 (3.5–32.5) | **0.008** |
| DMARDs and Corticosteroids naïve, n (%) | 38 (37) | 15 (45) | 23 (33) | 0.216 |
| csDMARDs+bDMARDs*, n (%) | 45 (44) | 20 (61) | 25 (36) | **0.007** |
| **The 1st month** | | | | |
| LDA, n (%) | 17 (17) | 9 (27) | 8 (11) | **0.043** |
| Remission, n (%) | 17 (17) | 9 (27) | 8 (11) | **0.043** |
| Normal physical function, n (%) | 70 (70) | 30 (91) | 40 (57) | **0.001** |
| **The 3rd month** | | | | |
| LDA, n (%) | 17 (17) | 4 (12) | 13 (19) | 0.411 |
| Remission, n (%) | 32 (31) | 18 (55) | 14 (20) | **<0.001** |
| Normal physical function, n (%) | 70 (77) | 31 (94) | 40 (69) | **0.004** |
| **The 6th month** | | | | |
| LDA, n (%) | 21 (20) | 5 (15) | 16 (23) | 0.365 |
| Remission, n (%) | 50 (37) | 22 (67) | 16 (23) | **<0.001** |
| Normal physical function, n (%) | 88 (85) | 33 (100) | 55 (79) | **0.002** |
| **The 12th month** | | | | |
| LDA, n (%) | 22 (21) | 0 (0) | 22 (31) | - |
| Remission, n (%) | 36 (35) | 33 (100) | 3 (4) | - |
| Normal physical function, n (%) | 81 (79) | 33 (100) | 48 (69) | - |
| Non-radiographic progression, n (%) | 71 (69) | 33 (100) | 38 (54) | - |

*Compared between CDC-achieving group and CDC-non-achieving group by Mann-Whitney rank-sum test.
#Courses of bDMARDs therapy were 3–6 months in most of the patients.

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**Disclosure of Interest:** None declared
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## AB0218 RHEUMATOID FACTOR IS ASSOCIATED WITH MORE PARAMETERS OF THE DISEASE ACTIVITY THAN ANTI-CITRULLINATED PEPTIDE ANTIBODIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an evolving disease. In order to have a tight control and treat it to target, different markers for the measurement of disease activity have been investigated. A new hope emerged with the appearance of the new diagnostic anti-citrullinated protein antibodies (ACPA), such as anti-CCP and antibodies against mutated citrullinated vimentin (anti-MCV).
**Objectives:** The aim of this study was to evaluate the association of ACPA and RF with the parameters of the disease activity and composite disease activity indices.
**Methods:** We performed a cross-sectional study with 220 participants: 95 RA patients, 95 Non-RA patients with systemic inflammatory diseases and 55 healthy controls (HC). Demographic data, laboratory data and physical examination were performed and radiographies taken. ACPA antibody were measured with ELISA method and RF was measured with conventional Latex test.
**Results:** The mean age of the patients was 50, mean disease duration 4,8 years and average disease activity DAS 28 4,83. The sensitivity and specificity of the Anti-MCV, anti-CCP and RF regarding Non-RA patients were as follows: sensitivity 0.72, 0.71 and 0.69 and specificity 0.82, 0.88 and 0.86, respectfully with the area under the curve 0.77, 0,80 and 0,77. Anti-MCV and Anti-CCP antibody positivity was associated with 8 parameters of the disease activity. The common parameters for all the 3 antibodies were ESR, CRP, DAS28 and SDAI. Anti-MCV positivity was associated with Anti-CCP ($p$<0,001) but not with RF positivity, with higher platelet number, morning stiffness and swollen joint count with $p$<0,05. Anti-CCP positivity was associated with anti-MCV and RF positivity and titer ($p$<0,001) and it was exclusively associated with the higher Sharp van der Heijde radiography scores. RF positivity was associated with anti-CCP and anti-MCV positivity and titer, ($p$<0,05 and 0,04), patient assessment of pain, SJC, TJC, DAS28, CDAI, SDAI and HAQ DI ($p$<0,05).
**Conclusions:** ACPA antibodies should be further evaluated in association with parameters of RA disease activity but RF should not be neglected as well.
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**Disclosure of Interest:** None declared
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## AB0219 PREVALENCE AND RISK FACTORS FOR LUNG DISEASE IN RHEUMATOID ARTHRITIS

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**Background:** Lung disease is the most common extra-articular location of Rheumatoid Arthritis (RA).
**Objectives:** This study aims to evaluate the prevalence and risk factors for lung disease in Rheumatoid Arthritis.
**Methods:** A cross-sectional study of 72 patients fulfilling RA ACR/EULAR criteria was conducted over one year. Epidemiological data and RA parameters were collected. Pulmonary function tests, chest X-ray and high resolution computed tomography (HRCT) were performed. Data analysis was carried out using the SPSS 20 Software. $p<0.05$ was considered statistically significant.
**Results:** Means of age and disease duration were 51.39± 12.40 and 11.76±8.17 years respectively. Smoking was active and passive in 8.3% and 9.7% of cases respectively. RA was seropositive in 70% of cases. Means of DAS28, HAQ, Scharp were 4.59±1.80, 1.19 ±0.96 and 71, 05±43.62 respectively. 58.82% of patients were under Methotrexate, 18.1% under Salazopyrine and 81.9% under prednisone. Only 29.2% were symptomatic on the respiratory level. 12.5% had abnormal physical examination. Chest radiography showed abnormalities in 46% and pulmonary function tests were abnormal in 47% of cases. 55.3% of patients had a lung disease confirmed by HRCT and dominated by interstitial disease (19.4%). RA respiratory functional signs were statistically related to the duration time and positive ACPA. Abnormal HRCT was significantly related to age (p=0.01), activity by DAS 28 (p=0.02) and VS (0.04), severity by RF rate (p=0.04) and HAQ (p=0.01). On multivariate analysis, interstitial disease, rheumatoid nodules, emphysema and pleurisy were respectively associated with smoking, sex, respiratory functional signs and age greater than 40 years.
**Conclusions:** Respiratory disease affects one in two patients in our RA population. It would be related to age and female gender, but also smoking, activity and severity that we should control.
**Disclosure of Interest:** None declared
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## AB0220 WHAT PROPORTION OF PATIENTS FAIL TO ACHIEVE CDAI AND AND SDAI REMISSION BASED ON PHYSICIAN GLOBAL ASSESSMENT? AN ANALYSIS FROM A PROSPECTIVE, OBSERVATIONAL REGISTRY

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**Background:** Physician's Global Assessment of Disease Activity (MDGA) is a measure that is frequently incorporated in disease activity indices which reflects the physician's perception of disease activity in rheumatoid arthritis (RA).
**Objectives:** The aim of this analysis was to assess the proportion of patients failing to achieve CDAI and SDAI remission based on MDGA in a real-world, routine clinical care setting in Canada.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, ankylosing spondylitis (AS), or psoriatic arthritis (PsA) with infliximab (IFX) or golimumab (GLM). Eligible patients for this analysis included RA patients treated with IFX or GLM between 2005 and 2015. Modified versions of CDAI (mCDAI) and SDAI (mSDAI) were calculated by omitting MDGA from the formulas. Correlation of the standard and modified versions of each index was assessed with the Pearson's correlation coefficient. ROC curve analysis was used to identify new thresholds for the modified versions of low disease activity (LDA) and remission. Cross-tabulations with the Chi-square test were used to assess the agreement between the standard and modified definitions of remission and LDA.
**Results:** A total of 1206 patients were included in the analysis with a mean (SD) age of 56.1 (13.4) years and a disease duration of 8.4 (8.9) years.
A strong positive correlation was observed between the standard and modified versions of CDAI ($r=0.99$; $P<0.001$) and SDAI ($r=0.99$; $P<0.001$). Based on ROC analysis the new thresholds for remission and LDA were: CDAI (remission=2.65, LDA=10.05) and SDAI (remission=3.31, LDA=10.73). The proportion of patients achieving remission by both indices was 17.8% and 19.5%, patients not achieving remission by both indices was 75.3% and 74.4%, and patients achieving remission by the new thresholds only was 6.9% and 6.1%, for CDAI and SDAI, respectively. Cross-tabulation of the standard and modified thresholds showed that an additional 8.4% and 7.6% of non-remission cases for CDAI and SDAI, respectively, would be classified as remission with the modified definitions. Similarly, an additional 17.6% and 15.1% of non-LDA cases for CDAI and SDAI, respectively, would be classified as LDA.
**Conclusions:** The results of this analysis showed that MDGA could account for up to 8% of non-remission cases and up to 18% of non-LDA cases as measured by CDAI and SDAI. Omission of MDGA from these disease activity indices could have a significant impact on patient management in preventing overtreatment with DMARDs and biologics and avoiding unnecessary switching of DMARDs and biologics.
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## AB0221 PREDICTIVE VALUE OF POWER DOPPLER ULTRASONOGRAPHY (PDUS) IN THE DIAGNOSIS OF VERY EARLY RHEUMATOID ARTHRITIS

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**Background:** There is a short window of opportunity for early diagnosis and treatment of rheumatoid arthritis, that may be crucial for reaching remission and a low rate of radiographic progression. High resolution power doppler ultrasonography (PDUS) is helpful in early detection of synovitis and allows an accurate classification of patients with joint inflammation.
**Objectives:** To establish wether the presence of basal power doppler signal in patients with very early arthritis may be helpful in order to establish the risk of final diagnosis of rheumatoid arthritis according ACR criteria 1987 at a year of follow up.
**Methods:** We studied the presence of ultrasonographic Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, knees) and 44 joints (28 joints and in addition hips, Tarsus, ankles and MTPs), with a mid-range equipment GE L5, in 40 patients with suspected early arthritis The patients were included with at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes with $<12$ weeks of duration of the symptoms. Presence or not of basal high acute phase reactants and basal erosions (score $\geq 2$ in at least one joint by modified Sharp method) for each patient were registered (37 patients with completed hands and feet radiology available). Presence of RF and/or ACPA positive were recorded as well. At one year follow-up was established whether patients met criteria for RA according1987 ACR or not. Statistical study: Chi-square, Fisher exact test, p univariant and Odds Ratio calculation.
**Results:** The presence of basal power doppler signal in $\geq 1$ joints of 44 (PD44) in baseline visit shows statistically significant association to RA diagnosis at 12 months by ACR 1987 classification criteria, p=0.008, OR=10,72 (1,76–65,24) but the presence of at least one joint with power doppler signal of 28 joints (PD28) did not (p=0.246). FR/ACPA were positive in only 20% and 15% of patients respectively, and were not associated to RA final diagnosis (p=0.236, p=0.152). Presence of basal radiographic erosions were associated to RA, $p<0.0005$ and OR 28,28 (3,05–261,87), as well as high CRP p=0.045 OR 4,63 (1,62–13,25) and ESR p=0.046, OR 4.5 (1.08–18,69). 17/17 (100%) of patientes with PD44 basal and radiographic erosions had final diagnosis of RA at 12 months.

| BASAL VARIABLES n=40 | | AR (ACR 1987) YES | p univariate | OR | IC 95 % |
|---|---|---|---|---|---|
| PD 28 | YES | 22/30 (73,3%) | NS | - | - |
| | NO | 5/10 (50%) | 0.246 | | |
| PD 44 | YES | 25/32 (78,1%) | 0.008 | 10,72 | (1,76-65,24) |
| | NO | 2/8 (25%) | | | |
| PD 44+ERORX (n=37) | YES | 17/17 (100%) | <0.0005 | NC (=) | - |
| | NO | 8/20 (40%) | | | |
| EROSION RX (n=37) | YES | 18/19 (94,7%) | < 0.0005 | 28,28 | (3,05- 261,87) |
| | NO | 7/18 (38,9%) | | | |

**Conclusions:** The presence of at least one joint with power doppler signal of 44 joints (PD44) on baseline visit may help to predict the RA diagnosis at 12 months of follow up according to criteria ACR 1987, in patients with very early RA. Presence of positive acute phase reactants and radiographic basal erosions increased the risk of RA as well. Moreover 100% of patients with PD44 in addition to radiographic basal erosions developed RA at 12 months.
**Disclosure of Interest:** None declared
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## AB0222 BODY MASS INDEX, SMOKING STATUS AND RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS: A REAL LIFE STUDY

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**Background:** Several studies have demonstrated that obesity and smoking could have a negative influence on the response to anti-TNFα in Rheumatoid Arthritis (RA). Very few data are available about the impact of body mass index (BMI) and smoking status on other biologic agents.
**Objectives:** To evaluate the influence of BMI and smoking status on response to Rituximab (RTX) in RA.
**Methods:** A total of 68 RA patients treated with RTX were included in this monocentric retrospective study. BMI was calculated at the initiation of treatment. After six months of treatment, C-reactive protein level, tender and swollen joints, change of DAS28 from baseline, rates of EULAR good response and rates of remission were evaluated.
**Results:** At baseline, the median [interquartile range] BMI was 25.04 [21.4–28.8] kg/m$^2$. The number of patients with normal weight, overweight and obesity was 34, 22 and 12, respectively. The number of patients smokers, past smokers and never smoked was 12, 17 and 38, respectively. Baseline characteristics did not differ between the three subgroups of BMI and smoking status. After six months, the number of RA patients with DAS28 decrease $\geq$1.2, EULAR good response and remission was 20 (29.41%), 13 (19,11%) and 12 (17.64%), respectively.
The median BMI did not differ between responders and non-responders for DAS28 decrease $\geq$1.2 (25.7 [22.28–28.63] vs. 24.7 [21.09–29.3], p=0.49), EULAR good response (24.22 [20.91–39.75] vs. 25.1 [21.23–28.99], p=0.96) and remission (24.08 [21.84–28.24] vs. 25.1 [21.22–29.3], p=0.81). The percentages of smokers, past smokers and never smoked did not differ between responders and non-responders for DAS28 decrease $\geq$1.2 (smokers 15%, past smokers 25%, never smoked 60% vs. smokers 19,15%, past smokers 25.53%, never smoked 55.32%, p=0.9), EULAR good response (smokers 15,38%, past smokers 30,77%, never smoked 53,85% vs. smokers 18,52%, past smokers 24,07%, never smoked 57,41%, p=0.87) and remission (smokers 25%, past smokers 41,67%, never smoked 33,33% vs. smokers 16.36%, past smokers 21.82%, never smoked 61.82%, p=0.18).
Multivariate analysis performed on data corrected for age, sex, disease duration, concomitant treatments, and previous anti-TNFs, confirmed that BMI, body weight, and smoking status did not influence the clinical response to RTX ($p>0.05$ for all outcome variables considered).
**Conclusions:** This monocentric evaluation of RA patients demonstrated that there is no influence of BMI and smoking status on response to RTX in RA. However, larger and prospective studies are needed to confirm these results that could be useful for the selection of biologics in obese and smokers RA patients.
**Disclosure of Interest:** None declared
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## AB0223 NEOPTERIN IN EARLY ARTHRITIS: DISEASE ACTIVITY AND SERUM MARKERS OF INFLAMMATION, CORRELATION INTO THREE TIME PERIODS, AN EXPERIENCE IN ARGENTINA

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**Background:** Neopterin is a molecule produced by monocytes by stimulation of Interferon Gamma. It is elevated in infections, autoimmune diseases, malignancies, transplant rejection, neurodegenerative, and cardiovascular conditions such as pregnancy [1,2].
**Objectives:** To investigate the serum levels of neopterin in patients with early arthritis (EA) and establish its relationship with activity disease.
**Methods:** Non-experimental, prospective and longitudinal study was conducted in patients with EA (<2 years of evolution) and >18 years of age. On days 0, 6 and 12 months physical examination and analysis of parameters of activity within 7 days of the blood sample (DAS28, HAQ, EVA and ESR, CRP, FR, anti-CCP and ANA) were performed. Neopterin determination was made by ELISA reagent kit Gen Way Biotech Inc and calculated with Logit-log. Normal value below 10 nmol/l was considered.
Radiographs of hands and feet at the initial visit and 12 months through SENS method (score of grips and erosions) were evaluated.
Neopterin values were compared to a control population of 47 healthy individuals. Stata 9.0 for data analysis. Fisher 2 to chi-2.
**Results:** Twenty-seven patients (36±13 years), 19 (70%) women and 8 (30%) males were evaluated. At first the mean value of neopterin in EA Group was 7.51 (5.5–11.4) vs 5.32 (3.5–6.44) in the control grou p (p=0.0004). It was correlated with scores of activity, and the activity measured by DAS28 was observed that in the initial period: Neopterin >10 nmol/L (n=8): 3.37 [2.53–4.36] vs Neopterin standard value (n=19): 3.86 [3.24 -4.54] (p=0.34).At 6 months: Neopterin>10 (n=5): 3.33 [2.14–4.33] vs Neopterin standard (n=22): 2.96 [2.66–3.73] (p=0.6); and at 12 months: Neopterin >10 (n=9): 3.08 [2.49–3.79] vs Neopterin standard (n=18): 2.90 [2.34–3.27] p=0.53. No correlation was found between neopterin and DAS 28.
**Conclusions:** In this study the results showed no correlation between disease activity (DAS28) and high concentrations of serological marker (neopterin) compared in the three periods or with other international assessment rates. Correlation was observed between DAS 28 and acute phase reactants (ERS and CRP) in the three periods. It would require studies with more patients to confirm these data.
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**Disclosure of Interest:** None declared
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## AB0224 ROLE OF ANTI-RA33 AS A BIOMARKER FOR DIAGNOSIS IN COLOMBIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Accurate and early diagnosis of rheumatoid arthritis (RA) is vital for the timely implementation of a comprehensive treatment aimed at halting or slowing its progression (1). The sensitivity of existing biomarkers, rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (anti-CCP) is low (2). It requires a new diagnostic biomarker with better performance in RA.
**Objectives:** To evaluate the diagnostic value of anti-RA33 (3) test in a simple of RA patientes and controls of Bogotá, Colombia, by measuring its sensitivity, specificity, positive and negative likehood ratio compared to RF and anti-CCP. Additionally, to asses the association between clinical and serological variables with the functional impairment degree in patients with RA.
**Methods:** A cross-sectional study in a sample of 80 RA patients and 20 controls without RA who attended to outpatient service in two hospitals of Bogotá from 2014 until 2015 was conducted by measuring their sociodemographic characteristics, arthritis activity degree by DAS-28 index, functional ability by HAQ-DI score and serological status for anti-RA33, RF and anti-CCP. A statistic analysis with proportions, summary and dispersion measures, contingency tables for measure of sensitivity, specificity, likehood ratios, ROC curves and multiple linear regression analysis was performed.
**Results:** Sensitivity score for anti-RA33, RF and anti-CCP was 15%, 85% and 93% respectively; while specificity was 100%, 90% and 85% respectively. The positive likelihood ratio was 8.5 for RF and 6.2 for anti-CCP. Finally, negative likelihood ratio was 0.87 for anti-RA33, 0.16 for RF and 0.08 for anti-CCP. The anti-RA33 seropositive patients were greater arthritis activity and functional disability as well as higher titers of RF and anti-CCP although these differences were not statistically significant. Finally, a moderately strong positive correlation was found between DAS-28 and HAQ-DI scores ($R^2$ =0.51). In the multiple linear regression model, DAS-28 index was the only predictor variable that explained the changes in the HAQ-DI functional ability score.
**Conclusions:** Findings suggest that anti-RA33 test does not seem to have any clinical utility for the diagnosis of RA in Colombian population. The importance of DAS-28 activity index as a score of association with functional disability in patients with RA was confirmed.
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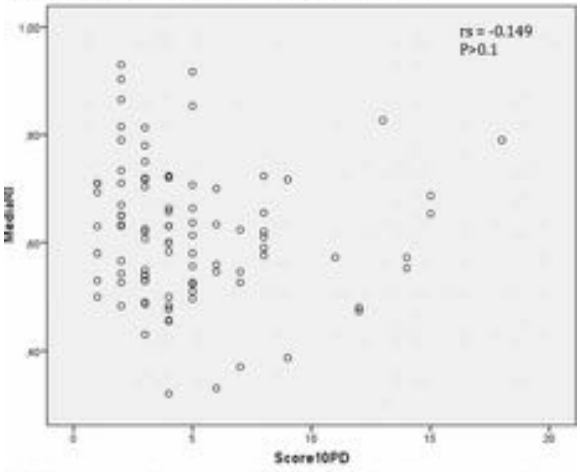
## AB0225 ASSOCIATION OF SPECTRAL DOPPLER RESISTIVE INDEX WITH POWER DOPPLER AND DAS28 IN ESTABLISHED RHEUMATOID ARTHRITIS

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**Background:** Angiogenesis and vasodilatation play a crucial role in the development and perpetuationof synovitis in rheumatoid arthritis (RA). Ultrasonography (US) is an useful tool for evaluation of pannus vascularization in active RA. Differently from US power Doppler (pD), the resistive index (RI) of spectral Doppler provides a quantitative analysis of vascular inflammation. As the musculoskeletal structures are characterized by high-resistance flows, the RI has a value of 1 in normal conditions; a decrease in the RI is registered in case of inflammation.
**Objectives:** To investigate a possible association of the RI spectral Doppler with other US parameters of synovitis and clinical measures of disease activity in established RA.

**Methods:** 95 pD-positive RA patients (1987 ACR criteria) were consecutively evaluated and scanned in this prospective cross-sectional study. Disease acitivity and disability were measured using Disease Activity Score in 28 joints (DAS28) and Health Assessment Questionnaire (HAQ), respectively. US examination was performed by ultrasound-trained rheumatologists in 10 hand joints (the wrists, 2nd and 3rd metacarpophalangeal and 2nd and 3rd proximal interphalangeal joints) using high-resolution equipment (MyLab 60, Esaote). Clinical and US evaluations were performed in a blinded fashion. Gray-scale (GS) and pD were searched using a semi-quantitative scale (0–3). For each patient, the most inflammed joint on US examination was identified and, then, RI was measured at least on three different sites of the sinovial area. The sum of the individual joint scores for GS and pD (10-joint score GS or pD) and the mean RI of the most US-affected joint were calculated. Kappa statistics was used to evaluate interobserver reability. Mann-Whitney test and Spearman correlation coefficient (rS) were used for statistical analysis.
**Results:** Patients' features were mean age, 55.6±11.8 years; female gender 79%, positive rheumatoid factor, 58%; median disease duration, 7 (range, 1–36) years; mean DAS28, 4.33±1.66; mean HAQ, 1.04±0.88. Real-time US interobserver kappa was 0.77 for GS, 0.87 for pD, and 0.68 for RI. RI was not significantly associated with 10-joint pD-score (rS=-0.15, 95% CI -0.33 to 0.05, p=0.15; figure 1), 10-joint GS-score (rS=-0.14, 95% CI -0.31 to 0.04, p=0.17), DAS28 (rS=0.05, 95% CI -0.17 to 0.26, p=0.61) or HAQ (rS=-0.01, 95% CI -0.22 to 0.20, p=0.95). There was also no association of RI with the presence of bone erosions (p=0.72).

Figure 1: Correlation of the 10-joint PD score with Resistive Index




MediaRI - mean value of resistive index, Score10PD - sum of all joint value in power Doppler semi-quantitative score, rs = Spearman correlation coefficient

**Conclusions:** RI was not either clinically or statistically correlated with clinical measures of disease acitivity, US inflammatory parameters, and structural damage in our study. Adding the RI to musculoskeletal US evaluation does not seem to improve US performance in PD-positive patients with established, long standing RA.
**References:**
[1] Terslev L et al. 2008;35(1):49–53
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4385

## AB0226 ONE YEAR EXPERIENCE OF A BDMARD SPACING PROTOCOL IN REAL LIFE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Current guidelines about rheumatoid arthritis (RA) management might admit tapering schedules of biologic disease modifiying drugs (bDMARDs) when disease activity control has been achieved and maintained, in line with growing scientific evidences [1]. Great heterogeneity in target populations, end-points, study designs, therapeutic protocols, criteria for bDMARD discontinuation and resumption globally prevents from univocal interpretation of study results [2]. Real life data might provide additional information on the topic, which could be better extended to routine care.
**Objectives:** To analyze the impact of a bDMARD down-titration strategy (spacing) on clinical and sub-clinical disease activity control over time (12 months) in real life RA patients attending a single Italian Rheumatologic Unit.
**Methods:** RA patients with at least 1 year of bDMARDs treatment and a well-controlled disease (at least low disease activity/LDA according to DAS28 criteria for at least 6 months) were offered to undergo a spacing (doubling the inter-administration period) of their ongoing bDMARD (anti-TNF, Abatacept/ABA, Tocilizumab/TCZ) medication. When present, concomitant conventional synthetic DMARDs (csDMARDs) and/or low dosage (less than 7,5 mg/d prednisone-equivalent) oral corticosteroid (CS) were admitted and maintained: Group A= CS-on patients; Group B= CS-off patients. Disease activity was monitored every 2 months through DAS28 in order to detect any clinical relapse (>LDA): relapsing Group A patients immediately resumed original bDMARD schedule, relapsing Group B patients started firstly low dose CS (5 mg/d) while keeping on bDMARD spacing. At the same time-points, ultrasonographic (US) assessment (Gray Scale/GS and power Doppler/PD scores) was performed on dorsal view of bilateral hands and wrists. Clinical and US results were analyzed either globally and by CS-co-medication, as to detect any bDMARD sparing effect.
**Results:** Thirty-seven RA patients consented to the bDMARD spacing. Most patients were on anti-TNF agents (4 TCZ, 1 ABA) in association with csDMARDs (7/37 csDMARD free), and without CS co-medication (30/37 CS free). At time of spacing overall clinical (mean DAS28±sd 1,92±0,59), lab (median ESR [IQR] 10,50 [7–16] mm/h, median CRP [IQR] 0,14 [0,10–0,49] mg/dL) and US parameters (median GS score [IQR] 9 [6–13,5], median PD score [IQR] 0 [0–0]) were consistent with disease control; more than half patients had negative prognostic factors. Globally, trends over time of either clinical and US parameters did not significantly differ between groups, regardless of CS co-administration. Nevertheless, over the first year of observation more CS-off than CS-on patients experienced disease relapse (12 versus 4 patients, respectively, p=0,99); this occurred sooner in CS-off patients, too (mainly in the first 6 months of follow up).
**Conclusions:** The feasibility of bDMARDs step-down schedules in RA patients should be clarified in real life setting, as well as in clinical trials. bDMARD spacing might be a possible choice, especially when low dosage CS are co-administered: their eventual bDMARD sparing effect should be confirmed with larger and longer observations, together with complete evaluations about cost-effectiveness and risk-to-benefit profiles.
**References:**
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[2] Yoshida K, et al. AnnRheumDis 2014;73:595–599.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5302

## AB0227 VALIDATION OF PATIENT-DERIVED DISEASE ACTIVITY SCORE IN CHINESE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The current standard of care for rheumatoid arthritis (RA) is treat to remission or low activity state. This underlines the need of regular assessment of disease activity. Patient-derived Disease Activity Score (PDAS) is one of the tools that have been developed and validated to allow patients with RA to self-assess disease activity.[1] Two versions of PDAS are available: PDAS1 (with ESR) and PDAS2 (without ESR). The corresponding cut-off points of RA activity statuses had been reported.[2] PDAS was developed in English speaking patients.
**Objectives:** To explore the validity of PDAS in Chinese speaking RA patients.
**Methods:** 100 RA patients were recruited from rheumatology specialist clinic in Hong Kong. They were asked to complete in Chinese version of questionnaires before clinic which included functional status (Health Assessment Questionnaire)[3], self assessed swollen and tender joint count, morning stiffness and global assessment. Standard disease activity score DAS28ESR and CDAI were assessed by Rheumatologists at these visits. Correlation with PDAS1 and 2 was done with Spearman rank test and categorical agreement by kappa statistics. The study was approved by local ethics committee.
**Results:** Patient characteristics are as follows: mean age 60 years (standard deviation SD 12), mean RA disease duration 14 years (SD 9), 90% female, 71% seropositive, 48% patients in remission or low disease activity while 52% in moderate or high disease activity. PDAS in Chinese patients showed equally high correlation with DAS28ESR and CDAI. Spearman rank correlation coefficients were similar to those in original PDAS derivation (in brackets) (all P<0.0001):

| | DAS28ESR | CDAI |
|---|---|---|
| PDAS1 | 0.86 (0.85) | 0.67 (0.69) |
| PDAS2 | 0.70 (0.70) | 0.77 (0.73) |

When comparing RA activity statuses ([remission or low] versus [moderate or high activity]) using kappa statistics, PDAS showed considerable agreement with DAS28ESR, noting that within this patient group, the agreement of DAS28ESR with CDAI itself was only 0.60:

| | DAS28ESR | CDAI |
|---|---|---|
| PDAS1 | 0.52 | 0.58 |
| PDAS2 | 0.28 | 0.53 |

In particular for PDAS2, a formula without the need of blood test, has good sensitivity (96%) of picking up DAS28 remission or low activity, and good negative predictive value (89%) to signal moderate or high activity.
**Conclusions:** PDAS can be adapated to Chinese language speaking RA patients

in routine clinical setting. PDAS2 is useful in two aspects: informing patients that they are well treated-to-target; and concuring with patients having moderate or high disease actiivity.

**References:**
[1] Choy EH et al. Arthritis Rheum. 2008 Feb 15;59(2):192–9
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[3] Koh ET et al. J Rheumatol. 1998 Sep;25(9):1705–8

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3814

## AB0228 ARTHRITIS WITH CHILDHOOD ONSET IN ADULT PATIENTS: LONG-TERM OUTCOMES AND SOCIAL ADAPTATION

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**Background:** Follow-up care and social adaptation issues in adult patients with childhood onset arthritis are highly relevant, as the prognosis and long-term outcomes of the disease are not sufficiently studied.
**Objectives:** To assess long-term outcomes and social status of adults with childhood onset arthritis.
**Methods:** Establishment of the adult patients with childhood onset arthritis database, covering the period from 2003 year to 2015 year, allowed to analyze the disease activity, the radiographic stage and functional class (using *Steinbrocker method*), complications, used pharmacotherapies, as well as social status (education, professional activity, marital status).
**Results:** The database includes 235 patients: 176 females, 59 males, mean age 27.7±8.0 years, disease duration 18.1±8.5 years. Persisting arthritis was found in 72% patients. Radiographic stage II was established in 139 patients, stage III – in 49, stage IV – in 47 patients. Functional class II predominates in the majority of patients. The most common disease-modifying anti-rheumatic drug (DMARD) used was methotrexate – in 73% of patients, each 3rd patient was taking sulfasalazine, each 4th - leflunomide, 15% of patients had never used whatever DMARDs. 53 patients were administered biologic drugs: 30 patients received 1, 16 patients – 2, 6 patients – 3, 1 patient received 4 of biologic drugs. Glucocorticoids (GCs) were administered in 55% of patients, more than 60% continue on GCs, including 42 patients using GCs for >10 years. Aseptic bone necrosis (predominantly of femoral head) was reported in 25% of patients. Bone fractures were documented in 8 patients. Joint prosthetics were required in 23 patients: single joint – in 9, 2 joints – in 11, 3 joints – in 2, 4 joints - in one patient. Arterial hypertension, requiring medication, was found in 12 patients. Nanism was diagnosed in 27 patients, primary amenorrhea – in 11, secondary amenorrhea – in 2, steroid diabetes – in 2 patients. Light perception visual acuity was documented in 2 patients, poor vision was reported in 3 patients. Amyloidosis was found in 2 cases. At present higher education was finished or in the process of continuation by 49 patients (including 2 patients – in medical institute), special education was finished or in the process of continuation by 169 patients. Only school education has 17 patients. Out of those with full education (127 patients) 85 are working (including 2 rheumatologists and 1 pediatrician), while 42 patients are in dependence. 52 patients have family (93% - women), 36 patients (91% - women) have children: one – 27, two – 7, three – 1, six – 1.
**Conclusions:** Only 1/3 of adult patients with childhood onset arthritis have satisfactory long-term clinical outcomes; at the same time the majority of patients are well adapted socially.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3960

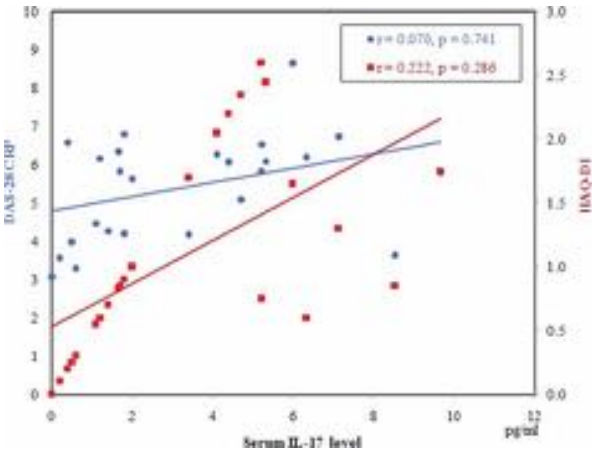
## AB0229 DOES SERUM LEVEL OF IL-17 AFFECT DISEASE ACTIVITY AND FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS PATIENTS? RELATION BETWEEN SERUM IL-17 LEVEL, DAS-28 AND HAQ-DI

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**Background:** Rheumatoid arthritis (RA) is a chronic, progressive, systemic inflammatory disease. Interleukin-17 (IL-17) is a cytokine that is expressed in inflammatory and autoimmune diseases and expected to play an important role in the pathogenesis of RA. Many years, the measurement of disease activity in RA has been held by Disease Activity Score-28 (DAS-28). Regarding the correlation between serum level of IL-17 and disease activity, some authors found a good significant correlation between these parameters,while others stated that DAS-28 values for expressing disease activity in RA patients may be flawed by coexisting fibromyalgia lead to higher total scores. Health Assessment Questionnaire – Disability Index (HAQ-DI) has been usually used for disability assessment in RA patients. It is one of the most widely used comprehensive, validated and patient-oriented outcome assessment instruments.
**Objectives:** To study the relation between serum IL-17 level, DAS-28 CRP and HAQ-DI in RA patients.
**Methods:** The study included 25 RA patients and 20 healthy controls. Serum IL-17 was measured by ELISA, disease activity by DAS-28 CRP and functional disability by HAQ-DI.
**Results:** Serum IL-17 level among RA patients was significantly higher than healthy control ($p$ <0.001). Serum IL-17 levels showed insignificant correlation with DAS-28 CRP and HAQ-DI of RA patients.

Table 1

| | Serum IL-17 | |
|---|---|---|
| | r | p |
| DAS-28 CRP | 0.070 | 0.741 |
| HAQ-DI | 0.222 | 0.286 |




**Conclusions:** IL-17 doesnot correlate with disease activity and functional disability in RA patients.

**References:**
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[2] Rosu A, Margaritescu C, Stepan A, Musetescu A, Ene M. IL-17 patterns in synovium, serum and synovial fluid from treatment-naive, early rheumatoid arthritis patients. Rom J Morphol Embryol 2012; 53(1):73–80.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1345

## AB0230 CENTROMERE PATTERN EXHIBITS A SPECIFIC DISTRIBUTION OF TITERS AMONG ANTI-NUCLEAR ANTIBODIES (ANAS) AND CHARACTERIZES A DISTINCT SUBSET IN RHEUMATOID ARTHRITIS

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**Objectives:** Centromere pattern is a staining pattern of anti-nuclear antibodies (ANAs). Here, we characterize the titer distribution of centromere pattern and analyze clinical and genetic features of centromere pattern-positive rheumatoid arthritis (RA).
**Methods:** We examined ANA by indirect immunofluorescence for 9,575 healthy volunteers and 1,211 RA patients without systemic sclerosis in Kyoto University Hospital. HLA-DRB1 was genotyped for 285 RA patients. We compared distributions of titers among ANA and analyzed associations between centromere pattern

and clinical or genetic features in the subjects. For validation, we recruited another cohort of 2,424 RA patients in Tokyo Woman's Medical University Hospital to confirm the associations between centromere pattern and clinical features.
**Results:** Eighty seven healthy volunteers (0.91%) and 25 RA patients (2.76%) were positive for centromere pattern of ANA. Centromere pattern was the only ANA staining pattern that demonstrated a definite bimodal distribution of levels in both healthy volunteers and patients with RA. Centromere pattern showed significantly higher levels than the other ANA patterns in the subjects positive for each ANA ($p<0.0001$). Centromere pattern-positivity was associated with old age and females in both healthy population and patients with RA.
Centromere pattern-positive patients with RA showed lower positivity of rheumatoid factor (RF) ($p=0.0011$) that is one of risk factors for bone destruction. Centromere pattern was associated with Raynaud's phenomenon and complication of Sjögren's syndrome and primary biliary cirrhosis ($p\leq0.0052$). No HLA-DRB1 alleles were significantly associated with centromere pattern.
In validation study, 82 RA patients (2.41%) were positive for centromere pattern. Centromere pattern-positivity was again associated with old age, females and negativity of RF ($p\leq0.0044$). Information of complications and symptoms was not available in the replication cohort. Centromere pattern-positive patients tended to show higher Total Sharp Score in spite of lower frequencies of RF in both cohorts.
**Conclusions:** Centromere pattern showed a specific distribution of levels among ANA. Centromere pattern-positive RA is a distinct subset with specific clinical features and complications. Centromere pattern is a possibly new risk factor of bone destruction in RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3857

## AB0231 HIGHER PEAK DISEASE ACTIVITY WAS IMPLICATED AS A RISK FACTOR IN THE DEVELOPMENT OF VERTICAL SUBLUXATION IN RA PATIENTS

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**Background:** Instability of the upper cervical spine is common in patients with rheumatoid arthritis (RA) and can lead to sudden death in worst case scenarios.
**Objectives:** The aim of this study was to evaluate the relationship between upper cervical spine instability and clinical factors, especially focusing on disease activity of RA.
**Methods:** The study included patients who had been enrolled in the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort study within two years from the onset of RA symptoms and who had cervical spine radiographs taken as part of the preoperative testing for elective joint surgery (e.g. joint replacement surgery) at the institute between April 2010 and March 2013. The anterior atlantodental interval (ADI) and Redlund-Johnell (R-J) values were measured to diagnose atlantoaxial subluxation (AAS) and vertical subluxation (VS), respectively. We obtained clinical data from the IORRA cohort study collecting various clinical data biannually, starting in October 2000.
**Results:** Finally, the current study included 56 patients. Nearly half of the patients had AAS (27 patients, 48.2%) and 12 patients (21.4%) had VS. In total, 59.6% of the patients had upper cervical instability. There was no significant correlation between the ADI and R-J values ($\rho$= -0.025; P=0.8). Multiple linear regression analysis revealed the maximum Disease Activity Score in 28 joints (DAS28) during the study period and height were significantly related to R-J values. No variable was significantly associated with the ADI. Univariate logistic regression analyses indicated only the maximum DAS28 during the study period was significantly associated with developing VS, and no variables were shown to be significant in relation to the development of AAS. Median (IQR) values for the maximum DAS28 during the study period in patients with and without VS were 6.1 (5.0 to 6.6) and 5.1 (4.6 to 5.5), respectively. The area under the ROC curve (AUC) showed the predictions using the maximum DAS28 (cutoff = 5.56, specificity = 79.1%, sensitivity = 69.2%, and AUC =0.714) were moderately accurate (Figure 1).

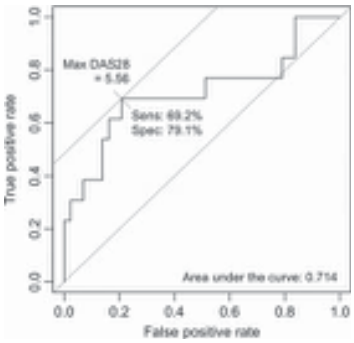


Figure 1

**Conclusions:** Higher peak disease activity was implicated as a risk factor in the development of VS in RA patients. We suggest that tight control of disease activity is desirable to reduce the risk of VS.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1040

## AB0232 NEUROPATHIC PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

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**Background:** Rheumatoid arthritis (RA) pain is traditionally attributed to peripheral inflammation of the joints. However, pain control is often inadequate, even when inflammation appears to be well controlled. This suggests that neuropathic pain (NP) may also be present in patients with RA.
**Objectives:** The objective of this study was to examine NP symptoms and associated factors in patients with RA.
**Methods:** Patients with RA according to ACR 1987 or ACR/EULAR 2010 classification criteria were included in this cross-sectional study. Demographic data and RA characteristics were collected. Pain was measured using a visual analogue scale (VAS). Disease activity was assessed by the Disease Activity Score (DAS 28). Functional disability was evaluated by the Health Assessment Questionnaire (HAQ). Joint destruction was assessed by the Van der Heijde-modified Sharp Score. NP symptoms were assessed using the DN4 questionnaire. Data analysis was carried out using the SPSS 20 Software. $p<0.05$ was considered statistically significant.
**Results:** Eighty-four patients with a mean±SD age of 50.6 ±12.29 years were enrolled. Eighty-nine per cent were female. Mean±SD duration of symptoms was 11.24±8.91 years. Thirty one per cent had NP and 96.2% of them were taking steroids. In the NP group, means±SD of VAS pain, DAS28, HAQ, sharp score were 3.85±2.73, 3.21±2.21, 1.00±0.95 and 63.27±43.52 respectively. NP patients did not significantly differ from those with no NP symptoms in terms of age, disease duration, disease activity, VAS pain, functional disability and joint destruction. The regression analysis showed that there was no significant correlation between NP and the RA parameters.
**Conclusions:** The prevalence of NP was 31% in our RA population. It is important to consider the existence of NP in the assessment and treatment of RA pain. However, larger studies are needed to investigate factors associated with NP in RA patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5049

## AB0233 ANTERIOR ATLANTOAXIAL SUBLUXATION IN RHEUMATOID ARTHRITIS: PREVALENCE AND PREDICTIVE FACTORS

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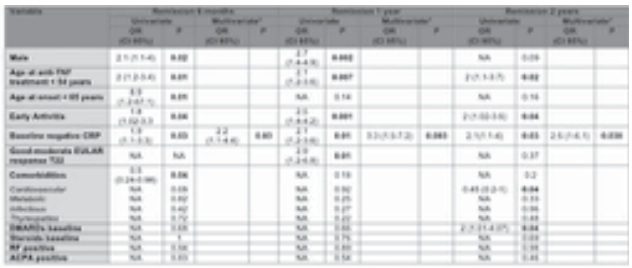
**Background:** Cervical spine involvement is common and potentially severe in patients with Rheumatoid Arthritis (RA). The most common abnormality is anterior Atlanto Axial Subluxation (aAAS), which has been reported in 19–70% of patients.
**Objectives:** The aim of this study was to determinate the prevalence of aAAS by plain radiographs and to assess its predictive factors.
**Methods:** A cross-sectional study was carried out with RA patients diagnosed according to ACR 1987 or ACR/EULAR 2010 classification criteria. Demographic characteristics and features of disease were collected. Pain was measured using a visual analogue scale (VAS). RA activity was assessed by the Disease Activity Score (DAS 28). Functional disability was evaluated by the Health Assessment Questionnaire (HAQ). Joint destruction was assessed by the van der Heijde-modified Sharp Score. aAAS was assessed on lateral radiographs taken in flexion. The diagnosis was based on an anterior atlantodental interval (AADI) greater than 4 mm. Data analysis was carried out using the SPSS 20 Software. $p<0.05$ was considered statistically significant.
**Results:** One hundred and sixteen patients with a mean±SD age of 49.07±13.23 years were recruited. Eighty-five per cent were female. Mean±SD duration of symptoms was 11.3±9.30 years. The diagnosis of aAAS was made in 11 (9.5%) of cases. RA patients with aAAS had longer disease duration, higher Sharp scores, and higher functional disability. On regression analysis, significant predictors of aAAS were disease duration ($p=0.008$), joint destruction ($p=0.002$), functional disability ($p=0.028$) and presence of coxitis ($p=0.038$). The multivariate analysis showed that structural damage was a predictive factor of aAAS ($p=0.007$ OR: 1.02, 95% CI 1.006–1.035) adjusted to functional disability and presence of coxitis.
**Conclusions:** The prevalence of aAAS was 9.5% in our RA population. Larger studies are required to identify the profile of RA patients at high risk of cervical spine involvement.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5064

## AB0234 PREDICTIVE RISK FACTORS OF REMISSION AND LOW-DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ANTI-TNF DRUGS IN REAL PRACTICE: RESULTS FROM A SINGLE CENTRE

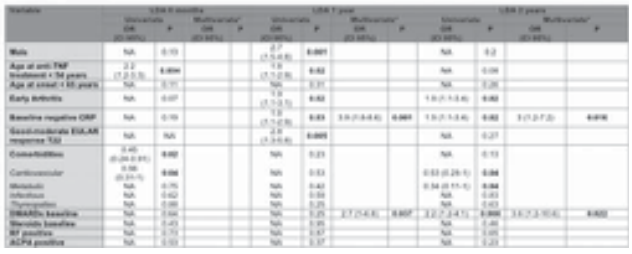
P. Conigliaro, M. Tonelli, P. Triggianese, M.S. Chimenti, F. Sunzino, R. Perricone.
*Rheumatology, Allergology and Clinical Immunology, University of Rome Tor Vergata, Rome, Italy*

**Background:** The goals of treatment in Rheumatoid Arthritis (RA) are remission and low disease activity (LDA); therefore, it is important to identify reliable predictive factors of these targets so that treatment can be tailored.
**Objectives:** We aimed at identifying positive and negative predictive factors of remission and LDA in RA patients treated in real practice with first line anti-TNF drugs.
**Methods:** Retrospective analysis of DAS28 remission/LDA in 308 RA patients treated for two years with first line anti-TNF drugs from January 2008 to December 2014: [female n=251 (81.5%), age 55±13 years, disease duration 7.6±8.4 years, rheumatoid factor (RF, n=220 (71.4%)), anti-citrullinated antibodies (ACPA, n=214 (69.5%)), baseline C-reactive protein (CRP, 11.4±16.5 (mg/L)), baseline DMARDs (n=225 (73.1%)), baseline steroid (n=160 (51.9%)), Adalimumab (n=109 (35.4%)), Etanercept (n=177 (57.5%)), other anti-TNF (n=22 (7.1%))]. Predictive factors considered for achievement of remission and LDA were: gender, age at the time of anti-TNF treatment (cut-off >54 yrs old, n=139 (45.1%)), age at onset >65 yrs old (n=27 (8.8%)), early arthritis (n=99 (32.1%)), baseline negative CRP (n=150 (48.7%), RF/ACPA positivity, good/moderate EULAR response at 6 months (n=169 (54.9%)), presence of any comorbidity (n=210 (68.2%)), cardiovascular comorbidity (n=83 (26.9%)), metabolic syndrome (n=26 (8.4%)), infectious (n=49 (15.9%)), thyreopathies (n=64 (20.8%)), concomitant DMARDs/steroid treatment. Intention to treat, ROC-curve, univariate and multivariate analysis by logistic regression were performed. Selection of the variables to be included in the multivariate analysis was performed on the basis of their statistical significance in the univariate analysis.
**Results:** In the univariate analysis positive predictors of remission and LDA at 6 months, 1 year and 2 years of anti-TNF treatments were identified as follows (Figure 1A): male gender, age at the time of anti-TNF treatment <54 yrs old, age at onset <65 yrs old, early arthritis, baseline negative CRP levels, good/moderate EULAR response at 6 months and concomitant DMARDs treatment. Negative predictors were presence of any comorbidity, cardiovascular comorbidity and metabolic syndrome. In the multivariate analysis the only significant positive predictor of remission and LDA at 6 months, 1 and 2 years of treatment was the negative CRP levels at baseline (Figure 1B).

A



B



**Conclusions:** Negative CRP levels prior to commence anti-TNF treatments in RA patients appeared to be a reliable predictor of remission and LDA in clinical practice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3629

## AB0235 EFFECT OF TOCILIZUMAB COMBINED WITH METHOTREXATE ON BLOOD-BASED NEOEPITOPE BIOMARKERS IN THE RADIATE STUDY

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease with elevated extracellular matrix (ECM) turnover. It is important to determine the efficacy of a therapy quickly to ensure that patients are given the right treatment. Biomarkers of ECM turnover could be such possible biomarkers. Matrix metalloproteinase degraded fragments of type III and IV collagen and C-reactive protein (C3M, C4M and CRPM) have previously found to be dose-dependently inhibited to tocilizumab (TCZ) and could identify ACR50 responders.
**Objectives:** 1) Confirm that TCZ have a dose dependent effect on the circulating biomarkers C3M, C4M, and CRPM and 2) investigate if these biomarkers are associated with disease activity and pain in RA patients undergoing TCZ treatment.
**Methods:** RA patients (n=217) fulfilling the American College of Rheumatology (ACR) criteria were included from a phase III randomized controlled trial (RADIATE). Patients received either TCZ+MTX (4mg/kg; TCZ4 or 8mg/kg; TCZ8) or placebo+MTX (PBO) every 4 weeks. C3M, C4M and CRPM were assessed in serum at baseline (BL) and week 16. Difference of a biomarker level over time was tested by paired t-test. Difference between the treatment groups was examined by one-way ANOVA. Correlation between biomarkers and clinical observations was investigated with Spearman's correlation. Bonferroni correction was used to find the critical p-value<0.0071 for correlations.
**Results:** C3M significantly decreased (p=0.027) at week 16 compared to BL for TCZ8. TCZ8 and TCZ4 was decreased in both C4M (p=0.0001) and CRPM (p<0.0001) at week 16 compared to BL. A dose dependent decrease was observed for C4M and CRP as the difference between TCZ8 and TCZ4 (p=0.031 and p=0.02), TCZ8 and PBO (p<0.0001 and p<0.0001), and TCZ4 and PBO (p=0.002 and p=0.004)Changes to week 16 in the biomarker levels of all patients were found to correlate with the changes in HAQ-QI (C3M: ρ=0.26, C4M: ρ=0.33, CRPM: ρ=0.33), DAS28 (C3M: ρ=0.36, C4M: ρ=0.38, CRPM: ρ=0.39), VAS pain (C3M: ρ=0.32, C4M: ρ=0.35, CRPM: ρ=0.32), CRP (C3M: ρ=0.5, C4M: ρ=0.55, CRPM: ρ=0.55) and ESR (C3M: ρ=0.51, C4M: ρ=0.54, CRPM: ρ=0.58). The CRPM BL level correlated negatively with the changes in HAQ-QI (ρ=-0.21). C3M, C4M and CRPM BL levels correlated negatively with changes to week 16 in VAS pain (C3M: ρ=-0.23, C4M: ρ=-0.28, CRPM: ρ=-0.26), CRP (C3M: ρ=-0.29, C4M: ρ=-0.36, CRPM: ρ=-0.34) and ESR (C3M: ρ=-0.17, C4M: ρ=-0.23, CRPM: ρ=-0.27).
The changes in C4M and CRPM levels were significantly higher in ACR20 and ACR50 responders (C4M: p=0.011 and p=0.009, respectively and CRPM: p=0.004 and p=0.025, respectively) compared to non-responders.

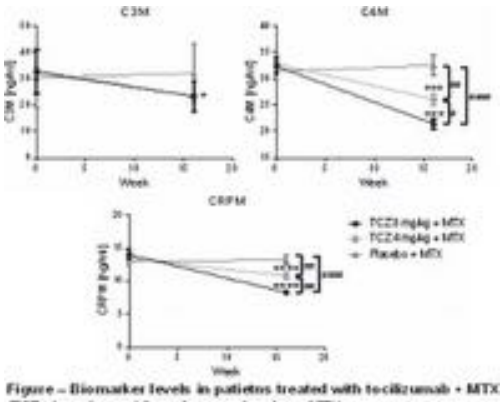



**Figure – Biomarker levels in patients treated with tocilizumab + MTX (TCZ: 4 mg/kg and 8 mg/kg, or placebo + MTX.**

**Conclusions:** C4M and CRPM decreased in a dose dependent manner in response to TCZ, while C3M was significantly reduced by TCZ8. Changes to week 16 in C3M, C4M and CRPM levels correlated with changes in disease activity and VAS pain. These findings support that ECM biomarkers are predictive biomarkers of treatment benefit. This was furthermore supported by the finding that there were difference between ACR20 and ACR50 responders in C4M and CRPM levels. Overall, these data confirm that ECM biomarkers are applicable as predictive tools in RA.
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[1] A.C. Bay-Jensen et al. SAR 43 (2014) 470–478
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4008

## AB0236 THE ROLE OF VITAMIN D RECEPTOR IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a disease characterized by chronic inflammation of synovial tissue, and progressive destruction of the joints. In RA patients a high prevalence of serum vitamin D deficiency/insufficiency was described. Vitamin D has a central role in the immune system and also correlates with increased levels of estrogen receptor α.
**Objectives:** The study analyzed the relationships between polymorphisms in the gene for vitamin D receptor (VDR) and the development and/or progression of the disease.

**Methods:** A total of 156 patients were enrolled with a diagnosis of RA (median age 55.6 years; 78% of them women; control group of 50 subjects). Development of the disease was scored by positive antibodies against cyclic citrullinated peptide (anti-CCP), rheumatoid factor (RF), CRP. Disease progression was assessed by the modified Sharp-van der Heijdeovou method Total Sharp Score (TSS). Polymorphisms were detected by PCR and subsequent restriction analysis (rs4516035 EcoRV; rs7975232: ApaI; rs731236: TaqI).
**Results:** The results show the relation of polymorphism VDR rs4516035 to seropositivity for anti-CCP in the distribution of genotypes (P=0.03), with a higher prevalence of the TT genotype when compared to the CC + CT variants (p=0.007, OR =3.2). The relationship was found also in the frequency of alleles (p=0.04). Further, a borderline relationship of this polymorphism to RF IgA levels (P=0.06) was detected. A relationship of polymorphism VDR rs731236 with the disease progression evaluated by TSS (p=0.02) was demonstrated, with the highest TSS in the patients carrying the GG variant.
**Conclusions:** The results show that the GG variant of VDR rs731236 polymorphism was associated with a worse prognosis of RA. Moreover, the VDR rs4516035 polymorphism was related to the seropositivity for anti-CCP, with a significant prevalence of TT genotype in positive RA patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3836

## AB0237 GRADATION OF CHANGES IN AXIAL AND PERIPHERAL SKELETON WITH RESPECT TO THE AGE AT RHEUMATOID ARTHRITIS (RA) ONSET

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**Background:** Patient's age at RA onset predefines the course of the disease, rate of progression and severity of erosive-destructive changes in hand and feet joints, mineral bone density (BMD) and deformities of the spine vertebrae.
**Objectives:** To compare the changes in axial and peripheral skeleton in pts in relation to the age of RA onset.
**Methods:** 164 females with RA aged 20 -65 y. were included. Mean age was 47,9±12,9 y., RA duration - 12,1±9,3 y. Genant semiqiantitative radiographic morphometry of lumbar and thoracic spine was obtained for all patients, erosive and destructive changes assessed using Sharp/van der Heijde scoring system. BMD was measured at lumbar spine level (L1–4), femoral neck (FM) and distal forearm (DF) of a non-dominant arm using Hologic "Discovery A" system. Data analysis was made with Statistica 6.0 software.
**Results:** All pts were grouped into 3 arms depending on the age at RA onset: Group 1 – 63 (38,4%) pts, whose age at RA onset was $\geq$18 $\leq$30 y., Group 2 – 78 (47,6%) pts, $\geq$31 $\leq$50 y. age at RA onset, Group 3 – 23 (14,0%) pts, $\geq$51 y. age at RA onset. Mean age of pts from Group 1 was 37,8±12,7 y, Group 2 – 51,9±7,8 y., Group 3 – 62,1 ±2,6 y ($p<0.05$), disease duration - 15,1±12,3 y., 11,0±6,6 y., and 7,1±3,1 y., respectively ($p<0.05$). Menopause was established in 30% of pts in Group 1, in 60% - in Group 2, in 100% - in Group 3; peripheral fractures in past medical history were documented in 19 (30%), 28 (36%), and 11 (49%) pts from Groups 1, 2, and 3, respectively ($p>0.05$), 50% of fractures occurred before RA onset. The groups were comparable in terms of the number of RF-positive pts, receiving DMARDs, the duration and cumulative dose of GCs. DAS28 RA activity score, the number of pts with extra-articular RA manifestations and the number of pts taking GCs by the moment of examination were less in Group 1vs Group 2 ($p<0.05$). Lumbar vertebral deformity scores (VDS), BMD values of L1–4, FN, DF, narrowed joint spaces and total Sharp score were comparable in all groups (p>0,05). Number of erosions in Group 1 was 46,3±59,7 scores, in Group 2 - 30,8±38,5 scores, in Group 3 - 19,3±27,4 scores (Groups 1 and 3 $p<0,05$). Vertebral deformities were found in 19% pts from Groups 1 and 2, and in 39% pts from Group 3 (Groups 2–3 $p<0,05$). Thoracic VDS was 0,78±0,08, 0,78±0,07 and 0,73±0,13, respectively (Groups 3 and 1; 3 and 2 $p<0,05$).
**Conclusions:** RA onset during attainment of peak bone mass and long lasting disease produced negative effect on axial and peripheral skeleton. Despite young age and absence of menopause the majority of pts presented with OP, peripheral fractures, BMD in all skeletal sites, and lumbar VDS values that were comparable to those in pts with later onset of the disease. Pts with RA onset after menopause and shorter duration of the disease present with equal to pts with early onset degree of joint space narrowing and total Sharp score, but not with similar number of erosions. Early onset of RA and therefore longer duration of disease is associated with more amount of erosions.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3145

## AB0238 THE PERFORMANCE OF A SINGLE CENTRE INTERVENTIONAL CLINIC IN EARLY RHEUMATOID ARTHRITIS

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**Background:** In early rheumatoid arthritis (RA), first assessment by a rheumatologist and/or initiation of disease-modifying anti-rheumatic drugs (DMARD) within 12 weeks of symptom onset are associated with a significant benefit in long-term disease outcome.[1,2]
**Objectives:** To determine the proportion of patients with newly diagnosed RA in whom first rheumatology assessment and/or initiation of DMARD therapy was within the desired time frame.
**Methods:** A retrospective chart review of adult patients diagnosed with RA during year 2014 and the first half of year 2015 was performed at our rheumatology department, which is a part of an integrated secondary/tertiary teaching hospital that provides rheumatology services for a population of more than 500.000 residents. Potential cases were identified by searching the electronic medical records for ICD-10 codes M05.* and M06.* Electronic and paper records of patients were then thoroughly reviewed. Dates were recorded for onset of inflammatory joint symptoms, referral to rheumatologist, initial assessment by a rheumatologist and initiation of DMARD therapy. The percentage of patients assessed by a rheumatologist and/or treated with a DMARD within 12 weeks of symptom onset and the median times for delay were then calculated.
**Results:** Between 01.01.2014 and 30.06.2015, 188 new cases of RA were identified at our Department of Rheumatology. Of those, 153 (81.4%) were referred to our early interventional clinic. Within 12 weeks of symptom onset, 89 (47.3%) new RA patients were examined by a rheumatologist and 68 (36.2%) were started on DMARD therapy; the median time from symptom onset to consultation was 12.8 (IQR 4.9–27.7) weeks, median time from referral to consultation was 1 (IQR 1–3) day and median DMARD treatment delay was 16.1 (IQR 8.6–32.8) weeks.

Table 1. Demographic data, clinical history, and delays

| | |
|---|---|
| Gender (female/male) (%) | 143/45 (76/24) |
| Age, years (mean ± SD) | 62.4±15.4 |
| DAS28 3v (mean ± SD) | 5.3±1.3 |
| Patients fulfilling 2010 ACR/EULAR classification criteria for RA, # (%) | 177 (94.1) |
| Time from symptom onset to first rheumatologist assessment, weeks (median) | 12.8 (IQR, 4.9–27.7) |
| Time from referral to first rheumatologist assessment, weeks (median) | 0.14 (IQR, 0.14–0.43) |
| Time from symptom onset to glucocorticoid initiation, weeks (median) | 13.0 (IQR, 5.8–27.2) |
| Time from symptom onset to DMARD initiation, weeks (median) | 16.1 (IQR, 8.6–32.8) |

Legend: SD: standard deviation, IQR: interquartile range.

**Conclusions:** 47% of new RA patients were assessed by a rheumatologist and 36% were treated with a DMARD within the recommended time frame of 12 weeks. Most of the treatment delay was due to the time elapsed between symptom onset and referral to a rheumatologist. These results substantiate the efficacy of our early interventional clinic in diagnosing and treating patients with early RA: despite the heavily protracted nationwide waiting times for first rheumatologist assessment and significantly (40%) lower number of rheumatologists per capita compared to European Union average, the percentage of timely treated patients was comparable to recent reports.
**References:**
[1] Van der Linden MPM, et al. Arthritis Rheum, 2010;62(12):3537–3546.
[2] Raza K, et al. Ann Rheum Dis, 2011;(70)10:1822–1825 [MT1].
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1679

## AB0239 ASSOCIATION OF A TRAF1 GENE POLYMORPHISM WITH JOINT DESTRUCTION IN ANTI-CITRULLINATED PEPTIDE ANTIBODY-NEGATIVE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Many studies show that heritability plays a part in joint destruction in rheumatoid arthritis (RA); however, the details are poorly understood. In the recent report by van Steenbergen et al., 43 polymorphism in a 66 Kb region spanning tumor necrosis factor receptor-associated factor 1 (*TRAF1*) were associated with radiographic progression in anti-citrullinated peptide antibody (ACPA)-negative patients with RA in a multicohort study from Europe and North America. Specially, the polymorphisms were located in the area downstream of the complement component 5 (*C5*)-*TRAF1* region and upstream to the *TRAF1*-PHD finger protein 19 (*PHF19*) region. We were intrigued by these findings and curious to know the relevance in Asian populations. Thus, we investigated the association of the 66 Kb region within *C5-TRAF1-PHF19* with progression of joint destruction in Japanese patients with RA.
**Objectives:** The purpose of this study was to identify genetic variants associated with progression of joint destruction in Japanese ACPA-negative patients with RA.
**Methods:** We studied 120 ACPA-negative patients with RA for whom Sharp/van der Heijde scores (SHS) of the hands were available at 5-year disease duration. DNA samples of the subjects were obtained from the Institute of Rheumatology Rheumatoid Arthritis cohort study (IORRA) DNA collection. All of the patients consented to participate in this study in accordance with the process approved by the Tokyo Women's Medical University Genome Ethics Committee. Identification of tag single nucleotide polymorphisms (SNPs) in the *C5-TRAF1-PHF19* region

was performed using Haploview (version 4.2; minor allele frequency >0.05, pairwise $r^2$>0.8). A total of 12 tag SNPs were selected and genotyped. We used rs2900180 as a proxy for rs7021880 ($r^2$=1.0), which was the polymorphism with the lowest *P*-value found by van Steenbergen et al. Linear regression analyses were performed to examine the association between each SNP and log-transformed SHS.

**Results:** The A allele of rs3761847 in *TRAF1* was significantly associated with SHS in the recessive model (*P*=0.00099, Table 1). The other SNPs had no association with SHS.

Table 1. Association of each SNP with Sharp/van der Heijde scores of hands in the first 5 years after onset of ACPA-negative RA.

| SNP | Tested model | Allele (minor/major) | MAF (in CEU*) | β | SE | *P*-value |
|---|---|---|---|---|---|---|
| rs933003 | Additive | A/G | 0.36 | 0.03 | 0.092 | 0.78 |
| | Recessive | | (0.05) | -0.12 | 0.092 | 0.21 |
| rs1837 | Additive | T/C | 0.47 | 0.04 | 0.092 | 0.70 |
| | Recessive | | (0.31) | 0.02 | 0.092 | 0.80 |
| rs1056567 | Additive | T/C | 0.40 | 0.03 | 0.094 | 0.72 |
| | Recessive | | (0.37) | 0.06 | 0.094 | 0.53 |
| rs10818477 | Additive | G/T | 0.29 | -0.04 | 0.094 | 0.68 |
| | Recessive | | (0.06) | -0.13 | 0.093 | 0.18 |
| rs6478488 | Additive | T/C | 0.21 | -0.18 | 0.091 | 0.056 |
| | Recessive | | (0.01) | -0.13 | 0.092 | 0.16 |
| rs2301334 | Additive | T/G | 0.26 | 0.02 | 0.092 | 0.82 |
| | Recessive | | (NA) | 0.11 | 0.092 | 0.22 |
| rs3761847 | Additive | G/A | 0.51 | -0.22 | 0.090 | 0.018 |
| | Recessive | | (0.48) | -0.30 | 0.088 | 0.00099 |
| rs2900180 | Additive | T/C | 0.30 | -0.05 | 0.093 | 0.58 |
| | Recessive | | (0.39) | -0.11 | 0.092 | 0.24 |
| rs12004487 | Additive | C/T | 0.20 | -0.11 | 0.093 | 0.25 |
| | Recessive | | (0.10) | -0.08 | 0.093 | 0.37 |
| rs7026551 | Additive | C/A | 0.17 | -0.09 | 0.093 | 0.32 |
| | Recessive | | (0.22) | -0.03 | 0.093 | 0.75 |
| rs7037673 | Additive | T/C | 0.47 | -0.11 | 0.092 | 0.23 |
| | Recessive | | (0.38) | -0.17 | 0.091 | 0.064 |
| rs4837805 | Additive | G/A | 0.31 | -0.08 | 0.093 | 0.41 |
| | Recessive | | (0.40) | -0.05 | 0.093 | 0.58 |

*MAF in CEU was based on HapMap-CEU phase 3.
MAF, minor allele frequency; CEU, Utah residents with ancestry from Northern and Western Europe; SE, standard error; NA, not applicable.

**Conclusions:** Our study demonstrated that the A allele of rs3761847 in the *TRAF1* gene was associated with joint destruction. We previously reported that the same allele was associated with an increased risk for development of RA in the Japanese population. Although the association between rs2900180 and joint destruction in RA patients was not validated in our study, we show that an association between *TRAF1* locus and joint destruction might exist in Japanese ACPA-negative patients. Our results contribute to the understanding of the pathogenesis of RA, especially in ACPA-negative patients.

**References:**

[1] van Steenbergen HW, Rodriguez-Rodriguez L, Berglin E, Zhernakova A, Knevel R, Ivorra-Cortes J, et al. A genetic study on C5-TRAF1 and progression of joint damage in rheumatoid arthritis. Arthritis Res Ther. 2015;17:1.

**Acknowledgement:** We thank all DNA donors for making this study possible. We appreciate the members of Institute of Rheumatology, Tokyo Women's Medical University for their effort on the IORRA cohort. We are also grateful to Ms Kaori Arai for her technical assistance.

**Disclosure of Interest:** None declared

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## AB0240 MMP-3 AS A BIOMARKER OF DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS

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**Background:** Measurement of serum MMP-3 levels has been considered useful to estimate the disease activity of rheumatoid arthritis (RA). We have shown that serum MMP-3 was significantly correlated with DAS28 (CRP) and could be a useful marker in predicting joint destruction[1,2]. CXCL13 attracts CXCR5-expressing B and helper T cells to the follicle and probably has central roles of ongoing immune activation in RA development[3]. Serum MMP-3 and CXCL13 have been reported as biomarkers for detecting the disease activity and predicting the therapeutic outcomes of RA[4].

**Objectives:** The aim of this study is to confirm the clinical significance of serum MMP-3 and CXCL13 measurement in the evaluation of disease activity and prediction of therapeutic outcome in RA patients treated with biologics.

**Methods:** Serum MMP-3 was serially measured by MMP-3 Latex kit (Sekisui Medical Co.) for 146 RA patients before and after treatment with biologics. Number of patients treated with each biologic were 39, 28, 19, 17, 26, and 17 patients treated with abatacept, adalimumab (ADA), etanercept, golimumab, infliximab (IFX), and tocilizumab, respectively. CXCL13 was measured by ELISA kit (Quantikine human CXCL13, R&D systems) for patients treated with ADA and IFX before and 24 weeks after treatment. The patients were classified into 61 responders (good) and 85 non-responders (moderate and none) by ACR/EULAR definition of remission criteria weeks after treatment.

**Results:** Serum MMP-3 before the treatment was significantly increased in 146 RA patients as compared with 196 healthy subjects (196.0± 197.4 vs 58.6±27.4 ng/ml, p<0.001), and showed significant positive correlation with DAS28 (Rs=0.3842, p<0.001), but no significant difference was found between 61 responders (210.6±213 ng/ml) and 85 non-responders (185.6±186.3 ng/ml). As shown in Figure 1 (left), the MMP-3 levels gradually decreased 4, 12, and 24 weeks after successful treatment with biologics (p=0.04, p<0.001, and p<0.0001, respectively), and extent of the decrease were significantly bigger in responders than non-responders 12 and 24 weeks after treatment. Serum CXCL13 level before the treatment significantly correlated with MMP-3 levels (Rs =0.4648, p<0.001) as well as DAS28 (Rs =0.5182, p<0.001). After treatment with ADA, serum CXCL13 was significantly decreased after 24 weeks in responders as compared with non-responders (Figure 1 right, p<0.05). However, such difference was not found in patients treated with IFX. Patients with lower serum CXCL13 levels (<82.7 pg/ml) before the treatment were shown to become non-responders (p<0.07), especially their serum MMP-3 levels were low (<69.1 ng/ml).

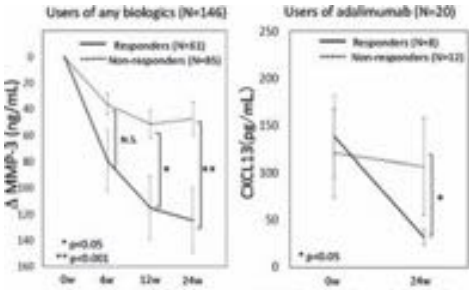



Figure 1. Time course of serum MMP-3 levels and CXCL13

**Conclusions:** Serum MMP-3 and CXCL13 was shown to be useful as disease activity markers, and serial measurement were helpful to evaluate the effect of treatments with biologics. CXCL13 may be useful in evaluating and predicting the therapeutic outcome of some kinds of biologics.

**References:**

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**Disclosure of Interest:** S. Kumagai Consultant for: Sysmex Co, Y. Uemura: None declared, T. Saito: None declared, R. UMEDA: None declared, A. Muta: None declared, M. Izumi: None declared, K. Abe: None declared, S. Sendo: None declared, G. Tsuji: None declared

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## AB0241 PLASMA MICRO-RNAS POTENTIALLY ASSOCIATED WITH THE INCREASE RISK FOR CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) patients are at increased risk for cardiovascular diseases and an accelerated atherogenesis is considered the cause of this increase. MicroRNAs (miRs) are small, non-coding RNA molecules which negatively regulate gene expression. Plasmatic miRs have been identified as biomarkers in a wide range of cardiovascular diseases (CVD).

**Objectives:** To identify plasmatic miRs in RA patients that can facilitate earlier diagnosis of CVD and provide insight regarding the increase risk for CVD in these patients.

**Methods:** We compared plasmatic profiles of 754 miRs in 7 RA patients without CVD, in 7 patients with acute myocardial infarction (AMI) but without RA, and in 7 healthy controls with the objective to find miRs commonly expressed in the two groups of patients but at different levels from the controls. All participants were male and were matched for age and for classical cardiovascular risk factors. Plasma profile of miRs were analyzed by real time PCR using validated TaqMan® OpenArray® MicroRNA panels which enables the quantification of 754 human miRNAs. Differential expression was analyzed with Expression Suite software. Selected miRs were further analyzed with $2^{-DDct}$ method. Kruskal-Wallis test and Dunns post- test were used for the statistical analyses.

**Results:** We were able to measure in the three groups, 50% (379) of the

miRs represented in the array. Plasma profile of circulating miRs in RA and AMI patients were different from the controls. Plasma miRs that were commonly expressed in AR and AMI and expressed significantly different versus controls were: mir-Let-7a, miR-96, miR-381, miR-451, miR-518d, miR-425–5p, miR-572, miR-190b, miR-708, and miR1180. Interestingly, all 10 miRs were down-regulated compared with controls. Furthermore, 9 miRs were differentially expressed in AMI patients versus controls and 16 miRs in RA patients versus controls.
**Conclusions:** In the present study we have identified a group of 10 miRs that potentially can be involved in the increase risk for CVD seen in RA patients. Among all these miRs, miR-451 and Let-7a have been previously associated with CVD and it might be the best candidates for future validation studies.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2518

## AB0242 IL6 GENETIC VARIANTS AND IGA-RF AS MARKERS OF EROSIVENESS AT ONSET IN EARLY RHEUMATOID ARTHRITIS

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**Objectives:** To determine whether genetic variants in the loci of interleukin-6 (IL-6) are associated with clinical and biologic phenotypes of Rheumatoid Arthritis (RA).
**Methods:** Three hundred and forty five early RA (ERA) patients were enrolled in this study (76.2% female; mean age: 54.4±14.1 years; 33.6% VERA). 239 patients (69.3%) were seropositive for at least one antibody: 62.9% ACPA, 48.7% RF -IgM and 33.0% RF-IgA positive, respectively. At diagnosis, 101 subjects (29.3%) had detectable erosions in hands and feet radiographs. All patients were treated according to a tight control strategy (Methotrexate for 3 months, and if an incomplete response was reached after 3 months a combination with Tumor Necrosis Factor (TNF) blockers was started) and at each visit, clinical remission was evaluated according to ACR/EULAR criteria (Felson DT et al. Arthritis Rheum 2011). ERA patients were genotyped for IL6–174G/C polymorphism by PCR and compared with a cohort of healthy subjects (n=293).
**Results:** The frequency of C allele of the IL-6–174G/C SNP was higher in ERA patients (30.7%) compared to healthy controls [23.7%; OR (95%CIs): 1.43 (1.11–1.83)], while the GG genotype was present in 49.6% of ERA and in 59.4% of control subjects [OR (95%CIs): 0.67 (0.49–0.92)] respectively. At baseline, ERA patients carriers of the GG genotype were more likely seropositive compared to patients carrying the C allele [74.9% vs 63.8%, p=0.03], mainly for the IgA-RF positivity [38.6% vs 27.7%; OR (95%CIs): 1.64 (1.04–2.57)]. At diagnosis, IgA-RF positive ERA patients were more likely erosive than IgA-RF negative ones [33.1% vs 25.2%; OR (95%CIs):1.80 (1.11–2.95)]. Conversely, radiographic damage was not associated with gender, symptoms duration, smoking habit, positivity for ACPA or IgM-RF antibodies and disease activity. The percentage of erosive disease increased to 39.6% in ERA patients IgA-RF + carrying the GG genotype compared to the others (24.7%; OR (95%CIs): 2.002 (1.23–3.26)], with a lower presence of radiographic damage in carriers of C allele and IgA-RF negative (12.5%). Finally, patients carrying C allele of IL6–174G/C SNP and IgA- RF negative at diagnosis, were less prone to develop erosions over time than subjects with at least one risk factor (8.0% vs 19.1%, respectively, p=0.02).
**Conclusions:** In our cohort of ERA patients, the presence of C allele of IL6–174G/C SNP associates with RA susceptibility whereas the GG genotype associates with seropositivity for IgA-RF and erosions. These data add new information about the biology underlying the development of radiographic damage in the early phases of RA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4629

## AB0243 THE IMPORTANCE OF BIOMARKERS (RF, ACPA AND MMP-3) SERUM LEVELS OF RHEUMATOID ARTHRITIS (RA) IN PREDICTION BONE EROSIONS IN PATIENTS WITH EARLY RA AND NO VISIBLE RADIOGRAPHIC STRUCTURAL DAMAGES-AN ECHOSONOGRAPHIC STUDY

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**Background:** Rheumatoid factor (RF) and autoantibodies against citrullinated peptides/proteins (ACPA) has been recognized as an important predictor of more severe structural joint damage. Baseline matrix metalloproteinases 3 (MMP-3) serum levels were described as a predictor for the development of joint erosions.Ultrasonography is more sensitive than X-ray in detecting erosions in RA.
**Objectives:** to assess the importance of the RF, ACPA and MMP-3 serum levels in prediction of hands and feet bone erosions, detected by ultrasound (US) examination, in patients with early rheumatoid arthritis, without structural damage visible on X-ray.
**Methods:** A group of 65 patients (56 female, mean age 53.8±14.6 yrs.) with early RA (Eular/ACR 2010 classification criteria) and ≤1 year duration, (mean duration 3.8 month), were enrolled in the cross sectional clinical study. All patients had been disease-modifying anti-rheumatic drug (DMARDs) and glicocorticoid therapy naïve and had no visible structural damage on hands and feet X-ray. The serological markers of RA were measured: RF (normal concentration<16 U/ml), ACPA (normal concentration<20 IU/ml) and total MMP-3 (normal cut-off range for females: 18–60 ng/ml and males: 24–120 ng/ml). The levels above normal were reted as positive. Ultrasound examination of both hand (wrist, MCP2, MCP5 joints) and MTP5 joints was performed by Esaote My Lab 70 machine using 18 MHz linear probe. Findings of bone erosion were determined according to OMERACT US group definition. Collected data were analyzed in SPSS 16 system.
**Results:** Joint bone erosions were found in 59 (90.8%) pts. by US examination. Forty-two (64.6%) pts. were RF positive (mean concentration 88.8±108.2). The mean 2.1 vs.1.6 US bone erosions were detected in RF positive in comparison to RF negative pts. respectively. Forty-six (70.7%) pts. were ACPA positive (mean concentration 467.0±454.4) with mean bone erosions 1.9 vs.1.8 bone erosions in ACPA negative pts. Forty-six out of 63 (73.0%) pts were MMP-3 positive (mean concentration 185.1±241.0) with mean bone erosions 2.1 vs.1.5 bone erosions in MMP-3 negative pts. The 0.500 value of the area under the ROC curve is found for RF, 0.443 for ACPA and 0.627 value for MMP-3. The 75.4% sensitivity, 67% specificity (cut of 99.2 ng/ml) of MMP-3, 71.9% sensitivity, 50% specificity (cut of 232 IU/ml) of ACPA and 66.7% sensitivity, 67% specificity (cut of 79.5 U/ml) of RF were established in predicting US bone erosion.
**Conclusions:** Early RA patients with no visible structural damages on X-ray, and increased RF, ACPA and MMP-3 serum levels had higher number of bone erosions assessed by US. Baseline MMP-3 serum levels had the highest sensitivity in predicting joint bone erosions assessed by ultrasound examination.
**Disclosure of Interest:** None declared
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## AB0244 MIR-155 EXPRESSION IN B CELLS OF RHEUMATOID ARTHRITIS PATIENTS IS RELATED TO FOLLICULAR SYNOVITIS AND MIRRORS B CELL SUBPOPULATIONS CHANGES AFTER IL-6R INHIBITOR TREATMENT

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**Background:** MicroRNA-155 (miR-155) was shown to be a key regulator of B cell biology. The fine-tuning of the transcription factor PU.1 by miR-155 is required for high-affinity IgG1 production and B cell maturation. However, the role of miR-155 in the activation of B cells in Rheumatoid Arthritis (RA) has not been explored.
**Objectives:** To investigate miR-155 expression in RA B cells and its association with B cell subpopulations distribution, synovial histological pattern and anti-IL6R treatment response.
**Methods:** 42 RA patients naive to treatment who underwent synovial tissue (ST) biopsy were enrolled and 30 RA no responder to MTX (MTX-IR) and 15 Osteoarthritis (OA) patients were used as comparison. Based on immunostaining for CD68, CD21, CD3 and CD20 cells, ST samples were categorized as diffuse or follicular pattern. CD19+ cells were isolated from peripheral blood (PB) and B cells subpopulations were assessed by FACS using IgD/CD27 classification. In 14 MTX-IR ERA patients starting TCZ (8 mg/kg), PB-derived CD19+ cells were tested for B cells subpopulations at baseline and after 3–6 and 12 months in association with miR-155 and PU.1 expression by qPCR. IL-6 receptor (IL6-R) was experimentally confirmed as miR-155 target by Luciferase assay. PB-derived CD19+ cells of HC were stimulated with IL-6 (20 pg/mL) and miR-155 expression was checked after 24–48 and 72h respectively.
**Results:** At study entry, naive RA and MTX-IR patients showed higher incidence of follicular synovitis than OA patients (p=0.001 and p=0.002 respectively). Moreover, RA patients with follicular synovitis were more likely ACPA positive (p=0.001) compared to patients with diffuse pattern. At baseline, PB derived B cells of RA patients were characterized by higher $IgD^{-}CD27^{-}$ cells (p=0.05) percentages compared to HC. Moreover, PB-derived CD19+ cells of RA patients with follicular synovitis showed an activated memory phenotype compared to patients with diffuse pattern (p=0.01). Finally, PB-derived CD19+ cells of naive and MTX-IR RA patients with follicular synovitis showed significantly higher expression of miR-155 compared to HC (p=0.001 and p=0.002 respectively) mainly in ACPA positive patients (p=0.001). During IL-6R inhibitor treatment, we found that $IgD^{-}CD27^{-}$ cells percentage significantly decreases after 12 months ($p<0.05$) follow-up compared to baseline. miR-155 expression in PB-derived CD19+ cells was significantly down-regulated after 3 (p=0.01), 6 (p=0.002) and 12 (p=0.001) months of TCZ treatment respectively. Conversely, PU.1 expression in PB-derived CD19+ cells was significantly up-regulated after 12 months (p=0.04) of TCZ treatment. Finally, miR-155 was found to be an inducible miR after IL-6 stimulation ($p<0.05$).
**Conclusions:** B-cells of naïve and MTX-IR RA patients with follicular synovitis show a memory phenotype and a high expression of miR-155 which is related with ACPA positivity. Moreover, miR-155 expression in PB-derived B cells of RA patients significantly decreases during IL-6R inhibitor treatment mirroring the

changes of B cell subpopulations distribution. Thus, miR-155 may represent a key regulator of B-cells in RA through IL-6 pathway.
**Disclosure of Interest:** None declared
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## AB0245 UNMET NEEDS AND BURDEN OF ILLNESS IN PATIENTS CURRENTLY RECEIVING BIOLOGIC TREATMENTS FOR RHEUMATOID ARTHRITIS: A COMPARISON OF PHYSICIAN PERCEPTION OF REMISSION AND DAS28-MEASURED REMISSION IN A REAL WORLD STUDY

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**Background:** Biologics have greatly improved the management of rheumatoid arthritis (RA), demonstrating efficacy and safety in alleviating symptoms, inhibiting bone erosion, and preventing loss of function.[1] The current study hypothesis was that despite significant improvement in patient (pt) outcomes since the introduction of biologics, significant unmet need and burden of illness remains.
**Objectives:** The main objective was to test our primary hypothesis. Secondary objectives were to explore patterns of physician use of disease activity measures and compare degree of reported unmet need as ascertained by subjective physician assessment and objective disease activity measures.
**Methods:** Descriptive analyses of the following outcomes were performed using ADELPHI RA Disease Specific Program (DSP) data for US and EU5 pts who had been receiving biologic therapy ≥3 months: remission based on DAS28 ESR (<2.6), physician-reported remission, disease severity, satisfaction with current control of pt's RA, and rating (100-point VAS) of pt's overall condition. Data were evaluated for the overall population receiving biologics and separately for pts receiving 1st- and 2nd-line biologics.
**Results:** After ≥3 months on biologics (n=1299), 56% of pts were in remission based on physician judgement, while 31% were in remission based on DAS28 ESR (<2.6; Table). Objective measures of disease activity were not calculated for 30% (389/1299) of pts overall (higher in the US, 63% [274/437] vs EU5, 13% [115/862]; $P<0.0001$). Physicians reported that 29% of pts had moderate to severe disease; 16% of pts had no improvement in disease severity or worsened with treatment; and 41% of pts taking biologics were in worse overall condition than the average (64.8 [100-pt VAS]) for all RA pts enrolled in the DSP (n=3379). 23% (304/1299) of physicians were dissatisfied with current control of the pt's RA on biologic treatment. Levels of unmet need were similar for 1st-line biologic pts relative to the overall group of biologic-treated pts and higher for 2nd-line biologic pts.

Table 1. Clinical outcomes for pts taking biologics

| Outcome, n (%) | Any biologic (n=1299) | 1st-line biologics (n=876) | 2nd-line biologics (n=403) |
|---|---|---|---|
| Remission | | | |
| Based on physician's assessment | 727 (56) | 539 (62) | 182 (45) |
| Based on DAS28[a,b] | 259 (31) | 181 (46) | 78 (37) |
| Additional physician's assessments | | | |
| Moderate to severe disease | 378 (29) | 218 (25) | 149 (37) |
| No improvement in RA severity with treatment | 204 (16) | 131 (15) | 66 (16) |
| Worse overall condition than DSP average | 530 (41) | 327 (37) | 191 (47) |

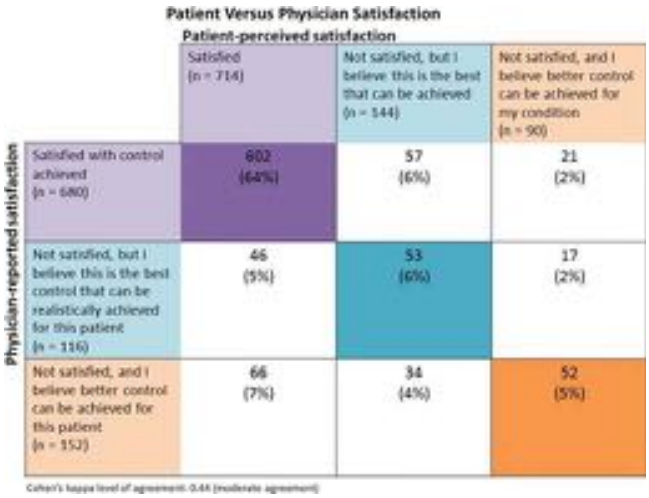
[a]Remission defined as DAS28 <2.6. [b]Any biologic, n=839; 1st-line, n=392; 2nd-line, n=210.

**Conclusions:** There are significant unmet needs among RA pts on biologic treatment, regardless of line of therapy, suggesting the need for biologics with novel mechanisms of action. Remission based on physician judgement appeared to be over-reported as compared to remission indicated by disease activity measure DAS28. Clinical disease activity measures were not used consistently by physicians. Future study is warranted to explore whether under-utilization of disease activity measures is associated with the discrepancy between physician subjective judgement and clinical measurement.
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[1] Smolen JS, et al. Ann Rheum Dis. 2014;73(3):492–509.
**Disclosure of Interest:** S. Peterson Shareholder of: Janssen, Employee of: Janssen, E. Sullivan Employee of: Adelphi Real World, D. Kielar Shareholder of: Janssen, Employee of: Janssen, N. Li Employee of: Janssen
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## AB0246 DISCREPANCY BETWEEN PHYSICIANS' AND PATIENTS' SATISFACTION WITH RHEUMATOID ARTHRITIS DISEASE CONTROL

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**Background:** An important element of the management of rheumatoid arthritis (RA) is the discussion of the degree to which patients are currently satisfied with their disease control. However, satisfaction with treatment disease control is not always aligned between patients and physicians.
**Objectives:** To explore the degree of discrepancy between physicians' and patients' satisfaction regarding RA disease control and to understand factors that may contribute to this discrepancy.
**Methods:** A multivariate logistic regression analysis was performed using ADELPHI RA Disease Specific Program (DSP) data in the US and EU5. Age and gender were forced in the model, and other covariates were included if the univariate $P$ value was <0.20. The missing indicator method was used to handle missingness.
**Results:** A total of 948 patients were included in this analysis. Overall, there was a discrepancy between physicians' and patients' perspectives on RA disease control in 26% of physician/patient pairs (Figure). Of 90 patients who rated their satisfaction as "*not satisfied, and I believe better control can be achieved for my condition*," 23.3% (n=21) had physicians who reported being satisfied with the RA disease control achieved. In contrast, of 714 patients who reported being satisfied with the RA disease control achieved, 9.2% (n=66) had physicians who rated their satisfaction as "*not satisfied, and I believe better control can be achieved for my condition*". After controlling for other covariates, some patients were more likely to disagree with their physicians' assessment of RA disease control, including those with the following disease characteristics: (1) longer disease duration (adjusted odds ratio [95% CI], 1.01 [1.00, 1.02]; $P=0.03$); (2) compared to DAS28 (CRP) ≤2.6 as reference level, higher disease activity (based on DAS28): DAS28 >2.6 to ≤3.2 (1.84 [0.96, 3.53]); DAS28 >3.2 to ≤5.1 (2.65 [1.45, 4.84]); DAS28 >5.1 (2.42 [1.02, 5.78]; all $P\leq0.05$); (3) greater activity impairment (based on the WPAI questionnaire; 1.10 [1.03, 1.17]; $P=0.003$). In contrast, patients who were in remission were more likely to agree with their physicians' assessment of disease control (0.43 [0.32, 0.60]; $P<0.0001$). In the multivariate analysis, a significant predictor of worse assessments of disease control by patients versus their physicians was greater activity impairment, based on the WPAI (1.31 [1.18, 1.44]; $P<0.0001$). In contrast, a significant predictor of better assessment of disease control by patients versus their physicians was a lower EuroQol-5 Dimension health status index score (indicating worse health status; 0.40 [0.17, 0.94]; $P=0.04$).




**Conclusions:** Results of this analysis showed a discrepancy between physicians' and patients' perspectives on RA disease control. Patients whose condition (objectively measured by longer disease duration, higher disease activity, and greater activity impairment) was worse were more likely to disagree with their physicians regarding their disease control. More impaired utility and health economic measurements were strongly associated with patients having a worse assessment of disease control than physicians. These results highlight need for further research to identify causes of this discrepancy in stated satisfaction.
**Disclosure of Interest:** S. Peterson Shareholder of: Janssen, Employee of: Janssen, E. Sullivan Employee of: Adelphi Real World, D. Kielar Shareholder of: Janssen, Employee of: Janssen, N. Li Employee of: Janssen
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## AB0247 A NEW DISEASE ACTIVITY BIOMARKER ALTERNATIVE TO CRP UNDER TOCILIZUMAB THERAPY FOR RHEUMATOID ARTHRITIS VIA PEPTIDOMIC ANALYSIS

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**Background:** Tocilizumab, anti-IL-6 receptor monoclonal antibody, is widely used for patients with rheumatoid arthritis. IL-6 is essential for production of C-reactive

protein (CRP). Tocilizumab fully inhibit the production of CRP. Therefore, we have difficulty in objective assessment of infection and disease activity because the level of CRP is suppressed under tocilizumab therapy. The development of new biomarker alternative to CRP is needed for daily practice.

**Objectives:** To discover new biomarkers alternative to CRP under tocilizumab therapy for rheumatoid arthritis.

**Methods:** We registered patients with rheumatoid arthritis treated with tocilizumab. We collected serum samples from those patients at baseline, 4 weeks after the first tocilizumab administration when patient's CRP level is almost normal, and 1 year later. And we measured CRP, ESR and clinical disease activity index (CDAI) score.Serum peptidomic analysis was conducted by newly-established one-step direct transfer technology (BLOTCHIP-MS analysis), a rapid quantitative technology for peptidomic analysis. All sample measurements were repeated four times. Statistical analyses of MS spectral data were conducted using ClinProTools version 2.2 (Bruker Daltonics).

**Results:** We registered 14 patients and their background is shown in Table 1. The levels of CRP were 1.16±0.99 mg/dl at baseline, 0.02±0.01 mg/dl at 4 weeks and 0.01±0.01mg/dl at 1 year, respectively. Their CDAI score were 22±9.2 at baseline, 15±8.9 at 4 weeks and 3±2.6 at 1 year, respectively. CRP titer decreased to almost normal level at 4 weeks regardless whether CDAI score did not fully decrease.

We detect 6 biomarkers, named as PRSJ01 to PRSJ06, by the peptidomic analysis (Table 2). The AUC of diagnostic value of these markers is from 0.742 to 0.858. For example, the level of PRSJ06 significantly decreased 4 weeks (Wilcoxon singed-rank test, $p$=0.02) and 1 year (Wilcoxon singed-rank test, $p$=0.003) after first tocilizumab administration (Figure 1). and it was inversely-correlated with CDAI score.

Table 1. Patient background at baseline

| | |
|---|---|
| Sex (n) | Female 10, Male 4 |
| Age (years) | 55.7±14.2 |
| CRP (mg/dl) | 1.16±0.99 |
| ESR (mm/h) | 33.4±24.1 |
| CDAI | 22±9.2 |
| MTX use (n) | 9/14 |
| MTX dose (mg/week) | 9.33±1.41 |

All values indicate mean ± SD.

Table 2. Diagnosis performance of biomarkers

| marker | Baseline vs 4W | | | Baseline vs 1Y | | |
|---|---|---|---|---|---|---|
| | AUC | SN | SP | AUC | SN | SP |
| PRSJ01 | 0.858 | 80 | 87 | 0.871 | 73 | 87 |
| PRSJ02 | 0.84 | 80 | 80 | 0.756 | 100 | 40 |
| PRSJ03 | 0.836 | 80 | 80 | 0.853 | 80 | 80 |
| PRSJ04 | 0.822 | 67 | 93 | 0.858 | 87 | 73 |
| PRSJ05 | 0.742 | 87 | 60 | 0.707 | 80 | 60 |
| PRSJ06 | 0.742 | 73 | 73 | 0.849 | 93 | 73 |

Figure 1. Level of PRSJ06 at each period.

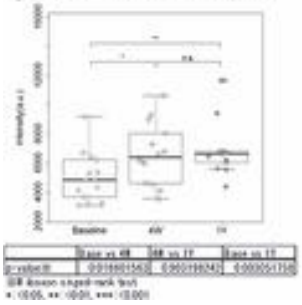
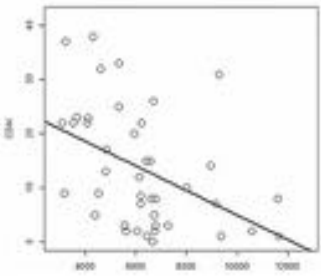


Figure 2. Correlation of PRSJ-6 and CDAI score



**Conclusions:** We detect new disease activity biomarkers alternative to CRP under tocilizumab therapy for rheumatoid arthritis. It is useful for exact evaluation of disease activity and infection during tocilizumab therapy.

**Disclosure of Interest:** None declared

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## AB0248 CIRCULATING CELL FREE DNA; A MARKER TO PREDICT THE THERAPEUTIC RESPONSE FOR BIOLOGICAL DMARDS IN RHEUMATOID ARTHRITIS

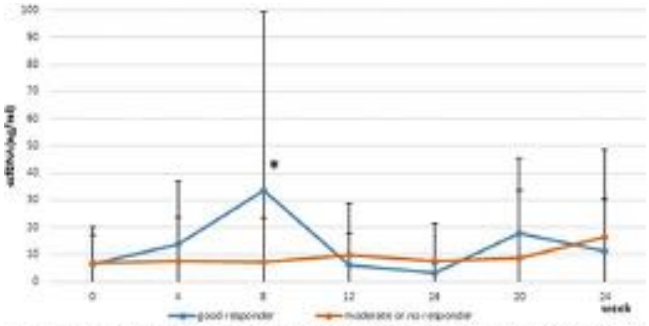
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**Background:** DNA is fragmented and released into blood circulation as results of damage or death of cells from peripheral bloods as well as organ tissues, and circulating cell-free DNA (ccfDNA) has been recognized as biomarkers of several medical conditions [1]. In patients with rheumatoid arthritis (RA), serum concentration of ccfDNA has been reported to be elevated [2], however, the relation between ccfDNA and the pathogenesis of RA remains unclear.

**Objectives:** To evaluate the correlation between ccfDNA in plasma and clinical disease activities in patients with RA.

**Methods:** The study group included 29 patients with RA who started biological DMARDs therapy. The concentration of ccfDNA in plasma was measured by quantitative real-time PCR at baseline to 24 weeks in every 4 weeks-period from 29 patients, and 21 healthy individuals. We also evaluated the correlation between ccfDNA and the clinical activities or the response for biological DMARDs, using disease activity score of 28 joints erythrocyte sedimentation rate (DAS28ESR) and the european league against rheumatism (EULAR) response criteria. In addition, synovial fluid samples of knee joint were collected from 14 patients with RA and12 with osteoarthritis (OA) to measure ccfDNA

**Results:** The concentration of ccfDNA in RA patients at baseline was higher than healthy controls (p=0.016).When evaluated the concentration of ccfDNA, it was increased until 8 weeks-period from the baseline, and then decreased after 12weeks-period. The average of DAS28ESR was improved in all patients enrolled. At 12weeks-period after treatment, 15 patients were good responders of the EULAR response criteria, 9 showed the moderate response and 5 showed no response. The concentration of ccfDNA in good responder was increased until 8weeks while those of moderate or no responder were not (P=0.042) (figure), and there was no significant difference between ccfDNA at baseline and other parameters in all patients. In joint fluid of RA patients, the concentration of ccfDNA was remarkably increased as compared to those from OA (P=0.00011).




The concentration of ccfDNA in good responder and moderate or no responder from baseline to 24 weeks-period.
*P<0.05

**Conclusions:** Increase of ccfDNA at 8 weeks-period was associated with improvement of disease activity. Compared with the biomarkers reported before, ccfDNA is possible to predict the early therapeutic effects of biological DMARDs in RA patients.

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**Disclosure of Interest:** None declared

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## AB0249 ROUTINE USE OF SYNOVIAL BIOPSIES FOR DIAGNOSIS AND TREATMENT GUIDANCE

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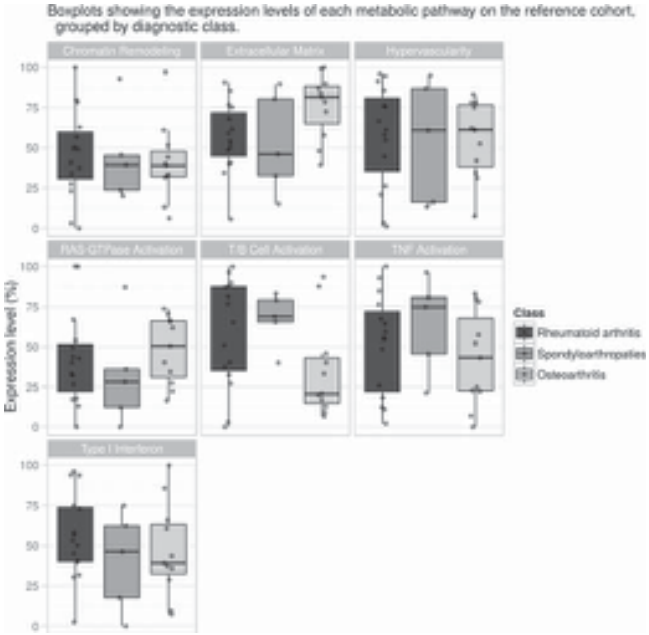
**Background:** Previous work [1] reports a differential diagnostic solution for patients with undifferentiated arthritis (UA) based on synovial gene expression. This diagnostic model uses a previously established signature of 96 genes [2] and 3 clinical variables (skin psoriasis, rheumatoid factors, hand arthritis), achieving 93.5% sensitivity and 86.8% specificity for the diagnosis of rheumatoid arthritis among UA patients. The signature covers 7 metabolic pathways involved in the pathogenesis of rheumatic conditions.

**Objectives:** To show the feasibility and relevance of a routine diagnostic test based on clinical and transcriptomic data from synovial biopsies, relying on a mathematical model, a central laboratory and an online software.

**Methods:** Kits for sample transportation, containing vials of RNA-preserving solution (RNAlater, Thermo Fisher Scientific) were sent to clinicians who harvested synovial tissue ($\leq$0.3cm$^3$) via needle-arthroscopy or an ultrasound-guided approach from the patient's joint (mostly knees, a few MCPs). Samples were shipped on an individual basis to a central laboratory (BE) using next day transportation at ambient temperature. No data about the patient or the doctor were provided to the laboratory aside from a sample ID.

RNA was extracted with RNEasy mini kit (Qiagen). Purity and concentration were checked with NanoDrop (Thermo Fisher Scientific). Retro-transcription was performed, followed by a qPCR (TLDA, 7900HT, Applied Biosystem). Four samples were analysed on each 384-well plate. The lab operator uploaded the PCR data on a dedicated secure web platform. In parallel, clinicians filled the 3 clinical values on that web platform. Based on both sources of information the software computed the differential diagnosis and the expression level of the 7 metabolic pathways, to feed doctor's therapeutic choices. PDF reports were then automatically sent via email to the doctor in charge of each patient. The software also managed all administrative aspects in order to get a fully functional portal.

**Results:** Synovial biopsies of 21 patients underwent the whole process. 19 (90.5%) showed satisfactory RNA quality. For the remaining 2, back up samples (harvested at the same time as the initial ones) could be analysed. One other sample (4.8%) could not be analysed due to insufficient RNA concentration. Gene expression values, diagnostic and pathways outputs were thus obtained for 20 samples (95.2%). The correlation between diagnosis and pathways expression levels was consistent with descriptions found in the literature [3,4] (Figure)




**Conclusions:** The routine implementation of a multi-gene RT-qPCR diagnostic test based on synovial biopsies in a real-life setting is successful. The operations put in place allowed a hassle-free management for the clinicians, thereby increasing the availability and reproducibility of the test. Early results with ultrasound-guided biopsy seem promising but require additional confirmation.

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**Disclosure of Interest:** None declared

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## AB0250 ASSESSMENT OF BALANCE AND ITS RELATION WITH CLINICAL PARAMETERS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid Arthritis (RA) one of the deformitive disease for feet. Patients generally need the special care, shoes and assistive devices because of their feet deformities.

**Objectives:** To evaluate the static and dynamic balances of the RA patients and to assess its relationship with clinical, functional and radiological parameters.

**Methods:** Patients diagnosed with RA according to ACR 2010 criteria were recruited into the study. A*ge and gender matched* healthy subjects were into the control group. The demographic (age, sex) and clinical properties (BMI, DAS28 etc) of patients were recorded. The state of balance of the patients was evaluated by means of "Berg Balance Scale" (BBS) and also 3 static and 4 dynamic balance tests with 25 parameters were assessed via the "*Neurocom Balance Master*" device. Radiographic assessments of feet were done to consider the deformities. "Foot and Ankle Outcome Score" (FAOS) was applied for foot function assessment. The level of fatigue (MAF: Multidimensional Assessment of Fatigue), depression (Beck Depression Inventory) and sleep disorders (Pitsbourg Sleep Quality Index) of all patients were evaluated and corelated with balance parameters.

**Results:** This study included 165 cases that consist of 81 RA group (66 female, 15 male) and 84 healthy control group (70 female, 14 male). The mean age of patients and controls were 48.90±10.36 and 45.89±12.07 years, respectively. Age, sex and BMI data of both groups were similar ($p>0.05$). There was a significant difference between the static and dynamic balance test results of the patient and the control groups ($p<0.05$). It was deduced that 66.7% of patients have depression, 64.2% sleep disorders and 93.8% fatigue according to surveys; however there was no correlation between these symptoms and presence of balance disorders. Although 92.4% of patients were established with foot deformities, these deformities were not correlated with FAOS and balance disorders. The presence of the swollen joint was determined as the most relevant factor about the balance disorders of RA patients.

**Conclusions:** Although RA patients have balance disturbances when we compared them with healthy controls, this disturbances has not significant relation with clinical, functional and radiological parameters. Balance problems are an important finding independently from other parameters during the course of the disease

**Disclosure of Interest:** None declared

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## AB0251 EARLY ONSET OF BENEFIT BY PATIENT-REPORTED OUTCOMES (PROS) WITH SARILUMAB TREATMENT IN RA

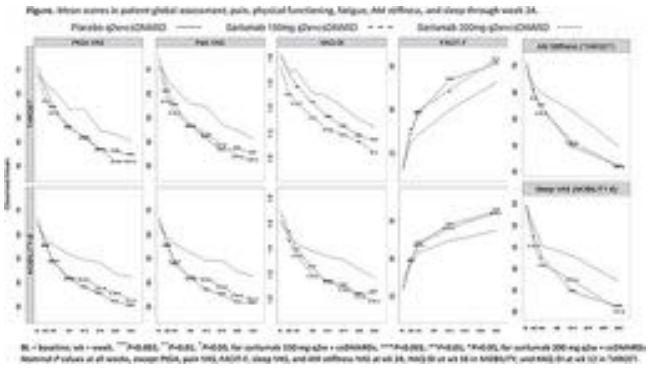
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**Background:** Efficacy, including improvements in patient-reported outcomes (PROs), was demonstrated in 2 phase 3 trials, MOBILITY[1] (NCT01061736) and TARGET[2] (NCT01709578), of sarilumab, an investigational human anti–interleukin 6 receptor monoclonal antibody. The most common treatment-emergent adverse events in both studies were infections, neutropenia, injection site reactions, and increased transaminases.

**Objectives:** To evaluate the early onset of benefit of sarilumab treatment measured by PROs.

**Methods:** In both studies, adults with moderate-to-severe, active rheumatoid arthritis (RA) were randomized to 1 of 3 groups receiving placebo, sarilumab 150 mg, or sarilumab 200 mg subcutaneously (SC) every 2 weeks (q2w) plus methotrexate (MTX; MOBILITY) or conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; TARGET). PROs assessed as early as week 2 included patient global assessment of disease activity (PtGA), pain assessed by visual analog scale (VAS), Health Assessment Questionnaire–Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F), sleep by VAS (MOBILITY), and AM stiffness by VAS (TARGET). Changes from baseline were analyzed using mixed-model repeated measures with region, number of prior tumor necrosis factor inhibitors (TNFis) (TARGET) or prior biologic use (MOBILITY), visit, treatment, treatment-by-visit interaction, and baseline PRO scores as covariates.

**Results:** Greater improvements were reported by patients treated with sarilumab 150 and 200 mg SC q2w vs placebo as early as week 2 in PtGA, pain VAS, HAQ-DI, FACIT-F, sleep VAS, and AM stiffness VAS (nominal $P<0.05$) (Figure) and sustained through week 24. Between-group differences were statistically significant for FACIT-F and sleep VAS at week 24 in MOBILITY and for HAQ-DI at week 12 (TARGET) and week 16 (MOBILITY).



**Conclusions:** Sarilumab treatment rapidly improved a broad range of PROs in patients with RA with inadequate response to MTX (MOBILITY) or TNFis (TARGET); these improvements were observed as early week 2 and maintained through week 24. The results demonstrate the early benefit of sarilumab treatment based on patients' own assessments of their disease.

**References:**

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**Acknowledgement:** This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

**Disclosure of Interest:** V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, Biogen, BMS, Celgene, Celltrion, Consortium of Rheumatology Researchers of North America (CORRONA), Crescendo/Myriad Genetics, EMD Serono, Genentech/Roche, GSK, Janssen, Eli Lilly, Novartis, Pfizer Inc, Regeneron Pharmaceuticals, Inc, Sandoz, Sanofi, and UCB, C. Chen Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, P. Mahajan Shareholder of: Sanofi, Employee of: Sanofi, M. Kosinski Consultant for: Sanofi and Regeneron, E. Mangan Shareholder of: in Pfizer Inc and Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, H. van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, N. Graham

Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, Y. Lin Shareholder of: Sanofi, Employee of: Sanofi, E. Keystone Consultant for: has consulting agreements/advisory board membership with Abbott, AstraZeneca, Biotest, BMS, F. Hoffman-La Roche, Genentech, Janssen, Eli Lilly, Merck, Pfizer Inc, and UCB; and has speaker honoraria agreements with Abbott, Amgen, AstraZeneca, BMS Canada, F. Hoffman-La Roche, Janssen, Pfizer Inc, and UCB., J. Braun Grant/research support from: received honoraria for talks, advisory boards, paid consultancies, and grants for studies from AbbVie (Abbott), Amgen, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer Inc (Wyeth), Roche, Sanofi-Aventis, and UCB, Consultant for: received honoraria for talks, advisory boards, paid consultancies, and grants for studies from AbbVie (Abbott), Amgen, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer Inc (Wyeth), Roche, Sanofi-Aventis, and UCB

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## AB0252 BENEFIT OF SARILUMAB WITH CSDMARDS ON PATIENT PRODUCTIVITY IN WORK, HOUSEHOLD WORK AND FAMILY, SOCIAL, LEISURE ACTIVITIES IN TNF-IR RA PATIENTS

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**Background:** The effect of active rheumatoid arthritis (RA) on participation, active and meaningful engagement by patients in activities important to them, has significant individual and societal costs. Sarilumab is an investigational human anti–interleukin 6 (IL-6) receptor monoclonal antibody. In the phase 3 TARGET study (NCT01709578), sarilumab + conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) demonstrated efficacy in adults with moderate-to-severe, active RA and inadequate response to TNF inhibitors. The most common treatment-emergent adverse events were infections, neutropenia, and increased transaminases; laboratory changes were consistent with IL-6 signaling blockade.

**Objectives:** To evaluate the effect of sarilumab treatment on patient productivity within and outside of the home; requirement for outside help; and family, social, or leisure activities in the past month as assessed by the RA-specific Work Productivity Survey (WPS-RA).[1]

**Methods:** The intent-to-treat population included 546 patients randomized 1:1:1 to placebo, sarilumab 150 mg, or sarilumab 200 mg every 2 wks (q2w) subcutaneously (SC) + background csDMARDs. The WPS-RA was assessed for patients employed outside of (completed all 8 items) and within the home (completed only the 5 items related to productivity within the home and participation in family, social, and leisure activities) at baseline and wks 4 (not reported), 12, and 24. Mixed-model repeated measures analyses were used to evaluate differences in individual WPS-RA items at a significance level of 0.05 if O'Brien's global test[2] showed significance ($P<0.025$).

**Results:** At baseline, 544 patients were administered the WPS-RA, 33.1%, 33.7%, and 35.7% (placebo, sarilumab 150, and sarilumab 200 mg q2w SC, respectively) of whom were currently employed outside of the home. Global testing indicated significantly greater overall improvement in patients treated with sarilumab 150 mg q2w SC (wk 12, $P$=0.0010; wk 24, $P$=0.0004) and sarilumab 200 mg q2w SC (wk 12, $P$=0.0036; wk 24, $P$=0.0003) vs placebo. At wk 24, patients currently employed outside of the home receiving sarilumab 200 mg q2w SC reported significantly greater reductions in number of work days missed due to RA and less interference with work productivity. Patients receiving both doses reported significantly greater reductions in number of days missed engaging in household work, days requiring hired help, and rate of arthritis interference in household work and less time missed engaging in family, social, and leisure activities.

**Conclusions:** Sarilumab treatment was associated with significant improvements in participation in work; household work; and family, social, and leisure activities. Improvements in productivity outside of the home were also significant among patients in the sarilumab 200 mg q2w SC group vs placebo, although only a proportion of patients worked outside of the home. These data indicate important improvements in overall participation following sarilumab treatment.

**References:**

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**Acknowledgement:** This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

**Disclosure of Interest:** V. Strand Consultant for: has received consulting fees from AbbVie, Amgen, AstraZeneca, Biogen, BMS, Celgene, Celltrion, Consortium of Rheumatology Researchers of North America (CORRONA), Crescendo/Myriad Genetics, EMD Serono, Genentech/Roche, GSK, Janssen, Eli Lilly, Novartis, Pfizer Inc, Regeneron Pharmaceuticals, Inc, Sandoz, Sanofi, and UCB., P. Mahajan Shareholder of: Sanofi, Employee of: Sanofi, C. Chen Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc,

Table 1. Change From Baseline in WPS-RA—Individual Items at Weeks 12 and 24

| Item | Week 12 Placebo + csDMARD (n=181) | Week 12 Sarilumab 150 mg q2w + csDMARD (n=181) | Week 12 Sarilumab 200 mg q2w + csDMARD (n=184) | Week 24 Placebo + csDMARD (n=181) | Week 24 Sarilumab 150 mg q2w + csDMARD (n=181) | Week 24 Sarilumab 200 mg q2w + csDMARD (n=184) |
|---|---|---|---|---|---|---|
| Work days missed (n) | (54) | (54) | (56) | (32) | (43) | (45) |
| LS mean | -1.2 | -2.0 | -3.0* | -2.0 | -2.9 | -3.2* |
| Days with work productivity reduced by ≥50% (n) | (54) | (54) | (56) | (32) | (43) | (45) |
| LS mean | -1.7 | -4.2* | -3.2 | -3.6 | -4.3 | -4.3 |
| Rate of interference with work (n) | (53) | (54) | (56) | (32) | (42) | (45) |
| LS mean | -10.4 | -19.2 | -18.7 | -16.3 | -24.2 | -27.3* |
| Household work days missed (n) | (170) | (164) | (169) | (101) | (126) | (133) |
| LS mean | -2.1 | -5.5* | -5.5* | -3.5 | -6.1* | -6.2* |
| Days with household work productivity reduced by ≥50% (n) | (169) | (163) | (169) | (101) | (125) | (133) |
| LS mean | -2.6 | -4.0 | -4.0 | -3.4 | -4.6 | -4.9 |
| Rate of interference with household work productivity (n) | (170) | (164) | (167) | (100) | (126) | (132) |
| LS mean | -12.1 | -27.7* | -24.0* | -19.7 | -31.0* | -32.7* |
| Days with outside help hired (n) | (170) | (164) | (169) | (101) | (126) | (133) |
| LS mean | -0.8 | -3.17* | -2.9* | -1.6 | -3.9* | -3.9* |
| Days with family, social, or leisure activities missed (n) | (170) | (164) | (169) | (101) | (127) | (133) |
| LS mean | -2.2 | -2.5 | -3.3 | -2.0 | -3.5* | -4.1* |

*Asterisk indicates $P<0.05$ vs placebo.

H. van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, E. Mangan Shareholder of: an employee of Regeneron Pharmaceuticals, Inc, and may hold stock and/or stock options in Pfizer Inc and Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc, O. Hagino Shareholder of: Sanofi, Employee of: Sanofi, N. Graham Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, G. da R.C. Pinheiro Consultant for: has received consulting fees from AbbVie, AstraZeneca, GSK, Hospira, Janssen, Pfizer Inc, Roche, RuiYi, and Sanofi., A. Kivitz Consultant for: has received consulting fees from Celgene, Genentech/Roche, GSK, Janssen, Pfizer Inc, Regeneron Pharmaceuticals, Inc, Sanofi, and UCB.

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## AB0253 FACTORS ASSOCIATED TO POOR HAND FUNCTION PERFORMANCE IN A COHORT OF RA PATIENTS: THE IMPACT OF DISEASE ACTIVITY

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**Background:** Small joints of the hands and wrists are universally affected in rheumatoid arthritis (RA) and hand function (HF) may be impaired; few indices include HF assessment, beyond swollen and tender joint counts.

**Objectives:** To evaluate HF in RA patients from an early arthritis clinic initiated in 2004, to compare it with HF from paired controls and to identify factors associated to impaired function.

**Methods:** From February 2014 to June 2015, 139 patients currently attending the clinic (97.2% of the cohort) had disease activity scored (DAS28) and tip-, key- and palmar-pinch and grip strength measured as recommended (1); in addition, patients completed the Michigan Hand Outcome Questionnaire (MHQ) (2) and the Disabilities of the Arm, Shoulder and Hand Outcome Measure (DASH) (3). Sixty-nine paired (according to age ±5 years and gender) controls had same evaluations (but DAS28). Cut-offs for normal tests were obtained from normative data and controls values (median + 1 SD). Descriptive statistics and regression analysis were used. Patients and controls signed informed consent.

**Results:** Patients were more frequently middle-aged (44.1± 13.1 years) female (89.2%) with median disease duration of 7 years (IQR: 3–9 years) at HF assessment; of them, 91 patients had DAS28-remission, 16 low disease activity, 23 moderate and 9 patients had high disease activity. Controls (age: 43.8±11.5 years, 89.9% female) scored better HF tests and questionnaires than patients with (any) disease activity; nonetheless, remission patients had similar DASH and key pinch than controls but worse MHQ (92.5 vs. 98.9), grip strength (18.7 vs. 22.3), tip pinch (3.8 vs. 4.5) and palmar pinch (5 vs. 6), (p=0.000 for all comparisons). DAS28 was consistently associated to HF impairment (β coefficient from 2.2 to 2.7, $p\leq0.05$); additional predictors were age and gender. Cut-off for DAS28 to predict normal HF varied (according to HF assessment, i.e, MHQ, DASH, grip strength or pinches) from 1.8 to 2.9. MHQ and DASH were highly correlated; pinches had moderate correlations with questionnaires and grip strength had the best correlation (rho=0.6 for either MHQ or DASH).

**Conclusions:** Disease activity consistently predicted HF in a cohort of RA patients with variable follow-up. Additional predictors were age and gender.

Remission's patients showed similar HF performance to controls, when evaluated by DASH and key pinch although the MHQ and grip strength measurement identified impairment of their HF. Routine assessment of RA patients should include a comprehensive evaluation of HF; according to our results, we propose grip strength and MHQ to assess it.

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**Disclosure of Interest:** None declared

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## AB0254 SEVERITY AND IMPROVEMENT OF MORNING STIFFNESS INDEPENDENTLY ASSOCIATE WITH TENOSYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Morning stiffness has long been recognized by both patients and rheumatologists as a characteristic feature of rheumatoid arthritis (RA). However, morning stiffness is no more included in 2010 ACR/EULAR Classification Criteria for RA [1] or in major instruments for evaluating disease activity of RA such as Disease Activity Score (DAS) [2] and 2011 ACR/EULAR Provisional Definition of Remission [3] for the lack of solid evidence for its independent value.

**Objectives:** We aimed to clarify the associations between morning stiffness and synovial inflammation and determine the independent value and the optimal measurement of morning stiffness in patients with RA.

**Methods:** We enrolled 76 consecutive RA patients who underwent musculoskeletal ultrasound and agreed to participate in the study. In addition to asking the duration of morning stiffness, we asked patients to complete a diagram which represents the time course of their morning stiffness in the dominant hand. We also determined the activity of synovitis in 11 joints and tenosynovitis in 8 tendons/tendon compartments in the same hand by using power Doppler (PD) ultrasound with a semiquantitative score (0–3).

**Results:** Study patients were predominated by women (78.9%) with a mean age of 58.4 (SD 14.6) years and a median disease duration of 24 (IQR 8–63.75) months. Rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA) had been positive in 84.2% and 77.6%, respectively. For synovitis, swollen/tender joint counts more strongly correlated with total PD scores ($\rho$=0.379–0.561, $p \leq 0.001$) than did any parameters of morning stiffness ($\rho$=0.217–0.314, p=0.006–0.021) (Table 1). For tenosynovitis, however, the severity on awakening and the improvement of morning stiffness more strongly correlated with total PD scores ($\rho$=0.503–0.561, $p<0.001$) than did swollen/tender joint counts ($\rho$=0.276–0.388, p=0.001–0.016) (Table 1). Multivariate analyses identified the severity on awakening and the improvement but not the duration of morning stiffness as factors that independently associate with the total tenosynovial PD score.

**Table 1. Correlations between clinical manifestations and ultrasound scores in dominant hand**

| | Joint count | | Morning stiffness | | | | |
|---|---|---|---|---|---|---|---|
| | Swollen joint | Tender joint | Duration | Severity VAS on awakening | Improvement of VAS at 1/4 | Improvement of VAS at 1/2 | Improvement of VAS at bedtime |
| Intra-articular synovial power Doppler score | | | | | | | |
| $\rho$* | 0.561 | 0.379 | 0.265 | 0.314 | 0.217 | 0.266 | 0.306 |
| p value* | < 0.001 | 0.001 | 0.021 | 0.006 | 0.060 | 0.020 | 0.007 |
| Tenosynovial power Doppler score | | | | | | | |
| $\rho$* | 0.388 | 0.276 | 0.280 | 0.503 | 0.505 | 0.561 | 0.538 |
| p value* | 0.001 | 0.016 | 0.014 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

*Spearman's correlation coefficient
VAS, visual analogue scale

**Conclusions:** Our data demonstrate a pathophysiological link between morning stiffness and tenosynovitis and also give an insight into the optimal measurement of morning stiffness. Our data support an independent value of evaluating morning stiffness in the management of RA.

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## AB0255 THE ASSOCIATION BETWEEN RHEUMATOID FACTOR POSITIVITY AND EFFECTS OF TREATMENT WITH A FIRST BIOLOGIC AGENT IN RHEUMATOID ARTHRITIS

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**Background:** The presence of rheumatoid factor (RF) plays an important role in diagnosis for patients suspected with rheumatoid arthritis (RA) [1]. However, it remains unclear whether RF positivity is related to the effects of treatment with biologic disease-modifying antirheumatic drugs (DMARDS).

**Objectives:** The objective of the current study was to determine whether RF positivity was associated with the effects of treatment with biologic DMARDS among bio-naïve RA patients.

**Methods:** We used demographic and clinical data from the Tsurumai Biologics Communication Registry, which comprises Nagoya University and 20 affiliated hospitals in Japan. Patients aged 20–80 years who fulfilled the ACR 1987 revised classification criteria or the 2010 ACR/EULAR classification criteria for RA were selected; those with prior exposure to biologic DMARDS were excluded. The RF status was divided into negative (0–15 IU/ml) or positive (>15 IU/ml). Multivariate logistic regression analysis was used to assess the association between RF positivity and the possibility of sufficient response to biologic DMARDS treatment, as defined by good response at week 16 in the EULAR response criteria, based on DAS28. Crude and adjusted odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs) were calculated. Adjustment variables included sex, age, whether or not tumor necrosis factor inhibitor had been used, baseline use of methotrexate (MTX) and glucocorticoids, and baseline stage and class as defined by the Steinbrocker classification.

**Results:** The demographic and disease characteristics of the patients at baseline were comparable between RF-negative (n=120) and RF-positive (n=557) groups. The mean age was 57 years; 81% were women. Patients had longstanding RA (mean 9.3 years), and the baseline DAS28 was 5.1. Among the patients, 80% and 61% received MTX and glucocorticoids, respectively. A good response as per EULAR response criteria was identified in 73 (60.8%) RF-negative patients and 268 (48.1%) RF-positive patients. The crude OR for the association between RF positivity and the possibility of good response as per EULAR response criteria was 0.60 (95% CI 0.40–0.89) compared with RF negativity. After adjustment for the aforementioned covariates, RF-positivity was associated with a decreased possibility of good response to biologic DMARDS compared with RF-negativity (OR 0.64, 95% CI 0.41–0.98).

**Table 1. Association between RF status and the possibility of good response as per EULAR response criteria, as determined by binary logistic regression analysis***

| | Crude OR (95% CI) | Adjusted OR (95% CI)† |
|---|---|---|
| RF status | | |
| negative | 1.00 (referent) | 1.00 (referent) |
| positive | 0.60 (0.40–0.89) | 0.64 (0.41–0.98) |

* OR = Odds ratio; 95% CI = 95% confidence interval. RF = rheumatoid factor
† Adjusted for sex, age, whether or not tumor necrosis factor inhibitor had been used, baseline use of methotrexate and glucocorticoids, and baseline stage and class as defined by the Steinbrocker classification.

**Conclusions:** This study demonstrated that RF-positivity was independently associated with a decreased possibility of good response to biologic DMARDS in bio-naïve RA patients.

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[1] P.Y. Chang, C.T. Yang, C.H. Cheng, K.H. Yu, Diagnostic performance of anti-cyclic citrullinated peptide and rheumatoid factor in patients with rheumatoid arthritis, Int J Rheum Dis, (2015).

**Disclosure of Interest:** None declared

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## AB0256 VERY EARLY RESPONSE TO ABATACEPT COULD BE A PREDICTIVE FACTOR FOR REPAIR OF BONE EROSION IN PATIENTS WITH RHEUMATOID ARTHRITIS ASSESSED BY MRI

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**Background:** There is no report investigating predictive factors for MRI erosion change in treatment of rheumatoid arthritis (RA) with abatacept (ABT), because very little data are available on the efficacy of ABT assessed by MRI.
**Objectives:** The aim of this study is to examine the efficacy of ABT in patients with RA assessed by MRI and identify factors associated with change of bone erosion score.
**Methods:** Thirty-five RA patients were included in this prospective study. MRI of bilateral hands and conventional radiographs (CR) of bilateral hands and feet were performed at baseline and month 12 of treatment with intravenous ABT. MRI images were scored for synovitis, osteitis and bone erosion according to the Rheumatoid Arthritis MRI Scoring System. CR images were assessed according to the van der Heijde modified total Sharp score.
**Results:** Thirty-one patients completed this study. Mean Simplified Disease Activity Index (SDAI) and Health Assessment Questionnaire Disability Index (HAQ-DI) at baseline were 23.4±12.0 and 1.1±0.6 respectively. At the group level, mean MRI synovitis and osteitis scores showed statistically significant reductions through 12 months of treatment with ABT (from 17.1±7.0 to 11.4±6.2 ($p<0.0001$) and from 5.1±8.2 to 1.9±2.5 ($p=0.003$), respectively). On the other hand, mean MRI erosion scores showed no change throughout the study period (from 28.2±38.6 to 28.7±39.2). Mean CR erosion scores also showed no change (from 17.3±42.5 to 17.6±42.6). However, at the patient level, reductions of MRI erosion score were observed in 13% of patients, whereas no patient showed reduction of CR erosion score. The functional remission rates, which is defined as HAQ-DI$\leq$0.5, of patients with regressive, unchanged and progressive MRI erosion score were 100%, 71% and 33%, respectively. On multiple regression analysis, SDAI response rate at month 1 and CRP at baseline were identified as the predicting factors for changes of erosion score (regression coefficient; -0.70 ($p<0.001$)/0.42 ($p=0.02$), respectively). Optimal cutoff value of SDAI response rate at month 1 was 0.524 ($p=0.019$). It is interesting that patients with regression of MRI erosion had high titer of rheumatoid factor (median: 591IU/ml) and anti-CCP antibody (median: 254U/ml) at baseline.
**Conclusions:** This study demonstrated ABT has a strong inhibitory effect on joint damage reducing synovitis and osteitis and not progressing bone erosion in RA patients. Over 10% patients showed repair of bone erosion assessed by MRI, which resulted in functional remission. SDAI response rate at month 1 could be a predictive factor for repair of bone erosion.
**Disclosure of Interest:** Y. Kukida Grant/research support from: Bristol-Myers Squibb, A. Kasahara: None declared, T. Seno: None declared, T. Inoue: None declared, N. Kamio: None declared, R. Sagawa: None declared, T. Kida: None declared, A. Nakabayashi: None declared, H. Nagahara: None declared, A. Yamamoto: None declared, S. Morita: None declared, H. Ito: None declared, M. Kohno: None declared, Y. Kawahito Grant/research support from: Bristol-Myers Squibb
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## AB0257 CLINICAL OUTCOME OF 2 YEARS TREATMENT OF THE EARLY PHASE RHEUMATOID ARTHRITIS

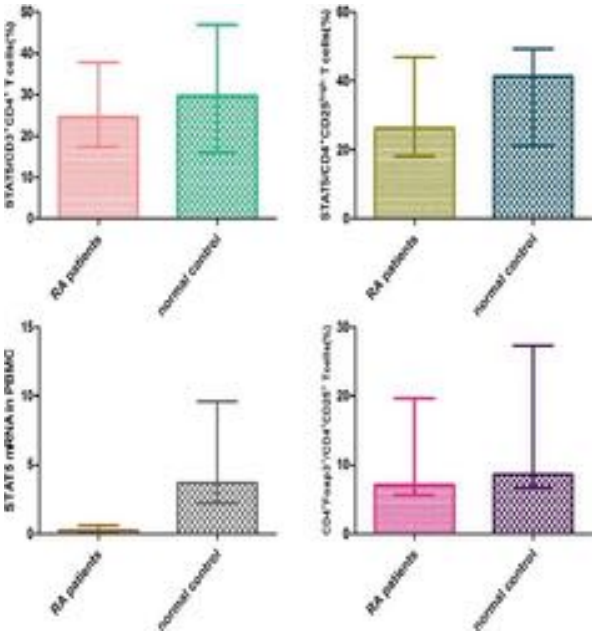
Y. Sugimura[1], S. Miyamoto[2], T. Kashiwagura[3], M. Kobayashi[4], N. Miyakoshi[1], Y. Shimada[1]. *[1]Orthopedic Surgery, Akita University Graduate School of Medicine; [2]Orthopedic Surgery, Nakadori General Hospital; [3]Rehabilitation Medicine, Akita City Hospital; [4]Orthopedic Surgery, Hiraka General Hospital, Akita, Japan*

**Background:** Few studies have reported long term clinical outcome of patients with early phase rheumatoid arthritis (RA).
**Objectives:** The objectives of this study were to investigate outcome of 2 years treatment for RA which was started less than 12 months after RA symptoms first appeared and to evaluate prediction factors of poorly controlled patients at 2 years.
**Methods:** From a total of 1663 RA patients registered in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) in 2012, 66 patients were treated within the first year of RA appearance, and enrolled in this study. Sex, age, RA disease duration, Steinbroker's stage, Steinbroker's class, medications and DAS28-CRP at the baseline and 2 years post-treatment were evaluated. Furthermore, we compared the group of remission (REM) or low disease activity (LDA) with the group of medium disease activity (MDA) or high disease activity (HDA) at 2 years.
**Results:** At the baseline, the patients included 13 males and 53 females. Mean age and RA disease duration were 59 (21–85) years and 7 (1–11) months, respectively. Fifty-four, 8, 4 and 0 patients were classified into Steinbroker's stage I, II, III, and IV, respectively. Thirty-nine, 25, 2 and 0 patients were classified into Steinbroker's class I, II, III, and IV, respectively. Thirty-seven (56%), 24 (36%), and 16 (24%) patients were treated with MTX, DMARDs, and PSL, respectively. In DAS28-CRP, 19 (29%), 13 (20%), 32 (48%), and 2 (3%) patients showed REM, LDA, MDA, and HDA, respectively. Forty-four patients were followed-up for 2 years. At 2 years, 30, 7, 5, and 2 patients were classified into Steinbroker's stage I, II, III, and IV, respectively. Thirty-one, 12, 1, and 0 patients are classified into Steinbroker's class I, II, III, and IV, respectively. In DAS28-CRP, 33 (75%), 4 (9%), 7 (16%), and 0 (0%) patients showed REM, LDA, MDA, and HDA, respectively. Compared with the group of REM or LDA, the group of MDA or HDA had significantly older age (P=0.018), higher Steinbroker's stage (P=0.012) and higher DAS28-CRP (P=0.049) at the baseline.
**Conclusions:** At 2 years, 75% of patients with early phase RA achieved REM. Older age, higher Steinbroker's stage and higher DAS28-CRP at the baseline could be prediction factors of poorly controlled patients at 2 years.
**Acknowledgement:** We wish to thank the members of AORA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5371

## AB0258 DECREASED PHOSPHOSTAT5 CONTRIBUTED TO IMPAIRMENT OF CD4+CD25+FOXP3+ TREGS IN RA PATIENTS

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**Background:** Our previous research has demonstrated decreased expression of $CD4^+CD25^+Foxp3^+$ regulatory T cells (Tregs) enrolled in the pathogenesis of rheumatoid arthritis (RA). Anti-TNF-$\alpha$ mAb therapy could improve Tregs expansion in RA and associate with clinical amelioration of RA patients. STAT5 is reported to have effects on many aspects of immune function, particularly in regulatory T cell development.
**Objectives:** In this study, we aim to monitor phosphoSTAT5 expression in Tregs and investigate its role in RA disease.
**Methods:** Flowcytometry was employed to detect the phosphorylation level of STAT5 in $CD3^+CD4^+$ T cells, $CD4^+CD25^{high}$ regulatory T cells and the expression of $CD4^+CD25^+Foxp3^+$Tregs in peripheral blood of 20 patients with RA disease and 20 age and gender-matched normal controls. STAT5 mRNA expression in peripheral blood mononuclear cells (PBMC) were also monitored of these RA patients and normal controls.
**Results:** Phosphorylation level of STAT5 deceased in RA patients both in $CD3^+CD4^+$ T cells and in $CD4^+CD25^{high}$ regulatory T cells, along with reduction of expression of $CD4^+CD25^+Foxp3^+$ Tregs. Detection of mRNA also confirmed STAT5 down regulation in Tregs in RA patients.




**Conclusions:** Compared with normal controls, the expression of $CD4^+CD25^+Foxp3^+$Tregs decreased in RA patients. PhosphoSTAT5 reduction in $CD3^+CD4^+$ T cells, mainly in $CD4^+CD25^{high}$ regulatory T cells contributed to impairment of $CD4^+CD25^+Foxp3^+$ regulatory T cells in RA.
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[1] Niu Q, Cai B, Huang ZC, Shi YY, Wang LL. Disturbed Th17/Treg balance in patients with rheumatoid arthritis. Rheumatol Int. 2012 Sep;32(9):2731–6.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4760

## Rheumatoid arthritis - comorbidity and clinical aspects

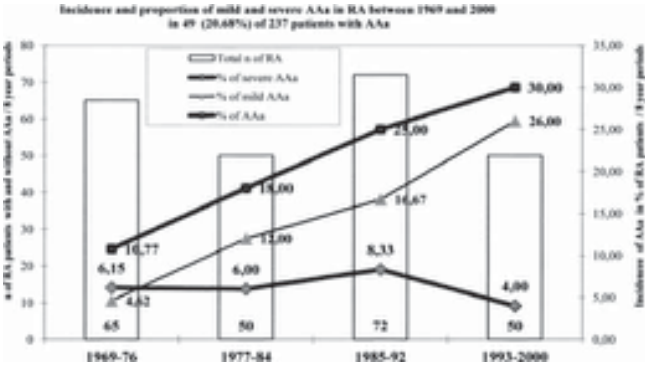
### AB0259 THE CHANGING FACE OF RHEUMATOID ARTHRITIS AND AA AMYLOIDOSIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 237 RHEUMATOID ARTHRITIS PATIENTS

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**Background:** According to some clinicians the course of rheumatoid arthritis (RA) has been changing in the last decades. However, AA amyloidosis (AAa) remains one of the most important complications of RA [1].
**Objectives:** The aim of this study was to verify this clinical impression, the "changing face of RA", characterized by AAa.
**Methods:** At the National Institute of Rheumatology 12138 patients died between 1969 and 2000; among them 237 with RA, and all of them were autopsied.
This non-selected autopsy population of 237 was the subject of present study. In 49 (20.68%) of 237 patients, RA was complicated by AAa.
**RA** was confirmed clinically according to the criteria of the American College of Rheumatology (ACR). The existence of AAa was determined histologically. The extent of amyloid A deposition/patient was evaluated by semi-quantitative visual estimation on a 0 to 3 plus scale. The average incidence of AAa was calculated in percentage of the number of RA patients, who died during four periods of time (8–8–8-8 years) covering 32 years (between 1969 and 2000).
**Results:** Demographics, duration and onset of disease (in years) of RA patients with AAa is summarized in Table 1, as well as the average incidence of AAa in RA between 1969 and 2000 in Figure 1.

| Years of death | 1969–1976 | 1977–1984 | 1985–1992 | 1993–2000 |
|---|---|---|---|---|
| Average age of RA pts. in years | 56.71 | 59.56 | 66.06 | 64.08 |
| Average onset of disease in years | 46.50 | 45.44 | 48.94 | 42.43 |
| Average disease duration in years | 12.00 | 14.11 | 17.11 | 20.71 |

During these four periods of time (1969 to 2000) the average age of the RA patients with AAa continuously increased somewhat (from 56.71 to 64.08 years). In the four periods RA was diagnosed increasingly earlier in life (42.43 years versus 46.5) and the course of the disease became longer (20.71 years versus 12.00).
The average incidence of AAa continuously increased (from 10.77% to 30.0%) between 1969 and 2000. This was due to the raised prevalence of mild AAa (the proportion of cases with severe AAa decreased (from 6.15% to 4.0%).




**Conclusions:** The earlier onset of RA and the longer life span may explain the changing face of RA and/or the more effective therapy. The increased incidence of AAa may be related to the longer duration of the inflammation.
The changing proportion of severe and mild amyloid deposition, i.e. the decrease of severe cases has likely been related to the introduction of more effective immunosuppressive therapy.
Our data from the end of the last century allow comparison with the changes following the introduction of the much more effective biological therapy of the present.

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**Disclosure of Interest:** None declared
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### AB0260 MULTIMORBIDITY IN RHEUMATOID ARTHRITIS PATIENTS: IMPORTANCE OF RENAL FUNCTIONAL CONDITION

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**Background:** RA pts commonly present with multiple concurrent chronic disease, compromising pts quality of life, limiting the use of potential therapies, contributing into disability, rate and costs of hospitalization [1–3].
**Objectives:** To identify the prevalence and extent of multi-morbid background in RA pts (ACR 1987 y) and relate pts multimorbidity status with RA activity and duration.
**Methods:** 209 RA pts (F-70,6%, mean age 67,0±11,3y), admitted to rheumatology division, were included into analysis. RA duration was 20 [6;109] mo, average disease activity (DAS28) - 5,2±1,7, radiographic stage 1–2 was identified in 54,5% (n=114) pts using the Steinbrocker scoring system. The severity of multimorbid environment was rated using Charlson Comorbidity Index (CCI) and Cumulative Illness Rating Score (CIRS). CCI was calculated using the rating scale with 19 nosological entities, ICD-10 (0–36); CIRS was calculated using the 5 score scale (0–4) to assess 14 major organ systems of the body (0–56). Values of CCI>5 and CIRS>4 were considered as important clinical and prognostic factors in RA pts.
**Results:** Mean CIRS value in RA pts was 15 [10;19] scores, and CCI value - 7 [4;10] scores. There was an obvious correlation between the two indices (r=0,86, $p$=0,005). CIRS and CCI values were independent of the RA duration (r=-0,43, $p$=0,53; r=-0,12, $p$=0,82, respectively) and RA activity (r=-0,12, $p$=0,08; r=0,02, $p$=0,7). The strongest correlation of the two indices was found with eGFR (using CKD-EPI formula), (CIRS r= -0,61, CCI r= -0,49; $p$<0,01), and with age (r=0,57, r=0,49; $p$<0,05). CIRS and CCI values also correlated ($p$<0,05) with MAP (mean arterial pressure) (r=0,48; r=0,37), excess body weight (r=0,28; r=0,35), creatinine levels (r=0,44, r=0,39), uric acid levels (r=0,32, r=0,31), as well as with hemoglobin level (r=-0,28, r=-0,25) and HAQ scores (r=0,31; r=0,32). No correlation was found between CIRS and gender, VAS score, and ESR, CRP, cholesterol and liver transaminases levels ($p$>0,05).
**Conclusions:** High multimorbid burden was established in the absolute majority of RA pts. RA duration and activity had no impact on the level of multimorbid burden, measured with CCI and CIRS indices (objective measure of cumulative physical illness burden). Compromised renal function, apart from the age, is of dominant importance in pts management issues, limiting the range of available effective therapies, thus, aggravating RA natural course on one side, and inducing and catalyzing the severity of dysmetabolic syndrome, AH and anemia – on the other.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4741

### AB0261 DOES THE PRESENCE OF RHEUMATOID FACTOR AND/OR ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY POSITIVITY AFFECT THE MANIFESTATIONS OF RHEUMATOID ARTHRITIS?

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**Background:** Since the 2010 revision of the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Classification Criteria and the availability of anti-cyclic citrullinated peptide antibody (ACCP) testing, patients newly diagnosed with rheumatoid arthritis (RA) are commonly tested for both rheumatoid factor (RF) and ACCP. Patients with ACCP or RF positivity are reported to have worse clinical and radiographic outcomes; however, the presence of ACCP may confound the effects of RF and vice versa.
**Objectives:** To determine if there were any differences at study baseline in RA patients who were ACCP-positive, RF-positive, doubly positive and doubly negative in terms of demographics, clinical, functional, laboratory features and radiographic erosions in a multi-ethnic cohort of RA patients in a tertiary rheumatology centre in Singapore.
**Methods:** This cross-sectional study was conducted at Tan Tock Seng Hospital in Singapore. 1206 patients fulfilled the ACR 1987 criteria for RA, of whom 475 were excluded due to a lack of both ACCP and RF status. Serum levels of ACCP and RF were analysed for differences in demographics (gender, ethnicity, age, smoking status, disease duration before study entry), clinical activity (Disease Activity Score-28 (DAS-28)), functional status (Health Assessment Questionnaire (HAQ) score), quality of life (Short-Form 36 (SF-36) physical and mental components), haemoglobin levels (Hb), erythrocyte sedimentation rate (ESR), hand radiographic erosions, and the use of prednisolone and disease modifying anti-rheumatic drugs (DMARDs) at study entry.
**Results:** 731 patients were studied of whom 491 were ACCP+RF+, 54 were ACCP+, 82 were RF+ and 104 were doubly negative. Mean disease duration of RA

prior to study entry was similar among the groups at 97.8–105.1 months (p=0.971) and mean disease duration before first DMARD was 38.8–42.7 months (p=0.966). 24.4% of the ACCP+RF+ patients were in remission (DAS-28 <2.6) compared to 36.6–39.4% in the other groups (p<0.05). ESR was higher (40.4mm/hour) in the ACCP+RF+ group compared to 30.6–30.9 mm/hour in the others (p<0.05). The use of prednisolone and number of DMARDs was higher in the ACCP+RF+ group (1.40±0.71) compared to the doubly negative group (1.13±0.59) (p<0.05). There were no differences in demographics, radiographic erosions, functional status and quality of life scores.

**Conclusions:** Patients who had dual positivity for ACCP and RF had lower remission rates and required more corticosteroid and DMARD treatment at baseline. However, this did not seem to have an impact on their functional status, quality of life and radiographic erosions. Future prospective studies would be useful to determine if the prognosis of patients with RA are affected by ACCP and RF positivity.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.3779

## AB0262 VERIFICATION OF ANTIBACTERIAL EFFECT OF SULFASALAZINE IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Sulfasalazine (SSZ) might have antibacterial effect, because it contains sulfa residue. However, its clinical usefulness in patients of rheumatoid arthritis (RA) has been unclear.

**Objectives:** Our aim was to evaluate whether SSZ could prevent bacterial infections especially in newly diagnosed RA patients.

**Methods:** The adult patients who were newly diagnosed with RA at St. Luke's International Hospital, Tokyo, Japan from January 2006 to December 2013 were included in this retrospective open cohort study. The patients were divided into two groups, either SSZ group in which the treatment was started with SSZ or non-SSZ group in which the treatment was started with DMARDs except for SSZ. The diagnosis of infections was defined by the prescription of antibiotics. We investigated whether SSZ group showed lower incidence rate of infections compared to non-SSZ group by multivariate logistic regression analysis for well-known risk factors for infections, such as age and other immunosuppressive DMARDs use.

**Results:** There were 179 eligible patients in SSZ group and 157 patients in non-SSZ group. Mean ages were 57.3±15.8 and 55.1±15.1 years old, and male percentages were 23.0 and 17.8% in SSZ group and non-SSZ group, respectively. Percentages who had received additional immunosuppressive agents including csDMARDs and bDMARDs were 68.2 and 86.0% for each groups. Incidence rate of bacterial infection was prone to be lower in SSZ group than in non-SSZ group in univariate analysis (17.7 per 100 person-years vs. 26.3 per 100 person-years, p=0.07). However, prevalence of infections in SSZ group did not differ from that of non-SSZ group both in univariate and multivariate analysis (0.30 vs. 0.30, p=0.49, 95% CI 0.51–1.37).

**Conclusions:** SSZ did not prevent bacterial infections in newly diagnosed RA patients.

**Disclosure of Interest:** A. Kitada Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, C. Min Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, Y. Kataoka Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, S. Kaneshita Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, M. Suda Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, K. Takasugi Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, Y. Ohara Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, R. Rokutanda Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, H. Shimizu Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, T. Tsuda Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, M. Kishimoto Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, K. Yamaguchi Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none, M. Okada Shareholder of: none, Grant/research support from: none, Consultant for: none, Employee of: none, Paid instructor for: none, Speakers bureau: none

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## AB0263 AGREEMENT BETWEEN DAS28, ACR/EULAR, SDAI, CDAI AND ULTRASOUND REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING BIOLOGICAL TREATMENT IN ROUTINE CARE

C.H. Brahe[1], L. Terslev[1], S. Krabbe[1], M. Østergaard[1], H. Røgind[1], H.S. Jensen[1], A. Hansen[1], J. Nørregaard[1], S. Jacobsen[2], K. Ellegaard[2], V. Fana[1], L. Juul[1], T. Huynh[1], D. Jensen[1], N. Manilo[1], K. Asmussen[1], P.B. Frandsen[1], S.T. Pedersen[1], N.S. Krogh[3], M.L. Hetland[1]. *[1]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet; [2]The Parker Institute, Copenhagen University Hospital at Frederiksberg; [3]ZiteLab ApS, Copenhagen, Denmark*

**Background:** Different remission criteria are available for patients with rheumatoid arthritis (RA). None of the criteria includes imaging remission, even though studies have shown that many RA patients in sustained clinical remission have synovitis detectable by ultrasound (US), i.e. grey scale synovial hypertrophy and/or Doppler signal in the synovium.

**Objectives:** We aimed to investigate the agreement between different clinical remission criteria and remission defined by US in patients with RA receiving biological therapy in routine care.

**Methods:** A total of 117 RA patients in sustained remission (i.e. DAS28 ≤2.6 for ≥1 year and no radiographic progression the last year) on biological therapy were recruited. All patients underwent US of 24 joints for grading of grey scale (GS) synovial hypertrophy (0–3) and synovial Colour Doppler activity (CD) (0–3). Imaging remission was defined in two ways: either GS=0 and CD=0 in all 24 joints, or GS≤1 and CD=0 in all 24 joints.

**Results:** Baseline characteristics are shown in table 1. At baseline patients received the following disease-modifying antirheumatic drugs (DMARDs): methotrexate (MTX; 72%), sulphasalazine (3%), azathioprine (2%), leflunomide (2%), no DMARDs (21%) and the following treatment with biological therapy: abatacept (2%), adalimumab (28%), certolizumab (3%), etanercept (28%), golimumab(3%), infliximab (27%), tocilizumab (9%).

For patients fulfilling DAS28 remission criteria, US defined remission was present in 9% (GS=0 and CD=0 in all 24 joints, termed "very strict" US remission) or 29% (GS ≤1 per joint and CD=0 in all 24 joints, termed "strict" US remission) and 24% had CD>1 in at least 1 joint (table 1). For patients fulfilling other criteria for clinical remission (CDAI, SDAI and ACR/EULAR remission), patients were in very strict US remission in 12%, 12% and 10%, respectively and in strict US remission in 28%, 29% and 20%, respectively. CD activity >1 in at least 1 joint was present in 22%, 25% and 22% of patients, respectively. The anatomical distribution of the GS synovial hypertrophy was 31% in metacarpophalangeal joints, 27% in metatarsophalangeal joints, 19% in wrists, 10% in knees, 7% in elbows and 6% in ankles. Thus, 33% of the total GS synovial hypertrophy was observed in the feet, which are not included in the DAS28 remission criteria.

There were no significant differences in US findings (GS or CD) between patients

Tabel 1: Baseline characteristics and agreement between clinical remission and ultrasound remission

| Characteristics | DAS28 remission | CDAI remission | | | SDAI remission | | | ACR/EULAR remission | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Yes (n= 117) 100% | No (n=52) 27% | Yes (n=85) 73% | P-values | No (n=34) 29% | Yes (n=83) 71% | P-values | No (n=68) 58% | Yes (n=49 42% | P-values |
| Age (years) | 60 (48-68) | 61 (48-67) | 60 (48-68) | 0.8 | 61 (50-68) | 60 (48-68) | 0.6 | 60 (48-68) | 60 (48-67) | 0.6 |
| Female gender | 84% | 71% | 87% | 0.6 | 85% | 70% | 0.4 | 74% | 87% | 0.2 |
| IgM-RF positive | 66% | 66% | 66% | 0.3 | 65% | 66% | 0.3 | 66% | 65% | 0.7 |
| X-ray erosions | 70% | 78% | 67% | 0.5 | 82% | 65% | 0.2 | 78% | 59% | 0.06 |
| Disease duration (years) | 11 (7-18) | 12 (9-26) | 11 (6-16) | 0.02 | 12 (8-23) | 10 (6-16) | 0.05 | 12 (7-20) | 10 (6-15) | 0.1 |
| SJC28 | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0.1 | 0 (0-0) | 0 (0-0) | 0.1 | 0 (0-0) | 0 (0-0) | 0.8 |
| TJC28 | 0 (0-0) | 0 (0-1) | 0 (0-0) | <0.001 | 0 (0-1) | 0 (0-0) | <0.001 | 0 (0-0) | 0 (0-0) | 0.008 |
| CRP (mg/dL) | 5 (2-6) | 5 (2-9) | 5 (3-6) | 0.6 | 5 (3-9) | 5 (3-5) | 0.008 | 5 (3-6) | 5 (3-6) | 0.4 |
| Pt. VAS global | 13 (4-30) | 37 (26-43) | 8 (3-17) | <0.001 | 35 (25-40) | 8 (3-15) | <0.001 | 25 (17-36) | 4 (1-7) | <0.001 |
| Total GS score | 7 (3-13) | 8 (3-14) | 7 (3-13) | 0.7 | 8 (4-13) | 7 (3-13) | 0.5 | 8 (3-17) | 6 (3-10) | 0.4 |
| Total CD score | 1 (0-2) | 0 (0-3) | 0 (0-2) | 0.8 | 0 (0-2) | 0 (0-2) | 0.8 | 0 (0-2) | 0 (0-2) | 0.9 |
| CD = 0 | 34% | 59% | 43% | 0.5 | 59% | 43% | 0.8 | 57% | 61% | 0.5 |
| CD ≤1 | 76% | 72% | 78% | 0.5 | 79% | 75% | 0.8 | 75% | 78% | 0.8 |
| GS =0 | 10% | 6% | 12% | 0.4 | 3% | 13% | 0.09 | 10% | 10% | 0.9 |
| GS ≤1 | 39% | 41% | 39% | 0.9 | 38% | 40% | 0.9 | 44% | 33% | 0.2 |

| Characteristics | US remission GS=0 and CD=0 | | | US remission GS≤1 and CD=0 | | |
|---|---|---|---|---|---|---|
| | No (n=106) 91% | Yes (n=11) 9% | P-values | No (n=83) 71% | Yes (n=34) 29% | P-values |
| Age (years) | 61 (48-68) | 49 (46-63) | 0.2 | 62 (50-69) | 51 (45-61) | 0.002 |
| Female gender | 87% | 82% | 0.5 | 84% | 74% | 0.4 |
| IgM-RF positive | 67% | 55% | 0.4 | 70% | 62% | 0.3 |
| X-ray erosions | 73% | 46% | 0.1 | 76% | 59% | 0.3 |
| Disease duration (years) | 11 (7-19) | 6 (4-12) | 0.01 | 12 (8-20) | 11 (5-14) | 0.02 |
| SJC28 | 0 (0-0) | 0 (0-0) | 0.2 | 0 (0-0) | 0 (0-0) | 0.9 |
| TJC28 | 0 (0-0) | 0 (0-0) | 0.4 | 0 (0-0) | 0 (0-0) | 0.9 |
| CRP (mg/dL) | 5 (2-6) | 5 (3-5) | 0.4 | 5 (3-8) | 5 (3-5) | 0.8 |
| Pt. VAS global | 13 (4-26) | 10 (6-18) | 0.5 | 11 (4-25) | 16 (7-28) | 0.3 |
| Total GS score | 8 (4-14) | 3 (0-9) | NA | 9 (5-15) | 2 (0-3) | NA |
| Total CD score | 1 (0-2) | 0 (0-0) | NA | 1 (0-2) | 0 (0-0) | NA |
| CD = 0 | 50% | 100% | NA | 37% | 100% | NA |
| CD ≤1 | 79% | 100% | NA | 68% | 100% | NA |
| GS =0 | 1% | 100% | NA | 1% | 32% | NA |
| GS ≤1 | 33% | 100% | NA | 15% | 100% | NA |

Values are median (IQR) unless otherwise indicated. Mann-Whitney U test for continuous data. Pearson-Chi square test for binomial data. US included bilateral scan of the following 24 joints: elbows, wrists, metacarpophalangeal joints 2-5, knees, ankles, metatarsophalangeal joints 2-5. NA: Non applicable

in remission vs patients not in remission, no matter which clinical remission criteria were used.
**Conclusions:** Subclinical synovitis was frequently detected by US in RA patients treated with biological drugs in routine care showing poor agreement between the clinical remission criteria and US remission. Further studies are needed to evaluate the benefit of US remission as a goal for treat to target strategies on patient-reported outcomes and radiographic progression.
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## AB0264 FATTY LIVER INDEX PREDICTS GLUCOSE METABOLISM DISTURBANCE IN INFLAMMATORY ARTHRITIS PATIENTS

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**Background:** Several studies reported an increased prevalence of nonalcoholic fatty liver disease (NAFLD) in subjects with rheumatic diseases [1]. NAFLD can be evaluated non-invasively and reliably by magnetic resonance spectroscopy, computed tomography and ultrasound. However, these methods are time consuming or associate with high costs. Thus, alternative estimates of NAFLD based on routine risk factors and serum biomarkers have been proposed [2]. Interestingly, these surrogate indices associate with insulin resistance and risk of type 2 diabetes in the general population [3]. To date, no data are available about a possible association between surrogate indices of NAFLD and glucose metabolism disturbance in the setting of inflammatory arthritis.
**Objectives:** To analyze the relationship between sierological markers of liver fat accumulation and 2-hours plasma glucose concentration (2hPG) in a population of rheumatic disease subjects undergoing an oral glucose tolerance test (OGTT).
**Methods:** For our aim, we recruited 45 subjects diagnosed with inflammatory arthritis (rheumatoid arthritis, RA; psoriatic arthritis, PsA; undifferentiated spondiloarthritis, uSpa). Exclusion criteria were: current diabetes, severe renal and hepatic disease. After overnight fasting, OGTT was performed by oral administration of a standard dose of 75 g anhydrous glucose dissolved in water. Plasma glucose levels were measured in a fasting state and again two hours after its administration. Other laboratory analyses included: lipids, complete blood count, erythrocyte sedimentation rate (ESR), high sensitivity C-Reactive Protein (hsCRP), serum alanine transaminase (ALT), aspartate transaminase (AST) and and gamma-glutamyltransferase (GGT). The liver fat score (LFS), the hepatic steatosis index (HSI) and fatty liver index (FLI) were employed as serum NAFLD indices as previously described [2]. Pearson's or Spearman's correlation analyses were used as appropriate to test the associations between continuous variables. Not normally distributed variables were log-transformed before analysis.
**Results:** 20 AR, 15 PsA and 10 uSpa composed our sample. Of these 16 were males and 29 were females. The mean age was 54±9.1. According to the OGTT results: 31 subjects were classified as NGT, 9 had IGT and 5 had diabetes. In simple correlation analyses, Ln2hPG significantly correlated with Age ($r=0.48$, $p=0.001$), BMI ($r=0.44$, $p<0.01$), HSI ($r=0.43$, $p<0.01$), LFS ($r=0.37$, $p=0.01$) and FLI ($r=0.54$, $p<0.001$). After controlling for BMI and age only FLI associated with 2hPG.
**Conclusions:** Our data demonstrate an association between 2hPG and NAFLD surrogate indices in a population of inflammatory arthritis patients. Among these FLI seems better associate with glucose metabolism disturbance.
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## AB0265 NON-CANONICAL NF-κB SIGNALING IN MICROVESSELS OF ATHEROSCLEROTIC LESIONS IN CORONARY ARTERIES IS ASSOCIATED WITH INFLAMMATORY CELL INFILTRATION AND MYOCARDIAL INFARCTION

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**Background:** Patients with chronic inflammatory diseases (CID) have higher risk of developing cardiovascular disease which may be in part due to increased systemic inflammatory burden. In atherosclerosis, extensive neovascularization is associated with plaque instability and increased chance of myocardial infarction (MI). We have established that non-canonical NF-κB signaling, and its central regulator NF-κB inducing kinase (NIK) in endothelial cells (EC) contributes to angiogenesis in synovial tissue of patients with various types of arthritis. Thus, we hypothesized that NIK$^+$ EC may also contribute to neovascularization in atherosclerotic lesions.
**Objectives:** Evaluate the expression of NIK in microvessels in atherosclerotic lesions from patients with and without CID and determine if it is associated with inflammatory cell influx, systemic inflammation or involvement of coronary arteries in MI.
**Methods:** Atherosclerotic lesions from 11 individuals with CID along with 11 matched controls, isolated from parts of the coronary artery implicated in MI (CA+) or not (CA-), were immunohistochemically stained with antibodies against NIK, CD31/34 (EC), myeloperoxidase (neutrophils), CD45 (lymphocytes), CD68 (macrophages) and tryptase (mast cells). NIK vessel density (NIK$^+$VD) and immune cell density (ICD) were subsequently calculated.
**Results:** NIK$^+$EC were present in atherosclerotic lesions of all coronary arteries. NIK$^+$VD significantly correlated with ICD of all characterized immune cells: leukocytes ($r=0.5227$; $p<0.0001$), macrophages ($r=0.3397$, $p<0.0001$), mast cells ($r=0.4205$, $p<0.0001$) and neutrophils ($r=0.2129$, $p=0.0016$). No significant differences were found in NIK$^+$VD in CID patients versus healthy, however, influx of leukocytes and macrophages per NIK$^+$ microvessel was significantly higher in CID lesions. Increased NIK$^+$ microvessels were also noted in CA+ as compared to CA- tissues ($p=0.0139$) in both healthy and CID patients.
**Conclusions:** NIK$^+$ microvessels are present in high numbers in atherosclerotic lesions and are strongly associated with the influx of inflammatory cells. Systemic inflammation is not a prerequisite for activation of this pathway in EC in atherosclerotic lesions, but our findings suggest that non-canonical NF-κB signaling is more pronounced in patients with CID resulting in the attraction of more immune cells that may further enhance progression of atherosclerotic lesions. Since activation of the non-canonical NF-κB pathway in EC induces angiogenesis and NIK$^+$ vessels are increased in coronary arteries associated with MI, non-canonical NF-κB signaling in EC may drive neovascularization and plaque instability, thus increasing the chance of developing a (fatal) MI.
**Disclosure of Interest:** None declared
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## AB0266 TREAT-TO-TARGET BIOLOGIC THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS HAS A SAFER PROFILE COMPARED TO DELAYED INITIATION OF BIOLOGICS

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**Background:** Rheumatoid arthritis (RA) is a chronic disease with involvement of small and large joints. Treat-to-target strategy aims to improve the outcome and rapidly reduce disease activity by using properly and aggressively all the therapeutic options.
**Objectives:** To estimate the safety of bDMARDs in RA patients, when administered according to international recommendations, compared to delayed initiation of bDMARDs in usual care.
**Methods:** All adverse events (AEs) and their severity were recorded. Cox proportional-hazards models were performed examining the association of treatment groups, with the risk of 1st AE. A separate analysis was performed for new cases of cancer during administration of bDMARDs.
**Results:** There were 250 patients in usual care and 113 patients in T2T group (*Table 1*). Delayed bDMARD administration was accompanied by more frequent and severe AEs, compared to T2T strategy (*Table 2*). In the 1st group 155 patients were recorded with at least one AE (56 patients with serious), of which 80 patients had at least one infection (30 a serious one). In T2T group, there were 47, 9, 11 and 2 patients with at least one AE, serious AE, infection and serious infection respectively. The IRR for the T2T group was 0.78 for the 1st AE, 0.56 for the 1st serious AE, 0.41 for the 1st infection and 0.23 for the 1st serious infection. *Table 3* illustrates the AEs (irrespective of AEs per person) in both groups.
A greater incidence of cancer was noticed in patients of usual care group. There were 15 new cases of cancer (non-melanoma skin=2 lung=2 lymphoma=5 breast=2 urinary tract=3 blood=1) compared with only one (urinary tract) in T2T group. The IR of the 1st group was 1.99/100PY compared to 0.4/100PY of the 2nd group ($p=0.027$). Nine of 16 cases had no risk factors for cancer. Mean

duration of sDMARDs, before bDMARDs, was 113 months and mean duration of bDMARDs 41 months.
The risk of 1st infection (irrespective of severity) was significantly higher for the usual care group compared to T2T group (p=0.002 for 1st infection, p=0.03 for 1st serious infection, *Figure 1*). The risk for 1st AE and serious AE was marginally non-significant (p=0.069 and 0.077 respectively) in usual care group.
After controlling for potential confounders, the risk for a serious AE remained significantly higher for usual care group (HR=0.42, p=0.041) (*Table 4*). Patients in T2T group were more likely to have a reduced risk for infection (HR=0.49 for 1st infection, HR=0.24 for serious one), although the findings were marginally non-significant (p=0.052 and 0.065 respectively).
Extra-articular manifestations increased the risk for any AE (irrespective of severity), progression of age was important for the 1st AE (mild or serious) and 1st serious infection, whereas patients with ESR >40mm/h were more vulnerable to infections.
**Conclusions:** Frequency and severity of AEs, especially infections, were substantially reduced in T2T group. A greater incidence of cancer was noticed in patients with delayed administration of bDMARDs.
**Disclosure of Interest:** None declared
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## AB0267 NO REMARKABLE DIFFERENCES ON SONOGRAMS OF WRIST, METACARPOPHALANGEAL AND PROXIMAL INTERPHALANGEAL JOINTS BETWEEN RHEUMATOID FACTOR NEGATIVE RHEUMATOID ARTHRITIS AND RHEUMATOID FACTOR POSITIVE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** It is reported RF-negative Rheumatoid Arthritis (RF-nRA) had distinct genetic background and pathogenesis mechanism leading to different prognosis and therapy response from RF-positive Rheumatoid Arthritis (RF-pRA). Ultrasound (US) of wrist, metacarpophalangeal (MCP) and proximal interphalangeal joints (PIP) which are the classical zone of RA involvement might verify whether the joint destruction would be different in both group.
**Objectives:** To verify whether the joint destruction would be different in RF-negative Rheumatoid Arthritis (RF-nRA) and RF-positive Rheumatoid Arthritis (RF-pRA) patients.
**Methods:** It is a blinded, controlled trial. All cases including RF-nRA group and RF-pRA group satisfied 2009 classification criteria with abnormal swollen or pain in wrists, AMCPs or PIPs. RF-pRA group should have x-ray or MRI evidences The most affected side of joints including the 2nd, 3rd MCPs, Athe 2nd, 3rd PIPs and wrists were examined. US examination and scoring system referred to Backhaus's US7 scoring system related regions. In addition, synovitis in gray-scale US (GSUS) on dorsal side of the 2nd, 3rd MCPs and PIPs (0–3 grade) and bone erosions on dorso-median, ulnar, palmo-median sides (0 or 1 if absent/present) of wrist in GSUS were also counted in to get a total of 0–106 scores. DAS 28 (3 variables) was employed to divide each of the 2 groups into 4 subgroup to assess the sonograms in different disease activity levels.
**Results:** 1) 15 RF-nRA cases and 41 RF-pRA cases were enrolled. Mean age (53.8yrs, 57.2yrs), female-male ratio(29:12,16:9), and disease duration(7.53,7.88) of 2 groups were described as above. DAS-28>5.1 subgroups in both 2 groups had the most cases (RF-nRA/RFpRAremission:low:moderate:high=3:2:4:6/1:5:15:20).
2) DAS-28 had highly positive correlation(r=0.95) to US sum scores while poor positive correlation with synovitis GDUS sum scores or synovial Power Doppler(PD) signals sum scores alone.(r=0.57,0.62)
3) No significant differences between RF-nRA and RF-pRA in aspect of synovitis in GDUS, synovial PD signals, and bone erosions in GDUS in wrists, MCPs, PIPs respectively in different levels.
**Conclusions:** Our study has not found any distinctions in most affected joints between RF-nRA and RF-pRA patients.
**Disclosure of Interest:** None declared
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## AB0268 CORONARY ARTERY STENOSIS IN PATIENTS WITH RHEUMATIOD ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a systemic inflammatory disease characterized by increased cardiovascular morbidity and mortality. Coronary angiography (CAG) is the gold standard to identify and assess the degree of coronary artery (CA) involvement. CA diseases (CAD) development in RA patients (pts) is associated with the accumulation of traditional risk factors and immunological disorders.
**Objectives:** To determine the incidence and predictors of CA stenosis development in RA pts with suspected CAD.
**Methods:** To analyze 63 RA pts (male/female 25/38, mean age 58 [52; 63] years, with long-standing RA (10,5 [7; 23] years), moderate to high clinical disease activity DAS 28 =4,7 [3,3; 5,8]). All pts underwent CA angiography. Multiple regression analysis was used to determine the risk of CA stenosis in RA pts.
**Results:** CA stenosis was detected in 22 (35%) of the 63 pts, male/female 15/7 (I group), including single vessel involvement - in 15 (68%) pts, three-vessel damage - in 7 (32%) pts, without cases of documented two vessels lesions. The most common stenosis location was the middle segment of the left anterior descending artery (11 (50%) pts), the right coronary artery (RCA) was more rarely involved, and RCA stenosis was observed in 7 (33%) pts, stenosis of the middle RCA segment - in 9 (41%) out of 22 pts. In 41 (65%) out of 63 pts hemodynamically insignificant stenoses (<50%) or intact CA was documented, male/female 10/31 (II group). Groups were comparable in terms of age, disease duration and DAS 28 scores. Males prevailed in Group 1: 68% vs 24% in Group 2 ($p<0,05$). Detection rates of carotid artery atherosclerotic plaques and thickening of the intima-media were similar in Groups 1 and 2 (19/16% and 53/56% pts). The prevalence of traditional risk factors was also similar in both groups: hypertension - 77% and 88%, dyslipidemia - 26% and 33%, diabetes mellitus - 5% and 17%, smoking – 45% and 17%, physical inactivity - 58% and 42%, obesity - 45% and 32% pts in Group 1 and 2, respectively. Serum HDL cholesterol concentrations in Group 1 (1,2 [1,0;1,5]mmol/l) was lower, than in Group 2 (1,55 [1,3;2,0]mmol/l, $p$ =0,03), while concentrations of cholesterol, LDL cholesterol and triglycerides did not differ in between the groups. There were no differences in therapeutic and dosing regiments (disease-modifying antirheumatic drugs (DMARDs), GEBAs and oral glucocorticoids (GCs)), with the only exclusion: the duration of GCs therapy was higher in Group 1 pts (5,3 [4;12] years) vs (3,1 [1,5;8], $p<0,05$) Group 2. The multiple regression analysis did not establish any direct relationship between CA stenosis and gender, age, RA activity, cholesterol and LDL cholesterol concentrations, use of DMARDs and oral GCs. Age was the strongest, but not statistically significant variable predicting stenosis (odds ratio (OR) 0,85; 95% CI [0,72–1,0], $p$ =0,05), with the following HDL-C <1,2mmol/L for women and <1,0 mmol/L for men (OR 0,82; 95% CI [0,64–0,90], $p$ =0,09).
**Conclusions:** Male gender, low HDL cholesterol levels and long-term GCs use seem to increase the risk of coronary artery stenosis in RA pts.
**Disclosure of Interest:** None declared
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## AB0269 CARDIOVASCULAR RISK ASSESSMENT IN PERSONS WITH AUTOIMMUNE RHEUMATIC DISEASE: A PILOT STUDY OF NON-INVASIVE ARTERIAL HEALTH TESTING

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**Background:** Persons with rheumatoid arthritis (RA) have increased mortality attributable to atherosclerotic cardiovascular disease (ASCVD) events. While a heightened risk of ASCVD events exists in patients with RA, we have yet to uncover an accurate method for estimating that risk. It is unknown how the current state of disease activity affects arterial function in early subclinical ASCVD.
**Objectives:** Our goal is to determine the effect of the current state of inflammatory disease activity, as measured by the Simplified Disease Activity Index (SDAI) and Health Assessment Questionnaire (HAQ) score, on arterial health in patients with RA, using an innovative non-invasive testing package developed at Mayo Clinic in Rochester, Minnesota.
**Methods:** We recruited a cohort of 50 patients with RA as defined by the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria, and conducted non-invasive arterial health testing on the same day as a rheumatologic assessment of clinical disease activity, which was classified in terms of tender/swollen joint counts, SDAI score and HAQ score. This arterial health testing package includes measurements of endothelial function (brachial artery reactivity testing, BART), arterial stiffness (pulse wave velocity, PWV), and early atherosclerosis (carotid intima-media thickness, CIMT, and carotid plaque presence).
Statistical analysis was performed with Spearman Correlation Coefficients between the rheumatologic disease activity scores and arterial health testing parameters.
**Results:** Our 50 patients had mean (SD) disease duration of 7.0 (±4.0) years, mean age of 57.2 years, and 38 (76%) were female. The average disease activity was moderate, with mean (SD) SDAI of 21.4 (±17.4); 27 patients had either moderate or high disease activity by SDAI. A statistically significant correlation emerged between the SDAI score and the following measures: corrected aortic augmentation index (r=0.35, p=0.012); and the CIMT of the right common carotid artery (r=0.28, p=0.048). The correlation between SDAI and aortic PWV was borderline (r=0.26, p=0.067). The HAQ score correlated significantly with the corrected aortic augmentation index (r=0.33, p=0.019), but not with PWV or CIMT measures of right and left common carotid artery.
**Conclusions:** We identified significant correlations between SDAI, and measures of arterial stiffness (i.e., corrected aortic augmentation index), and subclinical atherosclerosis (i.e., CIMT). The HAQ score significantly correlated with the corrected aortic augmentation index. This study suggests that the current state of disease activity in RA does significantly influence several measures of arterial health using this testing package.
**Disclosure of Interest:** None declared

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## AB0270 WORSENING OF DIAGNOSTIC DELAY IN EARLY ARTHRITIS DURING THE LAST 10 YEARS: A SINGLE CENTER EXPERIENCE

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**Background:** The reduction of the diagnostic delay in patients with early arthritis, in order to start treatment as early as possible and to improve outcomes, has required a considerable effort during the last 15 years.
**Objectives:** To evaluate the diagnostic delay, between 2004 and 2015, at our Early Arthritis Clinic (EAC).
**Methods:** 943 patients with rheumatoid arthritis (RA) (according to 1987 and/or 2010 classification criteria) or undifferentiated arthritis (UA) evaluated at our EAC between September 2004 to September 2015 were recruited (disease duration <12 months) and divided into 2 groups according to the time of diagnosis (group 1: 2004–2009; group 2: 2010–2015). A comparison among demographic features, diagnostic delay and disease activity (DAS28) at first evaluation was performed.
**Results:** A total of 943 patients were evaluated: 469 patients into the group 1 (74.4% women, mean age 58 ys) vs. 474 patients into the group 2 (74.7% women, mean age 57 ys). No differences were found in terms of serologic positivity and diagnosis. At baseline, patients in the group 2 showed lower disease activity as for DAS28 (4.86±1.17 vs. 4.32±1.24; p=0.0001), number of tender joints (6 IQR 2–11 vs. 4 IQR 2–8; p=0.0001), swollen joints (6 IQR 4–11 vs. 4 IQR 2–7; p=0.0001), ESR (22 IQR 13–40 vs. 16,5 IQR 8–33; p=0.0001). In contrast, patients in the group 1 showed lower time from the onset of symptoms to the diagnosis (111 days IQR 67–200 vs. 129 IQR 77–228; p=0.008). Data about the diagnostic delay comparing DAS28 categories are showed in figure 1: particularly in the group 2 there was a reduction in the number of patients in high disease activity-DAS28 who have the diagnosis established within the first 90 days after the onset of the disease (p=0,0026). 40% of patients in group 1 vs. 31% in group 2 had the diagnosis established within 90 days (p=0.005); however, the delay from the referral to the first evaluation at our EAC was similar in the two groups (21 days IQR 12–31 vs. 21 IQR 14–29; p=ns).

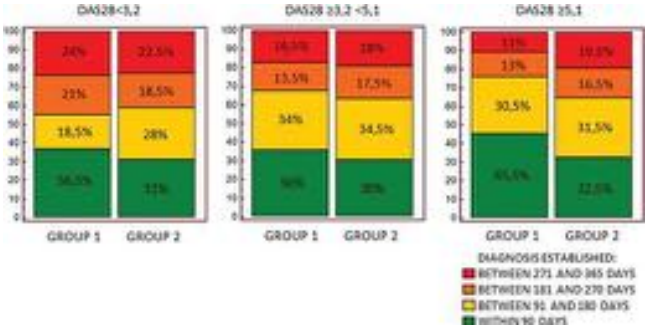



Figure 1

**Conclusions:** Currently, about 70% of the diagnosis is still not made within the so-called window of opportunity (90 days from the onset of symptoms). Moreover, a slight but significant worsening in the diagnostic delay has been observed; the delay doesn't seem to be related neither with time elapsing from referral to the first evaluation at the EAC nor to a lower disease activity at the beginning. Education programs at patients' and general practitioners' level should be implemented in order to reduce the delay and further improve the outcome.
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**Disclosure of Interest:** None declared
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## AB0271 EFFECTS OF GLUCOCORTICOIDS ON ENDOTHELIAL FUNCTION: FOCUS ON RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is the most common systemic autoimmune disease characterized by reduced life expectancy due to accelerated atherogenesis. Endothelial dysfunction (ED) precedes and initiates atherosclerosis, and its correction is associated with reduced CV risk. ED is present in RA and appears as a seminal target for reducing CV risk in RA. Despite the dramatic changes that occurred in the treatment approach in RA, majority of patients still use glucocorticoids (GCs). The potential harmful CV effects of GCs are "well-known" in the general population. In inflammatory diseases such as RA, the effects of GCs on CV risk is still a matter of debate. On the one hand, GC might increase CV risk by increasing CV risk factors but on the other hand, GC might reduce CV risk by decreasing the systemic and/or vascular inflammation.
**Objectives:** To provide the available data regarding the effects of GC on endothelial function, with a special focus on RA.
**Methods:** Systematic review of the literature on the PubMed database with the following keywords: "Glucocorticoids", "rheumatoid arthritis", "endothelial function" and "vascular function".
**Results:** In the vascular system, GC receptors are expressed by intact arteries, cultured vascular smooth muscle cells (VSMC) and endothelial cells. In physiological conditions, experimental data provide evidence of harmful effects of GCs on endothelial function, due to decreased Nitric oxide synthase activity/expression, decreased production of endothelium-derived hyperpolarizing factor (EDHF) and prostacyclin, the three main vasorelaxant endothelium-derived factors, associated with increased production of endothelin-1, an endothelium-derived vasoconstrictor. These experimental data were not unanimously confirmed by the few studies in healthy controls, which reported negative or not effect of GCs on endothelial function. Effect of GCs is totally different in inflammatory conditions in which GC reduced endothelial dysfunction and slowed progression of atherosclerotic plaques in animal models. Only 6 clinical studies were performed in RA. The available data suggested that low dose GC (5 mg/d) did not change endothelial function while a high dose for a short period (7 days) improved endothelial function in RA patient. No harmful effect of GC on endothelial function were reported in RA.
**Conclusions:** Data from experimental models highlighted the Janus face of GCs since they can exert deleterious effects on endothelial function when applied in "normal" cells/animals although they seem to be protective under inflammatory conditions. In RA patients, data are scarce and highly controversial due to methodological weaknesses. However, contrary to common believe that GCs deteriorate CV function, no effect and even positive effect of GCs on endothelial function have been reported. As more RA patients are starting GCs early in their disease course, there is an urgent need to perform clinical trials specifically-designed to define the best GCs strategy to prevent CV risk in RA.
**Disclosure of Interest:** None declared
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## AB0272 ANTI-RHEUMATIC TREATMENT IS NOT ASSOCIATED WITH REDUCTION OF PENTRAXIN 3 (PTX3) IN RHEUMATOID ARTHRITIS (RA), PSORIATIC ARTHRITIS (PSA) AND ANKYLOSING SPONDYLITIS (AS)

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**Background:** PTX3, an important component of the innate immune system,has been proposed as a useful biomarker of inflammation and cardiovascular (CV) risk, but its role in inflammatory rheumatic diseases (IRDs) is still uncertain [1,2].
**Objectives:** The aim of this study was to examine if methotrexate (MTX) and/or anti-tumor necrosis factor treatment (anti-TNF) treatment reduced serum PTX3 (s-PTX3) levels in IRDs (RA, PsA and AS), and if s-PTX3 levels were related to other markers of inflammation and to endothelial function (EF).

| | IRD (n=114) | RA (n= 64) | PsA (n=30) | AS (n= 20) |
|---|---|---|---|---|
| Number of patients treated with MTX monotherapy | 50 | 34 | 16 | 0 |
| PTX3 (ng/ml), Baseline | 3.9 (1.1-22.1) | 3.8 (1.2-22.1) | 4.2 (1.1-14.7) | 4.0 (1.9-8.5) |
| PTX3 (ng/ml), 6 weeks | 3.4 (0.7-11) | 3.3 (0.7-10.3) | 4.1 (0.9-11.1) | 3.2 (1.6-7.4) |
| PTX3 (ng/ml), 6 months | 3.9 (1.2-10.2) | 3.8 (1.2-9.3) | 4.4 (1.3-10.2) | 3.4 (1.5-8.4) |
| CRP (mg/L), Baseline | 8 (1-157) | 8 (1-78) | 5 (1-99) | 10 (1-157) |
| CRP (mg/L), 6 weeks | 2 (1-54) | 2 (1-54) | 3 (1-23) | 1 (1-34) |
| CRP (mg/L), 6 months | 2 (1-67) | 2 (1-67) | 2 (1-20) | 1 (1-14) |
| ESR (mm/h), Baseline | 13.0 (1-87) | 18.5 (1-81) | 8 (2-48) | 11 (2-87) |
| ESR (mm/h), 6 weeks | 7 (1-62) | 10.5 (2-62) | 6 (2-37) | 4 (1-12) |
| ESR (mm/h), 6 months | 7(2-37) | 9.5 (2-37) | 6 (2-22) | 3 (2-23) |

Values are presented as median (range).Reference range for s-PTX3 in serum are 1 ng/ml to 3 ng/ml.

**Methods:** From the biobank of PSARA, an observational study, we examined samples from 114 IRD patients starting with either MTX or anti-TNF with or without MTX (anti-TNF±MTX) due to active disease, who completed a 6 months follow up. s-PTX3 (enzyme-linked immunosorbent assay), EF (finger plethysmography) and established inflammatory biomarkers were evaluated at baseline and after 6 weeks and 6 months of therapy.
**Results:** The s-PTX3 levels in IRD and all the diagnostic subgroups were above the upper limit of the reference range. In contrast to established inflammatory markers, in particular C- reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (all p-values $<0.05$), s-PTX3 levels did not change significantly after 6 weeks and 6 months of anti-rheumatic therapy (all $p>0.2$). The effect of MTX monotherapy and anti-TNF±MTX on s-PTX3 levels was similar. Changes in CRP, ESR and EF were not related to changes in s-PTX3 levels neither in univariate analyses nor in analyses adjusted for potential confounders.
**Conclusions:** IRD patients have increased s-PTX3 levels, which, in contrast to other inflammatory markers, do not seem to improve within 6 months of therapy with MTX and/or anti-TNF. Thus, in theory, s-PTX3 might reflect a persisting immune process, even a causal factor of the inflammation, not inhibited by the standard anti-rheumatic treatment. Furthermore, even though PTX3 is thought to be a strong predictor of CV prognosis, it was not related to EF.
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**Disclosure of Interest:** None declared
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## AB0273 DISEASE CHARACTERISTICS AND CHANGE OF ARTHRITIS ACTIVITY ACCORDING TO TREATMENT IN HEPATITIS B SURFACE ANTIGEN POSITIVE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) treatment may differ according to hepatitis B state and consequently bring about different outcome of arthritis. Only a small number of studies have addressed the differences in disease characteristics and treatment patterns of RA in relation to hepatitis B state. However, it has not yet been elucidated whether hepatitis B affects treatment outcome such as disease activity.
**Objectives:** We investigated possible differences in change of arthritis activity between RA patients according to concomitant hepatitis B virus (HBV) infection.
**Methods:** A retrospective analysis of 40 hepatitis B surface antigen (HBsAg)-positive RA patients and 112 HBsAg-negative RA patients was conducted. The longitudinal relationship between HBsAg-positivity and RA activity/medication use was analyzed using generalized estimating equations in regression models.
**Results:** There were no significant differences in group for baseline characteristics. In regression analysis, RA activity-related outcomes showed follow-up time-dependent improvement during study period. We observed significant interaction between time and HBsAg-positivity for disease activity score in 28 joints with 3 variables (DAS28–3; $P$ =0.026), that means decreases in DAS28–3 with time influenced by HBsAg-positivity. But this interaction did not remain significant after adjustment. For tender joints, erythrocyte sedimentation rate, and C-reactive protein levels, there were no interaction between time and HBsAg-positivity, while swollen joints showed significant interaction ($P$ =0.017). The time-association and group differences were not observed in alanine aminotransferase (ALT) level. Over all visits, HBsAg-positive patients were less likely to receive methotrexate (OR 0.09 [95% CI 0.04–0.19], $P$ <0.0001) and more likely to receive sulfasalazine (OR 3.67 [95% CI 1.94–6.95], $P$ <0.0001). In HBsAg-positive RA patients, initial hepatitis B state was related to use of DMARDs, especially methotrexate ($P$ =0.040). Hepatitis reactivation occurred in 4 patients (10%) in HBsAg-positive RA patients. Among the patients who experienced HBV reactivation, only one patient had received previous antiviral treatment at baseline, but the patient exhibited lower adherence to drug. All patients who experienced HBV reactivation showed positive HBV DNA at baseline. There were no cases of hepatic failure or death.
**Conclusions:** There were no significant differences over time in DAS28–3, tender joints, inflammatory markers, according to HBsAg-positivity, while swollen joints showed significant difference over time. ALT level did not showed time-association and group differences. HBsAg-positive RA patients were less likely to receive methotrexate and more likely to receive sulfasalazine.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1193

## AB0274 THE INTERDEPENDENCE BETWEEN CLINICAL FEATURES OF RHEUMATOID ARTHRITIS, THYROID GLAND FUNCTION, AND THE ANTI-HORMONAL ANTIBODIES

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**Background:** According to the common notions, rheumatoid arthritis (RA) is an immunopathological condition with complex autoimmune response, directed presumably to synovial tissue. Besides that, there are some organ involvements in RA, that can strongly affect the extent of the autoimmune reactions. One of this organs is thyroid gland, because changes of its function, either increase or decrease, modulate activity of immune cells and inflammation level on the whole. Production of antibodies, directed to T3 and T4, is a candidate mechanism of the thyroid involvement.
**Objectives:** The objectives of our study are detection of different thyroid conditions in RA including determination of lesion type and function assessment, as well as searching for interdependence between the clinical features of RA, type of thyroid involvement, and the level of the anti-hormonal antibodies.
**Methods:** The research was carried out in agreement with the principles of the World Medical Association Declaration of Helsinki (1997). Approval for the investigation was got from the Regional Medical Ethics Committee. We enrolled adult patients with RA, verified using ACR/EULAR criteria (2010). RA activity was determined by means of DAS28 index. Thyroid involvement was detected by clinical, ultrasound, and laboratory assessment, including TSH, free T3, free T4, and anti-TPO. Anti-T3 and anti-T4 antibodies were measured using ELISA and calculated in terms of optical density units (ODU). The positive cutoff values, 0.098 ODU for anti-T3 and 0.093 ODU for anti-T4, have been found using healthy controls (n=39). Results were expressed as means±standard errors, the differences were considered significant at $p<0.05$.
**Results:** 75 patients with RA have been enrolled, including 61 (81.4%) women and 14 (18.6%) men, their age was from 25 to 78 years. Mean RA activity was 3.2±1.4 DAS28 points. Different visceral involvements were detected in 20 (26.7%) cases, and 5 (6.7%) of them had an overt clinical picture of thyroid lesions. The signs and symptoms for 4 of them were similar to Hashimoto's thyroiditis with hyperfunction, the remaining one was complied to the mixed toxic goiter. All these 5 patients had low TSH and quite high DAS28 score (4.8±1.9). However, the prevalence of subclinical thyroid disorders in RA was considerably higher. Virtually all the patients (n=73) have been revealed anti-T3 (0.128±0.047 ODU) and/or anti-T4 antibodies (0.152±0.050 ODU). There was no relationship between these antibodies and organ involvement, other than thyroid gland; RF titers also had no significant influence. We found some rather unexpected dependencies of these markers with X-ray RA stages, as well as with RA activity. There was a clear trend of elevation of mean anti-T4 concentration together with higher Steinbrocker stage (p=0.034, ANOVA), the inverse tendency have been observed for anti-T3 (p=0.047, ANOVA). Correlations of DAS28 score with anti-T4 (r=0.525, p=0.031) and anti-T3 (r=-0.391, p=0.040) were also opposite. There was another significant inverse correlation of DAS28 score and TSH concentration (r=-0.330, p=0.046).
**Conclusions:** Our data suggest that though anti-T4 concentration is tended to be elevated, high RA activity can promote hyperthyroidism. This is probably due to either influence of these antibodies to T4 and T3 production, or immune disturbances caused by thyroid hyperfunction itself.
**Disclosure of Interest:** None declared
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## AB0275 DIFFERENCES IN THE CLINICAL EVALUATION OF JOINTS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SECONDARY SJÖGREN SYNDROME

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**Background:** Secondary Sjögren syndrome (sSS) is classified as a connective tissue disease characterized mainly by xerophthalmia and xerostomia, and accompanied by various autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus, scleroderma, vasculitis, mixed connective tissue disease, primary biliary cirrhosis or autoimmune thyroiditis.
**Objectives:** To investigate whether a difference exists between DAS28 from CRP and DAS28 from ESR in patients with rheumatoid arthritis (RA) and secondary Sjögren syndrome (sSS).
**Methods:** The study included patients with rheumatoid arthritis (RA) and secondary Sjögren syndrome (sSS). The inclusion criteria have been specified as follows: radiological confirmation of rheumatoid arthritis, presence of data on DAS28-CRP and DAS28-OB, presence of at least one subjective and one objective symptom of dryness, and also presence of specific antibodies or at least focus score one in biopsy.
**Results:** Disease activity score 28 (DAS28) was assessed using both ESR and CRP in 60 patients with RA and sSS and 59 patients with RA alone. Although concordance between these two methods was good (Cohen's kappa coefficient

κ=0.60, 95% of CI (0.45–0.75) in first group and κ=0,71, 95% of CI (0.56–0.86) in control group). In the group with RA and sSS mean value of DAS28-ESR=5.2, whereas mean value of DAS28-CRP=4.7 ($p<0.0001$). In the group with RA alone mean DAS-ESR=4,7 while mean DAS-CRP=4,6, no significant difference was identified. Moreover, in RA patients with sSS mean ESR=39mm/h compared with mean CRP at 25mg/dl. 79% of all patients demonstrated dysproteinemia. There were connections between higher ESR and dysproteinemia. In control group there were no significant difference between CRP and ESR.

| parameter | RA patients with sSS | RA patients |
|---|---|---|
| age [yr], mean (SD) | 57 (11) | 51,6 (13,7) |
| ESR [mm/hr], median | 34,5 | 15 |
| CRP [mg dl], median | 14 | 16 |
| VAS [mm], median | 51 | 60 |
| tender joints, median | 8 | 8 |
| swollen joints, median | 4 | 3 |
| DAS-28 from ESR, mean (SD) | 5.2 (1.3) | 4,7 (1,3) |
| DAS-28 from CRP, mean (SD) | 4.7 (1.2) | 4,6 (1,4) |

Table 1 Baseline characteristics of the patients with RA and sSS
SD – standard deviation.

**Conclusions:** Both DAS28-ESR and DAS28-CRP are useful outcome measures in RA. However, in patients with RA and sSS DAS28 should be evaluated based on CRP or SDAI.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5422

## AB0276 PSYCHOLOGICAL STATUS IS ASSOCIATED WITH HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) as one of the most common autoimmune diseases is known to be one of the leading causes of disability.
**Objectives:** This study aimed to investigate the relationship between psychological disorders (depression, anxiety and insomnia) and quality of life in patients with rheumatoid arthritis patients.
**Methods:** A total of 50 patients were included with the diagnosis of rheumatoid arthritis meeting ACR 1987 criteria, in a prospective study. In a questionnaire, the characteristics of the disease and sociodemographic patient were collected.
Also psychiatric assessment was done using the insomnia severity index score (ISI) and the Hospital Anxiety and Depression scale (HAD). In addition, patients answered a Health Assessment Questionnaire (HAQ) to assess their functional capacity and the SF-12 to evaluate the quality of life.
**Results:** The female was found in 80%, the average age was 52,8 years. The average duration of disease progression was 8,79 years (0,5–30). The mean value of the DAS 28 was 5,03 [1.7 to 7.9].
Extra-articular manifestations were reported in 72% of patients: secondary Sjögrens syndrome in 54%, osteoporosis in 42%, pulmonary fibrosis in 12%. 80% of patients received methotrexate and 38% of patients were treated with biotheraby.
Radiological destruction was observed in 96% of cases. Joint deformities were reported in 56% of cases. The most prevalent comorbidities in this population were anemia (28%), hypertension (18%), and diabetis (18%).
On the psychological level, 12% of patients had an anxiety, 6% had depression. According to the ISI, 34% of patients had Subthreshold insomnia, 40% had moderate insomnia and 6% had severe insomnia. The mean value of the HAQ was 1.49 (0.2–3).
A significant positive correlation was found between the disease activity and the presence of insomnia (p=0.019), the presence of depression (p=0.009) and anxiety (p=0.049). Also, we found a significant positive correlation between the HAQ and depression (p=0,003).
The mean value of the physical health was 40.51 (16–59.2) and for the mental health was 48.13 (26–60).
**Conclusions:** Psychiatric illness is a relatively common disorder in patients with RA, it affects their quality of life. The treatment of those patients must consider psychiatric disorders, as part of a global approach.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1535

## AB0277 COMPARISON BETWEEN INTIMA-MEDIA THICKNESS AND CORONARY ARTERY TOMOGRAPHY IN SUBCLINICAL ATHEROSCLEROSIS DETECTION IN RHEUMATOID ARTHRITIS

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**Background:** Intima media thickness (IMT) and coronary artery calcification (CAC) quantification using multidetector computed tomography (MDCT) scanner are useful in detecting subclinical atherosclerosis and are good surrogate markers of cardiovascular morbidity and mortality in general population and in rheumatoid arthritis (RA)
A good correlation between these methods has been reported in RA, being CAC a slightly more sensitive technique (1)
**Objectives:** Our aim is to determine the value of IMT that better predicts the presence of coronary atherosclerosis, using CAC as reference and assuming CAC value of 100 as the cut-off point indicating high cardiovascular risk.
**Methods:** We evaluated 127 RA patients without previous cardiovascular events. Carotid ultrasonography was performed by a MyLab 70 scanner (Esaote; Genoa, Italy), equipped with 7–12 MHz linear transducer and the *automated software guided technique radiofrequency – Quality Intima Media Thickness* in *real-time* (*QIMT*, *Esaote*, *Maastricht*, *Holland*). According to data from non-rheumatic patients and also from RA patients, an IMT≥0.90 mm is a good predictor of high cardiovascular risk. To determine CAC score, a CT Imaging of coronary arteries using a 32-slice MDCT scanner (Lightspeed, Pro 32, GE Healthcare, USA) was performed.
**Results:** Patients with IMT below 0.90 mm had CAC values of 88±210 whereas patients with IMT≥0.90 mm had mean CAC values of 190± 272 (p=0.066). We found a positive correlation between IMT and CAC (correlation coefficient 0,303; p=0.001).
The IMT cut-off value ≥0.90 mm had a sensitivity of 32% for detecting CAC ≥100. ROC curve analysis showed and area under the curve of 0.664. The IMT cut-off value of 0.80 mm had a sensitivity of 40% and a specificity of 71.3%. Lowering the IMT cut-off point to 0.70, we reached a sensitivity of 76% and a specificity of 51.5% for CAC ≥100 detection. The positive predictive value for the IMT cut-off point of 0.70 mm was 76% in our population, being the negative predictive value 49.5%

| Variable | | Variable | |
|---|---|---|---|
| Age (mean ± SD) | 58. 57±9.7 | IMT ≥0.7 mm, n (%) | 71 (56) |
| Female sex, n (%) | 92 (72.,4) | CAC score (mean ± SD) | 103.4±222.6 |
| IMT ≥0,9 mm, n (%) | 19 (15) | CAC score ≥100, n (%) | 26 (20.5) |

**Conclusions:** IMT values ≥0.70 mm predict coronary artery calcification score above 100 with a sensitivity of 76%. According to that, the IMT value considered as predictor of high cardiovascular risk would be 0.70 mm instead of 0.90 mm.
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[1] Corrales A et al. “Cardiovascular risk stratification in rheumatic diseases: carotid ultrasound is more sensitive than coronary artery calcification score to detect subclinical atherosclerosis in patients with rheumatoid arthritis” Ann Rheum Dis. 2013,72 1764–1770.
**Disclosure of Interest:** None declared
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## AB0278 ARE THERE DIFFERENCES IN BASAL COMORBIDITIES BETWEEN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT AND THOSE TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS?

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**Background:** Rheumatoid arthritis (RA) patients frequently report concomitant comorbidities that could worsen their prognosis. Tumour necrosis factor inhibitors (TNFi), the most common biological agents used, have shown efficacy in RA patients, although use in RA patients with certain comorbidities warrant caution (1). Abatacept, a biologic agent with a different mechanism of action, inhibiting the co-stimulation of T-lymphocyte, has demonstrated differentiated safety profile (2), that could influence the biological agent prescribed in RA patients with some associated comorbidities
**Objectives:** To analyse differences in the frequency of baseline comorbidities in

RA patients treated with abatacept compared with those treated with TNFi
**Methods:** Patients with RA recruited into the BIOBADASER 2.0 register from January 2008 to December 2014 and treated with abatacept or TNFi with comorbidities were selected. Comorbidity was defined as ≥1 of the following at initiation of biological therapy: ischemic heart disease; malignancy (except lymphoma); diabetes; chronic pulmonary obstructive disease (CPOD); smoking; hypercholesterolemia; hypertension; heart failure; renal failure; lymphoma; osteoporosis; Epstein Barr, hepatitis B or C virus infection; and others. We analysed the frequency of each comorbidity, and differences in the rate of baseline comorbidities in the two groups were compared using t-test
**Results:** From January 2008 to December 2014, 640 and 252 RA patients treated respectively with TNFi or abatacept were included in the BIOBADASER 2.0 register, of whom 51.6% had ≥1 comorbidity at baseline. Frequencies for every basal comorbidity described are shown in Table 1. There was a significantly higher rate of heart failure in abatacept than in TNFi patients. Other comorbidities showed no significant differences.

Table 1

| Comorbidities | Abatacept group | TNFi group | p-value |
|---|---|---|---|
| Ischemic heart disease | 1 (2.27) | 14 (2.11) | 0.940 |
| Malignancy (except lymphoma) | 1 (2.27) | 13 (1.95) | 0.883 |
| Diabetes | 6 (13.64) | 46 (6.92) | 0.098 |
| CPOD | 2 (4.55) | 16 (2.41) | 0.382 |
| Smoking | 8 (18.18) | 109 (16.39) | 0.757 |
| Hypercholesterolemia | 9 (20.45) | 111 (16.69) | 0.519 |
| Hypertension | 10 (22.73) | 148 (22.26) | 0.942 |
| Epstein Barr infection | 0 (0) | 1 (0.15) | 0.797 |
| Heart failure | 4 (9.09) | 6 (0.9) | <0.001 |
| Renal failure | 0 (0) | 8 (1.2) | 0.464 |
| Lymphoma | 0 (0) | 0 (0) | |
| Osteoporosis | 7 (15.91) | 89 (13.38) | 0.635 |
| Hepatitis B virus infection | 1 (2.27) | 13 (1.95) | 0.883 |
| Hepatitis C virus infection | 0 (0) | 1 (0.15) | 0.797 |
| Others | 22 (50) | 292 (43.91) | 0.431 |

**Conclusions:** RA patients treated with abatacept had a higher baseline rate of concomitant heart failure compared with patients treated with TNFi, probably reflecting different recommendations on biological use. Even though abatacept has demonstrated a differentiated safety profile, overall no differences in other baseline comorbidities were found between groups
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[1] Singh et al. Arthritis Rheum 2016;68:1–26.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4625

## AB0279 PERIODONTAL DISEASE AND RHEUMATOID ARTHRITIS – COMPARISON OF TWO ASSESSMENT TOOLS, AND THEIR VALUE IN THE DETERMINATION OF THE ASSOCIATION BETWEEN THE TWO DISEASES

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**Background:** Periodontitis is involved in the pathogenesis of rheumatoid arthritis (RA), and a worse periodontal status has been proposed to correlate with the inflammatory activity of RA and to have an impact on its responsiveness to therapy. Human studies have been hampered by the lack of well-standardized assessment tools of the severity of periodontal disease (PD).
**Objectives:** The authors' aim was to compare the accuracy of two scoring systems of PD in RA patients, and to correlate the findings with multiple variables of RA activity and severity.
**Methods:** Eighty-one RA patients (mean age: 57 years, range: 28–82) were consecutively recruited. Disease activity was measured with DAS28, ESR, CRP, and swolllen and tender joint counts. Disease severity was assessed by the health assessment questionnaire (HAQ), anti-citrullinated peptide (mutated citrullinated vimentin) antibody and rheumatoid factor titers, and average DAS28 and average corticosteroid dose in the preceding year. The scoring of the severity of PD was assessed by means of the Community Periodontal Index of Treatment Needs (CPI) and the periodontal status classification, proposed by Fernandes et al. CPI scores PD severity on a 0–4 scale according to the presence of calculus and bleeding on probing (BOP) and probing depth, whereas the other index categorizes the severity as healthy-early-moderate-severe on the basis of clinical attachment level (CAL) and probing depth. Smoking status was also recorded.
**Results:** RA patients had a median score of 3 on the CPI index, and the median severity was moderate according to the periodontal status scale. The two systems had excellent correlation (Spearman r=0,966, p<0.0001), and there was also a negative correlation between the number of teeth and the CPI score (r=0,254, p<0.05) and the periodontal status score (r=0,210, p=0.059). A worse periodontal status (assessed with higher CPI score) was associated with a higher average DAS28 (despite therapy) measured during the year before the dental examination (r=0,376, p=0,022), with smoking (Kruskal-Wallis: p=0.014), and with higher DAS28 at the time of the examination (r=0.198, p=0.07). When assessed with the 4 staged periodontal status score, the association between PD severity and current DAS28 was significant (r=0.409, p=0.01).
**Conclusions:** CPI seems to have better performance than the periodontal status score proposed by Fernandes et al for the examination of the severity of PD in RA patients, and confirms the correlation between the severity of PD and RA activity and severity. This method is recommended for the research on the impact of periodontal status and of its correction on RA outcome.
**Disclosure of Interest:** None declared
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## AB0280 DEPRESSION AFFECTS NEGATIVELY QUALITY OF LIFE RELATED TO HEALTH OF COLOMBIAN PATIENTS WITH RHEUMATIC ARTHRITIS

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**Background:** Rheumatic arthritis (RA) causes deterioration on the health-related quality of life (HRQOL) and a negative impact on the emotional sphere of the affected individuals (1).
**Objectives:** Owing to scarce information existing in Colombia on the subject we decided to know the prevalence of depression on patients with RA and quantify its impact as well as the impacts of other variables on the HRQOL.
**Methods:** Design of Study: analytical cross sectional study.
Population of study: 100 individuals with ages 18 years or more, diagnosed with RA according ACR/EULAR 2010 criteria (2), which attended to outpatient service of the University hospital in the city of Neiva (Colombia) during 2013.
Gathering of information (data): through personal surveys that included socio-demographic and clinics variables; evaluation of depression prevalence using the Zung questionnaire (3) and HRQOL using the QOL-RA scale in spanish version (4).
Statistical analysis: summary measures, mean with standard deviation were used. An analysis of multiple lineal regression to identify predicter variables of HRQOL was made. For data analysis IBM SPSS 19. version was used. The research project was approved by the bioethical committee of the Universidad Surcolombiana in Neiva.
**Results:** 84% of participants were women, with mean age 53 years. 85% belong to 1 and 2 (lower) social strata, and 61% live with stable partners, depression prevalence of 23% was found. The mean outcome was 6.38. According dimension, the higher outcomes were familiar support (8.34), social interaction (8.24), and mood (6.49), while the lower outcome were perceived pain (4.97), arthritis (5.01) and physical ability (5.57). Likewise, the patients with depression had significantly lower outcomes of HRQOL (4.94) than those without depression (6.82) (p<0.001). With the multiple lineal regression model the only variable that predicted the HRQOL outcome was depression.
**Conclusions:** Colombian RA patients have high HRQOL outcomes in social interaction and familiar support dimensions and low in pain and arthritis dimensions; likewise patients with depression had lower HRQOL outcomes than those without depression, indicating that depression affects negatively all dimensions that comprise the QOL-RA scale.
HRQOL of Colombian RA patients are negatively influenced by depression, which stresses the importance of early detection and treatment of depressive symptoms in that population.
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## AB0281 BODY IMAGE DISTURBANCE IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO REQUIRES SURGICAL INTERVENTION

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**Background:** Recent effective treatment with disease-modifying anti-rheumatic drugs (DMARDs) including biologic DMARDs (bDMARDs) improved the disease control of patients with rheumatoid arthritis (RA), and the change of body image

of the patients might influenced the surgical indication. Body image assessment tool (BIAT) has been reported to be a reliable and valid tool[1)]. Patients with RA had a worse body image than individuals without RA[2)], however, there are no evidence showed the body image of patients who requires surgical intervention.
**Objectives:** The current study aimed to investigate the body image of patients who requires surgical intervention and to examine the correlation with depressive condition.
**Methods:** 163 patients (16 male, 147 female) with RA were divided into two groups of patients who didn't require the surgical intervention (non-operative group) and who underwent surgery (operative group). The non-operative group and operative group included 88 and 75 patients, respectively. The mean age of the non-operative and operative group were 64.8 and 64.4 years, and the mean disease duration were 17.5 and 22.7 years, respectively. The clinical evaluation included the use of bDMARDs, pain VAS (0–100mm), Health Assessment Questionnaire Disability Index (HAQ-DI), disease activity (DAS28-CRP), depression assessed by Beck Depression Inventory-II (BDI-II), and body image assessed by BIAT. Statistical analyses were performed using the Mann-Whitney U test, and Fisher's exact test.
**Results:** The rate of use of bDMARDs was not significant between non-operative and operative group. In the operative group, pain VAS, HAQ-DI, DAS28-CRP and BDI-II were significantly higher ($p<0.01$, $p<0.01$, $p<0.01$ and $p=0.02$, respectively) and BIAT was significantly lower ($p=0.02$) when compared with non-operative group. Higher BDI-II significantly correlated with lower BIAT in both non-operative ($r=-0.69$, $p<0.01$) and operative group ($r=-0.61$, $P<0.01$).

Comparing the non-operative and the operative groups

| | Non-operative group (n=88) | Operative group (n=75) | P value |
|---|---|---|---|
| Pain VAS (mm) | 22.0 (0~88) | 39.1 (0~100) | <0.01 * |
| HAQ-DI | 0.75 (0~2.75) | 1.39 (0~3.00) | <0.01 * |
| DAS28-CRP | 2.24 (1.03~5.31) | 2.64 (1.11~5.14) | <0.01 * |
| BDI-II | 9.1 (0~32) | 12.0 (0~49) | 0.02 * |
| BIAT | 3.2 (1.6~4.0) | 3.0 (1.5~4.0) | 0.02 * |

* Mann-Whitney U test

**Conclusions:** The result of this survey found the body image of patients in operative group was disturbed than that of non-operative patients. Body image disturbance was highly correlated with depressive condition in both operative and non-operative patients. To assess the body image might be useful to understand the patients' expectation and proper indication of the surgery.
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## AB0282 PREDICTING THE RESPONSES TO BIOLOGICAL THERAPY BY TWO KINDS OF ANTIBODIES TITERS AGAINST PORPHYROMONAS GINGIVALIS IN RA PATIENTS

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**Background:** There is little evidence on prediction of clinical response to biologics in patients with RA. Recently, it has been suggested that clinical response to tumor necrosis factor (TNF) inhibitors was related to periodontal conditions, which might be affected by infection with *Porphyromonas gingivalis* (*P.g.*). Additionally, serum antibody responses to *P. g* were associated with RA and periodontitis.Newly established test of antibody against hemin binding protein 35 (HBP) of *P.g.*, which has an ability specifically bind to *P.g.* containing protein HBP, can be available.
**Objectives:** To evaluate whether serum antibody responses to *P.g.* antigens and periodontal conditions are associated with clinical response to biologics in patients with RA.
**Methods:** 20 patients with severe RA enrolled in this study were treated with biologics according to the usual regimen. Clinical background and disease parameters were assessed at entry. DAS28-CRP was evaluated at 6 months (reassessment) after the initiation of biologics. Periodontal conditions were also assessed at entry. Serum levels of antibodies against *P.g.* sonicated extracts (SE) and HBP of *P.g.* were determined by enzyme-linked immunsorbent assay, respectively.
**Results:** Their mean (SD) age was 57.2 (13.4) years. Patients were predominantly women (85%) with mean disease duration of 8.2 (6) years.10 patients were treated with TNF-i, 7 with IL-6 blocker and 3 with CTLA4-Ig, respectively. Most patients had active disease with DAS28-CRP 4.2 (0.9) at baseline, and showed an improvement of DAS28-CRP 2.87 (0.82) at reassessment. Seven patients (35%) achieved remission (DAS28-CRP $<2.3$) at reassessment. The mean serum levels of anti-CCP antibodies were 270.2 (221.9), and the mean serum levels of antibodies against *P.g.* SE and HBP were 15.9 (52.3) and 0.632 (0.276), respectively at baseline. Periodontal conditions of the patients were as follows; mean PD was 2.62 (0.51) (mm), mean CAL was 2.85 (0.77) (mm), mean PCR was 0.37 (0.23) (%), and mean BOP was 0.21 (0.17) (%) at baseline. No associations were observed between changes in DAS28-CRP (delta-DAS28-CRP) and serum and periodontal parameter values (serum levels of antibodies against *P.g.* SE and HBP, PD, CAL, PCR, and BOP). Antibody titers against *P.g.* SE gradually decreased, on the other hand, anti-*P.g.* HBP was increased during 6 months.
**Conclusions:** Antibodies titers against *P.g.* and periodontal conditions could not predict the responses to biologics, but further studies are required to evaluate this hypothesis. And to our knowledge, this is the first report describing the change of serum level of antibodies against *P.g.* after treatments with biologics except infliximab.
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**Disclosure of Interest:** None declared
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## AB0283 EFFICACY AND SAFETY OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS-RELATED BRONCHIECTASIS (RA-BR): RESULTS FROM A MULTICENTRE COHORT

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**Background:** Bronchiectasis (BR) is a significant pulmonary morbidity associated with Rheumatoid Arthritis (RA). Patients with RA-BR are susceptible to infection and this poses a challenge in the treatment of articular disease. Evidence of efficacy and safety of biological therapy is scarce as these patients are often excluded from clinical trials.
**Objectives:** To evaluate the efficacy and safety of B cell depletion therapy with rituximab in a large RA-BR cohort of patient drawn equally from two centres.
**Methods:** We conducted a retrospective observational study of consecutive patients with RA-BR (detected by HRCT prior to rituximab) using identical data collection methodology between centres. Each cycle (Cn) of rituximab consisted of 2x1000mg infusions, repeated on clinical relapse. Disease activity was assessed using DAS-28 at baseline and every 6 months after each cycle and EULAR responses were calculated. Safety assessments included the number and severity of acute exacerbations of lung disease per year, together with five year survival and causes of death.
**Results:** 61 sero-positive patients were studied (43 female, median age 67 years (range 38–91)), median RA duration 9 years (range 1–23) years and BR duration 6 years (range 1–67). 36/61 (60%) were non-smokers. 20 patients were TNF-IR (8 primary non-response, 5 secondary non-response and 7 had side effects). 67% were on concomitant DMARDs. Total follow up duration was 321 patient-years.
At baseline, median DAS-28 was 5.7 (IQR 4.3–7.6). In C1, 53/61 (87%) achieved moderate-good EULAR response with a median reduction in DAS28 scores of 2.1 (IQR 0–3.4) $p=0.007$ at 6 months. EULAR responses were maintained at C2 and C3; 91% and 86% respectively. Median duration of response for C1, C2 and C3 were 54, 50 and 52 weeks respectively. In the 12 months prior to RTX, there was a median of 3 (0–7) infective exacerbations per patient. After RTX, 13 patients (21%) had fewer exacerbations compared to baseline; 40 patients (66%) remained stable and 8 patients (13%) had increased exacerbations. Overall, the number of exacerbations rose in the first year to a median of 4 (0–10) but then fell in years 2 and 3 to 2 (0–6) and 1 (0–4) respectively. Rituximab was discontinued in 8 patients (4 were due to increased exacerbations and 4 were due to inefficacy). 6 patients (10%) subsequently required alternative biologics for the treatment of RA. Of the 9 (15%) deaths, 3 (5%) died from respiratory disease.
**Conclusions:** Rituximab is effective and has an acceptable safety profile in the treatment of RA-BR. A temporary increase in acute exacerbations of lung disease may occur in the first year following rituximab. After subsequent treatment cycles, pulmonary symptoms stabilised or improved in most patients. Rituximab may therefore be a particularly appropriate therapeutic choice for this group of patients.
**Disclosure of Interest:** None declared
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## AB0284 REPRODUCTIVE HEALTH IN ADULT WOMEN WITH JIA AND RA

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**Background:** Building a family is an important part of a full life for many women with rheumatoid arthritis (RA) and juvenile inflammatory arthritis (JIA).

**Objectives:** Our goal was to identify the differences and similarities between the reproductive health choices and practices of women with RA and JIA.
**Methods:** A cross-sectional survey was completed by women between age 18–39 with a diagnosis of RA and/or JIA seen in a university rheumatology clinic. Descriptive statistical methods were used.
**Results:** Of the 33 women that completed the survey, 22 were diagnosed with RA at or after age 18 and 11 were diagnosed with JIA. The average age at diagnosis and the time of the survey was higher for women with RA (see table). The majority of participants were white. Methotrexate (MTX) had been used by all women with JIA and 73% of women with RA. The average total lifetime dose and duration of MTX dose was significantly higher among women with JIA.
Contraception: 4 women with RA were trying to conceive at the time of the survey. Among the other women, the rates of effective contraceptive use was similar, but more women with RA used an IUD or surgery and more women with JIA were taking daily birth control pills.
Pregnancy: Women in both groups reported a similar ideal number of children. About 2/3 of the women had either tried to conceive or been pregnant. The average age of first attempted pregnancy was similar between women with RA and JIA. Of the women who had tried to conceive or been pregnant, both groups had a similar number of pregnancies and the rates of live births, miscarriages, ectopic pregnancies, and elective terminations were not significantly different between the groups.
Fertility: Of the women who tried to get pregnant or had a pregnancy, 19% with RA and 40% with JIA reported infertility (p=0.3) and 12.5% with RA and 60% with JIA had used a fertility treatment to attempt pregnancy (p=0.03). The age of menarche, the frequency of menstrual irregularities, and the number of menses per year were similar between the groups.

| | RA | JIA | p-value |
|---|---|---|---|
| Number of women | 22 | 11 | |
| Age at survey | 33.9 (range 24–39) | 28.3 (range 20–38) | 0.005 |
| Age at diagnosis | 26.7 (sd 4.1) | 8.3 (sd 6.2) | 0.000 |
| Duration of disease | 7.2 (sd 3.8) years | 20 (sd 8.4) years | 0.000 |
| Race | 64% white/23% black | 100% white | 0.02 |
| Effective contraception | 56% | 82% | 0.34 |
| IUD or surgery | 44% | 9% | 0.05 |
| Oral contraceptives | 33% | 82% | 0.01 |
| Tried to conceive and/or had a pregnancy | 73% | 45% | 0.12 |
| Age 1st tried to conceive | 27.2 | 26.6 | 0.8 |
| Ideal number of children | 2.5 (sd 1.0) children | 2.4 (sd 0.8) children | 0.7 |
| Number of pregnancies | 1.7 pregnancies | 1.8 pregnancies | 0.4 |

**Conclusions:** The reproductive goals of women with JIA and RA appear to be similar. The majority of sexually active women were using effective contraception, with women with RA using long-acting options and women with JIA relying on birth control pills. Pregnancy outcomes appeared to be similar. Infertility was increased, particularly among women with JIA.
**Disclosure of Interest:** M. Clowse Grant/research support from: Pfizer, G. McDaniel Grant/research support from: Pfizer
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## AB0285 EFFECT OF ANTI-RHEUMATIC TREATMENT ON PERIODONTAL STATUS IN RHEUMATOID ARTHRITIS PATIENTS: A PILOT STUDY

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**Background:** Overlapping molecular pathways of inflammation have been implicated in periodontitis and rheumatoid arthritis (RA). The presence of shared underlying inflammatory pathogenesis mediating the progression of periodontitis and RA could provide potentially important common therapeutic targets.
**Objectives:** The primary purpose of this observational study was to determine the effect of methotrexate (MTX) and anti-TNFα (etanercept) on clinical parameters of periodontitis. Influence of periodontitis on efficacy of medical treatment of RA was a secondary endpoint.
**Methods:** Fourteen treatment-naïve patients starting with MTX and 12 patients starting with anti-TNFα therapy, fulfilling the ACR/EULAR classification criteria for RA (2010), older than 18 years, and with natural dentition were included. One patient was excluded because of antibiotic use for oral infection <3 months prior to the study. Four patients stopped treatment with etanercept after the first follow up visit because of patient related factors. Before starting medical treatment for RA and after 2 months (MTX) or 3 months (anti-TNFα), periodontal inflammatory burden was quantified with the periodontal inflamed surface area (PISA) (Nesse et al. 2008). Subgingival presence of *P. gingivalis* was determined by anaerobic culture. In addition, radiographic intra-oral pathologies (furcation involvement, peri-apical pathology and cariës) were assessed on panoramic radiographs. Oral hygiene was measured using full mouth plaque scores. Efficacy of anti-rheumatic treatment was measured by change in RA disease activity (DAS28-ESR).
**Results:** Treatment with MTX of anti-TNFα significantly improved DAS scores (both $p<0.001$) and erythrocyte sedimentation rates (ESR) (both $p<0.05$). PISA did not change significantly after starting with treatment with MTX or anti-TNFα. Also, PISA or presence of other intra-oral pathologies were not associated with changes in DAS scores and ESR
**Conclusions:** Anti-rheumatic treatment did not have significant impact on clinical periodontal parameters. Within the limitations of this study (PISA scores were rather low) PISA and presence of other intra-oral pathologies were not of associated with efficacy of anti-rheumatic treatment.
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## AB0286 CLINICAL FEATURES AND THERAPEUTIC CONSIDERATIONS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS; A CROSS-SECTIONAL STUDY

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**Background:** Rheumatoid arthritis (RA)'s prevalence increases with age. The average life expectancy is getting longer and global population is becoming older. Physicians will be challenged with the recognition and treatment of RA patients who may have different physical conditions, comorbid diseases and using multi-drugs.
**Objectives:** The aim of this study was to evaluate the clinical characteristics and treatment modalities in elderly RA patients.
**Methods:** We assessed elderly RA patients (≥65 years) diagnosed according to 2010 American College of Rheumatology (ACR) criteria. Clinical and laborotary findings, treatment durations, dose of drugs and treatment related adverse effects were recorded into a pre-defined protocol. "Disease Activity Score" (DAS-28), "Physician Global Assessment" (PGA) and "Health Assessment Questionnaire" (HAQ) scores were used as composite indices for RA activity evaluation.
**Results:**
Seventy-four RA patients [54 patients (73%) were female] with a mean age of 71±5 (65–86) years were included into the study,. The mean total disease duration of these patients was 97±104 (9–600) months. Disease onset was in the elderly period for 40 (55%) patients. Small joints of hands were the most frequently involved joints (95%). Seropositivity rate was 66% and 56% of the patients had erosive disease. DAS-28 and HAQ scores were correlated with PGA scores (p:0,001). The proportion of patients with high and moderate disease activity was found as 79% according to DAS-28 scores. There was no association between age and antibody titers or activity indices. Non-steroidal antiinflammatory drugs (NSAIDs) were part of the treatment in 53 patients (71%) and no severe side effects associated with NSAIDs were observed. The mean cumulative prednisolone dose was 7617±10602 mg. Hypertension and osteoporosis were the most frequent comorbidities (64% and 48%, respectively). The most commonly used disease modifying antirheumatic drug (DMARD) was methotrexate (76%) and the rate of compliance was found high for all drugs except sulfasalazine (Table 1). While 60% of all patients were treated with DMARD monotherapy, combination DMARD therapy were used in 37% of patients. The rate of biologic theraphy was found as 12% (9 patients) in all study population.

Table 1. The anti-rheumatic treatments in elderly RA patients

| Drugs | n (%) | Mean ages | Starting in ≥65 age n (%) | Mean dose | Treatment duration* | Maintanence of the theraphy n (%) |
|---|---|---|---|---|---|---|
| Methotrexate | 58 (79) | 70,9±5 | 42 (73) | 11,2±4,7mg/w | 38,1±51 | 41 (72) |
| Hydroxychloroquine | 35 (48) | 71,9±5 | 25 (74) | 206±37mg/d | 30,8±37 | 31 (91) |
| Leflunomide | 28 (39) | 72±6 | 20 (74) | 18,4±3,5mg/d | 29,5±29 | 20 (77) |
| Sulfasalazine | 13 (18) | 71,3±5 | 7 (53) | 1,8±0,3g/d | 47,1±69,2 | 5 (45) |
| Rituximab | 5 (6,7) | 72,6±6 | 5 (100) | 1000mgx2/2w | 6,2±3 | 5 (100) |
| Etanercept | 2 (2,7) | 65,5 | 21 (50) | 50mg/w | 13,5±14,8 | 1 (50) |
| Abatacept | 1 (1,3) | 66 | 1 (100) | 125mg/w | 6 | 1 (100) |
| Adalimumab | 1 (1,3) | 71 | 1 (100) | 40mg/d | 24 | 1 (100) |

*The mean treatment duration as months.

**Conclusions:** In this preliminary data from our ongoing study, elderly RA patients had remarkable compliance with NSAIDs and DMARDs. Although patients treated with biologic agents constituted a small group, no serious side effect that required cessation of the treatment was observed. By the increasing numbers of elderly RA patients in our cohort, we expect to obtain more powerful data on compliance and safety issues of the treatment and particularly biologic agents.
**Disclosure of Interest:** None declared
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## AB0287 PSYCHIATRIC DISORDERS IN RA PATIENTS: RELATION WITH FATIGUE, SLEEP QUALITY AND QUALITY OF LIFE

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease that predominantly affects the synovial joints and the periarticular structures, leading to persistent pain, functional deterioration, disability, sleep disturbance, and lower quality of life. Psychiatric disturbances are frequently observed in these patients.
**Objectives:** The aim of this trial was to investigate I) the psychiatric disorders in RA and II) the effect of concurrent psychiatric disorders on pain, fatigue, disease activity, sleep quality and health-related quality of life (HRQOL).
**Methods:** The patients who fulfilled the American College of Rheumatology (ACR) criteria for RA were recruited. All the patients were interviewed by a psychiatrist. The psychiatric disorders were evaluated with the Turkish Structured Clinical Interview for DSM-VI Axis I Disorders (SCID-I). Sociodemographic data, disease activity (DAS 28 score) and disease duration were reported. Pain was evaluated with visual analogue scale (VAS), fatigue with Multidimensional Assessment of Fatigue (MAF), and quality of life with 36-item Short Form Health Survey (SF-36), and sleep quality with Pittsburgh Sleep Quality Index (PSQI).
**Results:** One hundred patients with RA were studied (90% women, mean age 52.02±12.74 years; disease duration 10.29±8.99 years). Forty-six (46.0%) patients were diagnosed with a psychiatric disorder. Adjustment disorder (n=15) and major depressive disorder (n=12) were frequently observed in these patients. When we divided the groups as the RA patients with psychiatric disorders and the RA patients without psychiatric disorders, RA patients with psychiatric disorders had significantly higher pain scores (p=0.035) and fatigue scores (p=0.005). There was no difference between groups regarding disease activity. The scores of all domains of the SF-36 were significantly lower in RA patients with psychiatric disorders ($p<0.05$ for all). While there was no significant difference between groups regarding sleep duration, usual sleep efficiency and sleeping aid use, significant differences in sleep quality, sleep latency, sleep disturbance, daytime sleepiness and PSQI total score were observed. These scores were higher in RA patients with psychiatric disorders ($p<0.05$).
**Conclusions:** The rate of psychiatric disorders in RA patients was found to be 46% in the present study. We also determined that concomitant psychiatric disorders in RA patients were associated with significantly lower sleep quality and HRQOL and higher fatigue. Early identification of psychiatric disorders in RA patients and early referral to a multidisciplinary psychiatric team are necessary to improve the quality of life, sleep quality, and to reduce fatigue.
**Disclosure of Interest:** None declared
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## AB0288 THE 24-MONTH STUDY OF TREATMENT WITH MONOCLONAL ANTIBODY TO RANKL ON BONE MINERAL DENSITY AND STRUCTURAL DAMAGE IN PATIENTS WITH OSTEOPOROSIS AND RHEUMATOID ARTHRITIS

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**Background:** Chronic synovitis and RANKL-dependent osteoclastogenesis in rheumatoid arthritis (RA) lead to bone damage, such as local and systemic bone destruction (osteoporosis (OP), erosions and joint space narrowing). RANK-ligand is essential for osteoclast development, activation, and survival. The addition of an anti-RANKL antibody (denosumab) to the traditional scheme of RA treatment is a potentiality to control and prevent joint destruction as well as inhibit systemic osteoporosis.
**Objectives:** The aim is to evaluate the effects of continuous treatment with denosumab on bone mineral density and structural damage in patients with RA and OP.
**Methods:** 27 postmenopausal women (mean age 58,4±7,4 years) with RA (mean duration of RA 19,5±11,8 years) and OP received subcutaneously denosumab 60 mg every 6 months pro 2 years. According to X-ray 8 (29,6%) patients had the 2nd, 8 (29,6%) – the 3rd and 11 (40,8%) – the 4th stage of RA. 17 patients (62,9%) continued glucocorticoids (GC). The primary end points were the change from baseline in BMD (by dual energy x-ray absorptiometry at three sites: lumbar spine (L1-L4), hip neck (HN) and distal forearm (DF), the change in Sharp/van der Heijde (SVH) score by X-ray of hands and feet and the change in X-ray morphometric analysis of deformations in vertebrae (Genant method). The change of pain severity in spine was assessed using VAS. The Statistica 6.0 was used.
**Results:** At L1-L4 the significant increase of BMD was noted both at 12- and 24-month point in comparison with baseline: 0,789±0,079 g/cm$^2$ vs 0,818±0,077 g/cm$^2$ ($p<0.001$) and 0,789±0,079 g/cm$^2$ vs 0,836±0,078 g/cm$^2$ ($p<0.001$), respectively. The same was noted at DF – the increase of BMD at 12- and then at 24-month: 0,480±0,102 g/cm$^2$ vs 0,493±0,095 g/cm$^2$ (p=0.01) and 0,480±0,102 g/cm$^2$ vs 0,511±0,104 g/cm$^2$ ($p<0.001$), respectively. At HN it was noted the stabilization in BMD (statistically nonsignificant improvement) at both points. After separation on groups based on GC intake, this trend was also seen at both points in both groups: increase of BMD at L1-L4 and DF, stabilization of BMD at HN.
The erosion and total SVH score were increased at 12- and 24-month ($p<0.05$), while the narrowing score was not changed significantly at both points.
The index of vertebral deformations was not changed after 24-month compared with baseline: 0,79±0,01 for lumbar site and 0,76±0,04 for thoracic site, respectively.
At baseline 13 patients had pain in thoracic site of spine, while after the treatment their number significantly decreased (p=0.019) more that 2-fold – 4 (mean VAS 41.1±16.9 and 31.2±8.5 mm, respectively), at lumbar spine pain was also reduced (p=0.09): 15 and 8 patients (44.3± 23.3 and 35.6±14.7 mm, respectively).
**Conclusions:** Throughout the 24 months of therapy with denosumab it was shown the continued increase of BMD at L1-L4 and distal part of forearm - the significant increase was observed both at the first and the following year of therapy regardless of GC intake. At HN it was observed the stabilization of BMD. The erosion and total SVH score were increased, but the narrowing score didn't change after two years of observation. The index of vertebral deformations remained stable. The frequency and severity of pain in spine were decreased.
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## AB0289 ANALYSIS OF JOINTS SUSCEPTIBLE TO RHEUMATOID ARTHRITIS (RA) AND THEIR RECOVERY SEQUENCE BASED ON DAS28 WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) IN CHINA: A PROSPECTIVE COHORT STUDY

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**Background:** The disease activity score in 28 joints (DAS28)[1] and health assessment questionnaire (HAQ) [2] are guides the treatment of rheumatoid arthritis (RA). Smart System of Disease Management (SSDM) is a series of mobile phone applications for chronic diseases management, which includes interfaces of both doctors' and patients' applications. After entry data of lab test, treatment regiments, and executing DAS28 evaluation entry by patients, all data can be synchronized automatically to the authorized rheumatologist' mobile tool. The rheumatologist can adjust treatment regiments base on patients' profile. We have confirmed that the results of self-assessment in DAS28 by RA patients with SSDM were consistent with professionals' assessment in our previous study[3].
**Objectives:** To evaluate the susceptible joints and the recovery sequence of swollen joint counts (SJCs) and tender joint counts (TJCs) based on DAS28 which self-assessed by Chinese RA patients with SSDM, and to describe the association between DAS28 and HAQ.
**Methods:** Since August 31, 2014, thirty-one rheumatologists from twenty-five hospitals participated in the study. Adult patients fulfilling the 1987 ACR (formerly the American Rheumatism Association) criteria for RA were recruited. Patients were taught to self-assess DAS28 and HAQ with SSDM at the baseline, and were asked to repeat the assessment once a month during the treatment.
**Results:** As of January 14, 2016, 636 RA patients self-assessed for 2,306 times. At the baseline, 1,628 joints were swollen and 2,761 joints were tender. The top five swollen joints were right wrist, right middle proximal interphalangeal, left wrist, right knee and left knee joints, and the top five tender joints were right wrist, left wrist, right knee, left knee and right shoulder joints. Table1 shows the proportion of different joint involvement at the baseline and the last assessment. After treatment, the top five recovery joints were left little metacarpophalangeal, left ring metacarpophalangeal, right index proximal interphalangeal, right little metacarpophalangeal and right middle proximal interphalangeal in tender, and



left little proximal interphalangeal, left little metacarpophalangeal, right little proximal interphalangeal, right little metacarpophalangeal and left index proximal interphalangeal in swelling.
HAQ score showed that the top two difficult functions of RA patients were "reaching" and "hygiene" at the baseline. At the last assessment, the degree of recovery about "hygiene", "dressing and grooming" function were quicker than "reaching" and "walking", which was matched with DAS28's joints recovery characteristic (Detailed see Table 2).
**Conclusions:** In this study, most involved joints in tender and swelling are hand and wrist joints, which co-related to the physical activity function of "hygiene" and "dressing and grooming". After treatment, hand joints recovered more quickly than other joints, which matched with HAQ assessment results.
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## AB0290 LYMPHOCYTE RESTORATION AND TRANSITION OF PERIPHERAL LYMPHOCYTES SUBSETS ASSOCIATES WITH SPONTANEOUS REGRESSION OF METHOTREXATE-ASSOCIATED LYMPHOPROLIFERATIVE DISORDER (MTX-LPD)

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**Background:** Methotrexate-associated lymphoproliferative disorder (MTX-LPD) is a relatively rare but well known complication among patients under MTX treatment. Spontaneous regression of LPD after MTX withdrawal is regarded as a distinct character of MTX-LPD. Although detection of Epstein-Barr virus encoded small RNAs (EBER) in the pathological tissue is reported as a predictor of regression, although it is not necessarily specific [1)].
**Objectives:** To investigate the factors involved in spontaneous regression of LPD following MTX withdrawal.
**Methods:** We retrospectively reviewed 43 rheumatoid arthritis (RA) patients complicated with MTX-LPD from January 2000 to October 2015 in our institution. Age, sex, RA duration matched 76 control MTX-treated patients were selected. MTX-LPD patients were divided into two groups regarding to the status of LPD after MTX cessation; regressive LPD (R group) and persistent LPD (P group), and clinical parameters were compared. Flowcytometric analysis of the whole blood was underwent in a part of the MTX-LPD patients (N=10, 7 regressive, and 3 persistent LPD) and controls (N=10). The time of MTX cessation (= time of LPD diagnosis) was defined as week 0, and whole blood sample was collected at week 0, 4 and 12. Epstein Barr Virus antigen specific CD8+ T cells (EBV specific CD8+) was defined as MHC/EBV peptide tetramer positive CD8+ T cells.
**Results:** At the time of MTX cessation (week 0), number of peripheral lymphocytes was significantly decreased in LPD group, compared to control group. Among the LPD group, significant increase of lymphocyte number following MTX withdrawal was observed only in the R group, but not in P group while MTX dose, EBER positivity rate and pathological phenotypes did not show significant difference. Flowcytometric analysis revealed significant decrease in proportion of effector memory CD8+ T cells (EM CD8+), EBV specific CD8+ and T helpler 1 (Th1) subset in R group compared to control group. Following MTX cessation, significant increase in proportion of these subsets were observed only in the R group, but not in P group. On the other hand, proportion of CD14-CD15+ cells in lymphocyte fraction, which include myeloid derived suppressor cells [2)] (MDSC) was significantly increased in LPD group at week 0, and significantly decreased following MTX cessation only in the R group, but not in P group. Proportion of CD14-CD15+ cells negatively and significantly correlated with the proportion of EM CD8+T cells.
**Conclusions:** Our study suggested that decreased lymphocytes at the time of LPD diagnosis and restoration following MTX withdrawal are associated with pathogenesis and clinical course of "regressive" MTX-LPD. Proportion of Th1 cells, EM CD 8+, EBV specific CD8+ and CD14-CD15+ cells was restored following MTX cessation, indicating their involvement in regression of MTX-LPD.
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**Disclosure of Interest:** S. Saito: None declared, K. Suzuki Grant/research support from: Eisai Co.,Ltd., Bristol–Myers K.K., K. Yamaoka Paid instructor for: Pfizer, Chugai Pharma, Mitsubishi-Tanabe Pharma, Takeda Industrial Pharma, GlaxoSmithKline, Nippon Shinyaku, Eli Lilly, Janssen Pharma, Eisai Pharma, Astellas Pharma and Actelion Pharmaceuticals, T. Shimizu: None declared, T. Mori Paid instructor for: Astellas Pharma,Chugai Pharma,Eisai Co.,Ltd.,Janssen Pharmaceutical K.K., S. Okamoto Grant/research support from: Astellas Pharma,Chugai Pharma,Eisai Co.,Ltd.,Bristol–Myers K.K., Takeda Pharmaceutical Co.,Pfizer, Paid instructor for: Astellas Pharma,Chugai Pharma,Eisai Co.,Ltd.,Bristol–Myers K.K.,Takeda Pharmaceutical Co., Pfizer, K. Amano: None declared, M. Tokuhira: None declared, T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co.,Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co.,Ltd., Teijin Pharma Ltd., AbbVie GK, 2,Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Paid instructor for: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co.,Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co.,Ltd., Teijin Pharma Ltd., AbbVie GK, 2,Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K.,
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## AB0291 AN ANALYSIS OF THE RELATIONSHIP BETWEEN CLINICAL ACTIVITY, MODE OF THERAPY AND DEPESSION IN RHEUMATOID ARTHRITIS

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**Background:** An ever increasing body of research confirm that rheumatoid arthritis is associated wuth depression.
**Objectives:**
- Assessment of presence and severity of depression in patients suffering from RA.
- Determination of the connection between depression with the activity of the disease, functional status, and radiological stage of the disease.
- To examine the effect of therapy on the severity of depression.

**Methods:** The examination was conducted with 276 patients with RA (82.24% women and 17.76% men), with the average age of 5563±14.46 years. The average duration of the disease was 48.4±20.3 months. The control group comprised 145 healthy examinees homogenous with the examined group in age and sex distribution. The activity of the disease was determined using the DAS 28 SE index, the functional status was determined on the basis of an HAQ questionnaire, while the degree of radiological damage was determined using the Larsen score (0–200).
The intensity of pain was determined by the examinees themselves on the visual-analog pain scale VAS (0–100mm). The degree of depressivity was determined through application of the Beck scale for depression.
The statistical data processing was performed in the SPSS package, version 15.0.
**Results:** The symptoms of depression were registered in 73.19% of patients, significantly more than in CG (21.34%), $p<0.01$. Mild depressivity was registered in 37.62% of patients, moderate in 28.71%, pronounced in 14.76%, and major depression in 8.91% of patients.
Out of the total number of examinees, 34.78% received combined therapy (MTX + biological therapy). 65.22% of patients were treated using monotherapy (MTX). The mean value of the Beck index of the patients receiving biological therapy was significantly lower than the value of the Beck index of the patients receiving monotherapy MTX (11.8±7.16 vs.16.86±8.09).
The connection between the ages of patients, the duration of the disease, DAS 28 SE, VAS of pain, Larsen score and HAQ index with the Beck index of depressivity was studied. The results of the univariant logistic regression show that the degree of depression is separately affected by the duration of the disease and the functional status of the patient. The multivariant model of logistic regression emphasizes the functional status as the most dominant predictor of depressivity (coef. Beta 0.764), $p<0.001$.
**Conclusions:** Depression is a frequently present manifestation of RA which is most prominently influenced by the degree of functional disability of RA patients. Apart from the medication therapy, the treatment of RA requires an individual psychosocial approach and wider social support.
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## AB0292 LOW SERUM ALBUMIN, GLUCOCORTICOID AND LEFLUNOMIDE USE WERE ASSOCIATED WITH PERMANENT DISCONTINUATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) is the first line therapy for treatment of rheumatoid arthritis (RA) because of high efficacy and saved cost. MTX has toxicities such as GI irritation, hepatitis, pneumonitis and cytopenia. However,

MTX toxicities usually mild and does not lead to discontinuation. MTX toxicities have never been studied in Thailand, which prevalence of hepatitis B infection was high (26%).
**Objectives:** To examine the prevalence and reasons of discontinuation of MTX in RA and to determine factors, especially previous hepatitis B infection, associated with MTX discontinuation.
**Methods:** All 197 RA patients according to American College of Rheumatology (ACR) 1987 and/or ACR and European league of Rheumatology 2010 between 2000 and 2015 were studied. Anti-hepatitis B core antibody (anti-HBcAb), hepatitis B surface antigen (HBsAg), chest film were revealed prior to start methotrexate. Patients with positive HBsAg were excluded. Measurements of aspartate aminotransferase (AST), alanine aminotransferase (ALT), complete blood counts, signs and symptoms of methotrexate toxicities were recorded. Potential risk factors for toxicity were recorded. Univariable and multivariated analyses were performed to identify associated factors for permanently discontinuation of MTX.
**Results:** One hundred and ninety-seven RA patients were followed for 2142 person-years of MTX exposure. MTX was discontinued permanently in 47 patients (24%). Reasons for discontinuation were as followed: leucopenia 12 patients (26%), anemia8 patients (17%), thrombocytopenia3 patients (6%), pneumoitis11 patients (23%), GI irritation8 patients (17%), mild hepatitis (AST40–80 IU/mL) 8 patients (17%), severe hepatitis (AST>80 IU/mL) 8 patients (17%), mucositis 5 patients (10%), alopecia1 patient (2%). Mean time (standard deviation) to discontinuation was 522 (26.9) days. Multivariate logistic regression analyses found that serum albumin level less than 3.5 mg/dL, leflunomide use of more than 10 mg/d and prednisolone use of more than 10 mg per day were significantly associated with methotrexate discontinuation (odd ratio and 95% confidence interval of 15.33 (1.37–171.23), 5.33 (1.40–20.27)2.97 (1.14–7.77), respectively). Previous resolved hepatitis B infection defined as patients with positive anti-HBcAb was not associated with methotrexate discontinuation.
**Conclusions:** MTX discontinuation occurred in almost one-fourth of patients. Low serum albumin, glucocorticoid and leflunomide use were associated with permanent discontinuation of methotrexate in patients with rheumatoid arthritis.
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## AB0293 CAROTID INTIMA MEDIA THICKNESS AND INTERLEUKIN -17 LEVEL IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid Arthritis (RA) patients are at risk of cardiovascular disease (CVD) and carotid intima media thickness (cIMT) is an excellent marker of subclinical atherosclerosis. However, cIMT and the CVD biomarkers among RA patients with low disease activity and remission are not well studied.
**Objectives:** To assess the carotid intima media thickness (cIMT) in RA patients who were in low disease activity state and lacking concomitant co-morbidities potentially influencing cIMT. This study was also aimed to determine the correlation between serum IL-17 with cIMT.
**Methods:** Rheumatoid Arthritis patients who were in low disease activity or remission (DAS28<3.2) from Rheumatology Clinic, National University of Malaysia Medical Centre were recruited. Patients with traditional CVD risk factors were excluded. Carotid ultrasound was performed in RA patients and their age and gender-matched healthy controls to determine the cIMT thickness. Serum IL-17 was measured using ELISA method.
**Results:** A total of 76 patients were screened and 22 RA patients who were in low disease activity or remission were included. Patients with RA had significantly higher median cIMT, 0.53 (IQR0.13) mm compared to controls, 0.47 (IQR 0.14) mm, p=0.01. In RA patients, the cIMT had significant positive correlation with age ($r_s$=0.84, p=0.00), systolic BP ($r_s$=0.45, p=0.04), waist circumference ($r_s$=0.43, p=0.04), total cholesterol ($r_s$=0.54, p=0.01), BMI ($r_s$=0.45, p=0.04) and serum IL-17 ($r_s$=0.45, p=0.03) but negative correlation with total HDL ($r_s$=-0.43, p=0.05).
**Conclusions:** Patients with RA had significantly higher cIMT as compared to healthy controls despite minimal disease activity and lack of traditional CV risk factors, suggesting that the vascular injury due to previous inflammation may not be reversible. Serum IL-17 was also found to be correlated significantly with cIMT, suggesting that it may play a role in atherogenesis among RA patients.
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**Disclosure of Interest:** None declared
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## AB0294 LYMPHOCYTE RECOVERY AFTER METHOTREXATE DISCONTINUATION RELATE TO SPONTANEOUS REGRESSION OF MTX-LPD IN RA PATIENTS

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**Background:** Rheumatoid arthritis (RA) patients have a high risk of onset of lymphoproliferative disorders (LPD). Especially, LPD develop in patients treated with methotrexate (MTX) is known as MTX-associated LPD (MTX-LPD). MTX-LPD is classified among the "immunodeficiency-associated lymphoproliferative disorders (ID-LPD)" as an "other iatrogenic ID-LPD" in the 2008 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (1). We previously reported that MTX is an independent risk factor for LPD onset in Japanese RA patients (2). Characteristic of MTX-LPD is that MTX withdrawal possibly results in spontaneous regression of the LPD. Furthermore, there are some reports that the Epstein-Barr virus (EBV) infection is related to spontaneous regression of MTX-LPD. However, enough evidence about the relation with EBV infection and spontaneous regression of MTX-LPD is not presented. In addition, biomarker predicting a spontaneous regression of MTX-LPD has not been clarified.
**Objectives:** We examined the clinical characteristics of MTX-LPD in Japanese RA patients and attempted to determine the predictive marker for spontaneous regression of MTX-LPD.
**Methods:** We enrolled 33 RA patients who developed MTX-LPD from Kagawa Prefecture, Japan between June 2010 and December 2015. Patients were diagnosed according to American College of Rheumatology 1987 classification criteria, and treated with disease modifying antirheumatic drugs (DMARDs) including MTX. We divided into patients who were followed-up after the discontinuation of MTX alone (MTX withdrawal group) and patients who were performed chemotherapy after one month or more of the MTX discontinuation (chemotherapy group). The following differences between the two groups were examined: 1) serum LDH; 2) serum CRP; 3) sIL-2 receptor; 4) lymphocyte counts before and after MTX discontinuation; 5) hemoglobin; 6) histological findings related to LPD; 7) EBV association; 8) number of LPD lesions and 9) outcome.
**Results:** There were 28 patients in the MTX withdrawal group and 5 patients in the chemotherapy group. Laboratory data such as LDH, CRP, sIL-2R, lymphocyte counts and hemoglobin showed no significant difference in two groups. Furthermore, there is no difference between two groups about EBV infection and number of LPD lesions. However, significant differences were found in the change ratio of lymphocyte between the two groups.
**Conclusions:** We revealed that the change of lymphocyte before and after the MTX discontinuation relate to spontaneous regression of the MTX-LPD. This data suggest that the recover of lymphocyte after the MTX discontinuation may become a predictive marker for MTX-LPD treatment strategy.
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**Disclosure of Interest:** None declared
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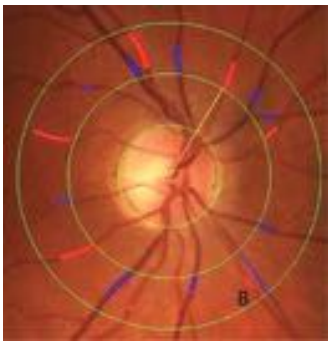
## AB0295 ABNORMAL CENTRAL RETINAL VEIN EQUIVALENT FOUND IN ACTIVE RHEUMATOID ARTHRITIS: A DIFFERENT PERSPECTIVE OF MICROVASCULAR HEALTH

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**Background:** Patients with rheumatoid arthritis (RA) have increased risk of cardiovascular disease. Retinal vascular caliber (RVC) is one of the new tools to determine the cardiovascular risk. RVC includes central retinal artery and vein equivalents (CRAE and CRVE). It is well known that CRVE is closely related with chronic inflammation (1).
**Objectives:** The objective of this study was to assess RVC score in RA patients and compared the data with those of SLE patients and age-sex-comorbidity equivalent population.
**Methods:** Forty-seven RA patient were enrolled in this study between July 2014 and January 2015. Demographic data of patients were recorded. Before the measurement of RVC, disease activity was measured by Disease Activity Score-

28 (DAS-28). Functional capacity assessed by Health Assessment Questionnaire (HAQ). Disease activity was categorized according to DAS-28 (DAS-28<3.2 low disease activity, DAS-28>5.1 high disease activity). Thirty-two SLE patients and 45 healthy controls constituted the control groups. RVC was measured from the dilated fundus photographs, and summarized as the central retinal artery and vein equivalents (CRAE- CRVE) using a semi-automated computer-assisted method (IVAN, Wisconsin University-Figure 1). Measurement of the retinal vascular caliber performed in between the 0,5–1 disc distance from the optical disc margin (Zone B, figure 1). Arterioles and venules were marked semi-automatically by the software (Red=arterioles, Blue=Venules). The largest 6 vessels width used in the previously accepted formula for calculating the CRAE and CRVE. Retinal photography was performed in all patients at baseline and 24 of RA patients were re-evaluated 5.2±2.1 months later.

**Results:** The mean age of RA, SLE patients and healthy controls were 52.1±11.9, 41.4±14.5, and 47.2±17.3 (p=0,008), respectively. Female sex (83%, 84%, and 80%, p>0.05), hypertension (40%, 31%, and 27%, p>0.05) and diabetes mellitus (8%, 3%, and 11%, p>0.05) frequencies were similar in all groups. CRAE score was similar in RA, SLE, and healthy controls (147.8±11.7 μm, 148.3±12.8μm, and 147.4±17.6μm), respectively. CRVE score was also similar (213.3±17.8 μm, 209.2±14,1μm, and 217.5±26.2μm). There was no correlation between DAS-28, HAQ score with RVC scores. At baseline, ten (21%) of patients had active disease, and 22 (47%) patients had low disease activity. CRVE score was higher in active RA patients than low disease activity patients (222.8±10.1 vs. 207.3±17.8, p=0.004). There was no correlation between the changes of DAS-28 and HAQ with the RVC changes during follow-up period.




**Conclusions:** CRVE is associated with systemic inflammation and possibly increased CV risk (1,2). Although, CRVE and CRAE were similar in RA, SLE and healthy control groups, however especially active RA patients had worse CRVE level. Measurement of retinal vein caliber is a sensitive methods for assessment of microvascular circulation. Further studies should be focused to importance of abnormal CRVE and cardiovascular status in rheumatic diseases.

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**Disclosure of Interest:** None declared

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### AB0296 CLINICAL CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS ACHIEVING NO DEPRESSION WITH 6 MONTHS OF BIOLOGIC TREATMENT

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**Background:** It is known that rheumatoid arthritis (RA) is comorbid with various diseases and especially concomitant depression is common with a high prevalence of approximately 20%. Even if RA disease activity is controlled, patients with persistent depression result in decreased activity of daily life (ADL) and quality of life (QOL).

**Objectives:** To study predictive factors for no depression status after using biologic agents for 6 months.

**Methods:** The study was 333 RA patients treated with biologic agents. The following patient's characteristics were investigated: age, gender, the number of previous drugs, disease duration, the type of biologic agents, baseline steroid dosage, MTX dosage, serum rheumatoid factor (RF), serum matrix metalloproteinase-3 (MMP-3), anti-cyclic citrullinated peptide antibody (anti-CCP antibody), tumor necrosis factor (TNF)-α, and interleukin (IL)-6. For evaluation we used Simplified Disease Activity Index (SDAI) for RA disease activity, Health Assessment Questionnaire (HAQ) for ADL, Short Form (SF)-36 for QOL, and Hamilton Depression Rating Scale (HAM-D) or Self-rating depression scale (SDS) for depression status. No depression was defined by HAM-D≦7 or SDS≦39 after 6 months of treatment. The subjects were divided into two groups according to the presence or absence of depression, and a retrospective study was performed. We excluded 101 patients due to loss to 6-month follow-up and 39 patients due to incomplete data; therefore, we included 193 patients in the analysis.

**Results:** Compared with a group of RA patients with depression (n=130), a group of patients without depression (n=63) had younger age (52.7± 14.8 vs. 59.8±14.3, p=0.002), more males (p=0.046), lower baseline steroid dosage (3.2±3.1mg vs. 5.0±4.4mg, p=0.002), lower SDAI (22.9±12.8 vs. 29.5±15.2, p=0.002), lower HAQ (0.43 ±0.47 vs. 0.75±0.62, p<0.001), higher SF-36 (p<0.05 in all categories), lower SDS (38.2±8.5 vs. 46.7±9.6, p<0.001), and lower HAM-D (5.0±4.0 vs. 9.3±6.0, p<0.001) were detected based on univariate analysis. On the other hand, younger age (p=0.0352), more males (p=0.0048), lower baseline steroid dosage (p=0.0459), lower titer of serum RF (p=0.0114), lower HAQ (p=0.0485) and lower "pain (p=0.0222)", "general health perception (p=0.0364)" and "social functioning (p=0.0078)" item of the SF-36 were detected based on logistic regression analysis.

**Conclusions:** It was suggested that RA patients with more male, lower disease activity, lower dosage of steroid, younger age, and higher ADL and QOL at baseline are more likely to achieve no depression status with biologic treatment.

**Disclosure of Interest:** Y. Miwa Grant/research support from: Tanabemitsubishi, Chugai, phizer, Ono, M. Hatano: None declared, A. Nishimi: None declared, S. Nishimi: None declared, T. Hayashi: None declared, R. Yanai: None declared, H. Furuya: None declared, M. Umemura: None declared, T. Kasama: None declared, M. Hosaka: None declared, K. Sanada: None declared

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## Rheumatoid arthritis - anti-TNF therapy

### AB0297 REAL-LIFE EFFECTIVENESS OF GOLIMUMAB IN BIOLOGIC-NAÏVE RHEUMATOID ARTHRITIS PATIENTS – DATA FROM REUMA.PT, A PORTUGUESE REGISTRY

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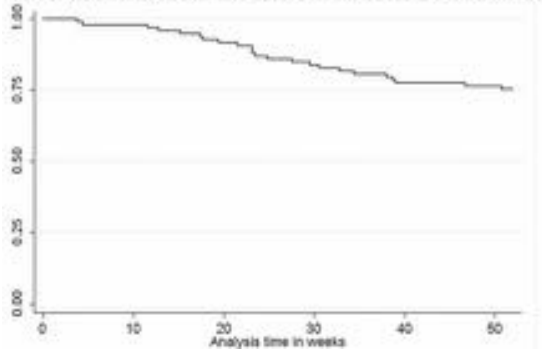
**Background:** Registries are becoming an increasingly important source of data, providing additional information on the use of biologics in clinical practice. The real-world clinical data currently available regarding the use of SC anti-TNFs is still limited. Therefore, it is of utmost importance to increase the knowledge of Golimumab (GLM) effectiveness in the clinical practice.

**Objectives:** This study was designed to access the effectiveness of SC GLM 50 mg/monthly + MTX through 52 weeks of treatment in biologic-naïve RA patients. The primary objective was to investigate the proportion of patients achieving clinical remission (DAS28ESR<2.6). The secondary objectives were the evaluation of: the treatment persistence rates; the proportion of patients achieving functional response (ΔHAQ>0.22); and the effect of treatment on DAS28 individual components.

**Methods:** This was a retrospective non-interventional study based on the Rheumatic Diseases Portuguese Register (Reuma.pt). It was conducted in a cohort of patients aged >18 years with active RA despite previous treatment with conventional DMARDs, biologic-naïve, who started SC GLM+MTX, from March 2011 to August 2015. The cumulative incidence of achieving clinical remission, treatment persistence and functional response/remission were estimated using survival analysis. Cox regression was used to calculate the hazard ratios.

**Results:** A total of 109 patients (86.3% female, mean age 55.5±13.2 years; mean age of diagnosis 45.5±13.5 years, rheumatoid factor 78% positive) met the study criteria. Ninety-three had a follow up of at least 52 weeks (i.e. all patients who started treatment before August 2014). At week 52, 38.3% of patients were on clinical remission, 91.9% achieved functional response and 35.2% were on functional remission (HAQ<0.5). The treatment persistence rate was 75.3% for the individuals who were in the study for ≥52 weeks (Figure 1). For functional remission, high CRP levels at baseline seem to be a determining factor (HR=0.54, *p*=0.026).

Figure 1: Kaplan-Meier survival estimate for Golimumab treatment persistence through 52 weeks



**Conclusions:** This is the first Golimumab data analysis generated from the Portuguese registry Reuma.pt. Our results are in agreement with data from other national registries and demonstrate the long-term effectiveness and the high treatment persistence rates of GLM through 52 weeks.
**Disclosure of Interest:** A. F. Mourão Consultant for: Merck Sharp & Dohme, C. Ribeiro: None declared, J. Borges: None declared, M. J. Gonçalves: None declared, M. Bernardes: None declared, S. Fernandes: None declared, R. Dezerto Employee of: Merck Sharp & Dohme, P. A. Laires Employee of: Merck Sharp & Dohme, P. Machado Employee of: Merck Sharp & Dohme, M. Eusébio: None declared, M. J. Santos: None declared, H. Canhão: None declared
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## AB0298 CURRENT STATUS OF CLINICAL DEVELOPMENT OF ANTI-TNF BIOSIMILARS: MAIN CHARACTERISTICS AND CURRENT TRENDS OF PHASE III TRIALS

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**Background:** The global development of a biosimilar product is methodologically complex, presenting potential design pitfalls and operational challenges with the risk of failing to demonstrate equivalence. The clinical development of anti-TNF biosimilars presents an additional challenge of selecting the most appropriate therapeutic indication(s) for the pivotal clinical trial(s) among those approved for the originator molecules.
**Objectives:** By reviewing the clinical development programs of biosimilars of adalimumab, etanercept and infliximab, we aimed to highlight the key features of pivotal clinical trials in terms of both study design and most suitable indications.
**Methods:** We performed a search of completed or ongoing Phase III global clinical trials for anti-TNF biosimilars in different clinical trials databases[1–3] as well as a search of literature on Medline for anti-TNF biosimilar clinical trials, and summarized the main features of study design of the retrieved trials.
**Results:** The pivotal efficacy and safety trials for anti-TNF biosimilars were either in rheumatoid arthritis (RA) or in psoriasis (PsO). In only a few cases, both indications were pursued for the same product in two pivotal trials. For etanercept and infliximab biosimilars, the most frequent indication of the pivotal trial was RA. For adalimumab either RA or PsO indications were investigated in approximately the same number of trials, with the most recent trials being all in PsO. All studies have an equivalence and not a non-inferiority design. However, considerable differences exist among these studies regarding key design elements such as the target patient population, background therapy, blinding, stratification, switch from originator to biosimilar product, primary dependent variable, and selection of equivalence margin. The differences of the study design of the Phase III biosimilar studies are summarized and discussed regarding the potential impact on demonstrating comparability and operational feasibility.
**Conclusions:** Most of the sponsors are conducting or have conducted the pivotal Phase III studies of anti-TNF biosimilars in one disease indication only, with a preference for PsO in most recent trials. This may suggest that PsO has become the indication of choice for pivotal trials for anti-TNF biosimilars. Potential advantages include 1) the greatest placebo-adjusted response rate is in PsO for the various TNF inhibitors among the licensed therapeutic indications[4,5], consistent with the need for a smaller sample size to demonstrate equivalence; 2) the primary study endpoint at week 16 or Week 12 for PsO compared to week 24 of RA allows for a shorter study duration; 3) a more favorable competitive environment leading to a faster trial execution; and 4) a more sensitive model to investigate immunogenicity compared to RA since PsO patients do not receive any immunosuppressive drug for the duration of the study.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3238

## AB0299 THE REASONS FOR WITHDRAWAL OF BIOLOGICAL DMARDS ACCORDING TO THE RUSSIAN REGISTRY OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Russian register of patients with inflammatory arthritis started in 2012 as a register of RA ("All-Russian register of Rheumatoid Artritis"- ARRA) now transformed into "Observational REgister of arthritis in cLinical practice" (OREL), including patients with rheumatoid arthritis (RA), psoriatic arthritis and adults with juvenile arthritis. (RA), psoriatic arthritis and adults with juvenile arthritis.
**Objectives:** To study reasons for withdrawal of biological DMARDs in patients with RA in clinical practice in Russia.
**Methods:** Data of 1398 pts with RA (286 men, 1112 women, medium age of 50,5 years), treated of biological DMARDs, were included in OREL registry from 01 Mar 2012 to 30 Mar 2015.
**Results:** 320 pts (22.8%) had withdrawals of biologics during this period. In 77 pts (23.4%) the reason for withdrawal was primary lack of efficacy or secondary loss of response; in 54 pts (16.9%) - adverse events (AE) or serious adverse events (SAE). In 80 pts (25.0%) biologic therapy has been stopped due to continuous remission; 109 pts (32.5%) had administrative reasons (lack of funding etc.).

Table 1. Main reasons for withdrawal biological DMARDs

| Biological DMARD | n | All reasons n (% )* | Continuos remission n (% )* | Lack of efficacy or loss of response n (%)* | AE/SAE n (%)* | Lack of funding n (% )* |
|---|---|---|---|---|---|---|
| Infliximab | 207 | 28 (13.5) | 0 | 11 (5.3) | 10 (4.8) | 7 (3.4) |
| Adalimumab | 253 | 64 (25.3) | 2 (0.8) | 25 (9.9) | 11 (4.3) | 26 (10.3) |
| Etanercept | 230 | 125 (54.3) | 74 (32.2) | 12 (5.2) | 8 (3.5) | 31 (13.5) |
| Certolizumab pegol | 47 | 12 (25.5) | 1 (2.1) | 1 (2.1) | 2 (4.3) | 8 (17.0) |
| Abatacept | 211 | 44 (20.9) | 0 | 17 (8.1) | 16 (7.6) | 11 (5.2) |
| Tocilizumab | 120 | 27 (22.5) | 1 (0.8) | 2 (1.7) | 6 (5.0) | 18 (15.0) |
| Rituximab | 330 | 20 (6.1) | 2 (0.6) | 9 (2.7) | 1 (0.3) | 8 (2.4) |

% relative to the total number of patients in the subgroup of drug.

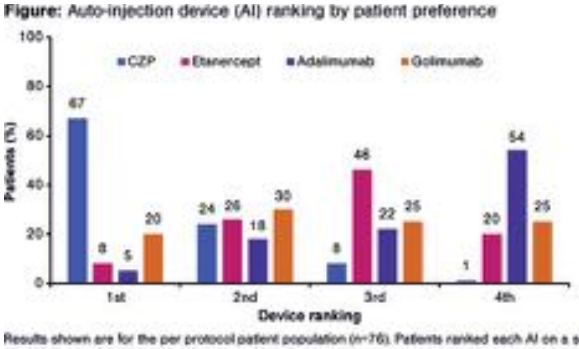
**Conclusions:** Frequencies of withdrawals due to lack of efficacy or loss of response among biological DMARDs were comparable. Etanercept has been withdrawn due to long term remission more often than other biologics. Lack of funding is still an important cause of withdrawal of biological therapy of RA.
**Disclosure of Interest:** None declared
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## AB0300 COMPARATIVE USABILITY STUDY FOR A CERTOLIZUMAB PEGOL AUTO-INJECTION DEVICE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Impaired manual dexterity is common in patients (pts) with rheumatoid arthritis (RA), often resulting in difficulties with drug self-administration when using pre-filled syringes.[1,2] Auto-injection devices (AIs) have been shown to provide a number of benefits, including reduced discomfort and greater ease of use compared with manual injections.[2,3] A new certolizumab pegol (CZP) device was created, based on pt insights and capitalizing on the benefits of existing AIs.
**Objectives:** To compare the usability of a new CZP AI with alternative anti-tumor necrosis factor (anti-TNF) devices (adalimumab, etanercept and golimumab) in patients with moderate to severe RA.
**Methods:** Eligible pts had moderate to severe RA (fingers, hands and/or wrists affected) and no prior experience of using an AI for RA. Each pt tested 4 AIs (CZP, golimumab, etanercept and adalimumab) in a randomized order by performing a simulated self-injection on a training skin pad strapped to the upper thigh or lower abdomen. All identifications were removed from the AI devices and respective instructions for use. Pts were provided with instructions for use for each of the AIs, but were not trained on device use prior to testing. Following utilization of all four AIs, pts were asked to rank them in order of preference from 1–4 (1=the most preferred) and to provide feedback on their usability (easy to use, easy to start the injection, easy to tell when injection was finished and willingness to use).
**Results:** Overall, 76 pts took part in this study. 67.1% pts ranked the CZP AI as their most preferred device; 23.7% ranked it as their second most preferred (Figure). The preference in the overall ranking of the CZP AI over each of the other devices was statistically significant ($p<0.001$). The majority of pts agreed, strongly agreed or very strongly agreed that the CZP AI was easy to use, easy to start the injection and that it was easy to determine when the injection was finished. Pts were significantly more willing to use the CZP AI compared with each of the other devices tested ($p<0.001$).

**Figure:** Auto-injection device (AI) ranking by patient preference




Results shown are for the per protocol patient population (n=76). Patients ranked each AI on a scale of 1–4 (1=the most preferred and 4=the least preferred).

**Conclusions:** In pts with moderate to severe RA, the CZP AI was the preferred

choice compared to the golimumab, etanercept and adalimumab AIs, and was associated with a high level of patient satisfaction.

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**Disclosure of Interest:** B. Domanska Employee of: UCB Pharma, L. Peterson Employee of: UCB Pharma, I. Mountian Employee of: UCB Pharma, M. Schiff Grant/research support from: UCB Pharma, Consultant for: UCB Pharma

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## AB0301 COMPARISON OF THE BIOAVAILABILITY OF A SINGLE DOSE OF CERTOLIZUMAB PEGOL INJECTED EITHER BY A PRE-FILLED SYRINGE OR BY AN AUTO-INJECTION DEVICE

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**Background:** Evaluation of the pharmacokinetic (PK) properties of certolizumab pegol (CZP) has shown a linear relationship between the dose administered (intravenous and subcutaneous [sc] routes), the maximum plasma concentration ($C_{max}$), and the area under the plasma concentration versus time curve (AUC).[1] In multiple clinical studies, the half-life ($t_{1/2}$) was approximately 14 days for all CZP dosage levels tested. CZP has also been demonstrated to have good bioavailability (approximately 80%) when given sc.[1]

**Objectives:** To compare the bioavailability of a single CZP 400 mg dose given as 2 x 200 mg injections injected by either a pre-filled syringe (PFS) or by an auto-injection device (AI), and to investigate the safety and tolerability of both methods of administration.

**Methods:** In this open-label phase I study, healthy volunteers were randomized into two parallel groups. On Day 1, study participants were injected with either 2 x 200 mg CZP via a PFS or 2 x 200 mg CZP via an AI. CZP plasma concentrations were measured pre-dose, and post-dose at 12h, 24h and Days 2, 3, 4, 5, 6, 7, 10, 14, 21, 28, 42, 56 and 84. Safety and tolerability were assessed by recording adverse events (AEs) and serious AEs (SAEs). In addition, the tolerability of the injection was assessed by a pain visual analog scale (VAS) and an injection site reaction questionnaire.

**Results:** 98 healthy volunteers were randomized to the PFS (n=49) and AI (n=49) groups. The mean plasma CZP concentration vs time profile of the AI was similar to that of the PFS. PK parameters were similar between the two modes of administration (Table). The 90% confidence intervals (CI) for the test/reference geometric mean ratios in $C_{max}$, $AUC_{(0\text{-}t)}$, AUC and $t_{1/2}$ were all contained in the bioequivalence range of 80–125%, and no statistically significant difference was found for $t_{max}$ between the two modes of administration (Table). Safety assessments showed that both methods of administration were equally well-tolerated. Injections performed with the AI appeared to be less painful immediately after administration than injections given by the PFS, as well as being associated with less burning and redness.

**Table:** Results of the bioequivalence analysis

| Parameter (unit) | Reference [a] | Test [a] | Test/Reference [c] | | CV (%) [d] |
|---|---|---|---|---|---|
| | CZP 400mg [b] PFS | CZP 400mg [b] AI | Point estimate | 90% CI | |
| $C_{max}$ (µg/mL) | 61.7 | 60.1 | 97.5 | 87.3–108.9 | 33.9 |
| $AUC_{(0\text{-}t)}$ (µg d/mL) | 1269.0 | 1239.9 | 97.7 | 89.1–107.2 | 28.1 |
| AUC (µg d/mL) | 1308.4 | 1325.8 | 101.3 | 92.8–110.6 | 25.9 |
| $t_{1/2}$ (days) | 10.4 | 11.3 | 108.9 | 96.4–123.0 | 36.7 |
| $t_{max}$ (days), median | 5.0 | 5.0 | 0.0 | 0.0–1.0 | n/a |

[a] Geometric least squares mean, unless otherwise noted; [b] CZP 400 mg dose was given as 2 x 200 mg injections; [c] Point estimate (90% CI) for the test/reference geometric least squares mean ratio (%) derived from the ANOVA; for $t_{max}$, median point estimate (90% non-parametric CI) of the difference test-reference; [d] ANOVA residual error, representing inter-subject variability. CI: confidence interval; CV: coefficient of variation.

**Conclusions:** CZP 400 mg dose is bioequivalent whether administered by AI or PFS. Overall, CZP injections were safe and well-tolerated for both administration methods.

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**Acknowledgement:** The authors acknowledge Costello Medical Consulting, funded by UCB Pharma, for writing and editorial assistance.

**Disclosure of Interest:** B. Astruc Employee of: Biotrial, S. Watanabe Employee of: UCB Pharma, G. Parker Employee of: UCB Pharma, R. Hulhoven Employee of: UCB Pharma

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## AB0302 INFLUENCE OF TAPERING BIOLOGICAL THERAPIES IN IMMUNOGENICITY IN A COHORT OF RHEUMATOID ARTHRITIS WITH LOW DISEASE ACTIVITY

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**Background:** Recent studies propose the use of a tapering strategy (dose reduction or discontinuation) of tumor necrosis factor inhibitors (TNFi) in rheumatoid arthritis (RA) patients (pts) in low disease activity (LDA) or clinical remission (R) without losing the disease control. One concern, when lower doses are used, is the appearance of anti-drug antibodies (ADA) with the consequent loss of efficacy.

**Objectives:** To evaluate the clinical influence of the tapering strategy of TNFi in a cohort of RA pts in LDA or R.

**Methods:** Of a total of 283 RA pts under TNFi, 52 patients treated with Infliximab (Ifx), Adalimumab (Ada) or Etanercept (Etn) were selected. All pts were in LDA or R (DAS28 $<$3.2 or $<$2.6, respectively) for at least 6 months prior to start the tapering strategy. Clinical activity (DAS28), drug levels (DL) and ADA were evaluated at baseline before tapering (pre-visit) and at the last available visit after 4 years follow-up (final-visit), this parameters were also evaluated at flares (DAS28$>$3,2 and $\Delta$DAS28$>$0.6). At flare, the biologic and non-biologic therapy could be intensified.

**Results:** In our cohort of 52 pts, 26 (50%) pts were treated with Ada, 16 (31%) with Etn and 10 (19%) with Ifx. Forty one (79%) were women and 41 (79%) pts were ACPA+ and RF+. Most patients received methotrexate concomitantly (69%), 25 (48%) pts other DMARDs and 22 (42%) prednisone. The mean follow-up was 43.76±8months, without statistically significance among TNFi (p=0.595). At pre-visit, 40 (77%) pts were in R and 12 (33%) LDA. The majority of patients remained in LDA or R at final-visit: 26 (50%) in R, 14 (27%) in LDA, 12 (23%) with DAS28$>$3.2, p=0.97). When a subanalysis in each TNFi was performed, it was confirmed that most pts were in LDA or R at final-visit (p=0.59 in Ada, p=0.26 in Ifx and p=0.78 in Etn). No differences in CRP levels between visit-pre and final visit were seen. 25 patients (48%) had flares during follow-up (13 (52%) had 1 flare, 10 (40%) had 2 flares and 2 (8%) had 3 flares. Most patients with flares were in LDA or R at final-visit (R=9 (36%), LDA=5 (20%)). Only 2 pts with flares dropped out the TNFi and were ADA + at final visit. All patients were ADA negative at the pre-visit and only 6 (11%) were positive at final-visit, 4 of them withdrawed therapy for maintaining clinical remission. A statistically significant decrease was observed in drug levels between the pre-visit and post-visit (Ada: 5251.9±1205.9 vs 1507.2±322.7, p=0.001; Etn: 2735.2±347.4 vs 1114.9±283.2, p=0.002; Ifx: 2358.4±728.5 vs 650.4±290.1, p=0.008).

**Conclusions:** The tapering strategy seems feasible in RA pts in LDA treated with TNFi, reducing the amount of drug administered with low incidence of ADA and without deterioration of disease activity. In most patients, flares appear to be controlled by changing the drug administration interval without the necessity of changing or stopping treatment.

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## AB0303 IDENTIFYING IMMUNOLOGICAL BIOMARKERS TO PREDICT TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS - PRELIMINARY RESULTS OF A PILOT STUDY

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**Background:** Good evidence shows that treating the inflammation of rheumatoid arthritis (RA) early leads to less disability and improved patient outcomes [1]. However, for patients receiving biologic therapies, only ~30% will have a good response to the first drug tried [2]; currently there is no way to predict which drug will be effective in each individual patient. As RA is an autoimmune disease, we hypothesise that the immunophenotype can be used to inform selection of the treatment most likely to be effective in individual patients.

The first step is to identify immunophenotypic differences between RA patients with very active disease and controls in order to inform hypotheses as to which immune markers may be important in informing selection of effective biologic therapy.

**Objectives:** 1) To compare the immunophenotype of RA patients about to start biologic therapy with controls.

2) To characterise the involvement of novel cell types such as invariant natural killer T (iNKT) cells and co-stimulatory pathways (CD200/CD200R) in RA compared to healthy controls.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were collected from patients about to be started on a biologic drug as part of the BRAGGSS study [3]. PBMCs were stimulated under a number of different conditions and analysed by 16-parameter flow cytometry for:

a) Cell surface profiles (major T and B cell subsets, classical and non-classical

monocytes, natural killer cells, dendritic cells, markers for iNKT cells and the expression of CD200 and CD200R), and
b) Intracellular cytokine quantification, following a stimulation assay (IFNγ, TNFα, IL-13, IL-10, IL-17A, GM-CSF, IL12-p40, IL-6).
**Results:** 7 RA patients and 9 healthy control samples were examined in this pilot study.
There were large differences in the number of IFNγ-producing T cells in all samples, in both RA patients and healthy controls (range 8.19% to 65.1% in RA and 17.9% to 49.0% in controls,). There were also differences in the number of IL-17A-producing T cells, although absolute numbers were lower (range: 1.2% to 12%). Samples could be placed into four phenotypes: 1) "IFNγ", 2) "IL-17A", 3) "double-hi", and 4) "low".
Interestingly, there was also a large range in number of IFNγ-producing B cells in all samples (mean fluorescence intensities (MFI) ranged from 202 to 1197).
Follow up data was available for 7 patients. Five had been started on an anti-TNF, one on tocilizumab and one on rituximab. Four had a good EULAR response, had been started on an anti-TNF, and had either the "double-hi", "IFNγ", or "low" phenotypes. One non-responder had been started an anti-TNF but had the "IL-17" phenotype. The other non-responder had been started on rituximab and had both the "IL-17" phenotype and a low IFNγ B cell signature.
**Conclusions:** RA patients may have very different B and T cell cytokine profiles on *ex vivo* stimulation of their PBMCs. This may be important in selecting the first biologic drug choice: For instance, a high IFNγ B cell phenotype might make rituximab a more attractive first choice, and so forth. These results require validation with larger sample numbers.
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**Disclosure of Interest:** None declared
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## AB0304 ADHERENCE TO DMARD AND SUBCUTANEOUS BIOLOGICAL THERAPY AMONG RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS AT BASURTO UNIVERSITY HOSPITAL

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**Background:** Combination therapy with DMARDs and Biological drugs is a common practice in the management of peripheral arthritis. The addition of Methotrexate to Biological agents provides better clinical response and decreased anti-drug antibodies production. This is well proved for patients with rheumatoid arthritis (RA), especially under therapy with anti-TNF antibodies, but not so clear for psoriatic arthritis (PsoA). Nevertheless a high percentage of patients may be non adherent, especially to DMARDs (Disease Modifying Antirheumatic Drugs), and this fact could have a negative effect on the course and management of the disease.
**Objectives:** To assess the adherence to subcutaneous Biological drugs and DMARDs in our patients with RA and PsoA under combination therapy, and to assess the relationship between the degree of adherence and different demographic and clinical aspects.
**Methods:** 179 clinical records of patients with PsoA and RA on Biologic treatment were reviewed. 61 patients on Biological monotherapy were excluded from the analysis. Demographic, clinical characteristics and comorbidities were collected. The level of adherence to DMARDS was obtained from the PRESBIDE monitoring system that estimates external pharmacy drug picking up for the last 8 months, and data of adherence to Biologicals from the Hospital Pharmacy registry (FARHOS). SPSSv22 software was used for statistical analysis.
**Results:** 109 patients included, 76% women, mean aged 57 years (range 19–86). 70% had RA and 30% PsoA. Disease evolution was longer than 10 years in 63% of the patients. 32% presented more than two comorbidities. Concerning DMARDs, 76% of patients received Methotrexate, 15.6%Leflunomide and 8.4% others. Average adherence to DMARDs was 65.5%, being good (>80%) in 49.5%, fair (60–80%) in 22% and low (<60%) in 28.4%. In 13 patients (11.92%) DMARD collection at the pharmacy was 0. Evaluated Biological drugs were mainly Adalimumab (30%) and Etanercept (39.5%). Adherence to Biologicals was excellent, average 91.8% (SD 9.78), significantly higher than the adherence to DMARDs (average 65.53, SD 32.79). ($p<0.001$, WR test). Disease activity estimated by DAS 28 was<2.6 in 57% of patients, 2.6–3.2 in 19,6% and >3.2 in 23.4%. There was no correlation between lack of adherence and resulting DAS 28. 47.7% of patients had received more than one DMARD previously, fact not being related to the current adherence. No relationship between the number of previous Biological drugs and adherence to DMARD was found.
**Conclusions:** Adherence to subcutaneous Biologic agents was good and statistically superior to Methotrexate. A high proportion of our patients (1/3) is non adherent to DMARDs, so that more than 10% are under unexpected monotherapy with Biological drugs because of noncompliance or withdrawal of the treatment. The reasons for this may be various, and the impact on the disease activity must be evaluated, as far as both negative and neutral effect had been described in the literature. The implementation of tools to monitor adherence and identification of non-compliant patients is useful in the search of solutions and clinical decision making.
**Disclosure of Interest:** None declared
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## AB0305 INFLUENCE OF DRUG LEVELS DURING THE FIRST ANTI-TNF THERAPY ON THE CLINICAL RESPONSE TO A SECOND BIOLOGIC IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The anti-tumor necrosis factor (anti-TNF) therapy has shown to be effective in rheumatoid arthritis (RA). Recent publications have shown the association between drug levels (DL) and clinical response to the anti-TNF therapies. For now it is not clear if the DL monitoring to the 1st anti-TNF in patients who discontinued due to inefficacy, can be useful to evaluate the clinical efficacy to the 2nd anti-TNF.
**Objectives:** To evaluate in a RA cohort (who stopped to the 1st anti-TNF due to inefficacy), the influence of the presence/absence of DL [infliximab (Ifx) y adalimumab (Ada)] at discontinuation, on the clinical response to the 2nd anti-TNF during the 1st year of therapy.
**Methods:** Seventy seven out of 182 RA patients who discontinued the Ifx or Ada therapy were recruited. All these patients dropped out the first anti-TNF due to inefficacy and switched to a 2nd anti-TNF (48 patients: 2 with Ifx, 4 with Ada, 40 with etanercept and 2 with certolizumab) or other biologics (OB) different to anti-TNF (29 patients: 17 with rituximab, 6 with tocilizumab and 6 with abatacept). Clinical activity was measured by DAS28 and clinical improvement by Delta-DAS28 adjusted to baseline clinical activity (baselineDAS-DAS (24weeks or 52weeks)/baselineDAS) at baseline, 24 weeks (24w) and 52 weeks (52w). DL were measured prior to drug administration at 24w and 52w by ELISA.
**Results:** Of the 77 RA patients, 82% (63/77) were women and the mean disease duration was 21±13 years. At the end of the 1st antiTNF, 54/77 (70%) had undetectable DL and 23/77 (30%) had detectable DL. At w24 of the 2nd biologic, patients treated with OB tended to be less active than patients treated with a 2nd anti-TNF but these differences were not significant at w52 (*DAS28 at w24:* 3.5±1.3 with OB vs 4.1±1.1 wirh 2nd anti-TNF, p=0.053; *Delta-DAS28 at w24:* 0.3±0.3 with OB vs 0.2±0.3 with 2nd anti-TNF, p=0.326; *DAS28 at w52:* 3.3±1.2 with OB vs 3.8±1.1 with 2nd anti-TNF, p=0.166; *Delta-DAS28 at w52:* 0.3±0.2 with OB vs 0.2±0.3 with 2nd anti-TNF, p=0.501). Patients with undetectable DL to first anti-TNF treated with a 2nd anti-TNF had better clinical response during the first year of therapy (*DAS28 at w24:* 3±1.1 with non DL vs 4.3±1.2 with DL, p=0.004; *Delta-DAS28 at w24:* 0.3±0.3 with non DL vs 0.2±0.3 with DL p=0.074; *DAS28 at w52:* 2.9±1.1 with non DL vs 4±1.2 with DL, p=0.015; *Delta-DAS28 at w52:* 0.4±0.2 with non DL vs 0.2±0.3 with DL, p=0.210). However, no differences in the clinical activity were observed between patients with undetectable or detectable DL who switched to OB (*DAS28 at w24:* 4.4±1.4 with non DL vs 3.8±1 with DL, p=0.247; *Delta-DAS28 at w24:* 0.2±0.2 with non DL vs 0.2±0.2 with DL, p=0.382; *DAS28 at w52:* 4.1±1.2 with non DL vs 3.5±0.7 with DL, p=0.122; *Delta-DAS28 at w52:* 0.2±0.2 with non DL vs 0.3±0.1 with DL, p=0.376).
**Conclusions:** In our cohort of RA patients with inefficacy to the 1st anti-TNF, a high proportion of patients discontinued the therapy with undetectable DL. The DL monitoring during the 1st anti-TNF seems to be a useful tool to define what patients have a better clinical response to the 2nd anti-TNF, although this effect does not influence on those patients who switch to OB.
**Disclosure of Interest:** None declared
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## AB0306 THE TIME WINDOW TO DETERMINE TROUGH VALUES OF ETANERCEPT IS IMPORTANT IN PERSONALIZED MEDICINE REGIME INDEPENDENTLY OF METHOTREXATE COADMINISTRATION

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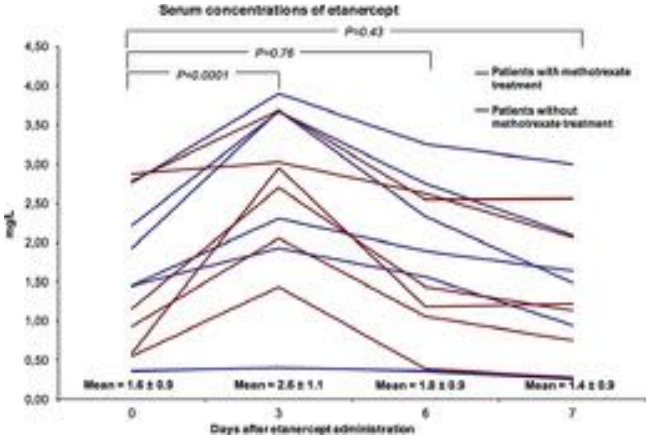
**Background:** Several studies show correlation between trough serum concentrations of TNF-alpha inhibitors and treatment efficacy (1,2). In spite of this, patients are treated with standard dosages as in "one size fits all". Individualised treatment based on trough value of etanercept might optimise treatment and reduce risk of adverse events. However, the time window to determine the trough value of etanercept in patients on standard dosing is not known. Based on the pharmacokinetics of etanercept ($t_{max}$ approx. 69 h, $t_{1/2}$ approx. 102 h) the purpose of this study was to challenge the window to determine trough values in patients treated with etanercept with and without concomitant methotrexate.
**Objectives:** To explore the time window to determine trough values of etanercept and whether concomitant treatment with methotrexate influence the width of the window.
**Methods:** Six arthritis patients with concomitant methotrexate and six arthritis patients without were included. Serum concentrations of etanercept were measured

before dosing, at day 3 ($t_{max}$), at day 6, and before next dosing at day 7 thus focusing on trough rather than peak values. Serum concentrations of etanercept were assessed by ELISA technique (3).

**Results:** The study included 12 female patients (10 diagnosed with rheumatoid arthritis and 2 with juvenile arthritis equally distributed between groups) treated with etanercept, with or without concomitant methotrexate. In the methotrexate group the average dosage was 15.4 mg/week (SD=6.4). For the whole study population, the age was 59.5 years (SD=15.4) with disease duration of 23.5 years (SD=7.4), and an average DAS28CRP of 2.2 (SD=0.6). There were no differences between the two subgroups in regard to age, disease duration, and years of treatment with etanercept, while the group treated without methotrexate tended to have a lower DAS28CRP (1.9 vs 2.5, p=0.06).

In a mixed-effect logistic regression model, methotrexate did not influence the serum levels of etanercept (P=0.6).

As expected there was a significant increase in serum level of etanercept on day 3 ($t_{max}$), while no difference was seen between day 0 and day 6 or 7 (compatible with the t½ of approx. 4 days), thus allowing considering extension of the window to determine trough values. However, a post hoc analysis confirmed a decline in concentrations from day 6 to day 7 of 0.32 mg/l (SD=0.29). In light of the rather narrow concentration ranges found in patient populations (1,2) it can not be ruled out as clinical irrelevant.




**Conclusions:** Concomitant methotrexate did not influence the serum levels of etanercept.

The day to day decrease in serum concentrations of etanercept at the end of a dosing interval must be considered when designing an algorithm for serum-concentration based personalized medicine.

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**Disclosure of Interest:** None declared

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## AB0307 NO CORRELATION BETWEEN BODY MASS INDEX AND CLINICAL RESPONSE TO INFLIXIMAB: POST-HOC ANALYSIS OF PLANETRA

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**Background:** Rheumatoid Arthritis (RA) patients with high body mass index (BMI) have been known to respond less well to anti-tumor necrosis factors (TNFs), especially infliximab. The post-hoc analysis of PLANETRA [1], a randomized controlled trial, was carried out to evaluate the influence of BMI on clinical response to infliximab (both infliximab originator and its biosimilar) in a large number of patients with RA.

**Objectives:** To investigate the association between BMI and clinical response to infliximab in patients with RA.

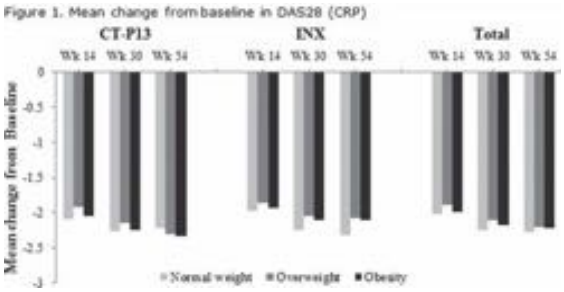
**Methods:** BMI was calculated before initiation of infliximab treatment in 606 patients with RA in PLANETRA. Patients were classified into 3 groups as normal weight (<25 kg/m$^2$), overweight (≥25-<30 kg/m$^2$) and obesity (≥30 kg/m$^2$) according to the WHO BMI categories. Changes in disease activity were assessed at weeks 14, 30 and 54 with the Disease Activity Score in 28 joints (DAS28 [CRP]), Health Assessment Questionnaire (HAQ), and Short Form Health Survey (SF-36) based on BMI categories.

**Results:** The proportion of patients with normal weight, overweight and obesity were 43.1%, 36.1% and 20.8%, respectively. Baseline characteristics were comparable among BMI subgroups in gender, height and weekly MTX dose given to patients. The mean DAS28 (CRP) at baseline was significantly higher in obesity group (5.80±0.87, 5.72±0.86 and 6.15±0.78 for normal weight, overweight and obesity, respectively; $P<0.0001$). But no significant differences were observed when comparing the mean change from baseline at Week 14 (-2.02 vs. -1.89 vs. -1.99), Week 30 (-2.25 vs. -2.10 vs. 2.17) and Week 54 (-2.27 vs. -2.20 vs. -2.22) among BMI subgroups. Similar results were observed when analysing biosimilar infliximab (CT-P13) and innovator infliximab (INX) separately up to Week 54 [Figure 1].

HAQ score was significantly higher in obese patients at baseline (1.55±0.55, 1.56±0.62 and 1.71±0.50, for normal weight, overweight and obesity, respectively; $P$=0.0278). However, there was no significant difference of mean change from baseline in HAQ at Week 14 (-0.56 vs. -0.48 vs. -0.55), Week 30 (-0.56 vs. -0.54 vs. -0.56) and Week 54 (-0.59 vs. -0.56 vs. -0.57) when assessed by BMI categories. In addition, improvements from baseline in both physical and mental component summary (PCS and MCS) scores were similar at weeks 14, 30 and 54 regardless of BMI (Table 1).

Table 1. Mean (SD) change from baseline in PCS and MCS of SF-36

| | <25kg/m$^2$ (n=261) | ≥25–<30kg/m$^2$ (n=219) | ≥30kg/m$^2$ (n=126) | P-value |
|---|---|---|---|---|
| Physical component summary (PCS) | | | | |
| Week 14 | 6.82 (7.36) | 6.25 (6.72) | 6.34 (7.57) | 0.6751 |
| Week 30 | 7.35 (7.75) | 6.76 (8.06) | 6.56 (7.68) | 0.6260 |
| Week 54 | 7.31 (8.48) | 7.56 (8.17) | 6.89 (8.57) | 0.8205 |
| Mental component summary (MCS) | | | | |
| Week 14 | 6.72 (10.82) | 5.61 (9.95) | 6.70 (9.84) | 0.4818 |
| Week 30 | 6.92 (10.10) | 6.41 (10.80) | 7.50 (9.95) | 0.6774 |
| Week 54 | 7.33 (10.79) | 6.31 (11.34) | 7.84 (10.22) | 0.4917 |




**Conclusions:** The BMI does not affect the clinical response to infliximab in patients with RA. No significant association was found between BMI and clinical response by DAS28 (CRP), HAQ and SF-36. Therefore, the weight-based dosing of infliximab is appropriate in RA patients.

**References:**

[1] Yoo D.H., et al. Ann Rheum Dis 2013;72:1613–20.

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## AB0308 A PHASE I PHARMACOKINETIC STUDY COMPARING PRE-FILLED PEN AND PRE-FILLED SYRINGE OF SB5, AN ADALIMUMAB BIOSIMILAR IN HEALTHY SUBJECTS

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**Background:** SB5 is developed as a biosimilar of the Adalimumab reference product (ADL). Equivalence in the pharmacokinetics (PK) between pre-filled syringe (PFS) of SB5 and PFS of ADL was demonstrated in a phase I study conducted in healthy subjects[1] and equivalent efficacy and comparable safety between PFS of SB5 and PFS of ADL up to week 24 were demonstrated in the phase III study conducted in patients with rheumatoid arthritis[2].

**Objectives:** To investigate and compare the PK, safety, and tolerability of the pre-filled pen (Pen) and PFS of SB5 in healthy subjects.

**Methods:** This study was a randomised, open-label, single-dose, 2-arm, parallel group study in healthy subjects. Subjects were randomised in a 1:1 manner to receive a single 40 mg dose of SB5-Pen or SB5-PFS by subcutaneous injection on Day 1 and then were observed for 57 days during which the PK, safety, and tolerability measurement were made. The serum concentration of adalimumab was measured using an enzyme-linked immunosorbent assay. The primary PK parameters were area under the concentration-time curve from time zero to infinity ($AUC_{inf}$), area under the concentration-time curve from time zero to the last quantifiable concentration ($AUC_{last}$), and maximum concentration ($C_{max}$). Equivalence for the primary PK parameters was to be concluded if the 90% confidence intervals (CIs) for the ratio of geometric least squares means (LSMeans) of the groups compared were completely contained within the pre-defined equivalence margin of 0.8 to 1.25 using an analysis of variance.

**Results:** Of 190 randomised subjects, 1 subject was excluded from the PK population in each arm (non-compliance with medication dosage in SB5-Pen and exclusion criteria met in SB5-PFS) and 188 subjects were analysed as PK population (n=94 in SB5-Pen and SB5-PFS each). Following single dose, the mean of $AUC_{inf}$, $AUC_{last}$, and $C_{max}$ were 2743.2 μg·h/mL, 2329.2 μg·h/mL, and 3.803 μg/mL for the SB5-Pen and 2503.3 μg·h/mL, 2182.2 μg·h/mL, and 3.673 μg/mL for the SB5-PFS. 90% CIs for the geometric LSMeans ratios of primary PK parameters for SB5-Pen and SB5-PFS were within the pre-defined equivalence margin of 0.8 to 1.25 (Table), confirming the bioequivalence between SB5-Pen and SB5-PFS. The proportion of subjects who experienced treatment-emergent adverse events (TEAEs) was comparable between the SB5-Pen and SB5-PFS (68.4% in SB5-Pen vs 60.6% in SB5-PFS). The most frequent TEAEs were upper respiratory tract infection (15.8% in SB5-Pen vs 19.1% in SB5-PFS). The majority of TEAEs were mild in severity. Only one subject in SB5-PFS experienced a moderate injection site reaction.

Table 1. Comparison of primary PK parameters between the treatments

| Comparison | PK parameters | Ratio | 90% CI |
|---|---|---|---|
| SB5-Pen vs SB5-PFS | $AUC_{inf}$ (μg·h/mL) | 1.104 | 0.9953; 1.2240 |
| | $AUC_{last}$ (μg·h/mL) | 1.070 | 0.9802; 1.1687 |
| | $C_{max}$ (μg/mL) | 1.021 | 0.9503; 1.0968 |

**Conclusions:** This study demonstrated PK equivalence between SB5-Pen and SB5-PFS in healthy subjects. Both SB5-Pen and SB5-PFS were generally well tolerated with similar safety profiles.

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**Disclosure of Interest:** D. Shin Employee of: Samsung Bioepis, Y. Lee Employee of: Samsung Bioepis, J. W. Kang Employee of: Samsung Bioepis, R. Ellis-Pegler Grant/research support from: Samsung Bioepis

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## AB0309 VALUE OF THE CLINICAL MEETINGS FOR AN ACCURATE BIOLOGICAL THERAPY ASSESSMENT IN RHEUMATIC DISEASES. THE EXPERIENCE OF THE BIOLOGICAL THERAPY ASSESSMENT COMMITTEE AT A TERTIARY HOSPITAL

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**Background:** Given the increasing use of biological therapies in rheumatologic diseases and the importance of their secondary effects, it has been promoted clinical Meetings for an accurate Biological Therapy Assessment (BTAM). In the BTAM rheumatologists consider the need to initiating biological therapy, changes in biological therapeutic targets, sustained biological treatment or their suspension.

**Objectives:** To assess the BTAM effectiveness in patients with rheumatic diseases in a Rheumatology Department in a tertiary-level hospital.

**Methods:** Prospective study including all consultations to BTAM between 2013 and 2015 in the Rheumatology Department of La Fe Hospital. Consultations were classified as: "therapeutic target modification", "route of administration modification", "dose treatment modification", "new biological treatment", "treatment continuation" and "treatment suspension". In order to evaluate disease activity, we used DAS28, BASDAI, serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Biostatistical analysis was performed using R software 3.2.3.

**Results:** We included 1683 BTAM consultations, corresponding to 517 patients with rheumatic diseases with a mean age of 39.94±14.88 and 13.37±8.75 years of disease progression. 51.6% of patients were rheumatoid arthritis, 27.9% spondyloarthritis, 15.3% psoriatic arthritis and 5.2% other diagnosis. 116 patients received a prior biological treatment. Disease activity evaluation of the 1683 BTAM consultations for the main categories is shown in the table.

| | Therapeutic target modification n (%) | Dose treatment modification n (%) | New biological treatment n (%) | Treatment continuation n (%) |
|---|---|---|---|---|
| TOTAL | 88 (5.2%) | 79 (4.7%) | 52 (3.1%) | 1405 (83.5%) |
| DAS28 | 4.32±1.68 | 2.74±1.39 | 4.78±0.97 | 2.8±1.23 |
| BASDAI | 6.3±1.71 | 3.03±1.89 | 6.74±1.28 | 4.29±2.36 |
| ESR | 26.12±28.13 | 17.47±18.43 | 17.26±11.99 | 13.79±12.54 |
| CRP | 10.21±15.23 | 4.15±4.41 | 8.22±9.04 | 3.88±6.41 |

Biostatistic analysis shows significant differences in Das28, BASDAI, CRP and ESR values between BTAM consultations for initiating new treatment or modify therapeutic target, and treatment continuation consultations ($P<0.0001$). There was also a significant association between the number of biological targets administered and the increase of DAS28 ($P<0.0001$) and BASDAI ($P=0.014$).

**Conclusions:** We observed a increased disease activity in cases where a new biological treatment or different therapeutic target is administrated, and values of disease activity in treatment continuation are compatible with low activity. In the 5.2% of consultations it has prescribed modification treatment, in order to avoid treatment ineffectiveness. Moreover, some continuation treatment consultations showed low activity scores, leading to a therapeutic optimization. BTAM consultations are useful for optimal management of these patients with biological therapy

**Disclosure of Interest:** None declared

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## AB0310 PROSPECTIVE STUDY OF 78 PATIENTS TREATED WITH INFLIXIMAB BIOSIMILAR REMSIMA®

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**Background:** In 2015 it began to be used in many EU countries the first biosimilar antiTNF (Infliximab) approved by the EMA. The Korean company owns the molecule under the trademark Remsima® was widely used for replacing existing treatments with infliximab molecule marketed since 1999 as Remicade in the approved indications in sheet for this purpose, RA, AS and PsA.

**Objectives:** Control the security and survival of the drug in patients Remsima® in which replaced the molecule Remicade infliximab. Settled visits every 3 months to monitor the occurrence of adverse events with possible association to the drug. Patients were followed in routine clinical practice for 8 different doctors.

**Methods:** 78 patients began treatment with Remsima® since March 2015. Of these, 25 were suffering from Rheumatoid Arthritis, Psoriatic Arthritis 8, SpA 41 and severe uveitis 2. 53 of these patients had already been treated with Remicade and 25 were "naive" to IFX, having been previously treated with other biological therapy or were naive to this.

**Results:** 37 patients, less than half have associated a DMARD in the 9th month of follow-up (70'2% MTX). 11 patients with Remsima not reached 37 weeks of follow-up and were removed (5 of these patients had replaced Remicade). None of them was removed for serious adverse effect. Overall 86% survival at 9 months. No patient dropped the sheet approved for disease Remsima 3mg/kg body weight or Remsima 5mg/kg dose before 6 months of treatment.

The reasons for medication discontinuation were in the 5 cases of replacement Remicade by Remsima: 4 loss efficacy and cutaneous leishmaniasis.

For patients naive to Remicade, 1 case of possible photosensitivity, 1 case of bronchospasm during infusion, one case of urticaria, 1 case of hip replacement surgery, one transfer to another country of residence and a loss of effectiveness.

The reasons for medication discontinuation were in the 5 cases of replacement Remicade by Remsima: 4 loss efficacy and cutaneous leishmaniasis.For patients naive to Remicade, 1 case of possible photosensitivity, 1 case of bronchospasm during infusion, one case of urticaria, 1 case of hip replacement surgery, one transfer to another country of residence and a loss of effectiveness. 4 patients showed in repeated infusions dizziness, headache or neck stiffness within 48 hours of infusion Remsima. However they asked to continue with medication.

Overall 86% survival at 9 months.Only 23% of patients needed glucocorticoid use at 9 months. 22% of patients required to reduce the infusion period IFX-Remsima 7 weeks or less. Finally in 4 patients an optimization of treatment extending to more than 8 weeks was achieved infusions. It is worth drawing attention to the small variation of CRP level ($\Delta$ <5mg/dl) at 9 months of initiation of Remsima treatment.

**Conclusions:** The results of safety and survival of biosimilar infliximab Remsima® are similar to those shown in their pivotal trials PLANETRAS and PLANETAS, both in patients with prior use of infliximab as another patient who has not used this. Although the follow-up period is too short, averaging 8.3 months and a standard deviation of 2, these data support an increasingly widespread use of this biosimilar in any patient profile.

**Disclosure of Interest:** None declared

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## AB0311 CLINICAL RESPONSES AND SYNOVIAL VASCULARITY IN OBESE RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ADALIMUMAB AND METHOTREXATE

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**Background:** Obese rheumatoid arthritis (RA) patients (pts) may have higher levels of inflammatory mediators, greater joint swelling and tenderness, and suboptimal response to therapy.

**Objectives:** We assessed disease activity and treatment response in obese RA pts, using ultrasonography (US) and clinical measures.

**Methods:** This *post hoc* analysis used observed data from the MUSICA trial[1] which evaluated the efficacy of high [20 mg/week (wk)] or low (7.5 mg/wk) doses of methotrexate (MTX) in combination with adalimumab (ADA) for 24 weeks (wks)

in RA pts with previous inadequate response to MTX who initiated ADA. Pts were grouped according to body mass index (BMI) at baseline (BL): normal BMI <25; overweight BMI ≥25-<30; obese BMI ≥30. Synovial vascularity and hypertrophy were measured by Power Doppler US and Greyscale respectively, bilaterally, at metacarpophalangeal (MCP) joints 2, 3, 5, metatarsophalangeal joint 5 (MTP5) and wrists. Swollen joint count (SJC) of 66 joints, tender joint count (TJC) of 68 joints, 28-joint count Disease Activity Score using C-reactive protein (DAS28-CRP), and numbers of pts reaching American College of Rheumatology (ACR) criteria, Clinical Disease Activity Index [CDAI] low disease activity (LDA,<10), DAS28-CRP low disease activity (LDA; DAS<3.2), were assessed at wks 12 and 24.

**Results:** Out of 308 pts at BL, 69 pts (22.4%) had BMI <25,102 pts (33.1%) had BMI ≥25-<30 and 137 pts (44.5%) had BMI ≥30. Disease characteristics and ultrasound disease assessments were similar for the 3 BMI subgroups at BL. At wks 12 and 24, compared with pts in the normal and overweight categories, obese pts tended to have numerically smaller mean changes from BL in SJC66, TJC68, DAS28-CRP, synovial hypertrophy and synovial vascularity (table). Compared to pts in the normal and overweight categories, significantly fewer obese pts reached ACR20/50 at wks 12 and 24. Significantly fewer obese pts reached CDAI LDA and DAS28-CRP LDA at wk 12; this difference was driven by those obese pts receiving low dosage of concomitant MTX (7.5 mg/wk), although by wk 24, the differences were no longer significant. There was low to no correlation between synovial vascularity/hypertrophy and clinical findings of swelling and tenderness. The proportion of pts with synovial vascularity=0 in the 3 BMI subgroups at wks 12 and 24 was not statistically different.

| | week 12 | | | week 24 | | |
|---|---|---|---|---|---|---|
| MTX mg/wk | Normal (BMI <25) | Overweight (BMI ≥25-<30) | Obese (BMI ≥30) | Normal (BMI <25) | Overweight (BMI ≥25-<30) | Obese (BMI ≥30) |
| Mean change from baseline in SJC66 | | | | | | |
| 7.5 | -8.7 (1.45) | -10.2 (1.24) | -7.3 (1.11) | -8.3 (1.70) | -11.2 (1.37) | -7.2 (1.29) |
| 20 | -12.1 (1.58) | -8.9 (1.26) | -9.9 (1.04) | -13.9(1.76) | -11.6(1.37) | -10.9 (1.16) |
| Overall | -10.4 (1.08) | -9.2 (0.88) | -8.9 (0.76) | -11.1 (1.22) | -11.4 (1.0) | -8.7 (0.85) |
| Mean change from baseline in TJC68 | | | | | | |
| 7.5 | -16.0 (2.24) | -14.5 (1.87) | -14.2 (1.67) | -16.7 (2.36) | -19.6 (1.90) | -15.8 (1.71) |
| 20 | -16.5 (2.38) | -15.4 (1.91) | -13.6 (1.56) | -18.1 (2.44) | -19.4 (1.91) | -17.3 (1.62) |
| Overall | -16.2 (1.64) | -15.0 (1.39) | -13.9 (1.15) | -17.4 (1.70) | -19.5 (1.35) | -16.6 (1.18) |
| Mean change from baseline in synovial hypertrophy | | | | | | |
| 7.5 | -1.1 (0.91)** | -2.9 (0.73)** | 0.7 (0.67)** | -1.8 (0.88) | -2.1 (0.71) | 0.3 (0.66) |
| 20 | -2.0 (0.94) | -1.0 (0.75) | -0.8 (0.61) | -0.8 (0.95)* | -1.3 (0.71)* | 1.0 (0.60)* |
| Overall | -1.6 (0.69)* | -2.0 (0.52)* | -0.1 (0.45)* | -1.3 (0.65) | -1.7 (0.50) | -0.3 (0.44) |
| Mean change from baseline in synovial vascularity | | | | | | |
| 7.5 | -1.7 (0.64) | -1.3 (0.52) | -0.7 (0.47) | -2.0 (0.59) | -1.2 (0.47) | -1.6 (0.44) |
| 20 | -2.3 (0.66) | -1.6 (0.53) | -1.5 (0.43) | -2.1 (0.64) | -1.3 (0.48) | -1.7 (0.40) |
| Overall | -2.0 (0.46) | -1.4 (0.37) | -1.1 (0.32) | -2.0 (0.43) | -1.3 (0.34) | -1.7 (0.30) |
| Patients reaching ACR 20, n/N (%) | | | | | | |
| 7.5 | 20/34 (58.8)* | 23/48 (60.4)* | 23/60 (38.3)* | 21/30 (70.0)** | 32/46 (69.6)** | 25/57 (43.9)** |
| 20 | 18/30 (60.0) | 24/47 (51.1) | 33/69 (47.8) | 18/28 (64.3) | 30/46 (65.2) | 36/69 (57.1) |
| Overall | 38/64 (59.4)* | 53/95 (55.8)* | 56/129 (43.4)* | 39/58 (67.2) | 62/92 (67.4) | 61/120 (50.8) |
| Patients reaching ACR 50, n/N (%) | | | | | | |
| 7.5 | 10/34 (29.4)* | 13/48 (27.1)* | 5/60 (8.3)* | 14/30 (46.7) | 17/46 (37.0) | 12/57 (21.1) |
| 20 | 13/30 (43.3) | 14/47 (29.8) | 15/69 (21.7) | 11/28(39.3) | 20/46 (43.5) | 20/69 (31.7) |
| Overall | 23/64 (35.9)** | 27/95 (28.4)** | 20/129 (15.5)** | 25/58 (43.1) | 37.9 (40.2) | 32/120 (26.7) |
| Patients reaching DAS28-CRP LDA, n/N (%) | | | | | | |
| 7.5 | 10/31 (32.3) | 10/46 (21.7) | 7/57 (12.3) | 12/29 (41.4) | 16/46 (34.8) | 13/55 (23.6) |
| 20 | 8/25 (32.0) | 14/42 (33.3) | 10/67 (14.9) | 7/24 (29.2) | 19/44 (43.2) | 22/58 (37.9) |
| Overall | 18/56 (32.1)** | 24/88 (27/3)** | 17/124 (13.7)** | 19/53 (35.8) | 35/90 (38.9) | 35/113 (31.0) |

*P* values for comparison between BMI subgroups. *p <.05, ** <.001. Chi-squared test was used for categorical variables, ANCOVA adjusting for baseline, treatment and BMI group was used for continuous variables.

**Conclusions:** Among obese RA pts initiating ADA, those on low dosage of concomitant MTX had poorer responses than pts in the normal and overweight categories, as measured clinically and by ultrasound imaging, although this effect was partly overcome by wk 24. Obese RA pts may have an improved clinical benefit if ADA is initiated with high (20 mg/week), rather than low dosage of concomitant MTX.

**References:**

[1] Kaeley et al. ACR/ARHP 2013 Annual Meeting. Boston, MA, USA

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## AB0312 PREDICTORS OF DISEASE COURSE AFTER THE DISCONTINUATION OF BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS PATIENTS WITH LONG-TERM REMISSION

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**Background:** The increasing number of patients treated with biologic therapies, the extending duration and costs of these treatments necessitate the development of strategies to the tapering or discontinuation of biologics in rheumatoid arthritis (RA) patients with long-standing remission on these agents. As flares occur frequently in patients in whom biologics are stopped, the identification of predictive markers for the preservation of long-standing remission after discontinuation is an important need. Several microRNA-s (miRNA) and SuPar (soluble urokinase plasminogen activator receptor) have been found to correlate with disease activity, and to be sensitive biomarkers of treatment response.

**Objectives:** The authors' aim was to prospectively follow the disease course after the permanent cessation of biologics, and to identify clinical and biochemical predictors of sustained biologic-free remission.

**Methods:** In this prospective, multicentre, controlled trial, eligible RA patients were treated with anti-TNF or IL6R-blocker, had a minimum of one-year remission (DAS-28<2.6), and no corticosteroid therapy. After discontinuation of the biologics, DAS28, HAQ, ESR and CRP were recorded at baseline, month 1, 3 and every 3 months thereafter. SuPar and soluble miRNA146a, miRNA16, miRNA155, miRNA223 and miRNA346 levels were measured by ELISA or QRT-PCR, respectively at baseline, month 1, 3, 6 and at relapse, if occurred. In the control group (n=5), patients had sustained remission on biologics, and had similar demographic and serological parameters, but the biologic therapy was not stopped.

**Results:** At present 23 patients with RA have been enrolled (average age: 59,95/35–79/ years).The mean duration of biologic therapy was 54,04 (25–84) months, and was started an average of 62,3 months (1–240 months) after the diagnosis. After the discontinuation, 14 patients are in biologic-free remission for an average of 5,21 (1–16 months). Relapse occurred in 9 cases an average of 5,20 (2–12) months after the discontinuation. miRNA146a levels at stop were higher in relapsers than in those with sustained remission (relative expression to cel miR39: -3,08 vs -7,87, p=0.009) (n=8 stopped patients, n=1 control). Circulating miRNA223, miRNA16, miRNA155 and miRNA346 levels were comparable in the two drug-cessation groups. SuPar levels were not different in the 12 patients in remission and 7 relapsers, in whom the measurements have been performed so far.

**Conclusions:** In RA patients with long-term remission on anti-TNF or IL6R-blocker, elevated level of miRNA146a may indicate a higher risk of relapse after stopping biologics. Further follow-up and the involvement of more patients are currently underway, and this may identify further predictive markers.

**References:**

[1] Toldi G, Kádár G et al. Soluble urokinase plasminogen activator receptor (suPAR) in the assessment of inflammatory activity of rheumatoid arthritis in patients in remission. ClinChem Lab Med 51(2):327–332. 2013

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## AB0313 SHORT-TERM EFFECTS OF TNF INHIBITORS ON BONE TURNOVER MARKERS AND BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS

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**Background:** TNFα inhibitors (TNFαI) exert positive effects on disease activity in rheumatoid arthritis (RA). Bone involvement is a major determinant of functional impairment in this disease.

**Objectives:** Here we investigated the short-term effects of TNFαI therapy on bone metabolism and density.

**Methods:** We studied 54 patients with RA starting a TNFI biologic drug, in whom any factor known to interfere with bone metabolism was excluded or rigorously accounted for. We measured at baseline and after 6 month therapy bone turnover markers (BTM): N-propeptide of type I collagen (P1NP), and bone alkaline phosphates (bAP) for bone formation and serum C-terminal telopeptide of type I collagen (CTX) for bone resorption. We also evaluated bone mineral density (BMD) at hip and lumbar by dual energy X ray absorptiometry (DEXA).

| | Absolute changes | P value | % changes | P value |
|---|---|---|---|---|
| P1NP (ng (ml) | 8.5±18 | 0.001 | 30.6±64.3 | 0.001 |
| bAP (μg/l) | 1±2.38 | 0.003 | 8.6±20.7 | 0.003 |
| CTX (ng/ml) | 0.047±0.188 | 0.07 | 44.9±130.6 | 0.01 |
| BMD Lumbar spine (mg/cm$^2$) | 4.1±50.7 | >0.1 | 0.2±5.2 | >0.1 |
| BMD Femoral neck (mg/cm$^2$) | −14.1±34.6 | 0.004 | −1.8±4.6 | 0.005 |

**Results:** All bone markers rose significantly and these changes were not dependent on steroids dosage; a significant decrease in femoral neck BMD was also observed (see Table).
**Conclusions:** These results indicate that TNFαI therapy in RA over 6 months is associated with an early increase in bone turnover and a decline in hip BMD.
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## AB0314 AWARENESS AND ACCEPTANCE OF BIOSIMILARS BY RHEUMATOLOGISTS IN ELEVEN EU COUNTRIES

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**Background:** The first infliximab biosimilar was approved in Europe in Sept. 2013 for all indications authorised for originator infliximab, including those in rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Confusion exists around differences between biologics and biosimilars, the definition of a biosimilar and the process by which they are manufactured. In addition, there are varying levels of comfort in the types of patients to whom biosimilars could be prescribed.
**Objectives:** We aimed to understand rheumatologists' current perspectives and knowledge on biosimilars, including regulatory aspects and manufacturing principles, as well as comfort with prescribing.
**Methods:** 222 rheumatologists chosen randomly across 11 countries (Finland, France, Germany, Hungary, Ireland, Italy, Norway, Portugal, Spain, Sweden, and UK) participated in a web-based survey from Jun. to Aug. 2015. Key eligibility criteria: being in a practice with at least 30% of patients with Rheumatoid Arthritis or 5% with Ankylosing Spondylitis; at least 15% of these treated with a biologic; physicians in the survey prescribed infliximab (originator or biosimilar) to at least one patient and have access to biosimilar infliximab (able to prescribe biosimilar infliximab). Most (72%) had prescribed biosimilar infliximab to at least one patient.
**Results:** 97% of rheumatologists indicated being familiar or very familiar with biosimilars. Despite a high level of familiarity, only 48% correctly identified the EMA definition of a biosimilar; the remainder incorrectly defined biosimilars as the equivalent of generics for biologics (16%) or as similar biologics having the same mechanism of action as the originator (36%). 65% of rheumatologists cited either limited or no knowledge of biologic manufacturing processes.
Most rheumatologists preferred to prescribe biosimilars to naïve patients or those who stopped responding to their current biologic. On a scale of 1 to 10 (10 = extremely comfortable), rheumatologists rated their level of comfort in prescribing biosimilars as 6.5 (significantly lower than gastroenterologists answering an identical question in a parallel survey; mean = 6.9, *p=0.002*). There was a general correlation between the length of exposure to biosimilars and willingness to prescribe, although exceptions were noted (e.g., Portugal, Spain). Knowledge regarding biosimilar manufacturing standards and comfort in prescribing were not correlated.
**Conclusions:** Knowledge and awareness of biosimilars is growing among EU rheumatologists and there are high levels of comfort in prescribing biosimilars; however, confusion still exists with regard to definitions, regulations and manufacturing standards.
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## AB0315 REDUCTION OF CONCOMITANT ORAL METHOTREXATE OR CORTICOSTEROIDS IN COMBINATION TREATMENT WITH ADALIMUMAB DOES NOT AFFECT EFFECTIVENESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** In rheumatoid arthritis (RA) patients (pts) receiving corticosteroids (CS) or methotrexate (MTX) with an anti-TNF, such as adalimumab (ADA), the concomitant CS or MTX dose may be reduced if pts respond well or have side-effects.
**Objectives:** To assess treatment effectiveness in pts whose MTX or CS oral dose was reduced over 10 years (y) of open label (OL) ADA treatment.
**Methods:** This was observed data from OL extensions (OLE) of the PREMIER and DE019 trials.[1,2] In PREMIER, MTX-naïve, early RA pts received ADA/MTX/ADA+MTX for 2y, and optional OL ADA for upto 8y. In DE019, biologic-naïve, established RA pts received 20 mg ADA+MTX/ 40 mg ADA+MTX/PBO+MTX for 1y and optional OL ADA+MTX for upto 9y. In both OLEs, MTX could be added/adjusted at the investigator's discretion, and oral CS dose could be tapered in pts who responded. Effectiveness at final visit (FV) was assessed by the numbers of pts achieving TJC68 =0, SJC66 =0, improvement from baseline in HAQ-DI $\geq$0.5 (HAQ-DI 0.5), ACR20/50/70 criteria and 28-joint disease activity score based on C-reactive protein (DAS28-CRP)$<$2.6. Additionally, in PREMIER, modified EULAR remission (REM) criteria [DAS28-CRP $<$2.6, TJC68 $\leq$1, SJC66 $\leq$1], "Good EULAR response" [DAS28-CRP $<$3.2 with a change from baseline $\leq$-1.2] were used.
**Results:** In *PREMIER*, by the pt's FV, out of 375 pts who had any oral CS, 220 (58.7%) were on ongoing CS; 155 (41.3%) had stopped. Among the 375 pts, 32% had a stable CS dose and 26.1% had a CS dose reduction. Dose reduction did not affect the proportion of pts reaching ACR criteria, HAQ-DI 0.5, and DAS28-CRP $<$2.6 by FV (table). Out of 497 pts in the OLE, 261 (52.5%) used concomitant MTX in the OLE, 236 pts did not. With/without MTX, the number of pts with DAS28-CRP$<$2.6 increased from 2 to 10y, and the proportion of pts with SJC or TJC=0, good EULAR response, or modified EULAR REM criteria, and the HAQ-DI scores were comparable in the +/– MTX groups. In *DE019*, by the pt's FV, out of 352 pts who received any oral CS, 207 (58.8%) were on ongoing CS and 145 (41.2%) had stopped CS. Among the 352 pts, 141 (40%) had a stable CS dose and 82 pts (23.3%) had a dose reduction. Out of 550 pts on MTX during the study, 497 (90.4%) were receiving MTX, and 53 (9.6%) had stopped by FV; 345/550 pts (62.7%) had stable MTX and 158 (28.7%) had a reduction. Reduction of CS or MTX did not affect the proportion of pts who reached the ACR criteria, HAQ-DI 0.5 and DAS28-CRP $<$2.6 by FV.

Table: Impact of dose changes in concomitant oral corticosteroids or MTX on effectiveness by final visit, n/N (%)

| | | |
|---|---|---|
| **PREMIER** | | |
| | **Stable CS dose** | **Decreased CS dose** |
| ACR20 | 66/117 (56.4) | 71/98 (72.4) |
| ACR50 | 44/117 (37.6) | 55/98 (56.1) |
| ACR70 | 26/117 (22.2) | 42/98 (42.9) |
| HAQ-DI 0.5 | 48/118 (40.7) | 48/98 (49.0) |
| DAS28-CRP <2.6 | 47/119 (39.5) | 57/98 (58.2) |
| | **With MTX use** | **Without MTX use** |
| TJC68=0 | 97/261 (37.2) | 115/234 (49.1) |
| SJC66=0 | 114/261 (43.7) | 129/234 (55.1) |
| Modified EULAR REM criteria | 87/261 (33.3) | 113/239 (48.5) |
| "Good" EULAR-CRP | 169/259 (65.3) | 177/232 (76.3) |
| Mean HAQ-DI at final visit | 0.7 (0.7) | 0.6 (0.7) |
| **DE019** | | |
| | **Stable CS dose** | **Decreased CS dose** |
| ACR20 | 164/323 (50.8) | 98/153 (64.1) |
| ACR50 | 109/323 (33.7) | 75/153 (49.0) |
| ACR70 | 63/323 (19.5) | 57/153 (37.3) |
| HAQ-DI 0.5 | 137/342 (40.1) | 75/158 (39.5) |
| DAS28-CRP <2.6 | 100/323 (31.0) | 188/524 (35.9) |
| | **Stable MTX dose** | **Decreased MTX dose** |
| ACR20 | 57/128 (44.5) | 45/78 (57.7) |
| ACR50 | 31/128 (24.2) | 38/78 (48.7) |
| ACR70 | 18/128 (14.1) | 26/78 (33.3) |
| HAQ-DI 0.5 | 54/139 (38.8) | 37/82 (45.1) |
| DAS28-CRP <2.6 | 29/128 (22.7) | 35/80 (43.8) |

MTX, methotrexate; CS, corticosteroid; ACR, American College of Rheumatology; HAQ-DI, health assessment questionnaire- disability index; DAS28-CRP, 28-joint count disease activity score based on c-reactive protein; TJC68, tender joint count at 68 joints; SJC, swollen joint count at 66 joints.

**Conclusions:** Overall, effectiveness associated with continuous ADA treatment was not sacrificed in pts in whom concomitant oral CS or/and MTX doses were reduced or discontinued, although many of these pts were likely responding well at the time of taper.
**References:**
[1] Keystone et al. J Rheum 2013;40:1487–97;
[2] Keystone et al. J Rheum, 2014;41:5–14
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**Disclosure of Interest:** E. Keystone Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Janssen, Pfizer, Roche, and UCB, Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Janssen, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, BMS, Janssen, Pfizer, Roche, and UCB, F. Breedveld Consultant for: Centocor, Schering-Plough, Amgen/Wyeth, and AbbVie, A. Kavanaugh Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Y. Zhang Shareholder of: AbbVie, Employee of: AbbVie, I. Sainsbury Shareholder of: AbbVie, Employee of: AbbVie, J. Kalabic Shareholder of: AbbVie, Employee of: AbbVie
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## AB0316 AN EXAMINATION OF DOSE ESCALATION AMONG INFLIXIMAB USERS IN THE US CORRONA RA REGISTRY

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**Background:** Limited data are available about infliximab (IFX) dose escalation.
**Objectives:** This analysis examines the frequency of dose escalation among IFX patients using data from the US CORRONA RA registry and describes the characteristics of patients who dose escalate vs those who do not.
**Methods:** RA patients initiating IFX at a dose of $\leq$5 mg/kg on or after 6/1/2009 with at least 1 follow-up visit with dose information were eligible for analysis. Subgroup analysis was performed among patients with follow-up at 1yr to compare characteristics between those who dose escalated vs those who did not. Dose escalation was defined as an increase of $>$1mg/kg in dose and/or a decrease in the frequency of dosing by at least 1 wk (e.g. q 8 wks to q7 wks). Censoring occurred if patients switched to another biologic or left the registry. Descriptive statistics were used to compare baseline characteristics of infliximab patients stratified by number of biologics, and also comparing those who dose escalated vs those who did not within the 1st yr after initiating therapy.
**Results:** A total of 716 patients initiated IFX after June 2009. Common characteristics included mean age (61yrs), women (78%), mean weight (83 kg), RF+ (70%) and CCP+ (67%), baseline CDAI (22.5), and insurance status (Medicare 46%, Medicaid 6%). Differences between those who initiated IFX as their 1st, 2nd, or 3rd biologic included RA duration (7.0, 9.6, 11.0 yrs, respectively, $p<0.001$), college education (50, 61, 66%, respectively, p=0.002), number of prior DMARDs (1.6, 1.8, 2.0; $p<0.001$), proportion receiving monotherapy (12, 15, 26%), and prednisone use (31, 29, 35%).
Over 3 yrs follow-up, the proportions of patients escalating IFX significantly differed, ranging from a low of 21% at 1 yr for patients using IFX as 1st line to a high of 81% at 3yrs for patients using it as 3rd line (Table, p=0.0024 for between-group differences). In patients with follow-up data at 12mo (n=608), there were some baseline characteristics associated with dose escalating vs not in the 1st yr of therapy including shorter RA duration (p=0.03), greater number of prior biologics (p=0.04), monotherapy (p=0.03), greater prednisone use (p=0.01), and higher CDAI (p=0.04) and related disease activity measures.

Table 1. proportion of patients increasing infliximab dose over time according to its use as a first, second, or third line biologic agent

| Follow-up time | First line (N=373) | Second line (N=210) | Third line (N=133) |
|---|---|---|---|
| 12 months, % | 21 | 31 | 30 |
| 24 months, % | 35 | 46 | 58 |
| 36 months, % | 49 | 62 | 81 |

**Conclusions:** Dose escalation of IFX is relatively frequent over time. Patients with more severe RA undergo dose escalation more commonly than those with less severe disease. Understanding long term benefits and persistence and related factors following dose escalation may help optimize dose escalation as a treatment strategy compared to switching.
**Acknowledgement:** This study is sponsored by Corrona, LLC. The Corrona RA registry has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, Astra Zeneca, BMS, Genentech, Horizon Pharma USA, Janssen, Eli Lilly, Novartis, Pfizer, and UCB.
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## AB0317 DRUG SURVIVAL OF BIOLOGIC AGENTS IN RHEUMATOID ARTHRITIS USING 10 YEARS OF DATA FROM THE NATIONAL HEALTH INSURANCE IN KOREA: A POPULATION-BASED STUDY AND COMPARISON WITH A SINGLE-INSTITUTION COHORT

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**Background:** Since 2004, Korean national health insurance began to cover the cost of biologic agents in rheumatoid arthritis (RA) patients experiencing treatment failure by conventional disease modifying antirheumatic agents. However, real-world issues such as selecting or switching among biologic agents in clinical practice became more complicated as types of the agents increased.
**Objectives:** To evaluate 1) first choice among biologic agents, 2) drug retention rate and duration and 3) switching rate and duration before switching of each biologic agent in RA.
**Methods:** We used prospective cohort data by the National Health Insurance Service (NHIS) in Korea, which consisted of more than one million subjects representing age, sex and income status of whole Korean population followed from 2004 to 2013. All RA patients with any experience of biologic agents were checked by the code of each drug and KCD9 code of diagnosis including all types of RA. To supplement the results of the population based study, we also compared and validated with the independent cohort of biologic agent users in Seoul national university hospital (SNUH).
**Results:** One hundred and seventy three patients were found to experience any of TNFa inhibitors from Jan. 2004 to Dec. 2013. Etanercept was the most frequent choice as first TNFa inhibitor (43.4%), followed by adalimumab (35.3%), infliximab (20.2%), golimumab (0.6%) and abatacept (0.6%). Among TNFa inhibitors, retention rates of etanercept (73.1%, 62.7%) at month 12 and 24 were significantly higher (p=0.039, both) than adalimumab (57.7%, 44.2%) and infliximab (45.5%, 36.4%). In SNUH cohort, etanercept (79.8%, 67.0%) also had better retention rate than adalimumab (51.3%, 48.7%) and infliximab (58.6%, 34.5%) at month 12 and 24 respectively. Mean duration of retention was almost twice longer in etanercept (3.42 years) than adalimumab (1.83 years, p=0.004) and infliximab (1.71 years, p=0.011). Similarly, etanercept (3.24 years) prescribed longer than adalimumab (1.98 years) and infliximab (1.63 years) with statistical significance in SNUH cohort. Etanercept also had lower switching rate (20.9%) than adalimumab (32.1%) and infliximab (38.5%, p=0.040) and the tendency were similar in SNUH cohort. Preferred biologic agents after switching were adalimumab (27.4%) and rituximab (24.2%). Etanercept users (1.35 years) had longer duration of use before switching than infliximab (0.60 years, p=0.050) but no significant difference was shown comparing with adalimumab (0.73years, p=0.483).
**Conclusions:** As golimumab, abatacept, tocilizumab were available relatively later than existing TNFa inhibitors and rituximab, more follow up period would be required to evaluate their value in treating RA. This research can be a pilot study before analyzing nationwide population cohort encompassing whole population of Korea. Conclusively, etanercept has been prescribed longer in general and the rate of retention till 2 years was also better then adalimumab and infliximab for 10 years after national insurance coverage.
**Disclosure of Interest:** None declared
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## AB0318 DOES CONCENTRATION OF ANTIBODIES TO ETANERCEPT AND ADALIMUMAB CORRELATES WITH PARAMETERS OF DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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**Background:** Introduction of tumor necrosis factor alpha (TNF) inhibitors has revolutionized therapy of rheumatoid arthritis (RA). Immunogenicity with consequent formation of antidrug antibodies (ADAb) is most responsible factor for secondary resistance. Adalimumab (ADA) as a fully humanized monoclonal antibody and Etanercept (ETN) as a fusion protein, are considered less immunogenic compared to other TNF inhibitors. In spite of this, various studies detected ADAb to ETN from 0% to 18% and for ADA from 0.04% to 87%.
**Objectives:** Our objectives were to determine the prevalence of ADAb to ETN and ADA in patients with RA and to evaluate correlations of ADAb with concentration of ETN and ADA and with parameters of disease activity.
**Methods:** Consecutive patients with established RA treated with ETN (25 patients) and ADA (20 patients) were enrolled in our cross-sectional study. Patients treated with ETN were older compared to patients treated with ADA (53.09±13.20 versus 47.06±12.54 years), had longer duration of disease (13.78±6.88 versus 9.11±6.91 years) and had longer duration of treatment (58.76±22.53 versus 20.3±14.11 years). Drug levels and concentration of ADAb were measured with commercially available ELISA kits from blood samples taken before next injection (trough values), and these levels were correlated with parameters of disease activity and compared between two groups.
**Results:** Both drugs had comparable efficacy according to DAS 28 SE (3.32±0.93 for ETN and 3.86±1.43 for ADA). Mean trough concentration of both drugs was satisfactory with values sevenfold greater than referent values: 240.23±502.64 ng/mL for ETN (referent values 0.0–35 ng/mL) and fourfold greater for ADA: 94.86±25.56 ng/mL (referent values 0.0–24.0 ng/mL). In spite of this, a more than a double concentration of ADAb was recorded in both groups: 326.96±292.51 IU/mL for ETN (referent values 0.0–142.06 IU/mL) and 23.21±56.87 IU/mL for ADA (referent values 0.0–10.00 IU/mL). Eight from 25 patients (32.4%) in ETN group and 8/20 (40%) in ADA group had elevated concentration of ADAb and this difference was not significant. Pearson correlation coefficient (r) showed weak negative correlation (r=-0.338) between concentration of ADAb to ETN and concentration of ETN and no correlation between ADAb to ADA and concentration of ADA. There were positive correlation of ADAb to ETN and Erythrocyte Sedimentation Rate (r=+0.482) and CRP (r=+0.411) but not with DAS 28 SE nor with the levels of RF and CCP Ab. The concentration of ADAb to ADA shoved only weak correlation with CCP Ab (r=+0.366) but not with any other parameter of disease activity.

**Conclusions:** Our data suggest that formation of ADAb after prolonged time of therapy is common even in the patients treated with TNF inhibitors considered as less immunogenic. But, a weak or even absent correlation with disease activity also suggest that not all of these ADAb are neutralizing with clinical consequences. These results also suggest that methodological aspects are of even more significance. There is a need for assay standardization and validation and consensus on the interpretation of serum drug and ADAb cut-off values with evidence based treatment algorithm useful for clinical practice.
**Disclosure of Interest:** None declared
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## AB0319 ANALYSIS OF LARGE JOINT DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED BY GOLIMUMAB

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**Background:** There is no investigation of large joint destruction treated with golimumab in rheumatoid arthritis. Especially what clinical factors related to the inhibition of large joint destruction was not reported so far.
**Objectives:** In order to investigate the inhibition of large joint destruction for rherumatoid arthritis in treated with golimumab, 450 large joints were assessed at baseline and 52 weeks after treatment with golimumab.
**Methods:** 450 large joints from 45 patients including elbow, shoulder, hip, knee and ankle by using ARASHI (Assessment of rheumatoid arthritis by scoring of large joint destruction and healing in radiographic imaging) scoring system (1) at baseline and 52 weeks after treatment with golimumab. Baseline data were mean age of 61.29±14.71 years, 91.1% of female, mean disease duration of 12.6±12.48 years, stage/class of I:7,II:10,III:9:,IV:19/2:18,3:26,4:1, mean MTX of 6.44±1.78 mg/weeks, mean PSL of 1.078±1.871 mg/day, 44.4% of 100 mg for golimumab, mean DAS28 (CRP) of 4.431±1.044. Rapid radiographic progression (RRP) and rapid radiographic improvement (RRI) were calculated and analysis of correlation for large joint destruction and clinical factors between baseline and 52 weeks.
**Results:** RRP was 21.9% in 450 large joints treated with golimumab. Therefore 78.1% were inhibited large joint destruction treated with goimumab in RA. RRI was 35.7% showing large joint improvement were obtained by golimumab. In clinical factors, baseline CRP affects ARASHI change score of knee at 52 weeks after treatment of golimumab.
**Conclusions:** Inhibition of large joint destruction were obtained in 78.1% for the patients treated with golimumab in RA.
**References:**
[1] Kaneko A, et al. Development and validation of a new radiographic scoring system to evaluate bone and cartilage destruction and healing of large joints with rheumatoid arthritis: ARASHI (Assessment of rheumatoid arthritis by scoring of large joint destruction and healing in radiographic imaging) study. Modern Rheumatology 23:1053–62, 2013.
**Disclosure of Interest:** None declared
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## AB0320 FACTORS ASSOCIATED WITH ACTIVE AND LATENT TUBERCULOSIS, TUBERCULIN SKIN TEST CONVERSIONS DURING ANTI-TUMOUR NECROSIS FACTOR THERAPY IN PATIENTS WITH RHEUMATIC DISEASES IN A MEXICAN COHORT

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**Background:** The Anti Tumour Necrosis Factor (aTNF) therapy in Rheumatics Diseases (RD) had changed the prognosis of theses conditions in the last decade. Unfortunately, aTNF therapy is associated a high-risk rate of infections, especially active tuberculosis (TB) [1]. The use of tuberculin skin test (TST) to detect and treat latent tuberculosis (LTBI) before to initiate aTNF therapy had reduced the risk of TB by 75 to 95% [2]. However, multiple factors as prevalence of TB by country, malnutrition, anergy, immunosuppressors, advanced age, BCG vaccination between others compromise the sensitivity and specificity (falsely negative and positive results) of the test to distinguish between remote and recent disease. These factors are also associated with frequency and progression of LTBI to TB and differ between populations [3]. Few studies have been performed in Mexicans with RD under aTNF therapy [4].
**Objectives:** To determine the frequency of TB and LTBI, TST conversions and associated factors during aTNF therapy in patients with RD from a Mexican cohort.
**Methods:** 151 patients ($\geq$14 years) from a Mexican cohort from 2011 to 2016 were examined. Ankylosing Spondylitis (AS), Juvenile idiopathic arthritis (JIA), Psoriatic Arthritis (PsA) and Rheumatoid Arthritis (RA) cases fulfilled Amor, ILAR, CASPAR and ACR/EULAR 2010 criteria respectively. TB and LTBI (TST induration $\geq$5 mm recorded to 72 hours) diagnosis occurred before to start aTNF therapy. Conversions happened in the second TST. Demographic factors, comorbidities and pharmacologic treatments were examined for patients without and with TB, LTBI and TST conversions under aTNF therapy. Variables were examined by univariable and multivariable analyses.
**Results:** Of 151 patients, 71 had AS, 68 had RA, 9 had JIA and 3 had PsA; of them 53% were women. The mean age [standard deviation (SD)] was 47.1 (12.5) years. The mean of time at onset of RD [standard deviation (SD)] was 12.3 (8.7) years. A total of 5 patients had TB for a crude prevalence of 3.3% and three of them used infliximab. TB was more common in patients with first TST negative and after TST conversion (OR 6.97, 95% CI 1.36–35.5, p=0.019). LTBI was detected in 57 (37.7%) patients and was more associated with lower wage (OR 0.2, 95% CI 0.52–0.98, p=0.047), to be healthcare workers (OR 57.1, 95% CI 2.67–1219.50, p=0.010), and smoking (OR 30.1, 95% CI 5.40–167.24, p$\leq$0.005). TST Conversions were presented in 43 (28.5%) cases and were more associated with treatment with $\geq$15 mg/d of prednisone (OR 3.7, 95% CI 1.54–9.21, p$\leq$0.005). No differences were found for patients with BCG vaccination and previous TB before aTNF therapy
**Conclusions:** This study suggests that patients with RD in this cohort from Mexico have a high prevalence of TB, LTBI and TST conversions compared to other studies. Also lower wage, to be healthcare workers and smoking were associated with LTBI, and TST conversion occurred more associated to use higher dose of glucocorticoids. The clinical significance of these TST conversions is unclear at the moment.
**References:**
[1] Rheumatol 2011;38:1234–43;
[2] J Rheumatol 2013;40;1938–1940;
[3] Clinical Infectious Diseases 2011;52(8):1031–1037;
[4] Rheumatol Int (2015) 35:1555–155.
**Disclosure of Interest:** None declared
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## AB0321 A TOTALITY-OF-THE-EVIDENCE APPROACH TO THE DEVELOPMENT OF GP2015, A PROPOSED ETANERCEPT BIOSIMILAR

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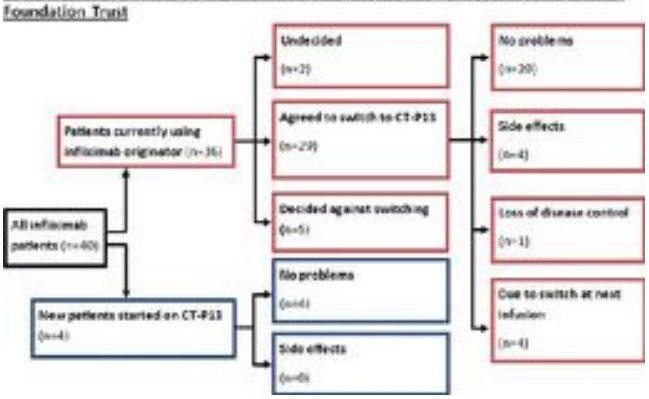
**Background:** Assessment of biosimilarity uses the "totality-of-the-evidence" concept, whereby a complete data package, comprising physicochemical, biological, nonclinical and clinical data, is used to evaluate and confirm biosimilarity between a proposed biosimilar and an approved originator (reference) product. A stepwise approach, using comparative analytical characterisation to inform next steps, is recommended. The totality-of-evidence derived from these data should demonstrate that the active substance of a biosimilar and its originator are essentially the same.
**Objectives:** To describe the development of a proposed etanercept biosimilar (GP2015).
**Methods:** To define the development target, multiple batches of the originator were characterised over time to understand quality attributes relating to protein structure, function, and amino acid modifications. An iterative, target-directed development process was used to design and produce a potential biosimilar product (GP2015) that fell within the variability range of the originator. Biosimilarity between GP2015 and the originator was confirmed at analytical, functional, nonclinical, pharmacokinetic (PK) and clinical levels using a stepwise approach. Biochemical attributes and functional properties were assessed using a comprehensive and sensitive state-of-the-art panel of analytical tools. Bioequivalence between GP2015 and the originator was assessed in vivo and in four PK studies in healthy volunteers. To confirm there were no clinically meaningful differences between GP2015 and the originator, a study of efficacy, safety and immunogenicity was performed in patients with moderate-to-severe chronic plaque-type psoriasis. This confirmative study assessed the Psoriasis Area and Severity Index response rate at Week 12 and at long-term timepoints.
**Results:** GP2015 was developed at the same dosage and strength as the originator. Multiple orthogonal analytical methods showed high similarity between GP2015 and the originator. The amino acid sequence was confirmed to be identical and protein folding was indistinguishable. Other attributes, such as glycosylation and product-related impurities, were highly-comparable with the originator. In vitro assays reflecting mechanisms of action and pharmacological properties showed GP2015 and the originator had similar bioactivity. PK bioequivalence between GP2015 and the originator was established in nonclinical and human studies. The study in patients with psoriasis confirmed similar efficacy and safety and comparable immunogenicity in a highly-sensitive indication. In all studies, no clinically meaningful differences between GP2015 and the originator were observed.
**Conclusions:** Analytical, functional, nonclinical and clinical data provide a comprehensive understanding of both GP2015 and the originator and demonstrate a high level of similarity between the two products in accordance with regulatory requirements. The totality-of-the-evidence is therefore believed to justify the use of the biosimilar in the same indications as the originator.
**Disclosure of Interest:** M. McCamish Employee of: Hexal AG, A. DaSilva Employee of: Hexal AG, R. Ernst Mayer Employee of: Sandoz Biopharmaceuticals, C. Fritsch Shareholder of: Novartis Pharma AG, Employee of: Novartis Pharma AG, M. Schiestl Employee of: Sandoz Biopharmaceuticals
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## AB0322 PRELIMINARY DATA ON THE INTRODUCTION OF THE INFLIXIMAB BIOSIMILAR (CT-P13) TO A REAL WORLD COHORT OF RHEUMATOLOGY PATIENTS

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**Background:** Infliximab is a chimeric monoclonal antibody against tumour necrosis factor alpha (TNF-α), used to treat autoimmune diseases such as rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis.[1] In 2015 NICE recommended the use of a new less expensive biosimilar CT-P13 (Remsima™; Inflectra™), based on its efficacy, safety and quality comparable to the reference infliximab product.[2] At Southend University Hospital NHS Foundation Trust, the use of CT-P13 has reduced treatment costs and allowed significant cost savings compared with reference infliximab.
**Objectives:** To review patient outcomes and estimate the cost savings of using CT-P13 as compared with reference infliximab.
**Methods:** Information packs were sent out to patients to inform them of the intended switch from Infliximab to CT-P13. Their understanding was further reinforced in a face-to-face session with the biologics pharmacist and any concerns were addressed. Additionally patients had access to a dedicated email account which was set up to deal with their queries. Written consent was obtained from patients prior to the switch. Patients were carefully monitored during the first infusion of CT-P13 and were advised to contact the rheumatology department if they developed any undue side-effects or loss of disease control. All eligible patients were offered a chance to recruit to BSR Biologics Register. All side-effects were reported to MHRA.
**Results:** 25 patients consented to the switch from infliximab to the biosimilar CT-P13. 20 patients reported no new side-effects or loss of disease control (80%, ±15.68). 4 patients developed side-effects after switching to CT-P13. 1 developed flu like symptoms, 1 developed inflamed foreskin and 2 developed pruritic rashes, (one patient after the first dose and the other patient after the 4th dose). All patients who developed side-effects were successfully switched back to reference infliximab. 1 patient reported loss of disease control and is due to switch back at their next infusion. None of the patients initiating CT-P13 first line have developed any side-effects to date. A paired t-test has revealed no statistically significant difference in CRP values taken before and after the switch (n=21, p=0.151). £70k is expected to be saved based on this reported use of CT-P13 in our rheumatology department over 12 months.

Flow diagram to demonstrate patient outcomes from CT-P13 usage at Southend NHS Foundation Trust




**Conclusions:** In our cohort of patients, switching from Infliximab to CT-P13 appeared to be safe for the majority of patients and represents a significant opportunity to provide a more cost effective service in rheumatology. The immunogenic nature of infliximab highlights the importance of having a robust safety net strategy when switching patients to biosimilars. Further multi-centre studies are needed to corroborate our findings.

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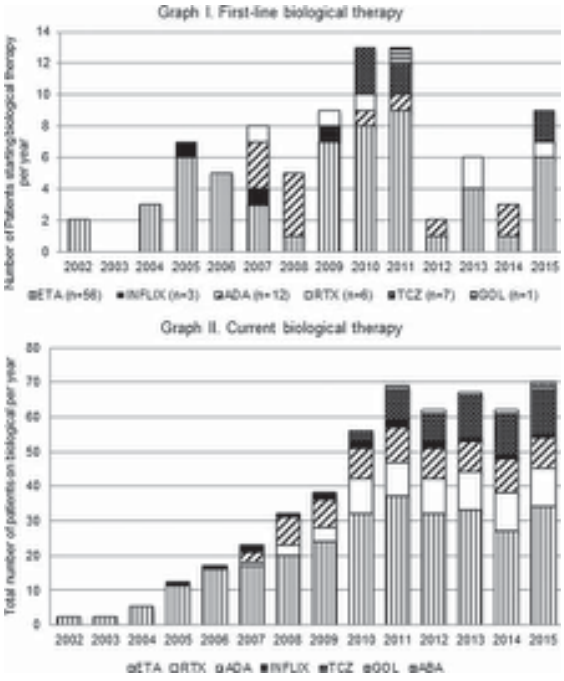
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## AB0323 PERSISTENCE OF BIOLOGIC THERAPY AND LONG TERM OUTCOMES AT 14 YEARS: OBSERVATIONAL DATA IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM A SINGLE CENTRE

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**Background:** Current recommendations for Rheumatoid Arthritis (RA) treatment focus on a treat to target approach [1, 2]. Long term individual drug persistence has been associated to factors such as type of biological agent and higher disease activity [3, 4]. Here we present data from a tertiary referral centre.
**Objectives:** To determine factors associated to drug persistence, switch or withdrawal of first-line biological therapy.
**Methods:** Retrospectively collected data (01/2002 to 12/2015) from our Unit included patients classified as RA according to ACR 1987 [5] and 2010 [6] criteria. The analysis included 288 patients, 29% (n=85) of which were lost to follow-up and 15% (n=44) of which were deceased. The present study was restricted to current biological therapy. We extracted baseline characteristics (age, gender, presence of RF and anti-CCP, duration of RA, year of initiation of therapy), first biologic and causes of switch or withdrawal, adverse events and treatment efficacy (according to DAS28). Data were collected through to December 2015. Outcomes were compared using the Man-Whitney test comparing those that maintained the same biologic to those that switched. We limited the analysis to patients treated with Etanercept (ETN), Adalimumab (ADA), Rituximab (RTX) and Tocilizumab (TCZ).
**Results:** A total of 85 patients (53%) were started on biological therapy (bDMARD), instituted after methotrexate (MTX) failure or intolerance (mean peak MTX dose 17 mg/week). Mean age [±SD]=59 [±10.2] years,79% female (n=65), mean disease duration 11.3 [±7.2] years (ranging from 1 to 37 years), 6 (7%) non-white, the majority positive for rheumatoid factor and/or anti-CCP (n=61, 72%). These patients were originally treated with ETN (n=56), Infliximab – INFLIX (n=3), ADA (n=12), RTX (n=6), TCZ (n=7) and Golimumab (n=1) (Graph I). After mean 4 [±2.9 [±SD] years of follow-up, ranging from 1 to 14 years (Graph II), 70 of 85 patients are currently still on bDMARD, mostly on ETN (n=34), TCZ (n=13), RTX (n=11) and ADA (n=9). Abatacept has been started on one patient. The median time of receiving ETN, ADA, RTX and TCZ was 5.0, 3.5, 2.0 and 4.0 years and retention rates were 71%, 67%, 83% and 86%, respectively. Overall, more than 95% of treatment switch was due to drug inefficacy. Severe infections occurred with ETN (one Pneumocystis pneumonia) and ADA (one genitourinary tuberculosis). Lack of efficacy due to TCZ was only seen in a single patient. There was no statistically significant differences between retention and non-retention groups.




**Conclusions:** Biological drugs for RA treatment in our Unit were determined by drug development and National Authority of Medicines and Health Products authorization. ETN was the most frequently used and for the longest duration with a 71% retention rate. Overall we found that the other agents were also well tolerated and effective in patients between 50 and 70 years of age. This information may be useful for clinicians with an ageing population.

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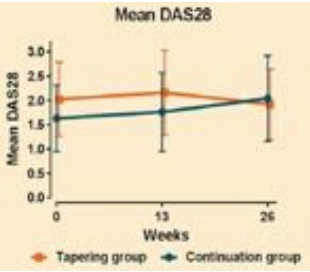
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**Acknowledgement:** Patients, Medical, Nursing and Administrative Staff of Unidade de Doenças Auto-imunes, Hospital Curry Cabral
**Disclosure of Interest:** M. Fernandes: None declared, I. Figueiredo: None declared, N. Riso: None declared, A. Panarra: None declared, M. F. Moraes-Fontes Grant/research support from: Roche, AbbVie, Pfizer, Biomarin, Actelion, Consultant for: Pfizer
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## AB0324 TAPERING OF ADALIMUMAB BASED ON THERAPEUTIC DRUG MONITORING IN RHEUMATOID ARTHRITIS

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**Background:** Treatment with biologicals is based on the principle of "one size fits all" without taking differences in dosing schemes, patients characteristics and pharmacokinetics into account.
**Objectives:** To compare disease activity 26 weeks after dose interval prolongation versus continuation of the regular dose in rheumatoid arthritis (RA) patients with high serum adalimumab concentration[1].
**Methods:** In the interim analysis of this open randomised controlled trial, patients with an adalimumab concentration >8 mL/L were randomly (1:1) assigned to continuation of adalimumab every other week (continuation group) or prolongation of the dosage interval to once every 3 weeks (tapering group), independently of disease activity score in 28 joints (DAS28). Patients were treated with adalimumab 40 mg subcutaneous every other week for at least 28 weeks before start of the study. Visits were scheduled at baseline, 13 and 26 weeks thereafter. The change in DAS28 (∆DAS28) after 26 weeks compared to baseline was taken as outcome measurement and a clinical relevant difference was defined as a ∆DAS28 >0.6. Based on an intention to treat analysis, an independent t-test was used to compare mean ∆DAS28 between the two groups. A total of 102 patients was calculated as a priori sample size.
**Results:** Fifty-three patients out of 142 screened patients (37%) had adalimumab concentrations >8 mL/L and were included in the study. All patients completed follow up. Twenty-six patients were randomly assigned to continuation group and 27 patients were assigned to tapering group. Patients characteristics at baseline did not differ significantly between the two groups. After 26 weeks, mean ∆DAS28 did not meet the criteria for a clinically relevant difference in both continuation group (0.29± 0.58 standard deviation (SD)) and tapering group (-0.06±0.58 SD) and did not significantly differ (p=0.06) between groups (see figure). Six patients in the continuation group developed active inflammation (defined as an increase of ≥1 swollen joint compared to baseline) during follow-up. In the tapering group, two patients developed active inflammation of whom one returned to standard dose of adalimumab. Despite the absence of inflammatory signs, eight other patients in the tapering group returned to standard dose on request of patient or treating rheumatologist.




**Conclusions:** This interim analysis shows that disease activity remains stable in RA patients with adalimumab concentrations >8 mL/L who prolonged their dose interval to once in the three weeks compared to patients who continued adalimumab every other week.
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**Disclosure of Interest:** M. l'Ami: None declared, A. Marsman Speakers bureau: Pfizer, C. Krieckaert Speakers bureau: Pfizer, J. Ruwaard: None declared, E. Kneepkens Speakers bureau: Pfizer, M. Nurmohamed Grant/research support from: AbbVie, BMS, Pfizer, UCB, Roche, Consultant for: Abbott, BMS, Pfizer, Roche, Speakers bureau: AbbVie, Pfizer, Roche, G. Wolbink Grant/research support from: Pfizer, Consultant for: Pfizer, AbbVie, UCB, Munidfarma, BMS, Speakers bureau: Pfizer, UCB
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## AB0325 COMPARISON OF THE EFFICACY OF SECOND TNF INHIBITOR VERSUS ALTERNATIVE BIOLOGICAL AGENT (RITUXIMAB/ TOCILIZUMAB/ABATACEPT) AFTER SECONDARY FAILURE TO INITIAL ANTI TNF THERAPY IN RHEUMATOID ARTHRITIS – A RETROSPECTIVE OBSERVATIONAL ANALYSIS

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**Background:** Treatment of rheumatoid arthritis (RA) has been revolutionized by the introduction of tumor necrosis factor inhibitors (TNFi). Nonetheless a significant proportion of patients fails to respond (primary failure) or may lose the initial response over time (secondary failure). Subsequent treatment for the patients who experienced secondary failure yet needs to be defined, particularly, as to whether a second TNFi or an alternative biological agent (non- TNFi), should be used.
**Objectives:** With the aim to assess and compare the efficacy of second TNFi versus non-TNFi after secondary failure to the first TNFi, we obtained data from patients with secondary failure who had started treatment with biologics from 2010 to 2015.
**Methods:** A pro-forma has been given to patients with secondary failure who were on either second TNFi or non-TNFi either in clinic or sent by post. Patients were excluded if they had missing or incomplete data, if the nature of the failure was unclear or if the treatment was changed due to infection, cancer, hepatitis, tuberculosis (TB) or Multiple Sclerosis (MS). Response was assessed by ACR20. Additionally, the clinical notes were reviewed and scrutinised aiming to gather as accurate as possible information on patients' clinical assessments. The response to treatment following secondary failure was further analysed according to the presence or absence of Rheumatoid Factor (RF) and Anti-CCP Antibodies (aCCP).
**Results:** Data from a total of 109 patients were obtained. 43 patients (M:F =1:3) were included in the analysis. Patient's mean age was of 61 years (SD ±10). From those patients excluded, 16 patients had incomplete data, 13 had unclear data, 19 patients had infection, 11 had cancer, 4 had hepatitis, 2 had TB, and 1 had MS. From the 43 patients analysed 20 were on a second TNFi [6 on Adalimumab (ADA), 5 on Certolizumab (CZP), 5 on Etanercept (ETA), 4 on Golimumab (GLM)] while 23 were on non-TNFi [12 on Rituximab (RTX), 6 on Tocilizumab (TCZ), 5 on Abatacept (ABT)].
A total of 24 of 43 patients (46.5%) responded to treatment after secondary failure. Of these, 8 patients (of 20; 40%) were from the TNFi group and 16 (of 23; 70%) from the non- TNFi group (p=0.05). Among the TNFi group, the response rate was 16% (1/6) for ADA, 60% (3/5) for CZP, 40% (2/5) for ETA, 50% (2/4) for GLM. In the non-TNFi group, the response rate was 75% (9/12) for RTX, 67% (4/6) for TCZ and 60% (3/5) for ABT.
When stratifying the response according to the presence or absence of RF or aCCP, seropositive patients showed significantly better response to non-TNFi compared to TNFi (70% vs 33%; p=0.03). Looking at responses according to drugs used after secondary failure, all patients who were seronegative responded to CZP and ABT (100% response) while seropositive patients showed 90% response to RTX.
**Conclusions:** Secondary failures to TNFi overall respond better to non-TNFi compared to second TNFi, especially if they are seropositive.Further studies are needed in order to guide the accurate pharmacological interventions.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4462

## AB0326 THREE-YEAR STUDY OF TNF-ALFA INHIBITORS USE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CONCOMITANT CHRONIC HEPATITIS B OR C

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**Background:** Managing patients with rheumatoid arthritis (RA) and concomitant hepatitis B virus (HBV) or hepatitis C virus (HCV) infections represents a major challenge in modern rheumatology.Due to a high risk of HBV, HCV infection reactivation and potential hepatotoxity the use of disease-modifying antirheumatic drugs (DMARDs) and corticosteroids is limited in such patients. Since biologic agents have been increasingly employed in patients with chronic inflammatory rheumatic diseases, their efficacy and safety need to be further investigated in patients with chronic HBV and HCV infection.
**Objectives:** To assess the safety and efficacy of TNF-alfa inhibitors (TNFi) in RA patients with concomitant chronic HBV and HCV infection.
**Methods:** From 2012 to 2015 we have been observing 10 RA patients (5 male, 5 female, mean age 45,4 years) with chronic HBV (6 patients) and HCV (4 patients) infection who were undergoing therapy with TNFi. Mean duration of the disease before initiating biologic agents was 8 years, mean follow-up period was 18,2 months. Criteria for starting biologics included high disease activity score (DAS28 - 6,7) with little response to non-biologic DMARDs (methotrexate, leflunomide, sulfasalazine) and/or low-dose corticosteroids (4–8 mg/day); intolerance of DMARDs or contraindications to them. 2 patients with RA and chronic HBV infection were given a preventive treatment with ribavirin and a concomitant treatment with alfa-inetrferon. One patient with RA and chronic HCV

infection recieved an antiviral preventive treatment with alfa-interferone. Hepatitis activity was monitored with viral load and liver function tests, RA activity was monitored with ESR, CRP, pain assessment with visual analogue scale (VAS) and disease activity score in 28 joints (DAS28). All tests were performed every 3 months during the first year and every 6 months beyond the first year of study. Patients were given standard doses of TNFi – adalimumab (2 patients with hepatitis C), etanercept (8 patients with hepatitis B, 2 patients with hepatitis C).
**Results:** Disease activity reduction was observed in all patients: mean pain VAS score decreased from 80 to 26.5 mm ($p<0,001$), mean ESR decreased from 32,8 to 12,5 mm/h, mean CRP level decreased from 4.2 to 0.3 mg/dl ($p<0,001$), mean DAS28 decreased from 6.25 to 3.36 ($p<0,001$). No viral load or liver enzymes increase was observed in our study. One patient with chronic hepatitis B and one patient with chronic hepatitis C had leukopenia on while being on etanercept and concomitant or preventive alfa-interferon therapy, which was successfully reversed with Leucostim
**Conclusions:** After 3 years of study TNF-alfa inhibitors (adalimumab and etanercept) appear to be effective and quite safe in patients with RA and concomitant chronic HBV and HCV infection. During the mean follow-up period of 18.2 months no viral load increase or signs of hepatitis virus reactivation have been noted. Althigh, TNFi-based treatment requires regular monitoring of HBV and HCV activity using PCR test.
**Disclosure of Interest:** None declared
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## AB0327 AN AUDIT OF THE USE OF BIOLOGIC THERAPIES AND DOSAGE TAPERING IN STABLE INFLAMMATORY ARTHRITIS PATIENTS: A REAL LIFE LOOK AT A DISTRICT GENERAL HOSPITAL'S PATIENTS

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**Background:** Rheumatology department at a South West England District General Hospital.
**Objectives:** To audit our use of biologic therapies in patients with inflammatory arthritis. To establish how many patients we are increasing the dosage interval, which patients we are choosing to do this for and what are the success rates from this. Evaluate what the financial implications are in doing this.
**Methods:** Using the "Homecare Patient List" patients with any inflammatory arthritis who were on a biologic medication were identified. Patients with a firm diagnosis of Rheumatoid Arthritis (RA) or Psoriatic Arthritis (PsA) were identified from this. Patients on one of 6 biologic medications (abatercept, adalimumab, certolizumab, etanercept, golimumab, and tocilizumab) were then included. Further inclusion criteria for the audit included being on a biologic medication for over 6 months (ie. Started before April 2015) and having regular follow up with our service (at least every 6 months).
148 patients were identified as suitable (108 Rheumatoid arthritis, 40 Psoriatic arthritis). Demographics were collected from hospital electronic records and then information regarding biologic medications and clinical status was taken from clinic letters using Epro records. Clinic letters prior to 2013 were not viewed. Results were collected in MS Excel template.
**Results:** Of the 108 RA patients; 76 female and 36 male, mean age was 61 years with a range of 32 years to 78 years. In 40 of these patients we attempted to taper the interval of their biologic medication. 87% of these patients were on methotrexate as an anchor medication. Biologic medications that were tapered included adalimumab, etanercept and certolizumab. In the 40 patients tapered this change has been maintained or increased in 28 patients, giving a success rate of 70%. 12 patients have returned to the original dosing regimen due to increased disease activity.
In the Psoriatic Arthritis patient group, there were 21 females, 19 males, with a mean age of 52 years (age range 31 years to 73 years). In 5 of these patients we have attempted to taper the interval of their medication. The majority of those tapered were on monotherapy adalimumab. The changes were maintained in 80% of patients.
**Conclusions:** In total we have attempted to taper 30% of RA and PsA patients on biologic therapies, 71% of these attempts have been maintained or increased. We are increasing the dosage intervals successfully by varying amounts, with a range from 16% to 55%, and by a mean of 30.58% over all medications included. Etanercept has successfully had the largest increase in interval with dosing intervals increasing by a mean of 55% compared to once every 7 day dosing. This has significant financial implications with an annual savings of £72,108.60 based on the data in this audit.
**Disclosure of Interest:** None declared
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## AB0328 WHAT COULD WE LEARN FROM THE SUB-ANALYSIS OF A SINGLE NATION COHORT IN A WORLDWIDE STUDY? LESSON FROM THE RESULTS OBSERVED IN THE ITALIAN COHORT OF THE GO-MORE TRIAL

R. Giacomelli [1], P. Ruscitti [1], V. Liakouli [1], P. Cipriani [1], M. Mecchia [2] on behalf of the Italian GO-MORE Investigators. *[1]Division of Rheumatology, University of L'Aquila, L'Aquila; [2]MSD Italy, Rome, Italy*

**Background:** GO-MORE Trial investigated the use of Golimumab (GLM) in rheumatoid arthritis (RA) in 3280 patients worldwide [1]. At present, the burden of arthritis is greater in poorer countries than in developed countries due to socioeconomic disparities [2], thus suggesting the usefulness of subgroup investigations.
**Objectives:** We evaluated the GLM as add-on therapy for RA patients in the Italian cohort of GO-MORE trial and we compared the baseline characteristics and efficacy after 6 months between Italian patients and the enrolled patients worldwide. A limit of these analyses is that they are *post hoc* in nature and many tests were performed without adjustments for multiplicity.
**Methods:** Ninety-eight Italian patients with active RA, fulfilling the 1987 ACR criteria, naïve for biologic drugs were enrolled. Statistical analyses were performed to assess: i. the differences in baseline characteristics; ii. the efficacy after 6 months; between Italian and Rest of the World GO-MORE populations.
**Results:** The majority of Italian patients were older than the worldwide patients ($p=0.01$). Compared to Rest of the World population, Italian patients showed a lower value of DAS28-ESR ($p=0.045$), DAS28-CRP ($p=0.0001$), and a significantly short disease duration ($\leq$2 years) ($p=0.045$). Differently from the Rest of the World patients, the large majority of Italian patients received biologic therapy after the failure of the first sDMARD ($p<0.0001$). Furthermore, a lower percentage of Italian patients were treated by high MTX dosage ($p<0.0001$). After 6 months of GLM treatment, the therapeutic response of the Italian patients did not differ from those observed in Rest of the World cohort. More than 90% of patients reported that the overall autoinjection experience was favourable and these results mirrored those observed worldwide [3].
**Conclusions:** The analysis of the Italian GO-MORE subset confirms that differences among patients may be shown, depending from different approaches in different health systems. The Italian cohort (early onset of the disease and already fulfilling the 1987 ACR criteria) is probably affected by a more severe disease with poor outcome [4], but the efficacy in this subset response rate of Italian subset did not differ from worldwide patients. GLM in the Italian patients showed a favourable benefit/risk profile and the positive autoinjection experience may help for patient's compliance and survival of the treatment.
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## AB0329 ULTRASOUND 7 VERSUS ULTRASOUND12 IN MONITORING THE RESPONSE TO ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Objectives:** This study aimed to assess the responsiveness of ultrasonography (US)-7 in patients with psoriasic arthritis (RA) non responders at only MTX terapy recruided with baseline ecographic positivity per disease activity. Sixty-two RA patients were recruited and followed up for 24 weeks.
**Methods:** The clinical, laboratory, and X-ray assessments, along with grayscale US (GSUS) and power Doppler US (PDUS) examinations were performed at baseline, 6, 14, and 24 weeks after adalimumab treatment GSUS for synovitis and PDUS for synovitis and paratendinitis/tenosynovitis were assessed by a semi-quantitative (0 to 3) score, while GSUS for paratendinitis/tenosynovitis and bone erosion was qualitatively assessed as absent or present (0 or 1). US scores in both 7-joint (US7) and 12-joint (US12) systems were evaluated.
**Results:** After 6, 14, and 24weeks of treatment with adalimumab, indices such as US scores in both 7-joint (US7) and 12-joint (US12) systems were evaluated. After 6, 14, and 24 weeks of treatment with adalimumab indices such as US scores, 28-joint disease activity (DAS28) score, and tender and swelling joint count were

all significantly improved compared to baseline. US7 scores were significantly correlated with that of US12. Strong correlations were identified between most US7 scores with DAS28, health assessment questionnaire (HAQ), and C-reactive protein (CRP) levels. When DAS28 was used as a reference, the US7 cutoff for disease remission was less than 35 for GS+PD and also less than 29 for GS and 1 for PD, respectively

**Conclusions:** Additionally, the positive percent agreement, negative percent agreement, and overall percent agreement for GS+PD were 77.78, 76.19, and 76.67%, respectively, which were all higher than that of GS or PD. US7 may be a feasible tool to assess the therapeutic response in RA patients.

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**Disclosure of Interest:** None declared

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## AB0330 ETANERCEPT ALTERNATIVE STORAGE AT AMBIENT TEMPERATURE

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**Background:** Introduction of biological disease-modifying antirheumatic drugs (DMARDs) that began with the approval of the tumour necrosis factor (TNF) inhibitor etanercept has revolutionized the management of patients with rheumatic diseases[1] and other inflammatory diseases.[2] Use of biological therapy, including TNF inhibitors, has improved outcomes for patients with RA, with sustained remission now considered the optimal treatment goal to prevent joint damage.[1] Therefore, flexible and convenient treatment options that are compatible with modern lifestyles are important aspects in helping patients maintain treatment and manage their disease. Since the introduction of etanercept, Pfizer has aimed to provide this through innovation in the form of lyophilized powder for solution injection, pre-filled syringe and pre-filled pen formulations.[3] Regulation of the manufacture of etanercept and other biologic drugs is governed by a requirement to perform robust analytical and stability testing to ensure quality is maintained.[4] Due to its structural complexity, etanercept, as with many other biologics, is typically stored under refrigerated conditions.[3] Here we describe the stability testing data that support an alternative storage condition for etanercept at ambient temperature, representing further innovation in the product lifecycle aimed at enhancing patient convenience.

**Objectives:** To generate a comprehensive analytical data package from stability testing of key quality attributes consistent with regulatory requirements that determine if the product profile of etanercept is maintained at an alternative storage condition of ambient temperature.

**Methods:** Test methods assessing the key attributes of purity (Size Exclusion High Performance Liquid Chromatography, Hydrophobic Interaction Chromatography), quality (appearance, pH, etanercept concentration by ultraviolet absorbance spectroscopy, particulate matter, reconstitution time, functionality), potency (cell-based TNF alpha-induced apoptosis bioassay) and safety (sterility, container closure integrity).

**Results:** Results and statistical analysis from stability testing across all etanercept presentations showed key stability indicating parameters were within acceptable limits through the alternative storage condition of 25℃ ±2℃ for a period of 1 month.

| Presentation | Stability study temperature (period in specification) | | |
|---|---|---|---|
| | 5℃ ±3℃ | 25℃ ±2℃ | 30℃ ±2℃ |
| 25mg PFS, 50mg PFS, 50mg PFP | 36 months | 1 month | ≥4 weeks |
| 25mg/vial | 36 months | 6 months | ≥4 weeks |
| 10mg/vial | 36 months | 24 months | ≥4 weeks |

PFS, pre-filled syringe; PFP, pre-filled pen.

**Conclusions:** Stability testing performed in line with regulatory requirements supported a single period of storage for etanercept at an alternative storage condition of 25℃ ±2℃ for up to 1 month within the approved expiry of the product. This alternative storage condition for etanercept provides greater flexibility for patients, particularly whilst travelling with etanercept, reflecting Pfizer's commitment to offer enhanced overall patient convenience.

**References:**

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**Disclosure of Interest:** S. Vicik Shareholder of: Pfizer, Employee of: Pfizer, J. Daffy Employee of: Pfizer, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, A. Paulson Shareholder of: Pfizer, Employee of: Pfizer, E. Shannon Employee of: Pfizer

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## AB0331 EARLY IMPROVEMENT OF MUSCULOSKELETAL ULTRASOUND FINDINGS CAN PREDICT FUTURE CLINICAL RESPONSE TO CERTOLIZUMAB PEGOL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Certolizumab pegol (CZP) is a PEGylated Fab' fragment of a humanized anti-TNF antibody and it brings rapid improvement of the signs and symptoms of RA. Musculoskeletal ultrasound (US) has been proved to be useful at assessing synovitis precisely in patients with RA. There are few reports, however, that verify the early response to CZP in RA patients by US. Moreover, it remains to be ascertained whether early US assessment of synovitis can predict future clinical response in treatment with CZP.

**Objectives:** In the present study we investigate whether US is useful for predicting future clinical response to CZP in RA patients.

**Methods:** Twenty patients with RA were treated with subcutaneous CZP 400 mg at weeks 0, 2, 4 followed by 400 mg every 4 weeks or 200 mg every 2 weeks. The mean age of patients was 55.2 years old and the mean disease duration was 5.9 years. The mean disease activity at baseline (week 0) was 4.91 for 28-joint disease activity score (DAS28). Fifteen (75%) patients were naïve to biologic agents. Seventeen (85%) and 9 (36%) patients were treated with methotrexate and glucocorticoids concurrently. At baseline and weeks 2, 4 and 12, US examination was performed at bilateral MCP, PIP, IP, and wrist joints. Gray-scale (GS) and pulse Doppler (PD) signal was recorded in each joint using semi-quantitative score (0 to 3). The sum of these scores obtained from each joint was used as GSUS and PDUS score.

**Results:** At weeks 0, 2, 4, and 12, mean GSUS score was 24.1, 20.4, 17.5, and 16.7, respectively. Mean PDUS score at weeks 0, 2, 4, and 12, was 14.6, 10.8, 10.8, and 9.9, respectively. Both GSUS and PDUS score were improved significantly as early as 2 weeks after treatment ($p=0.031$ and 0.011) and reduced by degrees during study period. At weeks 0, 4, 8, 12, and 24, mean DAS28 was 4.91, 3.61, 3.55, 3.50, and 3.05, respectively. DAS28 was significantly improved as early as 4 weeks after treatment ($p<0.001$). Clinical response was evaluated as achievement of DAS remission (DAS $<2.6$), and we classified 10 patients (50%) who achieved DAS remission at week 24 as "responders". The improvement in US assessment at week 2 was compared between responders and non-responders. Four patients showed a $>50\%$ reduction in PDUS score from baseline (PDUS 50 response) at week 2. At week2, none achieved a $>50\%$ reduction of GSUS score from baseline, whereas 8 patients indicated a $>20\%$ reduction in GSUS score from baseline (GSUS 20 response) at week 2. There was a marked high responder rate (80%: 4 out of 5) in the patients showing PDUS 50 response at week 2. Similarly, the responder rate (88%: 7 out of 8) of the patients showing GSUS 20 response at week 2 was remarkably high and significantly higher than that (25%: 3 out of 12, $p=0.020$) of the patients without GSUS 20 response.

**Conclusions:** Early response to CZP was confirmed by US examination and the early assessment of synovitis by US is useful to predict future clinical response to CZP in patients with RA.

**Disclosure of Interest:** None declared

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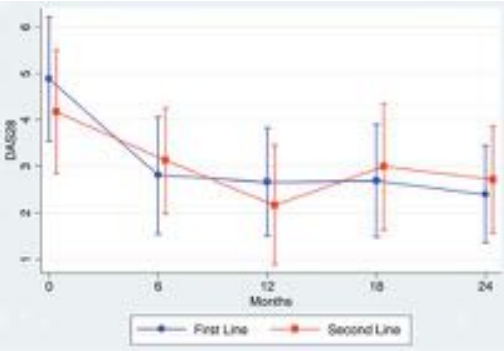
## AB0332 GOLIMUMAB EFFICACY IN RHEUMATOID ARTHRITIS AFTER CONVENTIONAL AND BIOLOGICAL TREATMENT: DATA FROM THE ITALIAN LORHEN REGISTRY

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**Background:** The efficacy of Golimumab (GLM) treatment in rheumatoid arthritis (RA) has been widely documented in clinical trials. Data are still needed to assess its efficacy and tolerability in everyday clinical practice.

**Objectives:** To assess the efficacy of the treatment with GLM in RA previously treated with conventional synthetic disease modifying antirheumatic drugs (cs-DMARDs) or biological DMARDs (bDMARDs) from a multicentric observational cohort (the LORHEN Registry).

**Methods:** All patients with a diagnosis of RA in the LORHEN database who started GLM from october 2010 up to september 2015, with at least one reported visit, were included.
We reviewed the data regarding the first 24 months of treatment, focusing on clinical efficacy.
The efficacy of GLM was assessed with DAS28, DAS28(CRP), SDAI and EULAR response criteria.
We executed intention-to-treat (ITT) and per-protocol analysis (PP).
We repeated the analysis for the subgroups of patients who received GLM as first or second bDMARD.
**Results:** We retrieved the data regarding 180 patients, with a mean (sd) age of 54,57 (13,62) years and a mean (sd) disease duration of 9,52 (9,32) years. Methotrexate was the concomitant csDMARD for 123 (68,3%) patients, while leflunomide, sulfasalazine and cyclosporine were given to 13 (7,2%), 5 (2,8%) and 4 (2,2%) patients respectively. 35 (19,4%) patients were treated with GLM monotherapy. 137 (76,1%) and 5 (2,8%) patients were given low dose (≤10mg prednisone equivalent a day) and medium dose (≥10 and ≤25) corticosteroid at baseline, with following tapering.
A total of 79 patients stopped the treatment with GLM due to inefficacy or adverse events before 24 months of treatment.
With the ITT design 55 (30,6%) and 44 (24,4%) patients achieved good or moderate EULAR response respectively at 6 months. The mean (sd) DAS28, DAS28(CRP) and SDAI progressively reduced, reaching 2,61 (1,11), 2,41 (0,72) and 4,62 (3,80) respectively at 24 months.
Within the PP scenario, 32 (66,7%) and 9 (18,8%) patients reached and maintained good or moderate EULAR response respectively to the end of the follow-up.
The clinical response to GLM therapy resulted slightly reduced when given as a second line bDMARD treatment, but the data did not met statistical significance.




**Conclusions:** GLM is effective in treating RA in everyday clinical practice. The efficacy increases significantly over the first 6 months and slightly during the following 18 months.
Interestingly enough, patients treated with GLM after a first bDMARD can still achieve low disease activity and clinical remission, with an overall efficacy of the treatment not statistically different to the first line.
**Disclosure of Interest:** None declared
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## AB0333 DRUG SURVIVAL OF TNF-α INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS IN DAILY CLINICAL PRACTICE: A RETROSPECTIVE COHORT RESEARCH

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**Objectives:** The aim of this study was to examine the frequency and reasons of discontinuation of TNF-α inhibitor treatment in rheumatoid arthritis (RA) patients in daily practice. We focused on (serious) infections, (skin) malignancies, (local) allergic reactions, inefficacy and remission. Furthermore, we investigated if the discontinuation was temporarily or permanent, if there were differences between the five TNF-α inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab pegol), if there was dose reduction during treatment and if there were differences between men and women.
**Methods:** This is a retrospective cohort study of RA patients treated with TNF-α inhibitors of the Rheumatology department Spaarne Gasthuis in Haarlem between January 2012 until January 2015. The variables of the database were tested with Kaplan Meier, Cox-regression and Chi-square test.
**Results:** In total 274 patients were included of whom 184 (67.2%) used etanercept, 63 (23%) used adalimumab and the groups treated with infliximab, golimumab and certolizumab pegol had each nine patients (3.3%). Of the 274 patients, 93 (33.9%) continued with the same TNF-α inhibitor treatment without interruption. The mean treatment duration in these patients was 30.1 months. Furthermore, 101 patients (36.9%) stopped treatment temporarily, of whom 95 stopped for less than 6 months. The reasons for the temporary stops were mild infections (64), newly diagnosed malignancies (2), local allergic skin reactions (1) and remission (6). Finally the first treatment episode in the study period was stopped permanently in the remaining 80 patients (29.2%), of whom 19 switched to another TNF-α inhibitor, 13 switched to another biological and 48 stopped biological treatment permanently. In table 1 reasons for stopping TNF-α inhibitor treatment are shown. Dose reduction of TNF-α inhibitor treatment was observed in 50 patients (18%), resulting in a relapse of RA in only 5 patients. Etanercept showed significantly more interruptions than the other TNF-α inhibitors. Other differences between the five TNF-α inhibitors and between men and women were not significant.

Table 1. Reasons for stopping TNF inhibitor treatment permanently (80 patients)

| | |
|---|---|
| Infections | 13 (11 mild and 2 serious) |
| Malignancies | 4 |
| Allergic skin reactions | 5 (3 local and 2 systemic) |
| Other side effects | 13 |
| Inefficacy | 21 |
| Remission | 5 |
| Lost to follow-up | 5 |
| Deceased | 5 |
| Other reasons | 9 |

**Conclusions:** Concluding, 71% of the RA patients stayed on the same TNF-α inhibitor, of whom 34% without interruptions and 37% with mostly short interruptions. This is in line with the literature (1). The remaining 29% of the patients stopped TNF-α inhibitor treatment permanently. Short treatment interruptions were found significantly more in the etanercept group. A plausible explanation for this finding is the higher injection frequency (once per week) of etanercept leading to more frequent interruptions. In conclusion, TNF-α inhibitor treatment in RA patients is safe and effective in more than 70% of the patients. Dose reduction may be an option in some patients, but stopping because of remission is rare and half of the patients flared within six months.
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[1] Monaco C, Nanchahal J, Taylor P, Feldmann M. Anti-TNF therapy: past, present and future. International Immunology. 2014;27(1):55–62
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5414

## AB0334 CLINICAL EFFICACY OF CERTOLIZUMAB PEGOL THERAPY IN PATIENTS WITH JAPANESE ACTIVE RHEUMATOID ARTHRITIS 52 WEEK RESULT ～A MULTICENTER REGISTRY STUDY～

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**Background:** Certolizumab pegol (CZP) is a polyethylene glycol (PEG)ylated Fc-free new anti-TNF α agent. However few data still reported clinical efficacy of CZP treatment in the routine practice.
**Objectives:** To evaluate the clinical efficacy of CZP in patients with Japanese active RA for 52 weeks.
**Methods:** Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria who had been prescribed CZP from Tsurumai Biologics Communication Registry (TBCR) between May 2013 and October 2014 were enrolled.The final study cohort of 80 RA patients. We reviewed the methods about the improvement of CRP, MMP3, DAS28-ESR and SDAI which was an index of disease activity of RA using Wilcoxon signed-rank, test and the rate of remission patients at Week4,8,12,24 and 52 by LOCF method.
**Results:** The group of patients included 15 males and 65 females. The mean age was 60.1±14.2 years old; the disease duration was 9.7±9.3 years; the patients of receiving methotrexate (MTX) was 59 cases (74%); the MTX dose was 11.0±3.5 mg/week and b-DMARD naïve patients was 51 cases (64%). Clinical findings related to RA were as follows: mean tender joint count, 5.7±4.9; swollen joint count, 5.4±4.2; patient's and physician's global assessment of disease activity, 51.7±26.5 and 44.7±23.2mm; CRP, 1.9 ±2.2 mg/dL; ESR, 48.9±34.0 mm/h; MMP3, 224±172 ng/ml; the rate of rheumatoid factor positive patients was 77%; DAS28 (ESR), 5.01±1.31; and SDAI, 22.7±11.3. The mean CRP improved to 1.0±1.4, 0.8±1.3, 0.7±1.1 and 0.5± 1.0 at Week 4, 12, 24 and 52 ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$), mean MMP3 improved to 153±132, 165±169, 119± 131 and 105±96 at Week 4, 12, 24 and 52 ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$), the mean DAS-ESR improved to 3.70±1.35, 3.47±1.43, 3.47±1.46 and 3.41±1.45 at Week 4, 12, 24 and 52 ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$) and the mean SDAI improved to 12.3±9.2, 10.6±9.1, 10.7±9.4 and 9.9±9.6 at Week 4, 12, 24 and 52 ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$) significantly (Fig.1). At Week 4, 12, 24 and 52 the rate of patients who achieved remission were each 22.7, 28.9, 30.0, 31.3% and 7.4, 26.0, 30.2, 31.8% in DAS-ESR and SDAI criteria (Fig.2). Also at Week 4, 12, 24 and 52 the rate of patients who achieved low disease activity (LDA) were each 41.3, 47.3, 48.6, 55.2% and 55.9, 58.9, 60.4, 71.2% in DAS-ESR and SDAI criteria. We used logistic models in order to determine predictive factors to achieve remission and LDA at Week52. Even after adjusting for other risk factors, b-DMARD naïve and MTX combination

remained significant and independent to achieve remission at Week52 (HR 3.88; 95%CI 0.95–15.89; p=0.059)(HR 4.06; 95%CI 0.79–20.88; p=0.094), and b-DMARD naïve and DAS-ESR at baseline remained significant and independent to achieve LDA at Week52 (HR 6.41; 95%CI 1.41–29.17; p=0.016)(HR 0.47; 95%CI 0.25–0.87; p=0.017) in the multivariate logistic analysis.

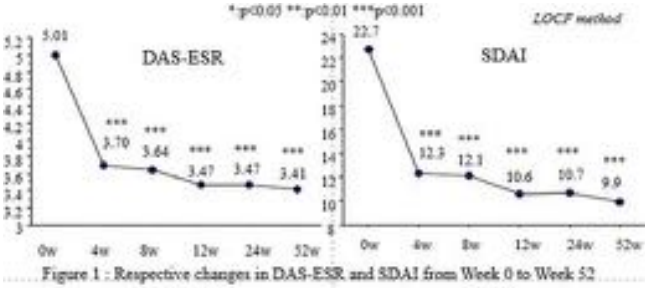



Figure 1 : Respective changes in DAS-ESR and SDAI from Week 0 to Week 52

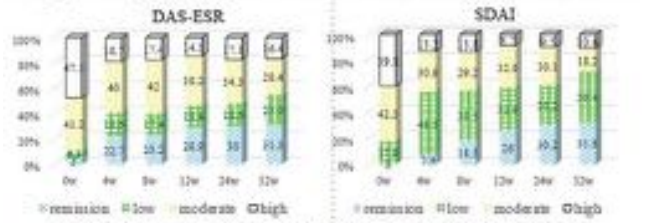



Figure 2: Time course of disease activity criteria using DAS-ESR and SDAI (Cut-off value was 5.1-3.2-2.6 and 23-11-3.3)

**Conclusions:** This study suggested that the new TNF-antagonist therapy of CZP was effective early and rapidly in patients with active Japanese RA. Especially lower DAS-ESR at baseline, MTX combination and b-DMARD naïve patients could expect higher efficacy of CZP treatment.

**Disclosure of Interest:** Y. Kanayama: None declared, A. Kaneko Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, Chugai Pharma, Abbott, Bristol-Myers Squibb, UCB, Janssen, and Pfizer., N. Takahashi Speakers bureau: Abbvie Japan Co. Ltd, Eisai Co. Ltd, UCB Japan Co. Ltd, MitsubishiTanabe Pharma Corporation, Takeda Pharmaceutical Company Ltd, Pfizer Co. Ltd, Chugai Pharmaceutical Co. Ltd, Janssen Pharmaceutical K.K., and Bristol-Myers Squibb Co. Ltd., T. Kato: None declared, Y. Hirano Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, and Bristol-Myers Squibb., Y. Hattori: None declared, N. Asai: None declared, N. Ishiguro Grant/research support from: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai Pharmaceutical, Mitsubishi Tanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan, Speakers bureau: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai Pharmaceutical, MitsubishiTanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan., T. Kojima Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, AbbVie, Bristol-Myers Squibb, and Pfizer, Janssenn Pharmaceutical Companies, Astellas Pharma and Chugai Pharma.

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## AB0335 PREVALENCE OF RESIDUAL INFLAMMATION IN RHEUMATOID ARTHRITIS PATIENT AFTER ONE YEAR OF ADALIMUMAB THERAPY

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**Background:** Studies have previously demonstrated that ultrasound detected power Doppler (PD) activity (implying active synovial inflammation) may be present in a proportion of patients in clinical remission[1,2] and this can be used to accurately predict subsequent radiographic structural progression.[3] It may be hypothesised that such continued subclinical inflammation despite apparent remission as determined by traditional criteria may trigger a subsequent disease flare.

**Objectives:** Our study aimed to determine subclinical joint inflammation in patients with rheumatoid arthritis by power Doppler ultrasound in patients with rheumatoid arthritis at 12 months of adalimumab therapy.

**Methods:** Patients with RA who had received adalimumab therapy were enrolled. Patients underwent clinical, laboratory, and ultrasonographic assessment with power Doppler assessment of bilateral elbows (posterior recess), wrists (radiocarpal), second and third MCP joints (dorsal recess), MCP II and III, PIP II and III (dorsal recess), knee, ankle and MTPII and MTP V joint at 12th month.

**Results:** Power Doppler ultrasound was performed in 62 patients (87 females and 18 males; mean age: 57.09±9.96 years). The mean baseline DAS28 were 8.13±9.52. Baseline PD score (mean ±SD) were 0.852 ±1.051 and after 12 month of adalimumab therapy, the PD score decreased to 0.23±0.42. Ultrasound was performed 12th month at various parts, with the mean GS score: most prominent at right wrist (.810±.924) and left wrist (.774±.909) (Table).Logistical regression confirmed diabetes, positive anti-CCP, high DAS28 had more sonographic inflammation, while hypertension and positive rheumatoid factor (RF) had less sonographic inflammation. MTX, glucocorticoid and cyclosporin therapy had increased inflammation.

Table 1. Distribution of PD ultrasound score at various joints

| Joints | Mean score | SD | 95% Confidence interval |
|---|---|---|---|
| R't Elbow | 0.536 | 0.7854 | 0.325–0.746 |
| Left Elbow | 0.464 | 0.7126 | 0.273–0.655 |
| R't Wrist | 0.810 | 0.9246 | 0.608–1.010 |
| L't Wrist | 0.774 | 0.9098 | 0.576–0.971 |
| R't 2nd MCP | 0.268 | 0.5557 | 0.119–0.416 |
| L't 2nd MCP | 0.179 | 0.6062 | 0.016–0.340 |
| R't 3rd MCP | 0.125 | 0.3844 | 0.022–0.227 |
| L't 3rd MCP | 0.071 | 0.3223 | 0.015–0.157 |
| R't PIP II | 0.143 | 0.4013 | 0.035–0.250 |
| R't PIP IV | 0.071 | 0.2599 | 0.001–0.141 |

**Conclusions:** Our data confirm the evidence that even after 1 year of biological therapy, there were still persistent subclinical synovitis, more severe at wrist joints. Baseline high DAS28 and high PD activity had more prone to residual inflammation. So we recommended serial ultrasound follow up of PD ultrasound in patients with rheumatoid arthritis after adalimumab therapy.

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[3] Brown AK, et al. Arthritis Rheum. 2008;58(10):2958–67.

**Disclosure of Interest:** None declared

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## AB0336 ANTI-ATHEROSCLEROTIC EFFECTS OF BIOLOGIC AGENTS, TOCILIZUMAB AND ETANERCEPT, IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Epidemic studies have shown that endothelial dysfunction and accelerated atherosclerosis lead to increased cardiovascular morbidity and mortality in patients with rheumatoid arthritis (RA). Cardio ankle vascular index (CAVI) measures arterial stiffness independent of blood pressure and it is superior to brachial ankle pulse wave velocity as an index of arterial stiffness. The aim of our study was to examine inhibitory effects on atherosclerosis of RA patients by biologic agents.

**Objectives:** We studied 36 RA patients with moderate or more disease activity as defined by the European League Against Rheumatism (EULAR) disease activity score (DAS28-ESR) in spite of MTX treatment.

**Methods:** We measured their CAVI before and after treatment with biologic agents (tocilizumab (TCZ) plus methotrexate (MTX)(n=11), etanercept (ETN) plus MTX (n=12), or MTX alone (n=13)) for one year.

**Results:** Each groups of characteristics (DAS 28, CRP, age, gender, disease duration) at baseline are no significantly different. Treatment with TCZ (9.62±1.56 and 9.05±1.42%, $P<0.05$), ETN (9.72±1.68 and 9.18±1.34%, $P<0.05$), but not MTX (9.88±1.63 and 9.79±1.87%; P=0.77) attenuated the CAVI significantly from baseline to 1 year follow-up.

**Conclusions:** TCZ and ETN but not MTX therapy may have a beneficial effect on preventing the progression of subclinical atherosclerosis and arterial stiffness. It remains unknown whether this effect is specific to TNF-alpha antagonists or relates to better control of inflammation irrespective of the disease modification strategy by which this is achieved.

**Disclosure of Interest:** None declared

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## AB0337 INCIDENCE RATE OF TUBERCULOSIS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TNF-α INHIBITORS-DATA FROM THE SLOVENIAN NATIONAL BIORX.SI REGISTRY

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**Background:** Treatment with TNF-α inhibitors (TNFi) is associated with an increased incidence rate (IR) of tuberculosis (TB).[1] Proper screening can reduce TB IR.[2,3] Recent reports suggest comparable TB IR for certolizumab (CZP) and monoclonal TNF-α inhibiting antibodies adalimumab ADA, golimumab (GOL) and infliximab (IFX) (0.47–0.69 vs 0.29–0.50 per 100 person years (PY), respectively).[4] Etanercept (ETA) was associated with a TB IR of 0.009–0.08 per 100 PY.[5–7] In February 2012 we showed that in our setting with a background annual TB IR of 8.4 per $10^5$ persons and stringent screening for latent tuberculosis infection prior to the initiation of the first TNFi since 2002 a TB IR of 0.16 (95% CI 0.02–0.58) per 100 PY in RA patients treated with TNFi.[8]

**Objectives:** To compare the TB IR in patients treated for RA with different TNFi.
**Methods:** In February 2015 we cross-linked the data from the mandatory BioRx.si and the national TB registries to identify cases of TB in patients who were ever treated with TNFi to avoid underreporting. TB IR for RA patients were calculated and compared for different TNFi.
**Results:** At the time of data extraction the BioRx.si contained data for 1693 RA, ankylosing spondylitis (AS) and psoriatic arthritis (PsA) patients treated with at least one TNFi for 4574 PY. There were no TB cases among the patients with AS and PsA. In 945 RA patients treated with TNFi for 2453 PY (41% ADA, 9% CZP, 36% ETA, 4% GOL, 10% IFX) 5 cases of TB were identified (Table 1) which translates into an overall IR of 0.20 (95%CI 0.07–0.47) in RA patients. There were no TB cases in RA patients on GOL or IFX, but 3 on CZP, 1 on ADA, and 1 on ETA. The TB IR for CZP was 1.39 (95% CI 0.29–4.02) per 100 PY which is significantly higher than TB IR for ADA at 0.10 (95% CI 0.002–0.55; p=0.002) per 100 PY or ETA at 0.11 (95% CI 0.003–0.63; p=0.005) per 100 PY or all TNFi other than CZP combined at 0.09 (95% CI 0.01–0.32; p=0.006) per 100 PY.

Table 1

| Age (years) | Sex | TST (mm) | CXR | QF | CP | TNFi | MP ever | MP (mg qd) |
|---|---|---|---|---|---|---|---|---|
| 54 | F | 18 | – | – | yes | ETA | yes | 8 |
| 57 | F | 20 | – | + | yes | CZP | yes | 4 |
| 62 | M | 0 | – | ND | no | ADA | yes | 4 |
| 70 | F | 10 | – | – | no | CZP | no | 0 |
| 80 | F | 0 | – | ND | no | CZP | yes | 4 |

F, female; M, male; MP, methylprednisolone; ND, not done; WNL, within normal limits; pts, patients; TNFi, tumor necrosis factor inhibitor; ADA, adalimumab; CZP, certolizumab; ETA, etanercept; RA, rheumatoid arthriti;, CP, tuberculosis chemoprophylaxis; TST, tuberculin skin test; QF, Quantiferon TB Gold test; CXR, chest X-ray suggestive of tuberculosis.

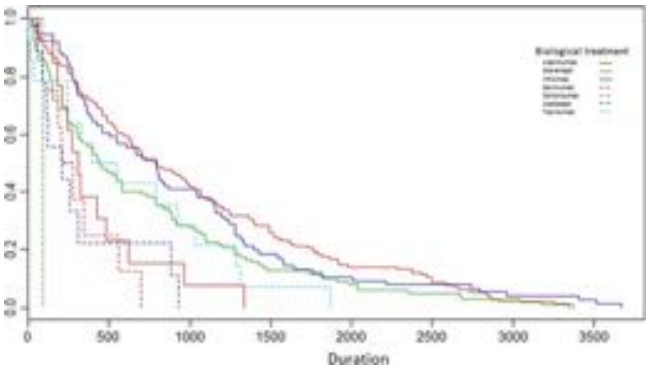
**Conclusions:** In our TNFi treated observational RA cohort, admitting all the shortcomings of the registry data, we observed a very strong signal suggesting a significantly higher TB IR in patients treated with CZP than those treated with any other TNFi.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1903

## Rheumatoid arthritis - other biologic treatment

### AB0338 SURVIVAL OF BIOLOGICAL DRUGS IN THE TREATMENT OF CHRONIC INFLAMMATORY ARTHROPATHIES

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**Objectives:** To analyze the survival of treatment lines with different biologics in a cohort of patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (AP), ankylosing spondylitis (AS) and other spondyloarthropathies (O).
**Methods:** Retrospective observational study.All patients who had been treated with a biological drug for at least six months during the period between 01/01/2009 and 31/08/2014, for any of the previously specified indications were included.In addition to demographic data, all lines of treatment received from the diagnosis and the duration of them were collected.It has been analyzed whether there were differences in the duration of treatment depending upon the drug and the disease. A survival analysis of all lines of treatment was performed using the Kaplan-Meier curves for each drug, including those who had not finished.It was represented on the vertical axis the percentage of patients who had each treatment and in the other axis, duration in days.It was analyzed whether there were differences between these curves using the log-rank test.
**Results:** We studied 484 patients with a mean age of 56 years (SD 14.4), 54.3% women. 742 lines of treatment were analyzed. Drug distribution: Adalimumab 344, etanercept 219, infliximab 96, golimumab 20, certolizumab 6, abatacept 20 and tocilizumab 26. In the cutoff point of the study (31.AUG.2014) had completed 342 of these lines.
The average duration of treatment in days (± SD) was calculated with the following results: Adalimumab: 1034 (±864)days; Etanercept: 735 (±768)days; Infliximab: 959 (±845) days; Golimumab: 302 (±225)days; Certolizumab: 90±0 days; Abatacept: 429 (±360)days; Tocilizumab: 328 (±337)days. The average length of treatment depending on the pathology (± SD) was also calculated. AR: 989 (±853)days; AP: 975 (±843)days; EA: 766 (± 677)days and O: 912 (±920)days.Given the standard deviations found, a survival analysis was performed using the Kaplan-Meier curves.Significant difference were observed when comparing the drugs 2–2 for the following pairs:adalimumab and infliximab have longer lines comparing to golimumab, certolizumab, abatacept and tocilizumab ($p<0.05$) and etanercept longer than golimumab, certolizumab and tocilizumab ($p<0.01$).




**Conclusions:** The duration of treatment lines is variable in all drugs and for all conditions tested. No differences were found with regard to the length of the lines between the three drugs analyzed with a longer time since its commercialization: adalimumab, etanercept and infliximab.
Supported by an unrestricted grant from Pfizer.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5126

### AB0339 CORRELATION BETWEEN CLINICAL AND ANTI-DESTRUCTIVE EFFECTS OF RITUXIMAB (RTM) AND B-CELLS COUNT IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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**Background:** Rheumatoid arthritis is a chronic autoimmune disease characterized by inflammation of the synovial tissue and destruction of the cartilage and bone. Antirheumatic treatment plays a important role in controlling the inflammation of rheumatoid arthritis and in minimizing joint damage. Rituximab has been successfully used to treat rheumatoid arthritis. It is a chimeric monoclonal antibody that targets the CD20 molecule expressed on the surface of B cells. Noteworhty, clinical and antidestructive effects often did not coincide.
**Objectives:** To study the impact of B-cells depleting therapy (RTM) on joint destruction in correlation with clinical effects and B-cells counts.
**Methods:** The study included 61 RA pts (average disease duration 10,1±7,7 y., mean DAS28 6,3±0,94, RF-positive 87%, ACCP–positive 93%) undergoing RTM therapy. Clinical effect was scored by EULAR criteria, radiographic progression was assessed using Sharp/van der Heijde (SvH) modified scoring method. B-cell level was measured with flow cytometry.
**Results:** By Week 48 after 2 RTM courses good response was documented in 29,7% pts, good and satisfactory in 85,3%; remission was achieved in 14,6% pts. There was no radiographic progression in remission pts., in 83% of pts with low disease activity and in 33% - with moderate disease activity. Of note, further progression in joint space narrowing was more pronounced than bony tissue destruction - in 32% and 25%m respectively. Clinical and anti-destructive effects were often dis-matching: bone destruction was abrogated without any clinical improvement in 54% of pts. There was no significant difference in clinical effects of RTM dosing regimens (1000mg x2 or 500mg x2). More potent anti-destructive effect was documented in pts getting higher RTM dose values. No significant influence of B-cells depletion on radiographic progression of the disease was noticed. Although, in RA pts achieving remission B-cell depletion was more notable (Median, IQR 0% (0–1.133) as compared to pts with active disease (Median, IQR 0.8% (0.2–4.8, p 0.001).
**Conclusions:** Clinical and anti-destructive effects of B-cell depletion therapy are not always equivalent. Therapeutic effect of two dosing regimens was similar, but the anti-destructive one was more pronounced with higher RTM doses. Radiographic progression did not show any correlation with the degree of B-cells depletion. Most pronounced B-cells depletion was documented in pts achieving remission.
**Disclosure of Interest:** None declared
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## AB0340 TAPERING STRATEGY IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOCILIZUMAB

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**Background:** Clinical trials have demonstrated the efficacy of Tocilizumab (TCZ) for patients with rheumatoid arthritis (RA). Several studies have demonstrated that dose tapering of TNF-inhibitors is a feasible therapeutic option in rheumatic patients with low disease activity (LDA). Nevertheless, few reports analyse the effectiveness of dose-tapering of TCZ.
**Objectives:** To evaluate the clinical outcome and incidence of flares in patients with RA in remission or LDA under a tapering strategy with TCZ and to analyse the influence of the tapering on serum drug levels.
**Methods:** Of a cohort of 34 adult patients with RA under therapy with TCZ, 13 patients with sustained LDA or remission (DAS 28-ESR <3,2) under a tapering strategy were included. Clinical disease activity (DAS-28-ESR, CDAI and SDAI), serological data (C-reactive protein, erythrocyte sedimentation rate) and serum TCZ levels were evaluated at the visit prior to starting tapering strategy (V0) and at the last visit available during a three-year follow-up period (LV). The tapering strategy consisted in a progressive interval prolongation and/or dose reduction. A flare was defined as an increase of the DAS28 greater than 3.2 plus a delta-DAS28 (related to pre-tapering DAS28) lower than -0.6. The number of flares, time to first flare and the activity in the worst flare were collected. In the case of a flare, the concomitant therapy and TCZ dose could be intensified. Blood samples were collected just before the infusion and serum drug levels were measured by ELISA.
**Results:** The baseline demographic and clinical characteristics are shown in Table 1. No differences in the clinical activity (DAS28: 2,28± 0,8 at V0 vs 2,5±0,7 at LV, p=0,25; CDAI 4,71: ±5,1 at V0 vs 5,71±5,1 at LV p=0,08; SDAI (4,99±5,3 at V0 vs 5,0 ±4,8 at LV, p=0,052), number of swollen joints (1,69±3,2 at V0 vs 1,46±1,8 at LV; p=0,091) and tender joints (0,69± 1,1 at V0 vs 0,62±0,96 at LV; p=0,243) and acute-phase reactants (CRP: 0,48±0,6 at V0 vs 0,54±0,6 at LV, p=0,219; ESR: 7,69±3,1 at V0 vs 10,3±5,4 at LV, p=0,152) between V0 and LV were observed. The decrease of drug levels between V0 and LV was not significant (15,4±9,31 vs 3,02±5,99, p=0,867). During the follow-up period, 6 (43%) patients presented flares. The number of flares after the tapering strategy was 1,2±1,6 and the time to the first flare was 1±0,4 years. The following clinical and disease activity data and serum TCZ levels were registered at the worst flare: STJ: 6,7± 7,4 and TJC: 1,83±1,2; DAS28: 3,99±0,6, CDAI: 14,7± 8,2 and SDAI: 14,5±9,08; TCZ levels: 0,86±1,78. Most patients after having a flare (4/6) reached remission or LDA at the end of the study, and no significant differences in LDA were observed between those with or without flares (DAS-28 LV<3,2:4/11 (36,4%) vs 7/11 (63,6%), p=0,097; CDAI LV <10: 4/10 (66,7%) vs 6/10 (85,7%), p=0,42; SDAI LV <11: 4/11 (36,4%) vs 7/11 (63,6%), p=0,097, respectively). All of the patients continued on tapering strategy and no patients dropped out because of inefficacy.

| | |
|---|---|
| Age, years ± SD | 55 ± 12,2; |
| Female [n/N (%)] | 13 (100%) |
| Disease duration (years) | 8,38 ± 4,9 |
| RF/ACPA positive, [n/N (%)] | 8/13 (62%); 11/13 (84%) |
| Erosive Arthritis [n/N (%)] | 7/13 (53%) |
| DAS 28-ESR, mean ± SD<br>CDAI, mean ± SD<br>SDAI, mean ± SD | 5,45 ± 0,93;<br>29,43 ±9,7;<br>30,9 ±11 |
| SJC and TJC ± SD | 10,3 ± 4,9;<br>6,98 ± 3,9 |
| CRP and ESR, mean ± SD | 11,5± 14,7;<br>21,8±9,1 |
| Time from diagnosis to TCZ initiation (years) ± SD | 5,1 ± 4,4 |
| Naive [n/N (%)] | 12/13 (92%) |
| Monotherapy [n/N (%)] | 0% |
| Co-therapy [n/N (%)]: 1 (MTX); 2; Other DMARDs only; 3(corticotherapy) | 1. 10/13 (77%);<br>2. 5/13 (38%).<br>3 8/13 (61%) |

**Conclusions:** The tapering strategy in patients with RA with LDA or remission receiving TCZ appears to be feasible, resulting in a low proportion of patients with flares and a good longterm clinical disease activity control.
**Disclosure of Interest:** C. Tornero Grant/research support from: Funded by an unrestricted medical grant from Pfizer., C. Plasencia: None declared, D. Pascual: None declared, T. Jurado: None declared, I. Monjo: None declared, M. B. Paredes: None declared, E. Moral: None declared, A. Pieren: None declared, L. Nuño: None declared, G. Bonilla: None declared, D. Peitedo: None declared, E. M.Mola: None declared, A. Balsa: None declared
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## AB0341 FAVORABLE EFFECTS OF SIRUKUMAB TREATMENT ON PHYSICAL FUNCTION AND REDUCTIONS IN MORNING STIFFNESS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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**Background:** Improvement in physical function and morning stiffness are important goals of rheumatoid arthritis (RA) treatment. Sirukumab, a selective human anti-IL6 monoclonal antibody, has recently been evaluated in a global, Phase 3 study for the treatment of RA in patients (pts) with active disease that did not respond adequately to conventional, synthetic disease-modifying antirheumatic drugs (DMARDs).
**Objectives:** To evaluate the effects of sirukumab treatment on physical function and morning stiffness in pts with active RA refractory to DMARDs.
**Methods:** In this study, eligible pts with active RA and inadequate response to DMARDs were randomized (1:1:1) to treatment with sirukumab SC 50mg q4w, sirukumab SC 100mg q2w, or placebo SC q2w. In the placebo group, pts with insufficient (<20%) improvement at Wks 18 or 40 or still on placebo at Week 52 were re-randomized to receive 1 of the 2 sirukumab doses. Pts completed the HAQ-DI at baseline (BL) and 16 subsequent study visits from Week 2 to 52. A clinically meaningful improvement in HAQ-DI from BL was defined as a change (reduction) of 0.22 in HAQ-DI,[1] and a normal HAQ-DI score was defined as ≤0.5. The average duration of daily morning stiffness during the previous week in minutes (0–1440 minutes) was evaluated at the same visits as the HAQ-DI.
**Results:** A significantly greater improvement from BL in the mean HAQ-DI score was observed for both doses of sirukumab compared with placebo at all time points from Wk 2 through to Wk 52 (all $P \leq 0.006$; Table). Improvements from BL in the HAQ-DI score were clinically meaningful (change of –0.22) for a significantly greater proportion of pts with sirukumab (both dose regimens) compared with placebo from Wk 4 onwards (all $P<0.001$). At Wks 24 and 52, a significantly greater proportion of pts achieved a HAQ-DI score of ≤0.5 with both doses of sirukumab compared with placebo (all $P<0.001$). In addition, there was a significantly greater reduction from BL in the duration of morning stiffness with both doses of sirukumab compared with placebo at Wks 16, 24, and 52 (all $P \leq 0.022$).

Table 1. HAQ-DI and morning stiffness outcomes at week 52[a]

| Outcome | Placebo (n=556) | Sirukumab 50mg q4w (n=557) | Sirukumab 100mg q4w (n=557) |
|---|---|---|---|
| HAQ-DI, mean (SD) change from BL | –0.23 (0.57) | –0.45 (0.61)[b] | –0.47 (0.60)[b] |
| Clinically meaningful improvement from BL in HAQ-DI, n (%)[c] | 263 (47.1) | 353 (63.4)[b] | 359 (64.5)[b] |
| HAQ-DI ≤0.5, n (%) | 69 (12.4) | 153 (27.5)[b] | 163 (29.3)[b] |
| Duration of daily morning stiffness (min), mean (SD) change from BL[d] | –67.3 (196.98) | –99.1 (233.82)[e] | –97.7 (231.53)[e] |

[a]n values are based on initial treatment assignment. [b]$P<0.001$ vs placebo. [c]Minimum clinically meaningful improvement, change of –0.22 from BL. [d]Placebo, n=552; sirukumab 50 mg q4w, n=552; sirukumab 100 mg q2w, n=555. [e]$P \leq 0.022$ vs placebo.

**Conclusions:** Sirukumab treatment in pts with active RA refractory to DMARDs was associated with early, sustained, and clinically meaningful improvement in both physical function and morning stiffness, which are key treatment goals for pts with RA.
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[1] Maska L, et al. Arthritis Care Res. 2011;63(S11):S4-S13.
**Disclosure of Interest:** C. Thorne Grant/research support from: Abbvie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant for: Abbvie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: Medexus/Medac, T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahikasei Pharma Corp., and Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., and Asahi Kasei Medical K.K.,abbivie GK, Daiichi Sankyo Co.,Ltd., Bristol–Myers K.K., Nipponkayaku Co.Ltd., Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co,. Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Astellas Pharma, and Diaichi Sankyo Co., Ltd., Celtrion, Nipponkayaku Co. Ltd, G. Karpouzas Consultant for: Janssen, Speakers bureau: Janssen, K. McQuarrie Employee of: Janssen Research & Development, LLC, S. Sheng Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, W. Xu Employee of: Janssen Research & Development, LLC, S. Peterson Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research

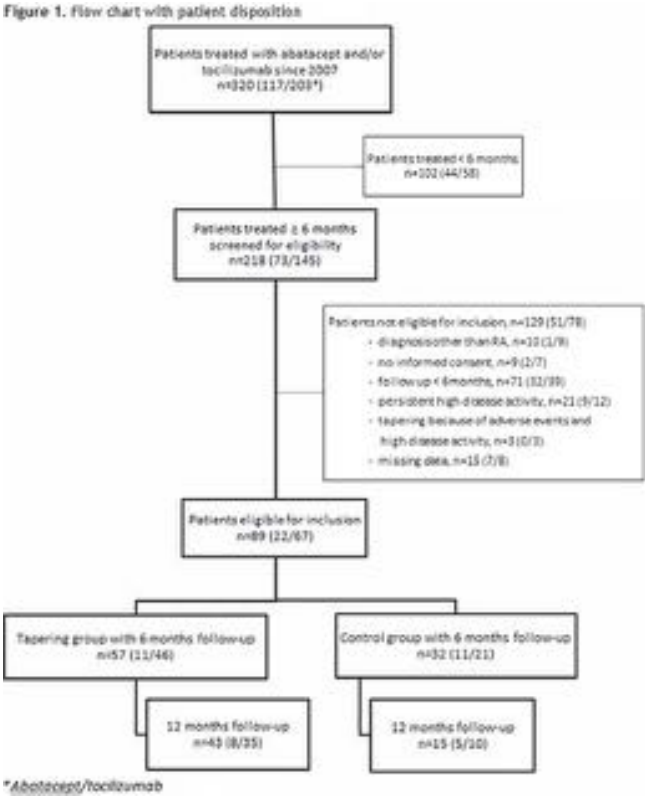
& Development, LLC, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, C. Han Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, K. Fei Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC
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## AB0342 STUDY ON ABATACEPT AND TOCILIZUMAB ATTENUATION (SONATA) IN RHEUMATOID ARTHRITIS PATIENTS: A RETROSPECTIVE, EXPLORATIVE COHORT STUDY

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**Background:** Disease activity guided tapering of tumor necrosis factor inhibitors (TNFi) has been shown to be feasible, safe and cost-effective in rheumatoid arthritis (RA) patients with stable low disease activity. However, data on biologics with another mode of action, like abatacept (ABA) and tocilizumab (TCZ), is scarce. Moreover, most studies are clinical trials, leaving uncertainty on the feasibility of tapering in daily clinical practice.
**Objectives:** To assess the difference in mean change (∆) between baseline and 12 months follow-up in DAS28 and HAQ-DI between eligible RA patients that attempted to taper ABA or TCZ compared to eligible patients that did not attempt to taper.
**Methods:** In this retrospective, explorative cohort study, data on clinical outcome measures were collected from all patients eligible to taper ABA or TCZ at the outpatient clinic of a specialized rheumatology hospital. Patients were eligible when fulfilling the 1987 and/or 2010 ACR RA criteria and/or clinical diagnosis by the treating rheumatologist, and when reaching low disease activity (DAS28 $<3.2$) after $\geq 6$ months of treatment with ABA or TCZ. Patients that attempted to taper were included in the tapering group and patients that did not attempt to taper were included in the control group. Tapering was done according to the local protocol, in which the dose was stepwise reduced or the injection interval was prolonged until discontinuation. Successful tapering was defined as using ABA or TCZ on lower than baseline dose and having low disease activity at 12 months. Outcome measures were mean ∆DAS28 and mean ∆HAQ-DI (positive figures mean increase) and differences between groups were tested using an (unpaired) t-test.
**Results:** From January 2007 until June 2015, 320 patients were treated with ABA and/or TCZ of whom 58 patients could be included (figure 1). Tapering was successful in 37% of ABA patients and 35% of TCZ patients. Mean ∆DAS28 at month 12 was 0.92 (95% CI -0.46 to 2.31) in the ABA tapering group versus 1.32 (95% CI 0.00 to 2.65) in the control group (p=0.05)and 0.31 (95% CI -0.24 to 0.85) in the TCZ tapering group versus 0.28 (95% CI -0.59 to 1.16) in the control group (non-significant (NS)). Mean ∆HAQ-DI at month 12 was 0.16 (95% CI -0.48 to 0.89) in the ABA tapering group versus -0.41 (95%CI -0.51 to 0.69) in the control group (NS) and 0.02 (95% CI= -0.40 to 0.44) in the TCZ tapering group versus 0.24 (95% CI= -0.31 to 0.79) in the control group (NS).

**Figure 1.** Flow chart with patient disposition




**Conclusions:** Tapering of ABA or TCZ appears to be feasible in RA patients in daily clinical practice, with no significant difference in change of disease activity or functioning between patients that tapered and patients that did not taper, although confidence intervals are relatively large in this small study. However, the percentage of successful tapering is lower compared to studies on tapering of TNFi. Also, numbers of patient that start tapering are suboptimal, possibly explained by the perception of a more refractory patient population in which treatment is continued longer, since ABA and TCZ are reserved for patients that fail on TNFi in our clinic.
**Disclosure of Interest:** None declared
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## AB0343 TREATMENT OF RHEUMATOID ARTHRITIS PATIENTS WITH PARENTERAL STAPHYLOCOCCAL PROTEIN A (PRTX-100): AN OPEN-LABEL SINGLE-SITE EXTENSION TRIAL

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**Background:** Staphylococcal protein A (SpA) is a bacterial B-cell superantigen that binds with high affinity to the Fc region of most immunoglobulins (Igs) and to the Fab framework region of Igs in the $V_H3$ gene family. PRTX-100, a highly purified form of SpA, has exhibited an acceptable safety profile when administered intravenously to small numbers of subjects at doses of up to 12 μg/kg.[1] SpA forms multimeric Ig complexes (MIgCs) with human antibodies which interact with and modulate cells of the monocytic lineage via FcR1 receptors.[2] However, the effects of SpA in rheumatoid arthritis (RA) are not fully understood.
**Objectives:** To expand the safety experience of parenteral PRTX-100 given to patients with RA, including retreatment. To describe PRTX-100 immunogenicity and pharmacodynamics as well as the feasibility of ultrasound joint count measurements.
**Methods:** This open-label trial enrolled 11 seropositive patients with RA who had previously participated in a Phase I trial[1] and responded (n=9) or had been given placebo (n=2). Patients were treated with 6 μg/kg PRTX-100 with four weekly intravenous infusions followed by five monthly infusions. Safety and disease activity were monitored monthly. Anti-PRTX-100 antibodies were measured. Patients were evaluated by standard clinical assessments and by ultrasound power Doppler joint counts (UPD).[3] Pharmacodynamic alterations in MIgC concentrations were assessed via cryoglobulin levels.
**Results:** The preliminary results indicated that PRTX-100 exhibited an acceptable safety profile. Adverse events (AEs) included fatigue (9% of patients), and headache (9%). Worsening of RA following initial infusions were observed in 82% of patients but diminished with subsequent infusions of PRTX-100. One patient discontinued therapy due to worsening of RA symptoms. One patient discontinued treatment due to perceived lack of improvement. No serious AEs were reported. At study day 196, 1 month after final infusion, all 11 patients demonstrated a reduction of DAS28CRP. There was a reduction in the UPD score of 26% (p=0.0054) and a correlation between the UPD and DAS28CRP of r=0.630 ($p<0.0001$). In addition, 55% of patients demonstrated increases in their MIgCs during treatment
**Conclusions:** Treatment with PRTX-100 in nine patients for the second time and two patients for the first time demonstrated an acceptable safety profile. A single subject discontinued the trial due to worsening of RA symptoms, although RA disease activity was improved in the majority of patients by the end of the study compared to baseline levels. Some subjects exhibited an increase in MIgCs after infusion of PRTX-100. The incorporation of ultrasound joint count methodology into small open-label trials might offer enhanced assessment of clinical efficacy.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2540

## AB0344 A RETROSPECTIVE NON-INTERVENTIONAL STUDY ON THE USE OF BIOLOGICS IN THE TREATMENT OF AUSTRALIAN PATIENTS WITH RHEUMATOID ARTHRITIS-THE REAL STUDY

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**Background:** Medication choices offered to rheumatoid arthritis (RA) patients are based in part on results from randomised controlled trials (RCTs). While

these trials form a valuable evidence-base for rational prescribing, extrapolation of RCTs data to every day clinical practice is hampered by the highly selected patient (pt) groups that are accepted into RCTs. The comparative effectiveness of biologic treatment regimens in a real world Australian population is unknown.
**Objectives:** To assess effectiveness of biologic (b) DMARDs, as monotherapy, in combination with conventional (c) DMARDs other than MTX and in combination with cDMARDs regimens including MTX in the Australian OPAL database.
**Methods:** A retrospective non-interventional study. Data was extracted from participating Australian rheumatology centres using point of care software. Pts ≥18 years (yrs) with probable/definite RA, who had been prescribed a bDMARD and have had a visit recorded 12 months prior to and at least 12–40 weeks (wks) after commencement of a bDMARD were included. Bouts of treatment (BTs) refer to cycles of continuous, individual biologics prescribing in individual pts; if pts change biologics then this was defined as a new BT. Wk12 (-4/+8) analyses included any measurement between wk8 and wk20 post bDMARDs initiation and wk24 (-4/+8) included any measurements between wk20 and wk32.
**Results:** 2971 pts met criteria; median age 60 yrs (min 19, max 94) and median disease duration prior to 1st bDMARD of 6.1 yrs (min 0.2, max 58.3). Median number of bDMARDs per pt was 1 (min 1, max 8). At least 1 bDMARD was taken by 2971 pts, 1177 received 2 bDMARDs and 507 received 3 or more. There were 4923 bDMARD BTs recorded for this population with median treatment duration of 0.7 yrs (min 0, max 11.8). Median duration of 1st bDMARD (n=2971 pts)=0.8 yrs (min 0, max 11.8); 2nd bDMARD (n=1177)=0.6 yrs (min 0, max 9.9) and 3rd bDMARD (n=507)=0.6 yrs (min 0, max 6.4). The most commonly used bDMARDs were etanercept (n=1358), adalimumab (n=1098), abatacept (n=642) and tocilizumab (n=629); median duration of BTs=0.7 (min 0, max 11.8), 0.8 (min 0, max 10.5), 0.7 (min 0, max 6.1) and 1.0 (min 0, max 7.4) yrs respectively. bDMARD monotherapy (no cDMARD overlap) was administered in 10% BTs (n=488); bDMARDs + MTX +/– other cDMARD(s) were administered in 74% BTs (n=3639) and bDMARDs + cDMARD(s) other than MTX were administered in 16% BTs (n=796). Median CDAI and DAS28 by biologic presented in Table 1.

Table 1: Median CDAI and DAS28 by biologic. BL= baseline; wk= weeks on treatment.

| CDAI | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Monotherapy | | | Combo MTX +/-cDMARDs | | | Combo cDMARDs only | | | |
| bDMARD | Time | n | Median | Min/Max | n | Median | Min/Max | n | Median | Min/Max | |
| Etanercept | BL | 40 | 19 | 0/58 | 403 | 24 | 0/70 | 123 | 33 | 0/70 | |
| | 12 wk | 16 | 5 | 0/36 | 263 | 5 | 0/64 | 85 | 5 | 0/67 | |
| | 24 wk | 6 | 2 | 0/4 | 77 | 5 | 0/48 | 25 | 3 | 0/28 | |
| Adalimumab | BL | 59 | 8 | 0/61 | 292 | 21 | 0/72 | 91 | 30 | 0/48 | |
| | 12 wk | 21 | 5 | 1/19 | 192 | 5 | 0/60 | 57 | 10 | 0/51 | |
| | 24 wk | 8 | 9 | 1/11 | 69 | 5 | 0/37 | 16 | 7 | 0/29 | |
| Abatacept | BL | 31 | 15 | 0/62 | 284 | 17 | 0/70 | 26 | 23 | 2/60 | |
| | 12wk | 16 | 6 | 1/28 | 144 | 7 | 0/56 | 16 | 7 | 0/34 | |
| | 24 wk | 8 | 9 | 2/37 | 72 | 6 | 0/54 | 4 | 7 | 2/19 | |
| Tocilizumab | BL | 40 | 25 | 0/66 | 144 | 19 | 0/69 | 42 | 25 | 0/47 | |
| | 12 wk | 23 | 7 | 0/60 | 84 | 6 | 0/47 | 29 | 4 | 0/22 | |
| | 24 wk | 7 | 5 | 0/22 | 31 | 6 | 0/23 | 8 | 2 | 0/10 | |
| DAS28 | | | | | | | | | | | |
| | | Monotherapy | | | Combo MTX +/-cDMARDs | | | Combo cDMARDs only | | | |
| bDMARD | Time | n | Median | Min/Max | n | Median | Min/Max | n | Median | Min/ Max | |
| Etanercept | BL | 47 | 3.9 | 0.1/7.4 | 527 | 4.8 | 0.5/8.6 | 158 | 5.5 | 1.0/8.7 | |
| | 12 wk | 18 | 2.5 | 1.0/6.4 | 196 | 2.5 | 0.6/7.9 | 102 | 3.1 | 0.3/8.5 | |
| | 24 wk | 5 | 2.5 | 1.1/3.4 | 112 | 2.5 | 0.5/6.9 | 32 | 2.6 | 1.1/4.8 | |
| Adalimumab | BL | 73 | 3.2 | 0.5/7.1 | 388 | 4.6 | 0.6/8.5 | 119 | 5.2 | 0.6/8.2 | |
| | 12 | 27 | 2.8 | 0.6/4.4 | 247 | 2.7 | 0.6/8.4 | 73 | 3.2 | 0.6/7.5 | |
| | 24 wk | 8 | 3.0 | 0.6/4.3 | 83 | 2.5 | 0.8/7.4 | 17 | 3.8 | 1.1/4.4 | |
| Abatacept | BL | 32 | 4.1 | 1.0/7.2 | 329 | 4.3 | 0.5/8.7 | 26 | 4.4 | 1.3/6.9 | |
| | 12 wk | 16 | 3.2 | 2.0/6.6 | 166 | 2.9 | 0.1/7.5 | 16 | 3.4 | 1.1/6.4 | |
| | 24 wk | 8 | 2.9 | 1.6/5.7 | 72 | 2.7 | 0.5/6.3 | 3 | 3.3 | 2.2/4.2 | |
| Tocilizumab | BL | 56 | 4.4 | 0.6/8.7 | 204 | 4.1 | 0.6/8.4 | 61 | 4.7 | 1.1/8.8 | |
| | 12 wk | 28 | 2.2 | 0.5/5.2 | 116 | 2.1 | 0.6/6.5 | 34 | 2.2 | 0.5/5.7 | |
| | 24 wk | 10 | 2.7 | 1.1/5.4 | 51 | 2.4 | 0.1/7.4 | 13 | 1.5 | 0.6/3.1 | |

**Conclusions:** The majority in this cohort of Australian RA pts receive 1 line of bDMARD. Pts tend to persist longer on 1st bDMARD than subsequent biologics. bDMARDs as monotherapy or in combination (+/– MTX) are valid treatment strategies in the real world.
**Acknowledgement:** The study was sponsored by Roche Products Pty. Limited. Medical writing was provided by Dr Joseline Ojaimi from Roche.
**Disclosure of Interest:** D. Nicholls: None declared, H. Griffiths: None declared, R. Barrett Employee of: Roche Products, Pty. Limited, P. Button Employee of: Roche Products, Pty. Limited, M. Truman Employee of: Roche Products, Pty. Limited, P. Bird: None declared, L. Roberts: None declared, K. Tymms: None declared, G. Littlejohn: None declared
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## AB0345 COMPARATIVE EFFECTIVENESS OF BIOLOGIC AGENTS FOR PATIENTS WITH RHEUMATOID ARTHRITIS – PRIMARY ANALYSIS FROM THE US CORRONA CERTAIN STUDY

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**Background:** Comparative effectiveness research (CER) can inform decisions regarding the choice of biologics for the treatment of RA.
**Objectives:** To compare the efficacy of tumor necrosis factor inhibitors (TNFis) and non-TNFis (nTNFis) in real-world patients with RA previously treated with ≥1 TNFi.
**Methods:** CERTAIN was a CER study nested within the US Corrona registry.[1] Adult patients with RA with moderate to high disease activity (CDAI >10) starting a TNFi or nTNFi (physician-driven choice of agent) were enrolled. For the primary analysis, only patients previously treated with ≥1 TNFi were included. The primary outcome was achievement of low disease activity (LDA) at 12 months (CDAI ≤10). A propensity score (PS) for the probability of treatment with a TNFi vs nTNFi was generated; patients outside the common area of support in the PS were excluded. Response rate was modeled using a mixed-effect logistic regression model with start of a biologic as the unit of analysis, adjusting for a priori and imbalanced baseline factors and to account for the clustering of patients within practice sites. As a sensitivity analysis, patients were matched 1:1 on the PS within each site.
**Results:** Of the 2795 biologic starts captured, 1142 biologic naive and 562 nTNFi experienced were excluded, leaving 1091 biologic starts in 998 patients for analysis of response after a TNFi. After PS trimming, 1081 starts (566 [52.4%] nTNFi and 515 [47.6%] TNFi) remained. Patients who started nTNFis were significantly more likely to have longer disease duration, higher patient fatigue scores, Medicare insurance and more prior TNFi use. At 12 months, 29.4% of nTNFi and 24.3% of TNFi initiators were in LDA. In the adjusted analysis (Table), patients on nTNFis were significantly more likely to achieve LDA. However, when adjusting for site clustering, the results were no longer significant.

Table 1. Adjusted ORs of achieving LDA after failure of ≥1 prior TNFi

| nTNFi vs TNFi Initiation* | OR (95% CI) | *P* Value |
|---|---|---|
| Partially adjusted logistic regression model (n=963) | 1.55 (1.12–2.13) | 0.008 |
| Fully adjusted mixed model with adjustment for site q clustering (n=963) | 1.17 (0.82–1.67) | 0.382 |
| Sensitivity analysis, 1:1 matching on PS within site (n=292) | 0.81 (0.48–1.36) | 0.428 |

LDA, low disease activity; nTNFi, non-TNFi; OR, odds ratio; PS, propensity score; TNFi, tumor necrosis factor inhibitor. *Adjusted for number of prior TNFis, duration of RA, seropositivity, fatigue, baseline CDAI, insurance status, baseline methotrexate and steroid use.

**Conclusions:** In this large, real-world study, after ≥1 TNFi failure, switch to a nTNFi was favored over treatment with a subsequent TNFi, but was not statistically significant after adjusting for site clustering. Results warrant further study.
**References:**
[1] Pappas DA, et al. BMC Musculoskeletal Disord. 2014;15:113.
**Acknowledgement:** The Corrona CERTAIN study is sponsored by Corrona, LLC, with support from the AHRQ (R01HS018517). The majority of funding for CERTAIN was derived from Genentech, with additional support for substudies from Eli Lilly, Momenta Pharmaceuticals and Pfizer. CERTAIN investigators also receive support from the NIH [JRC AR053351, JDG AR054 412].
**Disclosure of Interest:** D. Pappas Employee of: Corrona, LLC, Paid instructor for: Novartis, A. John Employee of: Genentech, Inc, J. Kremer Shareholder of: Corrona, LLC, Consultant for: Abbvie, Amgen, BMS, Genentech, Lilly, Pfizer, Employee of: Corrona, LLC, G. Reed Employee of: Corrona, LLC, T. Sommers Employee of: Corrona, LLC, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: AstraZeneca, Celgene, Genentech, Janssen, Novartis, Pfizer, Employee of: Corrona, LLC, J. Curtis Grant/research support from: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, AbbVie, Consultant for: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, Abb Vie
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## AB0346 TESTING FOR ANTI-CITRULLINATED PEPTIDE ANTIBODIES IN US CLINICAL PRACTICE SETTINGS IN PATIENTS NEWLY DIAGNOSED WITH RA – DATA FROM THREE DATABASES BETWEEN 2007–2014

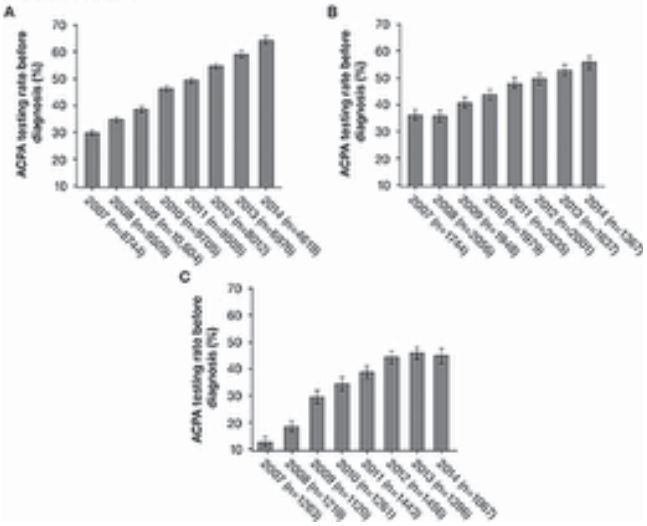
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**Background:** Current clinical guidelines recommend testing for anti-citrullinated protein antibodies (ACPA) at the time of RA diagnosis.[1] However, there is a lack of information about the frequency of ACPA testing at RA diagnosis or thereafter.
**Objectives:** To describe the frequency of ACPA testing over time and to investigate the potential differences in demographics, co-morbidities and hospitalizations between patients who received ACPA tests versus those who did not.
**Methods:** Data from the three following US commercial healthcare claims databases were analysed: IMS PharMetrics Plus (database A), Optum Clinfor-

matics Data Mart (database B) and Optum Clinformatics Data Mart Medicare (database C). Patients with two diagnosis codes for RA from 1 January 2007 to 31 December 2014, treatment with a DMARD, and continuous enrolment for at least 12 months before and 6 months after the index date were included. ACPA and RF testing claims identified by current procedural terminology codes were included in the analysis. ACPA testing rates were evaluated as number of patients with tests divided by total number of patients with and without tests. Multinomial logistic regression was used to evaluate baseline covariates associated with single ACPA test before the index date, single ACPA test after the index date and multiple ACPA tests.

**Results:** A total number of 67,674 patients newly diagnosed with RA in database A (age 18–64 years), 14,767 in database B (age 18–64 years) and 10,225 in database C (age ≥65 years) met the study inclusion criteria. The overall ACPA testing rate (95% CI) was 70.6% (70.3, 70.9) in database A, 72.2% (71.5, 72.9) in database B and 63.5% (62.5, 64.4) in database C. The ACPA testing rates increased from 2007 to 2014 for all three databases (Figure). The corresponding RF testing rates were 75.4% (75.1, 75.7), 85.1% (84.5, 85.6) and 77.8% (77.0, 78.6), respectively. Patients tested and not tested had similar characteristics, with a standardized difference of >0.10 in only a few co-morbidities. The odds ratio (OR) for pre-diagnosis testing for each year increase from 2007 to 2014 was 1.26 (95% CI: 1.25, 1.28) in database A, 1.19 (1.17, 1.22) in database B and 1.27 (1.23, 1.31) in database C. Women were more likely to have multiple tests in database A (OR: 1.15; 95% CI: 1.08, 1.21) and in database B (OR: 1.29; 95% CI: 1.14, 1.45), but not in database C (OR: 0.93; 95% CI: 0.80, 1.08). Patients who received ACPA tests, versus those who did not, had a lower rate of 1-year hospitalization; the hazard ratio (95% CI) after adjustment for covariates was 0.76 (0.71, 0.80) in database A, 0.86 (0.75, 0.98) in database B and 0.76 (0.68, 0.85) in database C.

**Figure 1.** ACPA Pre diagnosis Testing Rate 2007-2014 (A=PharMetrics; B=Optum; C=Optum Medicare




**Conclusions:** The ACPA testing rate, especially pre-diagnosis testing, increased significantly from 2007 to 2014. Women aged 18–64 years were more likely to have multiple tests. A slightly lower rate was seen in RA patients ≥65 years old.

**References:**

[1] Aletaha D, et al. Ann Rheum Dis 2010;69:1580–8.

**Disclosure of Interest:** E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, L. Burns Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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## AB0347 THE RETENTION RATES OF THE SECOND BIOLOGIC AGENTS IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO TNFα INHIBITORS, SINGLE-CENTER, RETROSPECTIVE, OBSERVATIONAL STUDY

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**Background:** There are few data about the safety of biologics switching for rheumatoid arthritis in clinical practice conditions.

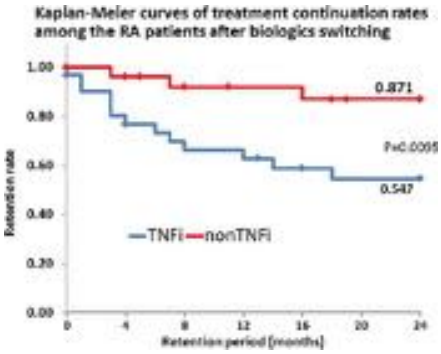
**Objectives:** To analyze the retention rates of biologics switch therapies for rheumatoid arthritis patients after inadequate response to TNFα inhibitors.

**Methods:** Data was collected retrospectively from medical records of RA patients in our center. We divided the RA patients with inadequate response to TNFα inhibitors into the two groups. The first group is consists of the patients who switched to other TNFα inhibitors. The other is consists of the patients who switched to non-TNFα inhibitors. We analyzed the retention rate of each group by Kaplan-Meier curves and log-rank test.

**Results:** In the "*another TNFα inhibitor*" group (31 cases, 59.4±14.8 years, women: 90.3%, ACPA-positive 74.2%, MTX use 93.3%, oral steroid use 30.0%), infliximab (IFX): 11, etanercept (ETN): 7, adalimumab (ADA): 9, golimumab (GLM): 2 and certolizumab pegol (CZP): 2 are administered as the first biologics, discontinued due to adverse events: 4, inadequate efficacy:26 and other: 1 respectively), IFX: 4, ETN: 17, ADA: 3, GLM: 2 and CZP: 5 were chosen as the second biologics. The cumulative retention rates of the second biologics in 12 and 24 months were 0.628 and 0.547 respectively. The reasons for discontinuation of secondary used TNFα inhibitors were adverse events: 4 and inadequate efficacy: 9.

In the "*non-TNFα inhibitor*" group (27 cases, 64.0±14.2 years, women: 83.3%, ACPA-positive 92.6%, MTX use 57.7%, oral steroid use 30.8%, IFX: 8, ETN: 13, ADA: 4, GLM: 1 and CZP: 1 are administered as the first biologics, discontinued due to adverse events: 7, inadequate efficacy: 20 respectively), tocilizumab (TCZ): 8 and abatacept (ABT): 19 were chosen as the second biologics. The cumulative retention rates of the second biologics in 12 and 24 months were 0.920 and 0.871 respectively. Three TCZ used patients were discontinued biologics within 24 months due to adverse events: 2 and inadequate efficacy: 1.

There was a significant difference in the retention rates in the two groups (log-rank test, p=0.0095) (figure). In the "non-TNFα inhibitor" group, the cumulative retention rates of TCZ and ABT in 24 months are 0.822 and 1.000 respectively. There is no significant difference (log-rank test, p=0.277).




**Conclusions:** Our data suggested that non-TNFα inhibitors can be used for a long period for the RA patients with inadequate response to TNFα inhibitors.

**References:**

[1] Hirabara S, et al. Clin Rheumatol. 2014, 33: 1247–54
[2] Deighton C. Nat Rev Rheumatol. 2009, 5:596–7

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.5157

## AB0348 A RETROSPECTIVE REVIEW OF DISPENSING OF CONCOMITANT GLUCOCORTICOIDS WITH BIOLOGICS PRESCRIBED FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN THE AUSTRALIAN POPULATION

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**Background:** The treatment of Rheumatoid arthritis (RA) in Australia is consistent with the current international guidelines of starting a biologic (b) DMARD in combination with methotrexate (MTX) where possible and/or other synthetic DMARDs with or without glucocorticoids (GCs). There is limited data available on the effects of various bDMARDs on oral GCs consumption in a real world data setting and in the same patient population.

**Objectives:** The objective of the study was to investigate the usage of concomitant GCs with bDMARDs for the treatment of RA patients over time.

**Methods:** Concessional (government subsidised) RA patients ≥18 years of age for whom bDMARDs were first dispensed for their RA (between 01August 2010 and 31July 2013), and who were in the Australian Medicare 10% sample database provided by the Department of Health and Aging through an Australian healthcare consulting company (PROSPECTION) were followed for a period of 2 years (until 31 July 2015). bDMARDs included: abatacept (IV and SC), adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and tocilizumab. Data were analysed using descriptive statistics for continuous variables and frequency counts for categorical variables. Individual anti-TNFs were equivalent in all analyses and therefore were combined for simplicity.

**Results:** Data from 269 patients were analysed. Of the patients who received oral GCs at some point during the study period (86%; n=230), 49% were ≥65 years old and 51% were 18–64 years old. The majority (81%) were females. For all patients, median dose of oral GCs was 4.1 (min 0, max 21) mg/day at one year prior to initiation of a bDMARD, 2.9 (min 0, max 22.2) mg/day and 2.0 (min 0, max 17.3) mg/day at 1 and 2 years, respectively, post-bDMARDs initiation. Daily GCs doses across the analysis time points and by drug group are presented in Table 1. Daily dose changes at 1–2 years post initiation of bDMARDs from 1 year before initiation of bDMARDs were statistically significant for all bDMARDs

(p<0.0001), all anti-TNFs (p<0.0001) and tocilizumab (p=0.0002). Percentage of patients who stopped GCs at any time post initiation of a bDMARD was 43% for all RA bDMARDs, 44% for all anti-TNFs, 27% for abatacept and 39% for tocilizumab. 31 percent of patients who remained on biologics for the observation period in the "all RA bDMARDs" group had an increase in GCs dose and 60% had a decrease after 1-year and 65% after 2 years; percentage increase and decrease in GCs doses for all groups are listed in Table 2.

**Table 1:** Daily glucocorticoids dosage

| Drug group | Time period | N | Mean (mg/day) | SD | Median (mg/day) | Min | Max |
|---|---|---|---|---|---|---|---|
| All RA bDMARDs | 1 yr before | 230 | 4.4 | 3.5 | 4.1 | 0 | 21.0 |
| | 1 yr after | 230 | 3.5 | 3.6 | 2.9 | 0 | 22.2 |
| | 1-2yr after | 230 | 2.8 | 3.1 | 2.0 | 0 | 17.3 |
| All RA anti-TNF | 1 yr before | 145 | 4.7 | 3.7 | 4.1 | 0 | 21.0 |
| | 1 yr after | 145 | 3.5 | 3.6 | 2.9 | 0 | 22.2 |
| | 1-2yr after | 145 | 2.5 | 2.9 | 1.8 | 0 | 15.2 |
| Abatacept | 1 yr before | 45 | 4.8 | 3.6 | 4.1 | 0 | 14.0 |
| | 1 yr after | 45 | 4.3 | 3.4 | 4.1 | 0 | 15.7 |
| | 1-2yr after | 45 | 4.8 | 3.9 | 4.9 | 0 | 17.3 |
| Tocilizumab | 1 yr before | 62 | 5.4 | 5.7 | 3.8 | 0 | 32.1 |
| | 1 yr after | 62 | 4.4 | 4.5 | 3.2 | 0 | 18.1 |
| | 1-2yr after | 62 | 3.2 | 3.9 | 1.9 | 0 | 18.2 |

**Table 2:** Proportion of patients with glucocorticoids dose changes from 1 year before to 1 and 1-2 years after initiation of bDMARDs.

| | Time period | N | Increased N (%) | Decreased N (%) | No change N (%) |
|---|---|---|---|---|---|
| All RA bDMARDs | 1 yr after | 230 | 72 (31) | 137 (60) | 21 (9) |
| | 1-2yr after | 230 | 63 (27) | 149 (65) | 18 (8) |
| All RA anti-TNF | 1 yr after | 145 | 46 (32) | 90 (62) | 9 (6) |
| | 1-2yr after | 145 | 34 (23) | 101 (70) | 10 (7) |
| Abatacept | 1 yr after | 45 | 19 (42) | 21 (47) | 5 (11) |
| | 1-2yr after | 45 | 18 (40) | 23 (51) | 4 (9) |
| Tocilizumab | 1 yr after | 62 | 23 (37) | 34 (55) | 5 (8) |
| | 1-2yr after | 62 | 14 (23) | 43 (69) | 5 (8) |

**Conclusions:** In the Australian setting, the majority of RA patients who were taking oral GCs had reductions in their daily GCs doses after initiation of bDMARDs; which continued for up to 2 years post treatment initiation.

**Acknowledgement:** The study was sponsored by Roche Products Pty. Limited. Medical writing was provided by Dr Joseline Ojaimi from Roche.

**Disclosure of Interest:** G. Jones: None declared, S. Hall: None declared, G. Littlejohn: None declared, E. Chung Consultant for: Roche Products, Pty. Ltd, R. Barrett Employee of: Roche Products, Pty. Ltd, P. Button Employee of: Roche Products, Pty. Ltd

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## AB0349 DENOSUMAB VERSUS BISPHOSPHONATES FOR TREATMENT OF RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA), caused by upregulation of proinflammatory cytokines, is characterized by overexpression of receptor activator of nuclear factor kappa-B ligand (RANKL) in the synovial membrane, which promotes osteoclast differentiation and thus increases bone resorption. Denosumab, an antibody against RANKL, prevents RANKL/RANK interactions and inhibits osteoclast-mediated bone resorption. This study investigated whether denosumab can prevent the inflammation caused by excessive bone resorption in RA patients in comparison with bisphosphonates, which directly prevent osteoclast-mediated bone resorption.

**Objectives:** RA patients in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry included 58 and 49 newly denosumab-treated and bisphosphonate-treated patients, respectively.

**Methods:** For RA, the Steinbrocker classification was measured at pretreatment and use of glucocorticoid, methotrexate, and biological agents, DAS28-ESR, simplified disease activity index (SDAI), erythrocyte sedimentation rate, and matrix metalloproteinase 3 were measured at pre-treatment and 6 and 12 months post-treatment. For bone metabolism, bone-specific alkaline phosphatase (BAP), indicating bone formation, tartrate-resistant acid phosphatase 5b (TRACP-5b), indicating bone resorption, and bone mineral density (BMD) of the lumbar and femoral neck were measured at pre-treatment, and 6 and 12 months post-treatment.

**Results:** For RA, the Steinbrocker class and stage were significantly higher in the denosumab group compared with the bisphosphonate group (p<0.0001 and p=0.0004, respectively). Use of biological agents was also significantly higher in the denosumab group compared with the bisphosphonate group at pre-treatment and 12 months post-treatment (p=0.006 and p=0.0467, respectively). There were no significant differences in DAS28-ESR and SDAI between the periods for denosumab or bisphosphonates (Figure). For bone metabolism, denosumab reduced BAP at 6 and 12 months post-treatment compared with pre-treatment (p=0.006 and p=0.0132, respectively) (Figure). There were no significant differences in BMD of the lumbar and femoral neck between the periods for denosumab or bisphosphonates, but denosumab revealed a tendency toward increases and bisphosphonates revealed a tendency toward decreases.

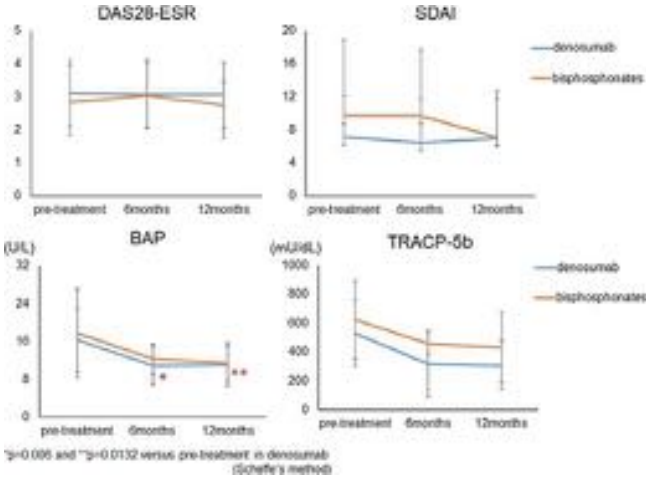



Figure 1

**Conclusions:** Denosumab and bisphosphonates did not suppress RA activity, but denosumab prevented excessive bone turnover more effectively than bisphosphonates.

**References:**

[1] Cohen SB, Dore RK, Lane NE, et al. Denosumab treatment effects on structural damage, bone mineral density, and bone turnover in rheumatoid arthritis: a twelve-month, multicenter, randomized, double-blind, placebo-controlled, phase II clinical trial. Arthritis Rheum 58 (5): 1299–1309, 2008.

**Acknowledgement:** We thank all the patients and AORA members who participated in this research.

**Disclosure of Interest:** None declared

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## AB0350 RITUXIMAB SEEMS OUTSTANDING BIOLOGICAL OPTION IN LATE ONSET RHEUMATOID ARTHRITIS: HUR-BIO REAL LIFE RESULTS

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**Background:** Rheumatoid arthritis (RA) can be categorized into late-onset RA and young-onset RA. Age at disease onset may implicate on disease activity, disease severity, comorbidity and also may have an impact on physicians' treatment choices.

**Objectives:** The aim of this study was to assess clinical and laboratory features, disease activity, response, and biological treatment choices according to late-onset RA and young-onset RA patients.

**Methods:** Hacettepe University Biologic Registry (HUR-BIO) is a single center biological registry since 2005. HUR-BIO biological dataset included demographic and clinical data and disease activity parameters. A total of 1087 (79.4% female) patients from the HURBIO registry were analyzed. Patients were categorized into two groups: young-onset RA (n=990, <60 years of age) and late-onset RA (n=97, ≥60 years of age) at disease onset. DAS-28 remission (<2.6) and low disease activity (<3.2) were assessed at last outpatient visit.

**Results:** The female gender was similar in both age group (77.3% vs. 79.6%, p>0.05). Mean age of patients were 71.4±6.0 years in late-onset RA and 51.6±11.7 years in young-onset RA group. The median age at diagnosis of patients were 64 (range 60–85) years in late-onset RA and 40 (range17–59) years in young-onset RA patients. Mean disease duration between diagnosis of RA and first biologic therapy was longer in young-onset RA patients [7.7±7.3 vs. 2.7±2.6 years, p<0.001], but mean biologic duration was similar in both groups [29.9±27.5 vs. 38.4±37.1 months, p>0.05]. Rheumatoid factor and anti-citrullinated peptides positivity in late-onset RA and young-onset RA patients were; 56.2% vs. 63.8% (p>0.05) and 45.9% vs. 63.2%, p=0.008, respectively. At the baseline level, anti-TNF (61 (61.9%) vs. 827 (73.6%), p=0.014) drugs were less frequently used in late-onset RA, rituximab (21 (21.6%) vs 111 (11.3%), p=0.003) was more frequently used in late-onset RA, and abatacept (16 (16,5%) vs. 148 (15,1%), p>0.05) was used similar in both group. Change in DAS-28 score was similar [1.55±1.14 vs. 1.79±1.45 (p>0.05)], in late-onset RA and young-onset RA patients. Remission (29.5% vs. 38.6%, p>0.05) and low disease activity (52.5% vs. 55.4%, p>0.05) were similar in late-onset RA and young-onset RA patients. Biological switch ratio was significantly lower in late-onset RA group, 18.6% vs. 35.2%, p<0.001.

**Conclusions:** Age may influence the clinician choice based on the efficacy and

safety profile. Biologic drugs are effective in late-onset RA, as well. Rituximab was relatively more preferred in late-onset RA patients; may be related with administration of every 6 months and safety profile in malignancy risk. Patient and physician opinion on these choices should be evaluated in further studies.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4656

## AB0351 BIOLOGIC TAPERING IN RHEUMATOID ARTHRITIS: INITIAL EXPERIENCES IN AN ENGLISH DISTRICT GENERAL HOSPITAL

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**Background:** Biologics are effective therapies in the treatment of Rheumatoid arthritis (RA)[1]. However, they are expensive and may have potentially serious side effects including infection[2]. There is growing evidence that biologic doses may be tapered down in patients with well-controlled RA, and good disease control may be retained[3].
**Objectives:** To ascertain if biologic tapering in patients with RA retain good disease control when biologic doses are tapered down, in a small district general hospital rheumatology department.
**Methods:** Patients taking biologics and with quiescent RA were selected prospectively on attendance to rheumatology follow up clinics, commencing in June 2015, and consented to participation in dose tapering. Eligible patients must not be taking corticosteroids. They must have disease remission for at least 2 years (defined as DAS28CRP $<2.6$). Alternatively, they may have disease remission for 12 months and no evidence of synovitis on ultrasound. Rituximab dose was decreased to one 1g infusion every 6 months. Infliximab, Abatacept and Tocilizumab infusion doses were reduced by 25%. Frequency was prolonged by 50% in subcutaneous TNF inhibitors. Patients were followed up at 6-monthly intervals with support from rheumatology help line in between for flares of disease.
**Results:** Between June 2015 and January 2016, 25 patients with RA have had biologic doses tapered. 6 month follow up appointment data is currently available for 10 patients. One female patient was found to have active disease at 6 month follow up, and one male patient had a flare up 1 month before his clinic appointment, so both have reverted back to standard dose biologic.
Mean DAS change for the 9 patients seen 6 months after dose tapering was +0.39 (-0.24: +2.03), which was skewed largely by the one female patient who had a flare at follow up. Median DAS change was +0.1. Mean GVAS before tapering was 29.8, and 33.7 at 6 month follow up. Mean CRP pre-tapering was 5.75 and at 6 months was 4.7. Two patients had a DAS 28 $>3.2$ at 6 months: one of whom had recent surgery which was felt to have contributed to disease flare so reduced dose Rituximab was continued. 6 out of the 9 patients had no swollen joints at 6 month follow up
**Conclusions:** So far 2 out of 25 patients have needed to revert back to original dose of biologic after tapering, which is promising. 7 of the 9 patients followed up on tapering had static disease activity. This suggests that dose tapering can be successfully achieved in a majority of RA patients who have achieved disease remission.
**References:**
[1] Callhoff J; Impact of biologic therapy on functional status in patients with rheumatoid arthritis – a meta-analysis; Rheumatology 53, 29; doi: 10.1093/rheumatology/ket266
[2] Ding T et al; BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies; doi: 10.1093/rheumatology/keq249b
[3] Smolen JS et al; EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update; Ann Rheum Dis; doi: 10.1136/annrheumdis-2013-204573
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5551

## AB0352 THE CHANGING FACE OF SEPTIC ARTHRITIS COMPLICATING RHEUMATOID ARTHRITIS IN THE ERA OF BIOTHERAPIES. RETROSPECTIVE SINGLE-CENTER STUDY OVER 35 YEARS

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**Background:** Rheumatoid arthritis (RA) is a risk factor for septic arthritis (SA), and anti-TNF therapy doubles the risk of SA.
**Objectives:** The purpose of this study was to see whether the frequency and features of SA complicating RA have changed over the last 35 years.
**Methods:** This retrospective single-center study included the full register of all patients hospitalized at the rheumatology department of Clermont-Ferrand – CHU between 1979 and 2013 for septic arthritis bacteriologically documented by synovial fluid and/or blood culture samples. The periods 1979–2002 (period before biotherapies) and 2003–2013 (last decade in the era of biotherapies) were compared.
**Results:** Between 1979 and 2013, 64/514 (12.5%) SA presented with a RA – 21/153 (13.7%) in the 2003–2013 period and 43/361 (11.9%) in the 1979–2002 period. Over the past decade, median age of SA–RA patients increased (61 *vs* 68 years; $p<0.02$) and predominant gender became males (52% *vs* 40%). The features of the RA remained unchanged: history (18 years (8–29) *vs* 16 (8–25)), rheumatoid factor (95% *vs* 87%), and corticosteroids (91% *vs* 81%) at the same mean dose (10 mg/d). 71% in the period before biotherapies and 63% in the last decade received a DMARD. Over the last decade 24% (*vs* 0; $p<0.003$) of patients received a biologic DMARD: etanercept (n=2), adalimumab (n=1), rituximab (n=1), tocilizumab (n=1). Proportion of polyarticular infection had decreased (9.5% *vs* 37%; $p<0.02$), down to the same level as SA-non-RA cases (8%). Proportion of *S. aureus* infections had stabilized (62% *vs* 74%) in SA-RA patients but was higher than SA-non-RA (47% and 53%). MRSA infections became more frequent in SA-RA (31% *vs* 6%; $p<0.05$) in contrast to SA-non-RA cases (8% *vs* 16%; ns). Gram-negative bacilli infections have tended to become more frequent (19% *vs* 5%; $p=0.08$). Blood cultures less often tested positive (29% *vs* 47%; ns). Mortality rates has fallen slightly (5% *vs* 9%; ns), in contrast to SA-non-RA cases (7% *vs* 6%; ns).
**Conclusions:** This study brings reassuring findings – in the era of biotherapies, the frequency of septic arthritis complicating rheumatoid arthritis has stabilized, and the most severe septic polyarticular forms are on the decline.
**Disclosure of Interest:** None declared
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## AB0353 SURVIVAL AND EFFECTIVENESS OF RITUXIMAB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS IN DAILY CLINICAL PRACTICE

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**Background:** Recently registry data provide evidence about long-term safety and efficacy of TNF inhibitors. However, data on Rituximab (RTX) treatment in daily clinical practice is limited.
**Objectives:** Our aim was to describe survival rate and effectiveness of RTX therapy in real-life practice conditions in a big cohort of patients with RA from Colombia
**Methods:** We included patients with RA treated at Medicarte IPS from May 2008 and November 2015. Medicarte is a referral center for the integral medical care and pharmacosurveillance of patients under biologic therapies in 13 cities in Colombia. Only those patients with systemic rheumatic diseases were enrolled. We only included those patients with at least 1 complete cycle of RTX treatment. Clinical information was obtained from electronic clinical records and medical claims. We defined survival of RTX treatment only those cases who started RTX treatment before 2015 and persist on RTX during the last visit.
**Results:** From a total of 1064 patients treated with Rituximab, 901 patients had a systemic rheumatic disease. 754 (86%) of patients had a diagnosis of RA. The majority of patients were female (87%); mean age was 55.0± 14.1 years and mean disease duration was 14.7±9.1 years. 57 patients were excluded as they had received less than 1 cycle, leaving 697 patients valid for full analysis. Of these, 80.2% received RTX as a first biological therapy. The mean number of cycles was 1.8 cycles (range 1–8). Adverse effect was reported in 85 (11.2%) patients. 318 patients received only 1 cycle, 185 patients 2 cycles, 91 patients 3 cycles, 30 patients 4 cycles, 18 patients 5 cycles and 8 patients 6 or more cycles. A total of 193 (25.5%) of patients remain on RTX treatment. At the last visit, mean DAS-28 score was 2.9± 1.4 and mean HAQ 0.97±0.71. 66% of patients had a low disease activity (DAS-28 $<3.2$) and 49% of patients were on remission (DAS-28$<2.6$). A 64% of patients had a good index of functionality (HAQ $<1.0$). We did not find differences in terms of clinical response or functionality among patients who used RTX as a first line therapy vs patients with previous biologic treatment (Table).

Table 1. Comparison among patients with RTX as a first agent vs patients previously treated with biologic therapy

| | RA treated with with RTX N=754 | RTX as a first agent N=605 | Previous treatment with biologic agents N=147 | P value |
|---|---|---|---|---|
| Female gender (%) | 87 | 88 | 85 | NS |
| Age (years) | 55±14 | 53±14 | 55±13 | NS |
| Mean disease duration (years) | 15. ±9.6 | 15.13±9.8 | 14.7±9.47 | NS |
| BMI | 25.2±3.9 | 25.2±3.8 | 24.9±4.4 | NS |
| Number of cycles | 1.8±1.1 | 1.7±1.0 | 2.0±1.4 | 0.002 |
| Duration of RTX treatment (years) | 1.55±1.70 | 1.35±1.36 | 3.24±1.9 | 0.001 |
| Last DAS-28 | 2.93±1.43 | 2.93±1.44 | 2.93±1.39 | NS |
| Last HAQ | 0.97±0.71 | 0.98±0.70 | 0.95±0.76 | NS |
| Remission (DAS28$<2.6$ )% | 48 | 49 | 47 | NS |

In 2 patients no information about previous biologic treatment was available.

**Conclusions:** In our cohort with more than 700 Colombian patients with RA treated with RTX, the rate of survival-on-drug in those with more than 1 cycle was 25%. Around half of patients under RTX treatment were on remission with an adequate physical function.
**Disclosure of Interest:** J. A. Gómez-Puerta Speakers bureau: Roche, Pfizer and BMS. Roche was not involved in the design, protocol, data collection or statistical analysis of this study, L. Uribe Botero: None declared, J. Urrego: None

declared, L. A. González: None declared, C. Cerón: None declared, C. Ochoa: None declared, M. A. Saldarriaga: None declared, A. Uribe Toro: None declared, O. J. Felipe Diaz: None declared
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## AB0354 SUBCUTANEOUS ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A REAL-LIFE EXPERIENCE

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**Background:** Therapeutic guidelines draw heavily on evidence from randomized controlled trials undertaken in well-characterized, highly-selective populations and managed in tightly-controlled settings. As such, the extent to which therapeutic efficacy in real-life populations and routine care settings is often unclear [1–2].
**Objectives:** To assess subcutaneous (SC) abatacept (ABA) efficacy and safety in a real-life setting.
**Methods:** This was a retrospective and single center study in which 94 patients (1987 ACR) were assessed from April 2014 to January 2016. The patients were stratified according to their treatment background: (n=39) biologic-naïve, (n=22) switched from IV to SC ABA administration (125mg-wk), and (n=33) inadequate response to TNF inhibitor (TNF-IR). The primary and secondary endpoints were change in DAS28-CRP, and Routine Assessment of Patient Index Data (RAPID3) from baseline to 6 months, respectively. A linear mixed effects model was made to account for correlation among repeated measures. Adverse events (AEs) were assessed and recorded at each visit to the rheumatology center.
**Results:** Baseline characteristics of patients were as follows: female gender 86%, mean age 55.2±12.3 years, median disease duration 12.5 (IQR 14) years, Rheumatoid Factor positive 94%, Anti-Cyclic Citrullinated Peptide Antibodies 84%, mean DAS28-CRP 5.4±0.72, and mean RAPID3 15.6±5.0. SC ABA monotherapy, concomitant use of methotrexate (MTX), and leflunomide were reported in 10%, 48%, and 27%, respectively. Demographics and disease characteristics were similar in all groups, except for baseline DAS28-CRP ($p<0.0001$), and RAPID3 ($p<0.0001$) in switch group. After 6 months of administration, the DAS28-CRP score change was statistically significant irrespective of group. The scores changed from 5.4±0.9 to 3.8±1.3 ($p<0.0001$, biologic-naïve group), from 3.1±1.2 to 2.7±1.2 (p=0.002, switch IV-SC group), and from 4.6±1.9 to 3.2±1.4 (p=0.0305, TNF-IR group). The RAPID3 scores changed from 18.1±5.4 to 12.1±6.3 ($p<0.0001$, biologic-naïve group), from 10.4±6.6 to 9.2±7.0 (p=0.0114, switch IV-SC group), and from 16.1±5.7 to 11.8±7.1 (p=0.284, TNF-IR group). No patients relapsed or needed to return to the IV administration. Infections, headache, and constitutional symptoms, occurred in 48%, 37% and 32% of patients, respectively. Serious infections were reported only in 2% of patients (i.e., herpes zoster). Local injection-site reactions occurred in 13% of patients. Most of AEs reported were reversible and mild. There were no treatment discontinuations. No deaths and malignancies were reported.
**Conclusions:** Our results disclose an improvement in RA disease activity and physical function, during 6 months administration of SC ABA. Patients switching from IV to SC formulation of ABA had lower activity and functional impairment at baseline, and efficacy was maintained through follow-up. SC ABA demonstrated a good safety profile, consistent with previously published data.
**References:**
[1] Reggia R, et al. J Rheumatol 2015;42(2):193–5.
[2] Nüβlein H, et al. Arthritis Rheum 2012;64(Suppl10):S199.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5165

## AB0355 REAL CLINICAL EXPERIENCE WITH ABATACEPT, FROM INTRAVENOUS TO SUBCUTANEOUS

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**Background:** Abatacept, a fusion protein CTLA4Ig1 that selectively modulates coestimulation of T lymphocites, was approved for the treatment of active rheumatoid arthritis (RA) in 2010 as an endovenous (e.v.) biologic therapy. Three years later was approved the subcutaneous (s.c.) abatacept for RA. The efficacy and safety of both types of administration of abatacept is similar[1]. Also switching from e.v. to s.c. administration of abatacept is effective and safe according to clinical trials[2]. Real clinical practice sometimes differs from clinical trials results. To the best of our knowledge, there is a lack of studies based on real clinical experience about RA patients who switched from e.v. to s.c. abatacept.
**Objectives:** To describe the efficacy of switching from e.v. to s.c. abatacept in our RA patients, evaluated by clinical and ultrasound examination
**Methods:** This observational study was conducted at the rheumatology department of Hospital Gregorio Marañón, Madrid, Spain. Patients diagnosed with RA under treatment with e.v. abatacept in whom rheumatologist and patient consensually decided to switch to s.c. abatacept were included in the study.
Subcutaneous abatacept was started one month later to the last e.v. administration, corresponding to baseline in the study. At baseline and three months later, all patients were clinically assessed and underwent to ultrasound (US) examination. US examination consisted on a reduced joint count (elbows, wrists, 2nd and 3rd metacarpophalangeal, knees and ankles) and tendon examination (2nd, 4th and 6th extensor compartments and tibialis posterior and peroneal tendons). Global synovitis was calculated on B mode and Power Doppler (SBM and SDM), also for tenosynovitis (TBM and TBM). After one year from the switching, clinical reports were reviewed to collect clinical data.
All patients signed an informed consent before to be included. This study was approved by our ethics committee.
**Results:** We included 23 RA patients, from them 21 (91.3%) are still on s.c. abatacept. Twenty-two from 23 (95.7%) were females, mean age 60 years old (range 44.1–82.4) and mean time on e.v. abatacept was 2 years (range 0.8–7.1). SBM was greater at 3 months after switching in 81.9% (18/22) of patients. No differences between SDM, TBM nor TDM were seen at three months. One patient had active synovitis on US both at baseline and three months. She stopped abatacept after US at three months.
Four patients were receiving half dose of e.v. abatacept (5 mg/kg every month) and switched to s.c. abatacept 125 mg every other week. All four patients are still on the same regimen.
Table 1 shows clinical and ultrasound data at baseline and follow-up.

| | Baseline (n:23) | 3 months (n:22) | 12 months (n:21) |
|---|---|---|---|
| DAS28crp (median, IR) | 2.87 (2.24, 4.12) | 2.28 (1.59, 3.1) | 2.37 (1.96, 3.79) |
| ESR mm/1ªh (median,IR) | 15 (9, 27) | 9.5 (6, 16.3) | 11 (3.5, 17.3) |
| CRP mg/dl (median, IR) | 0.46 (0.26, 0.74) | 0.3 (0.2, 0.6) | 0.4 (0.2, 0.6) |
| VAs global (mean, SD) | 4 (2.4) | 3,8 (2.3) | 2,8 (2.2) |
| TJC (median, IR) | 1 (0, 5) | 0.5 (0, 2) | 0 (0, 7.5) |
| SJC (median, IR) | 1 (0, 1) | 0 (0, 1) | 0 (0, 1) |
| SBM (median, IR) | 2 (2, 5) | 9 (4.75, 11) | NA |
| SDM (median, IR) | 0 (0, 1) | 0 (0, 1.25) | NA |
| TBM (median, IR) | 0 (0, 0) | 0 (0, 1) | NA |
| TDM (median, IR) | 0 (0, 0) | 0 (0, 0) | NA |

**Conclusions:** Switching from e.v. to s.c. abatacept in our RA patients was succesful at 12 months. Ultrasound on B mode showed more synovitis at 3 months after swiching, without relation with flares at 12 months.
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[1] Genovese MC. J Rheumatol. 2014;41:629–39
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[3] Naredo E. Arthritis Rheum. 2008;59:515–22
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4301

## AB0356 HOW DOES FIRST-LINE ABATACEPT COMPARE TO OTHER BIOLOGICS? DATA FROM A RHEUMATIC DISEASE REGISTRY

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**Background:** Observational studies are critical in assessing medication safety and effectiveness in the real world. Non-random assignment can provide insight to how and when medications are prescribed. Since the US introduction of TNF inhibitors (TNFi) in 1998, several newer biologics with varying mechanisms of action are available to patients and physicians. Most physicians prescribe TNFi prior to another biologic, however this trend may be changing.
**Objectives:** To compare the characteristics and outcomes (serious infections and malignancies) of patients who receive abatacept (ABA) vs TNFi as a first biologic.
**Methods:** Participating patients with RA in the National Data Bank for Rheumatic Diseases (NDB) provided treatment and other characteristics (sociodemographics and comorbidities) through self-reported biannual questionnaires. Only responses from 2005–2014 were used for greater comparability. Initiators of biologics were stratified by type (ABA vs. TNFi) and by number of previously exposed biologics. All patient-reported outcomes were verified by medical record review except non-melanoma skin cancer. Patients who had an outcome in the 180 days before treatment initiation were excluded from the analysis for that outcome. Marginal structural models were used to estimate the effect of treatment on the outcome by an appropriate control for the effects of time-dependent confounders using stabilized weights. Variables included sex, employment, marital status, smoking, education, income, select comorbidities, and medications prescribed. These results are reported as adjusted hazard ratios (HR). We repeated the analysis comparing ABA with all other biologics.
**Results:** A total of 3,088 RA patients initiated a first biologic during the study. Of these, 348 received ABA without any prior biologics, having a mean (median) time in the study of 2.6 (1.9) years with a total of 900 patient-years of follow-up. For patients who initiated a TNFi, 3.4 (2.4) years was the mean (median) time in the study with a follow-up of 9296 patient-years. The ABA patients were older, smoked more, and used more prednisone and less MTX compared to those starting their first non-ABA biologic. They also tended to have worse disease activity measured by HAQ and PAS. The crude and adjusted HR of hospitalized infections were: 0.7 (0.2–2.3) and 0.5 (0.2–1.6) and for all malignancies: 1.5 (0.84–2.8) and 1.1 (0.7–2.0), respectively. The results were similar when compared to all biologics (N=2,900).

| | ABA (N=348) | TNFi (N=2740) |
|---|---|---|
| Age, yrs - mean (SD) | 62.5 (13.1) | 57.9 (12.9) |
| Male sex - % | 17 | 20 |
| Education, yrs – mean (SD) | 13.8 (2.2) | 13.8 (2.4) |
| RA duration, yrs – mean (SD) | 11.9 (11.2) | 12.2 (11.1) |
| HAQ (0-3) - mean (SD) | 1.2 (0.7) | 1.0 (0.7) |
| Pain VAS (0-10) - mean (SD) | 4.5 (2.9) | 3.8 (2.8) |
| Global VAS (0-10) - mean (SD) | 4.2 (2.4) | 3.7 (2.6) |
| PAS (0-10) - mean (SD) | 4.2 (2.2) | 3.6 (2.2) |
| Cancer ever - % | 19 | 18 |
| Current smoker - % | 14 | 13 |
| Past smoker - % | 59 | 51 |
| IV antibiotics - % | 4.0 | 3.5 |
| Methotrexate (MTX) - % | 54 | 64 |
| DMARDS not MTX - % | 35 | 33 |
| Hydroxychloroquine - % | 19.5 | 19.8 |
| Prednisone - % | 37.6 | 29.9 |
| Any NSAID - % | 39.6 | 46.3 |
| Hypertension - % | 39.5 | 34.3 |
| Diabetic - % | 13.8 | 11.5 |

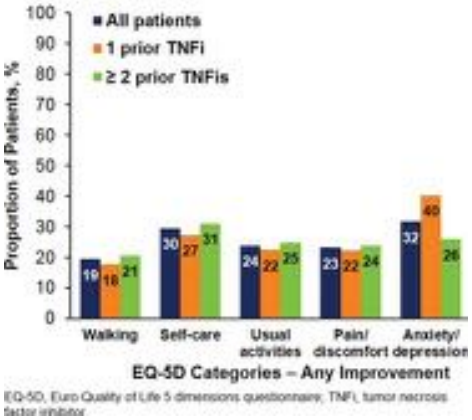
The table shows baseline characteristics comparing Abatacept and TNFi initiators.
**Conclusions:** In this RA cohort receiving a first biologic therapy, there appears to be a trend of channeling with ABA. Patients starting ABA tended to be older and have worse disease outcomes. Despite the baseline differences, there was no difference in hospitalized infections and cancers between the groups. This was still true when the comparison was made between ABA and other biologic initiators.
**Disclosure of Interest:** None declared
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## AB0357 IMPACT OF RITUXIMAB ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM THE US CORRONA REGISTRY

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**Background:** Patients with rheumatoid arthritis (RA) experience diminished quality of life, including increased disability and RA-related comorbidities. Patient-reported outcomes (PROs) are increasingly being recognized as important measures in determining response to therapy in patients with RA.
**Objectives:** To examine the impact of rituximab on PROs in the Corrona registry, a national US observational cohort of >40,000 patients with RA.
**Methods:** Between March 1, 2006, and September 1, 2015, patients with RA who had prior exposure to ≥1 tumor necrosis factor inhibitor (TNFi) and newly initiated rituximab while not in remission (Clinical Disease Activity Index [CDAI] >2.8) with a follow-up visit at 1 year (± 3 months) were identified. Changes in PROs, assessed 1 year from baseline and stratified by prior TNFi use, included patient global assessment of disease, pain and fatigue (visual analog score; 0–100); morning stiffness (hours); modified Health Assessment Questionnaire (mHAQ; 0–3) and Euro Quality of Life 5 dimensions questionnaire (EQ-5D). Improvement in EQ-5D domains was defined as patients reporting improvement or resolution of impairment among patients who reported impairment at baseline. Outcomes between the 1 and ≥2 prior TNFi groups were compared using $\chi^2$ or *t*-tests, as appropriate.
**Results:** Of the 667 patients initiating rituximab included, 284 (43%) had received 1 prior TNFi and 383 (57%) had received ≥2 prior TNFis. Overall, the median (IQR) age was 59 (50–66) years; 79% of patients were female. Baseline mean (SD) CDAI was 25.6 (13.9). Baseline PROs showed that patients were substantially impaired by their disease and were mostly similar between the 1 and ≥2 prior TNFi groups, although patients in the 1 prior TNFi group tended to have longer duration of morning stiffness and greater fatigue scores. At baseline, patients reported median (IQR) global assessment, pain, fatigue and mHAQ scores of 50 (35–73), 60 (31–75), 65 (40–80) and 1 (0.6–1.6), respectively, and a median (IQR) of 1 (0.5–2) hour of morning stiffness. Of the 667 total patients, 63% received rituximab retreatment and persisted on rituximab through 1 year. At 1 year, improvements were reported in all PROs with no significant difference between patients with 1 or ≥2 prior TNFis. Median (IQR) improvements in patient global assessment, pain and fatigue were 7 (–10 to 25), 7 (–5 to 25) and 9 (–5 to 20), respectively. Improvement in EQ-5D categories is shown (Figure). 51.7% of patients reported no improvement in morning stiffness, 28.5% reported improvement of 1–60 minutes and 19.8% reported improvement of >60 minutes.
**Conclusions:** Real-world data showed that quality of life in this cohort of patients with long-standing, refractory RA was substantially impacted by the disease. One year after initiation of rituximab, improvements were reported in all PROs, such as self-care and usual activities, and were similar between patients with exposure to 1 or ≥2 prior TNFis.
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**Figure.** Improvement in EQ-5D categories at 12 months among rituximab initiators who reported impairment at baseline




EQ-5D, Euro Quality of Life 5 dimensions questionnaire; TNFi, tumor necrosis factor inhibitor

## AB0358 EFFICACY AND SAFETY OF INTRAVENOUS AND SUBCUTANEOUS TOCILIZUMAB IN A COHORT OF PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS IN REAL-LIFE

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**Background:** Tocilizumab (TCZ) is a humanized monoclonal anti-interleukin-6 receptor antibody, used for the treatment of moderate to severe rheumatoid arthritis (RA). Although TCZ has been proved to be highly effective and safe in RA patients in large clinical trials, few data are available from real-life practice [1].
**Objectives:** To evaluate efficacy, safety and retention rate of intravenous (IV) and subcutaneous (SC) TCZ in a real-world setting.
**Methods:** We evaluated patients affected by moderate-to-severe RA and treated with TCZ from April 2010 to December 2015. Data of patients treated with IV-TCZ until December 2014 were collected retrospectively, while patients treated with either IV or SC-TCZ from January 2015 were included in a prospective cohort

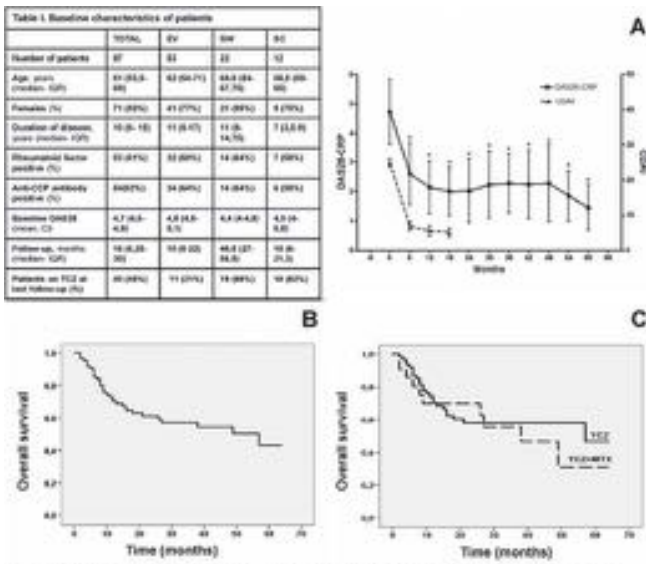



**Figure. Table I** shows baseline characteristics of the patients enrolled in the study. **Panel A** shows mean DAS28 of all the patients during a follow-up of 60 months (continuous line) and mean CDAI of 12 patients treated with SC-TCZ in the prospective phase (dashed line). **Panel B** shows the overall TCZ survival curve estimated by means of Kaplan-Meier method. **Panel C** shows the survival curve of patients treated with TCZ in monotherapy (continuous line) vs patients treated with TCZ in combination with MTX (dashed line). *p<0.001

and assessed for disease activity, quality of life, treatment discontinuation and/or onset of adverse events (AEs). DAS28-CRP, CDAI and SDAI were used for activity assessment. Treatment retention rate was estimated by Kaplan-Meier method.
**Results:** We evaluated 87 patients, 53 treated with IV-TCZ (8 mg/kg every 4 w), 12 with SC-TCZ (162 mg every week) and 22 patients who switched from IV to SC during follow-up (71 females, median age 61 y, median duration of disease 10 y, median follow-up 16 months). Sixty-six patients (76%) were treated in monotherapy and 21 (24%) in combination with methotrexate; 16 (18%) patients were naïve for previous biologic drugs.
At baseline, disease activity was severe in 36% of patients, moderate in 59% and mild or inactive in 5%; at month 6, 49% of patients achieved a clinical remission. The mean overall DAS28 was 4.72 at baseline and 2.61 at 6 months ($p<0.001$ for all comparisons between baseline and subsequent assessments, see Figure).
Thirty-three patients (38%) discontinued TCZ because of inefficacy (67%), AEs (24%) or other reasons (9%). Seventy-three infectious AEs occurred in 38 patients (45.1/100 person-years), 3 cases of pneumonia were severe and only one required treatment discontinuation. Other AEs were mild neutropenia (29%), mild hypertransaminasemia (22%), hypercholesterolemia (39%) and hypertriglyceridemia (10%). Infusion reactions were reported in 5/75 IV-TCZ patients, while injection site reactions in 8/34 SC-TCZ patients.
We observed an overall high retention rate (85.2%, 70.2%, 61.3%, 54.6%, 43.2% at 6, 12, 24, 48 and 60 months respectively); no significant difference was found between combination or monotherapy (p=0.58) or between IV or SC at 22 months (p=0.51). In multivariate Cox regression analysis longer duration of disease (HR 1.06, 95%CI 1.02–1.11), presence of ≥1 comorbidities (HR 2.25, IC95% 1.39–3.64) and previous treatment with ≥2 biologic drugs (HR 1.55, IC95% 1.04–2.31) were associated with treatment discontinuation.
**Conclusions:** TCZ is effective, well tolerated and safe in a population of RA patients followed in a real-life setting.
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[1] Gabay C, Riek M, Hetland ML, Hauge EM, Pavelka K, Tomšič M, et al. Effectiveness of tocilizumab with and without synthetic disease-modifying antirheumatic drugs in rheumatoid arthritis: results from a European collaborative study. Ann Rheum Dis. 2015 Sep 15.
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## AB0359 TREATMENT EFFECTIVENESS FOR RHEUMATOID ARTHRITIS AFTER SWITCHING FROM A TUMOR NECROSIS FACTOR INHIBITOR TO ANOTHER AGENT

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**Background:** When tumor necrosis factor inhibitor (TNFi) therapy fails in rheumatoid arthritis (RA), a majority of patients switch to another TNFi instead of a non-TNFi biologic disease-modifying antirheumatic drug (bDMARD).[1] The effectiveness of TNFi cycling compared with switching to a non-TNFi agent is not well established.
**Objectives:** This study examined treatment effectiveness among patients with RA in a large, commercially insured population who cycled to another TNFi ("TNFi cyclers") compared with those who switched to a non-TNFi agent ("non-TNFi switchers").
**Methods:** Administrative claims from January 2010 to September 2014 were analyzed from the Truven Health MarketScan Commercial database. Eligible patients received a TNFi in the 12 months before the "index" drug (a different TNFi or non-TNFi [bDMARDs or tofacitinib]). The study included adults ages 18 to 64 years with ≥12 months of continuous medical and pharmacy enrollment pre- and post-index, and ≥1 claim for RA (ICD-9-CM 714.0x) pre-index or 30 days post-index with no other autoimmune condition. Treatment effectiveness was defined using a validated algorithm[2] that was applied to medical and pharmacy claims for 12 months post-index for each patient. Treatment was considered to be effective if the patient satisfied all 6 algorithm criteria in this period: (1) ≥80% adherence (subcutaneous medication possession ratio or number of intravenous infusions); (2) no increase in dose; (3) no switch to another bDMARD; (4) no new conventional DMARD; (5) no new/increased oral glucocorticoid; and (6) less than 2 glucocorticoid injections in the first 90 days after the index date. Logistic regression was used to compare effectiveness rates by treatment cohort, controlling for baseline demographic and clinical characteristics, including number of prior biologic therapies.
**Results:** Of the 6,945 patients who switched from a pre-index TNFi, 5,020 (72.3%) were TNFi cyclers and 1,925 (27.7%) were non-TNFi switchers. Achievement rates for all 6 algorithm criteria combined and for individual criteria in the 12 months post-index are shown in the table. In the logistic regression model, non-TNFi switchers were 1.25 times as likely as TNFi cyclers to achieve all algorithm criteria for effectiveness (odds ratio, 1.248; 95% CI, 1.103–1.414; $P<0.001$).

| Achievement of treatment effectiveness criteria 12 months post-index | TNFi cyclers (n=5,020) | Non-TNFi switchers (n=1,925) | *P* value |
|---|---|---|---|
| Achieved all criteria | 24.0% | 27.8% | 0.001 |
| ≥80% Adherence | 40.0% | 41.7% | 0.182 |
| No dose increase | 88.3% | 96.7% | <0.001 |
| No switch to another bDMARD | 65.4% | 70.3% | <0.001 |
| No new conventional DMARD | 84.7% | 85.6% | 0.353 |
| No new/increased oral glucocorticoid | 85.7% | 84.7% | 0.285 |
| <2 Glucocorticoid injections in first 90 days | 90.6% | 90.6% | 0.968 |

**Conclusions:** On the basis of a claims-based algorithm of treatment effectiveness for RA, it appears that patients who switch from TNFi to non-TNFi agents are more likely to achieve treatment effectiveness criteria for 12 months after switching than patients who cycle to another TNFi.
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## AB0360 IMPACT OF ABATACEPT ON DISEASE ACTIVITY AND FUNCTIONAL STATUS IN PATIENTS WITH DIFFERENT DURATION OF RHEUMATOID ARTHRITIS

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**Background:** Abatacept (ABA) is a selective co-stimulation modulator, which is widely used in treatment of RA. There isn't enough data about its effectiveness and impact on functional status in patients with early (ERA) and long-standing (LS) rheumatoid arthritis (RA).
**Objectives:** To assess the impact of ABA on disease activity and functional status in patients with different duration of RA.
**Methods:** 85 patients (pts) with active RA and an inadequate response to synthetic DMARDs or biologics were enrolled in the study. They were grouped into 2 arms based on RA duration: less than three years (early RA) and more than three years (LS RA), i.e. 51% and 49% pts in each group, respectively. Most of them were middle aged females (48,8±13,5 years) with high disease activity (DAS28=5,25±1,15), RF-positive (76,7%) and ACPA-positive (73,1%). ABA (10 mg/kg) was administered intravenously following the adult intravenous dosing regimen. Disease activity was assessed by DAS28, functional status by HAQ-DI and results by EULAR criteria every 12 weeks.
**Results:** Before treatment DAS28 in ERA pts was 5,1±0,9, in LS RA – 5,3±1,3 and HAQ-DI in ERA pts was 1,3±0,6, in LS RA - 1,6±0,9. In three months after ABA therapy initiation a significant improvement in DAS28 and HAQ-DI was achieved in both groups ($p<0,05$). Improvement by EULAR response criteria was registered in 80% of pts with ERA and 67% of pts with LS RA. There was no significant difference between two groups after 3 and 6 months of treatment in achieving a good EULAR response: 27,5% and 43,75% – in early RA pts, 28,57% and 38,4% – in LS RA pts. There was a comparable percentage of non-responders after 3 and 6 months of therapy in both groups (at 3 months – 20% in early RA group, 31,4% – in LS RA group; at 6 months – 18,7% and 19,2% respectively). After 3 months and 6 months the improvement of HAQ-DI in ERA group was significantly higher, than in LS RA group ($p<0.05$). 28 adverse events (AEs) in 17 (20%) pts were registered. The most frequent AE were upper respiratory tract infections – 10 (11,8%) pts. Serious AEs (SAEs) occurred in 4 (4,7%) pts.
**Conclusions:** ABA has shown significant improvement in reduction of disease activity and improvement in functional status in pts with RA. No significant difference was seen between the groups of ERA and LS RA by EULAR criteria. However, pts in ERA group had significant improvement of HAQ-DI comparing with LS RA group. ABA has good safety profile, adverse events were registered only in 20% of patients.
**Disclosure of Interest:** None declared
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## AB0361 EVALUATION OF BASELINE CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT OR TUMOR NECROSIS FACTOR INHIBITORS IN CLINICAL PRACTICE IN SPAIN

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**Background:** Biological therapies have demonstrated efficacy in patients with rheumatoid arthritis (RA) improving the prognosis. The most widely used biological agents are tumor necrosis factor inhibitors (TNFi), although other biological agents with different mechanisms of actions, such abatacept, have been approved. Although all these drugs are indicated in RA, there is limited data on their use and whether differences in baseline characteristics of RA patients treated with different biologics

**Objectives:** To analyze differences in baseline characteristics of RA patients treated with abatacept, a T-cell co-stimulation inhibitor, compared with those treated with a TNFi

**Methods:** All BIOBADASER 2.0 register patients diagnosed with RA and treated with abatacept from January 2008 to December 2014 were selected. Baseline sociodemographic and clinical characteristics were analyzed compared them with RA patients treated with TNFi during the same period. Variables analyzed: age; gender; disease duration; positivity of rheumatoid factor; disease activity at initiation of biological measured by the DAS-28 score; number of previous biological agents (0, 1, ≥2); and concomitant glucocorticoid treatment. Differences between abatacept and TNFi patients in baseline DAS28 were analyzed according to the number of previous biological drugs received

**Results:** From January 2008 to December 2014, 252 RA patients treated with abatacept and 640 with TNFi were included in the BIOBADASER 2.0 register. Baseline characteristics are shown in Table1. At baseline, patients treated with abatacept were significantly younger; had a longer disease duration; had received a greater number of previous biologics; and had a higher DAS-28 (significant in patients who had received 1 previous biologic) than those treated with TNFi

| Variable | Total (n=892) | Abatacept group (n=252) | TNF inhibitor group (n=640) | p-value |
|---|---|---|---|---|
| Age at initiation of first biologic (years), mean (SD) | 55.3 (13.5) | 52.2 (13.1) | 54.6 (13.7) | **0.018** |
| Women, n (%) | 705 (79.0) | 208 (82.5) | 497 (77.6) | 0.107 |
| Disease duration (years), mean (SD) | 8.7 (8.3) | 12.1 (8.15) | 7.3 (8.0) | **<0.001** |
| Number of previous biological agents | | | | |
| 0 | 605 (67.8) | 27 (10.7) | 578 (90.3) | **<0.001** |
| 1 | 151 (13.6) | 71 (28.2) | 50 (7.8) | |
| ≥2 | 166 (18.6) | 154 (61.1) | 12 (1.9) | |
| Concomitant glucocorticoids (%) | 512 (57.4) | 134 (53.2) | 378 (59.1) | 0.109 |
| Rheumatoid factor (%) | 752 (84.3) | 214 (84.9) | 538 (84.1) | 0.751 |
| Basal DAS28 score, mean (SD) | | | | |
| Clustered | 4.74 (1.63) | 4.86 (1.74) | 4.73 (1.63) | 0.597 |
| Number of previous bDMARD = 0 | n=667* | n=44* | n=623* | 0.495 |
| | 4.70 (1.63) | 4.86 (1.74) | 4.69 (1.63) | |
| Number of previous bDMARD = 1 | n=490* | n=71* | n=419* | **<0.001** |
| | 4.28 (1.93) | 5.20 (1.53) | 4.09 (1.95) | |
| Number of previous bDMARD >2 | n=484* | n=137* | n=347* | 0.412 |
| | 4.74 (4.17) | 4.99 (1.46) | 4.59 (5.17) | |

*Number of treatments available to calculate DAS28 mean.

**Conclusions:** Patients with RA treated with abatacept have more active disease and a poorer prognosis that those treated with TNFi, significantly longer disease duration, have failed more previous biological agents and have higher baseline inflammatory activity

**Disclosure of Interest:** None declared

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## AB0362 SERUM LIPID LEVEL CHANGES ASSOCIATED WITH TOCILIZUMAB TREATMENT: OUR EXPERIENCE IN TWO UNIVERSITY HOSPITALS

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**Background:** Tocilizumab (TCZ) is a humanised monoclonal antibody against the Interleukin-6 (IL-6) receptor effective in patients with rheumatoid arthritis (RA) with an inadequate response to conventional DMARDs or an anti-TNF biologic. Among its side effects, a change in the serum lipid profile due to an increase of low density lipoproteins (LDLc) and of high density lipoproteins (HDLc) has been previously described. Its impact and proper management is still uncertain.

**Objectives:** To analyze the changes in serum lipid levels in patients under TCZ treatment.

**Methods:** Retrospective review. Patients treated with TCZ and complete serum lipid profile (total cholesterol, LDLc, HDLc, triglycerides) in two different rheumatology units were selected. Three time-points were established: 1) baseline; 2) one month after the start of TCZ; 3) six monthts after the start of TCZ. Epidemiologic and clinical data on al patients and laboratory findings (C reactive protein – CRP, erythrocyte sedimentation rate – ESR) at the given time-points were also recorded. A before-after comparative anlaysis using Wilcoxon's test, an a correlational analysis with inflammation laboratory parameters using Spearman's Rho test were performed.

**Results:** Thirty-five patients were included: 34 patients with rheumatoid arthritis and one with idiopathic retroperitoneal fibrosis. Patients were a mean (p25–75) of 57.5 years (51.8–63.3) old, and 30 (86%) were women. Table 1 shows the variations in lipid parameters at the different timepoints. A mild increase in HDLc levels was observed after one month of treatment which was maintained at 6 months later, but with no statistical significance (p=0.36). A significant elevation was observed in the remaining lipid paramenters (total cholesterol, LDLc, triglycerides) after one month of treatment, which dissapeared after 6 months of treatment. Inflammatory markers decreased significantly and persistently after the beginnig of TCZ treatment. In the correlation analysis no association was found between lipid levels and inflammatory markers (p>0.05 for all comparisons).

| | Baseline | Month 1 | p | Month 6 | p |
|---|---|---|---|---|---|
| Total cholesterol | 213.0 (193.5–47.0) | 242.5 (199.7–273.5) | **0.002** | 214.0 (179.0–37.0) | 0.36 |
| HDLc | 60.5 (46.0–78.0) | 64.0 (42.5–79.0) | 0.54 | 63.0 (53.0–81.0) | 0.36 |
| LDLc | 124.5 (97.0–150.2) | 143.5 (107.2–170.7) | **0.008** | 116.0 (79.0–140.0) | 0.66 |
| Triglycerides | 118.0 (74.5–170.5) | 137.5 (78.0–211.0) | 0.06 | 123.0 (82.0–209.0) | 0.15 |
| CRP | 2.6 (0.9–7.1) | 0.9 (0.9–1.75) | **0.002** | 0.9 (0.7–0.9) | **<0.001** |
| ESR | 29.0 (10.5–56.0) | 7.0 (3.0–18.0) | **<0.001** | 6.0 (2.0–12.0) | **<0.001** |

Units en mg/dL (unless mm/h for VSG). Data shown as median (p25–75). HDLc: high density lipoproteins, LDLc: low density lipoproteins, CRP: reactive C protein, ESR: erythrocyte sedimentation rate.

**Conclusions:** With TCZ, most lipid parameters show a significant but transitory increase. A mild though non-significant increase in HDLc levels was also observed. The antiatherogenic benefit of TCZ might be mediated by qualitative changes in the HDLc molecule. Prospective and larger studies are needed to characterize these results better.

**Disclosure of Interest:** None declared

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## AB0363 THE POSSIBILITY OF ESTIMATING THE THERAPEUTIC OUTCOME OF ABATACEPT FROM CHANGES IN CD4+/CD25+HIGH FRACTION

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**Background:** Cytotoxic T-lymphocyte antigen (CTLA) 4 is a molecule that suppresses T-cell activation and is expressed on the surface of regulatory T cells. Abatacept (ABT), a fusion protein fused to CTLA-4, is used in the treatment of rheumatoid arthritis (RA).

**Objectives:** The purpose of this study was to analyze the effect of ABT therapy on the CD4+/CD25+$^{high}$ fraction, which is thought to include regulatory T cells in the peripheral lymphocyte fractions of RA patients, and to elucidate whether this can be correlated to therapeutic outcome.

**Methods:** The subjects were 32 RA patients who were currently being treated with ABT therapy. The patients' background characteristics were as follows: age ranging from 39 to 81 years (mean: 62±12 years.), stage II disease in 8 patients, stage III disease in 14 patients, and stage IV disease in 10 patients. Sixteen patients were switched from other biological preparations, and 16 patients were ABT naive. Changes in CD4+/CD25+ and CD4+/CD25+$^{high}$ expression levels in blood tests prior to ABT administration were determined by using fluorescein isothiocyanate and phycoerythrin double stain, and measured by using flow cytometry in 5 points: 0 (prior to first ABT administration), 4, 12, 24, and 52 weeks.

**Results:** CD4+/CD25+ (%) showed a slight elevation at week 12 with subsequent decline followed by a slight elevation at week 52, although no significant differences were observed. Measured values at weeks 0, 4, 12, 24, and 52 were 26.4±1.6, 26.7±1.5, 28.9±1.7, 26.8±1.6, and 28.1±1.6, respectively. No significant differences in these values were observed between the switched and naive groups. However, our analysis of the CD4+/CD25+$^{high}$ distribution revealed that in the naive group, an interim decline occurred at week 52, but significant elevations were observed in the switched group starting at week 12. Analysis of the responders (10 cases) and non-responders (6 cases) to ABT in the switched group indicated that the responders showed significant declines in CD4+/CD25+$^{high}$ levels between weeks 12 and 52, as did the cases in the naive group. However, the non-responders showed significant elevations in this fraction from initial ABT administration until week 52.

**Conclusions:** Based on the fact that CTLA-4 is expressed on the surface of regulatory T cells, considering that ABT is a fusion protein that fuses CTLA-4 and immunoglobulin and regulatory T cells are present in the CD4+/CD25+$^{high}$ fraction, as well as the results of this study, we believe that in cases in which satisfactory

therapeutic effects were obtained through the use of ABT, the expression level of regulatory T cells declined. However, patients who were refractory to ABT therapy experienced CTLA-4 deficiency, which we believe caused regulatory T cells to be expressed. Based on these results, changes in the CD4+/CD25+$^{high}$ fraction can be used to measure the therapeutic efficacy for RA from the perspective of CTLA-4.

**Disclosure of Interest:** None declared

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## AB0364 A NOVEL APPROACH FOR RHEUMATOID ARTHRITIS: RESULTS OF THE ONGOING CLINICAL TRIALS WITH THE FULLY HUMAN IMMUNOCYTOKINE DEKAVIL (F8-IL10)

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**Background:** F8-IL10 (Dekavil) is a human immunocytokine composed of the vascular targeting antibody F8, specific to the extradomain A of fibronectin, fused to the cytokine interleukin-10. F8-IL10 is being investigated in a dose-finding, PK phase Ib study and in a randomized, double blind, placebo-controlled phase II study, as a new therapeutic strategy for rheumatoid arthritis (RA).

**Objectives:** The primary objective of the phase Ib study is to determine the safety, tolerability and MTD of Dekavil in combination with methotrexate (MTX). The primary objective of the phase II study is to assess the superiority of Dekavil plus MTX over MTX by measuring the mean change from baseline of DAS28-CRP. Immunogenicity of F8-IL10 and its PK and PD profile will also be explored.

**Methods:** Patients with active RA despite MTX therapy and who failed anti-TNF$\alpha$ treatment are the target population of both studies. In the phase Ib, cohorts of 3–6 patients are treated with escalating doses of Dekavil (6, 15, 30, 60, 110, 160, 210, 300, 450 and 600 $\mu$g/kg) in combination with a fixed dose of MTX (10–15 mg). In the phase II, patients are randomized to Dekavil 30 or 160 $\mu$g/kg plus MTX or placebo plus MTX. Dekavil is administered by s.c. injection once weekly for a maximum of 8 weeks in both studies.

**Results:** The first 9 cohorts of the phase Ib study have been completed, 32 patients were treated and 31 are evaluable for DLT. One DLT (G2 purpura) was observed in one patient of the 9th cohort. The same patient had G1 thrombocytopenia and G3 ALT increase. Both events were considered related to the study drug and resolved within ten days. Neither SUSAR nor treatment-related deaths occurred. Mild injection site reactions were reported in 59% of patients and 2 cases of anemia (G2 and G3) were considered related to the study drug. All adverse reactions resolved after the end of treatment. Currently, the MTD has not been reached and the 600 $\mu$g/kg dose is ongoing. To date, 59.3% of the 27 patients analyzed for efficacy had ACR and EULAR responses, 29.6% and 11.1% had ACR50 and ACR70, respectively, at the low dosages of 15, 30 and 60 $\mu$g/kg. Two patients benefited from ACR70 response for 12 months after the last drug administration. In the phase II study, 13 out of 87 patients have been enrolled so far. To date, neither SUSAR nor treatment-related deaths were recorded.

**Conclusions:** The promising safety and efficacy results, even at low dosages, of Dekavil in the phase Ib study led to the start of the phase II study to verify the efficacy of Dekavil in combination with MTX in the same patient population. The currently available data suggest that the targeted delivery of IL-10 to the sites of inflammation is a promising therapeutic approach for RA.

**Disclosure of Interest:** M. Galeazzi: None declared, R. Voll: None declared, G. Sebastiani: None declared, L. Bazzichi: None declared, O. Viapiana: None declared, J. Dudler: None declared, P. Sarzi-Puttini: None declared, E. Selvi: None declared, A. Iuliano: None declared, M. Pedretti Employee of: Philogen, L. Giovannoni Employee of: Philogen, I. Bindi Employee of: Philogen, C. Bettini Employee of: Philogen, N. Ravenni Employee of: Philogen, J. Wilton Employee of: Philogen, P. Zufferey: None declared, G. Ferraccioli: None declared, R. Caporali: None declared, C. Specker: None declared, J. Wollenhaupt: None declared, D. Neri Shareholder of: Philogen

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## AB0365 THE EFFICACY AND SAFETY OF ABATACEPT AS A FIRST BIOLOGICS IN JAPANESE RHEUMATOID ARTHRITIS PATIENTS COMPLICATED BY PULMONARY INVOLVEMENT

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**Background:** In clinical practice, it is not rare that we encounter patients with rheumatoid arthritis (RA) complicated by lung involvement. Clinically, lung involvement that accompany RA can be divided into: 1) lung lesions developing as extra-articular symptoms of RA, 2) drug-induced lung lesions caused by the drugs used for RA treatment, 3) opportunistic infection developing during RA treatment, and 4) others including lung lesions without causal relationship to RA. Then, starting the treatment, lung involvement is an important factor to select the disease-modifying anti-rheumatoid drugs (DMARDs) including biologics. There are many unfavorable reports to use tumor necrosis factor-$\alpha$ inhibitor, tocilizumab and rituximab in RA patients with lung involvement. Until now there are few reports whether or not abatacept induced serious respiratory adverse events (SRAE) and exacerbated RA associated ILD (RA-ILD).

**Objectives:** To compare the efficacy and safety of abatacept as a first biologics in RA patients between complicated with and without pulmonary involvement.

**Methods:** This is a prospective observation study. Thirty eight RA patients, who have never used biologics, were enrolled in this study. Pulmonary involvement was evaluated by high resolution computed tomography (HRCT). At 48 weeks after the enrollment of the study, clinical efficacy, safety, and continuation rate were compared between RA patients with pulmonary involvement and without pulmonary involvement.

**Results:** All patients are Japanese and eight patients were male and thirty patients were female. The mean age was 59.0±14.1 year-old, the mean prednisolone dose was 3.89±3.35 mg/day, and the mean methotrexate dose was 5.37±3.78 mg/week. DAS28-CRP was 4.24±1.33 and SDAI was 24.01±12.32 at enrolment. Eleven patients showed pulmonary involvement (8 patients: airway disease, 3 patients: interstitial lung disease). At 48 weeks, SDAI was significantly improved in both group (patients with pulmonary involvement: 25.3±14.56 to 14.23±12.31; p=0.023, patients without pulmonary involvement: 23.48±11.55 to 7.69± 6.70; $p<0.001$). $\triangle$DAS28-CRP was no significant difference between patients with pulmonary involvement and without pulmonary involvement (mean change, -1.20 vs -1.81; p=0.47). There was no change in LDH and KL-6 level in both group. Continuation rate was 81.6% and there was no difference between patients with pulmonary involvement (90.0%) and without pulmonary involvement (77.8%). There were no patients with exacerbating interstitial lung disease.

**Conclusions:** Abatacept as a first biologics is safe and effective in RA patients regardless of the presence or absence of pulmonary involvement. Furthermore abatacept did not lead the exacerbation of the existing pulmonary involvement.

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## AB0366 SWITCHING IN 1ST ANTI-TNF FAILURES TO 2ND ANTI-TNF AND OR ALTERNATIVE BIOLOGIC

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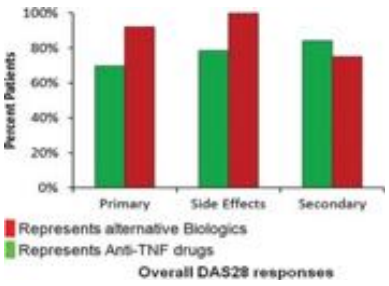
**Background:** When patients fail 1st anti-TNF & continue to have high disease activity, clinicians face a choice of switching to 2nd anti-TNF or alternative biologic. We set out a study using real world data from a clinical cohort in secondary care hospital in the United Kingdom

**Objectives:** To assess DAS response between the patients who have failed the 1st anti-TNF & compare switching to 2nd anti-TNF & or alternative biologic

**Methods:** We undertook a retrospective, observational study using a routine care biologics database. RA was diagnosed by consultants based on ACR criteria. The patients who failed to respond to a first anti-TNF were selected (including primary & secondary non-responders). Patients were dichotomised into either those who received either 2nd anti-TNF & or an alternative biologics (rituximab, abatacept or tocilizumab). The primary outcome measure was DAS response at 6 months following at dose initiation. A secondary outcome was safety. Statistical analysis compared rates in 2 groups by using Fischer's exact test

**Results:** 136 adult patients, who failed their 1st anti-TNF were included from January 2012 to December 2014. 56 (41.2%) patients received a 2nd anti-TNF & 13 (23.2%) had DAS non-response whereas 43 (76.8%) had DAS response. 19 patients failed second anti-TNF & had alternative biologic (including 6 with adverse events), whereas 37 continued. 99 (72.8%) received the alternative biologic in total. DAS response rates were 54%, 77% & 85% in the 3 groups. We further looked into the reasons for failure. Primary inefficacy was seen in 52 (38.2%), 23 (41%) & 38 (38.3%) patients in each of the cohorts respectively. Failure due to adverse

events were seen in 24 (17.6%), 14 (25%) and 13 (13.1%) patients in each of the cohorts respectively. Secondary inefficacy was seen in 60 (44.1%), 19 (33.9%) & 48 (48.4%) patients. Further analysis of 61 patients of primary inefficacy, 23 patients received 2nd anti-TNF, 16 responded & 7 did not, 38 received alternative biologic, 35 responded & 3 did not. Fischer's exact test showed P-value of 0.032 for the patients on alternative biologic, which is statistically significant. The adverse events group had 27 patients, 14 received 2nd anti-TNF, 11 responded and 3 did not.13 patients received alternative biologic with DAS response. P-value was 0.222 which is statistically not significant. Out of 67 secondary inefficacy patients, 19 received 2nd anti-TNF, 16 responded and 3 did not. 48 patients received alternative biologic, 36 responded & 12 did not with P-value of 0.527.
Overall, when the responses were compared for primary inefficacy, adverse events & secondary inefficacy, 2nd anti-TNF group had a total response of 77% (70%, 79% & 84% respectively), whereas alternative biologic group had 85% (92%, 100% & 75% respectively).There were no observed differences in safety signal between any of the groups




**Conclusions:** The study suggested that primary inefficacy patients respond better to alternative biologic, whereas 2nd anti-TNF group did not have statistically significant result. Adverse events group respond well to alternative biologics but the numbers were small. The disease duration and smoking status has shown to correlate with the biological treatment as well. Over all, this study should be repeated with large number of patients

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**Disclosure of Interest:** None declared
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## AB0367 ADHERENCE TO THE BIOLOGICAL THERAPY (BT) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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**Objectives:** To study the adherence to biologic therapy (BT) in patients with RA.
**Methods:** *Design* :Cross-sectional study. *Patients:* Consecutive sampling stratified by route of administration in the biological therapy unit (UTB). *Protocol:* Patients with sc BT are alternately reviewed every 3 months in general and specific (only BT pts) outpatient clinic. Iv BT patients are checked each time the drug is infused. Both groups of pts are reviewed according to a predetermined protocol of data collection. At the start of BT all subjects are interviewed by a nurse who explains the mode of application of drugs and emphasizing the importance of adherence to the effectiveness and safety of BT. *Outcome variables:* (1) level of adherence evaluated by Morisky-Green Test (MGT) and withdrawal drug in hospital pharmacy or drugstore (medication possession ratio [MPR]). Good adherence was considered when 4 responses indicative of adherence were given in MGT and a MPR>80%. The attendance rate to infusions was handled as equivalent to the medication possession ratio. *Other variables:* Demographics, comorbidities, clinical-analytical and synthetic DMARDs reclaim in the drugstores using "XXI electronic prescription"(a software used to control the dispensations in the public health system in Andalusia) in the last 6 months. *Statistical analysis:* Bivariate analyses were performed using T student test, Mann Whitney U test and Ji square test, followed by binary logistic regression (BLR).
**Results:** The main characteristics of the patients (n=178) are shown in the table. One hundred and twelve (63%) were with sc BT, 66 (37%) with iv BT and 49 patients (27.5%) were in monotherapy. 123/178 (69%) showed good adherence to BT and 67/129 (52%) took correctly concomitant synthetic DMARDs. Good adherence to BT was associated in the bivariate analyses with better control of the disease measured by DAS28 ($p<0.001$) and HAQ (p=0.006), fewer comorbidities (p=0.061), lower multimorbidity (p=0.014) and iv administration.However, in the multivariate analysis of poor adherence to BT as dependent variable identified only moderate to high activity DAS28 (OR [95% CI] = 4.51 [1.78 to 11.38]; p=0.001) and poor adherence to DMARDs (OR [95% CI] = 5.42 [2.18 to 13.24]; $p<0.001$) as independent predictors.

| Variables | Value |
|---|---|
| Sex (woman), n (%) | 138 (77,5) |
| Any comorbidity, n (%) | 111 (62,4) |
| Multimorbidity, n (%) | 76 (42,7) |
| Some traditional cardiovascular risk factors, n (%) | 113 (63,5) |
| Positive rheumatoid factor, n (%) | 153 (86,0) |
| Positive anti–cyclic citrullinated peptide antibodies, n (%) | 142 (79,8) |
| DAS28 at protocol, mean (DE) | 2,99 (1,3) |
| DAS28 average, mean (DE) | 3,04 (1,2) |
| HAQ at protocol, mean (DE) | 1,20 (0,7) |
| HAQ average, mean (DE) | 1,19 (0,7) |

**Conclusions:** Adherence to BT of patients with RA in a specific unit is moderate (69.1%) and adherence to the concomitant synthetic DMARDs is bad (52.7%).Patients with moderate or high activity in the previous 6 months, have 4.5 odds of having a bad adherence to FAMEb compared to those who are in remission or have low activity. Likewise, patients who do not take in proper manner associated biological DMARDs are 5.4 times more likely to have bad adherence to FAMEb.

**Disclosure of Interest:** None declared
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## AB0368 AC-CUTE: AN OPEN-LABEL STUDY TO EVALUATE NON-PROGRESSION OF STRUCTURAL JOINT DAMAGE IN PATIENTS WITH MODERATE TO SEVERE ACTIVE RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB

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**Background:** Clinical efficacy of subcutaneous tocilizumab (SC-TCZ) has been demonstrated in rheumatoid arthritis (RA); however the effect of SC-TCZ on joint damage has not yet been assessed. AC-CUTE (NCT01951170) aimed to evaluate the effects of weekly SC-TCZ on structural change in patients (pts) with moderate-severe active RA, who were inadequate responders to MTX/MTX-intolerant or inadequate responders to a single anti-TNF.
**Objectives:** To assess radiographic and MRI progression at week 24, in pts receiving SC-TCZ as monotherapy or in combination with MTX and/or conventional (c) DMARDs.
**Methods:** An open-label, multi-centre, prospective, single-arm study. Pts received TCZ 162mg weekly, single fixed dose SC injection, monotherapy or in combination with MTX or other cDMARDs. Primary endpoint was absolute change in radiographic Genant-modified Sharp Score (mTSS) between screening and week-24. Secondary endpoints were absolute change from baseline in RAMRIS of MRI erosions, synovitis and osteitis, and MRI cartilage loss (CARLOS). Efficacy parameters included change from baseline (initiation of SC-TCZ) in mTSS, DAS28, CDAI, SDAI and ACR20/50/70. The full analysis set population included pts who received at least 1 dose SC-TCZ, and was used for reporting safety, tolerability and efficacy. Subgroup analyses were split into SC-TCZ monotherapy [SC-TCZM: SC-TCZ monotherapy or SC-TCZ+cDMARDs other than MTX] and SC-TCZ in combination [SC-TCZC: SC-TCZ+cDMARDs including all MTX regimens].
**Results:** 52 pts enrolled from 10 Australian sites; majority females (79%), median age 59 yrs (min 28, max 79) and 5 yrs (min 0, max 31) median duration of RA. Pts in SC-TCZM had longer disease duration at baseline and higher mTSS score. 29 pts completed 24 weeks of treatment. Mean change from baseline for erosion/JSN/mTSS was 0.162/0.485/0.647 in SC-TCZM and 0.124/0.238/0.362 in SC-TCZC respectively; changes relative to baseline and between subgroups were not significant ($p>0.05$). Mean changes from baseline in MRI erosion/cartilage loss/synovitis/osteitis were 0.794/0.0882/-1.56/-2.88 for SC-TCZM and 0.955/0.1439/-1.68/-3.77 for SC-TCZC. Change from baseline for each MRI measure within SC-TCZC was significant ($p<0.05$); however no significant differences were observed between the 2 subgroups ($p>0.1$). At 24 weeks, decrease in DAS28 from baseline was significant for both subgroups (p=0.004 for SC-TCZC; $p<0.0001$ for SC-TCZM); however no significance was observed between subgroups (p=0.3). The proportion of pts achieving DAS28 remission (<2.6) over 24 weeks ranged from 65% for SC-TCZC to 89% for SC-TCZM. 3 pts reported serious adverse events, asthma, anaemia and Weber B Ankle Fracture; deemed unrelated to study medication.
**Conclusions:** There was no significant radiographic progression during the study period across groups. Mean changes in MRI variables were not significant in SC-TZM. MRI changes in SC-TCZC were significant for joint damage progression, as well as regression of synovitis and osteitis.

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None declared, R. Barrett Employee of: Roche Products, Pty. Ltd, P. Button Employee of: Roche Products, Pty. Ltd
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## AB0369 COMPARATIVE EFFECTIVENESS ABATACEPT, ADALIMUMAB AND RITUXIMAB IN PATIENTS WITH LONG-STANDING RHEUMATOID ARTHRITIS IN A REAL-LIFE SETTING

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**Background:** Clinical response in patients with rheumatoid arthritis (RA) using biologics is well-known. However, there is no direct comparison between biologics in cohorts of patients with long-standing RA in real-life settings, which could have implications in treatment decisions and health economics.
**Objectives:** The aim of this study was to describe a direct comparison in effectiveness between three different biological agents in their mechanism of action and its application in patients with long-standing RA in a cohort of real-life.
**Methods:** A descriptive retrospective study was performed. Were included 242 patients with at least 12 visits to rheumatologist in last 24 months. Clinical follow-up was according to DAS28: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it. We divided patients in two groups: remission-low disease activity (Rem/LDA) patients and moderate-severe disease activity (MDA/SDA) patients and the aim of the study was to analyze of patients who were in MDA/SDA disease activity how many reached a Rem/LDA status. Patients with diagnosis of RA and using Abatacept, Adalimumab and Rituximab were involved. Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson's statistics.
**Results:** 242 patients were included, 201 (83%) women and 41 (17%) men. Mean age was 58±10 years; patients with RA and using Abatacept, Adalimumab and Rituximab were involved and treatments were distributed as follows: Abatacept 72 (30%), Adalimumab 96 (40%) and Rituximab 74 (30%); At 24 months was observed an increase in percentage of patients in Rem/LDA and a decrease in percentage of patients in MDA/SDA disease activity statistically significant. For Abatacept at beginning the mean DAS28–3.8 and 24 months later DAS28–2.7; for Adalimumab at beginning the mean DAS28–3.2 and 24 months later DAS28–2.6; for Rituximab at beginning the mean DAS28–3.7 and 24 months later DAS28–2.5; although the HAQ reduction had clinical relevance there was no statistically significance. Between these biologics were not differences statistically significant in effectiveness. A very important issue was that at the end of the follow-up there was no patients in severe disease activity.

DISEASE ACTIVITY (DA) AT BEGINNING (AB) AND 24 MONTHS LATER (24 ML)

| | Remission AB n(%) | Remission 24 ML n(%) | Low DA AB n(%) | Low DA 24 ML n(%) | Moderate AB n(%) | Moderate 24 ML n(%) | Severe AB n(%) | Severe 24 ML n(%) |
|---|---|---|---|---|---|---|---|---|
| Abatacept | 20 (30) | 21(27) | 11 (15) | 25 (35) | 25 (34) | 27(38) | 15 (21) | 0 (0) |
| Adalimumab | 44 (46) | 45 (47) | 13(13) | 34 (35) | 27(28) | 18 (19) | 11(12) | 0(0) |
| Rituximab | 17 (23) | 21(29) | 10 (14) | 29 (39) | 30(40) | 24 (32) | 17(23) | 0(0) |

**Conclusions:** Study shows no significant differences in effectiveness between three different biological agents in their mechanism of action and its application analyzed, but there was a clear improvement in all patients with respect to basal disease activity, which proves effectiveness of implementation of a T2T strategy in patients with long-standing RA independent of biological.
**Disclosure of Interest:** None declared
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## AB0370 REAL LIFE EXPERIENCE WITH ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM A REGIONAL CENTRE IN UK

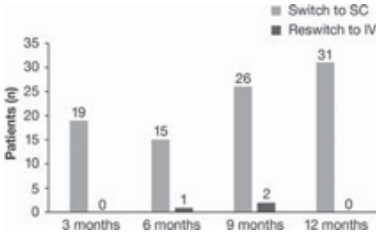
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**Background:** Abatacept is a biologic option for patient with Rheumatoid arthritis who have not responded to conventional disease modifying drugs as well as to TNF alpha inhibitors. It has been approved by the National Institute of Health and Clinical Excellence in UK.
**Objectives:** We share our experience with Abatacept in patients with Rheumatoid arthritis (RA) in routine clinical practice focussing on clinical response, disease remission and drug survival.
**Methods:** A retrospective analysis of RA patients on Abatacept from November 2012 to November 2014 was performed. Data collected included baseline demographics, number of previous synthetic and biologic DMARDs (Disease modifying drugs), baseline DAS 28 (Disease activity score) and change in DAS28 at 6 months.
**Results:** Total patients: 138 (100 females and 38 males, F: M ratio 2.63:1). Mean age of population was 63 years. Mean disease duration prior to abatacept was 12.8 years. Mean number of conventional DMARDs used before abatacept were 3.1 and biological DMARDs were 1.8. Abatacept was the first biological therapy used in 10 (7.2%) patients. At last follow up 59 (42.8%) and 57 (41.3%) patients were on intravenous and subcutaneous abatacept.
Mean DAS score before starting abatacept 5.89. Clinical response with a change in DAS 28 >1.2 was seen in 76% patients on Abatacept at 6 months. 15.9% Abatacept patients achieved remission at 6 months. 22 (15.9%) patients discontinued abatacept. Drug survival over 6 months was seen in 102 (73.9%) patients.
**Conclusions:** Abatacept showed response rate of 76% similar to reported in literature. Drug survival beyond 24 weeks was higher compared to other studies. Abatacept is safe, well tolerated and clinically effective in RA patients in real life.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6154

## AB0371 IS SWITCHING FROM IV TO SC ABATACEPT THERAPY SUSTAINABLE IN THE REAL WORLD? 1-YEAR ANALYSIS OF THE PROSPECTIVE, INTERNATIONAL ACTION STUDY

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**Background:** Open-label clinical trials have shown that patients with RA can switch from IV to SC abatacept therapy with no efficacy loss or safety concerns;[1,2] however, findings from single-centre, real-world studies are unclear.[3,4]
**Objectives:** To examine characteristics at baseline and before switching, and reasons for switching, in patients who switched from IV to SC abatacept in the real-world ACTION study.
**Methods:** ACTION is a 2-year, prospective, observational study of patients with moderate-to-severe RA who initiated IV abatacept across Europe and Canada. Enrolment periods: May 2008–Dec 2010 (biologic naïve or failed prior biologics); Sept 2010–Dec 2013 (biologic naïve); Oct 2011–Dec 2013 (failed prior biologics). This was an interim analysis of 1-year data. Assessments: baseline characteristics; reasons for switching; efficacy at the time of switch measured by EULAR response, DAS28 (ESR), DAS28 (CRP), CDAI and SDAI.
**Results:** 2364 patients were enrolled and 2350 were evaluable. A total of 91 patients (3.9%) switched from IV to SC abatacept during their first study year: 19 were biologic naïve and 72 had failed prior biologics at study entry. Compared with non-switchers, the switch group had numerically higher percentages of patients with BMI ≥35 kg/m$^2$, ≥1 co-morbidity and ≥2 prior anti-TNF failures, and lower mean disease activity, at baseline. Most patients (62.6%) who switched did so after >6 months in the study (Figure). Reasons for switching from IV to SC abatacept were available for 86 patients (94.5%; some patients had >1 reason): patient wish (53.5%), physician's preference (24.4%), safety (9.3%), poor compliance (4.7%), efficacy (2.3%), remission (2.3%), surgery (1.2%) and other (16.3%). Only 3/91 (3.3%) patients re-switched to IV abatacept; reasons were: patient wish, safety, efficacy (1 patient each). Prior to switching to SC abatacept, 64% of patients had a good/moderate EULAR response. According to mean (SD) values, disease activity before switching was moderate: DAS28 (ESR) 3.85 (1.09), DAS28 (CRP) 3.46 (1.07), CDAI 12.49 (7.70) and SDAI 13.6 (8.13).




**Conclusions:** Few patients switched from IV to SC abatacept and most who did so switched after >6 months allowing them to first achieve stable disease activity. Switching from IV to SC abatacept was primarily driven by patient or physician preference for the SC formulation. The very low rate of return to IV (3.3%) suggests that switching from IV to SC abatacept had no adverse clinical impact.
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**Disclosure of Interest:** R. Alten Grant/research support from: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, H. Nüßlein Consultant for: Bristol-Myers Squibb, AbbVie, Celgene,

Chugai, UCB, Pfizer, MSD, Novartis, Roche, Speakers bureau: Bristol-Myers Squibb, AbbVie, Celgene, Chugai, UCB, Pfizer, MSD, Novartis, Roche, M. Galeazzi: None declared, H. M. Lorenz Consultant for: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, Sobi, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, Speakers bureau: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, Sobi, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, X. Mariette Grant/research support from: Biogen, GSK, Pfizer, Speakers bureau: Bristol-Myers Squibb, GSK, Pfizer, sanofi, UCB, A. Cantagrel Grant/research support from: UCB, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Chugai, Lilly, MSD, Novartis, Pfizer, Roche, M. Chartier Consultant for: Bristol-Myers Squibb, Y. Elbez Employee of: Bristol-Myers Squibb, C. Rauch Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Le Bars Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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## AB0372 TREATMENT TO TARGET FOLLOWING INITIATION OF TREATMENT WITH RITUXIMAB IN RHEUMATOID ARTHRITIS: REAL LIFE EXPERIENCE

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**Background:** Rituximab (RTX) is an effective and relatively safe treatment for rheumatoid arthritis (RA). Following treatment initiation there is still controversy on how best to optimise further retreatment while limiting risks of cumulative immunosuppression and cost. There is evidence that retreatment at 6 months in patients with initial response but still have active disease can lead to further improvement[1,2].
**Objectives:** Evaluate how often is retreatment with RTX at 6 months associated with further improvement in disease activity in patients with RA that responded to 1 cycle of RTX.
**Methods:** Retrospective study of patients in the UCLH/UCL cohort:RA patients retreated with RTX (2x1000mg) at 6 months for improvement of initial response were selected and divided into 2 groups:patients that improved further (group A), and patients that did not (group B). Clinical and laboratorial data were assessed.
**Results:** Out of 40 selected patients, 32 (80%) improved further while 8 (20%) did not. Median age was 54 years with median disease duration (MDD) of 13 years in group A, and 51 years with 19 years MDD in group B. In both groups:75% were female, more than 87% were seropositive and more than 75% anti-cyclic citrullinated peptide antibody positive. In group A:10 received RTX alone, 11 with Methotrexate (MTX), 4 MTX and prednisolone, and 7 other immunosuppressants/immunomodulators. In group B:3 received RTX alone, 4 with MTX, and 1 with Etanercept. At baseline, group A presented a mean swollen joint count (mSJC) of 7.81, mean tender joint count (mTJC) 15.56, mean erythrocyte sedimentation rate (mESR) 41.5 and mean C-reactive protein (mCRP) 25.5, giving a median baseline DAS28 of 6.13 (IQ 5.23–7.21). Group B recorded:mSJC of 8.5, mTJC 16.9, mESR 44.25, mCRP 42.25, giving a median DAS28 of 6.49 (IQ 5.32–7.6). After the 1st RTX cycle group A recorded a median DAS28 decrease of 1.83 (IQ 1.11–2.5):4 (12%) achieving low disease activity, 22 (69%) moderate activity and 6 (19%) still high activity scores. While group B also presented improvement, the decrease in DAS28 was only a median of 1.07 (IQ 0.76–1.94): 1 patient (13%) achieving remission,2 (25%) moderate activity and 5 (62%) remaining with high disease activity. After the 2nd RTX cycle,in group A median DAS28 decreased a further 0.6 (IQ-0.12–1.3): 11 (35%) achieving remission or low disease activity, 19 (59%) moderate activity and 2 (6%) remaining with high disease scores. In group B DAS28 recorded a median decrease of 0.04 (IQ 0.72–0.67): 6 (75%) presenting high disease scores, 2 (25%) moderate and none remission or low disease activity.
**Conclusions:** Not all patients treated with RTX will achieve remission or low disease activity, but the majority that improve after 1 RTX cycle will improve even further after a 2nd cycle[1,2]. In our group 80% of patients improved further after a 2nd RTX cycle, with more than a third achieving remission or low disease activity and more than half moderate activity. There was a suggestion that patients who responded less well to their 1st cycle were less likely to improve further
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4989

## AB0373 DOSE RESPONSE MODELING IS A USEFUL TOOL TO DETERMINE DOSES FOR PHASE 3: EXPERIENCE FROM OLOKIZUMAB

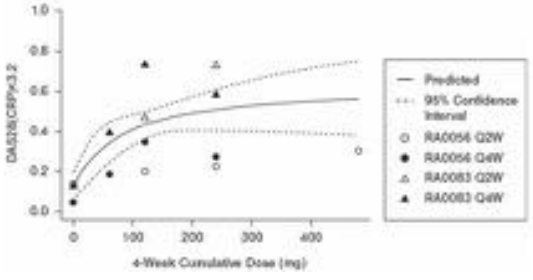
R. Reeve[1], A. Krotkova[2], D. Weilert[3], S. Fatenejad[4]. *[1]Quintiles Inc., Durham, United States; [2]R-Pharm CJSC, Moscow, Russian Federation; [3]Quintiles Inc., Kansas City; [4]Fatenejad Consultancy, Miami, United States*

**Background:** Olokizumab (OKZ) is an anti-interleukin-6 (IL-6) monoclonal antibody in development for the treatment of rheumatoid arthritis (RA). In phase 2 studies, treatment with OKZ+MTX resulted in significant improvements in disease activity compared to placebo (PBO)+MTX.[1,2] Here, we used dose-response modeling based on efficacy and safety data from phase 2 to determine the most appropriate OKZ doses for phase 3 development. This modeling approach utilizes all available data, and ensures that the decision is scientifically-based.
**Objectives:** To test the dose-response relationship of OKZ with clinical efficacy and safety, and identify the optimal doses for phase 3.
**Methods:** The nonparametric Jonkheere-Terpstra (JT) test was fitted to DAS28(CRP) data obtained from two double-blind, randomized, phase 2 dose-ranging (60 to 480mg 4-week cumulative dose [cd]) studies (RA0056 [NCT01242488] and RA0083 [NCT01463059]) to test for a monotonic dose-response curve without any assumptions on curve shape. The JT tests indicated that a dose-response model was statistically significant, allowing the Hill parametric model to be used, with study as a categorical covariate that affected both the $ED_{50}$ and $E_{max}$ parameters. Mean and 95% confidence intervals for the response were calculated. The Hill model was used since it fit the data adequately, and allowed estimation of the response curves using all available information. To select an appropriate dose, safety as well as efficacy must be included, and a balance between the two achieved. Thus, a dose-response model for the incidence of adverse events (AEs) was also required. A logistic regression model was fitted to the 17 most commonly observed preferred terms across pooled phase 2 data.
**Results:** The JT test indicated a statistically significant monotonic dose-response relationship: $p<0.005$ for all dosing regimens (every 2 weeks [wks; Q2W] and every 4 wks [Q4W]) in each study, and across pooled data from the two studies. Categorical DAS28(CRP) endpoints also indicated a monotonic dose-response relationship (Table). A parametric dose-response curve fitted using a Hill model[3] to combined data from the studies (Figure) adequately described the data, with an inflection point of 120mg 4-wk cd. This is the smallest dose that attains a response near the maximum. Dosing frequency had a small, non-statistically significant effect on categorical DAS28(CRP) response.
Logistic regression analysis of AEs did not indicate any evidence of a dose-related increase in AEs examined vs PBO+MTX, with the exception of injection site reaction.

**Table:** Probability of a monotonic dose-response relationship, based on the Jonkheere-Terpstra test

| Categorical endpoint | Dosing frequency | JT p-value |
|---|---|---|
| DAS28(CRP) < 2.6 | Q4W | 0.0001 |
| DAS28(CRP) < 2.6 | Q2W | 0.0003 |
| DAS28(CRP) < 3.2 | Q4W | <0.0001 |
| DAS28(CRP) < 3.2 | Q2W | 0.0020 |

**Figure:** Model for proportion of patients with DAS28(CRP)<3.2 at Week 12 as a function of 4-week cumulative dose, based on the Hill model




**Conclusions:** Efficacy increased with dose, without an increase in safety events, and plateaued at approximately 120mg cd. Modeling data were robust, with comparable results for individual studies vs pooled data, and continuous vs categorical responses. Thus a dose at the inflection point (128mg 4-wk cd given as 64mg Q2W) and a dose below the inflection point (64mg 4-wk cd) were selected for inclusion in the phase 3 program.
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**Acknowledgement:** The authors acknowledge Costello Medical Consulting and ELM Group for medical writing and editorial assistance, funded by R-Pharm CJSC.
**Disclosure of Interest:** R. Reeve Employee of: Quintiles Inc, A. Krotkova Employee of: R-Pharm CJSC, D. Weilert Employee of: Quintiles Inc, S. Fatenejad Consultant for: R-Pharm

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## AB0374 ANALYSIS OF SPACING OF THE INTRAVENOUS ADMINISTRATION OF TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Although the biologic disease modified anti rheumatic drugs (bDMARDs) are the most effective treatment of rheumatoid arthritis (RA), the costs are much higher than those of conventional synthetic DMARDs (csDMARDs). A number of studies on discontinuation, dose reduction or spacing of bDMARDs have been performed, but there is almost no report of the spacing of tocilizumab (TCZ) so far.
**Objectives:** To analyze the efficacy of spacing of the intravenous (iv) administration of TCZ in patients with RA.
**Methods:** Enrolled were 63 patients (11 male, 52 female) who were administrated iv TCZ for more than 1 year. Eleven patients had shifted to subcutaneous injection and the data at the last iv infusion were analyzed.
**Results:** Mean age was 57.4 years old (30–78), mean body weight was 55.5kg (37–85.5), mean duration of illness was 10.7years (0–32), Steinbrocker's Stage were 4/12/20/27, Class were 0/41/22/0, and the number of the former biologics were 0.9 (0–3), and duration of TCZ was 46.9 months (13–83). The intervals of administration were 4 weeks: 28.6%, 5 weeks: 38.1%, 6 weeks: 17.5%, 7 weeks: 6.0%, 8 weeks: 7.9%, 10 weeks: 1.6%. Tender joint count, swollen joint count, erythrocyte sedimentation rate (ESR), C-reactive protein, matrix metalloproteinase-3, patient's visual analogue scale (VAS), doctor's VAS, disease activity score (DAS) 28-ESR, simplified disease activity index (SDAI), and clinical DAI (CDAI) were significantly ameliorated. The remission rats were DAS28-ESR 90.5%, CDAI 44.4%, SDAI 42.9%, respectively. The number of patients with prednisolone (PSL) wer decreased from 50 patients at the initiating TCZ treatment to 38 patients ($p=0.031$), 4.2 (0–10) to 1.7 (0–5) mg/day ($p<0.0001$). Methotrexate (MTX) were used in 46 to 32 patients ($p=0.017$), 6.0 (0–18) to 3.3 (0–14) mg/weeks ($p<0.0001$). There were no changes in the usage of other csDMARDs.
**Conclusions:** Spacing of the TCZ administration were done in 71.4% of the patients,even though it significantly reduced disease activity and reduced PSL and MTX. TCZ is the most inexpensive bDMARDs in Japan, but with spacing, it is possible to reduce more cost with a good control of RA. Further study of the analysis of the prevention of joint destruction by spacing is necessary.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2417

## AB0375 BIOSIMILARS IN RHEUMATOLOGY CLINICAL PRACTICE-GAINING ACCEPTANCE IN DEVELOPING WORLD-EXPERIENCE FROM SOUTH INDIA

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**Background:** Biologic disease modifying anti-rheumatic drugs (DMARD) have revolutionized the management of several rheumatic disorders. A decade of experience in the west has gained insights in to the safety and efficacy of these cytokine inhibitors in inflammatory rheumatological disorders. However, the access to biologics has been restricted by the cost, in the developing world.
Bio-similars [(1)] have been developed in the Far East including India and the efficacy and safety have been comparable to their reference products, with affordable cost, with huge benefit to the patients.
**Objectives:** To review the use of synthetic DMARDs- Biosimilars in two centres of Rheumatology in south India and assess the efficacy/safety profile among the patients.
**Methods:** All Biologic users for a period of one year in the Rheumatology centre in Velammal Medical College Hospital, Madurai and Aruna Hospitals, Tirunelveli were reviewed (Oct 14-Oct 15). All patients should satisfy ACR criteria for diagnosis and would have failed classic DMARDs. They were all screened for TB, Hepatitis as per UK-NICE guidelines. All had 3 months review and are under regular follow up.
**Results:** Data from 15 patients were collected in this retrospective review. (Indications below)

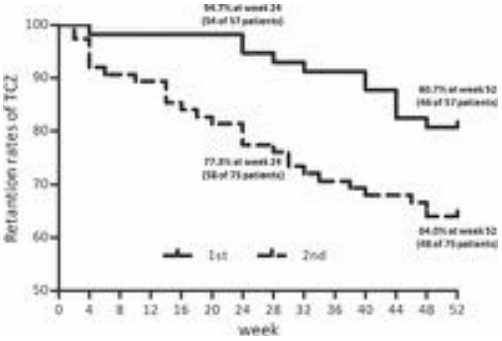
| Indications | No. of patients | Bio similar drug |
|---|---|---|
| Rheumatoid arthritis | 7 (6+1) | Intacept and Ritux (1) |
| Spondyloarthritis | 5 | Exemptia |
| SLE | 1 | Mabtas |
| ANCA associated vasculitis | 1 | Ritux RA |
| Psoriatic arthritis (but CCP positive) | 1 | Exemptia |

All 7 patients with RA were Bio-naive, received the biosynthetic DMARDS and achieved remission in 3 months. Pre treatment average DAS score was 5.65 and 3 months following treatment, the average DAS 28 score was 2.01, which shows significant improvement. The girl with SLE has responded dramatically following Mabtas therapy. In the Spondyloarthropathy group, all but one had spinal disease only. Pre treatment average BASDAI was 6.64 and 3 months following biosimilars BASDAI was 2.6. To date no infective complications were reported. All are maintained on oral DMARDS either Methotrexate or Leflunomide without steroids.
**Conclusions:** Biosimilars have been developed in the developing world with affordable cost. They are increasingly being used in different complex inflammatory rheumatologic diseases. It has gained reasonable acceptance. The rheumatologist should be aware of safety and use in a diligent manner.
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**Acknowledgement:** Special thanks to all the patients and The Velammal hospital rheumatology and medicine team.
**Disclosure of Interest:** None declared
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## AB0376 RETENTION RATES AND CLINICAL EFFICACY OF TOCILIZUMAB AS FIRST-LINE BIOLOGICS COMPARED TO SECOND-LINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** To date, biologic disease-modifying anti-rheumatic drugs (bDMARDs) targeting cytokines such as tumor necrosis factor (TNF)-$\alpha$ or interleukin (IL)-6 have been established as a standard therapy for rheumatoid arthritis (RA) patients with insufficient responses to conventional synthetic DMARDs such as methotrexate (MTX). The IL-6 receptor blocking monoclonal antibody, tocilizumab, is included as one of the first-line bDMARD in the latest European League against Rheumatism (EULAR) recommendations [1]. However, there has been few data as the retention rates of tocilizumab.
**Objectives:** This study aimed to investigate the retention rates and clinical efficacy of tocilizumab as first-line bDMARD compared with second-line treatment in patients with RA.
**Methods:** This is a retrospective study. All RA patients who treated with tocilizumab were included this analysis. These patients were divided into two groups. In the first group, tocilizumab was used as a first-line bDMARDs (1st group). Patients in the other group received tocilizumab as a second-line or more treatment (2nd group). Retention rates and clinical efficacy assessed by disease activity score in 28 joints (DAS28; on the basis of the erythrocyte sedimentation rate, ESR) and clinical disease activity index (CDAI) from week 0 to week 52 were assessed. The discontinuation ratio of glucocorticoid and MTX was also evaluated. Moreover, the effect of tocilizumab for bone was assessed by bone mineral density (BMD) of lumber spine and hip, and bone metabolic marker (BMM) of urinary type I collagen cross-linked N-telopeptide (NTX) and bone-specific alkaline phosphatase (BAP).
**Results:** Fifty-seven patients in 1st group and 75 patients in 2nd group were analyzed in this study. Retention ratio at week 24 and 52 was 94.7 and 80.7% in 1st group and 77.3 and 64.0% in 2nd group, respectively. Of 11 discontinued patients in 1st group, only 2 patients were withdrawal due to inadequate response. DAS28 remission rates were 17.4, 45.7, 50.0, 41.3 and 39.1% in 1st group and 8.3, 22.9, 29.2, 33.3 and 37.5% in 2nd group at week 4, 12, 24, 36 and 52, respectively. CDAI remission rates were 8.7, 10.9, 13.0, 23.9 and 15.2% in 1st group and 0, 6.3, 10.4, 14.6 and 10.4% in 2nd group at week 4, 12, 24, 36 and 52, respectively. The dose of MTX was reduced in 11 patients and MTX was withdrawal in 4 patients among 34 patients of 1st group using MTX at week 0. The dose of glucocorticoid was reduced in 16 patients and glucocorticoid was withdrawal in 10 patients among 20 patients of 1st group using glucocorticoid at week 0. BMM was not significantly changed and BMD was kept in both groups.




**Conclusions:** High retention rates and clinical efficacy of tocilizumab as first-line biologic treatment was found in retrospective research. Moreover, dose reduction and withdrawal of MTX or glucocorticoid was achieved in some patients with tocilizumab.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.1871

## AB0377 DIFFERENCES IN BASELINE PREDICTIVE FACTORS FOR REMISSION AT 52 WEEKS BY CONCOMITANT MTX USE DURING TOCILIZUMAB TREATMENT USING PROPENSITY SCORE MATCHED GROUPS

T. Kojima[1], S. Asai[1], N. Takahashi[1], Y. Yabe[2], Y. Hirano[3], Y. Kanayama[4], A. Kaneko[5], T. Takemoto[1], N. Asai[1], T. Watanabe[1], K. Funahashi[1], M. Hayashi[6], N. Ishiguro[1] on behalf of TBCR Study Group. *[1]Orthopedic Surgery, Nagoya University Hospital, Nagoya; [2]Rheumatology, JCHO Tokyo-Shinjyuku Medical Center, Tokyo; [3]Rheumatology, Toyohashi Municipal Hospital, Toyohashi; [4]Rheumatology, Toyota Kosei Hospital, Toyota; [5]Orthopedic Surgery, Nagoya Medical Center, Nagoya; [6]Rheumatology, Nagano Red Cross Hospital, Nagano, Japan*

**Background:** In the treatment of rheumatoid arthritis, concomitant use of methotrexate (MTX) should be a critical factor for decision of treatment now. Tocilizumab, IL-6 receptor antibody has been reported to have good efficacy even without concomitant MTX in clinical trials and observational study. However, there is an important clinical question that concomitant MTX use could have any impacts on predictive factors of achievement of good clinical goal.

**Objectives:** To explore the differences in predictive factor for achievement of remission by concomitant MTX use during TCZ treatment. In observational study, it is important to match background of the patients for comparison. We used propensity score matching, which is useful statistical tool for comparison in clinical practice.

**Methods:** This study included 240 RA patients who received TCZ (concomitant MTX use: MTX(+) 117: no use: MTX(–) 123) in the multicenter observational cohort (Tsurumai Biologics Communication Registry; TBCR, 2827cases treated with biologics were registered until 2014). We prepared matched groups by concomitant MTX use using propensity score (matched factors, age, sex, previous biologics use, glucocorticoid use, Steinbrocker stage and class, disease duration, DAS28 at baseline). We determined the baseline predictive factors for remission (DAS28) at week 52 by the matched groups using multivariate logistic regression analysis. Especially, association of DAS28 at baseline to achievement of remission was compared using area under the curve (AUC) of ROC curve.

**Results:** Sixty-nine patients were matched between groups. Baseline characteristics were shown in Table 1. Rate of remission was 55.2% in MTX(+) group and 44.8% in MTX(–) group (p=0.39). Independent predictive factors at baseline for remission were disease duration [OR:0.90, 95%CI (0.83–0.97)] in MTX(+) group while DAS [OR:0.49, 95%CI (0.29–0.83)] in MTX(–) group based on multivariate analysis. We also showed significant difference in association of DAS at baseline to remission between groups using AUC of ROC curve (AUC 0.59 vs 0.73, Fig. 1). Interestingly, after matching baseline characteristics, achievement of remission in MTX(–) group depended on disease activity at baseline while that in MTX(+) group did not. The cut-off value of DAS28 at baseline for achievement of remission was 4.87 (sensitivity 0.61, specificity 0.84) in MTX(–) group.

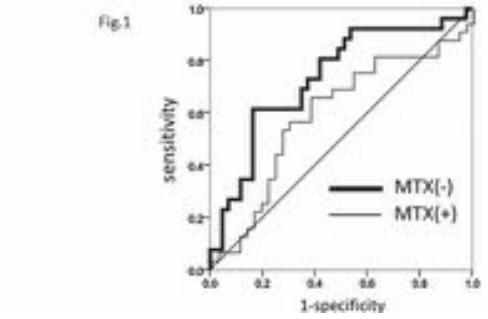
**Conclusions:** There is significant difference in baseline predictive factors for good clinical results by concomitant MTX use during TCZ treatment. The results should be taken into consideration to predict clinical response in clinical practice.

**Disclosure of Interest:** T. Kojima Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, AbbVie, Bristol-Myers Squibb, and Pfizer, Janssenn Pharmaceutical Companies, Astellas Pharma and Chugai Pharma., S. Asai: None declared, N. Takahashi Speakers bureau: Abbvie Japan Co. Ltd, Eisai Co. Ltd, UCB Japan Co. Ltd, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Company Ltd, Pfizer Co. Ltd, Chugai Pharmaceutical Co. Ltd, Janssen

Table 1. Baseline characteristics of patients by concomitant and no concomitant use of methotrexate with tocilizumab.

| | | | Before matching | | | | After matching | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Concomitant MTX | No concomitant MTX | | | Concomitant MTX | No concomitant MTX | | | |
| Variables | | | n=117 | n=123 | p-value | | n=69 | n=69 | p-value | | |
| Age (years) | Mean | (SD) | 56.8 | (12.4) | 59.2 | (13.0) | 0.19 | 58.8 | (13.0) | 59 | (14.9) | 0.93 |
| Male | n | (%) | 18 | (15.5) | 28 | (22.8) | 0.12 | 11 | (15.9) | 11 | (15.9) | 1 |
| Disease duration (years) | Median | (IQR) | 7.3 | (3.5-14.8) | 8.7 | (3.8-14.2) | 0.91 | 9.6 | (4.8-16.4) | 9.4 | (4.2-15.8) | 0.39 |
| Steinbrocker Stage I–II | n | (%) | 42 | (35.9) | 46 | (37.4) | 0.82 | 42 | (60.2) | 38 | (55.1) | 0.49 |
| Steinbrocker Class I–II | n | (%) | 79 | (67.5) | 84 | (52.0) | 0.02 | 37 | (53.6) | 43 | (62.3) | 0.47 |
| Previous biologics | n | (%) | 86 | (73.5) | 77 | (62.6) | 0.07 | 48 | (69.6) | 46 | (66.7) | 0.86 |
| Concomitant GC | n | (%) | 86 | (73.5) | 78 | (63.4) | 0.09 | 52 | (75.4) | 50 | (72.5) | 0.85 |
| DAS28 | Mean | (SD) | 5.5 | (1.2) | 5.8 | (1.3) | 0.09 | 5.7 | (1.09) | 5.5 | (1.27) | 0.35 |

MTX, methotrexate, GC, glucocorticoid.




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## AB0378 IMPROVEMENTS IN MEASURES OF WORK PRODUCTIVITY/INTERFERENCE AND GENERAL HEALTH STATUS WITH SIRUKUMAB TREATMENT IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE DISEASE-MODIFYING ANTI-RHEUMATIC DRUG TREATMENT

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**Background:** Treatment-related improvements in the ability to perform work and general health status are key outcomes from the perspective of a patient with rheumatoid arthritis (RA). Sirukumab is a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity and is under development for RA and other diseases.

**Objectives:** To evaluate the effects of sirukumab on work productivity/interference and general health status in patients with active RA refractory to conventional, synthetic disease-modifying anti-rheumatic drugs (DMARDs).

**Methods:** In a randomized, double-blind, Phase 3 global study, patients with active RA and inadequate response to DMARDs were randomly assigned (1:1:1) to treatment with sirukumab SC 50 mg q4w, sirukumab SC 100 mg q2w, or placebo SC q2w. Patients on placebo with insufficient (<20%) improvement at Weeks 18 or 40 or who remained on placebo at Week 52 were re-randomized to receive treatment in 1 of the 2 sirukumab groups. The Work Limitations Questionnaire (WLQ) was used to evaluate health-related job limitations and productivity loss. The 3-level EuroQol-5 Dimension (EQ-5D) questionnaire was used to measure 5 dimensions of health status (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression). The changes from baseline in the WLQ scores, EQ-5D index score (based on UK TTO), and EQ-5D health state visual analog scale (VAS) scores at Weeks 24 and 52 were evaluated as secondary endpoints.

**Results:** Mean WLQ production loss scores improved significantly from baseline for both sirukumab 50 mg q4w and 100 mg q2w compared with placebo at Weeks 24 and 52 (all $P<0.001$). In addition, significantly greater improvements from baseline were also observed in all 4 mean WLQ domain scores (mental-interpersonal, output, physical demands, time management) for both doses of sirukumab compared with placebo at Weeks 24 and 52 (all $P<0.05$). Both the mean EQ-5D index and health state VAS improved significantly from baseline with both sirukumab doses compared with placebo at Weeks 24 and 52 (all $P\leq0.002$).

Table 1. Mean (SD) change from baseline in WLQ and EQ-5D scores at week 52[a]

| Outcome | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w |
|---|---|---|---|
| *WLQ* | *(n=227)* | *(n=223)* | *(n=221)* |
| Production loss (total) score | –0.73 (5.03) | –3.06 (4.53)[b] | –2.94 (4.39)[b] |
| Domain scores | | | |
| Mental-interpersonal | –1.39 (21.09) | –8.45 (19.23)[b] | –8.69 (19.37)[b] |
| Output | –2.47 (24.17) | –12.39 (23.03)[b] | –12.18 (22.38)[b] |
| Physical demands | –4.70 (23.29) | –12.91 (22.27)[b] | –8.70 (21.00)[c] |
| Time management | –5.75 (25.52) | –16.54 (24.41)[b] | –16.38 (23.79)[b] |
| *EQ-5D* | *(n=556)* | *(n=557)* | *(n=557)* |
| Index[d] | 0.13 (0.34) | 0.20 (0.33)[b] | 0.20 (0.33)[b] |
| Health state VAS | 8.30 (26.14) | 16.80 (28.60)[b] | 17.14 (28.33)[b] |

[a]n values are based on initial treatment assignment and varied slightly for WLQ domain scores. [b]$P<0.001$. [c]$P=0.047$. [d]Based on UK TTO.

**Conclusions:** In patients with active RA refractory to DMARDs, sirukumab treatment was associated with significant improvements in work-related productivity and general health status, consistent with disease improvement demonstrated with sirukumab treatment.

**Disclosure of Interest:** T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahikasei Pharma Corp., and Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., and Asahi Kasei Medical K.K.,abbivie GK, Daiichi Sankyo Co.,Ltd., Bristol–Myers K.K., Nipponkayaku Co.Ltd., Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co,. Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Astellas Pharma, and Diaichi Sankyo Co., Ltd., Celtrion, Nipponkayaku Co. Ltd, G. Karpouzas: None declared, C. Thorne Grant/research support from: Abbvie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant for: Abbvie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: Medexus/Medac, K. McQuarrie Employee of: Janssen Research & Development, LLC, S. Sheng Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, W. Xu Employee of: Janssen Research & Development, LLC, S. Peterson Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, C. Han Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, K. Fei Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC

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## AB0379 TAPERING OR STOPPING OF METHOTREXATE IN NON-TUMOR NECROSIS FACTOR THERAPY (TOCILIZUMAB AND ABATACEPT) IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Non-tumor necrosis factor (TNF) agents, such as tocilizumab (TCZ) and abatacept (ABT), were widely used in the treatment of rheumatoid arthritis (RA). It seems that non-TNF agents are slightly different from anti-TNF agents in respect to dependency on methotrexate (MTX). Although MTX is a very important concomitant drug in anti-TNF therapy, MTX may not be so in non-TNF therapy for majority of patients. MTX have many severe adverse events (AE) such as interstitial pneumonia, severe infection, and myelosuppression. Tapering or stopping of MTX have been tried in our institute to avoid AE of MTX when RA patients treated with non-TNF agents reached at sustained remission. We report the preliminary results of MTX tapering in non-TNF therapy in this study.

**Objectives:** This retrospective study evaluated tapering or stopping of MTX in non-TNF therapy (TCZ and ABT) and impact of it to RA treatment in clinical practice.

**Methods:** 27 RA patients who initiated TCZ or ABT with concomitant MTX and continued non-TNF agents for 2 years were used. Time-course of disease activity (DAS28-CRP and CDAI), arthritis marker (serum MMP-3), activity of daily living (mHAQ), joint destruction ($\Delta$mTSS per a year) and tapering concomitant drug (MTX and prednisolone) were investigated. MTX was tapered depending on physicians decisions and stopped if possible.

**Results:** 20 females and 7 males with mean age of 60 years were used in this study. Mean RA duration was 11.8 years. TCZ was continued for 2 years in 16 cases and ABT in 11 cases. MTX of mean dosage of 9.0mg/week (4.0–16.0 mg/w) was prescribed in all patients at baseline. Mean DAS28-CRP was 4.57 at baseline, 2.26 at 1 year and 2.00 at 2 years. There were significant decreases not only from baseline to 1 years ($p<0.0001$) but also from 1 year to 2 years ($p=0.04$). Significant decrease and sustainment were also observed in CDAI, serum MMP-3 and mHAQ) (Fig. 1). Although $\Delta$mTSS at baseline was )10.0, it was significantly improved to 1.5 from baseline to 1 year ($p=0.0001$) and to 0.5 from 1 year to 2 years ($p<0.0001$). Mean MTX dosage was significantly decreased from 9.0mg/w at baseline to 4.8mg/w at 1 year ($p=0.0003$) and to 2.9mg/w at 2 years ($p<0.0001$). There was a significant difference of MTX dosage between at 1 year and 2 years ($p=0.049$). Although MTX was concomitant in all patients at baseline, it was used in only 66.7% at 1 year and only 40.7% at 2 year. Mean PSL was also tapered from 3.5mg/day at baseline to 1.2mg/d at 2 years (Fig. 2). Similar trends were observed in both patients treated with TCZ and ABT.

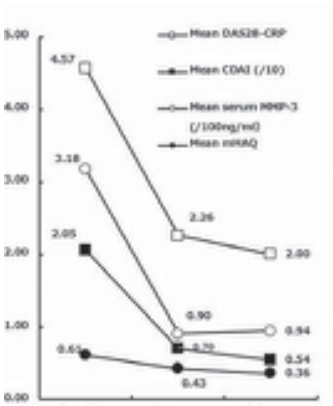



Fig1. Time courses of evaluated parameters

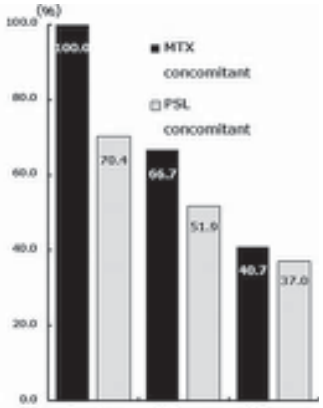



Fig2. Rates of concomitant MTX & PSL

**Conclusions:** This study suggested that concomitant MTX may be tapered or stopped in RA patients treated with TCZ or ABT and reached to sustained remission without worsening disease activity and joint destruction. Information of prospective large studies was necessary in the future.

**Disclosure of Interest:** None declared

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## AB0380 EXPERIENCE WITH RITUXIMAB IN THE MANAGEMENT OF RECURRENT TOCILIZUMAB INDUCED MACROPHAGE ACTIVATION SYNDROME IN AN ADULT PATIENT WITH SYSTEMIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS (STILL'S DISEASE)

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**Background:** Macrophage activation syndrome (MAS) is a potentially fatal complication of Still's disease (SD). The use of *biologic disease-modifying antirheumatic drugs* (bDMARDs) has significantly improved the prognosis in SD pts, although most recent reports on MAS linked to use of bDMARDs in SD patients raise certain concern.

**Objectives:** To share the experience from the use of bDMARD for management of MAS, induced by other bDMARDs in an adult patient with SD.

**Methods:** Description of a case of successful rituximab therapy for MAS, induced by tocilizumab in an adult SD patient.

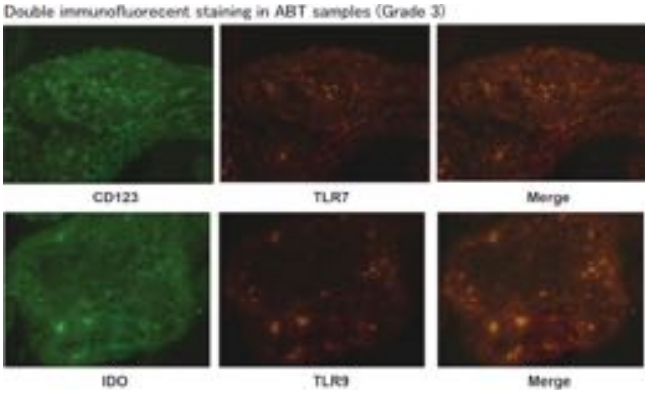
**Results:** In a patient Sh.,18 yo, the onset of SD occurred in December 2008y (at the age of 14 y.o.), manifesting with fever 39°C, arthralgia, lymphadenopathy, hepatosplenomegaly, neutrocytosis, maculopapular rash, ESR up to 40 mm/h, CRP 48 mg/L. Prednisone (50 mg/day) was discontinued shortly due to emergence of multiple duodenal ulcers (EFGDS), which resulted in increasing CRP up to 154 mg/L, anemia (nv-89 g/L), neutrocytosis up to $14{,}7x10^9$, elevated ALT and AST >120 EU/L, LDH 735 U/L, and ferritine >12000 μg/L. This condition progressed to tonic-clonic seizures and coma, leucopenia ($4{,}5x10^9$), and thrombocytopenia ($33x10^9$). MAS was documented. GCs were re-administered (prednisone 50 mg/day, methylpred pulse-therapy), sandimmun was also commenced at 200 mg/day dose. By 2013 y. the dose of prednisone was down-titrated to 2,5 mg/day and of sandimmun - to 100 mg/day. At this dose level a relapse of fever 38,5° C, arthralgia, pharyngalgia and rash on the forearms occurred. The dose of prednisone was up-titrated to 20 mg/day, but arthralgia and ubnormal lab parameters of active disease persisted (ferritine, CRP, ESR), necessitating administration of tocilizumab (8 mg/kg). But second infusion of tocilizumab caused severe adverse reaction (dyspnea, drop of BP, nausea, dizziness) with MAS reoccurrence (fever 39,5° C, thrombocytopenia, anemia, elevated liver

enzymes, ferritine, hypofibrinogenemia, hypertriglyceridemia), necessitating up-titration of methylpred dose up to 40 mg/day, pulse therapy with methylpred and dexamethasone, IVIG (2.5 g/kg total dose), SAMe. Associated pneumonia was successfully cured with antibiotics (CT verified). Rituximab 1000 mg was administered i/v by drop infusion, and repeated after 6 mo. Currently the patient does not voice any specific complaints, her lab parameters are constantly normal (remission), the methylpred dose was down-titrated to 4 mg/day.
**Conclusions:** Presented case, on one side, raises the appropriateness of updating the summary of product characteristics&directions for tocilizumab use in package circular/prescribing info, and on the other side, confirms the usefulness of rituximab for refractory Still's disease, complicated with MAS.
**Disclosure of Interest:** None declared
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### AB0381 EXPRESSION OF TOLL-LIKE RECEPTORS AND DISTRIBUTION OF IMMUNE-CELLS IN RHEUMATOID SYNOVIAL TISSUES OF THE PATIENTS TREATED BY ABATACEPT

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**Background:** Rheumatoid arthritis (RA) is a progressive chronic autoimmune and autoinflammatory disease affecting multiple joints simultaneously[1]. Abatacept (ABT) which is cytotoxic T-lymphocyte-associated protein (CTLA) 4-Ig agent is one of biologics[2].
**Objectives:** The aim of this study is to examine the effect of ABT for evaluating immune-reactive cells with toll-like receptors in the synovial tissue samples of RA patients with ABT therapy (ABT groups) compared to them with non-biological therapy (Non-BIO groups).
**Methods:** Synovial tissue samples of 20 RA (10 ABT and 10 Non-BIO samples) were immunohistochemically stained with TLR+ and immune-reactive cells including T cells (CD2), B cells (CD20), macrophage (CD68), conventional dendritic cells (cDC; S100, DC-LAMP), regulatory T cells (FoxP3) and indoleamine 2,3-dioxygenase+ cells (IDO). Positive cells were counted per 10 fields (x 200) by microscopy. TLR positive cells were analyzed by double Immunofluorescent methods with T cell, B cell, macrophage, cDC and plasmacytoid DC (pDC; CD123)-markers and IDO. Synovial inflammation was estimated by Krenn grading score.
**Results:** ABT and non-BIO group was shown the similar grading scores (2.3 vs 2.0), DAS28CRP4 (5.1 vs 4.3) and CRP (1.3 vs 0.9). IDO+ and FoxP3+ cells, not CD3+, CD20+ and CD68+ cells were correlated significant with DAS28CRP (4) in lymphoid aggregation in ABT groups ($p<0.01$). TLR immunoreactivity was also confirmed in pDCs and IDO+ cells by immunofluorescent staining (Fig. 1).




**Conclusions:** ABT was reported the similar remarkable effect with other biologics. We have already shown the residual inflammation of synovitis with TLR expressions in the RA patients who were received TNF-blockers[3]. TLR+ cells were observed with T cells and B cells related local inflammatory grading in ABT groups, however regulatory immune-cells might be increased and regulate inflammatory simultaneously. CTLA-4 and IDO was recently revealed the generation of osteoclast [4,5]. IDO+ cells increased in synovial tissues of ABT group compared to no-BIO group. ABT may not only regulate the immunosuppression but also suppress the activation of osteoclast in RA.
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## Rheumatoid arthritis - non-biologic treatment and small molecules

### AB0382 PREVENTION OF VENOUS THROMBOEMBOLISM (VTE) AFTER TOTAL KNEE REPLACEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** In this study, we analyzed incidences of VTE in patients with rheumatoid arthritis (RA) and osteoarthritis (OA) after total knee or hip arthroplasty, compared schemes of drug prevention and evaluated their efficiency.
**Objectives:** To evaluate the efficiency of prevention of VTE in patients with rheumatoid arthritis and osteoarthritis after total knee replacement under comparable conditions
**Methods:** We studied 151 patients operated in V.A. Nasonova Research Institute of Rheumatology for the period 2014–2015. Of these, 72 patients with RA (47.7%) and 79 patients with OA (52.3%). For a comparative analysis of the efficiency of anticoagulant therapy, each patient group was divided into 2 subgroups by type of drug therapy. The first - nadroparin calcium (the drug therapy was started for 12 hours after the operation at a dose of 0.1 ml per 10 kg of body weight one time per day), the second - nadroparin calcium with transfer to dabigatran etexilate (the first stage of 4 hours after the operation was started therapy by nadroparin calcium, and then after the removal of the epidural catheter moved to the dabigatran etexilate).Doppler ultrasonography (DUS) was routinely performed preoperatively and on postoperative day 7, 14, then 1 time a month for diagnosing a deep venous thrombosis (DVT). Time of observation was 6 months.
**Results:** VTE were reported in 6 (3.9%) patients, 1 of them (0.7%) with RA and 5 (3.3%) with OA. Distal deep vein thrombosis developed on 15 days after total knee replacement in RA patient. He received nadroparin calcium only. 4 patients with VTE after surgery from OA group used nadroparin calcium and 1 patient was on combined drug therapy. Of the 6 cases of VTE 4 (66.7%) were asymptomatic and 2 (33.3%) with development of clinical and laboratory picture. The case of thrombosis in a group of RA was asymptomatic. In a perioperative period of clinically significant bleeding was not seen.
**Conclusions:** Cases of VTE in patients with RA, despite the large number of risk factors, under comparable conditions is significantly lower than patients with OA. The number of asymptomatic deep vein thrombosis prevails over the development of clinical and laboratory complex of symptoms in both groups. In patients with RA and OA who were from the first group have reported 5 cases of VTE and only 1 case of VTE have reported in patients who were from second group. Combined drug VTE prevention in patients with RA and OA has been most effective and safe.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2882

### AB0383 WHAT'S DIFFERENT ABOUT RHEUMATOID PATIENTS ON LONG TERM STEROIDS?

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**Background:** Corticosteroids have been in and out of fashion as treatment in rheumatoid arthritis (RA) since their introduction in the 1940s. Current EULAR recommendations suggest using oral prednisolone at initiation and then for up to 6 months (1). However, studies suggest up to 30% of RA patients remain on prednisolone for much longer periods (2). We were interested in the characteristics of these long term current prednisolone users, and aimed to compare them to a cohort of RA patients not currently using oral prednisolone using data from our regional audit group.
**Objectives:** To describe the characteristics of RA patients currently taking oral prednisolone for more than 12 months (COP), and to compare to them to a cohort of RA patients not taking prednisolone (NOP).
**Methods:** 7 centres in our regional audit network submitted consecutive RA patients until we had achieved 100 patients in each group. We analysed demographics, duration of RA, use of second line medication, total number of medications, co-morbidities (ischaemic heart disease, hypertension and type 2 diabetes), bone density and RA activity measures.
**Results:** The table below shows key results. The mean daily steroid dose in the COP group was 6.6mg and the mean duration of current steroid use was 4.9 years. Similar numbers of patients in the COP and NOP groups were also using a conventional DMARD and/or biologic (85% and 86% respectively). 39% of both groups had one or more of the 3 comorbidities we looked for. 4% of the COP group had all 3 comorbidities compared to none of the NOP group and 5% of the COP group had 2 out of 3 comorbidities compared to 8% in the NOP group.

DEXA scans were available for 61% of COP and 31% of NOP patients. The mean T score in the COP group was -1.2 compared to -1.05 in the NOP group.

| | Current users | Non-current users |
|---|---|---|
| Number | 100 | 100 |
| Average Age (years) | 64.7 | 61.5 |
| Female (%) | 71 | 78 |
| Mean duration of RA (years) | 11.3 | 8.9 |
| Mean DAS28 score | 3.8 | 3.4 |
| Mean ESR (mm/hr) | 27 | 16 |
| Mean CRP (mg/L) | 21.5 | 9.2 |
| Mean total number of current medications | 8 | 5 |
| Total number on non-biologic DMARDs | 50 | 67 |
| Total number on biologic DMARDs | 12 | 3 |
| Total number on both non- biologic and biologic DMARDs | 23 | 17 |

**Conclusions:** This study provides a snapshot of an important group of 'real world' steroid-using RA patients who are perhaps under-represented in the literature. In our audit RA patients on long term prednisolone tended to be a little older, have a longer duration of RA, greater polypharmacy and greater disease activity. Interestingly, the prednisolone users were taking at least as much other second line medication as the non users, suggesting prolonged steroid use may suggest difficult to control RA rather than avoidance of polypharmacy. Co-morbidities seemed similar between groups. The relatively long duration of prednisolone treatment suggests that RA patients on steroids for more than one year are likely to stay on steroids longer term.

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**Disclosure of Interest:** None declared

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## AB0384 THE EFFECTS OF PENTOXIFYLLINE ON RHEUMATOID ARTHRITIS ACTIVITY ACCORDING TO THE DAS28 CRP DISEASE ACTIVITY SCORE

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**Background:** Treatment of rheumatoid arthritis (RA) prior to "Treat to target" is difficult enough, forcing researchers around the world look for ways to improve the effectiveness of RA treatment.

**Objectives:** To explore the possibilities of reducing RA activity on the disease activity score DAS28 CRP by adding pentoxifylline to the methotrexate treatment.

**Methods:** This study included women (n=101) with RA longer than 1 year in duration, have a seropositive rheumatoid factor, and DAS28 CRP activity score of 3.2–5.1. Middle aged – 45.04±5.24 years old. All patients received a 15.50±2.50 mg oral dose of methotrexate per week. Patients were divided into two groups - those who only had methotrexate (n=50) and those who were treated with an oral dose of methotrexate and 1200 mg of pentoxifylline per day (n=51).

**Results:** The baseline for both groups of RA patients did not differ significantly in terms of the level on the DAS28 CRP (p=0.812). On 14th day of the group who were taking pentoxifylline, the DAS28 CRP disease activity score was significantly lower by 12.5% ($p<0.001$). After 28 days, the users had a DAS28 CRP disease activity score index difference. The difference between two groups is statistically significant. In the group that were treated with pentoxifylline in addition to methotrexate (p=0.001) the index was found to be 8.3% lower. For 28 days, the methotrexate group's disease activity according to the DAS28 CRP activity score significantly decreased by 14.3% from the baseline ($p<0.001$). For 28 days, the pentoxifylline + methotrexate group also achieved a statistically significant reduction in the index according to the DAS28 CRP activity score by 20.5% ($p<0.001$)

The disease activity index for the two groups for 14 and 28 days is shown in the table.

DAS28 CRP Index in the two groups of RA patients

| Groups of patients and observation time | Group Methotrexate (n=50) | Group Methotrexate + Pentoxifylline (n=51) | Statistical significant differences between the two groups |
|---|---|---|---|
| Baseline | 3.11±0.05 | 3.13±0.05 | p=0.812 |
| For 14 days | 3.06±0.05 | 2.69±0.06 | $p<0.001$ |
| For 28 days | 2.71±0.04 | 2.48±0.06 | p=0.001 |

**Conclusions:** Thus, converting the monotherapy methotrexate to pentoxifylline will significantly reduce the activity of RA, while avoiding many of the adverse effects of the other combination therapies. This data requires further long-term research.

**Disclosure of Interest:** None declared

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## AB0385 TOFACITINIB IN RHEUMATOID ARTHRITIS: RESULTS OF POST-APPROVAL INVESTIGATOR INITIATED TRIAL

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**Background:** Tofacitinib (TOFA) was approved in Russia for treatment of patients with rheumatoid arthritis (RA) in 2013, but published information about its post-approval use limited to some individual clinical observations.

**Objectives:** To study the efficacy and safety of TOFA in patients with severe active RA in clinical practice.

**Methods:** We present the preliminary results of ongoing investigator initiated study "Local open label multicenter observational study of efficacy and safety of Tofacitinib in patients with active rheumatoid arthritis with insufficient response to DMARDs", a part of a research program "Russian investigation of methotrexate and biologics in early active inflammatory arthritis" (REMARCA). We included 120 patients (pts) with severe active RA (97 females, 23 males), with median age 51,0 [41,25; 59,0] years and disease duration 60,0 [24,25; 120,0] months, 92 (76,7%) RF positive, 91 (75,8%) ACPA positive, who were non-responders to methotrexate (MTX) at least 15 mg/week and/or other synthetic DMARDs, and biological DMARDs (b-DMARDs). 9 of 30 b-DMARDs non-responders had 2–4 biologics in history. Tuberculin test and chest X-ray were performed in all pts before TOFA prescription. We use TOFA in all the pts in starting dose 5 mg BID per os with possibility to increase the dose to 10 mg BID if needed. The use of TOFA in combination or as monotherapy was a prerogative of the rheumatologist. By January 2016, 91 patients received TOFA for 3 months and 55 pts – for 6 months.

**Results:** TOFA used in combination with MTX in 84 (70%) pts, with Leflunomide in 12 (10%), as monotherapy – in 24 (20%) pts. Dose escalation to 10 mg BID was carried out in 25 (20,8%) pts. Results presented in the table. 20 episodes of adverse events (AEs) in 14 pts observed: liver test 2-fold elevation – 4 cases, Herpes simplex – 3, skin rash – 2, erysipelas – 1, Herpes zoster – 1, latent TB activation – 1, bronchitis – 1, nasopharyngitis – 1, cystitis – 1, hemorrhoids – 1, headache – 1, nausea – 1. No serious AEs were reported. TOFA has been withdrawn in 4 pts: three due to lack of efficacy, one due to allergic skin rash.

Table 1

| | Baseline (n=120) | Month 3 (n=91) | Month 6 (n=55) |
|---|---|---|---|
| DAS28-ESR | 5,92 [5,15; 6,62] | 4,53 [3,47; 5,44]* | 3,88 [2,93; 4,44]* |
| DAS28-ESR remission/LDA | 0/0 | 10 (11%)/11 (12,1%)* | 10 (18,2%)/3 (5,5%) |
| SDAI | 32,2 [25,9; 43,8] | 15,7 [10,2; 23,8]* | 16,5 [11,1; 26,2]* |
| SDAI remission/LDA | 0/0 | 7 (7,7%)/20 (22%)* | 3 (5,5%)/10 (18,2%)* |
| CDAI | 28,3 [21,0; 37,9] | 12,0 [7,0; 19,0]* | 9 [5,0;16,0]* |
| CDAI remission/LDA | 0/0 | 7 (7,7%)/29 (31,9%)* | 3 (5,5%)/25 (45,5%)* |

*$p<0,01$ in comparison with the baseline values in the same pts.

**Conclusions:** TOFA was effective in clinical practice for control of disease activity in patients with severe RA with multiple resistance to synthetic and biological DMARDs during short-term follow up. Safety was satisfactory; there were no cases of serious AEs.

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**Disclosure of Interest:** None declared

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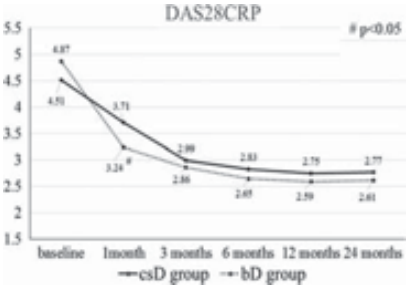
## AB0386 EFFECTIVENESS OF TRIPLE THERAPY USING TACROLIMUS, MIZORIBINE AND METHOTREXATE (MTX) FOR RHEUMATOID ARTHRITIS PATIENT RESISTANCE TO MTX – COMPARISON TO BIOLOGIC AGENTS

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**Background:** The advancement in biological agents and improvement in treatment strategy enabled many patients with rheumatoid arthritis to achieve remission or low disease activity. On the other hand, the cost of biological agents has become major problem in health economics and for some patients biological therapy is not affordable. Therefore recently, combination of conventional disease-modifying anti-rheumatic drugs (DMARDs) therapy have been reconsidered and some studies proved that triple therapies could be as efficacious as biologic agents.

**Objectives:** To compare retrospectively the triple therapy consisting of methotrexate (MTX), tacrolimus (TAC) and Mizoribine (MZR) with biologic agents in patients with established rheumatoid arthritis with no improvement despite the treatment with MTX.

**Methods:** Fifty one established RA patients with a disease duration more than 2 years were included. They showed no improvement the despite treatment with MTX for at least 3 months. We classified patients in 2 groups, one group with the addition of TAC and MZR (csD group) and the other with TNF inhibitor (bD group). There were no significant differences between the backgrounds of the two groups. We evaluated DAS28CRP scores, the van der Heijde-modified total sharp scores [1] and ARASHI change scores [2] which is a scoring system of large joint destruction and compared them between both groups for 2 years. Moreover we performed questionnaire of patient's satisfaction for the therapies.
**Results:** There were no significant differences of DAS28CRP at baseline. Both groups had significant improvement of the scores at final evaluation. There was a significant difference of the improvement rate in DAS28CRP of the bD group in comparison with the csD group at 1 month after treatment. However, no significant difference was observed between the two groups at 3 months and beyond after the treatment (Figure). There was a significant difference in the radiographic progression of small joints between both groups at the final evaluation (csD 0.53/year and bD 0.19/year). Main reasons for the discontinuation the treatment was the adverse events in csD group (csD 23.1% and bD 6.9%), as opposed to patient's intension in bD group. Although patient's satisfaction for improvement of disease activity was simila between the two groups, patient's intension to continue the therapy in csD group was higher than in the bD group. Many patients in bD group complained of the treatment expense.




**Conclusions:** Triple therapy using TAC, MZR and MTX enabled good clinical benefit even in comparison with the biologic agents. Moreover the triple therapy showed rapid effect which was significant within 3 months. However we should also focus on the mechanism for inferior effect on preventing the small joint destruction.
**References:**
[1] van der Heijde D, et al. J Rheumatol. 2000;27:261–3
[2] Kaneko A, et al. Mod Rheumatol. 2013;23:1053–1062
**Disclosure of Interest:** None declared
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## AB0387 EFFICACY OF 12-MONTH THERAPY WITH METHOTREXATE SOLUTION FOR SUBCUTANEOUS INJECTION (SC MTX) IN PATIENTS WITH EARLY RA WITH DIFFERENT BODY MASS INDEX (BMI)

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**Background:** The levels of inflammation markers, specifically C-reactive protein (CRP), are known to be elevated in patients with excessive body weight.
**Objectives:** To evaluate the efficacy of 12-month therapy with SC MTX in patients with recently emerged RA with different BMI.
**Methods:** MTX-naive patients with active early RA (<6 months) diagnosed in accordance with ACR/EULAR 2010 or ACR 1987 (DAS28>3.2) before inclusion were eligible for the 12-month open study. Patients were divided into 3 groups depending on the BMI: I ≤25 kg/m$^2$, II =25–30 kg/m$^2$, III ≥30 kg/m$^2$. Monotherapy with SC MTX once weekly was administered to all patients; starting dose – 10–15 mg per week with escalation of 5 mg every 1–2 weeks (maximum dose – 30 mg per week) until treatment targets were reached (DAS28≤2.6) or adverse events (AE) appeared. Given that patients received almost identical single doses of SC MTX, but had different BMI, we have calculated the dose in mg per m$^2$, calling it the actual dose (AD). Folic acid was administered at the dose of at least 5 mg per week on any day(s) except for the date of SC MTX administration. Disease activity was determined using $DAS28_{ESR}$, $DAS28_{CRP}$ and SDAI. Remission was determined in accordance with ACR/EULAR 2011 criteria.
**Results:** 47 patients (38 female, 9 male) with mean RA duration of 4.2±1.7 months and mean age of 51.0±13.2 years were included. There were no differences between groups defined on the basis of BMI in gender, disease duration, rheumatoid factor, baseline disease activity. The majority of patients have not received DMARD or glucocorticoids (GC) before. After 3, 6 and 12 months of monotherapy with SC MTX we received different results between groups (see table). AE were similar in all groups at each time point.
**Conclusions:** Treatment effect of SC MTX in patients with recently emerged RA correlates with BMI and is significantly increased in patients with normal BMI (≤25 kg/m$^2$) than in patients with excessive body weight or obesity.
**Disclosure of Interest:** None declared
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## AB0388 RISK OF NON ADHERENCE TO ORAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS. ARCO STUDY

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**Background:** Lack of adherence to medication in rheumatoid arthritis (RA) can worsen disease activity.
**Objectives:** To evaluate the risk of non-adherence to disease modifying antirheumatic drugs (DMARD) in RA patients treated with subcutaneous (SC) biological therapy.
**Methods:** ARCO was a retrospective study in RA patients ≥18 years-old from 42 Spanish hospitals on SC biological therapy. The risk of non-adherence to oral DMARD was evaluated using the Compliance Questionnaire in Rheumatology (CQR), a questionnaire validated against an electronic medication-monitoring system, for a cut-off point of taking ≤80% of the doses. Patients completed the Beliefs About Medicines Questionnaire (BMQ) and the Carbonell satisfaction

Risk of non-adherence to DMARD according to socio-demographic characteristics

| | | Risk of non-adherence | p |
|---|---|---|---|
| Age (years) | Q1: (≤48) | 37.4% | <0.001 |
| | Q2 (>48–56) | 15.0% | |
| | Q3 (>56–63) | 11.1% | |
| | Q4 (>63) | 21.7% | |
| Gender | Men | 26.5% | 0.361 |
| | Women | 20.3% | |
| Ethnic group | Caucasian | 20.5% | 0.107 |
| | Others | 38.1% | |
| Risk of alcoholism (AUDIT) | No | 21.0% | 0.429 |
| | Yes | 30.4% | |
| Educational level | Primary | 16.0% | 0.143 |
| | Secondary | 24.2% | |
| | Professional | 21.6% | |
| | University | 30.5% | |
| Employed | No | 17.8% | 0.039 |
| | Yes | 27.2% | |
| Comorbidities | No | 29.6% | 0.050 |
| | Yes | 18.5% | |

**Abstract AB0387** – Table 1. Efficacy of 12-month therapy with SC MTX in patients with recently emerged RA with different BMI

| Group (n) | 1 (20) | 2 (17) | 3 (10) |
|---|---|---|---|
| 3 months of treatment | | | |
| AD, mg/m$^2$, M±σ ($p_{1-2}$=0.03; $p_{1-3}$=0.0009; $p_{2-3}$=0.07) | 12.7±1.9 | 11.3±1.6 | 10.3±1.1 |
| Remission according to ACR/EULAR 2011 | 4 (20%) | 1 (6%) | 0 |
| 6 months of treatment | | | |
| $DAS28_{CRP}$, M±σ ($p_{1-2}$=0.05; $p_{1-3}$=0.03; $p_{2-3}$=0.27) | 2.1±0.96 | 2.6±0.7 | 3±0.8 |
| SDAI, median [25; 75] ($p_{1-2}$=0.3; $p_{1-3}$=0.03; $p_{2-3}$=0.2) | 4.3 [2.2; 7.5] | 5.5 [3.0; 8.6] | 10.0 [7.1; 13.6] |
| AD, mg/m$^2$, M±σ ($p_{1-2}$=0.002; $p_{1-3}$=0.0001; $p_{2-3}$=0.006) | 13.3 [12.5; 14.3] | 11.5 [10.5; 12.0] | 9.4 [8.3; 10.4] |
| Remission according to ACR/EULAR 2011 ($p_{1-2}$=0.2; $p_{1-3}$=0.3; $p_{2-3}$=0.6) | 6 (30%) | 4 (24%) | 1 (10%) |
| 12 months of treatment | | | |
| $DAS28_{ESR}$, M±σ ($p_{1-2}$=0.03; $p_{1-3}$=0.2; $p_{2-3}$=0.27) | 2.0±0.7 | 2.9±0.9 | 2.4±0.7 |
| $DAS28_{CRP}$, M±σ ($p_{1-2}$=0.02; $p_{1-3}$=0.2; $p_{2-3}$=0.6) | 1.7±0.6 | 2.4±0.8 | 2.3±0.6 |
| SDAI, median [25; 75] ($p_{1-2}$=0.03; $p_{1-3}$=0.01; $p_{2-3}$=0.8) | 1.2 [0.5; 4.0] | 3.3 [2.3; 9.9] | 4.3 [2.6; 7.0] |
| CRP, mg/l, median [25; 75] ($p_{1-2}$=0.01; $p_{1-3}$=0.007; $p_{2-3}$=0.6) | 1.1 [0.2; 3.1] | 3.7 [1.6; 7.9] | 4.0 [2.2; 9.4] |
| AD, mg/m$^2$, M±σ ($p_{1-2}$=0.08; $p_{1-3}$=0.001; $p_{2-3}$=0.09) | 13.1±2.2 | 11.5±2.0 | 10.2±1.7 |
| Necessity of bDMARDs usage, % ($p_{1-2}$=0.02; $p_{1-3}$=0.002) | 23% | 60% | 60% |
| Remission according to ACR/EULAR 2011 ($p_{1-2}$=0.1; $p_{1-2}$=0.07; $p_{1-2}$=1) | 12 (60%) | 5 (30%) | 3 (30%) |

questionnaire (Spanish validated questionnaire on satisfaction with medication).
**Results:** 364 patients were included (mean age 54.9 years [SD 12.5]; 77.5% women median RA duration 7.8 years). Complete CQR was available for 304 patients, of which 21.7% showed risk of non-adherence to oral DMARD (95% CI: 17.4 – 26.7%). The percentage was similar in men and women, and greater in extremes of age (>63 and ≤48 years-old), in those currently working and in patients with no comorbidities (Table). There was a trend to a higher percentage at risk of non-adherence in non-Caucasian patients, those with higher educational level and in those with risk of alcoholism (AUDIT questionnaire) (Table). The percentage with risk of non-adherence was similar in patients with 1, 2 or >2 oral drugs for RA, and in those treated or not with SC methotrexate, and it was higher in those who considered that the effect of their treatment for RA on the symptoms had been less than expected (38.1% vs 17.9% in those who thought it had been greater, p=0.029). No differences were seen with regard to the result of the BMQ.
**Conclusions:** In patients with RA treated with SC biological therapy, 21.7% showed risk of non-adherence to DMARD according to the CQR (taking ≤80% of the doses). The percentage was higher in extremes of age, patients with university degree, employed, without comorbidities and in those who considered that the treatment effect on RA had been lower than expected.
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**Disclosure of Interest:** None declared
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## AB0389 METHOTREXATE TREATMENT FOR RHEUMATOID ARTHRITIS IN POLAND: RETROSPECTIVE ANALYSIS OF PATIENTS IN ROUTINE CLINICAL PRACTICE

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**Background:** Methotrexate (MTX) is a folic acid antagonist which has both an antiproliferative and an anti-inflammatory action. It is the most commonly prescribed DMARD (disease-modifying antirheumatic drug) and is considered the "anchor drug" in rheumatoid arthritis (RA).
**Objectives:** Our study reviews RA treatment with MTX in Poland.
**Methods:** Presented study was based on a retrospective analysis of a cohort of 1957 patients with RA in routine clinical practice. The study was conducted among 100 rheumatologists from different centers that have been selected to reflect the structure of the treatment of RA in Poland. Each physician received 20 questionnaires that were filled on the nearest visit of consecutive 20 patients with RA. Data was collected using pre-defined questionnaire.
**Results:** MTX was taken by 91% of patients and 80% of them continued the treatment both as monotherapy (65%) or concomitantly with other DMARDs. In general, the therapy was initiated within 6 months after diagnosis in 60% of cases. However, MTX was introduced at the very beginning of the treatment for the majority of patients diagnosed after 2009. Methotrexate was given mostly orally, nevertheless in case of 18% of patients it was administered subcutaneously. During MTX treatment dose modifications could be observed in 76% cases and were contingent on different factors. Lack of efficacy was the major reason for increase, while the most common cause of reduction the dose was intolerance of MTX or presence of adverse events, like the most prevalent nausea and vomiting, weakness, increase in activity of liver enzymes and hair loss. Initial dose of MTX was mostly 10 or 15 mg/week. An increase in dosage to 25 mg/week was observed in 36% cases and was continued for 27% of patients. Medium maximum dose that was achieved during treatment was 20.2 mg/week (median 19.3 mg/week). Patients who currently take MTX primarily use a dose of 25 mg/week (27%), 20 mg/week (24%) or 15 mg/week (21%). Treatment interruption was noted in 21% patients predominantly due to intolerance to MTX, however in 13% of cases it was patient's decision. More than half of patients (61%) treated for 3–6 months with MTX achieved remission or low disease activity based on DAS-28.
**Conclusions:** MTX when used according to current recommendations is a effective drug, taking into account the efficacy and adverse effects.
To optimize the MTX therapy regular control visits are required
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## AB0390 SAFETY AND EFFICACY OF ABT-494, A NOVEL SELECTIVE JAK1 INHIBITOR, IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE OR INTOLERANCE TO ANTI-TNF BIOLOGIC THERAPY

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**Background:** ABT-494 is a novel selective JAK1 inhibitor.
**Objectives:** The safety, efficacy, and dose response of ABT-494 were characterized vs placebo (PBO) in patients (pts) with moderately to severely active RA and an inadequate response to ≥1 anti-TNF biologic therapy (TNF-IR).
**Methods:** This was a phase 2b, 12-week, double-blind PBO-controlled study; TNF-IR pts receiving stable background methotrexate (MTX) were randomized 1:1:1:1:1 to ABT-494 3, 6, 12, and 18 mg twice daily (BID) or matching PBO. The primary efficacy endpoint was the proportion of pts who achieved an ACR20 response at week 12.
**Results:** All 276 pts had failed ≥1 anti-TNF therapy prior to enrollment; 28% had received ≥2 anti-TNF biologics and 20% had also received non–anti-TNF biologics. Baseline (BL) characteristics were similar in all treatment groups. The proportion of pts achieving ACR20 at week 12 was significantly higher for all ABT-494 groups vs PBO (Table 1). There was a significant ($P<0.01$) dose response between PBO and all ABT-494 treatment groups for ACR20 response rates (non-responder imputation) at week 12. ACR50 and ACR70 responses were statistically significantly higher at doses of ≥6 mg BID. Changes in DAS28(CRP) from BL were significantly greater for all doses of ABT-494 vs PBO. Onset of action was rapid, with significant differences in ACR20 and change in DAS28(CRP) from BL at week 2 ($P\leq0.007$) for 6, 12, and 18 mg BID vs PBO. Low disease activity and clinical remission per DAS28(CRP) criteria were achieved statistically significantly more often in the 12-mg BID dose group vs PBO. The incidences of AEs were numerically higher in ABT-494 dose groups, with some trend towards dose dependency (Table 2). The majority of infections were mild. There was one serious infection ("bronchiectasis") in the PBO group and none in the ABT-494 treatment groups were reported. Five pts had non-serious events of herpes zoster: 1 pt each in the ABT-494 3 mg, 12 mg, and 18 mg BID treatment groups, and 2 pts in the PBO group. One pt in the 6-mg BID dose group reported 2 events of non-melanoma skin cancer (basal cell and squamous cell carcinomas). There was 1 report of anemia in the 18-mg BID dose group. No deaths were reported during the study.

**Table 1. Efficacy Endpoints at Week 12**

| | PBO (n=66) | ABT-494 3 mg BID (n=66) | ABT-494 6 mg BID (n=65) | ABT-494 12 mg BID (n=66) | ABT-494 18 mg BID (n=66) |
|---|---|---|---|---|---|
| ACR20, % | 34 | 53* | 68*** | 74*** | 67*** |
| ACR50, % | 15 | 24 | 35* | 42*** | 39** |
| ACR70, % | 6 | 13 | 26** | 32*** | 32** |
| DAS28(CRP), mean change from baseline† | -1.1 | -1.9*** | -2.2*** | -2.5*** | -2.3*** |
| CR (DAS28 <2.6, %) | 13 | 24 | 28 | 33* | 27 |
| LDA (DAS28 <3.2, %) | 25 | 33 | 36 | 49** | 42 |
| LDA (CDAI ≤10, %) | 25 | 27 | 31 | 40 | 40 |

ACR20/50/70, 20%/50%/70% improvement in American College of Rheumatology score; BID, twice daily; CDAI, Clinical Disease Activity Index; CR, clinical remission; CRP, C-reactive protein; DAS28, 28-joint Disease Activity Score; LDA, low disease activity
Non-responder imputation (NRI) unless otherwise noted.
*, **, *** statistically significant at the 0.001, 0.01, and 0.05 levels.
†Last observation carried forward.

**Table 2. Adverse Events Summary**

| Number of pts, n (%) | PBO (n=66) | ABT-494 3 mg BID (n=66) | ABT-494 6 mg BID (n=65) | ABT-494 12 mg BID (n=66) | ABT-494 18 mg BID (n=65) |
|---|---|---|---|---|---|
| Any AE | 25 (38) | 26 (39) | 31 (48) | 37 (56) | 28 (43) |
| Serious AE | 1 (2) | 2 (3) | 2 (3) | 0 | 1 (2) |
| Severe AE | 2 (3) | 1 (2) | 2 (3) | 2 (3) | 1 (2) |
| AE leading to discontinuation | 2 (3) | 0 | 6 (11) | 2 (3) | 3 (5) |
| Infections | 13 (20) | 11 (28) | 12 (22) | 22 (48) | 21 (38) |
| Serious infection | 1 (2) | 0 | 0 | 0 | 0 |
| Anemia | 0 | 0 | 0 | 0 | 1 (2) |
| Herpes zoster | 2 (3) | 1 (2) | 0 | 1 (2) | 1 (2) |
| Hepatic disorder | 1 (2) | 0 | 0 | 0 | 2 (3) |
| Neutropenia | 0 | 0 | 0 | 1 (2) | 1 (2) |
| Malignancy | 0 | 0 | 1 (2) | 0 | 0 |

AE, adverse event; BID, twice daily

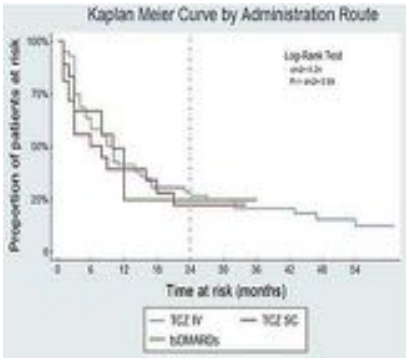
**Conclusions:** This phase 2b study demonstrated the clinical efficacy of ABT-494 vs PBO when dosed in combination with MTX in TNF-IR pts with active RA. ABT-494 had an acceptable safety and tolerability profile.
**Acknowledgement:** The design, study conduct, analysis, and financial support of the clinical trial (NCT01960855) were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the content. All authors had access to all relevant data. Mariana Ovnic and Michael J. Theisen of Complete Publication Solutions, LLC, provided medical writing support paid for

by AbbVie. This presentation contains information on the investigational product ABT-494.
**Disclosure of Interest:** J. M. Kremer Shareholder of: Corrona, Grant/research support from: AbbVie, Lilly, Novartis, and Pfizer, Consultant for: AbbVie, Lilly, Pfizer, Medimmune, Sanofi, and Regeron, Employee of: Corrona, E. C. Keystone Grant/research support from: AbbVie and Lilly, Consultant for: AbbVie and Lilly, Speakers bureau: AbbVie and Lilly, P. Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Samsung, Lilly, and Takeda, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Samsung, Lilly, and Takeda, H. S. Camp Shareholder of: AbbVie, Employee of: AbbVie, A. Friedman Shareholder of: AbbVie, Employee of: AbbVie, L. Wang Shareholder of: AbbVie, Employee of: AbbVie, A. A. Othman Shareholder of: AbbVie, Employee of: AbbVie, N. Khan Shareholder of: AbbVie, Employee of: AbbVie, S. Jungerwirth Shareholder of: AbbVie, Employee of: AbbVie
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## AB0391 SUSTAINED REMISSION AND RATE OF RELAPSE AFTER WITHDRAWAL OF BIOLOGIC OR NON-CONVENTIONAL DMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** Rheumatoid arthritis (RA) treatment has changed considerably over the last decade with the introduction of biologics and target synthetic non-conventional DMARDs. In spite of algorithms about when to begin using these drugs, data about when to stop them are scant.
**Objectives:** To assess the length of remission in patients with RA who had to discontinue a biological or a non-conventional DMARD because a clinical trial ended, and to compare survival remission curves.
**Methods:** A prospective cohort study of RA patients assembled at the time of their last dose of any of the following drugs: tocilizumab subcutaneous (TCZ-SC), TCZ intravenous (TCZ-IV), or targeted synthetic oral drugs (tsDMARDs) tofacitnib or baricitinib p.o. All patients were in RA remission (DAS-28 $<2.6$ and absence of swollen joints). Patients were followed at our clinic in the following way: 1) each patient had a structured telephone interview based on the COPCORD questionnaire every eight weeks by a senior medical student; 2) each patient was instructed to communicate with our center immediately if they were experiencing swollen joints, and 3) All patients had in-office assessments with the same rheumatologists every four months. The primary outcome was RA relapse, defined as the time (months) when the patient presented at least one swollen joint. Survival remission curves were calculated per type of drug (TCZ vs. tsDMARDs) and per route of administration (PO, SC or IV). A Long Rank Test was used to assess differences among survival curves and $p<0.05$ was considered significant. A Cox analysis was used to assess baseline predictors for relapse times.
**Results:** 99 patients were included, 88% female, with a mean age of 47±13 years. Sixty patients were treated with TCZ-IV, 18 with TCZ-SC and 21 with tsDMARDs-PO. Over the following 165 person-years, 27 (27%) remained in RA remission and 73% developed flare-ups (9 months was the median period for a flare-up). There were no significant differences among the three types of administration (IV, SC, and PO) or between the two classes of drugs (biological vs. tsDMARD). None of the baseline variables were significant as predictors of flare-ups.




**Conclusions:** Long-term clinical remission is possible in a number of patients with RA after suspending a biological or non-conventional DMARD. This feature has also been reported with other biological agents, but not with tsDMARDs. Additional data are required to support recommendations for discontinuing a biological agent after achieving remission.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2971

## AB0392 SAFETY AND TOLERABILITY OF IGURATIMOD IN RHEUMATOID ARTHRITIS WITH COMORBID ILLNESSES

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**Background:** Iguratimod, a member of the family of methanesulfonanilide, is a relatively new oral anti-rheumatic medication. Although most of the members of this family act as cyclooxygenase 2 inhibitor, iguratimod has been considered to be a novel immunomodulator agent. Little data exists regarding its safety and tolerability in patients with comorbid illnesses.
**Objectives:** To determine the safety and retention rate of Iguratimod in high risk patients.
**Methods:** For the period from December 2012 to July 2015, a retrospective review of medical records was performed at our institution for all patients who had been treated with Iguratimod for rheumatoid arthritis (RA). Baseline characteristic and clinical course were reviewed. For the analysis, using Kaplan-Meier curves, a comparison of adverse events and the number of treatment switches by each risk category (history of malignant neoplasms, latent tuberculosis infection (LTBI), underlying pulmonary disease, and estimated glomerular filtration rate (eGFR $<60$ mL/min/1.73m$^2$)) was conducted.
**Results:** A total of 173 patients were included in this study. The mean age was 68.7 yrs, and the disease duration was 12±10 yrs. Positivity of ACPA was 79% (the mean titer was 127.3 U/mL). Thirty nine patients (22.5%) have history of neoplasms (over 5 years before: n=13, within 5 years: n=14, on current treatment or on best supportive care (BSC): n=12). Thirty eight patients (22%) have LTBI, 46 patients have underlying pulmonary disease (Interstitial pneumonia: n=30, others: n=16). Estimated eGFR$<$60ml/min were seen in 28 patient.
Adverse effects (AE) include rash (n=4), gastrointestinal symptoms (n=10), liver function test abnormality (n=12), renal impairment (n=9), and interstitial pneumoniae (n=3).
None of the patients developed tuberculosis or HBV reactivation during the follow-up period. During the study period, 8 out of the 12 patients with current neoplasms were able to continue Iguratimod. Three patients who currently had neoplasms died during the study (all of whom were BSC patients at the baseline, and the follow-up periods were 199, 378, and 610 days, respectively). One patient was taken off Iguratimod due to an abnormality in the liver function test.
There was no statistical significance on the log-rank analysis for AE, and the number of treatment switches was LTBI (p=0.183), neoplasms (p=0.185), underlying pulmonary disease (p=0.136), and eGFR $<$60ml/min (p=0.373). For AE, LTBI (p=0.239), neoplasms (p=0.953), underlying pulmonary disease (p=0.158), and eGFR $<$60ml/min (p=0.322).
**Conclusions:** This study demonstrated the safety and tolerability of Iguratimod for established high-risk RA patients.
**References:**
[1] Lu LJ, et al. Multicenter, randomized, double-blind, controlled trial of treatment of active rheumatoid arthritis with T-614 compared with methotrexate. Arthritis Care & Research 2009; 61 979–987
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**Disclosure of Interest:** None declared
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## AB0393 METOTHREXATE PLUS LEFLUNOMIDE STEP-UP THERAPY IN EARLY RHEUMATOID ARTHRITIS PATIENTS WITH NON RESPONSE TO INITIAL METHOTREXATE IN MONOTHERAPY

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**Background:** Treatment of patients with rheumatoid arthritis (RA) must be directed to remission, and in some patients minimum activity, can be an option. The strategy most studied is the early and intensive treatment, associated with a strict monitoring. Half of these patients respond to initial monotherapy with methotrexate (MTX), and in non-responders, additive treatments with other synthetic DMARDs are an option.
The utility of the combined and additive strategy (Step-up) of MTX and Leflunomide (LEF) is not well defined in early RA.
**Objectives:** The objectives of this study was to estimate theproportion of clinical remission achieve by the Step-up strategy with LEF in patients with early RA that did not respond to initial monotherapy with MTX, the time to achieve remission, and estimate the state of remission in the last follow-up evaluation.
**Methods:** An observational study of consecutive case series was performed by including a cohort of patients from Early Arthritis Argentine Consortium (CONAART) with RA of less than 2 years of disease duration, with no response to MTX in monotherapy according to medical judgment, and in whom treatment was additive with LEF. Assessment and data collection was performed every 3 months. Sociodemographic characteristics, functional status, disease activity and treatment were included. "Time to result" was assessed since the date of the beginning with the combination of MTX plus LEF to remission or last control. The

state of remission was evaluated by DAS28. The Kaplan-Meier method was used to estimate the probability of each outcome.
**Results:** A total of 106 patients were included. The mean duration of the disease at the time of inclusion was 4 months (IQR 2–8). The average age was 50±12 years and 83% were women. 68% were positive for RF and 65% for CCP. Median follow-up was 34±18 months (300 patient-years). After addition of LEF, 95 (90%) patients weren't in remission. The mean DAS28 was 4.61 (±1.61), HAQ =0.9 (±0.76), dose of prednisone =7.31 (±4.25). The median time in months of use of MTX was 6.7 (IQR 3.4–14.4), and 64% had doses greater than 20 mg of MTX during follow-up, 47 (50%) of patients achieved clinical remission in an average time of 8 months. The remaining patients did not achieve remission. The overall probability of remission for patients-month follow-up was 0.49. Twenty-seven of the 47 patients (58%) were still in remission at the last visit. Median follow-up after achieving remission was 20 months (IQR 3–29).
**Conclusions:** In this early RA cohort study, 50% of patients with lack of response to MTX who added LEF achieved remission assessed by DAS28 at a median time of 8 months. 6 out of 10 of these patients were in remission at 2 years of follow-up.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3056

## AB0394 EARLY EFFECT OF TOFACITINIB ON OSTEOCLAST REGULATOR IN RHEUMATOID ARTHRITIS

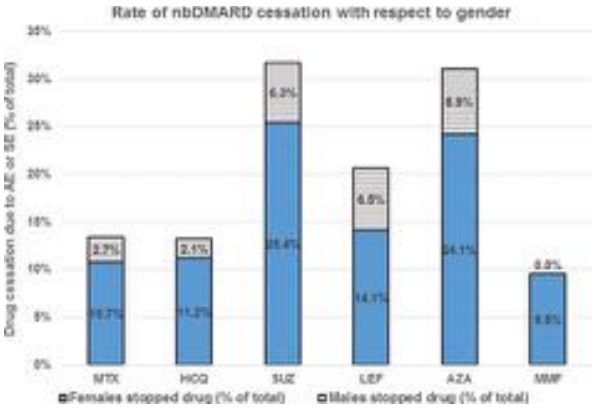
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**Background:** The selective Janus kinase (JAK) inhibitor tofacitinib has demonstrated excellent efficacy for rheumatoid arthritis (RA). These results suggest the possibility that tofacitinib improves osteoclastic bone destruction of RA. However, the detailed mechanism of tofacitinib for osteoclastogenesis in RA is pooly understood. In this study, we investigated the effect of tofacitinib on serum biomarkers related to osteoclast regulation such as soluble receptor activator of NF-kappa B ligand (sRANKL) and osteoprotegerin (OPG) in patients with RA.
**Objectives:** To clarify the effect of tofacitinib on osteoclast regulator in RA.
**Methods:** Fourteen patients with active RA who inadequate response to disease-modifying antirheumatic drugs (DMARDs) (mean age: 54.6 years, mean disease duration: 4.1 years, mean simplified disease activity index: 26.9, ACPA positive: 86%, oral steroid use: 29%, mean oral steroid dose: 10mg/day, MTX use: 93%, mean MTX dose:10.9mg/week, biologic DMARDs naïve: 57%) were started on treatment with tofacitinib 5mg twice daily (BID). Disease activity was assessed using the 28-joint count disease activity score-C-reactive protein sedimentation rate (DAS28-CRP) and simplified disease activity index (SDAI). Next, circulating levels of sRANKL and OPG were examined by enzyme-linked immunosorbent assay (ELISA) (sRANKL: human RANKL ELISA kit, Biomedica, OPG: human osteoprotegerin ELISA kit, Biomedica respectively) at the baseline, week 2, 4 and 12.
**Results:** After treatment of tofacitinib, SDAI score among all fourteen patients decreased significantly from 26.9±12.4 (mean±SD) at the baseline to 14.7±9.9 at week 4 ($p<0.0001$), to 8.3±6.1 at week 12 ($p<0.0001$). Baseline levels of sRANKL were significantly correlated with the levels of CRP (Spearman $r^2=0.488$, P=0.0054). Average of sRANKL levels decreased immediately from 0.15±0.11 pmol/L at the baseline to 0.09±0.05 pmol/L at week 2 ($p=0.0097$), to 0.11±0.10 pmol/L at week 4 ($p=0.0311$), to 0.08±0.05 pmol/L at week 12 ($p=0.0014$). On the other hand, statistically significant changes in OPG levels were not observed during 12 weeks. Consequently, average of sRANKL/OPG ratio decreased significantly from 4.81±4.82 at the baseline to 2.62±1.84 at week 2 ($p=0.0186$), to 3.11±2.81 at week 4 ($p=0.0191$), to 2.11±1.72 at week 12 ($p=0.0052$). Interestingly, decreasing effects of sRANKL levels or sRANKL/OPG ratio were greater in patient with high sRANKL level at the baseline.
**Conclusions:** Here, we show for the first time that tofacitinib has improved inflammatory bone destruction immediately through the regulation of sRANKL levels and sRANKL/OPG balance in RA. This mechanism might be a control of RANKL induction via JAK pathway inhibition in activated CD4+ T cells and synovial fibroblasts
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1413

## AB0395 ONE YEAR RETROSPECTIVE ANALYSIS OF SIDE EFFECTS OF NON-BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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**Background:** Non-biologic disease modifying anti-rheumatic drugs (nbDMARDs) (e.g. Methotrexate (MTX), Sulfasalazine (SUZ) and Leflunomide (LEF)) are used as initial treatment for autoimmune conditions; such as rheumatoid arthritis and psoriatic arthritis. However, there is limited evidence upon the proportion of patients who have to stop medication due to side-effects. Infoflex (CIMS) is an electronic system implemented at Derriford Hospital, May 2014. This system was used to record Rheumatology drugs started and stopped and causes for drug cessation[1].
**Objectives:** Our aim was to determine the proportion of patients who had to stop taking nbDMARDs due to adverse events (AE) or side-effects (SE), document the commonest reactions and examine whether there were gender differences in drug cessation.
**Methods:** A retrospective search was performed using Infoflex for all Rheumatology patients at Derriford Hospital for patients who had been started on nbDMARDs for a one year period between 01/12/2014–30/11/2015. Patients were selected for inclusion if they were continuing on the drug or had stopped it due to AE or SE. Patients were excluded if they had stopped their drug due to inefficacy.
**Results:** 1424 patient records were documented from a total of 1080 patients that met the inclusion criteria. Patients included were treated for a variety of rheumatological conditions with the following nbDMARDs; MTX (n=588), Hydroxychloroquine (HCQ) (n=385), SUZ (n=303), LEF (n=92), Azathioprine (AZA) (n=29), Mycophenolate Mofetil (MMF) (n=21), Cyclophosphamide (n=2), Gold (n=2), Cyclosporine (n=1), Tacrolimus (n=1).
The percentage and number of patient records that ceased medication due to AE or SE was; MTX 13.44% (n=79), HCQ 13.25% (n=51), SUZ 31.68% (n=96), LEF 20.65% (n=19), AZA 31.03% (n=9), MMF 9.5% (n=2). The nbDMARD dosage did not have any relationship to the rate of SE or AE.
Mean length of usage for each drug before stopping due to AE or SE was: MTX (95.9 days), HCQ (57.2 days), SUZ (57.1 days), LEF (68.2 days), AZA (69.8 days), MMF (175.5 days).
The most common AE or SE was found to be gastrointestinal for all drugs, except MMF.
The female to male ratio for those who discontinued MTX, HCQ and SUZ was increased in comparison with the female to male ratio for overall drug usage.




**Conclusions:** SUZ had the highest percentage of patients stopping medication (31.68%) with the shortest duration of usage (57.1 days). MMF had the lowest percentage of patients stopping medication (9.5%) with the longest duration of usage (175.5 days).
The commonest reported AE or SE for all drugs (except MMF) were within the gastrointestinal category; principally gastrointestinal intolerance and nausea.
The strengths of our data lie in the amount of information captured and its real world setting. Its weakness is the characterisation of SE is insufficiently specific and we have been unable to classify by disease. Future data collection is required to fully capture the patients who will discontinue nbDMARDs within the current study population. However, these data could potentially aid clinicians in advising rheumatology patients of the potential risks of different nbDMARDs.
**References:**
[1] Chameleon Information Management Services Ltd (CIMS). http://www.infoflex-cims.co.uk/cims/news/2015/11/plymouth_rheumatology
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**Disclosure of Interest:** None declared
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## AB0396 SAFETY OF TOFACITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN PATIENTS FROM LATIN AMERICA AND THE REST OF THE WORLD

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA).
**Objectives:** To assess the safety of tofacitinib in patients from Latin America (LA) and the rest of the world (ROW).
**Methods:** Data were pooled from patients who received tofacitinib 5 or 10 mg twice daily ± conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) from two Phase 1, nine Phase 2, six Phase 3 and two long-term extension (LTE) studies (one LTE was ongoing at time of analysis, data as of March 2015). Incidence rates (IR; patients with events/100 patient-years) and 95% confidence intervals (CI) for safety events of special interest pooled for both tofacitinib doses were calculated and compared between LA and ROW patient populations. LA countries that enrolled patients were: Argentina, Brazil, Chile, Colombia, Costa Rica, the Dominican Republic, Mexico, Peru and Venezuela.
**Results:** The analysis included 1037 LA patients (91.2% female; mean age 49.5 years; 7.5 years mean RA duration; 67.1 kg mean weight; 6.5 mean baseline Disease Activity Score for 28-joint counts based on erythrocyte sedimentation rate [DAS28-4(ESR)]; 71.3% baseline concomitant steroid use) and 5157 ROW patients (81.0% female; mean age 53.7 years; 8.1 years mean RA duration; 71.9 kg mean weight; 6.3 mean baseline DAS28-4 [ESR]; 63.8% baseline concomitant steroid use). IRs for safety events of special interest were generally similar for LA and ROW populations with overlapping 95% CIs (Table).

Table. Number of patients with events, IR and 95% CIs for safety events of special interest for all tofacitinib-treated patients

| Patients with events (IR, patients with events/100 patient years [95% CI]) | Latin America N=1037 (3251.3 patient-years total exposure) | Rest of the world N=5157 (16254.4 patient-years total exposure) |
|---|---|---|
| Discontinuations due to AEs | 211 (6.6 [5.7, 7.5]) | 1229 (7.5 [7.0, 8.2]) |
| Serious infection events (all patients) | 80 (2.5 [2.0, 3.1]) | 447 (2.8 [2.5, 3.1]) |
| Serious infection events (patients without baseline corticosteroid use) | 14 (3.7 [2.0, 6.2]) | 100 (3.8 [3.1, 4.6]) |
| Tuberculosis | 4 (0.1 [0.0, 0.3]) | 12 (0.1 [0.1, 0.1]) |
| Opportunistic infections (excluding tuberculosis) | 13 (0.3 [0.2, 0.5]) | 46 (0.3 [0.2, 0.4]) |
| Herpes zoster (serious and non-serious) | 111 (3.7 [3.0, 4.4]) | 592 (4.0 [3.6, 4.3]) |
| Serious herpes zoster | 5 (0.2 [0.1, 0.4]) | 48 (0.3 [0.2, 0.4]) |
| Malignancies (excluding NMSC) | 9 (0.3 [0.1, 0.5]) | 164 (1.0 [0.8, 1.2]) |
| Lymphoma | 0 (0.0 [0.0, 0.1]) | 19 (0.1 [0.1, 0.2]) |
| MACE[1] | 6 (0.2 [0.1, 0.4]) | 65 (0.4 [0.3, 0.5]) |
| All-cause mortality[1] | 13 (0.4 [0.2, 0.7]) | 38 (0.2 [0.2, 0.3]) |

[1]Adjudicated events; [2]deaths occurring within 30 days of the last dose of study drug
AE, adverse event; CI, confidence interval; IR, incidence rate; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer

**Conclusions:** In this analysis of pooled data from tofacitinib RA trials, the safety profile of tofacitinib in the LA and ROW populations was similar.
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**Disclosure of Interest:** O. Castañeda Grant/research support from: AbbVie, Bristol-Myers Squibb, GlaxoSmithKline, IQfarma, Janssen, MSD, Novartis, Periñán, Pfizer Inc, Roche, Roemmers, UCB, Consultant for: AbbVie, Bristol-Myers Squibb, GlaxoSmithKline, IQfarma, Janssen, MSD, Novartis, Periñán, Pfizer Inc, Roche, Roemmers, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, GlaxoSmithKline, IQfarma, Janssen, MSD, Novartis, Periñán, Pfizer Inc, Roche, Roemmers, UCB, J. Jaller Consultant for: Amgen, Bristol-Myers Squibb, Glaxo-SmithKline, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, Speakers bureau: Amgen, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, G. Citera Grant/research support from: AbbVie, Bristol Myers Squibb, Pfizer Inc, Consultant for: AbbVie, Bristol Myers Squibb, Pfizer Inc, Speakers bureau: AbbVie, Bristol Myers Squibb, Pfizer Inc, S. Radominski Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, M. Cardiel Grant/research support from: Pfizer Inc, Roche, Amgen, Bristol-Myers Squibb, Astellas, Janssen, Eli Lilly, Anthera, Consultant for: Pfizer Inc, Roche, AbbVie, Merck, Eli Lilly, Bristol-Myers Squibb, Speakers bureau: Pfizer Inc, Bristol-Myers Squibb, Roche, C. A. Zerbini Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, R. Guzmán Consultant for: MSD, Pfizer Inc, Roche, Novartis, UCB, Speakers bureau: Pfizer Inc, UCB, G. Solano Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Belini Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Maniccia Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kwok Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Rojo Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Ponce de Leon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
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## AB0397 TREATMENT REFRACTORY RHEUMATOID ARTHRITIS: IS REPOSITORY CORTICOTROPIN INJECTION (RCI) AN EFFECTIVE OPTION IN PATIENTS RESISTANT TO BIOLOGIC THERAPIES? (A PILOT STUDY)

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**Background:** Despite the availability of therapeutic options for RA, including DMARDs and biologic agents, there are many patients who are resistant to current therapy and remain inadequately controlled. We hypothesized that 12-week repository corticotropin injection (RCI) treatment may provide relief of RA and acute exacerbations in patients refractory to treatment with DMARDs and at least three biologics (including 1 tumor necrosis factor inhibitor).
**Objectives:** The objective of this study was to assess the efficacy and safety of RCI in this patient population.
**Methods:** This was a 12-week prospective, multicenter, open-label study with 9 patients. Patients were maintained on stable doses of a biologic, other DMARD therapies and prednisone of at least 7.5 mg daily; RCI was adjunctive therapy. RCI 40 U was given subcutaneously daily for 7 days. If an adequate response (>1.2 point reduction in the Disease Activity Score 28 using C-Reactive Protein [DAS28-CRP]) was achieved, the dose was decreased to 40 U twice weekly through week 12. If the response was inadequate, patients received 80 U once daily for 7 days, followed by 80 U twice weekly through week 12. The primary endpoint was >1.2 point reduction in DAS28-CRP at week 12. Secondary endpoints included improvements in American College of Rheumatology 20%, 50%, and 70% (ACR20, 50 and 70), decrease in Health Assessment Questionnaire Disease Index (HAQ-DI) score, and improvement in Functional Assessment of Chronic Illness Therapy (FACIT) and health-related quality of life (HRQOL) questionnaires.
**Results:** We report results for 9 patients (44–60 years). A total of 66% (6/9) of patients met the primary endpoint. The mean DAS improvement at 12 weeks on 40 U of therapy was numerically greater than that in patients increasing their dose to 80 U. Improvements were also noted in secondary endpoints, particularly over the first 4–8 weeks of treatment. Five of 9 patients maintained improvement in HAQ-DI and in the FACIT fatigue scale at week 12 (Table). There did not appear to be a clear pattern or association between cortisol levels and RCI response. No serious adverse events (AEs) occurred. Mild AEs included Cushingoid features (n=2), mild hyperglycemia (n=1), herpes zoster (n=1), and pedal edema (n=1).

Table 1

| Measure | Dose (U) | n | Mean baseline value | Mean change from baseline | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Week 1 | Week 2 | Week 4 | Week 8 | Week 12 |
| DAS28-CRP | 40 | 5 | 5.43 | –1.99 | –2.32 | –1.94 | –2.08 | –1.99 |
| | 80 | 4 | 5.26 | –0.73 | –1.63 | –1.53 | –0.56 | –1.64* |
| HAQ-DI | 40 | 5 | 1.05 | –0.20 | –0.25 | –0.17 | –0.03 | –0.10 |
| | 80 | 4 | 1.85 | 0.06 | –0.34 | –0.12 | –0.17 | –0.19* |
| FACIT | 40 | 5 | 29.60 | 4.80 | 9.40 | 6.20 | 4.00 | 5.60 |
| | 80 | 4 | 22.00 | 5.75 | 10.0 | 6.25 | –0.75 | 0.50* |

A decrease in DAS28-CRP and HAQ-DI, and an increase in FACIT indicate improvement. *Data for 2 patients are not reported here as they dropped out due to inadequate response. DAS28-CRP, the Disease Activity Score 28 using C-Reactive Protein; HAQ-DI, Health Assessment Questionnaire-Disease Index; FACIT, Functional Assessment of Chronic Illness Therapy.

**Conclusions:** RCI produced a rapid and clinically meaningful reduction in markers of disease activity and improved quality of life. RCI demonstrated a favorable safety profile; there were no serious adverse events and cortisol levels did not increase for most patients. For patients who are refractory to common RA therapies, the response rate to RCI was substantial and shows great promise in this difficult to treat population.
**Disclosure of Interest:** P. Fischer Grant/research support from: Mallinckrodt, Genetech, Paid instructor for: Mallinckrodt, R. Rapoport Paid instructor for: Amgen, Abbvie, Union Chimique Belge, Exagen
**DOI:** 10.1136/annrheumdis-2016-eular.4239

## AB0398 EFFICACY OF ADALIMUMAB AND TOFACITINIB IN RHEUMATOID ARTHRITIS: POST-HOC ANALYSES FROM A PHASE 3 STUDY

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). In a Phase 3, 12-month (Mo) study (ORAL Standard) including RA patients (pts) on stable background methotrexate (MTX), tofacitinib and adalimumab (ADA) demonstrated significant improvements in efficacy outcomes compared with placebo (PBO).[1]

**Objectives:** To evaluate the efficacy of tofacitinib and ADA based upon American College of Rheumatology (ACR) component scores in a post-hoc analysis of ORAL Standard.

**Methods:** ORAL Standard (NCT00853385) was a randomised, multicentre, Phase 3 study investigating the efficacy of oral tofacitinib 5 and 10 mg twice daily (BID) or ADA 40 mg administered subcutaneously (SC) every two weeks vs PBO in MTX inadequate responders. All pts received background MTX. Effects of tofacitinib 5 mg BID vs ADA 40 mg SC were evaluated in exploratory, post-hoc analyses at Mo 3, 6, 9 and 12 of the proportion of pts achieving ACR 20/50/70 response as well as the change from baseline in each of the following ACR components: Health Assessment Questionnaire-Disability Index (HAQ-DI), tender and swollen joint counts (TJC and SJC), Patient's Global Assessment (PtGA), erythrocyte sedimentation rate (ESR), Physician's Global Assessment (PGA), C-reactive protein (CRP) and Pain. For ACR response rates, pts who withdrew before Mo 12 were considered non-responders from that visit onward. The normal approximation approach to binomial proportions was used to analyse the ACR response. A mixed-effect model was applied to analyse the change from baseline data. Treatment differences for tofacitinib 5 mg BID vs ADA 40 mg SC were reported along with 95% confidence intervals. All analyses were descriptive and were not adjusted for multiplicity.

**Results:** Overall, ACR20/50/70 response rates were numerically higher for tofacitinib 5 mg BID vs ADA over the 12 mo. At Mo 6 ACR20/50/70 rates for tofacitinib were 60.6%, 38.9%, 19.7% vs 57.9%, 28.9%, 9.1%, for ADA. At Mo 12 ACR20/50/70 rates for tofacitinib were 59.6%, 43.5%, 24.9%, vs 61.4%, 38.6%, 16.8% for ADA. Comparable changes from baseline were reported for tofacitinib vs ADA in HAQ-DI, ESR, TJC, SJC, CRP, PtGA, PGA and Pain over time, with numerically higher improvements observed for tofacitinib in the majority of ACR components (Table). Previously published safety data from this study showed that infections and infestations were the most frequent AEs reported over 12 mo in both tofacitinib and ADA treatment groups.[1] Serious infection events were more frequent in tofacitinib 5 and 10 mg BID treatment groups (3.4% and 4.0%, respectively) compared with ADA (1.5%), over 12 Mo.[1]

LS mean change from baseline (difference from comparator) [95% CI treatment differences for tofacitinib 5 mg BID vs ADA 40 mg SC] in efficacy parameters at Months 3, 6, 9 and 12 for tofacitinib 5 mg BID and ADA 40 mg SC (FAS, longitudinal model).

| Efficacy | Month 3 | | Month 6 | | Month 9 | | Month 12 | |
|---|---|---|---|---|---|---|---|---|
| Parameter | Tofacitinib 5 mg BID (N=185) | ADA 40 mg SC (N=188) | Tofacitinib 5 mg BID (N=172) | ADA 40 mg SC (N=178) | Tofacitinib 5 mg BID (N=156) | ADA 40 mg SC (N=169) | Tofacitinib 5 mg BID (N=147) | ADA 40 mg SC (N=157) |
| HAQ-DI | -0.54 | -0.50 | -0.61 | -0.56 | -0.68 | -0.58 | -0.71 | -0.64 |
| | (-0.64) [-0.15, 0.06] | | (-0.07) [-0.18, 0.04] | | (-0.10) [-0.21, 0.01] | | (-0.07) [-0.18, 0.04] | |
| TJC | -13.76 | -13.68 | -16.06 | -15.21 | -18.58 | -16.07 | -19.51 | -18.46 |
| | (-0.70) [-2.89, 1.49] | | (-0.83) [-3.09, 1.39] | | (-2.51) [-4.80, -0.22] | | (-1.05) [-3.40, 1.30] | |
| SJC | -9.74 | -8.91 | -11.28 | -10.30 | -12.51 | -10.31 | -12.89 | -11.87 |
| | (-0.82) [-2.04, 0.40] | | (-0.98) [-2.23, 0.26] | | (-2.20) [-3.48, -0.92] | | (-1.02) [-2.33, 0.29] | |
| PtGA | -23.55 | -21.34 | -25.83 | -24.51 | -29.35 | -23.25 | -31.07 | -27.14 |
| | (-2.22) [-4.69, 1.25] | | (-1.32) [-3.89, 3.25] | | (-6.16) [-11.19, -1.81] | | (-3.92) [-8.72, 0.87] | |
| PGA | -31.38 | -28.79 | -36.27 | -33.33 | -40.71 | -35.45 | -42.45 | -40.83 |
| | (-2.59) [-6.34, 1.16] | | (-2.94) [-6.78, 0.89] | | (-5.26) [-9.19, -1.33] | | (-2.10) [-6.13, 1.94] | |
| Pain | -26.75 | -22.67 | -28.70 | -23.72 | -31.51 | -25.44 | -31.48 | -29.96 |
| | (-4.08) [-8.45, 0.29] | | (-2.97) [-7.41, 1.50] | | (-6.07) [-10.65, -1.48] | | (-1.52) [-6.19, 3.16] | |
| ESR, mm/hr | -12.83 | -15.65 | -15.67 | -15.11 | -13.74 | -17.02 | -12.79 | -14.95 |
| | (2.82) [-1.29, 6.93] | | (1.44) [-2.76, 5.63] | | (3.28) [-1.02, 7.58] | | (2.16) [-2.23, 6.54] | |
| CRP, mg/L | -9.70 | -8.42 | -11.17 | -8.66 | -11.44 | -8.07 | -9.71 | -8.67 |
| | (-1.28) [-4.21, 1.65] | | (-2.51) [-5.52, 0.50] | | (-3.37) [-6.47, -0.26] | | (-1.04) [-4.25, 2.16] | |

ADA, adalimumab; BID, twice daily; CRP, C-reactive protein; CI, confidence interval; ESR, erythrocyte sedimentation rate; FAS, full analysis set; HAQ-DI, health assessment questionnaire-disability index; LS, least square; PtGA, patient global assessment; PGA, physician global assessment; SJC, swollen joint count; TJC, tender joint count. N' number of patients given in the column headers are based on HAQ-DI analysis, other endpoints could have slightly different numbers of patients due to data collection and availability. Analyses were based on the full analysis set (FAS) which includes all patients who were randomised and received ≥1 dose of study drug, with the exclusion of data from two study sites (one site was identified after completion of the study report) due to GCP violation. A negative value of treatment difference indicates the effect is in favour of tofacitinib.

**Conclusions:** These post-hoc analyses show that efficacy was generally similar in comparing tofacitinib with ADA, with numerical differences in favour of tofacitinib in some efficacy parameters. The ORAL Standard study was not designed or powered for statistical comparisons between ADA and tofacitinib. Prospective studies to investigate the effect of tofacitinib compared with ADA are under way.

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## AB0399 REAL-WORLD EXPERIENCE WITH TOFACITINIB VS ADALIMUMAB (ADA), ETANERCEPT (ETN) AND ABATACEPT (ABA) IN BIOLOGIC-EXPERIENCED PATIENTS WITH RHEUMATOID ARTHRITIS (RA): DATA FROM A US ADMINISTRATIVE CLAIMS DATABASE

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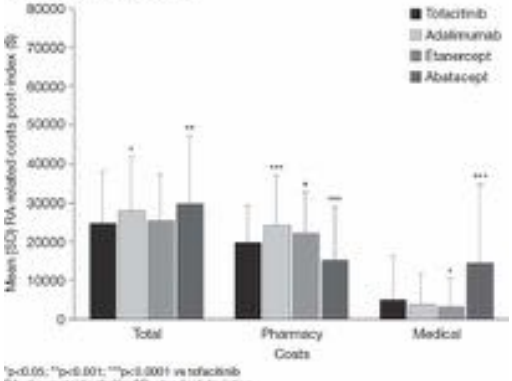
**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of RA. Limited real-world data exist comparing tofacitinib with biologic DMARDs (bDMARDs) in biologic-experienced (BE) RA patients (pts).

**Objectives:** To compare pt characteristics, treatment patterns and costs in BE RA pts receiving tofacitinib vs ADA, ETN and ABA using US claims data.

**Methods:** This retrospective cohort study included pts aged ≥18 years with RA (ICD9: 714.0x–714.4x; 714.81) and ≥1 tofacitinib (identified first) or bDMARD claim in the Truven MarketScan® Commercial and Medicare Supplemental healthcare claims database (01/11/2012–31/10/2014). Pts were continuously enrolled for ≥12 months (mos) pre- /post-index and had 1 bDMARD pre-index (due to greater imbalance in number of tofacitinib/bDMARD pts with ≥2 prior bDMARDs). Monotherapy was defined as absence of select conventional synthetic DMARDs within 90 days post-index. Outcomes were treatment persistence (index refills without a 60-day gap after prescription/administration days' supply expiration), adherence (proportion of days covered [PDC]), and 12-mo pre-/post-index RA-related costs. Adjusted analyses were performed using generalized linear models, which included demography, disease status/duration and pre-index therapy variables; 12-mo pre-index costs were included for cost-related dependent variables.

**Results:** 392 tofacitinib, 178 ADA, 118 ETN and 191 ABA pts met selection criteria. 12-mo pre-index bDMARD use was most common for tofacitinib (78%) vs ADA (60%), ETN (49%) and ABA (48%) pts (all $p<0.0001$). TNFi were the most common prior bDMARDs for tofacitinib (74%), ADA (92%), ETN (86%) and ABA (93%) pts. Pts who received tofacitinib at index had greater RA-related total/pharmacy costs vs ADA, ETN and ABA pts (all $p<0.05$) and medical costs vs ADA and ETN pts (both $p<0.0001$) in 12 mos pre-index, and highest percentage of index monotherapy use (53%) vs ADA (48%), ETN (48%) and ABA (41%; $p<0.05$) pts. The proportion of pts persistent with index therapy was similar for tofacitinib (43%), ADA (38%), ETN (42%) and ABA (44%) pts and remained so in adjusted analyses. Mean (SD) PDC was 0.55 (0.30) for tofacitinib pts vs 0.57 (0.30) for ADA, 0.59 (0.31) for ETN and 0.44 (0.39) for ABA ($p=0.0003$) pts. In adjusted analyses, ABA use vs tofacitinib was associated with lower mean PDC; increasing age and commercial insurance coverage were associated with higher PDC. Tofacitinib pts had lower post-index RA-related total costs vs ADA and ABA pts, pharmacy costs vs ADA and ETN pts, and medical costs vs ABA pts (all $p<0.05$) (Figure). In adjusted analyses, ABA, ETN and ABA use, commercial insurance coverage and number of pre-index rheumatologist visits were associated with higher total RA-related costs; North Central/Southern regions were associated with lower costs.

**Figure.** Mean (SD) RA-related total, pharmacy and medical costs in the 12-month post-index period




*p<0.05; **p<0.01; ***p<0.0001 vs tofacitinib
RA, rheumatoid arthritis; SD, standard deviation

**Conclusions:** More BE pts started tofacitinib vs ADA, ETN and ABA after recent (prior 12 mos) bDMARD use; BE tofacitinib pts had the highest proportion of monotherapy use. Persistence and adherence were at least similar for tofacitinib and bDMARD pts. Tofacitinib pts had lower adjusted RA-related total costs post-index vs bDMARD pts.

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**Disclosure of Interest:** J. Harnett Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Gerber Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Gruben Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Koenig Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Chen Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

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## AB0400 OPEN LABELED, MULTICENTER 24-WEEK STUDY TO ASSESS THE EFFICACY AND SAFETY OF TACROBELL® IN ACTIVE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is chronic inflammatory disease characterized by persistent synovitis and structural joint damage with T cell-driven inflammation. Tacrolimus suppress activation of T cells through the inhibition of calcineurin.

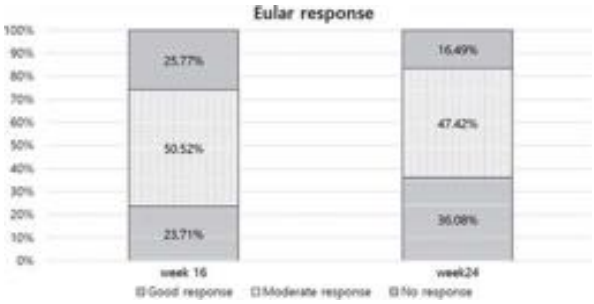
**Objectives:** We evaluated the efficacy and safety of Tacrobell® (Tacrolimus from Chong Kun Dang Pharma Inc.) in Korean active RA patient who had inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) including Methotrexate (MTX).

**Methods:** During the study period from Aug. 2012 to Jun. 2015, in this open labeled, multicenter study, 111 patients were enrolled. Patients were in active disease state with Disease Activity Score28 (DAS28) $\geq$3.2 despite previously taken at least one conventional DMARD including MTX. Patients had wash out period with DMARDs, except MTX. Patients received Tacrobell® during 24 weeks. The initial dose was 1 mg once daily and was increased to 3mg once daily by 1mg, every 4 weeks.

The disease activity was measured by the DAS28-ESR at 4, 8, 16, 24-week after the add on Tacrobell®. Simplified Disease Activity Index (SDAI), Korean Health Assessment Questionnaire (KHAQ)-20, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and the safety was assessed.

**Results:** Data from 97 patients were evaluated in full set analysis. At week-24, EULAR response rate were 83.5% (81 of 97) with improvements from week-16 in 74.2% (72 of 97). Mean DAS28-ESR was continuously decreased of 5.64 at baseline, 4.14 (±1.22, $p<0.001$) at week-16 and 3.66 (±1.39, $p<0.001$) at week-24. Efficacy rates according to SDAI were 89.7% (87 of 97) and KHAQ-20 score decreased -2.42 (±4.37, $p<0.001$) from baseline 7.27 (±4.59) at week-24. Mean ESR was decreased -10.97 (±24.16, $p<0.001$) at week-16, -14.77 (±24.57, $p<0.001$) at week-24 from baseline 46.05 (±23.22). Mean CRP was decreased from 2.86 (±7.85, $p=0.0578$) at baseline to 1.34 (±3.02, $p=0.0367$) at week-24.

The most common adverse events were in gastrointestinal (18 of 108; 16.679%) and respiratory disorder (12 of 108; 16.67%). In serious adverse events (6 of 108, 5.56%), two cases (pneumonia, high glucose level) were related with Tacrobell® and recovered with treatment. At laboratory exam, no abnormal findings with increased BUN or Cr as known common Tacrolimus side effect. Systolic blood pressure increased 2.12 mmHg at week-8.




**Conclusions:** This study demonstrated the efficacy of add on Tacrobell® therapy to MTX in patients with active RA.

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**Disclosure of Interest:** None declared

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## AB0401 COMPARATIVE EFFICACY OF INJECTION AND TABLET METHOTREXATE FORMS IN RHEUMATOID ARTHRITIS TREATMENT

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**Objectives:** To evaluate comparative efficacy of injection and tablet methotrexate forms in rheumatoid arthritis treatment.

**Methods:** 23 patients were included in study group (19 women, 4 men) with moderate (47.8%) and high activity (52.2%), receiving methotrexate subcutaneously in a dose of 10 -15 mg (average dose - 11 1±5,21) 1 time per week: 11 patients were switched from methotrexate tablet form, 2 patients received leflunomide previously, 10 patients received methotrexate initially. Comparison group - 20 patients (17 women, 3 men) taking methotrexate (10 -15 mg/week, the average dose 11,6±4,89) in tablets. The groups were comparable on key parameters. Effectiveness evaluation (ACR and EULAR criteria) and tolerability of treatment was carried out every 4 weeks for 6 months.

**Results:** Significant clinical and laboratory improvement (ACR 20) was achieved in 23 patients (main group) and in 14 patients - the control group. The appearance of the first effect (ACR 20) of methotrexate subcutaneously was observed after 2 weeks of treatment in 8 (34.8%), one month therapy - 17 (73.9%) patients, in the control group at 2 weeks - in 1 (5%), after 1 month at 7 (5%) patients respectively. After 6 months of methotrexate subcutaneously treatment decrease in activity ($DDAS28_{ESR}$ 2,3±0,9, initial $DAS28_{ESR}$ 5,3±2,9) corresponds to good effect, and treatment was significantly ($p<0.05$) better compared to the group receiving methotrexate in tablet form ($DDAS28_{ESR}$ 1,3±1,0, initial $DAS28_{ESR}$ 5,2±2,6). Adverse events occurred in 5 (21.7%) patients of the main group (alopecia, itching at the injection site, increased transaminases less than 1.5 normal) did not require discontinuation of the drug, in the control group - in 11 (55%) patients: dyspepsia, alopecia, increased transaminases, 2 (10%) patients refused from therapy

**Conclusions:** Subcutaneous administration of methotrexate in RA patients demonstrated more rapid and pronounced effect, better tolerability compared with taking the drug inside.

**Disclosure of Interest:** None declared

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## AB0402 EFFICACY OF IGURATIMOD ALONE OR IN COMBINATION WITH METHOTRXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** It has reported that Iguratimod (IGU), one of methanesulfonanilide of anti-inflamamatory agents, can inhibit anti-arthritic activity of rheumatoid arthritis (RA). IGU was approved for rheumatoid arthritis patients with inappropriate response to conventional treatments in Japan in September 2012.

**Objectives:** We aimed to assess the efficacy of IGU alone or in combination with Methotrxate (MTX) in patients with rheumatoid Arthritis

**Methods:** Patients who had an inadequqte response to MTX were enrolled. From December 2012, forty nine patients treated with IGU were analyzes retrospectively; 17 of 49 patients were treated with only IGU, 32 of 49 patients were treated with add-on IGU in combination with MTX. Disease activity and clinical response were assessed by disease activity score 28/ESR (DAS28-ESR) and EULAR response criteria, respectively. The DAS28-ESR, CRP, SDAI, CDAI at 1, 2, 3, 6, 12, 24 months from administration of IGU were examined.

**Results:** The average amount of IGU is 40.7mg in MTX group and 41.3mg in non-MTX group. The average amount of MTX was 7mg. After follow up 24 months, escape cases was six cases. The DAS28-ESR. After 12 months of treatment, The DAS28-ESR was decreased from4.32 to 2.37 significantly in MTX group ($P<0.01$), and also decreased from4.23 to 2.37 significantly in non-MTX group ($P<0.01$). According to EULAR response criteria at 12 months, The DAS28-ESR remission was observed in 46.9% of patients in MTX group and 52.9% in non-MTX group. CRP decreased from1.9 to 0.7 significantly in MTX group ($P<0.01$), and also decreased from 2.1 to 0.8 significantly in non-MTX group ($P<0.05$).There was no significant difference between the two groups.

**Conclusions:** Based on these results, we can conclude that the treatment of IGU is effective and well tolerated, and represents a new option for RA patients, including patient with inadequqte response to MTX.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2506

## AB0403 WHAT IS THE PLACE OF CORTICOSTEROIDS IN THE TREATMENT OF PATIENTS WITH EARLY ARTHRITIS?

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**Background:** While the 2013 EULAR recommendations for the management of rheumatoid arthritis (RA) mention that low-dose corticosteroids (CS) should be considered as part of the initial treatment strategy in association with DMARDs and should be tapered as soon as possible (1), the 2015 ACR Guidelines for the treatment of RA recommend CS for early RA (ERA) patients only if the disease flares (2).
**Objectives:** The aim of this study is to determine what forms of CS are used for patients with ERA and if the use of CS influences the outcome of this patients.
**Methods:** We have evaluated data obtained from patients with early arthritis (duration of less than 12 months), either ERA or early undifferentiated arthritis not classifiable as other disease, referred to the Early Arthritis Research Center of "Dr. I. Cantacuzino" between 2010 and 2014. Patients were treated according to the current guidelines. Parameters were evaluated at baseline and after 1 year of follow up.
**Results:** 73 patients were enrolled in this study and 60.3% were female. The mean age was 49.81±15.93 years. The mean duration of symptoms was 3.39±3.42 months. The parameters evaluated at baseline and after 1 year of follow up (median value and interquartile range) are described in Table 1.

Table 1. Parameters evaluated during the study

| Parameter | Baseline Median (Interquartile range) | 12 months Median (Interquartile range) |
|---|---|---|
| CRP (mg/l) | 8.63 (2.63–18.44) | 1.91 (0.91–4.19) |
| ESR (mm/h) | 27.00 (11.00–47.00) | 12.00 (7.00–17.00) |
| VAS patient (mm) | 64.00 (52.50–76.00) | 15.50 (0.00–26.00) |
| VAS physician (mm) | 50.00 (30.00–60.00) | 10.00 (0.00–10.00) |
| DAS28 | 4.75 (3.63–5.35) | 1.61 (1.17–2.59) |
| SDAI | 26.12 (14.94–32.13) | 2.67 (0.31–5.32) |

61.7% of patients received treatment with DMARDs and 56.2% of patients received CS, associated with DMARDs. The types of CS used at baseline and the percent of patients who received each type were: Prednisone (42.5%), Dexamethasone i.m. (4.1%), Betamethasone administered intra-articularly (8.2%) and pulse therapy with Methylprednisolone (1.4%). At 12 months only 10 patients (13.7%) still received CS and the only form of CS used was low-dose Prednisone. The number of patients who required CS decreased significantly during the study ($p<0.001$ – Wilcoxon test). All the parameters evaluated decreased significantly during the study ($p<0.001$ – Wilcoxon test), but CS didn't influence any of them ($p>0.05$ – linear regression) regardless of dose or mode of administration.
**Conclusions:** In a relatively small cohort of patients with early arthritis, there was no significant influence of CS treatment on the variation of parameters reflecting disease activity at 12 months. The doses and modes of administration at baseline varied, but that didn't influence the outcomes. On short-term, patients who receive CS, at baseline, have an subjective improvement of symptoms assessed by VAS, but at 12 months there is no significant difference between those who received at baseline DMARDs associated with CS and those who received DMARDs monotherapy. The number of patients who required treatment with CS decreased significantly during the follow up period and the few patients who still required CS at 12 months were receiving only low-dose Prednisone.
**References:**
[1] Smolen JS et al. Ann Rheum Dis. 2014;73:492–509
[2] Singh JA et al. Arthritis&Rheumatology; 2016;68(1):1–26
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2529

## AB0404 ULTRASONOGRAPHIC EVALUATION OF IGURATIMOD THERAPY IN PATIENTS WITH JAPANESE RHEUMATOID ARTHRITIS

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**Background:** Iguratimod (IGU) is a small-molecule antirheumatic drug that was approved in Japan in September 2012. IGU suppressed tumor necrosis factor-alpha-induced production of interleukin (IL)-6, IL-8, and monocyte chemoattractant protein 1 via inhibition of nuclear factor kappa B activation in cultured human synovial cells and human acute monocytic leukemia cells. We reported the clinical efficacy of IGU at ACR2014 and EULAR2015. However there is still few studies of improvement of ultrasonographic findings in RA treated with IGU.
**Objectives:** To evaluate the clinical efficacy of IGU therapy patients with rheumatoid arthritis (RA) using ultrasonography (US).
**Methods:** Participants comprised 51 Japanese RA patients who had recently received IGU. All patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria. Patients underwent clinical and laboratory assessments every 4 weeks from baseline to 24 weeks, and US assessments at baseline, 12 and 24 weeks. Gray scale (GS) and power doppler (PD) signals were scored using a semi-quantitative scale from 0 to 3 at 26 (0–78) synovial sites (22 joints) in the following joints: bilateral first to fifth metacarpopharangeal (MCP) joints (dorsal recess); first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) (dorsal recess) joints; and the wrists (dorsal radial, median and ulnar). We evaluated the improvement of GS and PD score from baseline to week 24.
**Results:** The patients included 15 males and 36 females. The mean age was 65.4±11.6 years; the mean disease duration was 9.1±11.0 years; and the number of MTX combination, other DMARD excluded combination, IGU monotherapy and Biologics combination were each 30, 9, 8 and 4 cases.
Clinical findings related to RA were as follows: tender and swollen joint count, 4.2±2.9 and 3.2±2.2; patient's and physician's global assessment of disease activity, 39.7±23.3 and 39.7±18.9mm; CRP, 1.1±1.3 mg/dL; ESR, 31.4±18.6 mm/h; DAS-ESR, 4.37±0.85; DAS-CRP, 3.80±0.74; CDAI, 15.3±6.4 and SDAI, 16.4±6.8. The mean CRP improved to 0.7±1.0 and 0.5±0.8 at Week 12 and 24 ($p<0.001$, $p<0.001$), mean MMP3 improved to 147.7±140.4 and 161.8±254.5 at Week 12 and 24 ($p<0.001$, $p=0.003$), the mean DAS-ESR improved to 3.39±0.93 and 2.91±0.83 at Week 12 and 24 ($p<0.001$, $p<0.001$) and the mean SDAI improved to 8.6± 6.0 and 5.8±4.8 at Week 12 and 24 ($p<0.001$, $p<0.001$) significantly. The mean GS score changed from 16.8±12.4 at baseline to 15.7±11.0 ($p=0.158$) and 14.5±9.8 ($p=0.043$) at week12 and 24. The mean PD score changed from 7.9±6.8 at baseline to 6.0±6.1 ($p=0.001$) and 5.3±5.5 ($p=0.006$) at week12 and 24 (Fig.1).
In the with MTX (n=30) and monotherapy or with csDMARD patients (n=17), the respective changes in GS and PD scores from baseline to 12 or 24 weeks were as follows: ΔGS score: -2.3±7.0 vs 1.3±5.8 ($p=0.118$) at 12 weeks and -3.9±9.2 vs 0.3±8.8 ($p=0.158$) at 24 weeks; and ΔPD score: -2.8±6.7 vs -0.5±2.6 ($p=0.053$) at 12 weeks and -4.0±6.8 vs 0.1±5.0 ($p=0.016$) at 24 weeks (Fig.2).

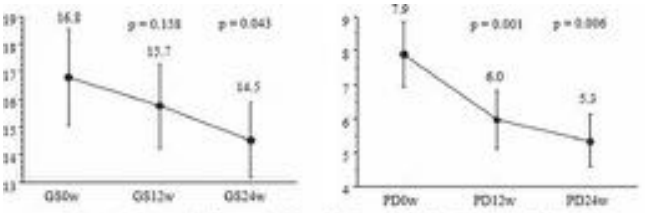


Figure 1 : Respective changes in GS and PD score from baseline to Week 24

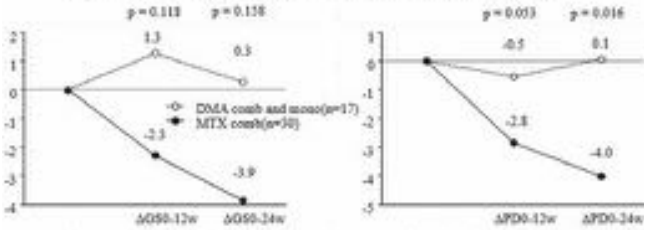


Figure 2 : Respective changes in ΔGS and ΔPD score from baseline to Week 24 in MTX combination and csDMARD combination or IGU monotherapy patients

**Conclusions:** The present study provides evidence supporting the IGU therapy improved not only the disease activity not also the inflammatory synovitis. Especially MTX combination patients could expect higher efficacy of IGU treatment.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6076

## AB0405 EFFECTS OF ATORVASTATIN ON DYNAMICS OF BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** There are some data indicating that statins produce a pleiotropic effect and can increase bone mineral density. It is also known that some statins (pravastatin, simvastatin) have an anti-inflammatory effect. Simvastatin has been shown to be effective in the treatment of rheumatoid arthritis (RA) in humans. We failed to find any research data indicating that atorvastatin has anti-inflammatory effects.

**Objectives:** To study the effect of Atorvastatin on the dynamics of bone mineral density and inflammatory markers of osteoporosis (OP) in patients with RA.
**Methods:** We examined 170 RA patients aged 22 – 75 years (128 females (75.3%) and 42 males (24.7%)). Bone mineral density was measured with dual-energy X-ray absorptiometry (DEXA) (Lunar DPX-Pro, GE, USA). Additionally, we measured serum osteocalcin levels and urine CrossLaps with ELISA test.
We divided the patients into two groups to study the effectiveness of Atorvastatin in the treatment of patients with RA/OP and osteopenia. Group 1 included 38 individuals who received Atorvastatin for 6 months at a dose of 20–40 micrograms per day. The experimental group included 29 patients with OP and osteopenia. They received calcium supplements at a dose of 1000 mg per day.
**Results:** We revealed that 84 (51.5%) out of 170 patients with RA had significantly lower Z- and T-scores values. We noted that 17 (20.2%) patients were diagnosed as having osteoporosis, while 67 (79.8%) had osteopenia. The most common manifestations of OP in RA patients included fractures, bone and back pain, as well as decreased muscle strength.
We measured biochemical markers of bone turnover at baseline and after 6-month of the treatment. There was significant positive dynamic of clinical and laboratory parameters during a 6-month treatment with Atorvastatin in OP patients with RA. In this patients we observed BMD and muscle strength increasing, reducing of bone and back pain, decreasing of C-reactive protein. Urinary CrossLaps were significantly decreased. Atorvastatin was well tolerated. There were few of insignificant side effects which were reduced after the drug dose decreasing. Symptomatic improvement occurred within 2–3 months after starting of atorvastatin therapy. Second group patients who received calcium monotherapy showed signs of progressive OP: bone mineral density continued to decrease (mean -2.7±0.18%), while bone pain and biochemical markers of bone metabolism remained unchanged.
**Conclusions:** We concluded that Atorvastatin may be used in the treatment of RA patients and can help to stabilize bone mineral density and improve the OP symptoms.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1107

## SLE, Sjögren's and APS - treatment

### AB0406 CLINICAL EXPERIENCE FROM ABATACEPT USE IN SYSTEMIC LUPUS ERYTHEMATOSUS: EFFECTIVENESS AND SAFETY

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**Background:** Biologicals therapies have been used for the treatment of Systemic Lupus Erythematosus (SLE) but only Belimumab has been approved by the European Medicines Agency. Abatacept (ABA), a T-cell co-stimulation blocker, has been proposed as an effective treatment for SLE due to its mechanism of action. Three randomised clinical trials have been performed with ABA in patients with SLE. Although any of these trials met the primary outcome of efficacy, it is still considered as an "off-label" option when none of the other conventional therapies have worked.
**Objectives:** To assess effectiveness and safety of ABA in patients diagnosed of SLE in a Rheumatology service from a tertiary care hospital in Madrid, Spain.
**Methods:** We performed an observational retrospective study in patients with SLE (according to the 1997 American College of Rheumatology classification criteria) who received treatment with ABA. We recorded demographic, clinical and laboratory parameters at the beginning of treatment, and after 6 and 12 months of treatment. We also recorded adverse events.
**Results:** We included 8 patients, all of them women. The median age was 45.13 years (range 30–67 years) and the median time from SLE diagnosis to ABA treatment was 12.12 years (range 3–21 years). Three patients had an overlap disease with Rheumatoid Arthritis. The most frequent symptoms were arthritis (n=5), cutaneous (n=3) and neurological symptoms (n=5), specifically organic brain syndrome (n=4) and lupus headache (n=3). None of the patients had renal disease. In all patients ABA was use after anti-TNFα or Rituximab treatment. One patient discontinued ABA after 2 months due to inefficacy, so she was excluded from statistical analysis.
Table 1 shows clinical and laboratory parameters at the beginning of treatment and after 6 and 12 months of treatment. After 6 months of treatment, disease activity according to SLEDAI decreased. One patient persisted with organic cerebral syndrome. After 12 months of treatment neurological symptoms showed a substantial improvement in every patient that presented them at the beginning. Four patients showed significant improvement of arthritis. Two patients experienced serious infections that required hospitalization.

Table 1. Clinical and laboratory parameters

| | 0 months (n=7) | 6 months (n=7) | 12 months (n=7) |
|---|---|---|---|
| SLEDAI (median) | 13.71 | 3.71* | 1.43* |
| Prednisone dose (mg/ day) (median) | 6.78 | 5.71 | 3.57 |
| Anti-DNA antibody levels (UI/ml) (median) | 80.61 | 22.77* | 20.21 |
| C3 (mg/dl) (median) | 95.94 | 94.13 | 98.94 |
| C4 (mg/dl) (median) | 11.63 | 15.13* | 14.88 |

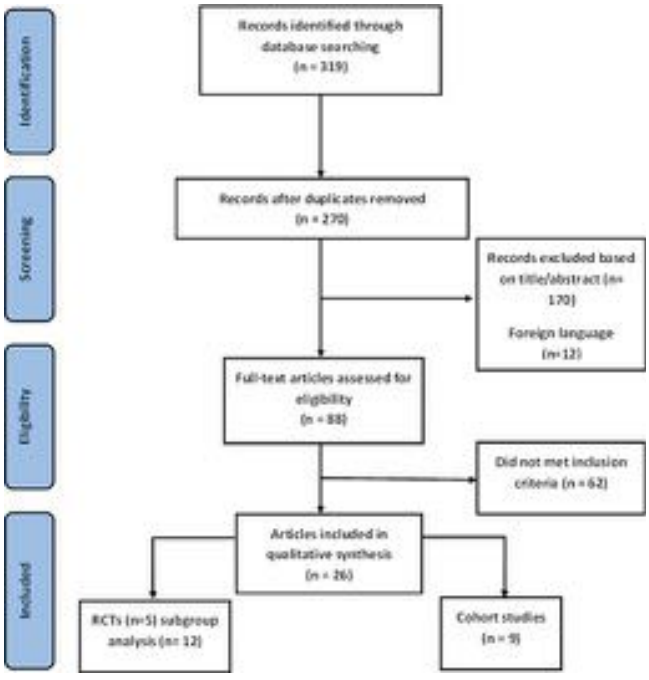
*Wilcoxon's Signed Rank Test, *p<0.05. Baseline vs 6 months after treatment and baseline vs 12 months after treatment.

**Conclusions:** ABA was effective in our SLE patients. Clinical response was evident at 6 months and persisted at 12 months. ABA may be a therapeutic option in SLE patients with inadequate response to conventional therapies, specially if arthritis or neurological symptoms are present.
**References:**
[1] Aringer M. Expert Opin Drug Saf. 2015;14:243–51.
[2] Ikeda K. Clin Dev Immunol. 2013;2013:697525.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4881

### AB0407 CAN WE IDENTIFY WHO BENEFITS FROM MYCOPHENOLATE MOFETIL IN SYSTEMIC LUPUS ERYTHEMATOSUS? A SYSTEMATIC REVIEW

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**Background:** Mycophenolate mofetil (MMF) has been shown to be a good therapeutic option in systemic lupus erythematosus (SLE), particularly lupus nephritis (LN). There is, however, evidence of variation in the response. Knowledge of predictors of response could aid patient selection for this therapy.
**Objectives:** The aim of this systematic review was to summarize the evidence examining factors measured at baseline and during treatment associated with a response to MMF in SLE.
**Methods:** We searched Medline, Embase, Web of Science and Cochrane Central Registers for Controlled Trials until November 2015 for relevant studies (Fig. 1). Studies included were randomized clinical trials (RCTs) with subgroup analysis and cohort studies involving SLE patients administered MMF with factors measured at baseline and during treatment that may predict treatment outcome. The overall quality of studies included was assessed independently by two reviewers. The quality of RCTs and cohort studies was assessed using the Cochrane Collaboration risk of bias tool and the QUality In Prognosis Studies (QUIPS) assessment tool, respectively. The quality of subgroup analysis was also evaluated. The Grading of Recommendations Assessment, Development, and Evaluation working group approach summarized the quality of evidence (QoE).
**Results:** Although the methodological quality of RCTs was good for primary outcome, most were compromised by lack of power for subgroup analyses and lack of an explicit test of the interaction. Very-low to low QoE suggested a comparable efficacy and safety of MMF among White, Black, Hispanic and Asian patients. Very- low to low QoE indicated that adolescent patients had neither a better LN response at 24 weeks or treatment failure rates at 36 months compared with adults. Patients with membranous LN or poor renal function (<30 mL/min/1.73 $m^2$) may have a renal improvement at 6 months with MMF according to low QoE. Moderate QoE suggested patients with extrarenal manifestations



may show control of disease activity and significant reduction in corticosteroid dose at 6 and 12 months. One moderate QoE study showed that LN patients with a mycophenolic acid area under the curve (MPA AUC) ≥30 mg/h/L-1 may have a better renal response at 1 year. Several studies of varying quality indicated a better response to therapy at 6 and 12 months in LN patients with an early reduction in proteinuria or early normalization of C3 and C4. However, an early reduction in anti–double-stranded DNA was not predictive of the renal response at 6 months.

**Conclusions:** In SLE patients, evidence for predictors of outcomes with MMF is limited. The results of this review should be treated with caution due to the heterogeneity of studies, and the risks of bias identified. Future studies of predictors measured at baseline and during treatment should be designed with "a priori" hypotheses and adequate statistical power.

**References:**

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[2] Huguet A, et al. Judging the quality of evidence in reviews of prognostic factors research: adapting the GRADE framework. Syst Rev. 2013;2:71

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**Disclosure of Interest:** None declared

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## AB0408 FACTORS THAT INFLUENCE THERAPY IN PATIENTS WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE

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**Objectives:** To compare clinical and immunological characteristics in patients with undifferentiated connective tissue disease (UCTD) treated with hydroxychloroquine (HCQ) in a large academic clinical practice.

**Methods:** This cross-sectional study included all patients diagnosed with UCTD according to the preliminary classification criteria (1), that seen at the Columbia University Lupus Clinic in New York, from January to December 2015. Clinical and immunological variables were ascertained by clinical evaluation and chart review. Chi squared tests were used to compare the following characteristic between treated and untreated patients: demographic characteristics, number of ACR criteria, SLICC criteria, individual symptoms and laboratory values.

**Results:** Eighty-three patients were identified; 93% were female, mean age at diagnosis of 44 years ±14.9; 67% were Caucasian, 20% Hispanic and 11% Black/African American; median disease duration of 3.91 years ±5.35. The most prevalent symptoms that required medical attention were arthralgia (81%), arthritis (46%), Raynaud (41%), fatigue (32%) and sicca symptoms (30%). All patients had positive antinuclear antibody (ANA) titers, 87% had titers above 1:640, with speckled pattern in 71% of patients. Interestingly, 16% of the patients studied met SLICC SLE criteria. Half of the patients, 42 (51%) were treated with HCQ and 41 (49.3%) were not treated.

The patients treated with HCQ were more likely to meet SLICC criteria (10 vs. 3, respectively; p=0.03), have a history of arthralgia (38 vs. 29; p=0.02), arthritis (28 vs. 10; p=0.0001), and fatigue (25 vs. 14; p=0.02). A history of low complement was more prevalent in the treated group (12 vs. 3, p=0.01).

**Conclusions:** Data from this single-center cohort of patients with UCTD show that patients treated with HCQ by their rheumatologist are more likely to have multiple clinical criteria and low complement compared to those that were not treated. These data suggest that rheumatologist treat pre-clinical autoimmunity in the setting of clinical symptoms. None of patients were treated based on serologies alone. Longitudinal studies are needed to evaluate the long-term impact of HCQ on outcomes in patients with UCTD.

**References:**

[1] Mosca M, Neri R, Bombardieri S. Undifferentiated connective tissue diseases (UCTD): a review of the literature and a proposal for preliminary classification criteria. Clin Exp Rheumatol 1999;17:615–20.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.6011

## AB0409 MODIFIED HOMA-IR INDEX IN PATIENTS WITH RHEUMATIC DISEASES RECEIVING GLUCOCORTICOID THERAPY

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**Background:** HOMA-IR index is widely used in current clinical practice for the evaluation of insulin resistance (IR). Elevation of HOMA-IR index is an indirect marker of IR progression.

**Objectives:** To evaluate the role of modified HOMA-IR index in patients with rheumatic diseases receiving glucocorticoid (GC) therapy.

**Methods:** The study included 98 patients with rheumatic diseases, including systemic lupus erythematosus (SLE) - 53 patients and systemic vasculitis (SV) – 45 patients. The first group included 52 patients receiving GC pulse-therapy (GC-PT) (prednisolone 10–15 mg/kg a day i/v, on 3 consecutive days), the second group included 46 patients receiving oral prednisolone 15–30 mg/day. The first group included 31 (59.6%) women and 21 (40.4%) men aged 18–69 years. Control group included 27 (58.7%) women and 19 (41.3%) men aged 19–63 years. All patients underwent standard clinical evaluation and an oral glucose tolerance test (OGTT): patients receiving GC-PT underwent OGTT 72 hours after the end of PT course, patients receiving oral GC – during the time of inpatient treatment. According to OGTT results patients were divided into 4 groups: no carbohydrate metabolism disturbance (CMD), impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and diabetes mellitus (DM). IR calculation according to HOMA-IR index was performed according to a formula proposed by X. Li et al. (2004): Homa-IR =1,5 + fasting blood glucose (mmol/l) x fasting C-peptide level (pmol/l) /2800.

**Results:** CMD developed in 10 (33.3%) patients in SLE group receiving GC-PT, compared to 18 (81.8%) patients receiving oral GC (p=0.002). In SV patients CMD was more prevalent in those receiving oral GC compared to GC-PT (4 (19.1%) vs. 19 (79.2%) patients, respectively (p=0.035). HOMA-IR index, reflecting the degree of IR, was elevated in patients with IGT and DM at baseline, during maximal blood glucose level and after GC-PT, compared to patients without CMD and IFG ($p<0.05$). IR was more pronounced in patients receiving oral GC and IGT and DM after OGTT ($p<0.05$), which demonstrates that a more pronounced IR during GC therapy predisposes to the development of more pronounced CMD.

**Conclusions:** GC therapy results in the development of IGT and DM in patients with elevated IR after GC-PT or prolonged oral GC treatment. CMD is more prevalent among patients receiving prolonged oral GC therapy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4748

## AB0410 THE INFLUENCE OF MAGNETIC PROPERTIES OF THE ADSORBENTS ON EFFICIENCY OF EXTRACORPOREAL THERAPY IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH ANTIPHOSPHOLIPID SYNDROME

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**Background:** Due to magnetic properties an installation which creates physiological magnetic field holding granules in suspension to prevent particle adhesion of sorbent and contribute to better blood contact was used.

**Objectives:** To remove pathogenic antibodies to cardiolipin in patients with systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS), constant hemocompatible antigenic drugs with magnetic properties (immobilized granulated antigen drugs – IGAD) were created.

**Methods:** To determine antibodies level to cardiolipin (AKA) the indirect ELISA was used. Magnetic adsorbents were created using technique of 3D oriented antigen fixation.

**Results:** When carrying out sorption of antibodies to cardiolipin (CL) in vitro, its decrease in all cases of EGAD use was observed (before sorption of antibodies to CL – 0.390±0.021, after – 0.141±0,006, $p\leq0.001$) unlike hemosorption with activated coal (before coal hemoadsorbent (HSC) – 0.52±0.05, after – 0.44±0.04, $p>0.05$). The use of activated carbon was accompanied by significant damage of formed blood elements: erythrocytes ($10^{12}$ /l) 3.8±0.02 – prior to sorption, 3.3±0.02 – after sorption; leukocyte count ($10^9$ /l) 5.4±0.12 before sorption, 4.0±0.09 after sorption; platelets ($10^9$/l) 203±1.14 – prior to sorption, 146±0.97 – after sorption that wasn't observed when IGAD used (erythrocytes ($10^{12}$ /l) – prior to sorption 3.8±0.03; after sorption 3.8±0.03; leukocytes ($10^9$ /l) – prior to sorption 5.4±0.12; after – 5.3±0.14; platelets ($10^9$/l) – prior to sorption 203±1.17; after 200±1.53.

Thrombosis frequency in the column free of magnetic field made 8 cases out of 20, and in 4 of them prevented blood flow. When carrying out immunoadsorbtion procedure in installation mentioned, 1 case out of 20 microclots were detected, which were not an obstacle to successful completion of immunoadsorbtion ($\chi^2$ =7.03, p=0.009). As a result of sorption procedure a significant decrease in circulated immune complexes (CIC) concentration from 12.4±1.2 to 4.6±0.5% was observed, at the same time changes in the concentration of total protein, immunoglobulin G, A, M classes were insignificant ($p<0.05$).

**Conclusions:** Thus, the adsorbent magnetic properties allow to avoid formed blood elements destruction as well as to increase extracorporal immunoadsorbtion efficiency, especially in cytopenic syndrome often observed in patients with SLE with APS.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.2676

## AB0411 RAPID REDUCTION OF ANTIBODIES AND IMPROVEMENT OF DISEASE ACTIVITY BY IMMUNOADSORPTION IN CHINESE PATIENTS WITH SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Immunoadsorption (IAS) has been used to treat patients with SLE for many years. Efficacy was proved for case report or series with SLE after IAS treatment, while case-control studies are so far lacking.
**Objectives:** We aim to evaluate the efficacy and safety of IAS as an addition to aggressive immunosuppressive treatment in Chinese SLE patients with severe disease activity.
**Methods:** Patients with SLE disease activity index 2000 (SLEDAI 2k) >15 were enrolled. The number of patients in IAS group and non-IAS group was 52, including 22 with lupus nephritis (LN), 10 with severe thrombocytopenia (<10 platelets/$\times 10^9$/l), 10 with neuropsychiatric lupus and 10 with a large pericardial effusion, respectively. Observation study was performed for every individual in either group for 3 months. Corticosteroid pulse therapy (CSPT, intravenous methylprednisolone 250 mg/day for 3 days) was given to each patient consecutively, followed by a daily oral dose of 1 mg/kg bodyweight of corticosteroid. Corticosteroid were tapered by 10% every 1~2 weeks after 4 weeks. IAS was initiated on the second day of CSPT. Other immunosuppressant included intravenous cyclophosphamide pulse therapy (IVCY, targeting 0.5 g/m$^2$ body surface area) every 2 weeks for 3 months. IVCY was initiated after 3 days' of CSPT.
**Results:** In total 52 SLE patients, the improvement of C3 level, dsDNA and AnuA titer after treatment at different visits compared with baseline was discovered in both groups, while the overall changes of these markers in IAS group were all more significant than those in non-IAS group. Similar results were observed in subgroup analysis. SLEDAI score dropped significantly after 1 week of treatment both in IAS group (from 24.46±4.14 to 12.65±3.85, p=$1.13\times10^{-27}$) and non-IAS group (from 24.46±4.07 to 14.67±3.42, p=$5.41\times10^{-24}$), while the significance was more prominent in IAS group (p=0.004). The dosage of steroids used at 3 months was significantly lower in IAS group (13.46±4.12mg) than that in non-IAS group (15.10±3.77mg) (p=0.037). No severe side effect occurred in our study.
**Conclusions:** This is the first report of the application of phenylalanine immunoadsorption to treating patients with SLE in China. In combination with corticosteroid therapy and immunosuppressant, IAS would appear to be an effective and safe treatment optimal for SLE, without consideration of its high cost.
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**Disclosure of Interest:** None declared
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## AB0412 EXPLORATORY RESULTS FROM THE BLISS AND ILLUMINATE TRIALS SUPPORT THE DESIGN OF THE CHABLIS-SC1 TRIAL, A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF BLISIBIMOD ADMINISTRATION IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Targeted, biologic inhibitors of B-cell Activating Factor (BAFF) have been evaluated in 4 large Phase 3 clinical trials in nearly 4000 patients with Systemic Lupus Erythematosus (SLE). Data from these studies identify that greatest treatment effect is discernable using more stringent endpoints in patients who enter with higher disease activity scores, taking more corticosteroids, and/or have anti-double-stranded DNA (dsDNA) and low complement C3 or C4[1,2,3].
**Objectives:** The CHABLIS-SC1 study (NCT01395745) has completed enrollment and will be the first trial to prospectively evaluate the impact of treatment on the above "responder populations" using the BAFF inhibitor, blisibimod.
**Methods:** CHABLIS-SC1 enrolled subjects positive for anti-nuclear and/or anti-dsDNA antibodies with SELENA-SLEDAI≥10 despite corticosteroid therapy. Subjects were randomized to have blisibimod or placebo added to their background medications. Efficacy will be evaluated using the SLE Responder Index-6 (SRI-6) at Week 52, defined as: ≥6 point reduction in SELENA-SLEDAI; no new BILAG A or 2 new BILAG B organ domain scores; and no worsening in Physician's Global Assessment.
**Results:** Table 1 identifies that the baseline characteristics of the 442 subjects enrolled into the CHABLIS-SC1 study more frequently meet all descriptions of "responder populations" identified previously[2–7]. In previous studies, the SRI-6 was associated with lower placebo responder rates and greater benefit of BAFF inhibitors over placebo.

Table 1. Estimated baseline disease characteristics of subjects in the CHABLIS-SC1 study and in Phase 3 trials with other BAFF inhibitors

| | Blisibimod (CHABLIS-SC1) | Belimumab (BLISS Trials) | Tabalumab (ILLUMINATE Trials) |
|---|---|---|---|
| Total randomized (N) | 442 | 1664 | 2288 |
| Mean age (years) | 36.3 | 35.3 | 40.7 |
| Female (%) | 93.9 | 94.1 | 91.9 |
| Mean SELENA- SLEDAI | 13.6 | 9.7 | 10.3 |
| Receiving corticosteroids (%) | 100 | 86.3 | 75.3 |
| ANA ≥1:80 (%) | 98.9 | 93.0 | – |
| +Anti-dsDNA (%) | 85.5 | 69.4 | 59.2 |
| Low C3 <90mg/dL (%) | 53.9 | 45.0 | 39.4 |
| Low C4 <16mg/dL (%) | 48.2 | 56.1 | 22.5 |
| +Anti-dsDNA & Low C3/C4 (%) | 59.7 | 52.6 | 35.0 |
| Protein:Creatinine ≥1g/g (%) | 19.7 | 13.1 | [Pr:Cr ≥0.4 10.4%] |
| Protein:Creatinine >2g/g (%) | 9.5 | 5.9 | – |

**Conclusions:** BAFF inhibitors are known to be at least modestly effective in SLE and impact B Cell-driven immunopathology such as autoantibodies. The CHABLIS-SC1 study design will determine whether enrichment for the hypothesized "responder population," patients with more severe, immunologically active SLE, will robustly discriminate treatment impact of blisibimod when background therapy is maintained.
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**Acknowledgement:** We wish to thank all of the patients, Investigators and study personnel participating in this trial.
**Disclosure of Interest:** J. Merrill Consultant for: Anthera Pharmaceuticals Inc, V. Strand Consultant for: Anthera, C. Hislop Shareholder of: Anthera, Employee of: Anthera, M. Gangal Shareholder of: Anthera, Employee of: Anthera, R. Martin Shareholder of: Anthera, Employee of: Anthera, K. Kalunian Consultant for: Anthera
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## AB0413 SYSTEMIC THERAPY IN PRIMARY SJÖGREN SYNDROME PATIENTS

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**Background:** Primary Sjögren syndrome (pSS) is a systemic autoimmune disease involving mainly the exocrine glandular system. Nevertheless, its clinical spectrum includes the development of multiple extra-glandular manifestations which will be determinant for the use of systemic therapy.
**Objectives:** The aim of our study was to describe the systemic therapy in a pSS cohort assisted in Spanish Rheumatology Departments and its association with the involvement of different organs.
**Methods:** This is a multicenter descriptive transversal study of pSS patients fulfilling European/American consensus criteria. Patients were included by randomization from thirty-three Rheumatology departments. Data were collected by reviewing clinical records and interviewing the patients. Informed consent was obtained and local ethics committees approved the study. Variables were analysed by descriptive statistical methods, using means, medians, and rates. Chi-square was used to establish the statistical associations, being considered a p<0,05 as significant.
**Results:** Four hundred and thirty-seven patients were included. Ninety-five percent of them were women. The median age of the cohort was 58 years. Eighty-four percent of the patients have been treated (currently or previously) with non-steroidal anti-inflammatory drugs (NSAID), 49% had been treated with glucocorticoids (GC), 7% with boluses of GC, 51% with antimalarial, 13% with methotrexate (MTX), 10% with azathioprine (AZA), 4% with mycophenolate mofetil (MM) and 3% with cyclophosphamide (CF). NSAIDs were significantly used more frequently in patients with joint involvement. GC were significantly used more frequently in patients with joint, pulmonary, central and peripheral nervous system (CNS and PNS) involvement and cytopenia. GC boluses were used significantly

more frequently in patients with musculoskeletal, pulmonary and nervous system involvement. Antimalarials were significantly used more frequently in patients with joint involvement. MTX was significantly used more frequently in patients with joint, CNS involvement and cytopenia. AZA was significantly used more frequently in patients with lung and CNS involvement and cytopenia. MM was significantly used more frequently in patients with renal, lung and PNS involvement, and cytopenia. CF was significantly used more frequently in patients with joint, pulmonary, CNS and PNS involvement.

**Conclusions:** Despite the absence of clinical controlled studies demonstrating efficacy and safety, systemic therapy use in SSp patients is very frequent. Its use is mainly associated with the presence of musculoskeletal, neurological, pulmonary and haematological manifestations.

**Disclosure of Interest:** None declared

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## AB0414 MYCOPHENOLATE MOFETIL AND DEFLAZACORT IN NEUROPSYCHIATRIC LUPUS: A RETROSPECTIVE STUDY

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**Background:** Mycophenolatemofetil (MMF) is an effective therapeutic agent with high safety profile in the management of lupus nephritis.

**Objectives:** This retrospective study was conducted to assess the efficacy and side effect profile of MMF and deflazacort in patient with neuropsychiatry lupus (NP SLE).

**Methods:** Patients of SLE by SLICC 2012 between January 2005 and May 2015 satisfying ACR 1997 criteria for NP SLEwere recruited from department of Clinical immunology & Rheumatology, Christian Medical College, Vellore, India. Patients consistently using MMF as the second line agent were enrolled. Clinical response, SLEDAI and side effect profile were noted from electronic medical records. Clinical improvement was defined as remission of presenting neurological symptom with no new neurological symptom.

**Results:** Of the 140 patients with NP SLE, 88 fulfilled the inclusion criteria. Mean age of the cohort was 25.51±7.82 years with female to male ratio of 84: 4. Median duration of neurological symptoms prior to presentation was 90 (17.5 – 317.5) days. Median duration of follow up was 33 (3–129) months. Among the various NP SLE manifestations, seizure was the most common presentation (n=37, 42.05%). Renal involvement was seen in 49 (55.7%) patients. MRI findings varied from white and grey matter hyper -intensities to ventricular dilatation and brain atrophy. Of the 88 patients on MMF, 13 were pulsed with 1 gm methylprednisolone for 3 days and 8 were pulsed with oral dexamethasone pulse of 40 mg/day for 5 days. Subsequently, oral steroids was started at a dose of 1 mg/kg & tapered after 8–12 weeks to mean deflazacortdose (prednisoloneeqyuivalent) of 11.07±7.77 (9.33±5.88) mg at the end of 1 year.

IMAGE: Showing various parameters at baseline and follow up as below.

Major adverse events included lower respiratory tract infection in 2 patients and 1 fatality due to sepsis from gastroenteritis.

Of 68 patient with median duration of follow up of 33 (3–129) months, 17 were only on MMF without any steroids, 14 not on either steroids or MMF and 6 were only on maintenance low dose steroids.

Table 1. Comparing side effect profile of patients on deflazacort and prednisolone (n=88)

| | Deflazacort | Prednisolone | P value |
|---|---|---|---|
| Number of patients | 70 | 18 | 0.001 |
| Cushingoid habitus | 7 | 16 | 0.000 |
| Serious Infections | 0 | 3 | 0.006 |
| Steroid induced hypertension | 1 | 4 | 0.000 |
| Steroid induced diabetes | 4 | 6 | 0.001 |

Deflazacort was equally efficacious and had better toxicity profile than prednisolone.

| Parameters | Baseline | Follow up at 3 months (%) | Follow up at 1 year (%) | Last follow up (%) |
|---|---|---|---|---|
| Number of patients | 88 | 78 (88.6%) | 76 (86.4%) | 68 (77.3%) |
| Mean steroid dose – deflazacort ( prednisolone equivalent) | 49.82 ± 14.65 ( 41.51 ± 12.21) | 33.42 ± 13.80 ( 27.85 ± 11.50) | 11.07± 7.77 ( 9.33 ± 5.88) | 3.63± 1.27 ( 3.03 ± 1.06) |
| Patients with clinical improvement (%) | NA | 68 (87.2%) | 71 (93.4%) | 66 (97.1%) |
| Patients with relapse or new onset neurological symptoms (%) | NA | 3 (4.42%) | 1 (1.3%) | 2 (2.9%) |
| Patients with unchanged neurological status | NA | 7 (8.98%) | 4 (5.3%) | 0 |
| Mean SLEDAI score | 21.99 ± 7.52 | 4.29 ± 2.81 | 2.27± 1.22 | 1.19± 0.82 |

**Conclusions:** In patients of NP SLE, MMF is efficacious in inducing remission and preventing relapse of disease with a good safety profile. Deflazacort was found to have superior toxicity profile with equal efficacy as to prednisolone in NP SLE patients.

**Disclosure of Interest:** None declared

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## AB0415 THE EFFECT OF VITAMIN D SUPPLEMENTATION ON ANTIPHOSPHOLIPID ANTIBODIES LEVEL IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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**Background:** Vitamin D is regarded as modulator of the immune response [1]. Treatment with $1,25(OH)_2D$ can ameliorate autoimmune disorders in rodent models of experimental allergic encephalitis, nephritis, inflammatory bowel disease, and diabetes mellitus [2,3]. Vitamin D deficiency is common among patients with antiphospholipid syndrome (APS) and is associated with clinically defined thrombotic events [4].

**Objectives:** To evaluate the effects on antiphospholipid antibodies level of an oral Cholecalcipherol supplementation for 3 months in APS patients.

**Methods:** The study included 16 patients (men - 4, women - 12) with APS (Sidney, 2006) mean age 34±6,4 years treated with warfarin – 5,0–7,5 mg/day and acetylsalicylic acid – 75 mg/day. 3 patients were diagnosed with vitamin D insufficiency, 13 – with deficiency [5]. Cholecalciferol - 1000 IU/day was added to the therapy for 3 months. Anticardiolipin (aCL) and anti-β2-glycoprotein I (aβ2GPI) IgG and IgM antibodies, serum 25(OH)D level were tested using commercially available ELISA kits before and after treatment with Cholecalciferol. Lupus anticoagulant was not investigated due to possibility of false positive results in warfarine-treated patients.

**Results:** Baseline level of aCL IgG was median 6,21 intarquartile range 2,72–65,77 GPL, aCL IgM – 85,30 (12,66–154,26) MPL, aβ2GPI IgG –16,40 (7,99–44,32) U/ml, aβ2GPI IgM – 15,89 (6,24–67,60) U/ml, serum 25(OH)D - 15,04 (13,00–19,00) ng/ml. After treatment with Cholecalciferol for 3 months the levels of antiphospholipid antibodies and vitamin D were the following: aCL IgG – 4,69 (2,91–12,42) GPL, aCL IgM – 7,38 (4,42–110,35) MPL, aβ2GPI IgG – 9,43 (5,42 - 13,04) U/ml, aβ2GPI IgM – 29,97 (8,13–71,30) U/ml, serum 25(OH)D - 27,16 (23,06–32,90) ng/ml. We found significant increase in serum 25(OH)D level (p=0,007) and decrease in aβ2GPI IgG level (p=0,038) after treatment with Cholecalciferol. The level of other antiphospholipid antibodies did not differ significantly ($p>0,05$) before and after Cholecalciferol treatment.

**Conclusions:** Our preliminary results indicate that vitamin D supplementation might be associated with decreased serum aβ2GPI IgG level. This can indicate a possible correlation between vitamin D status and thrombotic risk in APS.

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## AB0416 RELIABILITY AND SAFETY OF A NOVEL AUTOINJECTOR FOR SELF-ADMINISTRATION OF SUBCUTANEOUS BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** The ability to self-administer subcutaneous (SC) belimumab would enhance treatment options for patients with SLE.

**Objectives:** The reliability and safety of a novel autoinjector for self-administration of belimumab SC was examined in patients with SLE.

**Methods:** Study 200339 (NCT02124798) enrolled adults with SLE who had received at least three prior intravenous (IV) doses of belimumab 10 mg/kg plus standard care, or who had completed the open-label continuation phase of a randomised, controlled trial of belimumab SC (prefilled syringe). Open-label belimumab 200 mg SC (1 mL) was self-administered weekly (thigh or abdomen) using an autoinjector, under clinic observation at Weeks 1, 2, 4, 8 and at home at Weeks 3, 5, 6, 7. Patients assessed and recorded injections using a diary. Investigators assessed clinic injections. The primary endpoint was the proportion of patients who successfully administered the first two injections. Secondary endpoints included success at Weeks 4 and 8 within the clinic and success at Weeks 3, 5, 6, and 7 at home.

**Results:** 95 patients enrolled: 91 completed the study (3 withdrew due to AEs, 1 patient was lost to follow-up). 88 (93%) patients were female; mean (SD) age was 44.8 (12.5) years. Overall, 94% (89/95) of patients successfully administered belimumab at Weeks 1 and 2 using the autoinjector. Five patients completed their 1st injection with assistance from clinic personnel.

Of 736 attempted injections 720 (98%) were considered to be successful. Of the 16 injections reported to be incomplete, 14 (4 from 1 patient) were associated

| | Self-injection success or failure | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 | Week 7 | Week 8 |
| Was the drug successfully injected?[a] | | | | | | | | |
| n | 95 | 90 | 93 | 88 | 90[b] | 93 | 90 | 92 |
| Yes | 95 (100) | 89 (99) | 92 (99) | 87 (99) | 89 (99) | 90 (97) | 87 (97) | 91 (99) |
| No | 0 | 1 (1) | 1 (1) | 1 (1) | 1 (1) | 3 (3) | 3 (3) | 1 (1) |
| Did you inject the study medication yourself? | | | | | | | | |
| n | 95 | 90 | 93 | 88 | 91[a] | 93 | 90 | 91 |
| Yes | 90 (95) | 90 (100) | 93 (100) | 88 (100) | 91 (100) | 92 (99) | 90 (100) | 91 (100) |
| No, clinic staff completed injection | 5 (5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

[a] Five patients had a successful 2nd injection after an unsuccessful 1st attempt; the 2nd attempt is included in this summary. [b] For 1 patient, injection was performed at Week 5 per patient recall but no patient diary was available and no record was entered into the Interview Guide.

with use errors, 13 of which were concluded to be related to not holding the autoinjector in place until the injection was completed. Use errors were repeated by only 1 patient.

Reported pain levels were low and diminished over time. A total of 39 (41%) patients reported at least one adverse event (AE) and 15 (16%) patients reported an AE considered to be drug related. Four (4%) patients reported 7 serious AEs: anaemia/neutropenia/pneumonia/pyrexia, postoperative abscess, pulmonary embolism and deep vein thrombosis. Four (4%) patients reported injection site reactions: erythema (2), pruritus, rash, injection-related reaction and site reaction. No serious systemic reactions or deaths were reported.

**Conclusions:** Patients with SLE successfully administered belimumab SC using a novel autoinjector.

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## AB0417 PREVALENCE AND CLINICAL MANIFESTATIONS OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS IN A COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disease of unknown etiology affecting different organs and systems, and requiring the use of immunosuppressors (IS), which increases the risk of infections such as tuberculosis (TB) and its deliberate search is mandatory. Patients with SLE are prone to infections as a consequence of either intrinsic immunologic defects or the IS mainly steroids. The prevalence of TB is higher in SLE patients compared with the general population and has been reported in endemic areas up to 5%.

**Objectives:** To determine the prevalence of pulmonary TB - extrapulmonary and associated factor in SLE patients.

**Methods:** we performed a retrospective study in a cohort of 328 SLE patients between 2010–2015 in tertiary level hospital. We included SLE patients with TB diagnosis which was made by PCR, culture, histopathology (HP), acid fast bacillus (AFB) and therapeutic trial (TT). We investigated associated factors for TB: IS drugs 6 months prior diagnosis of Tb (steroids, cyclophosphamide pulse (CY), azathioprine, mycophenolate mophetil (MM) and rituximab), comorbidities (diabetes mellitus, chronic renal disease, arterial hypertension). We also investigated previous exposure and vaccination for TB, type of TB: pulmonary and extra pulmonary. Time evolution, organ involved and SLEDAI at time of diagnosis of Tb were analyzed. Descriptive statistics were performed descriptive statistical.

**Results:** We found 13 SLE patients with TB (mean age 43.5± 9.06 years, mean disease evolution of SLE: 6.6±3.2 years). SLE organ involvement: Renal: 7, hematological: 4 Neuropsychiatric: 2; joint -mucocutaneous 6. Active SLE: 9 (SLEDAI 11.5±4.9), inactive SLE: 4. Use of IS: MM 6, Azathioprine: 7, Cy: 5, steroid: 13 (prednisone: median 2.5, range 2.5 to 50 mg/day and methylprednisolone pulse 3g bimonthly in 2 patients), Rituximab: 3. Prevalence of TB was 13 of 328 (4%) patients, extrapulmonary:10 (77%) renal: 4, meningeal: 3, cerebral tuberculoma: 1 peritoneal: 1 disseminated: 1, and pulmonary TB: 3 (23%). Manifestation associated with TB: Fever 12 (92%) appetite loss: 3 (23%), weight loss 5 (38%), asthenia 8 (61%) headache: 3 (23%), hematuria: 2 (15%). TB diagnosis: AFB: 9 (69%), HP: 1 (7.5%), culture and PCR: 2 (15%), TT: one patients with miliary TB who died.

**Conclusions:** The prevalence of TB in SLE patients was about 4% and its main form was extrapulmonary. The presence of tuberculosis in patients LES constitute a chalence and should be identified in promptly in order to initiate an adequate treatment. TB diagnosis in patients with active SLE is difficult because both diseases share clinical and laboratory manifestations.

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## AB0418 SECONDARY SJÖGREN'S SYNDROME AND SICCA SYNDROME IN SYSTEMIC SCLEROSIS IN MEXICAN POPULATION

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**Background:** Systemic sclerosis (SSc) and Sjögren's syndrome (SS) are autoimmune diseases, which can coexist with sicca syndrome due to accumulation of collagen or chronic inflammation of the exocrine glands (salivary and endocrine). The prevalence of secondary SS to SSc ranges from 4 to 60%.

**Objectives:** To determine the prevalence of SS and sicca syndrome in Mexican patients with SSc.

**Methods:** Cross-sectional study. Seventy seven patients with SSc were studied at a tertiary hospital. SS and sicca syndrome were investigated according to the 2002 revised international criteria for Sjögren's syndrome by the American European Consensus Group (AECG). All patients underwent minor salivary gland biopsy, and the results of fibrosis andinflammation were classified according to Tarpley's classification with a score $\geq$1. Anti-Ro/SSA and Anti-La/SSB antibodies were quantified in 34 patients with positive histological findings for SS. All patients with ocular symptoms were also performed Schirmer's I test to evaluate the ocular manifestations.

**Results:** Infiltration characteristic of SSc, and 21 (27%) revealed SS lymphocytic infiltrate. Isolatedxerostomia was found in 17 (22%) patients, and isolated xerophthalmia in 5 (7%) patients.Five (6.5%) patients referred parotid glands swelling. Anti-Ro/SSA and/or anti-La/SSBautoantibodies were found in 28.5% (6/21) of patients with SS. 21 (27%) patients met the2002 revised criteria for classification for SS by the AECG, Schirmer's I test revealed dryeye severity level 2 in 4 (19%) patients, level 3 in 12 (57%) patients and level 4 in 5 (23.8%) patients.

**Conclusions:** The prevalence of sicca syndrome was 71%, 44 per cent related to systemic sclerosis's collagen infiltration, and 27% due to Sjögren's syndrome's lymphocytic infiltrate. It is important to give a treatment to improve symptoms and considering the high frequency of non Hodgkin lymphoma in patients with SSc and SS.

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## AB0419 AURION STUDY: PRELIMINARY RESULTS OF VOCLOSPORIN IN LUPUS NEPHRITIS

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**Background:** In lupus nephritis (LN), complete or partial remission (PR) is associated with better patient and renal survival. However, studies demonstrate that subjects who did not achieve a 25% reduction in proteinuria within 8 weeks of starting induction immunosuppression were unlikely to achieve even a PR. Recent studies suggest that a combination of calcineurin inhibitors (CNi's), MMF and low dose steroids may be effective in LN patients. Voclosporin (VCS) is a next generation CNi intended for the treatment of autoimmune diseases and prevention of transplant rejection, with a predictable pharmacokinetic-pharmacodynamic profile. An ongoing study (AURA-LV) is a global double-blind, prospective study comparing 2 doses of VCS with placebo. This study, AURION, is an exploratory study of VCS in active LN in combination with MMF and steroids.

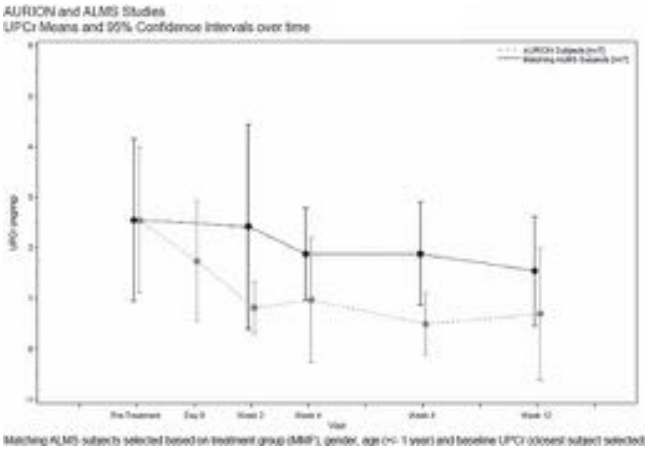
**Objectives:** The AURION study assesses the ability of biomarkers measured at 8 weeks to predict clinical response over 24 and 48 weeks. In addition complete remission is assessed at week 24, defined as a protein/creatinine ratio of $\leq$0.5 mg/mg and estimated glomerular filtration rate (eGFR,CKD-EPI equation) $\geq$60 mL/min/1.73 $m^2$ or no decrease from baseline in eGFR of $\geq$20%.

Participating subjects with active lupus nephritis will take voclosporin 23.7 mg BID in combination with standard of care. We report preliminary biochemistry data.
**Methods:** Eligibility criteria includes: renal biopsy within 2 years of screening; SLE by ACR criteria; laboratory features consistent with active LN; and eGFR >45ml/min/1.73m$^2$. VCS 23.7 mg po BID is administered in combination with MMF 1–2g/day and a reducing course of corticosteroids. UPCr assessments are made at each visit, together with biomarker (C3, C4 and anti-dsDNA) data at regular intervals. Proteinuria reduction over time is presented for the first 7 subjects enrolled in this pilot study, together with renal function, C3, C4 and anti-dsDNA plots.
To understand the impact of MMF/steroids alone, UPCr data is presented below with historical data from age/sex/UPCr matched patients from ALMS[1].
**Results:** (Mean±SD) Pretreatment UPCr was 2.5±1.6 mg/mg and eGFR was 115±34 ml/min. By week 8 mean UPCr had fallen to 0.5±0.5 mg/mg; a reduction in mean UPCr of 81%. eGFR at the same time-point was 113±10 ml/min. Expected increases in C3, C4 and decreases in anti-dsDNA were seen in this population.

Baseline demographics

| Demographics | (n=7) |
|---|---|
| Age (years) | 29.0±4.8* |
| Race | Asian |
| Sex (F/M%) | 100/0 |
| Time from SLE to LN diagnosis (years) | 1.6±2.6* |
| Time from SLE to study entry (years) | 6.1±3.0* |
| LN Class at study entry (n,%): Class III | 2 (29%) |
| Class IV | 2 (29%) |
| Class V | 3 (42%) |
| MMF Naïve (%) | 57.1 |
| eGFR at study entry (ml/min/1.73m$^2$) | 115±34* |
| Urine Protein/Creatinine Ratio | 2.54±1.56* |

*Mean ± SD.




**Conclusions:** Preliminary data from this this pilot study indicates that MTT using VCS, in combination with MMF and steroids, produced consistent reductions in proteinuria with preservation of renal function in the first 7 subjects enrolled with active LN. The results of the confirmatory global AURA-LV study using similar treatment patterns will be available later this year.
**References:**
[1] Appel GB, Contreras G, Dooley MA, et al. Mycophenolate mofetil versus cyclophosphamide for induction treatment of lupus nephritis. J Am Soc Nephrol. 2009 May;20(5):1103–12.
**Disclosure of Interest:** R. Yahya Grant/research support from: Aurinia Pharmaceuticals, A. H. B. A. Gafor Grant/research support from: Aurinia Pharmaceuticals, R. Huizinga Shareholder of: Aurinia Pharmaceuticals, Employee of: Aurinia Pharmaceuticals, T. M. Chan Grant/research support from: Aurinia Pharmaceuticals, Consultant for: Aurinia Pharmaceuticals, N. Solomons Shareholder of: Aurinia Pharmaceuticals, Employee of: Aurinia Pharmaceuticals
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## AB0420 SATISFACTION AND UNMET NEED AMONG SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS TAKING STANDARD OF CARE MEDICATIONS (SOC) IN A REAL WORLD SETTING

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**Background:** Limited data exists to assess drivers of treatment satisfaction and areas of unmet need among patients with SLE.
**Objectives:** Primary: Assess physician and patient reported treatment satisfaction and unmet need amongst SOC patients treated ≥3 months. Secondary: Describe factors associated with satisfaction among SLE patients treated with SOC. SOC is defined as ≥1 of the following treatments: anti-malarials [AMs], corticosteroids, [CS] immunosuppressants [IMs] or non-steroidal anti-inflammatory drugs [NSAIDs].
**Methods:** Cross-sectional study of 88 US rheumatologists and their next five, SLE patients. Patient record forms (PRFs) were completed by physicians and patients provided data via self-completion forms (PSCs). Clinical burden, quality of life and satisfaction data were collected from both parties. Descriptive and bivariate analysis was used to profile SOC patients. Backwards stepwise logistic regression was used to assess drivers of physician and patient reported treatment satisfaction.
**Results:** Rheumatologists provided 369 SOC PRFs; 228 corresponding PSCs were completed by SOC patients (mean age 44.0, majority female [86%], Caucasian [56%] and working/studying [63%]).
Current SLE disease severity for a majority of SOC patients was described as mild by their physician, however 25% were described as moderate/severe. Current SLE status was described by physicians as deteriorating/unstable for 12% of SOC patients and physicians reported dissatisfaction with treatment in 18% (a figure matched by PSC patients).
A significant correlation existed between decreased satisfaction (patient & physician) and increased disease severity ($p<0.001$) and/or deteriorating disease status ($p<0.001$).
Significant associations with physician satisfaction were observed in the following covariates; musculoskeletal involvement (vs. no involvement) (OR: 0.05, $p<0.001$), disease status (deteriorating vs. improving/stable) (OR: 0.06, $p<0.001$), reduction in activities of daily living (ADLs) (vs. no reduction) (OR: 0.14, $p<0.001$), improvement in general symptomatology (vs. no improvement) (OR: 10.66, $p<0.001$).
Significant associations with patient satisfaction were observed in the following covariates; Number of symptoms (OR per additional symptom: 0.88, p=0.020), reduction in ADLs (vs. no reduction) OR: 0.34, p=0.030, improvement in general symptomatology (vs. no improvement) (OR: 3.44, p=0.017), frequency of medication administration (satisfied vs. dissatisfied) (OR: 7.07, $p<0.001$).
**Conclusions:** Clinical burden (disease severity/disease deterioration) continues to impact over a quarter of current patients on SOC. This burden has a significant bearing on both physician and patient satisfaction with treatment, particularly among moderate/severe & deteriorating patients. These findings are worthy of further exploration to ensure best clinical practice and ways to enhance physician and patient communication.
**Acknowledgement:** Study (202146) funded by GSK
**Disclosure of Interest:** S. Ramachandran Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, K. Pascoe Employee of: GlaxoSmithKline employee at time of the study, B. Hoskin Employee of: Adelphi Real World, S. Lobosco Employee of: Adelphi Real World, D. Bell Employee of: Adelphi Real World, B. Pobiner Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, Y. Asukai Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline
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## AB0421 EVALUATION OF THE EXPERIENCE, SATISFACTION AND OUTCOMES OF AN AUTOINJECTOR FOR SELF-ADMINISTRATION OF SUBCUTANEOUS BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** A US, phase IIb study (#200339) found the belimumab autoinjector (BAI) was reliable and well-tolerated for home administration. This separate follow-up study (#201816) was conducted at the end of the phase IIb study to capture patient experiences with the various delivery devices-the BAI, intravenous belimumab (BIV) and belimumab prefilled syringe (BPS).
**Objectives:** To assess patient experiences with the BAI, with belimumab in general, and with switching to the BAI from BIV or BPS. Preference for administration route and the impact on activities of daily living were also explored.
**Methods:** Patients were recruited at their final week 8 study visit. The study consisted of a 43 item online (or paper) questionnaire followed by qualitative telephone interviews in a subset of patients. IRB approval was obtained and patients gave informed consent. The telephone interview captured further information from the patients' online survey responses. Quantitative data were analyzed using descriptive statistics and the qualitative data were transcribed and analysed using a content analysis approach.
**Results:** This study included a total of 43 patients who were representative of those that completed the phase IIb BAI study. Patients reported a high level of confidence in their ability to use the BAI correctly the first time they used it on their own. Overall satisfaction and satisfaction with the frequency of administration was higher for the BAI compared with BIV, and 76% preferred the BAI. The BAI was considered more convenient than BIV due to shorter administration time, less travel time, less interference with work, portability, and less/no pain. In telephone interviews, 62% (n=13) reported some disadvantages with the BAI (discomfort, inconvenience, not ergonomic). Patients reported a high level of satisfaction with belimumab regardless of administration route; 74% were satisfied or very

satisfied. All patients stated they would have preferred to initiate belimumab at an earlier stage of their disease and all patients wanted to continue receiving belimumab. The majority of patients reported improvements in overall symptoms, flare frequency and severity, and fatigue, since starting belimumab; many reported improvements in activities of daily living. Of those patients who worked, 59% reported the BAI had a positive impact on their ability to work and 40% of all patients reported the BAI improved their ability to carry out daily activities.
**Conclusions:** Patients were positive regarding their experience with adding belimumab to standard of care therapies, and favoured the BAI over BIV administration. Given only 2 patients were on the BPS, it was hard to draw any meaningful conclusions for this group. Self-selection bias, recall bias and small sample size should be considered limitations of this study design. The results of this study suggest that the availability of the BAI will be a welcome treatment option. The potential benefits of the BAI identified in this study should be explored in a long-term evaluation of the device to assess clinical and patient reported outcomes.
**Role of the study sponsor statement:** The research presented in this abstract was conducted by Evidera Inc. and was funded by GlaxoSmithKline.
**Disclosure of Interest:** E. Dashiell-Aje: None declared, G. Harding: None declared, K. Pascoe: None declared, J. DeVries: None declared, P. Berry Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline during the conduct of the study, S. Ramachandran Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline during the conduct of the study
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## AB0422 SELECTIVE FACTOR XA INHIBITORS IN TREATMENT AND PREVENTION OF THROMBOSES IN PATIENTS WITH RHEUMATIC DISEASES

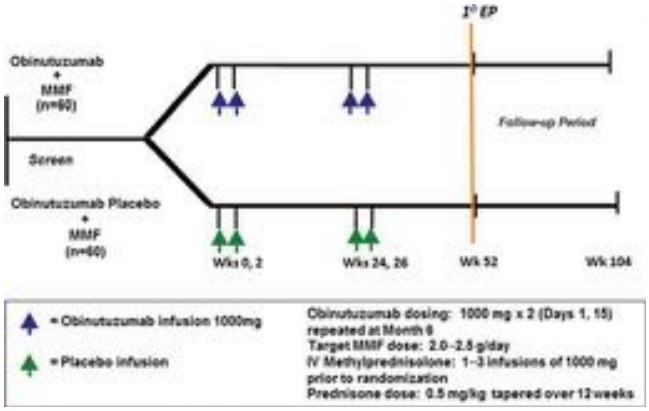
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**Background:** Due to the smaller size of the molecule and low affinity for platelet factor (f) 4, fondaparinux (F) does not cross react with heparin-induced-thrombocytopenia- antibodies [1]. Also F has some more beneficial mechanisms: reduction of aPl-production (BAFF/Blys) and tissue f expression, C3/C5-inactivation, fXa-C3 cleavage blocking, increase of angiogenic process [2]. This can lead to classify F as pathogenic treatment option for rheumatic diseases (RD) as well as anticoagulant.
**Objectives:** To evaluate the affectivity and safety of F in treatment and prevention of thromboses in patients (pts) with RD.
**Methods:** The study included 54 pts suffered from the next RD: 8 systemic lupus erythematosus (SLE), 7 rheumatoid arthritis (RA), 4 antiphospholipid syndrome (APS), 25 SLE+APS, 4 systemic sclerosis, 1 osteoarthritis, 2 ANCA-associated vasculitis and 1 Behcet's disease. All the pts were treated with anticoagulants - 24 pts with F, 25 pts with nadroparin, 1 pts with enoxaparin and 4 pts with rivaroxaban - for different reasons: deep vein thrombosis (DVT), trophic ulcer, thrombotic cerebral microangiopathy, postthrombotic pulmonary hypertension, hypercoagulability due to nephritis, thrombosis prevention in SLE+APS pts with low platelets. Incidences of thrombosis, bleeding events and platelets levels were monitored. 10 pts (RA + vasculitis) had initial high fibrinogen levels. 12 pts with SLE+APS had baseline aPTT elevation from lupus anticoagulant (LA). Direct anti-fXa level monitoring (anti-Xa) was performed.
**Results:** All the pts demonstrated clinical improvement. Low anti-Xa was registered in 6 (12%) pts, normal anti-Xa – in 37 (69%) pts and high anti-Xa – in 11 (19%) pts. Pts with low anti-Xa underwent dose correction and none of them had new incidence of thrombosis. Most of pts did not have bleeding complications. Only 1 pt with SLE+APS treated with F developed multiple cutaneous haemorrhages. We discharged F for 24 hours and started again in a half dose. anti-Xa monitoring showed level decrease from 1.73 to 1.3 units/mL. In pts with APS and/or SLE F did not influence on aPL, fibrinogen and aPTT. 3 SLE+APS pts who had distal gangrene and cutaneous necrosis intentionally were treated with high dose of F with anti-Xa ~2 units/mL. That led to a good clinical response and blood flow recovery in ischemic tissues. There were no any signs and symptoms of bleeding.
**Conclusions:** Fondaparinux is an effective and save drug for the treatment and prevention of thrombosis in pts with RD. During the therapy routine coagulation monitoring is not representative because of LA and inflammation. We recommend to monitor signs of bleeding and anti-Xa and to expand its normal rate up to 2 units/mL in pts with distal gangrene and cutaneous necrosis due to SLE and APS.
**References:**
[1] Smythe MA, Priziola J, Dobesh PP et al. Guidance for the practical management of the heparin anticoagulants in the treatment of venous thromboembolism. J Thromb Thrombolysis. 2016 Jan;41(1):165–86. doi: 10.1007/s11239-015-1315-2.
[2] Alijotas-Reig J, Ferrer-Oliveras R. Management of refractory obstetric antiphospholipid syndrome: from pathogenesis to novel immunomodulatory therapies. Proceeding of the 9th Meeting of the European Forum on Antiphospholipid Antibodies; 2013 May 16–18; Krakow, Poland. Krakow: Medycyna praktyczna; 2013.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5939

## AB0423 NOBILITY, A PHASE 2 TRIAL TO ASSESS THE SAFETY AND EFFICACY OF OBINUTUZUMAB, A NOVEL TYPE 2 ANTI-CD20 MONOCLONAL ANTIBODY (MAB), IN PATIENTS (PTS) WITH ISN/RPS CLASS III OR IV LUPUS NEPHRITIS (LN)

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**Background:** B cells infiltrate the kidneys of LN pts, and leukocyte-rich tubulointerstitial infiltrates are associated with greater risk for progression to renal failure. High-sensitivity flow cytometry (HSFC) analysis suggests incomplete B-cell depletion in systemic lupus erythematosus (SLE) is associated with nonresponse to rituximab (RTX). Obinutuzumab (Obi) is a glycoengineered type 2 anti-CD20 mAb that binds CD20 differently from RTX, a conventional type 1 anti-CD20 mAb, and depletes B cells to a greater degree than RTX. In preclinical studies, Obi displayed significantly increased antibody-dependent cellular cytotoxicity and enhanced direct cell death over type 1 anti-CD20 mAbs. In the CLL11 trial, which led to FDA breakthrough designation and its licensing in chronic lymphocytic leukemia, Obi demonstrated greater progression-free survival and greater minimal residual disease negativity over RTX even in protected microenvironments such as bone marrow. Double-blind randomized controlled trials demonstrated that type 1 anti-CD20 mAbs added to mycophenolate mofetil (MMF) or cyclophosphamide (CYC) increased the proportions of pts achieving partial renal response (PRR) but had no impact on complete renal response (CRR) rates at 12 months. Although these studies with RTX and ocrelizumab did not meet their respective primary endpoints, EULAR and ACR LN guidelines recommend RTX if treatment with CYC or MMF fails.
**Objectives:** The phase 2 study NOBILITY is designed to test the hypothesis that Obi may generate superior CRR rates in pts with active proliferative LN based on its ability to deplete B cells to a greater degree than type 1 anti-CD20 mAbs. The primary objective of this study is to evaluate the effect of Obi compared with placebo (PBO) when added to MMF in pts with class III or IV LN as assessed by the proportion of pts who achieve CRR at wk 52. Key secondary objectives relate to overall response (CRR + PRR), PRR, change in biomarkers of LN disease activity, and time to CRR.
**Methods:** Randomized, double-blind, PBO-controlled study to evaluate safety and efficacy of Obi added to MMF and corticosteroids (CS) in pts with ISN/RPS 2003 class III or IV LN.
**Results:** The study design is as follows: NOBILITY is a global multicenter study enrolling ~120 pts with biopsy-proven ISN/RPS 2003 class III or IV LN in the United States, Mexico, Columbia, Argentina, Spain, Israel, Brazil, and France. All pts will be on MMF up to 2.5 g/d and a combination of IV and oral CS to be tapered to 7.5 mg/d by wk 12. All pts will be followed up until wk 104, with the primary endpoint evaluation at wk 52 (figure). NOBILITY also features interim analyses at wk 4 for depletion of peripheral $CD19^+$ B cells by HSFC, centralized evaluation of the renal biopsy, and repeat renal biopsy on the basis of clinical status and local practice.




**Conclusions:** NOBILITY, a phase 2 trial evaluating Obi in LN, is grounded on the hypothesis that a type 2 anti-CD20 mAb will induce greater B-cell depletion in the kidneys and associated secondary lymphoid structures, translating to significant CRR rates.
**Disclosure of Interest:** T. Schindler Employee of: F. Hoffmann-La Roche, B. Rovin Grant/research support from: Genentech, Consultant for: Genentech, R. Furie: None declared, M. Leandro Grant/research support from: Roche, Consultant for: Roche, Genentech, Chugai, Lilly, BMS, M. Clark Grant/research support from: AbbVie, Consultant for: Genentech, P. Brunetta Shareholder of: Genentech, Employee of: Genentech, J. Garg Shareholder of: Roche, Employee of: Genentech
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## AB0424 RETROSPECTIVE EVALUATION OF MYCOPHENOLATE MOFETIL INFECTIOUS SIDE EFFECTS ON LUPUS NEPHRITIS PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disease driven by auto-reactive immune cells, in particular B cells that target multiple organ systems leading to severe complications. A main complication of SLE is nephritis, formally known as lupus nephritis (LN). MMF is a selective, non-competitive and reversible inhibitor of inosine monophosphate dehydrogenase. MMF provided to be useful in the treatment of patients affected by SLE, especially in those with LN. MMF demonstrated a more favorable safety profile compared with cyclophosphamide, especially in terms of alopecia and infertility rates. Nonetheless, the use of MMF in LN has not been extensively evaluated in terms of safety and infection rates.
**Objectives:** To study the prevalence of infections complications in a cohort of adult LN patients under MMF maintenance therapy.
**Methods:** Retrospective study, enrolling patients attending a Rheumatology/Nephrology department, diagnosed with SLE (American College of Rheumatology criteria) and LN, under MMF maintenance therapy. Drug variables: dose of MMF, time of exposure. Clinical variables: age, gender, race, disease duration, histological classification (renal biopsy), specific organ involvement, other therapeutics for SLE, serum urea and creatinine, 24h proteinuria, and urinary sediment. Statistical analysis with Microsoft Excel 2010; appropriate statistical tests were used; $p$ value$<0.05$ with a 95% confidence interval will be assumed.
**Results:** 44 SLE patients were enrolled, 37 were female (84.1%); mean age was 38.4±11.9 years and mean disease duration was 122.9±108 months. All the patients were white. 35 patients (80%) had class 4 LN, 5 had class 5 and histological classification was unknown in 4 patients. 34 (77%) patients had extra renal disease, 23 with joint disease and 14 with cutaneous involvement. Mean MMF dose was 1018±876mg. 35 (79%) patients were doing steroid therapy, mean dose 5.58±3.87mg and 39 (88.6%) patients under Hidroxicloroquine therapy. We identify 25 infectious events, 4 (16%) needing hospitalization, none death. Mean time to infection after MMF introduction was 12.16±16.3 months. The most frequent infections include urinary tract infections (UTI) (8 patients), cutaneous Herpes Zoster (4 patients) and respiratory tract infections (4 patients). We found a positive correlation between the occurrence of infection in the first 8 months of therapy and 24h Proteinúria and dsDNA in the beginning of therapy (p=0.04 and p=0.03, respectively). Hidroxicloroquine seem to have a protective effect against infections, but no statistic association was found. We found no association between infections and MMF/steroid dose or renal function.
**Conclusions:** We found significant morbidity associated with an increase incidence of infection after introduction of MMF, especially in the first months of therapy and patients with more active disease in the beginning of MMF. No mortality was associated with these infectious complications, and the hospital admission rate was low.
**References:**
[1] Afzali B, Shah S, Chowdhury P, et al. Low-dose mycophenolate mofetil is an effective and safe treatment to permit phased reduction in calcineurin inhibitors in chronic allograft nephropathy. Transplantation 2005; 79: 304–309.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5961

## AB0425 TAC-TIC USE OF TACROLIMUS-BASED REGIMENS IN LUPUS NEPHRITIS

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**Background:** Current guidelines do not mention tacrolimus as a treatment option and no consensus has been reported on the role of tacrolimus in active LN. Recent clinical trials have reported positive effects of tacrolimus-based (TAC) regimens for treatment of lupus nephritis (LN).
**Objectives:** With this systematic review and meta-analysis, we aimed to translate recent outcomes on tacrolimus-based regimens for LN treatment into clinical practice.
**Methods:** We identified from various databases every clinical studies investigating TAC regimens in LN. Studies were summarized on the basis of treatment target (induction or maintenance), concomitant immunosuppression and quality of the data. A meta-analysis was performed for the efficacy of TAC regimen as induction treatment, maintenance treatment as well as safety.
**Results:** 239 studies were identified from which 24 were clinical studies performed in LN patients: 6 case series, 9 cohort studies, 3 case-control studies (CCS) and 6 randomized controlled trials (RCTs). Further analysis of the 9 controlled trials showed that 7 studies investigated tacrolimus in combination with steroids and 2 tacrolimus with mycophenolate plus steroids. 4 RCTs investigated TAC regimens as induction treatment and 2 RCTs as maintenance treatment. Strikingly, there was no consensus in any of the studies regarding tacrolimus dosing and target trough levels. Importantly, all the studies were performed in LN patients of Asian ethnicity. A meta-analysis of TAC regimens for induction treatment showed a significantly higher complete response (RR 1.18, 95% CI 1.04–1.34, p=0.01) and a significantly lower no response rate (RR 0.71, 95% CI 0.56–0.90, p<0.01). With respect to safety, no clear differences between TAC regimens and conventional treatment were observed.
**Conclusions:** Current studies on TAC regimens for LN are limited, heterogenous and predominant uncontrolled studies in patients of Asian ethnicity. A significant, clinical efficacy of TAC regimens as induction treatment was found however cannot be extrapolated beyond Asian LN patient groups. Clearly, these results mandate further confirmation in multi-ethnic, randomized trials.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4313

## AB0426 RISK OF PNEUMOCYSTIS CARINII PNEUMONIA INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE POPULATION COHORT STUDY

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**Background:** Pneumocystis carinii pneumonia (PJP) infection often affects immunocompromised patients may cause severe morbidity and mortality. PJP may be preventable by prophylactic antibiotics in high risk patients. However, the epidemiology and risk factors for PJP in patients with systemic lupus erythematosus (SLE) are not full studied.
**Objectives:** This nationwide population-based study aimed to evaluate the risk of PJP in patients with systemic lupus erythematosus in Taiwan.
**Methods:** We identified 23,378 SLE patients from the National Health Insurance research database between 1997 and 2012 and compared the incidence rate (IR) of PJP infection with that of 93,512 age- and gender-matched non-SLE cohort. A Cox multivariable proportional hazards model was applied to evaluate the risk of PJP infection in the SLE cohort. Risk factors of PJP infection were also analyzed.
**Results:** The SLE cohort had a significantly higher IR of PJP infection (SLE IR=2.49, control IR=0.10, incidence rate ratio = 26.06, p<0.001). Male (Hazard ratio [HR] = 2.05, p=0.039), end stage renal disease (HR=1.88, p=0.035), use of mycofenolate mofetil (HR=5.11, p<0.001), intravenous steroid pulse therapy (HR=96.23, p<0.001).

Table 1. Risk factors of PJP infection in patients with SLE

| Variable | Univariate analysis | | | Multivariable analysis | |
|---|---|---|---|---|---|
| | HR (95% CI) | *P*-value | | HR (95% CI) | *P*-value |
| Male | 2.61 (1.33–5.13) | 0.005 | | 2.05 (1.04–4.04) | 0.039 |
| Comorbidity | | | | | |
| Diabetes mellitus | 0.55 (0.20–1.53) | 0.251 | | | |
| End-stage renal disease | 3.80 (2.15–6.72) | <0.001 | 1.88 (1.05–3.39) | 0.035 | |
| ILD | 2.02 (0.80–5.09) | 0.137 | | | |
| Stroke | 1.77 (0.92–3.40) | 0.088 | | | |
| Malignancy | 0.71 (0.40–1.25) | 0.237 | | | |
| Medications | | | | | |
| Hydroxychloroquine | 0.622 (0.35–1.12) | 0.108 | | | |
| Azathioprine | 1.86 (1.01–3.42) | 0.043 | – | - | |
| Mycofenolate mofetil | 14.58 (7.23–29.41) | <0.001 | 5.11 (2.48–10.50) | <0.001 | |
| Cyclosporine | 7.55 (3.21–17.77) | <0.001 | – | - | |
| Cyclophosphamide | 7.26 (3.80–113.89) | <0.001 | – | - | |
| MTX | 0.619 (0.09–4.49) | 0.632 | | | |
| Steroid | | | | | |
| Intravenous | 182.3 (65.31–508.8) | <0.001 | 96.23 (33.46–276.82) | <0.001 | |
| Oral daily dose over 7.5m† | 15.87 (7.07–35.64) | <0.001 | 3.83 (1.66–8.82) | 0.002 | |

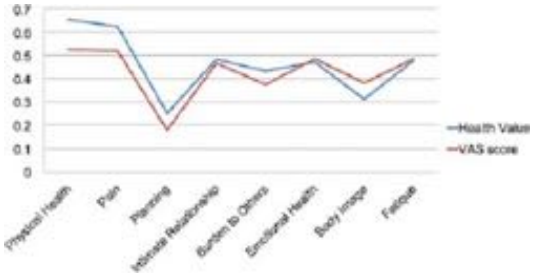
**Conclusions:** Higher risk of PJP infection was observed in SLE patients. Risk factors for PJP infection include male, end stage renal disease, use of mycofenolate mofetil, intravenous steroid pulse therapy and an oral daily steroid dose over 7.5mg.
**References:**
[1] Ratchaya Lertnawapan, Kitti Totemchokchyakarn, Kanokrat Nantiruj, Suchela Janwityanujit. Risk factors of Pneumocystis jeroveci pneumonia in patients with systemic lupus erythematosus. Rheumatol Int 2009;29:491–496.
[2] Michael M. Ward, Fiona Donald. Pneumocystis carinii pneumonia in patients with connective tissue diseases. Arthritis & Rheumatism 1999;42:780–789.
[3] Chia-Tse Weng, Ming-Fei Liu, Meng-Yu Weng, et al. Pneumocystis jirovecii Pneumonia in Systemic Lupus Erythematosus From Southern Taiwan. J Clin Rheumatol. 2013;19:252–8.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6131

## SLE, Sjögren's and APS - clinical aspects (other than treatment)

### AB0427 HEALTH-RELATED QUALITY OF LIFE IN THAI LUPUS PATIENTS. COMPARISON OF THE EUROPEAN QUALITY OF LIFE SCALE (EQ-5D) AND THE LUPUS QUALITY OF LIFE QUESTIONNAIRE (LUPUSQOL)

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**Background:** SLE mostly affects the working-age population. The disease burden has a significant impact to the quality of life.
**Objectives:** To assess the HRQoL in SLE patients by using the EQ-5D and the LupusQoL and to evaluate their correlation.
**Methods:** 248 patients were recruited. Demographic and clinical data including the SLEDAI were collected. We also evaluated the patients' preference in terms of the language, the precision of questions, and time consume. The correlation was examined by Pearson's correlation.
**Results:** 94.6% of patients were female. Mean age was 37.5±11.9 with the median disease duration of 5.1 years. The mean SLEDAI score was 3.6±0.4. The mean of EQ-5D health value and VAS scores were 0.65±0.20 and 78.1±20.2. Most patients reported that SLE had mild effect to their health status. 28.1 and 18.3% of patients reported moderate to severe problems in the mental components of pain/discomfort and anxiety/depression. The mean LupusQoL score was 78.9±16.3. Both EQ-5D health value and VAS were significantly correlated with all LupusQOL domains, strongly correlated with physical health and pain but poorly correlated with planning and body image. The patients preferred to use the EQ-5D over LupusQoL.




**Conclusions:** HRQoL in most SLE patients was generally good. The EQ-5D score was significantly correlated with the LupusQoL score particularly in the domains of physical health and pain. The EQ-5D is a simple and more convenient tool to assess the general health and can be used as a brief evaluation of lupus-specific HRQoL in daily practice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4542

### AB0428 CARDIAC INVOLVEMENT IN SYSTEMIC SCLEROSIS – A PORTUGUESE REALITY

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**Background:** Systemic sclerosis (SSc) has a wide spectrum of cardiovascular manifestations, being pulmonary hypertension (PH) one of the most lethal complications. Echocardiography is a pivotal screening test for patients at risk for PH that allows prompt identification of those with high estimated pulmonary artery systolic pressure (PASP).
**Objectives:** We conducted a retrospective analysis of patients with SSc followed in our Rheumatology department aiming to characterize those with estimated PASP≥35 mmHg.
**Methods:** Clinical and laboratory features, including dyspnea according to New York Heart Association (NYHA) classes, N-terminal pro-Brain Natriuretic Peptide (NT-proBNP) serum levels, uricemia, anti-nuclear antibody (ANA) specificities, 6-minute walk test (6MWT), and right heart catheterization (RHC), if required, were assessed.
**Results:** In total, 87 out of 103 SSc patients had available echocardiography results (females 93.1%; mean age 57.8 years; mean disease duration 10.3 years). Eight patients were classified as having NYHA class≥3. The median value of NTproBNP was 104 pg/mL (19 to 15902). Twenty one (24%) had estimated PASP≥35 mmHg (in 16 patients PASP could not be estimated), of whom16 performed RHC. PH (mPAP≥25 mmHg) was confirmed in 7 (44%) cases; 3 were classified as group 1, 1 as group 2, 2 as group 3 and 1 as group 5, according to the ERS/ECS 2013 classification. The group with elevated PASP included 11 patients with limited SSc, 7 with diffuse SSc, 1 sine scleroderma and 2 overlap syndromes. Comparison of patients with PASP≥35 mmHg with those with PASP<35 mmHg put in evidence the following differences (Table bellow).

| | PASP≥35 mmHg N=21 | PASP <35 mmHg N=66 | p-value |
|---|---|---|---|
| Age | 64.9 | 45.3 | 0.595 |
| Disease duration (years) | 10.1 | 11.5 | 0.571 |
| NYHA ≥3 | 35% | 0% | <0.001 |
| Mean NTproBNP (pg/mL) | 2549 (35–15,902) | 225 (19–3,042) | 0.083 |
| Mean uricemia (mg/dL) | 5.2 | 4.8 | 0.446 |
| Anti-Scl70 antibody | 42.1% | 18% | 0.055 |
| Raynaud phenomenon | 80% | 82% | 0.507 |
| Carbon monoxide diffusion (DLCOsb) <75 | 66.7% | 76.4% | 0.359 |
| Restrictive pulmonary disease (FVC <70%) | 44.4% | 4.8% | <0.001 |
| Mean distance in 6MWT (m) | 345 (150–530) | 398 (310–610) | 0.349 |

**Conclusions:** PASP is elevated in one quarter of SSc patients. This subgroup present more frequently higher NYHA classes, elevated NTproBNP levels and Scl70 positivity. About 44% of them had restrictive pulmonary disease. It is essential to closely monitor cardiorespiratory function in order to rule out cardiac involvement as early as possible.
Our results suggest that there is still need to increase physicians' awareness of systematic cardiovascular screening, since fewer patients than are nowadays recommended had a complete evaluation.
**Acknowledgement:** Cardiology department Hospital Garcia de Orta
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2703

### AB0429 PURE RED CELL APLASIA IN PATIENTS FROM SLE REGISTRY FROM THE SPANISH SOCIETY OF RHEUMATOLOGY (RELESSER)

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune systemic rheumatic disease that, in our area, presents hematologic manifestations in approximately 70% of cases[1]. Some of them are very rare, there are no large series whose analysis could provide relevant information.
**Objectives:** To study the characteristics of patients with Pure Red Cell Aplasia (PRCA) in a large sample of SLE patients.
**Methods:** SLE patients from RELESSER database were studied. We analysed the clinical and analytical SLE manifestations at 12 different domains (mucocutaneous, renal, musculoskeletal, constitutional, haematologic, vascular, cardiac, respiratory,

**Abstract AB0429** – Table 1

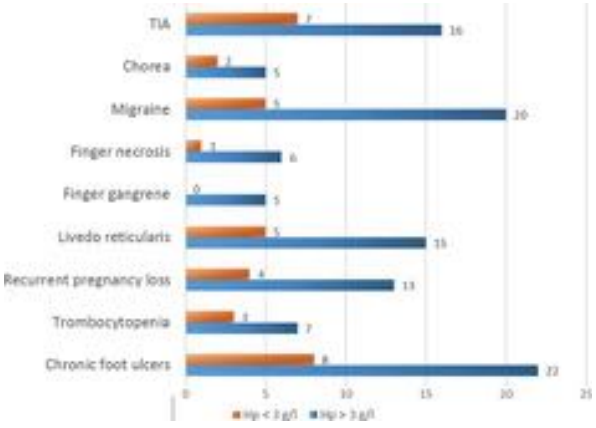
| | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
|---|---|---|---|---|---|
| Number of organ systems affected by SLE before PRCA diagnosis | Not applicable | 6 | 6 | 4 | 7 |
| Number of organ systems affected by SLE at PRCA diagnosis | Not applicable | 1 | 1 | 1 | 6 |
| Number of organ systems affected by SLE until last assessment | 3 | 3 | 5 | 1 | 2 |
| Haemoglobin levels at PRCA diagnosis (g/dl) | 7 | 4.9 | 4.9 | 4.5 | 6.3 |
| Bone Marrow biopsy or aspirate | Selective aplasia/hypoplasia of the red series, without changes in other series | | | | |
| SLEDAI / SLICC-ACR DI at PRCA diagnosis | Not applicable | 4 / 1 | 2 / 1 | 0 / 0 | 20 / 0 |
| SLEDAI / SLICC-ACR DI 1 year after PRCA | Not applicable | 0 / 1 | 2 / 1 | 2 / 0 | 4 / 0 |
| SLEDAI / SLICC ACR DI at last assessment | 0 / 0 | 6 / 3 | 0 / 2 | 0 / 0 | 0 / 0 |
| Number of treatment lines | 2 | 2 | 2 | 1 | 4 |
| Treatments administered | 1st: Oxitosona<br>2nd: Inmunoglobulins | 1st: Glucocorticoids<br>2nd: Inmunoglobulins & RBC transfusion | 1st: Glucocorticoids<br>2nd: Ciclosporin A | Glucocorticoids | 1st: Glucocorticoids<br>hydroxicloroquine<br>3rd: Rituximab<br>2nd: Belimumab<br>erythropoietin<br>4th: Darbepoetin α |
| Total number of treatments administered | 2 | 3 | 2 | 1 | 6 |
| Relapse | No | | | | |
| Death | No | | | | |

neuropsychiatric, gastrointestinal, ophthalmic and serological) before, during and after PRCA diagnosis and until the last available assessment. We also studied activity (SELENA-SLEDAI) and damage (SLICC/ACR DI)indices at each of those times.
We evaluated the treatment received, PRCA recurrences and the number of deaths by this entity.
**Results:** 3,656 patients from 45Rheumatology Units across Spain were studied. 5 cases of PRCA were found (<0.5%of total)
There were not viral infections in relation with the PRCA.
All patients had a good response to treatment, reaching complete remission without relapses or deaths. The mean number of treatment lines (± SD)that were necessary was 2.2 (±1.01)and the mean (± SD)number of treatments used was 2.8 (±1.92). Except for the patient diagnosed with PRCA before SLE, all of them received glucocorticoids as initial treatment. Of these 4patients only 1achieved complete remission without requiring immunosuppressive therapy.
The following table shows the characteristics of each patient:
**Conclusions:** PRCA is a very rare cause of anemia in SLE. In most cases it appears several years after the diagnosis of SLE. It is a serious manifestation but in our series, with a proper management showed a favourable response.
**References:**
[1] Pego-Reigosa JM et al. Analysis of disease activity and response to treatment in a large Spanish cohort of patients with systemic lupus erythematosus. Lupus 2015;24:720–9.
**Disclosure of Interest:** A. Lois-Iglesias: None declared, I. Rúa-Figueroa: None declared, C. Erausquin: None declared, D. Grados: None declared, A. Olivé: None declared, V. Quevedo: None declared, J. Alegre: None declared, J. Calvo: None declared, F. López-Longo: None declared, M. Galindo: None declared, F. deToro: None declared, C. Mouriño: None declared, J. Pego-Reigosa Grant/research support from: Work supported by Spanish Society of Rheumatology, FIS/ISCIII (PI11/02857), BIOCAPS from the EU 7th Framework Programme/REGPOT-2012–2013.1 (316265), GSK, Roche, Novartis, UCB.
**DOI:** 10.1136/annrheumdis-2016-eular.2133

## AB0430 CARRIAGE FREQUENCY OF HAPTOGLOBIN PHENOTYPES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME AND THEIR ASSOCIATION WITH CLINICAL MANIFESTATIONS

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**Background:** At present, in 30–35% systemic lupus erythematosus (SLE) patients antiphospholipid antibodies (aPL) are associated with the development of secondary antiphospholipid syndrome (APS), including venous and/or arterial thrombosis and other systemic disorders. Practitioners still face certain difficulties in differential diagnosis of the APS positive SLE and are in need for efficient tests to verify the diagnosis. Hp (haptoglobin) is a hemoglobin-binding glycoprotein of α2-globulin serum proteins fraction induced by seromucoids at the early stages of an inflammatory process. There are three phenotypic variants of Hp: Hp 1–1, Hp 2–1 and Hp 2–2. The practical value of Hp test in SLE patients is the possibility to diagnose a genetic predisposition to APS to predict severity of the disease.
**Objectives:** Determine the carriage frequency of different Hp phenotypes in SLE patients with APS, and reveal a correlation between the level of serum Hp and clinical manifestations of APS in SLE patients.
**Methods:** The study is based on the follow-up results of 103 SLE patients under treatment at the Republican Centre of Rheumatology, Tashkent Medical Academy. Entry criteria of patients in the study: reliable diagnosis of SLE, verified in accordance with SLICC (2012) criteria and the informed consent to participation. The secondary APS (SAPS) was based on the Sydney (2006) Classification Criteria for APS. Haptoglobin test was performed using disc polyacrylamide gel electrophoresis (PAGE).
**Results:** We have defined APS in 44 of 103 (42.7%) SLE patients. In 29 of 44 (65%) cases the APS diagnosis was based on major manifestations, and in 15 of 44 (35%) – by the presence of two or more additional signs. Distribution of SLE patients with APS, depending on the Hp phenotype: 38 (86.4%) patients with APS had Hp 1–1, 6 (13.6%) – Hp 2–1, 0 (0%) - Hp 2–2 phenotype (P<0.01, 95% CI). Distribution of SLE patients without APS depending on the Hp phenotype: 23 (39%) patients – Hp 1–1, 27 (45.8%) – Hp 2–1, 9 (15.3%) – Hp 2–2 phenotype. After distribution of the patients into groups by the Hp level, more than 3 g/l (I group) and less than 3 g/l (II group), we have analysed the correlation between Hp and clinical manifestations of APS: thrombocytopenia: I – 7 (22,5%), II – 3 (23,07%), HM – I – 13 (41,9%), II – 4 (30,7%), livedo reticularis: I – 15 (48,3%), II – 5 (38,4%), finger gangrene: I – 5 (16,1%), II – 0 (0%); finger necrosis: I – 6 (19,3%), II – 1 (7,6%); migraine: I – 20 (64,5%), II – 5 (38,4%); chorea: I – 5 (16,1%), II – 2 (15,3%); transitory ischemic attack (TIA): I – 16 (51,6%), II – 7 (53,8%); chronic ulcers of lower extremities: I – 22 (70,9%), II – 8 (61,5%) (P<0.05, 95% CI).




**Conclusions:** Results of our investigation showed that development of SLE and APS is characteristic for Hp 1–1 phenotype, apparently, being a predisposing factor to the autosensitisation and a genetic marker for APS. Furthermore, there is an expressed correlation between Hp level and clinical manifestations of APS.
**References:**
[1] Reshetnyak TM. Antiphospholipid syndrome: state of the art and future tasks. J Nauchno-prakticheskaya revmatologiya. 2013. 11–14:51–1.
[2] Erkan D, Aguiar CL, Andrade D, Cohen H, Cuadrado MJ, Danowski A. 14th International Congress on Antiphospholipid Antibodies: task force report on antiphospholipid syndrome treatment trends. Autoimmun Rev. 2014 13(6):685–96.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5317

## AB0431 ANTIBODIES TO THE ENZYME OF ADENINE BRANCH OF PURINE METABOLISM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** In the pathogenesis of SLE an important place is given to immune mechanisms with many uncertain aspects. Adenosine deaminase (ADA), 5-nucleotidase (5-NT), adenosine kinase (ADK) and xanthine oxidase (XO) are the main enzymes of adenine branch of purine metabolism (PM), the activity of which is closely related to the immunological processes in the body. The role of antibodies to enzymes PM in systemic lupus erythematosus (SLE) is not defined and poorly studied.
**Objectives:** The purpose of our work was to study antibodies to enzymes of adenine branch of PM in SLE patients and to detect correlations between studied antibodies and clinical and laboratory indices of pathological process.
**Methods:** 30 healthy individuals aged 18 to 40 years (20 women and 10 men) and 60 SLE patients aged 22 to 58 years (55 women and 5 men) were included into the research. The diagnosis of SLE was verified using the ACR criteria of the 1997. The object of research was blood serum. IgG antibodies to ADA (anti-ADA), 5-NT (anti-5NT), ADC (anti-ADC) and XO (anti-XO) were determined in the method developed by us for indirect ELISA-assay using an immobilized form of the correlative enzyme as antigen matrix. Positive results were considered greater than 2 standard deviations of figures obtained during the examination of healthy persons (0.106 Unit for anti-ADA; 0.1 Unit for anti-5NT; 0.47 Unit for anti-ADC; 0.097 U for the anti-XO). The results were expressed as mean ± σ, differences were considered significant when p<0.05. Person correlation coefficient (r) was also used.
**Results:** According to the results of the research the number of SLE patients with elevated levels of anti-ADA was 51.6%, anti-5NT - 41.7%, anti-ADK - 46,7%, the anti-XO - 53.3%. Comparison between the positive and negative for the presence of anti-ADA groups of patients with SLE showed a statistically significant increase in the detection rate of chronic headaches (p=0.01), lymphopenia (p=0.025) and the definition of increased values of antibodies to phospholipids (p=0.014).
Comparison between the positive and negative for the presence of blood serum anti-5NT groups of SLE patients showed an increase in the frequency of kidney damage (p=0.031) and vessels (p=0.053). Analysis of anti-5NT in relation to laboratory data allowed to identify a number of statistically significant correlations: with proteinuria (r=0,27; p=0,039), leukocyturia (r=0,35; p=0,012) and red blood cell (r=0,29; p=0,026). These data allow us to consider the anti-5NT as an additional indicator of lupus nephropathy.
Among patients with the presence of anti-ADK a significant number of patients with vascular disease (p=0,023) was revealed. A bit more often, but not statistically significant, patients with the presence of anti-ADC pulmonary injury (p=0,113) and the autonomic nervous system (p=0,124) were observed.
Comparison between the positive and negative for the presence of anti-CA groups of patients with SLE demonstrated a statistically significant increase in the frequency of signs of kidney (p=0.032) and blood vessels injury (p=0.042).
**Conclusions:** Determination of antibodies to enzymes PM can be used as additional laboratory tests in the diagnosis of complex SLE to characterize the clinical variants of the disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4868

## AB0432 HIGH PREVALENCE OF METABOLIC SYNDROME IN SOUTH AFRICAN SLE PATIENTS

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**Background:** Against a background of urbanisation and widespread poverty, the prevalence of the metabolic syndrome (MetS) is increasing in South Africa, and atherosclerotic cardiovascular diseases are emerging as a major cause of mortality. Patients with systemic lupus erythematosus (SLE) are at increased risk of the MetS and its complications, but there are no published studies of the prevalence or associations of the MetS amongst sub-Saharan Africans with SLE.
**Objectives:** To investigate the prevalence and associations of the MetS amongst recent-onset SLE patients.
**Methods:** A cross-sectional study of baseline features of an inception cohort of recent onset (<5 years' disease duration) SLE patients. All patients met the SLICC SLE classification criteria and were attending the rheumatology clinic in a state-sector tertiary academic hospital. The MetS was defined by Joint Interim Statement criteria[1].
**Results:** Of 90 patients, the mean (SD) age was 36.7 (12.2) yrs, disease duration was 24.7 (22.9) months, 81 (87.8%) were female, and of these 67 (82.7%) were premenopausal. In terms of ethnicity, 70.0% were of mixed ethnic ancestry and 25.6% were Black Africans. Patients were of poor socio-economic status: 31.1% were unemployed, with a mean (SD) schooling of 10.2 (2.6) yrs. The mean (SD) SLEDAI score was 5.9 (3.4), and 94.4% were ANA positive, and 15 (16.7%) had lupus nephritis. The majority of patients were prescribed chloroquine (97.8%) and low dose corticosteroids (67.1%). The mean (SD) BMI was 26.2 (6.8) kg/m$^2$, and 53.3% were smokers. The overall prevalence of MetS in this cohort was 33.3%, and increased waist circumference and reduced HDL- C were the most frequently observed features (Table). There was a trend toward more females having MetS (OR 0.2 (95%CI 0.02–1.4, p=0.09), but there was no association between the MetS and age, menopausal status, disease duration, ethnic group nor with SLEDAI score, presence of dsDNA, hypocomplementaemia, or with organ involvement including nephritis. Surprisingly, neither the use of corticosteroid or their dose was associated with MetS.

| Frequency of the MetS components (n, %) | Overall cohort (n=90) | Patients with MetS (n=30) |
|---|---|---|
| Hypertension | 37 (41.1) | 21 (70.0)) |
| Increased waist circumference | 62 (68.9) | 30 (100.0) |
| Hypertriglyceridemia | 22 (24.4) | 17 (56.7) |
| Low HDL-cholesterol | 50 (55.6) | 24 (80.0) |
| Diabetes | 6 (6.7) | 5 (16.7) |

**Conclusions:** South Africans with recently diagnosed SLE are at particularly high risk of atherosclerotic cardiovascular disease due to the high prevalence of the MetS and cigarette smoking. This calls for aggressive primary prevention strategies.
**References:**
[1] Alberti KG et al. Circulation 2009
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3721

## AB0433 DISEASE CHARACTERISTICS, SURVIVAL ANALYSIS AND MORTALITY IN A SINGLE CENTRE COHORT OF 240 PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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**Background:** Antiphospholipid syndrome (APS) is an autoimmune disease characterized mainly by thrombosis and/or pregnancy morbidity in the presence of antiphospholipid (aPL) antibodies. Significant mortality and morbidity has been reported in patients with APS.
**Objectives:** To characterize a single center cohort of patients with APS (including non-criteria manifestations) and to assess their survival rates, causes of mortality and associations with disease characteristics.
**Methods:** Records of 240 patients with APS were studied. Demographic characteristics, cumulative clinical and laboratory features, autoantibody profiles were retrieved from the existing database. Unattending patients were contacted by telephone and were searched on the national death information system (NDIS). Patients who were non-responsive to telephone calls, not seen in the outpatient clinic within the last 6 months and could not be traced on the NDIS were considered lost-to follow-up.
**Results:** There is a total of 240 patients in this cohort 118 of whom had primary APS and 122 had APS associated with SLE. 83% of the patients were female. The mean age at diagnosis was 41±12, duration of disease and follow-up were 110±85 and 92±82 months respectively.
Of 240 patients, 65% had vascular thrombosis (VT), 24% had pregnancy morbidity (PM), 10% had both VT and PM and 3 had catastrophic antiphospholipid syndrome. Overall 29% patients had thrombotic risk factors among which smoking followed by homozygous factor V Leiden mutation were the most prevalent. Of patients with VT 49% had arterial (a), 38% had venous (v) and 13% had both a and v thrombosis. 95 patients experienced a single thrombotic episode whilst 62 had more than once, most commonly v followed by a thrombosis. In the PM group, there were 31 patients with fetal deaths beyond 10 weeks, 39 with 3 or more abortions before 10 weeks, 18 with premature labour and 14 with pre-eclampsia. Overall, 46% of patients had aCL IgG, 36% had IgM and LA was present in 54%. Anti-β2GPI was tested in 117 patients and 38% were positive for IgG and 25% for IgM. Of the non-criteria manifestations of APS, the most common presentation was heart valve lesions followed by thrombocytopenia.
In total there were 25 deaths and 19 patients were lost to follow-up. Survival rates were 94, 86, 78 and 71% at 5, 10, 15 and 20 years respectively. Comparison of survival between patients with VT and PM displayed a marked reduction in the VT group (p=0.04) whilst primary and lupus associated APS patients had similar rates. Causes of death could be identified in 19 patients. Myocardial infarction, alveolar hemorrhage and pulmonary hypertension were the leading causes of death. Mortality was significantly associated with LA positivity (p=0.02).
**Conclusions:** In this cohort, the most prevalent manifestation of APS was arterial thrombosis. Long-term follow up revealed that patients with APS had significant mortality and APS-related manifestations dominated the causes. Thrombotic patients had a reduced survival relative to PM patients. No single aPL test was sufficiently sensitive in the evaluation of APS. LA positivity was a risk factor for reduced survival.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5888

## AB0434 THE ROLE OF IGG ANTI β2-GPI IN THE CLINICAL MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Beta 2 GPI is an important antigenic target for antiphospholipid antibodies. The role of IgG antibodies to β2 glycoprotein I [Anti-β2-GPI] has been well defined in antiphospholipid antibody syndrome but its role in the clinical manifestions of SLE remains elusive.
**Objectives:** To investigate the role of Anti-β2-GPI in the clinical manifestations of SLE
**Methods:** IgG Anti-β2-GPI was measured in 184 patients with SLE (93% women, mean age 28 years). IgG Anti-β2-GPI (>18 GPL units) was found in 19 patients (10.3%). Associations were determined with clinical manifestations of SLE and with components of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index
**Results:** Of the patients with SLE who demonstrated IgG Anti-β2-GPI, 31% had at least one thrombotic event (OR 4.2, p=0.01), 26% had pulmonary hypertension (OR 3.2, p=0.02) and 26% had recurrent abortions (OR 4.1, p=0.02). IgG Anti-β2-GPI was protective against lupus nephritis (OR 0.31, p=0.02). No other manifestations were significantly higher in patients with IgG Anti-β2-GPI positivity

| Clinical Manifestation | | Anti-β (2)-GPI | | |
|---|---|---|---|---|
| | | Positive | Negative | |
| Recurrent abortions | Present | 5 | 13 | OR 4.1 p=0.02 |
| | Absent | 14 | 152 | |
| Thrombotic events | Present | 6 | 16 | OR 4.2 p=0.01 |
| | Absent | 13 | 149 | |
| Pulmonary hypertension | Present | 5 | 15 | OR 3.2 p=0.02 |
| | Absent | 14 | 150 | |
| Lupus nephritis | Present | 6 | 98 | OR 0.31 p=0.02 |
| | Absent | 13 | 67 | |

**Conclusions:** In SLE, IgG Anti-β2-GPI is associated with thrombotic events and pulmonary hypertension, but may have a protective effect against lupus nephritis. Large scale studies are required to confirm these findings.
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## AB0435 IMMUNOSIGNATURE TECHNOLOGY IDENTIFIES SYSTEMIC LUPUS ERYTHEMATOSUS FROM A DROP OF SERUM

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease characterized by production of pathogenic autoantibodies. These autoantibodies form immune complexes that can deposit in tissues causing organ damage. The clinical heterogeneity of SLE, and its manifestations that overlap other diseases, pose a diagnostic challenge (1–3). Early identification of disease and disease activity is key to curtailing permanent organ damage (3–5). More accurate diagnosic tools than those in current clinical use would have a significant impact on patient care.
HealthTell has developed a high density peptide array platform to diagnose a disease based on differential Ab binding called ImmunoSignatures (IS). The IS technology uses arrays of hundreds of thousands of unique peptides designed to survey an individual's Ab repertoire from a drop of blood, plasma, or serum (6). Differential binding profiles of the Ab on the array between patients with the disease of interest and control groups are selected as input to develop classification algorithms. The technology holds promise for detecting the presence of any disease that generates a specific B-cell response. Furthermore, for autoimmune diseases the technology has the potential to provide accurate differential diagnosis as well as detection of disease activity and progression.
**Objectives:** To establish the feasibility of the IS technology in identifying subjects with SLE.
**Methods:** Two well-annotated cohorts of serum samples were used representing i) 45 SLE cases and ii) 45 age, gender and race-matched normal donors. All SLE patients met ACR criteria, and as their primary clinical manifestation had joint (53%), renal (38%), skin (2%), or inactive disease (7%). Serum samples were diluted and applied on to the arrays. Ab-peptide binding was detected with fluorescently-labeled goat anti-human IgG. Peptide binding signal was quantified and features with significant differences in intensity between cases and controls were identified by Bonferroni adjusted t-test and log odds ratios. Support vector machine classification algorithms were trained using the most distinguishing peptides. Classifier model performance was evaluated by applying 100 iterations of a four-fold cross-validation routine that included feature selection, model training, and model testing.
**Results:** The cross-validated performance metrics of the 500-peptide IS classifier included an area under the Receiver Operator Curve of 0.99 (95% confidence interval (CI) 0.98–0.99) and an overall accuracy of 93% (95% CI 91%>96%) at equal sensitivity and specificity.
**Conclusions:** ImmunoSignature identification of SLE is feasible and highly accurate based on the preliminary cross-validated performance. These results need verification in larger cohorts and validation in blinded studies. Future studies will include control samples relevant to SLE differential diagnosis such as inflammatory and non-inflammatory rheumatic diseases, as well as active and inactive SLE.
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## AB0436 ALL THE "HISPANICS" ARE NOT EQUAL. THE SEVERITY AND ACTIVITY OF PATIENTS WITH SLE IS HIGHER IN MESTIZOS LATIN AMERICAN VS. EUROPEAN CAUCASIAN. LESSONS FROM RELESSER

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**Background:** SLE is a known disease for the study of ethnic and gender minorities. In Spain, from 1998 to 2011, occurred a significant immigration from Latin American people. The English speakers consider "Hispanics" as the same ethnic group. But there are differences between the Hispanics from Spain (with ethnicity European Caucasian) and the Hispanics from Latin America (with ethnicity Mestizo Latin American).
**Objectives:** To know the demographic, clinical, severity, activity, damage, mortality and comorbidity of SLE in Hispanics with ethnicity European Caucasian (EC) and in Hispanic Mestizos from Latin American (MLA) residents in Spain. To identify differences between the groups.
**Methods:** Design: observational, multicentric, crossover study. Patients with SLE (ACR 1987) and <16 years old were included in 45 rheumatology Units in Spain. The RELESER methodology has been informed. Statistical analysis: we grouped the patients from the registry in two groups: EC and MLA and descriptive, univariate and multivariate statistics were done.
**Results:** 3,490 patients with SLE were included, 90% females; 3,305 (92%) Hispanics EC y 185 (5%) Hispanics MLA. The Table shows the main variables. Patients MLA had higher levels of activity (SLEDAI), severity (KATZ INDEX) and number of admissions to the hospital for SLE activity. The damage index (SLICC), mortality, and comorbidity Index showed no differences. In the multivariate analysis several models were constructed with adjusted for age, sex and disease duration. The patients MLA had a higher risk for Severity (Katz Index >3) OR 1,45 (1,038 – 2, 026, p=0,02. This differences were not found for activity: OR 0,98 (0.30 - 1.66), may be for collinearity.

Table 1

| Variable | European Caucasian n, % | Mestizos Latin American n, % | p |
|---|---|---|---|
| Total | 3.305, 92 | 185, 5 | |
| Women | 2.891, 90 | 176, 95 | 0.02 |
| Myositis | 113, 3 | 15, 8 | 0.001 |
| Hemolytic anemia | 271, 8 | 24. 14 | 0.01 |
| Lupus nephritis | 952, 29 | 79, 44 | <0.0001 |
| Serositis | 49, 1 | 9, 5 | <0.001 |
| Admissions related to LES activity | 1.741, 54 | 120, 67 | 0.0001 |
| | Median (IQR) | Median (IQR) | |
| Age at SLE diagnosis (years) | 35.5 (24.3–44.5) | 30.5 (22.6–36.9) | 0.001 |
| Age at the study inclusion | 32.8 (22–42) | 28.6 (21–36) | <0.001 |
| SLA disease duration (years) | | | |
| 1st symptom to diagnosis | 12.5 (5.7–17.5) | 7.9 (2.5–10.7) | <0.0001 |
| Activity (SLEDAI) | 2.5 (0–4) | 3.8 (0–4) | 0.01 |
| Severity (KATZ) | 2.6 (1–3) | 2.9 (2–4) | 0.01 |
| Damage (SLICC) | 1.1 (0–2) | 0.9 (0–1) | 0.6 |
| Comorbidity (Charlson) | 2.3 (1–3) | 1.7 (1–2) | 0.2 |

**Conclusions:** The SLE of Hispanics MLA patients had clinical differences when it was compared with Hispanics EC patients, mainly higher severity and activity. This shows that all the Hispanics are not equal.
**Disclosure of Interest:** None declared
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## AB0437 COMPLICATIONS OF THE MINIMALLY INVASIVE BIOPSY OF THE MINOR SALIVARY GLAND

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**Background:** The diagnosis of Sjogren Syndrome (SS), requires fulfillment of the American- European classification criteria, which include the obligatory presence of antibodies or a compatible histology. Numerous labial salivary gland biopsy techniques have been described, with variations in the size and shape of incision, as well as the need for suturing. Nowadays, the tendency is to use less invasive techniques
**Objectives:** To evaluate the frequency of complications of the minimally invasive biopsy of minor salivary glands
**Methods:** Transversal study of 159 biopsies of the minor salivary gland. *Inclusion Criteria:* patients with dry syndrome. *Biopsy technique:* anesthesia with ultracain and epinephrine, vertical incision (≤5 mm) of the internal surface of the lower lip using a scalpel and whitout suture, followed by the application of a gauze with topical procoagulant for 30 minutes. *Variables studied:* 1) clinical: age, sex, presence and duration of the symptoms; 2) diagnostic: Schirmer test, salivary scintigraphy, ANA, RF, anti-SSA and anti-SSB. 3) biopsy complications: a) immediate: bleeding and lipothymia; b) acute (<1 month): dysesthesia, hematoma, swelling, infection, pain, speaking and eating difficulties, scarring disorders (granuloma, keloid) and c) chronic (>1 month): dysesthesia, scarring disorders (granuloma, keloid), 4) histological: a) degree of atrophy: absent, light, moderate and severe b) Chisholm-Mason scale (I-IV)
**Results:** The characteristics of the sample group were; age 59.9 ±12.43 years, 91% women, 88% xerostomia, 89% xerophthalmia for a period of 49±37 months, 45% positive salivary scintigraphy, 54% positive Schirmer, 54% ANA, RF 22%, anti-SSA and anti-SSB of 28% and 6.2%, respectively. The complications were: immediate (n=16; 8%): bleeding (n=13; 81%), lipothymia (n=3; 18%); b) acute (n=93; 58%): dysesthesia (n=2; 1.2%) for a period of 2.5±0.7 days, hematomas (n=23; 14%)) for a period of 4±2.5 days, swelling (n=69; 43%) for a period of 3±2.4 days, infection (0%), 37% pain (26% mild, 9% moderate, 2% severe) for a period of 3±2.5 days, speaking difficulties (n=13;8.1%) for a period of 3±3.6 days, eating difficulties (n=20; 12%) for a period of 2.3±2.8 days and granuloma (n=10; 6.2%); c) chronic (n=4; 2.5%): dysesthesia (0%) and granuloma (n=4; 2.5%) without clinical repercussion. Material for histology was obtained in 92.5%. The development of chronic complications (granuloma) was not related to the presence of acute complications except temporal dysesthesia (18% vs 1%;

p<0.001). Also chronic complications was not related to the degree of histological atrophy or age, but a tendency was observed in younger patients (49±4.5 vs 60±12.4; p<0.09)
**Conclusions:** The minimally invasive biopsy of the minor salivary gland is a technique which is easy to carry out and complications are rare. Moreover, it also offers success rates to obtain material which are similar to those of other techniques. Given the ease of the technique and the fact that complications are rare, it is worth evaluating its incorporation into those centres where it is not being used and it should be performed by rheumatologists.
**Disclosure of Interest:** None declared
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## AB0438 CHEMOKINES AND RENAL COMPLICATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** We and others have performed cluster analyses of patients with systemic lupus erythematosus (SLE) and revealed several prognostically distinct clinical patterns. Certain clusters of patients present with lupus nephritis (LN) while others remain LN free in the course of their disease. [1] This observation suggests different immunopathogenic mechanisms may be in play in the various disease manifestations of lupus. Chemokines recruit immune cells and have been proposed as biomarkers for LN.
**Objectives:** This study aimed to investigate if changes in the serum levels of various chemokines were abnormal in patients with a clearly defined history of LN and non-LN (NLN). Chemokines, including interferon-γ-induced protein-10 (IP-10), RANTES and macrophage inflammatory protein-1α (MIP-1α) were examined.
**Methods:** Patients were said to have LN if they had at least 1 episode of biopsy-confirmed Class III, IV or V (or any combination of these 3 classes) nephritis, while those who had not exhibited any renal diseases after at least 10 years of follow up were designated NLN. The LN patients were further divided into those with inactive LN (ILN) and active LN (ALN). ALN patients were recruited at the time of renal biopsy before immunosuppressive drug treatment. Enzyme-linked immunosorbent assay (ELISA) was used to measure the concentration of RANTES, MIP-1α and IP-10 in serum of the 3 groups of patients.
**Results:** 80 patients were studied. 32 had ILN, 8 ALN and 40 NLN. Preliminary data show the serum levels of RANTES and MIP-1α were significantly lower in the LN group (including ALN and ILN) when compared with NLN SLE patients. (LN vs NLN: RANTES 3.3±5.7 ng/ml vs 7.6±9.9 ng/ml, p=0.0003; MIP-1α 39±106 pg/ml vs 86±158 pg/ml, p=0.03; IP-10 284±342 pg/ml vs 300±534 pg/ml, p=n.s.) There were no significant differences in the serum concentrations of RANTES and MIP-1α between the ALN and ILN subgroups (ALN vs ILN: RANTES 4.3±8.3 ng/ml vs 3.0±5.0ng/ml, p=n.s.; MIP-1α: 27±23 pg/ml vs 42±112 pg/ml, p=n.s.) For IP-10, no significant differences were found among the ILN, ALN and NLN groups. (ILN: 256±264pg/ml, ALN: 398±569pg/ml, NLN: 300±534pg/ml, all p =n.s.)
**Conclusions:** LN patients had lower serum levels of RANTES and MIP-1α when compared with patients with clearly no LN disease. These chemokines may have an immunopathogenic role in the development of renal complications in SLE. That no differences in the serum levels of RANTES, MIP-1α and IP-10 were observed between ILN and ALN patients may suggest these chemokines are not implicated in LN disease progression although a larger cohort study with serial follow-up of patients before and after the development of LN and the use of immunosuppressive treatment is needed. This is underway. In addition, more candidate chemokines and related cytokines will be studied.
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**Disclosure of Interest:** None declared
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## AB0439 ADVERSE EVENTS AFTER SURGERY IN PEDIATRIC PATIENTS WITH SLE: A NATIONWIDE STUDY

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**Background:** Little was know about the outcomes after surgery in pediatric patients with systemic lupus erythematosus (SLE).
**Objectives:** Our purpose is to investigate the postoperative adverse events among surgical pediatric patients with preoperative SLE in a nationwide population-based study.
**Methods:** We used Taiwan's National Health Insurance Research Database to identify pediatric inpatients with SLE and 258294 controls receiving major surgery. Sociodemographic characteristics, preoperative comorbidities, postoperative 30-day in-hospital major complications and mortality were analysed among surgical patients with and without SLE.
**Results:** Pediatric patients with SLE had a higher prevalence of preoperative coexisting medical conditions and postoperative major complications. The OR of 30-day postoperative mortality for surgical patients with SLE was 8.55 (95% CI 2.65–27.6) after adjustment. Among pediatric patients, SLE was associated with postoperative pneumonia (OR 8.79, 95% CI 5.54–13.9), acute renal failure (OR 30.6, 95% CI 14.8–63.2), admission to intensive care unit (OR 2.16, 95% CI 1.55–3.00), prolonged length of stay (OR 2.45, 95% CI 1.78–3.38) and increased medical expenditure (OR 2.64, 95% CI 1.92–3.63).
**Conclusions:** Among pediatric population, SLE significantly increased the risks of surgical complications and mortality after major surgery. Our findings demonstrated the need for integrated care and revised protocols for perioperative management to improve outcomes for pediatric patients with SLE.
**Disclosure of Interest:** None declared
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## AB0440 SERUM URIC ACID LEVELS PREDICT NEW RENAL DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Renal involvement is one of the most serious and frequent manifestations of systemic lupus erythematosus (SLE) and is associated with increased morbidity and mortality. Uric acid levels have been associated with the progression to subsequent end-stage renal disease in patients with chronic kidney disease [(1)]. Uric acid has been reported to be associated with new onset lupus nephritis [(2)]; however, the association between uric acid levels and renal damage has not been reported in SLE patients.
**Objectives:** To determine whether uric acid level predicts new renal damage in SLE patients after adjusting for known confounding factors.
**Methods:** This longitudinal study was conducted in consecutive SLE patients seen in our Rheumatology Department since 2012. Every patient had a baseline visit; follow-up visits were conducted every 6 months. For the purpose of this study, patients with at least two visits were included. Patients with end-stage renal disease (regardless of dialysis or transplantion) were excluded for this analysis. Renal damage was ascertained using the SLICC/ACR damage index (SDI). Uric acid was measured in mg/dl. Survival analyses using univariable and multivariable Cox-regression models were performed to determine the risk of new renal damage. The multivariable model was adjusted for age at diagnosis, gender, disease duration, socioeconomic status, SLEDAI, SDI, serum creatinine, use of prednisone, antimalarials and immunosuppressive drugs at baseline.
**Results:** One hundred and eighty-six patients were evaluated; their mean (SD) age at diagnosis was 36.8 (13.7) years; nearly all patients were Mestizo. Disease duration was 7.7 (6.8) years. Time of follow-up was 2.3 (1.1) years. At baseline, uric acid levels were 4.5 (1.3) mg/dl, the SLEDAI was 5.2 (4.3) and the SDI 0.8 (1.1). Sixteen (8.6%) patients had one point in renal domain at baseline and 2 (1.1%) had two. During the follow-up 16 (8.6%) patients developed at least one new point in the renal domain of the SDI. In univariable and multivariable analyses uric acid level at baseline predicted the development of new renal damage [HR: 2.24 (1.50–3.34), p<0.001; HR: 3.21 (1.39–7.42), p=0.006; respectively].
**Conclusions:** Higher uric acid levels predict the development of new renal damage in SLE patients even after adjusting for other well-known risk factors.
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**Disclosure of Interest:** None declared
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## AB0441 NEUROPSYCHIATRIC MANIFESTATIONS OF ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Evaluation of the diversity of Neuropsychiatric (NP) manifestations of adult-onset Systemic Lupus Erythematosus (SLE) for the period 2012–2014 (extended 2014–2015) is presented. The most common complications are migraine, cognitive and motor disorders, seizures, cerebrovascular disease
**Methods:** Complete clinical, rheumatological and neurological evaluation was performed using SLEDAI-2K, BILAG 2004, SLICC/ACR Damage Index test batteries. Immunological blood tests include C3, C4, Serum Cryoglobulins, ANA, anti-β2 GP I-Ig G, anti-β2 GP I-Ig M, Anti-double stranded DNA, anti-RNP/Sm, anti-His., Ro (SSA), La (SSB), anti-CENT B, anti-ribosomal P, ANCA followed by lumbal puncture, neuropsychological testing, Doppler sonography, EMG and EEG, brain MRI/CT.

**Results:** A total of 220 patients were longitudinally observed in 4 years period - 185 female, (84%), 35 men (16%). 82 (37%) patients presented NPSLE during the first 6 months. Consequent NP manifestations include: central vertigo (73.5%), headache (66.5%), cognitive impairment (33.2%), psychiatric disorders (18.7%), seizures (7.3%), cerebrovascular disease (10.6%), and polyneuropathy (3.5%). Positive anti-DNA antibodies (50%), anti-ribossomal P (20%), anticardiolipin antibodies (50%) were identified in NPSLE patients.
**Conclusions:** Patients with SLE present with different NP manifestations. It is still difficult to provide accurate differential diagnosis between NPSLE and chronic cerebrovascular disease or MS especially when NP manifestations are the first symptoms of SLE.
**Disclosure of Interest:** None declared
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## AB0442 SPECTRUM AND DRUG RESISTANCE OF BACTERIA ISOLATED FROM HOSPITALIZED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** In recent decades, the leading cause of death in patients with *systemic lupus* erythematosus (SLE) has changed from active disease to infection. The spectrum of infectious agents in SLE patients varies significantly among different ethnic groups. Furthermore, multiple drug resistance (MDR) pathogens have become the biggest concern worldwide, and the situation is even more serious in China.
**Objectives:** To investigate the spectrum and antibiotic resistant pattern of bacterial infection in patients hospitalized with SLE.
**Methods:** We collected the clinical and microbiological data from hospitalized SLE patients with bacterial infection between June 2005 and June 2015 and then conducted retrospective analyses.
**Results:** Among our sample of 3815 hospitalized patients, 258 episodes had microbiological defined bacterial infection. In terms of isolated microorganisms, gram-negative bacteria (GNB) were predominant over gram-positive bacteria (GPB) (178 isolates vs. 90 isolates). In the GNB, Escherichia coli (24.6%) was the most common isolate, followed by Acinetobacter baumannii (13.4%) and Klebsiella pneumoniae (9.0%). For GPB, coagulase negative Staphylococcus (CNS, 13.4%) was most commonly documented followed by Staphylococcus aureus (11.2%) and other GPB. Overall, MDR bacteria were detected in 26.9% of the isolates. Extended-spectrum beta-lactamase (ESBL) producers were expressed mainly in Escherichia coli (30/66, 45.5%) and Klebsiella pneumoniae (7/24, 29.2%). The proportion of multi-drug resistant acinetobacter baumannii (MDR-AB) in the sample was 36.1%. Eight of Staphylococcus aureus (8/30, 26.7%) were found to be methicillin-resistant Staphylococcus aureus (MRSA), and fourteen of CNS (14/36, 38.9%) were considered methicillin-resistant CNS (MRSCNS).
**Conclusions:** Predominance of GNB with emerging of MDR isolates was the notable features of bacterial infection in Chinese SLE patients. Therefore rational use of antibiotic will be urgently needed to reduce the morbidity and mortality of patients with SLE.
**Disclosure of Interest:** None declared
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## AB0443 RELATION BETWEEN ACCUMULATIVE DAMAGE AND DISABILITY RECOGNICED BY THE INSS* IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Systemic Lupus Erythematosus (SLE) in a multisystemic and autoimmune disease that specially affects young women during the second and third decade, and is able to injure different organs and or systems, being the most common one affected the musculoskeletal system. Events attributed to SLE itself and other related to the disease may impact negatively in the quality of life, unemployment, disability and mortality. Recent data show that 3.8% of SLE patients have comorbidities and 59.2% of them were receiving a disability pension. In Spain, the evaluation of disability and the assignation of the mentioned pension is given by the National Social Security Institute of Spain (INSS: Instituto Nacional de la Seguridad Social).
**Objectives:** To assess the relationship between cumulative damage regarding to the affected organ and the percentage of disability recognized by the INSS in SLE patients in Spain.
**Methods:** Cross-sectional prospective study of SLE patients according to the SLICC-2012 criteria, from the Rheumatology Service of Arnau de Vilanova Hospital and La Fe Hospital. We collected clinical and demographic data through personal interview and the SLIC-ACR questionnaire.
**Results:** A total of 140 patients were evaluated; of them, 95% were women with 33.39±13.63 year-old average at the diagnosis time with a 10.05±1.42 year-evolution of SLE. Clinical characteristics of each group are described in the table.

| | Without disability | With disability |
|---|---|---|
| N | 98.00 | 42.00 |
| Disability (%) | 0 | 53.14±23.7 |
| SLICC | 0.75±0.98 | 1.8±1.10 |
| Age at SLE diagnosis | 34.6±14.8 | 30.7±10.4 |
| SLE evolution (years) | 13.9±10.7 | 20.7±8.10 |
| Nervous system damage (%) | 12.24 | 28.57 |
| Musculoskeletal damage (%) | 88.78 | 90.48 |
| Mucocutaneus damage (%) | 72.45 | 76.19 |
| Serositis (%) | 7.14 | 14.29 |
| Cardiovascular damage (%) | 13.27 | 19.05 |
| Cytopenia (%) | 42.86 | 47.62 |
| Renal damage (%) | 13.27 | 19.05 |
| Raynaud's (%) | 29.59 | 47.62 |
| Antiphospholipid synd. (%) | 7.14 | 11.90 |
| Sjögren synd. (%) | 16.33 | 23.81 |
| Vasculitis (%) | 1.02 | 4.76 |

**Conclusions:** We observed a positive correlation between percentage of recognized disability and the SLICC-ACR index score. Musculoskeletal system is, in general, the most affected one, without differences between both groups; but we found a higher proportion of damage in nervous system, renal and vasculitis in patients with a recognized disability.
**Disclosure of Interest:** None declared
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## AB0444 EVALUATION OF CUMULATIVE DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AS A NEW CARDIOVASCULAR RISK FACTOR

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**Background:** The first cause of mortality in patients with Systemic Lupus Erythematosus (SLE) is cardiovascular disease (CVD). Accelerated atherosclerosis that occurs in SLE is considered one of the fundamental mechanisms of the increase of cardiovascular mortality in this group of patients. Among the factors that contribute to the accelerated atherosclerosis process, we include the classical CVD risk factors, as well as the inflammatory and specific SLE factors.
**Objectives:** To assess the CVR in SLE patients and the possibility of modifying it based on the accumulative damage and the disease activity.
**Methods:** Cross-sectional prospective study of SLE patients according to the SLICC-2012 criteria, from the Rheumatology Service of Arnau de Vilanova Hospital and La Fe Hospital. All patients had a complete blood-test with autoimmunity markers, and clinical, biometrics and treatment data were collected. Biostatistical analysis was performed with the *R* software version 3.2.3.
**Results:** 140 patients were evaluated; (95% women) with 33.39±13.63 year-old average at the diagnosis time with a 10.05±11.42 year-evolution of SLE. 15% of patients had had some kind of CVD; in them, we observe an increase of the classical cardiovascular risk factors comparing to the group who hadn't had any CVD manifestation.
We found a statistically significant association between high scores in the SLICC-ACR index ($P<0.001$), dyslipemia (P=0.04), diabetes (P=0.02) and the presence of CVD in our patients. In addition, though it didn't get statistical significance, we observed a tendency to the association between CVD with the presence of hypertension, high levels of LDL-cholesterol and high scores in the SELENA-SLEDAI activity index.
Finally, and also without statistical significance, we observed a marked difference between levels of IgM anticardiolipin and IgM beta2-glicoprotein, finding higher levels in the group of patients that had suffered any manifestation of CVD.
**Conclusions:** The CVD rate among our group of patients is 15%, clearly higher than the general Spanish population (8.53%). We confirm the weight of classical cardiovascular risk factors as a trigger of CVD in SLE; however, the accumulative damage of the disease calculated with the SLIC-ACR index has a determinant paper in the cardiovascular risk of our patients. Therefor it could be proposed as an additional factor of cardiovascular risk in SLE patients.
On the other hand, the disease activity calculated with the SELENA-SLEDAI index seems to have a tendency of correlation between higher scores and the presence of CVD, though the years of disease evolution don't seem to influence in CVD. Nevertheless, more independent studies are needed to confirm this hypothesis.
**Disclosure of Interest:** None declared
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## AB0445 OCULAR POSTERIOR SEGMENT FINDINGS IN ANTIPHOSPHOLIPID SYNDROME

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**Background:** Antiphospholipid Syndrome (APS) can affect all vessels in the body. Ocular complications are seen most commonly in posterior segment of the eye in these patients. The purpose of this study is to evaluate the posterior segment signs in APS patients and to compare these signs between Primary APS, Secondary APS and Systemic Lupus Erythematosus (SLE) patients without APS.
**Methods:** We have included 11 Primary APS, 2 Sjogren's Syndrome/ 27 SLE patients diagnosed as Secondary APS and 29 SLE patients without APS followed at Marmara University, Division of Rheumatology Outpatient Clinics in this study. All of the patients had a detailed ophthalmological examination, including dilated fundus examination and color fundus imaging. 10 patients with Primary Antiphospholipid Syndrome, 23 patients with Secondary APS and 23 patients with SLE had fundus fluorescein angiography imaging.
**Results:** Mean age of the patients was 34.8±12.5 years in Primary APS, 38.3±11.1years in Secondary APS and 38.3±10.9 years in SLE group. In Primary APS 45.5% of patients had venous thrombosis, 45.5% had arterial thrombosis and 72.7% had obstetric complications. In Secondary APS, 44.8% patients had venous thrombosis, 27.6% had arterial thrombosis and 72.4% had obstetric complications. Venous tortuosity was observed in 6 eyes of 3 patients in Primary APS group and 8 eyes of 4 patients in Secondary APS group. One patient with Secondary APS had bilateral branch retinal arterial occlusion. The most common ocular finding of the FFA was pigment epithelial window defect and was observed totally in 19 eyes of 12 patients. There was no statistically significant difference of ocular findings between the Primary APS, Secondary APS and SLE patients.
**Conclusions:** In this study, ocular posterior segment findings of Primary APS had been observed less commonly than previous studies. The lower prevalence of ocular complications in this study can be the result of early diagnosis and better control of relapses in these patients.
**Disclosure of Interest:** None declared
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## AB0446 CONTRACEPTIVE PRACTICES AND KNOWLEDGE AMONG WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN A PORTUGUESE TERCIARY CARE HOSPITAL

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**Background:** Systemic Lupus Erythematosus (SLE) is a disease that primarily affects women of reproductive ages. Unplanned pregnancy in women with SLE can have various complications both for the child and the woman, due to the disease itself or to eventual exposure to teratogenic medications. Most of these patients are candidates for extremely effective contraceptive methods, including implants, intrauterine devices (IUD) or permanent sterilization. However, some of these patients do not receive proper counseling and these methods are often underutilized.
**Objectives:** To determine contraceptive use, knowledge and counseling among patients with SLE attending a portuguese terciary care hospital.
**Methods:** Cross-sectional study in which women aged 15–50 followed in our Rheumatology Department with a diagnosis of SLE were approached to complete a researcher-administered survey.
**Results:** 74 women were included, median age 34 years (range 15–50), with median disease duration of 9.0 years (range 0.50–30.0). 8 patients were in menopause, 2 were pregnant at the time of the survey, and 18 had not been sexually active with a man in the 3 months prior to the survey. 46 women (62.1%) were sexually active and were considered to be at risk for unintended pregnancy. 41.3% (n=19) of these patients were using extremely effective contraceptive methods with a typical use failure rate of $\leq$3% (10 of them using (IUD), 7 permanent sterilization, and 2 implants), 32.6% (n=15) were using highly effective contraceptive methods with a typical use failure rate of $\geq$3% but $\leq$10% (combined oral contraceptive in 7 and progestatin-only oral contraceptive in 8) and 26.1% (n=12) were using either no method, or low effective methods with a typical use failure rate of $>$10% (masculine condom in 11 and one patient was not using any method).
52.2% (n=24) of the sexually active women were taking one or more of methotrexate, mycophenolate mofetil, cyclophosphamide or warfarin. Amongst these soubgroup of patients one third was using extremely effective contraceptive methods, one third was using highly effective methods and another third was using low effective methods either or no method.
Among women at risk for unintended pregnancy 13% (n=6) were not aware of the complications associated with pregnancy in their medical condition, and in patients using teratogenic medications 8.3% (n=2) were not aware of the the risks and 37.5% (n=9) had never been counseled about contraception. In women using teratogenic medications and low effective methods, 87.5% (n=7) were aware of the risks of pregnancy but 87.5% (n=7) had never been counseled about contraception.
**Conclusions:** In this study, most women with SLE who are at risk for unintended pregnancy were aware that their medical condition increases the health risks for themselves and their fetuses. However a significant number of patients, especially those under potencially teratogenic medications did not receive any contraceptive counseling. It is essential to educate these women about their reproductive health and contraceptive options and risks.
**Disclosure of Interest:** None declared
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## AB0447 ANTI-PHOSPHOLIPID POSITIVITY IN HEALTHY SUBJECTS: EVALUATION OF RISK FOR THROMBOTIC EVENT AFTER A 5 YEARS FOLLOW-UP

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**Background:** Antiphospholipid syndrome (APS) is defined by the presence of thrombosis and/or pregnancy morbidity in combination with the persistent positivity of antiphospholipid antibodies (aPL): lupus anticoagulant (LA), anticardiolipin (aCL) and anti b2glycoprotein I antibodies (anti-b2GPI). These autoantibodies could be detected in other pathological conditions, such as autoimmune diseases (i.e. Systemic Lupus Erythematosus - SLE -), infectious diseases or cancer. Moreover, aPL could be identified in asymptomatic subjects (aPL carriers). Concerning this group, several questions are still unsolved, such as the risk of developing thrombotic events and the need of a prophylactic treatment. To date, the aPL carriers who are considered at higher risk of thrombosis are those with LA positivity, with triple positivity (LA+aCL+anti-$\beta$2GPI) and those with persistently positive aCL at high/medium titer. Data from the literature reported a risk ranging from 0 to 3.8% after a mean follow-up period of 2.3–8.7 years. It should be considered that 70% of the evaluated aPL carriers showed a concomitant autoimmune disease, which represents a risk factor for thrombotic events.
**Objectives:** In this prospective study, we evaluated a cohort of aPL positive healthy subjects, in order to define the risk of developing thrombotic events, in comparison with a group of primary APS (PAPS) patients.
**Methods:** In this longitudinal study, we consecutively enrolled 29 aPL carriers (M/F 3/26; mean age±SD 45.0±10.9 years) and 21 PAPS (M/F 5/16; mean age±SD 41.8±12.1 years). According with the study protocol, all patients underwent clinical assessment (collection of anamnestic data and traditional risk factors for cardiovascular disease) and laboratory evaluation (aCL, anti-$\beta$2GPI, LA, antinuclear antibody – ANA –, C3 and C4 serum levels; thrombophilic screening). Data concerning the familial cardiovascular history were collected. All subjects were evaluated every 6 months.
**Results:** The comparison between aPL carriers and PAPS patients demonstrated as LA was significantly more frequent in aPL carriers (P=0.0001) while a similar percentage of triple positive patients was identified. Seventeen (58.6%) aPL carriers were treated with low dose aspirin (LDA), 2 (6.9%) with hydroxychloroquine. After a mean follow-up of 67.0 months (range 12–228), we identified an absolute risk to develop a thrombotic event of 0.03 (95% CI 0.001–0.238) and a relative risk of 0.7 (95% CI 0.02–6.44). In particular, a 55 years old female, treated with LDA, developed a thrombotic event after 84 months of follow-up, consisting in a minor stroke. The patient, without other risk factors, tested positive for LA and aCL at high/medium titer.
**Conclusions:** To the best of our knowledge, this is the first study specifically designed to evaluate only aPL positive healthy subjects. The longitudinal evaluation identified, after a mean follow-up higher than 5 years, an absolute risk for thrombotic events of 0.03, with a relative risk of 0.7. As suggested by the case described, the presence of multiple aPL positivity, with high/medium titer antibodies, requires particular attention.
**Disclosure of Interest:** None declared
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## AB0448 REAL TIME SONOELASTOGRAPHY IN PRIMARY SJÖGREN'S SYNDROME CORRELATES WITH MORPHOLOGICAL ULTRASONOGRAPHIC FEATURES AND GLANDULAR ACTIVITY BUT NOT WITH MINOR SALIVAR GLAND FIBROSIS

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**Background:** Real time sonoelastography (RTS) is a novel imaging option involving tissue stiffness assessment that might be a useful in primary Sjögren's syndrome (PSS).
**Objectives:** To evaluate the stiffness of parotid and submandibular glands using RTS, and to correlate with a morphologic ultrasonographic (US) score, profibrotic chemokines and cytokines, and gland fibrosis among patients with PSS.
**Methods:** We included 26 PSS patients with salivary gland biopsy within 5

years previous the US evaluation. B-Mode US and RTS (ARFI technique) were performed by a trained radiologist. Parotid and submandibular glands were individually rated for parenchymal echogenicity, homogeneity, hypoechogenic areas, hyperechogenic reflections and clearness of borders using the Hocevar scale (Global B-mode sum score 0–48 points). RTS was conducted at both parotid and submandibular glands (8 areas of each gland to obtain a median value) and then reported a median global RTS score in m/seg. We assessed the ESSDAI, ESSPRI, non-stimulated whole salivary flow rate (NSWSF), C3 and C4 levels, RF, anti-Ro/La antibodies and salivary levels of CXCL14, CCL28, TRAIL and TGb measured by ELISA. We also evaluated the presence of fibrosis in biopsies with the Masson's trichrome staining.

**Results:** The mean age was 51.1±11 years, median disease duration of 6.1 years, 92.8% were females and 92.8% had oral symptoms. The global B-mode score was 22.2 points (13–44) and the RTS global score 2.5 (1.64–3.28) m/seg. We found a correlation between the RTS global score and the global B-mode score (t=0.53, p=0.001), the RTS global score between both parotids (t=0.58, p=0.0001) and both submandibulars (t=0.50, p=0.0001); but not between parotids and submandibular glands. The RTS global score correlated with the NSWSF (t=-0.53, p=0.001), ESSDAI (t=0.31, p=0.03), glandular ESDDAI domain (t=0.36, p=0.02), C4 levels (t=-0.32, p=0.04), but not with the rest of serological variables, chemokines and cytokines levels.

We found fibrosis in 7 patients (26.9%), and these patients were not different when compared to the group without it, regarding the RTS global score, B-mode global score, age and chemokine and cytokines levels, but tended to have a longer disease duration. At the linear regression analysis, the glandular ESSDAI domain (B=0.49, p=0.04), the C4 level (B=-0.02, p=0.05) and the disease duration (B=0.04, p=0.04) were associated with the RTS global score.

**Conclusions:** The elastrographic evaluation correlated with the US morphologic score and glandular activity but not with fibrosis.

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## AB0449 COUPLING ANTI-SM ANTIBODY DETECTION AND ANTI-CHROMATIN ANTIBODY DETECTION IMPROVES THE DIAGNOSIS AND PROGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Autoantibody (Ab) detection including anti-nuclear Ab (ANA) plus anti-dsDNA/Chromatin Ab and/or anti-Sm Ab is central in the diagnosis and prognosis of systemic lupus erythematosus (SLE) and several methods can be used to detect them.

**Objectives:** Our objective was to compare diagnostic accuracy for several anti-dsDNA Ab, anti-chromatin Ab and anti-Sm Ab detection.

**Methods:** Accordingly, we compared different methods for anti-dsDNA Ab [indirect immunofluorescence using *Crithidia Luciliae* (CLIFT), anti-dsDNA by ELISA, anti-dsDNA by chemiluminescence (CLIA; IDS-ISYS, IDS) and anti-chromatin Ab (dsDNA-NCX, Euroimmun)] and anti-Sm Ab by ELISA (Immuno concept) and by CLIA (IDS-ISYS, IDS)]. The evaluation was performed in 49 SLE and 98 autoimmune disease controls including rheumatoid arthritis, scleroderma, vasculitis and Sjögren's syndrome.

**Results:** In SLE patients, Ab sensitivity (and specificity) was 97.9% for AAN, 61.2% (92.9%) for anti-chromatin Ab, 36.7% (93 9%) for anti-dsDNA Ab by CLIA, 32.6% (95.9%) for anti-dsDNA Ab by ELISA, and 30.6% (100%) by CLIFT. For anti-Sm Ab, CLIA improved its detection (sensibility 18.4% versus 8.2% by ELISA; specificity 100% both). The best associations were found for anti-chromatin Ab and CLIFT (sensitivity 67.3% and specificity 91.8%), and for anti-chromatin and anti-Sm Abs by CLIA (sensitivity 53.1% and specificity 95.2%). Several associations were identified, including, for anti-chromatin Ab, articular [Odds ratio (OR)=28,41; p=0,002] and cardio vascular disease [OR=9,47; p=0,032], plus leucopenia [OR=13,72; p=0,049]; and for anti-Sm Ab by CLIA lupus glomerulonephritis [OR =5.0, p=0.05], and pleuropulmonary manifestations [OR =25.3; p=0.004].

**Conclusions:** Combining anti-chromatin Ab detection by ELISA and anti-Sm Ab detection by CLIA contribute to improve the diagnosis and the prognosis of SLE.

**Disclosure of Interest:** None declared

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## AB0450 SYSTEMIC LUPUS ERYTHEMATOSUS: A FRENCH EXPERIENCE FOR 6 YEARS OF MULTIDISCIPLINARY CONSULTATION IN BREST

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**Background:** Systemic lupus erythematosus (SLE) is a complex disease and its diagnosis and treatment can require multiple capabilities easily available for the patients.

**Objectives:** Our objective was to set up a multidisciplinary consultation enabling patient support in occidental Brittany.

**Methods:** Given the complexity for the management of patients with systemic lupus erythematosus (SLE), a multidisciplinary consultation was set up to ensure optimal care for SLE patients at Brest University Medical School. This consultation was set on a quarterly base and gather rheumatologists, dermatologists, nephrologists, gynecologists and internal medicine physicians. A close collaboration with the immunology laboratory for biological diagnosis and follow-up was also set up. Clinical and biological data were collected.

**Results:** Of the 49 SLE patients followed since 2009, 45 were women (91.8%). The mean age was 47.1±17.7 years. Eighteen patients had malar rash (37.5%), 21 (43.8%) photosensitivity, 7 (14.6%) oral ulcers, 6 (12.5%) alopecia, 43 (89.6%) diffuse articular pain or arthralgia, 10 (20.8%) tenosynovitis, 15 (31.25%) lupus glomerulonephritis, 7 (14.3%) pericarditis, 2 (4%) cardiac vegetations, and 3 (6.1%) pleurisy. The mean SLEDAI score was 2.7±3.5, with values ranging from 0 to 17. Twenty patients were referred for diagnostic opinions (40.8%), 31 (63.3%) for therapeutic advice, 3 (6%) for pregnancy monitoring, and 16 (32.6%) for comorbidities management. The main comorbidities were cardiovascular risk factors and osteoporosis.

**Conclusions:** In conclusion, the multidisciplinary consultation helps to provide diagnostic and therapeutic aid due to the presence of experts from several disciplines. Patient enrollment for several services enables the creation of a valuable database whose analysis is ongoing.

**Disclosure of Interest:** None declared

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## AB0451 CLINICAL AND SEROLOGICAL FEATURES OF SJÖGREN'S SYNDROME ASSOCIATED WITH SSB/LA

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**Background:** Sjögren's syndrome (SS) is an autoimmune disease associated with focal lymphocytic infiltration in the epithelium of exocrine glands, and may develop systemic manifestations in about 80% of the patients. Typical antibodies present in SS are antinuclear antibody (ANA), rheumatoid factor, SSA/Ro and SSB/La. SS classification criteria includes SSA/Ro and SSB/La, and their presence is associated with extra-glandular manifestations. The prevalence of SSA/Ro in SS is 30–70%, and is related to increased frequency of dermatologic symptoms, scleritis and interstitial lung disease. The relationship between SSB/La and clinical manifestations has not been previously well established, though it can be found in 5–50% of SS, and may co-exist with SSA/Ro half of the times. SSB/La is found isolated in a very low percentages of SS.

**Objectives:** To evaluate the correlation between the presence of SSB/La antibody with distinct clinical, demographic and serological characteristics of SS.

**Methods:** Adult patients evaluated in the Rheumatology Section (Buenos Aires British Hospital) who fulfilled American European Consensus Group (AECG) SS criteria were included. Three groups were compared according to the antibodies present: 1. Positive SSA/Ro and negative SSB/La 2. Both positive 3. Negative SSA/Ro and positive SSB/La. Mann-Whitney and Fisher tests were used according to variables; those with $p<0.05$ were introduced in a multivariable analysis by logistic regression.

**Results:** Among 195 patients with SS, 93.8% (n=183) were female. Mean age was 54.7 years and the mean total disease duration was 68.5 months. We excluded from analysis 16/8.2% patients due to missing data, and 29/14.9% patients that were negative for both antibodies. Two groups were finally compared (Group 3

| Features | Group 1 n=67 (%) | Group 2 n=80 (%) | p |
|---|---|---|---|
| Sialoadenitis | 9 (13.4) | 30 (37.5) | **0.0019** |
| Palpable purpura | 1 (1.5) | 13 (16,3) | **0.0058** |
| Neuropathy | 8 (11.9) | 10 (12.5) | 0.56 |
| Interstitial lung disease | 4 (6) | 5 (6.3) | 0.6 |
| Raynaud phenomenon | 12 (17.9) | 12 (15) | 0.63 |
| Arthritis | 27 (40) | 35 (43) | 0.79 |
| Hypocomplementemia | 9 (13.4) | 39 (48.8) | **0.00001** |
| Hypergammaglobulinemia | 22 (32.8) | 55 (68.8) | **0.00003** |
| Rheumatoid factor | 28 (41,8) | 55 (68,8) | **0.0018** |
| ANA | 61 (90) | 80 (100) | 0.05 |
| Leucopenia | 7 (10.4) | 18 (22.5) | 0.08 |
| Cryoglobulinemia | 2(3) | 4 (5) | 0.42 |

**Group 1: Positive SSA/Ro and negative SSB/La; Group 2: Both positive**

excluded due to low prevalence, n=3/1.5%): 80/41% patients with positive SSA/Ro and negative SSB/La; and 67/34.3% positive SSA/Ro and SSB/La. In the univariate analysis, positive SSA/Ro and SSB/La was statistically found to be associated with recurrent sialoadenitis and palpable purpura. Serological findings associated with this group included positive rheumatoid factor, hypocomplementemia and hypergammaglobulinemia. Poor prognosis features such as palpable purpura (OR 9.5 IC 95% 1.1–79 p 0.037), recurrent sialoadenitis (OR 3.1 IC 95% 1.2–7.7 p 0.011), hypocomplementemia (OR 3.6 IC 95% 1.4–9.4 P 0.0075) and hypergammaglobulinemia (OR 2.7 IC 95% 1.2–6.1 p 0.01) were also statistically significant in the multivariate analysis. Cryoglobulinemia and leucopenia were not found to be associated in both of the analysis.
**Conclusions:** In our population, the presence of SSB/La in patients with positive SSA/Ro was related to recurrent sialoadenitis, palpable purpura, hypocomplementemia, hypergammaglobulinemia and reumathoid factor. Although previous studies are contradictory, our study might justify the systematic search of this antibody due to its clinical relevance and link to poor prognosis factors in SS.
**Disclosure of Interest:** None declared
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## AB0452 ANALYSIS OF CLINICAL MANIFESTATIONS, COURSE OPTIONS, OUTCOME OF SLE ACCORDING TO THE PROSPECTIVE STUDY AMONG RESIDENTS OF KYRGYZSTAN

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**Background:** Systemic lupus erythematosus (SLE) is a devastating disease affecting different organs, ultimately leading to organ failure and death. To date, there are no data regarding the real-life picture of SLE in Kyrgyzstan.
**Objectives:** To study of clinical symptoms, course and outcome of SLE according to the prospective study among residents of Kyrgyzstan.
**Methods:** An 2-year prospective analysis of patients with SLE with a specially developed research base (BLIPS 8, ADS-Limathon). 60 patients with definite diagnosis of SLE (ACR, 1997; SLICC, 2012), were treated in the department of rheumatology of NCCIM and observed from 2012 to 2015. They were evaluated by sex, age, disease duration, activity of SLE according the SLEDAI-2K, irreversible organ damage by SLICC Damage Index (SDI), quality of life using the SF-36 questionnaire, LupusQoL, HADS, FACIT, therapy, with monitoring of all parameters every six months for 2 years. From the data of the immunological studies immune linear (immunoblot) “ANA-LIA-Max 17” were analyzed with a purpose of detecting the antibodies of double-stranded DNA, Sm D1 antigen and antibodies of double-stranded DNA-linked immunosorbent analyisis (ELISA), C3-C4 components complement, indirect immunofluorescence of the antinuclear antibody cells of line Hep-2.
**Results:** Patients were mainly from the northern region of the republic (81.7%). The vast majority were women (86.7%), with average age 30 years old, with disease duration of about 1.0 years. Periods to verify the diagnosis ranged from 1 month to 9 years. The clinical course was dominated by patients with acute version (47%) and high activity (57%). In the debut of the disease most common clinical symptoms were cutaneous and articular syndrome (84.2% and 72.3%, respectively), the defeat of the serous membranes (88%) and kidney (68%). All patients received glucocorticoids (GC), 79% of them in the form of pulse therapy with methylprednisolone. From immunosuppressive drugs most commonly were used CP (48%), AZA (21%), MTX (10.4%) and plaquenil (11%), to a lesser extent MMF (8%). The proportion of patients receiving biologic therapy (rituximab) was only 2%, IVIG (Octagam) - 3.3%.The development of irreversible organ damage was recorded in half the patients (46%), at average of 6 months from the onset of the disease, mostly with low (36.7%) and the average SDI (21.7%). During the period of 2-year prospective study not only a significant reduction in the activity of the pathological process in many patients ($p<0,001$) is noted, but also the lack of clinical activity in 18% of patients. In 35% of cases minimal disease activity represented immunological activity. At 2-year follow-up there were 14 fatal cases (19.4%). They were mostly women (72%) with average age 37.9 years, with disease duration around 4 years. The main causes of death were active SLE and its complications: kidney disease (29%), central nervous system (CNS)-21.4% and combined CNS and lung (21.4%).
**Conclusions:** In the debut of the SLE acute onset and high disease activity, which led to the rapid development of organ damage in half the patients was recorded. In the structure of mortality among Kyrgyz cohort of SLE patients with renal involvement prevailed, CNS and CNS combined with lungs.
**Disclosure of Interest:** None declared
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## AB0453 THE QUALITY OF LIFE OF THE KYRGYZ COHORT OF PATIENTS WITH SLE ACCORDING TO THE PROSPECTIVE STUDY

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**Background:** Systemic lupus erythematosus (SLE) is a devastating disease affecting different organs, ultimately leading to organ failure and death. To date, there are no data regarding the real-life picture of SLE in Kyrgyzstan.
**Objectives:** The goal of the study is evaluation of the quality of life among Kyrgyz cohort of patients with SLE according to the prospective study.
**Methods:** 60 patients with definite diagnosis of SLE (ACR, 1997; SLICC, 2012) were treated in the department of rheumatology of NCCIM and observed from 2012 to 2015. They were evaluated by sex, age, disease duration, activity of SLE according the SLEDAI-2K, irreversible organ damage by SLICC Damage Index (SDI), quality of life using the SF-36 questionnaire, LupusQoL, HADS, FACIT, therapy, with monitoring of all parameters every six months for 2 years. From the data of the immunological studies immune linear (immunoblot) “ANA-LIA-Max 17” were analyzed with a purpose of detecting the antibodies of double-stranded DNA, Sm D1 antigen and antibodies of double-stranded DNA-linked immunosorbent analyisis (ELISA), C3-C4 components complement, indirect immunofluorescence of the antinuclear antibody cells of line Hep-2.
**Results:** Patients were mainly from the northern region of the republic (81.7%). The vast majority were women (86.7%), with average age 30 years old, with disease duration of about 1.0 years. Dates of illness onset to verify the diagnosis ranged from 1 month to 9 years. The clinical course dominated patients with acute one (47%) and high activity (57%). The clinical symptoms of were cutaneous and articular syndrome (84.2% and 72.3%, respectively), the defeat of the serous membranes (88%) and kidney (68%). Before the treatment, according to the overall SF-36 questionnaire all SLE patients had lower QOL revealed. Marked limitation of life activity of patients was due to the presence of physical and emotional problems with severe anxiety and depression affects on their social functioning. After 2 years significant improvement in quality of life on many scales, except for the scale of mental health is noted. Attention is drawn to the deterioration of quality of life on the scale of “viability”, which characterizes the patient a sense of lack of strength and energy for the period of the disease. The lowest quality of life is reported among Kyrgyz patients in the comparative analysis to QOL of patients with SLE in other 3 countries of Europe (UK, France and Italy) and Russia. Despite the reduction of disease activity ($p<0,001$) among Kyrgyz cohort of patients the baseline QOL of Russian SLE patients for a period of two years of careful clinical supervision was not achieved.
**Conclusions:** The low quality of life among Kyrgyz cohort of patients with SLE is associated with poor physical, emotional and social functioning. Despite the reduction of disease activity during the treatment, quality of life on the scale of “viability, lack of improvement of mental health component is identified as declining”.
**Disclosure of Interest:** None declared
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## AB0454 THE OUTCOME OF SLE RESIDENTS OF KYRGYZSTAN ACCORDING TO THE PROSPECTIVE STUDY

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**Background:** Systemic lupus erythematosus (SLE) is a devastating disease affecting different organs, ultimately leading to organ failure and death. To date, there are no data regarding the real-life picture of SLE in Kyrgyzstan.
**Objectives:** To study the outcomes of SLE according prospective study among residents of Kyrgyzstan.
**Methods:** An 2-year prospective analysis of patients with SLE with a specially developed research base (BLIPS 8, ADS-Limathon).60 patients with definite diagnosis of SLE (ACR, 1997; SLICC, 2012), were treated in the department of rheumatology of NCCIM and observed from 2012 to 2015. They were evaluated by sex, age, disease duration, activity of SLE according the SLEDAI-2K, irreversible organ damage by SDI, therapy, with monitoring of all parameters every six months for 2 years. From the data of the immunological studies immune linear (immunoblot) “ANA-LIA-Max 17” were analyzed with a purpose of detecting the antibodies of double-stranded DNA, Sm D1 antigen and antibodies of double-stranded DNA-linked immunosorbent analyisis (ELISA), C3-C4 components complement, indirect immunofluorescence of the antinuclear antibody cells of line Hep-2.
**Results:** The vast majority were women (86.7%), with average age 30 years old, with disease duration of about 1.0 years. Periods to verify the diagnosis ranged from 1 month to 9 years. The clinical course was dominated by patients with acute version (47%) and high activity (57%). In the debut of the disease most common clinical symptoms were cutaneous and articular syndrome (84.2% and 72.3%, respectively), the defeat of the serous membranes (88%) and kidney (68%). The

development of irreversible organ damage recorded in half the patients (46%), on average of 6 months from the onset of the disease, preferably with low (36.7%) and the average SDI (21.7%). Among the irreversible organ damage leading place is occupied by respiratory failure (53.5%) of them with pulmonary fibrosis (21.4%) and pulmonary hypertension (25%). Second place takes kidney disease (50%) with severe forms of nephritis (nephrotic syndrome and chronic renal failure). Irreversible changes in the central nervous system were observed in 21% of patients. Over the whole period there were 14 fatal cases (19.4%). They were mostly women (72%) with average age 37.9 years, with disease duration around 4 years. The main causes of death were active SLE and its complications: kidney disease (29%), central nervous system (CNS)-21.4% and combined CNS and lung (21.4%). During the two-year observation, despite the significant decrease in disease activity ($p<0,001$), the progression of SDI ($p<0,0001$), deterioration of whom are independent from both the activity and the variant of the disease ($r=0.18$, $p=0.2$; $r=0.03$, $p=0.8$ respectively) is noted. However, the degree of organ damage depended on the duration of illness ($r=0.27$, $p<0,03$) and the age of patients ($r=0.29$, $p=0.02$).

**Conclusions:** Irreversible organ damage of the respiratory organs (pulmonary fibrosis, pulmonary hypertension), renal, and CNS were the main predictors of adverse outcome of SLE among the residents of Kyrgyzstan.

**Disclosure of Interest:** None declared

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## AB0455 DYSLIPIDEMIA AND ATHEROGENIC RISK IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Dyslipidemia is a common comorbidity in patients with systemic lupus erythematosus, it is favored by central obesity, nephrotic syndrome, glucocorticoids and immunosuppressants.

**Methods:** 51 patients, who were determined the lipid profile were included. Variables associated with the disease and the drugs used were recorded. Atherogenic risk was calculated. Chi square was used for categorical variables. ANOVA was performed to determine the relationship between mean lipid profile and a logistic regression model to determine the association of the variables with the presence of dyslipidemia.

**Results:** 68.6% had dyslipidemia. Significant difference between the presence of dyslipidemia and Activity index measured by SLEDAI ($p=0.021$) was found, the presence of lupus nephritis ($P=0.021$), use of prednisone $\geq$20 mg/day ($p=0.0009$), evolution disease $<$3 years ($P=0.027$). Significance between the absence of dyslipidemia and use of hydroxychloroquine ($P=0.021$) was found. Activity index $\geq$4 (RR 6.34; $p=0.038$) and the use of prednisone $>$20 mg/day (RR 6.67; $p=0.036$) were independently associated with the presence of dyslipidemia. The average of Castelli rate was 5.02±1.8, the Kannel index was 2.97±1.4 and triglyceride/HDL-C ratio was 5.24 ±3.3.

**Conclusions:** Patients with systemic lupus erythematosus have a high prevalence of dyslipidemia and a high atherogenic rate, which increases cardiovascular risk significantly.

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## AB0456 COMPARATIVE STUDY OF RISK FACTORS FOR VENOUS AND ARTERIAL THROMBOSIS IN CARRIERS OF ANTIPHOSPHOLIPID ANTIBODIES

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**Background:** Previous studies on factors predicting thrombosis in antiphospholipid syndrome (APS) show that vascular risk factors impact mainly on arterial thrombosis, while antiphospholipid antibodies (aPL) exert more influence on pure vein thrombosis or mixed thrombosis (venous and arterial).

**Objectives:** To investigate and compare factors associated with occurrence of venous and arterial thrombosis in carriers of aPL.

**Methods:** Prospective observational study of a cohort of patients with medium-high titers of aPL according to current recommendations on APS, enrolled in the outpatient clinic of a tertiary care hospital. Association between venous or arterial thrombosis and several factors such as age, sex, arterial hypertension, hypercholesterolemia, diabetes mellitus, smoking, obesity, oral contraceptives, platelet count, mean platelet volume (MPV), lupus anticoagulant (LA), IgG/IgM anticardiolipin antibodies (aCL), IgG/IgM anti-β2-glycoprotein I and partial aPL-score was assessed by univariate analysis (Pearson's $X^2$ and Fischer exact tests if qualitative variables, *T*-student and *U* Mann Withney tests if quantitative variables), following by a logistic regression.

**Results:** Seventy-one patients (50 females, baseline age 51±17 years), of which 40 fulfilled definite classification criteria for APS (29 primary APS, 11 secondary APS), were followed for 4.2±4 years. Thirty-two patients developed 46 thromboses (24 in venous bed, 22 in arterial bed), of which 14 were recurrences. In univariate analysis, patients with venous thrombosis showed a higher prevalence of diabetes mellitus (3/5 vs 15/66, $p=0.06$) and LA (14/40 vs 4/31, $p=0.05$) and a lower platelet count (134.8±71.0 vs 168.1±73.3x$10^3$/$mm^3$, $p=0.09$), whereas patients with arterial thrombosis were more frequently men (8/20 vs 9/51, $p=0.04$) of advanced age (59±14 vs 50±15 years, $p=0.04$), and had a higher prevalence of diabetes mellitus (3/5 vs 14/66, $p=0.08$) and higher levels of IgG aCL (72.7±122.2 vs 34.8±58.2 GPL, $p=0.08$) and MPV (10.8±2.0 vs 9.8±1.3 fL, $p=0.02$). The logistic regression identified male sex, age, diabetes mellitus and IgG aCL as predictors of arterial thrombosis, while positivity to LA as the only predictor of venous thrombosis (Table 1).

Table 1. Odds ratio (95% CI) of independent factors associated with venous and arterial thrombosis ($p\leq0.05$)

| | Male sex | Age | Diabetes | LA positive | IgG aCL |
|---|---|---|---|---|---|
| Venous thrombosis | | | | 4.46 (1.12–17.73) | |
| Arterial thrombosis | 5.25 (1.36–20.27) | 1.05 (1.001–1.098) | 7.54 (1.00–59.05) | | 1.008 (1.001–10.160) |

**Conclusions:** In carriers of aPL, vascular risk factors such as male sex, age and diabetes predispose to arterial thrombosis together with IgG aCL, while the presence of LA is more specific of patients who experience venous thrombosis.

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## AB0457 HOW MUCH DIFFERENT IS JUVENILE ONSET SYSTEMIC LUPUS ERHYTEMATOSUS? DATA FROM A ROMANIAN COHORT

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**Background:** Systemic Lupus Erhytematosus (SLE) is a multiorgan disease in which pattern of evolution is linked to activity and damage. When the disease starts at an early age, all the outcomes might be influenced by this.

**Objectives:** The main focus of this study is to describe the differences between juvenile and adult onset SLE in a Romanian cohort.

**Methods:** 101 SLE patients were evaluated between March 2015 and December 2015. Patients were diagnosed with SLE according to ACR classification criteria and splited in 2 groups, taking into account age at disease onset: before and after 18. All patients agree to participate in this study. Data about demographic, clinical or serological characteristics, activity (SLEDAI) or damage (SLICC damage index SDI), treatment were collected. Statistical analisys was performed with SPSS 20.0.

**Results:** Our cohort was made from 18 patients with juvenile onset SLE and 83

with adult onset SLE. Mean age at diagnosis was 14.05 versus 37.89. The juvenile onset SLE group had significant more autoimmune disease as family background, mainly SLE and rheumatoid arthritis (33.3% versus 12.04%, p 0.025), significant more severe organ involvement during the disease evolution: SLE related neurologic involvement 33.3% versus 12% (p 0.025) and renal involvement 50% versus 16.8% (p 0.023), more frequent anti dsDNA Ab positives 88.8% versus 60.24% (p 0.021). This more severe pattern of evolution is also reflected by immunosuppressant therapy, Cyclophosphamide being used in juvenile subgroup in 66% cases versus 35.3% in adults (p 0.014). Interesting, there were no differences between cumulative damage between groups, as measured by SDI (p 0.24), with the mention that in juvenile onset patients, SDI>1 was more frequent SLE related. This is in line with the fact that side effects of the corthicotherapie were identified more in adult onset SLE 61.44% versus 33.3% in juvenile onset (p 0.029).

**Conclusions:** Our data clearly show that juvenile onset SLE has more genetic background and it is more prone to a severe disease, renal and neurologic involvement being more frequent than in adult onset form. Severity seems to be related both to the activity, but also to fast damage accrual over time. Controlling the disease activity must be our goal, since cumulative irreversible damage is mainly SLE related for our patients.

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**Disclosure of Interest:** None declared

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## AB0458 SERUM FERRITIN AS A BIOMARKER OF CLINICAL AND HISTOPATHOLOGICAL RESPONSE TO TREATMENT IN LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) is a major organ manifestation of Systemic Lupus Erythematosus (SLE). Renal biopsy is the current gold standard for assessment of renal pathology in LN, as non-invasive reliable markers are lacking. Ferritin is found in most tissues as a cytosolic protein that stores iron. Small amounts are secreted into the serum, where ferritin functions as an iron carrier. Ferritin is considered an acute phase protein, as it increases in response to stresses. Studies have reported elevated serum concentrations in patients with active compared to patients with inactive SLE, and also associations with LN.

**Objectives:** We assessed serum ferritin levels in patients with LN, in order to clarify its role in this SLE subset.

**Methods:** Serum levels of ferritin were determined by ELISA (Raybiotech Inc.) in 64 patients with biopsy-proven active LN (52 proliferative LN, PLN; 12 membranous LN, MLN), before and after completion of induction treatment. Post-treatment renal biopsies were performed after a median time of 7.7 months. Clinical responders (CR) were defined by $\geq$50% reduced proteinuria, normal or $\geq$25% improved estimated glomerular filtration rate, and inactive urinary sediment. Histopathological responders (HR) were defined by $\geq$50% improvement of renal Activity Index in post-treatment biopsies.

**Results:** Serum levels of ferritin decreased following induction therapy for LN in the entire cohort ($p<0.001$) and in patients with PLN ($p<0.001$), but not in patients with MLN (p=0.35). In the entire cohort, ferritin levels decreased in both CR ($p<0.001$) and clinical non-responders (CNR; p=0.030). They also decreased in HR ($p<0.001$), but remained stable in histopathological non-responders (HNR; p=0.06). In PLN, ferritin levels decreased in CR ($p<0.001$) and in CNR (p=0.003), as well as in HR ($p<0.001$) and HNR (p=0.011). In MLN, ferritin levels decreased in CR (p=0.03) and HR (p=0.046), but neither in CNR (p=0.69) nor in HNR (p=0.89). In patients with MLN, both baseline and post-treatment ferritin levels were higher in CNR (baseline median: 172.9 ng/mL, range: 15.9–486.3; post-treatment median: 309.7 ng/mL, range: 8.4–714.8) than in CR (baseline median: 59.8 ng/mL, range: 24.4–200.9; post-treatment median: 32.3 ng/mL, range: 4.9–43.2; p=0.03 and p=0.005, respectively); however, they did not differ between HR and HNR (p=0.79 and p=0.43, respectively).

**Conclusions:** Our data suggest ferritin as a marker of histopathological response to induction treatment in patients with LN. In patients with MLN in particular, high baseline ferritin levels predicted unfavourable clinical response to induction treatment, and, despite being initially lower, baseline ferritin levels decreased in CR. This implies a role of ferritin in the pathogenesis of this LN subset and warrants further investigation.

**Disclosure of Interest:** None declared

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## AB0459 TUBERCULOSIS AMONG SYSTEMIC LUPUS ERYTHEMATOSUS MEXICAN MESTIZO PATIENTS

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**Background:** Tuberculosis (TB) represents a major global health problem. TB has a higher incidence among patients with autoimmune rheumatic diseases than in the general population. The incidence and severity of TB in patients with systemic lupus erythematosus (SLE) varies greatly among different series (2.5–13.8%).

**Objectives:** To investigate the frequency and characteristics of TB in Mexican mestizo patients with SLE.

**Methods:** We reviewed the charts of 123 patients with SLE in our lupus clinic. Patients who developed TB after the diagnosis of SLE were identified. Data of all SLE patients followed up in our clinic were retrospectively analyzed. Clinical and demographic characteristics and treatment before diagnosis of TB were recorded.

**Results:** A total of 123 SLE patients were analyzed, 89.43% (n=110) woman. Seven cases (5.69%) of TB infection developed after the diagnosis of SLE. Pulmonary TB was reported in 3 patients (2.44%). Extra-pulmonary TB infecction was reported in 3 (2.44%) patients (one case of tuberculous pleurisy, one case of meningeal TB, and 1 case of cutaneous TB). Also, we found 1 SLE patient (0.81%) with latent TB infection. All patients had good response to treatment. No one received biologic therapy at the time of the diagnosis of TB infection. We did not found any case of disseminated infection or mortality related to TB infection.

**Conclusions:** These results suggest that in a country with high TB burden, TB screening and treatment of latent TB would be useful since the diagnosis of SLE is made.

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**Disclosure of Interest:** None declared

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## AB0460 CAUSES OF EARLY AND LATE DEATH OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS OVER A 10-YEAR PERIOD

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**Background:** Causes of death (CODs) of patients with systemic lupus erythematosus (SLE) comprise active SLE and comorbidities that develop as a result of SLE and immunosuppressive therapy: infections, cardiovascular disease and malignant tumors. Active disease and infections are typical causes of early death, while cardiovascular disease typically causes late death. However, COD frequencies depend on the source population and data ascertainment method.

**Objectives:** To identify and compare causes of early and late death of SLE patients deceased during a ten-year period.

**Methods:** We retrospectively identified SLE patients followed-up by our Department, deceased between 2002 and 2011, and included patients with $\geq$4 classification criteria of the American College of Rheumatology (ACR), $\geq$18 years of age and Croatian residency at the time of death. Death and causes of death were retrospectively identified using patient medical records, as well as death certificates and autopsy reports, when available. We also matched data on all SLE patients that visited our Department from 2002 to 2011 with the National Mortality Database. We classified CODs into five categories: active SLE, cardiovascular disease, infection, malignant tumor and other. More than one COD category was possible in a single patient. We compared the frequencies of each COD category between patients deceased within and after 5 years following diagnosis (early vs. late death). Frequencies were compared using the $\chi^2$ and Fisher's exact test, and continuous variables using the t-test and Mann-Whitney U test. The study was approved by the local ethics committee.

**Results:** We identified 90 deceased patients (68 females, 22 males; 21 in the

| Cause of death | Patients deceased (N=90) | % | Early death (N=21) | Late death (N=69) |
|---|---|---|---|---|
| Active disease (SLE) | 26 | 29 | 8 | 18 |
| Infection | 30 | 33 | 9 | 21 |
| a) Sepsis | 20 | 22 | 6 | 14 |
| b) Pneumonia | 18 | 20 | 5 | 13 |
| c) Urinary tract infection | 8 | 9 | 3 | 5 |
| Cardiovascular disease | 36 | 40 | 6 | 30 |
| a) Myocardial infarction + ischemic heart disease | 12 (7+5) | 13 | 1 | 11 |
| b) Myocardial infarction | 5 | 6 | 1 | 4 |
| c) Stroke | 8 | 9 | 0 | 8 |
| d) Pulmonary embolism | 3 | 3 | 1 | 2 |
| Malignant tumor | 15 | 17 | 1 | 14 |
| Other | 10 | 11 | 4 | 6 |
| Unknown | 8 | 9 | 1 | 7 |

early death group (EDG), 69 in the late death group (LDG)). EDG patients were older than LDG patients at diagnosis (mean age±SD: 56±15 vs. 46±17 years; p=0.005), but there was no difference between the age at death (mean age±SD: 58±15 years for all patients). Patients were followed-up for a median of 10 years (IQR: 5–15 years). LDG patients fulfilled a higher number of ACR criteria compared to EDG patients (median, IQR: 6, 5–7 vs. 5, 4–6; p=0.018). No difference between COD category frequencies was detected between EDG and LDG. Nevertheless, infections and active SLE were leading causes of early death (9/21 and 8/21, respectively), while cardiovascular disease was the most frequent cause of late death (30/69), followed by infection and active SLE (21/69 and 18/69, respectively)(Table). SLE was mentioned in the death-related medical records of only 41/90 patients.

**Conclusions:** Infections and active SLE are leading causes of early death, while cardiovascular disease is the most frequent cause of late death in SLE. Lack of recording of SLE in death-related medical records requires matching of clinical data with a complementary source, such as a population-based mortality database, to identify deceased SLE patients.

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**Disclosure of Interest:** None declared

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## AB0461 A RETROSPECTIVE STUDY OF PRIMARY SJOGREN'S SYNDROME PATIENTS WITH CANCER IN CHINESE POPULATION: A SINGLE-CENTER EXPERIENCE

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**Background:** With the development of modern therapies, better care of patients with primary Sjogren's syndrome has been achieved. However, primary Sjogren's syndrome may share an association with risk of lymphoproliferative disease or other malignancy.

**Objectives:** To investigate the clinical features of primary Sjogren's syndrome (pSS) patients with malignancies.

**Methods:** We studied clinical features of the pSS patients coexist with malignancies in the Third Affiliated hospital of Sun Yat-sen University from 2002 to 2015. Thirteen out of 918 patients with pSS developed malignancies, both solid tumors and lymphomas. Student's t test was used to compare patients'age and age of onset.

**Results:** The ratio of pSS with malignancies was 1.4% (13/918) in these patients. 6 were lymphoma, including 5 diffuse large B-cell lymphoma (DLBCL) and one mucosa associated lymphoid tissue type (MALT) Lymphoma. 7 were solid tumors, including one Colon cancer, one Hepatocellular carcinoma, one cervical carcinoma, one ovarian cancer, and one breast cancer, one cervical lymph nodes of squamous cell carcinoma and one peritoneal metastasis of unknown origin. The onset age of pSS was 44.5±19years,and onset age of malignancies was 47±18.4years. it seems that the age of pSS patients with solid tumors (53.6±18.9 years) was older than the age of pSS patients with lymphoma (34±13.9 years),but there was no significant difference.

**Conclusions:** The most frequent cancer associated with pSS is Lymphomas. the age of pSS patients with solid tumors might be older than the age of pSS patients with lymphoma.

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## AB0462 THE RISK OF CANCER IN SYSTEMIC LUPUS ERYTHEMATOSUS IN CHINESE POPULATION: A SINGLE-CENTER EXPERIENCE

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**Background:** It was reported that incidence rate of malignant tumor in general population was 0.24% in China in 2010. Cyclophosphamide is widely used in the treatment of systemic lupus erythematosus. Long term use of CTX may lead to increase the risk of tumor. However, whether the Cyclophosphamide risk of cancer will increase is not clear.

**Objectives:** To investigate the risk of cancer in systemic lupus erythematosus patients.

**Methods:** We studied retrospectively systemic lupus erythematosus patients coexist with malignancies hospitalized in the Third Affiliated hospital of Sun Yat-sen University from 1999 to 2015. The study included 2530 systemic lupus erythematosus patients.

**Results:** The ratio of systemic lupus erythematosus with malignancies was 0.24% in these patients (6/2530). Compared to general population, no increase in tumor incidence was found in systemic lupus erythematosus. The onset age of SLE was 47±17.8years,and the age of the patients with cancer were 50.7±14.9years.There were 6 solid tumor in our study, including three thyroid carcinoma, one nasopharyngeal carcinoma, one nerve glioma, and one meningioma.

**Conclusions:** The incidence of tumor in SLE patients was similar to the general populations.

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**Disclosure of Interest:** None declared

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## AB0463 CLINICAL CHARACTERISTICS OF ELDERLY PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Sjögren's syndrome is a common autoimmune disorder with the majority of cases occurring in midlife. Although the clinical presentation of primary Sjögren's syndrome (pSS) is known to differ by age, clinical characteristics of elderly patients with pSS have not been well described.

**Objectives:** To identify clinical characteristics of patients with pSS based on age group.

**Methods:** We retrospectively identified all patients with biopsy-proven lymphocytic sialadenitis and/or positive anti-SSA/Ro antibody who were treated at a tertiary medical center in Japan between 2005 and 2015. Data were collected on their clinical and laboratory features. Definite pSS was defined by the fulfilled American-European Consensus (AEC) criteria for pSS and probable pSS was determined by any 3 of the 6 AEC criteria without other collagen diseases. Clinical and laboratory characteristics of patients aged 60 years or older were compared with those of their younger counterparts.

**Results:** We identified 402 Japanese patients with biopsy-proven lymphocytic sialadenitis and/or positive anti-SSA/Ro antibody. 147 (37%) had pSS, 36 (9%) were undifferentiated, and 219 (54%) had at least one or more antinuclear antibody-associated collagen diseases. The median age of the pSS patients was 52 years (range 17–89); 41% (60 patients) were aged 60 years or older, and 91% were female (Table). Compared to the younger age group, the older patients were more likely to have dry mouth, primary biliary cirrhosis, lymphoma and thrombocytopenia. The younger patients had a greater likelihood of arthritis and a photosensitive rash ($p<0.05$).

| | Younger group | | Older group | | | Total |
|---|---|---|---|---|---|---|
| | (N=87) | % | (N=60) | % | P | % |
| Age, yr (range) | 40 (17-59) | | 72 (61-89) | | | |
| Female sex | 83/87 | 95 | 51/60 | 85 | 0.04† | 91 |
| Definite primary Sjögren's syndrome | 40/87 | 46 | 30/60 | 50 | 0.74 | 48 |
| Clinical features | | | | | | |
| Dry eye | 34/82 | 41 | 24/53 | 45 | 0.72 | 43 |
| Dry mouth | 42/83 | 51 | 42/53 | 79 | <0.01† | 62 |
| Parotitis | 12/87 | 14 | 5/60 | 8.3 | 0.43 | 12 |
| Arthralgia | 38/87 | 44 | 12/60 | 20 | 0.25 | 34 |
| Arthritis | 12/87 | 11 | 1/60 | 1.7 | 0.02† | 8.8 |
| Peripheral neuropathy | 6/87 | 6.9 | 1/60 | 1.7 | 0.47 | 4.8 |
| Aseptic meningitis | 4/87 | 4.6 | 0/60 | 0 | 0.15 | 2.7 |
| Renal tubular acidosis | 1/87 | 1.1 | 3/60 | 5 | 0.31 | 2.7 |
| Photosensitive rash | 17/87 | 20 | 1/60 | 1.7 | <0.01† | 12 |
| Interstitial lung disease | 1/87 | 1.1 | 4/60 | 6.7 | 0.16 | 3.4 |
| Chronic thyroiditis | 6/87 | 6.9 | 7/60 | 12 | 0.38 | 8.8 |
| Primary biliary cirrhosis | 3/87 | 3.4 | 13/60 | 22 | <0.01† | 11 |
| Lymphoma | 2/87 | 2.3 | 7/60 | 12 | 0.03† | 6.1 |
| Congenital heart block | 1/87 | 1.1 | 0/60 | 0 | 1 | 0.7 |
| Laboratory features | | | | | | |
| Leukopenia (<4,000/mm$^3$) | 33/87 | 38 | 22/60 | 37 | 1 | 37 |
| Lymphopenia (<1,500/mm$^3$) | 52/87 | 60 | 38/60 | 63 | 0.73 | 61 |
| Thrombocytopenia (<100,000/mm$^3$) | 7/87 | 8 | 15/60 | 25 | <0.01† | 15 |
| Low C3 and/or C4 | 29/72 | 40 | 17/44 | 39 | 1 | 40 |
| Positive anti-SSA/Ro and/or SSB/La antibody | 82/87 | 94 | 53/60 | 88 | 0.38 | 92 |
| Positive rheumatoid factor | 26/47 | 55 | 20/36 | 56 | 1 | 55 |
| Antinuclear antibody titer ≥1:320 | 30/77 | 39 | 23/52 | 44 | 0.41 | 50 |

**Conclusions:** Clinical characteristics of pSS may differ between younger and elderly patients. In elderly patients with pSS, careful evaluation for coexisting primary biliary cirrhosis or lymphoma is recommended.

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## AB0464 THE RATE OF AND RISK FACTORS FOR FREQUENT HOSPITALIZATION IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE KOREAN LUPUS NETWORK REGISTRY

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**Objectives:** The survival rate of patients with systemic lupus erythematosus (SLE) has improved in the last few decades, but the rate of hospitalization and health care costs for these patients remain higher than in the general population. Thus, we evaluated the rate of hospitalization and associated risk factors in an inception cohort of Korean patients with lupus.
**Methods:** Of the 507 patients with SLE enrolled in the KORean lupus NETwork (KORNET registry), we investigated an inception cohort consisting of 196 patients with SLE presenting within 6 months of diagnosis based on the ACR classification criteria. We evaluated the causes of hospitalization, demographic characteristics, and laboratory and clinical data at the time of SLE diagnosis of hospitalized patients and during a follow-up period. We calculated the hospitalization rate as the number of total hospitalizations divided by the disease duration, and defined "frequent hospitalization" as hospitalization more than once per year.
**Results:** Of the 196 patients, 117 (59.6%) were admitted to hospital a total of 257 times during the 8-year follow-up period. Moreover, 22 (11.2%) patients were hospitalized frequently. The most common reasons for hospitalization included disease flares, infection, and pregnancy-related morbidity. In the univariate regression analysis, malar rash, arthritis, pericarditis, renal involvement, fever, SLE disease activity index >12, hemoglobin level <10 mg/dl, albumin level <3.5 mg/dl, and anti–Sjögren's syndrome A (SS-A) positivity were associated with frequent hospitalization. Finally, multivariate analysis showed that arthritis, pericarditis, and anti–SS-A antibody positivity at the time of diagnosis were risk factors for frequent hospitalization.
**Conclusions:** Our results showed that frequent hospitalization occurred in 11.2% of hospitalized patients and arthritis, pericarditis, and anti–SS-A antibody positivity at the time of diagnosis were risk factors for frequent hospitalization.
**Disclosure of Interest:** None declared
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## AB0465 IS IT POSSIBLE TO ESTABLISH A PREDICTIVE PROFILE FOR LUPUS NEPHRITIS?

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**Background:** Lupus nephritis (LN) is one of the most common and serious complications of Systemic Lupus Erythematosus (SLE). There are several factors that are considered related to the development of LN like malar erythema, anti-dsDNA and low serum complement. However not all patients with high level of anti-dsDNA or low level of serum complement present LN.
**Objectives:** To determine if patients with low serum complement, high level of anti-dsDNA and malar erythema are more likely to have NL and analyze other clinical and immunological characteristics associated with NL.
**Methods:** This is an observational, retrospective study in which 30 patients with LN, diagnosed with renal biopsy are compared with 61 SLE patients without LN, followed in the Rheumatology Unit of the University Hospital Ramón y Cajal in the last 15 years. We excluded the patients diagnosed with other non lupus nephropathy or other associated autoimmune disease. The triad we've studied was the simultaneous presence of malar erythema, low level of serum complement (C3 and/or C4, <90 mg/dl and <10 mg/dl respectively) and high level of anti-dsDNA title (more than 3 times the normal limit as the standard technique >45 IU/ml by EliAUniCAP). Clinical and immunological data were collected following a review of medical records and analyzed using bivariate and multivariate methods in SPSS version 20.
**Results:** Patients with NL were significantly younger at diagnosis of SLE than the control group (26.4±10.7 years vs 32.7±12.5 years), p=0.022. There were no differences between gender, ethnicity and time of evolution of SLE. In bivariate analysis, significant associations between NL and malar erythema (OR 6.25, p=0.0001), oral ulcers (OR 2.68, p=0.029), leukopenia (OR 2.97, p=0.034), lymphopenia (OR 5.5, p=0.001), serositis (OR 3.4, p=0.013) and fever (OR 2.56, p=0.045) were observed. Among the immunological parameters that are associated with NL were anti-dsDNA>45 U/ml antibody (Cramer's V =0.360, p=0.001), anti-U1RNP (OR 3.2, p=0.013), and low level of complement (OR 10.3, p=0.008). Chronic cutaneous lupus erythematosus and rheumatoid factor had a negative association with LN (p=0.02; p=0.049 respectively). The LN type IV was significantly associated with the studied triad (p=0.013). In the multivariate analysis the patients who had the triad were more likely to have LN (OR 42.5, 95% CI 7.7 to 233, p=0.0001); in 75% of these patients the time from the onset of the triad to the onset of LN was equal to or less than 10.2 months. The triad has higher specificity than anti-dsDNA alone (93.4% vs 55%), but lower sensitivity (76.6% vs 96%), the positive predictive value of the triad was 85% and the negative predictive value was 89%.
**Conclusions:**
The presence of the triad (malar erythema, low level serum complement and anti-DNAds) is an important predictive factor for the development of lupus nephritis and more specific than the presence of each of these alterations separately. Given these results, although larger studies are needed to confirm this profile, special care must be taken to the patients with this clinical and analytically features.
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## AB0466 DAMAGE INDEX IN PATIENTS WITH THROMBOTIC ANTIPHOSPHOLIPID SYNDROME: RETROSPECTIVE COHORT STUDY

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**Background:** The antiphospholipid syndrome is an autoimmune-acquired thrombophilia, the thrombotic manifestations are associated with an important risk of organ damage.[1] A new index for assessment of thrombotic accumulative damage in APS has been proposed, it is called *Damage Index in patients with Thrombotic Antiphospholipid Syndrome* (DIAPS).[2]
**Objectives:** Explore the DIAPS change in patients with primary and secondary APS in a long-term retrospective cohort.
**Methods:** Clinical records of patients with APS according to the Sapporo[3] classification criteria and/or Sydney[4] were reviewed. The DIAPS instrument with 38 items was applied. Comparison of the initial and final DIAPS was performed using the Wilcoxon test and the changes in the follow up were analyzed with T Student. The main treatments were analyzed before and after with the NcNemar test.
**Results:** Fifty clinical charts were reviewed, 12 had to be excluded for not fulfill classification criteria or incomplete information. Initial and final DIAPS was recorded in 38 patients (13±5 years of follow up), 78.9% were female, with a mean age at diagnosis 44.2±12.4 years. A total of 57.9% had primary APS. Thirty four patients remain alive with 3 to 23 years of follow up. The initial DIAPS was 3±2 and the final score was 5±3 ($p$ <0.0001). The magnitude of change in the DIAPS was similar in primary and secondary APS ($p$ =0.243). During follow up, 31/38 patients had oral anticoagulation at the beginning and 33/35 at the end ($p$ =0.687). At the beginning of the study hydroxychloroquine was recorded in 14/38 patients and in 24/38 at the end ($p$ =0.021). Aspirin was used by 17/38 patients during the follow up ($p$ =1.000).
**Conclusions:** The change in DIAPS suggests cumulative damage in patients with APS despite treatment. The DIAPS is a useful tool to estimate accrued damage in patients with primary and secondary APS.
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## AB0467 ANTIBODIES TO DOUBLE STRANDED DNA: COMBINED STANDARD ELISA AND HIGH-SALT ELISA ASSAYS FOR THE DETECTION OF SLE DISEASE ACTIVITY

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**Background:** Serological markers in systemic lupus erythematosus (SLE) are crucial objective measures included in disease activity indices. Antibodies to double stranded DNA (anti-dsDNA) are included in composite outcomes, and changes in titers in response to therapy are frequently reported in clinical trials. Despite this, there are multiple disparate methods to evaluate anti-dsDNA. The classic Farr immunoassay for anti-dsDNA employs high concentrations of ammonium sulfate, detecting only high-avidity antibodies, binding in high ionic strength. The salt-resistant anti-dsDNA assay is considered highly specific for the diagnosis of SLE and reliable as a disease activity marker. In contrast, most ELISAs are performed with buffers of relatively low ionic strength, detecting both low-avidity and high-avidity antibodies. We screen for anti-dsDNA using the standard ELISA, and follow-up with a modified high salt ELISA which detects only higher avidity antibodies. Use of both forms of anti-dsDNA has not been evaluated as an additive tool for the assessment of disease activity.
**Objectives:** To evaluate the sensitivity and specificity of anti-dsDNA measurement

by standard and high-salt ELISA assays for SLE disease activity (SLEDAI ≥4). To gauge the additive value of the high salt assay, performed as a reflex, in those with a positive ELISA evaluation, for the assessment of disease activity.
**Methods:** Patients fulfilling ACR classification criteria for SLE were identified in rheumatology clinic. Demographic data and disease activity (SLEDAI) were recorded. Anti-dsDNA titers were evaluated initially by standard ELISA. With a positive ELISA, a high salt assay was performed reflexively. Those with disease activity (SLEDAI≥4) were compared to those with quiescent disease. Statistical analysis involved the calculation of sensitivity, specificity, positive and negative predictive value of each assay.
**Results:** Seventy-seven encounters were evaluated (69 patients), mean age 41 (SD 14) years, 64 (92.8%) were female. The group was mostly Caucasian, 39 (56.5%), 10 (14.5%) were African-American, 9 (13.0%) Asian and 8 (11.6%) were Hispanic. Forty-two (54.5%) assessments were of active disease, 26 (33.7%) had active renal disease.
The sensitivity of antibodies to dsDNA for disease activity, by standard ELISA, was 90.5% with a specificity of 35.1%. The high salt avid assay resulted in a lower sensitivity (47.6%) and higher specificity, (78.4%). When considered in combination, given that both are performed, the sensitivity of our protocol was 90.5% with a specificity of 78.4% for disease activity.
The correlation between the standard and high-salt anti-dsDNA assay taking all cases where both was performed was moderate (r=0.53), often with substantial discordance in results in individual patient specimens.
**Conclusions:** With an increasing focus on novel markers to evaluate SLE disease activity, there has been little focus on the optimal use of pre-existing tools. Here we demonstrate the clinical utility of a screening ELISA followed by a reflex high salt anti-dsDNA assay. We show high sensitivity and specificity for SLE disease activity through the use of a standard anti-dsDNA ELISA, and a high-salt modified assay which avoids the need for radioactivity and can be readily employed.
**Disclosure of Interest:** None declared
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## AB0468 CARACTERISTICS OF RENAL INVOLVEMENT IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Renal involvement is one of the most common manifestations of primary Sjögren's syndrome (pSS) and has no specific symptoms.
**Objectives:** - Identify the clinical and biological characteristics of patients with renal involvement in pSS.
- Identify the immunological profile of these patients.
- Specify the adequate treatment.
**Methods:** Fourty five patients with pSS admitted inCharles Nicolleuniversity Hospital from 2005 to 2015 were enrolled. All the patients met the validated European-American co-criteria of 2002 for pSS. No patients with secondary SS were included.
**Results:** Fourty five patients were enrolled in our study. Nine of them had renal involvement: eight women and 1 man. The mean age was 44,5 years. Time from onset to diagnosis was about 2,33 years. Concerning the kidney damage, 4 of the patients developed renal tubular acidosis (RTA), 3 of them developed others tubulo-interstitial disorders and 2 were diagnosed with glomerular disorder withhigh proteinuria. One of the nine patients had diabetis insipidus. Laboratory examinations showed 3 cases of hyperchloremia and 6 cases of hypokaliemia. One patient had hypokaliemic paralysis. Six patients had creatinincleranceunder 50 ml/mn.
All patients received symptomatic treatment. Seven patients were treated with corticosteroids and 3 patients received hydroxylchloroquine.
**Conclusions:** Patients with pSS commonly present with renal impairment.Tubular disorders are the main renal involvementespecially RTA. Glomerular lesions might be predominant. Morbidity of chronic renal failure might account for a certain proportion of pSS. Corticosteroids therapy might improve the prognosis.
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## AB0469 EVOLUTION OF ANTHROPOMETRIC PROFILE AND HABIT FOOD AFTER 10 YEARS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune inflammatory disease that affects various organs and systems. Cardiovascular disease is a common complication and is associated with factors inherent to the SLE and environmental factors such as overweight and poor eating habits. In addition, obesity has been speculated as a contributing factor to the onset and progression of autoimmune diseases.
**Objectives:** Evaluate the anthropometric profile and food habit after 10 years of follow-up of a group of patients with SLE and identify possible association with chronicity index and disease activity.
**Methods:** We evaluated 55 patients with SLE in two moments with an interval of 10 years, coming from a care referral center for SLE in Hospital de Clínicas de Porto Alegre, Brazil. For chronicity and activity was used Systemic Lupus International Collaborating Clinics (SLICC) index and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), respectively. Body Mass Index (BMI), Body Fat Percentage (BFP) and waist circumference (WC) were the anthropometric data collected in accordance with the standards of the World Health Organization (WHO). The total cholesterol, LDL, HDL and triglycerides were performed as routine care. The study was approved by the Ethics Committee of the Universidade Federal of Rio Grande do Sul (UFRGS) and all patients who agreed to participate in the study met the consent and informed.
**Results:**

| Variables | First | After 10 Years | p |
|---|---|---|---|
| BMI (kg/m$^2$) | 26.8±5.4 | 28.3±6. | 0.096 |
| BFP (%) | 25.7 (21.1, 33.5) | 33.8 (27.8, 39.6) | 0.054 |
| WC (cm) | 83.9±11.2 | 96.2±14.3 | 0.001 |
| Consumption of sweets (portion/day) | 0.143 | 0.286 | 0.286 |
| HDL cholesterol (mg/dL) | 56.0 (43.7, 72.3) | 48.5 (41.0, 55.0) | 0.026 |

**Conclusions:** Our study revealed a worsening in the lipid profile and a higher concentration of abdominal fat in patients with SLE after 10 years of follow-up, although diet has remained stable. Factors related to disease or treatment may have influenced these results, but were not assessed in this study. These findings serve as a warning to us take better care of the nutritional status and lipid profile of our patients.
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## AB0470 SEROLOGICAL EVOLUTION IN FERTILE WOMEN WITH POSITIVE ANTIPHOSPHOLIPID ANTIBODIES

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**Background:** Antiphospholipid syndrome (APS) is an autoimmune disease characterized by the presence of aPL and at least a clinical event defined as recurrent venous thrombosis, arterial thombosis or pregnancy morbidity. The titers of aPL usually fluctuate, they frequently decrease and eventually become negative during follow-up period, thus reducing the risk of thrombotic events.
**Objectives:** The aim of this study was to explore the clinical and serological course of fertile women with positive aPL, as well as the factors and the potential therapeutic implications associated with aPL negativization.
**Methods:** We conducted a retrospective study including women attending the obstetric autoimmune pathology clinic of a tertiary-facility serving a population in about 350,000 in Northern Spain. We included 105 women with a confirmed positive APL serology according to Sydney Criteria between October 1995 and December 2013. Patients were classified into 3 different groups: A) patients with primary APS (49), B) patients with a positive serology for APL, not meeting clinical criteria (42) and C) patients with systemic lupus erythematosus and a positive serology for APS (14). They were also classified, according to the serological APL evolution: patients with persistently negative aPL, transiently

positive serology and persistently positive serology according to previously established criteria.
**Results:** After a mean follow up of 114,4±37,2 months, 59% patients had persistently negative antibodies, while 25,7% patients presented persistently positive aPL serology. After the multivariate analysis only the tobacco use (OR 3,5 p=0,013) was confirmed as an independent risk factor. The load of antibodies, specially the presence of triple positivity (OR: 2,4; IC: 0,16–2,36), was close to statistical significance (p=0,162). No other factors, including traditional cardiovascular risk factors, treatments or clinical manifestations reached statistical significance. Persistent positivity was associated with higher risk for further pregnancy morbidity (41 vs 52%; p=0,328). In 17 patients, with persistently negative serology who were asymptomatic, treatment with low dose aspirin was discontinued. No clinical events related to APS were reported after treatment withdrawal, during a 119,9 months follow-up period.
**Conclusions:** Our study suggests that among fertile women, antiphospholipid antibodies remain persistently positive only in one quarter of patients, being tobacco use an independent risk factors for its persistence. Among patients with persistently negative serology and with a low-risk profile discontinuation of antiplatelet therapy could be considered a safe choice.
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## AB0471 RISK FACTORS FOR PREGNANCY MORBIDITY IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES WITHOUT A DEFINED CLINICAL ANTIPHOSPHOLIPID SYNDROME

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**Background:** Antiphospholipid syndrome (APS) is an autoimmune disease characterized by the presence of either thrombosis or pregnancy morbidity and antiphospholipid antibodies (aPL), such as anticardiolipin (ACL), anti b2 glycoprotein (AB2GLP1) and lupus anticoagulant (LA). The prevalence of aPL is around 10% in the general population, increasing up to 50% in lupus patients. However, the frequency of pregnancy morbidity and the influence of the antibody profile in patients with positive APL serology without a defined APS is not well established.
**Objectives:** 1) To define the frequency of pregnancy morbidity in women with positive aPL who do not fit the clinical criteria for APS; 2)To analyze the influence of the serological profile and the load of antibodies associated with these complications, and 3) To determine the efficacy of prophylactic treatment in preventing adverse pregnancy outcome.
**Methods:** We retrospectively analyzed 92 pregnancies in 39 women with a confirmed positive serology for aPL (ACL, AB2GLP1 and LA) according to Sydney criteria. Then, we analyzed a subgroup of 15 women who had 38 pregnancies after a positive serology was confirmed.
**Results:** Overall, 54% of the 39 pregnant women suffered morbidities: one early pregnancy loss (7), two pregnancies losses (7), fetal death* (1), premature birth* (1), preeclampsia (2) and intrauterine growth restriction (3). After a mean follow-up of 146±60,3 months, only 2 patients developed obstetric APS* and none of them developed thrombotic APS. We found no association between the antibody profile and pregnancy morbidities. There was no association between pregnancy complications and the load of antibodies either. Regarding prophylactic treatment, only 8 women received AAS, combined with LWH in 3 of them, we found a non-significant tendency to prevent obstetric events.
When analyzing the 92 pregnancies, we found 28 obstetric events in 26 pregnancies. Mean age for pregnant women was 29,9±5,8 years, gestational age was 38,2±1,8 weeks, birth weight was 3108±482 g and mean Apgar was 8,7±1,1. Regarding treatment influence there was a non significant tendency to prevent obstetric events (OR 0,32, CI 95% 0,87–1,20; p=0,081), that reached statistical significance when analyzing early pregnancy losses (OR 0,12; IC 0,02–0,95; p=0,019). When we restricted the analysis to the 38 pregnancies that were posterior to the positive serology result, we found a significant protective effect of prophylactic treatment (OR=0,15; CI 95% 0,02–0,85; p=0,021), thus conferring a 6.5-fold higher risk of pregnancy complications in the untreated women (IC 95% 1,2–36,33; p=0,032).
**Conclusions:** a) Pregnancy morbidity rate in women with positive antiphospholipid antibodies was 54% when analyzing the total number of pregnancies, and 32% when analyzing the pregnancies after confirmed positive serology. b) We didn't find a profile of antibodies specifically related with obstetric complications. c)Prophylactic drug therapy is effective in preventing early pregnancy losses and achieving a higher live birth rate.
**Disclosure of Interest:** None declared
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## AB0472 ASSESSMENT OF MEAN PLATELET VOLUME AS A MARKER OF DISEASE ACTIVITY IN SLE PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is a multisystem inflammatory autoimmune disease that evolves with periods of remission and exacerbation activity, whose intensity can be measured by the SLEDAI. This tool is complex and has limitations. The mean platelet volume (MPV) is a marker of platelet activation and has been shown to be associated with inflammation, which makes it a potential biomarker to aid in the assessment of disease activity in SLE.
**Objectives:** To evaluate VPM in SLE patients at the active and inactive stages according SLEDAI and assess a possible correlation between VPM with SLEDAI, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complement 3 (C3), and complement 4 (C4).
**Methods:** This cross-sectional study consisted of 40 patients with SLE, according to American College of Rheumatology (ACR) classification criteria, that were evaluated in Rheumatology Clinic of the Hospital de Clínicas de Porto Alegre in the second half of 2015. Interview during medical consultation and medical chart review were used to collect demographic, clinical and laboratory data. Disease activity was assessed with SLEDAI and chronicity was assessed with SLICC damage index (SDI). The blood count and platelets are measured in automation equipment Sysmex XE 5000. Platelets are analyzed by impedance, and the mean platelet volume is an index calculated by the machine when the examination of platelets. VSG was carried out by automated method by capillary photometry kinetics, PCR and C3 and C4 complement were determined in automation by immunoturbidimetry with intensification of reaction particles. Comparisons between groups were made with t-test or Mann-Whitney test.
**Results:** All patients studied were female, 25 (62.5%) were classified as European-derived, mean age was 42.7±12.6 years and the average age at diagnosis was 29.9±9.9 years. At the time of the study, the median (IQR) for SLEDAI was 1.50 (0.0,4.0) and for SDI was 0.0 (0.0,1.0). Patients were divided into two groups (SLEDAI=0 and SLEDAI>0). The VPM had an inverse significant correlation with SLEDAI ($r$=-0.38; p=0.01). However, the MVP did not correlate significantly with ESR, CRP, C3 and C4. Patients were divided into two groups (SLEDAI=0 and SLEDAI>0) and the results for classification criteria were similar, but lymphopenia was most prevalent in group SLEDAI>0.
**Conclusions:** There is a correlation between the VPM and the SLEDAI in our SLE patients, making it a possible tool to be used in the evaluation of disease activity.
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## AB0473 QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS MEASURED BY THE SF36

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**Background:** Systemic Lupus Erythematosus (SLE) and rheumatoid arthritis (RA) are autoimmune diseases that mainly affect people in the reproductive stage of their life; it is interesting to investigate the impact of both diseases have in patient's quality of life.
**Objectives:** The main objective of this study was to evaluate the quality of life of patients diagnosed with SLE and RA using the SF36 questionnaire and the factors that influence it
**Methods:** Analytical, observational cross-sectional study of a cohort of SLE and RA patients. A large number of clinical and epidemiological variables were recorded (i.e. years of evolution, the age at diagnosis, disease activity, gender, marital status, etc). Quality of life was determined by SF36 questionnaire. Statistical analysis was performed with SPSS19.0 program. Qualitative variables were expressed as percentages and frequencies while quantitative were informed as mean and standard deviation. Association was analyzed with X2 test and Student T test. Pearson's test was used for correlation analysis.
**Results:** 112 patients were studied, 50.9% (57/112) patients had SLE and

49.1% (55/112) RA. 69.6% (78/112) of patients came from the capital city and metropolitan area. 87.5% (90/112) were female, 57.14% (64/112) were living in couple and 49.1% (55/100) had basic education. 43.8% (49/97) perceive less or equal to the minimum wage monthly income. 42% (47/98) were living with 3 or fewer inhabitants in the house and 58.9% (66/108) had ≥40 years old at disease onset. The mean value of physical (PCS) component of SF36 questionnaire in SLE and RA was 45.13±12.5 and 47.7±12.5 respectively and the difference between them was significantly (p=0.01). On the other hand, the mean value of mental (MCS) component was 47.7±12.5 and 46.4±12 respectively but no significant difference was found (p=0.58). In relation to the 8 SF36 components we found significant difference between them, principally in the components that measures body pain (p=0.0001) and health perception (p=0.047). In SLE patients, a significant negative correlation it was found between PCS and HAQ (p=0.00018) and SLEDAI (p=0.0020). No significantly correlation with MCS was found. Regarding the SLICC Score, a statistically negative correlation was found with MCS (p=0.036). In RA patients, a significant negative correlation was found between PCS and HAQ (p=0.0001), no association with the DAS28 was found. But, a negative correlation between the MCS and DAS28 (p=0.03) was found. No significant correlation was observed with HAQ.

**Conclusions:** In this cohort revealed that physical and mental component of SF36 are influenced by the disease activity and functional impairment.

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## AB0474 A PROSPECTIVE EVALUATION OF ENDOTHELIAL DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITHOUT PREVIOUS CARDIOVASCULAR EVENTS: PRELIMINARY RESULTS

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**Background:** Cardiovascular disease (CVD) due to premature atherosclerosis is a leading cause of morbidity and mortality in Systemic Lupus Erythematosus (SLE) patients. Early identification of patients with subclinical disease and tight control of cardiovascular risk factors are essential to reduce such complication [1,2].

**Objectives:** To assess the prevalence of endothelial dysfunction (ED) by a non invasive procedure in SLE patients with early disease without history of CVD.

**Methods:** SLE patients, according to 2012 Classification Criteria, with a disease duration less than 5 years, followed in the Rheumatology and Nephrology Unit of our Hospital were proposed to perform a cardiologic evaluation. Exclusion criteria were represented by: history of CVD, diabetes, chronic renal disease (creatinine clearance<60 ml/min), not controlled systemic arterial hypertension, current smoking or smoking in the last 3 years, hypercholesterolemia (total cholesterol>240 mg/dl), obesity (body mass index ≥30), statin or beta-blocker use. Each patient underwent a clinical and serological evaluation, a transthoracic doppler echocardiogram and an evaluation of endothelial function by endoPAT technique. Patients with ED, defined as reactive hyperemic index ≤2, were compared to those without ED by Fisher, T student or Mann-Whitney tests as appropriate.

Table I Disease characteristics and treatment of 17 SLE patients

| | |
|---|---|
| Cutaneous, n (%) | 9/17 (53) |
| Mucosal, n (%) | 5/17 (29) |
| Renal, n (%) | 7/17 (41) |
| Articular, n (%) | 12/17 (71) |
| Neurological, n (%) | 1/17 (6) |
| Serositic, n (%) | 5/17 (29) |
| Hematological, n (%) | 12/17 (71) |
| Antiphosphslipid Syndrome, n (%) | 1/17 (6) |
| Antinuclear antibody positivity, n (%) | 17/17 (100) |
| Anti-double stranded DNA positivity, n (%) | 7/17 (41) |
| Anti-extractable nuclear antigen positivity, n (%) | 10/17 (59) |
| Anti-cardiolipin IgG positivity, n (%) | 1/16 (6) |
| Anti-cardiolipin IgM positivity, n (%) | 4/16 (25) |
| Anti@2Glycoprotein I IgG positivity, n (%) | 1/16 (6) |
| Anti@2Glycoprotein I IgM positivity, n (%) | 2/16 (12) |
| Lupus anticoagulant positivity, n (%) | 5/17 (29) |
| C3 mg/dL, mean (SD) | 86,5 (20,7) |
| C4 mg/dL, mean (SD) | 13,2 (6,8) |
| Systemic Lupus Erythematosus Disease Activity Index 2K, mean (SD) | 4,06 (3,13) |
| Systemic Lupus International Collaborating Clinics Damage Index., median (range) | 0 (0-3) |
| Steroids, n (%) | 16/17 (94) |
| Antimalaric, n (%) | 15/17 (88) |
| Disease Modifying Antirheumatic Drugs, n (%) | 10/17 (59) |
| Belimumab, n (%) | 1/17 (6) |
| Low dose aspirin, n (%) | 8/17 (47) |
| Oral anticoagulant, n (%) | 2/17 (12) |
| Anti-hypertensive drugs, n (%) | 7/17 (41) |

**Results:** We enrolled 17 SLE patients (100% female, 88% caucasian) with a median disease duration of 14 months (0–68), a mean age of 41 years (±16), and a mean age at diagnosis of 39 years (±17). Five patients (29%) had a systemic hypertension that was well controlled by treatment. No other cardiovascular risk factors were present. Disease characteristics and treatment are shown in Table I. Echocardiogram showed diastolic dysfunction in 3 patients. EndoPAT identified 7 patients (41%) with ED. We did not find any significant association between the presence of ED and demographic-clinical-serological characteristics of patients or treatments or echocardiografic findings. A tendency for an association with an history of renal disease was observed (57% versus 0%, p:0.058).

**Conclusions:** A significant proportion of SLE patients showed signs of ED despite a recent disease and the absence of significant cardiovascular risk factors.

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## AB0475 SHRINKING LUNG SYNDROME IN SYSTEMIC LUPUS ERYTHEMATOSUS – A RARE COMPLICATION

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**Background:** Pleuropulmonary involvement in Systemic Lupus Erythematosus (SLE) occurs in 60 to 80% of patients. Shrinking lung syndrome (SLS) is a non-exclusive, rare manifestation of SLE. The pathogenesis and treatment of SLS are not well established.

**Objectives:** We describe the clinical, immunological and radiological features and the therapeutic management of a series of 8 cases of SLS.

**Methods:** This study is a retrospective, descriptive study of a series of 8 cases of patients diagnosed with SLE in the Rheumatology Unit of Ramón y Cajal Hospital and Severo Ochoa Hospital.

**Results:** Of the 8 patients, 7 were women with a mean age at diagnosis of 40 years. Only 2 patients had severe visceral involvement. All patients had a history of serositis. All patients had positive ANA, 87.5% anti-DNA positive and 100% had low complement at some point in the evolution of the disease. 62.5% had anti-Ro and 50% had anti-RNP. 37.5% of patients were already in treated with low or intermediate doses of corticosteroids at the time of diagnosis, 37.5% received dolquine, 25% were treated with azathioprine and one patient had epratuzumab.In relation to diagnostic studies, 100% of patients had elevating one hemidiaphragm or both on chest radiography and basal atelactasis. The most common findings on the CT scan were: elevation of the diaphragm, pleural effusion and the presence of basal atelectasis. All cases had a restrictive pattern in PFT and in the cases in which the results were available, the carbon monoxide gas transfer capacity was reduced. Regarding the therapeutic management, 62.5% were treated initially with intermediate-high doses of oral corticosteroids (mean dose 17.5 mg/day), in 25% was added Chloroquine, in 25% of cases Azathioprine and MMF in one patient. Only one patient received treatment with Beta-2 agonists. The evolution was favorable only in the patient receiving MMF with clinical and radiological improvement of stabilization on clinical and radiological findings over the time. In 62.5% of patients the pleuritic chest pain persisted and 37.5% presented later infectious respiratory complications.

**Conclusions:** SLS is a rare complication in patients with SLE. The pathogenesis of SLS is unknown. It was suggested the possible involvement of the anti-Ro antibody. In our series, 62.5% had anti-Ro positive and 50% anti-RNP positive. The SLS must be suspected when a SLE patient star with unexplained dyspnea and/or pleuritic chest pain and a loss of lung volume in the imaging studies and development of a restrictive pattern in PFT. The treatment is not well established. In most published series, as in our case, the initial treatment is represented by the oral corticosteroid (30–60 mg/day). In several studies it has been proposed the use of Beta-2 adrenergic agonists and Theophylline, although their effectiveness has not been well demonstrated. In refractory cases the use of other immunosuppressive has been successfully reported. In our series, the addition of Chloroquine or Azathioprine was not associated with radiological improvement but with clinical stabilization in time. The MMF was associated with clinical and radiological improvement but a conclusion cannot be taken. The clinical outcome in most of the series is usually favorable, with subjective improvement in pain and dyspnea and with progressive improvement in lung function tests.

**Disclosure of Interest:** None declared

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## AB0476 SERUM LEVELS OF PROLIFERATION-INDUCING LIGAND, B-CELL ACTIVATING FACTOR, ANTINUCLEAR AUTOANTIBODIES AND MARKERS OF INFLAMMATION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME COMPARED TO PATIENTS WITH SICCA SYMPTOMS WITHOUT DIAGNOSIS OF PSS AND WITH HEALTHY SUBJECTS

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**Background:** The proliferation-inducing ligand (APRIL) and B-cell activating factor (BAFF) are associated with primary Sjögren's syndrome (pSS), because they affect B-cell activity – possible key factor in the pSS pathogenesis.
**Objectives:** The study aimed at determining the correlation between serum concentrations of APRIL /BAFF and markers of pSS and of systemic inflammation.
**Methods:** We evaluated 3 groups: (i) 41 patients with established pSS diagnosis (according to AECG criteria and ACR criteria 2012); [the mean age 51±15.3; 82,9% female (F), 17.1% males (M)]; (ii) 32 subjects with symptoms of dryness (other connective tissue diseases were excluded)[the mean age 56±12,46; (93,75%) F, 2 (6,25%) M], and (iii) 24 healthy volunteers [the mean age 43±12,4; 19 (79,2%), F and 5 (20,8%)M]. Laboratory tests were performed, including establishing inflammatory parameters: erythrocyte sedimentation rate (ESR), serum concentration of C-reactive protein (CRP) (range 0–10 mg/l), concentrations of gamma globulins (g/dl). ANAs titers and patterns were determined by an indirect immunofluorescence method with HEp2 slides. Anti-SSA and anti-SSB antibodies were detected by a dot-blot method allowing semi-quantitative evaluation. Serum concentration of APRIL and BAFF were measured using an enzyme-linked immunosorbent assay. Minor salivary gland biopsies evaluating the number of inflammatory infiltrates foci [focus score (FS) of mononuclear cells above 50] were performed. The study was approved by the Ethics Committee of NIGRR. Differences between groups were analyzed using U Mann-Whitney test (continuous variables). Correlations between variables were assessed with the Spearman correlation coefficient. Statistical significance was set at $p<0.05$
**Results:** pSS patients had significantly higher serum concentrations of BAFF and ANAs (Mann Whitney test $p<0,015$, $p<0,000$ respectively), but not of APRIL, compared to the healthy control (HC) group. There were no differences in serum concentration of BAFF and APRIL between pSS and sicca (S) group. Positive correlation between BAFF and APRIL serum concentrations was found in HC group ($r=0,469$;$p<0,05$), but not in pSS and S groups. In S group BAFF positively correlated with CRP ($r=0,446$;$p<0,05$) and ANAs positively correlated with a presence of anti-SS-A, anti- SS-B antibodies and a level of gamma globulins. In pSS group there was a statistically significant positive correlation between the concentration of APRIL and: (i) ANAs ($r=0,569$), (ii) anti-SS-A ($r=0,313$), (iii) anti -SS-B ($r=0,424$) and (iv) gamma globulins level ($r=0,408$). In pSS group ANAs positively correlated with FS ($r=0,455$).
**Conclusions:** 1. BAFF correlates more closely with an inflammatory reaction, while APRIL with a prolonged autoimmune response, that favoures the production of autoantibodies. 2. Lack of statistically significant differences in the concentrations of BAFF and APRIL between pSS and S group may be explained, based on other studies, by a local BAFF overexpression in salivary glands in pSS group or by an influence of EBV infection or reactivation in both groups (data not shown). 3. Positive correlation between FS and ANAs may suggest a role of ANAs in a local inflammation.
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## AB0477 ARTERIAL STIFFNESS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS PATIENTS AS A POTENTIAL PREDICTOR OF EARLY ATHEROSCLEROSIS

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**Background:** Cardiovascular disease (CVD) is one of the major cause of death in patients with SLE. Arterial stiffness is considered to be an independent risk factor of development CVD and a strong predictor of all-cause mortality. Increased arterial stiffness, due to premature vascular ageing, can be observed in patients with SLE as well as in patients with chronic kidney disease.
**Objectives:** To evaluate arterial stiffness determined as carotid – femoral puls wave velocity in systemic lupus erythematosus patients. The comparison of traditional risk factor of CVD and markers of subclinical atherosclerosis in SLE, patients with histologically proven Lupus nephritis (LN) and healthy controls.
**Methods:** We evaluate the data from 41 SLE patients, (37 females, 4 male, mean age 37, mean duration of the SLE of 8years). 21 of these patients with histologically proven Lupus nephritis and chronic kidney disease (CKD). Arterial stiffness, measured as carotid – femoral puls wave velocity (PWV) was established with the SphygmoCor system. This non-invasive technique uses the principle of applanation tonometry. Our control group counted 20 heathy male and female with no history of CVD, CKD or autoimmune disease. We evaluate the influence of traditional CV risk factors as age, smoking, BMI, diabetes mellitus, dyslipidemia, previous history of CV and cerebrovascular morbidity to PWV in SLE patients. Disease activity score (SLEDAI), the level of C3, C4 complement component and anti-dsDNA antibodies, renal function and antifosfolipid antibodies were measured at the same timepoint, correlated with PWV and carotid artery intima media thickness.
**Results:** Mean PWV in Lupus nephritis patients was numerically higher (6,5m/s) than that in other SLE patients (5,7m/s) and healthy controls but it lacked the statistical significance. PWV in LN was positively associated with carotid artery intima media thickness (IMT), hsCRP level, serum creatinine level, C4 complement component ($p<0,05$), presence of antiphopholipid syndome and SLICC score ($p<0,02$).
**Conclusions:** SLE patients are in increased risk of CV disease. PWV is considered as an independent risk factor of CVD and CKD. Despite we did not prove statistical significant difference in PWV in patients with Lupus nephritis in comparison to other SLE patients, there was a trend to increased PVW in this pilot study. The correlation to creatinin levels indicates relation of this parameter to renal function. It seems to be associated more with the fact of renal insufficiency that the pure presence of lupus nephritis. The PVW correlates with another test for early atherosclerosis and with the IMT. Further investigation is needed to establish the role of evaluation of PWV in SLE patients.
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## AB0478 GLUCOCORTICOID PREVENTS THE PROGRESSION OF ATHEROSCLEROSIS IN JAPANESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL PROSPECTIVE COHORT STUDY (NTMC-COHORT STUDY)

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**Background:** Several cross-sectional studies have shown a progression of atherosclerosis in systemic lupus erythematosus (SLE) was associated with the activity of SLE but not with glucocorticoid therapy. However, a few evidence showed the correlations between the progression of atherosclerosis in SLE and glucocorticoid therapy in longitudinal studies. Moreover, races and regions are known to be important in atherosclerosis.
**Objectives:** We conducted a longitudinal prospective cohort study to clarify relevant clinical factors to influence the progression of atherosclerosis in Japanese patients with SLE.
**Methods:** In our cohort of the patients with SLE who regularly visit our department, the patients who underwent echography of the carotid arteries twice or more, with an interval of two years or more, were enrolled into the present study.
Atherosclerosis was evaluated with echography of the carotid arteries. A mean of the bilateral intimal carotid artery media thickness (mIMT) was measured with the three-point method (TOSHIBA Xario200, Aplio400). The annual progression rate of mIMT (mIMT/y) was calculated from the difference between the baseline and the subsequent echo studies.
We analyzed clinical factors associated with mIMT and mIMT/y using multiple regression analysis. For mIMT, clinical factors assessed in the analysis were as follows: age, disease duration, smoking habits, comorbid conditions, total cumulative prednisolone dosage (tPSL), history of other medications, SLICC/ACR damage index (SDI), Ankle-Brachial Index, Cardio-Ankle Vascular Index, HbA1c, C-reactive protein, serum creatinine, high density lipoprotein cholesterol, and low density lipoprotein cholesterol at baseline. For mIMT/y, in addition to the factors above, we assessed mean daily prednisolone dosage during the follow-up period (mPSL) and other medications during the follow-up period.
The analysis was performed by SPSS version 20.
Data were represented as median (25–75 percentile).
**Results:** Thirty-nine Japanese patients with SLE were recruited in our study. Of these, 35 were women; age, disease duration, tPSL at baseline, and daily prednisolone dosage during the follow-up period (mPSL) were 60 (48–65) years, 25 (12–32) years, 58 (36–82) g and 5.0 (4.0–7.5) mg/day, respectively. The intervals of echo studies were 4.0 (2.7–6.1) years.
At baseline, the mIMT was 0.60 (0.50–0.75) mm. Age ($B=0.005$, $SE=0.002$, $p=0.011$) and SDI ($B=0.05$, $SE=0.02$, $p=0.019$) were selected as positive contributory factors for mIMT, while tPSL was selected as a negative factor ($B=-0.002$, $SE=0.001$, $p=0.007$).
For mIMT/y, mPSL ($B=-0.005$, $SE=0.002$, $p=0.004$) was a negative contributory

factor, and diabetes mellitus requiring medical therapy was a positive factor (B=0.032, SE=0.014, p=0.035).
**Conclusions:** These results suggested that glucocorticoid therapy might be protective against the progression of atherosclerosis in Japanese patients with SLE.
**Disclosure of Interest:** None declared
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## AB0479 MUSCULOSKELETAL MANIFESTATIONS ARE MAJOR DETERMINANTS OF IMPAIRED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Musculoskeletal (MS) manifestations are among the most frequent expressions of Systemic Lupus Erythematosus (SLE) being present in up to 90–95% of patients during disease course and in 60% of disease flares. They have been associated with impaired quality of life (QoL) in SLE patients. However, the role of different subtype of MS manifestations has not been investigated.
**Objectives:** To investigate the impact of different MS manifestations in SLE patients as major determinants of impaired health related QoL (HRQoL) in SLE.
**Methods:** One hundred twelve consecutive SLE patients (age 47.6± 16.8 years, disease duration 115.5±84.0 months; 6 male) diagnosed according to the 1997 ACR classification criteria were recruited in this cross-sectional study; 87 patients were sub-classified as affected by non-deforming non-erosive arthritis (NDNE), 15 as Jaccoud's arthropathy (JA) and 10 as rhupus syndrome (RS) according to clinical and radiographic features. Thirty-five patients affected with Rheumatoid Arthritis (RA) and 38 healthy controls (HC) were recruited as control groups. HRQoL was evaluated using three validated self-administered questionnaires: the Short Form 36 (SF36) health survey questionnaire, the Heath Assessment Questionnaire (HAQ) and the Fatigue scale v4 (FACIT-4).
The search for factors independently associated with low QoL included univariate analyses and stepwise multiple regression models. Explanatory variables tested were: age, disease duration, gender, occupation, arthropathy subtypes, SLEDAI, SLICC damage index, Body Mass Index, arthritis, discoid LE, neuropsychiatric symptoms, active nephritis, depression, fibromyalgia, osteoporosis with fractures, osteonecrosis. Multivariate models were fitted with covariates with $p<0.1$ to predict outcomes; Bonferroni's corrected $p<0.05$ was considered significant.
**Results:** SLE patients had worse results ($p<0.01$) than HC in SF36, HAQ, and FACIT-4. Patients classified as affected by JA and RS had worse results ($p<0.01$) in SF36, HAQ, and FACIT-4 than patients with NDNE and RA, but no differences were recorded between these two groups.
Factors independently associated with lower score in the physical summary components of SF36 were: JA ($p=0.01$), arthritis ($p<0.01$) and fibromyalgia ($p<0.01$). Factors independently associated with lower score in the mental summary components of SF36 were: JA ($p<0.01$), RS ($p<0.01$) and fibromyalgia ($p<0.01$). Factors independently associated with lower HAQ results were: JA ($p<0.01$), arthritis ($p<0.01$) and osteoporosis with fracture ($p<0.01$). Factors independently associated with lower FACIT-4 score were JA ($p<0.01$) and arthritis ($p<0.01$).
**Conclusions:** MS manifestations were confirmed as one the major factors associated with lower QoL in patients with SLE. In particular active arthritis, JA and fibromyalgia were associated with low levels of patient's perception in physical function evaluated with the HAQ and SF36, whereas JA and fibromyalgia were determinants of impaired mental health. Active arthritis and JA were associated with increased fatigue perception evaluated with FACIT-4.
**Disclosure of Interest:** None declared
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## AB0480 CANCER INCIDENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** In the latest study published by the SEOM (Spanish Society of Medical Oncology) in 2012, the most prevalent types of cancers in Spanish women are breast, colorectal, corpus uteri, lung and ovary. In addition, in Systemic Lupus Erythematosus (SLE) patients a higher incidence of cancer has been described, about 15–20% higher. Today, there is some controversy around the activity on SLE or even drugs employed such as cyclophosphamide could be an extra risk factor for cancer development in these patients. In fact, there are not many studies regarding cancer incidence in SLE.
**Objectives:** To analyze the cancer incidence in a series of SLE patients, as well as their clinical characteristics.
**Methods:** Cross-sectional retrospective study of SLE patients according to the SLICC-2012 criteria, coming from the Rheumatology Service of Arnau de Vilanova Hospital and La Fe Hospital. In all patients clinical and disease activity data were collected, using personal interview and medical history.
**Results:** A total of 140 patients were evaluated; of them, 95% were women with 33.39±13.63 year-old average at the diagnosis time with a 10.05±11.42 year-evolution of SLE. Of them, 6 patients (4.3%) have had some type of cancer, whose clinical characteristics are presented in the table.
**Conclusions:** The percentage of SLE patients who have developed any type of cancer was 4.3%, which doubles the rate for Spanish general population (2.12%). The types of found cancer are heterogeneous and don't correspond to the usual pattern described for general population in our country.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4134

## AB0481 DESCRIPTION OF A LATE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

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**Background:** The late-onset Systemic Lupus Erithematosus (SLE) has been defined as that one beginning after 50 years old, and supposes around 6–18% of the SLE patients. According to the literature, the most common clinical manifestations are interstitial lung disease, serositis, Sjögren's syndrome and cytopenias. Though the illness activity is lower in these patients, this population usually stands with more accumulative damage and has a higher mortality than the early-onset SLE patients.
**Objectives:** To study the differences between the late-onset SLE patients and the conventional-onset ones, regarding to the debut and actual manifestations, biomarkers of autoimmunity, accumulative damage and disease activity.
**Methods:** Cross-sectional prospective study of SLE patients according to the SLICC-2012 criteria, coming from the Rheumatology Service of Arnau de Vilanova Hospital and La Fe Hospital in Valencia, Spain. All patients had a complete blood-test with autoimmunity markers, and clinical and activity data were collected using the SLICC-ACR and SELENA-SLEDAI questionnaires.
**Results:** A total of 140 patients were evaluated; (95% were women) with 33,39±13,63 year-old average at the diagnosis time with a 10,05±11,42 year-evolution of SLE. Of them, 12% had a late-onset of the disease (diagnosis at >50 years old). In this group of patients we found a higher incidence of SS and Raynaud's phenomenon as the initial symptom (5,9% and 11,8% respectively), compared to the early-onset patients (2,4% and 4,1%). However, regarding to the actual manifestations, this group has a lower incidence of Raynaud's, as well as renal damage or cytopenias. We observe a higher proportion of SS between the late-onset group, although the ENAs levels are lower than in the early-onset group. In addition, the late-onset group has an incidence of cardiovascular events 4 times higher than the early-onset one.
**Conclusions:** We observe a concordance between the debut symptoms in our late-onset series and other series described previously in the literature, where SS presents with a higher proportion in these patients. On the other hand, we cannot distinguish if the higher proportion of cardiovascular events in this groups is due to the late-onset SLE characteristics itself, or to other factors regarding to the older age.
**Disclosure of Interest:** None declared
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**Abstract AB0480** – Table 1

| Case | Gender | SLE-onset age | SLE evolution (years) | Cancer type | Time from SLE-onset to cancer diagnosis (years) | Anti-dsDNA | ANAs | Anti-RO | Anti-LA | Anti-SM | Anti-RNP |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Female | 17 | 30 | Ovarian adenocarcinoma | 21 | – | + | + | – | – | – |
| 2 | Male | 47 | 18 | Thymoma | –2 | – | – | – | – | – | – |
| 3 | Female | 40 | 18 | Liposarcoma right leg | 3 | + | + | – | – | – | – |
| 4 | Female | 45 | 25 | Invasive ductal carcinoma left breast | 25 | – | + | + | – | – | – |
| 5 | Female | 29 | 10 | Cervical intraepithelial neoplasia (CIN-1) | 7 | – | + | + | + | – | – |
| 6 | Female | 27 | 23 | Ovarian tumor | 13 | – | – | – | – | – | – |

## AB0482 EVALUATION OF CURRENT AND AT THE ONSET CLINICAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Systemic Lupus Erythematosus (SLE) in a multisystemic autoimmune disease that specially affects young women during the second and third decade, and is able to injure different organs and or systems, being the most common one affected the musculoskeletal system.
**Objectives:** To analyse the influence of the time of evolution and age of the patient in the current clinical manifestations and the debut of the disease in patients with SLE.
**Methods:** Cross-sectional prospective study of SLE patients according to the SLICC-2012 criteria, coming from the Rheumatology Service of Arnau de Vilanova Hospital and La Fe Hospital. All patients had a complete blood-test with autoimmunity markers, and clinical, biometrics and treatment data were also collected from the personal interview and the medical history. Biostatistical analysis was performed using the *R* software version 3.2.3., using a simple, binomial and logistic lineal regression.
**Results:** A total of 140 patients were evaluated; of them, (95% were women) with 33.39±13.63 year-old average at the diagnosis time with a 10.05±11.42 year-evolution of SLE. We can find the clinical manifestations at the onset disease on the table.

| Onset manifestation | (%) | Onset manifestation | (%) |
|---|---|---|---|
| Musculoskeletal | 73.6 | Sjogren synd. | 2.9 |
| Skin | 39.3 | Raynaud's | 5 |
| Kidney | 5 | Other | 27.1 |
| Cytopenia | 7.9 | | |

We observe statistically significant differences in the musculoskeletal system involvement (P=0.008), and in the presence of vasculitis (P=0.01) in patients with a shorter time of disease evolution. There is also a direct relationship between cardiovascular (P=0.002) and renal (P=0.03) affection in younger patients. Finally, cytopenias are correlated both in young patients (P=0.0009) as well as with a shorter time of evolution (P=0.02).
**Conclusions:** We observe a concordance between our SLE series and those already described at the literature, where renal involvement occurs at younger ages, and the musculoskeletal system involvement occurs early in disease or even as the onset symptom.
**Disclosure of Interest:** None declared
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## AB0483 RISK FACTORS ASSOCIATED WITH GREATER DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: AN EGYPTIAN MULTICENTER STUDY

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**Background:** Systemic lupus erythematosus (SLE) is a prototypic multisystem autoimmune disorder. The total damage in a patient with SLE may result from SLE itself or any other pathologic process. The management of SLE targets immediate control of disease activity, but also it should include the prevention of organ damage from treatment and comorbidity by minimizing or controlling risk factors of organ damage.
**Objectives:** The aim of this study was to assess risk factors of greater damage in a sample of Egyptian SLE patients.
**Methods:** This is an Egyptian multicenter retrospective study. The study included 100 SLE patients: 64 patients from Cairo University Hospital and 36 patients from Zagazig University Hospital. The patients are classified according to the Systemic Lupus International Collaborative Clinics (SLICC) criteria for SLE. Systemic Lupus International Collaborative Clinics/ACR Damage Index (SLICC/ACR-DI) was used to measure damage in each patient. The period of data collection took 4 months. The collected data included demographic, clinical, serologic data and medications.
**Results:** 100 SLE patients (93% females and 7% males with mean age 33.44±8.6 and disease duration 6.25 (1–17) were included. The most frequent item in the damage index in our patients was retinal changes or optic atrophy (12%), followed by osteoporosis (11%). The total SLICC/ACR Damage Index Score ranged from 0 to 8. There was a significant positive correlation between the Damage Index and the patient's age, SLEDAI-2k at the onset and at the last visit ($P<0.05$). A higher Damage Index score was found in hypertensive patients compared to normotensive patients and among those with positive anti-phospholipid antibodies compared to those with negative anti-phospholipid antibodies and the difference was statistically significant ($P<0.01$). A statistically significant higher Damage Index score was found in cyclophosphamide users compared to non-users, and in those with proteinuria & seizures compared to those without ($P<0.05$). Comparing all variables; seizures was by far the most important predictor of Damage Index in the regression model (Beta=0.279, P=0.028), followed by SLEDAI at last visit (Beta =0.234, P=0.062) and then Antiphospholipid Syndrome (Beta =0.335, P=0.064).
**Conclusions:** Damage in SLE cannot be prevented completely as SLE is an aggressive disease treated by aggressive medications. Frequent ophthalmologic follow up is necessary for all SLE patients. SLE patients with hypertension and positive antiphospholipid antibodies develop higher damage scores so they need closer observation and control of these factors if possible. Rheumatologists should try to minimize damage as much as possible to maintain patients' health, functioning, and general wellbeing.
**Disclosure of Interest:** None declared
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## AB0484 IDENTIFICATION OF CLINICAL AND SEROLOGIC FACTORS ASSOCIATED WITH NEUTROPENIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Hematologic manifestations are common in systemic lupus erythematosus (SLE). Lymphopenia is most commonly found among leukopenia, but neutropenia is also found in about 50–60% of SLE patients. Most patients experience mild neutropenia while less than 5% of those experience moderate to severe neutropenia which can increase susceptibility to recurrent infection. Although it is crucial to understand risk factors associated with neutropenia in SLE patients, there is a paucity of clinical data regarding neutropenia in patients with SLE.
**Objectives:** This study was performed to identify the clinical and serologic factors that are associated with neutropenia in patients with systemic lupus erythematosus (SLE).
**Methods:** A total 160 admissions of 85 SLE patients between 2006 and 2013 were retrospectively reviewed. Neutropenia was defined as absolute neutrophil count (ANC) below 1,500/mm$^3$. Baseline characteristics of the patients were compared between patients who experienced neutropenia and those without. Clinical and serological factors related to neutropenia episode during admission were analyzed using generalized estimating equation (GEE) and multivariate analysis.
**Results:** Thirty two (37.6%) patients experienced neutropenia, and neutropenia episode was found in 35 (21.9%) of admissions. Most of the neutropenia episodes were mild to moderate. Severe neutropenia of ANC$<$500/ mm$^3$ occurred in 14.3% of the cases. Patients with neutropenia had higher frequencies of ANA (100.0 vs 86.8%, *P*=0.042) and anti-dsDNA (87.5 vs 60.4%, *P*=0.008), and satisfied more SLE classification criteria at the time of the diagnosis than those without (4.8 vs 4.1, *P*=0.014) Clinical characteristics at admission such as comorbidities, concomitant medications, and SLEDAI were not different between admissions with and without neutropenia episode. Anemia, leukopenia, thrombocytopenia and low complement levels were frequently associated with neutropenic episodes. Co-existence of chronic kidney disease (OR,16.91; 95% confidence interval (CI), 2.09–136.6; *P*=0.008) and Sjögren's syndrome (OR, 6.48; 95% CI, 1.46–28.66; *P*=0.014) was associated with increased risk of developing neutropenia.
**Conclusions:** This study demonstrates that most of neutropenia in SLE patients occur as part of hematologic and immunologic abnormalities. SLE patients with renal damage and Sjogren's syndrome should be closely monitored for development of neutropenia.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3334

## AB0485 ANTI-C1Q ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH RENAL PATHOLOGY OF LUPUS NEPHRITIS

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**Background:** There is a lack of serum markers for effective evaluation of renal lesion severity of systemic lupus erythematosus (SLE). Recent studies show that anti-Clq antibody has been associated with SLE and lupus nephritis (LN), but there were few data about the relationship between anti-Clq antibody and renal pathology of LN.
**Objectives:** To investigate the relationship between serum anti - Clq antibody and the disease activity of SLE as well as renal pathological characteristic.
**Methods:** Anti-C1q Ab were measured by enzyme-linked immunosorbant assay (ELISA) in 128 patients with SLE (including 58 cases with LN and 70 cases without LN), 103 patients with other autoimmune diseases (disease control group) and 60 healthy individuals (healthy control group). Renal biopsy was conducted in all LN patients.

**Results:** Prevalence of anti-C1q was 31.3% (40/128) in patients with SLE, significantly higher than that in disease control group and healthy control group (31.3% vs.4.9% (5/103), $P<0.01$; 31.3% vs. 0 (0/60), $P<0.01$). And the positive rate of anti-C1q Ab was significantly higher in patients with active SLE (37/54,68.5%), LN (35/58, 60.3%) and active LN (32/36, 88.9%) in comparison with patients with inactive SLE (3/64,4.7%), non-LN (5/60,8.33%) and inactive LN (3/22,13.6%), respectively. The incidence of renal involvement in SLE patients with positive anti-C1q Ab was higher than that in anti-C1q Ab negative group (87.5% vs 29.5%, $P<0.05$). 12 cases of renal biopsies were classified as WHO Class II. 13 cases Class III,18 cases Class IVCand 15 cases Class V. The serum anti-C1q Ab level in Class IV LN patients (63±10 RU/ml) was higher than that in Class II/III/V LN patients ($P<0.01$). There was no significant difference of the anti-C1q Ab level among the other pathological types of LN.The serum C1qAb level was significantly higher in the LN patients with renal deposition of C1q (++), IgG positive and C3 positive, in comparison with the deposition of C1q (+/–), IgG negative and C3 negative, respectively ($P<0.05$). The elevated levels of anti-C1qAb was significantly positively correlated with the deposition of C1q, IgG and C3 in the kidney.

**Conclusions:** The serum anti-C1q antibody, a simple and non-invasive marker, can reflect the disease activity of SLE, especially with regard to renal involvement. It is useful for SLE to predict renal lesion, particularly diffuse proliferative LN (iclass IV).

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## AB0486 PRESENTING MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A COHORT OF 100 SLE PATIENTS FROM A SINGLE CENTER

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**Background:** Systemic lupus erythematosus (SLE) is a multiorgan disease with protean manifestations and its diagnosis can pose a considerable challenge.

**Objectives:** The aim of the study was to analyze clinical and laboratory manifestations at the onset of SLE and to compare ACR and the SLICC criteria for the classification of SLE.

**Methods:** A retrospective study of a well characterized SLE cohort of 100 patients was undertaken. All patients met four or more updated ACR criteria (range 4–8). The following data were collected: age, gender, initial manifestations, time from the first symptom or disorder to definite diagnosis and clinical and laboratory features at the time of SLE diagnosis.

**Results:** Of the 100 patients analyzed 91 were women, the mean age at the time of diagnosis was 36.56±11.61 years. The most common presenting features were mucocutaneous (77%) and musculoskeletal (76%) manifestations, fatigue (74.6%), fever (52%) and non-scarring alopecia (34%). Median time from the first symptom/disorder to diagnosis was 10 months (range 1–120 months). At diagnosis most of the patients had elevated inflammatory markers ESR and CRP (87.4% and 50% respectively). Anemia and leukopenia was detected in 61% and 48% patients respectively. Serositis was observed in 24%, renal manifestations in 15% and psychosis or seizures in 7% of patients. Positive ANA were present in 97% of patients, anti-dsDNA antibodies in 66%, anti-Sm antibodies in 29.8%, aCL in 18.2%, aB2GPI in 13.8%, LA in 27% and low complement levels in 44.3%. All patients met also SLICC criteria (range 4–11), and significant number of them fulfilled items not contained in updated ACR criteria (non-scaring alopecia, low complement and other neuropsychiatric manifestations).

**Conclusions:** The prevalence of various clinical and laboratory features associated with SLE in our patients is comparable to findings of most major studies. We have shown that some patients could be diagnosed earlier using SLICC criteria. Furthermore, elevated inflammatory markers support SLE diagnosis.

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## AB0487 ANTIPHOSPHOLIPID SYNDROME AND EPILEPSY: WHERE DO WE STAND?

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**Background:** Epilepsy and seizures are commonly reported among the neurological manifestations of Antiphospholipid Syndrome (APS).

**Objectives:** To discuss the epidemiological, pathophysiological, laboratory, clinical, radiological, and therapeutic aspects of epilepsy/seizures in APS/ antiphospholipid antibody (aPL)-positive patients.

**Methods:** We searched the literature through Google Scholar and PubMed for all publications reporting on the epidemiology, pathogenesis, laboratory, imaging and associated clinical findings, and management of epilepsy/seizures in APS/aPL-positive patients. The following keywords were used: antiphospholipid, Hughes syndrome, anticardiolipin, lupus anticoagulant, anti-β2-glycoprotein I, partial, complex, generalized, and idiopathic epilepsy, seizure, and convulsion. All reports published between 1971 and 2015 were included.

**Results:** Temporal lobe epilepsy is particularly prominent in many APS cases. The prevalence of epilepsy/seizures in APS patients is approximately 8%, which is nearly 10 times the prevalence of epilepsy in the general population (0.5–1%). The pathogenesis is complex and may involve micro-thrombosis and/or immune-mediated neuronal damage. The association of seizures with aPL is more significant in the presence of SLE. Seizure patients with positive aPL tend to develop thrombocytopenia and livedo racemosa more frequently than those without aPL. The presence of SLE and the presence of neurological symptoms significantly correlate with the presence of white matter changes on MRI. In contrast, the correlation between aPL positivity and the presence of white matter changes is very weak. However, MRI can be normal in more than 30–40% of patients. New MRI techniques can better elucidate the pathology of brain damage in neuro-APS. The theurapeutic management of epileptic APS patients relies on anti-epileptic treatment and anticoagulant agents when there is evidence of a thrombotic event. The anti-thrombotic benefit of hydroxychloroquine and statins is supported by several studies.

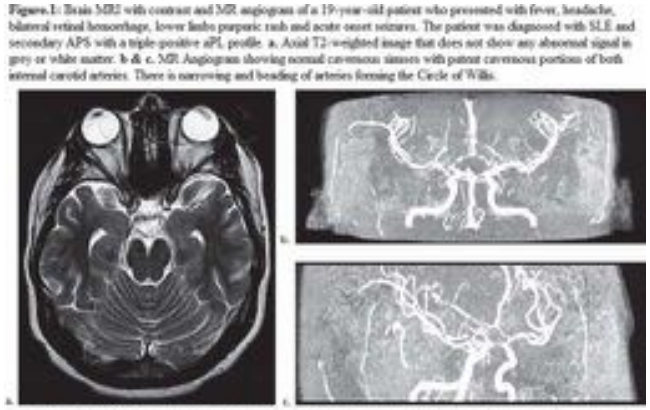


Figure.1: Brain MRI with contrast and MR angiogram of a 19-year-old patient who presented with fever, headache, bilateral retinal hemorrhage, lower limbs purpuric rash and acute onset seizures. The patient was diagnosed with SLE and secondary APS with a triple-positive aPL profile. a. Axial T2-weighted image that does not show any abnormal signal in grey or white matter. b & c. MR Angiogram showing normal cavernous sinuses with patent cavernous portions of both internal carotid arteries. There is narrowing and beading of arteries forming the Circle of Willis.

Legend: MRI, Magnetic resonance imaging; MR, Magnetic resonance; SLE, Systemic lupus erythematosus; APS Antiphospholipid syndrome; aPL, Antiphospholipid antibodies.

**Conclusions:** MRI remains the imaging modality of choice. aPL testing is recommended in young patients presenting with atypical seizures and multiple hyper-intensity lesions on brain MRI in the absence of other possible conditions. In the absence of consensual recommendations, the decision of lifelong anticoagulation in epileptic APS patients is discussed on a case-by-case basis.

**Disclosure of Interest:** None declared

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## AB0488 CLINICAL, BIOLOGICAL AND IMMUNOLOGICAL FEATURES OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A GROUP OF TUNISIAN PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease with wild spectrum manifestations. Disease severity and outcome are variable in different ethnic groups. The aim of this study was to describe clinical, biological and immunological features of SLE in a group of Tunisian patients.

**Objectives:** A retrospective study, including patients with SLE (Revised criteria of the American College of Rheumatology), followed in a department of Internal Medicine from 2000 to 2013. Data for demographic, clinical, biological and immunological characteristics of patients were recorded and analyzed. Treatment and outcome were described.
**Results:** Two hundred and forty six patients with SLE were included. The sex-ratio M/F was 0.14. The mean age at the disease onset was 32.96 years (ranges 6–72 years). The mean delay to diagnosis was 20±40. 3 months. Arthralgia, arthritis and cutaneous manifestations were noted in 90.2, 46.3 and 76% of cases respectively. Pleural effusion was observed in 25.6% of cases and pericarditis in 37% of patients. Lupus nephritis was diagnosed in 104 patients (42.3%). In the 81 patients who underwent renal biopsy, class IV nephritis was the most frequent (27 cases). Neuropsychiatric manifestations were observed in 20.6% of cases and 7.3% patients had peripheral neuropathy. Biological data revealed anemia in 73.2% of cases (Among them, 83.4% had a positive Coombs test), leucopenia (44.7%), lymphopenia (78%) and thrombocytopenia in 24% of cases. Antinuclear antibodies were positive in 97.2% of cases. Anti-dsDNA antibody was positive in indirect immunofluorescence and in ELISA in 141/190 and 76/91 patients respectively. Autoantibodies to extractable nucleair antigens were positive in 165/194 cases; anti-Sm antibodies were positive in 96/152, anti-nucleosome in 26/31, anti-histone in 48/82 and anti-ribosome in 16/67 cases (they weren't systematically screened). Low rate complement was observed in 83/140 cases. Chloroquine or hydroxychloroquine were given to 234 patients and 91.4% of patients were treated with corticosteroids (mean treatment duration: 64.13±50.83 months). Immunosuppressive drugs were added in 59.3% of patients; Cyclophosphamide (n=80), Azathioprine (n=52), Methotrexate (n=11) and Mycophenolate mofetil (n=3). The mean treatment duration of immunosuppressive therapy was 37.1±33.17 months. Relapses occurred in 62.8% of cases with a mean delay of 33.4±34.45 months. Mean follow up duration was 75.65±57.26 months. Remission was noted in 133 (54%) of patients. Twenty four patients died and 43 patients were lost to follow up. End stage renal disease was observed in five patients. Infections occurred in 143 cases. SLE was associated to Sjogren syndrome (n=41), antiphospholipid syndrome (n=29), systemic sclerosis (n=10), primary biliary cirrhosis (n=5), celiac disease (n=4) and to Kikuchi disease in 3 cases.
**Conclusions:** In our series, SLE patients had a high prevalence of cutaneous and articular manifestations. Nephritis lupus prevalence was similar to other African, Afro-american and Hispanic groups and lower than Asians. Global outcome was good with more than a half remission. Infections were frequent in our group (58%) because most of our patients had poor socio-economic conditions, in addition to their immunosuppression.
**Disclosure of Interest:** None declared
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## AB0489 CENTRAL NEUROLOGICAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Central neurological manifestations are a serious and common complication of systemic lupus erythematosus (SLE).
**Objectives:** The aim this study was to determine the prevalence of central neurological manifestations in a group of Tunisian patients and to describe their clinical, imaging findings, their treatment and outcome
**Methods:** A retrospective study conducted in an Internal Medicine department over a period of 14 years (from 2000 to 2013). SLE patients with central neurological manifestations (criteria of the American College of Rheumatology) were included. Clinical, laboratory data and imaging features of these patients were analyzed.
**Results:** Fifty one patients had central neurological and /or psychiatric manifestations (20.7%). The mean age at diagnosis was 33.6±14.16 years. Sex ratio M/F was 0.10. Neurologic manifestations revealed the disease in 3.2% of SLE patients. The mean delay from SLE diagnosis to neurological manifestations was months 11.7±47.9 months. Clinically, headache was reported in 42.1% of cases and seizures in 39.4% of cases. Physical exam found: pyramidal syndrome (n=12), reflecting meningeal irritation (n=9), paraplegia (n=4) and chorea (n=2). Psychiatric manifestations were associated to neurological manifestations in 23.07% of patients: depression (n=8), anxiety disorder (n=7) and catatonia (n=2). Thirteen patients had only psychiatric manifestations: depression (n=9), anxiety disorder (n=5), catatonia (n=1). Antinuclear antibodies, anti-Sm and anti-Ribosome were positive in 49/50, 17/31 and 2/16 respectively. Aseptic meningitis was found in nine patients; lymphocytic (n=7) or polynuclear predominance (n=2). Magnetic resonance imaging (MRI) confirmed central nervous system involvement in 31 cases. Demyelinating aspect with high intensity signals were found in different localizations: periventricular (n=9), frontal (n=6), parietal (n=5), centrum semiovale (n=5), occipital (n=3). Cortical atrophy was observed in two patients. Two patients presented with stroke and one patient had cerebral venous thrombosis. MRI was normal in three patients. Antiphospholipid syndrome and Sjogren syndrome were associated to SLE in six and nine patients respectively. Patients had also arthralgia (96.1%), cutaneous manifestations (80.4%), pericarditis (31.4), pleural effusion (17.6) and lupus nephritis (37.2%). Patients were treated with antimalarial drugs (90.2%), corticosteroids (88.2%) and antiplatelet drugs (23.5%). Thirty two patients received immunosuppressive therapy: Cyclophosphamide (n=22), Azathioprine (n=9) and Methotrexate (n=1). Neurologic relapses were noted in 23, 7% of cases with a mean delay of 42.2 months. Remission was noted in 68.4% of patients with sequel in 38.4% of cases. Mean follow duration was 74.8±52.3 months.
**Conclusions:** Prevalence of central neurological and psychiatric manifestations in systemic lupus erythematosus varies widely in different studies (20 to 97%), depending on the studies style and the including criteria. They are a real challenge for clinicians because they need to exclude other related conditions (infections, drugs, ...) and primitive psychiatric disorders.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4448

## AB0490 PLASMA VITAMIN D LEVEL IN PRIMARY SJOGREN'S SYNDROME – TUNISIAN COMPARATIVE STUDY OF 66 PATIENTS

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**Background:** Beyond its critical function in calcium homeostasis, vitamin D has recently been found to play an important role in the modulation of the immune/inflammation system. Increasing numbers of study have established that vitamin D insufficiency contributes to a number of diseases, suggesting a range of physiological functions of vitamin D. Recent findings seem to show that low vitamin D levels in patients with Sjogren Syndrom could be associated with severe complications such as peripheral neuropathy.
**Objectives:** The purpose of this study was to evaluate plasma vitamin D level in Primary Sjogren's Syndrome (PSS) and comparing it with healthy controls.
**Methods:** North Africans patients (Tunisian patients) with PSS were diagnosed in an internal medicine department. All patients with PSS meet the revised AECG criteria 2002 and/or ACR proposed criteria 2012. We proceed in this prospective study with a comparison of plasma vitamin D between two groups, with a matched age and sex, one of patients with a Primary Sjogren's Syndrome (PSS) and a second of healthy control subjects. Sixty six patients with PSS were enrolled. Sex ratio was 0.11 (59 female (89.4%) and 7 male (10.6%)).Mean age at diagnosis was 49.07 years ±12.56 (range 26 -73years). Forty eight healthy controls were included. Sex ratio was 0, 14 (42 females (87.5%) and 6 males (12.5%). Registration and statistical analysis of data were done with SPSS. Plasma 25-hydroxyvitamin D (25-OHD) concentrations were measured by a competitive chemiluminescence immunoassay using the Liaison Analyzer (DiaSorin Inc., Stillwater, MN). The inter-assay CV was below 10%. Vitamin D deficiency was defined according to the most recent cut-points defined by The Institute of Medicine as 25-OHD concentrations $<10$ $\mu$g/L.
**Results:** Plasma vitamin D level of PSS patients was insufficient in 42.2% of cases (plasma vitamin D level $<30$ $\mu$g/L) and in 57.8% of cases plasma vitamin D level was lower than 10 $\mu$g/L. Plasma vitamin D was lower than 10 $\mu$g/L in 66.66% of healthy controls. There is no significant variation of plasma vitamin D levels according to sex, in the PSS group. Plasma vitamin D levels are not significantly decreased in patients with central and/or peripheral neurological manifestations compared to patients with no neurological symptoms. Plasma vitamin D levels are, however; significantly lower in male patients than controls.
**Conclusions:** The incidence of vitamin D deficiency seems more important for PSS patients than healthy controls. It might be interesting to study these patients to examine the outcome of the disease and its severity after a vitamin D supplementation therapy.
**Disclosure of Interest:** None declared
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## AB0491 PLEURAL AND PULMONARY INVOLVEMENTS IN SYSTEMIC LUPUS ERYTHEMATOUS

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**Background:** Pleural and pulmonary involvements (PPI) occur in almost half of the patients with systemic lupus erythematous (SLE). The aim of the study was to determine prevalence of these manifestations in a group of Tunisian SLE patients and to describe their clinical, biological, and immunological characteristics.
**Methods:** We conducted a retrospective study of patients who fulfilled the revised ACR criteria of SLE admitted in an Internal Medicine department over a period time of 14 years. Patients with PPI related to SLE were included. Infectious states were excluded. Respiratory involvements were evaluated using chest x-ray, computed tomography (CT) and pulmonary function tests.
**Results:** Sixty six SLE patients had PPI (27%). The mean age was 36 years (ranges 14 to 69 years). The sex-ratio M/F was 0.1. Clinical symptoms were dyspnea (6 cases), chest pain (4 cases) and fever (32 cases). The chest X-Ray was abnormal in 66 cases: pleural effusion (n=65), atelectasis (n=2) and parenchymal opacities (n=1). CT showed parenchymal bands in three cases and fluctuating multifocal opacities in one patient. Pleural fluid was lymphocytic in all cases. Pulmonary function tests showed restrictive syndrome in two cases.
PPI was found in 44 cases (67%) at the time of SLE diagnosis and revealed the

disease in 18 cases. In other cases, PPI occurred after mean disease duration of 44 months. Pleural effusion was confirmed in 65 patients. Two patients had Shrinking syndrome. Bronchiolitis obliterans was diagnosed in one patients and organizing pneumonia in another one. Pulmonary hypertension was noted in 4 patients. Other involvements were noted in all patients: pericardial effusion (77%), cutaneaous manifestations (74%), lupus nephritis (36%), neurological involvements (14%) and myositis (9%). Comparison of patients with and without PPI involvements showed that pericarditis was significantly more frequent in patients with PPI (76.2% vs 22.6%; $p<0.001$). Antibodies to extractable antigens and anti-SSB/La antibodies were more frequent in these patients (94% vs 82.6%; p=0.049 and 57.9% vs 28.4%; p=0.001 respectively).
Patients received steroids and immunosuppressant drugs in 88% and 51% of cases respectively. Pleural effusion was recurrent in 7 patients. Mean duration of follow up was 69 months (range 0–187).
**Conclusions:** SLE had a wide spectrum pulmonary manifestations; pleural effusion is the most frequent. PPI can be due to lupus itself or to other associated conditions. In all cases, possible infectious and drug-induced causes should be ruled out.
**Disclosure of Interest:** None declared
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## AB0492 MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS: CAUSES AND RISK FACTORS IN A GROUP OF TUNISIAN PATIENTS

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**Background:** Mortality risk in patients with (SLE) is higher than in general population.
The aim of this study was to determine mortality causes in a group of SLE patients.
**Methods:** A retrospective study of patients who fulfilled the revised ACR criteria of SLE and admitted in an Internal Medicine department from 2000 to 2013. Data were recorded and analyzed for clinical, biological manifestations, infections and complications. Mortality causes were noted.
**Results:** Twenty three patients out of 246 SLE patients died (9.3%). They were 22 female and 1 male. Mean age at disease onset 33.5±16.1 years. During SLE course, patients presented with arthralgia (n=21), pericardial effusion (n=15), lupus nephritis (n=14), pleural effusion (n=9), hepatitis (n=7), neurologic manifestations (n=6) and pulmonary hypertension (n=2).
Patients were given corticosteroid in 95.6% of cases and immunosuppressive drugs in 60.8% of cases. Immunosuppressive treatment were based on cyclophosphamide (n=10), azathioprine (n=7), mycophenolate Mofetil (n=2) and cyclosporine (n=1). SLE was in remission in 82.6% of cases when death occurred and four patients were in relapse without other conditions.
Death was related to infections in 13 cases: pneumonia (n=5), urinary tract infection (n=4), skin infection (n=2), tuberculosis (n=1) and pulmonary aspergillosis (n=1). Three patients had cancer (one lung cancer, one cecum cancer and one still indeterminate). Death occurred in two patients because of heart failure and was related to a severe pulmonary hypertension. Pericarditis (65.2% vs 36.9%; p=0.01), anti-histone antibodies (83.3% vs 49%; p=0.031) and infections (91.3% vs 60.1%; p=0.004) were statistically more frequent in dead patients. Lupus nephritis was also more frequent in these patients (63.6% vs 43%; p=0.068).
**Conclusions:** Pericarditis and lupus nephritis were a poor factor prognosis in our series. Infection was the main cause of mortality in our patients. In addition to immunosuppression, poor socioeconomic status and lack of health care access in some patients can explain this high prevalence.
**Disclosure of Interest:** None declared
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## AB0493 RETINAL VASCULOPATHY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is one of the most common autoimmune diseases affecting multiple systems and organs. Retinal vasculopathy (RV) in SLE patients has a reported incidence of 3–29%[1–2]and often leads to poor visual outcome. However, there are limited data to date on this condition in Chinese patients, which might underestimate the importance of SLE with RV in daily practice.
**Objectives:** To analyze medical records of SLE inpatients from January 2006 to January 2016 and compare the clinical characteristics of SLE patients with and without RV.
**Methods:** All patients admitted to Peking Union Medical College Hospital from January 2006 to January 2016 fulfilled the revised ACR classification criteria for SLE (1997)[3]. For each case, two controls were randomly selected from contemporaneous SLE patients without clinical ophthalmic complaints.
**Results:** (1) The prevalence of RV was 0.66% (35/5298) in our cluster of SLE patients. The median duration of SLE before clinical retinal vascular disease was 12 months (range 0–168months). Seven out of 35 (20%) SLE patients with RV complained of ophthalmic disorders before they were diagnosed with SLE. Two patients presented ophthalmological disorder as initial manifestation. A total of 60 eyes were involved in these patients. Most (48/60, 80%) eyes presented with a decrease of visual acuity, 7/60 eyes had visual field loss, and 3/60 eyes presented diplopia.
The ophthalmic examination revealed cotton-wool spots (30/60, 50%), retinal vascular stenosis (31/60, 51.6%), vaso-occlusion (16/60, 26.7%) and hemorrhage (41/60, 68.3%)(Fig. 1).
(2) The nervous system involvement (51.4 vs. 24.3%, P=0.005) and hematological disturbance (62.9% vs. 34.3%, P=0.005) presented more frequently in patients in the case group than the control group.Patients in the case group presented a much lower frequency of positive anti-SSA antibodies than the control group (34.3% vs. 67.1%, P=0.001).
The patients in the case group had a more active SLE disease index. The mean (± SE) SLEDAI score was 19.9±0.9 points in cases compared to 10.2±0.7 points in controls ($P<0.001$).
(3)Nervous system disturbance (OR =4.340, 95% CI 1.438, 13.094, P=0.009) and leukocytopenia (OR =6.385, 95% CI 1.916, 21.278, P=0.003) were the independent risk factors, while anti-SSA antibody positive (OR =0.249, 95% CI 0.087, 0.710, P=0.009) was a protective factor for RV in SLE patients.

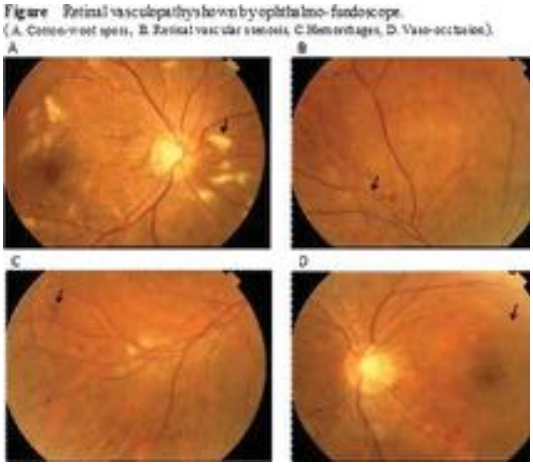


**Figure** Retinal vasculopathy shown by ophthalmo-fundoscope.
(A. Cotton-wool spots, B. Retinal vascular stenosis, C. Hemorrhages, D. Vaso-occlusion).

**Conclusions:** RV is one of serious ocular lesions in SLE patients not received enough attention yet in our Chinese clinical work. Fundus examination is recommended to be performed as soon as a patient is diagnosed with SLE to screen potential cases of RV in SLE patients. On the other hand, all RV patients with uncertain causes should be referred to a rheumatologist for further screening of SLE.
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**Disclosure of Interest:** None declared
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## AB0494 RISK FACTORS OF HEART DISEASE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Cardio vascular diseases are caused by premature development of atherosclerotic vascular lesions and thrombotic complications and the third leading cause to death in patients with systemic lupus erythematosus (SLE).
**Objectives:** Identify associated risk factors of cardiovascular disease in patients with SLE.
**Methods:** A total of 92 patients (9 men and 83 women) with a documented diagnosis of SLE according to the ARA criteria. The age of patients ranged from 18 to 55 years of age, disease duration ranged from 3 to 24 years. More than half part of patients with SLE have a subacute course of the disease (78.6%) and the average level of activity (80.2%). In clinical surveys were taken into account family history of cardiovascular disease, smoking, hypertension, diabetes mellitus (DM), body mass index, menopause in women, stress. It was detected biochemical blood tests to determine the lipid profile - total cholesterol, VLDL cholesterol, LDL cholesterol, HDL cholesterol, triglycerides. Also surveyed cerebral circulation according to Doppler ultrasound of the brachiocephalic vessels (SPL cylinder head).
**Results:** Classical cardiovascular risk factors (one or more) occurred in 85 (92.3%) patients. Thus, were the predominant dyslipidemia (78.7% of patients), mainly due to triglyceridemia, increase the level of total cholesterol and low

density lipoprotein. Hypertension was detected in 32.7% of patients, smoking - 13.6%, overweight - at 45.4%, family history of cardiovascular disease - at 27.2%, diabetes - at 4.5%, menopause in women - 15.8%, stress - 35% of patients. During the cylinder head ultrasound carotid artery vasoconstriction by type was detected in 77.2% of patients.

**Conclusions:** The results of this study confirm the high probability of the development of atherosclerosis and related complications in SLE patients, which calls for the timely detection and correction of modifiable risk factors.

**Disclosure of Interest:** None declared

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## AB0495 BIOMARKERS ASSOCIATED WITH INCREASED RISK OF THE PRESENCE OF ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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**Background:** Systemic lupus erythematosus is a common autoimmune disease occurring predominantly in women during reproductive age. Antiphospholipid syndrome (APS) is a prothrombotic, systemic autoimmune disease. Tumor necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK) is a recently identified proinflammatory cytokine of the TNF superfamily. The available evidences have indicated that TWEAK might be a target for therapeutic intervention in renal, vascular injury and neuropathy in systemic lupus erythematosus SLE. Hyperleptinaemia in the general population is also associated with atherosclerosis, hypertension and metabolic syndrome.

**Objectives:** Aim of the study was to evaluate the correlation between IMTand serum level of soluble TWEAK (sTWEAK), adipokine Leptin and traditional risk factors of atherosclerosis. Comparison between (sTWEAK) and Leptin in different studied groups.

**Methods:** The study is a case control study which conducted on 30 patients with SLE (A), 26 patients with secondry antiphospholipid syndrome (B), 14 patints with primary antiphospholipid syndrome (C) and 20 healthy volunteers with matched age and sex (D). All the study persons underwent full clinical assessment and investigations including Complete blood picture, ESR, kidney function tests, Lipid profile,body mass index.carotid duplex measuring intima media thickness (IMT). Serum soluble TWEAK and leptin using ELISA.

**Results:** The results showed high statistically signficant difference (P value $<0.001$) between group C and D, group B and C amd high statistically signficant difference (P value: 0.006) between group A and C as regards IMT. High statistically signficant difference (P value $<0.001$) between all groups as regards sTWEAK and leptin. With high level in those with antiphospholipid syndrome. There was no significant correlation btween (sTWEAK) and Leptin and IMT in different studied groups.

**Conclusions:** sTWEAK and leptin with other traditional risk factors can be a useful markers to predict and evaluate the presence of atherosclerosis in SLE and antiphospholipid patients.These findings should be taken into consideration as leptin contributes to increased oxidation, but further studies are required to determine whether hyperleptinaemia in patients with SLE contributes directly to increased oxidative stress.

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**Acknowledgement:** Many thanks for our dear patients, hoping for better health and life

**Disclosure of Interest:** None declared

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## AB0496 OCCURRENCE OF VASCULAR ACCESS THROMBOSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ON HEMODIALYSIS

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**Background:** In patients with lupus nephritis, the presence of antiphospholipid antibodies (aPL) is considered to be an indication of increased risk of thrombotic microangiopathy, a serious complication of SLE [1].

**Objectives:** To assess the occurrence of vascular access thrombosis in SLE patients on regular hemodialysis & its relation to the presence of antiphospholipid antibodies.

**Methods:** The study included 50 SLE female patients on regular hemodialysis; patients further subdivided into; *group A* included 34 patients with thrombotic history and/or fetal loss and *group B* included 16 patients without thrombosis and *group C* 20 female patients on regular hemodialysis with end stage renal disease caused by diseases other than SLE with age matching as a control group. All recruited from the dialysis units in Ahmed Maher Teaching Hospital, and Ain Shams University Hospital. After informed consent all the study population underwent full history taking, detailed clinical examination, measurement of anti-ds DNA, ANA, anticardiolipin IgG & IgM and lupus anticoagulant in addition to CBC, PT, PTT, Creatinine, ALT & AST and duplex on A-V fistula with measurement of intima media thickness.

**Results:** Age & dialysis duration matched groups were selected (37.24±8.88, 35.69±10.91 vs 37.15±9.21 yrs & 5±3.06, 5.06±3.04 vs 5.65±3.17 yrs respectively). We found that the level of anticardiolipin IgG & IgM and lupus anticoagulant were highly significantly higher in patients of group A than group B than group C (62.18±8.84 vs 20.74±5.73vs 13.41±5.70 u/ml, 46.96±9.72 vs 9.99±3.85 vs 7.12±2.68 u/ml, 63.26±12.05 vs 38.31±6.33 vs 2±0 respectively) ($p<0.001$). Also there was a highly significant thrombocytopenia in group A (132.41±15.10 vs 270.56±64.78 vs 264.05±67.80x$10^3$/$\mu$l) with prolonged PT and PTT (17.14±1.74 vs 13.47±1.55 vs 12.40±2.33 sec. and 45.24±6.32 vs 33.25±4.71 vs 29.55±3.62 sec) than group B & group C ($p<0.001$). There was a highly significant increase in intima media thickness of A-V fistula in group A than group B & group C (119.94±22.22 vs 51.19±15.58 vs 61.91±34.55 mm) ($p<0.001$).

**Conclusions:** SLE patients on regular hemodialysis with positive antiphospholipid antibodies have higher incidence of occurrence of vascular access thrombosis.

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**Acknowledgement:** We thanks all patients participating with us in this study.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4568

## AB0497 THE PREVALENCE OF AUTOANTIBODIES IN LYMPHOPROLIFERATIVE DISEASES AND THEIR CLINICAL IMPORTANCE

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**Background:** The association between lymphoproliferative diseases, like chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma (NHL), and autoimmunity is well-known. The risk of development of lymphoproliferative diseases, primarily lymphomas, is higher in autoimmune diseases, like systemic lupus erythematosus (SLE), Sjogren's syndrome (SS) and rheumatoid arthritis (RA). Until now, various studies evaluated markers of autoimmunity, like antinuclear antibody (ANA).

**Objectives:** We evaluated the frequency of some autoantibodies in CLL and NHL; and investigated their association with clinical findings.

**Methods:** Onehundred-and-ninetynine NHL patients (113 males, 86 females, mean age: 55.1+16.4) and 64 CLL patients were included into the study (36 males, 27 females, mean gae: 62.4+12.4). Blood samples were taken from the patients at the time of diagnosis. ANA, ANCA tests and ENA profile when deemed necessary were assessed by the immunofluorescence method by same technician. Rheumatoid factor (RF), anti-CCP were evaluated by the nephelometry method. The demographic and clinical features and outcome of patients were obtained from medical charts. In addition, the frequency of CLL and NHL in our RA and SLE cohort were evaluated.

**Results:** In NHL group, ANA was positive in 44 (22.1%); RF in 13 (6.5%); anti-CCP in 3 (1.5%); and ANCA in one patient. In CLL group, ANA was positive in 20 patients (31.7%), and RF in 7 (11.1%) patients; ANCA was positive in 3 patients; and anti-CCP was positive in 2 patients. Our NHL group included 3 RA (1.5% 3/199), one SLE (0.5%, 1/199) and one SS (0.5%, 1/199) patients. Our CLL patients included one RA (1.6%, 1/63), one SS (1.6%, 1/63) and one ANCA-associated vasculitis (1.6%, 1/63). In NHL patients, the frequencies of ANA positivity (29.1% vs. 16.8%) and RF positivity (11.6% vs. 2.7%) were higher in female patients (p values, 0.039 and 0.011). In CLL group, there was a trend to more frequent ANA positivity (40.7% vs. 25%); and less frequent RF positivity (3.7% vs. 16.7%) in female patients (p values$>$0.05). ANA positivity in NHL patients was at least at a titer of at least 1/100 in 25 cases; in 19 patients, it was positive at higher titers. In CLL patients, on the other hand, ANA was positive at a 1/100 titer in 11 cases; in 9 cases, it was positive at a higher titer. The frequencies of ANA and RF positivity were most common in subtypes of marginal zone lymphoma (30.8% vs. 23.1%). The mean age in NHL group was also significantly higher in RF- positive patients than in other patients (64.3±12.5 vs. 54.4±16.5, p=0.036). In CLL patients, the frequency of lymphadenopathy was significantly higher in RF-positive (15.6% vs. 0%, p=0.05) and ANA-positive (42.2% vs 5.6%, p=0.005) groups than in others.

**Conclusions:** ANA was the most commonly encountered autoantibody in both CLL and NHL patients. RF positivity was more frequent in CLL. RF and ANA were associated with the presence of lympadenopathy. The most common autoimmune disease in patients with lymphoproliferative diseases was RA.

**Disclosure of Interest:** None declared

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## AB0498 ETHNIC ASPECTS OF CHILDREN WITH SYSTEMIC LUPUS ERITHEMATOSUS

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**Background:** Clinical, genetic aspects of rheumatic diseases with a relation to the patients' ethnicity have increasingly become the subject of wide discussion in recent years. The significance of this problem is clearly seen in systemic lupus erythematosus (SLE).
**Objectives:** Explore ethnic, genetic features in children with SLE.
**Methods:** The basis of this work was aimed to survey results and data of archival materials of 153 SLE patients observed in the clinic of the Scientific Center of Pediatrics and Pediatric Surgery, the Republic of Kazakhstan. We studied the course and outcome of systemic lupus erythematosus in children of Kazakh and Russian population and features of distribution of HLA-class I loci in children Kazakh population.
**Results:** We observed 153 patients with SLE at the age from 3 to 15 years and older, including 120 children of Kazakh nationality (78.4%), and 33 - of Russian nationality (21.6%). Evaluating the activity of pathological processes, depending on the ethnicity, revealed that the highest activity (74.1% vs. 24.2%) and acute (69.2% vs. 33.3%) were in Kazakh children. In assessing the overall disease activity by SLEDAI scale, the children of the Kazakh population had 38,9±5,1 against Russian 22,1± 4,1 points. Thus, acute and the high degree of activity of SLE prevailed in Kazakh children ($P<0.05$).
Given the severity and outcome of SLE in the indigenous children, we studied the association between SLE and HLA - class I antigens in Kazakhs children. This study was carried out for the first time in Kazakh children. Antigens of HLA system loci A, B and C were determined in 62 Kazakh children between the 7–16 years with SLE. The control group included 277 healthy test donors of the same nationality. The most common alleles in locus HLA-A SLE was HLA-A1 ($p<0.001$); the highest rate in the locus B was found in: HLA-B5 ($p<0,01$), HLA-B7 ($p<0.01$), HLA-B15 ($p<0.01$), HLA-B35 ($p<0.01$); in the locus C: HLA-CW3 ($p<0.01$). Among them the increase of the frequency of antigen HLA-A1 and HLA-CW3 were significant (Pcorr.=0.01–0.08).
Compared with donors, the positive level of association was found in HLA - A1 ($\chi^2$=14,62, RR=3,04, $p<0,001$), HLA-B7 ($\chi^2$=6,16, RR=2,30, $p<0, 01$), HLA-B15 ($\chi^2$=6,61, RR=2,51, $p<0,01$), HLA-CW3 ($\chi^2$=7,91, RR=2,91, $p<0.01$) and negative association in HLA-B5 ($\chi^2$=6,29, RR=0,41, p=0,01), HLA-B35 ($\chi^2$=7,06, RR=0,26, p=0,01).
As a result of the studies, four tentatively called "risk" antigens were found and the severity of its clinical manifestations - HLA-A1, HLA-B7, HLA-B15 and HLA-CW3. HLA-B5 and HLA-B35 had the protective nature of SLE. Given the fact that the studies discovered four tentatively called "risk" antigens – HLA-A1, HLA-B7, HLA-B15, HLA-CW3 and two protector antigens – HLA-B5, HLA -V35, they were compared with the position of the risk attribute (etiologic and preventive fraction). It was found that the greatest contribution to the development of the disease was brought by the antigen HLA-A1 (RR=3,04, EF=0,32), and vice versa, a contribution to the resistance of the disease was made by HLA-B5 (RR=0,41, PF=0, 21).
**Conclusions:** Acute and the high degree of activity of SLE prevailed in children of Kazakh population. Determination of loci HLA- A1, HLA -B15, HLA-B7 and HLA-CW3 has a great importance in the prediction of severity and related tactics of management and treatment of patients.
**Disclosure of Interest:** None declared
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## AB0499 BONE MINERAL DENSITY IN POSTMENOPAUSAL MEXICAN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** It is accepted that patients with SLE exhibit an increased risk for low BMD and bone fractures; nevertheless, few studies have evaluated bone disorders in Latin American population. It is the first study that has evaluated frequency and correlations of low BMD in postmenopausal mestizo Mexican women with SLE
**Objectives:** To determine the frequency of osteoporosis and possible risk factor for low bone mineral density (BMD) in postmenopausal mestizo Latino American women with systemic lupus erythematosus (SLE)
**Methods:** A cross-sectional study was conducted among 100 postmenopausal patients with SLE. Patients were evaluated using a questionnaire about the follow variables: age at the time of the study, age at menopause, disease duration, disease activity, damage of the disease, cumulative corticosteroid dose, and history of fracture. Lumbar spine and hip measurements of BMD were performed by dual absorptiometry. Univariate and multivariate statistical analyses were used to assess relationship between risks factor and BMD.
**Results:** The mean age was 53.8±9.56 years and the mean SLE duration was 73.2±65 months. The mean BMD of the lumbar spine was 0.944±0.178 g/cm$^2$ and the hip was 0.915±0.135 g/cm$^2$. Osteopenia was present in 63% and osteoporosis in 31%. In the univariate analysis, age at the time of the study and menopause duration were associated with low BMD at the hip while age at the time of the study, menopause duration and damage of the disease were associated with low BMD at the lumbar spine. In the multiple regression analysis, low BMD in lumbar spine and hip were associated only with age (B= -0.0004, P=0.017; B= -0.0006, P= <0.05).
**Conclusions:** Osteopenia was found in 63% and osteoporosis in 31%. Risk factor for low BMD in both total hip and lumbar spine in postmenopausal SLE women was age.
**Disclosure of Interest:** None declared
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## AB0500 A NOVEL DNA-PEPTIDE COMPLEX DETECTS ANTI-DSDNA ANTIBODIES IN SLE SERA

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**Background:** The detection of anti-dsDNA antibodies is critical for the diagnosis and follow-up of SLE patients. The presently available assays are characterized by a non-optimal specificity (solid phase assays) or sensitivity (CLIF test).
**Objectives:** To overcome the limits of CLIFT and solid phase chromatin assays, we explored the diagnostic potential of an assay based on plasmid DNA containing a highly bent fragment of 211 bp from *Crithidia Luciliae* microcircles, complexed with histone peptides.
**Methods:** Electrically neutral complexes of PK201/CAT plasmid (PK) DNA and histone (H) 4 peptides were evaluated by electromobility shift assay. Complexes of H4 peptides and PK were absorbed to the solid phase to detect IgG antibodies in sera. Sera from 109 SLE patients, 100 normals and 69 disease controls (systemic sclerosis, Sjogren's syndrome, unclassified connective tissue disease) were tested.
**Results:** H4 (14–34) containing the consensus sequence for DNA binding interacts with PK retarding its migration. H4 (14–34)-PK complexes were used to test sera by ELISA; inhibition assays show that sera react with epitopes present on DNA or on the complex, not on the peptide. Anti-H4-PK antibodies were detected in 56% SLE sera (more frequently in patients with skin or joint involvement) vs 12% disease controls; antibody titer is correlated with ECLAM score and anti-C1q antibodies, negatively with C3 levels. Anti-H4-PK antibodies compared with CLIFT and solid phase dsDNA assays display moderate concordance.
**Conclusions:** The H4-PK assay is a simple and reliable test, endowed with high specificity and sensitivity, useful for the differential diagnosis and evaluation of disease activity of SLE patients. This assay increases the variety of anti-DNA antibodies that can be measured, complementing the assays currently used for the detection of anti-DNA antibodies.
**Disclosure of Interest:** None declared
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## AB0501 SJÖGREN SYNDROME, CANCER INCIDENCE AND MORTALITY IN VIGO AREA

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**Background:** Sjögren's syndrome (SS) is a systemic autoinflammatory disease with a well known epidemiological and laboratory characteristics. Its main symptoms are derived from exocrine glands affectation. Like other inflammatory diseases presents an increased incidence of malignancies. The diagnosis of this entity and subsequent identification of factors associated with the occurrence of tumors is important for early detection and management
**Objectives:** To analyze the epidemiological, clinical and laboratory characteristics and the occurrence of lymphoma and mortality in a cohort of patients in a tertiary hospital diagnosed with SS
**Methods:** Descriptive analysis of data collected retrospectively of patients with SS (criteria American-European 2002) between November 1989 and November 2012 the Hospital of Vigo
**Results:** We describe 58 patients with SS of which 86% were women with a mean age of 53±15 years.Mean follow-up time was 69 months (range5–343). Mean age at diagnosis was 50 years (range 26–87 years).Only 6 (10%) had a secondary SS associated with Lupus Erythematosus Systemic, Rheumatoid Arthritis, Scleroderma, Mixed Connective Tissue Disease and Sarcoidosis. We do not find any autoimmune disease associated with organ-specific.The 84.5% and 93% had ocular and oral symptoms respectively.The parotid scintigraphy

was performed in 25 (43%), which was pathological in 37 (68%).Salivary gland biopsy was performed in 30 (52%), 28 were diagnostic (93%).The most common extraglandular involvement was the joint (50%),followed the skin and lymph nodes (both 12%).24% have Raynaud's phenomenon with capilaroscopia nonspecific. Others, were central and peripheral nervous system (8.6% each one), respiratory (7%) and kidney (3%). None had muscle involvement. Anti-Ro was positive in 83% (59% also had anti-La) and anti-La was positive in only 48%.Antinuclear antibodies and rheumatoid factor were positive in 95% and 67% respectively. 22 (38%) had low C4 and 10 (17%) had low C3. Cryoglobulins were positive in 2 (3%). Only two patients have anti-Ro and anti-La negatives (they had xerostomia and xerophthalmia, parotid scan and biopsy compatible with the diagnosis). The cancer incidence was 10%, 2 were solid tumors (one pancreatic adenocarcinoma and another invasive ductal breast cancer) and 4 were hematologic (diffuse B lymphoma, angioimmunoblastic T lymphoma, Hodgkin's lymphoma and nodal MALT). All those who developed lymphoma they had previous lymphadenopathy. The mortality rate was 12%: 4 neoplasia (2 lymphomas, 1 pancreas and 1 breast), 2 infections, 1 cerebral hemorrhage.

**Conclusions:** The 89.6% of our series had a primary SS with the same collected clinical and serological features literature. The development of a neoplasm was the leading cause of death (57.1%). In our cohort over half the patients who had lymphadenopathy developed a hematologic malignancy. SS patients have a higher risk for hematologic malignancy, so based on our data, the occurrence of lymphadenopathy it is a warning sign which requires us to actively seek a lymphoproliferative process

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**Disclosure of Interest:** None declared

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## AB0502 PREVALENCE AND CLINICAL CHARACTERISTICS OF SECONDARY SJÖGREN'S SYNDROME AND SICCA SYMPTOMS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN DAILY CLINICAL PRACTICE

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**Background:** Patients with rheumatoid arthritis (RA) can develop sicca symptoms which may be related to secondary Sjögren's syndrome (sSS).

**Objectives:** To assess the prevalence and clinical characteristics of sSS in RA patients.

**Methods:** In this cross-sectional study, 96 consecutive established RA patients referred to our outpatient clinic were submitted to a complete diagnostic work-up for the presence of sSS according to the American-European Consensus Group criteria.[1] Patients underwent clinical examination including DAS-28 score, Schirmer's test and sialometry of submandibular/sublingual (SM/SL) glands and parotid (PAR) glands. In addition, patients were asked to complete the Health Assessment Questionnaire (HAQ), RAND-36 and Multidimensional Fatigue Inventory (MFI). Clinical characteristics were compared between RA patients fulfilling the criteria for sSS, RA patients with at least one sicca symptom of the eyes or mouth but no sSS and RA patients without sicca symptoms.

**Results:** Of the 96 included RA patients, 75 (78%) were female, mean age was 54±10 years and median disease duration of RA was 10 years (IQR 5–17). In total, 38 patients (39.6%) reported to have at least one sicca symptom of the eyes or mouth. Six patients (6.3%) were diagnosed with sSS. RA patients with sSS had higher disease activity, lower tears production and lower salivary flow rates compared to patients with and without sicca symptoms. Patients with sicca symptoms used more often xerogenic drugs, had higher disease activity and lower salivary flow rates than patients without sicca symptoms. No differences were found in the proportion of patients that were anti-SSA/SSB antibody positive between the groups. Furthermore, both patients with sSS and patients with sicca symptoms experienced worse physical functioning, lower health-related quality of life and more fatigue than RA patients without sicca symptoms (Table 1).

**Conclusions:** The prevalence of sicca symptoms and sSS was 39.6% and 6.3%, respectively, in our study group of established RA patients in daily clinical practice. Both the presence of sicca symptoms and sSS was associated with higher disease activity, impaired health-related quality of life and fatigue in RA patients.

Table 1. Clinical characteristics of RA patients with sSS, with sicca symptoms but no sSS, and without sicca symptoms.

| | sSS (n=6) | Only sicca (n=32) | Non-sicca (n=58) | P-value (overall) |
|---|---|---|---|---|
| Demographics | | | | |
| Female gender | 5 (83%) | 28 (88%) | 42 (72%) | 0.241 |
| Age (yrs) | 58 ± 7 (60) | 54 ± 8 (55) | 54 ± 12 (56) | 0.655 |
| Disease variables | | | | |
| Time since RA diagnosis (yrs) | 15 ± 9 (13) | 14 ± 9 (11) | 10 ± 8 (10) | 0.175 |
| RF positive | 6 (100%) | 28 (88%) | 48 (83%) | 0.481 |
| Anti-SSA positive | 1 (17%) | 2 (6%) | 4 (7%) | 0.661 |
| Xerogenic drug use | 4 (67%) | 26 (81%)* | 29 (50%) | 0.014 |
| Presence of erosions | 6 (100%) | 27 (84%) | 39 (67%) | 0.068 |
| Presence of EAMs | 4 (67%) | 17 (53%) | 25 (43%) | 0.421 |
| DAS-28$_{ESR}$ | 5.1 ± 1.4 (5.9)*† | 3.2 ± 1.1 (3.1)* | 2.7 ± 1.1 (2.6) | 0.001 |
| ESR | 38 ± 13 (38)*† | 22 ± 17 (21) | 19 ± 15 (15) | 0.018 |
| CRP | 27 ± 19 (24)*† | 10 ± 10 (6) | 10 ± 13 (5) | 0.016 |
| HAQ | 1.4 ± 1.0 (1.4)* | 1.0 ± 0.6 (1.0)* | 0.5 ± 0.6 (0.4) | 0.001 |
| Dryness | | | | |
| Schirmer's test (mm/5min) | 3.9 ± 1.8 (3.0)*† | 15.4 ± 11.4 (13.8) | 16.7 ± 10.5 (14.0) | 0.001 |
| SM/SL rest (ml/min) | 0.05 ± 0.04 (0.05)*† | 0.15 ± 0.10 (0.11)* | 0.27 ± 0.24 (0.18) | 0.001 |
| SM/SL stimulation (ml/min) | 0.11 ± 0.11 (0.07)*† | 0.38 ± 0.33 (0.34)* | 0.55 ± 0.32 (0.50) | 0.000 |
| PAR rest (ml/min) | 0.01 ± 0.02 (0.01)* | 0.04 ± 0.04 (0.03)* | 0.07 ± 0.06 (0.07) | 0.000 |
| PAR stimulation (ml/min) | 0.06 ± 0.04 (0.05)* | 0.14 ± 0.11 (0.10) | 0.18 ± 0.12 (0.16) | 0.013 |
| RAND-36 | | | | |
| Physical functioning | 38 ± 29 (40)* | 48 ± 24 (50)* | 69 ± 25 (75) | 0.000 |
| Role physical | 17 ± 41 (0)* | 35 ± 41 (25)* | 64 ± 42 (100) | 0.002 |
| Bodily pain | 37 ± 24 (38)* | 57 ± 21 (57)* | 70 ± 19 (67) | 0.001 |
| General health | 33 ± 14 (35)* | 42 ± 21 (35)* | 54 ± 22 (55) | 0.012 |
| Vitality | 31 ± 12 (33)*† | 54 ± 22 (50)* | 66 ± 18 (70) | 0.000 |
| Social Functioning | 50 ± 18 (44)* | 67 ± 25 (63)* | 81 ± 19 (88) | 0.001 |
| Role emotional | 56 ± 50 (67) | 73 ± 42 (100) | 81 ± 35 (100) | 0.434 |
| Mental health | 56 ± 18 (52)*† | 76 ± 20 (80) | 80 ± 15 (84) | 0.020 |
| MFI | | | | |
| General fatigue | 14 ± 2 (14)* | 12 ± 4 (12)* | 9 ± 4 (10) | 0.001 |
| Physical fatigue | 15 ± 3 (16)* | 12 ± 4 (13)* | 9 ± 4 (10) | 0.000 |
| Reduced activity | 14 ± 4 (16)* | 11 ± 5 (12)* | 9 ± 4 (8) | 0.004 |
| Reduced motivation | 15 ± 4 (16)*† | 10 ± 4 (10) | 9 ± 4 (8) | 0.003 |
| Mental fatigue | 12 ± 3 (12)* | 9 ± 5 (9)* | 7 ± 3 (6) | 0.006 |

Values are presented as number of patients (percentage) or mean ± SD (median).
*p<0.05 compared to non-sicca group.
†p<0.05 compared to only sicca group.

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**Disclosure of Interest:** None declared

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## AB0503 LARGE VESSEL VASCULITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS - A CASE SERIES FROM A SINGLE CENTRE IN SOUTH INDIA

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**Background:** In Systemic lupus erythematosus (SLE), vasculitis is seen in 11% to 36% of patients. Small vessel vasculitis is seen in upto 86% and medium vessel vasculitis in the rest, and rarely large vessels are involved. We present a series of 4 such patients which is unique in that aortitis and lupus were diagnosed at the first presentation.

**Objectives:** To study the clinical profile of SLE patients presenting with Large vessel vasculitis (LVV).

**Methods:** Patients presenting to Rheumatology department between January 2012 and February 2015 fulfilling ACR criteria for SLE with evidence of large vessel involvement clinically and by Doppler ultrasound, CT angiography or MR angiography were included and followed prospectively. Demographic, clinical, laboratory and imagelogy data were studied.

**Results:** All patients were females, between 21–37 years of age. All had clinical features suggestive of SLE with a positive serology for ANA and double stranded DNA. Mean age of the patients was 25.25±4 years, with median duration of disease of 34.5 (range 4 -60) months with mean SLEDAI of 22±7.

All patients had history of claudication of extremities. Imaging findings are described in table 1.

Patients 1, 2 and 4 had subclavian artery and aortic bruit. Patient 3, who presented with cerebrovascular accident had MR angiography showing multiple focal intracranial vessel stenosis along with large vessel involvement. Three patients had nephritis, one had CNS lupus. Three patients had high ESR 68,106,70 mm after one hour. One patient had a positive Anticardiolipin antibodies (1/3). Three had low complements (3/3). Patient 2 underwent renal biopsy, and found to have class V lupus nephritis.

Patient 1,2 and 3 received intravenous pulse cyclophosphamide therapy, Patient 4 was treated with azathioprine. Patient 1 underwent PTCA to aorta and subclavian artery in view of persistent claudication. After a mean follow up of 29±22 months all patients are stable.

**Abstract AB0503** – Table 1

| Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|
| CT angiogram | CT angiogram | CT angiogram | Doppler ultrasonogram |
| Circumferentially thickened descending aorta and left subclavian artery | Segmental stenosis (7cm) of descending thoracic aorta, upto level of aortic hiatus with post stenotic dilatation, stenosis of second part of left subclavian artery with irregularity of the wall. | Narrowing of the 1st and 2nd part of subclavian artey and entire left radial artey | Doppler showed reduced flow b/l subclavian brachial, radial, femoral, dorsalis pedis and posterior Tibial.A |



**Conclusions:** Large vessel involvement in SLE predominantly involves aorta and subclavian arteries and is associated with high disease activity.

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**Disclosure of Interest:** None declared

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## AB0504 HTR2A POLYMORPHISMS INFLUENCE IN SYSTEMIC LUPUS ERYTHEMATOUS CLINICAL, IMMUNOLOGICAL MANIFESTATION AND DAMAGE ACCRUAL

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**Background:** Serotonin receptor 1A and 2A genes polymorphisms (HTR1A and HTR2A) have been associated to increased risk of depression and suicide. Hypomethylated HTR1A has been associated to Systemic Lupus Erythematosus (SLE) patients manifestations. Preliminary results in our cohort showed an association between HTR2A polymorphisms and SLE manifestations development risk and depression risk in SLE patients.

**Objectives:** To investigate the association of 5-HTR2A polymorphisms (rs6314, rs6313) and clinical organ involvement, specific antibodies expression and damage accrual and time to damage accrual in SLE patients.

**Methods:** 75 SLE patients were evaluated for 5-HTR2A polymorphisms rs6314 and rs6313, by a Taqman assay and PCR-RFLP methodology, respectively. SLE diagnosis was based in ACR 1999 criteria, the organic involvement and specific antibodies were reviewed in the charts (Cumulative SLE manifestations for genetic studies) and damage was assessed by SDI (Systemic Lupus International Collaborating Clinics - Damage Index). Statistical analysis was made with SPSS 22.0.

**Results:** 75 SLE patients (70 female) with a mean age of diagnosis of 29.55 years old (SD 12.0) and mean follow-up time of 17,39 years (SD 7,70). Mucocutaneous involvement occurred in 88%, articular 85,3%, renal 46,7%, 30,7% neuropsychiatric. 38 patients (50,7%) had organ damage acrrual with a mean time to first damage accrual of 3,75 years (SD 6,88). 7 (9,3%) accrued renal damage and 15 (20%) neuropsychiatric. Polymorphism distribution was rs6313 (CC 22,7%, CT 54,7% e TT 14,7%) and rs 6314 (CC 86,7%, CT 13,3%). No association was found between these polymorphisms and any clinical involvement, cytopenias, antibodies, damage accrual or time to damage. Neuropsychiatric damage accrual was earlier in patients carrying CC rs6314.

**Conclusions:** Contradictory results are a very common phenomena in studies of complex diseases mainly due to the interaction fo several genes. Although poorly studied the serotonin receptor and transporter genes have been linked to SLE development and depression in SLE patients. In our study, there was no relation between any clinical or serological manifestations and the rs6313 and rs6314 HTR2A polymorphism but the earlier neuropsychiatric damage accrual opens a window of doubt of what might be the role of serotonin in SLE heterogeneity.

**Disclosure of Interest:** None declared

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## AB0505 PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Pulmonary arterial hypertension (PAH) is a rare disease characterized by the progressive increase in pulmonary artery pressures, leading to right heart failure. Systemic lupus erythematosus (SLE) is the second connectivity after Scleroderma can be complicated by PAH. This study aims to estimate the prevalence of PAH in SLE, detected by echocardiography.

**Methods:** This is a retrospective study of ten years about 80 patients with SLE fulfilling the criteria of the ACR (American College of Rheumatology), followed in our department of internal medicine. Echocardiography with measurement of pulmonary artery pressure was performed in 72 patients. Above 30 mmHg mean arterial pressure was used to define PAH.

**Results:** Ten patients (7% of cases) had pulmonary arterial pressure greater than 30mmHg. Two of them had lung disease (the first with emphysematous lung and the other a lupus interstitial lung disease). Three patients had mitral insufficiency. A syndrome of anti-phospholipid antibodies (APS) was noted in four patients (40% of cases). Five other lupus patients had isolated PAH (50% of cases). We noted a positive anti-Sm antibody in three patients (40% of cases).

**Conclusions:** PAH is a rare and severe complication of SLE and is a bad prognostic factor. Its detection is based on echocardiography. PAH lupus may be the expression of APS or secondary to pulmonary fibrosis or left valvulopathy. The treatment is based on corticosteroids and immunosuppressive association. Anticoagulants are indicated in cases of APS.

Due to the severity of PAH in SLE, a screening echocardiography should be systematically offered to patients with SLE to treat early this serious complication and to enhance prognosis.

**Disclosure of Interest:** None declared

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## AB0506 SYSTEMIC LUPUS ERYTHEMATOSUS: NEUROPSYCHIATRIC MANIFESTATIONS

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**Background:** Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by autoantibody production, complement activation and deposition of immune complexes in tissues and organs. According to different authors about 25–79% of the SLE patients have neuropsyhiatric involvement (NPSLE) at same point of the disease course. The latter could be the only and single disease manifestation but often NPSLE is present in patients with active disease.

**Objectives:** Our objective is to present the results from our study about the neuropsychiatric manifestations in patients with SLE. Based on its results we propose a new set of criteria for NPSLE. The use of these criteria for the last 5 years in Bulgarian patients with SLE proved their high sensitivity and specificity.

**Methods:** In order to determine the type and incidence of nervous system (NS) damages clinical, laboratory, and instrumental examinations were performed in a total number of 225 patients with SLE for a total period of 9 years. Depending on the specific features of the clinical course the patients were divided into three groups: with clinically manifested NS damages, without clinically manifested NS damages and with incomplete SLE. Patients with rheumatoid arthritis and healthy controls matched for age and gender were used as control groups.

**Results:** The study showed high percentage (64,44%) of neuropsychiatric manifestations in the SLE patients. Cognitive dysfunctions were found in 49,33% of the SLE patients. According to this set of criteria the NPSLE diagnosis should be made in the presence of at least one indicator from the first group of criteria (seizures, psychosis, cerebrovascular event, lesion of cranial nerves, motor disturbances, quantitative alterations of consciousness) and at least two indicators from the second group of criteria (cognitive dysfunction, headache due to lupus, peripheral neuropathy, MRI changes, EEG changes, ENMG changes, positive aRPA, positive aPL) after excluding other causes than SLE for their occurrence.

**Conclusions:** The use of the proposed criteria of NPSLE with high specificity and sensitivity is of practical value allowing earlier detection of NS damages and introduction of adequate pathogenic treatment.

**Disclosure of Interest:** None declared

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## AB0507 EARLY DETECTION OF ASYMPTOMATIC PLEUROPULMONARY MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS BY HIGH RESOLUTION CT AND PULMONARY FUNCTION TESTS

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**Background:** (SLE) is a prototype of an autoimmune disease with a broad variety of clinical manifestations, particularly affecting the kidneys and the central nervous

system. Autoantibodies against double strand DNA (Anti ds DNA) and a number of other nuclear and cytoplasmic antigens as well as spontaneous immunoglobulin producing cells are characteristic of SLE, reflecting an aberrant immune response (1). Patients may manifest serious and life threatening complications of the disease with relapses and remissions (2). Thoracic manifestations of the rheumatic diseases (RDs) are a significant cause of morbidity and mortality worldwide. The five RDs most frequently associated with pleuropulmonary disease are: Rheumatoid arthritis (RA), (SLE), Progressive systemic sclerosis (PSS), Polymyositis/dermatomyositis (PM/ DM), Sjogren syndrome (SS). The clinical presentation is highly variable, ranging from pleuritic pain alone to slowly progressive breathlessness accompanied by cough. On occasion RD may present acutely with overwhelming respiratory failure as the first pulmonary manifestation (3). Asymptomatic involvement is more common and abnormalities in pulmonary function tests have been cited in up to two thirds of patient with SLE in some studies.

**Objectives:** The aim of this study is the early detection of asymptomatic pleuropulmonary manifestation of systemic lupus erythematosus using high resolution CT and pulmonary function tests.

**Methods:** During study period (May 2013 to June 2015), 30 SLE patients (29 female and 1 male) were included in this prospective study. The patients were diagnosed according to the American College of Rheumatology criteria for the classification of SLE. All patients were asymptomatic for any pulmonary manifestations. Plain chest X-ray, HRCT and pulmonary functiontests (PFTs) were performed for all patients. Analysis of data was done by Compaq computer using SPSS (statistical program for social science version 14).

**Results:** The high resolution CT findings in the studied patients were positive in 12 (40%) out of 30 patients and negative in 18 (60%) out of 30 patients. The plain x-ray finding in the studied patients were positive in 3 (10%) out of 30 patients. The pulmonary function tests were as the following: restrictive disease in 5 (16.7%) out of 30 patients, the rest of patients were normal and no obstructive disease

**Conclusions:** The pulmonary manifestations are present in SLE patients even in asymptomatic cases, at some point of time during the course of the disease. Some of these manifestations may remain asymptomatic. The use of CT scan and pulmonary function tests will help in early recognition and introduction of the therapy will help in preventing the morbidity and mortality in such cases.

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## AB0508 SERUM AND URINARY INTERFERON-GAMMA-INDUCIBLE PROTEIN 10 IN LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) is one of the serious complications of systemic lupus erythematosus (SLE). Finding reliable non-invasive biomarkers for LN will help to improve disease outcomes. IFN-γ-inducible protein 10 (IP-10) is a pro-inflammatory chemokines which is involved in the immunopathogenesis of LN. Thus, we investigated the role of IP-10 as a potential marker of LN.

**Objectives:** To identify the sensitivity, specificity and cut-off value of serum and urinary IP-10 level in LN patients compared to albumin/creatinine ratio and anti-dsDNA.

**Methods:** We included 30 female SLE patients and 10 age-matched healthy female controls. SLE disease activity index (SLEDAI) was calculated. Active SLE was defined as SLEDAI $\geq$4. Patients were divided into 10 SLE patients with LN, 10 active SLE without LN and 10 inactive SLE patients. Serum and urinary levels of IP-10 were measured by ELISA. Anti-dsDNA and urine albumin/creatinine ratio were measured. Renal biopsy was performed to LN patients.

**Results:** Mean age of patients was 30±10 years versus 32±9 years in controls. Mean disease duration was 52±16 months. Mean SLEDAI was 10.2±3.6.

Active SLE patients had significantly increased serum IP-10 (324±224 pg/dl) and urinary IP-10 (172±206 pg/dl) as compared to inactive SLE (215±188 pg/dl and 121±150 pg/dl respectively) ($P<0.01$) and healthy controls (103±28 pg/dl and 32±13 pg/dl respectively) ($P<0.008$).

No significant difference was found in serum and urinary IP-10 levels between active LN and active non-renal patients, even in biopsy-proved proliferative LN patients.

Serum and urinary IP-10 positively correlated with SLEDAI ($r=0.416$; $P<0.02$) and ($r=0.448$, $P<0.01$) respectively.

By receiver operating characteristics (ROC) analysis, serum and urinary IP-10 could be used to diagnose SLE with serum IP-10 being better [p=0.011, AUC, 95% confidence interval (CI) = 0.772 {0.629–0.915}, P=0.018, AUC 95% CI = 0.753 (0.606–0.901) respectively].

A value of serum IP-10 116.5 pg/ml as a cut-off value is best in differentiating SLE patients from healthy controls with 76% sensitivity and 70% specificity. A value of urinary IP-10 37.9 pg/ml is best in indicating SLE with 70% sensitivity and 70% specificity.

Serum IP-10 could differentiate active from inactive SLE [P=0.007, AUC (95% CI = 0.753 (0.594–0.911)]. It is better than urinary IP-10, albumin/creatinine ratio and anti-dsDNA [AUC {95% CI = 0.654 (0.467–0.841); {0.529 (0.317–0.742)} {607 (402–812)}].

A value of serum IP-10 136 pg/ml is best in differentiating active from inactive SLE with 81% sensitivity and 71% specificity.

Serum and urinary IP-10 did not significantly differentiate either LN from SLE without LN [AUC 95% CI = 0.633 (0.430–0.837), 0.610 (0.397–0.823)], nor active renal SLE from active non renal SLE (AUC [95% CI = 0.533 (0.230–0.837), 0.700 (0.431–0.969)].

Albumin/creatinine ratio is a better marker in differentiating between SLE with LN and SLE without LN [P=0.008, AUC (95% CI = 0.803 (0.610–0.995)]

Any of the serum and urinary IP-10, albumin/ creatinine ratio, and anti-dsDNA didn't correlate with the class of lupus nephritis (P=0.658, 0.647, 0.807 and 0.069 respectively).

**Conclusions:** Serum and urinary IP-10 are useful markers of lupus activity; however, they are not indicative of renal activity. Albumin/creatinine ratio is superior in identifying LN and renal activity.

**Disclosure of Interest:** None declared

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## AB0509 SERUM DICKKOPF-1 (DKK1) AND ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

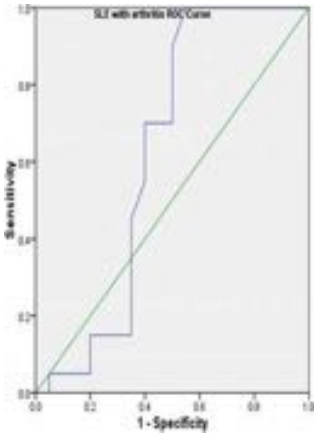
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**Background:** Systemic lupus erythematosus (SLE) is a chronic multi-organ autoimmune disease. Among the various clinical manifestations, arthritis is one of the most common features. Arthritis in SLE is usually considered mild and non-erosive; however, chronic pain and deformities are frequently reported by patients with longstanding disease. The underlying mechanism for arthritis and joint damage in SLE is not very clear. It is increasingly recognized that Wnt pathway is considered as a key signalling pathway in bone homeostasis. Dickkopf-1 (DKK-1) is an inhibitory molecule that regulates the Wnt pathway. The potential role of DKK1 in the pathogenesis of arthritis in SLE patients is not clearly understood. Therefore, we are investigating the relationship between serum DKK-1 and arthritis in patients with SLE aiming at finding new therapeutic targets in SLE patients.

**Objectives:** To identify the sensitivity, specificity and cut-off value of serum DKK1 in SLE patients with arthritis.

**Methods:** We recruited 84 subjects (44 SLE patients and 40 age and gender-matched healthy control subjects). SLE patients were divided into 2 groups; the first group included 22 SLE with arthritis and the second group included 22 SLE patients without arthritis or joint involvement. Arthritis was based on the American college of rheumatology (ACR) definition in the classification criteria for SLE.To be included in the analyses, the arthritis must have been documented by the treating physician and have been present for at least the two weeks preceding the clinic visit. We used SLE disease activity index (SLEDAI) for assessment of disease activity. Active lupus was defined as SLEDAI $\geq$4. Serum DKK1 was measured using ELISA. We measured anti-dsDNA, C3, C4, CRP and ESR. Plain X-ray was done to all patients.

**Results:** Mean age of the patients was 34.6±4.7 and mean age of the controls was 32.07±8.1. Most of the study groups were females (88.6% of the patients and



87.5% of the controls). Mean disease duration was 8.4±4.5 years. Mean SLEDAI was 10.7±6.8.
Patients with SLE had significantly increased serum DKK1 (2749±1675 pg/ml) compared to controls (2020±771 pg/ml) ($P<0.019$). SLE patients with arthritis had significantly higher levels of serum DKK1 than SLE patients without arthritis (2748±199 pg/ml and 2462±331 pg/ml respectively) ($P<0.042$).
Serum DKK1 didn't show any correlations with SLEDAI, CRP, ESR, C3, C4 or anti-dsDNA levels. No correlation was found between serum DKK1 and disease duration or age of the patients.
By receiver operating characteristics (ROC) analysis, serum DKK1 could be used to diagnose SLE patients with a diagnostic cut-off value of 1560 pg/mL [area under curve (AUC) 0.631 (95% CI, 0.509- 0.755)], sensitivity 82.5%, and specificity 45.5%. A value of serum DKK1 1920 pg/mL as a cut-off value is best in differentiating SLE patients with arthritis from SLE patients without arthritis with sensitivity 70%, and specificity 50% [(AUC) 0.622 (95% CI, 0.432- 0.813)]. Serum DKK1 couldn't differentiate between active and inactive SLE patients.
**Conclusions:** High serum DKK1 level is associated with arthritis in SLE patients. Therefore, DKK1 could have a role in the pathogenesis of arthritis in SLE patients and strategies that block DKK1 may be of potential therapeutic interest.
**Disclosure of Interest:** None declared
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## AB0510 CHRONIC DAILY HEADACHE DETERIORATES THE QUALITY OF LIFE IN KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Headaches is common in patients with systemic lupus erythematosus (SLE) [1]. However, the lack of specific clinical distinctions for headache in SLE has made it difficult to elucidate its pathophysiology. Chronic daily headache (CDH) is a category of headache disorders that occurs more than 15 days per month and is associated with a profound decline in the quality of life [2].
**Objectives:** The aim of this study is to investigate the clinical characteristics of CDH in patients with SLE and their association with disease severity and the quality of life.
**Methods:** A total of 40 consecutive patients with SLE participated in the survey. We investigated headache characteristics, visual analogue scale (VAS) for pain, and six-question headache impact test (HIT-6) to evaluate the impact of headache on the quality of life. The patients underwent required blood tests for assessment of disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI).
**Results:** Six patients (15%) met the criteria for CDH. The total score of HIT-6 is significantly higher in SLE patients with CDH than in those patients who suffered from headache without CDH (P=0.027). SLE patients with CDH in particular had a higher prevalence of "wish could lie down" than those who suffered from headache without CDH (P=0.017). The multivariate regression analysis indicates that the headache days per month was a predictor for headache-related disabilities.
**Conclusions:** As far as we know, this is the first study of its kind to evaluate the correlation of CDH and the quality of life in Korean patients with SLE. CDH may deteriorate the quality of life in patients with SLE.
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**Disclosure of Interest:** None declared
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## AB0511 MINOR SALIVARY GLAND (MSG) BIOPSY FINDINGS IN INDIAN PATIENTS WITH SJÖGREN'S SYNDROME AND THEIR CORRELATION WITH EXTRA-GLANDULAR MANIFESTATIONS

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**Background:** Minor salivary gland (MSG) biopsy has assumed greater importance in the classification of patients with Sjögren's syndrome fter publication of the ACR criteria[1]. In addition, germinal center (GC) like structures on MSG biopsy, have been reported to predict future risk of lymphoma[2]. Sjögren patients in India are younger and have more extraglandular features compared to western cohorts.[3] There has been no data regarding biopsy findings and ACR criteria utility in Indian patients.
**Objectives:** Determine utility of MSG biopsy in Indian Sjögren patients. Determine correlation of biopsy findings with extraglandular manifestations of Sjögren's syndrome.
**Methods:** After Institutional Ethics Committee approval, a retrospective review was done to determine all minor salivary gland biopsies in our hospital from July 2013 to Sept 2015.Among the biopsy specimens, patients diagnosed as Sjögren's were selected and their slides were reviewed by pathologist.Clinical characteristics were determined by retrospective chart review.
**Results:** A cohort of 26 patients emerged. Nearly all were female (25/26) and fulfilled the ACR criteria (25/26). The mean age was 56.9 years.Twenty one patients had an extra glandular manifestation.Arthritis was seen in 14 patients,2 patients had renal involvement 2 patients had vaculitis,3 patients had interstitial lung disease,1 patient had pulmonary artery hypertension, and hematological involvement was seen in 7 patients.Salivary gland biopsy was positive in 20. ANA was positive in 23 of 26 patients, RF in 16/25, anti-Ro antibody in 8/18 & anti-La in 7 of 18 patients.The mean focus score was 1.7/mm$^2$ with a maximum score of 9.57/mm$^2$.There was no statistical difference in proportion of positivity of biopsy (4/5) or mean focus score (2.01/mm$^2$)between patients with extra glandular involvement and those without (16/21 and 1.71/mm$^2$).Mean focus score and proportion of positive MSG biopsy was also similar between patients with arthritis and those without. Only 2 patients (7.7%) had germinal centers (GC) like structures in the biopsy.Both patients with GC like structures had extra glandular features, were biopsy positive and had a focus score of 6.175/mm$^2$. Among patients without GC like structures 19 out of 24 had extra articular features, 18 out of 24 were biopsy positive and the mean focus score was 1.41/mm$^2$. These patients are under follow up for possible progression to lymphoma.
**Conclusions:** In this small cohort of Indian Sjögren's patients who had undergone biopsy the ACR criteria was sensitive enough to be fulfilled in nearly all patients.Similar to previous Indian series, extra glandular features were more frequently observed compared to western cohort. Only two patients had germinal centers.(c.f. ~25% in Theander et al.[2]).Among patients with GC like structures there seemed to higher focus score and more extraglandular features.However, biopsy findings did not appear to correlate with extraglandular manifestations.
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## AB0512 USE OF NOMINAL GROUP TECHNIQUE TO FACILITATE ITEM REDUCTION FOR SLE CLASSIFICATION CRITERIA DEVELOPMENT

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**Background:** Criteria for the classification of SLE are being developed with the support of EULAR and ACR. Two independent exercises (expert-based Delphi exercise and data-driven cohort evaluation of early SLE and controls) were undertaken to generate candidate criteria, and then reduce them to a smaller set.
**Objectives:** To select a set of items that maximizes the likelihood of SLE in a person with an uncertain diagnosis.
**Methods:** A panel of seven international SLE experts (reflecting practice in Spain, France, Germany, United States, Canada and Mexico) was asked to rank 41 candidate criteria nominated in the Delphi and cohort studies. The rankings were presented at a face-to-face meeting of the expert panel and steering committee. A consensus meeting using nominal group technique (NGT) was conducted to reduce the list of criteria for consideration. Redundant or poorly performing criteria were removed.
**Results:** This expert panel NGT exercise reduced the candidate criteria for SLE classification from 41 to 21. The panel distinguished potential "entry criteria", which would be required for classification, from other potential "additive criteria", summarized in Table 1. Entry criteria were ANA by hep 2 immunofluorescence ≥1:80, and low C3 and/or low C4.
Additional work is needed to refine definitions*, to evaluate their independence and relationships within domains, and to ascertain item weights.
**Conclusions:** This expert panel NGT exercise resulted in 21 candidate SLE

Table 1. Additive criteria

| Lupus nephritis by renal biopsy with immune deposits |
|---|
| Rash with dermoepidermal interface changes and/or immunoglobulin and/or complement deposition on immunofluorescence |
| Anti-dsDNA antibody |
| Anti-Smith antibody |
| Presence of multiple autoantibodies* |
| Antiphospholipid antibodies (*LA, anti-Cardiolipin, anti-beta2GPI, or prolonged RVVT*) |
| Leukopenia (<4000/mm$^3$on 2 or more occasions) |
| Thrombocytopenia <100,000 on 2 or more occasions |
| Autoimmune hemolytic anemia |
| Active urine sediment (without UTI) |
| Persistent proteinuria (>0.5g/day) |
| Acute cutaneous lupus: SLICC definition |
| Chronic cutaneous lupus: SLICC definition |
| Alopecia with associated scalp inflammation |
| Arthritis (inflammatory arthritis tender or swelling)* |
| Serositis *(pleural, pericardial effusion, pleurisy, pericarditis, peritonitis)* |
| Oral mucosal lesions on the hard palate |
| CNS manifestations *(seizures, psychosis, chorea, myelitis, optic neuritis, stroke or acute confusional state*) |
| Fever* |

classification criteria. Refinement of definitions, ability to cluster criteria into domains and weighting of criteria will be ascertained in the next phase.

**Acknowledgement:** This work was supported by EULAR and ACR

**Disclosure of Interest:** None declared

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## AB0513 PREGNANCY OUTCOME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is associated with increased pregnancy complications. In addition, pregnancy may lead to disease exacerbations in SLE. Another problem is infertility and early menopause caused by drugs, like cyclophosphamide.

**Objectives:** In this study, we aimed to evaluate pregnancy complications and menstrual problems in SLE patients.

**Methods:** Out of 400 regularly followed SLE patients, 73 patients with 86 pregnancies during the last 5-year period from 2 centers were included. SLE patients were questioned about the presence of pregnancy, history of menstrual cycle, the method of contraception, status of fertility and exacerbation of SLE during pregnancy. Their medical records were evaluated to retrieve data about the pre-mentioned questions

**Results:** During this period, 10 SLE patients had come to hospital for the treatment of infertility. 7 of them became pregnant by in vitro fertilization. 52 of SLE patients planned pregnancy before conception. Fetal loss developed in 18 patients, 6 patients experienced preeclampsia during pregnancy. Premature delivery developed in 5 patients. The frequency of fetal loss tended to be higher in SLE patients with unplanned pregnancy (38.5 vs. 25%, p>0.05). Fetal loss was significantly higher in anti-phospholipid syndrome group (35% vs. 4.2%, p=0.002) and in SLE patients with hypocomplementemia (47.1% vs. 20.9%, p=0.059).

SLE flares were observed in 15 patients and nephritis (8 patients) was the most common finding of exacerbation. SLE flare group during pregnancy had a significantly higher rate of hypocomplementemia (84.6% vs. 30.8%, p=0.001), premature delivery (27.3% vs. 2.3%, p=0.023), and APS (27.3% vs 7%, p=0.056).

**Conclusions:** In our cohort, fetal loss and SLE flares were relatively higher. APS and hypocomplementemia were associated with fetal loss and disease flares.

**Disclosure of Interest:** None declared

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## AB0514 ASSOCIATION OF ANTI-RO (SSA) SPECIFICITY WITH CLINICAL MANIFESTATIONS IN A SPANISH POPULATION

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**Background:** The Ro/La system is considered as an heterogeneous antigenic complex, constituted by three different proteins (52 kDa Ro, 60 kDa Ro and La) and four small RNAs particles. Anti-Ro are the most prevalent specificity among many autoimmune diseases. There is controversy regarding the relation between the different subunits of Ro antibody and the appearance of certain clinical aspects both in patients with autoimmune diseases and in healthy people[1].

**Objectives:** To analyse antiRo Ab subtypes of people with or without autoimmune diseases criteria and determine whether there is a relation with any type of involvement.

**Methods:** We reviewed patients medical records who had more than one positive determination of anti-Ro, between 2010 and 2012 in the hospital of Merida, Spain. We collected data to support the existence of xerophthalmia and xerostomia, mucosal ulcers, Raynaud's phenomenon, arthritis, interstitial lung disease (ILD), serositis, neurological involvement (polyneuropathy, mononeuritis multiplex and central involvement), nephritis and cutaneous lesions (SCLE, DLE, photosensitivity, malar rash and alopecia). We use Xi2 and, when necessary, Yates correction, to determine if there exist significative relation between the described pathologies and antibodies to 52 kDa Ro, 60 kDa Ro and La.

**Results:** Data of the relation of each pathology with the anti Ro subunits are represented in Table 1. From the 131 patients, the frequency of antibodies was found: 11 anti-Ro52 Ab, 33 antiRo 60 Ab, 73 antiRo52/60 Ab, 14 patients with unknown pattern and 47 also had associated anti-La Ab. We found statistically significant in the following cases: Xerophthalmia and xerostomía with anti-La (p<0.01), mucosal ulcers with anti-La (p<0.05), ILD with antiRO52 (p<0.05), neuropathy anti-Ro52/60 (p<0.01) and antiLa (p<0.05); skin lesions with the abscence of anti-Ro52 (p<0.01) and the presence of anti-La (p<0.01). Of the 10 cases of ILD, three of them progressed to pulmonary fibrosis, all of them with antiRo 52, therefore with a relation statistically significant (p<0.01).

Table 1

| | Anti Ro antibody (n=285) | | | | Anti La & anti Ro Ab (n=121) | All patients (n=285) |
|---|---|---|---|---|---|---|
| | Ro 52+ (n=21) | Ro 60+ (n=63) | Ro52/60+ (n=177) | Unknow n=24 | | |
| Xerophtalmia-Xerostomia | 6 (9.4%) | 12 (18.7%) | 41 (64.1%) | 5 (7.8%) | 31 (48.4%) | 64 (100%) 48.8% |
| Mucosal ulcers | 3 (7.1%) | 8 (19.1%) | 28 (66.7%) | 3 (7.1%) | 21 (50%) | 42 (100%) 32.1% |
| Raynaud | 4 (12.1%) | 8 (24.2%) | 19 (57.6%) | 2 (6.1%) | 9 (27.3%) | 33 (100%) 25.2% |
| Artritis | 4 (10%) | 8 (20%) | 21 (52.5%) | 7 (17.5%) | 15 (37.5%) | 40 (100%) 30.5% |
| ILD | 3 (30%) | 3 (30%) | 4 (40%) | 0 | 3 (30%) | 10 (100%) 7.6% |
| Serositis | 1 (7.1%) | 2 (14.3%) | 8 (57.1%) | 3 (21.4%) | 5 (35.7%) | 14 (100%) 10.7% |
| Neuropaty | 0 | 0 | 10 (22.2%) | 0 | 7 (77.8%) | 10 (100%) 7.6% |
| Nephritis | 0 | 4 (26.7%) | 10 (66.7%) | 1 (6.7%) | 6 (40%) | 15 (100%) 11.5% |
| Skin involvement | 0 | 18 (31.6%) | 36 (63.2%) | 3 (5.3%) | 24 (42.1%) | 57 (100%) 43.5% |

**Conclusions:** We found that the anti-La Ab, was associated with sicca symptoms, mucosal ulcers, neuropathy and skin lesions. Ro52 subunit had a positive association with the occurrence of ILD and its progresion to fibrosis and negative association with skin lesions. Anti-Ro60 positivity was unrelated to any involvement. AntiRo52/60 positivity were associated with the onset of neurological symptoms. Studies bigger and with a larger sample of patients to confirm these results are needed.

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**Disclosure of Interest:** None declared

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## AB0515 VITAMIN D, IL-10, IL-17, AND IL-23 AS BIOMARKER FOR DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic, autoimmune, inflammatory disease and the prototype of multisystem autoimmune diseases. Several cytokines such as interleukin (IL)-10, IL-17, IL-23, and vitamin D have been suspected in the pathogenesis of SLE. However, the association between these cytokines, vitamin D and disease activity is unknown.

**Objectives:** We aimed to determine the association between IL-10, IL-17, IL-23, vitamin D and SLE disease activity index (SLEDAI) score.

**Methods:** We included 40 patients with SLE (mean age: 35.5±13.41 years, 95% female) and 20 healthy controls (mean age: 36.1±14.76 years, 70% female) in the study. Clinical and laboratory parameters and, SLEDAI score were evaluated. Serum IL-10, IL-17 and IL-23 were measured by nephelometry and vitamin D by HPLC (high-performance liquid chromatography). Mann-Whitney U and Kolmogorov-Smirnov test were used for statistical analysis. P<0.05 was accepted as statistically significant.

**Results:** The level of vitamin D was significantly lower (p=0,003), and IL-23 was significantly higher (p=0,001) in SLE patients compared to healthy controls. There was no significant difference for IL-10 and IL-17 between both group (p>0,05). However, a significant correlation between vitamin D and disease duration (p=0,02), and between IL-23 and vitamin D (p=0,019) were found among SLE patients. Vitamin D levels were correlated with SLEDAI score and IL-23 in patients group.

**Conclusions:** Although there are studies suppporting the role of IL-10 and IL-17 in the pathogenesis of SLE in the literature, there was no significant difference between patients and healthy controls in our study. IL-23 levels were significantly higher, whereas vitamin D levels were significantly lower in SLE patients than in the control group. Also vitamin D levels were negative correlated with duration of

disease and IL-23. Levels of IL-23 may be used to evaluated the disease activity, or may be a promising therapeutic approach for SLE patients.
**Disclosure of Interest:** None declared
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## AB0516 SERUM LEVELS OF FAS/APO-1 AND FAS LIGAND (FASL) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Apoptotic defects have been proposed to explain the pathogenesis of systemic lupus erythematosus (SLE). Fas/APO-1 and FasL, members of the tumor necrosis factor (TNF) families, are involved in apoptosis. They are expressed in membrane-associated as well as soluble forms (sFas/APO-1 and sFasL).
**Objectives:** The aim of this study is to determine serum levels of sFas/APO-1 and sFasL in patients with SLE.
**Methods:** The study included 48 pts (90% females, age 30,0 [27,0–44,5] years (median [interquartile range 25%>75%]) with SLE (ACR criteria, 1997) and 10 controls (100% females without any rheumatic and infectious diseases, age 39,5 [31,0–45,0] years, $p>0,05$). SLE-related factors, including disease duration, clinical features, SLE Disease Activity Index (SLEDAI 2K) and Systemic Lupus International Collaborating Clinics (SLICC) damage index were evaluated in parallel with relevant laboratory findings (blood and urine tests, CRP, immunoglobulins G, A and M, complement C3 and C4 fragments and others), autoantibodies (ANA, antiDNA, ENA-SSA, -SSB, -Sm, -RNP-70, aPL). Serum levels of sFas/APO-1 (pg/ml) and sFasL (ng/ml) were measured by ELISA (Bender MedSystem GmbH, Austria). Statistical analyses were performed with STATISTICA program, version 8.0.
**Results:** Mean SLE duration was 5,0 [1,0–12,0] years, SLEDAI 2K score - 9 [4–15], SLICC damage index score - 0 [0–1]. SLE pts had lower levels of sFas/APO-1 vs control (669,65 [487,90–791,40] vs 1456,90 [426,50–2060,80] pg/ml, $p<0,01$) and higher levels of sFasL vs control (0,10 [0,01–0,03] vs 0,07 [0,05–0,10] ng/ml, $p<0,05$). In SLE pts serum sFas/APO-1 level correlated with platelets absolute count (r=-0,292, $p<0,05$), creatinine (r=0,538, $p<0,0001$), urea (r=0,431, $p<0,01$), uric acid (r=0,698, $p<0,000000$), proteinuria (r=0,311, $p<0,05$), cylindruria levels (r=0,365, $p<0,05$), glomerular filtration rate (r=-0,341, $p<0,05$) and systolic blood pressure (r=0,327, $p<0,05$), SLEDAI 2K (r=0,342, $p<0,05$), antiSSA (r=-0,467, $p<0,001$), antiSSB (r=-0,338, $p<0,05$), ACL IgG (r=0,434, $p<0,01$), CRP concentrations (r=0,446, $p<0,01$) and ESR (r=0,428, $p<0,01$). We divided SLE pts into two groups: Group 1 included pts with lupus nephritis (n=24 (50%)), Group 2 – SLE pts without nephritis (n=24 (50%)). Pts from Group 1 had higher, but not statistically significantly, levels of sFas/APO-1 as compared to Group 2 levels (706,15 [601,35–974,05] vs 591,90 [464,25–754,85] pg/ml, $p>0,05$).
**Conclusions:** The increased level of sFasL (a marker of apoptosis) and reduced level of sFas/APO-1 (apoptosis inhibitor that blocks binding of sFas/APO-1 to sFasL) in the study group is indicative of up-regulated apoptosis in SLE patients. Established correlation of sFas/APO-1 concentration with indicators of kidney damage and SLEDAI 2K score allows us to consider sFas/APO-1 as a marker of lupus nephritis and high SLE activity.
**Disclosure of Interest:** None declared
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## AB0517 SEASONAL DISEASE ACTIVITY IN LUPUS NEPHRITIS IN NORTHERN PORTUGAL – RETROSPECTIVE STUDY

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**Background:** Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disease driven by auto-reactive immune cells that target multiple organ systems leading to severe complications. A main complication of SLE is nephritis, formally known as lupus nephritis (LN) that is classified as a secondary form of glomerulonephritis. Exposure to sunlight is one of the environmental factors involved in the pathogenesis of systemic lupus erythematosus. Previous studies of a seasonal influence on SLE activity have conflicting results, suggesting that there was only an increased incidence of photosensitive rashes in the summer months, whereas others found more articular pain in the winter and spring. A study of renal biopsies found that the prevalence of class V lupus nephritis was significantly higher in Winter and Spring.
**Objectives:** To determine, in a cohort of adult LN patients, whether there is any seasonal variation in the activity of LN, and possible correlations between specific organ involvement, gender and disease duration.
**Methods:** Retrospective study, enrolling patients attending a Rheumatology/Nephrology outpatient department, diagnosed with SLE (according to the American College of Rheumatology criteria) and LN. Fixed variables: age, gender, race, disease duration, LN treatment phase, histological classification (renal biopsy), specific organ involvement and therapeutics for SLE, including glucocorticoids. Clinical variables evaluated 2 times for year (one in winter; one in summer, without change in therapeutics): anti-dsDNA antibodies, serum urea and creatinine, urinary sediment and protein-to-*creatinine* ratio (UPr/Cr). Statistical analysis with Microsoft Excel, version 2010; appropriate statistical tests was used, and a $p$ value$<0.05$ with a 95% confidence interval will be assumed.
**Results:** 73 SLE patients were enrolled in the study, 61 were female (84%); mean age was 40±11.5 years and mean disease duration was 118±102 months. All the patients were white. 51 patients (70%) had class 4 LN. 58 (79%) patients had extra renal disease, 34 with joint disease and 23 with cutaneous involvement. Mean UPr/Cr was superior in summer than winter (0.443±0.66mg/g Vs 0.401±0.84mg/g), this increase being statistically significant (p=0.04). Patients with SLE cutaneous involvement had higher renal activity in summer and higher seasonal variation (p=0.02). Mean dsDNA was superior in summer, but this difference wasn't statistically significant. No association was identified between seasonal disease activity and sex or disease duration.
**Conclusions:** Despite the reduced size of our cohort, we confirmed a seasonal pattern for Lupus Nephritis and renal disease activity in Northern Portugal, being higher in summer time, in possible correlation with an increase in temperature and duration of sunshine, expecially in SLE patients with cutaneous envolvement.
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## AB0518 CLINICAL THROMBOTIC MANIFESTATIONS IN SLE PATIENTS WITH AND WITHOUT ANTIPHOSPHOLIPID ANTIBODIES: A TEN-YEAR FOLLOW-UP

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**Background:** Systemic lupus eyrthematosus can bge associated with antiphospholipid syndrome. Years ago our study team investigated the thrombotic risk factors and complications in 272 lupus patients with and without antiphospholipid antibodies. At baseline, three groups were created, an aPL- group with 107 aPL negative patients, an aPL+ group with 81 aPL positive patients without clinical manifestations and a secondary antiphospholipid syndrome (APS) group with 84 aPL+ patients who met the Sapporo criteria.
**Objectives:** The objective of this study was to investigate of new thrombotic events, SLE activity,.co-morbidities, and mortality in total of 272 lupus patients for ten years of follow up.
**Methods:** The above mentioned 272 patients with SLE registererd in the Division of Clinical Immunology, University of Debrecen have been followed up prospectively for ten years.
**Results:** A total of 28 out of the 272 patients were lost to follow up. A total of 22 new thrombotic complicatons occurred, two in the aPL negative group, three in the aPL+ group. New antiphospholipid antibodies appeared in these patients. 77.3% of the new thrombotic complicatins reoccurred in the APS group despite the adequat anticoagulant and/or anti-platlet therapy. SLE activity was the most common in the APL+ group but the difference was not significant. A total of 27 out of 84 APS (32%), 14 out of 81 aPL positive and 10 out of 107 aPL negative patients died during the follow up. The causes of death were thrombotic events or complications in 40.7% in patients with APS.
**Conclusions:** Our data confirm recurring thrombotic events in lupus patients with antiphospholipid syndrome. Antiphospholipid syndrome seems to negatively influence the survival of the patients with systemic lupus erythematosus.
**Disclosure of Interest:** None declared
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## AB0519 QUALITY OF LIFE OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH DISEASE ACTIVITY AND ORGAN DAMAGE

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**Background:** In order to assess adequately the success of treatment of patients with systemic lupus erythematosus (SLE), the patient's individual perception of his physical and mental health and degree of integration into the community is required. The most commonly used standardized quality of life questionnaire, involving physical, mental and social acpects, is The Medical Outcome Survey Short Form 36 (SF-36). The results regarding the correlation of activity index and degree of organ damage in SLE patients with quality of life have so far been contradictory.
**Objectives:** Our aim was to evaluate the quality of life of SLE patients using the SF-36 questionnaire, and to establish the correlation of Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), organ damage index - SLICC/ACR Damage Index (SDI) with quality of life.
**Methods:** The study enrolled 85 SLE patients aged 45.3±9.7 years on the

average, out of which 78 (91.8%) women and 7 (8.2%) men, with average disease duration of 10.4±8.0 years, hospitalized at the Clinic of Rheumatology, "Niška Banja" Institute, in whom the diagnosis was made based on the revised 1997 ACR criteria. Disease activity was assessed using the SLEDAI questionnaire, organ damage using the SDI, and quality of life using the SF-36 questionnaire. The control group consisted of 30 healthy examinees. Both groups were homogenous as to the factors of gender and age.
**Results:** Our results showed that there was significantly worse quality of life in all SF-36 domains in SLE patients compared to controls ($p<0.001$). The domain of physical functions in SLE patients had poorer results compared to mental functions (36.68 vs. 49.14), and average results were below 52% in all SF-36 domains. There were no significant differences in the values of all SF-36 domains between the group with lupus nephritis and those without it. The mean value of SLEDAI was 11.38±7.55, median was 8, minimum value 0 and maximum value 36. In the assessment of correlation between the SLEDAI and quality of life represented via the SF-36 questionnaire, we found only a negative correlation between limitations due to physical difficulties and SLEDAI ($r=-0.216$; $p<0.05$). The mean SDI value was 1.81±1.98, median 1, minimum value 0, maximum value 9. Our study demonstrated a negative correlation between all SF-36 domains and SDI ($p<0.001$ in most domains), with the exception of emotional status and SDI, where a correlation was not found.
**Conclusions:** Quality of life of SLE patients measured by the SF-36 index was significantly worse compared to healthy individuals. There was no difference in quality of life in any of SF-36 domains between those with and without lupus nephritis. Quality of life measured by the SF-36 index was not correlated with disease activity measured by the SLEDAI in most of the domains. Poorer quality of life was associated with a higher SDI, except for the emotional status domain.
**Disclosure of Interest:** None declared
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## AB0520 MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS IN A ARGENTINIAN COHORT

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease associated with a high morbidity and mortality. The specific causes of death may vary among ethnic groups.
**Objectives:** To examine mortality rates related to SLE in a single Argentinian population.
**Methods:** A retrospective cohort study was designed. Clinical Record of SLE patients treated between 2000 and 2005 and followed until 2015 in a tertiary no academical hospital that does not attend pediatric population were reviewed, including demografic and clinical data. The cause of death was searched from the medical records and deaths certificates from the Public Health Archives. Continuous data was expressed in median and interquartile range (IQR), categorical data in frequency and percentage. Chi-square test or Fisher's test was used to analyse categorical data and Mann-Whitney or Student's T-Test for continuous data. Kaplan – Meier survival curves were calculated. A p value $<0.05$ was considered as significant.
**Results:** Fifty- five patients were enrolled, 48 women (87%), with a median age of 37 years (IQR:29–44.5), median disease duration of 9 years (IQR:3–12.3) and a total follow-up of 500 patients- years.Thirty- five patients (63%) were diagnoses after the first visit. Two (3.6%) were smokers, 16 (29.1%) had hypertension, 8 (14%) were diabetics and 9 (16.7%) has dyslipidemia. Treatments included glucocorticoids ($>10$ mg/ day of prednisone) in 47 (85%), immunosuppressive therapy 27 (49.1%) and anti-malarial 44 (80%). Renal involvement was found in 30 (54%) patients.
**Conclusions:** Long-term survival in a single center of SLE argentinian patients was low in comparation with oteher studies. An cumulative survival from diagnosis of 81% at 5 years and 61% at 10 years was observed. Infection and SLE activity were the main causes of death
**Disclosure of Interest:** None declared
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## AB0521 QUALITY OF LIFE IN PATIENTS WITH SLE AND CUTANEOUS INVOLVEMENT

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**Objectives:** To establish the relationship between cutaneous involvement and Quality of Life (QoL) in patients with systemic lupus erythematosus
**Methods:** Cross-sectional study of SLE patients with cutaneous involvement, fulfilling SLICC/ACR 2012 classification criteria. Cutaneous involvement was assessed by Cutaneous Lupus Erithematosus Disease Area and Severity Index (CLASI), disease activity – by SLEDAI and SLAM and QoL by SF-8 questionnaire. The Pearson correlation coefficient was calculated between the variables.
**Results:** The study included 92 Caucasian SLE female patients with a mean age of 40,0±12,6 yrs and a mean disease duration of 5,1±5,8 yrs. The mean age at the disease onset was 33,5±11,4 yrs and the mean SLICC/ACR criteria number – 6,1±2,8 points. The disease activity by SLEDAI and SLAM was appreciated as high with 1,24±10,4 and 12,1±8,6 points, respectively. The SLICC/ACR DI constituted 1,47±1,6 points. The cutaneous involvment by CLASI showed a mean activity of 4,7 points and a damage of 3,0 points, mean CLASI score being appreciated with 7,2 points. The QoL by SF-8 demonstrated low indices, compared to general population, in both domains: Physical Component Summary (PCS) and Mental Component Summary (MCS) with a mean value of 37,74 and 38,72 points, respectively. The analysis of Pearson coefficient between the QoL and CLASI did not show significant correlation ($r\leq0,2$, $p>0,05$). The PCS og the QoL correlated inversely with the disease activity ($r=-0,58$ for SLAM and $r=-0,45$ for SLEDAI, $p<0,05$) and the MCS correlated inversely with SLICC/ACR classificatino criteria ($r=-0,45$, $p<0,05$). CLASI activity index correlated with SLAM and SLEDAI ($r=0,45$ for SLAM and $r=0,37$ for SLEDAI).
**Conclusions:** The QoL is dicreased in SLE patients by both components: physical and mental. The severity of cutaneous involvment did not correlate with the QoL's indices. Meantime, CLASI activity score correlated with disease activity and the MCP pf the QoL correlated with the number of SCLICC/ACR 2012 classification criteria.
**Disclosure of Interest:** None declared
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## AB0522 ON THE POSSIBLE PROTECTIVE ROLE OF COMPLEMENT SYSTEM IN IMMUNE COMPLEX LUPUS NEPHROPATHY

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**Background:** The links between complement and SLE are complicated and fascinating. After many years of study, hypotheses are developing which may begin to explain these apparent paradoxical findings.
**Objectives:** To assess correlation between complement? Circulating immune complexes and organ pathology in SLE.
**Methods:** Of 277 patients enrolled, 252 were female (91%) and the mean age of the patients was 46.6 years (range 18 to 70). 194 patients (70%) had active disease defined as SLEDAI score. All patients met $\geq$4 ACR SLE criteria. Complement activity in serum was detected by hemolytic method in CH50 units. For the assay of immune complexes (CIC), polyethylene glycol (PEG) precipitation method was used. As a control we used sera from 100 healthy donors.
**Results:** During a long observation of SLE patients we identified variants of hypocomplementemia dynamics. In the group 1 there was almost continuous and increasing hypocomplementemia (75 patients). In the group 2 hypocomplementemia arose during exacerbation of the disease and the complement level was restored under the influence of treatment (67 patients). In the group 3, the activity of complement constantly corresponded to the normal level (135 patients). Glomerulonephritis was diagnosed in 50% of patients in the first group and 46% in the 2nd and in 35.3% in the third group. Renal failure was more frequent among patients in groups 1 and 2. In the group 3, it appeared significantly less often, because of long course of the disease. The average activity of the complement, depending on the group of patients differed, and the average concentration of CIC was highest in the group 3 and in groups 1 and 2 it was statistically less high and was almost the same in both groups. However, signs of inflammation, such as fever and ESR, CRP were higher in patients of the group 3. The activity of complement was the most low and CIC levels were high in patients with renal insufficiency. A decrease of complement activity in patients with the maximum degree of activity of SLE in 56% and 57%, respectively. When calculating the number of units of CH50 per number of units of CIC we get a new integral indicator of the activity of the disease in more than 89% of cases.
**Conclusions:** According to the activity of the complement system in SLE represents a heterogeneous group. The low level of activity of the complement system, characteristic for a certain group of patients contributes to the appearance of glomerulonephritis. High level of complement has a protective effect against renal pathology. The ratio of activity of the complement system and the level of circulating immune complexes has a specific pathogenic role in SLE.
**Disclosure of Interest:** None declared
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## AB0523 CUTANEOUS MANIFESTATIONS IN PRIMARY SJOGREN'S SYNDROME

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**Background:** Cutaneous manifestations are one of the most common extraglandular manifestations of Sjogren's syndrome (SS). Entities such as as Annular erythema, Sweet syndrome, erythema nodosum and vasculitis have been described. Vasculitis was reported in approximately 10% of SS patients, with histologically characterized by lymphocytic or leukocytoclastic vasculitis.
**Objectives:** Describe cutaneous manifestations in patients with primary SS, registered in the GESSAR (Argentine Study Group for the Sjogren Sydrome) database and determine their association with systemic and laboratory clinical manifestations.

**Methods:** Observational, analytical case-control study. Patients aged 18 years and older with a diagnosis of primary SS. Demographic, clinical and serological data about patients included in the GESSAR database was collected, from the moment of joining until June 2015. Cases (patients with cutaneous manifestations) and controls (patients without cutaneous manifestations) were included with a relationship 1:4. Cutaneous manifestations were described. In addition, patients with purple were compared to the rest of the patients included in the study. For the analysis of continuous variables t or Mann Whitney tests were used, according to distribution and sample size. Categorical variables were analyzed using chi-square or Fisher exact test, according to the expected frequency distribution table. Multivariate logistic regression analysis was performed.
**Results:** 335 patients were included, 67 with cutaneous manifestations, with an average age of 53 years (SD 15). 95% are female and the average diagnosis age is 47 years (SD 17). In the group of patients who had cutaneous manifestations, 60% had purple, 19% urticaria, 19% petechiae, 16% ulcers, 7% erythema multiforme, 4% erythema nodosum and 9% subcutaneous nodules. No statistically significant differences in age, sex and time of evolution of the disease between the two groups were found. In univariate analysis differences were found in: arthritis (47% vs 31%, p=0.01), neuropathy (21% vs 9%, p<0.01), decrease in C4 levels (34% vs 18%, p<0.01), decrease in C3 levels (25% vs 10%, p<0.01) and positive cryoglobulins (27% vs 9%, p<0.01). In the multivariate analysis no independent association of these variables was found. With respect to purple, significant differences were found with: arthritis (49% vs 31%, p=0.02), neuropathy (9% vs 25%, p<0.01), anemia of chronic disorders (34% vs 17%, p<0.01), decreased C3 (37% vs 10%, p<0.01) decrease in C4 level (49% vs 15%, p<0.01), anti LA (66% vs 47%, p<0.03) and positive cryoglobulins (37% vs 10%, p<0.01). In multivariate analysis, the decrease in C4 levels (OR 4.5; 95% CI 1.6–12.9, p<0.05) and positive cryoglobulins (OR 5.6; 95% CI 1.7–18.6, p<0.05) were independently associated with the presence purple.
**Conclusions:** No independent associations were found regarding demographic, clinical and serological characteristics between patients with and without cutaneous manifestations. Purple is the most common cutaneous manifestation. The group of patients with Purple is most often associated with decreased C4 levels and the presence of cryoglobulins.
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**Disclosure of Interest:** None declared
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## AB0524 INCIDENCE AND RISK ANALYSIS OF OSTEOMYELITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A NATIONWIDE COHORT STUDY

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**Background:** Fever and musculoskeletal pain are manifestations of systemic lupus erythematosus (SLE). These symptoms might be confused with the presentations of osteomyelitis, especially in SLE patients. On the other hand, SLE patients may have higher risk to get infection, including osteomyelitis, due to immunodeficiency.
**Objectives:** This study aimed to investigate the epidemiology and risk factors of osteomyelitis in SLE patients.
**Methods:** We conducted this population-based cohort in entire Taiwanese by using Taiwan National Health Insurance Research Database. Patients with SLE and age- and sex-matched control group without SLE were enrolled. The primary endpoint was the first occurrence of osteomyelitis. The risks of osteomyelitis in SLE patients were analyzed with Cox proportional hazards regression models, including age, sex, comorbidities and medications.
**Results:** From 2000 to 2012, we identified 18472 SLE patients (88.6% women, mean age of 37.5 years) and 73888 control patients. Compared with the controls, the osteomyelitis incidence rate ratio (IRR) (95% CIs) among all SLE patients were 8.23 (6.76–10.05). The IRR between young SLE patients (18–40 years) and their controls was 22.87 (15.59–34.44). Multivariable Cox regression analyses in SLE patients indicated that older age, being male, with disease of peripheral artery disease (PAOD), chronic kidney disease (CKD), bone fracture, performing orthopedic surgery in recent 6 months, and daily prednisolone equivalent to or more than 7.5 mg are strongly related to osteomyelitis. In contrast, the use of hydroxychloroquine was a protective factor for osteomyelitis.

Table 1. Risk factors of osteomyelitis in patients with systemic lupus erythematosus

| Variables | Univariate analysis | | Multivariable analysis[a] | |
|---|---|---|---|---|
| | HR (95% CI) | p value | HR (95%CI) | p value |
| Age | 1.029 (1.020–1.039) | <0.001 | 1.027 (1.017–1.037) | <0.001 |
| Male, n (%) | 2.014 (1.436–2.825) | <0.001 | 1.766 (1.255–2.484) | 0.001 |
| Comorbidity | | | | |
| Diabetes mellitus | 4.25 (1.735–10.409) | 0.002 | | |
| Chronic kidney disease | 4.300 (2.429–7.613) | <0.001 | 2.750 (1.536–4.921) | 0.001 |
| PAOD | 5.408 (1.988–14.710) | 0.001 | 3.628 (1.342–10.102) | 0.011 |
| History of septic arthritis | 3.755 (0.526–26.828) | 0.187 | | |
| Orthopedic surgery | 4.277 (2.681–6.823) | <0.001 | 2.047 (1.165–3.597) | 0.013 |
| Bone fracture | 6.991 (4.256–11.482) | <0.001 | 4.327 (2.387–7.843) | <0.001 |
| Drugs | | | | |
| Steroid (day dose≥7.5)[b] | 1.931 (1.505–2.477) | <0.001 | 2.639 (2.017–3.454) | <0.001 |
| Hydroxychloroquine | 0.516 (0.393–0.677) | <0.001 | 0.579 (0.437–0.766) | <0.001 |
| Azathioprine | 0.735 (0.574–0.942) | 0.015 | 0.721 (0.547–0.949) | 0.02 |

**Conclusions:** SLE patients had a higher incidence rate of osteomyelitis, especially those who were older, male, had history of PAOD, CKD, bone fracture and orthopedic surgery and used a high dose of corticosteroid.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4125

## AB0525 CORRELATION ANALYSIS OF SERUM CYSTATIN C AND LIPIDS LEVELS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Objectives:** To discuss the correlation between the level of serum cystatin C and lipids in patients with systemic lupus erythematosus.
**Methods:** Used automatic biochemical analyzer to detect serum cystatin C (CysC), triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein (LDL-C) and hsCRP levels in 136 cases of SLE patients and 113 cases of healthy people. Data obtained using SPSS13.0 software to carry on statistical analysis.
**Results:** Outcome of SLE patients group comared with healthy controls, hsCRP (13.5±4.85 mg/L vs 2.03±0.88 mg/L), CysC (2.63±1.95 mg/L vs 0.85±0.37 mg/L), LDL-C (3.06±1.21 mmol/L vs 2.33±0.41 mmol/L), TC (5.32±2.63 mmol/L vs 4.02±1.67 mmol/L) and TG (1.92±0.83 mmol/L vs 1.44±0.8 mmol/L) were significantly different between the two groups. Compared with healthy controls, HDL-C (1.12±0.31 mmol/L vs 1.52±0.85 mmol/L) was decreased (P<0.01). In SLE patients group, the serum CysC level and hsCRP, TC, TG and LDL-C were positively correlated, and the level of HDL-C was negative to the level of CysC. The health control group was no significant corretation.
**Conclusions:** Serum lipid levels of SLE patients were positive to the level of CysC. Suggest that joint detection of SLE patients serum CysC and blood lipids index is helpful to the diagnosis of SLE treatment and condition monitoring.
**References:**
[1] Ganda A, Magnusson M, Yvan-Charvet L. Mild renal dysfunction and metabolites tied to low HDL cholesterol are associated with monocytosis and atheroselerosis, Circulation, 2013,127(9):988–996
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**Disclosure of Interest:** None declared
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# Vasculitis

## AB0526 SERUM FERRITIN AS A MARKER OF ACTIVITY IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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**Background:** ANCA-associated vasculitides (AAVs) are a group of systemic inflammatory disorders with substantial morbidity and mortality. Alveolar hemorrhage and gastrointestinal involvement are major causes of death in these disorders. Markers that measure activity and predict prognosis are needed. Serum ferritin levels are shown to be associated with activity and prognosis of certain rheumatic diseases such as antiphospholipid syndrome, dermatomyositis and systemic lupus erythematosus.
**Objectives:** To investigate association between serum ferritin with acute phase reactants and major disease manifestations in AAV.To investigate association between serum ferritin with acute phase reactants and major disease manifestations in AAV.
**Methods:** Retrospective charts of 40 patients (22 males, mean age 49±15 years) with AAV were utilized. Patients fulfilling Chapel hill classification criteria for AAV and those with at least 6 months of follow up were included. Disease activity of AAV was assessed with Birmingham vasculitis activity score (BVAS). Serum ferritin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and creatinine values were obtained from hospital records. Creatinine clearance (CrCl) was calculated with MDRD formula. Association between serum ferritin

with acute phase reactants and major disease manifestations were analyzed with Spearman rank and Mann Whitney U tests.
**Results:** Among 40 patients with AAV, 14 had pulmonary hemorrhage, eight had end stage renal disease, three mesenteric ischemia and four died in the follow up (two due to alveolar, one cerebral and one GI hemorrhage). Serum ferritin was not correlated with ESR and CRP. However, there was a significant correlation between BVAS and initial CrCl ($r=0.61$, $p<0.001$ and $r= -0.59$, $p<0.001$, respectively). Serum ferritin values were higher in patients with pulmonary hemorrhage (median (IQR), 65.8 (207) vs 1041 (1281) ng/mL, $p<0.001$) and in those four patients who died in the initial six-moths follow up period (206.8 (556) vs 1362 (1292) ng/mL, $p<0.014$).
**Conclusions:** Serum ferritin could be used as a marker of activity because of its ability to reflect disease severity which has already been shown in other systemic inflammatory disorders. Association between serum ferritin with other manifestations of AAVs remain to be elucidated in the large population studies.
**References:**
[1] Chen, Y.X., et al., Analyzing fatal cases of Chinese patients with primary antineutrophil cytoplasmic antibodies-associated renal vasculitis: a 10-year retrospective study. Kidney Blood Press Res, 2008. 31(5): p. 343–9.
[2] Hogan, P.C., et al., Biomarkers Predict Relapse in Granulomatosis with Polyangiitis. J Biomark, 2014.
**Disclosure of Interest:** None declared
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## AB0527 COMPARISON OF TWO INITIAL PREDNISONE DOSE REGIMENS IN GIANT CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is a vasculitis affecting large vessels and it is the most frequent type in patients over 50 years old. Although glucocorticoids (GC) still remain the mainstay of treatment in all these cases there is no yet clear evidence about optimal initial dose, regimen and relapses predictors and treatment [1, 2].
**Objectives:** To assess the characteristics of treatment, relapse and outcomes of a biopsy-proven GCA patients and to compare these items between groups based on initial oral prednisone dose.
**Methods:** We performed a retrospective review of all patients diagnosed of biopsy-proven GCA in our institution (Complejo Hospitalario Universitario de Vigo) between 1 January 2000 and 31 December 2014. Additionally, they fullfilled at least 2 of other 4 1990 ACR classification criteria. Epidemiological, clinical and laboratory data, treatment and outcome of all these patients at diagnosis and during follow-up were analysed. We also compared groups by initial oral prednisone dose ($\leq$40mg/day vs $>$40mg/day) using Cox models.
**Results:** During study period 70 patients were identified and analysed. Mean age at diagnosis was 77±7 years old and fifty-one (73%) were female. Charlson index was $\leq$1 in 83% of cases. Most frequent presenting symptoms were headache (87%), polymyalgia rheumatica (57%) and jaw claudication (48.6%). Ischaemic manifestations at diagnosis were seen in ten patients (14.3%). Median ESR and CRP was 88±26mm/h [31–140] and 92±88mg/dL [4–326] respectively. Median delay time from first symptom until diagnosis was 2 months [0–72]. We also analysed patients divided in two groups based on initial oral predisone dose ($\leq$40mg/day [17 patients] vs $>$40mg/day [53 patients]). No differences was seen in sex, age, comorbidities (including cardiovascular risk factors), antiagregants/ immunosupressive therapy use or laboratory markers. Nevertheless prednisone dose at first month (30.2mg/day vs 48.6mg/day; p=0.001), time to reach $\leq$5mg/day of prednisone (11.8 vs 16 months; p=0.045) and total prednisone dose (7.2 vs 11.5 grams; p=0.001) were significantly higher in $>$40mg/day group although we did not see more GC-related adverse effects in this group (p=0.38). During follow-up period (median 29 months [3–140]) 18 patients had at least one relapse, however we did not observe statiscal differences between both groups (18% in $\leq$40mg/day vs 28.8% in $>$40mg/day; p=0.35). Time to first relapse (12±11.3 months in $\leq$40 vs 16±12.9 months in $>$40; p=0.67) and total treatment time (28±23.5 in $\leq$40 vs 35±25.1 months in $>$40) were similar in boths groups. We could not identified any factor that was related to relapses in our multivariate analysis. Twenty-two patients died during follow-up period but none were related with GCA.
**Conclusions:**
- High-dose prednisone was the most frequent initial treatment of GCA patients.
- Lower doses regimen could be as safe and effective as the high-dose regimen.
- Relapses were seen in ¼ of patients but we could not identified any factor associated with them.

**References:**
[1] Salvarani C, Cantini F, Hunder GG. Polymyalgia rheumatica and giant-cell arteritis. Lancet 2008; 372: 234–45.
[2] Les I, Pijoan JI, Rodríguez-Álvarez R et al. Effectiveness and safety of medium-dose prednisone in giant-cell arteritis: a retrospective cohort study of 103 patients. Clin Exp Rheumatol 2015; 33 (Suppl 89): S90–97.
**Disclosure of Interest:** None declared
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## AB0528 ORGAN INVOLVEMENT WITH SYSTEMIC VASCULITIS OF AUTOIMMUNE AND OF SEPTIC ORIGIN – A COMPARATIVE POSTMORTEM STUDY OF 38 RHEUMATOID ARTHRITIS PATIENTS

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**Background:** In rheumatoid arthritis (RA) circulating immune complexes lead to systemic vasculitis of autoimmune origin (A-SV) which may involve various organs. RA as well as autoimmune diseases may be complicated by septic infections (SI) and accompanied with systemic vasculitis of infectious origin (S-SV). In case of systemic vasculitis the identification of its origin is of crucial importance because of the basic differences in therapy.
**Objectives:** The aim of this study was to compare the prevalence, average incidence and severity of A-SV and S-SV in various organs of RA patients.
**Methods:** At the National Institute of Rheumatology 12138 patients died between 1969 and 2000; among them 234 with RA and all of them were autopsied. Lethal septic infection (SI) was observed in 31 (13.25%) of 234 patients. SI was accompanied in 5 patients with S-SV. The clinically identified pathogenic agents and the strong, significant and positive correlation between S-SV and SI (association coefficient: 1, $c^2=26.1881$, $p<0.00007$) supported the infectious origin of SV.
The prevalence, average incidence and severity of S-SV in twelve organs of these 5 RA patients was determined histologically and compared with 33 RA patients with A-SV of our previous study [1].
**Results:** The prevalence in % and the average incidence and severity of A-SV (n=33) and S-SV (n=5) in various organs of 38 RA patients are summarized in the table.

| RA | A-SV | | | | S-SV | | | |
|---|---|---|---|---|---|---|---|---|
| Organs | A-SV/ organ (n=33) | Prevalence/ organ in % | Average incidence/ organ | Average severity/ organ | S-SV/ organ (n=5) | Prevalence/ organ in % | Average incidence/ organ | Average severity/ organ |
| Heart | 22 of 33 | 66.67 | 0.303 | 0.566 | 5 of 5 | 100.0 | 0.400 | 0.567 |
| Lung | 15 of 31 | 48.39 | 0.194 | 0.349 | 2 of 5 | 40.0 | 0.167 | 0.267 |
| Liver | 12 of 32 | 37.50 | 0.115 | 0.214 | 2 of 5 | 40.0 | 0.200 | 0.300 |
| Pancreas | 9 of 25 | 36.00 | 0.160 | 0.320 | 1 of 5 | 20.0 | 0.133 | 0.267 |
| Kidney | 17 of 33 | 51.52 | 0.197 | 0.313 | 3 of 5 | 60.0 | 0.300 | 0.600 |
| Adrenal gland | 12 of 28 | 42.86 | 0.149 | 0.280 | 1 of 4 | 25.0 | 0.125 | 0.208 |
| G-I tract | 11 of 29 | 37.93 | 0.161 | 0.293 | 4 of 5 | 80.0 | 0.333 | 0.567 |
| Spleen | 12 of 28 | 42.86 | 0.155 | 0.292 | 1 of 5 | 20.0 | 0.167 | 0.300 |
| Skeletal muscle | 15 of 28 | 53.57 | 0.190 | 0.375 | 5 of 5 | 100.0 | 0.400 | 0.740 |
| Nerve | 12 of 23 | 52.17 | 0.138 | 0.254 | 2 of 3 | 66.67 | 0.167 | 0.333 |
| Skin | 8 of 23 | 34.78 | 0.072 | 0.094 | 1 of 3 | 33.33 | 0.056 | 0.056 |
| Brain | 3 of 32 | 9.38 | 0.021 | 0.042 | 0 of 5 | 0.0 | 0.0 | 0.0 |

**Conclusions:** The involvement (prevalence in %) of various organs, the average incidence and severity of A-SV and S-SV are basically determined by the systemic circulation and blood supply of various organs, by circulating immune complexes and other agents, furthermore by their possible elimination. The source of infection may have a modifying effect regarding the organ manifestation of S-SV.
**A-SV** was most dominant in the heart, skeletal muscles, lung, pancreas, and kidneys, the main targets of circulating immune complexes in RA. In septic RA patients the S-SV dominated in the heart, skeletal muscles, kidneys, and gastrointestinal tract, which may be due to the complex effect of circulation and source of septic infection (e.g. high prevalence of urogenital and gastrointestinal infections in our autopsy population).
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1096

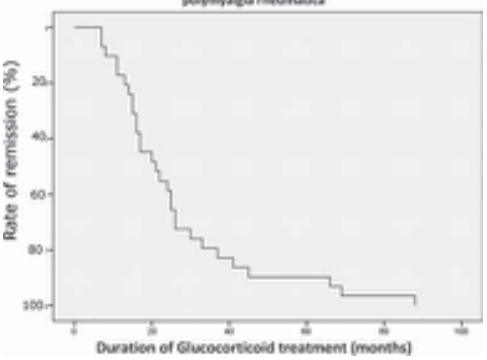
## AB0529 LONG-TERM GLUCOCORTICOID MONOTHERAPY CAN LEAD TO REMISSION IN JAPANESE PATIENTS WITH POLYMYALGIA RHEUMATICA WITHOUT NOTABLE ADVERSE EFFECTS

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**Background:** Polymyalgia rheumatica (PMR) is a common inflammatory condition of elderly persons. Clinical symptoms are improved by low-dose glucocorticoids (GCs). However, most patients require long-term GC therapy, because relapses are common. The recent recommendations for the management of PMR[1)] suggested early introduction of methotrexate (MTX) in addition to GCs in patients with a relapse, and/or without a significant response to GC, or experiencing GC-related adverse events.
**Objectives:** The aim of this study was to evaluate the duration of GC monotherapy until remission of PMR patients, and the adverse events of long-term GC treatment.

**Methods:** We conducted a retrospective study of 29 PMR patients who had achieved remission in 3 hospitals in Japan. All patients met EULAR/ACR classification criteria. None of the patients had clinical symptoms or signs of giant cell arteritis. Patients who had been treated with methotrexate in addition to GCs were excluded. Remission was defined as the absence of symptoms and normal levels of Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) after the discontinuation of GC. Treatments to prevent GC related adverse event, especially osteoporosis, were left up to each physicians.
**Results:** 20 (69%) were women. The mean (SD) age at the diagnosis was 75.7 (8.14) (range 61–90) years. The median and mean (SD) of initial prednisolone (PSL) dose was 15 and 13.1 (4.15) mg daily. The median duration of GC treatment until remission was 21 months (range 7–88). Three patients achieved remission after longer than 5 years of GC treatment (66, 69, and 88 months)(Figure). For analysis, patients were divided into 2 groups; those who achieved remission within 24 months (early remission group; 17) and those who required GC treatment for more than 25 months (long treatment group; 12). A comparison of the 2 groups was done. No difference was observed in clinical features and laboratory data at diagnosis. Furthermore, there was no significant difference in the starting dose of GCs or GCs tapering speed. Most female patients received vitamin D and/or bisphosphonate. Serious GC adverse events, such as osteoporosis associated fractures, and infections, were rare, and the frequencies of adverse events did not differ between the 2 groups.

Figure Duration of glucocorticoid therapy until remission in 29 patients of polymyalgia rheumatica




**Conclusions:** Most patients have achieved a remission within two years. However, some patients required longer-term treatment. The risk factors for prolonged therapy were reported; female sex, elevated ESR, and peripheral inflammatory arthritis. In this study, any clinical factors at diagnosis were not associated with the duration of PSL treatment until remission.
Our results indicate that low-dose GC therapy might be safer than was previously reported, as long as efforts are made to prevent GC-related adverse events. The rate of MTX adverse events in elderly is not low. Further studies are necessary to determine the risk and benefit of GC monotherapy
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3444

## AB0530 25-HYDROXYVITAMIN D3 DEFICIENCY: PREVALANCE AND ITS IMPACT ON DISEASE ACTIVITY IN SMALL-MEDIUM VESSEL VASCULITIS

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**Background:** Growing evidence suggests that vitamin D has important immunomodulatory effects and plays key roles in endothelial dysfunction, atherosclerosis and pathogenesis/progression of some of the inflammatory rheumatic diseases such as rheumatoid arthritis and systemic lupus erythematosus. Although recent data indicated that vitamin D deficiency is quite prevalant and affects endothelial dysfunction in Behcet's Disease and Takayasu's arteritis, vitamin D levels in small/ medium vessel vasculitis and its effects on disease course have not been evaluated.
**Objectives:** To determine the prevalance of 25-hidroxyvitamin D3 [25(OH)D3] deficiency and to investigate its effects on disease activity in patients with small and/or medium vessel vasculitis.
**Methods:** In this cross-sectional study, 25(OH)D3 levels were measured in adult patients with systemic small-medium vessel vasculitis including ANCA-associated vasculitis (AAV), cryoglobulinemic vasculitis (CryV), IgA vasculitis (IgAV) and polyarteritis nodosa (PAN), and sex-matched healthy subjects (HS). All patients' baseline demographics, disease characteristics, acute phase reactants, medications and disease extents (DEI), disease activities (BVAS) and damage scores (VDI) were determined. 25(OH)D3 level <30ng/ml and <20ng/ml were regarded as insufficiency and deficiency, respectively.
**Results:** Forty five patients (29% new diagnosis) with systemic vasculitis and 63 HS were included (*Table 1*). The mean 25(OH)D3 level was 21.8±14.3 ng/mL in patients with vasculitis and 56.7±23.9 ng/mL in HS ($p<0.001$). Vitamin D insufficiency and deficiency were significantly higher in patients with vasculitis compared to HS (*Table 1*). Thirty eight patients (84.4%) were active (BVAS≥1) at the time of recruitment. 25(OH)D3 levels were not different in active (21.6±14.8) and inactive (23.1±12.1) patients (p=0.79). Of the 24 vitamin D deficient patients 23 (95.8%) had renal involvement. Vitamin D deficient patients had slightly higher BVAS (6.5±6.7 vs 3.7±3.7), VDI (3.8±1.4 vs 3.2±1.3) and DEI (3.0±2.8 vs 1.8±2.4) scores at recruitment but the differences were not statistically significant ($p>0.05$). Likewise there was no difference in acute phase reactants according to vitamin D status.

Table 1. Baseline characteristics of patients with vasculitis and healthy subjects*

| | Patients with vasculitis* (n=45) | Healthy subjects (n=63) | P value |
|---|---|---|---|
| Age, years | 51.9±16.0 | 38.3±6.1 | <0.001 |
| Male, n (%) | 39 (86.7) | 32 (50.8) | 0.10 |
| Disease duration, years | 4.8±4.7 | - | - |
| Organ involvement | | | |
| Cutaneous | 25 (55.6) | - | - |
| Upper airway | 18 (40) | - | - |
| Ocular | 5 (11.1) | - | - |
| Pulmonary | 25 (55.6) | - | - |
| Renal | 39 (86.7) | - | - |
| Gastrointestinal | 5 (11.1) | - | - |
| Neurologic | 12 (26.7) | - | - |
| Cardiovascular | 1 (2.2) | - | - |
| BVAS, median (range) | | | |
| BVAS new/worse (0-63) | 0 (0-22) | - | - |
| BVAS persistent (0-33) | 1 (0-31) | - | - |
| DEI (0-23), median (range) | 2 (0-9) | - | - |
| VDI (0-59), median (range) | 4 (1-6) | - | - |
| 25-Hydroxyvitamin D3 level, ng/mL | 21.8±14.3 | 56.7±23.9 | <0.001 |
| <30ng/mL, n (%) | 35 (77.8) | 8 (12.7) | <0.001 |
| <20ng/mL, n (%) | 24 (53.3) | 2 (3.2) | <0.001 |

*The values are presented as mean±SD, unless indicated otherwise ¶ Systemic vasculitis included AAV (n=34, GPA=23, MPA=11), CryV (n=3), IgAV (n=7), PAN (n=1)

**Conclusions:** Vitamin D insufficiency and deficiency are quite common in patients with small/medium vessel systemic vasculitis. In this preliminary study we could not demonstrate any association with vitamin D deficiency and disease activity in patients with vasculitis. However, prospective followup of a larger sample would better clarify the role of vitamin D on disease activity. Considering also the use of high dose glucocorticoid treatment, these patients should be adequately evalauted and treated for vitamin D deficiency.
**Disclosure of Interest:** None declared
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## AB0531 THE ROLE OF HYDROXYCHLOROQUINE IN ANCA POSITIVE AND NEGATIVE VASCULITIS

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**Background:** There is an unmet need for a less toxic, corticosteroid sparing therapy in ANCA vasculitis (AAV), as up to 50% of patients relapse by 5 years and 20% have sub-optimal disease control. Hydroxychloroquine (HCQ) has been effective and safe in autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis. There is mechanistic rationale for the effectiveness of hydroxychloroquine in vasculitis, considering its effect on immune mediators involved in pathogenesis, including B cell activating factors, Toll-like receptors, autoreactive T cells and cytokines.
**Objectives:** To assess retrospectively the efficacy and safety of hydroxychloroquine (HCQ) in patients with systemic vasculitis
**Methods:** Patients were identified by searching our departmental vasculitis database including 248 patients in total and electronic clinical records. Twenty-six patients received hydroxychloroquine along with corticosteroids and immunosuppressants. We assessed the effect of hydroxychloroquine on clinical symptoms and the median dose of corticosteroids required.
**Results:** Twenty six patients with various vasculitides were treated with hydroxychloroquine (median dose 200 mg OD): 6 patients with Henoch Schonlein

purpura (HSP), 6 urticarial vasculitis, 6 with ANCA+ vasculitis (AAV) (4 PR3-ANCA, 2 MPO-ANCA), 1 Eosinophilic Granulomatosis with Polyangiitis (EGPA), 2 Takayasu arteritis, 2 Behcet's disease, 1 adult Still's disease (AOSD), 1 relapsing polychondritis, 1 polyarteritis nodosa (PAN). The female: male ratio was 21:5. Median age was 53 years. The median duration of HCQ treatment was 3 years. Sixteen patients experienced a reduction in arthralgia, skin rashes improved in 8 patients and completely resolved in a further 4. Eight patients could reduce corticosteroid doses (from 9 mg to 6 mg) and 3 discontinued corticosteroids. Four patients developed fewer vasculitic relapses, 6 felt less fatigued, 2 patients no longer experienced abdominal pain and diarrhoea, 2 improved their mood and ability to think clearly. The 6 patients with AAV experienced improvement in arthralgia, reduced their prednisolone doses by a third, had fewer relapses and felt less tired. One patient developed asymptomatic QT prolongation and stopped the hydroxychloroquine, with no other adverse events reported.

| Additional immunosuppressive therapy | Patient No. | Diagnosis |
|---|---|---|
| Nil | 8 | 3 Behcet 2, HSP, 1 AAV, 1 PAN,1 urticarial vasculitis |
| Methotrexate + prednisolone | 5 | 2 HSP, 1 AAV, 1 AOSD, 1 polychondritis |
| Azathioprine + prednisolone | 3 | 1 HSP, 1 AAV, 1 urticarial vasculitis |
| Mycophenolate mofetil + prednisolone | 2 | 1 urticarial vasculitis, 1 EGPA |
| Mycophenolate mofetil | 2 | 1 AAV, 1 Takayasu |
| Methotrexate | 2 | Urticarial vasculitis |
| Azathioprine | 1 | Takayasu |
| Prednisolone | 1 | AAV |
| Mepacrine | 1 | HSP |
| Rituximab | 1 | AAV |

**Conclusions:** All 26 patients reported symptomatic benefits associated with hydroxychloroquine treatment, especially improvement in joint pains, fatigue, rash. Vasculitic relapses were less frequent, with a reduction in corticosteroid doses. Hydroxychloroquine was generally well tolerated.
**Disclosure of Interest:** None declared
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## AB0532 PROFILE OF HENOCH SCHONLEIN PURPURA (HSP) NEPHRITIS: 23 YEARS EXPERIENCE AT A TERTIARY CARE CENTRE IN NORTH INDIA

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**Background:** HSP is one of the most common vasculitides of childhood. Glomerulonephritis is seen in approximately 30–50% of the patients and is the principal cause of morbidity and mortality in HSP patients.
**Objectives:** We describe our experience of managing children with HSP Nephritis (HSPN).
**Methods:** 314 children were registered in Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, PGIMER, Chandigarh with a diagnosis of HSP based on EULAR/PRINTO/PRES criteria during the period from January 1993 to June 2015. A retrospective case review of all patients with HSPN with respect to clinical features, pathological findings and treatment was done. HSPN was defined based on urine erythrocyte >5/HPF and/or proteinuria >150mg/24 hr. Patients were divided into four clinical types according to the laboratory results: (1) isolated hematuria (urine erythrocyte >5/HPF and proteinuria <150 mg/24hr); (2) minimal proteinuria (150 mg/24hr ≤ proteinuria <25 mg/kg); (3) moderate proteinuria (25 mg/kg ≤ proteinuria <50 mg/kg); (4) massive proteinuria (≥50 mg/kg). The severity of the renal pathological findings was determined based on the classification of the International Study of Kidney Disease (ISKDC), from grades I – VI [(1)].
**Results:** Renal involvement was seen in 64 patients (20.4%) after a mean duration of 32.3 days from the onset of symptoms of HSP. Renal manifestations developed in 57.8% of the patients within 4 weeks of symptom onset, in 84.4% within 8 weeks and in 100% within 6 months. Massive proteinuria was the most common clinical feature seen in 56.7% of the patients followed by minimal proteinuria in 21.7%, moderate proteinuria in 15% and isolated hematuria in 6.7% of cases. Hypertension was seen in 24 patients. 4 patients had deranged renal function tests.13 patients developed a clinical relapse of the renal disease after a mean interval of 551.5 days from the remission of first episode. Albuminuria with microscopic hematuria was the most common presentation of second episode (77%) followed by isolated albuminuria (23%).
Kidney biopsy was done in 48 patients. Three fourth of the patients had histological grade II or IIIa. 75% of patients with grade ≥ IV had gross hematuria at presentation. 25 patients received prednisolone alone, 31 received azathioprine in addition to prednisolone, while cyclophosphamide and mycophenolate mofetil were used in 5 and 1 patient respectively. Patients were followed up for a mean period of 3.6 years during which 13 were lost to follow up, 1 expired while 3 patients each are currently on prednisolone and azathioprine. Nephritis resolved in 48 patients (75%) with mean duration of renal involvement being more in patients with nephritis at presentation (429 days) as compared to patients who develop nephritis in follow up (321 days).
**Conclusions:** In our cohort of HSPN, 100% of the patients developed renal involvement within 6 months of the onset of symptoms of HSP with massive proteinuria being the most common clinical feature. Grade II and IIIa were the most common renal pathological grades seen in 75% of the patients.
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**Disclosure of Interest:** None declared
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## AB0533 SYSTEMATIC REVIEW: "EFFICACY AND SAFETY OF BIOLOGICAL THERAPY COMPARED TO IMMUNOSUPPRESSIVE THERAPY VS PLACEBO IN THE TREATMENT OF UVEITIS ASSOCIATED WITH BEHÇET'S DISEASE"

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**Background:** Systemic treatments used in ocular involvement in Behçet's disease are corticosteroids, synthetic and biological immunosuppressants. Because of irreversible ophthalmic complications, it's a priority to know the efficacy of these drugs.
**Objectives:** To analyze the efficacy and safety of biological therapy vs cyclosporine A (CyA), azathioprine (AZA) or placebo in reducing the rate of uveitis and improving the visual prognosis of Behçet's.
**Methods:** A systematic search of literature on MEDLINE,EMBASE,and Cochrane Central Register of Controlled Trials was conducted from inception to July 2015.A hand search was performed by reviewing the references of the included studies and the international congress.Criteria for study selection:1)adults with Behçet's-uveitis,2)Biological therapies,3)placebo or active comparator with CyA or AZA,4)outcome measures to evaluate effectiveness as a number (no) of recurrence of uveitis,visual prognosis,cystic macular edema, retinal vasculitis,vitritis,hypopyon,etc; and/or adverse events.Meta-analyses,systematic reviews,clinical trials and observational studies of>10 patients with comparator were included.The selection,review and evaluation of quality of the articles was independently conducted by 2 reviewers.The Oxford Level of Evidence scale was used to determine the quality of the studies.
**Results:** Of 195 articles,5 met the inclusion criteria:2retrospective observational studies and 3randomized clinical trials in 235 patients with Behçet and refractory uveitis.Age range was 12–69 years with male dominance,and follow up was 1–72 months.Evidence with infliximab (IFX) (2 studies) is weak and suggests more effective than CyA in reducing the rate of uveitis in short-term (6m) and more effective than CyA+AZA or methotrexate (MTX) to reduce the no. of retinal vasculitis relapse,and severe complications and to improve visual acuity in long term (LE4).The weak and insufficient evidence of rituximab (RTX) associated with MTX (1study) suggested similar efficacy to cyclophosphamide (CYM) associated with AZA, improving the total adjusted rate of disease activity without improvement in short-term visual acuity (6m)(LE 3b).Regarding secukinumab and daclizumab vs placebo (1 study respectively), the small but acceptable level of evidence suggests ineffectiveness in reducing relapses and in the improvement of visual acuity,with sparing effect on immunosuppressants in short-term for secukinumab (LE2a-2b). Available evidence reveals few significant adverse events. All studies could be applicable in clinical practice.
**Conclusions:** With the limited evidence found, IFX appears to be safe and more effectiveness than CyA alone or in combination with other immunosuppressants in reducing short term uveitis relapse and the number of severe long-term complications.RTX is similar to CYM paired with AZA in improving rates of inflammatory activity in short term.Secukinumab as well as daclizumab is not effective in reducing relapses of uveitis but could spare immunosuppressants.The results of this review support the benefit of carrying out further well-designed comparative studies with IFX and RTX.
**Disclosure of Interest:** None declared
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## AB0534 THE RELATIONSHIP OF PENTRAXIN-3 LEVELS IN BEHCET DISEASE WITH IL-17, DISEASE ACTIVITY AND ATHEROSCLEROTIC RISK FACTORS

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**Background:** Several factors have been implicated as contributing to the risk of atherosclerosis in patients with BD. (1) These include inflammatory mediators

such as cytokines and adhesion molecules and traditional cardiovascular risk factors such as age, high blood pressure, and dyslipidemia.(2) PTX3 also acts as a modulator of inflammatory processes and is involved in the development of atherosclerotic lesions. It is produced by endothelial cells in atherosclerotic plaques.
**Objectives:** With this study we aimed to identify the levels of the proteins like Pentraxin and Fetuin-A which are thought to have a role in the progress of atherosclerotic and cardiovascular disorders in Behçet disease and the relationship of these with disease activity, inflammatory cytokine, insulin resistance and dyslipidemia.
**Methods:** This study included 58 patients (36 female, 22 male) with Behçet disease and 20 healthy controls. Serum pentraxin-3, fetuin-A, IL-17 and insulin concentrations were determined. Also, HOMA-IR values were calculated. Disease activity was assessed with Behcet's Disease Current Activity Form (BDCAF).
**Results:** PTX3 and fetuin-A levels were not correlated with ESR, CRP, and any domains of BDCAF scores. IL-17 levels were significantly positively correlated with arthritis of BDCAF scores. there wasn't any significant relationship between the lipid profile and PTX3, IL17 and fetuin-A levels. There wasn't any correlation between PTX and IL 17, fetuin-A, insulin, HOMA IR levels ($p>0.05$).
**Conclusions:** Just like CRP, PTX3 is an acute-phase reactant and it is considers as an inflammatory and atherosclerotic biomarker. In this study, we presented that PTX3 can increase like IL-17 but there aren't any relation between the disease activity and coronary risk factors such as serum lipids, glucose intolerance and obesity. Since this is a cross sectional study, to determine higher levels of pentraxin in BD patients who also have higher cardiovascular disease incidences, the patients have to be followed in the longer run. To identify these long-term studies to quantified atherosclerosis are required.
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## AB0535 ASSESSMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH GRANULOMATOSIS WITH POLIANGIITIS USING THE SCORE RISK INDEX

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**Background:** anulomatosis with Poliangiitis (GPA) is an inflammatory disease characterized by destruction of small vessels. Patients with rheumatic diseases particularly with high inflammatory activity such as rheumatoid arthritis have increased morbidity and mortality due to cardiovascular (CV) disease.
**Objectives:** To analyze the prediction index of 10-year risk of a fatal cardiovascular disease events in GPA patients versus controls using the systematic coronary risk evaluation (SCORE) risk index.
**Methods:** Thirty-five GPA patients older than 40 years (18 males, mean age 54.7±9.8 years) and thirty age and sex matched healthy controls seen at the rheumatology clinic were studied. The American College of Rheumatology and Chapel Hill Consensus Conference criteria were used for the diagnosis of GPA. Information on demographics, classic CV risk factors, and clinical features of GPA were obtained by standardized forms. Disease activity of GPA was calculated with Birmingham vasculitis activity index/Wegener (BVAS/WG). Disease and control groups were compared with non-parametric tests.
**Results:** Calculated SCORE values of GPA patients were significantly higher compared to age and sex matched control group (Median (IQR) 2 (3) vs 1 (0), p==0.022). Seven GPA patients (20%) were above the threshold of high risk for the Turkish population. 30 out of thirty seven (81%) patients were newly diagnosed when the SCORE was calculated. There was no correlation between initial BVAS values and SCORE index.
**Conclusions:** We found that GPA patients have a higher 10-year risk of a fatal cardiovascular disease event than healthy controls. However, the use of additional tools or modifications in the SCORE might be considered to fully identify the GPA patients with high CV risk.
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## AB0536 CAN RHEUMATOLOGISTS DIAGNOSE AND MANAGE GIANT CELL ARTERITIS BETTER THAN NON RHEUMATOLOGISTS

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**Background:** Giant cell arteritis (GCA) is the commonest vasculitis affecting large and medium vessels. GCA presents with varying symptomatology which makes timely diagnosis and management challenging. A number of guidelines for the management of GCA have been published.[1,2] In clinical practice, patients present to various specialists including general practitioners, general physicians, neurologists, rheumatologists and ophthalmologists which may result in wide variations in clinical care.
**Objectives:** To establish the incidence of GCA in the Maltese population and whether rheumatologists are able to diagnose and manage giant cells arteritis better than non rheumatologists.
**Methods:** This was a population observational study of Maltese patients between 2012 and mid 2015. All patients who underwent a temporal artery biopsy (TAB) were recruited and their case notes reviewed.
**Results:** There were 122 patients (80 females) who underwent a TAB over 3.5 years for suspected GCA and out of these, 29 were positive. The incidence of biopsy proven temporal arteritis in Malta was 6.4 per 100,000 inhabitants aged over 50 years. Mean age was 72.6 (SD 10.5) years. An additional 27 patients were treated for GCA on clinical grounds. Median CRP was 31 mg/L (IQR 6–87) and ESR 81 mm/hr (53.5–102.5).
A total of 53 patients presented to the rheumatologists and 69 patients to non rheumatologists, and a positive TAB was obtained in 32% and 11.6% of patients respectively. Glucocorticoids were initiated before taking a TAB in 39.6% by rheumatologists and 34.7% and non rheumatologists. Overall (including TAB negative patients) 60.4% of patients presenting to the rheumatologists and 33% of patients presenting to non rheumatologists were treated as GCA.
The starting dose of Prednisolone was between 40–60mg in 82% of rheumatologist treated patients compared to 65% by non rheumatologists. The tailoring regimes varied widely and documentation was poor for many patients treated by non rheumatologists. Rheumatologists treated 50% of patients with a Prednisolone dose of 40 mg or greater for at least a month, 37.5% were given lower doses while the treatment regimen was unclear in 12.5%. Non rheumatologists treated 20.8% with a Prednisolone dose of 40 mg or greater for at least a month, 33.3% were given lower doses and in 45.8% regimen was unclear. The main differential diagnoses were sepsis/infection (7 cases), PMR (4 cases), pyrexia of unknown origin (4 cases) and cluster headache (2 cases).
**Conclusions:** Malta seems to have a low incidence of GCA comparable to other Mediterranean countries but lower than northern European countries.[3]
GCA presents to a wide variety of specialists leading to a broad variation in treatment regimens. Non rheumatologists seem to have a lower threshold for TABs and possibly perform a number of unnecessary TABs.
In order to ensure timely and appropriate management rheumatologists should take the lead and set up interspecialist pathways based on international guidelines that work in the local context. These pathways should include guidance about access, diagnosis, investigations and treatment and be disseminated to other clinical colleagues in both primary and secondary care.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3314

## AB0537 ISOLATED AORTITIS OR AORTITIS RELATED WITH RETROPERITONEAL FIBROSIS: A SINGLE CENTER EXPERIENCE OF 12 PATIENTS

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**Background:** Aortitis is the inflammation of aortic wall and it can result from infectious or non-infectious conditions. Retroperitoneal fibrosis (RPF) may be accompanied by idiopathic aortitis.
**Objectives:** In this report, we aimed to retrospectively evaluate in terms of clinical course, treatment and outcomes of 12 patients with isolated aortitis or aortitis related with RPF.
**Methods:** We reviewed files of our patients diagnosed with non-infectious aortitis or aortitis with RPF between Jan-1998-Dec-2015. Their clinical presentations, co-morbidities, location of aortic involvement, treatment features and outcomes were recorded. The diagnosis of aortitis and RPF were based on positron

emission tomography (FDG-PET-CT) scan and/or computed tomography. The presence of RPF was confirmed by biopsy in 4 patients.
**Results:** The study group consisted of 12 patients (8 M, 4 F). The mean age at the time of diagnosis was 60 yrs (42–70 yrs). Isolated aortitis was found in 5 patients, RPF plus aortitis in 6 patients, pure RPF in 1 patient. 6 patients with RPF plus aortitis presented with hydronephrosis and 1 patient with pure RPF presented with cystocele. In patients with isolated aortitis, 4 patients had subclavian and thoraco-abdominal involvement, 1 patient had bilateral subclavian and abdominal aorta involvement. 5 patients with RPF plus aortitis had only abdominal aorta involvement, 1 patient had thoraco-abdominal involvement. 1patient with abdominal aorta involvement had aortic aneurysm. Constitutional symptoms including fever, weight loss, and fatigue existed in all patients at the first admission. Hydronephrosis and post-obstructive renal failure were treated with double J stent and steroid treatment in 6 patients with RPF. Acute phase reactants increased in all patients. Ig G4 levels were determined in 8 patients and only 1 patient had increased level of Ig G4. All patients were given only prednisolone or prednisolone plus immunosuppressive drugs such as azathioprine or methotrexate. Clinical manifestations and increased acute phase reactants resolved in a reasonable time. 2 patients passed away due to sepsis and intra-cerebral infection, respectively. One of these 2 patients had many co morbidities.
**Conclusions:** While constitutional symptoms were a dominant complaint in isolated aortitis, hydronephrosis and acute renal failure as well as back pain were the chief manifestations of RPF. The presence of co-morbidities may play a role in mortality.
**Acknowledgement:** None
**Disclosure of Interest:** None declared
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## AB0538 ASSESSMENT OF NEUROLOGICAL MANIFESTATIONS IN TEMPORAL ARTERITIS

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**Background:** Temporal Arteritis (TA) is a vasculitis characterized by systemic and ischemic symptoms that concern fundamentally supraaortic blood vessels. The neurological clinic can be expressed as: headache, visual alterations, affection of cranial nerves, transient ischemic attack (TIA) or ischemic stroke in carotid or vertebrobasilar territory. The ocular affection is the most frequent but other neurological ischemic affections, not retinals, are not rare but they often occur unnoticed and are attributed to atherosclerosis given the age of the patients. Being a treatable and preventable process, there is an opportunity to improve the diagnosis of this affection.
**Objectives:** Assess the vascular events of supraaortic blood vessels, ocular vessels and non ocular vessels in our vasculitis surgery.
**Methods:** A retrospective study was carried out on the clinical history of the patients sent to our vasculitis surgery on suspicion of TA. The diagnosis of arteritis or nonarteritic neurological affection was realized in agreement with usual clinical criteria. The variables registered were age and sex, cardiovascular risk factors (CVR), clinical manifestations,VSG and PCR values, the final diagnosis and the results of the biopsy and the ultrasound examination, as well as the number of affected branches, brain TAC and MRI. The statistical analysis was realized by means of the software program SPSS Statistics version 20.0.
**Results:** Of the 163 patients studied, 112 were women and 51 men (31,3% vs 68,7%). One hundred thirteen patients (59,32%) had definite diagnosis of TA while 50 (30,68%) presented other diagnoses. Of the total of the patients, 59 (24 men and 35 women) presented neurological clinic: diplopía 10, loss of vision 48, TIA 7 and ACVA 4. Of these 42 were diagnosed with arteritic neurological affections (secondary to TA): 6 diplopía, 35 loss of vision, 4 TIA and 2 ACVA. Among the patients with nonarteritic and arteritic neurological events no differences were found for sex, VSG, PCR, blurry vision, fever, loss of vision, diplopía, TIA, ACVA, CVR, smoking and atrial fibrillation (AF): there was only significant differences for age. The analysis of the patients diagnosed with TA, withand without neurological events, appear in the table.

| | AT with neuroischemic events (n=42) | AT without neuroischemic events (n=71) | P< |
|---|---|---|---|
| Age (mean) | 81.29 | 71.29 | 0.001 |
| Sex ♀/♂ | 20/22 | 51/20 | 0.030 |
| VSG (mean) | 58.58 | 55.53 | 0.845 |
| PCR (mean) | 35.86 | 25.04 | 0.435 |
| Headache (no/yes) | 25/17 | 21/49 | 0.002 |
| Constitutional syndrome (no/yes) | 37/5 | 58/12 | 0.322 |
| Fever (no/yes) | 40/2 | 61/9 | 0.143 |
| Jaw claudication (no/yes) | 36/6 | 61/9 | 0.521 |
| Pulse temporal arteries (no/yes) | 15/2 | 20/1 | 0.419 |
| Polymyalgia rheumatica | 39/3 | 60/10 | 0.203 |
| Cardiovascular risk (no/yes) | 11/31 | 6/11 | 0.140 |
| Smoking (no/yes) | 28/12 | 56/10 | 0.196 |
| Number of affected branches | 2.88 | 3.43 | 0.018 |

**Conclusions:** Non ocular central neuroischemic events are frequent and affect 10,62% of the patients with TA. Among the patients with TA the neuroischemic risk associates to being a male, advanced age, a greater number of affected branches in ultrasound examination and to the presence of headache.
**Disclosure of Interest:** None declared
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## AB0539 TOFACITINIB FOR POLYARTERITIS NODOSA – A TAILORED THERAPY

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**Background:** Tofacitinib is a novel inhibitor of Janus kinase (JAK) 3 and JAK1 [1]. The JAK inhibitors are in the focus of research in myriad of other inflammatory diseases as it seems the JAK- (signal transducer and activator of transcription) STAT pathway has a central role in cytokines' signal transduction. We herein describe a case of refractory polyarteritis nodosa (PAN) successfully treated with tofacitinib.Preliminary evidence for the role of JAK-STAT pathway in vasculitis has been recently published [2].
A 28 years-old man had been diagnosed with PAN at the age of 14. He presented with livedo reticularis, arthritis and skin nodules with fibrinoid necrosis, as confirmed by biopsy. Immunologic panel at the time of diagnosis was negative for ANCA, ANA, SSA, SSB, RF, and complement levels were normal. He was treated with azathioprine and methotrexate for several years and was in complete remission. Three years prior the initiation of tofacitinib his disease flared and he began suffering from necrotizing vasculitis of the scrotum and calves, abdominal pain and polyarthritis with high CRP levels (160–300 mg/l) for which he received recurrent intravenous solumedrol pulses and oral prednisone therapy of 40–60 mg daily in between pulses. Numerous treatments including, infliximab, adalimumab, rituximab, etanercept, tocilizumab, potassium iodide and cyclophosphamide intravenous and oral failed to achieve remission. Subsequently, he was hospitalized for reevaluation and was treated by plasma exchange for 3 weeks with partial remission, but had to discontinue the treatment due to central line sepsis. At this point he was in severe long standing inflammatory state for 3 years with high CRP levels low albumin (3 mg/dl) and ongoing leukocytosis.
**Objectives:** To evaluate the activity of the JAK-STAT pathway guiding the treatment with tofacitinib.
**Methods:** We have profiled his peripheral blood cells using mass cytometry (CyTOF), a single cell proteomics platform capable of simultaneously measuring the expression up to 45 proteins on each cell and on millions of cells. This provided a high-dimensional immune cell type profile of his immune system, both in cell abundance as well as the activity of the JAK1 and 3 along with STAT 3 pathways in response to stimulation with interleukin 6, specifically in CD4+ and CD8+ T cells subsets (figure 1).
**Results:** We initiated treatment with tofacitinib 10 mg BID that resulted in prompt normalization of his CRP, albumin and leukocyte count, resolution of skin ulcers and relief of pain. Prednisone therapy was soon tapered from 60 mg to 10 mg daily. Reevaluating the response of the JAK-STAT pathway to IL-6 stimulation after treatment confirmed attenuated response of the CD8+T and CD4+T cell (figure 1). After one year of follow-up the patient remained in complete remission.

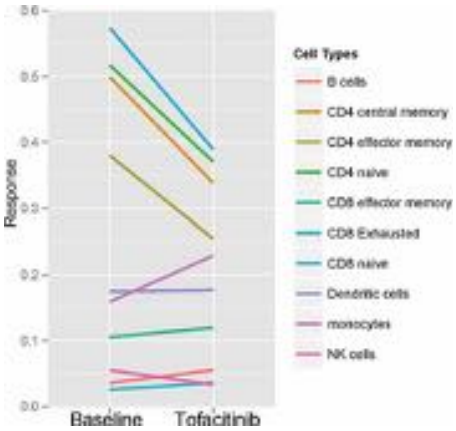


Figure 1

**Conclusions:** In conclusion, this is the first report in the literature of treatment of refractory PAN vasculitis with tofacitinib. Using high resolution mass cytometry technology we were able to tailor and monitor therapy.
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**Disclosure of Interest:** None declared
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## AB0540 POST-THROMBOTIC SYNDROME AND VENOUS DISEASE SPESIFIC QUALITY OF LIFE IN PATIENTS WITH VASCULAR BEHÇET'S DISEASE

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**Background:** Behçet's disease (BD) is a systemic disease characterized by oral aphthosis, genital ulcers, ocular lesions and systemic involvement including major vessels. Vascular Behçet's disease (VBD) is observed in up to 40% of BD. It is one of the major causes ofmorbidity and mortality in BD. Deep venous thrombosis (DVT) is the most common form of vascular involvement in Behcet's disease (BD). Post-thrombotic syndrome (PTS) develops in up to one-half of patients with DVT and is associated with impaired quality of life (QoL). There is no data on severity of DVT related PTS and its impact on quality of life in patients with Vascular Behçet's Disease (VBD).
**Objectives:** We aimed to evaluate frequency of PTS and venous disease spesific QoL in VBD and to compare it with patients having DVT associated with non-Behçet's disease (NBD) causes.
**Methods:** This study included 50 patients (Male/Female: 41/9) with VBD and 31 age and gender-matched individuals (Male/Female: 22/9), with DVT associated with non-BD causes. Villalta scale was used to assess of PTS. Venous Disability Score (VDS) and Venous Clinical Severity Score (VCSS) were used for the assessment of venous disease. Venous disease-specific QoL was measured through Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom questionnaire (VEINES-QoL/Sym). Behçet Syndrom Activity Score (BSAS) questionnaire was used to assess disease activity.
**Results:** We observed significantly lower risk of PTS together with significantly better VEINES-QoL, VEINES-Sym and VDS in VBD group compared to NBD group. When VBD patients with PTS were compared to patients without PTS; VEINES-QoL, VEINES-Sym VCSS were significantly worse. BSAS was also significantly higher in patients with PTS. An inverse correlation was found between VEINES-QoL and BSAS in multivariate analysis. There were no differences between anticoagulant users and non-users regarding the presence of PTS and scores of all venous assessment tools.

Table 1. Venous assessment and quality of life parameters in study groups

| | Vascular Behçet disease (n=50) | Non-Behçet group (n=31) | P value |
|---|---|---|---|
| VEINES-QoL | 85.6±17.1 | 74.9±18.6 | 0.01 |
| VEINES-Sym | 37.7±9.4 | 33.1±10.1 | 0.04 |
| VCSS | 5.2±5.1 | 6.2±4.5 | 0.346 |
| CEAP | 2.4±1.7 | 2.3±1.5 | 0.747 |
| VDS | 1.1±0.6 | 1.5±0.5 | 0.002 |
| SF-36 MCS | 45.3±9.6 | 41.9±10.8 | 0.163 |
| SF-36 PCS | 42.1±10.7 | 41.2±9.6 | 0.726 |

VEINES-QoL/Sym: Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symphtom questionnaire, VCSS: Venous Clinical Severity Score, CEAP: Clinical, Etiologic, Anatomic, Pathophysiologic) classification, VDS: Venous Disability Score MCS: Mental component of SF-36, PCS: Physical component of SF-36.

**Conclusions:** We found lower PTS risk and better venous disease spesific QoL, symptom severity and venous disability scores in VBD compared to NBD group. Venous disease spesific QoL negatively correlated with disease activity. Effective control of vascular inflammation through treatment in VBD might explain lower PTS and better venous QoL outcomes in VBD patients. Our results suggest that successful control of disease activity might decrease development of PTS, improve venouse disease spesific QoL as well as preventing the relapses in VBD.
**Disclosure of Interest:** None declared
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## AB0541 THE PROGNOSTIC SIGNIFICANCE OF THE BIRMINGHAM VASCULITIS ACTIVITY SCORE (BVAS) IN PATIENTS WITH SYSTEMIC VASCULITIS TRANSFERRED TO THE INTENSIVE CARE UNIT (ICU)

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**Background:** Systemic vasculitides represent a heterogeneous group of diseases that share clinical features including respiratory distress, renal dysfunction, and neurologic disorders. These diseases may often cause life-threatening complications requiring admission to an intensive care unit (ICU) [1]. Birmingham Vasculitis Activity Score (BVAS) is the most widely used generic tool to quantify disease activity in systemic vasculitis. Acute Physiology And Chronic Health Evaluation (APACHE II) is a simple and accurate assessment scale of the severity of disease in critically ill patients newly admitted to ICU.
**Objectives:** The aim of this study was to identify possible prognostic biomarkers for patients with vasculitis admitted to ICU.
**Methods:** A retrospective study was carried out from 2004 to 2014 in patients with systemic vasculitis admitted to the Rheumatology division and transferred to ICU due to clinical worsening, with a length of stay beyond 24 hours. An additional group of patients admitted to ICU, and without history of systemic vasculitis, were used as a matched-control group. A total of 25 patients were included in the analysis.
**Results:** ICU mortality was significantly associated with higher BVAS scores performed in the ward ($p<0.01$) and at the admission in ICU (p=0.01), regardless of the value of APACHE II scores (p=0.50). We used receiver-operator characteristic (ROC) curve analysis to evaluate the possible cutoff value for the BVAS in the ward and in ICU and we found that a BVAS $>8$ in the ward and that a BVAS $>10$ in ICU were significantly related to the mortality in ICU ($p<0.01$).
**Conclusions:** BVAS appears to be an excellent tool for assessing ICU mortality risk of patients with systemic vasculitides admitted to specialty departments. Our experience has shown that performing the assessment at admission to the ward is more important than determining the evaluation before the clinical aggravation causing the transfer to ICU.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3502

## AB0542 DO AGE-RELATED VARIATIONS REMAIN IN HENOCH-SCHÖLEIN PURPURA CURRENTLY?

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**Background:** Henoch-Schölein purpura (HSP) is a generalised vasculitis characterised by various combinations of skin, joint, gastrointestinal and renal involvement. The diagnosis HSP is based on clinical and histological features. HSP can occur at any age, but is most common in childhood. The etiology remains unknown, although it is quite common upper respiratory tract (URT) infections as a precedent.
**Objectives:** To describe the prevalence of the clinical manifestations in adults and children at the time of diagnosis of HSP.
**Methods:** A retrospective study of the case records of all admitted patients identified by the HSP diagnosis in the Hospital Universitario Severo Ochoa (Madrid, Spain) between January 1976 and June 2015 was undertaken. Classification criteria proposed by Michel et al were used for the diagnosis - including age $<20$ years at onset (1). Demographic, clinical and laboratory data at the time of diagnosis of the patients with HSP were extracted from their clinical records according to a specifically designed protocol and stored in a computerized file. Continuous data were described as mean and standard deviation (mean, SD), or median and interquartile range (IQR) and categorical variables as percentages. Means and incidence rates were compared using the Student t test. To compare categorical data we performed the chi-square test.
**Results:** We identified 51 patients, mainly male (64.7%), with a median age at the onset of symptoms of 18 (IQR 13–41) years old. Thirty nine were younger than 20 years old. In 51% a history of URT infection before the onset of HSP was found, particularly in children (56.4%), without statistical significance (p=0.19). Palpable purpura was the initial manifestation of the disease in all patients. Differences in the distribution of cases by joint and abdominal manifestations between adults and children were not statistically significant. Joint involvement was presented in 66.7% (34 patients), where arthritis was recorded up to 41.2%, mostly children having arthritis in 84.21% (p=0.5). Abdominal manifestations were presented in 60.8% (47% adults and 13% children) (p=0.8). Renal manifestations were hardly recorded at onset, whereas up to 66.7% had no renal involvement described (31 children and 3 adults) (p=0.001). Hematuria and proteinuria were observed in 3.9% and 2% of the study population respectively, while the association of both renal manifestations was observed in 21.6%.
**Conclusions:** Although the simple size is small, our study shows several differences at the onset of HSP between adults and children. The disease is observed predominantly in childhood, where joint involvement was frequent. Renal involvement, generally manifested as hematuria either isolated or in association with proteinuria, constitutes the most serious feature of HSP in adulthood.
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[1] Michel BA, Hunder GG, Bloch DA, Calabrese LH. Hypersensitivity vasculitis and Henoch-Schonlein purpura: A comparison between the 2 disorders. J Rheumatol 19: 721–8, 1992
**Disclosure of Interest:** None declared
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## AB0543 RISK FACTORS FOR MORTALITY IN ANCA-ASSOCIATED VASCULITIDES

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**Background:** Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides (AAV) are necrotizing small-vessel vasculitides in conjunction with autoantibodies to neutrophil constituents. Diffuse alveolar hemorrhage (DAH) and

renal involvement are the most serious manifestations, and higher five factor score (FFS) has been associated with higher mortality rate. Although the introduction of cyclophosphamide and corticosteroids has changed the natural history of disease from an almost fatal condition to a relapsing and remitting one with greatly increased survival, patients with AAV still have a 9-fold increased risk of death in the first year of disease. Furthermore, reported causes of death (COD) and risk factors for mortality vary between studies, which indicate the need of further investigation.

**Objectives:**

To investigate the COD and risk factors for mortality in patients with AAV.

**Methods:** A retrospective study was conducted in 44 patients with microscopic polyangiitis (MPA) and 12 granulomatosis with polyangiitis (GPA) from January 1999 to December 2011. All patients fulfilled the Chapel Hill Consensus Conference 1992 definition and Sorensen's diagnostic criteria for MPA and GPA. We reviewed medical records of patients including basic demographic characteristics, cumulative clinical features, treatment agents, and causes of death. The primary COD was defined as the main clinical and pathological process directly responsible for death and then categorized into 3 groups: vasculitis-related, vasculitis-unrelated, and unknown.

**Results:** Renal involvement and DAH were observed in 73.2% (41/56), and 30.4 (17/56), respectively, in all the patients with MPA or GPA. The mortality rate was 41.1% (23/56) with 5 deaths (41.6%) in patients with GPA and 18 (40.9%) with MPA. Among the significant risk factors for mortality on univariate analysis, which include DAH, renal involvement, $\geq$4 organ involvements, $\geq$2 FFS scores, and $\geq$4 treatment modalities, a multivariate regression analysis identified DAH as an independent predicting factor (HR, 10.28; 95% CI, 2.58–40.56; $p<0.001$). In an analysis of COD, two deaths (8.6%) were related to vasculitis, while 19 (82.6%) were related to infection. The most common COD was pneumonia (17/23, 73.9%) which, in turn, was associated with DAH (OR, 27.18; 95% CI, 4.30 - 171.80; $p<0.001$) and $\geq$4 organ involvement (OR, 7.62; 95% CI, 1.54 - 37.71; $p=0.013$) as independent risk factors. Bacteria were the most frequent microorganisms causing pneumonia (n=43, 68.2%), followed by fungi (n=8, 12.7%) and *Pneumocyctis jirovecii* (n=7, 11.1%). Most frequently isolated bacteria were *Acinetobacter baumanii* (6 cases), and *Staphylococcus aureus* (MRSA, 6 cases). The mean number of isolated pathogens in patients with pneumonia was 3.33 ±2.11. There were no significant difference in the mean number of pathogens between patients who survived and dead (3.00±0.00 vs. 3.37±2.24).

**Conclusions:** The result of present study implicated that early intervention of pulmonary infection may be critical to increase survival rates in AAV patients with DAH and or severe disease.

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## AB0544 SERUM BETA 2-MICROGLOBULIN LEVELS IN BEHÇET'S DISEASE

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**Background:** Behçet's disease (BD) is a systemic vasculitis characterized by oral ulcer, genital ulcer, skin lesion and uveitis. Because there is no reliable biomarker, the evaluation of BD disease activity is dependent on the extent of clinical manifestation and usually assessed by questionnaires, such as Behcet's Disease Activity Score (BSAS) or Behcet's Disease Current Activity Form (BDCAF).

**Objectives:** This study was performed to investigate the association of serum beta 2-microglobulin level and clinical manifestation or disease activity in BD.

**Methods:** The study population consisted of 63 patients with BD and 21 healthy controls. Patients with BD were assessed by disease duration, currently involved organ, BSAS, BDCAF, ESR and CRP.

**Results:** Serum beta 2-microglobulin levels of patients with BD were found to be significantly higher than those in the healthy controls (median 1.67 mg/L and 1.44 mg/L, p=0.003). In further analysis in BD patients, it was significantly correlated with ESR (rho =0.289, p=0.025) and CRP (rho =0.364, p=0.004) but not correlated with BD activity represented by BSAS (rho = -0.039, p=0.761) and BDCAF (rho =0.011, p=0.929). Serum beta 2-microglobulin levels were significantly increased with age (rho =0.459, $p<0.001$) but did not have correlation with BD duration (rho =0.161, p=0.212). There was no difference in the serum beta 2-microglobulin levels according to the presence of oral ulcer, genital ulcer, skin lesion, uveitis and arthritis.

**Conclusions:** Serum beta 2-microglobulin was elevated in patients with BD and correlated with ESR and CRP, but was not correlated with BD clinical manifestation or disease activity.

**Disclosure of Interest:** None declared

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## AB0545 INTERFERON ALPHA2A VERSUS CYCLOSPORIN A FOR THE TREATMENT OF SEVERE OCULAR BEHCET'S DISEASE – A PROSPECTIVE, RANDOMISED, SINGLE BLIND, NATIONAL MULTICENTER TRIAL (INCYTOB)

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**Background:** Behcet's disease (BD) is a variable vessel vasculitis. To date, there are only retrospective case series showing efficacy of interferon alpha for ocular BD. This trial was started in 2007.

**Objectives:** To prove that interferon alpha2a is at least as effective as cyclosporin A.

**Methods:** Maintenance dosage of IFN was 3 to 9 Mill iU 3x/week, CSA dosage 3 to 5 mg/kg, adapted to response every two weeks. In case of nonresponse, the patients were switched to the alternative treatment arm after week six. Efficacy was measured by Posterior Uveitis scoring system (PUS), Behcet's disease current activity form (BDCAF), Health assessment questionnaire (HAQ) and Beck depression Inventory (BDI) were also used. Primary endpoints were time to remission by PUS and number of cross over from one arm to the other.

**Results:** The study was stopped in 2013 after 37 patients due to slow recruitment. 13 patients per treatment arm (n=26, 65% male, 35% female, 38% German, 50% Turkish, 12% other, mean age 30.5 years) were evaluated. All 13 patients with primarily IFN achieved remission of their ocular disease, 9 of 13 in the CSA arm (p=0.096). The median time to complete PUS remission was 84 vs. 72 days, p=0.899. The probability to achieve remission after one year was 0.92 for IFN (95% CI 0.49–0.99) and 0.62 for CSA (95%CI 0.24–0.81). There were significantly more switches from CSA to IFN (n=7) than vice versa (n=1) (p=0.030). The main reasons were inefficacy (n=4 for CSA) and/or side effects (n=3 for CSA). PUS of the affected eyes improved significantly in both arms during the first year ($p<0.001$). Visual acuity at baseline was significantly better in the CSA arm than in the IFN arm, hence a significant improvement over time could only be shown in the IFN arm ($p<0.003$ week 30). BDCAF improved in both arms ($p>0.001$), as did HAQ (p=0.047). Safety analysis revealed more hair loss (p=0.004) and cytopenia ($p<0.001$) in the IFN and hypertension (p=0.048) in the CSA arm.

**Conclusions:** Both treatments are effective for ocular and extraocular BD. There is a tendency towards superiority of interferon alpha considering that there were more switches from CSA to IFN due to inefficacy and side effects. Due to the small sample size, this did not reach significance. A prospective international multicenter trial may help to overcome these limitations.

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## AB0546 SHOULD A RHEUMATOLOGIST MANAGE PATIENTS WITH GIANT CELL ARTERITIS?

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**Background:** Temporal arteritis (TA) is the commonest vasculitis characterised by inflammation of large and medium vessels. It predominantly affects the cranial arteries arising from the aortic arch and requires early recognition and treatment to ensure the avoidance of ischaemic neuro-ophthalmic complications.

**Objectives:** 100% compliance with the British Society of Rheumatology guidelines for TA: Ø Diagnosis criteria Ø Urgent referral for specialist evaluation Ø Inflammatory markers checked before steroid started Ø Temporal artery biopsy (TAB) advised for all the patients with a suspicion of TA Ø Analyse the correlation between inflammatory markers and TAB results Ø and the complex management of this patients.

**Methods:** Retrospective analysis of electronic records of patients that were discharged from acute services with a diagnosis of TA from Brighton and Sussex University Hospital between 1st August 2012 and 31st July 2015.

Patients' blood and TAB results were checked. Specialist letters (Rheumatology, Ophthalmology, Care of the Elderly, TAB clinic) were reviewed electronically. We analized the discharge medication and the advice following specialist review and investigations performed.

**Results:** There were a total of 39 patients with a proposed diagnosis of TA 37 of which had data available for analysis. The average age was 77, 74% were female. Two patients (5%) were referred by the GP for TAB. One of them (50%)

had a positive TAB but was not referred for a rheumatology review. Only 62% had TAB from which 46% were positive. 91% of positive biopsies had an ESR>50 and 100% had a CRP>5. All the patients seen in hospital were immediately started on steroids. Only 79% were on Calcium and Vitamin D3, 67% were on Bisphosphonates, 27% were on Antiplatelet treatment and 74% were on a proton pump inhibitor (PPI). 54% of the patients were seen by a Rheumatologist with the diagnosis being confirmed in 86%, even though 44.5% did not have a TAB and 11% had a negative result. One third of the patients had no evidence of secondary care follow up, 13% were seen by Ophthalmology and 2.5% by Elderly Care. From the 46% not seen by a Rheumatologist 11% had a positive TAB and 33% did not undergo TAB. From 8 patients seen by Ophthalmogist 37% were referred for a rheumatology review and only 50% of those with a positive biopsy.
**Conclusions:** In order to achieve 100% standards as set by BSR guidelines based on ACR criteria we need to reinforce GP's to directly refer to Rheumatologist. We recommend that all those patients seen by the medics in hospitals should be referred for Rheumatology review directly as well as those patients seen by an ophthalmologist. Rheumatology review should focus more on the supportive medical management to ensure the BSR guidelines are appropriately implemented. We have proposed a pathway for the investigation, management and specialist review for those patients suspected of Giant Cell Arteritis that will be attached to the discharge letter from the hospital and from the TAB clinics.
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[1] The NICE and British Society of Rheumatology guidelines.
**Disclosure of Interest:** None declared
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## AB0547 DIAGNOSTIC DELAY FOR GIANT CELL ARTERITIS (GCA). A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** The diagnosis of giant cell arteritis (GCA) remains difficult, with patients often presenting with non-specific and atypical symptoms. Such ambiguity can lead to delays in the diagnosis of GCA, which in-turn may result in the patient experiencing preventable and life-altering outcomes, including blindness. Despite the seriousness of such diagnostic delay, the extent of this, though frequently highlighted, has seldom been the primary focus of GCA research. Without a clear understanding of the extent to which GCA diagnosis is delayed, it is difficult to quantify the current problem and how this may then impact on patient outcomes.
**Objectives:** To determine the average time-period between the onset of GCA symptoms and receiving a GCA diagnosis.
**Methods:** We conducted a systematic review and meta-analysis to identify research literature which has examined diagnostic delay of GCA and to determine the extent of this delay. Literature searches were conducted in the following bibliometric databases; MEDLINE, EMBASE, CINAHL, PsycInfo and ISI web of knowledge. A single reviewer (HR) initially performed a title screen; abstracts were then reviewed by two reviewers (HR & JP) and finally, two reviewers (JP & CM) assessed the remaining articles in full. Final article selection was based on pre-specified inclusion criteria and from these data on a multitude of factors was extracted. The primary outcome of interest was the "average number of weeks between onset of GCA symptoms and GCA diagnosis", with other extracted data including; lead author, year of publication, sample size, gender, age, country, healthcare setting, method of GCA diagnosis and the definition of diagnostic delay. Where diagnostic delay was reported as 'days" or "months", data were converted to "weeks" to provide a standardised dataset for analysis. Standard deviations were also converted to standard errors (SE) for use in a meta-analysis. Random-effects meta-analysis was used to report the mean number of weeks (95% confidence interval (CI)) between symptom onset and GCA diagnosis.
**Results:** 4,128 articles were initially identified, 185 were reviewed in full and 34 articles were included in the final systematic review. Of these, the average age ranged from 65.2 to 81.6 years and GCA samples from 31 articles were recruited from secondary care. GCA diagnosis was defined by a positive temporal artery biopsy in 25 articles, using the 1990 ACR criteria in 4 articles, with the remaining articles either using clinical judgement or not providing a definition. Delay was determined by the article reporting "how many days, weeks or months had occurred between GCA symptom onset and receiving a diagnosis of GCA". 16 articles were included in the meta-analysis, resulting in a mean number of weeks between symptom onset and GCA diagnosis of 8.87 (95% CI 6.4 to 11.3) ($I^2$ =95.8%, p<0.001).
**Conclusions:** On average, patients experience approximately a 9-week delay between the onset of their symptoms and receiving a diagnosis of GCA. The reasons for this are yet to be understood, but could provide important insight and inform future strategies to improve outcomes for patients. Our research provides the current benchmark for diagnostic delay of GCA for which future efforts to reduce this problem can be measured against.
**Disclosure of Interest:** None declared
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## AB0549 ANCA TESTING IN A COHORT OF PATIENTS FROM A SINGLE CENTRE

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**Background:** Antineutrophil cytoplasmic antibodies (ANCA) are autoantibodies directed against constituents of primary granules of neutrophils. ANCA are the serological marker of some idiopathic systemic vasculitides, predominantly involving small and medium-sized blood vessels, such as granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA), which are known as the ANCA-associated vasculitis (AAV). Although ANCA are the serological hallmark of AAV, ANCA have been reported in a number of other conditions including infections, malignancies, connective-tissue diseases, liver and gastrointestinal diseases, renal diseases, and other vasculitides. Many studies have evaluated the clinical value of ANCA testing, but few analyze ANCA utility under actual routine conditions in unselected patients with the usual laboratory techniques.
**Objectives:** Our aim was to evaluate the positive predictive value (PPV) of ANCA testing in a cohort of unselected patients from a Spanish tertiary hospital.
**Methods:** We reviewed the clinical charts of patients with positive ANCA testing between January 2014 and December 2014 at the Immunology Department from a 1.000-bed tertiary teaching hospital from Barcelona (Spain). Detection methods included indirect immunofluorescence (IIF) for all testing request and chemiluminescent immuno-assay (CLIA) for antibodies against mieloperoxidase (MPO) and proteinase 3 (PR3) in patients with positive IIF.
**Results:** Out of 1615 patients with ANCA testing request, 298 (18.5%) tested positive. Atypical pattern (X-ANCA) was the most frequent (50.3%) over perinuclear pattern (P-ANCA) (27.5%) and cytoplasmatic pattern (C-ANCA) (22.1%). 35.4% of P-ANCA and 36.4% of C-ANCA were positive for MPO-ANCA and PR3-ANCA, respectively, whereas 97.3% of X-ANCA tested negative by CLIA. 53 (18.2%) patients with positive ANCA had a diagnosis of ANCA-associated vasculitis (AAV). Other diagnosis were the following: 26 (8.9%) connective tissue diseases, 13 (4.5%) vasculitides non-AAV, 13 (4.5%) autoimmune liver diseases and 11 (3.8%) inflammatory bowel disease. The combination of IIF and CLIA showed the best diagnostic accuracy. P-ANCA with anti-MPO had a PPV of 75% for AAV, and PPV of C-ANCA with anti-PR3 was 70.8% for GPA.
**Conclusions:** This study proves that ANCA testing with modern commonly commercially available methods has an elevated PPV for AAV in routine clinical practice.
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**Disclosure of Interest:** None declared
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## AB0550 HUGHES-STOVIN SYNDROME: SUCCESSFUL USE OF INFLIXIMAB IN LIFE THREATENING BEHCET'S, WITH PULMONARY INVOLVEMENT IN 3 CASES IN AN UNIVERSITY HOSPITAL

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**Background:** Hughes-Stovin Syndrome (HSS) is described as a very rare vascular manifestation of Behcet's disease in medical literature. HSS is a very rare clinical disorder and around 40–60 published cases of HSS have been described in medical literature so far.
**Objectives:** To illustrate the use of Infliximab in three cases.
**Methods:** Case1: A 25 year old male presented with optic nerve emboli, oral ulcers and CT scan revealed pulmonary artery aneurysms within the right lower lobe and pulmonary emboli (image). This was treated with Endovascular coiling, pulsed cyclophosphamide, mycophenolate and prednisolone. He had ongoing episodes of haemoptysis that were treated with Infliximab. The patient is now well controlled on Infliximab, mycophenolate and prednisolone.
Case2: A 34 year old male with history of genital and mouth ulcers, presented with haemoptysis and CT scan showed multiple pulmonary emboli with aneurysms. He was treated with pulsed Methyl-prednisolone and infliximab 5mg /kg at weeks 0,4,6 and 8, followed by every 8 weeks and Methotrexate. He later developed a DVT, therefore the methotrexate was switched to Azathioprine 2.5mg/kg/day

and he received Methyl-prednisolone. Infliximab dose was increased to every 2 weeks. After ongoing review he was switched from Infliximab to Adalimumab and he is now in remission.
Case3: A 19 year old male admitted with haemoptysis and respiratory compromise and was intubated in ICU. His CTPA showed bilateral pulmonary emboli with aneurysms. He had erythematous macules, follicular papules, oral ulcers and weight loss with positive pathergy. He was treated with IV methyl prednisolone and infliximab 5mg/kg every 2 weeks.He was extubated 24 hrs after starting treatment and he was discharged home within 9 days of treatment.He is maintained on Adalimumab and Azathioprine and he is now in remission.
**Results:** Although case 1 did not fulfill the ISG criteria for Behcet's disease, case 2&3 fulfilled the criteria. Case1 had a protracted course although managed as per Behcet's pathway by Behcet's centres of excellence in UK and Infliximab was used as a step up treatment. Case 3 presented very unwell, but he was extubated 24 hrs after starting treatment and Infliximab was used as an induction treatment.



**Conclusions:** Early diagnosis and timely intervention is crucial in improving the prognosis of patients with HSS. Our experience of these 3 rare cases suggests that Infliximab should be used as induction treatment in managing life threatening HSS.
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## AB0551 CLINICAL APPLICATION OF TWO DIFFERENT DISEASE ACTIVITY SCORES FOR ENT INVOLVEMENT IN GRANULOMATOSIS WITH POLYANGIITIS

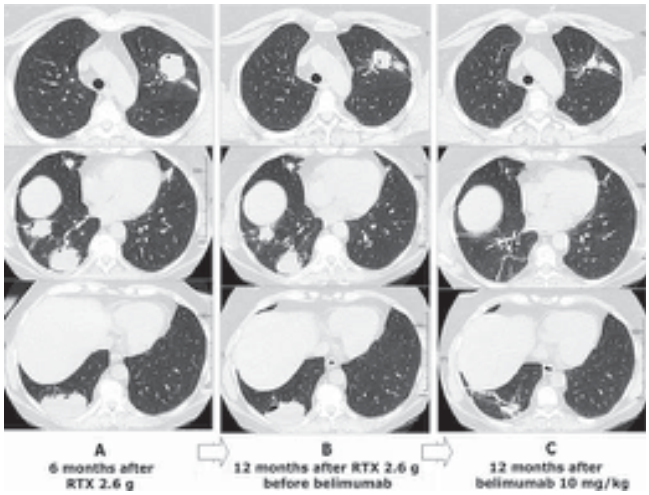
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**Background:** In the management of Granulomatosis with Polyangiitis (GPA), is critical to assess correctly the disease activity in each organ to define the better therapeutic approach and follow up strategy. This statement is also valid for ENT involvement, that we decide to assess with two different organ specific disease activity scores, the already validated Del Pero ENT/GPA DAS[1] and a new ENT score developed by our Otolaryngology Unit (Padova,ENT/GPA DAS), composed by 8 items: nasal crusting, reported bloody rhinorrhea, nasal inflammation, laryngoscopy inflammation, objective stridor, inflamed TM/middle ear, siero-mucous otitis and hearing loss.
**Objectives:** Compare the accuracy of two different ENT scores (ENT/GPA DAS and Padova ENT/GPA DAS) and correlate them with the most commonly used GPA Activity Indexes and identify if they are effective to predict relapses that require therapeutic changes.
**Methods:** We selected retrospectively the GPA patients with ENT involvement followed by Rheumatology and Otolaryngology Units from 2006 to 2015. Each ENT evaluation of our patients were matched with temporally nearest Rheumatologic visit to assess the ENT/GPA DAS, the Padova ENT/GPA DAS, the Birmingham Vasculitis Activity Scores (BVAS v3, BVAS-WG), the Physician Global Assessment (PGA), the Vasculatis Damage Index (VDI), the serological biomarkers (ESR and CRP) and treatment strategy.
For statistical analysis, we used Mann Whitney test, Spearman test and Fisher test.
**Results:** The selected ENT/GPA patients were 25 (41.6% of all GPA patient cohort), mainly middle aged (51.7±14.9 years), women (64%) and ANCA positive (80%) with PR3 specificity (75%). The total of ENT assessment were 67, so some patient were seen more than once (mean 2.68, min 1, max 8). The two considered ENT scores presented a significant difference ($p<0.0004$) from each other and the correlation analysis showed that ENT/GPA DAS was directly correlated to ESR ($p<0.0001$), CRP ($p=0.03$), BVAS v3 ($p=0.005$), BVAS-WG ($p=0.004$) and PGA ($p<0.0001$), while our Padova ENT/GPA DAS presented a significant correlation only with VES ($p<0.0001$) and PGA ($p=0.027$).
The therapeutic strategies analysis observed that, in all cohort, the change of the immunosuppressive drug (32/67) presented higher BVAS v3 ($p<0.0001$), BVAS-WG ($p<0.0001$) and PGA ($p<0.0001$). Furthermore, in follow up visits of patient in maintenance therapy or induction of remission therapy, excluded those with Cyclophosphamide or Rituximab (25/44), we observed a significant increased rate of therapeutic change in those with ENT/GPA DAS higher than 0 ($p=0.025$, OR 5.8 IC95% 1.16–24.9)
**Conclusions:** Our analysis showed that ENT/GPA DAS is more performing than Padova ENT/GPA DAS to reflect the disease activity. This is probably a consequence that some items considered in our ENT/GPA DAS, such as all type of hearing loss, express better the damage than active disease. Moreover, the data showed that ENT/GPA DAS could identify patients with an active disease worthy of therapeutic changes, especially in particular patient subsets. This data should be confirmed with further evidences on larger GPA patients cohorts and prospective studies.
**References:**
[1] Del Pero MM et al Laryngoscope, 123:622–628, 2013.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4577

## AB0552 SUCCESSFUL EXPERIENCE WITH BELIMUMAB IN THE TREATMENT OF REFRACTORY GRANULOMATOSIS WITH POLYANGIITIS

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**Background:** Anti-CD20 antibody rituximab (RTX) has proved beneficial in ANCA-associated vasculitis (AAV). However, granulomatous features typical for the granulomatosis with polyangiitis (GPA) can be resistant to RTX, primarily after a single course. Local production of B-cell activating factor (BAFF) in granulomatous lesions and elevated levels of serum BAFF in AAV provide a rationale for BAFF-targeted therapies. The anti-BAFF monoclonal antibody (belimumab) has shown efficacy in SLE, and its role as a relapse prevention agent in AAV is being assessed in a randomized trial (BREVAS), but whether BAFF-neutralization can be used to induce remission of AAV remains unsolved.
There is some evidence for increasing of BAFF levels after RTX treatment (Holden et al., 2011) and high levels of BAFF are associated with a shorter duration of the RTX-induced B-cell depletion. Thus, addition of belimumab should potentially enhance B-cell suppression.
**Objectives:** Here we present the first clinical case report of effective belimumab use for remission induction in GPA with severe pulmonary granulomatous inflammation, which was refractory to cyclophosphamide (CYC) and one course of RTX.
**Results:** A 56-year-old woman with 6-month history of fever, rhinitis, otitis, cough, polyarthralgia and cranial nerve affection was admitted to hospital. A chest X-ray revealed bilateral nodules. Fiberoptic bronchoscopy revealed infiltration in the subglottic area and ulcerated lesions along the tracheobronchial tree. She also had elevated inflammatory markers (ESR 24 mm/h, CRP 48 mg/dL), thrombocytosis (PLT $781\times10^3$/mm$^3$) and cytoplasmatic pattern positive ANCA by indirect immunofluorescence screening. GPA was diagnosed. Induction therapy included prednisolone (40 mg/day) and pulses of CYC and methylprednisolone.
6 mo later CYC total dose (TD) was 6.2 g, prednisolone 15 mg/day. A CT scan revealed new focuses of granulomatous inflammation in lungs. Birmingham Vasculitis Activity Score (BVAS)=8. ESR 45 mm/h, CRP 13 mg/dL, platelets $323\times10^3$/mm$^3$, ANCA was negative. RTX (TD 2.6 g) was administered due to the refractory GPA and resulted in B-cell depletion.
After 6 mo of RTX clinical improvement was achieved, however, a CT scan



revealed persistence of pulmonary lesions (A). BVAS=6. CRP 2 mg/dL, CD19+ B-cells 0%. Mycophenolate mofetil 1 g/day was initiated but soon discontinued due to nausea and replaced by azathioprine 100 mg/day. As there was no significant improvement after 12 mo of RTX (B), treatment with belimumab was initiated (800 mg/wk N2, then 800 mg/mo).

CT monitoring showed consistent improvement of pulmonary lesions after administration of belimumab (C), but at 12 mo the lesions failed to resolve completely, necessitating the prolongation of Belimumab to total 18 mo, then due to poor tolerability (emerging stomatitis) it had to be discontinued. Thus, RTX was restarted at 500 mg twice with 6 mo interval, providing further improvement in CT images.

**Conclusions:** Belimumab can be useful in treatment of patients with GPA, who are refractory to CYC and RTX. Combined approach to B-cell targeting with both anti-CD20 and anti-BAFF treatment can represent promising strategy for patients with severe refractory GPA.

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**Disclosure of Interest:** None declared

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## AB0553 SYSTEMIC VASCULITIS OF AUTOIMMUNE AND SEPTIC ORIGIN – A COMPARATIVE POSTMORTEM STUDY OF 38 RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Systemic vasculitis of autoimmune origin (A-SV) is of critical importance in the pathogenesis of rheumatoid arthritis (RA). RA may be complicated by septic infections (SI) accompanied with systemic vasculitis of septic origin (S-SV). The correct clinical diagnosis of A-SV and S-SV is essential because of essential differences in therapy.

**Objectives:** The aim of this study was to characterize the A-SV and S-SV by the type, incidence and severity of vasculitis involving blood vessels of different caliber.

**Methods:** At the National Institute of Rheumatology 12138 patients died between 1969 and 2000; among them 234 with RA and all of them were autopsied. RA was confirmed clinically according to the criteria of the ACR. Lethal septic infection (SI) was observed in 31 (13.25%) of 234 patients. SI was accompanied in 5 patients with S-SV. The clinically identified pathogenic agents and the strong, significant and positive correlation between S-SV and SI (association coefficient: 1, $c^2$=26.1881, $p<0.00007$) supported the infectious origin of SV.

The average incidence and severity of S-SV in twelve organs of these 5 RA patients was analyzed and compared with 33 RA patients with A-SV of our previous study [1]. The negative value of association coefficient and the lack of significant correlation between A-SV and lethal SI (association coefficient: -0.3249 $c^2$=0.6052, $p<0.44$) supported the direct autoimmune origin of SV in patients without SI [1].

The incidence (existence), severity, and the types of vasculitis (non- specific – Ns, fibrinoid necrotic – Fn, granulomatous – Gr) in blood vessels of different calibers (arteriole – a, small artery – A, medium size artery – AA, venule – v, small vein – V, medium size vein – VV) were determined visually in histological slides [1]. Severity of vasculitis was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale (based on the number of involved vessels/light microscopic field x40).

**Results:** The incidence and severity of A-SV and S-SV in absolute number is summarized in Table.

| N of RA patients with SV | Type of vasculitis | | | Size of involved blood vessels | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | Ns | Fn | Gr | a | A | AA | v | V | VV | |
| A-SV (n=33) | | | | | | | | | | |
| A-SV incidence | 216 | 64 | 45 | 169 | 106 | 32 | 6 | 9 | 3 | 325 |
| A-SV severity | 395 | 119 | 80 | 322 | 191 | 55 | 9 | 13 | 4 | 594 |
| S-SV (n=5) | | | | | | | | | | |
| S-SV incidence | 50 | 17 | 0 | 27 | 23 | 15 | 0 | 0 | 2 | 67 |
| S-SV severity | 87 | 27 | 0 | 53 | 40 | 18 | 0 | 0 | 3 | 114 |

**Conclusions:** The clinical course of RA characterized by acute exacerbations and relapses corresponds to the relapsing nature of autoimmune vasculitis. A-SV and S-SV may exist in different stages of inflammation at the same time [1]. A-SV is more severe and shows variegated histologic changes, versus S-SV which is less severe and more monotonous.

Non-specific and fibrinoid necrotic vasculitis may exist in A-SV and S-SV as well. Granulomatous vasculitis was never detected in S-SV; the presence of granulomatous vasculitis refers to A-SV.

Arteries of all calibers may be involved in both systemic vasculitis with more pronounced involvement of medium size arteries in S-SV. Veins were never involved in S-SV; the inflammation of veins supports A-SV.

Histological differences may help in identification of autoimmune or septic origin of vasculitis.

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**Disclosure of Interest:** None declared

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## AB0554 AN AUDIT OF THE PREVENTION OF LONG TERM COMPLICATIONS IN PATIENTS WITH AN ANCA-ASSOCIATED VASCULITIS

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**Background:** ANCA–associated vasculitis (AAV) is a potentially life threatening condition which requires immediate intervention with immunosuppressive treatment. Although patient survival from disease had improved, unfortunately patients survive to experience long term complications of both the disease and the treatment. The major cause of early mortality in this population is infection with increased later risks of malignancy and cardiovascular disease. Patients are also at risk of other treatment related morbidity such as impaired fertility. These complications are a major cause of morbidity and mortality in these patients, therefore it is vital to implement all the available preventative measures when indicated

**Objectives:** The aim for this audit was to assess whether patients were receiving the correct adjuvant treatment and counselling in order to protect them against the long term complications of ANCA-associated vasculitis and the side effects from treatment.

**Methods:** Patients under the Rheumatology/Renal vasculitis clinic at the University Hospital of South Manchester (UHSM), with a diagnosis of an AAV, were identified. Audit standards were set using 2008 EULAR recommendations and BSR/BHPR guidelines for management of patients with vasculitis, therefore patients diagnosed before the publication of the 2008 EULAR recommendations (April 2008) were excluded from this audit. Standards were set at 100% unless stated otherwise. Data was collected retrospectively from patient's medical records and electronic secondary care records.

**Results:** We identified 22 patients diagnosed with AAV at UHSM after April 2008, comprising of 12 male and 10 female patients, ranging from 23 to 70 years of age. The median age is 51 and the interquartile range is 22.5. Of these patients, 25% were assessed for their risk of tuberculosis prior to treatment and 77.2% and 72.7%, were given the influenza and pneumococcal vaccines respectively. Only 4.76% of patients had a full cardiovascular risk assessment in the 12 months prior to this audit. This comprised of monitoring the patients' blood pressure (95.24%), weight (90.48%), cholesterol (80.95%) and HbA1c/ fasting glucose levels (76.19%) and counselling patients about smoking cessation (0% documented) and exercise (23.81% documented). Of the 13 patients treated with intravenous cyclophosphamide, 87.5% received Mesna, 91.6% were monitored for bladder cancer with a urinalysis and 40% of women were documented to have been advised to have cervical smears. 37.5% of patients were informed about the risk of infertility; however, no male patients had a documented offer of sperm banking.

**Conclusions:** Optimal preventative management for the complications of disease and treatment were not uniformly applied to patients with AAV. Awareness and screening for cardiovascular risks were good however areas for improvement include counselling these patients about possible risks associated with treatment of the disease, such as infertility and encouraging uptake of protective measures

**Disclosure of Interest:** None declared

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## AB0555 AMOUNT OF PROTEINURIA IS RISK OF FLARE FROM BVAS REMISSION AMONG MICROSCOPIC POLYANGIITIS PATIENTS IN JAPAN

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**Background:** Microscopic polyangiitis (MPA) is a common form of ANCA associated vasculitis in Japan. Renal involvement is frequent in MPA and an important factor with respect to therapeutic methods and outcomes.

**Objectives:** To determine the association between renal characteristics at diagnosis and the relapse.

**Methods:** A retrospective review was conducted in 28 patients who were newly diagnosed as MPA. (January 2007 to August 2015) Baseline characteristics are collected include urine profile and renal pathology. The primary endpoint is the first flare. Disease flare is defined an increase in at least one major Birmingham vasculitis activity score (BVAS) items. Furthermore, analysis on other outcomes, such as end stage renal failure, induction of hemodialysis and death has been conducted.

**Results:** Of the 28 patients with MPA, all patients had renal vasculitis. 18 achieved BVAS remission, and relapse occurred among 5 patients (19.2%). Cox

multivariate analysis showed that amount of proteinuria on admission was a predictor of relapse (HR 4.2; 95% CI, 0.13–10.5). In renal biopsy, those relapsed five cases tend to have more intensive glomerulonephritis, according to the European Vasculitis Study Group (EUVAS) classification, though no statistical significance was performed.

**Conclusions:** Amount of proteinuria is a risk factor for relapse in MPA.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.5013

## AB0556 HLA REVISITED IN EGYPTIAN PATIENTS WITH BEHÇET'S SYNDROME:NEW ASSOCIATIONS OF HLA ALLELES WITH SUSCEPTIBILITY, PROTECTION, PRESENTATION AND SEVERITY OF THE DISAESE

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**Background:** Behçet's syndrome is a multisystem autoimmune syndrome that has a male predominance. Its manifestations usually start in the young adulthood with target organ damage affecting mainly the skin, eyes, Brain and blood vessels [(1)]

**Objectives:** The aim of the study was to investigate HLA class I genotyping in a cohort of Egyptian patients with Behçet's syndrome and comparing them with HLA genotyping in healthy population (control group) to estimate possible association between HLA and syndrome susceptibility as well as syndrome presentations.

**Methods:** Fifty-seven Egyptian patients with Behçet's syndrome fulfilling the International study group criteria for Behçet's syndrome[(2)] were recruited from the Rheumatology department, Cairo University teaching hospitals.HLA class I genotyping was done for all patients via sequence specific oligonucleotides probes at the National Cancer Institute. HLA class I genotyping data of normal control group was obtained from case control studies done on Egyptian population with a total of 221 individual. [(3–4)]

**Results:** The studied 57 patients were divided into 50 males and 7 females. The mean age of patients was 35.28±9.73 years with mean disease duration of 9.26±7.36 years. The main clinical features were oral ulcers (100%), genital ulcers (100%), eye involvement (54%) neurological involvement (29%) and vascular involvement (36%) furthermore (33%) had bilateral visual acuity $\leq$6/60 fulfilling the diagnosis of legal blindness.

Certain HLA genotypes were significantly associated with susceptibility for Behçet's syndrome, the odds ratio (OR) for HLA-A68 was 8.4 (CI=2.9–25.9), HLA-B15 was 6.7 (CI=2.9–15.6), HLA-B51 was 6.6 (CI=3.4–13.0), HLA-A24 was 4.0 (CI=1.5–10.2) and HLA-A2 was 2.1 (CI=1.1–3.8). On the other hand HLA A3 genotype was found to be significantly protective with odds ratio of 0.003 (CI=0.01–0.6).

HLA B51 was significantly associated with ocular disease with odds ratio of 3.47. Furthermore HLA B51 was associated with legal blindness with a significant odds ratio of 5.21.

**Conclusions:** HLA A68, B15, B51, A24 and A2 are associated with Behçet's syndrome susceptibility in the present cohort of Egyptian patients and A3 was found to be protective.

HLA B51 is associated with ocular involvement and more important the blinding eye disease and can be considered as a poor prognostic marker for ocular disease.

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**Disclosure of Interest:** None declared

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## AB0557 BEHÇET'S DISEASE IN WOMEN: A TUNISIAN SERIES OF 135 PATIENTS

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**Objectives:** The aim of this study was to describe clinical and genetic characteristics of Behçet's disease (BD) in women and to compare them with those in men.

**Methods:** 430 cases of patients with BD (fulfilling criteria of the International Study Group for BD) were studied. Clinical and genetic characteristics of women with BD were noted, than compared to those observed in male BD patients. Data were compared using the Chi2 test and the Fisher exact test.

**Results:** 135 women were studied; the mean age at the onset of the BD was at 28.7 years. The average age at BD diagnosis was 34.64 years. Genital aphtosis was noted in 71.9% of patients and skin lesions in 83% (pseudofolliculitis: 63.7%, erythema nodosum: 28.9% and positive pathergy test: 56.6%). Ocular involvement in type of uveitis was noted in 43% of patients and retinal vasculitis in 23.7% of them. 65% of women complained of arthralgia while only 7.4% of them presented arthritis. Neurological manifestations were objectified in 31.9% of patients. Deep vein thrombosis (DVT) and arterial disease were noted respectively in 15.6% and 0.7% of cases. HLA B51 was present in 47.7% of women with BD in our series. Compared to male patients, women had significantly less genital aphtosis (71.9% vs 83%, p=0.008), pseudofolliculitis (63.7% vs 79.6%, $p<0.0001$), DVT (15.6% vs 33.2%, $p<0.0001$) and arterial disease (0.7% vs 9.2%, p=0.001). On the contrary, arthralgia (65% vs 47.5%, p=0.007) and erythema nodosum (28.9% vs 11.6%, $p<0.0001$) were significantly more frequent in women.

**Conclusions:** Our results were similar to other BD series regarding the high incidence of erythema nodosum and joint manifestations in women, and the lower frequencies of genital aphtosis and vascular involvements compared to men.

**Disclosure of Interest:** None declared

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## AB0558 JUVENILE-ONSET BEHÇET'S DISEASE: CLINICAL AND GENETIC FEATURES COMPARED WITH ADULT ONSET-DISEASE

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**Background:** Behçet's disease (BD) is are in children.

**Objectives:** The aim of this study was to describe clinical spectrum of BD in childhood in comparison to adult onset-disease.

**Methods:** We conducted a retrospective study over 10 years including 430 patients with the diagnosis of BD according to the criteria of the International Study Group. The patients were placed into two groups based on the age of the disease onset: group1: juvenile-onset ($\leq$16 years) and group 2: adult-onset disease (age $>$16 years). Clinical, genetic and therapeutic characteristics of juvenile patients were analyzed and compared with adult patients

**Results:** There were 38 cases with juvenile onset disease (24 males, 14 females; gender ratio M/F: 1.7). A family history of BD was found in 3 patients. The mean age of the disease onset in this group was 12.8 years ±2.9 and the average age at BD diagnosis was 21.55 years ±7.47. Genital ulcers were observed in 71% of cases. Skin lesions were found in 76.3% of patients and positive pathergy test in 70.4%. Nineteen patients (50% of cases) had ocular involvement (uveitis: 18 cases, retinal vasculitis: 10 patients) which was complicated of blindness in 2 cases. Neurological involvement was observed in 8 patients (21% of cases). Eight patients presented vascular lesion (superficial venous thrombosis: 5 cases, deep venous thrombosis: 3 cases), no cases of arterial involvement was noted. HLA B51 was found in 62.5% of cases. Comparative study of the 2 groups showed that children with BD had significantly less deep venous thrombosis and more superficial venous thrombosis. The ocular involvement was relatively less severe in children (blindness: 15.4% vs 32.5%). Treatment was based in colchicine, corticosteroids (73.7%) and immunosuppressant agents. Cyclophosphamides were more used in adults (45.6% vs 26.3%; p=0.02) and azathioprine in children (46% vs 33%; p=0.08).

**Conclusions:** Behçet's disease in children is characterized in our series by the frequency of superficial venous thrombosis and seems to run a less severe course (less DVT and blindness, no arterial involvement and less use of cyclophosphamide). An appropriate and early treatment would prevent the occurrence of serious visceral complications in these patients.

**Disclosure of Interest:** None declared

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## AB0559 RELIABILITY AND VALIDITY OF THE TURKISH TRANSLATION OF THE BELIEFS ABOUT MEDICINES QUESTIONNAIRE (BMQ-T) IN PATIENTS WITH BEHÇET'S DISEASE

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**Background:** Behçet's disease (BD) is a multisystem vasculitis with unknown etiology characterized by the heterogeneous nature of organ involvement and a fluctuating disease course. There are various effective treatment alternatives, while, the first and essential step for a successful treatment is patients' adherence to therapy. Efforts to improve treatment outcomes require a better understanding of the particular barriers to and facilitators of adherence to therapy, and of patient experiences of taking treatment. Treatment adherence is influenced by many factors, among them: i) route of administration, ii) psychosocial factors, iii) fear of side effects, iv) lack of an immediate feeling of benefit, and v) patient attitudes to health and disease and beliefs about medicines.
**Objectives:** The aim of this study was to evaluate the reliability and validity of the Turkish translation of the Beliefs about Medicines Questionnaire (BMQ-T)© for patients with Behçet's disease.
**Methods:** This methodological study enrolled a sample of 125 patients. The scale was adapted to Turkish through a process including translation, comparison with versions in other languages, back translation, and pretesting. Construct validity was evaluated by factor analysis. Medication adherence evaluated as poor, moderate and good according to the Morisky Medication Adherence Scale (MMAS). BMQ-T scores compared along medication adherence status groups.
**Results:** In our study, as in the original scale, the factor analysis confirmed that the BMQ-T had a four-factor structure explaining 54.73% of the total variance. The BMQ-T had acceptable internal consistency (Cronbach's alpha coefficient: Specific Necessity = 0.812; Specific Concerns = 0.672; General Harm = 0.677; General Overuse = 0.656), adequate test–retest reliability (intraclass correlation coefficients: Specific Necessity = 0.715; Specific Concerns = 0.680; General Harm = 0.678; General Overuse = 0.327). Specific Necessity and Specific Concerns scores were significantly different between medication adherence status groups.
**Conclusions:** The psychometric properties of the BMQ-T were consistent with those reported in the original study. The BMQ-T was found to be a valid and reliable tool for evaluating beliefs about medicines in patients with Behçet's disease.
©Professor Rob Horne.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4884

## AB0560 CLINICAL FEATURES OF ARDIOVASCULAR INVOLVEMENT IN BEHCET'S DISEASE

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**Background:** Behcet's disease is a kind of systemic vasculitis. Multiple organs including derma, mucosae, articulation, neurologic system, gastrointestinal tract and cardiovascular system might be involved. Vital organ complications lead to poor outcomes. Cardiovascular involvement in Behcet's disease is estimated to range from 7% to 40%, with fatality rate reaches up to 29% [1–3].The characteristics of Chinese Behcet's disease patients with cardiovascular lesions were rarely reported before.
**Objectives:** To investigate the clinical characteristics of cardiovascular involvement in Behcet's disease.
**Methods:** We reviewed 35 medical records of patients of Behcet's disease with cardiovascular lesions in Anzhen Hospital, Capital Medical University between January 2002 and January 2014. All the patients fulfilled the international Behcet's disease study group criteria [4].
**Results:** (1) The mean (±SD) age when the cardiovascular disorders flare-up was 36.9±9.6 years. 27/35 (77.1%) of the patients were male.
(2) The clinical spectrum of cardiovascular abnormalities included valvular regurgitation (20,57.1%, among these patients, two patients complicated with infectious endocarditis, and five patients had perivalvular leakage after primary valvular surgery), conduction system disturbances (10,28.6%), intracardiac thrombosis (1,2.9%), aneurysms of the arteries (13,37.1%), artery stenosis or occlusion (5,14.3%), pulmonary vascular diseases (3,8.6%), venous thrombosis (4,11.4%). 20 patients had more than one of these lesions simultaneously.
(3) Clinical manifestations were varied from shortness of breath (17,48.6%), febrile (9,25.7%), chest pain (5,14.3%), dizziness (4,11.4%), cough (4,11.4%), limb ischemia (4,11.4%), palpitation (3,8.6%), hemoptysis (3,8.6%), seroperitoneum (2,5.7%), facial edema (1,2.9%), dysphagia (1,2.9%), to asymmetric blood pressure (1,2.9%).
(4) Inflammatory indicators erythrocyte sedimentation rate and C-reactive protein were not significantly different between the different subgroups (P=0.26 and P=0.972, respectively).
(5) Ten patients received corticosteroids and immunosuppressive drugs treatment. Intervention therapy (aortic coated stent lumen isolation) was administered on one patient. Operations (including valve replacement, valular annulus reconstruction, Bentall, aorta replacement and heart transplantation) were performed on 12 patients. One patient (2.9%) died from multiple organ dysfunction during hospital stay.
**Conclusions:** Cardiovascular involvement in Behcet's disease is a serious systemic lesion deserved attention. Corticosteroids and immunosuppressive drugs together with intervention therapy or operations are effective remedies for Behcet's disease patients with cardiovascular lesions.

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**DOI:** 10.1136/annrheumdis-2016-eular.2595

## AB0561 HEART INVOLVEMENT IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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**Background:** Cardiac involvement is factor of poor prognosis in eosinophilic granulomatosis with polyangiitis (EGPA). Due to current data, heart lesions in EGPA are associated with higher peripheral eosinophilia. However, data about cardiac manifestations of EGPA are limited.
The aim of the study was to evaluate the frequency of occurrence of heart involvement in patients with EGPA, and to study interrelation of heart lesion and peripheral eosinophilia and other signs of the disease.
**Objectives:** Were analyzed 19 case histories of patients with EGPA (13 women and 6 men, mean age ± SD – 49.8±14.8 years, mean disease duration – 4.6±3.76 years). The patients were treated in Saratov regional hospital, rheumatology department.
**Methods:** Were used clinical tests and echocardiography.
**Results:** 7 (36.8%) patients had features of heart damage. In 2 patients were found clinical signs of myocarditis, confirmed with echocardiography (ejection fraction 48 and 50%, respectively). In 1 patient was found fibrosis of atrioventricular valves, in 3 patients – signs of valvular insufficiency, in 1 – was diagnosed coronariitis.
Eosinophils number was increased in 11 patients: in 4 from 7 patients with cardiac involvement and in 8 from 11 without heart lesion. The highest number of eosinophils was found in 2 patients with miocarditis (40 and 43%, respectively). Improvement in miocarditis and ejection fraction under the treatment was associated with decrease of eosinophils count.
In other patients during the treatment (12–24 month of follow-up) eosinophils count was normalized. There were no new features of cardiac involvement under the treatment.
**Conclusions:** Patients with EGPA frequently have cardiac involvement. Miocarditis is associated with high eosinophils' count. Heart involvement is reversible and has no trend to progression under the treatment.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4357

## AB0562 DEMOGRAPHIC CHARACTERISTICS AND DISTRIBUTION OF THE VASCULITIDES FREQUENCIES: A REAL- LIFE EXPERIENCE OF VASCULITIS CENTER FROM EASTERN MEDITERRANEAN

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**Background:** Vasculitides are a heterogeneous group of diseases. The distribution of the type of vasculitis changes not only with age and sex but according to the geographic area as well. The prevalence of each vasculitis is important in guiding the local medical education and raising awareness of doctors and policy makers etc.
**Objectives:** This study is aimed to present the distribution of vasculitides in the Pediatric and Adult Vasculitis patient Groups.
**Methods:** Hacettepe University is one of the main referral centers in the country. Executive committee of our Vasculitis center consist of physicians from Pediatric

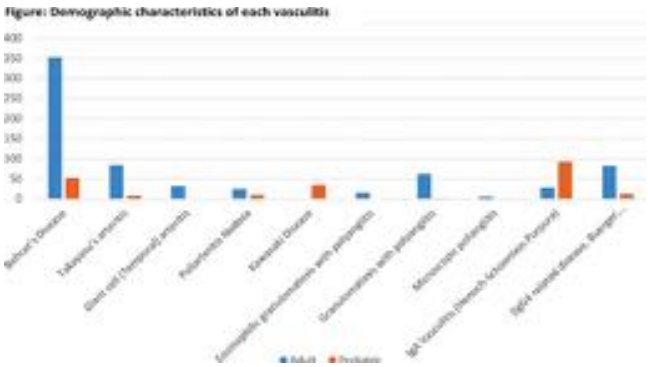
and Adult Rheumatology, Nephrology, Radiology and Pathology Departments. Multidisciplinary approach improves management of our patients. All patients starting from October 2014 have been included and defined according to the 2012 revised Chapel Hill nomenclature criteria.

**Results:** A total of 882 patients had been newly diagnosed/followed in this period. 205 (23.2%) of them were pediatric patients. The leading vasculitis among adult patients was Behcet's Disease whereas in pediatric patients it was HSP (Figure). More than half of the adult Behcet's patients (58.4%) had uveitis/neurologic/vascular involvement.

Takayasu arteritis was more frequent than giant cell arteritis among the adult patients. There was a female predominance in patients with large vessel vasculitis. Granulomatous polyangiitis was the most common small vessel vasculitis in adults. Finally 23 adult cases of Immunglobulin G4 related disease have been seen.

Table 1. Demographic characteristics of each vasculitis

| | Adult patients Mean age (SD) | Pediatric patients Mean age (SD) |
|---|---|---|
| Behçet's disease | 42.8 (12.9) | 11.8 (4.0) |
| Female, % | 52.5% | 46.1% |
| Takayasu's arteritis | 38.9 (14.2) | 14.3 (4.1) |
| Female, % | 91.6% | 100% |
| Giant cell (temporal) arteritis | 69.5 (8.2) | – |
| Female, % | 74.2% | |
| Poliarteritis nodosa | 40.1 (15.3) | 11.3 (7.3) |
| Female, % | 39.1% | 50.0% |
| Kawasaki disease | – | 4.7 (3.0) |
| Female, % | | 26.4% |
| Eosinophilic granulomatosis with polyangiitis | 52.9 (19.3) | 10 |
| Female, % | 60% | 100% |
| Granulomatosis with polyangiitis | 54.1 (15.9) | 8.5 |
| Female, % | 46.5% | 50% |
| IgA Vasculitis (Henoch-Schoenlein purpura) | 38.3 (18.5) | 7.3 (4.9) |
| Female, % | 46.1% | 47.7% |
| IgG4related disease | 47.8 (17.8) | – |
| Female, % | 52.2% | |
| Others (secondary vasculitis, Buerger, cryoglobulinemic vasculitis, aortitis, etc.) | 47.4 (15.6) | 13 (5.1) |
| Female, % | 50% | 50% |




**Conclusions:** We describe the demographic characteristics and distribution of vasculitides in the eastern Mediterranean. Behcet's disease has a high frequency as expected. Also Takayasu arteritis is more frequent than Giant cell arteritis. Microscopic polyangiitis is very rare. Among children Kawasaki was less and Behçet disease markedly more when compared to western Europe figures. The observed differences may be due to genetic modifiers or environmental factors.

**Disclosure of Interest:** None declared

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## AB0563 TAKAYASU'S ARTERITIS: EXPERIENCE FROM A TERTIARY CARE CENTRE IN WESTERN INDIA

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**Background:** Takayasu's arteritis (TA) is a rare, granulomatous panarteritis of aorta and its major branches, most commonly presenting before the age of 40 years. There is limited data regarding epidemiology of TA from India.

**Objectives:** To describe the clinical profile and outcome of patients with Takayasu arteritis from a tertiary care centre in western India.

**Methods:** We analysed medical records of TA patients satisfying the 1990 Criteria of American College of Rheumatology for the Classification of Takayasu Arteritis attending Rheumatology Department from 2009 to 2014.Demographic, clinical, laboratory, imaging features and intervention done were noted.

**Results:** Forty Eight patients were included. Mean ESR at first visit of patients was 51mm/hr and last visit was 28 mm/hr. Mean ITAS at first visit was 10.9 and last visit was 0.6.CT angiography was used in 41%, PET was done in 70% and repeat PET was done in 35%.

Table 1. Disease characteristics

| | |
|---|---|
| Female:Male ratio | 2.69:1 |
| Mean age at diagnosis (mean±SD) (years) | 34.18±11.65 |
| Fatigue | 20 (41.6%), |
| Malaise | 18 (37%), |
| Headache | 12 (25%), |
| Hypertension | 10 (20%), |
| Pulse loss | 33 (68%). |
| Bruit | 35 (72%), |
| Aortic incompetence | 4 (8%) |
| Renal artery stenosis | 5 (10%) |
| Most common pulse loss | Brachial |
| Most common bruit | Carotid |
| Most common class of disease (as per angiographic classification) | Class V |
| Most common steroid sparer used | Methotrexate 28 (58%) |
| Change of steroid sparer required in patients due to lack of efficacy | 13 (27%) |
| Surgical intervention required. | 13 (27%) |
| Patients suffered stroke during the course of illness | 7 (14%) |
| Patients diagnosed in pre pulseless stage of disease | 12 (25%) |
| Uneventful pregnancy | 4 |

**Conclusions:** 1. 12 (25%) patients were diagnosed in pre pulseless stage of disease. 2. As per angiographic classification class V disease was most common seen in our cohort. 3. 27% patients were refractory to treatment requiring surgical intervention.

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**Disclosure of Interest:** None declared

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## AB0564 SHORT-TERM RESULTS OF THE NEW ANTI-TNF TREATMENT WITH CERTOLIZUMAB PEGOL IN REFRACTORY TAKAYASU'S ARTERITIS

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**Background:** Takayasu's arteritis (TAK) has a prolonged chronic course and requires long-term immunosuppressive treatment with different results. Tumor necrosis factor (TNF) alpha is a promising target for treatment in patients with TAK, though clinical experience is limited. Certolizumab pegol (CER) is a pegylated Fab' fragment of a humanized TNF inhibitor monoclonal antibody.

**Objectives:** To evaluate the efficacy and safety of treatment with CER in patients with TAK refractory to standard immunosuppressive treatment.

**Methods:** Four patients with type 5 [generalized] TAK (all females, median age 30.5 years [20–33]) were treated with CER for the average of 10.5 months (8–12). TAK was diagnosed according to the ACR criteria and CHCC2012. CER was administered subcutaneously at a dosage of 400 mg every 4 weeks (with loading dose 400 mg every 2 weeks for the first month). Prior to CER administration all patients were treated with combination of immunosuppressive drugs (PRED + median 3 cytotoxic agents [MTX=4, MMF=3, CYC=2, LEF=1, AZA=1] and 1 biologic agent [INFL=2, TOCI=1] for 7.5 years [1–12]). Criteria of efficacy included complete and incomplete remission and relapse of arteritis. Activity of disease was evaluated using the NIH criteria and the Indian Takayasu Clinical Activity Score (ITAS2010).

**Results:** Median duration of disease before CER administration was 12 years (11–16). High activity of TAK was confirmed by standard laboratory tests (median ESR 38 mm/h, CRP 21 mg/L) and MR-angiography/US. All patients improved, including complete and partial remission in 3 (75%) and 1 (25%) patients, respectively. Median PRED dose was reduced from 15 mg (10–25) to 5 mg daily (≤5 mg daily in 3 patients, discontinuation in 1). 2 patients discontinued MTX and MMF, in 1 patient MTX dose was decreased from 20 to 10 mg/wk, 1 patient continued CER monotherapy for 6 months. After treatment average ESR and CRP were 10 mm/h and 1.2 mg/L, respectively. Repeated US and MRA confirmed low or absence activity of disease in all patients. Median ITAS score decreased from 4 (2–10) to 0 (0–2) and median Kerr index decreased from 2 (1–3) to 0 (0–1). CER administrations were well-tolerated; we observed 1 case of community-acquired pneumonia (after 4 months of CER) and 1 case of post-operative abscess of foot (after 5 months of CER). During treatment with CER there were no relapses of TAK. All patients continue CER treatment.

**Conclusions:** CER is effective in case of active systemic inflammation in patients with TAK that was refractory to other immunosuppressive therapies, including biologic agents (INFL, TOCI). In one case CER monotherapy was sufficient to control disease activity for at least 6 months. As in case of other TNF inhibitors the risk of infections should be taken into account. Long-term results with clinically important end-points (surgical interventions, occlusions or stenosis progression, long-term survival etc.) are awaited.

**Disclosure of Interest:** None declared

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## AB0565 DIFFUSE ALVEOLAR HEMORRHAGE, DIAGNOSIS, TREATMENT AND 3-YEAR PROGNOSIS IN A GROUP OF 32 CASES OF TERTIARY CENTRE

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**Objectives:** Diffuse alveolar hemorrhage (DAH) is severe, life-threatening syndrome, affecting the patients with systemic vasculitis and other systemic connective tissue diseases. It can be often the first manifestation of systemic disease. Frequently DAH is the acute incident, which often leads to the rapidly emerging respiratory and/or renal failure with requirement of ventilatory support and with high mortality rate.
**Methods:** Diffuse alveolar hemorrhage was diagnosed on the basis of bronchoscopy and CT examination in patients with rapidly progressive respiratory insufficiency or newly emerged hemoptysis. Artificial ventilation was started in majority of cases.Therapeutically were used high doses of steroids i.v. (1000 mg 3–5 times in the iv infusion), Cyclophosphamide pulse, and plasmapheresis in some cases.
**Results:** The group of patients consisted of 32 cases; the average age of patients was 54 years (20–71) years. In half of patients was the episode of DAH the first manifestation of the disease. 16 patients were pro3 ANCA-positive, 7 patients MPO-ANCA positive, 6 patient had known systemic connective tissue disease 46.8% of patients survive 3 years from the acute episode of DAH, including two with repeated hemorrhage. 15 patients died during the acute phase of the disease, 3 more died during next 3 years, two of them on an opportunistic infection. Steroids were used for all patients, cyclophosphamide in 71, plasmapheresis in 56%, and i.v. immunoglobulins for 6.25 percent of patients. Patients who survive 3 years after the acute episode, had significantly lower necessity of artificial ventilation (40 vs. 93%) against the fatal cases, unfavorable prognostic sign was long term connective tissue disease. Residual lung impairment is present in 53% of the surviving patients; the signs of pulmonary arterial hypertension are present in 20% of the surviving group.
**Conclusions:** Diffuse alveolar hemorrhage is a sudden life-threatening event with a high mortality rate (46%) in the acute phase and during the first 3 years after the acute episode (20% of survivors). Up to half of patients the episode of DAH may be the first manifestation of the disease. Survival of patient depends on rapid diagnosis and the initiation of intensive immunosuppressive therapy. Respiratory failure is the major negative quoad vitam prognostic factor.
Suspect the diffuse alveolar bleeding is necessary always in the case of a rapidly progressive respiratory failure. Acute bronchoscopy and x-ray examination give diagnosis of DAH, which further specify the acute examination of ANCA antibodies (71% of the report was ANCA antibodies positive.
**Disclosure of Interest:** None declared
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## AB0566 OUTCOMES OF TAKAYASU'S ARTERITIS IN CHILDREN AND ADOLESCENTS

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**Background:** Takayasu's arteritis (AT) in children and adolescents is ranked number third in frequency among the vasculitis and is one of the common causes of renovascular hypertension. It is believed that the sickness rate of AT is more common in Asian ethnic group. In this disease, vascular stenosis has been found in 90% of cases and 45% of them is the aneurysm. In this regard, early diagnosis and adequate treatment are important to avoid the development of stenosis, aneurysms, vascular thrombosis, ischemia of organs and an adverse outcome.
**Objectives:** To conduct a retrospective analysis of the course and survival in children and adolescents with Takayasu's arteritis.
**Methods:** A retrospective analysis of the course and survival in patients with Takayasu's arteritis observed in the clinic of the Institute since 2005 was conducted. Total: 9 patients. Age: 10–17 years. The ratio of girls/boys was 3.5:1. Takayasu's arteritis was diagnosed according to the diagnostic criteria recommended by the EULAR/ PRINTO/ PRES (2010).
**Results:** All patients were patients of Kazakh nationality. None of relatives of the 1st and 2nd relationship degree had any cases of vasculitis or autoimmune diseases. Chronic nasopharyngeal infection, carious teeth were identified in all patients, which could be a trigger factor for the occurrence of Takayasu arteritis. But, no any cases of relation between Takayasu arteritis and TB infection were identified. On average, from the appearance of disease symptoms and before diagnosis of the disease 14 months had left (8 months ÷ 2 years 2 months). In all patients, Takayasu's disease was diagnosed at advanced stage, characterized by lesions of the arteries extending from the aorta, which was confirmed by angiography. Vascular disease Type III was revealed in 7 patients, type IV in 2. Secondary shrinkage of both kidneys due to a complete occlusion of the renal arteries developed in one 13 years old patient. All patients had undertaken active anti-inflammatory (glucocorticoids) and immune suppressive therapy (methotrexate 10–15mg/m$^2$, tocilizumab 12 mg/kg), symptomatic therapy. During the therapy, unstable and partial regression of general inflammatory symptoms were observed, hypertension was not completely stopped in 8 patients (88.9%), including a patient with end-stage of renal failure. Given the nature (III and type IV) of vascular lesions, unstable and partial anti-inflammatory effect of the therapy, the prognosis for life was unfavorable. Since diagnosis, survival rate in patients under 7 years was 22.2% (2), under 5 years – 44.4% (4) under 2 years – 22.2% (2) and at one year – 11.1% (1). The cause of death was: end stage of renal disease – 11.1% (1), stroke – 55.5% (5), myocardial infarction – 22.2% (2) and aortic aneurysm rupture of 11.1% (1).
**Conclusions:** Thus, the diagnosis of AT in children and adolescents was revealed late, which delayed an early prescription of adequate immunosuppression and contributed to the development of severe complications and death
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5830

## AB0567 AORTIC INVOLVEMENT IN A RETROSPECTIVE COHORT OF LARGE VESSEL VASCULITIS PATIENTS

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**Background:** Large vessel vasculitis include Giant cell arteritis (GCA) and Takayasu's disease. Both these conditions can be associated with aortic inflammatory involvement, detectable by FDG-PET. Aortitis is an indicator of a more severe clinical course of disease.
**Objectives:** We aimed to evaluate the different clinical phenotypes of large vessel vasculitis in a retrospective cohort of patients followed-up at our immunorheumatology outpatient clinic. We further aimed to identify predictors of aortic disease.
**Methods:** We retrospectively reviewed all the clinical records of patients receiving a diagnosis of large vessel vasculitis from 1st January 2010 to 1st January 2016. Clinical, laboratory, hystopathological and imaging data were collected. Non-parametric statistical analysis was performed.
**Results:** We recorded 42 diagnosis of large vessel vasculitis along a 5-year follow-up. Out of them 6 patients were not included in the analysis because of the lack of clinical informations. Median age of general population was 72.5 [64.0–76.0]; at onset, median ESR was 56 mm/h [44–75], while CRP was 6.9 mg/dl [3.4–12.1]. Median follow-up was 12 months [6–28]. 25/36 patients were female (69.4%); headache was the commonest onset symptom (28 cases, 77.8%), while polymyalgia rheumatic was diagnosed in 10 patients (27.8%). Half of the patients underwent a PET to rule out aortitic involvement, which was detected in 14/18 patients. The prevalence of aortic involvement was higher in male (7/11, 63.6%) than in female (7/25, 28%; p=0.04). Headache was always reported in uncomplicated GCA, while it was less frequent in aortitic patients (6/14 patients, 42.8%; p=0.0007). No differences were found with respect to age and laboratory data between patients with and without aortic involvement.
**Conclusions:** Large vessel vasculitis are quite common diseases in elderly people. A subset of patients, characterized by aortic involvement and a more severe prognosis can be detected. The absence of headache and male sex are risk factors for aortitis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4891

## AB0568 GIANT CELL ARTERITIS AND MALIGNANCY – MORE THAN JUST A COINCIDENCE?

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**Background:** Malignancy associated vasculitis represents 2–5% of systemic vasculitides. While there have been reports of increased incidence of malignancy in patients with giant cell arteritis (GCA) no definite association has yet been established.
**Objectives:** To determine the proportion patients with GCA and past/concurrent/subsequent malignancy.
**Methods:** We conducted a prospective longitudinal analysis of patients diagnosed with GCA from September 2011 to December 2015 at a single secondary/tertiary rheumatology centre. The proportion of patients with past, concurrent, and successive malignancy (diagnosed within 1 year of follow-up) was determined. Crude incidence rate (CIR) of malignancy in general population aged 50 years and above from the same geographical region in year 2011 and 2012 (final accessible reports based on complete yearly data) was acquired from Slovenian Cancer Registry for comparison.
**Results:** During the observation period 106 new GCA cases were identified (Table 1). Nineteen patients (17.9%) were diagnosed with a malignancy at any point in time (Table 2). In 7 patients (6.6%) malignant disease was found concomitantly with GCA (4/7) or within one year of follow-up (3/7). With respect to location of these 7 newly diagnosed malignancies, there were 4 cases (3.8%) of urinary bladder cancer (Table 2). There was 1 death due to cancer during the follow-up. None of the 12 patients with a history of past malignant disease had a recurrence of cancer at GCA diagnosis or during the follow-up. CIR for malignancy in comparably aged population of the same geographical region was 1.51%, with cumulative CIR for urinary tract malignancy of 0.08% and specific CIR for bladder cancer of 0.04%.

Table 1. Characteristics of GCA patients

| | |
|---|---|
| Age, years (median (IQR)) | 73.9 (67.3–78.8) |
| Gender (female/male) (%) | 75/31 (71/29) |
| Smoking (current and/or past), # (%) | 42 (39.6) |
| General symptoms, # (%) | 78 (73.6) |
| – in patients with concurrent/successive malignancy, # (%) | 1/7 (14.3) |
| – in patients with past history of malignancy, # (%) | 2/12 (16.7) |
| – in patients without known malignancy, # (%) | 16/87 (18.4) |
| Positive temporal artery biopsy, # (%) | 71/88 (80.7) |
| Positive temporal artery ultrasound, # (%) | 81/105 (77.1) |
| Large vessel vasculitis, # (%) | 42/97 (43.3) |

Legend: IQR, interquartile range.

Table 2. Location of malignancy and temporal relationship to GCA

| Location | P | C | S |
|---|---|---|---|
| Renal | 1 | 0 | 0 |
| Bladder | 0 | 3 | 1 |
| Stomach | 0 | 0 | 1 |
| Colon | 3 | 0 | 0 |
| Ovarian/uterine | 3 | 0 | 0 |
| Haematologic | 1 | 1 | 0 |
| Breast | 2 | 0 | 0 |
| Prostatic | 1 | 0 | 0 |
| Melanoma | 1 | 0 | 1 |
| Total | 12 | 4 | 3 |

Legend: P, past; C, concurrent; S, successive.

**Conclusions:** In our study, 6.6% of GCA patients were found to have a concurrent malignant disease compared to 1.5% of similarly aged general population. Additionally, we detected an increased incidence of urinary bladder cancer in our GCA cohort.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2845

## AB0569 DOES THE AGE AT DISEASE ONSET INFLUENCE THE CLINICAL PRESENTATION AND LONG-TERM OUTCOME OF ANCA-ASSOCIATED VASCULITIDES? RESULTS FROM A SINGLE-CENTRE COHORT

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**Background:** ANCA associated vasculitides (AAV) are a group of diseases that can transversally affect all age groups (1).
**Objectives:** To identify peculiar characteristics in clinical presentation and long-term outcome of patients with AAV according to age at diagnosis.
**Methods:** Medical records of patients followed at our Department up to December 2015 with a diagnosis of AAV were analysed. Patients were stratified according to age at diagnosis $<65$ or $\geq 65$ years old.
**Results:** A total of 96 patients with AAV were identified. General characteristics of the study population are presented in table 1. 72.91% of patients were diagnosed before the age of 65 (group A), while 27.09% presented with an elderly-onset disease (group B). Mean age at symptoms onset was 43.09±12.55 and 68.49±8.03, respectively ($p<0.0001$). Mean follow up was 70.19±73.41 without significant differences between the two groups. The diagnosis of granulomatosis with polyangiitis (GPA) was more frequent in group A (33.33% Vs 9.37%; p=0.03). Accordingly, c-ANCA (PR3) were significantly more detectable in group A (p=0.03). Eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyangiitis (MPA) were more represented in group A without reaching statistical significance. The clinical presentation at disease onset was characterised by a higher rate of ocular and musculoskeletal involvement in group A (p=0.004) and more frequent systemic symptoms (p=0.01) and peripheral nervous system involvement (p=0.008) in group B. A compromised renal function due to the vasculitic process was more reported in the elderly-onset group (p=0.007). Comorbidities were more relevant in group B ($p<0.0001$). Treatment approach did not differ between the two groups, except for a lower mean corticosteroid (CS) dosage in the elderly group at induction, counterbalanced by a lower rate of CS suspension at the end of follow up. Rituximab was only prescribed to 3 female patients of group A. Despite the different organ involvement, indices of disease activity, prognosis and damage did not differ between the two groups. Outcome was generally favorable in both groups, with a 2% mortality rate in group B.
**Conclusions:** Elderly-onset AAV shows some peculiar characteristics of organ involvement at disease onset, a higher rate of comorbidities, and slightly different therapeutic approach compared to younger-onset patients; nevertheless, long-term outcome is generally equally favorable.

Table 1. General characteristics of the study population

| Clinical characteristics N (%) | Total population N=96 | Group A (<65 yrs) N=70 | Group B (≥65 yrs) N=26 | p |
|---|---|---|---|---|
| Sex: (M/F) | 43/53 (44.79%/55.21%) | 31/39 (44.28%/55.71%) | 12/14 (46.15%/53.84%) | ns |
| Type of AAV: | | | | |
| EGPA | 55 (57.29%) | 38 (39.59%) | 17 (17.71%) | ns |
| GPA | 38 (39.58%) | 29 (41.43%) | 9 (9.37%) | 0.006 |
| MPA | 3 (3.12%) | 3 (4.29%) | 0 | ns |
| p-ANCA (MPO) | 33 (34.37%) | 22 (40.43%) | 11 (42.31%) | ns |
| c-ANCA (PR3) | 28 (29.17%) | 25 (35.71%) | 3 (11.54%) | 0.03 |
| FFS positivity | 37 (38.54%) | 28 (40%) | 9 (34.61%) | ns |
| BVAS at onset (mean ± SD) | 14.83±7.57 | 14.60±7.67 | 15.46±7.17 | ns |
| BVAS at the end of follow up (mean ± SD) | 1.52±1.85 | 1.68±1.93 | 1.09±1.57 | ns |
| VDI at the end of follow up (mean ± SD) | 1.24±1.07 | 1.30±1.08 | 1.08±1.04 | ns |

FFS: Five Factor Score, BVAS: Birmingham Vasculitis Activity Score, VDI: Vasculitis Damage Index.

**References:**
[1] Scott DG, Watts RA. Epidemiology and clinical features of systemic vasculitis. Clin Exp Nephrol 2013;17:607–10.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3319

## AB0570 IGG4 RELATED DISEASE: PROTEAN CLINICAL MANIFESTATIONS AND A DIAGNOSTIC CONUNDRUM

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**Background:** -
Immunoglobulin G4-related disease (IgG4-RD) is a multisystemic fibro-inflammatory condition characterized by tumefactive lesions, dense lympho-plasmacytic infiltrate, storiform fibrosis and obliterative phlebitis. Serum IgG4 levels are usually elevated in 70–90% of cases. The mean age at diagnosis is 60 years with a striking male preponderance. (Male:Female – 8:3)
**Objectives:** To present a single center experience with IgG4-RD and the diagnostic and therapeutic challenges encountered.
**Methods:** A retrospective case review at an urban teaching hospital was done over a year after the availability of quantitative assessment of IgG4 levels and tissue immuno-histological staining techniques. This revealed four cases of IgG4-RD involving the pancreas, retroperitoneum, kidney and meninges demonstrating its multi-systemic nature.
**Results:** We encountered a M:F ratio of 3:1 with mean age at presentation being 66 year
Case 1: A 76-year-old male with significant weight loss, erroneously diagnosed with pancreatic tail malignancy, underwent distal pancreatectomy and was subsequently diagnosed with AIP on biopsy.
Case 2: A 71-year-old male s/p left partial nephrectomy 4 years ago with an incidental finding of right kidney mass (2x2x2cm). After undergoing right partial nephrectomy, he was diagnosed with IgG4-related kidney disease.
Case 3: A 56-year-old male with abdominal pain and worsening renal function had MRI findings of a heterogeneous retroperitoneal mass attached to the right kidney. Biopsy revealed a diagnosis of IgG4-retroperitoneal fibrosis.
Case 4: A 57-year-old female presented with headache, bilateral lower extremity weakness and gait abnormality. Elevated serum IgG4, leptomeningeal enhancement on MRI and dural biopsy all suggested IgG4-related pacchymeningitis.
**Conclusions:** IgG4-RD often presents as a diagnostic conundrum. There is a need to increase clinician awareness of IgG4-RD, since early identification and subsequent treatment with immunomodulators may prevent disease progression and prevent complications and/or unnecessary surgeries. PET/CT may prove to be a useful adjunctive imaging technique to investigate for multi-system involvement. Over reliance on serum IgG4 levels for screening may result in missed diagnosis in a significant percentage of patients.
**Disclosure of Interest:** None declared
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## AB0571 A CROSS-SECTIONAL STUDY OF HEALTH-RELATED QUALITY OF LIFE ASSESSED BY THE SF-36 AND THE EQ-5D-5L IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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**Background:** Health-related quality of life (HRQoL) is an important outcome of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), and the Medical Outcomes Study Short Form-36 (SF-36) is usually used as a generic measure of HRQoL. However, there are only several published reports focusing on HRQoL among patients with AAV. In addition, another popular measure of HRQoL, the 5-level EuroQoL 5-Dimensions Questionnaire (EQ-5D-5L), which is often used for the calculation of quality-adjusted life years (QALYs) has received less attention in the field of AAV.
**Objectives:** We aimed to cross-sectionally investigate the relationship between HRQoL assessed by the SF-36 and the EQ-5D-5L, and clinical background and indices among AAV patients.
**Methods:** Patients with AAV were defined and classified according to the European Medicines Agency algorithm. Patients were approached during their outpatient attendance in our university clinic from July through December 2015. Some of the hospitalized patients during the study period were also eligible to

the study. Patients were asked to complete the SF-36, the EQ-5D-5L, and other related demographic questionnaires. The SF-36 contains 36 items scored in 8 domains. Using the national norm score and its SD, the "0–100 score" of each domain of the SF-36 was transformed to the norm-based score (NBS) so that each had a mean of 50 and a SD of 10 in the national population sample. In addition, 2 summary scales were calculated based on NBS: physical (PCS) and mental (MCS) component summary scores. A lower score in SF-36 indicates poorer health or greater disability. The EQ-5D-5L comprises the 5 dimensions of HRQoL, and each dimension has 5 levels. An EQ-5D-5L health state was converted to a single summary index by applying the formula and ranges from 0 to 1; 0 meaning death and 1 complete health. Physicians were asked to complete the Birmingham Vasculitis Activity Score (BVAS) and the Vasculitis Damage Index (VDI) simultaneously and record other medical information.

**Results:** A total of 34 Japanese patients with AAV (microscopic polyangiitis 23, granulomatosis with polyangiitis 8, and eosinophilic granulomatosis with polyangiitis 3) participated. In the study population, the mean age was 66, 29 were women, the mean disease duration was 7 years, the mean prednisolone dosage was 10.9 mg/day, the mean BVAS was 5.2, and the mean VDI was 2.7. The mean scores in 7 out of the 8 domains of the SF-36 were significantly lower than those of the age- and sex-matched national norms ($p<0.05$). The mean PCS and MCS scores of the SF-36, and the mean EQ-5D-5L index value were 29.4, 48.0, and 0.72, respectively. The mean PCS score and the mean EQ-5D-5L index value were significantly lower than those of the age- and sex-matched national norms ($p<0.05$), whereas the mean MCS score was not. The PCS score and the EQ-5D-5L index value had moderate inverse correlation with age, the prednisolone dosage, the BVAS, and the VDI ($r$= -0.41 to -0.62), whereas the MCS score did not. Sex and AAV classification were not significantly associated with the PCS and MCS scores or the EQ-5D-5L index value.

**Conclusions:** In the study population, the PCS score and the EQ-5D-5L index value in patients with AAV were lower than the national norm and inversely correlated with age, the prednisolone dosage, the BVAS, and the VDI, whereas the MCS score was not.

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## AB0572 IMPACT OF AGING ON THE CLINICAL FEATURES AND TREATMENT OF ANCA ASSOCIATED VASCULITIS IN THE ELDERLY

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**Background:** ANCA associated vasculitis (AAV) usually occurs in elderly patients, but only a few studies regarding clinical features and treatment of elderly onset AAV have been reported so far[1,2].

**Objectives:** To compare clinical features and treatment of AAV between elderly patients (≥75) and younger patients (<75) in Japanese patients.

**Methods:** Patients who met the criteria for granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and Churg-Strauss syndrome (CSS) were included in this study. AAV patients (N=31) who were initially treated at Fukushima Medical University Hospital (Fukushima, Japan) from 2004 to 2015 were retrospectively reviewed. These patients were divided into 2 groups (elderly, N=9 and younger, N=22) and compared for the following clinical features, laboratory data and treatment: age at diagnosis, sex, Birmingham Vasculitis Activity Score (BVAS), symptoms, liver and renal function, hemoglobin, serum ferritin levels, IgG, ANCA (MPO/PR3) positivity, and therapy (prednisolone and immunosuppressive therapy).

**Results:** Following 31 AAV patients were identified: 8 cases of GPA, 20 cases of MPA, and 3 cases of CSS. Elderly group showed significantly lower frequency of skin manifestation and significantly higher frequency of kidney symptoms. In laboratory data, elderly group showed significantly lower serum AST, LDH and Ferritin levels. As to therapy, elderly patients received significantly lower prednisolone doses and frequency of cyclophosphamide (CYP) administration. Mortality rates (1 year) were significantly higher in elderly group (33.3%) than younger group (4.6%). Four patients died: all patients were MPA and the main causes of death were vasculitis progression (alveolar hemorrhage) and infection.

| Clinical features | Elderly, N = 9 | Younger, N = 22 | *p* value |
|---|---|---|---|
| Age (years old) | 78.2 | 61.1 | - |
| Sex (Female, %) | 77.8 | 45.5 | 0.053 |
| BVAS | 17.9 | 17.3 | N.S |
| Symptoms (%) | | | |
| ENT | 33.3 | 40.9 | N.S |
| Lung | 77.8 | 40.9 | N.S |
| **Kidney** | **88.9** | **50.0** | **0.023** |
| Nervous system | 33.3 | 54.5 | N.S |
| **Skin** | **0** | **27.3** | **0.043** |
| Laboratory Data | | | |
| **AST (IU/L)** | **27.2** | **44.8** | **0.049** |
| ALT (IU/L) | 25.3 | 46.5 | 0.081 |
| **LDH (IU/L)** | **181** | **264** | **0.028** |
| CRP (mg/dL) | 11.37 | 9.33 | N.S |
| Creatinine (mg/dL) | 1.03 | 1.02 | N.S |
| Hemoglobin (g/dL) | 9.77 | 10.6 | N.S |
| **Ferritin (ng/mL)** | **257** | **486** | **0.009** |
| IgG (mg/dL) | 1885 | 1802 | N.S |
| ANCA (MPO/PR3) positivity (%) | 100 | 81.8 | N.S |
| Therapy | | | |
| **PSL doses (mg/day)** | **34.4** | **45.9** | **0.028** |
| **CYP therapy (%)** | **0** | **27.3** | **0.043** |
| **Mortality rates (1 year, %)** | **33.3** | **4.6** | **0.016** |

**Conclusions:** This study shows that the clinical features of elderly AAV patients are comparable to those of younger patients in Japan, except for lower skin manifestations and higher kidney symptoms. Lower AST, LDH, and ferritin levels in elderly AAV may indicate that elderly patients show milder organ damage on admission. Higher mortality rates in elderly AAV may be associated with lower PSL doses and frequency of CYP administration. Proper immunosuppressive therapy should be considered to reduce mortality rates for vasculitis progression or severe infection in elderly AAV.

**References:**

[1] Hoganson et al. J Clin Rheumatol. 2008.
[2] Weiner et al. Clin J Am Soc Nephrol. 2015.

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## AB0573 THE DISEASE ASSOCIATIONS OF TAKAYASU'S ARTERITIS

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**Background:** Case reports or small case series suggest that Takayasu arteritis (TA) can co-exist with various chronic inflammatory disorders. Inflammatory bowel disease [(IBD; Crohn's disease (CD) or ulcerative colitis (UC)] has been the most common association.

**Objectives:** We conducted a formal study to look specifically at the frequency of association of such chronic inflammatory disorders in a large cohort of patients with TA followed at a single tertiary center.

**Methods:** There were 226 (200 F/26 M) patients registered with a diagnosis of TA at the Rheumatology Department of Cerrahpasa Medical Faculty, between 1977 and December 2015. Of these, 17 (8%) had died and 15 (7%) were lost to follow-up. The remaining 194 patients were called back at the outpatient clinic for an interview and for a physical examination. A standardized form sought whether the patient was also diagnosed as IBD, ankylosing spondylitis (AS), Behçet's syndrome (BS), amyloidosis (AA), uveitis, rheumatoid arthritis (RA), systemic lupus erythematosus, systemic sclerosis, Sjögren syndrome, psoriatic arthritis, myositis, small vessel vasculitis, a demyelinating or any other autoimmune or inflammatory disorder. The presence of skin-mucosa lesions ascribed to BS and inflammatory back pain were also specifically sought for. In addition to the self-reported information, patient charts and all medical documentation available such as hospitalization reports, imaging studies and blood work were used as a source of information.

**Results:** One hundred and fifty-three (136 F/17 M) patients were studied. The mean age at the onset of symptoms was 31±11 years and at the time of TA diagnosis was 34±12 years. Subclavian artery was the most common involved artery (83%), followed by common carotids (75%) and aorta (64%). Currently, while 25 (16%) patients were off treatment, 72 (47%) patients were using glucocorticoids, 47 (31%) azathioprine, 32 (21%) methotrexate and 44 (29%) biological agents.

We identified 11 (7%) patients with IBD (CH/UC:7/4), 11 (7%) with AS, and 9 (6%) with BS. Ten patients (6 IBD and 4 BS) were diagnosed simultaneously. The onset of TA preceded AS in 6 patients, IBD in 2, and BS in 1 as shown in Table. Among the remaining 122 patients, when the 31 patients with IBD, AS and BS were excluded, recurrent oral ulcers were present in 19 (16%), erythema nodosum in 13 (11%), arthritis in 12 (10%), papulopustular lesions in 5 (4%), uveitis in 5 (4%), and genital ulcer in 1. Inflammatory back pain was reported by 44 (36%) patients; this was usually in the dorsal spine level alone (n=30), less commonly in both dorsal and lumbar spine (n=10) and in the lumbar spine alone (n=4).

Table. Demographic features of 31 TA patients with IBD, AS or BS

| Concomitant disease | F/M | Mean age at TA diagnosis (SD) | Mean age at concomitant disease (SD) | The time of TA diagnosis in relation to concomitant disease |
|---|---|---|---|---|
| AS (n=11) | 9/2 | 31 ±8 | 27±11 | TA preceded (n=6)<br>AS preceded (n=5) |
| IBD (n=11) | 10/1 | 33±9 | 31±9 | Simultaneous (n=6)<br>TA preceded (n=2)<br>IBD preceded (n=3) |
| BS (n=9) | 7/2 | 35±13 | 32±13 | Simultaneous (n=4)<br>TA preceded (n=1)<br>BS preceded (n=4) |

In addition, 3 patients had secondary amyloidosis, 1 had RA and 1 morphea. We also observed 2 patients with autoimmune hepatitis and 2 with psoriasis, all having onset after anti-TNF treatment.
**Conclusions:** This survey shows that TA co-occur with IBD, AS or BS in about 1/5 of the patients, at least in a hospital setting and this seems to be without a clear temporal pattern. The rather high prevalence of inflammatory back pain in the dorsal spine in TA needs further scrutiny.
**Disclosure of Interest:** None declared
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## AB0574 FECAL CALPROTECTIN LEVEL LOOKS PROMISING IN IDENTIFYING ACTIVE DISEASE IN BEHÇET'S SYNDROME PATIENTS WITH GASTROINTESTINAL INVOLVEMENT: A CONTROLLED AND PILOT STUDY

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**Background:** The fecal calprotectin (FC) level is widely used as a non-invasive method for identifying patients with active Crohn's disease (CD) and ulcerative colitis. Gastrointestinal involvement of Behçet's syndrome (GIBS) shows clinical and endoscopic similarities to CD. A previous study in a small number of Behçet's syndrome (BS) patients with mainly mucocutaneous lesions showed that serum calprotectin levels did not differ between active and inactive patients (1). Another study suggested that FC may help to diagnose GIBS patients (2). We are not aware of studies addressing whether FC levels help to distinguish active GIBS patients from those in remission.
**Objectives:** To determine whether FC levels help predict active disease in GIBS patients.
**Methods:** We collected fecal specimens from 23 GIBS (11 M, 12 F and mean age 44±9 years) patients before colonoscopy. The reasons for colonoscopy were assessing active disease in patients presenting with abdominal pain (with or without diarrhea) (n=9) or confirmation of a remission in asymptomatic patients (n=16). Four symptomatic and 3 asymptomatic patients had active ulcers by endoscopy. On the other hand, 5 symptomatic and 13 asymptomatic patients did not have ulcers by endoscopy. We also included 22 active and 25 inactive CD patients as controls. We used 150 μg/g as the cut-off for a positive FC level. We also looked at the correlation between FC and serum CRP levels, Crohn's disease activity index (CDAI) and disease activity index for intestinal Behçet's disease (DAIBD) scores.
**Results:** FC was >150 μg/g in all of the 7 GIBS patients with ulcers compared to 4/16 of GIBS patients without ulcers (OR, 95%CI: 42 to 888). The mean FC was 1125±800 μg/g (95%CI: 341 to 1908) among symptomatic patients with ulcers (n=4) and 209±213 μg/g (95%CI: 22 to 396) among symptomatic patients without ulcers (n=5). On the other hand, the mean FC was 243±73 μg/g (95%CI: 158 to 328) among asymptomatic patients with ulcers (n=3) and 95±160 μg/g (95%CI: 0.4 to 189) among asymptomatic patients without ulcers (n=11). Among CD patients, 16/25 active patients and 3/22 patients in remission had FC level >150 μg/g (OR, 95%CI: 11 to 49). There was a low correlation between FC and serum CRP levels (r=0.3, p=0.1), a moderate correlation between FC levels and CDAI scores (r=0.5, p=0.02) and very low correlation between FC and DAIBD scores (r=0.01, p=0.9). Among the 4 GIBS patients who had high FC levels despite being in remission for gastrointestinal involvement, 1 had active mucocutaneous lesions, 1 had concomitant macrophage activation syndrome, and 1 had polycythemia vera with trisomy 8. None of the patients were receiving NSAIDs that could increase FC levels.
**Conclusions:** Pending the study of more number of patients, FC may turn out to be a useful non-invasive tool for ruling out active gastrointestinal lesions in asymptomatic GIBS patients. A high FC level demands caution for the presence of active ulcers especially in symptomatic patients, but whether the presence of other BS manifestations can cause false positive results remains to be studied.
**References:**
[1] Oktayoglu P et al. Scand J Clin Lab Invest. 2015
[2] Kim DH et al. ECCO.2014
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3318

## AB0575 STEROID USE IS PROTECTIVE OF OSTEOPOROSIS IN POLYMYALGIA RHEUMATICA PATIENTS: A CASE-CONTROL STUDY

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**Background:** The treatment of polymyalgia rheumatica (PMR) requires long-term corticosteroid therapy, which is known to induce bone mineral density loss and predispose patients to fracture. Therefore, we hypothesise that patients with PMR are more likely to suffer from osteoporosis (OP), as defined by a T-score threshold of ≤-2.5.
**Objectives:** To ascertain whether steroid use in PMR patients is associated with an increased propensity to OP, and whether other factors increase the propensity.
**Methods:** Study subjects were recruited from patients attending for DEXA scan at a scanner in the North West of England from 2004–2014. Patients with PMR were identified from this cohort for a case-control study: cases were defined as OP on DEXA scan, and controls were patients with T-score >-2.5; the exposure was steroid use (current, previous or ever). Odds ratios within the case-control study were estimated using Stata v13.1, which was used for all statistical analysis. A logistic model was fitted with OP as the dependent variable and age, gender, co-morbidities, medication predisposing to OP and risk factors for OP as the explanatory variables. Following univariate analysis, variables with p<0.2 were fitted into a multivariate logistic model, which was stratified by OP overall, and OP of either the femoral neck or lumbar spine.
**Results:** 649 patients with PMR were identified. There were 108 patients with OP (cases), of whom 95 patients (87.96%) were female, and 541 controls, of whom 388 patients (71.72%) were female (p=4.11E-04). Mean age in cases was 74.59 years (SD 8.78) and 70.18 years (SD 8.49) in controls (p=1.23E-06).
"Current" and "ever" use of steroids were associated with reduced odds of OP: OR 0.62 (95% CI 0.26–1.10, p=0.07) and OR 0.16 (95% CI 0.04–0.58, p=3E-04), respectively. There was no association with "previous" steroid use.
Following multivariate logistic regression, any history of steroid use ($OR_{adj}$ 0.14 [95% CI 0.04–0.44]), age >70 years ($OR_{adj}$ 2.37 [95% CI 1.51–3.72]) and female gender ($OR_{adj}$ 3.05 [95% CI 1.64–5.66]) were significantly associated with OP overall. This model retained significance in lumbar spine OP: steroid use $OR_{adj}$ 0.24 (95% CI 0.08–0.78), age >70 years $OR_{adj}$ 1.72 (95% CI 1.08–2.75) and female gender $OR_{adj}$ 2.83 (95% CI 1.46–5.48). Steroid use was not associated with femoral neck OP, whilst age>70 years ($OR_{adj}$ 7.01 [95%CI 2.93–16.79]) and female gender ($OR_{adj}$ 2.68 [95% CI 1.11–6.49]) retained their significant association.
**Conclusions:** This study demonstrates that steroid use is protective of OP in PMR patients, despite the increased risk of OP with chronic steroid use. This may be because clinicians are more diligent in prescribing bone protection in these patients, due to awareness of the increased iatrogenic risk of OP that long-term corticosteroid use predisposes to.
**Disclosure of Interest:** None declared
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## AB0576 OPHTALMOLOGIC FINDINGS IN PATIENTS WITH TAKAYASU'S ARTERITIS

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**Background:** Takayasu's Arteritis (TA) is a large vessel vasculitis of young females. Ophtalmologic findings as wreath-like arteriovenous anastomosis around the optic disc are the firstly described clues for TA. Opthalmologic pathologies could have negative impact on quality of life but, there are limited data about ocular manifestations of TA.
**Objectives:** To investigate the ophthalmologic manifestations of TA.
**Methods:** In this cross-sectional study 33 TA (F/M: 29/4) patients were evaluated. Demographic and clinical findings were recorded from hospital files. Addition to routine examination, anterior segment and fundus of eyes were assessed.
**Results:** The median age at the time of ocular examination was 38 (min-max:19–62) years and mean disease duration was 5.7±5.5 years. Two (6.1%) patients had diabetes mellitus, 13 (39.4%) patients had hypertension. Only one patient had cranial involvement of TA. Most of the patients had been taking immunosuppressive agents addition to corticosteroids [Methotrexate (n=11, (33.3%)), cyclophosphamide (n=9, (27.3%)), azathiopurine (n=5, (15.2%)), one patient for each mycophenolate mophetil, infliximab, tocilizumab]
Of patients 15 (45.4%) had pathologic findings in opthalmologic examinations. Twelve patients (36.4%) had anterior segment pathology, 10 (30.3%) patients had posterior segment pathology. Of these patients 7 (21.2%) had both anterior and posterior segment pathology. Distribution of anterior segment pathologies were; 9 (27.2%) patients had cataract, 2 (6.1%) patients had dry eyes and one patient had congenital disgenesis.
In fundoscopic examination of posterior segment, hypertensive retinopathy was the most frequent pathologic finding as 12.1% (n=4) Three of these patients have had diagnosis of essential hypertension and were treated with anti-hypertensive medication One patient had ocular ischemic syndrome which is typical for TA (Table 1).

Table 1. The Fundoscopic Examination Findings of 33 patient with TA

| Fundoscopic Examination Findings | N | % |
|---|---|---|
| Normal | 23 | 69.7 |
| Stage 1 hypertensive retinopathy | 4 | 12.1 |
| Foveal pigment epithelial alterations | 1 | 3.0 |
| Ocular ischemic syndrome | 1 | 3.0 |
| Hard exudate and microhemorrhage | 1 | 3.0 |
| Delayed mfERG (multiphocal electroretinography) responses | 1 | 3.0 |
| Drusen formation | 1 | 3.0 |
| Exudate and subretinal fluid | 1 | 3.0 |

**Conclusions:** In the early results of our study, disease or treatment related ocular pathologic findings were frequent in TA. Periodic consultation and ophthalmologic

examination of TA patients might be rational approach in follow up of these patients.
**Disclosure of Interest:** None declared
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## AB0577 SLEEP QUALITY IN BEHCET'S DISEASE IS ASSOCIATED WITH DISEASE ACTIVITY, DEPRESSION, AND QUALITY OF LIFE IN KOREAN POPULATIONS

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**Background:** Behcet's disease is a chronic, systemic vasculitis that can involve all sizes of blood vessels. Those complicated symptoms lead to the patient's impairment of life quality as well as psychological problems. Sleep disturbance is one of the most particular concerns in patients with Behcet's disease. It has been known that the disease activity of rheumatoid arthritis and ankylosing spondylosis is associated with the sleep quality. However, studies about the sleep quality of patients with Behcet's disease in Korean population are limited.
**Objectives:** The purpose of this study was to find out the effects of sleep quality on Behcet's disease in Korean population. We also investigated the relationship between depression, quality of life, other clinical findings of Behcet's.
**Methods:** The study was performed by cross-sectional design in two tertiary hospitals. We met one hundred patients with Behcet's disease, surveyed them face-to-face and conducted the chart review for more clinical informations. Sleep quality was assessed by the Korean version of Pittsburgh sleep quality index (PSQI). Disease activity of Behcet's disease was evaluated by Behcet's disease current activity form (BDCAF). Depression was assessed by the Korean version of Beck depression inventory second edition (BDI-2). Quality of life was assessed by the Korean version of the Leeds Behcet's Disease Quality of Life Measure (BDQoL).
**Results:** Among 100 patients, median age was 51 [44.5–56.0] years, median disease duration was 77.5 [24.0–136.0] months and 31% were male. Those who met the diagnostic critera of fibromyalgia were 28 patients. The frequency of poor sleep quality (PSQI $>5$) was 67%. Patients with poor sleep quality tend to have higher BDI2, BDCAF and pain VAS score ($P<0.001$, $P=0.028$, and $P=0.011$). Female rate was significantly higher, and BDQoL was lower in poor sleeper group ($P=0.004$ and $P<0.001$). Among 7 PSQI components, daytime dysfunction was higher in patients with high disease activity ($P=0.03$). Total PSQI score were strongly correlated with BDCAF score, BDI-2 score, BDQoL score, and pain VAS score ($P=0.02$, $P<0.001$, $P<0.001$, and $P<0.001$, respectively).
**Conclusions:** The low quality of sleep is associated with disease activity, depression and quality of life in Korean patients with Behcet's disease. We expect better disease control will improve the sleep quality.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4674

## AB0578 SUCCESSFUL TOTAL HIP ARTHROPLASTY IN PATIENTS WITH SEVERE ANCA- ASSOCIATED VASCULITIS: SINGLE- CENTER EXPERIENCE

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**Objectives:** We evaluated the postoperative morbidity in patients with severe ANCA- associated vasculitis (AAV) undergoing primary total hip arthroplasty (THA).
**Methods:** Retrospective analysis of interventional case series, single referral center study. Four patients with severe AAV due to destructive hip damage (5 affected hips) were selected for 5 THA.
**Results:** The mean age of our cohort was 45 years (27- 66 years), 75% female. Two patients had microscopic polyangiitis (MPA), 1- granulomatosis with polyangiitis (GPA) and 1- eosinophilic granulomatosis with polyangiitis (EGPA). All patients had severe AAV and Five-Factor Score (FFS)=1. Short course of hemodialysis was required in one patient with MPA and rapidly progressive glomerulonephritis. In another case was the age of MPA onset $>65$ years. The GPA patient had a history of nephrectomy for hydronephrosis, which complicated afterwards with kidney and ureter granulomatous vasculitis and occlusive thrombosis of the femoral veins in the active phase of the disease. EGPA patient was overweight (BMI 28) and had EGPA-associated cardiomyopathy. Destructive hip damage was caused by osteonecrosis in 3 patients, and fracture of the proximal femur in 1 patient with osteoporosis. At the time of THA procedure all patients were in remission phase (BVAS=0) with normal serum creatinine levels, all comorbidities were controlled by medications. In two cases AAV remission was induced by rituximab.
All implants were radiographically stable without osteolysis. In all cases THA has been clinically effective, with functional gain such as improved mobility as well as pain reduction and was not associated with postoperative serious complications (except for blood transfusion requirements) or AAV relapse.
**Conclusions:** Elective THA is a safe and effective procedure for destructive hip damage in the AAV patients, including cases with the history of severe vasculitis and unfavorable prognostic factors (FFS=1). AAV remission must be achieved and comorbidities identified and treated to minimize postoperative complications.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2090

## AB0579 NON-INFECTIOUS AORTITIS ASSOCIATED WITH POLYMYALGIA RHEUMATICA: WHAT IS THE BEST DIAGNOSIS AND THERAPEUTIC OPTION? EXPERIENCE IN A LOCAL HOSPITAL

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**Background:** Non-infectious aortitis associated with polymyalgia rheumatica (PMR) is a rare entity (1). Sometimes the conventional immunosuppressive therapy is not enough, forcing us to find new therapeutic options (2,3). We present our experience in a local hospital.
**Objectives:** To evaluate symptoms, clinic, diagnosis and therapeutic options.
**Methods:** During the years 2010–2015 we search for patients diagnosed with PMR which at the same time were diagnosed with non infectious aortitis. Their medical records were reviewed and the following data were collected: initial clinical diagnosis, diagnosis method used, time elapsed since the onset of symptoms to diagnosis, ESR and CRP at diagnosis and after the use of treatment.
**Results:** 5 patients were found: 4 women and 1 man. The average age onset of initial symptoms was 67.2 (74–58) years and the average delay in the diagnosis of the disease was 26 (1–50) months.
The most common onset clinic was classic PMR symptom. Patients 2, 3, 4 and 5 also showed parietooccipital or parietal headache. Other symptoms were lower limb claudication, temporomandibular joint pain, dyspnea, fatigue and pseudofibromyalgia.
All patients underwent temporal artery biopsy. In patient 5 bilateral temporal artery biopsy was performed.
The definitive diagnosis test was PET (4). In patient 2 PET was compatible with aortitis being angioMRI negative.
The average ESR at the beginning and after the treatment was 87.4 (114–65) and 10.2 (15.6) respectively. The initial and final average CRP (mg /dL) was 8.03 (14.54–1.86) and 1.2 (3 to 0.5) respectively.
All patients underwent autoimmune analytical battery, being this study negative.
1,2,3 and 4 patients performed concomitant weekly methotrexate (MTX) with maximum dose of 25 mg weekly sc. Patients 1 and 5 made concomitant treatment with steroids and azathioprine at doses of 100 and 150 mg daily, respectively.
Patients 1,2,3 and 5 were treated with tozilizumab which was well tolerated and without adverse effects to date. The average time from diagnosis of the disease until the start of treatment was 9.75 months (2,3). Patient 4 at the time of publication of these data remained asymptomatic with weekly MTX 15 mg sc and 5 mg of prednisone.
**Conclusions:** Non-infectious aortitis associated with PMR may go unnoticed due to high variability of presentation. This can make, sometimes, a delayed diagnosis (1). PET seems to be a good tool for the diagnosis (4) and tozilizumab seems to be a suitable treatment for those patients refractory to steroids and DMARDs (2,3). More patients are needed to generalize these data.
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**Disclosure of Interest:** None declared
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AB0580 **A PROSPECTIVE OPEN-LABEL SINGLE CENTER STUDY OF ADALIMUMAB IN BEHCET ARTHRITIS**

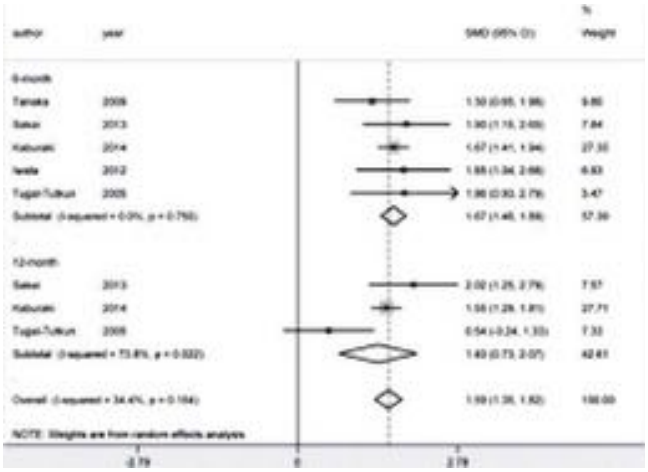
Y. Braun-Moscovici, Y. Tavor, D. Markovits, M. Naffaa, K. Toledano, A. Rozin, R. Beshara-Garzoz, M.A. Nahir, A. Balbir-Gurman. *B Shine Rheumatology Unit, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion-Israeli Institute of Technology, Haifa, Israel*

**Background:** Behcet's disease is a multisystemic chronic relapsing inflammatory disease, classified among the vasculitides. The clinical manifestations include mucocutaneous lesions, articular, ocular, vascular, gastrointestinal and/or central nervous system involvement. The aetiology of Behcet's disease is unknown. TNF-α may play an important role in the pathogenesis of the disease. Short term studies reported the efficacy of anti-TNFα therapy, particularly regarding ocular and mucocutaneous involvement in Behcet's.
**Objectives:** The primary end point was to assess efficacy and safety of Adalimumab (ADA) in patients with active Behcet's arthritis not responding to one or more DMARDS. The secondary end point was to assess the impact of treatment on other disease manifestations.
**Methods:** Eligible patients with active arthritis were enrolled in a 24 weeks single center prospective open-label study. Patients who relapsed within 12 weeks following ADA discontinuation could enter a 3 year extension study. The efficacy was assessed by 68 tender and 66 swollen joint count, patient visual analogue scale (VAS) for pain, physician overall disease activity VAS, health assessment questionnaire (HAQ), Behçet's Disease Current Activity Form (BDCAF), C reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Statistical methods: descriptive statistics, T test, Mann-Whitney U test.
**Results:** Ten patients (6 females),age (mean, standard deviation – SD) 45 (8.4) years, with a disease duration of 11.6 (10) years, met the inclusion, exclusion criteria and were treated with subcutaneous ADA 40mg every 2 weeks for 24 weeks. The clinical manifestations included arthritis, oral and urogenital aphtae in all patients, erythema nodosum (3 patients) and other skin involvement (3 patients), uveitis (1 patient) and deep vein thrombosis (1 patient). Prior to ADA therapy they failed treatment with3.2 (1.3) different DMARDs. A statistically significant improvement was observed in swollen joint count (mean (SD) at baseline 4.6 (4.2) vs 0.4 (0.6) at 24 weeks, p=0.006), physician VAS (51.5 (18.5) vs 24.5 (16), p=0.002) and BDCAF (5.4 (1.6) vs 2.1 (1.4), p=0.001), but not in tender joint count (19 (18.7) vs 10.9 (12.6), p=0.14) or HAQ (1.76 (0.85) vs 1.59 (0.99), p=0.14). Resolution of oral and urogenital ulcers was achieved in all patients. Significant reduction of pain was reported by 40% of patients. No relapse of uveitis or other disease manifestations occurred during the study. The treatment was well tolerated: there were no serious adverse events; there were no injection related site reactions. Four infective episodes (2 cases of pneumonia and 2 of sinusitis), were treated ambulatory and did not require ADA withdrawal. The disease relapsed in 9 out of 10 patients, within 4–6 weeks following ADA interruption, 7 patients enrolled into the extension study.
**Conclusions:** ADA treatment was well tolerated and achieved a significant improvement in arthritis and mucocutaneous manifestations in all study patients but only 40% reported significant pain reduction. A subset of patients with insufficient improvement in joint tenderness and generalized pain may require comprehensive pain management besides anti-inflammatory therapy.
**Acknowledgement:** ABBVIE donated the study medication
**Disclosure of Interest:** None declared
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AB0581 **INFLIXIMAB THERAPY IN PATIENTS WITH REFRACTORY UVEITIS OF BEHÇET'S DISEASE: A META-ANALYSIS**

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**Background:** Behçet's disease is a chronic inflammatory vasculitis that can affect multiple systems. Ocular involvement is common and often cause significant morbidity, such as loss of sight, and offering challenge to management due to relapse. Off-label use of anti-tumor necrosis factor (TNF) agents for Behçet's disease (BD) is increasing. Especially for refractory uveitis
**Objectives:** To assess the effect of infliximab on refractory uveitis caused by Behçet's disease, we conducted a meta-analysis.
**Methods:** A comprehensive search of multiple databases was performed. Weighted Mean Difference (WMD) or standardized mean difference (SMD) and 95% confidence intervals (95%CI) were calculated to assess the efficacy. Q test was used to examine the inter-study heterogeneity, and the robustness of the results was tested through sensitivity analysis. Begg's funnel plot and Egger's test were operated to check the publication bias.
**Results:** A total of 9 articles were included in this meta-analysis. We observed that infliximab treatment significantly reduced uveitis attack in Behçet's disease patients (WMD=2.35, 95% CI: 1.74–2.96), which was confirmed by subgroup analysis on 6- and 12- month after treatment (WMD=2.51, 95% CI: 1.81–3.21; WMD=2.11, 95% CI: 0.62–3.60). Visual acuity was greatly improved by infliximab therapy (SMD=-0.31, 95% CI: -0.59 to -0.03). Moreover, infliximab therapy also decreased the macular thickness of Behçet's disease patients (SMD=1.75, 95% CI: 1.35–2.15).



**Conclusions:** Infliximab therapy is effective in the treatment of Behçet's disease patients with refractory uveitis.
**Disclosure of Interest:** Y. Qin Employee of: Yuxing Qin is employee of XIAN Janssen. The Janssen pharmaceutical companies did not provide any financial support for this work. The authors report no other conflicts of interest., X. zhang: None declared, P. Geng: None declared, R. luo: None declared, G. zhang: None declared
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## Scleroderma, myositis and related syndromes

AB0582 **MORTALITY IN PATIENTS WITH SYSTEMIC SCLEROSIS – A SINGLE CENTER EXPERIENCE**

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**Background:** Patients (pts) with systemic sclerosis (SSc) experience higher mortality rates.
**Objectives:** To assess the mortality and causes of death in SSc pts' cohort at our center.
**Methods:** The data were retracted from the Rambam EUSTAR database (220 pts, years 2004–2013) and completed from pts' files; demographic, clinical and laboratory data, malignancy cases, the reason of death were analyzed. Comparisons were made between the deceased pts and surviving pts with similar disease duration. Proportional hazards models of Kaplan-Meier survival analysis and student's T-test were used for statistical analysis. Data found to significantly affect survival in a first univariate analysis were entered in a multivariate Cox proportional hazards model. Causes of death were analyzed using standard descriptive statistics. Data characterized pts with malignancy were incorporated in the logistic regression model.
**Results:** 47 (21.4%) pts deceased (age 53±15 years, disease duration 9.8±11 years, females 76.6%, diffuse disease 27.6%). Causes of death were: pulmonary

**Abstract AB0581** – Table 1. Characteristic of the studies included in the meta-analysis

| First Author | Year | Country | No. of case | Gender F/M | Age | Infliximab dose (mg/kg) | Infliximab treatment time (weeks) |
|---|---|---|---|---|---|---|---|
| Hiroyuki Tanaka | 2009 | Japan | 22 | 2/20 | 39.9±12.9 | – | – |
| Tsutomu Sakai | 2012 | Japan | 20 | 8/12 | 45±14 | 5 | 0, 2, 6, and every 8 weeks |
| Toshikatsu Kaburaki | 2014 | Japan | 150 | 32/118 | 38.5±12.1 | – | – |
| Vanesa Calvo-RÍo | 2014 | Spain | 124 | 56/68 | 38.6±10.4 | 3–5 | 0, 2, 6, and every 4–8 weeks |
| Sultan Al Rashidi | 2013 | Saudi Arabia | 19 | 1/18 | 25.6±7.8 | 5 | 0, 2, 6, and every 8 weeks |
| L. Niccol | 2007 | Italy | 12 | 5/7 | 33±12.8 | 5 | 0, 2, 6, and every 8 weeks |
| Daiju Iwata | 2012 | Japan | 17 | 3/14 | 36.9 (15–58) | 5 | 0, 2, 6, and every 8 weeks |
| Fabrizio Cantini | 2012 | Italy | 36 | 21/15 | 31.6±10.9 | 5 | 0, 2, 6, and every 8 weeks |
| Ilknur Tugal-Tutkun | 2005 | Turkey | 13 | 0/13 | 18–65 | 5 | 0, 2, 6, and 14 |

fibrosis (PF), pulmonary arterial hypertension (PAH), right and left heart failure (CHF, 27.7% and 19.1%); infections (17.0%), malignancies (17.0%), renal crisis (6.4%), gastrointestinal complications (GIT) (2.1%), and others (10.64%). Survival was significantly affected by: older age at diagnosis (P=0.011), male gender (P=0.049), reduced lung volumes and diffusing capacity (P=0.014 and p=0.001), PF (P=0.002), PAH (P<0.001), CHF (P<0.001), use of diuretics (P<0.001), arrhythmias (P<0.001), malignancy (P=0.003), proteinuria (P=0.003), and GIT complications (P=0.027). Malignancy was reported in 14/47 (29.8%) pts: lungs 23.5%, GIT 17.7%, genitourinary tract 17.7%, other 41.2%. Malignancy was not an independent predictor of mortality.
**Conclusions:** In this study the leading cause of death in SSc pts was cardiopulmonary complications, followed by malignancy and infections; renal and GIT complications were less frequent. High index of suspicion and early diagnosis of main SSc complications will allow early intervention and may hopefully change the fate of SSc pts.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2460

## AB0583 LONG-TERM INTEGRATED TREATMENT WITH BOSENTAN AND ILOPROST INCREASES, INDEPENDENTLY FROM OTHER CLINICAL CHARACTERISTICS, THE ABSOLUTE NUMBER OF CAPILLARIES IN SYSTEMIC SCLEROSIS PATIENTS: A NAILFOLD CAPILLAROSCOPIC ANALYSIS

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**Background:** Iloprost (ILO) and bosentan (BOSE) integrated therapy was demonstrated to improve microvascular structure in systemic sclerosis (SSc) patients, in two long-term follow up studies [1].
**Objectives:** Since the alterations in capillary number seem to predict the incidence of clinical SSc complications [2], present study aimed to quantify, by nailfold videocapillaroscopy (NVC), long-term effects of BOSE treatment on nailfold capillary absolute number and their possible correlation with clinical parameters of the disease.
**Methods:** Thirty SSc patients entered the study, with a follow up of for 4 years. Fifteen patients were treated with ILO mono-therapy (80 μg/day, for 5 continuous days, every 3 months), while other 15 patients, because of the onset of systolic pulmonary hypertension (sPAP) or digital ulcers (DUs) were treated with BOSE (125 mg twice/day) and ILO integrated therapy (ILO+BOSE). Nailfold capillaries absolute number, DU incidence, diffusing capacity of the lung for carbon monoxide (DLCO), sPAP and renal artery resistive index (RI) were evaluated yearly. Friedman test, Cochran's q test, Marginal homogeneity and mixed modelling were used to study variables with repeated measures. A p value lower then 0.05 was considered significant.
**Results:** In the ILO+BOSE group, capillary absolute number was found to have a significant increase (p=0.01) from T0: 6.8±1.3 to T4: 7.8±1.5 (14.7%), whereas in the ILO group, a non-significant decrease in capillary number from T0: 7.18±0.5 to T4: 6.5±1.1 (9.4%) was found. According to multivariate analysis, the most significant associations, other then BOSE treatment, were observed between capillary number increase and baseline capillaroscopic "Early" pattern (p<0.0001), lcSSc subtype (p=0.001), while it was independent from other clinical characteristics. In the ILO+BOSE group there was a significant reduction in the annual incidence of new DUs from T0 (10/15 patients) to T4 (2/15 patients) (80%; p=0.0042) and no further negative significant changes were observed in DLCO and sPAP. On the contrary, in the ILO group, DLCO was significantly reduced (8.1%, p=0.039) and sPAP increased (15%, p=0.04) during the follow up. RI did not change significantly in both groups.
**Conclusions:** Capillary absolute number count seems a reliable parameter to evaluate long-term effects of BOSE on microvasculature in SSc. A significant reduction in the annual incidence of new DUs and stabilization of lung function was observed and appeared to be associated to the increased number of capillaries during a four-years integrated treatment with BOSE and ILO.
**References:**
[1] Cutolo M et al. 2013;40:40–5.
[2] Smith V et al. 2011;70:180–3.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4317

## AB0584 SYSTEMIC SCLEROSIS SINE SCLERODERMA: AN INFRA-DIAGNOSED DISEASE?

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**Background:** Systemic sclerosis (SSc) is a connective tissue disease of unknown origin, with heterogeneous clinic presentation and chronical and progressive evolution. There is a subtype of SSc without cutaneous presentation designated as systemic sclerosis sine scleroderma (ssSSc) that is difficult to diagnose with a delay on it producing worse prognosis.
**Objectives:** The objective of this study was analyzing demographic features, clinical presentations, the treatment and evolution of ssSSc patients from our hospital.
**Methods:** There were analyzed in a retrospective way the patients diagnosed of SSc in our center between 1990 and May 2015, selecting those with ssSSc.
**Results:** Among the 106 patients diagnosed of SSc in this period, only 5 patients (4.7%) had ssSSc. All of them were women with an average of 51 years. 3 patients (60%) had additionally an autoimmune hypothyroidism, other a polyglandular autoimmune syndrome and the other one had no autoimmune disease. Only one patient (20%) was HTA, another was smoker and another one had dyslipidemia. None of the 5 patients had suffered exposure to toxic elements. Average time delay for diagnosis was 10 years. For 3 patients initial diagnosis was in one case primary Raynaud phenomenon, other case pulmonary arterial hypertension (PAH) essential and in another one polyglandular autoimmune syndrome. 2 of the ssSSc diagnosis were done in 2006 (coincident with the opening of our monographic office of autoimmune systemic diseases). The reason for consultation in 4 of the patients (80%) was Raynaud phenomenon (RP) that was present in all of the patients during the tracking. Only one patient (20%) had digital ulcers, 2 patients (40%) esophagitis and 1 tendinopathy. 1 patient (20%) had PAH confirmed by right coronary angiography. All patients had antinuclear antibodies (ANA) positive, 80% anticentromere. A patient presented positivity to Anti Ro and another one to anticardiolipin antibodies. Nailfold capillaroscopy was made to 4 patients (80%), being all of them pathologic (Cutolo's pattern 3 active and 1 early). Spirometry was made in 4 patients (80%) founding diffusion alteration in 3 of them. The transthoracic echocardiogram performed to all patients was pathologic in the 3 of them (60%) (1 patent ductus arteriosus, 1 PAH and 1 valvular heart disease). Regarding treatment, 3 patients (60%) were treated with calcium antagonists and 2 (40%) received bosentan, without presenting none of them any serious adverse effect. It is important to highlight that 2 patients (40%) developed limited scleroderma after 9 and 4 years of diagnosis respectively. The patient with PAH died during the tracking because of right heart failure.
**Conclusions:** ssSSc diagnosis is difficult due to the absence of the main presentation, the cutaneous one. The most frequent beginning symptom is the RP, so including this symptom in the anamnesis and stablishing screening measures in patients with RP with detection of ANAs and periungual capillaroscopy is important for an early detection to allow diagnosis improvement.
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[2] Sophie P et al. The many faces of scleroderma sine scleroderma: a literature review focusing on cardiopulmonary complications. Rheumatol Int (2009) 29:861–868.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5776

## AB0585 INTIMA MEDIA THICKNESS AND ATHEROSCLEROTIC PLAQUES ARE ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS AND DEPRESSION IN SYSTEMIC SCLERODERMA

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**Background:** Atherosclerosis is a common cause of mortality and morbidity in many autoimmune diseases. There is not much evidence about the role of atherosclerosis in increase mortality in systemic scleroderma.
**Objectives:** The aim of study is detection of subclinical atherosclerosis measured by ultrasound detected intima media thickness in a group of systemic scleroderma patients and finding relation to traditional risk factors, clinical manifestation, immunological profile and selected laboratory markers.
**Methods:** From March 2015 to January 2016 55 patients with systemic scleroderma were included in the study. (9 men. 46 women, mean age - 59±10.5y., age of diagnosis 51.2±12.3y., duration of disease 5±8.5y., duration of Raynaud's phenomenon 8±12.1y.). In these patients data were collected on traditional atherosclerosis risk factors (smoking, BMI, arterial hypertension, Diabetes, lipid profile, family history of cardiovascular event), on the phenotype of scleroderma disease (lung manifestation, pulmonary hypertension, digital ulceration, involvement of gastrointestinal tract, myositis, renal crisis). The immunological profile of the disease was assessed by analysis of autoantibodies. All patients were tested by complex psychological test - MMPI-II (The Minnesota Multiphasic Personality Inventory test, standardized psychometric test of adult personality and psychopathology) and BDI-II test (Beck Depression Inventory test of depression). The presence of subclinical atherosclerosis was assessed by ultrasound measurement of intima media thickness (IMT) and by assessment of presence carotic plaque. Echocardiography aimed for detection of pulmonary hypertension, left ventrical function and valvlular disease was done. Statistical tests (descriptive statistic, Student t-test, Spearman test and ANOVA) were

performed to describe eventual relation of findings, p-value $\leq$0.05 considered as significant.
**Results:** Pathological IMT was detected in 31 (56.3%), plaques in 19 patients (34.5%). In this group was low incidence of cardiovascular events – 1 ischemic heart disease, 1 myocardial infarction and one stroke, prevalence presence of valvuvar disease (16 patients, 29.1%). IMT correlated with disease duration (p=0.01), positivity of anti Scl 70 (p=0.02), TC/HDL ratio (p=0.02), hsCRP (p=0.05), presence of PH (p=0.002), digital ulceration (p=0.007), gastrointestinal damage (p=0.04), but also with MMPI-II scale of depression (p=0.03) and hypochondria (p=0.01) and BDI-II summary score (p=0.04). Presence of plaques correlated with disease duration (p=0.05), diffuse form (p=0.01), TC and HDL ratio (p=0.02), hsCRP (p=0.02), digital ulceration (p=0.03) and MMPI-II measured scale of conversion hysteria (p=0.01) and BDI-II summary score (p=0.03).
**Conclusions:** Patients with scleroderma in our study had low presence of cardiovascular manifestation. Nevertheless prevalence of latent atherosclerosis detected by increase IMT and presence of atherosclerotic plaques of carotic artery is high and correlates with some organ manifestations (pulmonary hypertension, digital ulceration). Presence of atherosclerosis correlates also with subclinical depression assessed by complex psychological tests.
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**Disclosure of Interest:** None declared
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## AB0586 PREDICTORS OF INTERSTITIAL LUNG DISEASE IN 79 PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE

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**Background:** Interstitial lung disease (ILD) is a common complication of various connective tissue diseases, like scleroderma, polymyositis or mixed connective tissue disease (MCTD). The development of ILD is in many cases asymptomatic, although autopsy found lesions typical for the ILD in 90–100% [1]. In the case of MCTD ILD is the most common pulmonary involvement with incidence of 47,1% (active form- 66% of them) and its severe type - progressive fibrosis characterize 20.8% after 4.2 years mortality rate [2].
**Objectives:** The aim of the study was to estimate the prevalence of ILD and pulmonary fibrosis in a cohort of MCTD patients, and to identify clinical and immunological predictors of this complication.
**Methods:** The study included 79 patients (the median age =44 years, 83.5% of women), who fulfilled Alarcon-Segovia and Kasukawa sets of criteria for MCTD. Clinical features of MCTD, autoantibody profile and serum cytokine (IL-1, IL-10, IL-21, IL-23, TNF$\alpha$, IFN$\gamma$, VEGF) concentrations were assessed. Screening chest X-ray, and if needed pulmonary function tests and high resolution computed tomography (HRCT) were performed additionally.
ILD was defined as active, reversible interstitial lung disease with symptoms such as dyspnoea and dry cough, proven radiologically by presence of interstitial lesions in X-ray or ground-glass opacity in HRCT ± decrease in pulmonary function tests by 10% in forced vital capacity (FVC) or diffusing capacity of the lungs for carbon monoxide (DLCO).
**Results:** ILD and pulmonary fibrosis were present in 19% of MCTD patients and this group was characterized by older age, longer disease duration, more frequent systemic damage, and higher disease activity comparing to the rest of study group. The most common findings among patients with ILD were abnormal FEV1 (80% vs 15,4%) and oesophageal involvement (4,4 vs 19,7%). Concomitance of pulmonary arterial hypertension (PAH) and ILD in MCTD were observed in only 2,5% of examined patients. Moreover, patients with ILD were less often positive for anti-SmB antibody than the ILD-free subjects (11.1 vs 37.7%), but similar cytokine concentrations was stated in both groups.
**Conclusions:** In MCTD pulmonary involvement (ILD and/or pulmonary fibrosis) develops mostly in patients with long lasting, clinically severe disease, accompanied by low frequency of anti-SmB antibody presence.
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## AB0587 PULMONARY ARTERIAL HYPERTENSION AS A RISK FACTOR FOR MORTALITY IN CONNECTIVE TISSUE DISEASE WITH BIOPSY PROVEN INTERSTITIAL LUNG DISEASE

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**Background:** Connective tissue diseases (CTD) are a heterogeneous group of autoimmune systemic diseases characterized by circulating autoantibodies and varying degrees of organ involvement including interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH).[1–2] PAH in CTD is known to be associated with increased mortality. Whether ILD alone is associated with increased mortality is uncertain, but lung infections have been suggested to accelerate the development of ILD and impair the prognosis.
**Objectives:** To investigate a cohort of CTD patients with biopsy verified ILD and examine whether histopathologic ILD patterns, PAH and/or lung infections requiring hospital admission are independent predictors of mortality.
**Methods:** A retrospective cohort study of CTD patients with lung biopsy verified ILD. Data regarding ILD patterns were obtained from lung biopsies, PAH was evaluated with transthoracic echocardiography (TTE) using tricuspidal regurgitation $\geq$36 mmHg as a parameter for PAH. Data regarding lung infections requiring hospital admission and death were obtained from medical records. Survival was analyzed by age and gender adjusted multiple cox-regression analysis using SPSS version 22.
**Results:** Fifty-six CTD patients had ILD verified CTD, 21 (37%) with systemic sclerosis, 14 (25%) with polymyositis, 14 (25%) with undifferentiated connective tissue disease and 7 (13%) with mixed connective tissue disease. At the time of lung biopsy, the 56 CTD patients (50% females) had a mean (SD) age of 53.5 (11.3) years and disease duration of 4.4 (9.1) years. The follow-up after biopsy consisted of 203 person-years. Eight patients (14%) died during follow-up translating to a mortality rate of 39.4 per 1000 person years. Non-specific interstitial pneumonia (NSIP) histopathological pattern was observed in 15 (27%), fibrosis in 16 (29%), while 25 (44%) had other histopathological patterns. Thirteen (23%) patients had PAH which was associated with increased mortality with a HR=5.3 [95% CI 1.2–24.2], p=0.03. The patients with histopathological NSIP and fibrosis patterns had a higher mortality than other types of ILD, nevertheless the histopathologic pattern of ILD and hospital admission requiring infections did not predict increased mortality.
**Conclusions:** PAH predicts poor outcome in CTD patients with ILD, irrespective of the histopathological ILD pattern. In CTD with interstitial lung disease early PAH screening and initiation of treatment is paramount for optimizing survival among patients with CTD and ILD.
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## AB0588 RISK FACTORS FOR THROMBOEMBOLIC EVENTS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** Patients with Idiopathic Inflammatory Myopathies (IIM) have an increased risk of thrombotic event (TE) compared with the general population (1). The role of traditional thrombotic risk factors, IIM disease activity, presence of antiphospholipid antibodies (aPL) and adhesion molecules, in the pathogenesis of TE is unknown.
**Objectives:** *We* aimed to investigate the prevalence of TE (pulmonary embolism (PE), deep venous thrombosis (DVT), myocardial infarction (MI), stroke, transitory ischemic attack (TIA) or peripheral arterial thrombosis (PAT)) in IIM patients. We also compared clinical and serological characteristics of IIM patients with and without TE.
**Methods:** 286 IIM patients followed between 1993–2014, with and without TE, were identified. Information on traditional risk factors for TE, autoantibody profiles, disease activity and medical treatment was retrieved from registries and medical records. Serum levels of anti-$\beta$2-glycoprotein I (anti-$\beta$2-GPI) and anticardiolipin antibodies (aCL) as well as serum levels of adhesion molecules i.e. vascular cell adhesion molecule 1 (VCAM), intercellular adhesion molecule 1 (ICAM) and e-selectin were analysed on stored sera. Sera of patients with TE were screened for levels of adhesion molecules at the time of IIM diagnosis and at the time of TE. Levels of adhesion molecules were also analysed in 40 healthy individuals.
**Results:** Sixty-seven (23.4%) of the 286 IIM patients suffered from at least one TE, 33 presented with arterial thrombosis (MI, Stroke, TIA, PAT), 31 with venous

thrombosis (DVT, PE), 3 with both. Among traditional risk factors for TE, higher age at diagnosis ($p<0.001$), male gender ($p<0.05$) and hypertension ($p<0.05$) occurred more frequently in patients with TE than in those without. No other significant differences in terms of prevalence of risk factors, disease activity, medical treatment or autoimmune profile were found. Significantly higher levels of VCAM, ICAM and E-selectin ($p<0.001$, $p<0.001$ and $p<0.05$, respectively) were found in patients with IIM compared to controls. However, there was no significant difference in the levels of any of the investigated adhesion molecules between IIM patients with TE and those without. Moreover, no significant difference in the levels of adhesion molecules at the time of IIM diagnosis and at the time of TE was observed.

**Conclusions:** The main finding of this study is the striking prevalence of thrombotic events in patients with IIM. The fact that 1 out of 5 patients suffered from a TE should alert the clinician to screen for TE when clinically indicated as well as to consider prophylactic treatment in risky situations, including surgery, immobilisation or pregnancy. Male gender, higher age at IIM diagnosis and hypertension should be taken into account when estimating TE risk. High disease activity or aPL positivity were not specific features of IIM patients with TE, nor were elevated serum levels of adhesion molecules. The mechanisms leading to increased risk of TE in patients with IIM need further investigations.

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**Disclosure of Interest:** None declared

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## AB0589 HYPERCOAGULABLE STATE MIGHT BE INDUCED BY ALVEOLAR-ENDOTHELIAL DAMAGES IN INTERSTITIAL LUNG DISEASE ASSOCIATED WITH POLYMYOSITIS/DERMATOMYOSITIS

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**Background:** Polymyositis and dermatomyositis (PM/DM) are often complicated by interstitial lung diseases (ILD), which is an important cause of death. It has been reported that endothelial damages are likely to exist in PM/DM patients with ILD (PM/DM-ILD). Endothelial damages and oxidative stress induced hypercoagulable state in many connective tissue diseases (CTD) such as rheumatoid arthritis, systemic lupus erythematosus and systemic scleroderma. Recent evidence suggested that anticoagulation therapies might contribute to improve the disease activity of pneumonia related to CTDs.

**Objectives:** The purpose of this study was to clarify the association between the disease activity of ILD and blood coagulation disorders in patients with PM/DM.

**Methods:** This study is retrospective observation study. The medical records of 22 patients who were diagnosed as having PM/DM admitted to our hospital from April 2012 to March 2015 were reviewed in present study (median age: 50.5, female ratio: 81.8%). Diagnosis of ILD was evaluated by chest high-resolution CT. We reviewed the laboratory findings and autoantibody profile associated with PM/DM.

**Results:** Eighteen of 22 (81.8%) patients with PM/DM were diagnosed as having ILD. Autoantibodies associated with PM/DM were evaluated in 14 patients among 18 patients with PM/DM-ILD. Anti-aminoacyl-tRNA synthetases (ARS) and anti-MDA5 antibody was positive in 8/14 patients (57%) and 4/14 patients (29%), respectively. Anti-Jo-1 antibody was detected in 3 patients (38%), anti-PL7 in 3 patients (38%), anti-OJ in one patient (12%), and anti-EJ in one patient (12%) in 8 patients with anti-ARS antibody positive PM/DM-ILD. The levels of creatinine kinase (CK) in anti-ARS antibody positive PM/DM-ILD patients was higher than those in anti-ARS antibody negative PM/DM-ILD patients (median CK 2464 v.s 106 IU/ml, p=0.01). The levels of serum KL-6 and plasma D-dimer in anti-ARS antibody positive PM/DM-ILD patients tended to be higher than those in anti-ARS antibody negative PM/DM-ILD patients (median KL-6 691 v.s 489 IU/ml, D-dimer 2.57 v.s 1.96 ug/ml). Additionally, there is significantly positive correlation in the levels of between serum KL-6 and plasma D-dimer (R=0.58, p=0.0008). However, there is no correlation between the levels of serum KL-6 and blood coagulation tests, such as prothrombin time (%) and activated thromboplastin time.

**Conclusions:** These results suggest that anti-ARS antibody, especially anti-Jo-1 and anti-PL7, seems to be associated with the severity of muscular manifestation and alveolar-endothelial damages. The level of plasma D-dimer reflects the disease activity of ILD in patients with PM/DM. The hypercoagulable state might be induced by alveolar-endothelial damages and oxidative stress in PM/DM-ILD.

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## AB0590 EVALUATION OF DERMAL THICKNESS BY THREE DIFFERENT TECHNIQUES IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Skin involvement is critical for sub-classification of systemic sclerosis into different subsets (1).

**Objectives:** The aim of this study was to identify possible correlations between modified Rodnan skin score (mRSS), high frequency skin ultrasounds (US) and plicometer skin test (Plicometry) in the evaluation of dermal thickness (DT) in patients with (SSc).

**Methods:** 63 SSc patients (mean age 63±12SD years, mean SSc duration 6±5 years) and 63 healthy subjects (mean age 65±15SD years) were enrolled. The three methods were employed in the seventeen areas of the skin usually evaluated by mRSS (face, fingers, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs and feet) and the total score calculated, as previously reported (2,3). US was performed by a 18 MHz probe (Esaote, Italy) reporting DT as millimetres, and Plicometry (Gima, Italy) adopting a 0–3 score as for mRSS assessment (4). Nailfold videocapillaroscopy (NVC) was performen in SSc patients to assess the proper pattern of microangiopathy.

**Results:** A statistically significant positive correlation was found between the three methods to evaluate DT in the SSc patients (mRSS vs US $r=0.53$, $p<0.0001$; mRSS vs Plicometry $r=0.98$, $p<0.0001$; US vs Plicometry $r=0.53$, $p<0.0001$). In particular, US showed that all SSc patients had a statistically significant higher DT in the 17 areas when compared with control subjects ($p=0.0001$). DT measurements were found progressively higher in patients with “Early”, “Active” and “Late” NVC pattern of microangiopathy.

**Conclusions:** This study demonstrates a significant relationship between mRSS, US and Plicometry in dermal thickness evaluation in SSc patients. At the level of the seventeen skin areas analyzed by US, all SSc patients showed a statistically significant higher DT than controls.

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## AB0591 NAILFOLD VIDEOCAPILLAROSCOPY MAY NOT REFLECT CHANGE OF DIGITAL ULCERS STATUS IN A SHORT TERM EVALUATION OF SYSTEMIC SCLEROSIS PATIENTS

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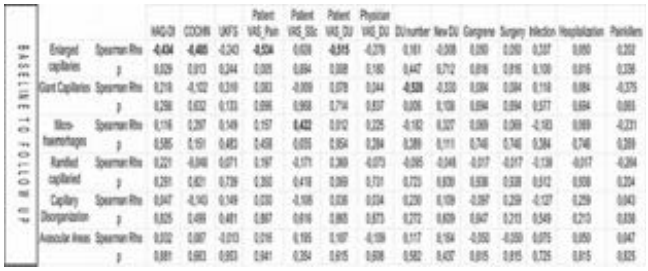
**Background:** Nailfold videocapillaroscopy (NVC) is a useful tool in systemic sclerosis (SSc) patients, useful not only for the diagnosis but also to predict the development of organ and vascular complications, such as the utility of the recently proposed semi-quantitative scoring for digital ulcers (DU) [1].

**Objectives:** to prospectively evaluate the change of prevalence of NVC microvascular alterations and their possible correlations with changes in patients-reported outcomes (PROs) and clinical-reported outcomes (CROs) and prevalence of clinical characteristics related to DU in SSc patients.

**Methods:** SSc patients presenting at least one DU and attending the Rheumatology Wound Care Clinic of the Florence University Hospital or the London Royal Free Hospital were enrolled. Patients were assessed with PROs (HAQ-DI, UKFS, Cochin scale, VAS for pain, DU status and general disease status) and CROs (VAS for DU status) at baseline and after 16 weeks. DU number, appearance of new DU, presence of gangrene, infection, need for hospitalization or surgery procedures, painkillers use were recorded at each visit. NVC was performed at both visit and the presence of micro-haemorrhages, giant capillaries, irregularly enlarged capillaries, ramified capillaries, capillary disorganization and loss of capillaries was scored according to the previously proposed score (0 = no changes, 1 = from 0 to 33%; 2 = from 33% to 66%, 3 = more than 66%). Correlations were tested through Spearman test.

**Results:** twenty-five SSc patients were eligible for the study. No significant correlation was seen at baseline; when analysing changes between baseline and follow-up, a negative correlation was seen between irregularly enlarged capillaries and the majority of PROs; moreover, changes of number of DU showed negative correlation with changes of giant capillaries, possibly reflecting the evolution of microvascular damage.

**Conclusions:** NVC is useful tool to predicting DU development, but may not reflect short term change in DU status; therefore a longer-term evaluation may be necessary to detect NVC modifications paralleling DU changes in SSc patients.



| BASELINE TO FOLLOW UP | | MAG-DI | CDDMN | UKFS | Patient VAS_Pain | Patient VAS_SSc | Patient VAS_DU | Physician VAS_DU | DUnumber | New DU | Gangrene | Surgery | Infection | Hospitalization | Painkillers |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Enlarged capillaries | Spearman Rho | -0,434 | -0,465 | -0,243 | -0,534 | 0,639 | -0,515 | -0,279 | 0,161 | -0,308 | 0,293 | 0,293 | 0,337 | 0,000 | 0,202 |
| | | p | 0,029 | 0,013 | 0,244 | 0,005 | 0,894 | 0,008 | 0,165 | 0,447 | 0,712 | 0,016 | 0,016 | 0,109 | 0,016 | 0,336 |
| | Giant Capillaries | Spearman Rho | 0,218 | -0,102 | 0,218 | 0,063 | -0,000 | 0,079 | 0,044 | -0,528 | -0,330 | 0,084 | 0,084 | 0,118 | 0,084 | -0,375 |
| | | p | 0,298 | 0,632 | 0,133 | 0,696 | 0,999 | 0,714 | 0,837 | 0,005 | 0,109 | 0,694 | 0,694 | 0,577 | 0,694 | 0,065 |
| | Micro-haemorrhages | Spearman Rho | 0,116 | 0,297 | 0,149 | 0,157 | 0,422 | 0,012 | 0,225 | -0,182 | 0,327 | 0,069 | 0,069 | -0,183 | 0,069 | -0,231 |
| | | p | 0,585 | 0,151 | 0,483 | 0,458 | 0,035 | 0,954 | 0,284 | 0,389 | 0,111 | 0,748 | 0,748 | 0,384 | 0,748 | 0,269 |
| | Ramified capillaries | Spearman Rho | 0,221 | -0,048 | 0,071 | 0,197 | -0,171 | 0,369 | -0,073 | -0,095 | -0,048 | -0,017 | -0,017 | -0,139 | -0,017 | -0,264 |
| | | p | 0,291 | 0,831 | 0,739 | 0,350 | 0,418 | 0,069 | 0,731 | 0,723 | 0,830 | 0,938 | 0,938 | 0,512 | 0,938 | 0,224 |
| | Capillary Disorganization | Spearman Rho | 0,047 | -0,143 | 0,149 | 0,030 | -0,106 | 0,038 | 0,034 | 0,230 | 0,109 | -0,297 | 0,259 | -0,127 | 0,259 | 0,043 |
| | | p | 0,825 | 0,499 | 0,481 | 0,897 | 0,616 | 0,865 | 0,873 | 0,272 | 0,609 | 0,647 | 0,213 | 0,549 | 0,213 | 0,838 |
| | Avascular Areas | Spearman Rho | 0,032 | 0,097 | -0,013 | 0,016 | 0,195 | 0,197 | -0,159 | 0,117 | 0,164 | -0,552 | -0,359 | 0,075 | 0,059 | 0,047 |
| | | p | 0,881 | 0,663 | 0,953 | 0,941 | 0,354 | 0,915 | 0,606 | 0,582 | 0,437 | 0,015 | 0,015 | 0,725 | 0,815 | 0,825 |

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**Disclosure of Interest:** None declared

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## AB0592 EVALUATION OF ARTERIAL STIFFNESS IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS: A CASE-CONTROL STUDY

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**Background:** Systemic sclerosis (SSc) patients are characterized by premature cardiovascular (CV) mortality. In this setting, the disease represents an intriguing model to evaluate premature endothelial damage. Indeed, both macrovascular and microvascular damage characterizes subclinical atherosclerosis (ATS) in these patients (1). Traditional CV risk factors, SSc-related inflammatory and autoimmune mechanisms may contribute to accelerated ATS. Among indirect measures of subclinical ATS, aortic stiffness (AS), measured by carotid-femoral pulse wave velocity (cf-PWV), and augmentation index (Aix@75) are independent predictors of CV morbidity and mortality in several diseases. To date, studies evaluating subclinical ATS in SSc provided conflicting results. Moreover, factors influencing atherosclerosis in SSc have not been well defined.

**Objectives:** To evaluate cf-PWV and Aix@75 measures of AS in SSc patients and analyze relationship between disease-related features and AS.

**Methods:** Thirty-four consecutive female SSc patients (mean age 61±15 years) with mean disease duration of 17±12 years since Raynaud phenomenon and 34 healthy sex, age and arterial pressure (AP) matched controls (HC) were enrolled. Traditional CV risk factors, disease-specific clinical, metabolic and immunologic features were collected. Disease activity and severity were assessed by Valentini Disease Activity Index (VDAI) and Medsger Disease Severity Scale (MDSS), respectively. Cf-PWV was determined by means of applanation tonometry (SphygmoCor). AIx@75 was calculated as difference between the 2nd and 1st wave systolic peaks and standardised to 75 beats/min. The relationship between cf-PWV, AIx@75 and all variables was investigated with univariate (one-way ANOVA) and multivariate models.

**Results:** Mean blood AP was similar in patients and HC. About 1/3 patients were receiving immunosuppressive therapy, 33% iloprost, 41% calcium-chanel blockers, 9% beta-blockers, 9% angiotensin receptor blockers and 3% ACE-inhibitors. Mean VDAI was 1,37±1,32 and 15% of patients were characterized by high activity (score >3). Mean MDSS was 0,35±0,65 with 9% of patients who had a moderate-severe disease. Both absolute AIx (16,1±8 *vs* 11,5±7 mmHg; p=0,014) and AIx@75 (30,9±16 *vs* 22,2±12%; p=0,012) resulted significantly higher in SSc compared to HC, while cf-PWV was similar in the two populations. At multivariate analysis, age, mean AP and mean C-reactive protein resulted independent predictors of cf-PWV, while only age and mean AP of AIx@75. Of interest, limited SSc and anti-centromere positive patients were characterized by significantly higher AIx@75 in comparison to diffuse SSc and anti-Scl70 positive (p=0.045 and p=0.04, respectively).

**Conclusions:** Subclinical atherosclerotic damage in SSc seems to be mainly characterized by increased AIx, a measure of arterial stiffness that encompasses peripheral vascular reflectance and left ventricular ejection, thus reflecting a prevalent peripheral microvascular involvement. Moreover, several factors, including inflammatory state, may contribute to AS in these patients. Intriguing, the significant increase of AIx in limited SSc may suggest a more severe peripheral microvascular involvement in these patients.

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**Disclosure of Interest:** None declared

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## AB0593 CHOROIDAL INVOLVEMENT IN SYSTEMIC SCLEROSIS: COMPARISON BETWEEN SKIN BLOOD PERFUSION AND CHOROIDAL THICKNESS BEFORE AND AFTER ILOPROST TREATMENT

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**Background:** Systemic sclerosis (SSc) is characterized by progressive diffuse microvascular damage and decreased blood perfusion (BP) at skin and internal organs (1). Laser speckled contrast analysis (LASCA) evaluate skin BP in different areas of body (2). Histological studies and fluorescein angiography demonstrated choroidal involvement in SSc, and recently optical coherence tomography (OCT) measurement showed significantly thinner choroid thickness (CT) in SSc patients (3–5). Iloprost, a prostacycline analogue, is effective in the treatment of microvascular manifestations in SSc (7).

**Objectives:** To study skin BP and ocular CT in patients with SSc, before and after iloprost treatment.

**Methods:** After informed consent was obtained, twelve SSc patients according to ACR/EULAR classification criteria (8) (mean age 58±13 years, mean disease duration 5±3 years) underwent ophthalmologic evaluation by OCT and BP evaluation by LASCA, before after 8 hours of continuous iloprost i.v. infusion (0.5 ng/kg/min). OCT images were recorded by 3D-2000 OCT (Topcon, Japan) using protocol "line" that averages 50 B-scans and generates a horizontal 6 mm line. CT area measurements were performed manually using image J software. BP was assessed by LASCA at the level of fingertips, periungueal, whole face, perioral and periorbital area, and the average BP calculated as perfusion units (PU)(1). Statistical analysis was performed by non parametric tests.

**Results:** Both before and after iloprost therapy (T0-T1), statistically significant positive correlations between BP and CT were found at periorbital (T0 r=0.55, p=0.022, and T1 r=0.91 p=0.0002), fingertips (T0 r=0.69, p=0.004, and T1 r=0.63, p=0.01), and perioral skin areas (T0 r=0,75, p=0.002, and T1 r=0,61, p=0.012). Further correlations were observed at periungueal (T0 r=0.54, p=0.02, and T1 r=0.50, p=0.04) and whole face (T0 r=0.49, p=0.04, and T1 r=0.47, p=0.05). BP was found significantly increased after iloprost therapy in all examined areas (p=0.002). Patients did not show any visual/ocular symptom during and after iloprost infusion.

**Conclusions:** LASCA and OCT seem concordant tools in assessing the functional microvascularization status in SSc patients. Since LASCA is a reliable tool to assess skin BP, its observed correlation with the CT and the effects of iloprost treatment, suggest that the OCT evaluation could be included in periodical instrumental evaluation of SSc progression and effects of microvascular targeted treatments.

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**Disclosure of Interest:** None declared

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## AB0594 ANTI-RNA POL III ANTIBODIES IN SYSTEMIC SCLEROSIS - THE PREVALENCE AND USEFULNESS

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**Background:** Anti-RNA Polimerase III (a-RNA Pol III) antibodies are markers antibodies which are detected in sera of patients with systemic sclerosis (SSc). They are found in approximately 20% of SSc, particularly with diffuse subtype. According to literature a-RNA Pol III antibodies are strongly associated with scleroderma renal crisis (SRC). They are also correlated with higher rate of SSc-related mortality. Additionally, there are many data which reported that, a-RNA Pol III antibodies are associated with an increased risk of malignancy in patients with SSc.

**Objectives:** The aim of the study was assess the prevalence of a-RNA Pol III antibodies in patients with systemic sclerosis and to identify differences in the picture of the disease in patients with the presence of a-RNA Pol III.

**Methods:** The study was performed in 126 (98-female and 28-male) consecutive SSc patients treated in Department of Rheumatology. Patients fulfilled the ACR classification criteria of SSc (60 have diffuse SSc-dcSSc and 66 limited SSc – lcSSc). The subtype of SSc, incidence of internal organ involvement, the prevalence of malignancy, death and serological profile were determined in the whole data group. The study group were studied according to the presence of antibodies applying commercial test – EUROLINE Systemic Sclerosis Profile. Detection and interpretation of results was carried out electronically using the specific program Euroimmun– EUROLINEScan. Due to the presence of a-RNA

Pol III antibodies, patients were divided into two groups a-RNA Pol III(+) SSc – 19 pts and a-RNA Pol III(–) SSc – 107 pts.
**Results:** According to our data a- RNA Pol III antibodies were present in 19/126 patients with SSc (15%), including the a-RNA Pol III 11 were present in 16 and a-RNA Pol III 155 in 14. In this group of 13 (68,4%) pts had no other marker to SSc antibodies as a anticentromere, anti-topoisomerase I. Moreover, in our study group, a-RNA Pol III antibodies were more common in patients with dcSSc (p=0,049), compare to lcSSc. We also showed a significant positive association with a-RNA Pol III antibodies and occurrence of malignancy (p=0,007), SRC (p=0,001) and decreased DLCO (p=0,007). There was no relationship between the presence of a-RNA Pol III and other organ involvement, digital ulcerations or calcinosis.
**Conclusions:** 1. Anti- a-RNA Pol III antibodies are quite common in patients with systemic sclerosis, particularly with diffuse subtype.
2. In more than 50% of patients a-RNA Pol III antibodies may be present as the sole marker to SSc antibodies.
3. In SSc a-RNA Pol III antibodies are frequently associated with malignancy occurrence, kidney and lung involvement.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5032

## AB0595 DESCRIPTIVE ANALYSIS OF A SINGLE CENTER SERIES OF 23 PATIENTS WITH POSITIVE PM-SCL ANTIBODY

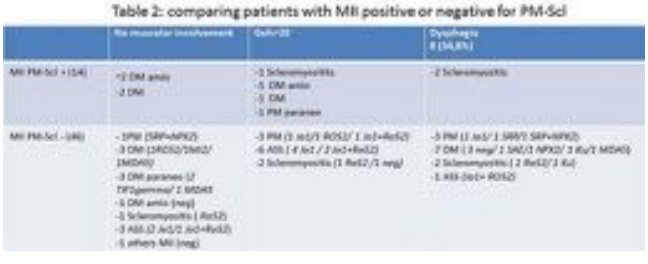
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**Background:** PM-Scl antibodies (abs) belong to the group of myositis-associated antibodies and typically determine a nucleolar or speckled pattern on immunofluorescence. These abs found in patients (pts) with Scleromyositis and, less frequently, in isolated forms of Systemic sclerosis (SSc), Polymyositis (PM) and Dermatomyositis (DM). In SSc pts PM-Scl +, pulmonary involvement seems less severe, while they show more frequent arthritis. Raynaud's phenomenon (RP), digital ulcers (DU) and gastroesophageal involvement appear to be less frequently expressed. In myositis the association with esophageal and lung involvement is well known.
**Objectives:** To characterize demographic and clinical features of a single center series of PM-Scl positive patients.
**Methods:** Sera from 48 SSc and 60 idiopathic inflammatory myophaties (MII) attending local outpatient clinic, detected with EUROIMMUNE Myositis Profile 4 kit, were tested to search PM-ScL antibodies. Demographic, laboratory and clinical data (RP, arthritis, DU, muscular involvement, disphagia) were retrospectively retrieved from available clinical charts. The presence of interstitial lung disease (ILD), was evaluated by HRCT (measured by using score of Goh for the extension) and functional respiratory testing (FVC and DLCO). Severe ILD was defined by: Goh score of>20 and FVC and DLCO <75%.
**Results:** 23 Pts (18 F) resulted positive for PM-Scl. The mean age was 60.5±9.4 years and the mean disease duration was 145.9± 76.3 months. 1 patient had negative ANA, 1 showed ANA anticentromere and 1 dot pattern; the remaining 20 patients (86,9%) were ANA+ showing nucleolar pattern. By applying available formal classification criteria 5 (21.7%) pts were diagnosed as DM, 2 (8.7%) as DM amyopathic, 3 (13.05%) as overlap Scleromyositis, 3 (13.05%) as PM, 1 (4.4%) as cancer associated PM, 9 (39.1%) as SSc (2 diffuse, limited 6, intermediate 1). 13 (56.5%) pts had no evidence of cytopathic muscle involvement (defined as normal CPK, myoglobin and LDH). 5 pts (21.7%) presented a Goh score >20, 1 FVC <75%, and 7 (30.4%) DLCO <75%.
4 pts presented arthritis. 14 (60.8%) had RP, 6 (26%) DU, 8 (34.8%), dysphagia (see images 1). When compared with patients with SSc and MII negative for PM-Scl, MII PM-Scl + pts did not show significant greater risk of developing ILD (Goh>20)dysphagia or minor muscle involvement. SSc PM-Scl + pts seem to have a greater risk of developing arthritis and DU than their corresponding SSc PM-Scl negative pts (p<0.05) while no differences did emerged about ILD (Goh>20) and dysphagia.

Table 1: comparing patients with SSc positive or negative for PM-Scl



Table 2: comparing patients with MII positive or negative for PM-Scl



**Conclusions:** The role of PM-Scl as a risk factor for ILD in MII pts is not confirmed, but should be considered the positivity in the control group of Jo1, representing per se a major risk factor for this complication (image 2). For patients with SSc is confirmed the role of PM-Scl as a risk factor for arthritis and digital ulcers but not for ILD.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4879

## AB0596 ASSESSMENT OF PULMONARY FUNCTION IN PATIENTS DIAGNOSED OF EARLY SYSTEMIC SCLEROSIS

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**Background:** Interstitial lung disease (ILD) is a frequent complication of systemic sclerosis (SSc) and is often progressive and has a poor prognosis. A restrictive ventilatory defect could suggest ILD either alone or in combination with pulmonary arterial hypertension. Nowadays, Early-SSc is well defined as preliminary stage of SSc. Patients who meet criteria for Early-SSc could benefit from an early diagnosis of pulmonary involvement.
**Objectives:** Our aim was to assess the pulmonary function in patients diagnosed of Early SSc.
**Methods:** Retrospective observational study of a wide and unselected series of patients diagnosed as Early-SSc from a single university hospital from June 2012 to August 2015. Patients were classified as Early-SSc following Le Roy criteria. In spite of this, patients already did not met 2013 ACR/EULAR classification criteria for SSc. We reviewed pulmonary function through conventional spirometry and diffusing capacity of lung for carbon monoxide (DLCO). Interpretation of the results of spirometry and DLCO was made according European Respiratory Society (ERS) and American Thoracic Society (ATS) standards
**Results:** We included a total of 41 patients with a mean age of 53±15.6 years (97.6% women; 2.4% men). No one of our patients evidenced a restrictive ventilatory pattern. DLCO was under normal limits in 11 patients (26.8%). Small airway obstruction expressed according decreased maximal (mid-) expiratory flow (MMEF) 25–75 was present in 13 patients (31.7%).
After a mean follow-up period of 26.1±16.6 months, 20 (48.8%) patients fulfilled 2013 ACR/EULAR criteria. The remaining 21 patients continued classified as Early-SSc following Le Roy criteria. The analysis of the subgroup of patients who progressed to SSc showed that DLCO was decreased in 7 of those 20 patients (35%) and also 8 of 20 patients (40%) presented decreased maximal (mid-) expiratory flow (MMEF) 25–75. Comparing with the subgroup of patients which not progressed to SSc no were significant differences (Decreased DLCO: 35% vs 26.8%; p=0.8 and Decreased MMEF 25–75: 40% vs 31.7%; p=0.9).
**Conclusions:** In our study, about a quarter of the patients classified as Early-SSc presented abnormal values of DLCO and/or signs of small airway obstruction without the presence of a restrictive ventilatory pattern. Moreover, the expression of this pulmonary dysfunction tends to be more frequent in patients who progressed to definitive SSc, although this was not statistically significant. An early assessment of pulmonary function in this context should be highly recommended.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5300

## AB0597 ADAPTATION OF UCLA SCLERODERMA CLINICAL TRIAL CONSORTIUM GASTROINTESTINAL TRACT 2.0 QUESTIONNAIRE INTO TURKISH

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**Background:** Nearly 90% of patients with scleroderma (SSc) have gastrointestinal tract (GIT) involvement in variable severities and is a challenging process for clinicians.
The University of California Scleroderma Clinical Trial Consortium Gastrointestinal Tract 2.0 (UCLA SCTC GIT 2.0) is a questionnaire including 34 items, 7 multi-item scales: reflux, distention/bloating, diarrhea, fecal soilage, constipation, emotional well-being and social functioning. By these parameters, a total GIT score is calculated (1). This scale translated in German, Italian, French, Polish, Spanish, Swedish, Dutch before, they are available in http://www.uclascleroderma.researchcore.org/ website (1–3). There is no Turkish version of this scale yet.
**Objectives:** Our aim is to make translation, cultural adaptation of the UCLA SCTC GIT 2.0 into Turkish, and assess reliability of the scale in patients speaking Turkish.
**Methods:** UCLA SCTC GIT 2.0 scale was translated into Turkish according

to international guidelines and applied to 97 SSc patients. The questionnaire repeated in 29 patients after an interval of 15 days for determining reliability. For internal consistency, Cronbach's alpha was calculated, reliability coefficient if item deleted and test-retest reliability also determined. External consistency was measured by comparing with the Short Form (SF)-36 by Spearman's correlation analysis (rho: ≤0.29 weak, 0.30–0.49 middle, ≥0.50 strong).

**Results:** 97 scleroderma patients were included in this study (female:87.6%, mean age:55.4±11.4). Internal consistency Cronbach's alpha was calculated as 0.89, reliability coefficient if item deleted was 0.89–0.90. External consistency of UCLA SCTC GIT 2.0 was measured by comparing with the SF-36, correlation was meaningful in medium level (Table 1,2).

Table 1. Descriptive statistics and internal consistency statistics

| UCLA SCTC GIT 2.0 scale | n | Mean score (SD) | Minimum score | Maximum score | Cronbach alpha | Floor effect % | Ceiling effect % |
|---|---|---|---|---|---|---|---|
| Reflux | 97 | 0.64 (0.54) | 0.0 | 2.6 | 0.83 | 17.5 | 0.0 |
| Distension | 97 | 1.02 (0.75) | 0.0 | 3.0 | 0.58 | 7.2 | 1.0 |
| Soilage | 97 | 0.30 (0.72) | 0.0 | 3.0 | 0.68 | 82.5 | 3.1 |
| Diarrhea | 97 | 0.28 (0.47) | 0.0 | 1.5 | 0.36 | 69.1 | 0.0 |
| Social Functioning | 97 | 0.17 (0.32) | 0.0 | 1.3 | 0.47 | 67.0 | 0.0 |
| Emotional Wellbeing | 97 | 0.30 (0.43) | 0.0 | 2.2 | 0.73 | 41.2 | 0.0 |
| Constipation | 97 | 0.63 (0.69) | 0.0 | 2.5 | 0.56 | 34.0 | 0.0 |
| Total GIT score | 97 | 0.45 (0.37) | 0.0 | 1.6 | 0.82 | 3.1 | 0.0 |

All scales are scored from 0.00 (better HRQOL) to 3.00 (worse HRQOL) except the diarrhea and constipation (range from 0.00–2.00 and 0.00–2.50, respectively). The UCLA GIT 2.0 provides a total score of GIT severity and calculated by summation of all scales (except constipation) and ranges from 0.00 to 2.83.

Table 2. External Consistency Statistics: Correlation Between SF-36 Items and Component Summaries and UCLA SCTC GIT 2.0 Items

| UCLA SCTC GIT 2.0 / SF-36 | PF | RP | RE | VT | MH | SF | BP | GH | PCS | MCS |
|---|---|---|---|---|---|---|---|---|---|---|
| Reflux | -,300** | -,436** | -,296** | -,421** | -,376** | -,285* | -,417** | -,312** | -,386** | -,318** |
| Distension | -,461** | -,422** | ,238* | -,465** | -,474** | -,340** | -,427** | -,408** | -,437** | -,354** |
| Soilage | -,237* | -,160 | ,001 | -,170 | -,165 | -,131 | -,328** | -,114 | -,254* | -,027 |
| Diarrhea | -,265** | -,258* | -,180 | -,214* | -,215* | -,146 | -,325** | -,083 | -,296** | -,176 |
| Social Functioning | -,208* | -,203* | -,242* | -,189 | -,271** | -,210* | -,400** | -,242* | -,300** | -,248* |
| Emotional Wellbeing | -,397** | -,379** | -,439** | -,334** | -,372** | -,337** | -,445** | -,263** | -,304** | -,368** |
| Constipation | -,163 | -,101 | -,199 | -,047 | -,063 | -,166 | -,299** | -,065 | -,167 | -,132 |
| Total GIT score | -,482** | -,453** | -,321** | -,492** | -,493** | -,369** | -,560** | -,395** | -,482** | -,349** |

p<0.05 * and p<0.01 ** PF: physical functioning, RP: role limitations due to physical health, RE: role limitations due to emotional problems, VT: vitality, MH: mental health, SF: social functioning, BP: bodily pain, GH: general health, PCS: physical component summary, MCS: mental component summary.

**Conclusions:** UCLA SCTC GIT 2.0 scale had strong internal consistency, good reliability and acceptable validity when adapted into Turkish. Turkish-speaking patients with scleroderma, this scale will be useful to assess GIT symptoms. The basic constraint of our study was, not using image procedures for objective GIT involvement evidences.

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**Disclosure of Interest:** None declared
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## AB0598 DOES THE PRESENCE OF ANTI-CITRULLINATED PROTEIN ANTIBODIES CHANGE THE PRESENTATION OF SYSTEMIC SCLEROSIS?

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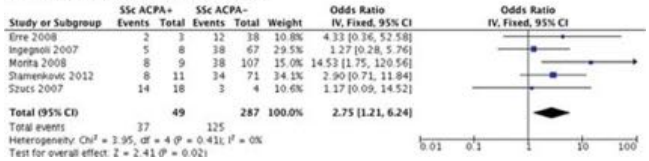
**Background:** Systemic sclerosis (SSc) is one of the most complex and heterogeneous systemic disease. The diagnosis can be helped by the positivity of different characteristic auto-antibodies steered toward topoisomerase I, centromeric protein, RNA polymerase and fibrillarin. Different presentations of the disease can be associated with some specificities of auto-antibodies. Recently, some studies have reported the presence of anti-citrullinated protein antibodies (ACPA) in patients with SSc.

**Objectives:** We have conducted a systematic literature review in order to define the prevalence of ACPA in SSc, and to observe their influence on clinical and paraclinical presentation of the disease.

**Methods:** Literature search was performed in PubMed Medline database on 15 february 2015. Publication were identified through a search that used the terms: ("systemic sclerosis"(MeSH) and "ACPA or anti-CCP or rheumatoid factor or cohort or value diagnostic"). In a first step, we have selected all cohorts over 50 patients with SSc and ACPA identification. In a second step we have included all studies in which the clinical profile of scleroderma was detailed according to their ACPA status. Meta-analyses were performed when there were two or more studies with similar clinical description.

**Results:** For the first question, we identified 13 observational studies merging 1231 patients with SSc. ACPAs were positive for 113 patients, giving a prevalence of ACPA in SSc of 9.2%. In a second step, we identified 9 studies reporting clinical and paraclinical aspects according to their ACPA status. Information was enough to perform a meta-analysis for arthralgia, arthritis, joint erosions, skin sclerosis, pulmonary arterial hypertension, pulmonary fibrosis and gastrooesophageal reflux. We found a significant association between ACPA positivity and the presence of arthritis (OR: 25.48 [11.82–54.47]), joint erosions on X-rays (OR: 13.06 [4.68–36.43]), pulmonary arterial hypertension (OR: 7.72 [2.38 – 25.5]), and pulmonary fibrosis (OR: 2.75 [1,21–6.24]) (Fig 1).

Figure 1 – Meta-analysis assessing the impact of presence of ACPA on pulmonary fibrosis in patients with SSc.




**Conclusions:** ACPA prevalence in scleroderma is 9.2%. Our systematic literature review shows a significant increased risk for erosive arthritis, pulmonary hypertension and pulmonary fibrosis in ACPA positive SSc. ACPA should be systematically included in the check-up of systemic sclerosis.

**Disclosure of Interest:** None declared
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## AB0599 INTERLEUKIN-35 IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** Interleukin-35 (IL-35) is a newly described heterodimeric cytokine that belongs to the IL-12 family and consists of p35 (IL-12a) and EBI3 (IL-27b) subunits. IL-35 exerts immunomodulatory activities in several autoimmune inflammatory diseases.

**Objectives:** The aim of this study was to assess IL-35 expression in muscle tissue of patients with idiopathic inflammatory myopathies (IIM) and to compare serum levels of IL-35 in patients with IIM to healthy controls and asses potential association with activity of IIM.

**Methods:** The expression of IL-35 was studied in a series of 19 muscle biopsy samples of idiopathic inflammatory myopathies (9 dermatomyositis, 10 polymyositis) and 10 non-inflammatory control muscle biopsies from patients with myasthenia gravis.Serum levels of IL-35 were measured in 23 PM, 28 DM and 15 cancer associated myositis patients as well as in 40 healthy controls.Disease activity was evaluated by the Myositis Disease Activity Assessment Tool (MYOACT) and by serum muscle enzymes.

**Results:** Both IL-35 subunits were found in immune cells of the inflammatory infiltrates in IIM muscle biopsies, no immunoreactivity was observed in muscle tissue of control patients.IL-35 serum levels were increased in all IIM patients compared to healthy controls ($p<0.001$). There were no differences in IL-35 serum levels between myositis subgroups. Serum IL-35 levels correlated with the overall MYOACT score, with extramuscular and muscle domains of MYOACT, with physician's global activity assessment and lactate dehydrogenase levels.

**Conclusions:** IL-35 subunits are overexpressed in inflammatory infiltrates in muscle tissue of IIM patients and elevated circulating IL-35 levels correlate with several disease activity parameters. These data suggest potential role of IL-35 in the pathogenesis of inflammatory myopathies.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3675

## AB0600 HIGH PREVALENCE OF REDUCED BONE MINERAL DENSITY AND UNDERTREATMENT OF OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis is a systemic inflammatory rheumatic disease with a very low prevalence, that has been associated with an increased risk of

low bone mineral density (BMD)[1], but data on risk factors associated with bone loss in systemic sclerosis are scarce.
**Objectives:** The objective of this study was to investigate the prevalence of and risk factors for low BMD in patients with systemic sclerosis.
**Methods:** Demographic and clinical data of 61 patients with systemic sclerosis were collected. BMD measurements of the lumbar spine, total hip and femoral neck were performed using DXA. Osteoporosis was defined as a T score less than -2.5 SD and osteopenia as a T-score between -1.0 and -2.5 SD, according to WHO definitions. Systemic sclerosis disease severity was defined by the Rodnan skin score and by the Medsger disease severity score[2]. Multiple linear regression analyses was used to assess factors associated with BMD.
**Results:** Patients were on average 56.7±12.4 years old and 72% were female of whom 77% postmenopausal. BMD measurements revealed osteopenia or osteoporosis in at least one measurement site in 67% of the patients, of whom 30% had osteoporosis. Low body mass index and postmenopausal state were significantly associated with low BMD in all skeletal sites. No significant associations were found between age, Rodnan skin score, Medsger disease severity score, glucocorticoid treatment and BMD. Of the 30% of patients who had an indication for anti-osteoporosis treatment, 91% did not receive anti-osteoporosis medication.

Table 1. Multiple linear regression analysis of BMD in the total hip, femoral neck and lumbar spine

| | Covariates | β | *p*-value | $r^2$ |
|---|---|---|---|---|
| Total hip | Postmenopausal state | –0.326 | 0.003 | 43% |
| | BMI | 0.406 | <0.001 | |
| | Medsger score general | –0.150 | 0.251 | |
| | Proteinuria | –0.229 | 0.085 | |
| Femoral neck | Postmenopausal state | –0.280 | 0.02 | 33% |
| | BMI | 0.351 | 0.004 | |
| | Medsger score general | –1.06 | 0.461 | |
| | Proteinuria | –0.146 | 0.342 | |
| | Physical activity | 0.146 | 0.247 | |
| Lumbar spine | Postmenopausal state | –0.301 | 0.015 | 37% |
| | BMI | 0.391 | 0.003 | |
| | Medsger score general | –0.07 | 0.640 | |
| | DcSSc subtype | –0.226 | 0.165 | |
| | Rodnan skin score | 0.204 | 0.199 | |
| | ESR | –0.152 | 0.282 | |

BMI = body mass index, DcSSc = diffuse cutaneous systemic sclerosis, ESR = erythrocyte sedimentation rate, β = standardized regression coefficient.

**Conclusions:** The results of this cross-sectional study demonstrate a high frequency of osteoporosis or osteopenia in 67% of our patients with systemic sclerosis and low body mass index and postmenopausal state were identified as the most important risk factors. No relationship between disease severity and BMD was found, which could be related to the sample size, although it can be argued that low BMI is, at least partly, a marker of disease severity. This study also shows a high frequency (91%) of undertreatment of osteoporosis in this patient group. These results underline the importance of monitoring and treatment of low BMD in systemic sclerosis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2774

## AB0601 SIGNIFICANT CARDIOLOGICAL CHANGES IN SYSTEMIC SCLEROSIS: AN ELECTROCARDIOGRAPHIC AND ECHOCARDIOGRAPHIC EVALUATION

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**Background:** Cardiac involvement in Systemic Sclerosis (SSc) is rather common and it can be considered a bad prognostic feature.
**Objectives:** In this study we aimed to evaluate this involvement performing electrocardiogram (ECG) and echocardiogram in a group of SSc patients, comparing their data with those of healthy volunteers (NC).
**Methods:** Seventy-one consecutive SSc patients (Group A) were compared to 60 NC (Group B), matched for age and sex. Both patients and NC were evaluated by anamnesis, physical examination, ECG and trans-thoracic echocardiogram, with Doppler and tissue-wave Doppler.
**Results:** Ten SSc patients and 3 NC were excluded (Group A: 4 patients for increased basal heart rate, 2 for TAPSE <17 mm, 3 for valvular disease and 1 patient for severe pulmonary hypertension. Group B: 3 subjects for high basal heart rate). Among SSc patients 22 (36.1%) had a diffuse cutaneous form (dcSSc), and 39 (73.9%) had a limited cutaneous form (lcSSc). In table 1 clinical-demographic and laboratory features of patients are described. QT dispersion (QTd) and QTc dispersion (QTcd) were significantly higher in Group A respect to Group B (QTd 49.83 vs 27.85 msec, p<0.0001; QTcd: 51.39 vs 29.73 msec, p<0.0001). Patients with dcSSc showed longer QTc values than controls (440.58±18.23 vs 427.64±23.12 msec, p=0.02). Left ventricular mass index (LVMI) mean values were significantly increased while left ventricular ejection fraction (LVEF) mean values were significantly reduced in Group A compared with Group B respectively (LVMI: 80.5 vs 61.54 g/$m^2$, p<0.0001; LVEF: 63.55 vs 68.42%, p=0.0001). No patient with LVEF<55% was found. In addition left atrial volume index for body surface (LAVI) mean values were higher in Group A (27.67 vs 18.78 ml/$m^2$, p<0.0001). The percentage of patients with left ventricular diastolic dysfunction (LVDD) was higher in Group A (70.5 vs 21.8%, p=0.0001). In Group A QTc prolungation, increased levels of QTcd and P wave duration were associated with LVDD. An increase of P-wave duration was also associated with higher values of LAVI (p=0.04).

Table 1. Main clinical-demographic and laboratory features of 61 SSc patients

| Features | |
|---|---|
| Age (years)(median, 25°p–75°p) | 66.5 (55–74.5) |
| Sex (F/M) | 57/4 |
| Disease duration (years)(median, 25°p–75°p) | 5.5 (4–12) |
| lcSSc/dcSSc | 39/22 |
| Modified Rodnan Skin score (median, 25°p–75°p) | 8.5 (4.75–14.25) |
| Active digital ulcers (n/%) | 8/13 |
| Interstitial lung disease (n/%) | 26/42.6 |
| Anti-nuclear antibodies positivity (n/%) | 58/95 |
| Anti-centromere antibodies positivity (n/%) | 23/37.7 |
| Anti-topoisomerase I antibodies positivity (n/%) | 22/36 |

**Conclusions:** Significant cardiological differences can be found in SSc, even in asymptomatic patients, respect to NC, thus confirming how ECG and echocardiogram are relevant instruments able to detect morpho-functional abnormalities suggestive of an early myocardial involvement in this disease.
**Disclosure of Interest:** None declared
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## AB0602 INCREASED STIFFNESS OF MEDIAN NERVE IN SYSTEMIC SCLEROSIS

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**Background:** The frequency of peripheral nerve involvement has been debated in systemic sclerosis (SS). Despite the patients have clinical symptoms such as numbness and paresthesia the electrodiagnostically proven neuropathy incidence is low.
**Objectives:** The aims of this study are to document peripheral neuropathies in a cohort of SS and compare the sonoelastrographic measurements of median nerves in systemic sclerosis, idiopathic carpal tunnel syndrome and healthy controls.
**Methods:** The clinical, electrophsiological and ultrasonographic assessments were done by three masked researchers. Patients with SS and CTS were assessed with nerve conduction studies. The sonoelastography and sonographic assessments of the median nerve were perfomed with 6–18 Mhz lineer transducer. The measurements of cross sectional areas (CSA)were performed at psiform and forearm level from axial US images. The sonoelastrography was performed with same transducer and same sonographer. The median nerve was visualized in axial view and kept in center of the screen. Seven-10 slight compressions were made periodically by the sonographer until the device determined that the proper elastographic view was obtained. The elastic ratio is the ratio of strain distribution in two selected region of interests (ROI). A round ROI was positioned in the center median nerve, while a same size of ROI was positioned in a homogeneously soft anatomical structure, which was considered as internal control. Second ROI was positioned on the flexor carpi radialis for the wrist level and flexor digitorum superficialis for the forearm level. The ROIs were fixed to 2 mm. By using this method, a higher elastic ratio reflects a lower elasticity of median nerve.
**Results:** The study was completed with 47 hands of 24 patients with SS, 53 hands of patients with CTS and 38 hands of health controls. According to electrodiagnostic testing 17 patients were normal, 4 patients were diagnosed as CTS and 3 patients were diagnosed as polyneuropathy in patients with SS. The CSA of CTS group was significantly higher than systemic sclerosis and control groups. The elastic ratio at psiform level and forearm levels of systemic sclerosis

| Group | Mean | SD | ANOVA | Tukey |
|---|---|---|---|---|
| Median nerve cross sectional area at psiform level | | | | |
| Control | 9.13 | 2.18 | F: 11.15 p=0.001 | Control/systemic sclerosis p=0.325 |
| Systemic sclerosis | 10.27 | 3.36 | | Control/CTS p=0.001 |
| CTS | 12.64 | 4.61 | | CTS/systemic sclerosis p=0.004 |
| Elastic ratio at psiform level | | | | |
| Control | 1.63 | 1.15 | F: 7.09 p=0.001 | Control/systemic sclerosis p=0.001 |
| Systemic sclerosis | 3.02 | 2.56 | | Control/CTS p=0.27 |
| CTS | 2.19 | 0.93 | | CTS /systemic sclerosis p=0.04 |
| Elastic ratio at forearm level | | | | |
| Control | 9.16 | 1.71 | F: 9.93 p=0.001 | Control/systemic sclerosis p=0.001 |
| Systemic sclerosis | 8.3 | .94421 | | Control/CTS p=0.24 |
| CTS | | | | CTS /systemic sclerosis p=0.001 |

SD, standard deviation.

group were significantly higher than the CTS and control groups. There was no statistical difference between CTS and control groups.
**Conclusions:** The frequency of peripheral neuropathy is increased in SS. The median nerves loose the elasticity in both wrist and forearm level where the CSA's are in the normal range. These results suggested that the increased peripheral nerve involvement in SS is about the increased stiffness of the nerves.
**Disclosure of Interest:** None declared
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## AB0603 MAJOR COMORBIDITIES OF IDIOPATHIC INFLAMMATORY MYOSITIS AFFECTING SURVIVAL AND FUNCTIONAL IMPAIRMENT: A POPULATION-BASED STUDY USING 11 YEARS OF FOLLOW UP FROM THE NATIONAL HEALTH INSURANCE IN KOREA

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**Background:** Patients with idiopathic inflammatory myositis (IIM) suffer from comorbidities such as interstitial lung disease (ILD), cancer, and infections related to immunosuppressive agents.
**Objectives:** To evaluate 1) incidence rate ratio (IRRs) of major comorbidities in IIM compared to non-IIM Koreans, and 2) impact of the comorbidities on survival and functional impairment.
**Methods:** A retrospective cohort study was performed using the 2002–2013 National Health Insurance Service (NHIS) database of weighted probability sampled one million cohort. IIM was identified by at least two visits to the tertiary hospitals under ICD9 code of IIM. Age- and sex-matched twenty subjects per patient, who never had ICD9 code at least for 1 year, were included as the unexposed. The occurrence of ILD, cancer, herpes zoster, and tuberculosis, severely disabled status, and death was captured using ICD9 code, disease-specific medication, and/or government-approved qualification for co-payment reduction on these outcomes.
**Results:** Ninety-one patients were newly diagnosed as IIM from 2003 to 2013. Most patients (>90%) defined as such were found to have muscle biopsy, electromyogram, or multiple laboratory examinations on muscle enzymes. Their incidence rate of the above outcomes was significantly elevated (Table); IRRs of ILD 31.8 [95% confidence interval: 13.2 – 76.7], cancer 2.36 [1.61–3.48], herpes zoster 1.75 [1.20–2.54], tuberculosis 2.08 [1.15–3.77], severely disabled status 4.79 [2.55–9.01], and mortality 3.47 [1.96–6.12]. Among IIM patients, the presence of ILD or cancer greatly deteriorated survival; mortality IRR of 73.2 [9.58–559.9] in ILD and 63.2 [17.6–226.7] in cancer. The occurrence of zoster and tuberculosis did not influence on the mortality. ILD and cancer also worsened functional impairment of IIM patients; IRR of 12.0 [2.64–54.9] for severely disabled status in ILD and 13.2 [4.19–41.6] in cancer.

Table 1. Incidence rate and incidence rate ratios of major comorbidities, severely disabled, and death in patients with idiopathic inflammatory myositis versus the matched control

| | Incidence rate (# of cases/1,000 person-year) | | Incidence rate ratio [95% Confidence interval] |
|---|---|---|---|
| | Myositis (n=91) | Control (n=1820) | |
| Interstitial lung disease | 33.0 (13/394.3) | 1.04 (8/7714.3) | 31.8 [13.2–76.7] |
| Cancer | 73.6 (29/394.3) | 31.1 (240/7714.3) | 2.36 [1.61–3.48] |
| Herpes zoster | 76.1 (30/394.3) | 43.6 (336/7714.3) | 1.75 [1.20–2.54] |
| Tuberculosis | 30.4 (12/394.3) | 14.6 (113/7714.3) | 2.08 [1.15–3.77] |
| Severely disabled | 30.4 (12/394.3) | 6.35 (49/7714.3) | 4.79 [2.55–9.01] |
| Death | 35.5 (14/394.3) | 10.2 (79/7714.3) | 3.47 [1.96–6.12] |

**Conclusions:** This is the first report of the nation-wide population based evaluation of IIM in Korea. The incidence of ILD, cancers, zoster, and tuberculosis was exceptionally higher in IIM than non-IIM. ILD and cancers significantly affected prognosis of IIM. More detailed analysis of comorbidities and their risk factors using the whole national database is underway.
**Disclosure of Interest:** None declared
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## AB0605 RIDAI.ORG/SSC: THE PORTUGUESE NATIONAL SYSTEMIC SCLEROSIS REGISTRY – FOCUS ON QUALITY OF LIFE AND DATA CONFORMITY

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**Background:** Registries have a major role in patient follow-up, prospectively collecting real life data, they help us to better understand rare diseases like scleroderma. These atabases allow standardization of daily clinical practice, introducing decision support tools and improving quality and health outcomes. They also allow drug and device surveillance; scientific societies, academia and regulatory authorities can analyze their selected core set of data.
**Methods:** Our web-based registry - RIDAI (Informatic Registry of Autoimmune Diseases; www.ridai.org), was created in 2003 by the Portuguese Society Internal Medicine to support all Autoimmunity Clinics in Portugal; currently collecting data from 40 centres, with 4825 patients with different diseases. It has been constantly developped to comprise all the updated tools to measure important domains in autoimmune diseases. Demographic and clinical data were collected and analysed in Microsoft Excel 2013.
**Results:** Short presentation and demonstration of RIDAI, online since 2013. The scleroderma cohort has 326 patients, 227 limited and 99 diffuse subtypes, 43 (13.2%) males, mean age 56.4 (range 3–90), longest follow-up since 1993.
Comorbidities are highly prevalent in our cohort: dyslipidemia in 46 patients, hypertension in 40, peripheral vascular disease in 22, osteoporosis in 20, heart failure in 13, diabetes in 10 and coronary heart disease in 3 patients.
Most frequently used tools include Modified Rodnan Skin Score (mRSS), Visual Analogic Scale (VAS), Joint Count, EUSTAR Systemic Sclerosis Activity Scale (EUSTAR SSAS), the UCLA Scleroderma Clinical Trials Consortium Gastrointestinal Scale (SCTC GIT), Health Assessment Questionaire (HAQ) and Short Form-36 (SF-36). MRSS has a mean value of 9.1. Patient VAS has a mean 39.6; physician VAS mean 38.6. Painful Joint Count has a mean value of 3.0; tender Joint Count mean 1.6. The EUSTAR SSAS has a mean value of 1.27. SCTC GIT mean value is 0.52. HAQ mean value is 1.0; SF-36 mean is 103.9.
Biological disease modifying drugs were prescribed off-label in 10 patients, for severe skin and joint disease.
**Conclusions:** The RIDAI is the largest portuguese scleroderma registry. It's a versatile application and can be articulated with other platforms, with direct contribution to international multicentric studies. The presentation of the first 326 patients illustrates the complexity and heterogeneity of systemic sclerosis and of this cohort of patients. Treating to target and using standardized monitoring tools, Portuguese Internal Medicine physicians confirm good treatment performance, with a positive impact on indexes, specially mean mRSS and quality of life (HAQ, SF-36); enabling comparision with best practices.
**Disclosure of Interest:** None declared
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## AB0606 FACTORS RELATED WITH THE DEVELOPMENT OF ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Different studies and meta-analysis have shown that subclinical atherosclerosis (AS) and vascular complications (VC) are higher in patients with Systemic Sclerosis (SSc) than in healthy population, a fact that has been fundamentally related to non traditional vascular risk factors (VRF).
**Objectives:** To identify VRF which shows to be independently related to the

existence of macrovascular affection (carotid ultrasound, ankle-braquial index [ABI]) in patients with SSc.
**Methods:** Transverse descriptive study with analytical components. Study population: cohort of 115 patients with SSc controlled in the Rheumatology Department of a tertiary hospital. Variables: 1) *Clinical variables*; 2) *Questionnaires and indices:* global VAS, HAQ, SF-36, CHFS (Cochin Hand Function Scale),MHISS (Mouth Handicap In Systemic Sclerosis scale), HOMA and SCORE; 3) *Analytical variables:* hemogram, classic vascular risk biomarkers, activity/inflammation biological markers, autoantibody profile, hemostasis/vascular disease markers; 4) *Vascular study:* ABI and carotid doppler ultrasound (ESAOTE MyLab XV70, 7–12 MHz linear transducer, software $^{RF}$QIMT) measuring intima-media thickness (IMT) and the presence of atheroma plaques (Mannheim Consensus); 5) *Other variables:* acro-osteolysis, ECG, functional pulmonary tests, lung HRCT and doppler echocardiography. A vascular surgeon measured ABI and the carotid doppler ultrasound was done by a vastly experienced rheumatologist, blind to the rest of findings, in a term of 3 months after the initial evaluation. Statistical analysis: IBM-SPSS Statistics v22.0 package.
**Results:** 115 patients where included, of which 108 were studied; with a mean age of 60,16 years (SD ±15,16); 99 women (91.7%) and 9 men (8.3%.) Mean SSc evolution time was 11.45 years (SD ±8,84). LSSc was most frequently diagnosed (50%), followed by SSc without scleroderma (18.5%), DSSc (16.7%), overlap syndrome (9.3%) and pre-SSc (5.6%). 38.9% of patients were hypertensive, 46.3% suffered a DL, and 6.3% were diabetic. 37% had a pathological carotid ultrasound and 39.8% had macrovascular damage (atheroma plaque and/or IMT$>$0.9 mm and/or ITB$<$0.9). The bivariate analysis showed a relation between macrovascular disease and several traditional and non traditional (related to the disease) VRF. In the multivariate analysis, age, HTA, DL, systolic pressure, glycaemia, renal function,VC history, SCORE values, SF36, duration of the SSc, coexistence of an inflammatory disease, diastolic dysfunction of the LV, ESR, D-dimer values, estimated PsAP values, and the use of different drugs (statins, ACEI, ARBs, endothelin receptor antagonists, rituximab) maintained a significant relationship with the different macrovascular disease variables.
**Conclusions:** Macrovascular disease in patients with SSc associates with traditional VRF (age, HTA and DL) as well as VRF related to SSc (prolonged duration, greater inflammatory load, elevated PsAP values, diastolic dysfunction of LV). A strict control of blood pressure values and the use of statins should be part of the regular protocol for treating selected, elderly patients.
**Disclosure of Interest:** None declared
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## AB0607 DETERMINANTS OF UNEMPLOYMENT AMONGST AUSTRALIAN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** The ability to work is a fundamental component of everyday life.
**Objectives:** To assess employment status, risk factors for unemployment and the associations of unemployment with patients' health related quality of life (HRQoL).
**Methods:** All patients completed in a systemic sclerosis (SSc) longitudinal cohort study, completed an employment questionnaire on enrolment. Clinical manifestations were defined based on presence at the time of enrolment. Summary statistics, chi-square tests, univariate and multivariable logistic regression were used to determine the associations of various risk factors with employment.
**Results:** Among 1587 SSc patients, 160 (20%) were unemployed at the time of cohort enrolment excluding retired patients. Of these, 63% had limited disease subtype. Mean (±SD) age at enrollment was 51.9 (±10.4) years; 13 years below the average retirement age in Australia. Mean (±SD) disease duration at recruitment was 11.1 (±10.9) years. Multivariable regression analysis revealed the presence of digital amputation (OR 3.9, 95%CI 1.7–9.1, p=0.002), diffuse disease subtype (OR 2.2, 95%CI 1.3–3.5, p-value=0.002), sicca symptoms (OR 2.7, 95%CI 1.6–4.4, p$<$0.001), a physical job (OR 1.8, 95%CI 1.1–3.1, p=0.03) and pulmonary arterial hypertension (OR 2.2, 95%CI 1.1–4.5, p=0.02) to be associated with unemployment. Unemployed patients had consistently poorer HRQoL scores in all domains (physical, emotional and mental health) of the SF-36 form than those who were employed.

Table 1. Risk factors associated with unemployment in multivariable analysis

| Characteristic | OR (95% CI) | p value |
|---|---|---|
| Physical job | 1.8 (1.1–3.1) | 0.03 |
| Diffuse disease subtype | 2.2 (1.3–3.5) | 0.002 |
| PAH | 2.2 (1.1–4.5) | 0.02 |
| Sicca | 2.7 (1.6–4.4) | $<$0.001 |
| Digital amputation | 3.9 (1.7–9.1) | 0.002 |

Abbreviation: OR = odds ratio; PAH = pulmonary arterial hypertension; 95% CI = 95% confidence interval.

**Conclusions:** SSc is associated with substantial work disability and unemployment, which is in turn associated with poor quality of life. Raising awareness, identifying modifiable risk factors and implementing employment strategies and work place modifications are possible ways of reducing this burden.

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## AB0608 CHARACTERISTIC ADVERSE EVENTS AND DEVELOPMENT OF DIGITAL ULCERS IN BOSENTAN-TREATED JAPANESE PATIENTS WITH DIGITAL ULCERS SECONDARY TO SYSTEMIC SCLEROSIS

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**Background:** Only a few medications have been approved for the prevention and treatment of digital ulcers in Japan. Ethnicity has been reported to affect the severity and occurrence rate of digital ulcers, which are potentially caused by more common autoantibody prevalence in the systemic sclerosis (SSc) patients of some ethnic groups; however, information on Japanese and Asian patients is limited. In the present study, the adverse events and development of digital ulcers were investigated when bosentan was administered to Japanese SSc patients. We focused on liver function test abnormalities, which are one of the characteristic adverse events of bosentan, baseline patient characteristics, and the onset/resolution time of the associated adverse events. The occurrence and healing of digital ulcers over time in each patient were also examined.
**Methods:** Twenty-eight (28) patients were enrolled in 9 study sites in Japan. This was a multi-center, single arm, open-labeled study conducted in order to investigate the safety and efficacy of bosentan in Japanese patients who had or had a previous history of SSc-related digital ulcers. The safety of the drug was monitored and the clinical course of digital ulcers was assessed up to Week 52 of the treatment.
**Results:** The adverse events observed in $\geq$5% of patients, i.e., at least two patients during the 52-week treatment period, were upper respiratory tract infections (14/28, 50.0%), liver function test abnormalities (12/28, 42.9%), the development of new digital ulcers (7/28, 25.0%), anemia (5/28, 17.9%), peripheral edema (4/28, 14.3%), diarrhea (3/28, 10.7%), urinary tract infections (2/28, 7.1%), arthralgia (2/28, 7.1%), constipation (2/28, 7.1%), and herpes zoster (2/28, 7.1%). Of the 12 patients (42.9%) with liver function test abnormalities, 4 (14.3%) showed AST and/or ALT elevations $>3\times$ the upper limit of normal, occurring before Week 16 for two patients and after Week 16 for the other two. All elevated liver enzymes normalized upon withdrawal of the drug. During the 52-week observation period, 25% (7/28) of patients developed new digital ulcers, the mean (± SD) number of which was 0.6±1.3.
**Conclusions:** The adverse events observed in the present study were similar to those previously reported with the use of bosentan, demonstrating the safety of the drug for Japanese patients; however, 4 out of 28 patients had adverse events associated with liver function disorders, which are one of the characteristic adverse effects of bosentan. These results indicate that liver function needs to be monitored regularly in patients treated with bosentan.
**Disclosure of Interest:** None declared
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## AB0609 RADIOGRAPHIC FINDINGS IN HAND X-RAY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Musculoskeletal involvement is major complication for patients with systemic sclerosis (SSc). Many radiographic abnormalities are observed, especially in hands, however, the detailed prevalence and the association with clinical features is still unclear.
**Objectives:** To clarify the characteristics of radiographic findings in hand X-ray and their association with clinical features in SSc.
**Methods:** Japanese SSc patients without rheumatoid arthritis who visit our hospital from 2011 to 2015 were included. Two directional hand X-ray was taken to evaluate joint and soft-tissue changes. Clinical and serological parameters were collected retrospectively from their medical records. The prevalence of abnormal findings in X-ray was examined, and the associations with clinical features, SSc subtypes and autoantibodies were analyzed.
**Results:** Sixty four patients including 16 diffuse cutaneous (dc) SSc and 49 limited cutaneous (lc) SSc were enrolled. The mean age was 66.7 years (range 31–88years), 87.5% were female and the mean disease duration was 13.9 years (range 1–37 years). Thirty four patients (53.1%) were positive for anticentromere antibody, 21 (32.8%) for anti-Scl-70 antibody, and 3 (4.7%) for anti-RNA polymerase III antibody. Fifteen (24.6%) were positive for rheumatoid factor (RF), and 1 (1.6%) for anti-cyclic citullinated peptide (CCP) antibody. Finding of hand X-ray showed acroosteolysis in 18.4%, erosive hand osteoarthritis in 15.4%, flexion contracture in 13.8%, and calcinosis in 10.8%. Acroosteolysis was significantly associated with digital tip ulcer (p$<$0.01), digital pitting scar (p$<$0.01), interstitial

lung disease ($p<0.05$), gastrointestinal involvement ($p<0.05$), and longer disease duration ($p<0.01$). Flexion contracture also showed the association with digital tip ulcer, digital pitting scar, and gastrointestinal involvement ($p<0.01$, $p<0.01$, and $p<0.05$, respectively). While acroosteolysis and flexion contracture were more frequent in dcSSc than lcSSc (43.8% vs 10.4%, $p<0.01$ and 31.3% vs 8.3%, $p<0.05$, respectively), erosive osteoarthritis was observed only in lcSSc (dcSSc 0% vs lcSSc 20.4%, $p>0.05$). Calcinosis and erosive osteoarthritis were not related with any other clinical features including age, sex, and disease duration. Assessing the relation between X-ray findings and autoantibody, acroosterolysis were associated with positivity for anti Scl-70 ($P<0.05$,), and flexion contracture with anti-RNA polymerase III ($P<0.05$), but no association was found between X-ray findings and RF/anti-CCP antibody positivity.

**Conclusions:** Various abnormal findings in hand X-ray were observed in patients with SSc. Of these, acroosteolysis was most prevalent. Both acroosteolysis and flexion contracture were associated with peripheral circulatory disturbance and the distinct characteristics of dcSSc, whereas erosive osteoarthritis was observed only in lcSSc. These results suggest that the difference of X-ray findings reflects the underlying pathogenesis of each patient with SSc.

**Disclosure of Interest:** None declared

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## AB0610 PLATELET FACTOR 4 AS A BIOMARKER IN KOREAN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a complex multi-organ autoimmune disease with chronic and heterogeneous clinical manifestations. There is an unmet need for a new biomarker for early diagnosis and classification of SSc. Recent technical advancements have indicated several biomarkers for SSc; among these, platelet factor 4 (PF4), also known as CXCL4, was suggested by a large-cohort proteomic study [1]. PF4 is a chemokine released from activated platelets and is involved in coagulation, inflammation, and angiogenesis, which are influential in SSc pathogenesis. Therefore, PF4 may be an effective biomarker for SSc.

**Objectives:** To investigate the efficacy of PF4 as a biomarker for the diagnosis, activity and severity of patients with SSc.

**Methods:** Thirty-nine SSc patients (36 female and 3 male; mean age, 58.8±10.42 years; mean disease duration, 7.15±3.92 years; 11 diffuse cutaneous SSc cases and 28 limited cutaneous SSc cases) and 30 healthy controls (HC; 25 female and 5 male; mean age, 46.43±14.43 years) were enrolled. To estimate the circulating PF4 level, levels of platelet poor plasma (PPP) PF4 as well as serum PF4 were measured using an ELISA kit (R&D, Minneapolis, USA). SSc patients were divided into 2 subgroups according to disease activity and based on the presence/absence of interstitial lung disease (ILD), pulmonary hypertension, digital ulcers, and autoantibodies (anti-centromere Ab and anti-Scl70 Ab). Differences between SSc and HC groups were compared by Student's *t*-test, and the subgroups were compared using the Mann-Whitney test. Predictive values of serum PF4 and PPP PF4 for SSc diagnosis were evaluated by the area under the receiver operating characteristic curve (AUROC).

**Results:** Serum PF4 levels of SSc were lower than those of HC (SSc, 5143.3±1777.5 ng/mL; HC, 5927.4±1348.5 ng/mL; $p$ =0.048) but no significant differences were observed PPP PF4 levels (SSc, 407.2±486.6 ng/mL; HC, 297.3±141.5 ng/mL; $p$ =0.187) between SSc patients and controls. Moreover, no significant differences were observed between active and inactive SSc subgroups and between subgroups with/without ILD, pulmonary hypertension, digital ulcers, and autoantibodies. The AUROC for serum PF4 and PPP PF4 levels was 0.628 (0.497–0.76, cuff of value 3998.5 ng/mL) and 0.491 (0.367–0.65, cuff of value 511.1 ng/mL), respectively.

**Conclusions:** In Korean patients with SSc, both serum PF4 and PPP PF4 levels are not efficient biomarkers for SSc diagnosis and do not appear to be associated with clinical activity and severity.

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**Disclosure of Interest:** None declared

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## AB0611 ULTRASOUND EVALUATION OF HAND ARTICULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS COMPARED TO PHYSICAL EXAMINATION

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**Background:** Musculoskeletal involvement, preferentially affecting hands and feet, represents a frequent feature and may lead to disability in patients with systemic sclerosis (SSc). The most common manifestations are arthralgia, stiffness, synovitis, and tenosynovitis. In a large multicentre study, synovitis, tendon friction rubs, and joint contractures were found in 16%, 11%, and 31% of 7286 SSc patients assessed by clinical examination [1]. However, several ultrasound (US) studies revealed a higher frequency of hand joint involvement [2].

**Objectives:** To investigate the frequency and severity of hand joint involvement in a cohort of SSc patients evaluated by US, and to compare the results of US synovitis detection with those of physical examination.

**Methods:** Over a 6-month period, all consecutive (new and old diagnosis) SSc patients (ACR/EULAR 2013 criteria) currently followed in our center underwent clinical and US hand examination. One rheumatologist expert in musculoskeletal US performed all examinations by using Esaote Technos MPX, MyLab 40, employing high frequency (12–18 MHz) transducers. Power Doppler (PD) parameters were adjusted (range of pulse repetition frequency 400–800 Hz; frequency 7–11.1 MHz). Patients were scheduled to be examined at the same hour of the day in the same room with an ambient temperature of 21°C. Hand and wrist joints were evaluated for synovitis, tenosynovitis, calcinosis, acro-osteolysis and distal vascularization. An independent rheumatologist made the clinical examination and US examiner was blind to clinical findings. US assessment of synovitis was scored according to the OMERACT–EULAR PD composite semiquantitative scale (0–3).

**Results:** 89 patients, 79F/10M, mean age 61.11±15.1, median disease duration 160 months (min: 2,max: 492), 83 (93%) with limited SSc and 6 (7%) with diffuse SSc were recruited. Synovitis was detected in 15 (16.8%) and in 35 (40.2%) of the cases by clinical examination and US, respectively ($p=0.019$). PD revealed grade 1 synovitis in 19/35 (54.3%) patients, grade 2 in 14 (40%) and grade 3 in 2 (5.7%). Tenosynovitis, calcinosis and acro-osteolysis were found at US 19 (21.3%), 14 (15.7%), acro-osteolysis in 11 (12.3%) and 8 (9%), respectively. Distal vascularization was detected in 60 patients (67%).

**Conclusions:** Confirming previous studies, our results show that hand synovitis in SSc may be underestimated by clinical examination only, while US examination provides an accurate assessment of the frequency and the degree of severity of synovial inflammation. However, synovitis in our cohort of SSc patients resulted mild in the majority of the cases.

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## AB0612 MULTICENTER REGISTRY ON INFLAMMATORY MYOPATHIES IN MADRID (REMICAM): DESCRIPTIVE ANALYSIS

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**Background:** Clinical manifestations, evolution and prognosis of idiopathic inflammatory myopathies (IIM) are very heterogeneous which, together with its low prevalence, limits the study of the disease.

**Objectives:** To analyze the clinical characteristics of patients diagnosed of IIM in a multicenter study.

**Methods:** A multicenter retrospective descriptive study from REMICAM[1] myositis study group was performed. All patients were diagnosed with IIM according to Bohan and Peter[2] criteria, were followed up sometime between January 1980 and December 2014 and were classified into 7 different clinical subgroups: primary dermatomyositis (DM), primary polymyositis (PM), juvenile dermatomyositis (JuvM), cancer associated myositis (CAM), overlap myositis (OM), inclusion body myositis (IBM) and necrotizing myositis (NM).

**Results:** 478 IIM cases were included. 74% of the cases was women, with an age at diagnosis of 43.7±22.6 years, and an average follow-up time of 9.7±8.3 years. The main IIM subgroups were primary myopathies (PM 28%, DM 22%, OM 19.9%, JuvM 19.2%, CAM 8.4%, NM 1.3%, BMI 1.3%). The connective tissue diseases more frequently associated in OM subgroup were MCTD (30%), systemic sclerosis (27%) and SLE (18,9%). The main extramuscular manifestations were cutaneous lesions (65%), arthritis (43%), general symptoms (39%) gastrointestinal complications (33%), and interstitial lung disease (ILD) (30%). Patients with OM had a higher prevalence of ILD (46.8% vs. 25.8%;$p<0.001$), Raynaud (67% vs. 19.4%;$p<0.001$), arthritis (70% vs. 35.8%;$p<0.001$) and cytopenias (55.9% vs. 21.5%; $p<0.001$), whereas JuvM patients developed more calcinosis (30.4% vs. 5.7%;$p<0.001$) but fewer serious infections (4.7% vs. 29.3%;$p<0.001$). During the period of study 114 patients died (24%), and the main causes of death were infections (24%), cancer (24%) and cardiovascular events (22%).

**Conclusions:** In this multicenter REMICAM registry 478 IIM cases have been included. The most common subtypes were primary myopathies, and the most frequent extramuscular manifestation were typical cutaneous lesions. Overlap myositis patients presented with more extramuscular manifestations than the other subgroups.

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**Disclosure of Interest:** None declared

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## AB0613 ANTI-C1Q AUTOANTIBODIES ARE FREQUENTLY DETECTED IN PATIENTS WITH SYSTEMIC SCLEROSIS AND LUNG FIBROSIS

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**Background:** Anti-C1q autoantibodies are associated with systemic lupus erythematosus (SLE) but their presence in other rheumatic diseases has not been investigated in great detail.
**Objectives:** We aim to assess the clinical significance of anti-C1q autoantibodies in systemic sclerosis (SSc).
**Methods:** Seventy five patients with SSc (median age 59 years; females, 61; diffuse cutaneous SSc 35, limited cutaneous SSc, 40) were studied. Thirty eight patients with SLE, 25 patients with Sjögren's syndrome (SjS), 19 with rheumatoid arthritis (RA), and 31 healthy individuals (NC) were also included. IgG anti-C1q antibodies were tested by ELISA. Anti-nuclear antibodies (ANA), and SSc-specific autoantibodies were also tested.
**Results:** A receiver operator characteristic curve (ROC) confirmed that the cut off at 20 RU/mL for the anti-C1q test (specificity, 0.94, 95% CI, 0.79 to 0.99, LR: 5.0) was appropriate. Anti-C1q antibodies were present in 32.0% of SSc patients compared to 16.0% SS, 10.5% RA patients ($p<0.05$, for all) and in 6.5% NC ($p<0.01$). The frequent presence of anti-C1q antibodies in SLE was confirmed (13/38, 34.2%). Amongst the 24 anti-C1q (+) SSc patients, 15 had high/moderate levels (>40 RU/mL). There was no association between anti-C1q antibodies and anti-topoisomerase I, anti-centromere, or anti-RNA polymerase III antibodies. Anti-C1q antibodies were associated with male sex (p=0.04) and lung fibrosis (LF) (p=0.008), and co-occurrence of LF and skin ulcers (p=0.006). Ulcers were more prevalent in anti-C1q(+) than anti-C1q(–) patients (64% vs 44%), but the difference did not reach statistical significance (p=0.1).
**Conclusions:** Anti-C1q antibodies were frequently detected in SSc, were associated with PF and co-occurrence of PF and skin ulcers and may contribute to the autoimmune process in SSc.
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## AB0614 A COMPHEHENSIVE ANALYSIS OF 12 DISEASE-SPECIFIC AUTOANTIBODIES IN GREEK PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Patients with systemic sclerosis (SSc) are characterized by ANAs against various autoantigens, none of which is 100% sensitive for the disease. The need for profiling testing based on a combination of the most important SSc-related autoantigens has led to the development of commercial SSc-profile assays.
**Objectives:** To determine the diagnostic and clinical relevance of systemic sclerosis (SSc)-related autoantibodies tested by a line SSc-profile assay in a well defined cohort of Caucasian SSc patients, all from Central Greece.
**Methods:** 98 consecutive patients with SSc (80 female, 18 male, mean age 57,9±14,9 y) including 60 patients with diffuse cutaneous SSc (dcSSc) and 38 with limited cutaneous SSc (lcSSc) were analyzed by a profile SSc line assay (Euroimmun) for autoantibodies against 12 autoantigens: Scl-70, Centromere (A, B), RNA polymerase III (subunits 11 & 155), fibrillarin, NOR90, Th/To, PM/Scl 100, PM/Scl75, Ku and PDGFR.
**Results:** ANA by indirect immunofluorescence was present in 98 (98%) patients with SSc. Overall, 81 (82.6%) patients had abs against at least one of the 12 autoantigens. Anti-Scl-70 abs were present in 49 (49.4%) SSc patients, anti-centromere A in 22 (22.5%), anti-centromere B in 22 (22.5%, all anti-centromere A positive) anti-RNA polymerase III RP155) in 18 (18.3%) anti-RNA polymerase III RP11 in 14 (14.3%), anti-fibrillarin in 3 (3.1%), anti-Ku in 5 (5.1%), anti-NOR90 in 7 (7.1%), anti-PM/Scl100 in 4 (4.1%), anti-PM/Scl75 in 7 (7.1%), anti-Th/To in 4 (4.1%) and anti-PGDFR in 1 (1%) SSc patients. Overall, the most frequent anti-Scl-70, anti-centromere or anti-RNA polymerase III abs were present in 81 (81%) SSc patients while 6 (6.1%) lacked those antibodies and were positive for at least one of the other 9. Anti-Scl-70 were associated with diffuse SSc and ACA with limited SSc ($p<0.001$ for both). Positivity of Scl-70 was also correlated with the presence of lung fibrosis (p=0.004) and tended to be associated with the presence of digital ulcers (p=0.073). Anti-centromere abs were less prevalent in SSc patients with lung fibrosis (p=0.004). Anti-PM/Scl75 abs tended to be associated with the presence of digital ulcers (p=0.055). Anti-NOR90 abs were more frequent in male SSc patients (p=0.019).
**Conclusions:** Anti-Scl70, anti-centromere and anti-RNA polymerase are by far the most dominant autoantibodies in SSc but other disease-related autoantibodies can also be present in SSc patients lacking those three autoantibodies. The presence of anti-Scl-70 abs identifies patients with lung fibrosis and along with anti-PM/Scl75 tend to be associated with the presence of digital ulcers.
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## AB0615 IS INCREASED SERUM INTERLEUKIN-35 LEVELS A DISEASE ACTIVITY MARKER IN DERMATOMYOSITIS AND POLYMYOSITIS?

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**Background:** Idiopathic inflammatory myopathies (IIMs) are a group of heterogeneous, systemic disorders [1].DM and PM are two main clinical subtypes of IIMs in Chinese population. The pathogenesis underlying myositis is complicated and yet not well clarified. In IIM, cytokines are secreted by immune cells, endothelial cells and muscle cells, and can exert pro-inflammatory or anti-inflammatory effects [2–3].Interleukin-35 (IL-35) is a heterodimeric cytokine composed of two subunits, p35 and EBI3 [4].To date, IL-35 has been studied in several kinds of autoimmune disease but its role remains controversial under the pathology conditions. Therefore, we measure IL-35 expression in circulation of IIM patients and to evaluate its association with myositis-related features.
**Objectives:** The purpose of this study was to assess the level of serum IL-35 in indiopathic inflammatory myopathies (IIMs) patients and to evaluate its association with IIM-related features.
**Methods:** Clinical data and serum samples were collected from76 DM, 28 PM and 43 healthy controls. Follow-up of 34 patients was also conducted. Serum IL-35 levels were detected by enzyme linked immunosorbent assay (ELISA). Disease activity of myositis patients was assessed according to the myositis disease activity assessment visual analogue scale (MYOACT).
**Results:** IL-35 serum levels were increased in myositis patients compared to healthy controls ($P<0.001$). No differences in IL-35 serum levels were found between DM and PM (P=0.468). Serum level of IL-35 with IIM was negatively correlated with disease duration (r =-0.231, P=0.019). Patients with dysphagia had higher IL-35 levels than those without (P=0.001). But, there was no statistically significant difference between IIM patients with interstitial lung disease (ILD) and without (P=0.997). Cross-sectional correlation analysis showed a positive correlation of serum IL-35 with CK (r=0.285, P=0.004), ESR (r=0.235, P=0.02), serum ferritin (SF) (r=0.471, P=0.001), LDH (r=0.401, $P<0.001$) and MYOACT scores (r=0.227, P=0.021). Serum IL-35 levels were significantly higher in ANA (P=0.026), anti-HMGCR (P=0.038) and anti-SRP (P=0.009) antibody positive patients than that in negative respectively. Follow-up study showed the change of IL-35 levels after treatment correlated with the change of MYOACT scores (r=0.375, P=0.029).
**Conclusions:** Serum IL-35 was elevated in both PM and DM patients and increased serum IL-35 was associated with dysphagia of myositis patients but not ILD. The serum levels of IL-35 also correlated with disease activity. These data suggest the increased serum IL-35 is a marker of disease activity and the risk for esophagus involvement in IIM. Finally, IL-35 may participate in the pathophysiological process of IIM.
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## AB0616 ADAPTATION INTO SPANISH OF THE HAND MOBILITY IN SYSTEMIC SCLEROSIS TEST (HAMIS) IN A GROUP OF PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Hand function in scleroderma patients can be assessed by specific instruments such as the Cochin scale and the Scleroderma Health assessment questionnaire (SHAQ), both self administrated. Sanqvist and Eklun designed the Hand Mobility in Systemic Sclerosis test (HAMIS), which is performed by the evaluation of a health professional. The original instrument was designed in English.
**Objectives:** The aim of this study was to adapt into Spanish the HAMIS test in

order to assess hand function in patients with systemic sclerosis and to evaluate its reliability and validity.
**Methods:** The study included 28 patients that met ACR/EULAR 2013 classification criteria for systemic sclerosis, who attended the Rheumatology Service from March 2014 to March 2015; 21 were diffuse and 7 limited. Patients with overlapping and sclerodermiform syndromes were excluded. Demographic data, clinical manifestations, laboratory studies including ANA by IIF (Hep2) were recorded. Different scores were performed: modified Rodnan, Medsger and Cochin. HAMIS was translated into Spanish and back translated into English. Four translators did not know the original English version of the test. A pilot test was conducted in 5 systemic sclerosis patients and adaptations were performed in order to obtain the final Spanish version. HAMIS test was assessed by an occupational therapist. Two weeks later, the study was repeated in 10 patients chosen randomly to assess stability (test-retest) and concordance according to Bland&Altman. Values of HAMIS and Cochin test were correlated (Spearman's Rank correlation coefficient).
**Results:** All 28 patients (27 female) had mean age at diagnosis of 49.6±13 years and median disease duration of 5 years (range=0–25). All patients developed Raynaud's phenomenon (mean age at onset of Raynaud of 45±17 years), 3 patients had puffy hands, 11 presented digital ulcers, 9 pitting scars and 23 telangiectasia. Through capillaroscopic evaluation, early pattern was found in 11 patients, active in 7 and late in 8 patients. When analyzing severity by Medsger score, such was normal in 1 patient, 11 presented mild involvement, 13 moderate and 3 severe. Median for Rodnan score was of 6 (range=2–27) and 8 for Cochin (range=0–38). Median for HAMIS was of 6 (range=0–21) with Cronbach's alpha of 0.81; in test-retest: mean of the difference was of 0.091 (range= -5 to +5). Correlation between HAMIS and Cochin was significant (r=0.65; p=0.0002)
**Conclusions:** An adapted Spanish version of HAMIS was developed, showing an acceptable reliability (Cronbach and stability) and criterion validity (correlation with Cochin test).
**Disclosure of Interest:** None declared
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## AB0617 CYCLOPHOSPHAMIDE VS MYCOPHENOLATE MOFETIL IN SCLERODERMA INTERSTITIAL LUNG DISEASE (SSC-ILD) AS INDUCTION THERAPY: A SINGLE CENTER, RETROSPECTIVE ANALYSIS

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**Background:** Scleroderma is an autoimmune disease characterized mainly by skin manifestations and various visceral organs involvement especially lungs. Lung involvement is the leading cause of mortality in this patients.Various studies have demonstrated efficacy of cyclophosphamide (CYC) and mycophenolate mofetil (MMF) in SSc-ILD but no head to head comparative data is available till date.
**Objectives:** To compare efficacy of CYC & MMF in patients with SSc-ILD in terms of improvement in lung function.
**Methods:** Patients more than 18 years of age fulfilling ACR 2012 classification criteria for Systemic sclerosis with significant ILD as defined by Forced vital capacity (FVC) $\leq$80 and Presence of ILD on thoracic high resolution computerized tomography were included.MMF group received upto 3gm daily and CYC group received 600mg/m$^2$ (Max 1.2 gm) for total duration of 6 months.Monthly clinical assessment and 3 monthly lung function (spirometry-FVC) were done for 6 months.Response was evaluated as per American Thoracic Society recommendations (improvement when increase in FVC $\geq$10%, stabilization when change in FVC $<$10% and worse reduction in FVC was $\geq$10%).Appropriate statistical tests were applied to analyse the data.
**Results:** 23 patients (18 female/5 male) in CYC and 44 patients (40 female/4 male) in MMF group were included with mean age of 46±10.34 years (mean disease duration of 6.04±5.96 years) and 45.54± 13.74 years (mean disease duration of 4.84±4.08 years) in respective groups.After 6 months of induction therapy,increase in mean percentage of FVC observed was 10.84±13.81% (p=0.003) in CYC and 6.07±11.92% (p=0.006) in MMF group.When the change in FVC at 6 months in both groups were compared to each other,no significance difference was found (p=0.373).
**Conclusions:** We support the use of mycophenolate for the patients for whom CYC is contraindicated or not tolerated, given the substantial toxicities and modest benefit of CYC as alternative.A prospective multicenter controlled trial of mycophenolate in SSc-ILD patients is warranted to support the above data.
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## AB0618 NAILFOLD CAPILLAROSCOPY CHANGES DURING PREGNANCY IN CONNECTIVE TISSUE DISEASES

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**Background:** Nailfold videocapillaroscopy (NVC) changes early appear in connective tissue diseases (CTDs): besides the "scleroderma pattern" of systemic sclerosis (SSc), abnormalities have been reported in mixed connective tissue disease (MCTD) and undifferentiated connective tissue disease (UCTD) [1]. Pregnancy can modify the course of of CTDs [2]. NVC changes during pregnancy have been described in healthy women [3], but no data are available regarding CTD subjects during pregnancy.
**Objectives:** Our study aimed to investigate if there is an impact of pregnancy on NVC changes, and of which kind, among CTDs patients.
**Methods:** After Local Ethic Committee approval and informed consent signature, we prospectively enrolled 29 consecutive pregnant women, with an established diagnosis of CTD (either SSc, MCTD or UCTD) and RP from at least 12 months. Pregnant women underwent a NVC examination at conception (defined as T0) and, after that, to a second one (T1), between the beginning and the end of the third trimester of gestation. The pregnant subjects are referred as "cases". In parallel, 29 non-pregnant women with the same diagnosis, comparable underlying disease duration and similar age of cases were matched in retrospect ("controls"). NVC was performed in all 29 couples of patients by the same operator, at baseline (T0) and follow-up (T1) (Videocap, DS MediGroup, Milan, Italy). The following capillaroscopic parameters were considered: number of capillaries per area; presence of ectasic capillary and megacapillaries; haemorrhages (hemosiderin deposits); loss of capillaries, disorganization of the microvascular array and capillary ramifications (combined, their constitute the "microangiopathy evolution score"-MES); tortuosity; edema. A semiquantitative rating scale was adopted to score each capillary abnormality (0=no changes; 1=less than 33% of capillary alterations/reduction; 2=33–66% of capillary alterations/reduction; 3=more than 66% of capillary alterations/ reduction) [4]. Statistical analysis was conducted by non-parametric tests.
**Results:** Among 29 cases (and 29 matched controls), we collected 14 UCTD, 10 MCTD and 5 SSc. Regarding capillaroscopic abnormalities, the two groups were homogeneous at T0, whereas statistically significant differences (excepted for ectasias and tortuosity scores) were observed at T1. Capillary number increased only among cases (pregnant women; $p<0.001$). Hemosiderin deposition and architectural subversion scores were reduced in cases and increased in controls (both, $p<0.05$). Megacapillary, MES, ramifications and edema scores progressed only in controls (all, $p<0.05$), while capillary number reduction score (consistently with absolute capillary number per mm$^2$) was abated in pregnant cases.
**Conclusions:** Our work investigated for the first time pregnancy influence on NVC aspects in CTDs; considering the number of statistical differences in capillaroscopic abnormalities between the two groups at the follow-up, it suggests that pregnancy could play a protective role against microvascular damage progression in CTDs subjects.
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## AB0619 AUTOLOGOUS NON-MYELOABLATIVE HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SYSTEMIC SCLEROSIS: THE BENEFIT OF QUANTITATIVE CHEST-CT ANALYSIS FOR RESPONSE OF LUNG INVOLVEMENT AND COMPARISON WITH RESULTS OF PULMONARY FUNCTION TESTS AND CLINICAL TESTS

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**Background:** Lung disease represents the leading cause of mortality and

morbidity in patients with systemic sclerosis (SSc). In patients with rapid progressive disease immunoreset by high-dose chemotherapy accompanied by autologous stem cell transplant (auto-SCT) represents a possible rescue. For accurate evaluation and monitoring of lung parenchymal changes in patients undergoing treatment for SSc, different modalities (clinical examination, respiratory functional tests) are used, but these are all prone to some inaccuracies. Quantitative-CT represents a novel, fully automated technique able to exactly quantify lung volume and changes in CT-attenuation of lung parenchyma induced by SSc. Parameters like high attenuation value (HAV) and mean lung density (MLD) as well as percentile ranges 200–300/and300–400 Hounsfield units (HU) reflect at best lung involvement with this disease.

**Objectives:** The aim of this study was to evaluate the course of SSc-related pulmonary changes following high-dose therapy & auto-SCT using quantitative chest-CT analysis and compare its results with those of established clinical and pulmonary function tests.

**Methods:** Non-enhanced chest-CT examinations were performed before, directly after (0.49±0.20y) and at mean 2.2±2.1y after auto-SCT in 26 patients with SSc that were enrolled between March 2001 and March 2015. Chest-CT quantitative analysis was performed using fully automated software calculating inspiratory total lung volumes (TLV), mean lung densit (MLD), high attenuation values (HAV) and their distribution in the lung core vs. peel. All patients underwent pulmonary functional tests. The course of cutaneous SSc was evaluated by modified Rodnan skin score (mRSS). Classification of response to auto-SCT was performed at mean 6mo after auto-SCT based on the course of forced vital capacity (FVC) into responders 10% increase or stabilisation of FVC and non-responders >10% decrease in FVC.

**Results:** The FVC course at 6mo classified the patients into responders 20 (76.9%) and 6 (23.1%) non-responders. Correspondingly, FVC, forced expiratory volume in 1s (FEV1s), vital capacity (VC) as well as single-breath diffusion capacity for carbon monoxide ($DLCO_{cSB}$) significantly improved (p=0.03/0.001/0.001/0.013). Mean modified Rodnan skin score (mRSS) improved from 27.35±9.25 before to 10.81±8.64 after auto-SCT (p=0.003) in responders. In non-responders no statistically significant improvement were registered. At CTD, total lung volume increased (p=0.018) whereas MLD (p=0.026) and HAV decreased (p=0.020) after auto-SCT only in responders. Improvement of CTH-parameters was stronger in the lung peel reflecting the typical localisation of SSc-fibroalveolitis. Changes of mRSS 6 months after auto-SCT correlate significantly with those 24 months after transplantation (r=0.575; p=0.031). Percental changes in MLD correlated well with FEV1 (r=0.733; p=0.016) in responders.

**Conclusions:** Quantitative-CT analysis of lung parenchymal attenuation and volume in SSc-patients presenting lung involvement is accurate, can be easily and quickly accomplished being less dependent on patient's compliance and results match those of pulmonary function and clinical tests.

**Disclosure of Interest:** None declared

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## AB0620 EVALUATION OF USEFULLNESS OF KLEBS VON DEN LUNGEN-6 AS A BIOMARKER OF INTERSTITIAL LUNG DISEASE WITH POLYMYOSITIS AND DERMATOMYOSITIS INCLUDING THAT IN THE SHORT TIME COURSE AFTER TREATMENT

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**Background:** Because of the extremely variable incidence and outcome of interstitial lung disease (ILD) in polymyositis/dermatomyositis (PM/DM), exploration and validation of biomarkers for diagnosis, prognosis, and response to treatment is mandatory. Lung epithelium-derived proteins such as Krebs von den Lungen-6 (KL-6) and surfactant protein-D (SP-D) are used as serum biomarkers for ILD. However, their usefulness in patients with PM/DM is not fully established.

**Objectives:** We aimed to evaluate the usefulness of KL-6 as a biomarker of ILD with PM/DM, including that in the short time course after treatment.

**Methods:** A total of 42 patients with active PM/DM who were admitted to our hospital from April 2010 through March 2015 were included: 22 with PM, 14 with classical DM, and 6 with clinically amyopathic dermatomyositis (CADM). PM/DM and CADM were diagnosed according to Bohan and Peter's criteria and Sontheimer's criteria, respectively. Overlap patients with other collagen tissue diseases were excluded to avoid potential confounding. ILD was defined as presence of a diffuse parenchymal lung disease on high-resolution CT such as reticular opacity, ground-glass opacity, and honeycombing. Clinical, radiological, and laboratory data were retrospectively collected from the medical records and statistically analyzed.

**Results:** Of the 42 study subjects, 30 patients had ILD on high-resolution CT: 24 with PM/classical DM, and 6 with CADM. There was no significant difference in age, sex, or disease duration between patients with and without ILD. On admission (pre treatment), % vital capacity (%VC) and % diffusing capacity of the lungs for carbon monoxide (%DLCO) were not significantly different between patients with and without ILD ($p$ =0.11 and 0.06, respectively). However, serum KL-6 and SP-D levels were already significantly higher in patients with ILD than in those without ($p$ <0.01 in both comparisons). In addition, levels of serum KL-6 and SP-D showed moderate inverse correlations with %VC and %DLCO ($r$ = -0.45 to -0.51). All the patients with ILD were treated with glucocorticoid. In addition, calcineurin inhibitors, namely cyclosporine and tacrolimus, and intravenous cyclophosphamide were administered simultaneously in 22 and 8 patients, respectively. Although 12 patients showed some clinical and/or radiological improvement in 4 weeks, levels of serum KL-6 were not significantly different between those at pre treatment and at 2 or 4 weeks post treatment ($p$ =0.78 and 0.81, respectively). Concordance rate between clinical or radiological amelioration and decrease in serum KL-6 levels after treatment was low (Cohen's $\kappa$ = -0.39).

**Conclusions:** The present study validated that serum KL-6 is a useful biomarker for the diagnosis of ILD associated with PM/DM. However, the levels of serum KL-6 did not respond immediately by treatment even in the cases with clinical improvement. Serum KL-6 should be used as a biomarker for ILD with PM/DM while understanding these strengths and limitations.

**Disclosure of Interest:** None declared

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## AB0621 FROM VEDOSS TO ESTABLISHED SYSTEMIC SCLEROSIS DIAGNOSIS ACCORDING TO THE NEW ACR/EULAR 2013 CLASSIFICATION CRITERIA: A FRENCH-ITALIAN CAPILLAROSCOPIC SURVEY

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**Background:** NailfoldCapillaroscopy (NC) is a diagnostic and sensitive tool in order to investigate Raynaud's phenomenon (RF) that is the hallmark of both Systemic Sclerosis (SSc) and Very Early Diagnosis Of ScS (VEDOSS) patients. Thus NC is largely used in patients with these conditions and NC specific abnormalities have become a minor criteria in ACR/EULAR SSc Criteria in 2013.

**Objectives:** Aim of our study was to monitor NC changes in a group of 66 VEDOSS patients, enrolled in two EUSTAR center.

**Methods:** We selected those patients who developed SSc at the follow-up. Moreover, we compared the NC features of these patients with NC of those VEDOSS patients who did not move to SSc, in order to find out NC features, if any, suitable as predictive risk factor for SSc at the time of VEDOSS diagnosis.

**Results:** In our 66 VEDOSS patients, 21 of them (19 females, mean age 55 yrs) shifted to SSc in a mean follow-up time of 31 months (range 6–60 months). Table 1 shows the main features of matched VEDOSS patients: Group A with unchanging diagnosis and Group B progressing into SSc. Table 2 shows the progression of NC abnormalities from VEDOSS to established SSc diagnosis in Group B patients.

Table 1

| Features | Group A (n=21) | Group B (n=21) |
|---|---|---|
| Age, yrs (range) | 50 (28–70) | 55 (27–77) |
| Sex (M/F) | 1/20 | 2/19 |
| Disease duration, month (range) | 51 (14–70) | 50 (21–70) |
| Follow up, months (range) | – | 31 (6–60) |
| Anti-centromere Ab (n) | 11 | 14 |
| Anti-Scl70 Ab (n) | 3 | 5 |
| ANA positivity (n) | 7 | 2 |
| NC Pattern | Normal = 11 (52.3%)<br>Early = 7 (33.3%)<br>Active = 2 (9.6%)<br>Late = 1 (4.8%) | Normal = 8 (38.1%)<br>Early = 8 (38.1%)<br>Active = 4 (19%)<br>Late = 1 (4.8%) |

Table 2

| NC Parameter | NC at baseline (VEDOSS diagnosis) | NC at follow-up (SSc diagnosis) |
|---|---|---|
| Loop diameter | 86 μm | 98 μm |
| Apex width | 176 μm | 187 μm |
| Capillary distribution | Slighty irregular = 11 (52.4%)<br>Disorganized = 4 (19%) | Slightly irregular = 14 (66.6%)<br>Disorganized = 6 (28.6%) |
| Capillary density (n/mm$^2$) | Normal = 12 ( 57.1%)<br>Reduced = 9 (42.8%) | Normal = 9 ( 42.8%)<br>Reduced = 12 (57.1%) |
| Capillary enlargement (enlarged = 20–50 μm; giant >50 μm | Enlarged loops = 10 (47.6%)<br>Giant loops = 10 (47.6%) | Enlarged loops = 6 (28.6%)<br>Giant loops = 11 (52.4%) |
| Avascular areas (n pts/%) | 2/9.5% | 6/28.6% |
| NC Pattern (n) | Early = 8 (38%)<br>Active = 4 (19%)<br>Late = 1 (4.7%) | Early = 5 (23.8%)<br>Active = 7 (33.3%)<br>Late = 2 (9.5%) |
| Score >1 (n pts) | 13 | 15 |

When we compared basal NC of Group A and Group B patients, in former VEDOSS developing SScwe found a significantly higher NC score (>1), 13 versus 5 cases (p<0.03) and a larger mean apex width, 177 μm (range 50–640) versus 104 μm (range 10–280) (p<0.005).

**Conclusions:** Our study describes a progression of NC changes during the evolution of early SSc. Moreover we identified some NC features, such as higher NC score and larger apex width, whose presence at the very early diagnosis of SSc may suggests its development in an established disease, thus underlying the relevance of specific NC abnormalities as possible predictive risk factors.

**Disclosure of Interest:** None declared

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## AB0622 ASSESSMENT OF OUALITY OF LIFE IN SYSTEMIC SCLEROSIS PATIENT WITH TRANSLATION, CROSS-CULTURAL ADAPTATION, AND VALIDATION OF THE SYSTEMIC SCLEROSIS QUESTIONNAIRE (SYSQ) INTO THE TURKISH LANGUAGE

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**Background:** Systemic Sclerosis (SSc) is a multisystem connective tissue disorder which decreases the life-expectancy and quality of life (QoL) of the patients.
**Objectives:** To determine the effects of SSc on physical and mental health of the patients as well as their QoL and translation, cross-cultural adaptation, and validation of the Systemic Sclerosis Questionnaire (SySQ) to the Turkish language.
**Methods:** We evaluated 88 SSc patients (F/M=77/11, mean age 49.8±12.4 and mean disease duration 7.2±6.0 years, limited/diffuse=60/28) and 81 healthy subjects (HS)(F/M=70/11, mean age 46.8±11.2 years) without a history of malignancy and infection. QoL, functional capacity, fatique, anxiety and depression were assessed by SF-36, SySQ, HAQ, UK SSc functional score (UKFS), FACIT-F and HADS, respectively. The SySQ was translated according to international guidelines and administered to all patients and controls. Internal consistency was tested by computing Cronbach's alpha. Test-retest reliability was determined by computing the intraclass correlation coefficient (ICC). Correlation of SySQ with SF-36, HADS, FACIT-F was assessed by using Pearson test.
**Results:** The internal consistency of SySQ was similar to the original study (1) and ranged from 0.812–0.937 for items. The interobserver reliability was also very good for each item (ICC: 0.88–0.97). QoL assessed by SySQ, anxiety and depression and fatique scores were significantly worse in SSc patients than healthy subjects (Table 1). All items of SySQ positively correlated with UKFS, HAQ, HADS scores, patient and physician global assessments of disease activity and negatively correlated with all parameters of SF-36 and FACIT-FT.

**Table 1:** Comparison of SF-36, SysQ, HAQ, HADS and FACIT-FT scores between SSc patients and healthy subjects*

| | SSc patients (n=88) | Healthy subjects (n=81) | *P* value |
|---|---|---|---|
| **SF-36 components** | | | |
| Physical functioning | 38.9±12.6 | 50.6±7.6 | <0.001 |
| Physical role functioning | 39.3±12.2 | 49.0±10.3 | <0.001 |
| Bodily pain | 43.3±13.2 | 52.0±12.0 | <0.001 |
| General health perceptions | 35.7±12.0 | 45.8±9.6 | <0.001 |
| Vitality | 45.2±12.1 | 52.5±10.4 | <0.001 |
| Social role functioning | 41.0±14.9 | 49.4±11.0 | <0.001 |
| Emotional role functioning | 38.6±13.6 | 41.5±13.6 | 0.17 |
| Mental health | 39.8±11.4 | 47.1±9.4 | <<0.001 |
| Physical component summary | 37.6±11.9 | 49.6±10.5 | <0.001 |
| Mental component summary | 42.3±11.6 | 45.3±12.0 | 0.09 |
| **Systemic Sclerosis Questionnaire (SysQ)** | | | |
| SysQ-General symptoms (0-24) | 10.3±5.7 | 2.3±3.8 | <0.001 |
| SysQ-Gastrointestinal system (0-21) | 6.3±5.3 | 1.5±1.9 | <0.001 |
| SysQ-Musculoskeletal system (0-33) | 8.7±7.9 | 1.0±1.9 | <0.001 |
| SysQ-Cardiopulmonary system (0-18) | 5.4±4.3 | 1.9±2.5 | <0.001 |
| **Hospital anxiety and depression scale (HADS)** | | | |
| HADS-Depression | 8.3±5.3 | 5.1±4.1 | <0.001 |
| HADS-Anxiety | 8.3±4.7 | 5.5±3.6 | <0.001 |
| **HAQ** | 1.13±0.94 | 0.13±0.26 | <0.001 |
| **Fatigue (FACIT-FT) score** | 94.0±29.0 | 124.2±22.3 | <0.001 |

**The values are presented as mean±SD, unless indicated otherwise*

**Conclusions:** Disease-specific QoL, mental and physical health of the SSc patients were significantly worse than healthy individuals in our study. Turkish version of SySQ is reproducible and valid for Turkish SSc patients.
Fatma Temiz, Merve Saganak, Nazife Enginar and Gulsen Ozen contributed equally to this research.
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**Disclosure of Interest:** None declared
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## AB0623 TREATMENT OF SCLERODERMA-RELATED DIGITAL ULCERS WITH ILOPROST: A COHORT STUDY

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**Background:** SSc is characterized by diffuse microangiopathy leading digital ulcers (DU) in almost 50% of patients. The treatment of non-healing DU is often very difficult. It includes both systemic (prostanoids, bosentan) and local (wound care) therapies. In clinical practice, therapy of DU should be tailored mainly on clinical symptoms and according to specific clinician's experience. At the moment, no guidelines for the use iloprost, a stable prostacyclin-analogue used for the management of DU in SSc, are not yet available.
**Objectives:** We report the therapeutical effects of our regimen for the use of iloprost in a cohort of SSc patients during a long-lasting follow-up period.
**Methods:** Fifty consecutive SSc patients recruited at two Rheumatology Units since January 2003, who received iloprost infusions for a time period >2 years were included in the analysis. Patients' features were: males/females ratio 7/43; mean age at SSc diagnosis 43.5±12.7SD years; median disease duration at the beginning of therapy 2 years (range 0–18); mean follow-up with iloprost treatment 10±4.2SD years; diffuse SSc cutaneous subset in 13/50 (30%) patients; anti-Scl70 and anticentromere autoantibodies in 25 (50%), and 14 (28%) subjects, respectively. For all patients epidemiological, clinical, laboratory, and instrumental data were available for the study period. Iloprost schedule consisted in monthly i.v. infusion at 0.8–1 ng/kg body weight/min with average cumulative dosage per each session of 25 μg, according to patients' tolerance. At the beginning of the treatment and in the presence of recent onset, severe and/or multiple DU at high risk of gangrene, patients were hospitalized for continuous infusion of iloprost (3 days, average 0.2 mg).
**Results:** 31/50 (62%) patients showed DU at the beginning of iloprost therapy: among them, 22 (71%) resolved during the follow-up, while the other 9 presented recurrent or chronic DU, despite the treatment. With regards the 19/50 patients without DU at baseline, only one developed skin lesions at the end of very long follow-up (8 years), when a general deterioration of clinical conditions, in particular severe pulmonary hypertension, lead to exitus.
Considering the 31 SSc patients with DU at baseline, a diffuse skin subset was present in 3 out of 22 patients with healed DU, and in 5 out of 9 who did not (13.6% vs 55.5%, Fisher's p=0.027); no other significant correlations were observed as regards visceral organ involvement and serological alterations. Finally, the concomitant administration of other vasoactive therapies seems to be scarcely relevant on the DU outcome.
**Conclusions:** Our data suggest that long term administration of iloprost seems to be effective for DU healing in SSc. Comparative studies with different treatment regimens are warranted to reach a consensus on standardized guidelines for the use of Iloprost for DU healing in SSc.
**Disclosure of Interest:** None declared
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## AB0624 CLINICAL CONSEQUENCES OF GLUCOCORTICOIDS (GCS) DISCONTINUATION IN PATIENTS WITH PERSISTENTLY INACTIVE SYSTEMIC SCLEROSIS (SSC)

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**Background:** Glucocorticoids (GCs) are widely used in the management of patients with systemic sclerosis (SSc), but are frequently discontinuated because of patient and/or physician concern. Clinical consequences of GCs discontinuation have never been investigated in SSc patients.
**Objectives:** To identify factors hampering GCs discontinuation in SSc patients with inactive disease who had been chronically (i.e. more than 3 months) treated with oral GCs.
**Methods:** Consecutive SSc adult patients fulfilling the 2013 ACR/EULAR criteria for SSc (1) were evaluated for the following inclusion criteria: - stable lung function and skin thickening during the previous year; - non inflammatory joint involvement; - no puffy fingers; - no serositis; - no CK increase; - no cutaneous vasculitis; - inactive disease, i.e. European Scleroderma Study Group Activity Index score<3 during the previous 6 months (2); - no co-morbidities requiring GCs. A slow GCs tapering regimen (reduction of 10% of weekly dose each week) was prescribed to achieve GCs discontinuation within 6 months (T6) from enrollment. At study entry, and at last evaluation the following self-administered patient outcomes were recorded: Short-Form-36 (SF-36), Health Assessment Questionnaire – Disability Index (HAQ-DI), VAS fatigue, VAS pain, VAS general health. Moreover, at study entry, after 3 and 6 months a complete history and clinical assessment were performed.
**Results:** Forty-eight SSc patients (46 females, 9 dcSSc, 17 anti-Scl-70 positive), with a mean±SD age of 56±14 years and a median disease duration of 10 years (range 2–22) satisfied the inclusion criteria and were enrolled in the study. Median baseline daily GCs dose was 5 mg (range 5–10).
At T6, 33 (68.7%) patients were free from GCs. In the remaining 15 patients, GCs were not discontinued because of the occurrence of inflammatory arthralgias

in 8, arthritis in 2, puffy fingers in 2, increase of CK in 2, and subacromial bursitis in 1 patient. At univariate logistic regression analysis baseline VAS-GH (OR 1.03, 95% CI 1.00–1.06; p=0.03), VAS-pain (OR 0.97, 95% CI 0.95–0.99; p=0.02), HAQ-DI score (OR 0.34, 95% CI 0.13–0.81;p=0.010), heart severity score (OR 0.28, 95% CI 0.08–0.97; p=0.018) resulted to be associated with the achievement of a GCs-free regimen. At multiple logistic analysis, baseline HAQ-DI resulted to be the only indipendent factor hampering GC discontinuation (OR 0.33, 95% CI 0.13–0.83; p=0.01). At ROC curve analysis, a HAQ-DI score$\leq$0.5 identified patients in whom discontinuation was successfully obtained with 77.5% sensitivity and 55% specificity; a HAQ-DI score $\leq$0.125 with 9.7% sensitivity and 86.7% specificity (positive likelihood ratio=5.23; negative likelihood ratio 0.35; AUC=0.764).

**Conclusions:** About one-third of SSc patients with inactive disease were not able to achieve a GC-free regimen. Disability as assessed by HAQ-DI was the leading factor hindering GCs discontinuation. A low HAQ-DI score can drive the physician choice to completely discontinue GCs in SSc patients.

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**Disclosure of Interest:** None declared

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## AB0625 THE CLINICAL SIGNIFICANCE OF ANTIPHOSPHOLIPID ANTIBODIES IN SYSTEMIC SCLEROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** The association between antiphospholipid antibodies (aPL) and systemic sclerosis (SSc) and its clinical manifestations is controversial, but owing to some shared pathogenetic pathways one expects that SSc patients with aPL will have more severe vascular manifestations that SSc without aPL.

**Objectives:** To evaluate whether different aPL are associated with SSc and some of its clinical manifestations and if so, whether aPL titre impact on the severity of those clinical manifestations.

**Methods:** Systematic review of EMBASE and PubMed databases from inception to October 2015 followed by meta-analysis according to the PRISMA guidelines.

**Results:** The relationship between between aCL (anticardiolipin) of IgG/IgM isotype and SSc was addressed in 8 studies yielding 725 controls and 484 SSc participants. The pooled prevalence of IgG aCL was 1.6% in controls and 15.4% in SSc patients with an odds ratio (OR) of 10.895 (95% CI 5.853, 20.282, $I^2$ =19.5%, p=0.003) and that of IgM was 0.6% and 5.1% respectively with an OR of 7.843 (95% CI 2.981, 20.633, $I^2$ =21.5%, p=0.002). The relationship between between IgG a$\beta_2$GPI of IgG/IgM isotype and SSc was addressed in 8 studies yielding 725 controls and 484 SSc participants. The pooled prevalence of IgG a$\beta_2$GPI was 1.6% in controls and 15.4% in SSc patients (OR 11.121, 95% CI 2.587, 47.812, $I^2$ =35.6%, p=0.0003) while that of IgM was 0.6% and 5.1% respectively (OR 12.185, 95% CI 1.563, 94.948; $I^2$ =67.5%, p=0.02). The relationship between aPL and thrombosis was addressed in 6 studies yielding 428 aCL negative and 88 aCL positive SSc: the pooled prevalence of thrombosis was 3.7% in the aCL negative group and 25% in the aCL positive group with a relative risk (RR) of 7.344 (95% CI: 4.089–13.191; $I^2$ =29.5%, $p$ =0.0001). The relationship between aPL and pulmonary arterial hypertension (PAH) was addressed in 7 studies yielding 1171 aCL negative SSc patients and 166 aCL positive SSc: the pooled prevalence of PAH in aCL negative patients was 11% and in aCL positive patients was 24.6% for a RR of 6.8 (95% CI: 3.110–12.280; $I^2$ =4.18; $p$ =0.0001). The relationship between aPL and renal involvement was investigated in 5 studies yielding 264 aCL negative and 83 aCL positive SSc patients: the pooled prevalence of renal involvement in aCL negative patients was 17% and in aCL positive patients was 40% for a RR of 1.993 (95% CI: 1.359–2.923; $I^2$ =0%, $p$ =0.0001).

**Conclusions:** There is a strong association between aPL and SSc; within SSc per se, aPL, with varying heterogeneity, relate to some vascular manifestations of SSc, such as thrombosis, DI, PAH and renal involvement. The analysis was carried out on the percentage of positive aPL per group, as very few studies reported aPL titres, precluding further assumptions on the relationships found

**Disclosure of Interest:** None declared

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## AB0626 CLINICAL PREDICTORS FOR DEVELOPMENT OF INTERSTITIAL LUNG DISEASE IN MCTD

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**Background:** Mixed connective tissue disease (MCTD) is an immune-mediated systemic disorder characterized by serum autoantibodies against U1-ribonucleoprotein and diverse multi-systemic clinical manifestations. Approximately 50% of patients with MCTD develop a radiological pattern of interstitial lung disease (ILD). In this study, we explore the phenotypic and clinical features in patients with MCTD that are associated with development of ILD.

**Objectives:** To explore the association of demographics, clinical features and serologic markers with the development of ILD in patients with MCTD.

**Methods:** We performed a retrospective case control study utilizing data from patients evaluated at a single tertiary care center between 2007–2014. Twenty-eight patients who met validated criteria for diagnosis of MCTD were included in the study. Out of these, 14 patients had high-resolution computed tomography or biopsy-proven ILD, and the remaining 14 had MCTD without any evidence of ILD. We performed a multivariate logistic regression with multiple demographic, clinical and serological predictor variables, and ILD as the outcome variable.

**Results:** Two clinical variables were found to have an association with development of ILD in patients with MCTD: 1. Dyshpagia with a $R^2$ value of 0.33 (p value $<$0.001); 2. Raynaud's phenomenon with $R^2$ value of 0.28 (p$<$0.001). We did not find a significant association between any other demographic, clinical or serological variables and development of ILD in patients with MCTD.

**Conclusions:** Dysphagia is one of the symptoms of esophageal involvement in patients with autoimmune connective tissue disorders. An association of dysphagia with the development of ILD in our study is in harmony with the existing literature, wherein esophageal dysmotility has been described in a cluster of patients with MCTD and ILD.

Scant data, primarily case reports, suggest an association of Raynaud's phenomenon with development of ILD in patients with undifferentiated CTD. To our knowledge, this is the first study highlighting the association of Raynaud's phenomenon with development of ILD in a subset of patients with MCTD.

This study is limited by its small size and retrospective nature. Additionally, the mechanistic aspects of this association between Raynaud's phenomenon and ILD remain unexplored.

The association of easily elicited historical and clinical features of MCTD with subtle, but worrisome, pulmonary pathology carries the promise of sensitizing the unsuspecting clinician about the entity of ILD in MCTD.

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## AB0627 PREDICTORS OF ILD AND ITS PROGRESSION IN A COHORT OF SCLERODERMA PATIENTS FROM WESTERN INDIA: A PROSPECTIVE OBSERVATIONAL COHORT STUDY

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**Background:** Pulmonary involvement, including both interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH), has become the primary cause of Scleroderma-related death. Little data has been published from India regarding the progression of ILD and Pulmonary arterial hypertension in Scleroderma.

**Objectives:** 1) To identify baseline factors predictive of ILD and its outcome in patients with Scleroderma. 2) To study the progression of ILD and PAH in scleroderma patients 3) To study the demographic and clinical profile of scleroderma patients from Western India.

**Methods:** Prospective observational study involving 68 patients. Patients were evaluated at 0,3,6,9 and 12 months. Patient's demographic and clinical details were recorded at baseline. Other than routine tests, Anti-nuclear antibodies (ANA), Spirometry, diffusing capacity of lung for carbon monoxide (DLCO) measurement, high resolution computed tomography (HRCT) of thorax, 6-minute walk test and echocardiography were done.

**Results:** Study included 68 individuals with Scleroderma (according to the American College of Rheumatology classification criteria for SSc) with majority of cases being females n=64 (94.1%). ILD was seen in 53 (77.9%) patients with a mean duration of 4.17 years. When we compared the mean change in FVC, DLCO and PAH from the time of onset of ILD/PAH to the values at last follow up, there was no significant change. ILD patients with UIP pattern on HRCT, showed a significant progression in terms of $>$10% fall in FVC as compared to NSIP subgroup. None of the baseline parameters were predictive of ILD and its progression. Older age predicted onset of PAH.

**Conclusions:** 1) None of the studied baseline variables were predictive of ILD and its progression. 2) Only age had statistically significant effect as a predictor for

Table 1. Disease characteristics

| Variables | No (%) |
|---|---|
| Raynaud's phenomenon | 62 (91.2) |
| Sclerodactyly | 49 (72.1) |
| Digital pits | 47 (71.2) |
| Calcinosis | 2 (2.9) |
| Telangiectasia | 9 (13.23) |
| Arthritis | 31 (45.6) |
| GERD | 49 (72.1) |
| Sicca symptoms | 10 (14.7) |
| Myositis | 6 (8.8) |
| ILD | 53 (77.9) |
| PAH | 21 (30.9) |
| ANA | 66 (97.05) |
| Anti-topoisomerase antibody | 35 (51.4) |
| Anti-centromere antibody | 17 (25) |
| **Variables** | **Average (mean ± SD)** |
| Age (years) | 40.9±10.4 |
| Modified Rodnan Skin score | 13.96±7.4 |

the occurrence of PAH. 3) The demographic and clinical profile of our cohort was comparable to other studies from India and western population. Calcinosis and telangiectasia were less frequently seen as compared with western population.

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**Disclosure of Interest:** None declared

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## AB0628 LUNG CANCER IN SYSTEMIC SCLEROSIS: CASES IN A HOSPITAL COHORT

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**Background:** Systemic sclerosis (SS) is a rare disease that leads to greater morbidity and mortality than in general population, but due to its unfrequency there are very few clinical and epidemiological data. Some meta-analysis[1] about the increased incidence of cancer in SS compared to the average population (Relative risk (RR) 1.75[1]) were published; even more relevant when it refers to lung cancer (RR 4.35[1]), compared to the general population; suggesting that interstitial lung disease (ILD) may be the cause of this increased incidence

**Objectives:** To provide our cases of lung cancer in patients with SS, describe the clinical, epidemiological and pathological features and assess the possible risk factors associated

**Methods:** Retrospective review of lung cancer cases of a 115 patients hospital cohort with SS. Clinical and epidemiological characteristics, timeline, SS subtype, histology and likely associated risk factors are described.

**Results:** The prevalence of cancer in our 115 patients serie with SS is 10.4% (12/115), lung cancer was the most frequent neoplasia (4/12, 33%)

Case 1. Woman, 36 years old, nonsmoker, diagnosed at 23 year old of diffuse SS (DSS) Scl70+, with recurrent ulcers. ILD (HRCT and biopsy: desquamative interstitial pneumonia, DIP) at 29 years old. Treatment: prednisone (7.5 mg/ average dose), azathioprine 100mg, calcium antagonists, bosentan and alprostadil. She presented intercostal pain and was diagnosed by biopsy and HRCT of well defined adenocacinoma with mucosecretory pattern and acinar areas, T3N0M0. Pneumonectomy was performed with good results.

Case 2. Woman, 72 years old, nonsmoker, diagnosed at 58 years old of DSS Scl70+ with recurrent ulcers and ILD (HRCT: nonspecific interstitial pneumonia, NSIP) at 64 years old. Treatment: calcium antagonists, bosentan and alprostadil. She presented abrupt clinical and PFT deterioration, biopsy and HRCT showed poorly differentiated non-small cell carcinoma T4N0M1b. Dyed six months after diagnosis.

Case 3. Male, 47 years old, nonsmoker, diagnosed at 43 years old of DSS and ILD (HRCT: NSIP) with recurrent ulcers. Treatment: prednisone (7.5 mg/d), calcium antagonists, bosentan and alprostadil. He presented constitutional syndrome and respiratory clinical worsening, diagnosed by biopsy and HRCT of large cell neuroendocrine carcinoma of the lung, T3N0M1b. Stable after 18 months of palliative chemotherapy.

Case 4. 57-years-old male, smoker, ESD diagnosis with rapid Raynaud's syndrome onset, HRCT and lung biopsy evidenced lung adenocarcinoma T2aN3M0. Improvement of skin symptoms after chemoradiation.

**Conclusions:** Lung cancer is the most common malignancy in our cohort. All of them had DSS. Most of them (3/4) had a previous diagnosis of ILD and were nonsmokers, with a mean time of evolution from the SS diagnosis to neoplasia of 9.6 years and 6.3 years from diagnosis of ILD. The other case, had simultaneous diagnosis of SS and lung cancer. Only one case had been previously treated with non-steroid immunosuppressant. These results force us to strictly control the risk of neoplasia in patients with SS, predominantly those with diffuse involvement and ILD diagnosis.

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**Disclosure of Interest:** None declared

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## AB0629 DESIGN OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 2 CLINICAL TRIAL OF THE TOLL-LIKE RECEPTOR ANTAGONIST IMO-8400 IN PATIENTS WITH DERMATOMYOSITIS

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**Background:** Dermatomyositis (DM) is a rare idiopathic inflammatory myopathy characterized by an auto-inflammatory immune response in muscle and skin. Multiple lines of evidence suggest Toll-like receptors (TLRs), central components of the innate immune system, play a key role in DM pathogenesis. A retrospective study evaluating muscle biopsy samples showed that TLR9, TLR4 and TLR2 were significantly over-expressed in skeletal muscle and infiltrating cells in DM subjects compared to controls. Over-expression of type I and type II interferons and other cytokines has been demonstrated in DM, suggesting involvement of the NF-κβ pathway. Expression of certain cytokines also had significant positive correlations with expression of TLR9 and TLR4. IMO-8400 is an investigational oligonucleotide-based antagonist of TLRs 7, 8 and 9 that has demonstrated clinical activity in patients with psoriasis. We hypothesize that inhibition of TLR activity in patients with DM with IMO-8400 has the potential to reduce chronic inflammation in affected tissue.

**Objectives:** Our objective was to design a Phase 2 clinical trial of IMO-8400 in DM patients using the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) as the primary efficacy endpoint. Specifically, we wished to estimate the placebo response for the CDASI and calculate optimal treatment effect in order to estimate optimal subject numbers and length of trial.

**Methods:** Retrospective analyses were conducted using longitudinal CDASI assessments for 115 unique DM patients seen at the Stanford University outpatient dermatology clinic. Patients with multiple assessments approximately 12 or 24 weeks apart were grouped by the first visit CDASI activity score ($<$15, 15–19, 20–24 and $\geq$25), and the change in CDASI activity score between the visits was assessed.

**Results:** Over 24 weeks, a 5 point or greater decrease in CDASI activity score was observed at 31.8% of patient visits, with the change in CDASI activity score ranging from -23 to +27 points across all patients. Because some patients experienced clinically meaningful changes of 4 to 5 points on the CDASI following treatment with standard of care therapies, a 7 point treatment effect was targeted for the IMO-8400 trial. Sample size calculations resulted in 10 patients per treatment group, assuming a standard deviation of 8.5 points over 24 weeks using a Repeated Measures Mixed Model analysis of change from baseline on monthly CDASI assessments ($>$80% power on a 1-sided test; alpha=0.05).

**Conclusions:** Based on these analyses, we initiated a double-blind, placebo-controlled, 24-week Phase 2 clinical trial in DM patients (NCT number: NCT02612857). Key entry criteria include adults with DM aged 18–75 years, CDASI activity score $\geq$15, clinical symptoms of active muscle disease, and abnormal serum CK or ALD, EMG, muscle biopsy or MRI. Additional outcome measures include MMT-8, timed function tests including 10-meter run walk, and exploratory biomarkers of disease activity.

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## AB0630 CARDIAC MAGNETIC RESONANCE IMAGING WITH PHARMACOLOGICAL STRESS PERFUSION IN ASYMPTOMATIC PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Systemic Sclerosis (SSc)-heart disease (SSc-HD), although often clinically silent, significantly reduces the life-expectancy in these patients [1]. The cardiac magnetic resonance (CMR) is recognized useful tool for the diagnosis of SSc-HD and cardiac stress tests might be a helpful technique to highlight the occult myocardial involvement, which cannot be detected at rest due to compensatory mechanisms [2,3].
**Objectives:** To evaluate the possible occult cardiac involvement in asymptomatic SSc patients by pharmacological stress, rest perfusion and delayed enhancement CMR, to identify as earlier as possible those patients at higher risk of cardiac related mortality and needing specific cardiovascular treatments.
**Methods:** Sixteen consecutive patients with definite SSc fulfilling the ACR/EULAR 2013 classificative criteria [4] in less than 1 year from the onset of Raynaud's phenomenon underwent pharmacological stress, rest perfusion and delayed enhancement CMR. No enrolled patient showed signs and/or symptoms suggestive for cardiac involvement, confirmed by both the 12-lead ECG examination and echocardiography. No patient showed traditional cardiovascular risk factors. Patients, in which CMR technique showed occult cardiac involvement, underwent to heart computed tomography (CT) scan to evaluate a possible coronary disease.
**Results:** Stress perfusion defects, in the left ventricle, were detected in 6 out of 16 (37.5%) patients. A sub-endocardial defects and/or a ventricular mid-myocardial layer stress perfusion defects were observed. Our results confirmed, in these 6 patients, a normal flow distribution of the explored coronary arteries by CT scan. The presence of CMR stress perfusion defects did not correlate with any clinical feature of patients.
**Conclusions:** Myocardial stress perfusion defects may be early detected, by pharmacological stress perfusion CMR, a reliable and sensitive technique for the non-invasive evaluation of SSc-HD, in patients with SSc of recent onset. These defects seems to be independent from traditional risk factors and associated comorbidities, suggesting that are a specific hallmark of the disease. An early detection of myocardial involvement might suggest starting of vasodilatative therapies in these patients.
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**Disclosure of Interest:** None declared
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## AB0631 PREVALENCE, SEVERITY AND CLINICAL SIGNIFICANCE OF PAIN IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Objectives:** To assess prevalence, severity and type of pain in patients with systemic sclerosis (SSc), and relationship with disease status, depression and quality of life.
**Methods:** 42 consecutive patients with SSc (38 women and 4 men), mean age 56.5 years, mean disease duration 9.5 years, were included in this study. 31 (73.8%) of patients had limited SSc (lSSc) and 11 (26.2%) diffuse form of disease (dSSc). ACA were positive in 15 (35.7%) and ATA in 17 (40.5%) patients. We assessed prevalence and severity of different types of pain (during attacks of Raynaud's phenomenon, pain caused by ischemic ulcers, odynophagia, arthralgia, headache, back pain and chest pain) in our patients. Presence of manifestations of neuropathic pain was assessed using the PainDetect questionnaire. Relationship among different types of pain with disease status, symptoms of depression and quality of life was estimated. Disease status was assessed using the Scleroderma Assessment Questionnaire (SAQ), occurrence of depressive symptoms by the Beck's Depression Inventory (BDI), whilst quality of life was evaluated using the EQ-5D index.
**Results:** Thirty nine patients (92.9%) reported different types of pain. 19 (45.2%) patients experience some form of pain every day. Arthralgia is the most common type of pain, present in 78.6% of patients, followed by pain during attacks of Raynaud's phenomenon (69%), back pain (47.6%), headache (31%), chest pain (23.8%), odynophagia (21.4%) and painful ischemic ulcers (19%). Pain caused by ischemic ulcers was reported as most severe (median 8.5 on a 0–10 scale). All types of pain were equally frequent in patients with lSSc and dSSc. However, joint pain was more intense (p=0.02) in patients with dSSc (7.6 vs. 5.5). The Index of Disease Statuts (IDS) positively correlated with severity of joint pain ($\rho$=0.66, $p<0.001$), but not with severity of other types of pain. Moreover, a significant correlation was noticed only between joint pain and the EQ-5D index ($\rho$=-0.52, p=0.009). On the other hand, a significant correlation between BDI index and intensity of pain during attacks of Raynaud phenomenon ($\rho$=0.49, p=0.007), pain caused by ischemic ulcers ($\rho$=0.81, p=0.016), odynophagia ($\rho$=0.73, p=0.026) and arthralgia ($\rho$=0.59, $p<0.001$) was observed. Compared to patients with intermittent pain, patients suffering from chronic pain have a significantly lower mean value of EQ-PD index (0.52 vs 0.79, z=-4.12, $p<0,001$) and a higer mean value of IDS (1.21 vs. 0.53, z=-3.32, p=0.001). Patient with manifestations of neurpathic pain have significantly higher mean values of IDS, BDI an EQ-5D index, than patients without neuropathic pain.
**Conclusions:** Pain is present in 92.9% of patients with SSc. Arthralgia is the most common type of pain. Although less frequent, pain caused by ischemic ulcers was reported as most severe. Intense joint pain, chronic pain and neuopathic pain are associated with more severe form of the disease and poorer quality of life. All types of pain have impact on development of depressive symtoms in patients with SSc.
**Disclosure of Interest:** None declared
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## AB0632 ASSOCIATION BETWEEN INTERSTITIAL PULMONARY INVOLVEMENT AND MICROVACULATURE CHANGES IN SYSTEMIC SCLEROSIS

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**Background:** Pulmonary disease is the leading cause of mortality in patients with systemic sclerosis (SSc). Baseline gas transfer (DLCO) and FVC levels have traditionally been used as measures of disease severity and reductions in both parameters have been associated with increased mortality in the interstitial lung disease of SSc. In SSc the reduced capillary density leads to a reduced blood flow, to tissue ischemia. Tissue hypoxia usually initiates the formation of new blood vessels from the pre-existing microvasculature. Nailfold capillaroscopy is a safe, noninvasive routine way for the microvascular investigation
**Objectives:** The aim of this study is to assess the association between capillaroscopic abnormalities and parameters of interstitial lung involvement in patients with SSc.
**Methods:** All patients underwent routine clinical examination (dyspnea, cough, crepitus), pulmonary function tests, DLCO (alveolitis grade and fibrosis), blood gases and HRCT scan of chest (1). Microvasculature changes were assessed using nailfold videocapillaroscopy (NVC) which was performed by two independent examiners. The obtained images were analysed anonymously by two investigators blinded for the clinical and serum status of SSc patients and classified as early, active and late pattern, non specific or normal picture (2). For statistical evaluation Poisson's correlation coefficient and T-test were used.
**Results:** Total 42 patients (38 females) were investigated: 30 individuals with limited form, 7 with diffuse, 3 patients with scleroderma sine scleroderma, 1 with overlap syndrome and 1 with undifferentiated connective tissue disease. The mean age ± standard deviation (SD) of the whole cohort was 51±22 years and the mean disease duration ± SD was 10±7 years. 3 patients (7.5%) had early NVC pattern, 12 patients (30%) had active, 10 (58%) late pattern, and 17 (37.5%) had nonspecific changes or normal picture. The patients with late NVC pattern exhibited more often mild to moderate alveolitis, decreased FEV1 and FVC and DLCO. When correlating NVC patterns with clinical findings, pulmonary function test and HRCT scans we found only an association of low significance with dyspnea and alveolitis grade (both $p<0.1$).
**Conclusions:** In our study NVC patterns did not seem to correlate with severity of interstitial lung disease in SSc patients
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**Disclosure of Interest:** R. Bečvář Consultant for: Actelion, M. Tomcik: None declared, S. Skacelova: None declared, J. Stork: None declared, A. Slovakova: None declared
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## AB0633 PERFORMANCE OF THE EULAR/ACR 2013 CLASSIFICATION CRITERIA IN A PORTUGUESE SYSTEMIC SCLEROSIS POPULATION

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**Background:** The 1980's ACR classification criteria for systemic sclerosis (SSc) show low sensitivity, especially in early or mild forms. A new set of classification criteria has been developed by ACR/EULAR in 2013. Applicability of the new criteria in clinical practice remains to be shown.
**Objectives:** To evaluate the performance of both set of classification criteria for SSc in a Portuguese SSc population.
**Methods:** Cross-sectional study including consecutive patients with clinical diagnose of SSc (based on expert opinion) followed in our rheumatology department. Clinical and demographic characteristics were collected by consulting the clinical files and national data base – Reuma.pt. The two sets of criteria were applied to all patients, sensitivity was calculated and Kappa coefficient was used to evaluate the agreement between them. Patients not fulfilling the old but fulfilling the new criteria were compared with those that fulfilled ACR criteria using Mann-Whitney, qui-square and fisher test (SPSS 23.0). Significance level was set as $<0.05$.
**Results:** 108 patients were included, 96 (88.9%) were female with mean age of 58.21 (±12.8) years and a median disease duration of 6 years (0–38). 96 (88.9%) had localized and 12 (11.1%) had diffuse disease form. The most prevalent criteria items were: Raynaud's phenomenon (93.5%), sclerodactyly of the fingers (85.2%) and antinuclear antibodies (94.4%).
For overall cohort, 53 patients (49.1%) fulfilled the old ACR criteria. These 53 patients and more 44 patients (97) fulfilled the new ACR/EULAR criteria, showing a sensitivity of 89.9% compared to 49.1% of the old ones. Kappa coefficient was 0.197 (p=0.01).
In patients with localized forms, the sensitive of ACR/EULAR criteria was 88.5% compared with 43.8% of ACR 1980 criteria and Kappa coefficient was 0.183 (p=0.02).
In diffuse forms, all 12 patients fulfilled both criteria set, showing an almost perfect agreement.
Patients not fulfilling the old but fulfilling the new criteria presented more frequently with capillaroscopic abnormalities (p=0.04) and anticentromere antiboy (p=0.01), but low incidence of anti-Scl70 antibodies ($p<0.001$) and interstitial lung disease ($p<0.001$).
**Conclusions:** Our study confirmed a greater sensibility of the new ACR/EULAR 2013 criteria compared with ACR 1980 criteria, especially in mild and localized SSc disease forms. In our patients with SSc not fulfilling the old criteria, the presence of capillaroscopic abnormalities and anticentromere antibodies among the new set of classification criteria were of the utmost importance in their reclassification as SSc patients. The application of the new criteria in clinical scenario allows an early classification and timely management of more SSc patients, ensuring a better prognosis.
**Disclosure of Interest:** None declared
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## AB0634 SURVIVAL AND CAUSES OF DEATH IN A PORTUGUESE POPULATION WITH SYSTEMIC SCLEROSIS

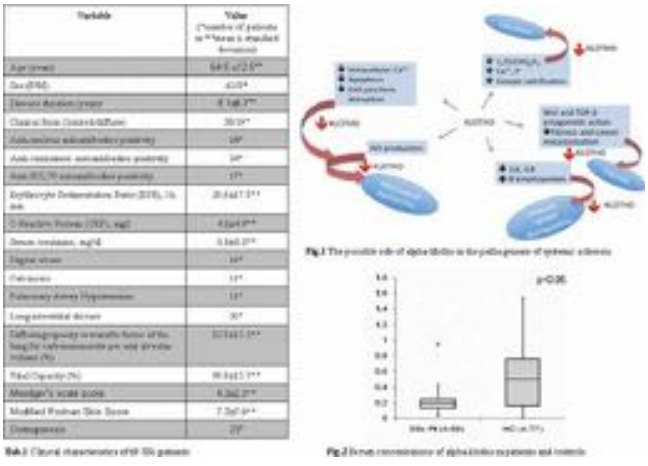
R. Fonseca[1], D. Rosa-Gonçalves[1], F. Aguiar[1], T. Meirinhos[2], T. Martins-Rocha[1], E. Mariz[1], M. Bernardes[1], L. Costa[1]. *[1]Rheumatology, São João Hospital Centre, Oporto; [2]Rheumatology, Centro Hospitalar do Baixo Vouga, Aveiro, Portugal*

**Background:** Systemic sclerosis (SSc) is known for its poor prognosis. However, it is apparent that subsets of patients have bad outcomes sometimes after a short time of disease duration whether some others will remain stable with a milder disease. The factors that have impact in the prognosis and mortality are yet to be determined.
**Objectives:** To study the causes of dead and survival predictors in a Portuguese SSc population.
**Methods:** Observational retrospective cohort study was performed including consecutive patients with clinical diagnosis of SSc (based on expert opinion), followed in our rheumatology department since 1990. Clinical and demographic characteristics were retrospectively collected by consulting the clinical files.
Patients who have died were compared with the others using Student t-test, Mann-Whitney test, Chi-square or Fisher test. Kaplan-Meier survival analysis and log rank were used to compare survival (SPSS 23.0). Significance level was set as $<0.05$.
**Results:** 114 patients were included, 99 (86.8%) females and 15 (13.2%) males, with a mean age of 57.61 (±11.3) and a median disease duration of 7 years (0–38). 100 (87.7%) had localized and 14 (11.1%) had diffuse disease form.
The mortality rate observed was 1.1 cases per 100 person-years. Among the 10 patients that have died, 60% (6) were female, 60% (6) had diffuse and 40% (4) had limited skin involvement, and 20% (2) had overlap syndromes (1 overlap with rheumatoid arthritis and 1 with systemic lupus erythematosus). The median age was 63.5 [57 – 84] years and median disease duration was 10 [1–20] years.
The causes of death were: infections in 5 (3 sepsis, 1 septic arthritis, 1 pneumonia), cardiovascular events in 3 (right heart failure secondary to pulmonary arterial hypertension) and neoplasia in 2 (1 brain metastases of occult tumour and 1 gastric adenocarcinoma).
Mortality occurred more frequently in male patients (26.7% compared to 6% in females, p=0.03), in patients with diffuse skin involvement (40% compared to 4% in limited forms, $p<0.001$), digital ulcers (16.7% compared to 5%, p=0.04), pitting scars (20.6% compared to 3.8%, p=0.007), pulmonary arterial hypertension (50% compared to 6.5%, p=0.009), interstitial lung disease (19.2% compared to 5.7%, p=0.04) and anti-Scl70 antibodies (20.8% compared to 5.6%; p=0.03).
Kaplan-Meier univariate analysis showed a lower survival in patients with diffuse skin involvement (log rank 14.2 $p<0.001$), interstitial lung disease (log rank 6.3 p=0.04) and positive anti-Scl70 antibodies (log rank 6.4 p=0.04).
**Conclusions:** Our results are in accordance with previous studies that show a high frequency of infections and cardiovascular events as major causes of death, but we also find malignancy as an important factor too. Diffuse skin disease, interstitial lung disease and positive anti Scl70 unfavourably influenced the survival and these patients are the ones in need for carefully evaluation and aggressive treatment.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4431

## AB0635 MEASUREMENT OF SERUM ALPHA-KLOTHO IN SYSTEMIC SCLEROSIS PATIENTS: RESULTS FROM A PIVOTAL STUDY

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**Background:** Systemic sclerosis (SSc) is a connective tissue disease characterized by microangiopathy and fibrosis involving skin and inner organs. Furthermore, an aberrant activation of the immune system may contribute, at least in part, to the pathogenesis of the disease. Klotho, expressed both as transmembrane and soluble protein, contributes to prevent ageing, hyperphosphatemia, fibrosis, arteriosclerosis, inflammation, and cancer development. Mice lacking klotho gene expression develop an accelerated ageing, with different phenotypes ranging from atherosclerosis and hyperphosphatemia to skin atrophy and emphysema. A deficiency in klotho expression could be responsible for microangiopathy, calcinosis and fibrosis, which represent common characteristics of systemic sclerosis (fig. 1).
**Objectives:** To evaluate the serum concentration of a-klotho in a group of SSc patients compared to healthy controls and to correlate its levels with the degree and the kind of organs involvement, assessed through Mesdger's scale score.
**Methods:** We enrolled 69 patients affected by SSc, according to ACR/EULAR 2013 criteria, and 77 matched HC. Blood samples obtained from both patients and controls were collected and analysed by an ELISA test for the determination of human soluble a-klotho by using an anti-human Klotho Mouse IgG (My Biosource, CA, USA). Scleroderma patients were assessed for disease activity through Mesdger's scale. Moreover, modified Rodnan Skin Score (mRSS), pulmonary function tests, 2D echocardiography, chest high resolution computerized tomography, serum creatinine level, ESR, and CRP were also assessed. Subjects suffering from uncontrolled diabetes, lung obstructive diseases or renal impairment not depending on systemic sclerosis were excluded.
**Results:** Our cohort consisted of 69 SSc patients (61 females, mean age 64.5±12.5 years, mean disease duration 9.1±6.7 years) and 77 healthy controls (28 females, mean age 49,7±10,2 years). Demographic data are reported in tab.1. Patients were treated with calcium channels blockers (21 cases), i.v.prostanoids (all), immunosuppressive drugs (prednisone in 22 cases; hydroxychloroquine in 14 cases; mofetilmycophenolate in 3 cases; methotrexate in 6 cases; cyclosporin A in 1 case; azathyoprine in 5 cases). Overall, SSc patients have lower serum



klotho concentration than healthy controls (0.45 + 0.43 ng/ml vs 0.59 + 0.39 ng/ml; p=0.023197; fig.2). However, in SSc patients Spearman test did not reveal a significant association between the serum concentration of klotho and Mesdger's scores. Furthermore, we did not find any association among klotho levels and mRSS, DLCO/AV, serum creatinine, disease duration, age of the patients, ESR and CRP.
**Conclusions:** To our knowledge, this is the first study aiming to investigate the serum concentration of klotho in SSc patients. Our data showed a lower concentration of klotho in the serum of SSc patients compared to healthy controls. However, klotho levels were not related to the severity of the disease, assessed through Mesdger scale, neither to lung or kidney functional impairment, skin fibrosis or systemic inflammation.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1683

## AB0636 INTERSTITIAL LUNG DISEASE IN SCLERODERMA PORTUGUESE PATIENTS

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**Background:** Systemic sclerosis (SSc) is a rheumatic disorder characterized by inflammation and fibrosis involving the skin as well as internal organs, including the lung.
**Objectives:** This study was conducted to characterize SSc patients with ILD and determine predictor features for the presence of ILD.
**Methods:** A retrospective evaluation of SSc patients from our Rheumatology department was undertaken. ILD was defined according to imaging findings in high-resolution CT (HRCT) combined with functional parameters. Demographic features, auto-antibodies, spirometry, diffusion capacity for carbon monoxide (DLCO) measurement, echocardiography and 6-minute walk test were compared between groups with and without ILD using parametric tests and non-parametric tests. Predictor factors were established by logistic regression analyses.
**Results:** One hundred and three SSc patients with current mean age of 60.2±14.1y and mean disease duration of 10.0±9.6y were evaluated. Thirty-four (35.8%) patients were diagnosed with ILD, of whom 13 had limited cutaneous SSc, 14 had diffuse cutaneous SSc, 2 sine sclerodema and 5 overlap syndroms. ANA was positive in 100% cases, anti-Scl70 was found in 55% and anti-centromere antibody positivity was found in 15% of patients. HRCT revealed diffuse parenchymal lung disease involvement >20% in 18 (53%) cases, with the majority showing a predominant honeycombing pattern. Spirometry showed a restrictive pattern in 8 patients and 1 had obstruction. The DLCOsb was abnormal in 7 patients. Three patients had pulmonary hypertension confirmed by right heart catheterization, 2 patients classified as group 1 and 3 and 1 patient of group 5. About 63% of ILD patients were ever treated with corticosteroids and 27% with cyclophosphamide, which were the most common drugs used. Two patients were also treated with rituximab. In this ILD-group, 5 deaths were recorded, 2 due to cancer, 1 abdominal sepsis, 1 pulmonary hypertension and 1 of unknown cause. Comparison of these ILD patients with non-ILD patients revealed some significantly differences (Table 1).

Table 1. Statistically significant distinctions between patients with and without ILD

| | ILD patients (n=34) | No-ILD patients (n=61) | *P* |
|---|---|---|---|
| Current mean age (years) | 61.8±14.5 | 58.6±13.2 | 0.330 |
| Mean disease duration (years) | 11.6±9.8 | 9.2±9.3 | 0.250 |
| Anti-centromere antibody (%) | 5 (15) | 48 (79) | **<0.001** |
| Anti-Scl70 antibody (%) | 18 (55) | 4 (7) | **<0.001** |
| Diffuse cutaneous disease (%) | 14 (41) | 5 (8) | **<0.001** |
| Digital ulcers (%) | 19 (54) | 11 (18) | **<0.001** |
| NYHA Functional Classification (%) | 23 (67) | 30 (49) | **0.017** |
| Tricuspid regurgitation (%) | 26 (84) | 24 (45) | **0.001** |
| DLCOsb <60 (%) | 7 (64) | 0 (0) | 0.056 |
| Hypoxemia at rest (%) | 8 (27) | 4 (7) | **0.013** |
| Gastrointestinal involvement (%) | 10 (48) | 9 (24) | 0.060 |
| Death (%) | 5 (16) | 1 (2) | **0.020** |

Multivariate analysis showed that digital ulcers (OR=31.6, 95% CI 3.09 to 321.91), Anti-Scl70 antibody positivity (OR=10.1, 95% CI 1.19 to 85.74) and anti-centromere antibody negativity (OR=0.08, 95% CI 0.01 to 0.83) were independently associated with the presence of ILD.
**Conclusions:** This study is one of the first studies carried out in Portugal regarding lung involvement in SSc. About one third of the patients had ILD, whose main characteristics are in accordance with other European cohorts. We confirmed that anti-SCL70 positivity, presence of digital ulcers as well as the absence of anti-centromere antibody is independently associated with ILD
**Disclosure of Interest:** None declared
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## AB0637 ILOPROST (ILO) IN SYSTEMIC SCLEROSIS (SSC): THE SAFETY EXPERIENCE OF TWO ITALIAN CENTRES

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**Background:** Iloprost (ILO) is a synthetic analogue of prostacyclin $PGI_2$ with a potent vasodilator action, an anti-proliferative effect on smooth muscle cells and inhibition of platelet aggregation. ILO is employed intravenously for the control of Raynaud Phenomenon and digital ulcers. Up to now, no agreement has been reached on the regimen (dosage and frequency) to be used in SSc patients.
**Objectives:** To identify the most common side effects that are developed during ILO infusion in SSc.
**Methods:** 81 SSc patients, classified according to ACR EULAR criteria, derived from two Italian centers, were submitted to ILO infusion: patients were subclassified according to the edematous or fibrotic/atrophic phase of the disease. ILO was infused (6–8 hour infusion, dose ranging from 0.5 to 1.0 ng/kg/ min) (1) with a progressive increase of the dosage up to the achievement of patient's tolerance: the infusion on pump was started at 5 ml/hour and increased every half an hour up to 20 ml/hour (a dose of 4 mcg/h which corresponds to 1ng/kg)according to patients tolerance and appearance of side effects.
**Results:** Out of 81 patients, 16 were in the *edematous phase* with puffy fingers (digital edema). In this cohort, 5 individuals (31.2%) developed diarrhea and 9 (56.2%) developed hypotension during the infusion. When the drug was withdrawn patients had an immediate amelioration but when ILO was restarted, they again developed diarrhea or hypotension that led to definitive interruption of the treatment. Moreover, 10/16 patients (62.5%) experienced significant and painful digital swelling which led to the tapering of the infusion dosage below 10 ml/hr (which corresponds to 0.5 ng/kg per min); out of 10 patients, only one could continue the treatment while the other 9 had to be withdrawn due to the maintenance of the intense digital pain due to vasodilation. Finally, 11 patients (68.7%) reported flushing and 7 (43.7%) headache, but they were always controlled with the reduction of the infusion below 10 ml/hr. Out of 81 patients, 65 were in the *atrophic/ fibrotic phase:* 10 patients (15.3%) developed diarrhea and 24 pts (37%) hypotension that led to temporary withdrawal: when ILO was restarted and kept below 10 ml /hr, no side effects were experienced. In 23 cases (35.3%) flushing and in 8 cases (12.3%) headache were experienced, but were well controlled with infusion reduction below 10 ml/hr.
**Conclusions:** ILO was well tolerated in SSc patients characterized by fibrotic phase, where side effects could be managed by reducing/modulating the infusion rate. In edematous patients, ILO infusion should be decided in case where the severity of Raynaud's phenomenon or the presence of digital ulcers strongly suggests its use.
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**Disclosure of Interest:** None declared
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## AB0638 A REDUCED LOWER ESOPHAGEAL SPHINCTER PRESSURE PREDICTS A HIGHER GASTROESOPHAGEAL REFLUX DISEASE QUESTIONNAIRE SCORE IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** A reduced basal lower esophageal sphincter (LES) pressure (LES<15 mmHg) is recognized as an early finding of esophageal involvement in systemic sclerosis (SSc) patients (1).
**Objectives:** We aimed to investigate potential associations of a reduced basal LES pressure at first observation with the development of new gastrointestinal symptoms and with self-administered questionnaires devoted to assess the impact of gastrointestinal involvement on quality of life during follow-up (FU) in SSc patients.
**Methods:** SSc patients meeting the 2013 ACR/EULAR criteria for disease classification with measurement of basal LES pressure at the first observation and at least one FU visit with complete clinical evaluation were enrolled. The gastroesophageal reflux disease questionnaire (GerdQ) (2, 3) was administered to explore the impact of esophageal symptoms on patient's disease perception and to estimate the risk for GERD. Associations between reduced basal LES pressure and new onset gastrointestinal symptoms at FU were analyzed by Fisher's exact test, while the GerdQ score in SSc patients with or without a reduced basal LES pressure was analyzed by Mann-Whitney U test.
**Results:** Fifty-nine SSc patients, aged 47±13 years, were investigated (75% females; median disease duration 7 years, range 0.5–43). Eighty % of patients had a limited SSc subset (lcSSc); 20% had a diffuse subset (dcSSc). All patients were ANA positive (36% had anti-centromere antibodies, 39% anti-Scl70+; 5% anti-RNApolymerase III; 1.7% anti-PmScl; 1.7% anti-U1RNP). All patients were

under proton pomp inhibitors ± prokinetics during FU. Forty-two % of patients had already esophageal symptoms at baseline; 32% developed new esophageal symptoms and 40% new gastric and/or intestinal symptoms during observation (median FU 4 years; range 0.5–15.5). Baseline basal LES pressure was reduced in 63% of patients. Out of these, 49% had also esophageal symptoms. Median GerdQ score at the end of FU was significantly higher in patients with baseline reduced LES pressure (7, range 3–14 versus 6, range 2–11; $p<0.001$). However, even though patients with baseline reduced LES pressure had a higher prevalence of a GerdQ score higher than 7, indicating an impact of esophageal symptoms on their quality of life (12/37 versus 4/22), this difference was not statistically significant.

**Conclusions:** Our data suggest that evaluation at baseline of esophageal involvement in SSc patients by esophageal manometry can predict the development of more severe symptoms over time, as evaluated by the association with a higher score at GerdQ also in initially asymptomatic patients. Larger studies need to be carried out to confirm this association.

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## AB0639 BONE MINERAL DENSITY IS DECREASED IN PATIENTS WITH SYSTEMIC SCLEROSIS AND CORRELATES WITH SERUM IPTH LEVELS: A CROSS SECTIONAL STUDY

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**Background:** Systemic sclerosis is a multisystemic disease with devastating consequences. It is believed that osteoporosis is common in systemic sclerosis with causation being ascribed to the altered GI motility, malabsorption, immobility, use of glucocorticoids among other factors. A few studies have looked at osteoporosis and associated factors in patients with systemic sclerosis, however results are conflicting [1–2].

**Objectives:** The aim was to study the bone mineral density (BMD) in patients with systemic sclerosis and its correlation with organ involvement.

**Methods:** Patients attending the Rheumatology Clinic at PGIMER, Chandigarh were screened and 100 patients meeting the American College of Rheumatology (ACR) criteria for systemic sclerosis were recruited for the study. In all such patients, BMD was measured using dual energy xray absorptiometry (DXA). Serum Vitamin D and iPTH levels were estimated.

**Results:** Most of the participants were females (8:1). The mean age of the participants was 42±12 years. The median disease duration prior to recruitment was 5 years (3–8 years). Thirty four of eighty nine women were post menopausal at the time of conducting the study. 48% of patients had interstitial lung disease while 18% had pulmonary arterial hypertension. 56% had received corticosteroids while 16% had received cyclophosphamide. Most patient received 7.5 mg of corticosteroids intitially and the dose was tapered to 5mg once a day and then to alternate days and subsequently was stopped. Cyclophosphamide was given as a monthly pulse for 6 months when indicated. Among patients included, 72% of patients had a low bone mass at the spine while 42% had a low bone mass at the femoral neck. In all, 28% had osteoporosis of the lumbar spine while 6% had osteoporosis of the femoral neck. 41 patients exhibited hypocalcemia. Serum iPTH levels were elevated with a median value of 76.24 (50.26–102.675) pg/ml. Serum iPTH correlated inversely with low bone mass at the hip ($p=0.023$, $r^2=0121$). We did not find a correlation with increasing age, postmenopausal status, low BMI, corticosteroid use, serum 25(OH) Vitamin D levels, disease duration, presence of ILD or PAH.

**Conclusions:** Low bone mass is highly prevalent in patients with systemic sclerosis and correlates inversely with Serum iPTH levels. Serum iPTH levels may be an important marker for early diagnosis of osteoporosis in these patients and may help in timely institution of anti resorptive measures, hopefully, before the occurrence of fragility fractures

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## AB0640 CAROTID INTIMA MEDIA THICKNESS IS INCREASED IN PATIENTS OF SYSTEMIC SCLEROSIS: CROSS SECTIONAL, CASE-CONTROL STUDY

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**Background:** Atherosclerosis is a leading cause of cardiac and non-cardiac related morbidity and mortality in SSc[1]. It is believed to occur secondary to chronic inflammation, altered lipid profiles and function, development of autoantibodies, and endothelial dysfunction. There is increasing evidence that atherosclerosis occurs prematurely in systemic sclerosis [2–3].

**Objectives:** The aim was to describe the parameters of subclinical vascular changes [Carotid Intima Media Thickness (cIMT), Flow Mediated Dilatation (FMD), Ankle Brachial Pressure Index (ABPI)] in patients with systemic sclerosis and compare them with age and sex matched controls.

**Methods:** 50 patients of systemic sclerosis aged 20–50 years were selected and compared with the same no. of age and sex matched controls. Patients with diabetes, hypertension, dyslipidemia, smoking and thyroid disorders were excluded. cIMT was calculated using a linear probe (L 12–5 MHz) on a Philips iU 22 ultrasound machine at a distance of 2 cm from the carotid bulb. A mean of the left and right cIMT was calculated. Endothelium-dependent FMD of brachial artery was expressed as the percentage change in brachial artery diameter from baseline. The average of the right and left brachial artery FMD was studied. ABPI of both right and left lower limb was measured (using Doppler) and the average value of ABPI was considered.

**Results:** The cases and controls were well matched in terms of age, blood pressure, B.M.I, renal and liver functions, and lipid profiles. 16 patients had limited cutaneous SSc while 36 had diffuse cutaneous SSc. cIMT was significantly more in SSc patients as compared to controls (0.585 mm *vs* 0.571 mm; p=0.001). FMD measurements in SSc patients were lower when compared to controls, but they did not achieve statistical significance (7.61% *vs* 8.03%; p=0.608). ABPI values were similar in SSc patients and controls (1.056 vs 1.036; p=0.398). cIMT did not show any correlation with age or duration of illness. ABPI showed significant inverse correlation with duration of illness (Rho= -0.385; p=0.006). However, none of these parameters varied as per the pattern of skin involvement (diffuse vs limited), presence or absence of digital infarcts or pulmonary fibrosis.

**Conclusions:** cIMT is increased in patients with systemic sclerosis as compared to matched controls and may serve as a useful marker for detection of subclinical atherosclerosis in these patients. ABPI varies inversely with disease duration in patients with systemic sclerosis.

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## AB0641 THE ROLE OF ORO-PHARYNGEAL-ESOPHAGEAL SCINTIGRAPHY IN THE EVALUATION OF THE SWALLOWING FUNCTION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: SHORT-TERM RESULTS OF AN ONGOING PROSPECTIVE STUDY

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**Background:** Dysphagia represents a major burden in IIM patients. OPES is a safe, reliable and repeatable technique, which allow a semi-quantitative scoring of oropharyngeal (OP) and esophageal (E) involvement. OPES is widely used in neuromuscular diseases and could replace other traditional imaging techniques, such as esophageal x-ray, which is difficult to repeat, allows only qualitative examination and exposes patients to risk of aspiration pneumonia.

**Objectives:** The primary aim of our study was to explore prevalence of upper gastrointestinal abnormalities in IIM using OPES. Secondary aim was to correlate the presence of alterations detected by OPES with disease activity and dysphagia in IIM patients.

**Methods:** Twenty-eight IIM patients were enrolled (M:F=3:25; 11 dermatomyositis, 15 polymyositis, 2 inclusion body myositis; mean age: 60±14.7 years; mean disease duration: 52±44 months). Each patient underwent a disease activity evaluation: physician's and patients' visual analogue scale (phVAS and ptVAS), health quality assessment questionnaire, manual muscle test 8 (MMT8) and serum creatine kinase. Dysphagia was assessed by a validated patients reported outcome questionnaire, the "MD Anderson dysphagia inventory" (MDADI), which classifies dysphagia as not present, mild, moderate, severe and total disability.

Dysphagia parameters, assessed by OPES after 10 ml liquid (L) or semi-solid (SS) bolus labelled with 99mTechnetium-nanocolloid intake, were: pre-deglutition penetration, aspiration, OP and E transit time and retention index (RI). OP-RI was classifiable by a 4 grade scale: no retention (<8% of the swallowed bolus), mild (9–20%), moderate (21–40%) and severe retention (>40%), while E-RI was classifiable by a 3 grade scale: no retention (<20%), mild (20–45%) and severe retention (>45%).

**Results:** According to MDADI score, 10 patients (36%) presented no dysphagia, 12 (43%) mild, 4 (14%) moderate and 2 (7%) severe disability.

OPES showed a normal OP and E transit time in all patients.
OP-RI or E-RI were altered in almost all patients, and, both after L and SS bolus, RI was altered in 25 patients. In the 10 patients with no dysphagia symptoms, IR alterations for L and SS bolus were detected respectively in 9 and 7 patients.
Correlations with statistical significance between disease activity parameters and MDADI index were found for phVAS and ptVAS ($p$=0.032 and $p$=0.017) and MMT8 ($p$=0.014), while E-RI correlated with MMT8 ($p$=0.007).
Moreover, 13 patients presented uncoordinated movement at proximal and medium esophagus and 2 patients presented SL bolus inhalation. No patients presented pre-deglutition penetration.
**Conclusions:** Dysphagia represents a major disabling feature in 64% of IIM patients and is associated with disease activity. From the clinical point of view, OPES allows to identify subclinical involvement in almost all patients examined, even if no symptoms were reported by the patients. Greater sample size and, above all, prospective clinical follow-up will clarify the clinical meanings of the alterations detected by OPES and their prognostic value.
**Disclosure of Interest:** None declared
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## AB0642 LARGE VESSEL INVOLVEMENT IN LIMITED AND DIFFUSE SYSTEMIC SCLEROSIS: A PULSE WAVE VELOCITY STUDY

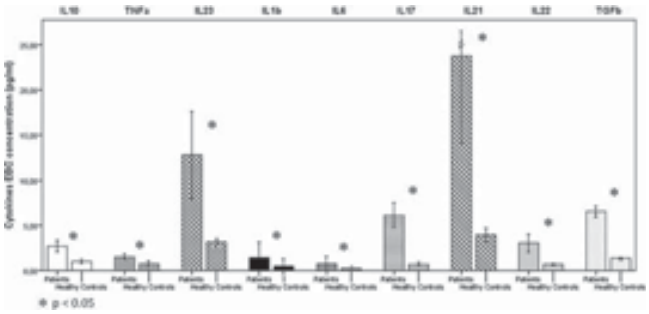
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**Background:** Systemic Sclerosis (SSc) is a chronic inflammatory autoimmune disease of the connective tissue characterized by vasculopathy and progressive fibrosis thickening of the skin and internal organs. Vascular damage is recognized as a diagnostic landmark in SSc, both in its limited and diffuse form. Micro- and macro-vascular damage have been involved in the pathology; early detection may be helpful in therapeutic planning and management. Subclinical cardiac damage can be detected with transthoracic echocardiography (TTE) while arterial stiffness can be measured by Pulse wave velocity (PWV). Both have been shown to have an independent predictive value in cardiovascular risk stratification. However it is not yet clear whether they are actually present and detectable in SSc patients, or if an association with a specific subtype exists (1).
**Objectives:** to evaluate the presence of subclinical cardiac organ damage in patients with limited and diffuse SSc, in comparison with a cohort of healthy individuals.
**Methods:** Patients with limited and diffuse SSc referred to the Rheumatology Unit in our Hospital, in according to 2013 ACR/EULAR Classification Criteria, were enrolled. The study was conducted in accordance with the Declaration of Helsinki and approved by our Ethics Committee. All patients underwent a complete transthoracic echocardiogram, and PWV evaluation, which were performed in agreement with the last International Guidelines (2). Past medical history and risk factors, clinical and biochemical data were collected. 23 healthy subjects, similar for demographic characteristics, were used as controls.
**Results:** 41 patients (35 female,age 56.9±13.6 years), 21 with diffuse and 20 with limited SSc were recruited. Past medical history, cardiovascular risk factors, gender distribution and disease duration were similar in the two subgroups with no statistically differences. Patients with limited SSc were mean of 10 years older than patients with diffuse SSc. TEE parameters – left ventricular remodeling, atrial enlargement, diastolic disfunction - and hemodynamic indexes – PWV (6.5 [6;6.8] vs 7.0 [6.2;8.5], p=0.24) and Augmentation index (145.6±14.2 vs 149±20.6,p=0.52) did not show significant difference. Indeed, in the regression analysis, PWV was correlated to age (rho=0.60,p<0.001). When compared with healthy controls, again no significant difference emerged, considering echocardiographic and hemodynamic indexes.
**Conclusions:** In SSc, PWV seems to increase in according to age, with no additional impact of the specific pathology nor subtype. Vascular damage in the SSc population is likely not reflected in increased arterial stiffness or subclinical cardiac damage. Evaluation of SSc patients with PWV and TEE should not be routinely performed.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3845

## AB0643 TH-17 CYTOKINES AND INTERSTITIAL LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS

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**Background:** T Helper 17 (Th17) cytokines play an important pathogenetic role in most of autoimmune diseases, but their role in lung impairment in systemic sclerosis (SSc) is still poorly known.
**Objectives:** We aim to evaluate whether Th17-related cytokines are detectable in serum and in exhaled breath condensate (EBC) of patients affected by SSc and whether their concentrations are related to clinical parameters of lung impairment in diffuse SSc.
**Methods:** The outpatients with SSc according to ACR criteria attending Clinic of Rheumatic Disease, Città della Salute e della Scienza in Turin, between May 2014 and March 2015 were enrolled into the study, as well as a group of healthy non-smokers subjects, enrolled as controls. The study was approved by ethical committee and each patient released his informed consent; smokers, patients with asthma, COPD, history of cancer or other autoimmune diseases, current corticosteroids or immunosuppressive drugs therapy, recent (last 8 weeks) or current airway or systemic infection were excluded from the study. All patients underwent pulmonary function tests: spirometry, flow-volume curves, residual volume and diffusing capacity of the lung for carbon monoxide (DLCO), thoracic CT-scan analysed according to Global Warrick score and six minutes walking tests (6MWT). EBC and blood samples were collected in all the patients and controls. Serum and EBC Th-17 related cytokines (IL-17A, IL-21, IL-22, IL-23, IL-1β), TGF-β, TNF-α, IL-6 and IL-10 were measured using an xMAP technology and analysed by a multiplex immunoassay.
**Results:** 29 outpatients affected by SSc were enrolled, as well as 20 healthy controls.
17 patients (1 male) were affected by limited SSc (lSSc) and 12 (no men) were affected by diffuse SSc (dSSc); the mean age was 64.5±15.5 yrs. All serum cytokines were significantly higher in patients than in controls ($p<0.05$), except for IL-1β (p=0.063) and TGF-β (p=0.900); all EBC cytokines were significantly higher in patients than controls ($p<0.05$). No difference in serum cytokines concentrations was observed between lSSc and dSSc, while all Th17-related cytokines in EBC were significantly higher in dSSc than in lSSc ($p<0.05$).
In dSSc, serum IL-10 levels were significantly correlated with CT Global Warrick score (p=0.007, r=0.730), with DLCO (r=-0.664, p=0.018) and with 6MWT (r=-0.857, p=0.001).
Serum TNF-α and IL-23 levels significantly correlated with the CT Global Warrick score (r=0.699, p=0.011 and r=0.659, p=0.020 respectively) and IL-23 also correlated with FVC (r=-0.578, p=0.049). In EBC, IL-1β significantly correlated with CT Global Warrick score (r =0.434, p=0.016) and with DLCO (r=-0.492, p=0.007), while IL-17 negatively correlated with DLCO (r=-0.394, p=0.042).




**Conclusions:** In conclusion, our results show a correlation between Th-17 cytokines measured in serum and in EBC, with interstitial lung involvement of patients with diffuse SSc, underlining the importance of targeting these cytokines in the development of new therapeutic approaches against lung fibrosis.
**Disclosure of Interest:** None declared
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## AB0644 SUBCLINICAL HEARING LOSS IN SYSTEMIC SCLEROSIS PATIENTS: RELATION TO DISEASE SEVERITY

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**Background:** Systemic sclerosis (SSc) is one of the most complex systemic autoimmune diseases[1]. Ear involvement is not uncommon and should be taken into consideration during diagnostic and therapeutic procedures of SSc[2]
**Objectives:** The aim of the present study was to assess hearing in asymptomatic SSc patients and correlate the findings with clinical characteristics and disease severity.

**Methods:** The study included 35 female SSc patients and 35 matched controls. Skin thickness was assessed using modified Rodnan skin score (mRSS) and disease activity by Medsger severity score (MSS). Audiological tests including pure tone audiometry, speech audiometry, impedance audiometry and auditory brainstem response (ABR) were performed
**Results:** The mean age of patients was 40.3±6.2 years, and disease duration 7.3±4.6 years. Mild bilateral symmetrical sensorineural hearing loss (SNHL) was present in 27/35 (77.1%) mostly at high frequencies. Hearing thresholds, pure tone average and speech reception threshold were significantly higher (p=0.001) in SSc patients than in control. In those with hearing loss, word discrimination score (WDS) was lower and ABR-I delayed compared to those without (p=0.001,p<0.0001 respectively) with consequently shorter inter-peak interval (IPI) I-III (p=0.01) and IPI I-V (p=0.004). In patients with hearing loss there was an increased frequency of acro-osteolysis (51.9%), telangiectasia (59.3%), arthralgia (70.4%) and peripheral neuritis (44.4%) compared to those with normal hearing. The MSS and mRSS significantly correlated with the high frequency hearing threshold and negatively with WDS. Audiometric parameters were comparable between patients with diffuse (n=14) and limited (n=21) cutaneous SSc.
**Conclusions:** Audiometric tests may detect subclinical SNHL mostly cochlear in SSc patients. The significant association between SNHL with telangiectasia and neuritis raises the likelihood that the SNHL may be due to an underlying vasculopathy or neuritis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1573

## AB0645 ANTI-SSA/RO ANTIBODIES IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS: THE ASSOCIATION WITH INTERSTITIAL LUNG DISEASE

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**Background:** Anti-SSa/Ro antibodies are among the common antibodies found in Systemic Sclerosis (SSc) patients (prevalence range 15–38%). Recent studies have suggested the association of anti-SSa/Ro with interstitial lung disease (ILD) as well as their prognostic role in SSc patients, however its definitive importance is yet to be determined.
**Objectives:** To determine the prevalence of anti-SSa/Ro antibodies in a cohort of SSc patients and its association with clinical and serological features.
**Methods:** Observational retrospective cohort study was performed including consecutive patients with clinical diagnosis of SSc (based on expert opinion) followed in our Rheumatology Department. Demographic, clinical and laboratorial data were obtained from clinical records. Lung involvement was considered if ILD was detected by an experienced radiologist in high-resolution computed tomography. Extractable Nuclear Antigen Antibodies, including ant-SSA/Ro, were measured in all the patients included, using enzyme-linked immunosorbent assay (ELISA) method. Patients with positive anti-SSa/Ro were compared with the other patients using Mann-Whitney, t-student, $\chi^2$ and Fisher tests (SPSS 23.0). Significance level was set as $<0.05$.
**Results:** 108 patients were included, 96 (90%) were females with a mean age of 58.2±12.8 years and a median disease duration of 6 years [0–38]. 12 (11%) patients had diffuse SSc and 96 (89%) limited SSc. Anti-SSa/Ro antibodies were present in 13 (12%) patients and were the third most common antibodies after anti-centromere (57%) and anti-Scl70 (20%). In the anti-SSa/Ro group, 11 (84.9%) were females and the mean age was of 61.1±12 years. Comparing to non-anti-SSa/Ro patients, both groups were similar regarding demographical data, disease duration and type of skin involvement. Anti-SSa/Ro group had more frequent SSc-Overlap syndromes (SSc-OS) (54% vs 15%, p=0.003). Anti-SSa/Ro group had significantly more frequent ILD (54% vs 18%, p=0.01) with no differences regarding the pattern of lung disease. No statistically significant differences were found regarding frequencies of myopathy, pulmonary hypertension, gastrointestinal, renal and cardiac involvement. There was a greater proportion of neoplasia and joint involvement in the anti-SSa/Ro group (23% vs 6% and 54% vs 27%, respectively), not reaching statistical significance. Anti-SSa/Ro patients had significantly more frequent anti-Scl70 antibodies (46% vs 17%, p=0.02) and Rheumatoid Factor (31% vs 6%, p=0.018), without differences regarding other antibodies. No differences in mortality were found between the groups.
**Conclusions:** Anti-SSa/Ro antibodies were among the most common antibodies in our cohort of SSc patients. Consistently with previous data, our study supports their association with SSc-OS and ILD without evidence for other clinical features. Finally, our study also demonstrates a greater proportion of anti-Scl70 antibodies in these patients.
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## AB0646 THE ROLE OF SERUM YKL-40 IN SYSTEMIC SCLEROSIS (SSC)

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**Background:** SSc is a refractory of connective tissue disease that causes fibrosis of the skin and various organs. 2013 ACR/EULAR classification criteria of SSc can diagnose early phase of skin involvement. Thus we considered that YKL-40 is known to be involved in inflammation, tissue fibrosis and remodeling, is an useful marker for evaluating early diagnosis and complications in SSc. YKL-40 is expressed in the synovial membrane and cartilage fibroblast cells in Rheumatoid Arthritis. However the relationship between SSc and YKL-40 is unclear.
**Objectives:** To clarify YKL-40 is useful marker in early diagnosis in the presence or absence of complications in Japanese SSc patients.
**Methods:** Study I: We measured serum level of YKL-40 by ELISA (Quantikine ELISA (R&D systems) ®) in 16 healthy controls and 26 SSc patients without complications: such as asthma, infection, diabetes, malignant disease, interstitial pneumonia (IP), pulmonary arterial hypertention (PAH), arthritis and other collagen disease. These complications may be increased YKL-40 levels. Study II: We measured serum level of YKL-40 by ELISA in 76 SSc patients: 42 patients without IP or PAH,17 patients with IP, 4 patients with PAH, 13 patients with IP and PAH. We were attention to IP and PAH complications as a factor involved in the prognosis in SSc.
**Results:** Study I: Serum YKL-40 levels were significant higher in SSc patients without complications than in healthy controls (77.3±15.8 vs 35.0±4.5ng/ml, P=0.01). On the other hand, there is no difference of YKL-40 levels due to gender, disease duration and disease type of SSc. Study II: Serum YKL-40 levels were significantly higher in SSc patients with IP and PAH than in SSc patients without IP and PAH (66.5±15.3 vs 193.4±45.3 ng/ml, P=0.01). Serum YKL-40 levels in SSc patients with IP was 92.9±28.5 ng/ml, and with PAH was 157.5±60.2 ng/ml.
**Conclusions:** We could show increase in serum YKL-40 levels with SSc excluding complications in Japan. In contrast, Montagna reported that serum YKL-40 levels in 40 SSc patients was median 75.5ng/ml (24.2–584) including the organ complications such as heart, lung, kidney, arthritis and high CRP cases (median 0.4mg/dl, 0.3–7.5). The Complications and other factors may be influent to level of serum YKL-40. And, Nordenbaek reported SSc patients with elevated serum YKL-40 had shorter survival than patients with normal serum YKL-40 and died more often due to extensive interstisial or vascular fibrosing processes. However, there is no report on YKL-40 in SSc patients with PAH. We thought that the measure of serum YKL-40 levels in SSc patients with organ complications such as IP and/or PAH is very useful marker. We showed that YKL-40 levels are useful marker in early diagnosis of SSc with or without complications.
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## AB0647 DISEASE SUBSETS, AUTOANTIBODIES AND CLINICAL FEATURES IN 176 ADULT ITALIAN PATIENTS WITH SYSTEMIC SCLEROSIS: A CROSS SECTIONAL STUDY

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**Background:** Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by vascular changes and progressive fibrosis of skin and various internal organs. A variety of circulating autoantibodies have been detected in SSc. Some of them are well-established tools strongly associated with SSc and useful for diagnosis and management of the disease (e.g. ANA, anti-centromere, anti-topoisomerase I, anti-RNA polymerase III – RNAP III). Other autoantibodies are less frequent and non-specific for SSc even if potentially useful to better assess clinical subsets and prognosis (e.g. anti-Th/To, anti-Ku, anti-PM/Scl).
**Objectives:** To investigate the prevalence of anti-Th/To, anti-Ku, anti-RNAP III and anti-PM/Scl antibodies as well as to study the associations between these antibodies and clinical features in Italian SSc patients.
**Methods:** Sera from 176 consecutive patients with SSc collected at two Italian sites were tested for anti-Th/To (anti-Rpp25 and anti-Rpp38), anti-Ku, anti-RNAP

III, anti-PM/Scl, and anti-centromere antibodies (anti-CENP-A and B) using QUANTA Flash chemiluminescence immunoassays (CIAs) on the BIO-FLASH instrument (Inova Diagnostics, San Diego, USA). Additionally, ANA screening was performed using QUANTA Flash CTD Screen Plus which includes the most relevant nuclear/cytoplasmic antigens. The Italian cohort included: women 162 (92%), limited cutaneous (lc-SSc) subtype 137 (78%), patients with present or past history of digital ulcers 56 (32%), calcinosis 25 (14%), lung fibrosis 69 (39%), heart involvement 22 (12.5%), pulmonary arterial hypertension 11 (6%) and esophageal involvement 84 (48%).
**Results:** 152 (86.4%) patients were CTD Screen Plus positive, 8 (4.5%) anti-Th/To positive, 8 (4.5%) anti-Ku positive, 20 (11.4%) anti-RNAP III positive, 0 (0%) anti-PM/Scl positive, 70 (39.8%) anti-CENP-A positive, and 87 (49.3%) anti-CENP-B positive. Anti-CENP-A, anti-CENP-B and anti-Ku antibodies were significantly associated with the lc-SSc subtype ($p<0.0001$, $p<0.0001$ and $p=0.0469$, respectively). None of patients positive for anti-Ku antibodies displayed digital ulcers ($p=0.0075$). Anti-Th/To (Rpp25) antibodies were associated with the presence of calcinosis ($p=0.0399$) while anti-RNAP III antibodies with its absence ($p=0.0353$). All patients positive for anti-Th/To were positive for the Rpp25 component while only one of them was also positive for the Rpp38 component.
**Conclusions:** The present study points out the low prevalence of anti-RNAP III and highlights a lower prevalence of anti-Th/To in Italian SSc patients. Several known associations between autoantibodies as SSc subsets have been confirmed while others could not be verified in the study. This supports the potential utiliy of autoantibodies to stratify SSc into clinical subsets. Large international multi-center studies are required to define and validate rare autoantibodies such as anti-Th/To, anti-Ku and anti-PM/Scl antibodies.
**Disclosure of Interest:** None declared
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## AB0648 ANTICENTROMERE ANTIBODIES: CLINICAL SIGNIFICANCE IN A LARGE COHORT OF PATIENTS WITH A LONG FOLLOW-UP

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**Background:** The presence of anti-centromere antibodies (ACA) has been associated with limited cutaneous systemic sclerosis (lcSSc), primary biliary cirrhosis (PBC), Sjogren's syndrome and less frequently with other autoimmune diseases (AID). However, given the low prevalence of ACA (<3% of positive ANA), the series published to date have included few patients and with little follow-up, so there have been mixed results (1, 2).
**Objectives:** The aim of the study was to establish the clinical significance of ACA in a large group of patients with a long follow-up.
**Methods:** The study was conducted at six affiliated University hospitals on all patients with positive ACA by indirect immunofluorescence on Hep-2 cells, between January 2011 and December 2014. Subsequently, the date of the first positive determination to ACA was identified in the patient's electronic file. Low titers of ACA were considered when the highest value was 1/320. Only those who have 2 or more positive determinations were included. All laboratory tests, echocardiography, CT of the chest and the final diagnosis were carefully reviewed.
**Results:** A total of 308 patients were studied, 269 were women (87%). The mean age was 70.21±13.5. The mean follow-up from the first determination of positive ACA was 125.43 months (range 11–276). High titers of ACA (>1/1280) were recorded in 94.5% of patients. The ACA was the only positive antibody in 219 patients (71.1%). On the other patients the associated antibodies were: AMA 15%, anti-Ro 6%, ASMA 2.2%, anti-Scl 70 1.5% and anti-gastric parietal cell in 2.9%. Regarding the diseases diagnosed in ACA patients: 57% had systemic sclerosis most of them lcSSc, 11% PBC, 6.6% Raynaud without systemic manifestations, 3% Sjogren's syndrome, 3% Arthritis, 2% Autoimmune hepatitis (AIH). Also, there was a 5.9% (17 patients) with overlap syndromes (lcSSc + PBC; AIH + PBC; AIH + Rheumatoid arthritis). Of the 175 patients with lcSSc 16% had pulmonary arterial hypertension, 10% interstitial lung disease and 5% suffered from digital ulcers. No autoimmune disease was diagnosed during the follow-up in 65 patients (21%). Among the 14 patients with low titers of ACA only 28.6% had AID.
**Conclusions:** The presence of anticentromere antibodies were associated with a high likelihood of developing anautoimmune dise ase (80%) mainly limited cutaneous systemic sclerosis, so these patients should be adequately evaluated and followed. However, low titers of ACA decrease the frequency of associated autoimmune diseases.
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**Disclosure of Interest:** None declared
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## AB0649 CLINICAL AND IMMUNOLOGICAL FEATURES OF PATIENTS WITH ANTI-PM/SCL ANTIBODIES: A RETROSPECTIVE STUDY OF 17 CASES

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**Background:** The PM/Scl autoantigen, which is currently known as the 'human exosome', is a macromolecular complex that consist of up to 16 proteins located primarily in the nucleolus and is involved in RNA processing and degradation. It has 2 major antigenic determinants called PM/Scl-100 and PM/Scl-75 based on their molecular weights. Anti-PM/Scl antibodies were initially reported in patients with systemic sclerosis (SSc)-polymyositis (PM) overlap syndromes but they are associated with a wide variety of autoimmune diseases including isolated SSc, PM, dermatomyositis (DM) and interstitial lung disease (ILD), and less frequently with systemic lupus erythematosus, primary Sjögren's syndrome (pSS) and undifferentiated connective tissue disease (UCTD).
**Objectives:** To describe the clinical and immunological features of PM/Scl-positive patients treated in a Spanish tertiary center.
**Methods:** We performed a retrospective study of patients with PM/Scl-100 and PM/Scl-75 positive antibodies seen in our center during the period 2007–2015. Positivity for these antibodies was detected by line immunoassay and confirmed by indirect immunofluorescence. Demographic and clinical data were obtained through review of their medical records.
**Results:** 17 anti-PM/Scl-positive patients were found during the study period, 12 of them women (70.6%) with a mean age at diagnosis of 57.5 years (range: 38–82). Positivity PM/Scl-75 was detected in 8 cases, for PM/Scl-100 in 4 cases and simultaneously for both antibodies in 5 cases. The diagnoses of these patients were: limited cutaneous SSc in 3 cases, SSc-PM overlap 2, SSc-DM overlap 1, isolated PM 1, isolated DM 1, unspecified myositis 3, isolated ILD 2, pSS 1, UCTD 1 and mitochondrial myopathy 1. The most common clinical manifestations were dyspnea (41.2%), Raynaud's phenomenon (RP) (35.2%), muscle weakness (29.4%), hand edema (23.5%) and arthralgia (23.5%). Three patients developed digital ulcers, 2 'mechanic's hands' and Gottron's papules and 1 calcinosis. No differences in clinical manifestations between PM/Scl-75 and PM/Scl-100 were found. ILD was diagnosed in 8 cases (47.1%) with radiological pattern of usual interstitial pneumonia in 2 cases, nonspecific interstitial pneumonia 2, organizing pneumonia 1, lymphocytic interstitial pneumonia 1 and no characteristic pattern 2. The acute phase reactants (erythrosedimentation rate, C-reactive protein) were elevated in 58.8% and muscle enzymes in 41.2% (creatine kinase mean value 658 IU/L, range: 184–1758), 4 cases had lymphopenia and 6 hypergammaglobulinemia. The antinuclear antibodies were positive in 13 patients, anti-Ro/SSA in 4 and anti-centromere, anti-SRP, and anti-Ku in 1 case each. None of the patients died or developed malignancy (mean follow-up: 70.6 months).
**Conclusions:** The patients in our series presented a heterogeneous clinical profile similar to other series in the literature and the most common manifestations were ILD, RP and myositis. Anti-PM/Scl antibodies have been traditionally associated with overlap syndromes, but we found a wide variety of diagnoses in our cases. Despite the high incidence of ILD in anti-PM/Scl-positive patients, the presence of these antibodies seems to be associated with good prognosis and infrequent development of malignancies.
**Disclosure of Interest:** None declared
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## AB0650 SURVIVAL AND ORGAN INVOLVEMENT IN PATIENTS WITH LIMITED CUTANEOUS SYSTEMIC SCLEROSIS AND ANTI-TOPOISOMERASE ANTIBODIES

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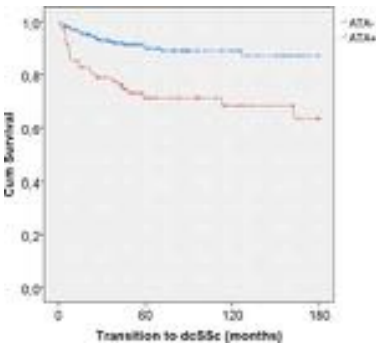
**Background:** In systemic sclerosis (SSc) there are two main subgroups based on skin involvement: limited cutaneous systemic sclerosis (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc). LcSSc is associated with the presence of anti-centromere antibodies (ACA) and a more subtle disease course, whereas dcSSc is associated with anti-topoisomerase antibodies (ATA) and often a more severe disease course. Nevertheless, despite the associations between clinical subtype and autoantibodies, there are quite a number of SSc patients who have limited skin involvement and antibodies associated to diffuse skin involvement (ATA). The question is whether these patients have a disease more like lcSSc or more like dcSSc.
**Objectives:** The aim of this study is to determine whether survival and organ involvement in lcSSc patients who are ATA positive are similar to lcSSc ATA negative patients or to dcSSc ATA positive patients. Furthermore, the relation between ATA positivity and time to transition from lcSSc to dcSSc was evaluated.

**Methods:** Data from The Nijmegen Systemic Sclerosis cohort were used. Survival analysis was performed to show cumulative survival and time to event for Interstitial Lung Disease (ILD), Pulmonary Arterial Hypertension (PAH), cardiac involvement, Scleroderma Renal Crisis (SRC), and transition to lcSSc. Cox proportional hazard modelling was performed to adjust for confounders.
**Results:** Survival up to 15 years of follow-up was highest in lcSSc ATA positive patients, whereas dcSSc ATA positive patients had lowest survival (table 1). Interstitial Lung Disease (ILD) occurred more frequently in lcSSc ATA positive patients compared to lcSSc ATA negative patients. However, a higher frequency of ILD was seen dcSSc ATA positive patients. No significant differences were seen between the four (table 1) subgroups in occurrence of PAH, cardiac involvement and SRC. At the moment of diagnosis, 343 patients were classified as lcSSc and 48 of these patients evolved from lcSSc to dcSSc, 24 (9%) in the ATA negative subgroup and 24 (29%) in the ATA positive subgroup (figure 1).

Table 1. Organ involvement and death during follow up

| | Total | lcSSc | | dcSSc | | p-value |
|---|---|---|---|---|---|---|
| | | ATA+ | ATA– | ATA+ | ATA– | |
| Death (%) | 85 (18.5) | 6 (10.3) | 44 (18.6) | 17 (21.8) | 18 (20.7) | 0.334 |
| Death or ASCT (%) | 102 (22.2) | 6 (10.3) | 44 (18.6) | 30 (38.5) | 22 (25.3) | <0.001 |
| ILD (%) | 131 (35.9) | 20 (48.8) | 48 (24.7) | 35 (60.3) | 28 (38.9) | <0.001 |
| PAH (%) | 32 (7.5) | 4 (7.0) | 21 (9.8) | 5 (6.7) | 2 (2.5) | 0.199 |
| Cardiac Involvement (%) | 49 (11.0) | 6 (11.1) | 19 (8.2) | 13 (17.1) | 11 (13.3) | 0.158 |
| SRC (%) | 14 (3.1) | 0 (0.0) | 3 (1.3) | 4 (5.3) | 7 (8.5) | 0.003 |

ILD: interstitial lung disease, PAH: pulmonary arterial hypertension, SRC: Scleroderma renal crisis, ASCT: autologous stem cell transplantation.




**Conclusions:** This study showed that lcSSc ATA positive patients differ from lcSSc ATA negative patients and dcSSc ATA positive patients concerning both survival and occurrence of ILD. Therefore, in everyday clinical practice, the prognosis of lcSSc ATA positive patients should be considered separately.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2842

## AB0651 USEFULNESS OF NEUTROPHIL TO LYMPHOCYTE RATIO IN PREDICTION OF LUNG INVOLVEMENT IN PATIENT WITH SYSTEMIC SCLEROSIS

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**Background:** Both neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte (PLR) are reported to be increased in various inflammatory diseases, but there clinical significance in systemic sclerosis (SSc) remains unclear
**Objectives:** The aim of the study is to evaluate usefulness of neutrophil to lymphocyte ratio in diagnosis of systemic sclerosis and in prediction of lung involvement such as pulmonary fibrosis.
**Methods:** The medical records of 88 SSc patients and 50 healthy controls were retrospectively reviewed. NLR, PLR between SSc patients and healthy controls were compared, and correlation between these indexes and lung involvement were analyzed. Exclusion criteria included active infection and/or the presence of any hematological, cardiovascular or metabolic disorder.
**Results:** The NLR and PLR were found to be significantly higher in SSc patients when compared to the healthy control (NLR: 3.95±6.59 vs 2.00±1.07, $p<0.01$, PLR: 163.87±101.12 vs 126.33 ±42.31, $p<0.05$). SSc patients with lung involvement had higher NLR and PLR levels than those without lung involvement ($p<0.01$, $p<0.05$). NLR was negatively correlated with forced vital capacity (FVC)(r=-0.341, $p<0.01$) but not diffusing capacity for carbon monoxide (DLCO). Receiver-operating characteristics analysis (ROC) of NLR to predict lung involvement in SSc showed that the area under the curve (AUC) was 0.763. The cut-off NLR value for prediction of lung involvement was determined as 2.59. (sensitivity, 0.700;specificity, 0.729; $p<0.01$)
**Conclusions:** NLR may be a promising marker that reflects lung involvement in patients with SSc and values greater than 2.59 were useful in prediction of lung involvement.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3384

## AB0652 GRANULOMATOSIS AND INFLAMMATORY MYOPATHY: CLINICAL SEROLOGICAL PATHOLOGICAL FEATURES AND PROGNOSIS

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**Background:** Case reports and short series ($n<7$) suggested that granulomatosis may be found in various inflammatory myopathies (IM) subtypes [1] but the clinical significance of this association is unanswered.
**Objectives:** To study clinical significance of granulomatosis in IM patients.
**Methods:** Patients with non-caseating granuloma (muscle or other tissue) were first identified among a monocentric cohort of 291 patients diagnosed with IM. 20 rheumatology and internal medicine practitioners were also contacted by electronic letters and asked to report their observations. Clinical, biological, histological features and evolution were retrospectively studied using a standardized questionnaire and compared with a control group of 14 randomly selected patients suffering from IM without identified granulomatosis.
**Results:** 14 IM patients with granulomatosis with a median follow-up of 77 months were included. Age at IM diagnostic was 54 years (16 to 70). Granuloma was identified 44 months before IM (23 years before to 4 after) in muscle (n=5), lymph node (n=5), skin (n=2), liver or spleen (n=1) tissues. Angiotensin converting enzyme amount was 114U/l (48 to 168).
7 patients (4 women, 57±14 years at IM diagnosis) were categorized as a defined IM subset because of typical histological and/or immunological features: antisynthetase syndromes (n=3), polymyositis (n=1), scleromyositis (n=1), dermatomyositis (n=1), inclusion body myositis (sIBM, n=1). These patients mostly presented with proximal weakness (n=6/7). Mean CK level was 780±390U/l. None had granumola in muscle biopsy. Extra-muscular involvements were arthralgia (n=4), interstitial pneumonia (n=4), mechanic's hand (n=1) and Raynaud's phenomenon (n=1). Patients received corticosteroids and meanly one another immunological drug (n DMARDs=1±0,8) with effectiveness except for the sIBM patient. None of these features was significantly different from the control group.
7 patients (4men, 54±12 years) did not met definitive criteria of a specific myopathy. As compared with the control group, they presented more often with distal weakness (n=3/7, p=0.002) and had lower CK level (260±56 vs. 2028±600U/l, p=0.006). Muscle biopsy most frequently revealed granuloma (n=5). Other lesions were endomyosial inflammatory cell infiltration (n=4), fibers atrophy (n=4), rimmed vacuoles (n=2). The patients experienced polyarthralgia (n=4), interstitial pneumonia (n=3), Raynaud (n=2). Despite a higher number of DMARDs as compared with the control group (2.7±0.4 vs. 1.3±0.2, $p<0.05$) and the patients with granolumatosis and defined IM ($p<0.05$), absence of muscle improvement was more frequent (n=5/7).
**Conclusions:** Half of IM patients with granulomatosis match diagnostic criteria for IM subtypes without clinical particularity aside from the granuloma. The unclassified others patients are characterized by an sIBM-like phenotype with distal weakness, low CK level and frequent unfavorable response to immunomoduling therapy despite not meeting criteria for definite sIBM. Clinicians should pay attention to auto-antibodies and muscle histology to tailor the care of IM patients with granulomatosis, which do not represent a homogeneous group.
**References:**
[1] Kenji Sakai,"Inclusion Body Myositis with Granuloma Formation in Muscle Tissue", Neuromuscular Disorders no9 (Sept 2015): 706–12.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1549

## AB0653 GASTRIC ANTRAL VASCULAR ECTASIA IN SYSTEMIC SCLEROSIS PATIENTS: LONG-TERM PROGNOSIS AND TREATMENT

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**Background:** Gastric antral vascular ectasia (GAVE) is characterized by a pathognomonic endoscopic pattern, mainly represented by red spots either organized in stripes radially departing from pylorus, defined as "watermelon stomach", or arranged in a diffused-way, the so called "honeycomb stomach". In

our previous work we found a prevalence of GAVE in 35% of systemic sclerosis (SSc) patients that had an upper gastrointestinal (GI) endoscopy for evaluation of symptoms. The main complication of GAVE is symptomatic anemia due to GI bleeding requiring blood transfusion. As the pathogenesis is unknown, the aim of the therapy is to decrease GI bleeding. Endoscopic therapy (endotherapy) is the mainstay of treatment with surgery reserved for severe refractory cases. The data on the efficacy of endotherapy and treatment requirements of SSc patients with GAVE is very limited.
**Objectives:** The aim of our study is to assess the treatment requirements of SSc patients with GAVE and the efficacy of endotherapy in particular.
**Methods:** Retrospective analysis of a prospectively maintained database of SSc patients followed in a tertiary referral center for SSc. Our cohort is part of the EUSTAR cohort. Statistical analysis: descriptive, student's T test, Mann-Whitney test.
**Results:** Fifty SSc patients were diagnosed with GAVE. Seventeen patients (34%) suffered of symptomatic anemia and were treated with argon plasma coagulation (APC) for a mean (SD) of 4.5 (4.3) sessions per patient. The mean (SD) hemoglobin was 9.4 (1.7) gr% in the group who required endotherapy compared to 11.5 (1.3) in the group which did not need any intervention. Four patients needed more than 6 sessions of treatment. Mean (SD) follow up was 4.1 (2.4) years. Nine patients required a total of 73 packed blood cells units and another 4 had intravenous iron replacement. Four patients died during the first 2 years after diagnosis, none of them due to bleeding complications. None of the patients that survived more than 2 years required further endotherapy or blood transfusions. No significant complications of APC occurred. Interestingly, all those who survived,had received immunotherapy with cyclophosphamide or mycophenolate mofetil due to multisystem involvement and disease activity.
**Conclusions:** Long term survivors among SSc patients with GAVE had an excellent response to APC and did not require blood transfusions or endotherapy after 2 years follow up. All the long term survivors received immunotherapy. This observation might hint to the pathogenesis of GAVE in SSc.
**Disclosure of Interest:** None declared
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## Spondyloarthritis - treatment

### AB0654 DRUG SURVIVAL AND SWITCHING RATE OF TNF INHIBITORS IN A COHORT OF PATIENTS WITH ANKYLOSING SPONDYLITIS WITH LONG TERM FOLLOW UP

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**Background:** Although the efficacy of TNF inhibitors (TNFi) in ankylosing spondylitis (AS) is well established, their long term survival (>5 years), baseline prognostic factors for their discontinuation and switching rate have not been adequately studied in daily clinical practice.
**Objectives:** To estimate the long-term survival, switching rate of TNFi as well as to identify baseline predictors for drug survival in a cohort of patients with AS in real life settings.
**Methods:** A retrospective systematic chart review of all AS patients treated with TNFi in our Rheumatology Unit from 1/1/2003 to 31/12/2015 was performed. Demographic, clinical and laboratory data were collected and analyzed. Drug survival was estimated by Kaplan-Meier analysis. The impact of several covariates on drug survival was analysed by Cox regression.
**Results:** 103 AS patients who had received etanercept (ETN, n=41), infliximab (INF, n=33), adalimumab (ADA, n=21), golimumab (GOL, n=7) or certolizumab pegol (CZP, n=1) were included. Patients were predominantly males (67%, n=69) with a mean age of 45±11.8 years and a median disease duration of 7 years. The patients were followed for a median time of 5 years (mean: 5.1±2.6 years). Peripheral arthritis was present in 42% (n=43) and extra-articular manifestations in 26.5% (n=27) of patients. The majority (94%, n=97) received TNFi as monotherapy. The mean overall survival of the first TNFi was 81.2±6.7 months (40% survival after 7 years). ADA demonstrated a longer survival (84±8.5 months) compared both to ETN (53±6 months, p=0.04) and INF (76±11 months, p=0.063). 43 patients (42%) discontinued the 1st TNFi due to adverse events (37%), inadequate response (35%) or other reasons (28%). 10% of patients were lost to follow up. No difference in discontinuation reasons was found among the different TNFi (p=0.125). 33 patients (32%) switched to a second TNFi (ADA: n=23, ETN: n=3, INF: n=3, GOL n=2, CZP n=1). Overall the retention to therapy was better for non-switchers compared to switchers' to a second TNFi (81.2±6.7 months vs. 42.8±7 months, p=0.086). Specifically for ADA, this difference was statistically significant (p=0.03). Among several baseline variables (age, disease duration, extra-articular manifestations, peripheral arthritis, HLA B27 status), none was predictive for therapy discontinuation. Although lower baseline CRP (HR=0.7, 95% CI: 0.5–1.3), longer disease duration (HR=1.1, 95% CI: 0.9–1.3), concurrent smoking (HR=4.9, 95% CI: 0.9–25) and male gender (HR=4.8, 95% CI: 0.8–26) were associated with higher risk for drug discontinuation, these did not prove to be statistically significant by multivariate analysis.
**Conclusions:** Only 40% of AS patients remain on their 1st TNFi 7 years after starting treatment. ADA demonstrated longer survival compared to ETN and INF as the 1st TNFi. Approximately one-third of patients switched to a 2nd TNFi which had a shorter survival compared to the 1st. In our patient cohort we did not identify any baseline predictors for longer drug survival.
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### AB0655 ANTI-TNF ALPHA DOSE REDUCTION IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Anti-Tumor Necrosis Factor (TNF)alpha drugs play a fundamental role in Ankylosing Spondylitis (AS) therapy. Nevertheless their use is associated to potential side effects, such as a higher frequency of infection, and high healthcare costs. On these bases, a dose reduction strategy (lengthening drug administration interval) is often attempted in clinical practice.
**Objectives:** 1) to retrospectively compare the features of anti-TNFalpha-treated AS patients who could lengthen the administration interval (group A) with those of patients who needed to maintain standard dosage (group B); 2) to evaluate the impact of dose reduction on infection frequency; 3) to evaluate cost-savings in group A.
**Methods:** All AS patients attending the spondyloarthritis outpatients clinic-Rheumatology Unit of University of Padova and of University of Rome "Tor Vergata" between January 2011 to April 2015 who were treated with anti-TNFalpha (infliximab, adalimumab, etanercept) at a standard dose for at least 6 months with a good control of disease activity (ASDAS <2.1) were prescribed a dose reduction regimen. Some patients were able to maintain the new regimen (group A), while others were not because of symptom flare-up (group B). Disease activity (ASDAS, BASDAI), inflammatory (CRP), functional and (BASFI) and metrologic (BASMI) indexes were recorded at baseline (t0), after 6 months (t6), then once a year (t12, t24, t36, t 48) for a 4-year follow-up.
**Results:** Data from 96 AS patients (25 females, 26.04%; mean age 47.62±13.39 years) were examined. Drug administration interval, which could be lengthened in 66 (68.75%) patients (group A) without flare-ups or functional worsening, was associated to an improvement in ASDAS [t0=2.1 (1.49) vs t48=1.00 (0.29); p<0.0001]; BASDAI [t0=39 (49.6) vs t48=9.5 (14); p<0.0001]; BASFI [t0=22 (35) vs t48=1 (11); p<0.0001]. At the end of the observation period (t48), group A showed better physical functioning and lower disease activity compared to group B [BASFI A vs B =1 (36.18) vs 17.5 (7.3), ASDAS 1 (0.3) vs 1.6 (1.15); CRP 2.15 (2.1) vs 3.1 (7.3) mg/L]. At t0 group A had a less severe inflammatory status [CRP A vs B 2.9 (3.3) vs 4.7 (6.4) mg/L; p=0.0134], and a negative family history for spondiloarthritis (p=0.0318), while no significant difference was observed for smoking, psoriasis, peripheral arthritis, dactylitis, uveitis, enthesitis in more than 4 sites and HLA B27. The number of patients who developed infections during the observation period was significantly lower in group A (p=0,007); the average cost saving at t48 for group A vs group B was: 7.060 vs 14.820 € for infliximab; 6357 vs 13.260 € for etanercept; 11840 vs 12.917 € for adalimumab.
**Conclusions:** Lenghtening anti-TNFalpha administration interval appears to be a valid approach in patients with a less severe inflammatory status, and a negative family history of spondyloarthritis. Dose reduction regimen is associated to lower infection frequency and less expense for National Health Care System.
**References:**
[1] Arends S, van der Veer E, Kamps FB, et al. Patient-tailored dose reduction of TNF-α blocking agents in ankylosing spondylitis patients with stable low disease activity in daily clinical practice. Clin Exp Rheumatol. 2015;33:174–80.
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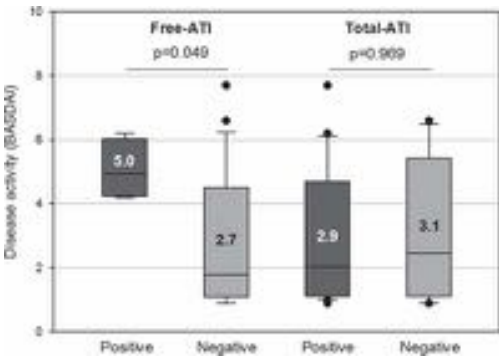
### AB0656 CLINICAL RELEVANCE OF MEASURING FREE VERSUS TOTAL ANTI-INFLIXIMAB ANTIBODIES IN PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** Antibodies to infliximab (ATI) are associated to loss of response, adverse effects and discontinuation of treatment in rheumatic patients[1]. However, the clinical relevance of measuring free versus total anti-drug antibodies (free plus drug-complexed antibodies) remains to be established.
**Objectives:** To analyse the association between the clinical response and ATI measured as free and total content of immunoglobulins in a cohort of patients with spondyloarthritis.
**Methods:** A retrospective pilot study was conducted including 12 patients with

spondyloarthropathies (9 ankylosing spondylitis (AS) and 3 spondyloarthritis (SpA)) under maintenance infliximab (IFX) therapy (3–5 mg/kg every 8 weeks). Disease activity was assessed by BASDAI score every 6 months. Trough serum samples were consecutively collected every two months during a follow up period of 1±0.1 years. In total 75 samples were collected (average of 6.3 per patient). Ten patients (83%) received concomitant therapy with methotrexate. IFX levels were measured with *Promonitor®-IFX* (Progenika-Grifols, Spain). Free and total-ATI were measured with *Promonitor® Anti-IFX* (Progenika-Grifols, Spain) (PR) and *IDKmonitor® Infliximab total ADA* (IDK) (Immundiagnostik, Germany) ELISA kits, respectively. Cut-point of PR and IDK ATI assays is 5 and 10 AU/mL, respectively. FDA guidance for comparing two diagnostic tests in the absence of a gold standard was followed[2].

**Results:** Five (41.7%) and (83.3%) patients were positive for free and total-ATI using PR and IDK assays, respectively. Overall, positive (PPA) and negative (NPA) percent agreements between the two assays were 52%, 16% and 100%, respectively. All samples with positive free-ATI (7) had undetectable IFX levels (0.0±0.0 μg/mL); however, 72% of total-ATI positive samples (43) were also positive for IFX levels (1.7±1.7 μg/mL, min 0.035 μg/mL and max 6.4 μg/mL). Both outcomes are coherent with the intended use of each kit, which also explains the low PPA. However, total-ATI are positive in 40% of the samples even when the patient responds (BASDAI<4), which questions the utility of total-antibodies in a clinical setting. This evidences a low clinical specificity of total-ATI measurement using the cut-off of 10 AU/mL recommended by the manufacturer and therefore that the presence of total-ATI in the presence of detectable drug has little utility. Patients without free-ATI had significantly lower BASDAI than patients with free-ATI (2.7±2.0 without antibodies vs 5.0±0.9 with antibodies, $p$=0.049), whereas no statistically significant difference was observed between patients when total-ATI were used (3.1±2.2 without antibodies vs 2.9±2.0 with antibodies, $p$=0.969) (Fig. 1).




**Conclusions:** Total-ATI do not correlate with disease activity in spondyloarthritis. The fact that many samples are positive to total-ATI even in patients with low disease activity makes very difficult interpretation of results. The explanation is that the fraction of ATI bound to IFX is not clinically relevant as long as there is free therapeutic drug in circulation.

**References:**

[1] Ducourau et al. Arthritis Res Ther 2011;13:R105
[2] Statistical guidance on reporting results from studies evaluating diagnostic tests. 2007.FDA

**Disclosure of Interest:** A. Ruiz del Agua Employee of: Employee of Progenika Grifols, J. Pascual Employee of: Employee of Progenika Grifols, N. Torres Employee of: Employee of Progenika Grifols, D. Pascual-Salcedo: None declared, A. Martínez: None declared, T. Jurado: None declared, C. Plasencia: None declared, A. Balsa: None declared, B. Ruiz-Argüello Employee of: Employee of Progenika Grifols, A. Maguregui Employee of: Employee of Progenika Grifols, A. Ametzazurra Employee of: Employee of Progenika Grifols, A. Martínez Employee of: Employee of Progenika Grifols, D. Nagore Employee of: Employee of Progenika Grifols

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## AB0657 DISCONTINUATION OF ANTI-TNF THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN CLINICAL PRACTICE: PREVALENCE AND CAUSES

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**Background:** The majority of patients with axial spondyloarthritis (SpA) response to anti-TNF therapy. However, discontinuation of this therapy due to different reasons is still a relevant problem. Currently, there is not enough data to know exactly which is the prevalence and causes of interruption of anti-TNF therapies in clinical practice.

**Objectives:** First, to evaluate the frequency and causes of discontinuating adalimumab or infliximab as the first anti-TNF in patients with axial SpA in clinical practice. Second, to investigate the influence of anti-drug antibodies (ADA) on these causes.

**Methods:** A total of 326 patients with axial SpA who had received adalimumab (34%) or infliximab (66%) as a first anti-TNF therapy were included in this retrospective, observational study performed in a tertiary hospital. Disease activity (BASDAI, ASDAS, CRP and ESR) was measured before starting anti-TNF therapy, after 6 months and when interrupting the therapy to assess properly whether the reason for discontinuation was primary or secondary failure. Serum drug levels and/or ADA were measured at 6 months visit and at the end of anti-TNF treatment.

**Results:** A total of 99 (30.4%) patients discontinued treatment. Mean (SD) under anti-TNF therapy until discontinuation was 2.5 (2.9) years. Characteristics of these patients when initiating anti-TNF therapy are shown in Table 1. The reason to interrupt treatment was: primary failure in 22.2%, secondary failure in 36.4%, side effects 32.3%), and other reasons in 9.1%. Serum drug levels and ADA were available in 83 patients. In most patients with ADA positive (14/17), the reason for discontinuation was secondary failure. Out of those patients who discontinued due to secondary failure, 38.9% had ADA positive.

| Demographic characteristics | Total (n=99) |
|---|---|
| Age (years) | 49.9 ± 11.9 |
| Sex (female) | 45 (45.5%) |
| BMI | 28.2 ± 5.1 |
| HLA-B27 positive | 50 (50.5%) |
| Disease duration (years) | 14.2 ± 8.5 |
| Drug levels 6 months | 39 (39.4%) |
| ADA levels 6 months | 12 (12.1%) |
| Drug levels endpoint | 53 (53.5%) |
| ADA endpoint | 25 (25.3%) |
| DMARDs | 50 (50.5%) |
| Baseline CRP | 10.2 ± 16.3 |
| Baseline ESR | 21.5 ± 18.9 |
| Baseline ASDAS | 3.1 ± 0.9 |
| Baseline BASDAI | 6,1 ± 1.9 |

**Conclusions:** In our cohort of patients with axial SpA treated with adalimumab/infliximab, 30% of patients discontinued anti-TNF therapy. The main reason to discontinue treatment was secondary failure, which was related to the presence of ADA in almost 40% of patients.

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## AB0658 INFLUENCE OF KNOWN RISK FACTORS ON SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS PATIENTS RECEIVING LONG-TERM TREATMENT WITH TNF INHIBITORS: RESULTS FROM THE GLAS COHORT

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**Background:** In ankylosing spondylitis (AS), the most important prognostic factor for spinal radiographic progression is the presence of syndesmophytes at study entry. In addition, male gender, older age, longer symptom duration, smoking, HLA-B27 positivity, and increased inflammatory markers were found to be associated with radiographic progression in AS.[1]

**Objectives:** To investigate the influence of known risk factors on spinal radiographic progression in AS patients receiving long-term treatment with TNF inhibitors.

**Methods:** Consecutive patients from the GLAS cohort receiving TNF inhibitors with baseline and biannual spinal radiographs untill 6 years of follow-up were included. Radiographs were scored in chronological time order by two independent readers according to the mSASSS. Single linear imputation of radiographic data was used in case patients had missing data at one or more intermediate follow-up visits. The influence of the earlier mentioned risk factors for radiographic progression was investigated using univariable and multivariable generalized estimating equations (GEE). Subsequently, radiographic progression

was modeled with different time functions (linear and non-linear) to provide the best fit for the data in patients with and without risk factors. A time function with $p \leq 0.05$ contributed significantly to the model and the estimated mean progression rates of the 2-year time intervals were calculated.

**Results:** Eighty patients were included; 70% were male, 78% HLA-B27+, mean age was 41±10 years, median symptom duration 14 (IQR: 8–24) years, mean BASDAI 6.0±1.7, mean ASDAS 3.8±0.8, and mean mSASSS 8.7±13.3.

During 6 years of follow-up, mean progression was 4.2±4.8 mSASSS units. GEE revealed that baseline syndesmophytes, gender, age, and symptom duration were significantly associated with radiographic damage over time. No significant associations were found for smoking, HLA-B27 status, and elevated CRP levels. The presence of baseline syndesmophytes was the only independent predictor for progression.

Baseline mSASSS was highest in AS patients with baseline syndesmophytes, male gender, age ≥40 years, and symptom duration ≥10 years. In these patients, mSASSS progression followed a non-linear course showing a reduction in estimated progression rates over time (Table 1). Most patients with syndesmophytes also had one or more other risk factors (e.g. male gender and symptom duration ≥10 years). A linear course with low estimated progression rates was found in patients without these risk factors (Table 1).

**Table 1.** Estimated mean spinal radiographic progression rates based on the best time model of AS patients (n=80) stratified for baseline risk factors.

| | | n | Baseline mSASSS | Best time model (linear or non-linear) | mSASSS progression scores 0-2 year | 2-4 year | 4-6 year |
|---|---|---|---|---|---|---|---|
| **Syndesmophytes** | **Yes** | 37 | 15.8 ± 14.9 | Non-linear | 2.8 | 2.5 | 1.6 |
| | **No** | 43 | 0.4 ± 0.8 | Linear | 0.4 | 0.4 | 0.4 |
| **Gender** | **Male** | 56 | 10.9 ± 14.6 | Non-linear | 1.8 | 2.1 | 1.2 |
| | **Female** | 24 | 3.5 ± 7.4 | Linear | 0.7 | 0.7 | 0.7 |
| **Age** | **≥40 years** | 43 | 12.3 ± 15.2 | Non-linear | 2.3 | 2.0 | 1.3 |
| | **<40 years** | 37 | 4.5 ± 9.1 | Linear | 0.9 | 0.9 | 0.9 |
| **Symptom duration** | **≥10 years** | 52 | 12.3 ± 15.2 | Non-linear | 2.3 | 2.0 | 1.3 |
| | **<10 years** | 25 | 2.1 ± 3.1 | Linear | 0.6 | 0.6 | 0.6 |

Values are presented as mean ± standard deviation; mSASSS: modified Stoke AS Spine Score.

**Conclusions:** In our cohort of AS patients receiving long-term treatment with TNF inhibitors in daily clinical practice, patients with known risk factors for radiographic progression (especially the presence of baseline syndesmophytes) showed the highest radiographic damage scores at baseline and the highest but reducing radiographic progression over time. In contrast, patients without these risk factors showed less baseline damage and low linear progression rates.

**References:**

[1] Arends S, et al. Curr Opin Rheumatol. 2014;26:259–68.

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## AB0659 EFFECT OF ETHNICITY ON RESPONSE TO ANTI-TNF BIOLOGIC THERAPY IN SEVERE ANKYLOSING SPONDYLITIS

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**Background:** Anti-TNF biological therapy has revolutionised management of Ankylosing Spondylitis (AS) however, variability in treatment response within the AS population exists and may possibly be influenced by ethnicity.

**Objectives:** To investigate the effect of ethnicity on treatment response to anti-TNF biologics by analysis of patient disease activity scores of severe AS patients by ethnicity.

**Methods:** Severe AS patients defined by a persistent Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of >4 and poor response to non-steroidal anti-inflammatory drugs (NSAIDs) were identified retrospectively from an anti-TNF therapy clinic database of patients treated by the Rheumatology Department between 2004 and 2014. Prescribed biologics were Infliximab, Etanercept, Adalimumab, Golimumab and Certolizumab. Patient clinical demographics and baseline BASDAI and spinal pain Visual Analogue Scale (VAS) scores from electronic records were collected pre-biologic treatment initiation and from 12 weeks post treatment follow-up. Data was analysed by non parametric descriptive statistics for changes in disease activity levels and compared by ethnicity. Adequate treatment effect was determined as a follow-up BASDAI score reduction with respect to the baseline of ≥2 units or 50% of the pre-treatment baseline score (BASDAI50) with a reduction of the spinal pain VAS by ≥2 cm. 99 of 256 available electronic records were complete at baseline and follow-up for BASDAI and corresponding VAS scores and were selected for analysis.

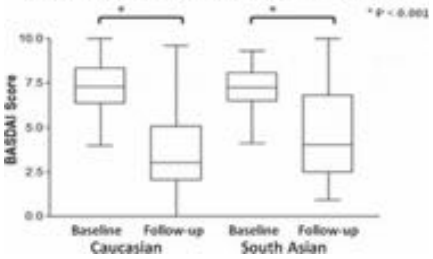
**Results:** Overall 59/99 (59.6%) of the 99 selected records achieved an adequate response. Interrogation of records by database ethnicity classifications showed the following groups to be present in the data set:

49: Caucasian – English, Scottish, Welsh, Irish, Any Other White Background
44: South Asian – Bangladeshi, Indian, Pakistani
3: Other Asian
1: Other Mixed
2: Other

By ethnicity an adequate response was achieved in:
36/49 (73.5%) of Caucasians,
20/44 (45.5%) of South Asians,
2/3 (66.7%) of the Asian other group,
1/2 (50%) of the Other group and 0/1 (0%) of the other mixed group.

Kruskal-Wallis multiple comparison testing showed statistical differences between baseline and follow-up mean BASDAI scores within Caucasian and South Asian ethnicities (*Figure 1).* Within the Caucasian group the baseline median=7.28 (IQR 6.3, 8.35), mean=7.31 (CI 6.92–7.70) versus follow-up median=3 (IQR 2, 5.1), mean=3.79 (CI 3.05–4.54). Within the South Asian subgroup the baseline median=7.25 (IQR 6.45, 8.06), mean=7.25 (CI 6.88–7.63) versus follow-up median=4.04 (IQR 2.45, 6.8) mean=4.62 (CI 3.8–5.44), both comparisons $P<0.001$. No significance was returned for comparisons between all ethnic groups at baseline and all at follow-up. "Other" group data subsets were too small to draw conclusions.

**Figure 1. Comparison of treatment response by ethnicity at baseline and 12 weeks post treatment initiation**




**Conclusions:** Therapy was efficacious in 59.6% of patients analysed. By ethnicity statistically significant BASDAI score improvements were achieved within Caucasian and South Asian populations respectively. Baseline scores between these ethnicities were similar however the patient proportion within each of these groups that achieved an adequate response was higher among Caucasians 73.5% versus 45.5% of South Asians. This preliminary study may suggest as yet undiscovered ethnic influences affecting treatment response that merits further investigation.

**Disclosure of Interest:** None declared

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## AB0660 PREDICTORS OF FLARE AFTER TAPERING ANTI-TNF THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** In most patients with axial spondyloarthritis (axSpA) achieving a clinical response after receiving standard dose of anti-TNF therapy, it seems possible to decrease anti-TNF dose without leading to flare of the disease. However, a minority of patients fails to this strategy and need to maintain standard dose of anti-TNF therapy in order to keep disease activity under control.

**Objectives:** To identify prognostic factors of flare after tapering anti-TNF therapy in patients with axSpA who achieve sustained clinical response with standard dose of this therapy.

**Methods:** This was a restrospective, observational study performed in a tertiary hospital. All patients with axSpA who had achieved sustained low disease activity for at least 6 months after receiving standard dose of a first anti-TNF drug and who had later decreased the dose of anti-TNF therapy were included. Low disease activity was defined as BASDAI <4 plus normal value of CRP. All patients were followed-up during 2 years after starting on tapering strategy. Collected data included: demographic (age, gender) and disease characteristics (HLA-B27, disease duration, peripheral involvement), smoking status, clinical disease activity measures (BASDAI, ASDAS, CRP) before starting and before decreasing anti-TNF therapy, time under anti-TNF therapy, concomitant treatment, and time in remission before tapering. Patients were followed-up during 2 years after tapering anti-TNF therapy. Flare was defined as BASDAI ≥4 plus elevated CRP (>5mg/L) and/or delta-BASDAI ≥2. To identify possible predictors of flare, univariable and multivariable logistic regression analyses were employed including all variables described within the collected data as independent factors.

**Results:** Fifty-three patients with axSpA receiving a tapering strategy after achieving low disease activity were included. Characteristics for these patients are presented in table 1. Four patients interrupted anti-TNF due to adverse effect before ending the study. In total, 8/49 patients (16%) had a flare during the 2-year follow-up period. In the univaribale analysis, only the age (OR=1.06; p=0.05), BASDAI before tapering (OR=2.64; p=0.01) and ASDAS before tapering (OR=4.12; p=0.08) were significantly associated with the occurrence of flare. In

| Characteristic | Mean ± SD/n (%) |
|---|---|
| Age years | 50.9±13.2 |
| Gender, males | 39 (74) |
| Smoking habit | |
| Non-smoker | 29 (57) |
| Smoker | 8 (16) |
| Past smoker | 14 (27) |
| Anti-TNF therapy | |
| Infliximab | 18 (34) |
| Adalimumab | 17 (32) |
| Etanercept | 14 (26) |
| Golimumab | 4 (8) |
| Time in remission before tapering, months | 16.9±12.6 |
| MTX pre-tapering | 13 (25) |
| SSZ pre-tapering | 18 (34) |
| BASDAI pre-tapering | 1.7±1.2 |
| ASDAS pre-tapering | 1.2±0.6 |
| CRP pre-tapering | 3.5±7.6 |

the multivariable analysis, only the BASDAI before tapering remained statistically significantly associated with flare (OR=2.39; p=0.03).
**Conclusions:** In patients with axSpA and sustained clinical response to anti-TNF therapy, a tapering strategy leads to flare in less than 20% of patients. The value of BASDAI before tapering anti-TNF therapy predicts the occurrence of flare. This may help us to select the appropriate patients and moment to implement a tapering strategy in patients with axSpA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3744

## AB0661 PREDICTORS OF RESPONSE IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH INFLIXIMAB OR GOLIMUMAB IN A REAL-WORLD SETTING

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**Background:** Recent studies have suggested that early and aggressive treatment of spondyloarthritis, including ankylosing spondylitis (AS) and psoriatic arthritis (PsA), may be associated with favorable patient outcomes, reducing synovial inflammation, delaying joint damage, and maintaining functional status.
**Objectives:** The objective of this analysis was to determine the predictive factors of ASDAS remission in AS patients treated with infliximab (IFX) or golimumab (GLM) in a Canadian routine clinical care setting.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis (RA), ankylosing spondylitis, or psoriatic arthritis with IFX or GLM. Eligible patients for this analysis included AS patients treated with IFX or GLM between 2005 and 2015. Variables associated with ASDAS remission (<1.3) were examined using univariate analysis and those showing a statistical trend (P<0.150) were considered in multivariate logistic regression analysis to identify independent predictors.
**Results:** A total of 582 patients were included in the analysis with a mean (SD) age of 45.8 (12.2) years and a disease duration of 8.3 (10.2) years. The majority of patients were male (57.2%). Upon 12 months of treatment statistically significant and clinically meaningful improvements were observed in ASDAS (3.6 vs. 2.3; P<0.001), BASDAI (6.2 vs. 3.8; P<0.001), BASFI (5.6 vs. 3.9; P<0.001), morning stiffness (74.2 vs. 42.8; P<0.001), and HAQ-DI (1.12 vs. 0.77; P<0.001). The proportion of patients who achieved ASDAS remission was 22.3% and 22.2% at 6 and 12 months, respectively. Sustained remission was achieved by 16.0%. In univariate analysis, male gender (male vs. female: 25.2% vs. 14.1%; P=0.073), previous use of a biologic (experienced vs. naive: 37.5% vs. 20.9%; P=0.129), lower ESR (P=0.096), lower BASFI (P=0.003), lower BASDAI (P=0.002), lower morning stiffness (P=0.120) and lower HAQ-DI (P=0.001) showed a statistical trend in their association with ASDAS remission at 12 months of treatment. Age, disease duration, CRP, psoriasis, peripheral arthritis, inflammatory bowel disease, uveitis, HLA-B27 and presence of enthesitis did not have an impact of ASDAS remission. Multivariate logistic regression analysis showed that, upon adjusting for covariates, non-exposure to a previous biologic (OR=3.40; P=0.078) approached statistical significance and lower HAQ-DI (OR=0.36; P=0.004) was a significant independent predictor of ASDAS remission.
**Conclusions:** Twelve-month treatment with IFX or GLM in a real-world setting was associated with significant improvements in disease parameters. Prior exposure to a biologic and lower HAQ-DI were identified as independent predictors of ASDAS remission upon adjusting for potential confounders.
**Disclosure of Interest:** L. Bessette: None declared, S. Kapur: None declared, M. Zummer: None declared, M. Starr: None declared, D. Choquette: None declared, M. Sheriff: None declared, W. Olszynski: None declared, E. Rampakakis Employee of: JSS Medical Research Inc;, E. Psaradellis Employee of: JSS Medical Research Inc;, B. Osborne Employee of: Janssen, K. Maslova Employee of: Janssen, F. Nantel Employee of: Janssen, A. Lehman Employee of: Janssen, C. Tkaczyk Employee of: Janssen
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## AB0662 INDIRECT COMPARISON OF TNF INHIBITORS FOR ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: META-ANALYSIS OF RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS

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**Background:** For ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) patients, tumor necrosis factor (TNF) inhibitors are recommended when disease activity persists despite non-steroidal anti-inflammatory drugs.
**Objectives:** To evaluate the efficacy and safety of TNF inhibitors in patients with AS and nr-axSpA.
**Methods:** Searching PubMed, Embase, Cochrane Library, CNKI and WanFang databases, we included all double-blind randomized controlled trials (RCTs) that compared a TNF inhibitor with placebo in AS/nr-axSpA patients. The efficacy endpoints included the proportions of patients reaching Assessment in Ankylosing Spondylitis 20% response (ASAS20), ASAS5/6, partial remission, and Bath Ankylosing Spondylitis Disease Activity Index 50% improvement (BASDAI50). We used adverse events (AEs), withdrawals due to AEs and severe AEs to evaluate the safety of biologics. TNF inhibitors were pooled to perform comparison with placebo and among themselves, calculating odds ratios (OR) with associated 95% credible intervals (CrI), probability of being best ($P_{best}$) and the surface under the cumulative ranking curve (SUCRA) as well as numbers needed to treat (NNT).
**Results:** Twenty-nine double-blind RCTs with 5200 patients were included in the analysis focusing on 6 TNF inhibitors, including etanercept, intended copies of etanercept, adalimumab, infliximab, golimumab and certolizumab. Compared with placebo, TNF inhibitors were efficacious in achieving ASAS20, ASAS5/6, partial remission and BASDAI50 responses, but with an increased risk of AEs and withdrawals due to AEs. No significant differences in efficacy were found among biologics, except that etanercept had a higher rate of ASAS20 response compared with golimumab in the Chinese patients (OR 4.78, 95% CrI 1.20–17.84). Among the Chinese population, etanercept was ranked the most efficacious therapy for ASAS20 with NNT of 2 ($P_{best}$ 93.6%, SUCRA 0.97).
**Conclusions:** Compared to placebo, TNF inhibitors are efficacious in controlling disease activity for AS and nr-axSpA patients without a higher risk of severe AEs. Although no significant differences in efficacy among biologics were found, the Chinese population had a better ASAS20 response to etanercept.
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**Disclosure of Interest:** None declared
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## AB0663 EFFICACY AND SAFETY OF ADALIMUMAB IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS - AN INVESTIGATOR-INITIATED RANDOMIZED PLACEBO-CONTROLLED TRIAL

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**Background:** This study investigates the effect of adalimumab (ADA) in patients with axial spondyloarthritis (axSpA).
**Objectives:** In an investigator-initiated randomized, placebo-controlled, double-blinded trial (NCT01029847) the efficacy of adalimumab was investigated in patients with axSpA according to the Assessment of Spondyloarthritis International Society (ASAS) criteria.(1,2)
**Methods:** 49 patients with axSpA, BASDAI≥4.0 despite treatment with NSAID and clinical indication for TNFα inhibitor treatment were randomized to s.c. placebo (PLA) or ADA 40 mg eow from baseline to week 6. All patients received ADA from weeks 6 to 24. At week 24, patients with a BASDAI reduction >50% or 2.0 were considered responders. MRI of the spine was scored according to SPARCC Spine Inflammation Index by an experienced reader blinded to all other data. Data from the randomized period (week 0–6) were analysed by Chi-square, unpaired t-tests and Mann-Whitney U tests as appropriate.

**Abstract AB0663** – Table 1

| | Adalimumab | | | Placebo | | | Comparison of treatment groups at week 6, p-value* | Comparison of treatment groups for change from baseline to week 6, p-value* |
|---|---|---|---|---|---|---|---|---|
| | Baseline | Week 6 | Change from baseline to week 6 | Baseline | Week 6 | Change from baseline to week 6 | | |
| BASDAI | 6.3 (1.2) | 3.9 (2.4) | –2.4 (2.2) | 6.4 (1.5) | 5.8 (2.2) | –0.6 (1.8) | 0.007 | 0.005 |
| BASFI | 5.2 (1.9) | 2.9 (2.1) | –2.3 (1.9) | 5.0 (2.1) | 4.9 (2.3) | –0.2 (1.3) | 0.005 | 0.000 |
| BASMI | 2 (1; 4) | 2 (1; 3) | 0 (–1; 0) | 3 (2; 4) | 2 (1; 5) | 0 (–1; 1) | 0.64 | 0.46 |
| VAS pain | 68 (19) | 36 (25) | –33 (31) | 65 (19) | 63 (24) | –2 (25) | 0.001 | 0.001 |
| VAS patient global | 70 (18) | 40 (28) | –32 (30) | 68 (19) | 63 (27) | –5 (26) | 0.007 | 0.002 |
| VAS physician | 55 (46; 78) | 26 (11; 53) | –18 (–44; –7) | 72 (48; 80) | 56 (35; 72) | –5 (–22; 8) | 0.004 | 0.028 |
| SPARCC spine | 7 (1; 15) | 1 (0; 12) | –2 (–12; 0) | 5 (2; 8) | 3 (2; 7) | 0 (–3; 1) | 0.21 | 0.046 |

Mean (SD) or median (IQR). *Unpaired t-tests for BASDAI, BASFI, VAS pain and VAS global. Mann-Whitney U tests for BASMI, VAS physician and SPARCC MRI spine score. P<0.05 is considered significant.

**Results:** Mean (range) age was 38 years (20–61), symptom duration 12 years (0–45) and time since diagnosis 3 years (0–38). 51% were males, 74% HLA-B27 positive, 20% had a history of uveitis, 4% of psoriasis and 6% of inflammatory bowel disease.
At week 24, a BASDAI reduction >50% or 2.0 was attained by 32 of 49 (65%) patients (58% and 72% in the PLA and ADA groups, respectively). 61% of patients achieved ASAS 20 response and 61% ASAS 40 response. From baseline to week 6, the SPARCC MRI spine score improved significantly more in the ADA group than in the PLA group, as did clinical variables (Table):
Treatment was discontinued in 5 patients due to adverse events during ADA treatment, due to rash (1), unspecified allergic reaction (1), paresthesia and reduced sensibility of 2 fingers (1), back pain worsening (1), and hospitalization due to myalgia and malaise (1).
**Conclusions:** Adalimumab significantly improved clinical and MRI measures of disease activity already at week 6 compared to placebo. 2/3 of patients achieved the clinical endpoint at week 24, confirming the clinical efficacy in axSpA.
**References:**
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[2] Rudwaleit et al. Ann Rheum Dis 2009;68:777–83
**Disclosure of Interest:** None declared
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## AB0664 HIGHER EXPRESSION OF MICRORNAS IN PERIPHERAL BLOOD MONONUCLEAR CELLS IN ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease characterized by inflammatory back pain and enthesis. MicroRNA (miRNA) are an abundant class of small RNA that can play an important role in gene regulation and participate in many physiological and pathological process[1]. According to the microarray results previously, our group found that the expression levels of miR-17–5p, miR-27a, miR-29a and miR-126–3p were higher in AS group than in healthy group. Moreover, the expression levels of miR-17–5p downregulated significantly after regular etanercept treatment, while the other 3 microRNAs slightly upregulated. Another study also reported elevated miR-29a expression in PBMCs of patients with AS[3], while no further study on investigating the treatment effect on miRNA expression.
**Objectives:** To investigate the expression level of the four miRNAs mentioned before in AS and healthy controls. The changes of microRNAs expressions after regular therapies are also the focus of our study.
**Methods:** We initially validated the expression levels of miR-17–5p, miR-27a, miR-29a, miR-126–3p in the PBMCs of AS (n=99) and healthy controls (n=39) using real-time quantitative reverse transcription PCR (qRT-PCR). Patients with AS were divided into 4 groups according to their different therapies, including 12-week Celecoxib/Etanercept /combination therapy and 24-week rh TNFR:Fc therapy (n=16, n=23, n=22 and n=38 respectively). Fold change for each reaction was calculated as $2 - \Delta\Delta Ct$.
**Results:** Significantly higher expression of the four miRNAs (miR-17–5p, miR-27a, miR-29a and miR-126–3p) were observed in AS ($\Delta Ct$ value: 4.40±2.02, 6.75±1.58, 1.52±1.12 and 2.34±1.58, $p<0.001$, respectively) than in healthy controls ($\Delta Ct$ value: 6.15±1.41, 8.05±0.86, 4.29±1.16, and 4.17±1.01, $p<0.001$, respectively). The corresponding fold changes were 3.34 (0.61–18.37), 2.47 (0.71–8.59), 6.82 (2.24–20.79) and 3.55 (0.96–13.06). Moreover, expressions of miRNAs were dramatically downregulated after 24-week etanercept therapy except miR-29a ($p$=0.013, $p$=0.043, $p$=0.025 and $p$=0.262 respectively). A 12-week celebrax therapy or combination therapy can significantly reduce the expression level of miR-126–3p ($p$=0.006 and $p$=0.016). There were no significant difference between AS patients before and after treatment in miR-17–5p, miR-27a as well as miR-29a.
**Conclusions:** We validated the 4 elevated miRNAs expression in PBMCs of patients with ankylosing spondylitis. Different treatments can reduce the expression of microRNAs to some extent.
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# Spondyloarthritis - clinical aspects (other than treatment)

## AB0665 IMPACT OF DISEASE ACTIVITY ON PSYCHOLOGICAL STATUS IN PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is a standard instrument regularly used to assess disease activity of patients with spondyloarthritis (SpA). However, the well-being of a patient is also affected by impairment of function as well as psychological status especially depression and anxiety.
**Objectives:** The aim of this study was to investigate the relationship between disease activity measured by the BASDAI and psychological variables.
**Methods:** This was a cross-sectional study at a rheumatology department over a twelve months period. Patients with diagnosis of SpA (ASAS 2009) were recruited. Respectively, disease status and psychological status were assessed by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Hospital Anxiety and Depression Scale (HADS). A statistical analysis was performed.
**Results:** A total of 100 patients were enrolled; mostly male (71%). The mean age of the sample was 41,72 (±13,57) years; the mean disease duration at study baseline was 11,87 (±10,3) years. Mean morning stiffness 30,26 minutes. The mean score on VAS pain was 60,3mm (±28,66). At baseline, the mean BASDAI score was 4,5 (±2,3); 57% have BASDAI greater than or equal to 4. The mean (SD) scores by the study participants on the HADS-Anxiety (HASD-A) and HADS-Depression (HADS-D) were 8,9 (±5,08) and 7,23 (±5,27), respectively. The prevalence of anxious symptomatology based on the HADS-A was 39%, 18% were classified as possible anxiety cases. Based on HADS-D scores, 31% of the patients presented symptoms of depression and 15% possible depression. BASDAI was positively correlated with both HADS-D ($r$=0.505, $p<0.0001$) and HADS-A ($r$=0.425, $p<0.0001$). The multivariate logistic regression analysis revealed that patients' whose BASDAI>4 at baseline was an independent risk factor associated with the risk of both depression (OR=4.9, 95%CI [1.7–13.9], p=0.002) and anxiety (OR=2.7, 95%CI [1.1–6.7], p=0.027).
**Conclusions:** This study underscore that high disease activity increased significantly the risk of depression and anxiety in SpA.
**Disclosure of Interest:** None declared
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## AB0666 PROGRESSION OF AORTIC AND VALVE ABNORMALITIES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Aortic and valve abnormalities are systemic inflammatory manifestations of ankylosing spondylitis (AS). Data on the prevalence, clinical significance and evolution are discrepant.

**Objectives:** To assess the dynamics of aortic and valve abnormalities detected by transthoracal echocardiography (TTE) in AS pts according to the results of prospective study.
**Methods:** 45 pts with AS (The New-York criteria) age <60 years, with the initial TTE - changes of aorta and valves and without concomitant cardiac diseases were assessed at the Institute of Rheumathology from 2008 to 2015. At baseline 15 pts had aortic root dilatation, 21 – aortic wall thickening, 32 – aortic valve thickening, 15 – mitral valve thickening. 5 pts had valve prosthesis (including 2 with both aortic and mitral prosthesis). 19 pts had aortic regurgitation (AR), 15 of them – 1–2 degree, 4 – 3–4 degree), 20 pts had mitral regurgitation (MR) 1–2 degree. Subaortic thickening ("bump") was detected in 10 pts. 16 of 45 pts used anti-TNF drugs during the observation period, 14 pts – only NSAID, 15 – NSAID and DMARD, including sulfaslazine (11 pts) and metotrexate (4 pts). All pts were underwent re-TTE after 1–4 years
**Results:** Negative dynamics was detected in 27 (60%) pts in total. Progression of aortic root dilatation from 1 to 6mm was detected in 12 of 15 pts (80%), in 2 - dilatation was first identified. 14 pts had first identified valve thickening (9 – aortic, 4 – mitral, 1 – both). 5 pts were underwent valve replacement: 4 – aortic, 1 – mitral. AR progression was detected in 10 pts (in 2 – of 2 degree, in 8 – of 1 degree), MR progression – in 6 pts of 1 degree). A negative correlation was found between anti-TNF- therapy and progression of aortic root dilatation (R=-0,329, P=0,03). "Subaortic bump" was first identified in 3 pts. Among 10 pts with subaortic bump initially, decrease from 8mm to 3mm was found in 1 pts, complete regression – in 2, all used biologics.
**Conclusions:** Aortic root and valve abnormalities tend to progression in most AS pts. Subaortic bump is able to regress if it is due to inflammatory edema and not fibrosis. Active anti-inflammatory therapy can protect in cardiac disease progression.
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## AB0667 HLAB27 ASSOCIATED UVEITIS TRENDS AND PATTERNS OF A MULTIETHNICITY COHORT: NEED FOR COMBINED RHEUMATOLOGY AND EYE SERVICES?

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**Background:** Uveitis is associated with systemic autoimmune disease and often present to Eye Department as an emergency. Uveitis can be a first presenting symptom of systemic autoimmune disease and often not followed up in Rheumatology services. Approximately 40% of patients with acute anterior uveitis (AAU) have undiagnosed spondyloarthritis (1). Previous studies in UK by Hamilton et al showing delay in diagnosing spondyloarthropathy (SpA) up to 8 years (2). Delay in referral of HLA B27 positive Uveitis by primary care and secondary care physicians to Rheumatology may be a reason for the delayed diagnosis (3,4).This can be better avoided if inter-speciality referral and pathways are established. To enable the best effective care delivered for Uveitis patients,we attempted to review the current trends of our own cohort of patients with HLAB27 Associated Uveitis
**Objectives:** - To review the cohort of HLA B27 positive uveitis in a busy tertiary care hospital serving multi ethnic patients.
- To observe the pattern and association of systemic autoimmune disease particularly spondyloarthropathy.
- To see how many cases been referred to Rheumatology services and how best they are managed with systemic immunosuppressive therapy.
**Methods:** The methodology includes retrospective analysis of data captured from the Uveitis Data Base maintained by ophthalmology department. The consecutive new cases of HLAB27 uveitis were identified for three-year period from 2011 to 2014. The clinical records, ophthalmology examination records, demographic details, ethnicity were reviewed. The type of uveitis, presenting symptoms and systemic associations were explored. Modes of treatment, complications and pattern of referral and input from other specialties were assessed as well treatment plans were collected. The data were captured by using standardized proforma. The captured data was analysed using excel spreadsheet.
**Results:** Total of 624 Uveitis patients 73 cases (105 eyes) of HLAB27 positive uveitis (11.7%) were identified.The most common systemic association in our cohort was Ankylosing Spondylitis (31.8%). 34%of the affected eyes did not develop anycomplications.88% had anterior uveitis with 38% showing chronicity.79% of the patients had better than 0.3LogMar acuity in the affected eye on presentation.
**Conclusions:** The data collected emphasizes the higher incidence of Ankylosing Spondylitis in patients, who presents with uveitis associated with positive HLA B27. Our result reiterates the need for establishing combined clinics to avoid delay in referrals enhancing patient management and experience.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3966

## AB0668 EFFECTS OF INFLIXIMAB TREATMENT IN TERMS OF METABOLIC PARAMETERS AND INSULIN RESISTANCE IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Risk of cardiovascular mortality is increased in patients with ankylosing spondylitis (AS). Chronic inflammation plays a crucial role in the development of accelerated atherosclerosis. TNFa is a pro-inflammatory cytokine which may be a key mediator in the pathophysiology of atherogenesis. This cytokine reduces the activity of insulin and causes insulin resistance (IR).
**Objectives:** We assessed the effect of infliximab treatment on insulin sensitivity and metabolic parameters in patients with AS.
**Methods:** In this prospective study, 20 consecutive AS patients (11 men and 9 women, mean age 39±10 and mean disease duration 12±7 years) fulfilling the modified 1984 New York criteria for AS were investigated. All patients were treated with iv infliximab (5 mg/kg, 0, 2, 6. week and ewery 8 weeks). A complete biochemical profile was obtained before and after 24 weeks of infliximab therapy (BASDAI, BASFI, ESR, CRP, hsCRP, lipid parameters, fasting glucose, insulin, HbA1C, waist circumference, weight, BMI, blood pressure). No patients were taking medications known to affect glucose, lipid metabolism and blood pressure. The Homoeostasis Model Assessment of Insulin Resistance Index (HOMA-IR) and Quantitative Insulin Sensitivity Check Index (QUICKI) were used to measure IR.
**Results:** After 24 weeks of infliximab treatment there was no statistically significant difference in fasting glucose levels, fasting insulin, HOMA-IR, QUICKI, HbA1C and blood pressure. Weight (84±18 vs. 87±16, p=0.002), body-mass index (29±6 vs. 30±5, p=0.001), waist circumference (101±12 vs. 104±11, p=0.014) and LDL level (112±42 vs. 127±36, p=0.014) increased significantly from baseline.
**Conclusions:** Infliximab treatment caused an increase in weight, BMI, waist circumference and LDL level but no change in IR. Cytokines associated with inflammation reduce appetite. Amelioration of anorexia with anti-TNF therapy may explain these results. Further studies are needed to clarify the role of factors that contribute to accelerated atherosclerosis in AS.
**Disclosure of Interest:** None declared
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## AB0669 12 MONTH FOLLOW-UP OF PATIENT SATISFACTION AND OUTCOMES OF A NOVEL ANKYLOSING SPONDYLITIS PATIENT CENTERED EDUCATION PROJECT

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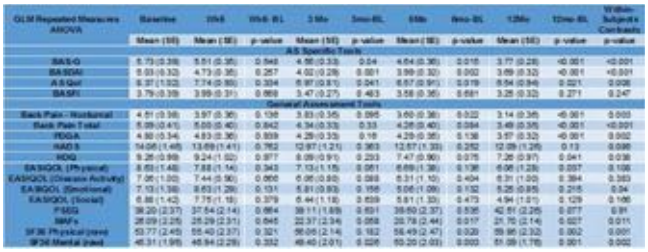
**Background:** Ankylosing Spondylitis (AS) specific patient centred interventions are rare. Following educational needs assessment, focus group consultation, and execution of a *Plan, Do, Study, Act* (PDSA) model, we developed and delivered a 6 weekly AS *education for Ankylosing Spondylitis* (AS-P) program to patients diagnosed with AS (New York criteria)
**Objectives:** Determine participant satisfaction and response to the AS-P intervention at 12 months.
**Methods:** Seventy-nine participants, mean age 43.5±14.5 years, diagnosed with AS were recruited for this study (AS-P). Intervention: 6-week group education program facilitated by health professionals. Program content included disease process, medication, pain management, stretches and strategies to cope with depression and fatigue. The program using patient centred approach is based on adult learning techniques and uses self-efficacy and self-management constructs. The SMAS was delivered in a small group setting delivery by interactive teaching and group discussions. The outcomes were measured post-intervention at 3, 6 and 12 months, 42 (of 79) patients completed the 12 month evaluation.
**Results:** At 12 months, 83.3% of patient made behaviour changes after the AS-P program, predominantly, increased exercise (n=7) and lifestyle modifications (n=6), with 94.3% of these patients sustaining these changes. 69% of patients continued to set and achieve goals related to their AS. 71.4% of patients felt that the AS-P gave them all the information they required to manage their condition. 95.2% of patients felt that attending the AS-P was worthwhile. 64.3% of patients reported never forgetting to take their medication, 23.8% forgot to take their medication a couple of times a month, 4.8% forgot to take their medication most of the time, and 7.1% didn't respond.
**Conclusions:** We have developed a program that is effective in improving patient related outcomes with high levels of satisfaction up to 12 months. Improved clinical outcomes are described in a separate abstract. The program is portable and sustainable and can be delivered in community or hospital settings. "Train the trainer program" workshops are planned for health professionals wanting to deliver this program.

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**DOI:** 10.1136/annrheumdis-2016-eular.3876

## AB0670 ANKYLOSING SPONDYLITIS (AS-P) PATIENT CENTRED EDUCATION PROGRAM IMPROVES DISEASE ACTIVITY AND QUALITY OF LIFE UP TO 12 MONTHS

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**Background:** Patient centered education interventions are rare. After a needs assessment, focus group consultation, and execution of a *Plan, Do, Study, Act* (PDSA) model, we developed and delivered a multidimensional *Ankylosing Spondylitis Education Program* (AS-P) to patients referred via a rheumatologist (meeting the New York criteria for AS).
**Objectives:** To examine the benefits of AS-P for people with Ankylosing Spondylitis (AS) in regards to health status, quality of life and disease activity.
**Methods:** 79 people were recruited in the intervention. Exclusion criteria: <18yo; non-English speaking; comorbid inflammatory musculoskeletal disease; and/or visual, auditory, or cognitive impairment. Participants attended a weekly 2.5 hour patient centered education session facilitated by same two health professionals over 6 weeks. The scripted content included multidimensional strategies including stretches; self-efficacy and self-management constructs and optional 7th week supervised exercise class.
Data collection included demographic, AS disease management characteristics, medication patterns, and outcomes, measured at baseline, 6 weeks, 3 months, 6 months and 12 months using GLM repeated measures ANOVA. Additional outcomes included the: BAS-G, BASDAI, AS-QoL, BASFI, back pain (VAS), PDGA, anxiety (HADs), health distress (HDQ), quality of life (EASIQoL), perceived health (GPH), pain (PSEQ), MAFs and SF-36.
**Results:** At baseline, 43.3% were male and the mean age was 43.5 ±14.5 years. The median time to AS diagnosis from the index symptom experience was 4 years IQR (1–11). The only significant change in medication usage occurred between Month 3 to Month 6 (p=0.018).
The BAS-G, BASDAI and the AS-QoL had improved between baseline to 3, 6 and 12 months (all $p<0.05$). Nocturnal and total back pain had improved between baseline and 12 months (all $p<0.05$). The PDGA and HDQ had improved between baseline and 12 months (all $p<0.05$). The EASI-QOL (physical health composite) had improved at 3 and 12 months ($p<0.05$). There was also a positive trend in the EASIQOL disease activity, emotional state and social composite scores ($p>0.05$). MAFs demonstrated a sustained improvement over 12 months (p=0.011). Similarly, the SF-36 physical (p=0.001) and mental (p=0.002) composite scores had improved 12 months post-intervention.
BASFI (p=0.271) and HADs (p=0.086) demonstrated no improvement 12 months post-intervention.



**Conclusions:** AS-P for AS is effective in improving AS specific disease activity, pain and QOL scores for up to 12 months.
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**Disclosure of Interest:** None declared
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## AB0671 DEGRADATION OF ISOMERIZED TYPE II COLLAGEN MAY SERVE AS A DISCRIMINATIVE BIOMARKER OF INFLAMMATION MEDIATED JOINT DESTRUCTION IN RHEUMATIC DISEASES

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**Background:** Collagen isomerization is a non-enzymatical process associated with tissue aging, and changes in levels of isomerized peptide fragments may reflect unique changes during pathological conditions. The D-G sequence in C2M is likely to undergo beta-isomerization over time, and may be altered in tissue turnover diseases affecting the joint. We therefore hypothesize that pathological conditions, such as ankylosing spondylitis (AS) or rheumatoid arthritis (RA), which affects the general turnover of cartilage may result in altered levels of isomerized collagen type II.
**Objectives:** The aims of this investigation were to develop a novel assay measuring an isomerized form of MMP degraded collagen II and to investigate whether it can be used as a clinical marker of joint deterioration in inflammatory joint diseases.
**Methods:** A solid phase competitive ELISA was developed applying a specific monoclonal antibody targeting an isomerized type II collagen fragment, C2Mβ. The biomarker was characterized by measuring its generation in vitro by cleavage of bovine cartilage with a range of proteases. Furthermore, the release of C2Mβ into the supernatant of bovine explants cultured ex vivo were measured under normal (without cytokines) and catabolic (TNF-α and oncostatin M) conditions. Serum samples from AS patients (n=28, age 25–76) or RA patients (n=149, age 15–86) were collected and C2Mβ measured. The change in C2Mβ after TNF-alpha treatment for 52 weeks was analyzed in AS patients. ROC curves were generated and the area under the curve calculated (AUC) to assess the assays capacity to distinguish between the diseases. Multivariable logistic regression was employed to correct for age and gender.
**Results:** The antibody against C2Mβ was specific towards the neo-epitope and did not recognize the non-isomerized form. C2Mβ was released from bovine cartilage when cleaved with MMP2 or MMP9 but not Cathepsin S. Levels of C2Mβ was increased in the supernatant of *ex vivo* cultured bovine cartilage explants in response to the catabolic cytokines TNF-α and Oncostatin M ($p<0.001$), compared to unstimulated explants which did not release C2Mβ. The addition of the MMP inhibitor GM6001 to catabolically activated explants completely abrogated the release of C2Mβ. C2Mβ was slightly decreased in AS patients treated with TNF-α inhibitors (10%), although the effect was not significant. C2Mβ was able to distinguish AS from RA with an AUC of 0.785, which increased to 0.905 when including age and gender
**Conclusions:** The C2Mβ neoepitope is released from catabolically activated cartilage and is measurable in human serum. C2Mβ is elevated in AS patients compared to RA patients and the marker can discriminate AS from RA with high diagnostic accuracy. Anti-inflammatory treatment in AS patients resulted in a trend towards a decrease in the marker compared to baseline. These findings suggest that systemic levels of C2Mβ may potentially serve as a joint specific biomarker for monitoring joint turnover and destruction as well as treatment efficacy in rheumatic diseases
**Disclosure of Interest:** C. Thudium Employee of: Nordic Bioscience A/S, Y. He Employee of: Nordic Bioscience A/S, N. Gudmann Employee of: Nordic Bioscience A/S, K. De Vlam: None declared, R. Lories: None declared, S. Hirata: None declared, Y. Tanaka: None declared, M. Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, A.-C. Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S
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## AB0672 PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS AND LOW BONE MINERAL DENSITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS IN HONG KONG: A CROSS-SECTIONAL STUDY

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**Background:** The disease process of ankylosing spondylitis (AS) is characterized by chronic inflammation. Osteoporosis is now known to be associated with chronic inflammation. Bone loss occurs early in AS increasing the risk of fracture, and is related mainly to the inflammatory process. This study aims to determine the relationship between AS and osteoporosis.
**Objectives:** To determine the prevalence and risk factors of low bone mineral density (BMD) in a local Hong Kong Chinese cohort of ankylosing spondylitis (AS) patients. Dual X-ray absortiometry (DXA) scan at different sites were compared and evaluated.
**Methods:** Ninety-two patients with AS were enrolled in this study. Clinical, demographic and radiological data were collected. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), Ankylosing Spondylitis Disease Activity Score (ASDAS), Patient and Physician global scores, Health Assessment Questionnaire (HAQ) and Bath AS Metrology Index (BASMI) were evaluated. BMD at the lumbar

spine via antero-posterior (AP) and lateral projections, neck of femur (NOF) and total hip were measured.
**Results:** Low BMD was found in half of the 92 Chinese AS patients. Factors associated with low BMD were BASDAI, BASMI, post-menopausal status, body mass index (BMI), alcohol use and family history of AS. Multiple logistic regression analysis by backward selection revealed that BASDAI (odds ratio (OR) 1.03, 95% confidence interval (CI)1.00–1.06; $p$ =0.031), post-menopausal status (OR 6.11, 95% CI 1.07–34.81; $p$ =0.041), BMI (OR 0.81, 95% CI 0.71–0.93; $p$ =0.003) and alcohol use (OR 4.79, 95% CI 1.49–15.38; $p$ =0.008) were significantly associated with low BMD. Total hip BMD was more sensitive than AP lumbar BMD in detecting low BMD in AS.
**Conclusions:** Low BMD in AS is not uncommon and often underdiagnosed. BASDAI, post-menopausal status, alcohol use and BMI were independently associated with low BMD in this study.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4163

## AB0673 ARTERIAL STIFFNESS, DISEASE ACTIVITY AND FUNCTIONAL IMPAIRMENT IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Cardiovascular risk is an important factor for increased morbidity and mortality in patients with ankylosing spondylitis. Currently, it is estimated that the cardiovascular risk from atherosclerotic origin in patients with ankylosing spondylitis is twice as high compared with aged-matched controls [1–4]. Arterial stiffness appears to contribute to the complex aetiology of cardiovascular disease and is regarded as a predictor of increased cardiovascular risk and all-cause mortality [5].
**Objectives:** To assess arterial stiffness in relation to the disease activity and functional limitation in patients with ankylosing spondylitis.
**Methods:** Twenty four patients (mean age: 45.8±11.7 years) suffering of ankylosing spondylitis (disease duration: 11.1±5.1 years) and twenty four gender and age-matched healthy controls were included in the study. Clinical, biological and functional status of ankylosing spondylitis patients was recorded. Arterial stiffness was assessed by measuring pulse wave velocity (PWV) and pulse wave analysis was performed using applanation tonometry.
**Results:** We found significant differences between ankylosing spondylitis patients and healthy controls in regard to PWV (p=0.047), aortic augmentation pressure - AP (p=0.028), augmentation index - AIx (p=0.038) and aortic augmentation index adjusted for heart rate - AIx75 (p=0.011). PWV and AIx75 were significantly associated with the disease functioning score - BASFI (p=0.012, r =0.504; p=0.041, r=0.421). Aortic AP and augmentation indexes (AIx and AIx75) were all associated to ASDAS score (p=0.028, r=0.448; p=0.005, r=0.549; p=0.025, r=0.455).
**Conclusions:** Our study showed that ankylosing spondylitis patients have a higher arterial stiffness than the age-matched controls, leading to an increased cardiovascular risk. We found that arterial stiffness is positively associated with disease activity and functional impairment. Chronic spondiloarthropaties should be screened for arterial stiffness, even in the absence of traditional cardiovascular risk factors, in order to benefit from primary prevention measures.
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**Disclosure of Interest:** None declared
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## AB0674 SECRETORY IGA: NEGATIVE CORRELATION WITH DISEASE ACTIVITY MEASURES IN HLA B27 POSITIVE SPONDYLOARTHRITIS PATIENTS

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**Background:** The human Major Histocompatibility Complex (*MHC*) encompasses a group of genes located in chromosome 6 (6p21.3); it encodes proteins expressed on the cell surface. The HLA-B27 is a MHC class I molecule associated with spondyloarthritis (SpA); many theories related to its natural function have been postulated to explain its pathogenic role.[1–2] Relevance of HLA-B27 molecule in the mucosal immune system, the gut mucosa inflammation, and secretory IgA (SIgA) production remains unresolved.
**Objectives:** The purpose of this study was to evaluate the correlation between serum SIgA levels and disease clinical activity in a cohort of HLA B27 positive and negative SpA patients with ReA and USpA, in a clinical center in Bogota Colombia.
**Methods:** The concentration of SIgA in serum was measured by an enzyme linked immunosorbent assay and the HLA-B27 was assessed by flow cytometry, followed by Polymerase Chain Reaction with sequence specific primers, in 46 patients with USpA and ReA. Clinical gastrointestinal manifestations and activity indices (BASDAI, ASDAS x CRP and ASDAS x ESR) were collected from each patient. Statistical analysis was performed using Stata 11.2 ® software for Windows; Pearson correlation was used to measure the degree of relationship between SIgA and clinical activity depending on the HLA B27 status. The study was approved by local hospital's ethics committee.
**Results:** 46 SpA patients completed the study with mean age of 34,8 ±12,3 years; 78,2% were men, 52,17% were HLA B27 positive, 60.9% of patients reported gastrointestinal symptoms such as diarrhea, abdominal pain, abdominal swelling and hematochezia. 63,6%, 88,6% and 100% of patients had disease activity evaluated by BASDAI, ASDAS-CRP and ASDAS-ESR scores, respectively, and 71,7% of patients had SIgA concentration above the upper normal range. The SIgA concentration was correlated with disease activity measures: BASDAI, ASDAS-CRP and ASDAS-ESR (-42% (0.0046), -37% (0.014) and -45% (0.0021) respectively); the negative coefficient correlation between SIgA and BASDAI, ASDAS-CRP and ASDAS-ESR was higher in HLA-B27 $^{+}$ patients -70% (0.0009), -58% (0.0093) and -57% (0.0083) than in HLA-B27 $^{-}$ patients.

| Correlation | HLA-B27 positive | | HLA-B27 negative | |
|---|---|---|---|---|
| | Pearson Coefficient | P value | Pearson Coefficient | P value |
| SIgA vs BASDAI | –70% | 0.0009 | –21% | 0.3397 |
| SIgA vs ASDAS-CRP | –58% | 0.0093 | –20% | 0.3579 |
| SIgA vs ASDAS-ERS | –57% | 0.0083 | –35% | 0.0992 |

**Conclusions:** These results suggest that SIgA levels in patients with ReA and USpA might be a correlate of disease activity measures based upon HLA-B27 status and might reflect an immunomodulatory role in these pathologies.
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## AB0675 IS THE PERIODONTAL CLINICAL AND MICROBIOLOGICAL CONDITION IN SPONDYLOARTHRITIS SIMILAR THAN RHEUMATOID ARTHRITIS?

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**Background:** The periodontal disease (PD) generates systemic impact given the increase in acute phase reactants related to the inflammatory. The relationship between Rheumatoid arthritis (RA) and PD is supported by pathological and immunological data but is not clear this association in Spondyloarthitis (SpA). The association between their respective disease activities and severities are less documented. Periodontal inflammation may affect disease activity and severity on patients with SpA.
**Objectives:** To evaluate the association between clinical indices of PD and markers of disease activity in SpA patients and compare these markers in patients with RA and controls.
**Methods:** The rheumatologic condition and periodontal status of 79 individuals with SpA, 59 patients with RA and 79 matched-controls were evaluated. *Porphyromona gingivalis (Pg)*, IgG1, and IgG2 to *Pg* were determined. The C-reactive protein-, erythrocyte sedimentation rate-, HLA B 27, rheumatoid factor-

RF, anti-citrullinated protein antibodies, and disease activity measures for SpA and RA were assessed. The rheumatologic Scores and periodontal condition were evaluated by two experienced and calibrated periodontists and rheumatologist. The groups were compared with Kruskal Wallis, Mann-Whitney U and Wilcoxon test's test and a paired t-test. The chi-square test was used to evaluate periodontal variables and SpA disease activity. The institutional Ethics Committee approved the study.

**Results:** 79 SpA patients with the following subtypes were included: Ankylosing Spondylitis (AS) (19), undifferentiated SpA (46), and reactive arthritis (ReA) (14). SpA patients had a considerable frequency of periodontitis (55.7%). Of them, 39.2% were classified as moderate and 2.5% as severe periodontal condition. No differences was found in frequency of periodontal condition between subtypes. SpA patients showed lower levels of insertion loss compared to RA patients and the control group ($p<0.05$). A significant association was observed in microbiological variables of SpA patients. The frequency of (*P gingivalis)* in the control group was 51.9% compared to 30% in SpA (p=0.015), especially in those with good response to NSAIDS ($p= <0.05$). Significant associations between the severity of periodontal involvement in RA patients was observed. 63.8% of RA patients had moderate severity disease (49.2%) and severe periodontitis (13.6%) (p=0.035) but not in SpA group. There were not association between disease activity measures in SpA, periodontal and severity condition.

**Conclusions:** As compared to RA and healthy controls, periodontal condition in SpA patients was similar. Lower grades of severity and bacterial load were found. This suggests that an interdisciplinary treatment between periodontists and rheumatologists may help to modulate periodontal condition and prevent systemic impact

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## AB0676 EVOLUTION OVER THIRTY YEARS OF THE PROFILE OF INPATIENTS WITH REACTIVE ARTHRITIS IN A TERTIARY RHEUMATOLOGY UNIT

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**Background:** Reactive arthritis (ReA) are sterile arthritis occurring after extra articular bacterial infection, mainly located in gut or genito urethral mucosa

**Objectives:** The aim of this study was to analyze, over 30 years, frequency as well as clinico-biological and therapeutic characteristics of ReA, comparing two periods.

**Methods:** In this retrospective monocentric study, the charts of all the patients followed in our unit between January 1st 1984 and April 2014 with the diagnosis or ReA, according to International Classification Criteria (1), were recorded and clinic biological features, management and outcome were analyzed, and compared between two periods: from January 1984 to December 1993, and from January 2004 to December 2013.

**Results:** 62 patients fulfilling international diagnosis criteria were analyzed. We found no significant differences (Table) between the two periods in incidence of new cases, clinical presentation (rheumatologic and extra articular features), biological and microbiological data or outcome. Change in therapeutic management was obvious with occurrence of anti TNF use in the recent period.

**Conclusions:** Reactive arthritis is still a current rheumatologic problem, with an apparently stable incidence in a developed country, with a need of early and tailored rheumatologic management.

| | 1984–1993 | 2004–2013 | p |
|---|---|---|---|
| Number of patients included | 15 | 31 | 0.4 |
| Number of patients hospitalized | 7,438 | 11,823 | |
| Men | 13 | 28 | 0.6 |
| Median age at diagnosis | 37 | 30 | 0.9 |
| HLA B27 + (%) | 91 | 63 | 01 |
| Delay between infection/articular symptoms (days), mean | 14.2 | 14 | 0.6 |
| CRP (mean) (mg/l) | 87,4 | 90,1 | 0.9 |
| Evidence of infectious agent (%) | 53 | 61 | 0.2 |
| TJC/SJC | 2.8/1.8 | 3.2/2 | ns |
| Dactylitis (%) | 13 | 29 | 0.3 |
| Enthésitis (%) | 40 | 26 | 0.5 |
| Extra articular features (%) | 47 | 35 | 0.4 |
| Axial symptoms (%) | 33 | 29 | 1 |
| DMARDs use (%) | 36 | 62 | 0.1 |
| Median delay of DMARD introduction (days) | 210 | 50.5 | ns |
| Biologic agents use (%) | 0 | 45 | 0.005 |
| Remission at last follow-up (%) | 57 | 47 | 0.6 |

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**Disclosure of Interest:** None declared

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## AB0677 COMPARATIVE CHARACTERISTICS OF RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS (NR-AXSPA) BASED ON DATA FROM 12 MONTH FOLLOW UP OF CORSAR COHORT

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**Background:** Clinical similarity of nr-axSpA and ankylosing spondylitis (AS) has been well established, but whether nr-axSpA is an initial stage of AS, or these two subtypes are nosologically self-determined entities is still being debated.

**Objectives:** To study the evolution of early axial spondyloarthritis (axSpA) in the Moscow axSpA cohort of patients (pts) - CoRSaR (Russian acronym from CohoRt of early axSpA pts).

**Methods:** Currently the CoRSaR cohort includes 94 axSpA pts with <5 years of inflammatory back pain duration (ASAS 2009y.criteria). 54 out of them with at least 12 months (mo) follow up pts (FUP) were included into preliminary analysis of axSpA evolution study. Evaluation of all pts at inclusion (Mo0) and FUP (Mo12) visits was similar and included: medical case history, clinical examination, X-ray of pelvis (and other segments of the back bone and joints, when necessary) - following ASAS guidelines, MRI of sacroiliac joints. Pts' mean age at Mo0 visit was 27,1±5,5 y., average disease duration - 22,4±15,1 mo, 49 (90,7%) pts were HLA-B27 positive.

**Results:** Pts were grouped into 2 arms to analyze axSpA evolution: Group 1 – nr-axSpA, Group 2 – AS. The table shows pts' baseline and FUP Mo12 visit characteristics. No significant difference has been found between the two groups – radiographic AS and nr-axSpA - in terms of prevalence of arthritis, enthesitis, BASDAI, ASDAS CRP, and BASFI scores. Radiographic sacroiliitis, i.e., AS, has developed in 9 (39%) out of 23 nr-axSpA pts during 12 Mo FUP.

**Conclusions:** No clinical differences between radiologically confirmed axSpA (i.e., AS) and nr-axSpA were established. AS has developed in 9 (39%) out of 23 nr-axSpA pts during 12 Mo.

**Disclosure of Interest:** None declared

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## AB0678 A COMPARISON OF DEPRESSION AND ANXIETY LEVELS IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHROPATHY WITH THOSE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** The concept of axial spondyloarthropathy (SpA) recently recommended by the ASAS includes patients comprising the early and late stages of the disease. This concept also includes patients not meeting the criteria for ankylosing spondylitis (AS) but classified as non-radiographic SpA on the basis of chronic lumbar back pain and other characteristics of SpA. Although this group is more heterogeneous and distinct from AS in terms of some characteristics, it still has a similar burden in terms of disease activity. Psychiatric symptoms can often

**Abstract AB0677** – Table 1

| | Mo0 visit (n=54) | | | FUP Mo12 visit (n=54) | | |
|---|---|---|---|---|---|---|
| | AS n=31 (57.4%) | Nr-axSpA n=23 (42.6%) | | AS n=40 (74.0%) | Nr-axSpA n=14 (26.0%) | *p* |
| Gender: m, % / f ,% | 17 (54.8%) / 14 (45.2%) | 7 (30.4%) / 16 (69.6%) | 0.07 | 20 (50.0%) / 20 (50.0%) | 4 (28.5%) / 10 (71.5%) | 0.16 |
| BASDAI score, Me [25%;75%] | 3.4 [1.6; 5.1] | 3.5 [2.0; 4.9] | 0.83 | 1.8 [0.80; 3.65] | 2.75 [1.2; 3.6] | 0.57 |
| BASFI score, Me [25%;75%] | 1.2 [0.3; 2.5] | 1.4 [0.3; 2.5] | 0.83 | 0.65 [0; 2.05] | 0.35 [0.1; 1.3] | 0.77 |
| ASDAS-CRP score, Me [25%;75%] | 2.5 [1.4; 3.1] | 1.8 [1.3; 3.1] | 0.4 | 1.35 [1.1; 2.05] | 1.3 [1.0; 2.1] | 0.78 |
| CRP, mg/L, Me [25%;75%] | 4.3 [1.0; 20.0] | 4.8 [0.6; 9.7] | 1.0 | 2.3 [0.85; 10.1] | 2.5 [0.8; 4.8] | 0.78 |
| ESR, mm/h, Me [25%;75%] | 13.0 [5.0; 24.0] | 8.0 [5.0; 14.0] | 0.4 | 7.5 [5.0; 21.0] | 6.5 [5.0; 8.0] | 0.38 |
| MASES score, Me [25%;75%] | 1.0 [0.0; 2.0] | 1.0 [0; 3.0] | 0.81 | 0 [0; 1.0] | 0 [0; 0] | 1.0 |
| SJC, Me [25%; 75%] | 0.0 [0; 0] | 0.0 [0; 0] | 0.28884 | 0 [0; 0] | 0 [0; 0] | 0.00000 |

be seen in patients during the course of AS. Depressive symptoms are seen at levels of 27.4–55.5% and anxiety symptoms at levels of 19.5–60.9%. Few studies have investigated this situation in the non-radiographic SpA group.
**Objectives:** To assess depression and anxiety levels in AS and non-radiographic SpA groups and to review potentially associated factors.
**Methods:** One hundred fifty-five (114 AS, 41 non-radiographic SpA) patients with axial SpA according to the ASAS definition were included in the study. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to assess activity, visual anolog scale (VAS) for spinal pain, the Bath Ankylosing Spondylitis Functional Index (BASFI) for functional capacity and the Ankylosing Spondylitis Quality of Life (ASQOL) for quality of life. The State-Trait Anxiety inventory (STAI), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were used to determine psychiatric symptoms.
**Results:** The AS patient group (mean age 39±10.8, male 73.4%) was older than the non-radiographic SpA group (mean age 35±10.1, male 54.8%), and had a greater preponderance of males.
No difference was determined between the two groups in terms of BASDAI, VAS spinal pain, ASQOL or BASFI scores. Psychiatric measurements were also similar between the AS and non-radiographic SpA groups.
The STAI, BDI and BAI exhibited good correlated with BASDAI, BASFI, ASQOL and VAS spinal pain (Table).

Table 1. Correlations between psychiatric symptoms and disease, functional capacity and quality of life scales

| | | BASDAI | BASFI | VAS spinal pain | ASQOL |
|---|---|---|---|---|---|
| STAI-I (state anxiety) | r | 0.432 | 0.343 | 0.373 | 0.481 |
| | p | <0.001 | <0.001 | <0.001 | <0.001 |
| STAI-II (trait anxiety) | r | 0.375 | 0.342 | 0.234 | 0.420 |
| | p | <0.001 | <0.001 | 0.005 | <0.001 |
| Beck anxiety inventory | r | 0.430 | 0.375 | 0.326 | 0.508 |
| | p | <0.001 | <0.001 | <0.001 | <0.001 |
| Beck depression inventory | r | 0.427 | 0.432 | 0.410 | 0.595 |
| | p | <0.001 | <0.001 | <0.001 | <0.001 |

**Conclusions:** Despite the presence of some clinical differences between the AS group and the non-radiographic SpA group, regarded as the early stage of the disease, the two group exhibit similar features in terms of psychiatric symptoms and disease activity. Psychiatric symptoms are closely associated with disease activity, functional capacity and quality of life.
**Disclosure of Interest:** None declared
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## AB0679 MARDRID SONOGRAPHIC ENTHESIS INDEX SCORING SYSTEM IS SENSITIVE FOR ASYMPTOMATIC PERIPHERAL ENTHESITIS IN EARLY AXIAL SPONDYLOARTHRITIS

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**Background:** Mardird sonographic enthesis index (MASEI) was one of the most wide used scoring systems for enthesitis not only used in spondyloarthropathy (SpA) but also in the other disease such as enthesitis in Behcet's disease. However, no articles mentioned its role in early diagnose in the early axial SpA without peripheral syndromes yet.
**Objectives:** Our study is to find out the role of MASEI in diagnosis of early axial SpA.
**Methods:** Ultrasound was performed by 2 observers blinded to the other examinations and the final diagnosis. All cases were diagnosed as early axial SpA fulfilling 2009 classification criteria but not 1996 New York Criteria with sacroilliac X-ray and MRI.US examination referred to MASEI related regions. BASDI, ASDAS were employed to assess disease activity. MRI was synchronized done for the position with positive findings by ultrasound to make sure the accuracy of the enthesitis.
**Results:** 1) 168 early axial SpA subjects without proof for peripheral enthesitis including physical examination or past history were screened by ultrasound.47 (28.0%) were made diagnosis as perpheral enthesitis by US and 45 (25.6%) were comfirmed by MRI. Mean age of 45 was 29.3 yrs, female-male ratio was 0.36:1, and disease duration was 0.89 yr. Positive HLA-B27 patients were more than HLA-B27negative ones (4:1).
2) The average of MASEI scores were low level (7.26±2.36). No significant differences between HLA(+) and HLA(–) groups. However, the scores for male patients group was higher than female ones (Sig=0.002), especially in respect of tendon thickness, tendon structure disturbance and bone erosion (Sig=0.000,0.001, 0.011).
3) The most common US findings were the chronic presentations as bone erosion, bone calcification. (75.6%, 84.4%) which suggested the enthesis aggression in asymptomatic patinets is a long-term slow change.
**Conclusions:** Our study found MASEI assessment is good tool for early diagnosis and follow up for peripheral enthesitis in early axial SpA and the US positive findings might be earlier than the clinical presentations.
**Disclosure of Interest:** None declared
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## AB0680 WHAT PATIENTS CLAIM TO BE HIP PAIN DOES NOT ALWAYS REFER TO THE ACTUAL HIP JOINT. RESULTS FROM A CLINICAL AND RADIOLOGICAL EVALUATION COHORT IN CLINICAL PRACTICE

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**Background:** The hip joint is a site of involvement in a number of rheumatic conditions. Patients are often complaining of hip pain. The "Hip" as a complaint or a joint involved in disease is being used, as a metric in a number of indices or questionnaires, to evaluate IBP (1) or Spondyloarthropathies (such as BASDAI question 2) (2). However, what patients are describing as "hip" pain is not always referred to the actual hip joint.
**Objectives:** To assess which structure(s) patients indicate when they are referring to hip pain.
**Methods:** A diagram has been developed which has been used as a proforma to design on the site of "hip pain" from patients (new and/or follow up) when seen in clinic. After detailed history and examination, an accurate description of the site referred to as "hip" was recorded. Radiological imaging was utilised, for those patients with either multiple sites or clinically unclear causes of "hip" pain, to confirm or exclude the clinical diagnosis for the pain. The study classified as an audit and took place at a single centre between August 2014 and September 2015.
**Results:** A total of 54 patients (M:F 10:44) have been assessed [mean age of 57.6 years (sd ±14.1)]. Total sites identified and evaluated were 72 as 14 patients of 54 (25.9%) indicated more than 1 site when describing their hip pain [10 patients:2 sites (18.5%), 4 patients (7.4%) 3 sites]. A total of 8 structures have been described by patients as the site of their hip pain. These (in addition to the hip joint) were: trochanterum, iliac crests (including anterior superior, posterior superior and anterior inferior) lumbar spine, sacroiliiac joint. Radiological evaluation performed on 40/54 patients (74%). From those, 23 patients had X-rays (57.5%), 13 patients had ultrasound (32.5%), 4 patients (10%) had MRI.
Following clinical and radiologic evaluation the structures identified and confirmed as the source of the hip pain were: Trochanterum (n=19; 26.3%), followed by hip joint (n=15; 20.8%), Iliac crest (n=13; 18%), Lumbo-sacral spine (n=6; 8.3%), posterior superior iliac crest (n=6; 8.3%), anterior superior iliac crest (n=5; 6.9%), Sacro-iliac joint (n=5; 6.9%), and anterior inferior iliac crest (n=3; 4.1%).
**Conclusions:** A total of 80% of patients presented with "Hip pain" were referring to a different structure than the hip joint in our study. The greater trochanter was the most commonly reported anatomical structure of pain from patients when they were referring to hip pain. The hip joint itself was 2nd in the frequency of reported hip pain, seen in only 1 in 5 patients coming to clinic complaining of hip pain. We therefore suggest the "hip pain" item, used in questionnaires that do not include clinical evaluation, has to be interpreted with caution.
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## AB0681 CAN CONVENTIONAL AND NON-CONVENTIONAL CARDIOVASCULAR MARKERS IDENTIFY DIFFERENT TYPES OF CARDIOVASCULAR INVOLVEMENT IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

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**Background:** Cardiovascular (CV) mortality is increased in patients with ankylosing spondylitis (AS) and psoriatric arthritis (PsA) but there are very few publications concerning CV morbidity. Furthermore, the findings of a number of studies indicate that AS and PsA are associated with different CV manifestations.
**Objectives:** The aim of the study was to use conventional and unconventional CV markers such as common carotid IMT (ccIMT), carotid pulse wave velocity (PWV), ejection fraction (EF) and global longitudinal strain (GLS) assessed by means of speckle tracking echocardiography (STE) to identify the different types of CV involvement in AS and PsA.
**Methods:** The study involved 30 outpatients satisfying the New York diagnostic criteria for AS (14 males and 16 females; mean age 53.07±10.73 years; mean disease duration 5.03±4.06 years), and 30 outpatients satisfying the CASPAR criteria for PsA (15 males and 15 females; mean age 54.27±9.63; mean disease duration 5.73±4.07 years), matched in terms of age, gender and other anthropometric characteristics. None of the participants had smoked cigarettes during the previous ten years or showed any signs or symptoms of CV disease, pulmonary involvement, or any other complication. All of the patients were treated with DMARDs and anti-inflammatory drugs, but none had received any biological or steroid therapy at baseline. They were therefore normal in terms of basal

ECG tracking, blood pressure (BP) values and glyco-lipid profiles (hypertension, dyslipidemia, diabetes and hyperuricemia were exclusion criteria). All of the patients underwent a clinical and standard echocardiographic examination, a carotid ultrasound study (including IMT and PWV assessment), and STE of the left ventricle (LV) using commercial QLAB Philips software.
**Results:** There were no differences between the AS and PsA groups in terms of EF and traditional echocardiographic parameters such as ccIMT (right: median right 0.64 mm, IQR 0.48–0.78 mm *vs* 0.64 mm, IQR 0.50–0.79 mm; $p$=0.07; and left: 0.64 mm, IQR 0.49–0.80 mm *vs* 0.64 mm, IQR 0.50–0.80 mm; $p$=0.08). However, PWV was higher in the PsA group (right: median 7.82, m/sec:, IQR 7.05–8.45, m/sec *vs* 7.08, m/sec, IQR 6.92–7.92, m/sec; $p$=0.04; and left: median 7.80 m/sec, IQR 6.99–8.41 m/sec *vs* 7.07 m/sec, IQR 6.93–7.92 m/sec; p=0.04), and GLS was lower in the AS group (median 19.83, IQR 16.00–24.40 *vs* 20.03, IQR 18.12–24.82; p=0.02).
**Conclusions:** The study findings show that our AS patients had impaired GLS in comparison with those with PsA, thus suggesting a myocardial alteration, and our PsA patients had higher PWV values than the AS patients, thus indicating endothelial dysfunction. There were no differences in ccIMT, EF or other conventional echocardiographic indexes between the two groups, but these findings suggest that AS and PsA patients are affected by different types of CV alteration, and the importance of identifying them in order to prevent CV events.
**Disclosure of Interest:** None declared
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## AB0682 CORRELATION BETWEEN DISEASE ACTIVITY AND CARDIOVASCULAR PARAMETERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** As cardiovascular (CV) involvement is frequent in patients with rheumatic diseases, it is important to implement strategies of early diagnosis, treatment and follow-up and to understand the relationship between this complication and disease activity.
**Objectives:** To investigate the correlations between the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and a series of conventional and unconventional CV markers in a group of patients with ankylosing spondylitis (AS).
**Methods:** We studied 30 patients with AS diagnosed using the New York criteria (14 males and 16 females with a mean age of 53.07±10.73 years), all of whom underwent a standard echocardiographic examination, a carotid ultrasound study (including IMT and PWV assessment), and speckle tracking echocardiography (STE).
**Results:** Our AS patients had impaired STE-measured LV myocardial longitudinal ε(median 19.83%, IQR 16.00–24.40% *vs* 21.46%, IQR 18.35–25.69%; $p<0.05$) and higher PWV (right: median 7.81 m/sec, IQR 7.03–8.45 m/sec *vs* 6.86 m/sec, IQR 6.42–7.99 m/sec; $p$=0.07: left: median 7.77 m/sec, IQR 6.97–8.38 m/sec *vs* 6.85 m/sec, IQR 6.28–7.88 m/sec; $p$=0.06) compared to healthy controls. Stepwise regression analysis revealed a weak correlation between BASDAI values and right (p=0.04) and left carotid PWV (p=0.05), whereas LV global longitudinal strain (GLS) assessed by means of STE very significantly correlated with disease activity (p=0.001). There was no correlation with common carotid IMT (cIMT) or ejection fraction (EF).
**Conclusions:** PWV and (especially) GLS are very important markers of CV damage and may identify CV involvement in AS patients earlier than conventional indices such as EF or cIMT, furthermore the are a correlation between these markers and disease activity. However, these findings need to be confirmed in a larger series of patients.
**Disclosure of Interest:** None declared
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## AB0683 HIP INVOLVEMENT IN SPONDYLOARTHRITIS PATIENTS: A FREQUENT AND SERIOUS MANIFESTATION

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**Background:** The prevalence of hip involvement in spondyloarthritis (SpA) patients varies from 7–50%. It is a cause of significant functional impairment and a marker of poor prognosis.
**Objectives:** The aim of this study was to compare demographic, clinical, laboratory and treatment data among SpA patients with and without hip involvement.
**Methods:** Cross-sectional study including 187 SpA patients that fullfilled the modified New York criteria. The patients completed a questionnaire assessing age at diagnosis, disease subtype, clinical presentation, disease-activity (BASDAI, ASDAS) and functional-indices (BASFI) and BASMI was calculated. The patients' records were consulted to asses the following parameters: presence of HLA-B27 antigen, inflammatory markers (ESR, CRP), radiographs of spine, hip and sacroiliac joints. Hip involvement was considered based on the BASRI-hip scoring system (hip involvement if $\geq$2). The statistical analysis was performed using SPSS 21.0 software, and $p<0.05$ was taken to indicate statistical significance. To compare the differences between the groups, Mann-Whitney U, $\chi^2$ and Fisher tests were used.
**Results:** 187 patients were included, with 55.6% males, median age 46.0 (range 21.0–79.0) years. In this study 75 (40.1%) patients had hip involvement, which was significantly more frequent in males (46.1% vs 32.5%, p=0.041). There were no statistically significant differences in age at diagnosis, age at evaluation, time of diagnosis, smoking habits, subtype of SpA, extra-articular manifestations or HLA-B27 positivity. Ankylosis of bilateral sacroiliac joints and syndesmophytosis were significantly more frequent in patients with hip involvement (56.2 vs 28.8% p<0.001 and 57.3% vs 38.7% p=0.009). Median disease duration was significantly greater in SpA patients with hip involvement (19.0 vs 14.0 years, p=0.001). BASMI, BASFI and ASDAS-CRP were significantly higher in patients with hip involvement (median 5.0 vs 3.8, p<0.001; median 5.1 vs 3.3, p=0.001 and 2.4 vs 2.0, p=0.038, respectively). Median BASDAI and ASDAS-ESR were also higher in these patients but this difference was not statistically significant (3.3 vs 2.8, p=0.361 and 2.3 vs 2.1 p=0.318, respectively). There were no differences in what concerns SpA treatment between the two groups.
**Conclusions:** This study shows that radiographic hip involvement is a frequent disease manifestation in SpA, and that it could be more common in male patients with long-standing disease. It also confirms that hip involvement reflects more severe disease, as it is associated with more axial damage and functional impairment.
**Disclosure of Interest:** None declared
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## AB0684 GENDER SPECIFIC DIFFERENCES IN ANKYLOSING SPONDYLITIS AT TREATMENT INITIATION IN PATIENTS TREATED WITH INFLIXIMAB OR GOLIMUMAB

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**Background:** The prevalence of ankylosing spondylitis (AS) is 2–3 times higher in men compared to women. Recent studies have suggested that clinical differences exist between both genders with women experiencing a higher burden of disease.
**Objectives:** This analysis examined gender-specific differences with respect to patient and disease parameters at initiation of infliximab (IFX) or golimumab (GLM) for the treatment of AS in a Canadian routine clinical practice setting.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis with IFX or GLM. Patients with AS treated with IFX who were enrolled since 2002 or with GLM enrolled since 2010 were included in this analysis. Between group differences were assessed with the Fisher's Exact test or the independent samples t-test, while linear regression was used to assess the independent association of gender with HAQ-DI, ASDAS, BASDAI, and BASFI improvements at 12 months.
**Results:** A total of 539 AS patients were included in this analysis; 188 (34.9%) patients were treated with GLM and 351 (65.1%) with IFX. The majority of patients were male (61.8%). Mean age and disease duration were comparable between genders for both GLM and IFX, (Table 1). Overall, disease parameters (ESR, PtGA, MDGA, HAQ-DI, ASDAS, and BASFI) were similar for GLM with the exception of BASDAI where higher disease severity was observed among females. Among patients treated with IFX, between gender differences were observed for CRP with significantly lower levels in female patients; however BASDAI and HAQ-DI where significantly higher in females compared to males. Other parameters (ESR, PtGA, MDGA, ASDAS, and BASFI) were similar for IFX between genders. Regression analysis showed that, upon adjusting for baseline levels, female gender (ΔBASDAI=0.603; P=0.035) was associated with increased BASDAI at 12 months of treatment as compare to males. HAQ-DI, ASDAS, and BASFI, on the other hand, at 12 months were comparable between genders.

Table 1. Patient characteristics at baseline by gender

| AS-GLM, mean (SD) | Male (n=115) | Female (n=73) | P-value |
|---|---|---|---|
| Age, years | 46.3 (15.2) | 44.4 (11.8) | 0.498 |
| Disease duration, yrs | 5.2 (10.0) | 6.0 (10.6) | 0.704 |
| CRP, mg/L | 12.6 (15.2) | 17.5 (50.5) | 0.389 |
| BASDAI | 5.6 (2.3) | 6.5 (1.7) | **0.007** |
| **AS-IFX, mean (SD)** | **Male (n=218)** | **Female (n=133)** | **P-value** |
| Age, years | 45.1 (12.0) | 47.0 (10.8) | 0.163 |
| Disease duration, years | 9.6 (10.3) | 8.8 (9.6) | 0.505 |
| CRP, mg/L | 19.2 (26.9) | 12.5 (17.6) | **0.012** |
| HAQ-DI | 1.11 (0.58) | 1.27 (0.63) | **0.019** |
| BASDAI | 6.0 (2.1) | 6.6 (2.1) | **0.013** |

**Conclusions:** Overall, at anti-TNF initiation, female AS patients experience greater disease activity relative to men at initiation of biologic therapy. Whether this represents a gender bias in prescribing, or a gender based difference in the acceptance of biologic treatment or disease assessment, requires additional research.

**Disclosure of Interest:** M. Starr: None declared, M. Zummer: None declared, D. Choquette: None declared, B. Haraoui: None declared, P. Rahman: None declared, M. Sheriff: None declared, E. Rampakakis Employee of: JSS Medical Research Inc;, E. Psaradellis Employee of: JSS Medical Research Inc;, B. Osborne Employee of: Janssen, A. Lehman Employee of: Janssen, K. Maslova Employee of: Janssen, F. Nantel Employee of: Janssen, C. Tkaczyk Employee of: Janssen
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## AB0685 NOVEL USE OF PULMONARY FUNCTION TESTING IN MEASUREMENT OF DISEASE STATUS IN ANKYLOSING SPONDYLITIS

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**Background:** Chest wall restriction is a common outcome in patients with ankylosing spondylitis (AS). Pulmonary function testing (PFT's) demonstrates a restrictive pattern of impairment. This impairment may be exacerbated when the subject is recumbent particularly when sleeping. It is not clear to what extent the specific FVC and FEV1 standing or lying values correlate with other commonly employed physical exam and functional outcome measures.We postulate that critical diminution of recumbent pulmonary function may have an adverse effect on sleep quality and functional outcome measures.
**Objectives:** To determine the utility of PFT testing in AS patients. To determine if FVC and FEV1 values in standing and recumbent postures correlate with other physical and functional outcome measures in AS patients.
**Methods:** 48 consecutive patients with AS had routine history and physical exams including the EDASMI (Edmonton Ankylosing Spondylitis Metrology Index). Standard AS questionnaires were administered BASG, BASDAI, BASFI and Epworth Sleepiness Scale was used to determine degree of daytime sleepiness as a measure of sleep quality. PFT's were performed in standing and recumbent posture. Statistical analysis was performed with SPSS software and included age, sex and smoking adjusted analysis of correlation of FVC standing, FVC lying, FVC difference between standing and lying (FVC delta), FEV 1 standing, FEV 1 lying and FEV1 difference between standing and lying (FEV1 delta).
**Results:** The population consisted of 15 women 10 of whom were smokers and 34 men 24 of whom were smokers. The mean age for the females was 50 years with a mean disease duration of 29.2 years. The mean age of the males was 51 years with a mean disease duration of 28.7 years. Mean BMI for the females was 29.4 and for the males 28.3.
There is a statistically significant correlation in men between FVC and FEV1 with chest expansion, EDASMI, BASFI and BASDAI. Tragus to wall measurement also correlated with FVC measurements. These relationship were observed even when controlling for age and smoking history. FVC delta did not correlate with measurements of AS outcome or the Epworth Sleepiness Scale. BASFI correlates with the Epworth Sleepiness Scale.
In the female cohort, FVC correlation with EDASMI almost reached statistical significance. The FVC in female smokers correlates with the age of onset and duration of disease. However, there was no correlation of FVC or FEV 1 with measurement of chest expansion, tragus to wall measurement, BASFI or BASDAI. The FVC delta did correlate with BASFI in females who have smoked. Correlation between FEV1 delta (but not FVC delta) with the Epworth Sleepiness Scale almost reached statistical significance in the female smoking group.
**Conclusions:** FVC and FEV1 are objective and reproducible measures of pulmonary function. In men, these correlated well with the standard physical examination measurements including chest expansion, tragus to wall measurement and the EDASMI. In turn all of these physical measurements correlated with the patient function as measured by BASFI and to a lesser extent BASDAI. Further study of this patient population is required to determine the utility of PFT testing as an independent outcome variable.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3299

## AB0686 CROSS SECTIONAL COHORT OF INFLAMMATORY BOWEL DISEASE RELATED ARTHRITIS IN RHEUMATOLOGY SECONDARY CARE

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**Background:** Joint involvement associated with inflammatory bowel disease (IBD) is well recognised within the concept of spondyloarthritis (SpA). There are two groups of articular manifestation in IBD: an axial arthropathy, including inflammatory back pain, sacroiliitis and ankylosing spondylitis (AS); and a lesser-studied peripheral arthritis, which is broadly divided into type 1 (oligoarthritis) and type 2 (polyarthritis). Previous data comes largely from cohorts of patients studied in gastroenterology secondary care, and identifies IBD related arthritis as a common and poorly understood condition.
**Objectives:** To describe the demographic characteristics, clinical features and current assessment and treatment of patients with Crohn's Disease (CD) or Ulcerative Colitis (UC) related arthritis in rheumatology secondary care.
**Methods:** One hundred consecutive patients with a physician diagnosis of IBD related arthritis were selected for inclusion. Data was collected retrospectively from patient notes, hospital electronic records and imaging software. Demographic, patient reported, clinical and treatment data was collected.
**Results:** In this group of 100 patients, mean age 48.8 years (range 22–86), mean disease duration 7.8 years was an equal proportion of men (54) and women (46) and IBD subtype (CD=53, UC=41, Indeterminate=5, other=3). Disease phenotype and radiographic damage are described in table 1. At the last clinic assessment only 36% of patients had a tender and swollen joint count documented. The burden of peripheral symptoms was small with an average tender joint count of 1.43 (range 0–12) and swollen joint count of 0.67 (range 0–14). Frequency of axial and peripheral symptom assessment was similar at 72% and 75% respectively. Gut symptoms were only assessed in 50% of patients. 21% of patients had a documented history of uveitis and 22% a history of enthesitis. In patients with axial symptoms the mean outcome measures were as follows: BASDAI =4.4 (range 0.9–7.1), BASMI =3.7 (range 0–7.4) BASFI =4 (range 0–8.6), back pain =4 (range 0–9), patient global assessment =3.3 (range 1–9). 79% of patients had a current or prior treatment history with one or more disease modifying anti rheumatic drugs (DMARD), and 37% with anti-TNF therapy. At least 11% had a history of non-steroidal anti-inflammatory use.

Table 1. Demographics and clinical features of 100 patients with IBD related arthritis patients in rheumatology secondary care

| | |
|---|---|
| **Demographics** | |
| Age (years) | 48.8 |
| Disease duration (years) | 7.8 |
| **Clinical features** | |
| HLA-B27 positive | 46.4% |
| Axial disease | 62% |
| Radiographic | 84% |
| Non-radiographic | 16% |
| Peripheral disease | 56% |
| Type 1 | 31% |
| Type 2 | 17% |
| Other | 8% |
| Arthralgia | 10% |
| Erosive disease | 7.6% |
| Radiograph not done | 36.4% |
| History of uveitis | 21% |
| History of enthesitis | 22% |

**Conclusions:** We report data describing a distinct but heterogeneous clinical phenotype of IBD associated arthritis in rheumatology secondary care. We found high rates of DMARD and anti-TNF use, little erosive peripheral disease and variable clinical assessment. We suggest there is a need for improved assessment of IBD associated arthritis to better quantify the burden of disease and natural history.
**Disclosure of Interest:** None declared
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## AB0687 CARDIOVASCULAR MORBIDITY AND MORTALITY OF PATIENTS WITH SPONDYLOARTHRITIS, RESULTS OF 10-YEAR PROSPECTIVE CONTROLLED STUDY

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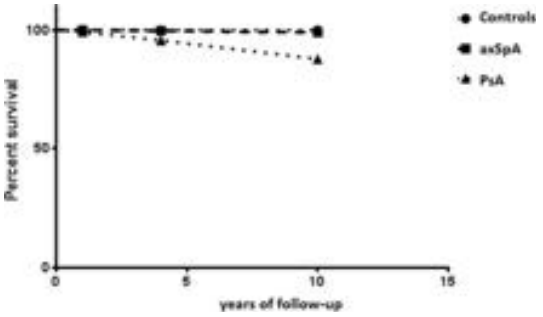
**Background:** Cardiovascular events are the leading cause of mortality in arthritis. However, data of cardiovascular (CV) morbidity and mortality in spondyloarthritis (SpA) are contradictory. Current data about CV mortality and morbidity in SpA in Russian population are limited.
**Objectives:** The aim of the study was to evaluate CV morbidity and mortality in patients with SpA.
**Methods:** 676 patients with SpA without CV diseases were involved, 160 healthy individuals included as controls. In 10 years of follow-up CV events (cardiac death, angina, myocardial infarction (MI), stroke, arterial hypertension (AH), arrhythmias or conduction disturbances) were recorded. Statistical analysis was performed using SPSS17.
**Results:** 313 patients and 10 controls had loss the follow-up. From 363 patients with 10-year results 278 had axial SpA (axSpA), 85 – psoriatic arthritis (PsA)). Mean age±SD was 40.1±14.1 years in SpA, 40.0±11.4 in axSpA, 40.55±10.6 in PsA, 39.0±11.2 in controls, $p \geq 0.05$ for all. Prevalence of male was recorded in axSpA compared with PsA (p=0.02), other groups were matched in gender, $p \geq 0.05$ (69.7% males in SpA, 76.3% in axSpA, 48.2% in PsA, and 56% in controls). Smoking was frequently occurred in axSpA (68%, $p < 0.05$ with all the other groups). Frequency of CV events is presented in table.

Table 1. Cardiovascular events in SpA during 10-years of follow-up

| | Angina, n | MI, n | AH, n | Cardiac death, n |
|---|---|---|---|---|
| SpA, n=363 | 57 | 41 | 188 | 9 |
| axSpA, n=278 | 36 | 28 | 132 | 2 |
| PsA, n=85 | 21 | 13 | 56 | 7 |
| Controls, n=150 | 13 | 3 | 32 | 0 |

Arrhythmias were recorded in 55 (15.2%), conduction disorders – in 48 (13.22%), stroke – in 9 (2.47%) SpA patients.

Odds ratio (OR) of death in SpA as compared to controls was 4.6 (95% confidential interval (CI) 0.4–10.6), $p>0.05$, in PsA OR=8.0 (CI 5.7–16.1) compared to controls and 9.9 (CI 6.0–18.1), compared to axSpA, $p<0.0001$ for all, image.
Relative risk (RR) of MI in axSpA was 1.77 (CI 1.5–2.1), in PsA – 4.3 (CI 2.5–14.5), compared to controls, $p<0.0001$ for all. In controls risk of MI was comparable with expected population level (RR 1.24, CI 0.96–1.59).
In axSpA RR for AH = 2.23 (CI 1.6–3.1), in PsA RR = 3.09 (CI 2.19–4.35), $p<0.0001$ compared to controls.




**Conclusions:** CV mortality in SpA and axSpA is comparable to population level, in PsA is higher, than in healthy controls and in ax-SpA. The incidence of angina, MI, AH in patients with ax-SpA and PsA exceeds the incidence in healthy controls.
**Disclosure of Interest:** None declared
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## AB0688 DISEASE ACTIVITY AND INFLAMMATORY MRI LESIONS IN PATIENTS WITH AXIAL AND PERIPHERAL SPONDYLOARTHRITIS

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**Background:** Relationship between inflammatory lesions on magnetic resonance imaging (MRI) and clinical disease activity measures is still unclear in patients (pts) with spondyloarthritis (SpA). In some studies MRI sacroiliac joints (SIJ) scores correlated negatively with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [1], but correlated neither with the Ankylosing Spondylitis Disease Activity Score (ASDAS) nor C-reactive protein (CRP) level. Another study showed a positive correlation between BASDAI and Spondyloarthritis Research Consortium of Canada (SPARCC) score [2].
**Objectives:** To evaluate the disease activity and correlations between clinical indices, CRP, erythrocyte sedimentation rate (ESR) and SPARCC MRI score in SpA.
**Methods:** 67 SpA pts (23 - axial (according to Assessment of Spondyloarthritis International Society (ASAS) 2009 criteria) and 44 – peripheral (according to ASAS 2011 criteria)) consulting a clinic for the first time were included. Mean age of pts (68.7% male) was 36.6+10.7, 88.4% of 43 pts were HLA-B27 positive. BASDAI (mm), Bath Ankylosing Spondilitis Functional Index (BASFI, mm), ASDAS, CRP (mg/l), ESR (mm/hr) and SPARCC MRI SIJ score (0–72, n=32) were evaluated. Spearman coefficients for correlation were calculated.
**Results:** In all SpA pts mean value ($M\pm\sigma$) of indices and laboratory parameters were: BASDAI – 4.76±1.89, BASFI – 3.3±2.2, ESR – 26.21±19.63, CRP – 27.48±54.83, ASDAS-CRP 3.11±1.02 and ASDAS-ESR 3.07±0.97.
ASDAS-CRP, ASDAS-ESR and BASDAI were higher in peripheral SpA than in axial SpA: 3.32±1.05 vs 2.72±0.83 (p=0.016), 3.29±1.01 vs 2.66±0.75 (p=0.005) and 5.12±2.02 vs 4.07±1.4 (p=0.01) respectively. The level of inflammatory lesions of SIJ was high: SPARCC MRI SIJ score was 25.97±12.89, without significant differences between axial (27.83±12.92) and peripheral (23.57±12.92) SpA.
The correlation analysis revealed that for all SpA pts BASFI positively correlated with the both, ESR (r=0.388, p=0.01) and CRP (r=0.357, p=0.003), but BASDAI was only with CRP (r=0.428, p=0.001). All disease activity and functional indices for all SpA showed a high correlation with each other: ASDAS-CRP and ASDAS-ESR with BASDAI and BASFI (r value from 0.502 to 0.745, p=0.001), and BASDAI with BASFI (r=0.426, p=0.015).
In pts with axial SpA ASDAS-CRP and ASDAS-ESR but not BASDAI and BASFI were correlated with laboratory activity: ASDAS-ESR with ESR (r=0.620, p=0.002) and CRP (r=0.516, p=0.012), ASDAS-CRP only with CRP (r=0.785, p=0.001). All clinical indices of pts with the involvement of peripheral joints showed significant ($p<0.05$) correlation with ESR and CRP (r value from 0.302 to 0.779).
SPARCC MRI SIJ score showed correlation with CRP (r=0.358, p=0.004) in all SpA, with CRP (r=0.496, p=0.036) in axial SpA and with BASFI (r=0.556, p=0.039) in peripheral SpA pts.
**Conclusions:** Disease activity according to ASDAS-CRP, ASDAS-ESR and BASDAI was significantly higher in pts with peripheral comparison with axial SpA. Clinical indices of pts with peripheral SpA showed better correlation with laboratory activity in comparison with axial SpA. SPARCC MRI score correlated with disease activity (only CRP level) of axial SpA pts and functional status (BASFI) of peripheral SpA pts.

**References:**
[1] Van der Heijde D. Arthritis Rheumatol. 2014;66(3):667–73.
[2] Zhang P. Clin Radiol. 2015;70(1):62–6.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1673

## AB0689 COMOPARISON BETWEEN MALES AND FEMALES WITH SPONDYLOARTHRITIS

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**Objectives:** The aim of our study is to describe the characteristics of women with spondyloarthritis though a comparison with men.
**Methods:** This is a retrospective observational study, conducted in the rheumatology department at CHU Hassan II Fez, analyzing the records of patients diagnosed spondyloarthritis during the period extending from January 2009 to June 2014.
We realized a descriptive study of our patients then we compared clinical and epidemiological profil of spondyloarthritis in both sex to emphasize the characteristics of morrocan women spondyloarthritis.
**Results:** A 136 patients were included, 86 men and 50 women. The mean age was 38,44±13,5 years with an average diagnostic delay of 4,71±5 years. Clinical symptomatology was dominated by axial involvement dorsolombalgie in 90,4% of cases.
Uveitis was the extra-articular manifestation most common in 5,1% of cases. 61,8% of patients had active disease, and 46,3% had severe disease.10,3% of patients had juvenile-onset, 24.1% patients had a hip involvement.
The comparison of women and men objectified significant association between female sex and late onset of disease ($p<0,001$), illiteracy (p=0,021), family antecedent of spondyloarthrtitis (p=0,025), arthritis (p=0,049), the use of sulfasalzine and methotrexate (p=0,042, p=0,006 respectively)
After logistic regression analysis the female sex was associated with late onset of disease ($p<0,001$, OR=0,93; IC=0,89–0,96) and the use of methotrexate (p=0,018, OR=0,14;IC=0,02–0,71) whereas male sex was associated with hip involvement (p=0,02, OR=3,3; IC=1,18–13,03) and tabac (p=0,004, OR=22,47; IC=2,76–182)
**Conclusions:** Women with AS appear to have both similarities and differences in disease expression when compared with men with spondyloarthritis. The causes of the differences are still unknown, although both sex and gender factors may explain some of them.
**Disclosure of Interest:** None declared
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## AB0690 PROFILE OF JUVENILE-ONSET COMPARED TO ADULT-ONSET SPONDYLOARTHRITIS

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**Objectives:** the aim of our study is to analyze the differences and similarities between a group of juvenile-onset spondyloarthritis (JOSpA) ($\leq$16 years) and a group of adult-onset spondyloarthritis (>16 years) (AOSpA).
**Methods:** This is a retrospective observational study, conducted in the rheumatology department at CHU Hassan II Fez, analyzing the records of patients diagnosed spondyloarthritis during the period extending from January 2009 to June 2014.
We realized a descriptive study of our patients (clinical and epidemiological parameters) then we compared JOSpA and AOSpA to emphasize the characteristics of juvenile onset spondyloarthritis.
**Results:** A 84 patients were included 22 with JOSpA and 62 with AOSpA. The mean age was 30,90±10,5 years with the average diagnosis delay of 5,68±5,74 years. Diagnosis according to ASAS criteria was in 73,8% of cases, according to AMOR criteria in 21,4% of cases and 4,8% according to NYM criteria. Clinical symptomatology was dominated by axial involvement dorsolombalgie in 89,3%.
Uveitis was the extra-articular manifestation most common in 8,3%.
The average Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was 4,62±1,907, the average Bath Ankylosing Spondylitis Functional Index (BASFI) was 4,56±2,485. 34.5% patients had a hip involvement.
The variables associated with JOSpA were lower limb arthritis (p=0.04), hip involvement (p=0,001), enthesitis chest pain (p=0,04) and the use of anti TNF alpha (p=0,008).
After logistic regression analysis the JOSpA was associated with enthesitis chest pain (p=0,011; OR=8,2, IC=1,62–41,34) and the use of anti TNF alpha (p=0,001; OR=9,1; IC=2,39–34,69)
**Conclusions:** Our study showed that JOSpA is associated with enthesitis and the use of anti TNF alpha. This characterization will help to understand the characteristics of the JOSpA patients and their needs in the long-term follow up.
**Disclosure of Interest:** None declared
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## AB0691 OBLIQUE VIEWS HAVE ADVANTAGES OVER ANTERO-POSTERIOR VIEW RADIOGRAPHS IN ASSESSING SACROILIITIS: AN IMAGING STUDY

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**Background:** Radiograph of antero-posterior (A-P) view of pelvis is usually used to diagnose sacroiliitis. Magnetic resonance imaging (MRI) can detect lesions early in the disease course before they can be seen on radiography. The severity of sacroiliitis may be different as detected by MRI or by A-P view X-ray. The oblique view of pelvis may provide additional information that makes it closer to the finding of MRI than A-P view X-ray.
**Objectives:** To record lesions of sacroiliac joint (SIJ) seen on A-P view and oblique views radiographs and MRI in patients with axial Spondyloarthritis (SpA), and to analyze whether oblique views have advantages over A-P view radiographs in assessing sacroiliitis.
**Methods:** Three readers blinded graded the sacroiliitis according to the modified New York criteria seen on A-P view, oblique views and MRI from 182 patients with axial SpA. We summarized the characteristics of scores assessed by three kinds of imaging methods and calculated the sensitivity, specificity, positive and negative likelihood ratio of A-P view and oblique views radiographs for diagnosing axial SpA with MRI as the gold-standard.
**Results:** The total accuracy of oblique views was higher than that of A-P view in assessing sacroiliitis as referred to the data of MRI (82.8% vs. 71.6%, $p<0.01$). The agreements were higher between oblique views and MRI than that between A-P view and MRI in the SIJs graded $\leq 2$, especially in patients with symptom duration less than 2 years (all $p<0.01$). But in the SIJs graded $>2$ and in patients with symptom duration more than 2 years, there were no differences using A-P view or oblique views to assess sacroiliitis (all $p>0.05$). Oblique views had high sensitivity, while A-P view had moderate sensitivity for diagnosing axial SpA in the SIJs graded $\leq 2$.
**Conclusions:** We recorded and analyzed the sacroiliitis assessed by A-P view, oblique views radiographs and MRI and found that oblique views had some advantages over A-P view radiographs in assessing sacroiliitis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1678

## AB0692 PARAMETERS ASSOCIATED WITH SEVERE AXIAL STRUCTURAL INVOLVEMENT: DATA FROM THE BAMBOO SPINE COHORT ON 133 SPONDYLOARTHRITIS PATIENTS

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**Background:** Several factors have been associated with the structural severity of axial SpA: older age, disease duration, HLA-B27 positivity, elevated C-reactive protein (CRP) levels, male gender and cigarette smoking status.
**Objectives:** This study aimed to depict the characteristics of the patients with severe axial involvement in 2016 in France, after a long disease duration, and their exposition to NSAIDs, and biologics during the course of their disease.
**Methods:** Patients with severe axial involvement were defined by the presence of at least one of the following criteria: two intervertebral adjacent bridges and/or fusion at lumbar spine and/or at cervical spine; three inter-vertebral adjacent bridges and/or fusion at thoracic spine. Patients have been identified through a nationwide effort involving 19 departments of rheumatology located in France and in Monaco (the ACTSPA network). Data have been retrospectively collected through a structured questionnaire.
**Results:** In the current study, 133 patients have been included between February 2015 and January 2016. Mean (±SD) age was 54 yrs ± 13 at inclusion and 32 years (±12.5) at diagnosis. The patients were mainly males (n=123), sex ratio male/female was 12/1. Mean duration since the diagnosis was 22 yrs (±12.6), but was 28 yrs (± 12.3) since the first axial symptoms. 73% were ever smokers, and 37% were active smokers (n=49; men 38%, women 20%). Mean BASDAI was 2.9/10 (±1.9) and mean BASFI 3.7/10 (±2.0). 42% of the patient reported chest wall pain, 75% buttock pain, 43% peripheral arthritis, 37% enthesitis, and 8% dactylitis. Most patients were HLA-B27 positive (n=96; 72%). 80% had increased CRP during the course of the disease. Anterior uveitis prevalence was 28%, of psoriasis 19%, of IBD 9.8%. 91% of the patients were exposed to NSAIDs during the course of their disease, for a mean exposure duration of 17 years (range 1- 42 yrs). Patients were exposed to biologics in 79% of cases; all of them with at least one TNF-Blocker (mean number of anti-TNF per patient 1.57; mean exposure to the treatment 7.5 yrs). 5 patients were exposed to other biologics (ustekinumab or tocilizumab)
**Conclusions:** This crude data analysis of patients with axial structural lesions shows patients' characteristics that were previously associated with disease severity such as high HLA-B27 prevalence, sex ratio biased toward male gender and systemic inflammation. Nevertheless, these data also demonstrate the potential huge impact of tobacco on disease severity since 73% of the patients from this cohort were ever smokers compared with 36% in DESIR cohort and 52% in the French male population (1). When considering the potential role of NSAIDs or TNF-blockers, further studies are required in particular by comparing this population to other existing cohorts of SpA patients with less structural damage. Moreover, among other mechanisms, epigenetic deregulation induced by smoking should be investigated as a potential disease severity paramer.
**References:**
[1] Tabac info service, 2000.
**Acknowledgement:** This work has been founded by The French Society of Rheumatology
**Disclosure of Interest:** None declared
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## AB0693 GENDER AS A DETERMINANT OF FUNCTIONAL STATUS AND DISEASE ACTIVITY MEASURES IN PATIENTS WITH LONGSTANDING ANKYLOSING SPONDYLITIS

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**Background:** Increasing evidence points to gender differences in disease presentation and course in Ankylosing Spondylitis (AS). This could reflect female specific AS characteristics or inequalities in health care provision.
**Objectives:** To investigate the impact of gender and remoteness on functional outcome, quality of life (QOL) and disease activity measures in an AS cohort with longstanding disease.
**Methods:** Cross sectional cohort study in TNFi naïve AS patients (n=227) in the Arctic region of Norway. Spinal function and functional indices (BASFI, Dougados Index), QOL measures (MHAQ, SF36) were obtained simultaneously with a range of biomarkers (ESR, CRP, IL-6, TNFa, IL-17, IL-23) during a research visit. Remoteness definition was living in a community with <10000 inhabitants. Associations between clinometric, QOL and serological findings were analysed by non-parametric methods.
**Results:** Despite similar age at and disease duration since symptom onset (280 vs 265 months, p=0.5) female patients (n=66) had better spinal flexion (median 40 vs. 36°, p=0.035) and finger floor distance (7 vs. 16 cm, p=0.015) compared to male patients (n=161). While global disease scores (BASFI, Dougados Index, MHAQ and ASDAS-CRP) and comorbidity prevalence were comparable, female patients were more often work disabled (61 vs 49%, p=0.01). IL-6 levels correlate with ASDAS (Rs 0.4, p=0.005), occiput wall distance (Rs 0.32,p=0.012) and inversely with Schober (Rs -0.36 p=0.004), spinal flexion (Rs -0.27, p=0.03) and lateral movement (Rs= -0.31, p=0.013) in female patients only.
**Conclusions:** While remoteness has little impact on the disease severity of AS in Northern Norway, the gender based variation in disease course in AS may be underpinned by differential activation of inflammatory cytokines.
**Acknowledgement:** The authors want to acknowledge the technical assistance of Kirsten Nilsen, bioengineer at Uito
**Disclosure of Interest:** None declared
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## AB0694 INERTIAL SENSOR FOR THE ASSESSMENT OF CERVICAL RANGE OF MOVEMENT IN AXIAL SPONDYLOARTHRITIS

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**Background:** Axial Spondyloarthritis (AxSpA) affects mainly the spine reducing patient mobility including neck. Several tools have been used to evaluate range of motion in AxSpA, but these tools have problems of reliability and accuracy. Motion capture [1], has been recently developed and validated, however a dedicated laboratory of movement is needed. IMU sensors (Inertial Measurement Unit) are a new and cheap kind of technology that allows knowing 3D orientation. These sensors could provide equivalent results to motion capture, with lower requirements, although validation processes are needed.
**Objectives:** To evaluate reliability of an inertial sensor IMU to assess cervical range of movement in patients with AxSpA.
**Methods:** 7 male patients with AxSpA (age 55.9±11.9, time of evolution 14.37±10.74) were included. An IMU sensor (Shimmer3©) placed on the patient's forehead was used. 4 reflective markers were attached to the head using a band (one above the sensor, two over the tragus, and one in the occiput). To detect movement of the trunk, 4 more markers were used (2 over the shoulders, 10 cm below C7 and average distance between L4 and C7). 3D reconstruction

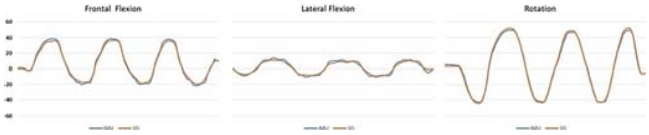
**Abstract AB0694** – Table 1

| | IMU1 | IMU2 | 3D | ICC-A* | ICC-B* | SME-A* | SME-B* | RMSE-A* | RMSE-B* | CV-A* | CV-B* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Frontal flexion (°) | 74.0 (51.0) | 74.1 (52.3) | 72.5 (53.4) | 0.999 (>0.995) | 0.994 (>0.975) | 2.53 | 5.36 | 2.35 | 5.21 | 3.42% | 7.29% |
| Lateral flexion (°) | 49.2 (44.5) | 50.6 (44.8) | 45.1 (43.5) | 0.999 (>0.998) | 0.995 (>0.978) | 1.39 | 4.21 | 1.87 | 5.72 | 2.82% | 8.60% |
| Cervical rotation (°) | 89.2 (62.5) | 91.3 (67.9) | 93.2 (63.2) | 0.993 (>0.967) | 0.996 (>0.981) | 7.88 | 5.73 | 7.64 | 6.67 | 8.90% | 6.45% |

IMU 1, IMU 2: results obtained by the IMU tests (mean (SD)) test/retest. 3D: results obtained by UCOTrack. ICC: intraclass correlation coefficient (value and >95% IC). SME: systematic mean error. RMSE: root mean square error. CV: coefficient of variation. A: comparison test/retest. B: Comparison IMU/3D.

was performed using the UCOTrack© system [1]. 3D orientation was obtained by the sensor and by the UCOTrack, both at 50 Hz. Patient made three bend movements (frontal, lateral and rotation). Measurements were repeated 5 minutes after. PRO questionnaires and structural damage (mSASSS) were also evaluated. Several statistical tests were performed to assess reliability of the sensor and its comparison with the Gold Standard.

**Results:** Affectation level was widely spread among the study participants (BASDAI: 3.4±2.9; BASFI 4.2±3.9; BASMI 5.3±2.2; UCOASMI: 6.1±2.5; mSASSS: 39.9±22.4; cervical mSASSS: 17.9±8.8). Table shows the measurements in the three ranges of cervical motion and statistical parameters analyzed.




**Conclusions:** Test/retest values were very similar, with excellent ICCs and low errors. Motion capture system detected some variations from 3° to 13° at the trunk. To place another IMU sensor at C7 to compensate it is recommended. Number of patients were very small and a model that analyzes the entire spine, not only the cervical part, must be developed. This pilot study shows that IMU sensor could be used, with results very similar to gold standard and with good reliability, improving metrology for AxSpA patients.

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**Disclosure of Interest:** None declared

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## AB0695 BONE QUALITY ASSESSMENT BY THE TRABECULAR BONE SCORE IN SPONDYLOARTHRITIS

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**Background:** Many patients affected by spondyloarthritis are at risk of fracture due to the bone's fragility although their bone mineral density (BMD) is not significantly decreased. Other tools are needed to assess changes in the bone of these patients. The Trabecular Bone Score (TBS) is a bone quality assessment tool that analyses variations of the grey level of a densitometric image. It was evaluated among post-menopausal women and in secondary osteoporosis. It may help to discriminate patients with osteoporosis fractures.

**Objectives:** To evaluate the TBS in a population of spondyloarthritis as a bone quality indicator and look for the clinical and biological factors correlating to the values of the TBS.

**Methods:** Patients who met the criteria of a spondyloarthritis diagnosis and who had a measure of BMD were selected. All these patients came for the setting up or the changing of a biotherapy. Clinical and laboratory data were collected at the same time as the BMD measurement.The TBS measurements were obtained immediately from dual-energy X-ray absorptiometry spinal images. A TBS was considered normal above 1.34, distorted between 1.34 and 1.2 and very distorted below 1.2.

**Results:** Ninety-eight patients participated in the study. The average age was 40.2 years and the average duration of the disease's evolution was of 8.2 years. A spinal BMD lower than -1 and -2.5 T-score was respectively observed in 17% and 3% of patients. The average TBS was lowered to 1.34. The spinal BMD correlated positively to the values of TBS (r=0.61), whereas the duration of the disease's evolution (r = -0.24), its activity level (r= -0.33) and the serum PTH levels (r= -0.27) correlated negatively to the TBS. This association persisted in multivariate analysis. More than half of patients with a BMD above the threshold of a -2.5 T-score had an altered TBS. The relashionship observed between the rates of the PTH and the TBS, which we do not find with the BMD, suggests that a part of the changes of the bone structure in inflammatory rheumatism such as the spondyloarthritis, would be under the dependence of the PTH regardless of the BMD.

**Conclusions:** This study shows that TBS provides additional and independent information from the simple BMD measure on bone status of patients with inflammatory rheumatism. It appears necessary to carry out studies on a larger scale to analyse the discriminating power of the TBS in the prediction of fragility fracture to a greater extent.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.3901

## AB0696 CLINICAL CHARACTERISTICS OF SPONDYLOARTHRITIS IN THE CZECH REPUBLIC: A SINGLE CENTRE COHORT

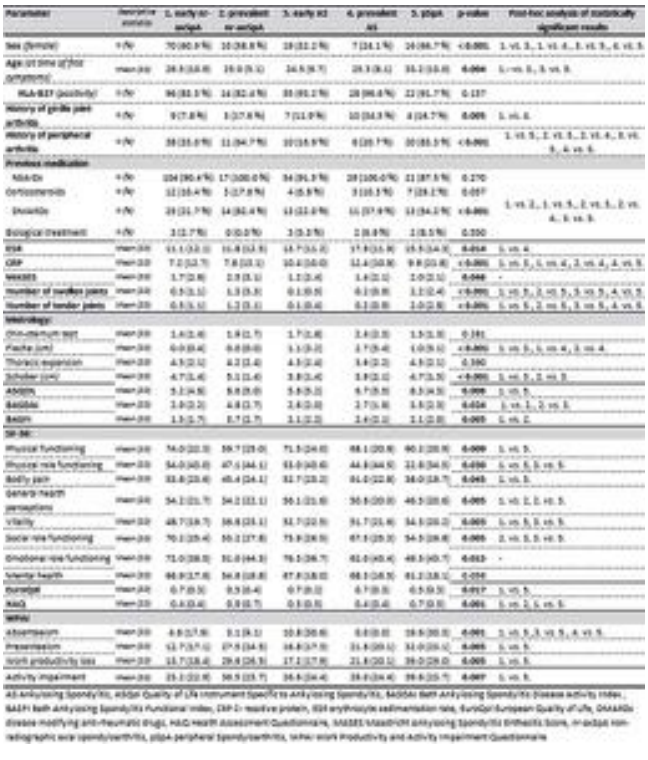
K. Grobelná[1], Š. Forejtová[1], M. Urbanová[1], K. Zegzulková[1], M. Hušáková[1], T. Philipp[2], J. Gatterová[1], J. Hořínková[1], K. Hejduk[3], L. Šenolt[1], K. Pavelka[1]. *[1]Rheumatology Institute in Prague; [2]Thomayer Hospital, Prague; [3]Institute of Biostatistics and Analyses, Brno, Czech Republic*

**Background:** Spondyloarthritis (SpA) is an inflammatory rheumatic disease with predominantly axial or peripheral involvement.

**Objectives:** To present baseline characteristics of different groups of SpA patients.

**Methods:** 244 patients diagnosed with SpA were examined between 2012–2015 and divided into 5 subsets: early non-radiographic axial SpA (nr-axSPA), prevalent nr-axSpA, early ankylosing spondylitis (AS) prevalent AS, peripheral SpA (pSpA), according to the time of diagnosis (more or less than 3 years from baseline examination) and according to the imaging arm of ASAS criteria for axSpA and for pSpA. The analysis included: gender, age/type of first symptoms, age at diagnosis, family history, inflammatory back pain, history of peripheral or girdle arthritis and extraarticular manifestations, previous/present medication (NSAIDs, DMARDs, glucocorticoids, biological agents), smoking, BMI, spinal mobility, *MASES*, swollen/tender joints, physician global assessment (MDGAS), ASDAS-CRP, BASDAI, BASFI, quality of life outcomes (ASQol, SF-36, EuroQol, HAQ, WPAI), HLA-B27, ESR, CRP. Kruskal-Wallis test and post-hoc analysis were used, data are presented as mean±SD.

**Results:** We found a significant difference in gender: majority of nr-axSpA patients as well as pSpA were females in contrast to subsets of AS patients. Patients with early AS developed first symptoms earlier compared to patients with early nr-axSpA and pSpA. Prevalent subsets had higher occurrence of girdle and peripheral arthritis compared to early subsets. Previous treatment with DMARDs was significantly higher in patients with prevalent nr-axSpA and pSpA compared to the remaining subsets. Patients in AS subsets compared to nr-axSpA subsets had significantly worse spinal mobility (fleche, modified Schober distance). BASDAI was significantly higher in prevalent nr-axSpA compared to early nr-axSpA and early AS. BASFI was significantly higher in prevalent nr-axSpA compared to early nr-axSpA. ASQol values were significantly higher in prevalent nr-axSpA and pSpA compared to early nr-axSpA. Almost all SF-36 values and EuroQol were significantly lower in pSpA compared to axSpA (especially early subsets). WPAI values showed worse work conditions (absenteeism, presenteeism, work productivity and activity impairment) in pSpA compared to all subsets of axSpA, especially nr-axSpA with significant differences in all parameters. CRP levels



were significantly higher in AS subsets compared to nr-axSpA subsets. We did not find significant difference in HLA-27 positivity across analyzed subsets, however nr-axSpA groups had tendency to lower percentage of HLA-B27 positivity compared to the remaining groups.
**Conclusions:** The results of our study are comparable to other SpA cohorts described in the literature. In addition, we demonstrated worse quality of life and work limitations in patients with pSpA than in those with axSpA.
**Acknowledgement:** Supported by MHCR 23728
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2802

## AB0697 DOES VITAMIN D AFFECTS THE SEVERITY OF THE DISEASE IN PATIENTS WITH ANKYLOSIS SPONDYLOARTHRITIS IN A SUNNY COUNTRY?

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**Background:** Vitamin D has been found to have a role in immune system function. It there's been many studies on the relationship between vitamin D and disease activity in ankylosing spondyloarthritis (AS). However, studies have concerned the groups based on vitamin D levels and determined the differences between these patients in terms of disease activity, functional status, quality of life, and others clinical parameters. The aim of this study was to compare 25-hydroxyvitamin D (25 (OH) D) in patients with AS and healthy subjects and to determine the relationship between 25 (OH) D and activity disease, functional status and quality of life.
**Objectives:** The aim of this study is to compare 25-hydroxy-vitamin D3 (25(OH)D3) levels in AS patients with those in normal healthy subjects and to determine the relationship between 25(OH)D3 levels and AS disease activity, functional status, and quality of life.
**Methods:** hundred twenty-five consecutive patients and 76 healthy volunteers were included in this study. After a comparison between the patient group and the control group, the group of patients was divided into normal subgroups, deficient and inadequate function of plasma 25 (OH) D3 levels for another comparison
**Results:** Level differences 25 (OH) D between the patients and controls were statistically significant. The number of patients with AS whose rates 25 (OH) D were classified as normal, insufficient and deficient were respectively 32, 51 and 38.
The sedimentation rate (ESR), C-reactive protein (CRP) and the scores Bath AS Disease Activity Index (BASDAI) were higher in the subgroup deficiency and 25OHD deficiency ($P<0.05$). Bath functional scores (BASFI) and the quality of life (ASQoL) were significantly different between the subgroup with normal 25OHD levels and deficient subgroups ($P<0.05$). Finally the level of pain, BASDAI, ESR and CRP were inversely correlated with 25OHD ($P<0.05$)
**Conclusions:** Plasma levels of 25 (OH) D may be reduced in patients with ankylosing spondyloarthritis and this can negatively affect the activity of the disease, the functional status and quality of life.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1561

## AB0698 CLINIMETRIC PROPERTIES OF THE ASAS HEALTH INDEX IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: VALIDATION IN AN ITALIAN COHORT

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**Background:** Over the last decades, many efforts have been conducted to develop useful tool for the evaluation of disease activity. However, since the development of Assessment of SpondyloArthritis international Society Health Index (ASAS HI), no specific freely available questionnaires to describe the overall picture of impairments, limitations and restrictions in activities or social partecipation.
**Objectives:** The aims of this study were to test the feasibility, reliability, and construct validity of the ASAS HI, in order to compare its clinimetric properties with the current available measures of disease activity, functional limitation and health status assessments in patients with axSpA.
**Methods:** A cohort of 140 consecutive axSpA has been the object of study. The feasibility has been determined by the percentage of patients who were able to complete the questionnaire by themselves and by the time employed to fill the ASAS HI. The reliability has been evaluated performing a test-rerest of the questionnaire within a week. The construct validity was examined in three ways. First, we examined construct convergent validity by correlating the scores of the ASAS HI with ASDAS-CRP/ESR, SASDAS, BASDAI, BASMI, BASFI, the ASQoL and EQ-5D. Secondly, we have created patient groups based on the patients' activity ranks (ASDAS-CRP and SASDAS categorisation) within the cohort to assess discriminative accuracy. Additionally, to distinguish patients with active and non-active disease and to assess their respective cut-off points values, the receiver operating characteristic (ROC) curve analysis was used. Thirdly, we analyzed the contribution of demographic (age, sex, and disease duration) and clinical variables (number of comorbidity and disease activity by ASAS-CRP) to the attainment of an ASAS HI condition by stepwise logistic regression.
**Results:** The mean time to complete the ASAS HI was 114.9± 45.2 seconds (range 48 – 210 seconds). Coefficients of agreement between ASAS HI scores on first and second administrations were excellent and all items showed very good agreement (ICC =0.976; range 0.966 to 0.982). The ASAS HI was correlated significantly with all other comparator scores ($p<0.0001$). The highest correlations were seen with ASQoL (rho 0.784; $p<0.0001$), BASFI (rho 0.671; $p<0.0001$) and SASDAS (rho 0.640; $p<0.0003$). On categorizing patients into different cut-off point of disease activity, with respect to the both ASDAS-CRP and SASDAS, ASAS HI scores were highly significantly different between the four categories ($p<0.0001$). An ASAS HI value of 4.0 resulted the cut-off with the highest combination of sensitivity and specificity (82.6% and 86.3%, respectively) to distinguish the inactive disease.
**Conclusions:** The results reported in this study confirm the feasibility, reliability and validity of the ASAS HI in Italian patients with axSpA. Of particular interest appears the cut-off value of 4.0, under which could be identified the inactive disease. This value could represent an easily applicable starting point in daily clinical practice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2932

## AB0699 ENTHESITIS AND SACROILIITIS PREVALENCE DETERMINED BY DOPPLER ULTRASONOGRAPHY AND MAGNETIC RESONANCE IMAGING IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Background:** Patients with inflammatory bowel disease (IBD): Crohn disease (CD) and ulcerative colitis (UC) can develop extraintestinal manifestations and ones of the most important are musculoskeletal affections. In published studies, the prevalence of Spondyloarthritis (SpA) stands from 10 to 20% but with a wide range of variation. These differences are related to the methods used for its determination.
**Objectives:** 1) To determine the prevalence of sacroiliitis with X-ray or magnetic resonance imaging (MRI) and of enthesitis with Doppler ultrasonography in patients with active IBD without following an immunosuppressant therapy 2) To check the prevalence of patients with positive ASAS criteria for axial and peripheric SpA.
**Methods:** Cross-sectional study in which a sample of patients diagnosed of active IBD, without previous diagnosis of rheumatic inflammatory disease and without any previous immunosuppressant therapy, underwent a comprehensive rheumatologic examination addressed to detect musculoskeletal SpA features. Data collected comprised: demographics, family medical history, IBD characteristics and comorbidities, axial symptoms, swollen and tender joint counts (44/46 joints), entheses and dactylitis examinations, BASDAI and BASFI questionnaires and CRP and HLAB27 blood tests. The following image techniques were also applied: cervical, lumbar column and pelvis X-ray, sacroiliac MRI with T1 and STIR sequence and ultra-sound exploration of entheses.
**Results:** 30 patients (16 women) with a mean age 39.8 (9,8) years have been studied. 16 had CD and 14 UC. 16% tested positive for B27. 14 patients referred chronic lumbar pain, 4 of them with inflammatory characteristics. 10 patients referred arthralgias, without joint swelling o redness and 3 patients had history of heel pain, although they were not explored for any physician. None of the patients did not refer past medical history of uveitis or psoriasis (family or own history). 36% of the patients had MRI signs of sacroiliac inflammation that met ASAS criteria. One of the patients had grade 3 radiographic sacroiliitis and one patient with inflammatory signs in sacroiliac joints by MRI did not refer chronic lumbar pain. Ultrasound alterations were found in at least one enthesis within 97% of the patients: entheses calcifications (72%), bursitis (61%) and erosion (5%).
**Conclusions:** In patients with active IBD not previously diagnosed with SpA, the existence of sacroiliitis and ultrasound alterations in entheses is frequent (36% and 97%, respectively). The prevalence of patients meeting axial SpA ASAS criteria is 32% and for peripheral criteria is 10%. The lower frequency of peripheral SpA can be attributed to an earlier diagnose of this form of presentation or to a lack of sensitivity of the peripheral SpA ASAS criteria on patients with IBD. Addition of ultrasound results in classification criteria could take into account patients with enthesitic signs earlier.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2516

## AB0700 BASELINE CLINICAL CHARACTERISTICS OF THE LEEDS SPARRO EARLY PSORIATIC ARTHRITIS COHORT: HIGH DISEASE AND RADIOGRAPHIC INVOLVEMENT ARE SEEN EARLY EVEN IN THE PRESENCE OF PRESERVED QUALITY OF LIFE

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**Background:** Data are mounting on the need to treat PsA early to improve long term outcome and prevent disability. There are few cohorts of early untreated PsA reported in the literature with variable characteristics and outcomes which may reflect different geographical and health economic backgrounds.
**Objectives:** To describe the baseline clinical characteristics of the early PsA cohort recently initiated as part of the Leeds SpARRO (Spondyloarthropathy Register for Research and Observation) study to assess how change in practice implemented through dedicated early synovitis and SpA clinics may affect outcome in SpA.
**Methods:** Observational study describing baseline clinical characteristics of the first 55 patients recruited to the Leeds SpARRO register with a new diagnosis of PsA. Data are presented as descriptive statistics including demographics, clinical disease activity measures, treatment and patient reported outcomes.
**Results:** Subjects recruited fulfilled CASPAR criteria [mean disease duration from symptom onset is 1.5±0.6 years]; F:M ratio 1.4; 66% white British; mean BMI 29±6 kg/m$^2$ and were DMARD naïve (90%) at presentation. The majority were negative for both RF and CCP antibodies (96% [n=53]; with an asymmetrical (67%), polyarticular joint phenotype (73%). Axial involvement was seen in 29% (n=16). As expected, the majority of the cohort was negative for HLA-B27 (76%, n=42). Prevalence of current skin psoriasis was high (91%) although extent and severity were mild (PASI median (IQR) 4 (0–27). Nail involvement was recorded in 50% (mNAPSI mean± SD 8±11). No extra-articular manifestations were seen apart from 1 case with Crohn's disease. Quality of life scores for skin and joints showed mild impairment [DLQI median (IQR) 4 (1–9)] and PsAQoL [median (IQR) 7.5 (3–12)] however, the PASDAS was consistent with high disease activity mean ±SD (5.6±1.2). Furthermore, baseline radiographic assessment (n=44) showed established change in 25% (n=11) [juxta-articular new bone formation (n=7) and erosions (n=4; all in MTP joints)] of subjects whilst 50% of the total population were smokers (22% n=12 current; 27% n=15 previous). HAQ score (median [IQR] was 0.75 [0.25–1.4]).

Table 1. Baseline clinical characteristics of early PsA patients

| Clinical characteristics | Values | Pt number |
|---|---|---|
| Age, mean ± SD years | 42±12 | 55 |
| Skin psoriasis duration (yrs) | 10±11 | 47 |
| Family history of psoriasis, n (%) | 32 (61%); unknown in 2 (4%) | 55 |
| Family history of PsA, n (%) | Yes 5 (9%); unknown 3 (5%) | 55 |
| DIP prominent disease, n (%) | 6 (11%) | 55 |
| Arthritis mutilans, n (%) | 0 (0%) | 55 |
| Dactylitis score, mean ± SD | 1±1 | 55 |
| MASES, mean ± SD | 2±3 | 55 |
| SJC76, mean ± SD | 4±6 | 55 |
| TJC78, mean ± SD | 12±15 | 55 |
| Early MS, mean ± SD | 101±167 | 54 |
| CRP level mg/L, mean ± SD | 11±22 | 55 |

**Conclusions:** Our cohort of early, untreated PsA shows relatively preserved quality of life at baseline highlighting the successful and timely identification of these patients through early arthritis clinics. Still, composite measures of disease activity and radiographic assessment confirm highly active disease and established damage in 25% of cases, emphasizing the need for prompt intervention to achieve immediate disease control and prevent disability and development of co-morbidities in this disease.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5856

## AB0701 THE DIAGNOSTIC VALUE OF SACROILIAC PROVOCATION TESTS IN SPONDYLOARTHRITIS AND THEIR RELATIONSHIP WITH MAGNETIC RESONANCE IMAGING FINDINGS

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**Background:** Sacroiliac provocation tests are used in cases with a suspected diagnosis of spondyloarthritis (SpA). However, all of the studies on the diagnostic value of these physical examination tests have been carried out in non-inflammatory sacroiliac (SI) joint pathologies, and the data about the contribution of these tests in the diagnosis of SpA is poor.
**Objectives:** To investigate the role of sacroiliac provocation tests in the diagnosis of SpA, and their relation with inflammatory findings in magnetic resonance imaging (MRI).
**Methods:** 51 patients (F/M=7/44) with chronic low back and/or hip pain admitted to the rheumatology clinic were included in the study. The history of patients participating in the study were taken by a rheumatologist, and another experienced rheumatologist who is unaware of the patient's medical information performed 5 different challenge tests for SI joints (sacroiliac compression test, sacroiliac distraction test, FABER-Patrick test, sacral thrust test, drop test) within a certain protocol. All patients were evaluated with sacroiliac MRI for the presence of acute inflammation. The sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratio (LR) and diagnostic accuracy of each physical examination methods were calculated with taking clinical diagnosis and sacroiliac MRI as the standard evidence of acute inflammation (2 different comparisons).
**Results:** 30 patients included in the study met the diagnostic criteria for SpA. Calculations related to diagnostic value of each examination method are summarized in Table 1.When data was analyzed for the diagnosis of SpA, the positive LR value of provocation tests ranged between 1.4–2.24.For the relationship between the examination findings and acute changes in SI joint MRI, LR values ranged positively between 1.1–2.79.Inflammatory back pain in history was associated with a positive LR value of 1.17 in predicting the diagnosis of SpA and a positive LR value of 1.37 in predicting acute changes in MRI.

Table 1. The diagnostic features of sacroiliac joint provocation tests (acute inflammation in MRI are taken as standard)

| | Sacroiliac compression test | | Sacroiliac distraction test | | FABER-Patrick | | Sacral thrust test | | Drop test | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Dx | MRI | Dx | MRI | Dx | MRI | Dx | MRI | Dx | MRI |
| Prevalance | 0.41 | 0.41 | 0.65 | 0.65 | 0.61 | 0.35 | 0.76 | 0.76 | 0.43 | 0.43 |
| Sensitivity | 0.43 | 0.53 | 0.71 | 0.77 | 0.46 | 0.43 | 0.79 | 0.87 | 0.61 | 0.53 |
| Spesifity | 0.61 | 0.76 | 0.43 | 0.52 | 0.78 | 0.76 | 0.26 | 0.38 | 0.78 | 0.71 |
| PPV | 0.57 | 0.76 | 0.61 | 0.70 | 0.72 | 0.72 | 0.56 | 0.67 | 0.77 | 0.73 |
| NPV | 0.47 | 0.53 | 0.56 | 0.61 | 0.55 | 0.48 | 0.50 | 0.67 | 0.62 | 0.52 |
| LR+ | 1.10 | 2.24 | 1.26 | 1.61 | 2.14 | 1.82 | 1.06 | 1.40 | 2.79 | 1.87 |
| LR- | 0.94 | 0.61 | 0.66 | 0.45 | 0.68 | 0.74 | 0.82 | 0.35 | 0.50 | 0.65 |
| Accuracy | 0.51 | 0.63 | 0.59 | 0.67 | 0.35 | 0.57 | 0.55 | 0.67 | 0.69 | 0.61 |

Dx, diagnosis; PPV, Positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

**Conclusions:** These results show that the contribution of SI provocation tests for predicting the findings of inflammation in MRI or SpA diagnosis is extremely limited.When compared to the diagnostic accuracy of similar tests in non-inflammatory conditions of SI joint in the literature, the predictive value of provocation tests in the diagnosis of inflammatory conditions seems to be lower.
**Disclosure of Interest:** None declared
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## AB0702 MEDIAL OLIVOCOCHLEAR REFLEX IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is a chronic systemic inflammatory disease. Via autoimmune mediators, AS can damage the auditory system similar to other systems. Otoacoustic emissions studies in patients with AS showed that the damage that causes hearing loss was in the outer hair cells. The medial olivocochlear (MOC) reflex is used to evaluate the medial olivocochlear efferent system (MOES), which includes the outer hair cells.
**Objectives:** The aim of this study was to evaluate the presence of subclinical damage in the inner ear with the aid of the MOC reflex test in patients with AS with no hearing complaints.
**Methods:** Thirty-four patients with AS and a control group of 30 healthy volunteers with similar demographic characteristics were evaluated in the study. Otoacoustic emission responses, MOC reflex results, and frequency-specific and total suppression findings were compared between the groups. The relationship between the clinical and laboratory findings for the patients with AS and the MOC reflex data were also investigated.
**Results:** Reduced MOC reflex response ($p$=0.04) and suppression ($p$=0.019) were detected in patients with AS. When the clinical and laboratory findings for the patients with AS and the MOC reflex test results were compared, a significant correlation was found only between the MOC reflex and the erythrocyte sedimentation rate (ESR).
**Conclusions:** The results showed that AS can damage the inner ear, especially the MOES, and can reduce the MOC reflex response without clinical hearing loss.
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## AB0703 PREVALENCE OF AXIAL AND PERIPHERAL SPONDYLOARTHRITIS IN A SAMPLE OF LEBANESE PATIENTS WITH PSORIASIS

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**Background:** Spondyloarthropathies (SpA) are a group of frequent inflammatory rheumatic disorders with usually delayed diagnosis. Extra articular manifestations such as psoriasis are frequently observed, therefore it is crucial to detect SpA at the dermatologist's clinic.
**Objectives:** The main objective is to evaluate the prevalence of axial SpA in a sample of Lebanese patients with psoriasis. Secondary objectives include evaluating the prevalence of inflammatory back pain (IBP) and peripheral SpA.
**Methods:** We evaluated a sample of consecutive patients, with cutaneous or nail psoriasis, diagnosed by a dermatologist at Hotel-Dieu de France hospital, and a control sample of patients consulting for other dermatologic symptoms. Patients and controls responded to a questionnaire including items corresponding to different sets of SpA criteria. Biology and imaging data were retrieved from the medical file.
**Results:** 80 patients were included, 48 psoriasis and 32 controls. Mean age was 39.3 years (SD 17.66), sex ratio was 1. Mean psoriasis duration was 12.9 years (SD 12.37). 14.6% of psoriasis patients were on systemic treatment, 0% had HLA B27 available, 4.2% had imaging and 12.5% had CRP results. In the psoriasis patients, the prevalence of axial SpA according to the ASAS criteria was 4.2% compared to 0 in the control group. However, according to Amor criteria, where imaging or HLA B27 are not mandatory, the prevalence of SpA was 29.2%, significantly higher than in the control group 0% (p 0.01). The prevalence of peripheral SpA (ASAS criteria) was 27.1%, higher than the control group 0%. The prevalence of IBP according (ASAS criteria) was numerically higher 14.6% in the psoriasis group compared to 3.1% in the control group (p 0.135). No significant correlation was found between age, gender, psoriasis duration and diagnosis of SpA. A statistically significant difference was found between psoriasis duration and IBP prevalence (p 0.049), between family history of SpA and axial SpA (OR 2.18, p 0.003) and IBP (OR 2.38 p 0.027). Nail psoriasis seemed to be associated with peripheral SpA (OR 2.5), however the association was not statistically significant (95% CI 0.62–10.05). The same trend was found for generalized psoriasis: OR 2.47 (95% CI 0.65–9.34).
**Conclusions:** The expected significantly higher prevalence of SpA in the psoriasis sample indicates the importance of raising the awareness of Lebanese dermatologists to early detection of SpA. From simple clinical hints (IBP, family history of SpA, nail psoriasis), the index of suspicion should be high enough to prescribe the appropriate tests and/or refer the patient to a rheumatologist.
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**Acknowledgement:** Dermatology Department, Hotel-Dieu de France hospital, Beirut
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## AB0704 DIFFERENTIAL EVALUATION OF SPONDYLOARTHRITIDES RADIOGRAPHIC FEATURES

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**Background:** Diagnosis and differential diagnosis of various forms of spondyloarthritides is primarily based on the clinical manifestations and radiographic features analysis. Clinical manifestations though can be quite similar, so imaging studies data play an important role in diagnosis.
**Objectives:** To evaluate the differences of certain forms of spondyloarthritides in terms of radiographic features and also the opportunity to establish differential diagnosis and prognosis of the disease on this basis.
**Methods:** The study enrolled 100 patients with spondyloarthritides. The first arm included 50 patients with ankylosing spondylitis (AS). The second arm included 50 patients with Chlamydia-induced spondyloarthritis (HiSPA). The diagnosis of AS was made on the basis of the modified New York criteria (1984). Mean patients' age was 34.0±10.9 years in the AS arm and 27.1±6.9 years in the HiSPA arm. All patients in both arms were males. Mean disease duration was 6.4±4.5 years [1.9; 10.9] in the AS arm and 5.6±4.7 years [0.9; 10.3] in the HiSPA arm. Patients underwent radiography of the sacroiliac joints (SIJ), lumbar, thoracic and cervical spine. We evaluated and compared the frequency of the following radiographic features: erosions/pseudodilation or irregular narrowing of the SIJ, SIJ ankylosis, symmetrical syndesmophytes in any region of the spine, asymmetrical syndesmophytes in any region of the spine.
**Results:** Our study showed the following rate of the individual radiographic features: erosions/pseudodilation or irregular narrowing of the SIJ: 11 (22.0%) in the first arm and 32 (64.0%) in the second arm ($p<0.05$); SIJ ankylosis: 28 (56.0%) in the first arm and 2 (4%) in the second arm ($p<0.05$); symmetrical syndesmophytes: 34 (68%) in the first arm and 3 (6.0%) in the second arm; asymmetrical syndesmophytes: 5 (10.0%) in the first arm and 21 (42.0%) in the second arm ($p<0.05$). Furthermore, in the AS arm radiography significantly more often revealed simultaneous involvement of all 3 spine regions (cervical, thoracic, lumbar): 17 (34.0%) vs. 2 (4.0%) in the HiSPA arm ($p<0,05$).
Thus, despite the general similarity of radiographic features, we have identified significant differences, which, in our opinion, are due to diversity of pathogenesis and can be considered predictors of structural disease progression rate. This observation can help in the diagnosis and disease prognosis establishment, as well as in the prediction of the skeletal dysfunction course in patients with spondyloarthritides.
**Conclusions:** Our findings suggest differences in AS and HiSPA radiographic features. In the first arm they were of more pronounced proliferative and progressive nature, and in the second had distinct inflammatory features with less progression while disease duration in both groups was quite comparable.
**Disclosure of Interest:** None declared
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## AB0705 FATIGUE, PAIN AND PATIENT GLOBAL ASSESSMENT ARE UNSTABLE IN SPONDYLOARTHROPATHY PATIENTS WITH STABLE DISEASE ACCORDING TO BASDAI

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**Background:** The use of patient-reported outcome measures has become routine in clinical practice and in clinical trials. In order to use a specific outcome measure in the daily clinic, the natural variation of the outcome measure must be known. Natural variation may also be characterized as measurement error and is assessed in individuals who are considered to be in "steady state".
**Objectives:** To examine natural variation of BASFI, patient global assessment (PaGl), pain, fatigue in patients with stable spondyloarthropathy (SpA).
**Methods:** 107 SpA patients treated in the daily clinic with a TNF-inhibitor and characterized by stable disease were identified in the Danish rheumatology registry (DANBIO). According to ASAS response criteria for biological treatment in SpA [1] and to previous reports on BASDAI measurement errors [2], stable disease was defined as a change in BASDAI $\leq$20 between two consecutive visits. Paired data from a single set of such two visits were extracted for each patient. Data comprised BASDAI, BASFI, PaGl, pain and fatigue scored on 0–100 VAS scales. Natural variation was examined using the Bland-Altman method with calculations of lower and upper 95% limits of agreement (LLoA;ULoA) between two consecutive assessments and the corresponding bias (mean of individual differences). Associations between intra-individual inter-visit differences ($\Delta$) were described by linear correlation (r) and stepwise multiple regression analyses (partial regression coefficients (rp) and standard errors of estimation (SEE)).
**Results:** Mean age was 44±14 years, mean inter-visit time duration 16±13 weeks (range 3 – 91) and mean $\Delta$BASDAI 0.0±10.5 (range -20 – 20, ns). Biases were close to 0 for all the variables indicating stable conditions on the group level between the two consecutive visits. On the individual level, differences were more pronounced (Table). LoA for BASFI corresponded to the predefined accepted limits for BASDAI (±20). However, LoA for fatigue, pain and PaGl approximated ±35. No significant correlations were found between the absolute $\Delta$values of BASDAI, BASFI, fatigue, pain or PaGl and the inter-visit time duration (r range -0.1 – 0.2, ns). $\Delta$BASFI, $\Delta$fatigue, $\Delta$pain and $\Delta$PaGl were weakly correlated with $\Delta$BASDAI (r range 0.30 – 0.60, $p<0.01$). In multiple regression analyses, $\Delta$BASFI was best predicted by $\Delta$pain, and $\Delta$fatigue, $\Delta$pain and $\Delta$PaGl by $\Delta$BASDAI (rp range 0.40 – 0.49, $p<0.0001$, SEE). Although the associations were highly significant, SEEs were high (range 10.8 – 15.6) illustrating poor agreement in individuals.

Table 1. Agreements between two consecutive measurements in SpA patients with stable disease (change in BASDAI $\leq$20)

| Level | Group (mean ± SD) | | | Individual | |
|---|---|---|---|---|---|
| | Visit 1 | Visit 2 | Bias | LLoA | ULoA |
| BASFI | 33.0±24.8 | 32.7±25.2 | –0.3±11.7 (ns) | –23.2 | +22.6 |
| Fatigue | 49.3±28.2 | 48.7±28.7 | –0.6±18.8 (ns) | –37.4 | +36.2 |
| Pain | 35.6±26.9 | 34.8±25.7 | –0.8±17.0 (ns) | –34.1 | +32.5 |
| PaGl | 40.8±27.9 | 39.4±27.9 | –1.4±17.5 (ns) | –35.7 | +32.9 |

**Conclusions:** Independently of time duration, fatigue, pain and PaGl fluctuated substantially and unpredictable in SpA patients with stable BASDAI. In the daily clinic, a change in these outcome measures of at least 35 may be considered as natural variation or "measurement error" with no clinically important relation to the disease activity.

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## AB0706 LIPID PROFILE AND ACTIVE SYSTEMIC INFLAMMATION MAY DIFFERENTLY AFFECT THE PATHOMECHANISM OF CARDIOVASCULAR DISORDERS IN ANKYLOSING SPONDYLITIS (AS) AND IN PSORIATIC ARTHRITIS (PSA)

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**Objectives:** To investigate lipid profile, inflammatory mediators, markers of endothelial activation and other clinical factors associated with cardiovascular risk in AS and PsA.
**Methods:** Lipid profile, atherogenic index (AI –the TC: HDL)), CRP level, disease activity (BASDAI and ASDAS), patients BMI and risk factors like smoking and hypertension were evaluated in 21 AS patients (6 female, 15 male, mean age 41,6±7,4 years, with disease duration of 6,5 ±10,1 years) and in 18 PsA patients (8/f, 10/m, mean age 46,1± 10,6 y., disease duration 6.1±7,5 y.). Serum concentrations of ICAM-1, RANTES, CD40 Ligand were measured using ELISA. The SCORE calculator was used for CV risk estimation.
**Results:** Mean values of BMI for AS and PsA patients, mean age and the disease duration did not differ significantly between the study groups. There were 9 smokers, 6 patients with hypertention and 3 patients with a coronary heart disease (CHD) in AS group and 5 smokers, 11 patients with hypertension, 3 with CHD in PsA. Mean values of BASDAI 5,9±1,9 SD in AS and 4,4±2,2 in PsA indicated active diseases. The SCORE CV risk above 5% was found in 4 patients (19%) with AS and in 3 PsA patients (16%). In AS AI (3.6±1) was significantly lower and HDL/LDL (0.51 ±0,1) higher vs. AI (4,4±1) and HDL/LDL (0,46± 0,1) in PsA ($p<0,03$).
14 (AS + PsA) smokers revealed higher serum levels of ICAM-1 (17,9± 7,7 ng/ml) comparing to 25 non –smokers (12,8±2,5 p=0.004). In AS we found significant ($p<0,05$) positive correlations between BASDAI values and HDL levels (r=0,4) and ASDAS and HDL (r=0,55) and negative correlations between BASDAI and AI (r= -0,60), ASDAS and AI (r= -0,50), BASDAI and CD 40 Ligand (r= -0,5). In PsA only BASDAI positively correlated with HDL levels (r=0,56). In non –smokers AI positively correlated with CD40 Ligand and CD40 Ligand negatively correlated with BASDAI. In smokers BASDAI and ASDAS positively correlated with HDL and BASDAI negatively with AI. We did not find any correlatinons between SCORE risk, disease activity, markers of inflammation and vascular injury.
**Conclusions:** In our opinion the SCORE calculator underestimates CV risk in AS and PsA. Higher activity of the disease is associated with elevated HDL levels and decreased AI (a lipid paradox), which may suggest, that mostly in active AS, factors other then cholesterol-related are associated with the pathogenesis of CV disorders.
Neither lipid alterations nor inflammatory mediators but smoking seems to be the strongest factor associated with a direct vascular injury.
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## AB0707 CHECKLISTS (MINIMUN AND EXCELLENCE) FOR THE EVALUATION OF PATIENTS WITH AXIAL SPONDIYOARTHRITIS IN DAILY PRACTICE: PERSONALIZA PROJECT

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**Background:** Currently there is great workload in rheumatologic clinics and a lot of variability in the type and number of potential measures for patients with axial SpA.
**Objectives:** To standardize axial SpA evaluation in daily practice through the generation of two checklists (one for minimum and another of excellence).
**Methods:** A qualitative study was performed. First, an expert panel was set up (8 rheumatologists with interest and experience in axial SpA). A focal group with patients was organized. Barriers and facilitators in the evaluation and management of patients with axial SpA was analyzed. A systematic literature review was performed in order to identify measures for axial SpA and methodological characteristics as their validity or impact in daily practice. All of this information was presented to the experts and discussed. As a result, a draft of variables for a proper evaluation of patients with axial SpA was proposed. Then, the experts evaluated different characteristics of these variables (validity, feasibility, impact, etc) and selected a feasible and relevant list of variables (minimum checklist, in case of busy clinics or less skilled professionals) and added some other interesting variables (excellence checklist, the ideal evaluation) to cover all the domains of the disease. With these variables an electronic and paper checklists were designed.
**Results:** Two checklists were generated. The minimum checklist includes a) Personal history (date of symptoms start, date of diagnosis, family history of Crohn disease/ulcerative colitis, psoriasis, reactive arthritis, uveitis, spondyloarthritis, smoking status, peripheral disease, enthesitis, dactylitis, extra-articular manifestations, profession, physical activity, inflammatory low back pain; b) Comorbidity (arterial hypertension, Diabetes Mellitus, hypercholesterolemia, cardiovascular disease, gastric ulcers, depression, osteoporosis, others); c) Physical examination (enthesis, synovitis, hips, dactylitis, modified Schöber, thoracic expansion, cervical rotation); d) Activity control (ASDAS, BASDAI, physician VAS, d) Function: BASFI; e) Labs and imaging (hemogram, ESR, biochemistry, CRP, urine, axial and sacroiliac x-ray, HLA B-27); f) Treatments (NSAID, biologic therapy, cessations and reasons, other treatments, physical activity). In the excellence checklist along with the previous, the following variables were included: blood pressure, cardiac frequency, weight, height, BMI, abdominal perimeter, BASMI, lipids, 25-OH Vitamin-D, glicohaemoglobina, microalbuminuria, DEXA.
**Conclusions:** These checklists for patients with axial SpA might help evaluate rheumatologists in daily practice in order to early recognition and management of comorbidities, disease activity and other outcomes.
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## AB0708 DELAY TO DIAGNOSIS IN ANKYLOSING SPONDYLITIS: A LOCAL PERSPECTIVE

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**Background:** The diagnostic delay in axial spondyloarthritis is reported to be improving after campaigns by ASAS and the rheumatology community to educate primary care physicians to refer patients for early assessment[1]. MRI scanning has also been in widespread use since 2000. We conducted a local study to assess if diagnostic delay was improving in our well-defined cohort of ankylosing spondylitis (AS) patients who are reviewed in our physiotherapy-led service, and to compare this with national trends.
**Objectives:** We set out to determine the time to diagnosis of AS in our cohort and to assess if this has changed over time. Our aim is to reduce diagnostic delay by educating local primary care clinicians about inflammatory back pain (IBP) and the importance of early recognition and referral.
**Methods:** Patients were identified from the physiotherapy database of 53 patients currently reviewed under the AS service at a district hospital in the North West of England. We assessed mean and median delay to diagnosis, gender, family history of AS, those diagnosed pre- and post-2000, patient age and date of first presentation to primary care with IBP, and date of first rheumatology review. Only those fulfilling diagnostic criteria for AS were included in the dataset.
**Results:** 44 males and 9 females with age range 28–83 years.
Mean delay to diagnosis was 8.94 years. Median delay to diagnosis: 8 years.
1962–1999 (10 patients) Mean 6.7 years. Median 7 years
2000–2004 (13 patients) Mean 9.5 years. Median 7 years
2005–2009 (15 patients) Mean 9.8 years. Median 8 years
2010–2015 (16 patients) Mean 9.1 years. Median 7 years
Range of diagnostic delay was 0 to 40 years. 15% were diagnosed in <2 years. 42% diagnosed in <5 years. 58% diagnosed in <10 years. The pre-2000 mean delay to diagnosis was 6.7 years, Post-2000 mean delay was 9.45. However, 81% of our AS patients were diagnosed post-2000.
42% of patients were on biologic therapy, the remainder were on NSAIDs. No significant difference was seen between the sexes. 19% of patients had a clear family history of AS, and no difference was seen in delay to diagnosis compared to those without family history.
**Conclusions:** Our findings closely reflect those of national data obtained in recent studies[2]. Diagnostic delay has not improved in the time frame of this local study, although AS diagnoses have proportionally increased, likely due to increased use of MRI. Why is the delay not improving? Back pain remains a common presenting complaint in primary care, with lack of recognition of associated extra-articular features. In conclusion, there remains a need for education on when to suspect axial spondyloarthritis and refer to secondary care.
To follow up this study we are holding a series of AS targeted educational meetings with primary care colleagues, a local AS patient support group and regional special interest group. We will assess this intervention and subsequent referrals with the aim of improving confidence in suspected AS cases.
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ankylosing spondylitis: results from the Danish nationwide DANBIO registry. Ann Rheum Dis 2015;74:e12.
[2] Sykes M, Doll H, Sengupta R, Gaffney K. Delay to diagnosis in axial spondyloarthritis: are we improving in the UK? Rheumatology 2015;54:2283–2284.
**Disclosure of Interest:** None declared
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## AB0709 NEUROPATHIC PAIN COMPONENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Axial spondyloarthritis (axSpA) comprises a heterogeneous group of diseases which predominantly involve the axial skeleton and have many overlapping clinical features. The axial SpA spectrum ranges from non-radiographic axial SpA (nr-axSpA) at one end to ankylosing spondylitis (AS) at the other. Chronic low back pain (LBP) is the presenting symptom in the majority of patients with axSpA. Different studies have revealed that 16 to 54% of patients with chronic LBP may have neuropathic pain (NeP) component. Although there is no gold standard for the diagnosis of NeP, use of neuropathic pain screening tools, and quantitative sensory testing may offer the reliable way to diagnose NeP.
**Objectives:** The aim of this study was first to assess NeP component in patients with axSpA, including nr-axSpA and AS; and secondly to assess potential interactions between NeP component and other variables and outcome measures.
**Methods:** Adult patients who met Assessment of SpondyloArthritis International Society (ASAS) axSpA classification criteria were consecutively recruited. Patients with a previous diagnosis or under treatment for NeP, or having diseases causing increased risk to develop neuropathic disorders like uncontrolled diabetes, neuroendocrine or neuro-vascular disorders were excluded. Patients were examined and evaluated for disease specific and generic outcome measures including disease activity parameters, physical functions, psychological status and health related quality of life measures. Neuropathic component of pain was evaluated using the DN4 interview and PainDetect questionnaire which were applied by the same experienced physician who was unaware of patients' other clinical and outcome data. Patients with a score $\geq$4 in DN4 were considered as "probable NeP" and $\geq$13 in PainDetect were considered as "possible or likely NeP". Clinical variables and outcome measures were compared patients with NeP and without NeP component according to two different criteria.
**Results:** One hundred and seven patients (51.4% male, 48.6% female) with axSpA (36 nr-axSpA, 71 AS) were included (mean age 35.9±10.2). The first presenting symptom was LBP in 80% of the patients. NeP component was present in 31.8% of patients with axSpA categorized according to DN4 (33.3% in nr-axSpA vs 31.0% in AS, p=0.805) and in 34.6% of patients categorized according to PainDetect (36.1% in nr-axSpA vs 33.8% in AS, p=0.813). Pain characteristics like burning, electric shock, tingling, pins and needles, itching, numbness and painful cold as well as pain course were quite similar between patients with nr-axSpA and AS. Patients with NeP component according to two assessment tools had significantly higher scores in VAS-pain, fatigue, BASDAI, ASDAS-CRP and poorer QoL and physical functions compared to patients with nonNeP. However after adjusting for confounding variables in a multivariable logistic regression analysis NeP was associated only with ASQoL (OR 1.14; 95% CI 1.05–1.25) in DN4 categorized and VAS-fatigue (OR 1.32; 95% CI 1.07–1.62) in PainDetect categorized patients.
**Conclusions:** This is the first study showing that nearly one third of patients with axSpA may have NeP component regardless of having nr-axSpA or AS. NeP component may contribute worsened QoL and fatigue and should be kept in mind while targeting the management.
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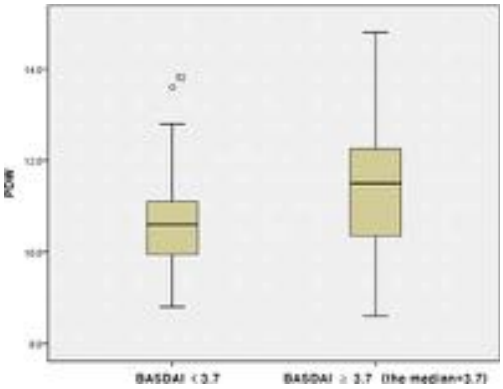
## AB0710 PLATELET DISTRIBUTION WIDTH AS AN ADJUNCTIVE INFLAMMATORY MARKER IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** With the recent introduction of biological drugs, remarkable improvements have been reported in treatment of ankylosing spondylitis (AS). Since those are most effective for delaying the progression when started sufficiently early in the disease course, more aggressive interventions are necessary at that time through evaluation of disease activity. Usually three methods for disease activity assessment are available for use in patients with AS: BASDAI (Bath AS Disease Activity Index), BASFI (Bath AS Disease Functional Index), and ASDAS (Ankylosing Spondylitis Disease Activity Score). However, these activity score have problem of depending too much on subjective assessment. Laboratory findings such as ESR and CRP also are not the good biomarkers since they have possibility of false positive and false negative. Thus, there is a high *demand* for additional and complementary marker that correlate with disease activity. Platelet distribution width (PDW) is specific marker of platelet activation. It can represent the heterogeneity of thrombocyte volume. Mean value of PDW was significantly higher in patients with preterm labor with asserted platelet activation compared to healthy persons suggesting the possible high grade inflammation in the pathology. In addition, an association between elevated platelet (PLT) counts and several autoimmune diseases is well known.
**Objectives:** We investigated whether PDW and PLT counts correlated with disease activity indices of AS and laboratory inflammatory markers and compared them between active and inactive AS patients.
**Methods:** We evaluated the disease activity in the 78 AS patients by using the BASDAI, ASDAS-ESR, and ASDAS-CRP. Laboratory inflammatory marker as acute-phase reactants, including ESR, and CRP levels were also measured in these AS patients. We divided all patients into 2 groups according to disease activity indices of AS: active groups were defined as BASDAI $\geq$3.7 (the median), ASDAS-ESR $\geq$2.1 (60.2%) and ASDAS-CRP $\geq$2.1 (43.6%).
**Results:** The mean (±SD) PDW was 11.0 (±1.3) %. The means (±SD) of PLT counts, ESR, CRP, BASDAI, ASDAS-ESR, and ASDAS-CRP level were respectively 263±57 x $10^9$/L, 21 (±18.6) mm/hr, 5.17 (±8.0) mg/l, 3.6 (±1.8), 2.39 (±1.03), and 2.08 (±1.02)] in the patients with AS (not shown). PDW significantly correlated with BASDAI, ASDAS-ESR, and ASDAS-CRP (r =0.390, p<0.01; r =0.287, p<0.05; r =0.295, p<0.001, respectively). On the other hand, PLT count showed no significant correlation with these parameters, but there was significant correlations with CRP (r =0.346, p<0.05) (Table). The Mean of PDW of patients with higher BASDAI were significantly higher when compared with that with lower activity (11.4±1.4 vs 10.6± 1.0%, p=0.007) (Figure).

| | ESR | CRP | BASDAI | ASDAS-ESR | ASDAS-CRP |
|---|---|---|---|---|---|
| PDW | 0.084 | 0.043 | **0.390*** | **0.287**# | **0.295*** |
| PLT count | 0.193 | **0.346*** | –0.060 | 0.117 | 0.084 |

PDW, platelet distribution width; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS, Ankylosing Spondylitis Disease Activity Score. r is determined by Spearman's rank correlation test Bold characters indicates a statistically significant difference with a *p*-value <0.05. #Statistical significance p<0.05. *Statistical significance p<0.01.




**Conclusions:** To conclude, we suggest PDW as supplementary novel marker to detect active AS that shows conventional inflammatory marker in normal range.
**Disclosure of Interest:** None declared
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## AB0711 BODY MASS INDEX IS RELATED WITH THE PRESENCE OF SYNDESMOPHYTE IN AXIAL SPONDYLOARTHRITIS: DATA FROM KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS (KOBIO) REGISTRY COHORT

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**Background:** Given that obesity might have a potent role in the regulation of the inflammatory response of spinal or peripheral joints in axial spondyloarthritis (axSpA), the detailed relationships between obesity and disease symptoms and activity should be addressed in patients with SpA
**Objectives:** We cross-sectionally investigated whether body mass index (BMI) is associated with parameters of disease activity and clinical manifestations in axSpA.
**Methods:** Demographic, clinical, and radiological features and disease activity indexes from 789 axSpA patients (619 males and 170 females) were obtained from the Korean College of Rheumatology Biologics (KOBIO) registry cohort. BMI (kg/m$^2$) was classified into normal (BMI <23.0), overweight (23.0 $\leq$ BMI <25.0), and obese (BMI $\geq$25.0). Disease activity indexes included ESR, CRP, ASDAS, BASDAI, and BASFI.

**Results:** The mean BMI in patients with axSpA was 23.8± 13.3. 50.2% of all patients were overweight or obese. Overweight/obese female patients showed higher ESR, CRP, ASDAS-ESR, and ASDAS-CRP than normal patients (p=0.045, p=0.011, p=0.035, and p=0.029, respectively). Patients with ASDAS score ≥2.1 showed higher BMI than patients with ASDAS score <2.1 (p=0.019). A greater increase in BMI was noted in patients with syndesmophyte than in those without syndesmophyte (p<0.001). Multivariate regression analysis showed that increased BMI was closely related with presence of syndesmophyte (β=0.932, p=0.002). In addition, syndesmophyte was found to be influenced by BMI (OR=1.087, 95% CI 1.033–1.145, p=0.007)

**Conclusions:** Our results imply that increased BMI was related with presence of syndesmophyte and in part associated with disease activity in axSpA.

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**Disclosure of Interest:** None declared

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## AB0712 ANALYSIS OF DIFFERENT MANIFESTATIONS IN THE CERVICAL SPINE INVOLVEMENT OF LONGSTANDING ANKYLOSING SPONDYLITIS: ATLANTOAXIAL ANKYLOSIS (AAA) AND ATLANTOAXIAL SUBLUXATION (AAS)

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**Background:** Atlantoaxial ankylosis (AAA) is another late manifestation of cervical spine involvement in longstanding AS and suggest that higher cervical mSASSS is more related with the development of AAA than atlantoaxial subluxation (AAS). AAA does not cause as much cervical instability as AAS.

**Objectives:** To analyze radiologic and clinical findings of atlantoaxial ankylosis and atlantoaxial subluxation in ankylosing spondylitis

**Methods:** A total of 150 AS patients (145 men, 5 women, mean age, 36.8 years) who had AAA (60 men and 2 women, mean age, 60 years) or AAS (85 men and 3 women, mean age, 34 years) were randomly gathered and underwent at least two plain radiographs of lateral cervical spine on flexion. The atlantodental interval more than 3mm was considered as AAS. Loss of atlantodental interval was considered as AAA. The plain radiographs of lateral cervical spine were independently analyzed by two radiologists. Interobserver reliability between reader 1 and 2 in scoring mSASSS in AS was analyzed. We compared the results of mSASSS between AAS and AAA to see if it was related to severity or duration of the disease.

**Results:** The mean mSASSS of AS patients with AAA and AAS were 40.1 and 16.5 respectively and the mean duration of AS patients with AAA and AAS were 19.3 and 13.7 years each. There was a significantly (p<0.05) higher total mSASSS, especially cervical spine mSASSS, for AS patients with AAA than those with AAS after mSASSS was corrected for age and duration. But, disease duration was not significantly related with the development of AAA compared with that of AAS.

**Conclusions:** We found that it has incidence as high as AAS and both are similar in that they are late presentation of AS and occur in patient with long duration. We found that AAA is another manifestation of cervical spine involvement in longstanding AS and is related to severity of the AS reflected by higher cervical mSASSS.

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**Disclosure of Interest:** None declared

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## AB0713 SPECTRUM OF ATLANTOAXIAL ANKYLOSIS (AAA) IN THE ANKYLOSING SPONDYLITIS (AS): IS IT REALLY CHRONOLOGICAL CHANGES THAT OCCUR WITH DISEASE PROGRESSION OR ARE THERE TWO COMPLETELY DIFFERENT PATHWAYS?

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**Background:** The morphologic characteristics of atlantoaxial ankylosis in AS patient and suggests different pathways of involvement resulting in atlantoaxial subluxation in AS patients

**Objectives:** To evaluate morphologic characteristics of AAA in AS patient and classify them into categories which reflects the end-stage manifestations of two differents disease pathways.

**Methods:** Plain radiographs of cervical spine in 62 AS patients with AAA were reviewed. We classified AAA in AS patients into three subtypes: loss of atlantodental interval (type I), ankylosis of facet joint (type II) and ankylosis of anterior longitudinal ligament or anterior atlantooccipital membrane with cervical spine (type III).

And then, we categorized 62 AS patients with AAA into two subgroups: group A (21 patients) with only synovial joint involvement of AS (type I or type II or both) and group B (41 patients) with enthesis involvement of AS with additional synovial joint involvement (type III plus type I or type II or both).

We compared the results of mSASSS and disease duration between group A and B.

**Results:** The mean cervical mSASSS of patients in group A and B were 27.3 and 16.0 each (p value, 0.196). The mean duration of AS patients in group A and B were 23.7 and 23.6 years each. There was no siginificant differences in cervical, lumbar and total mSASSS or disease duration between the two groups.

**Conclusions:** We propose that atlantoaxial joint involvement in the AS patients is not chronological changes that occur with disease progression, but rather it is end-stage manifestation of two different pathways: one only involving synovial joint and the other one involving both synovial joint and enthesis.

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[4] Laiho K, Kauppi M. The cervical spine in patients with ankylosing spondylitis. Clin Exp Rheumatol 2002;20:738

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## AB0714 NSAID PRESCRIBING PRACTICE IN PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** NSAID's are widely prescribed for patients with active spondyloarthritis. All NSAID's have the risks of adverse cardiovascular, GI, renal and thrombotic toxicity.

The Medicines and Healthcare Products Regulatory Authority (MHRA) as well as National Institute of Clinical Excellence (NICE) have issued guidance that applies to all traditional NSAIDs and selective COX-2 inhibitors.

**Objectives:** To review the prescribing of NSAID's in line with the MHRA/NICE recommendations.

**Methods:** This is a Trust-wide audit, looking into the NSAID prescribing practice in spondyloarthritis at the Royal National Hospital for Rheumatic Diseases.

The "AS database" was interrogated to define the total number of patients prescribed an NSAID to be taken continuously, from 1st Sept 2014 till 31st Aug 2015. Data was retrospectively collected from the database as well as the case records. Information regarding the definite indication for NSAID prescribed, contraindications and risk factors was collected. Pathology systems were accessed to check if renal function had been performed in the past 12 months of prescription.

**Results:** 69 patients with SpA taking regular NSAIDs were identified. A clear indication was identified in 44/69 (63.7%) patients (Table 1). No patients with

Table 1. Indications for prescribing NSAID's

| Indication | Number of patients |
|---|---|
| Inflammatory backache | 26 |
| Peripheral arthritis | 7 |
| Enthesitis | 3 |
| Osteoarthritis | 7 |
| Others | 7 |
| Fatigue | 2 |
| Greater trochanteric bursitis | 2 |
| Hip pain | 2 |
| Fracture | 1 |

Table 2. Risk factors for NSAID's

| Risk factor | Number of patients |
|---|---|
| Age >65 years | 15 |
| Ischemic heart disease | 3 |
| CVA | 0 |
| Peripheral vascular disease | 0 |
| CKD | 0 |
| Diabetes mellitus | 2 |
| Hypertension | 18 |
| Drugs which could increase the risk of bleeding when co-prescribed with NSAID's (SSRI) | 1 |
| Drugs increasing nephrotoxicity when co-prescribed with NSAID's | 17 |

contra-indications were prescribed the drugs. 22/69 (31.8%) had one or more risk factors for the drugs (Table 2). 49/69 (71.01%) patients were at risk of adverse GI effects. Of these, 27 (55.1%) were prescribed PPI's.
Renal function in the last 12 months was assessed in 40/69 (57.97%) patients. 8 patients who were receiving other concomitant nephrotoxic drugs had not had their renal function assessed in the past 12 months.
**Conclusions:** The proportion of patients with a documented indication for NSAID was moderately high. No patients with contra-indications to the drugs were prescribed the medication, which is in keeping with the guidance. The most common risk factors were age>65 years, hypertension and drug interactions involving ACE-I and ARB's, which increase the risk of nephrotoxicity. Only 55% of those at risk of adverse GI side effects were prescribed a PPI. Monitoring of renal function in addition, was moderate, being done in just over a half of the patients. Strategies to improve routine assessment of risk factors prior to commencing NSAIDs in AxSpA patients need to be addressed.
**Disclosure of Interest:** None declared
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## AB0715 CORRELATION OF CLINICAL SYMPTOMS AND INSTRUMENTAL FINDINGS IN AS COXITIS

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**Background:** Involvement of the hip joint (coxitis) is one of distinctive manifestations of ankylosing spondylitis (AS), resulting total hip arthroplasty in 5%>7% of cases.
**Objectives:** To correlate the clinical features of coxitis in AS pts with radiographic and ultrasonographic findings.
**Methods:** A total of 63 patients (mean age 31,7±12,7 years) with a diagnosis of AS (at the modified New York criteria 1984), having of pain in the hip joints, sequentially admitted for treatment at the clinic. Mean age of disease onset was 30,8±9,6 y. Hip pain was scored using VAS 100 mm. Coxitis was established on the basis of clinical symptoms - the presence of pain and/or limitation of motion in the hip joints at the time of admission of the patient to the clinic. Pelvic radiographs were taken in all pts to determine the severity of hip involvement using BASRI hip scale, and ultrasound examination was made using Sono Diagnost 360 (Philips) with linear (7,5 MHz) and convex (5,0 MHz) transducers. Joint effusion was set when the distance between the signals from the joint capsule and the inner part of the femoral neck was more than 7 mm.
**Results:** Synovitis on ultrasonography found in 53 (81%) pts out of 61. Pts were grouped into 2 arms based on radiologic findings, i.e. Group with radiographic signs of coxitis and Group without radiographic abnormalities. Two groups comparison data are presented in the Table

| Parameters | Pts with US verified coxitis | | P |
|---|---|---|---|
| | BASRI-hip 0–I (n=20) | BASRI-hip II–IV (n=33) | |
| Gender (M/F), n | 18/2 | 23/10 | 0,04 |
| AS duration, mo, Me [25%; 75%] | 93.95 [77–111.5] | 221 [176–321] | 0.03 |
| Age | 35.5 [25.7–43.2] | 46.3 [37.2–49.1] | 0.02 |
| US confirmed trochanteritis | 3 (15%) | 5 (12.1%) | 0.4 |
| BASDAI, Me [25%; 75%] | 4.85 [3.7–6.75] | 4.3 [3.3–5.4] | 0.2 |
| BASFI, Me [25%; 75%] | 4.8 [2.3–5.7] | 5.3 [4.3–6.9] | 0.03 |
| HLA-B27. n (%) | 19 (95%) | 30 (93.9%) | 0.6 |
| ASDAS (CRP) Me [25%; 75%] | 3.3 [2.95–3.85]* | 3.7 [2.4–4.7] | 0.6 |
| VAS mm Me [25%; 75%] | 60 [40–80]* | 40 [20–60] | 0.002 |
| ESR, mm/h, Me [25%; 75%] | 14.5 [10–35] | 20.5 [25–45] | 0.02 |
| CRP, mg/mL, Me [25%; 75%] | 22.52 [4.75–33.9] | 17.4 [5.3–27.5] | 0.03 |
| Bilateral coxitis, n (%) | 15 (75%) | 20 (60%) | 0.5 |
| Intermalleolar distance with maximally spread legs <100 cm | 1 (5%) | 3 (6%) | 0.8 |

**Conclusions:** Ultrasound allows hip joint to clarify the cause of pain with similar clinical and radiographic manifestations, localized in this area, as well as to determine if the patient has synovitis in the early stages of the coxitis. Patients with radiological coxitis have a longer duration of the disease, severe functional disorders of the index BASFI, with the defeat of the peripheral joints is less common.
**Disclosure of Interest:** None declared
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## AB0716 SOME CAUSES FOR DELAYED RECOGNITION OF ANKYLOSING SPONDYLITIS IN REAL CLINICAL PRACTICE IN RUSSIA: RESULTS OF A SINGLE MULTICENTER NON-INTERVENTIONAL STUDY – EPIKA 2

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**Objectives:** Recognition of ankylosing spondyloarthritis (AS) in current real clinical practice is often delayed. Identification of main causes of this peculiarity would help to propose administrative interventions to improve practices.
**Methods:** A single multicenter non-interventional study was conducted in spring 2015 y in order to ascertain the clinical features of AS in the real practice of a rheumatologist. 402 consecutive AS pts (meeting modified N-Y criteria) referred to a rheumatologist were evaluated following accepted standards during 2 mo at 10 clinical centers of Russia. All pts were evaluated, including those who attended because of deterioration, and pts coming for scheduled check-ups within the disease monitoring program. Patients' mean age was 40,8±11,5 y,. 292 (72,6%)-males, 82,6% were HLA-B27- positive.
**Results:** Time to establishing the AS diagnosis from the disease onset was 85,2±86,2 mo. In 32,3% of cases the diagnosis was made within 2 years from the onset, in 52,5% - within 5 years, and in 25,8% of pts the diagnosis was established in >10 years after AS onset. Association with specific clinical AS features at disease onset, such as axial or joint involvement (location, spatial extent of pain and synovitis) was not established. The AS diagnosis in 351 (87,3%) pts was established by rheumatologist, in 25 (6,2%) – by general practitioner, in 14 (3,5%) – by neurologist, and in remaining pts – by other specialists. During the first reference to a doctor the AS diagnosis was established in 3,7% (15 pts) cases, during 2–5 visits – in 25,1% (101), during 6–10 visits – in 25,1% (113), while 43,0% (173) of cases required >10 visits to establish the AS diagnosis. Probably due to established practices and pts' mentality in Russia all cases with back pain would be referred initially to neurologists and GPs, and only after multiple visits they may be referred to rheumatologists, which explains the fact of establishing AS during the first visit by neurologists and GPs, and only 6% input in AS verification from rheumatologists during Visits 2–5–6%. Generally before recognizing AS physicians were inclined to name it as spine degenerative disease (58%), reactive arthritis (21%), hernia of inter-vertebral disk (34%), osteoarthritis (6%), non-differentiated arthritis (10%), and oths. In almost half (42%) cases pts had to undergo 2–3 other diagnoses (not associated with spondyloarthritis) before AS was verified.
**Conclusions:** In real clinical practice the final AS diagnosis is usually established in 7 years average after AS onset. Pts are usually attended for quite a long period of time by other specialists, who are not sufficiently familiar with AS, therefore, AS is missed and other disease are being treated instead. Therefore, GPs and neurologists require improved and adjusted training, enabling them to suspect AS and timely refer a patient to a rheumatologist.
**Disclosure of Interest:** None declared
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## AB0717 CLINICAL CHARACTERISTICS OF ANKYLOSING SPONDYLOARTHRITIS IN REAL CLINICAL PRACTICE IN RUSSIA: RESULTS OF A SINGLE MULTICENTER NON-INTERVENTIONAL STUDY – EPIKA 2

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**Objectives:** Recognizing the clinical picture of ankylosing spondylitis (AS) in real practice would help to optimize healthcare services provided to this group of pts.
**Methods:** A single multicenter non-interventional study was conducted in spring 2015 y in order to ascertain the clinical features of AS in the real practice of a rheumatologist. 402 consecutive AS pts (meeting modified N-Y criteria) referred to a rheumatologist were evaluated following accepted standards during 2 mo at 10 clinical centers of Russia. All pts were evaluated, including those who addressed because of deterioration, and pts coming for regular check-ups within the disease monitoring.
**Results:** Patients' mean age was 40,8±11,5 y,. 292 (72,6%)- males, 82,6% were HLA-B27- positive. Age at AS onset was 27,6±12,3 y., in 65,4% AS onset occurred before the age of 30 y.o., and in 16,9% – before 16 y.o. Time to establishing the AS diagnosis was 85,2±86,2 mo. By the moment of evaluation inflammatory

back pain was present in 55,7% pts, peripheral arthritis - in 33,1%, enthesitis – in 37,1%, dactylitis – in 1,2%. Average BASDAI disease activity score was 4,3±2,1 (in 54,2% of pts it was >4, in 12,7% - >7, and in 18,2% - <2), and BASFI score – 4,1±1,8 (in 48,0% of pts it was >4,in 17,1%,- >7, and in 26,1% - <2). Extraskeletal manifestations were documented in 13,2% AS pts (including uveitis – in 45,3%, psoriasis – in 28,3%, Chrons disease – in 7,5%, IgA-associated neuropathy – in 5,7%, aortitis – in 3,8%). Such complications as amyloidosis were registered in 6 (1,5%) pts, cardiac arrhythmias – in 10 (2,5%) pts, aortal defect – in 1 (0,2%) patient. Most common comorbidities (verified by corresponding specialists) in this population were: arterial hypertension - in 25,1% AS pts, gastric ulcer – in 9,7%, ischemic heart disease – in 4,0%, diabetes mellitus – in 3,0%, chronic bronchitis – in 2,2%, bronchial asthma – in 2,0%, HCV hepatitis – 1,7%, HBV hepatitis – in 1,5%, tuberculosis – in 1,0%, oncologic diseases – in 0,2%, demyelinating conditions – in 0,2% pts. Comorbidities were not found in more than 50% (52%) of pts. Total arthroplasty procedures were documented in 19 (4,7%) pts, including 15 (3,7%) cases of hip replacement, and knee replacement in the rest. By the moment of evaluation another 6,7% of pts required total hip replacement procedure. 92% of pts were taking NSAIDs, sulfasalazine – 31,2%, methotrexate – 11,2%, peroral GCs s - 9,3%, TNF-α inhibitors– 19,1%.
**Conclusions:** In real clinical practice the final AS diagnosis is usually established in more than 7 years after AS onset, by that moment the disease has already reached high activity and pronounced functional impairments occurred. Various comorbidities are found in >40% of AS pts, but with much lower incidence as compared to other systemic rheumatoid diseases.
**Disclosure of Interest:** None declared
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## AB0718 IS THERE A RISK OF SERIOUS RHYTHM AND CONDUCTION DISTURBANCES, REQUIRING THE INSTALLATION OF A PACEMAKER, IN PATIENTS WITH SPONDYLOARTHRITIS?

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**Background:** There is a lot of conflicting data about the defeat of the cardiovascular system in patients with spondyloarthritis (SpA).
**Objectives:** Rate the frequency of pacemakers setting in patients with SpA compared with the frequency of pacemakers implanted in the population
**Methods:** A database of patients with established heart pacemakers in 2013–2014 years, residing in the territory of the Tatarstan Republic was analyzed, the results correlated with the number of population. The frequency of cardiac pacemakers establishing the Tatarstan Republic is 2 per 10,000 population. The population of Tatarstan Republic in 2014 - 3,855,258 people, of whom at the age of 18 to 50 years - 1,831,719 people. 2958 patients with SpA are observed in Rheumatology clinics in Tatarstan, 2355 from them - with ankylosing spondylitis (AS).
**Results:** Young working age patients with implanted pacemakers without heart disease history were selected from the database. Those aged 18 to 50 years - 123 people (0.7 per 10,000 population), of whom 59 (47.9%) had congenital heart disease and conduction abnormalities, 5 (4.1%) patients had rheumatic disorders, (2 (1.6%) - a history of acute rheumatic fever, 3 (2.4%) - SpA. Among patients with an established diagnosis of SpA, AS was established in 1 person, in 2 diagnosis of SpA was set retrospectively: in the history of the disease low back pain was found and further examination was conducted. Thus, the frequency of cardiac pacemakers implanted in patients with SpA in Tatarstan is 0.1% or 10 cases per 10,000 patients, and 0.04% or 4 cases per 10,000 in patients with AS.
**Conclusions:** In patients with SpA there is a risk of serious rhythm and conduction disturbances, in some cases requiring the establishment of a permanent pacemaker. The frequency of pacemaker implantation is higher than in the whole population.
**Disclosure of Interest:** None declared
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## AB0719 THE EFFECTIVENESS OF THERAPEUTIC STRATEGIES TO ACHIEVE THE GOAL (T2T) ON THE EXAMPLE OF KAZAN (RUSSIA) COHORT OF PATIENTS WITH SPONDYLOARTHRITIS

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**Objectives:** To rate the effectiveness of therapeutic strategies to achieve the goal (T2T) on the example of Kazan cohort of patients with spondyloarthritis (SpA) compared with routine practice
**Methods:** The main group of active observation by rheumatologist and regular correction of therapy according to the T2T criteria for spondyloarthritis included 42 patients: 27 (64.3%) with ankylosing spondylitis (AS) - New York criteria, 15 (35.7%) with axial SpA and positive MRI osteitis. High and very high activity (ASDAS) was at 54.8%, moderate - at 45.2% of patients. The comparison group - 40 patients (65% - AS, 35% - axial SpA) observed in the routine practice with a rheumatologist consultation as needed (just about once in 6 months). Patients were comparable for demographic and clinical characteristics, disease activity, duration of symptoms was not more than 10 years, the average 5,1±2,7. All patients received nonsteroidal anti-inflammatory drugs (NSAIDs), if necessary on a long constant reception. At baseline and after 3, 6 and 12 months BASDAI, ASDAS, BASFI, remission criteria (ASAS) were determined, adherence to treatment was evaluated.
**Results:** During the observation period in two groups a decrease ($p<0.05$) of mean values BASDAI, BASFI, $ASDAS_{CRP}$ was noticed. For the year of observation in the main group 95.2% of patients showed improvement on ASAS40 criteria, partial remission ASAS criteria was reached at 3 months - 47.6% of patients, at 6 months - 73.8%, at 12 months - 80, 9%, periods of exacerbation were observed in 19.1% of patients.
In the comparison group - 55% of patients showed improvement on ASAS40 criteria, after 3 months partial remission ASAS criteria was reached in 17.5% of patients, at 6 months - 35%, 12 months - 47.5% patients, periods of exacerbation were observed in 57.5% of patients.
The number of patients, regulary performed physical exercises, in the study group was 73.8%, in the control group - 35%. In the study group 76.1% of patients received NSAIDs continuously, in the control group - 37.5% of patients - only on request
**Conclusions:** The treatment strategy T2T SpA is an effective tool for the management of patients with this pathology, improves adherence to therapy, helps to control disease activity, improves functional status.
**Disclosure of Interest:** None declared
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## AB0720 THE CHARACTERISTICS OF ANDERSSON LESIONS (SPONDYLODISCITIS) BASED ON WHOLE SPINE MAGNETIC RESONANCE IMAGING IN ANKYLOSING SPONDYLITIS

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**Background:** Andresson lesions could cause debilitating pain and functional impairment in ankylosing spondylitis (AS) patients.
**Objectives:** The objective of this study was to identify the characteristics of Andersson lesions using whole spine magnetic resonance imaging (MRI) in AS.
**Methods:** A total of 62 patients with AS who had taken whole spine MRI were retrospectively enrolled in this study. Regional distribution in the entire spine and within the individual discovertebral unit (DVU) including the central, peripheral, and diffuse disc types of Andersson lesion was assessed. We compared the number of DVUs with Andersson lesion with clinical and radiographic indicies such as erythrocyte sediment rate (ESR), C-reactive protein (CRP), BASDAI, BASFI, and modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).
**Results:** Fifty-three patients (85.5%) had at least one Andersson lesion. We found a total of 129 DVUs with Andesson lesions (9.0%) in the entire spine levels. Andersson lesion at the lower thoracic spine (from T7–8 to T12-L1) was most commonly detected than other spine levels. Among the total 151 Andersson lesions, 41 lesions were identified at the central, 26 lesions at the anterior peripheral, 44 lesions at the posterior peripheral, and 40 lesions at the diffuse disc types. However, the number of Andersson lesions did not correlate with ESR, CRP, BASDAI, BASFI, and mSASSS in AS patients ($p>0.05$ of all).
**Conclusions:** Our study indicates that presence of Andersson lesion in AS patients is clearly underestimated. MRI provides more increased opportunity to detect earlier Andersson lesions than conventional radiography.
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**Disclosure of Interest:** None declared
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## AB0721 THE CLINICAL CHARACTERISTICS AND ASSOCIATED FACTORS OF CHINESE ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Ankylosing Spondylitis (AS) is the prototype of spondyloarthritis, with inflammatory back pain (IBP) as its most typical clinical characteristic and others including peripheral arthritis, anterior uveitis, dactylitis and so on. Human leucocyte antigen B27 (HLA-B27) status, gender and some other factors have been reported to be related with the disease clinical characteristics.

**Objectives:** We aim to describe the clinical spectrum of Chinese AS patients and investigate the influence of HLA-B27 status, gender and age at disease onset factors on the clinical features.
**Methods:** Chinese AS patients with complete clinical data and fulfilling the 1984 Modified New York criteria are studied. The recorded parameters include age, sex, HLA-B27 status, family history, age at AS onset, symptom at onset, disease pattern and presence of IBP, peripheral arthritis, hip joint involvement, anterior uveitis, dactylitis and enthesitis. Chi-square test and independent samples t-test are applied between groups of categorical and continuous variables respectively, using SPSS version 13.0 software.
**Results:** (1) A total of 1630 Chinese AS patients with a gender ratio of 3.36:1, average age of 27.84±9.07 and age at disease onset of 22.03±7.62 are included.17.2% have positive family history and 18.3% have juvenile onset AS (JoAS). (2) The overall HLA-B27 prevalence is 84.2%. HLA-B27 positive group has a younger age at onset (21.86±7.48 vs 22.92±8.31,p=0.041), higher presence of IBP (86.62% vs 78.35%, p=0.001) and hip joint involvement (53.12% vs 43.25%, p=0.004) than B27 negative group. (3) However, HLA-B27 positivity still shows some differences within different gender cohort. In the male group HLA-B27 positivity only shows higher prevalence of family history and IBP (86.62% vs 78.35%, p=0.001), while in the female B27 positivity has higher prevalence of hip joint involvement (48.98% vs 32.43%, p=0.011). (4) From the aspect of age at onset, although the JoAS and AoAS group have similar B27 positive rate and gender ratio, JoAS group has obviously higher prevalence of peripheral symptom at onset (52.70% vs 24.00%), enthesitis (34.38%vs23.17%) and peripheral pattern (68.56% vs 42.07%), with all P value $<0.001$.
**Conclusions:** HLA-B27 status, gender as well as age at disease onset are associated with the clinical manifestations of AS patients, which indicates the disease complexity and requires further attention in disease diagnosis. Larger scale studies and immunogenetic technology development are needed for better understanding of disease spectrum and mechanism.
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## Psoriatic arthritis

### AB0722 PSORIATIC ARTHRITIS PATIENTS WITHOUT SYMPTOMS OF CORONARY ARTERY DISEASE MAY HAVE HIGHER PRESENCE AND EXTENT OF CORONARY PLAQUES COMPARED TO CONTROLS BY CORONARY CT ANGIOGRAPHY

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**Background:** Patients with psoriasis and psoriatic arthritis (PsA) have an increased prevalence of cardiovascular (CV) risk factors, metabolic syndrome (Metsy), and higher risk for subsequent major CV adverse events[1]. Previous studies in rheumatoid arthritis have shown higher coronary plaque vulnerability in patients with coronary artery disease (CAD) compared to controls[2]. Far less is known about CAD in PsA. The extent and composition of coronary plaques have not been studied yet in PsA.
**Objectives:** (1) Study the presence, extent and type of coronary plaques as measured by coronary CT angiography (CCTA) in PsA without symptoms of CAD as compared to controls. (2) To compare plaque measurements between patients with Metsy to those without Metsy (NMetsy) and to controls. (3) Investigate the effect of disease related variables on coronary plaques.
**Methods:** 50 PsA patients (25 Metsy - 25 NMetsy) and 25 controls without CAD (age and sex-matched) underwent 64-slice CCTA. Scans were analysed by 2 readers, blinded to the patients' characteristics. Plaque localisation within the coronary tree, the number of patients with plaque and of affected coronary vessels were assessed. Plaque type was classified into calcified (CP), mixed (MP) and non-calcified plaque (NCP)[3]. Plaque volume was measured for each plaque type and was added to give a total volume (PV) in $mm^3$. The number of segments with plaque per patient (segment involvement score (SIS 0–15)) and segment stenosis score (SSS 0–60) were calculated. Kruskal-Wallis test, rank correlations and linear regression analyses were used to study the effect of Metsy and PsA related variables on coronary plaques.
**Results:** Mean age of PsA patients and controls was 58 (±8.3) and 57 (±5.6) years. PsA disease duration was 19 (±7.8) years. 4 (16%) controls had Metsy. 78% of PsA vs 44% of controls had plaques (P=0.007) and the number of affected coronary vessels were higher in PsA (P=0.015). There were more PsA patients with MP and MP volume was higher compared to controls (P=0.006). Mean PV, SIS and SSS were higher in patients with PsA (P=0.002, P=0.032, P=0.004; respectively). Skin and joint related parameters, and CCTA measurements were similar in Metsy vs NMetsy. Plaque presence, PV and SSS were significantly higher in both Metsy and NMetsy compared to controls. SIS (P=0.034) and MP volume (P=0.004) were higher in NMetsy vs controls.
Max CRP correlated with PV (r=0.39 P=0.006), SIS (r=0.41 P=0.003) and SSS (r=0.4, P=0.004). Disease duration, max TJC and max CRP had significant effect on the number of affected coronary vessels (P=0.034, P=0.049, P=0.022, respectively). Linear regression analyses revealed no significant relationship between PV and Metsy, whilst diagnosis of PsA (B=0.324 (CI95% 0.05–0.597) P=0.021) and max CRP (B=0.01 (CI95% 0.004–0.019) P=0.006) were independent predictors of PV.
**Conclusions:** This pilot study is the first to assess coronary plaques in PsA using CCTA. PsA patients asymptomatic for CAD had a higher presence and extent of plaques, particularly MP, compared to controls. Our results suggest that PsA may result in accelerated coronary plaque formation independent of metabolic disease.
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**Disclosure of Interest:** A. Szentpetery: None declared, D. Brady: None declared, G. Healy: None declared, C. Redmond: None declared, H. Fleming: None declared, J. Duignan: None declared, M. Haroon: None declared, J. Dodd: None declared, O. FitzGerald Grant/research support from: Pfizer, AbbVie, BMS, UCB, Consultant for: Pfizer, AbbVie, Janssen, MSD, Cellgene, Novartis, Speakers bureau: Pfizer, AbbVie, Janssen, UCB, Cellgene
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### AB0723 THE CLINICAL ASSESSMENT OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES IN PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disease in the spondyloarthropathy group with the history of psoriasis. Although some PsA findings are similar to rheumatoid arthritis (RA), RF negativity, some radiological and clinical findings are different in PsA. There is no spesific laboratory examination for diagnosis of PsA. On the other hand, anti-CCP antibody positivity is a spesific finding for the diagnosis of RA.
**Objectives:** We aimed in this study to analyse the frequency of anti-CCP positivity in PsA and the asscіaton with clinical and radiological findings.
**Methods:** The study group is consisted of 100 PsA patients, who fulfilled the CASPAR cirteria for PsA and 100 healthy controls (HC). We filled a form for all patients, which included clinical and laboratory findings of patients. We analyzed anti-CCP antibody with microELISA in the sera of patients.
**Results:** In our study, the anti-CCP positivity (40,9±63,5 IU/ml) was detected in 15% of PsA group and 4% of healthy controls. The difference was statistically significant (p=0,014; OR=4.24, 95% CI=1.35–13.25).Nine out of 15 anti-CCP positive patients were female, the remaining 6 were male. Thirteen patients (86,7%) had peripheral arthritis, 1 patient (6,7%)had sacroiliitis, 1 patient (6,7%) had peripheral arthritis and sacroiliitis. 42,8% of PsA patients with peripheral arthritis had asymetric olygoarthritis (6/14), 28,5% had monoarthritis (4/14) and 28,5% had symetric polyarthritis (4/14). Anti-CCP antibody positivity had no effect on the involvement of peripheral arthritis. Sacroiliitis and dactilitis were more frequent in the anti-CCP negative group. No patient with dactylitis had anti-CCP positivity (p=0.005). While, 43,5% of RF positive patients were detected anti-CCP positivity, 6,5% of RF negative patients were detected anti-CCP positivity (p=0,000).

Table 1. The frequency of disease findings in anti-CCP positive and negative groups

| | CCP(–) (n=85) | CCP(+) (n=15) | p | OR | 95% CI |
|---|---|---|---|---|---|
| Sex: Female / Male | 64.7% / 35.3% | 60% / 40% | 0.071 | 2.75 | 0.889–8.47 |
| Increased ESH | 32.9% | 46.7% | 0.178 | 1.78 | 0.587–5.4 |
| Increased CRP | 34.1% | 40% | 0.771 | 1.29 | 0.417–3.97 |
| RF >20 | 15.3% | 66.7% | 0.00 | 11.08 | 3.25–37.7 |
| Deformity | 21.2% | 26.7% | 0.736 | 1.35 | 0.385–4.76 |
| Sacroiliitis | 21.2% | 13.3% | 0.729 | 1.75 | 0.361–8.15 |
| Radiographic changes | 15% | 0% | 0.207 | 0.828 | 0.752–0.911 |
| Anti-TNF treatment | 31.8% | 26.7% | 0.077 | 0.78 | 0.228–2.67 |
| PSARC responce | 84.7% | 86.7% | 1 | 0.852 | 0.172–4.23 |

**Conclusions:** Our data reveals that anti-CCP positivity is more frequent in PsA compared to HC. We found no statisticall association between anti-CCP positivity and clinical or radiological findings.
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## AB0724 THE FREQUENCY OF THE METABOLIC SYNDROME AND COMPARISON OF HE RISK FACTORS FOR CARDIOVASCULAR DISEASE IN PSORIASIS, PSA AND RA GROUPS

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**Background:** Metabolic syndrome (MetS) increases the risk of developing cardiovascular disease at least two-fold. Various studies have suggested that MetS is associated with a state of chronic, low-grade inflammation (1).
**Objectives:** Our aim is to show relationships between MetS and chronic low grade inflammatory diseases, to determine frequency of MetS in psoriasis and psoriatic arthritis (PsA) against romatoid arthritis (RA).
**Methods:** 155 patients were included in this cross-sectional study. Fifty patients were psoriasis, 55 patients were PsA who was diagnosed according to the CASPAR criteria. Fifty patients were seropositive RA who was diagnosed according to the ACR/EULAR 2010 classification criteria. MetS was diagnosed by the 2005 criteria of IDF (2). Cardiovascular risk factors and MetS associated parameters were evaluated.
**Results:** Patients mean age, age at onset disease and diagnosing age of disease in the RA group were significantly higher compared with the psoriasis and PsA (p=0,002–0,000–0,000; respectively). Duration of psoriasis was 14,7±10,2 years in the PsA group and 12,1±11,7 years in the psoriasis group (p=0,000). Duration of arthritis were significantly longer in the RA group compared with the PsA group (p=0,000).
Insulin resistance showed no significant difference between the three groups (%70, %64, %66). Elevated triglyceride levels were higher in the psoriasis and PsA compared with the RA groups (%34, %32,7, %16; respectively; p=0,045). Hypertension ratio was higher in RA than PsA and psoriasis (p=0,011) (Table 1). CRP and HAQ which are parameters for used in the follow up disease activity were higher in the RA group.

Table 1. The frequency of the metabolic syndrome and the risk factors for cardiovascular disease in Psoriasis, PsA and RA groups

| n (%) | Psoriasis | PsA | RA | P |
|---|---|---|---|---|
| Sex (F/M) | 24/26 (48/52) | 39/16 (71/29) | 39/11 (78/22) | 0,04* |
| Smoking | 20 (40) | 17 (30,9) | 7 (14) | 0,04* |
| Alcohol Consumption | 4 (8) | 4 (7,3) | 1 (2) | 0,201 |
| Increased Fasting Glucose | 10 (20) | 14 (25,5) | 16 (32) | 0,172 |
| Increased HbA1c | 11 (22) | 17 (30,9) | 12 (24) | 0,82 |
| Increased Triglycerides | 17 (34) | 18 (32,7) | 8 (16) | 0,045* |
| Increased Total Cholesterol | 21 (42) | 32 (58,2) | 23 (46) | 0,69 |
| Increased LDL | 21 (42) | 22 (40) | 18 (36) | 0,54 |
| Decreased HDL | 3 (6) | 9 (16,4) | 16 (32) | 0,016* |
| Increased VLDL | 18 (36) | 14 (25,5) | 8 (16) | 0,023* |
| Increased Uric Acid | 5 (10) | 6 (10,9) | 5 (10) | 0,984 |
| MetS | 18 (36) | 16 (29,1) | 18 (36) | 0,684 |
| Insulin Resistance | 35 (70) | 35 (64) | 33 (66) | 0,785 |
| Hypertension | 8 (16) | 11 (20) | 19 (38) | 0,011* |

**Conclusions:** In all three groups, the MetS was shown to be higher than the general population. The differences between the groups could not be detected because of the small number of patients, and not equal distribution of population by age and gender.
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## AB0725 ANTI-TNF-α THERAPY IMPROVES ENDOTHELIAL FUNCTION AND ARTERIAL STIFFNESS IN PATIENTS WITH MODERATE-TO-SEVERE PSORIASIS: A 6-MONTH PROSPECTIVE STUDY

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**Background:** The risk of CV events is closely related to the severity of the psoriasis. The presence of severe psoriasis confers an additional 6.2% absolute risk of a 10-year rate of CV events compared with the general population. Studies on anti-TNF-α therapy indicate that these agents yield a reduction in the incidence of CV events in patients with psoriasis.
**Objectives:** To determine if the use of the anti-TNF-α monoclonal antibody adalimumab could improve endothelial function and arterial stiffness in patients with moderate-to-severe psoriasis.
**Methods:** Prospective study on a series of consecutive patients with moderate-to-severe psoriasis who completed 6 months of therapy with adalimumab. Patients with history of cardiovascular events, diabetes mellitus, kidney disease, hypertension or body mass index $\geq$35 kg/m$^2$ were excluded. Assessment of endothelial function by brachial artery reactivity measuring flow-mediated endothelial dependent vasodilatation (FMD%), and carotid arterial stiffness by pulse wave velocity (PWV) was performed at the onset of treatment (time 0) and at month 6.
**Results:** 29 patients were studied. Anti-TNF-α adalimumab therapy yielded a significant improvement of endothelial function. The mean±standard deviation (SD) FMD% values increased from 6.19±2.44% at the onset of adalimumab to 7.46±2.43% after six months of treatment with this biologic agent (p=0.008). Likewise, following the use of adalimumab, PWV levels decreased from 6.28±1.04 m/s at the onset of adalimumab to 5.69±1.31 m/s at 6 months (p=0.03).
**Conclusions:** Patients with moderate-to-severe psoriasis exhibit improvement of endothelial function and arterial stiffness following anti-TNF-α therapy. These findings are of potential relevance due to increased risk of cardiovascular disease in patients with severe psoriasis.
**Acknowledgement:** The study was supported by a research grant from Abbvie Inc.
**Disclosure of Interest:** None declared
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## AB0726 SEVERE OBESITY IS FREQUENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND IS ACCOMPANIED BY INCREASED CARDIOVASCULAR RISK

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**Background:** It is known that patients with psoriatic arthritis (PsA) are at increased risk of obesity and associated cardiovascular comorbidity, in particular those with severe and long-standing disease (>10 years). There is less information on the frequency of obesity and cardiovascular risk in patients with incident or medium-term disease.
**Objectives:** To investigate the prevalence of obesity compared to the population, disease presentation and the cardiovascular morbidity at onset of disease and after a mean of five years disease.
**Methods:** We selected two discrete groups of patients with a PsA diagnosis (M07.0-M07.3) enrolled in the national database of the German Collaborative Arthritis Centres between 2003 and 2014: patients with either short ($\leq$0.5 years) or longer disease duration (between 4 and 6 years). Stratified by BMI classes, disease activity and cardiovascular comorbidity, as well as the deviation of the BMI from the age- and sex-matched normal population were analysed.
**Results:** 421 patients were enrolled with incident disease (mean disease duration 3.0 months) and 965 with medium-term PsA (mean 5.0 years). Both the BMI distribution in general and the portion of patients with severe obesity (BMI$\geq$35, ~8%) were similar in incident and medium-term PsA. In comparison to the age- and sex-matched population, obesity was more frequent in patients with incident (23.5% vs. 16.1%) as well as in medium-term PsA (24.7% vs. 17.4%). Obesity was associated with higher disease activity, higher patient-reported burden and substantially higher prevalence of cardiovascular risk factors already in early PsA except for significantly lower smoking rates (Table1). In medium-term PsA, 23.6% of all patients (mean age 52 years) and 36.1% of the obese patients (mean age 54 years) presented with any cardiovascular risk factor (diabetes, hypertension, hypercholesterolemia or heart disease); in obese patients the prevalence of coronary heart disease (10.1%) was doubled compared to incident patients.
Table 1 shows patient characteristics in incident PsA.
**Conclusions:** One quarter of the patients with PsA are obese, already at the onset of the disease, and they present with more severe obesity than the age and

| | BMI 18.5-<25 | BMI 25-<30 | BMI≥30 |
|---|---|---|---|
| n of cases | 144 (34%) | 171 (41%) | 99 (24%) |
| Females | 57.6% | 42.1% | 59.6% |
| Mean age (years) | 45.1 | 51.7 | 47.6 |
| ESR (mm/Hg) | 17.4 | 16.5 | 26.5 |
| CRP (mg/dl) | 1.6 | 1.0 | 2.2 |
| Mean swollen joint count | 2.0 | 3.0 | 3.5 |
| Mean tender joint count | 1.4 | 2.1 | 3.3 |
| Moderate or high disease activity* (physician) | 38.0% | 39.0% | 50.5% |
| Poor patient global health* | 12.8% | 16.9% | 22.9% |
| Severe pain* | 17.2% | 22.6% | 26.1% |
| Current smoking | 32.5% | 34.5% | 20.3% |
| Diabetes | 1.6% | 4.6% | 17.4% |
| Hypertension | 8.8% | 17.8% | 28.3% |
| Hypercholesterolemia | .8% | 3.9% | 4.3% |
| Coronary/other heart disease | 2.4% | 4.6% | 4.3% |
| Any of the 4 cardiovascular risk factors | 10.4% | 24.3% | 35.9% |

*NRS 0-10; moderate = 4-6; high/severe/poor = 7-10

sex matched normal population. The high cardiovascular comorbidity at onset of PsA is further significantly increased in obese patients already after five years of disease. This should be considered in the treatment of these patients.

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**Disclosure of Interest:** None declared

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## AB0727 INCREASED RATES OF HYPERTENSION IN PATIENTS WITH PSORIATIC ARTHRITIS COMPARED TO PSORIASIS ALONE: RESULTS FROM THE UK BIOBANK

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with the presence of psoriasis. Lifestyle factors such as body mass index (BMI), smoking and alcohol consumption have been reported to contribute to the risk of both diseases. These risk factors also contribute to cardiovascular disease (CVD) which is a major cause of morbidity and mortality in patients with psoriasis and PsA.

**Objectives:** To compare lifestyle factors between individuals with PsA, psoriasis and a control group and to assess the association between these inflammatory diseases and CVD outcomes utilising the UK Biobank resource.

**Methods:** UK Biobank recruited 502,664 people aged 40–70 years in the UK between 2006 and 2010. Data on lifestyle, sociodemographics, health and medical history were collected at the assessment visit by questionnaire and interview by research nurse. Participants were asked if they have ever been diagnosed by a physician with a disease. Lifestyle factors including alcohol (current or past drinker) and smoking status (ever or never) were recorded and height and weight measured to calculate BMI. In this cross-sectional study, the frequency of these factors was compared between PsA, psoriasis and healthy controls using logistic or linear regression analyses depending on the outcome, adjusting for age and gender. Comparison between disease groups was performed by linear combinations of coefficients post estimation. Three CVD outcomes: heart attack, angina and hypertension, were tested for association with disease group using logistic regression including BMI, smoking, alcohol, age and sex as covariates. Odds ratios (OR) and β coefficients are reported with 95% confidence intervals (CI).

**Results:** 862 people with PsA, 4,761 with psoriasis and 465,371 control participants were included in the study (Table). Compared to the control group; both the PsA and psoriasis groups had higher BMI (β 1.43 (95% CI 1.11:1.75) and 0.72 (0.58:0.85) respectively), the psoriasis group smoked more (OR 1.63 (1.54:1.72)) and patients with PsA were less likely to be current drinkers (OR 0.68 (0.55:0.85)). Compared to patients with psoriasis, patients with PsA had higher BMI (β 0.69 (0.32:1.06)) and were less likely to be ever smokers and current drinkers (OR 0.70 (0.61:0.81) and 0.65 (0.51:0.83), respectively). Finally, hypertension was more prevalent in PsA compared to the control and psoriasis cohorts (OR 1.71 (1.48:1.97) and 1.55 (1.33:1.82), respectively).

Table 1. Characteristics of patients

| | Control (n=465,371) | Psoriasis (n=4,761) | PsA (n=862) |
|---|---|---|---|
| Age, mean (sd) | 56.4 (8.1) | 56.3 (8.1) | 56.1 (7.4) |
| Males (%) | 45.1 | 52.9 | 48.1 |
| BMI, mean (sd) | 27.3 (4.8) | 28.1 (5.0) | 28.9 (5.4) |
| Current drinkers (%) | 92.1 | 92.6 | 88.9 |
| Ever smokers (%) | 44.6 | 57.3 | 47.8 |
| Hypertension (%) | 26.9 | 29.2 | 37.7 |
| Heart attack (%) | 2.2 | 2.9 | 2.8 |
| Angina (%) | 3.1 | 4.0 | 4.3 |

**Conclusions:** Using a large population based cohort we show that self-reported CVD outcomes, in particular hypertension, are significantly higher in PsA compared to psoriasis independently of known CVD risk factors. The results contribute to our understanding of the lower quality of life reported by patients with PsA.

**Disclosure of Interest:** None declared

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## AB0728 RENAL DISORDERS IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Objectives:** To study clinical and laboratory changes in kidney patients with psoriatic arthritis (PA).

**Methods:** The study included 60 patients. The age of patients ranged from 22 to 60 years. All patients underwent clinical and laboratory study: functional kidney tests, general analysis of blood, Zimnitsky test, Reberg test, creatinine and urea levels.

**Results:** Kidney disease was diagnosed in 25 (41,7%) patients. Nephropathy is directly related to the underlying disease, was detected in 18 (30.0%) patients, including chronic glomerulonephritis in 10 cases and renal amyloidosis in 6 cases. We failed to verify the nature of kidney impairment in 2 patients. There was the prevalence of men among patients with psoriatic nephropathy (in 17). Renal disease is seen in patients with other systemic manifestations of the PA, including the expressed trophic disorders (in 9), prolonged fever (in 5), lymphadenopathy (in 2), heart disease (in 6) and liver (in 3).

Urinary syndrome was characterized by transient proteinuria and small haematuria (in 19 cases), a significant and persistent haematuria (red blood cells up to 30–40–50 in sight with episodes of gross haematuria) at extremely low values of proteinuria (in 5), regularly or occasionally high proteinuria above 3g/day (in 5). Extrarenal symptoms was presented with persistent oedema (in 4), hypertension (in 5). Nephritic syndrome was diagnosed in 12 patients. Reduced concentration ability of the kidneys was observed in 17 patients, and expressed presentation of chronic renal failure in 5 cases. Bladder syndrome was usually observed at the beginning of the PA, in exacerbations of joint syndrome with generalization process or the development of an advanced stage of dermatosis. In some cases, slight proteinuria and haematuria accompanied by acute syndromes was a comorbidity of main PA for many years without any development of kidney damage or azotaemia. Renal amyloidosis was characteristic for being accompanied by the nephritic syndrome. Daily protein loss reached 6–8g, and the amount of protein in a disposable examination of urine - 10,5 g/l. The total protein content in the serum was reduced to 49 g/l. Changes in urine, except for proteinuria, characterized microhaematuria (in 5 patients), small leukocytes (in 6), granular and wax cylinders.

**Conclusions:** Patients with PA in 41,7% cases had a variety of manifestations of the urinary syndrome. This represents the role of immediate diagnosis and correction of renal dysfunction; thus, chronic renal impairment may adversely affect prognosis of the disease.

**Disclosure of Interest:** None declared

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## AB0729 BASELINE LEVELS OF CTX-II AND GLUCOSYL-GALACTOSYL-PYRIDINOLINE IN PATIENTS WIH EARLY PSORIASIC ARTHRITIS: ASSOCIATION WITH DISEASE SEVERITY,DISABILITY, QUALITY-OF-LIFE, BIOLOGICAL TREATMENT REQUIRED AND PROGRESSION OF JOINT DESTRUCTION AT 5 YEARS OF FOLLOW UP

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**Background:** Although many efforts have been made to identify Psoriasic Arthritis (PsA)-specific biomarkers, none of the putative ones identified so far has resulted in a clinically relevant outcome and patient benefit.

In other diseases of the joints, elevated levels of urinary CTX-II (C-telopeptide fragments of type II collagen) and Glc-Gal-PYD (glucosyl-galactosyl-pyridinoline) have been associated with progression of damage.

**Objectives:** To analyze the association between the baseline levels of urinary CTX-II and Glc-Gal-PYD in patient with early PsA with disability, quality of life, biological treatment required and radiological damage at 5 years of follow up.

**Methods:** We included 36 patients who came to the service with some of the suggestive information of PsA and who later completed five years of follow-up and they fulfill nowadays PsA according to classification of psoriatic arthritis (CASPAR) criteria.

Urine samples were taken from all patients attending for the first time with suspected early PsA. Urinary excretion of CTX-II was determined by immunoassay

(ELISA) (ng/ml). Urinary excretion of Glc-Gal-PYD was determined by High performance liquid chromatography (HPLC). Because urinary levels were not normally distributed, all data were transformed into logarithms for analysis.
Association analysis was performed with the following five variables at 5 years:
- Disease Severity for the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): mild, moderate and severe.
- Health Assessment Questionnaire (HAQ).
- Study Short Form 36 (SF-36).
- Anti-TNF therapy: Yes/No.
- Sharp-van Der Heijde modified scoring method for PsA.

**Results:** Baseline levels of urinary excretion of CTX-II and Glc-Gal-PYD in patients presenting for the first time with suspected early SpA were significantly higher in those who had HAQ and SF-36 scores significantly worse, required biological treatment and in those due to moderate and severe disease severity at five years of follow up.
In a multivariable linear regression analysis, Baseline levels of urinary excretion of CTX-II and Glc-Gal-PYD in patients presenting for the first time with suspected early SpA were an important predictor of worse radiological score at the age of 5 (erosions, joint space narrowing, (subluxation, ankylosis, gross osteolysis, and pencil in cup phenomena).
**Conclusions:** Baseline levels of urinary excretion of CTX-II and Glc-Gal-PYD in patients with early SpA may be a prognostic biomarker since in our series it was associated with worse disease severity, disability, quality-of-life and progression of joint destruction at 5 years of follow up.
**Disclosure of Interest:** None declared
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## AB0730 PSORIATIC ARTHRITIS PATIENTS WITH WORK DISABILITY HAVE WORSE QUALITY OF LIFE COMPARED TO THOSE WHO ARE EMPLOYED

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**Background:** Work disability (WD) is an important functional outcome measure in inflammatory arthritis, which has been studied comprehensively in rheumatoid arthritis and ankylosing spondylitis, however limited data is available in psoriatic arthritis (PsA). A variety of WD measurement tools are available, but there are no validated and specific guidelines in PsA [1,2].
**Objectives:** In PsA patients with and without WD: (1) to compare patient-reported outcomes (PROs) and physician-assessed measures and (2) to assess whether there are gender-specific differences associated with WD.
**Methods:** Consecutive patients with PsA fulfilling the CASPAR criteria were enrolled. Patients on disability pension, those with early retirement due to arthritis, those unemployed, away from work due to sick leave were considered as having WD. Disease activity measures (TJC/68, SJC/66, ESR, CRP, PASI), economic data, patient-reported outcome measures (HAQ, EQ-5D, SF-36, BASDAI, BASFI, ASQoL, DLQI, pain VAS, average level of fatigue), radiographic damage, medication history and comorbidities were compared between employed and work-disabled patients in both genders using Mann-Whitney pairwise and chi-square test.
**Results:** 81 patients completed the economic questionnaire. Thirty-eight (17 male and 21 female) participations of working age had work disability versus forty-three (20 male, 23 female) employed patients. Out of 81 patients, 27 were biologic-naïve and 54 had ever been on biologic agents. We have found no significant differences in disease activity measures or in the number of erosions between work-disabled and employed patients. On the other hand patients with WD had significantly worse self-reported values in both gender groups, especially in females. The total number of comorbidities (p=0.020) and coexistent rheumatic diseases (p=0.025) were significantly higher among patients with WD. Work-disabled patients had more healthcare-related appointments and required more help (p=0.001), including home care and assistance travelling to the hospital.
**Conclusions:** Consistent with previous studies, in this cross-sectional cohort we have observed that rates of WD are high (46.9%) among patients with PsA with no difference between males and females. Despite similar disease activity and structural damage measures, patients with WD had worse physical function and overall reduced quality of life compared to employed patients. These differences were more pronounced in females, who had more physical and social limitations related to PsA.
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## AB0731 MUSCULOSKELETAL BUT NOT SKIN DISEASE ACTIVITY INFLUENCE RHEUMATOLOGISTS DECISION TO CHANGE DMARDS OR BIOLOGIC THERAPY IN PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a systemic inflammatory disease mainly characterised by arthritis, dactylitis, enthesitis and skin involvement. Recently issued therapeutic guidelines (1) suggest that treatment decisions should be driven by as many manifestations of disease as possible.
**Objectives:** The aim of this study was to determine, in a multicentre Italian cohort of PsA patients, which clinical or patient reported disease outcome influence physician decision to change DMARD or biologic treatment.
**Methods:** 173 consecutive patients with PsA (103 males and 70 females, mean age 52±12 years) were enrolled in a longitudinal observational study. Seven tertiary referral clinics with expertise in PsA and SpA were involved. Detailed clinical examination, including ACR joint count, presence or absence of dactylitis and enthesitis, PASI, were recorded. Patient perception of disease was evaluated by means of global, joint and skin specific VAS scales. Detailed treatment information were also recorded. According to study protocol clinical assessment was performed at baseline and after twelve weeks in order to identify two distinct groups: changed and unchanged DMARD or biologic therapy.
**Results:** A higher number of tender joints ($p<0.007$) and an higher number of swollen joints ($p<0.0003$) but not an higher PASI score (p=ns) were observed in the group of patients which were prescribed a change in DMARD or biologic treatment. Enthesitis and dactilytis were more frequent in the group with changes in treatment (p=0.001 and p=0.02 respectively). Patient global and joint perception of disease resulted more severe in the group where a change of therapy was decided, as shown by VAS global ($p<0.001$) and VAS joint ($p<0.02$) while no differences in the distribution in the two groups were observed considering patient perception of skin involvement. A significant difference was observed in the following joints: wrist (p=0.05), distal interphalangeal ($p<0.002$) and knee (p=0.03) involvement.
**Conclusions:** The results of this study, performed in an Italian cohort of PsA patients, suggest that rheumatologists, when they decide to change DMARD or biological treatment in PsA patients, are influenced by both objective evidence of musculoskeletal involvement and by patient reported global and joint outcomes. They do not seem to be influenced by the extent of skin dermatitis, possibly because of the generally low extent of skin involvement in PsA patient and/or because of a musculoskeletal orientated approach of rheumatologists.
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## AB0732 PERSISTENCE ON TREATMENT AND OPTIMIZATION AMONG ANTI-TNFα AGENTS IN PSORIATIC ARTHRITIS PATIENTS IN CLINICAL PRACTICE

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**Background:** As in rheumatoid arthritis some patients with psoriatic arthritis (PsA) can be refractory to anti-TNF-α therapy, may lose responsiveness, or develop drug intolerance over time and a switch to another TNFα antagonist can often restore therapeutic response.
**Objectives:** The study aim was to determine treatment persistence and to identify causes of discontinuation in PsA patients in clinical practice.
**Methods:** Patients with PsA (classified on the basis of CASPAR criteria) and treated with blockers of the TNF-α (following EULAR recommendations) adalimumab (ADA), etanercept (ETA), golimumab (GOL), infliximab (INF) or certolizumab (CTZ), between 2011–2015, were retrospectively included. Treatment persistence was analyzed and differences between therapies were assessed by means of an analysis of variance model (ANOVA), while a chi-square test was used to evaluate relationships between therapies and causes of treatment discontinuation and the administration of concomitant disease-modifying antirheumatic drugs (DMARDs) among therapies and types of disease.
**Results:** One hundred and ninety-six patients received: 98 ETA, 63 ADA, 22 GOL, 10 INF and 3 CTZ, with an age mean of 51.7±12.4 years old without differences among groups of therapies (p 0.993), and 111 were men (56.6%). Combination treatment with DMARDs was in 126 patients (64.3%) and no differences were observed among five anti-TNF therapies. One hundred and forty-three patients (73.0%) had persistence in first anti-TNF, mean 61.2 (12.8) months, and by groups was: 84.7% ETA, 60.3% ADA, 59.1% GOL, 70% INF and 66.7% CTZ, p 0.007,

without differences among clinical subtypes (p 0.978). Combination therapy with DMARDs was associated with a higher persistence in first anti-TNF, 67.8% vs 55.9%, but without statistical significance (p 0.108). Change of first anti-TNF occurred in 53 patients: failure to treatment was in 33 patients (62.3%) and discontinuation by adverse event was in 20 patients (37.7%) without differences among groups (p 0.535). Discontinuation by failure to treatment has happen with a mean of 66.1 (43.1) months and by adverse event in 53.4 (30.2) months (p0.235). In 68 (34.7%) patients without clinical activity dosing interval of treatment was increased and we have not observed differences among the groups (p 0.265).
**Conclusions:** In this cohort, anti-TNFα therapy was associated with high persistence at first anti-TNF therapy, mainly etanercept. Switching to another anti-TNF-α agent occurred in a quarter of patients, when treatment was suspended because of failure to response or an adverse event. Furthermore, treatment was optimized in one third of patients.
**Disclosure of Interest:** None declared
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## AB0733 MASEI SHOWS SUBSTANTIAL CHANGES IN THE ENTHESES OF YOUNG HEALTHY VOLUNTEERS – AMENDING ITS PD SCORE AND EXCLUDING KNEE ENTHESES THICKNESS PROVIDES BETTER DISCRIMINATION OF ENTHESITIS IN PSORIATIC ARTHRITIS PATIENTS

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**Background:** Tendon complaints are common in both healthy adults and patients with psoriatic arthritis (PsA). Ultrasound (US) could be used to investigate whether these are located at the enthesis and of inflammatory origin, as it is able to detect structural changes and inflammatory changes using Power Doppler.
**Objectives:** We aim to describe the difference in ultrasound abnormalities in the entheses of patients with recently diagnosed PsA, patients with established PsA and young healthy volunteers (20–30 years). using the MASEI US score
**Methods:** Consecutively newly diagnosed PsA patients participating in the Dutch south west Psoriatic Arthritis Registry (DEPAR), patients with >2 years PsA and healthy volunteers (aged 20–30 years) were asked to participate. An ultrasound was performed by one examiner unaware of clinical findings using an Esoate Mylab 60 (probe LA-435 and LA-523). The triceps, quadriceps, proximal and distal patellar and Achilles tendon insertion, plantar fascia (i.e. the locations of the Madrid Sonographic Enthesis Index; MASEI) and the tendon insertion at the lateral epicondyle of the elbow were investigated (1). In each location structural changes, erosions, calcifications, increased thickness and Power Doppler signal and is some locations bursitis were evaluated, resulting in a total score (range 0–158).
**Results:** In total, 25 newly diagnosed PsA patients (A), 25 established PsA patients (B) and 25 healthy volunteers (C) participated. The median of the MASEI+ score was for A 18 (IQR 15–30), for B 22 (IQR 15–27) and for C 10 (IQR 5–15) (Table 1).
Of note, the reference values for thickness of the Quadriceps tendon at the superior pole (6.1 mm), the inferior pole (4.0 mm) and the insertion at the tuberosity of the tibia (4.0 mm) were exceeded by 50%, 58% and 70% of the entheses of healthy volunteers (50 tendons). Also the degree of Power Doppler signal varied from one spot of signal to a confluent signal in large section of the enthesis, suggesting different levels of inflammation or possibly even false-positive findings. The images were re-evaluated for PD signal (assigning 1 point for one spot of signal, 1.5 for 2 or 3 spots, 2 for confluent small area or 3 points for confluent large area). When excluding increased thickness of knee entheses and using the re-evaluated PD scores the median MASEI was resp. 13 (IQR 10–22.5), 13.5 (IQR 9.5–18) and 3 (IQR 1.5–8) (Table 1).

**Table 1. Scores of the ultrasound evaluation in the three participant groups**

| | new PsA (n=25) | established PsA (n=25) | healthy volunteer (n=25) |
|---|---|---|---|
| MASEI | | | |
| MASEI + lateral epicondyle (median, IQR) | 18 (15-30) | 22 (15-27) | 10 (5-15) |
| MASEI* (median, IQR) | 13 (10-22.5) | 13.5 (9.5-18) | 3 (1.5-8) |
| PD | | | |
| 0 enthesis with PD (%) | 6 (24) | 1 (4) | 11 (44) |
| 1 enthesis with PD (%) | 7 (28) | 7 (28) | 3 (12) |
| 2 enthesis with PD (%) | 7 (28) | 9 (36) | 5 (20) |
| 3 enthesis with PD (%) | 1 (4) | 4 (16) | 3 (12) |
| >3 enthesis with PD (%) | 4 (16) | 4 (16) | 3 (12) |

PsA = psoriatic arthritis; IQR = interquartile range; MASEI = Madrid Sonographic Enthesis Index added with the lateral epicondyle score bilaterally (range 0-158);* MASEI and lateral epicondyle score, excluding increased thickness in knee entheses and using new scoring system to award points for PD: 1 point for one spot of signal, 1.5 for 2 or 3 spots, 2 for confluent small area or 3 points for confluent large area; PD = Power Doppler signal.

**Conclusions:** US structural changes and inflammation in the entheses are common in both early and established PsA patients using the MASEI. In healthy young adults US enthesitis was only observed around the knee. MASEI ultrasound score differentiated PsA patients from healthy volunteers when dropping the knee tendon enthesis thickness and applying a refined Power Doppler score. Our findings need to be confirmed in a larger cohort of healthy controls and patients.
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## AB0734 QUALITY OF LIFE AT BASELINE IN EARLY PSORIATIC ARTHRITIS RELATED TO INITIAL PRESENTATION OF MONO-, OLIGO-, AND POLYARTHRITIS AND TENDER ENTHESIS: RESULTS FROM THE DEPAR STUDY

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**Background:** Little data is available on quality of life in newly diagnosed psoriatic arthritis (PsA) patients and its relation to the extent of the disease.
**Objectives:** To describe quality of life in newly diagnosed PsA related to the extent of the disease as defined by the number of swollen joints and the presence or absence of tender enthesis.
**Methods:** Baseline data of consecutively recruited incident PsA patients was used from the Dutch south west Psoriatic Arthritis Registry (DEPAR) study between August 2013 to November 2015. Health-related quality-of-life (HRQoL) was assessed by the 8 subscales of the Short-Form 36 (SF-36) questionnaire (0–100, higher score represents a better HRQL) and the PsA-specific quality-of-life (PsAQoL) questionnaire (0–20, lower score represents a better HRQL). Patients were classified in the three arthritis subtypes (i.e. mono-, oligo- or polyarthritis) based on evaluation of the rheumatologist. A tender enthesis was defined as having at least one tender enthesis using the Leeds Enthesitis Index (LEI) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES).
**Results:** 209 patients with arthritis at time of inclusion completed the SF-36 questionnaire. Average age was 51.4 years (SD 13.7) and 55% were male. Of these patients 49 had monoarthritis, 92 oligoarthritis and 68 polyarthritis. At least one tender enthesis was present in 45%, 38% and 53% of the patients.
Mean scores of the subdomains in the SF-36 were similar across the different arthritis-groups, with better scores for monoarthritis compared to oligo and polyarthritis. However, when separating the groups based on the presence of a tender enthesis HRQoL decreased substantially for all groups across all subdomains of the SF-36, with a mean difference of 15 points (Figure 1). Mean scores of all subdomains were significantly lower in the tender enthesis group (n=106) compared to the non-tender enthesis group (n=131). Comparable results were observed for the PsAQoL scores (mono: 7.09 (SD 6.24) vs. 2.15 (SD 2.85); oligo: 7.11 (5.21) vs 4.18 (5.65) and 8.52 (6.04) vs 2.16 (2.90)

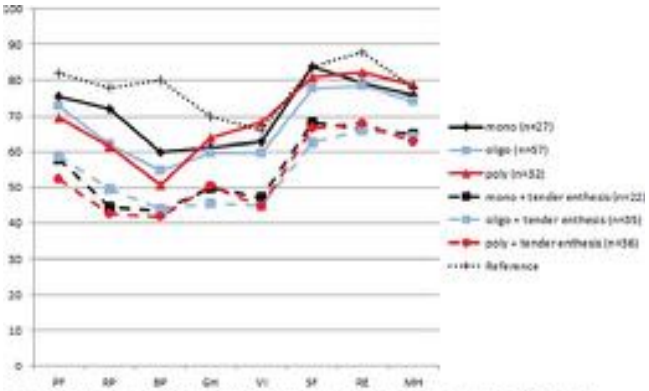



Figure 1. Health-related quality of life in patients with monoarthritis (mono), oligoarthritis (oligo), and polyarthritis, with and without presence of a tender enthesis, as measured by physical functioning (PF), physical role functioning (PR), bodily pain (BP), general health (GH), vitality (VI), social functioning (SF), emotional role functioning (ER), and mental health (MH) (SF-36).

**Conclusions:** Stratifying the HRQoL for the presence of tender enthesis, present in about half of newly diagnosed PsA patients, showed lower levels of health-related quality-of-life across both physical and mental scales, independent of arthritis classification, emphasizing the importance of the enthesis in PsA.
**Disclosure of Interest:** None declared
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## AB0735 THE ANNUAL INCIDENCE OF NEWLY DIAGNOSED PSORIATIC ARTHRITIS IN RUSSIAN PATIENTS WITH PSORIASIS IS SUSPECTED TO BE HIGHER THAN OFFICIALS REPORT: A POPULATION-BASED STUDY

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**Background:** Psoriatic arthritis (PsA) occurs in 6.2–42% of patients (pts) with psoriasis (PsO). The results range widely among different populations due to some difficulties in performing epidemiological studies, heterogeneous clinical presentations of PsA, and the lack of world accepted criteria and questionnaires and low awareness of the risk PsA in PsO pts among dermatologists.
**Objectives:** to estimate the mean annual incidence of PsA in Russian pts with PsO according to medical statistics record and to compare with direct interview results of pts with PsO in dermatologic clinics across Russian Federation.
**Methods:** Analysis of the number of newly diagnosed PsA among the adult and children above 14 years Russian pts with PsO coding in official medical records as L40.5+ by International Statistical Classification of Disease and Related Health Problems (ICD-10) between 2009 - 2013 years. 1091 pts with different clinical types of PsO at the same age were called to the dermatological offices to be direct interviewed by dermatologists and responded to follow questions: Do you have any joint pain? Do you have PsA confirmed by rheumatologists? The mean annual incidence of PsA in PsO pts were calculated by formula.
**Results:** Between 2009 - 2013 the mean annual incidence of newly diagnosed PsA in Russian pts with PsO estimated at 2.5% or 1.9/100.000 cases for whole Russian population. Among 1091 interviewed PsO pts in dermatologic offices 27.9% of pts have joint complaints and 8% of pts have PsA confirmed by rheumatologists.
**Conclusions:** The mean annual incidence of PsA in the Russian pts with PsO is lower than reported before in other populations due to under diagnosis, heterogeneous clinical presentations of PsA and coding problems in dermatological clinics. Iinterdisciplinary collaboration with rheumatologists is needed.
**Disclosure of Interest:** None declared
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## AB0736 THE BEPAS COHORT: A REAL-LIFE MULTICENTER PROSPECTIVE COHORT OF PSORIATIC ARTHRITIS IN BELGIUM: DEMOGRAPHICS AND BASELINE CHARACTERISTICS

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**Background:** Psoriatic arthritis (PsA) is a common form of chronic arthritis with major impact on the physical and psychosocial integrity of the patient. BEPAS (Belgian Epidemiological Psoriatic Arthritis Study) is a large prospective multicenter cohort set up in 17 Belgian rheumatology practices based in secondary and tertiary referral centers (private practice, non-academic and academic hospitals).
**Objectives:** (1) To generate a comprehensive database to characterize the clinical presentation and the frequency of the distinct PsA subtypes; (2) to estimate the severity of disease based on disease activity scores and structural damage; (3) to estimate the impact in terms of health-related quality of life of PsA in Belgium and (4) to evaluate progression of structural damage and loss of function in patients with PsA over time.
**Methods:** Patients with an existing or a new clinical diagnosis of PsA and fulfilling the CASPAR classification criteria were recruited. All patients gave informed consent. In the prospective study, patients are followed every year during the first 2 years with a possible extension for an additional 5 years. Demographics,clinical parameters, and data about QoL and disability were collected. X-rays of hands and feet are performed every year and axial X-rays every 2 years.
**Results:** 461 patients (mean age: 52.79 years (±12.29), male 57%) were recruited from December 2012 to July 2014. N = number of patients with data available.
**Conclusions:** This large cohort paints a real-life heterogeneous presentation of PsA in academic and non-academic centers in Belgium and contrast with other cohorts which are mainly academic cohorts. Further data collection will facilitate clinical and outcome studies iabout the impact and natural history of PsA in Belgium.
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| | N | Global | Male | Female |
|---|---|---|---|---|
| Age (yrs) | | 52.79 (±12.29) | 53.05 (±12.23) | 52.43 (±12.41) |
| Gender (m/f) | 461 | 263/198 | 263 | 198 |
| Symptoms duration | 450 | 11.91 (±10.83) | 11.37 (±9.79) | 12.64 (±12.08) |
| Disease duration (yrs) | 459 | 8.60 (±9.30) | 8.46 (±8.74) | 8.79 (±10.00) |
| Family historyPsA | 456 | 47 (10.3%) | 27 (10.3%) | 20 (10.3%) |
| Psoriasis type 1% | 444 | 287 (64.6%) | 165 (63.7%) | 122 (65.9%) |
| BSA (%) | 279 | 5.25 (±10.50) | 6.10±12.11 | 3.99 (±7.35) |
| Nail % | 459 | 122 (26.6%) | 85 (32.3%) | 37 (18.9%) |
| Clinical involvement at entry | | N of total | N of male (263) | N of female (198) |
| Dactylitis | 461 | 64 (13.9%) | 41 (15.58%) | 23 (11.61%) |
| Enthesitis | 461 | 111 (24.1%) | 51 (19.39%) | 60 (30.30%) |
| SJ count | 461 | 2.13 (±4.53) | 2.32 (±5.23) | 1.89 (±3.3) |
| TJ count | 461 | 4.10 (±7.31) | 3.72 (±6.79) | 4.61 (±7.95) |
| Abnormal CRP (≥5mg/l) | 430 | 125 (29.1%) | 64 (25.3%) | 61 (34.5%) |
| Physician Global | 429 | 24.61 (±21.18) | 22.84 (±20.72) | 27.00 (±21.62) |
| Patient global | 380 | 36.42±23.47 | 33.06 (±23.43) | 40.89 (±22.83) |
| HAQ | 460 | 0.72 (±0.64) | 0.64 (±0.63) | 0.83 (±0.63) |
| Workstatus: unemployed | 450 | 224 (49.8%) | 120 (46.7%) | 104 (539%) |

## AB0737 CLINICAL AXIAL INVOLVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS IS UNDERESTIMATED: IMPACT ON BURDEN OF THE DISEASE. DATA FROM THE BEPAS COHORT

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**Background:** Psoriatic Arthritis is often considered to be predominantly peripheral presenting with arthritis, dactylitis and enthesitis. Consequently randomized controlled trials, screening procedures for early detection and treatment strategies largely focus on peripheral disease. Axial involvement is considered less common. The BEPAS cohort (Belgian Epidemiological Psoriatic Arthritis Study) is a prospective multicenter real life cohort set up in 17 Belgian large academic and non academic rheumatology practices that offers a unique opportunity to study the axial involvement in this patient group.
**Objectives:** (1) To estimate the prevalence of axial involvement in patients with PsA in general (2) to estimate the prevalence of inflammatory back pain in patients with PsA; (3) to estimate the influence of disease duration on spinal manifestations.

| IBP_at inclusion | IBP(–) (304) | | IBP(+) (157) | | P |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | IBP(+) vs IBP(–) |
| Age at onset of PsA (yr) | 45.51 | 13.86 | 42.98 | 14.16 | 0.066 |
| Age at onset 1st PsA complaints (yr) | 42.58 | 14.45 | 38.71 | 14.46 | 0.007 |
| Disease duration PsA (yrs) | 8.30 | 8.95 | 9.19 | 9.93 | 0.332 |
| Sympt duration PsO (yrs) | 11.15 | 10.67 | 13.40 | 11.02 | 0.037 |
| BASMI | 17.49 | 5.71 | 20.49 | 6.06 | <0.01 |
| Sites with enthesitis (N) | 0.82 | 2.90 | 1.68 | 3.94 | 0.009 |
| Digits with dactylitis (N) | 0.27 | 1.01 | 0.32 | 1.01 | 0.586 |
| TJ78 | 2.65 | 4.77 | 6.82 | 9.90 | 0 |
| SJ76 | 1.70 | 3.99 | 2.92 | 5.23 | 0.006 |
| BSA | 3.50 | 9.07 | 5.21 | 10.35 | 0.107 |
| Actual use of anti-TNF | 0.47 | 0.50 | 0.42 | 0.49 | 0.316 |
| VAS PtGA (mm) | 35.50 | 26.03 | 51.79 | 25.30 | 0 |
| VAS PhGA (mm) | 19.04 | 18.68 | 31.53 | 20.41 | 0 |
| CRP (mg/L) | 3.46 | 6.55 | 5.63 | 14.33 | 0.03 |
| BASDAI | 3.03 | 2.18 | 5.02 | 2.21 | <0.01 |
| PASDAS | 3.33 | 1.40 | 4.46 | 1.38 | <0.01 |
| SF36 Phys Comp Sum | 42.25 | 10.12 | 35.81 | 9.27 | <0.01 |
| SF36 Mental Comp Sum | 47.10 | 12.43 | 40.39 | 13.28 | <0.01 |

**Methods:** Patients included in the BEPAS cohort were evaluated for the presence of a clinical phenotype indicating axial involvement, the specific presence of spinal complaints (reported by patients) and the presence of inflammatory back pain according the Rudwaleit criteria. Demographics and clinical features were recorded. BASDAI and BASMI were calculated.
**Results:** Among the 461 recruited patients (mean age: 52.79 years (±12.29), male 57%) 157 patients (34,1%) fulfilled the Berlin Criteria for inflammatory back pain with a higher prevalence in female patients (40,5% vs 28,9%, p=0.007) at inclusion.A family history of ankylosing spondylitis is reported in 3.3% of the patients. Clinical characteristics and demographics are listed in table 1.
**Conclusions:** The BEPAS cohort reports a substantial contribution of inflammatory axial involvement to the clinical and inflammatory burden of disease in PsA patients. Inflammatory axial involvement is a common clinical phenotype in PsA patients reporting higher disease activity and worse health status occurring more frequent in female patients, contrasting with other spondyloartropathies.
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## AB0738 ASSOCIATION BETWEEN ENTHESOPATHIC CHANGES AND BONE TURNOVER MARKERS IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** In patients with Psoriatic arthritis (PsA) there are changes in bone remodeling, not well established, that lead to a loss in bone mineral density (BMD) and to bone formation in the form of syndesmophytes and enthesophytes.
The enthesis, one of the most pathological findings that characterize PsA, can be studied with ultrasonography in a more sensitive and specific way than by clinical examination. Enthesopathic structural and inflammatory changes, which can be diagnosed by ultrasonography, are described in the OMERACT consensus and can be quantified by exploration indices such as MASEI.
**Objectives:** To evaluate the association between enthesopathical changes measured by MASEI index and bone remodeling markers in a population of patients with PsA.
**Methods:** Patients diagnosed with peripheral PsA and had been followed in a tertiary hospital, excluding those treated with vitamin D were included. Demographic, clinical, analytical (vitamin D (25OHD), bone turnover markers P1NP and βCTX, BMD (done with a maximum of 24 months before) data was collected. The entheseal affection count was determined by ultrasonography according to the MASEI index, which was re stratified in inflammation index and structure index, and by anatomical areas. Statistical study was done with the SPSS 17.0 program.
**Results:** 66 patients were included, 62.1% (41) were women, with a mean age of 56.8±11.9 years and mean duration of disease of 108.1 ±102.5 months; 84.8% (56) were treated with methotrexate and 33.3% (22) were receiving biological therapy (anti-TNF). Mean MASEI index was 13±9.7; mean structure index was of 9.3±5.9; and mean inflammation index 3.7±4.5. The quadricipital and achilles enthesis had higher mean MASEI indexes (4.2±3.4 and 2.9±2.1, respectively). MASEI and the structure index were positively associated with age ($r=0.31, p<0.05$ and $r=0.42$, $p<0.01$, respectively); contrary to the inflammation index.
Patients with osteoporosis had a mean age significantly greater than the rest of the sample.
No association was found between the results of BMD (stratified as normal, osteopenia and/or osteoporosis) and total MASEI index, structure score, inflammation score or each of the anatomical areas that were studied. As to bone turnover markers, P1NP and βCTX showed a tendency to an inverse relation with age. βCTX was inversely related to MASEI index of quadriceps and achilles ($p<0.05$). Likewise, when excluding patients treated with antiresorptive and anabolic agents the tendency maintains the same but is not statistically significant (p=0,078 and 0,076, respectively).No other associations were found between these bone remodeling markers and the rest of ultrasound indexes of enthesis.
**Conclusions:** Structural changes seen in the enthesis of our group of patients with PsA associate with a reduction of the bone turnover marker βCTX.
**Disclosure of Interest:** None declared
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## AB0739 ASSESSMENT OF SKIN INVOLVEMENT IN PATIENTS WITH POLYARTICULAR PSORIATIC ARTHRITIS AFTER 30 MONTHS OF BIOLOGICAL THERAPY OPTIMIZATION

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**Background:** Some patients with psoriatic arthritis (PA) in optimizing biological therapy present joint and/or skin activity, and they need to return to the standard dose of the drug. We present the articular and skin Activity Data in our cohort of patients with polyarticular psoriatic arthritis (PPA) in therapeutic optimization
**Objectives:** Assessment of the cutaneous activity by the PASI (Psoriasis Area Severity Index) and NAPSI (Nails Psoriasis Severity Index) scales and the analysis of the joint clinical course by DAS28 in PPA patients with biological treatment followed in the Rheumatology section of an university hospital of Jerez (Cadiz, Spain), which are undergoing therapeutic optimization.
**Methods:** An observational, descriptive, longitudinal and retrospective study by reviewing medical records, between January 2013 and January 2016, of PPA patients carrying at least 6 months in remission (DAS28 <2.6) or minimal activity (DAS28 2.6–3.2) and those who underwent optimization of biological therapy. Demographics, duration of PPA before the use of biological, biological time optimization, clinical evaluation by DAS28 pre and post-optimization, therapeutic strategy and assessment of skin activity by the PASI and NAPSI scales. Statistical analysis with the SPSS Statistics 22.0 software version is performed.
**Results:** From a total of 120 patients with PA in biological treatment, 26 of them with only polyarticular involvement (20.83%) were performed optimization of the therapy. 61.5% are male. Mean age 50±13 years. Average time optimized treatment dose: 31±14 months. 11 patients (42%) performed adalimumab 40 mg/15 days optimizing his administration every 21 days; 15 (57%) patients initially performed etanercept 50 mg/7 days were optimized to 25 mg/7 days (9 patients (34%)), 50 mg/10 days (2 (7%)) or 50 mg/15 days (4 (15%)). At the time of optimization, 25 (96.2%) patients presented remission DAS28 and 1 (3.8%) low activity, continuing in the same situation at the time of the end of the study (30 months after optimization). However, 5 patients (19.2%) (4 from etanercept group and 1 from adalimumab group) required to return to full doses of biologic drug for clinical worsening, agreeing worsening skin, remaining stable clinical joint. The skin evaluation was average PASI 1.95±2.13 (0–72) and medium NAPSI 11.19±11.38 (0–160), presenting patients who required back to initial biological dose PASI values between 1.6 and 5.8 and NAPSI values between 20 and 32, with prevalence of nail disease in the lower limbs. One patient (3.8%) required changing biological undesirable effects (anal fistula)
**Conclusions:** 77% of patients with PPA in remission or low activity subject to therapeutic optimization in our center remained stable at an average of 31 months of optimization, allowing continued the biological treatment in optimized doses. The main cause of return to full doses of biologic therapy in the remaining 33% of cases was worsening cutaneous involvement, remaining stable clinical joint in 100% of patients of our study
**Disclosure of Interest:** None declared
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## AB0740 THE EFFECT OF PREGNANCY ON DISEASE ACTIVITY OUTCOMES IN PSORIATIC ARTHRITIS PATIENTS

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**Background:** Psoriatic arthritis often affects patients at a childbearing age. The relationship between pregnancy and psoriatic arthritis (PsA), in terms of pregnancy outcomes and its effect on disease activity, has not been well studied.
**Objectives:** The aim of this study is to evaluate the effect of pregnancy on disease activity in psoriatic arthritis
**Methods:** A retrospective review of files of female patients followed at the Psoriatic arthritis clinic at the Tel Aviv Medical center was performed and patients with at least 1 pregnancy during follow up and one visit during or soon after pregnancy were included in this descriptive study. A thorough review of the files was performed which included the following data: age, disease duration, pattern of PsA, disease activity before during and after pregnancy, and record of treatment, including intra-articular injections before and during pregnancy. Postpartum period was defined as up to 1 year after pregnancy. PsA as well as psoriasis activity was defined by the treating physician as follow: no disease activity (no active synovitis), mild disease (up to 1 joint involved), moderate to severe disease (more than 2 joints involved). Accordingly, the follow up during and after pregnancy was classified as: improvement, worsening or stable
**Results:** 13 PsA women and 20 pregnancies were identified. 19 resulted in live healthy babies. The mean age at pregnancy was 31.6 years. Table 1 summarizes the status of disease activity before, throughout pregnancy and during the post partum period in the whole group. No significant change in disease activity was noticed throughout pregnancy while a significant proportion of patients flared at post partum
Before 12 pregnancies, the patients were treated with TNF α blockers. In 10, the biologic treatment was discontinued close to pregnancy or during the first trimester. In this group, 4 (40%) of patients were classified as mild to severe activity prior to pregnancy. This number increased up to 6 (60%), 7 (70%) and 10

(100%) during the 1st, 2nd trimester and postpartum period respectively. In the 2 patients in whom biologics were not stopped pregnancy, no change in the degree of disease activity was noticed.
Interestingly, in the group of non-TNFα treated patients, an improvement in disease activity was observed – the proportion of patients with mild to severe disease activity decreased from 100% close to pregnancy to 71% in the 1st and 2nd trimester and 43% in the 2rd one while an increase to 86% was observed after pregnancy.
During 5 pregnancies, corticosteroids (CS) were initiated or the dosage increased - all in pregnancies where TNF α blockers were stopped before pregnancy.

Table 1. Disease activity during pregnancy

| No (%) | Before pregnancy | 1st trimester | 2nd trimester | 3rd trimester | Post partum |
|---|---|---|---|---|---|
| No disease activity | 7 (37%) | 6 (32%) | 6 (32%) | 8 (42%) | 2 (10%) |
| Mild dis. Activity | 4 (21%) | 5 (26%) | 5 (26%) | 5 (26%) | 6 (32%) |
| Moderate to severe dis. activity | 8 (42%) | 8 (42%) | 8 (42%) | 4 (21%) | 11 (58%) |

**Conclusions:** Patients with PsA definitively flare after pregnancy. Our results suggest that stopping treatment with TNF α blockers before pregnancy is associated with flare during pregnancy and the post partum period. It seems that in terms of PsA disease activity, it is recommended to continue treatment with TNF α blockers throughout pregnancy
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## AB0741 DETECTION OF PSORIATIC ARTHRITIS IN PATIENTS WITH PSORIASIS IN DAILY ROUTINE CARE USING QUESTIONNAIRES FOR DIAGNOSIS OF PSORIATIC ARTHRITIS AND FLUORESCENCE-OPTICAL IMAGING TECHNIQUE: DIAGNOSTIC VALUE FOR DETECTION OF SUBCLINICAL SIGNS OF MUSCULOSKELETAL INFLAMMATION IN PSORIASIS?

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**Background:** Psoriasis (Pso) is one of the most common chronic inflammatory skin disease in Europe. Psoriatic arthritis (PsA) is closely associated to Pso; the skin manifestation appears usually years before PsA-related symptoms emerge. Up to 30% of Pso patients develop PsA; its concrete prevalence is still unclear. Questionnaires for detection of PsA (PASE, PEST, GEPARD) are validated tools for use in dermatology practice with different sensitivity and specificity levels. Fluorescence-optical imaging technique is a new method to detect changes in microvascularisation of the hands as potential early marker for subclinical musculoskeletal inflammation. Positive results of screening questionnaires in patients without current detection of PsA in rheumatological examination might have a diagnostic value to reflect subclinical disease activity of PsA.
**Methods:** This interims analysis includes 151 Pso patients (diagnosis confirmed by dermatologist) without pre-existing diagnosis of PsA but risk factors for its development (nail psoriasis and/or joint pain or swelling within the last 6 months) from a prospective, multicentre study (XCITING) in Germany. Patients are examined by rheumatologist (clinical examination and ultrasound) to determine PsA-diagnosis. FOI is performed additionally and analysed by an independent central reader. Results for PASE, PEST and GEPARD questionnaires as well as for FOI in comparison to the diagnosis of PsA by rheumatologist are compared to survey their value for clinical performance.
**Results:** In 81 out of 151 (53.6%) psoriasis patients with risk of development of PsA (as defined in inclusion criteria) PsA was diagnosed by rheumatologist using clinical examination and ultrasound. PsA confirmed patients were positive in 71.6% when using PASE, 32.1% when using PEST and 44.4% by GEPARD. Positive results in questionnaires despite negative results in rheumatologists assessment were seen in 28.4 – 67.9% of the used tools (67.9% PASE, 28.4% PEST, 55.6% GEPARD). In addition to PsA confirmed by rheumatologists, in 23.2% of Pso patients without clinical verified PsA a positive FOI-signal could be detected. In this group PASE was positive in 47.1%, PEST in 14.3% and GEPARD in 25.7% of the patients.
**Conclusions:** In this cohort of patients with active Pso and newly diagnosed PsA but with pre-defined risk of development of PsA, more than 50% of the patients were classified as PsA by rheumatologist. The sensitivity of detection of PsA by using questionnaires in early disease seems to be limited. False positive results in questionnaires in patients without clinical evident PsA might be influenced by signs of subclinical inflammation measured by FOI.
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## AB0742 EVOLUTION OF BIOLOGIC TREATMENT, SATISFACTION WITH CONTROL OF DISEASE, AND PATIENT-REPORTED OUTCOMES IN EUROPEAN PATIENTS WITH PSORIATIC ARTHRITIS: A REAL-WORLD STUDY

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**Background:** Patients with psoriatic arthritis (PsA) commonly receive therapy with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), either alone or in combination with biologics such as tumour necrosis factor inhibitors.[1]
**Objectives:** To assess the evolution of real-world biologic treatment patterns in patients with PsA by comparing patient data from two distinct patient surveys from 2014 and 2011.
**Methods:** This was a retrospective, cross-sectional analysis of data from two independent surveys (Adelphi Real World PsA Disease Specific Programmes) conducted in Q1 2011 and Q3 2014. Rheumatologists provided patient demographics, clinical details, treatment history and levels of satisfaction with disease control. Patient-reported outcomes included satisfaction with disease control, EuroQol-5 Dimension, Work Productivity and Activity Impairment (WPAI) and Alternative Health Assessment Questionnaire Disability Index (without aids/devices, HAQ-DI). Statistical differences were assessed using Mann-Whitney-U tests and Fisher's exact tests for quantitative and categorical outcomes, respectively. Missing data were not imputed.
**Results:** Patients with PsA receiving biologic treatment were similar in age, sex and body mass index in 2014 (n=325) and 2011 (n=326). The two independent cohorts showed no difference in time since diagnosis, severity of PsA prior to initiation of current treatment, disease progression prior to initiation of current treatment and time on current biologic treatment. The 2014 cohort had milder PsA vs the 2011 cohort (mild/moderate/severe: 72.6%/24.9%/2.5% vs 59.8%/35.0%/5.2%, respectively; P=0.0004), fewer patients who had ever experienced an acute episode (36.4% vs 56.6%, respectively; P<0.0001) or experienced an acute episode in the last 12 months (21.9% vs 31.4%, respectively; P=0.0074) and more patients with better current disease status (improving/stable/deteriorating slowly/deteriorating rapidly/unstable: 31.4%/56.7%/1.6%/7.2%/3.1% vs 27.3%/52.2%/14.4%/3.1%/3.1%, respectively; P=0.045). Patients did not receive biologic treatment any earlier in 2014 (median [interquartile range]; 36 [12, 72] months in 2014 vs 33 [15, 63] in 2011, P=0.2261). The number of csDMARDs received prior to initiation of biologic treatment did not differ significantly in 2014 vs 2011 (P=0.1551). Both physicians and patients were more satisfied with control of PsA in 2014 vs 2011 (81.5% vs 71.8%, P=0.0016 and 90.9% vs 67.3%, P=0.0002, respectively). The HAQ-DI score was significantly lower, indicating better health, in 2014 vs 2011 (0.38 [0.00, 0.88] vs 0.63 [0.27, 1.00], respectively; P=0.0065). WPAI scores showed nonsignificant improvements in outcomes in 2014 compared with 2011.
**Conclusions:** There were no significant differences in severity of PsA at initiation of treatment or treatment patterns in the patient samples analysed in 2014 vs 2011; however, patients' disease status was improved and both patients and physicians were more satisfied with the control of PsA in 2014 than in 2011. Further investigation is required to elucidate the reasons behind the improved outcomes observed over time.
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**Disclosure of Interest:** J. Lucas Employee of: Adelphi Real World, R. Wood Employee of: Adelphi Real World, J. Piercy Employee of: Adelphi Real World, J. C. Cappelleri Shareholder of: Pfizer, Employee of: Pfizer, B. Kola Shareholder of: Pfizer, Employee of: Pfizer, A. Chhabra Shareholder of: Pfizer, Employee of: Pfizer, R. Vasilescu Shareholder of: Pfizer, Employee of: Pfizer, M.-A. Hsu Shareholder of: Pfizer, Employee of: Pfizer
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## AB0743 CHARACTERIZATION OF PSORIATIC ARTHRITIS PATIENTS BY SKIN AND JOINT SEVERITY: RESULTS FROM THE CORRONA SPONDYLOARTHRITIS REGISTRY

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory condition affecting the skin and joints, and can lead to significant joint damage, disability and reduced quality of life. Disease severity varies among patients and is not well characterized in a real world setting.
**Objectives:** To characterize the PsA patients by skin severity (defined by body surface area, BSA) and joint (defined by modified disease activity score, mDAS)

in the Corrona PsA/Spondyloarthritis (SpA) registry, a large cohort of PsA-SpA patients in the US.

**Methods:** PsA patients enrolled in the registry between 4/2013 and 7/2015 were included. Patients were categorized by the level of skin involvement measured by BSA (low:BSA≤3%; moderate: BSA>3% & BSA≤10%; high:>10%) and joint severity as measured by mDAS (low:mDAS≤2.7; moderate:mDAS>2.7 & mDAS≤4.1 & high:mDAS>4.1). Patient characteristics at registry enrollment and biologic use were evaluated and one-way analysis of variance/Chi-square tests were used for continuous and categorical variables to evaluate differences.

**Results:** 1613 PsA patients were included, of which 1281 were categorized by BSA severity (low=64%, moderate=22%, high=14%) and 1331 by mDAS severity (low=21%, moderate=53%, high=26%). Overall, there were 53% females, mean (SD) age of 54 (13) yrs, mean (SD) disease duration of 12 (10) yrs. Majority of patients were referred by a primary care provider (40%) followed by self-referral (23%) or a rheumatologist (19%); 5% were referred by a dermatologist. Presence of dactylitis (10%, 13% and 22% in low, moderate and high resp.), and enthesitis (18%, 23% and 40% in low moderate and high resp.) were highly correlated with mDAS categories ($p<0.0001$), however similar correlation were not observed with categories of BSA. 61% of patients had prior biologic use and differences were observed in current biologic use by severity of BSA and mDAS categories: 62%, 59% and 97% ($p<0.001$) and 64%, 62% and 97% ($p<0.0001$) with low, moderate and high respectively, where app. one-third of the patients were on monotherapy. Among patients with moderate/high mDAS only 15% had high BSA (table).

| Skin involvement (BSA) | Joint severity (mDAS) | | | |
|---|---|---|---|---|
| | mDAS: Low (≤2.7) | mDAS: Moderate (2.7–≤4.1) | mDAS: High (>4.1) | Total |
| BSA: Low (≤3%) | 151 (67.4%) | 399 (70%) | 133 (47.8%) | 683 |
| BSA: Moderate (>3–≤10%) | 47 (21%) | 111 (19.5%) | 80 (28.8%) | 238 |
| BSA: High (>10%) | 26 (11.6%) | 60 (10.5%) | 65 (23.4%) | 151 |
| Total | 224 | 570 | 278 | 1072 |

**Conclusions:** Majority of PsA patients present to the rheumatologist with moderate/severe joint symptoms and mild skin symptoms, and are primarily referred by PCPs, self-referred, or other rheumatologists. mDAS severity was correlated with presence of dactylitis/enthesitis and the number of enthesitis sites. The majority of PsA patients (60%) were treated with biologic agents regardless of joint or skin severity; however over 90% of patients with high joint or skin severity were treated with biologic therapy.

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## AB0744 DEVELOPING THAI SIRIRAJ PSORIATIC ARTHRITIS SCREENING TOOL AND VALIDATED THAI PSORIASIS EPIDEMIOLOGY SCREENING TOOL AND THE EARLY ARTHRITIS FOR PSORIATIC PATIENTS

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**Background:** Majority of PsA patients present with Ps before onset of arthritis up to 10 years. Ps patients are generally taken care by general practitioners or dermatologists therefore they play a key role for early detection of PsA. There are a few screening tools available; however, it has been reported that they have a wide range of sensitivity and specificity around 24- 90% and 40–94%, respectively, in the different studies [1]. There is no screening tool which has been verified in Thai content. Furthermore, it would be essential to have a simple tool with good discriminating property.

**Objectives:** To validate Thai version of the Psoriasis Epidemiology Screening Tool (PEST)[2] and the Early ARthritis for Psoriatic patients' questionnaire (EARP)[3], and to develop the new tool for screening psoriatic arthritis (PsA) among psoriasis (Ps) patients.

**Methods:** This was a cross-sectional study. Ps patients visiting psoriasis clinic at Siriraj Hospital were recruited. They filled out EARP, and PEST, and were evaluated full musculoskeletal history, examination and radiography. Diagnosis of PsA was based on a rheumatologist's evaluation and fulfilled ClASsification criteria for Psoriatic Arthritis. Receiver operator characteristic (ROC) curves, sensitivity, and specificity were used to determine the performance of tools. Siriraj Psoriatic Arthritis screening Tool (SiPAT) was composed from the most relevant questions regarding peripheral arthritis, axial inflammation, enthesitis selected from multivariate analysis.

**Results:** A total of 159 patients, prevalence of PsA was 78.6%. The ROC curve analyses of the Thai EARP, PEST, and SiPAT were 0.90 (95%CI: 0.84, 0.96), 0.85 (0.78, 0.92), and 0.89 (0.83, 0.95), respectively. The sensitivities of SiPAT, Thai EARP and PEST were 91.0, 83.0, and 72.0%, respectively while the specificities were 69.0, 79.3, and 89.7%, respectively.

**Conclusions:** Thai EARP and SiPAT have diagnostic performance better than Thai PEST. SiPAT could be proposed as a simple and effective tool for screening PsA among Ps patients.

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## AB0745 DAPSA WITH TWENTY-EIGHT JOINT COUNTS MAY BE USEFUL FOR THE ASSESSMENT OF PSORIATIC ARTHRITIS

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**Background:** Disease Activity index for Psoriatic Arthritis (DAPSA) originally developed from patients with reactive arthritis (1). Subsequently, validation of DAPSA was also shown on psoriatic arthritis (PsA) patients (2). DAPSA includes swollen joint count (SJC) (66 joint), tender joint count (TJC) (68 joint), CRP (mg/dl), patient global assessment, and pain. However, it is well known that assessment of 28 joint is feasible than 66/68 joints especially in the rheumatoid arthritis trials.

**Objectives:** Objective of this study was to assess construct validity and sensitivity to change of DAPSA-28 in a single center biological registry.

**Methods:** Hacettepe University biological registry (HUR-BIO) is a single center biological registry. Since 2012, consequently all PsA patients with new started anti-TNF treatments were recorded. HUR-BIO included sex, age, PsA disease duration, education, body mass index (BMI). Before anti-TNF treatments, baseline disease activity parameters were recorded: SJC and TJC (28 joints), health assessment questionnaire (HAQ), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Bath ankylosing spondylitis activity index (BASDAI), visual analog scale 0–100 mm (VAS) of patient's global assessment of disease activity (PGA), pain, and fatigue. Original DAPSA calculated to sum of CRP (mg/dl), pain VAS (cm), PGA VAS (cm), SJC (66 joints), and TJC (68 joints). We used 28 TJC/SJC instead of 66/68 joints for calculation of DAPSA, which called DAPSA-28. At baseline, all DAPSA items completed in 78 patients. The subsequent clinical visit recorded in 53 patients (4.6±3.0 months after baseline). *Statistical analysis:* Internal consistency was evaluated using Cronbach's $\alpha$ coefficient. Construct validity was assessed by Spearman's correlation between the DAPSA-28 scores and other measures. Sensitivity to change assessed with standardised response mean (SRM). A SRM >0.8 is considered large.

**Results:** Overall, 58 of 78 (74.4%) were female, mean age was 43.1 (11.8) years, mean PsA duration was 6.4 (5.1) years. Mean DAPSA-28 score was 20.1 (8.1). Patients with low educational level (primary scholl 22.8 (9.6) vs high scholl 16.8 (5.7), p=0.009), and high BMI (BMI >30 kg/m$^2$ 22.4 (8.4) vs BMI <30 kg/m$^2$ 17.8 (7.2), p=0.011) had higher DAPSA-28 score. Mean of all DAPSA items were followed; PGA 5.8 (1.7), pain 6.3 (2.3), CRP 2.0 (2.8), SJC 1.9 (2.2), TJC 4.0 (3.6). DAPSA-28 domains had moderate internal consistency (Cronbach's $\alpha$ 0.61). Correlation of DAPSA-28 with other outcome measures followed; DAS-28 (r=0.86), TJC (r=0.78), SJC (r=0.73), PGA (r=0.48), pain VAS (r=0.47), CRP (r=0.44), fatigue VAS (r=0.38), HAQ (r=0.36), ESR (r=0.35), and BASDAI (r=0.31). DAPSA-28 had excellent SRM (1.14).

**Conclusions:** DAPSA domains are almost universal for all kind of inflammatory arthritis. Simple sum of those domains seem valid and feasible in PsA patients. Although assessment of 66/68 joints may be rational particularly patients with distal interphalangeal involvement, it has feasibility issue. Our results demonstrated that DAPSA-28 had excellent capacity at sensitivity to change for clinical trials. Unfortunately, we could not compare DAPSA with DAPSA-28, future studies are needed for these comparison.

**References:**
[1] Rheumatology 2000;39:148–55
[2] Ann Rheum Dis 2010;69:1441–7
**Disclosure of Interest:** None declared
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## AB0746 HIGH PREVALENCE OF CARDIOVASCULAR COMORBIDITY IN PATIENTS WITH PSORIATIC ARTHRITIS AND MODERATE-TO-SEVERY PLAQUE PSORIASIS: A RETROSPECTIVE DERMATOLOGICAL CLINIC-BASED STUDY

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**Background:** An association between inflammation, psoriasis (PsO), psoriatic arthritis (PsA) and increased cardiovascular comorbidity has still limited data.
**Objectives:** to evaluate the prevalence of cardiovascular comorbidity in patients (pts) with PsA and PsO without arthritis in the dermatological hospital cohort.
**Methods:** 592 pts (Male-348/Female-244) with moderate-to-severy plaque PsO, mean age 49.2±0.6 years, mean PsO duration 11.8±0.6 were included. PsO and PsA pts with cardiovascular disease (CVD), including coronary heart disease (CHD), arterial hypertension, (AH), atherosclerosis and cerebrovascular accident (CVA) were identify in the hospital Database reporting and coding by International Statistical Classification of Disease and Related Health Problems (ICD-10) between 2010 - 2011 years. M±m, t-test, (%) were calculated. All $p<0.05$ were considered to indicate statistical significance.
**Results:** 220 out of 592 pts (37.2%) had PsA and 372 out of 592 pts (62.8%) had PsO alone. PsA pts were older then PsO pts – 53.3±0.9 and 46.9±0.9 ($p<0.001$). In PsA pts CVD coding as I 00 – I 99 were found in significantly more cases than in PsO pts – in 155 out of 220 pts (70.5%)/in 200 out of 372 pts (53.5%) accordingly ($p<0.05$). In PsA pts AH coding as I 10 - I 15 was found in significantly more cases than in PsO pts - in 138 out of 220 pts (62.7%) and in 178 out of 372 pts (47.9%) accordingly ($p<0.001$). In PsA pts CVA coding as I 65 – I 66 found significantly often than in PsO pts - in 48 out of 220 pts (22%) and in 57 out of 372 pts (15.3%) accordingly ($p<0.05$). CHD and Atherosclerosis coding as I 70 were registered significantly often in PsA pts compared to PsO pts – in 40 out of 220 pts (18%) and in 35 out of 372 pts (9.3%) accordingly ($p<0.001$).
**Conclusions:** Cardiovascular comorbidity is common for PsA and PsO without arthritis pts. High frequency of CVD in PsA than PsO could be due to share inflammation pathways with atherosclerosis and age. Screening and accurate management of CVD risk factors in both diseases are needed.
**Disclosure of Interest:** None declared
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## AB0747 PSORIATIC ARTHRITIS REGISTRY OF TURKEY (PSART): RESULTS OF A MULTICENTER REGISTRY ON 1081 PATIENTS

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**Background:** PsART (PsA registry of Turkey) is a multicenter web-based registry.
**Objectives:** The objective of this registry is to assess characteristics of PsA and compare the differences among genders in our population.
**Methods:** PsART was established in 2014 including 32 rheumatology centers. Detailed data regarding demographics for the skin and joint disease, disease activity assessments and treatment choices were collected.
**Results:** One thousand and eighty-one patients (64.7% women) with a median (range) PsA duration for 3.7 (0–45) years were enrolled. Median psoriasis duration was 13 (0–59) years. The most frequent type of PsA was polyarticular 437 (40.5%) followed by oligoarticular 407 (37.7%) and axial disease 372 (34.4%). Patients with a combination of axial and peripheral disease had a longer disease duration than patients with one type of joint disease (52 (0–545) vs 42 (0–486) months, p=0.008). Mean (SD) swollen and tender joint counts were 1.7 (3) and 3.6 (4.8). 38.6% of patients were on csDMARD monotherapy, 7.1% were anti-TNF monotherapy and 22.5% were using anti-TNF plus csDMARD combinations. Within items included in the minimal disease activity, only 17.6%>67% of patients had inactive disease state. The major differences among genders were women being older (48.3 (12.8) VS 44.4 (12.5), $P<0.001$), more fatigue and higher HAQ scores (Table). Women also had more frequent peripheral arthritis than men and less axial disease (only peripheral vs axial vs combined, n (%): women: 479 (68.5%), 62 (8.9%), 158 (22.6%) respectively; men: 222 (59.4%), 41 (11%), 111 (29.7%) respectively; p=0.011). Women had significantly more history of psoriasis in their family compared to men (34.8% vs 25.7%, p=0.003).
**Conclusions:** PsART had similarities with the previously published registries, supporting its external validity. Women having more fatigue and worse functioning and as well as the high percentage of active disease state point out to the unmet need in treatment of PsA.

| | All patients (n=1081) | Female (n=702) | Male (n=379) | p |
|---|---|---|---|---|
| Inflammatory LBP n (%) | 275 (25.4) | 155 (22.3) | 120 (32.1) | 0.002 |
| Duration of morning stiffness | 37.9 (43.0) | 38.5 (43.8) | 36.7 (41.6) | 0.73 |
| Patient global assessment | 43.5 (24.9) | 44.3 (24.0) | 42.1 (26.6) | 0.22 |
| Fatigue VAS | 46.2 (26.2) | 48.5 (24.6) | 42.0 (28.6) | 0.002 |
| Pain VAS | 44.6 (27.1) | 45.5 (26.0) | 43.1 (28.9) | 0.21 |
| HAQ | 0.71 (0.65) | 0.74 (0.64) | 0.66 (0.67) | 0.014 |
| BASDAI | 39.4 (25.6) | 39.1 (24.5) | 39.9 (27.3) | 0.88 |
| BASFI | 29.0 (24.2) | 28.1 (23.7) | 30.7 (24.9) | 0.27 |
| PSI | 7.5 (7.2) | 7.4 (7.3) | 7.7 (7.1) | 0.57 |
| Physician global assessment | 35.6 (22.2) | 35.6 (21.1) | 35.8 (24.1) | 0.86 |
| Swollen joint counts | 1.7 (3.0) | 1.6 (3.1) | 1.8 (2.8) | 0.91 |
| Tender joint counts | 3.6 (4.8) | 3.7 (5.0) | 3.4 (4.3) | 0.93 |
| Body surface area | 6.1 (10.7) | 4.9 (8.0) | 8.4 (14.2) | 0.69 |
| Leeds enthesitis index | 0.2 (0.7) | 0.2 (0.8) | 0.2 (0.5) | 0.43 |

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## AB0748 NOVEL BIOMARKERS DISTINGUISH PSORIATIC ARTHRITIS FROM PSORIASIS

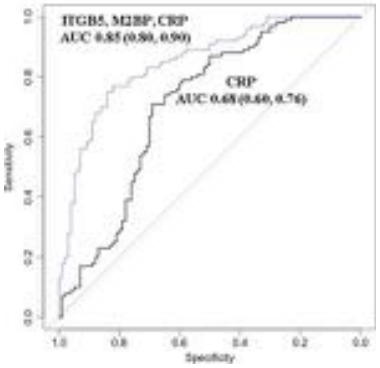
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**Background:** There is a high prevalence of undiagnosed psoriatic arthritis (PsA) in psoriasis patients. Therefore identifying soluble biomarkers for PsA will help in screening psoriasis patients for appropriate referral to a rheumatologist.
**Objectives:** Our purpose was to investigate whether serum levels of novel markers discovered by quantitative mass spectrometry (MS) of synovial fluid and skin biopsies, differentiate PsA patients from those with psoriasis without PsA (PsC).
**Methods:** Serum samples were obtained from 100 patients with PsA, 100 with PsC, and 100 healthy controls. Subjects were group matched for age and sex. No patient was undergoing treatment with biologics at the time of serum collection. Using enzyme-linked immunosorbent assays, four high-priority markers, previously discovered by quantitative MS of synovial fluid and skin biopsies, were analyzed in the serum: Mac-2-binding protein (M2BP), CD5-like protein (CD5L), Myeloperoxidase (MPO), and Integrin-β 5 (ITGB5), as well as previously established markers Matrix metalloproteinase-3 (MMP3) and C-reactive protein (CRP). Data were analyzed using logistic regression (LR), and receiver operating characteristic (ROC) curves were plotted.
**Results:** The 100 PsA patients (41 females, mean age 51 years) had mean psoriasis duration of 22.9 years, PsA duration of 14.6 years, swollen joint count 3.2, tender joint count 6, and PASI score of 4.7. The 100 PsC patients (45 females, mean age 50 years) had mean psoriasis duration of 20.3 years and PASI score of 4. The 100 controls (52 females) had a mean age of 35 years. Polychotomous LR showed that ITGB5, CRP and M2BP are markers that are significantly different between the three groups. The analyses also showed that CD5L, ITGB5, M2BP, MPO, MMP3 and CRP are independently associated with PsA, while CD5L, M2BP and MPO are independently associated with PsC. When comparing PsA to PsC, ITGB5, M2BP, and CRP were found to be independently associated with PsA (Table 1). ROC analysis (Figure 1) of this model showed an

Table 1. Logistic regression analysis comparing patients with PsA to PsC

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| Biomarkers | OR[a] (95% CI) | P-value | OR[a] (95% CI) | P-value |
| CD5L, ng/mL | 1.08 (0.92, 1.26) | 3.63E-01 | – | – |
| ITGB5, ng/mL | 4.07 (2.44, 6.81) | 8.36E-08 | 3.82 (2.18, 6.70) | 3.05E-06 |
| M2BP, ng/mL | 29.72 (5.88, 150.09) | 4.05E-05 | 32.32 (4.90, 213.32) | 3.07E-04 |
| MMP3, ng/mL | 1.59 (1.21, 2.11) | 1.00E-03 | – | – |
| MPO, ng/mL | 1.09 (0.83, 1.43) | 5.40E-01 | – | – |
| CRP, mg/mL | 1.93 (1.50, 2.48) | 2.55E-07 | 1.96 (1.46, 2.62) | 5.84E-06 |

[a]Odds ratios associated with a two-fold increase in the protein level.



area under the ROC curve of 0.85 (95% CI [0.80, 0.90]) that was superior to CRP only model (AUC 0.68 [0.60, 0.76]).
**Conclusions:** CD5L, ITGB5, M2BP, MPO, MMP3 and CRP are soluble PsA markers. However, only ITGB5, M2BP and CRP, differentiate PsA from PsC, and is superior to CRP alone.
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## AB0749 IMPACT OF PATIENT PERCEPTION OF PSORIASIS AND PSORIATIC ARTHRITIS SEVERITY ON PATIENT-REPORTED OUTCOMES: AN ANALYSIS FROM THE ADELPHI DATABASE

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**Background:** Patients (pts) with psoriatic arthritis (PsA) report experiencing different levels of skin involvement (psoriasis, PsO). The impact of pt perception of PsO and PsA severity on pt-reported outcomes (PROs) in PsA pts is not clearly understood.
**Objectives:** To examine the impact of perception of PsO and PsA severity (assessed by self-completion questionnaires) in PsA pts on PROs in real world setting.
**Methods:** This retrospective analysis extracted data from the Adelphi 2014 Rheumatology disease-specific programme (DSP).[1] The DSP is a large multi-center, multi-country, cross-sectional survey of pts with a physician confirmed diagnosis of PsA. Pts filled out a self-completion form providing an assessment of their symptoms, satisfaction with disease control and quality of life. Pts reported their perception of PsA severity as mild, moderate or severe, both at diagnosis and at the time of survey. Pts reported their perception of PsO severity on a numeric rating scale of 0–10 (0, No PsO; 1–3, Mild; 4–7, Moderate; 8–10, Severe) only at the time of survey. The self-assessment questionnaires also included Dermatology Quality of Life (DLQI), alternative Health Assessment Questionnaire – Disability Index (HAQ-DI), Work Productivity and Activity Impairment (WPAI), and Euro Quality of Life 5 Dimensions (EQ5D). Pts with PsA diagnosis were stratified by self-reported severity of both PsA and PsO. Statistical differences between the groups were evaluated using $\chi^2$ test (categorical variables) or analysis of variance (ANOVA, continuous variables).
**Results:** Of the 329 PsA pts analyzed from the Adelphi database, similar number of pts reported either mild (164, 50%) or moderate-to-severe PsA (165, 50%) symptoms, at the time of survey (Table 1a). At the time of PsA diagnosis, majority of pts (292, 88%) reported experiencing moderate-to-severe PsA symptoms. At the time of survey, greater number of pts reported mild-to-moderate PsO (223, 68%) and the remaining pts reported no PsO (69, 21%) or severe PsO (37, 11%) symptoms. There was a significant association between the perception of PsA and PsO severity at the time of survey (P<0.001). The frequency and severity of itching increased significantly with increasing perception of PsO and PsA severity (P<0.001, Table 1b). However, the severity of itching was much more pronounced in pts with severe PsO. DLQI and WPAI scores were significantly impacted by increasing severity of both PsA and PsO (P<0.001). The HAQ-DI and EQ5D scores were significantly influenced by severity of both PsA (P<0.001 for HAQ-DI and EQ5D) and PsO (HAQ-DI: P<0.05; EQ5D: P<0.01); however, a larger effect on HAQ-DI and EQ-5D scores were observed in pts with severe PsA.

Table 1a. PsA severity at diagnosis or at present stratified by PsO severity at survey[a]

| PsO Severity | PsA severity at diagnosis | | | Total | PsA severity at survey*** | | | Total[b] |
|---|---|---|---|---|---|---|---|---|
| | Mild | Moderate | Severe | | Mild | Moderate | Severe | |
| No PsO | 8 (2.4) | 33 (10.0) | 27 (8.2) | 68 (20.5) | 45 (13.7) | 19 (5.8) | 5 (1.5) | 69 (21.0) |
| Mild | 11 (3.3) | 49 (14.9) | 43 (12.4) | 101 (30.5) | 61 (18.5) | 34 (10.3) | 7 (2.1) | 102 (31.0) |
| Moderate | 13 (3.9) | 75 (22.7) | 34 (10.3) | 122 (36.9) | 42 (12.8) | 70 (21.3) | 9 (2.7) | 121 (36.8) |
| Severe | 7 (2.1) | 16 (4.8) | 17 (5.1) | 40 (12.1) | 16 (4.9) | 15 (4.6) | 6 (1.8) | 37 (11.2) |
| Total | 39 (11.8) | 173 (52.3) | 119 (36.0) | 331 (100) | 164 (49.8) | 138 (41.9) | 27 (8.2) | 329 (100) |

[a] n(%)
[b] Severity of both PsA and PsO at survey were reported by 329 patients
P-value for significant association between PsA and PsO severity at the time of survey ($\chi^2$ test): ***, P<0.001
Abbreviations: PsA=Psoriatic Arthritis; PsO=Psoriasis.

Table 1b. Summary of PROs stratified by PsA and PsO severity at survey[a]

| PROs | PsA severity at survey | | | PsO severity at survey | | | |
|---|---|---|---|---|---|---|---|
| | Mild | Moderate | Severe | No PsO | Mild | Moderate | Severe |
| Itch Frequency | 2.1±0.8 | 2.9±1.0 | 3.0±1.3 | 1.4±0.6 | 2.4±0.7 | 3.0±0.8 | 3.3±1.1 |
| | *** | | | *** | | | |
| Itch severity | 3.9±2.7 | 5.5±2.8 | 5.4±3.5 | 1.0±0.0 | 3.1±0.8 | 6.6±1.2 | 9.7±0.8 |
| | *** | | | *** | | | |
| DLQI | 2.7±3.8 | 6.2±5.6 | 8.7±6.2 | 0.8±1.5 | 3.4±3.8 | 6.7±5.5 | 8.5±7.9 |
| | *** | | | *** | | | |
| WPAI | 15.2±21.4 | 44.8±27.3 | 50.1±29.3 | 13.0±23.8 | 25.0±25.7 | 51.6±26.7 | 43.6±32.1 |
| | *** | | | *** | | | |
| HAQ-DI | 0.3±0.4 | 0.8±0.6 | 1.2±0.7 | 0.5±0.6 | 0.4±0.5 | 0.7±0.6 | 0.7±0.7 |
| | *** | | | * | | | |
| EQ5D | 0.9±0.1 | 0.7±0.2 | 0.5±0.3 | 0.8±0.2 | 0.8±0.2 | 0.7±0.3 | 0.7±0.3 |
| | *** | | | ** | | | |

[a] Mean ± SD
P-value for significant difference between PsA or PsO groups (ANOVA): ***, P<0.001; **, P<0.01; *, P<0.05.
Abbreviations: PROs=Patient Reported Outcomes; PsA=Psoriatic Arthritis; PsO=Psoriasis; DLQI=Dermatology Life Quality Index; Itch Frequency=Frequency of itching due to PsA; Itch severity=Rating of worst itching due to PsA skin symptoms on a 0-10 rating scale; HAQ-DI=Health Assessment Questionnaire-Disability Index; WPAI= Work Productivity and Activity Impairment; EQ5D=Euro Quality of Life 5 Dimensions questionnaire.

**Conclusions:** Pt perception of PsO severity mostly impacted the frequency and severity of itching, DLQI, and WPAI measures, while pt perception of PsA severity at survey negatively influenced all pt reported outcome (PRO) measures.
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# Osteoarthritis

## AB0750 ANALGETIC EFFECT OF NSAIDS IN CHRONIC KNEE OSTEOARTHRITIS WITH A "CLINICAL" CENTRAL SENSITIZATION

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**Background:** NSAIDs are widely used for therapy nociceptive pain in osteoarthritis (OA) patients. But in 27% - 61% case this treatment fails to reduce mean pain levels beyond minimal clinically important thresholds [1]. Recent studies have demonstrated that chronic knee OA mechanisms besides nociceptive pain also include central sensitization (CS) (neuroplastic changes in the posterior horn) [2]. CS characterized with neuropathic (NP) phenomena spontaneous and evoked (34% cases), referred hyperalgesia and neurophysiological changes (low pressure pain threshold).
**Objectives:** to evaluate the efficacy of NSAID in patients with "clinical" CS.
**Methods:** 40 women (age 55±75), II-III grade by Kellgren-Lawrence with chronic knee OA were included. Patients were divided in groups in accordance with the results of neuropathic test DN4 (screening test for CS): patients with positive DN4 (n=11) and patients with negative DN4 (n=29) and accordance with presence of spontaneous NP phenomena (for ex. burning, tingling, current rush): patients with spontaneous NP phenomena (n=29) and patients without spontaneous NP phenomena. Dynamic of OA severity by WOMAC (mm) and pain intensity by VAS (mm) were assessed between groups.
**Results:** There was no difference between sociodemographic factors in groups. Statistically and clinically significant reduction in pain score after one-month treatment (n=20) in patients with negative DN4 score was seen (mean pain relief 26mm vs 17 mm, p<0,05). Significant decrease of WOMAC from baseline to final evaluation in patients without spontaneous NP phenomena (mean WOMAC redaction 315 mm vs 199 mm, p<0,05) was demonstrated.
**Conclusions:** Patients with clinical signs of CS have suboptimal pain control. Targeting treatment including anticonvulsants or antidepressants to symptoms of CS in people with OA could lead to benefit.
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## AB0751 THE DEPENDENCE OF OSTEOARTHRITIS PROGRESSION FROM GLYCEMIC CONTROL IN PATIENTS WITH DIABETES

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**Background:** The influence of type 2 diabetes mellitus (T2DM) on development and progression of osteoarthritis (OA) has been proved. However, there is a lack of data from more detailed researches in such category of patients.
**Objectives:** To estimate the proinflammatory serum cytokine levels and the clinical features in patients with knee OA and T2DM depending on glycemic control.
**Methods:** Patients (n=45) who had bilateral knee OA according to ACR criteria and T2DM were divided into two groups according to the compensation degree T2DM taking into account parameters of glycated hemoglobin concentrations (HbA1c) which were assessed using liquid chromatography. Blood glucose level was also estimated. Group 1 (n=26) had control T2DM. Group 2 (n=19) had no control T2DM. All patients were comparable by age, sex and duration of OA. Serum cytokine levels (IL-1b, IL-6, IL-10, IL-18), NO, and adypokines

(adiponectin, leptin) using ELISA were assessed. Intensity of pain, general health, stiffness, physical functions were measured by visual analog scale (VAS),Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee injury and Osteoarthritis Outcome Score – (KOOS) and short form 36 (SF-36). U-Mann-Whitney test was applied to detect differences between groups. Correlation was assessed using Spearman correlation coefficient (rs).
**Results:** No significant difference has been found in parameters reflecting the functional disorders. Serum cytokines levels also were not different between the studied groups. Correlation analysis identified the relationships between clinical parameters and cytokines in OA patients with control and non-control T2DM. Certain data are presented (Table).

Table. Correlation between clinical parameters and serum cytokine levels in studied groups

| Cytokines | OA patients with control T2DM n=26 | | | OA patients with non-control T2DM n=19 | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Pain (KOOS) | Physical Function (WOMAC) | General health (SF-36 GH) | Pain (VAS) | Physician's assessment of disease (VAS ) | Pain (KOOS) | Physical Functioning (SF36-PF) | Bodily pain (SF36-BP) | Physical health (SF36-PH) |
| IL-1b (pg/ml) | 0.56 | 0.44 | 0.45 | 0.95 | 0.41 | 0.64 | **0.0002*** | **0.0001*** | **0.002*** |
| IL-6 (pg/ml) | 0.70 | 0.62 | 0.58 | **0.002*** | **0.02*** | **0.03*** | 0.13 | 0.13 | 0.30 |
| IL-10 (pg/ml) | 0.83 | 0.51 | 0.74 | 0.33 | 0.18 | 0.85 | 0.42 | 0.21 | 0.30 |
| IL-18 (pg/ml) | **0.03*** | **0.04*** | 0.61 | 0.62 | 0.23 | 0.61 | **0.04*** | 0.95 | 0.80 |
| NO (pg/ml) | 0.38 | 0.07 | **0.02*** | 0.54 | 0.18 | 0.78 | 0.35 | 0.95 | 0.80 |
| Leptin (ng/ml) | 0.73 | 0.87 | 0.67 | **0.003*** | **0.002*** | **0.01*** | **0.001*** | **0.04*** | **0.01*** |

Table legend: * - p<0.005;

**Conclusions:** The results show that depending on the glycemic control may change clinical and immunology parameters of OA in patients with T2DM, especially in group with non-control T2DM. These data should be verified by larger studies and may be useful for the development of a personalized approach to patients with comorbid disorders such as OA and T2DM in future.
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## AB0752 THE ASSOCIATION BETWEEN CLINICAL SYMPTOMS AND SERUM CYTOKINES LEVELS IN PATIENTS WITH KNEE OSTEOARTHRITIS AND COMORBIDITY

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**Background:** A number of factors influence development and progression of osteoarthritis (OA), including comorbid diseases. Such factors as obesity, impaired glucose tolerance, raised blood glucose level can affect clinical processes and also have similar mechanisms of immunopathogenesis with OA.
**Objectives:** To explore the symptoms and the proinflammatory serum cytokine levels in patients with knee OA and obesity, metabolic syndrome (MS) and type 2 diabetes mellitus (T2DM) and to estimate association between clinical and immunological features.
**Methods:** A study was performed on 128 persons with bilateral knee OA according to the ACR criteria who were divided into four groups. Group 1 (n=17) had obesity, group 2 (n=17) had MS, group 3 (n=56) had T2DM and group 4 (n=38) had only knee OA without comorbid diseases. All patients were comparable by age, sex and duration of OA. We assessed serum cytokine levels (IL-1b, IL-6, IL-10, IL-18), NO including adipokines such as adiponectin and leptin using ELISA. Intensity of pain, general health, stiffness, physical functions were measured by visual analog scale (VAS),Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee injury and Osteoarthritis Outcome Score – (KOOS) and with short form 36 (SF-36). U-Mann-Whitney test was applied to detect differences between groups. Correlation was assessed using Spearman correlation coefficient (rs).
**Results:** In the course of the comparative analysis of the groups of OA patients and concomitant diseases with a group of OA patients without comorbidity there were found many statistically significant differences in such scales and indexes as VAS, WOMAC, KOOS, SF-36. Patients with OA and obesity are characterized by the prevalence of symptoms OA of KOOS scale (median (Me) 61.1; interquartile range (IQR) 55.5–70.8; $p<0.001$). Patients from group 2 (MS) and 3 (T2DM) were significant worse parameters of general health and high levels of pain, morning stiffness and functional disoders of the knees. Differences in serum cytokine levels were found in patients with OA and T2DM (IL-6 p=0.0018; IL-18 p=0.0006; NO $p<0.001$). Patients with OA and obesity had high leptin level (p=0.03). Group 3 with OA and T2DM had significant differences in leptin (p=0.0002). Correlation analysis identified relationships between clinical parameters and cytokines in OA patients with obesity and T2DM. Some data is presented (Table).

Table. Correlations between clinical parameters and serum cytokine levels in studied groups

| Cytokines | OA patients with obesity n=17 | | | | | | OA patients with T2DM n=56 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Physician's assessment of disease (VAS ) | General health (VAS) | Total score WOMAC | Sport's activity (KOOS) | Bodily pain (SF36-BP) | Physical health (SF36-PH) | Pain (VAS) | General health (VAS) | Symptoms OA (KOOS) | Physical Functioning (SF36-PF) | General Health (SF36-GH) | Physical health (SF36- PH) |
| IL-1b (pg/ml) | 0.49 | 0.49 | **0.02*** | 0.05 | 0.41 | 0.10 | 0.79 | 0.69 | **0.03*** | 0.66 | 0.46 | 0.28 |
| IL-6 (pg/ml) | 0.35 | 0.13 | 0.13 | 0.24 | **0.01*** | **0.01*** | **0.02*** | 0.11 | 0.25 | **0.01*** | 0.47 | **0.04*** |
| IL-10 (pg/ml) | 0.20 | 0.80 | 0.35 | **0.01*** | 0.49 | 0.29 | 0.62 | **0.007*** | 0.42 | 0.13 | 0.08 | 0.13 |
| IL-18 (pg/ml) | 1.0 | 0.41 | 0.38 | 0.29 | 0.17 | **0.01*** | 0.02 | 0.80 | 0.41 | 0.45 | 0.25 | 0.47 |
| NO (pg/ml) | 0.41 | **0.03*** | 0.29 | 1.00 | 0.13 | 0.49 | 0.71 | 0.66 | 0.42 | 0.96 | **0.03*** | 0.73 |
| Adiponectin (pg/ml) | **0.01*** | 1.0 | 0.65 | 0.29 | 0.29 | 0.65 | 0.91 | 0.70 | 0.57 | 0.57 | 0.84 | 0.45 |
| Leptin (pg/ml) | 0.80 | 0.35 | 1.0 | 0.56 | 0.13 | 0.49 | **0.003*** | **0.03*** | **0.04*** | 0.05 | 0.05 | **0.01** |

Table legend: * - p<0.005;

**Conclusions:** According to the study, patients with obesity, MS and T2DM have special clinical and laboratory features of progression of OA. Such immunological parameters as serum cytokine concentrations may also be linked with symptoms of OA in patients with aforecited comorbidity. These data should be verified by larger studies.
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## AB0753 LONGITUDINAL STUDY ON CLINICAL WORSENING OF OSTEOARTHRITIS IN THE KNEE AND HIP OVER 2 YEARS: WORSENING AFTER STANDARDIZED NON-SURGICAL TREATMENT FOR 3 MONTHS IS A STRONG PREDICTOR FOR WORSENING AT 2 YEARS

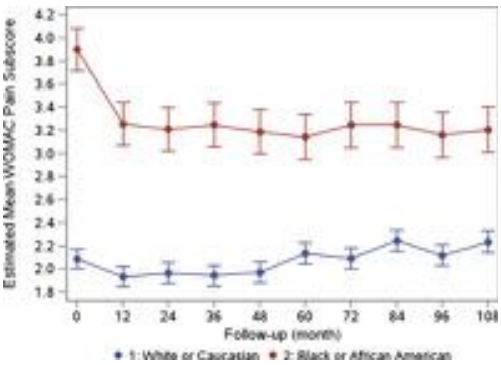
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**Background:** Despite the high incidence of clinically established knee and hip osteoarthritis (OA), few data are available on risk factors for clinical worsening.
**Objectives:** The aims are 1) to estimate the proportion of symptomatic knee and hip OA patients showing worsening at 2 years, after 3 months standardized conservative treatment, 2) to estimate the additional value of clinical criteria at 3 months in prediction worsening at 2 years compared to baseline values only.
**Methods:** All 302 patients in this longitudinal study in secondary care (CONTROL-PRO: patients fulfilling clinical ACR criteria for knee or hip OA and not yet deemed eligible for arthroplasty), received conservative treatment (the first 3 months standardized) which comprised education, physical therapy, step up analgesics and advice on weight reduction if indicated. The Western Ontario and McMaster Universities of Osteoarthritis Index (WOMAC) was used to measure pain and physical functioning as well as a numeric rating scale measuring patient global assessment. Measurements were performed at baseline, 3 months and 2 years. Worsening at 2 years was operationalized as fulfilling recently validated clinical worsening criteria for knee and hip OA or total joint replacement (TJR) in the index joint. Logistic regression was used to estimate the additional value of the determinant fulfilling clinical worsening at 3 months as predictor for worsening at 2 years.
**Results:** Baseline characteristics were 66% female, a mean age of 55.0 (SD 9.8) years, and median BMI of 27.9 kg/m$^2$ (IQR 25.3–32.9). Median duration of symptoms was 3.8 years (IQR 1.6–10.4), the majority addressed the knee joint (84.8%) as index joint and 211 patients (69.9%) had Kellgren and Lawrence scores $\geq$2. A total of 79 (27.8%) and 181 patients (59.9%) clinically worsened at 3 months and 2 years respectively. 75 Out of 181 patients (41.4%) who worsened at 2 years, had undergone a TJR in the index joint on average 1.1 years (SD 0.5) after inclusion. Of these 181 patients who worsened over time, a lower proportion of patients underwent a TJR of the knee than a TJR of the hip in their index joint (34.5% versus 72.7% respectively, $p<0.0001$). Patients who clinically worsened at 3 months showed an increased odds ratio of 5.8 to clinically worsen at 2 years as well (95% CI 2.2–15.6, $p<0.001$). Similar results were obtained when only TJR at 2 years as outcome measure was used.
**Conclusions:** A high proportion of knee and hip OA patients in secondary care who are not deemed yet eligible for surgery at inclusion, showed clinical worsening over 2 years, even after conservative treatment. At 2 years, we observed relatively less TJRs for knee OA than for hip OA. Our results show that clinical worsening at 3 months is a strong independent risk factor for worsening at 2 years. A short conservative treatment trial could thus be used in clinical practice to select patients in whom TJR should be considered.
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## AB0754 RACIAL DIFFERENCES IN KNEE OSTEOARTHRITIS PAIN, SYMPTOMS AND DISABILITY REPORTING

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**Background:** Manifestations and severity of knee osteoarthritis (KOA) vary across racial groups. Characterizing this variability allows identification of vulnerable groups and customizing interventions accordingly. Pain and functional limitations tend to be greater among African-Americans (AAs) than Whites (WHs) with KOA. Differential progression in KOA symptoms by race has not been well-described.
**Objectives:** To compare progression over 9 years in reported pain, disability and other symptoms of AAs and WHs with or at high-risk of KOA
**Methods:** Data from baseline to 108 months were gathered from the Osteoarthritis Initiative (OAI). The study rationale and inclusion criteria for OAI (people ages 45–79 with symptoms of and/or radiographic KOA, or with risk factors for developing KOA) have been described (http://oai.epi-ucsf.org/datarelease/). All AA and WH subjects were included in the study. Knee pain, disability and other OA symptom trajectories were based on: 1) WOMAC pain subscale score [range: 0–20], 2) Knee pain severity in the past 30 days based on a numerical rating scale (NRS) [range: 0–10], 3) WOMAC disability subscale score [range: 0–68], and 4) Knee Injury and Osteoarthritis Outcome (KOOS) other symptoms score [range: 0–100]. Higher scores indicate greater OA-related pain/disability in all measures, except for KOOS symptoms score. Mixed effect models for repeated measures were used to test for racial differences in mean values and mean change during follow-up. All models were adjusted for age, sex, body mass index [BMI], and education.
**Results:** A total of 3790 WH and 874 AA OI participants were included, and the majority (58.4%) were female. Mean (SD) age at baseline was 61.2 (9.2) years, and mean (SD) BMI was 28.7 (4.9) kg/m$^2$. Baseline WOMAC pain subscale score was higher in AAs (mean 3.90 [95% CI: 3.72 to 4.08]) in comparison to WHs (mean 2.09 [95% CI: 2.00 to 2.18]) ($p \leq 0.0001$). After the second administration of the questionnaires 1-year post-baseline, there was a significantly greater decline in mean WOMAC pain score among AAs compared to WHs (-0.64 [95% CI: -0.79 to -0.50] vs. -0.15 [95% CI: -0.22 to -0.08]; $p < 0.0001$), while the mean pain levels remained relatively stable between the 1 year and 9 year follow-up visits (Figure 1). Trajectories of mean pain severity measured with a NRS, WOMAC disability, and KOOS symptom score had similar patterns, with a significantly greater decline among AAs from baseline to the first year of follow-up, followed by relatively stable group means. Change in mean scores over the first year of follow-up for AAs, in comparison to WHs, were as follows: pain severity (-0.70 [95% CI: -0.83 to -0.56] vs. -0.14 [95% CI: -0.20 to -0.08]; $p < 0.0001$), WOMAC disability score (-1.70 [95% CI: -2.15 to -1.25] vs. -0.79 [95% CI: -0.99 to -0.58]; p=0.0003) and KOOS other symptoms score (2.16 [95% CI: 1.52 to 2.80] vs. 1.18 [95% CI: 0.89 to 1.48]; p=0.0064).




**Conclusions:** The results suggest that AAs report a precipitous drop in KOA-related symptoms between first administration at baseline and second administration 1 year later. Self-reported measures of symptoms are accepted as primary endpoints in randomized controlled trials (RCTs) and commonly used in observational studies. The implications for RCTs that rely on changes in these measures to demonstrate drug efficacy include obscured treatment effects among AAs, as well as biased selection for trial eligibility.
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## AB0755 THE PREDICTIVE ROLE OF HIGH SENSITIVE C-REACTIVE PROTEIN AND HIGH DENSITY LIPOPROTEIN IN DEVELOPMENT OF ROTATOR CUFF TEAR IN PATIENTS WITH HAND OSTEOARTHRITIS

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**Background:** Rotator cuff tear (RCT) and hand osteroarthritis (HOA) are commonly accompanied because they share a similar pathogenesis. However, there was no previous study investigating the relationship between RCT and HOA.
**Objectives:** To estimate the prevalence and associated factors of RCT in patients with HOA.
**Methods:** In this study, we enrolled 1150 farmers who lived in Gyeongnam province in Korea from June 2013 to December 2015. Physical examinations were performed by rheumatologists and orthopedists. Plain radiography of hands and magnetic resonance imaging (MRI) of shoulders were performed in all participants. Serum levels of high sensitive C-reactive protein (hsCRP) and high density lipoprotein (HDL) were checked. RCT was diagnosed by clinical examination and MRI findings. Diagnosis of HOA was made by the 1990 American College of Rheumatology classification criteria. Severity of HOA was defined as Kellgren–Lawrence (KL) grade $\geq$3 on plain radiographs. Erosive HOA was defined as having eroded 'E' or remodelled 'R' phase of the Verbruggen.
**Results:** The prevalence of RCT was higher in patients with HOA group (192/307, 62.5%) than those without HOA (410/827, 49.5%, $p < 0.010$). Among 307 with HOA, patients with RCT were older (62.69±7.04 vs. 59.11 ±7.69, $p < 0.001$) and showed higher hs-CRP (1.51±3.78 vs. 0.67±0.70, p=0.004) and lower HDL levels (55.66±15.46 vs. 60.48±12.45, p=0.003) compared to those without RCT. There were no significant differences in gender, smoking, comorbidities, work period, body mass index, number of affected joints, HOA severity, and prevalence of erosive HOA between both groups. Multiple logistic regression analysis showed significant associations of age (odds ratio [OR] 1.06; 95% confidence interval [CI] 1.02 - 1.10), serum levels of hsCRP (OR 1.37, CI 1.04 - 1.80), and HDL (OR 2.13, CI 1.14 - 3.98) with RCT in HOA patients.
**Conclusions:** The prevalence of RCT is high and age and serum levels of hsCRP and HDL have predictive roles in the development of RCT in HOA patients.
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## AB0756 LIVING WITH OSTEOARTHRITIS: REAL LIFE PERCEPTION UPON PAIN AND FUNCTION

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**Background:** Osteoarthritis (OA) is a prevalent condition for which treatments are based on analgesia and physical therapies. Despite that, most of the patients continue to have pain and limited function influencing there day by day life.
**Objectives:** Our objective was to evaluate pain perception in a cohort of participants, diagnosed with osteoarthritis.
**Methods:** 75 patients with osteoarthritis were enrolled in this study, conducted in Sf. Maria Hospital between 1 June and 30 December 2015. All patients signed an informed consent approved by local ethic committee. Data about demographics, joint involvement and treatment were collected. All patients completed a HAQ evaluation and a Visual Analogue Scale (VAS) for pain (0–10). We developed a questionnaire in order to capture patient perception about osteoarthritis symptoms and how this disease impact there life. They were asked about how pain interfere with usual activity (work, preparing meal, house kipping), with social activity (family interaction, friends) or how they perceived pain or efficacy of the treatment in the last month. They were also asked about there expectations related to this disease. Statistical analysis was made with SPSS.
**Results:** Mean age at evaluation was 63 with a female predominance (83%). 89.3% were taking NSAIDs and 73.3% acetaminophen. Functional status evaluated by HAQ showed that 24% patients had a score of 0, with 57% having a score of 1 and 19% a score of 2. VAS for pain was at least 5 for more than 80% of patients, despite treatment. Higher VAS was significant more frequent in female patients (p 0.001), in patients with family history of osteoarthritis (p 0.023) and in the one with sedentary life style (p 0.035). Most of the patients considered that pain interfere with daily activity, the impact being evaluated as moderate for 46.67% of patients and severe for 32%. Pain also had a negative impact on their social life, the percentage for moderate disturbance being of 38.67% and 18.67% for severe one. Only 11% of patients consider that the pain control is well managed. Despite these results, 40% of the patients do not expect that there quality of life will improve in the future.
**Conclusions:** Residual pain after treatment is present in most of the patients with osteoarthritis and these interfere significantly with daily living and quality of life. These patients enter in a vicious cycle related to worsening pain – low physical activity. Although this findings, there is a resumption of these patients in front of the disease.
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## AB0757 CLINICALLY IMPORTANT IMPROVEMENT THRESHOLDS FOR HARRIS HIP SCORE AND ITS ABILITY TO PREDICT REVISION RISK AFTER PRIMARY TOTAL HIP ARTHROPLASTY

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**Background:** Harris Hip Score (HHS) is the most commonly used instrument in the assessment of total hip arthroplasty (THA). Clinically meaningful thresholds for HHS have not been defined; limited data exist on responsiveness.
**Objectives:** To examine the clinically meaningful change thresholds, responsiveness and predictive ability of the Harris Hip Score (HHS) questionnaire.
**Methods:** We included a cohort of patients who underwent primary total hip arthroplasty (THA) and responded to HHS preoperatively and/or at 2- or 5-year post-THA to examine the clinically meaningful change thresholds (Minimal clinically important improvement, MCII; and moderate improvement), responsiveness (effect size (ES) and standardized response mean (SRM)) based on pre- to post-operative change and its predictive ability at 2- and 5-years post-THA for future revision.
**Results:** 2,667 patients with mean age of 64 years completed baseline HHS; 1,036 completed both baseline and 2-year and 669 both baseline and 5-year HHS. MCII and moderate improvement thresholds ranged 15.9–18 points and 39.6–40.1 points, respectively. ES was 3.12 and 3.02 at 2- and 5-years; respective SRM was 2.73 and 2.52. Compared to patients with HHS scores of 81–100 (score range, 0–100), patients with scores $<55$ at 2- and 5-years had higher hazards (95% confidence interval) of subsequent revision, 4.34 (2.14, 7.95; $p<0.001$) and 3.08 (1.45, 5.84; p=0.002), respectively. Compared to HHS score improvement $>50$ points from preoperative to 2-years post-THA, lack of improvement/worsening or 1–20 point improvement were associated with increased hazards of revision, 18.10 (1.41, 234.83; p=0.02); and 6.21 (0.81, 60.73; p=0.10), respectively.
**Conclusions:** HHS is a valid measure of THA outcomes, is responsive to change and predictive of revision risk post-primary THA. We have defined MCID and moderate improvement thresholds for HHS in this study.
**References:**
[1] None
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## AB0758 THE RELATIONSHIPS BETWEEN BONE MINERAL DENSITY AND RADIOGRAPHIC FEATURES OF HAND OR KNEE OSTEOARTHRITIS IN OLDER ADULTS: DATA FROM THE DONG-GU STUDY

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**Objectives:** The relationship between osteoarthritis (OA) and osteoporosis has exhibited contradictory features over the past four decades. The aim of this study was to evaluate this relationship using separate analysis of the radiographic features of OA whether various radiographic features of OA were associated differently with bone mineral density (BMD) in the Korean elderly.
**Methods:** Data were derived from the Dong-gu cohort; 2,354 subjects were enrolled in the present cross-sectional study. Baseline characteristics, the BMDs of the lumbar spine and femoral neck which was measured by DXA, and X-rays of knees and hands, were collected. A semi-quantitative grading system was used to estimate the severities of individual radiographic features. We adjusted for confounders using multiple linear regression modeling to analyze the relationships.
**Results:** After adjustment for confounders, hand and knee OA total scores were negatively associated with the BMDs of the lumbar spine and femoral neck, except for the total knee OA score and lumbar spine BMD. In detail, hand osteophytes and sclerosis exhibited positive relationships with the BMDs of the lumbar spine and femoral neck, except for hand osteophytes and femoral neck BMD. On the contrary, however, knee joint space narrowing (JSN), hand JSN, and hand subchondral cysts were negatively associated with the BMD of the lumbar spine and femoral neck. Knee JSN and hand subchondral cysts exerted the greatest effects on BMD.
**Conclusions:** Separate analysis of the radiographic features of OA better reveals associations of OA with the BMD of the lumbar spine and femoral neck.
**Disclosure of Interest:** None declared
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## AB0759 RELATIONSHIP BETWEEN COMORBIDITY INDEX AND HEALTH RELATED QUALITY OF LIFE IN SYMPTOMATIC KNEE OSTEOARTHRITIS PATIENT

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**Background:** Knee osteoarthritis (OA) is the most prevalent symptomatic OA among adults and is the leading cause of disability.[1] The ultimate treatment goal in such chronic disease is to achieve a good health related quality of life (HRQoL).[2,3] Since knee OA prevalence is increasing throughout age, comorbidity become common condition.[4,5] Comorbidity is presumed as contributing factor unto health related quality of life in knee OA patient.
**Objectives:** To evaluate the relation between comorbidity index and health related quality of life in symptomatic knee OA patient.
**Methods:** This was a cross-sectional study conducted in Rheumatology Policlinic Cipto Mangunkusumo Hospital, Jakarta. HRQol was measured with a self-assessment generic instrument Medical Outcome 36- Items Short Form (SF-36) Health Status Survey (figure 1).[6] Comorbidity index was measured by researcher with Cumulative Illness Rating Scale (CIRS).[7] Bivariate analysis was performed by using Chi-square test and its alternative Fisher Exact Test.
**Results:** Most subjects were woman with mean age of 62,62 years (SD8,02). The most prevalent risk factor was overwight or obesity. Mean value for body mass index in this study was 27,54 kg/m$^2$ (SD 4,44). Eighty six percent of subjects were having poor physical component summary (PCS) of HRQoL. Whereas 72,2% of subjects waere having good mental component summary (MCS) of HRQoL. Ninety eight point seven percent subjects were having $\geq$1 comorbidity(ies). The three top positive comorbidity system were endocrine- metabolic, vascular, and musculosceletal and integument. The median value of comorbidity index was 1,68 (0–2,33) which is resembled moderate comorbidity index. There was no relation has been found in bivariate analysis between comorbidity index and PCS (OR=1,11; CI95%=0,26–4,75), neither with MCS (OR=1,21; CI95%=0,41–3,61).

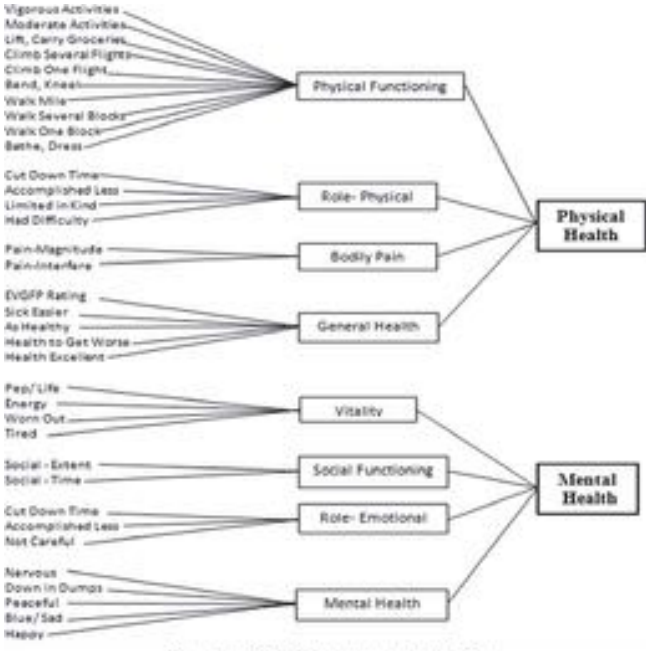



**Figure 1. SF-36 *Measurement Model**
*Ware JE, Sherbourne CD 1992*

**Conclusions:** There is no relation between comobidity index and HRQoL, both physically and mentally component in symptomatic knee OA patients. The homogenicity of comorbidity condition and HRQoL in subjects may contributed to the result.
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## AB0760 COMPARISON OF LIFE QUALITY, PAIN INTENSITY AND FATIGUE WITH PATIENTS SUFERRING FROM RHEUMATOID ARTHRITIS AND KNEE OSTEOARTHRITIS

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**Background:** It is well known that chronical rheumatoid diseases have negative impact on life quality. Pain and joint swelling, limited motion, stiffness and deformity from one side, as well as fatigue, poor sleep quality and depression, on the other hand, significantly reduce life quality.
**Objectives:** Comparison of life quality, pain intensity and fatigue intensity of patients with rheumatoid arthritis (RA) and knee osteoarthritis (knee OA).
**Methods:** 150 patients have been examined: 75 patients with RA and 75 patients with knee OA. Groups were homogenous regarding gender and age. Life quality has been estimated by means of questionnaire- Short Form Medical Outcomes Instruments (SF 36) SF 36F-physical sphere and SF 36M-mental sphere. Pain and fatigue intensity was estimated by scale VAS.
**Results:** Average value of SF 36F with patients suferring from RA was 35.62±21.73 in regard to patients suffering from knee OA 61.72±18.85, $p<0001$. Average value of SF 36M with patients suffering from RA was 44.79±24.18 compared to patients with knee OA having 68.12±20.77, $p<0001$. Pain intensity with patients with RA was 47.79±24.66 compared to patients with knee OA ranging 46.08±18.82, $p=0.622$. Fatigue intensity with patients suffering from RA was 48.28±25.64 compared to patients with knee OA having 29.23±15.58, $p<0001$.
**Conclusions:** Patients with RA have significantly less quality of life and greater fatigue intensity compared to patients with knee OA. Pain intensity was not statistically significantly different. Although patients with RA have poorer values of quality of life, taking into account a big number of patients with knee OA, a significant implication of this disease is recognized. Pain is significant predictor of poor quality of life.
**Disclosure of Interest:** None declared
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## AB0761 EFFICACY OF PER-CUTANEOUS ULTRASOUND GUIDED DRAINAGE OF DEGENERATIVE MENISCAL CYSTS IN KNEE OSTEOARTHRITIS PATIENTS

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**Background:** Meniscal cysts presented in about 4% of patients with knee osteoarthritis [1]. Meniscal cysts may result in pain and disability in the knee. Ultrasound may be used for therapeutic aspiration of the cyst [2].
**Objectives:** To evaluate the efficacy of ultrasound guided percutaneous drainage of symptomatic meniscal cysts in patients with knee osteoarthritis.
**Methods:** Ultrasound guided percutaneous drainage of symptomatic meniscal cysts were performed in 38 patients with Knee osteoarthritis in the period between January 2013 and December 2015. Thirty cysts were related to the medial meniscus and 8 cysts were related to the lateral meniscus. Cysts were injected with local anaesthetic before completion of procedure. All 38 patients were subsequently followed up one month and 6 months after the aspiration with the primary outcome measures were the Western Ontario and McMaster Universities OA Index total pain score WOMAC (a Likert scale), patient global assessment (PGA) questionnaires and musculoskeletal ultrasonography assessment.
**Results:** In every case the procedure was well tolerated. Complete aspiration of the cyst were performed in 15 patients (39.5%) and partial aspiration were performed in 23 patients (60.5%). Before aspiration US meniscal cyst measurements 29.5±9.2 mm * 13.6±4.5 mm. At the end of the 1st month, there was a reduction of 50% in the WOMAC pain score. 89.4% (34 patients) felt that their knee pain had improved compared to baseline. At this time point just US meniscal cyst measurements 19.5±5.2 mm * 11.6±4.1 mm. At the end of the 6th month post aspiration, there was a reduction in the WOMAC pain score of 30%. At this time point just 78.9% (30 patients) felt that their knee pain had improved compared to baseline. At this time point just US meniscal cyst measurements 25.5±6.2 mm * 13.6±3.6 mm. Patient outcomes did not significantly correlate with any meniscal cyst characteristic. Complete aspiration was associated with better outcomes.
**Conclusions:** Ultrasound-guided percutaneous aspiration of degenerative meniscal cysts is a well-tolerated, simple, and safe procedure for patients with knee osteoarthritis.
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**Disclosure of Interest:** None declared
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## AB0762 FFICACY AND SAFETY OF NEM® ARTRO(NEM®-STRATUM NUTRITION) BRAND EGGSHELL MEMBRANE IN PATIENTS WITH KNEE OSTEOARTHRITIS ACCOMPANYING WITH JOINT PAIN AND STIFFNESS. A MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER STUDY

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**Background:** Traditional treatments for pain and stiffness in osteoarthritis attempt to address only the symptoms associated with the diseases.
**Objectives:** To investigate the efficacy and safety of natural eggshell membrane Natural Eggshell Membrane (NEM) in patients with knee osteoarthritis having joint pain and stiffness.
**Methods:** This study is a Efficacy and Safety of NEM®ARTRO(NEM®-Stratum Nutrition) Brand Eggshell Membrane in Patients With Knee Osteoarthritis Accompanying With Joint Pain and Stiffness. A Multi-center, Randomized, Double-blind, Placebo-controlled, Crossover Study. This study was planned to include 200 female or male patients, however a total of 166 patients were screened and all the 166 patients were enrolled to the study. Median age of the medication group was 53 and in the placebo group was 57. The study was conducted as a multicenter, randomized, double blind, placebo controlled and crossover study. Patients aged $\geq$40 years having osteoarthritis complaints for 1–5 years and grade 2 or 3 knee osteoarthritis were included as 166 patients in total (32 male and 134 female). They were randomly assigned to receive either Natural Eggshell Membrane (NEM®) (drug group) or placebo (placebo group) for 30 days. After the evaluations on day 30, the placebo group was also initiated to Natural Eggshell Membrane (NEM®). Thus, at the end of 90 days, two groups (the 60-day and 90-day Natural Eggshell Membrane (NEM®) treatment groups) were evaluated. For pain and stiffness in patients, VAS and WOMAC scales and for quality of life SF-36 scale was used. The degree of pain and stiffness was evaluated at baseline and days 7, 30, and 90. Quality of life scales were evaluated in the baseline and in the end of treatment.
**Results:** There was no difference between the drug (n=83) and placebo (n=83) groups regarding demographics, baseline clinical findings, and pain (VAS, WOMAC) and stiffness (WOMAC) scores. At the end of 7- and 30-day treatment, the pain and stiffness scores were significantly lower in the drug group than in the placebo group.
A total of 8 adverse events in the medication group and 15 adverse events in placebo group were observed. It was seen that none of the conditions in medication group are serious.
WOMAC pain score has decreased 30% in the first month and 40% in the third month for medication group. VAS score was decreased 22% in the first month and 42% in the third month for medication group. WOMAC stiffness score has decreased 34% in the first month and same in the third month for medication group. SF-36 score was 39 for the first month and 46 for the third month for medication group.
**Conclusions:** In the treatment of patients with knee osteoarthritis, Natural Eggshell Membrane (NEM®) reduces pain and stiffness in early period and provides a significant progress in quality of life and maintains its efficacy in long-term.
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## AB0763 DOES DECREASED BONE MINERAL DENSITY AFFECT CLINICAL MANIFESTATION IN KNEE OSTEOARTHRITIS WOMEN?

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**Background:** Current studies and research support the role of bone mineral density (BMD) in knee osteoarthritis (KOA). However, few studies have focused on its impact on KOA parameters.
**Objectives:** The aim of this study was to investigate if decrease of BMD affect the intensity of pain, functional disability, and radiographic severity in KOA women.
**Methods:** We conducted a cross sectional study including confirmed radiographic knee osteoarthritis according to Kellgren and Lawrence scale, with normal and reduced BMD according to the classification of Report of a WHO Study Group. The two groups were compared on pain Visual Analogue Scale (VAS), Lequesne index, Womac function, and radiological grade after adjusting for significant covariates. Multiple regression analysis was used to identify the independent effects of each specific component for decrease of BMD on knee osteoarthritis parameters.
**Results:** One hundred forty women were included. The mean age was 55,28±8,08 [37–75] years, and the mean BMI was 30,18±2,43 [23–37] kg/m$^2$. The prevalence of decrease of bone mineral density was 55,7%. Women with and without osteoporosis had similar KOA parameters. Multiple regression analyses showed, after adjusting for all covariates, that decrease of BMD had a positive impact on pain VAS (p=0,002) and WOMAC (p=0,003), an indicator of restrictions on daily activity WOMAC (p=0,08), Lequesne index (p=0,001). Noted that lower parameters BMD was significantly associated with high level of CRP (p=0,04).
**Conclusions:** In patients KOA with a concomitant decrease in BMD revealed a distinct pain in the knee by VAS and index WOMAC, a strong indicator of restrictions on daily activity WOMAC, more high Lekena index and a higher level of CRP.
**References:**
[1] In addition to anti-inflammatory therapy, appropriate treatment of osteoporosis needs to become an important management strategy for knee pain and functional impairment.
**Disclosure of Interest:** None declared
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## AB0764 RADIOGRAPHIC CHARACTERISTICS OF THE HIP MAY PREDICT RESPONSE TO VISCOSUPPLEMENTATION IN PATIENTS WITH HIP OSTEOARTHRITIS. RESULTS OF A PROSPECTIVE OBSERVATIONAL, MULTICENTER, OPEN-LABEL, PILOT STUDY

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**Background:** Viscosupplementation by intra-articular injections of hyaluronic acid (HA) is used to alleviate pain and improve function in patients with hip osteoarthritis (HOA). However patients the more likely to be satisfied with the treatment are not well defined because predicive factors of success are still lacking.
**Objectives:** To identify radiological predictive factors of response to viscosupplementation (VS) in patients with hip osteoarthritis (HOA).
**Methods:** Prospective, multicenter, open-label trial, performed in daily practice conditions. Patients with hip OA were treated with a single IA injection of crosslinked HA+mannitol (CHAM), using fluoroscopy or ultrasonography guidance. Hip radiographs at baseline were scored by a single experienced observer using Kellgren-Lawrence (KL) grade and OARSI score for joint space narrowing (JSN), osteophytes and subchondral changes. Hips were classified according radiographic features such as JSN location (supero-lateral, supero-medial, axial, diffuse, posterior) and architectural abnormalities (dysplasia, coxa profunda, femoro-acetabular impigement FAI). Pain and function were assessed at baseline and day 90 using WOMAC index. Satisfaction with the treatment, decrease in analgesics consumption throughout the follow-up, and treatment efficacy were self-assessed by the patients at day 90. Association between these features and response to treatment (pain improvement>50% versus baseline) were assessed in univariate analysis, and then using logistic regression, adjusting confounded variables
**Results:** One hundred patients (59 females, 41 males, mean age 62) were included in the trial. Hip OA was bilateral in 39 patients. The median (range) WOMAC pain and function at baseline were 26 (7–42) and 79 (9–134) respectively. Response to treatment was obtained in 60 patients without any difference regarding gender, age and BMI but was better in the most symptomatic patients (p=0.014). In the 80 patients who completed the trial with fully available radiographic and clinical data, efficacy was inversely related to KL grade (p=0.02). Furthermore the percentage of success was highly dependent on the radiographic features. Regarding JSN severity, response was obtained in 100%, 59%, 55%, 41% of the cases for grade 0,1, 2 and 3 respectively. Regarding the femoral head migration, better results were obtained in axial (65%) and supero-medial (62%) JSN than in supero-lateral JSN (50%). Response was also more likely to be obtained in case of FAI (62%) and coxa profunda (69%) than in hip dysplasia (40%).
**Conclusions:** This pilot study, which need further confirmation by larger scale trials, suggests that radiological features might be of high importance for the decision of viscosupplementation in patients with hip OA.
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## AB0765 IDENTIFICATION OF NEUROPATHIC PAIN COMPONENT IN PATIENTS OF VARIOUS AGE WITH KNEE OSTEOARTHRITIS

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**Background:** Osteoarthritis-induced pain is a result of nociceptor stimulation, associated with local tissue damage and inflammation. Resent data suggest the presence of neuropathic pain symptoms in patients with osteoarthritis.
**Objectives:** The aim of this study was to estimate the structure of pain syndrome, reveal the presence of neuropathic pain (NP) component, symptoms and signs of NP in patients suffering from knee osteoarthritis.
**Methods:** We've examined 44 patients with knee osteoarthritis of the II-III stages by the Kallgrene-Lawrence scale aged 47–85 years (average age 66,1±1,5 years). Patients were divided according to age into next groups: 47–60, 61–74, 75–85 years. To assess the NP component, we used screening scales painDETECT, LANSS, DN4 questionnaires. To assess intensity of pain, visual analogue scale (VAS) was used. Besides WOMAC and EuroQol-5D questionnaire were applied. For statistical analysis of results, ANOVA, correlation and regression analysis, chi square ($\chi^2$) were applied.
**Results:** 72,7% of patients with knee osteoarthritis examined by painDETECT were unlikely to have the NP component, 22,7% might possibly, 4,6% – probably. LANSS scale: 25% were probably to have NP. DN4 scale: 31,2% probably had NP. Moderate to significant correlations were found between intensity of pain by VAS data and Neuropathic Pain Scales (painDETECT, LANSS, DN4) data (p<0,05). It was established than higher results of screening by painDETECT and DN4 positively correlate with a disturbance of physical function tested by WOMAC (p<0,05). PainDETECT data have moderate to significant correlations with EuroQol-5D questionnaire (p<0,01). Verbal descriptors as pins and needles, tingling, numbness and allodynia, pain from light touch which are revealed by 3 screening scales can significantly contribute to the likely neuropathic component in patients with knee osteoarthritis (p<0,05). Burning pain (p<0,01), pins and needles (p<0,05) can be associated with a more severe pain in patients with knee osteoarthritis.
**Conclusions:** Thus, in patients with osteoarthritis the pain syndrome may reveal NP features. Identification of these would promote a targeted treatment strategy.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1705

## AB0766 BAKERS' CYST AND TIBIOFEMORAL ABNORMALITIES ARE MORE DISTINCTIVE MRI FEATURES OF SYMPTOMATIC OSTEOARTHRITIS THAN PATELLOFEMORAL ABNORMALITIES

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**Background:** In knee osteoarthritis (OA) structural abnormalities can be present in all joint tissues and compartments. These abnormalities are not OA specific and co-occur in different joint locations. Which structural abnormalities can identify symptomatic OA is unclear.
**Objectives:** We investigated magnetic resonance (MR) abnormalities in the knee that can discriminate best between individuals with and without symptomatic OA.
**Methods:** The Netherlands Epidemiology of Obesity (NEO) study is a population-based cohort including 6671 individuals aged 45–65 years, of which 1284 participated in a MR imaging sub-study. Structural abnormalities (osteophytes, cartilage loss, bone marrow lesions (BMLs), subchondral cysts, meniscal abnormalities, effusion, Baker's cyst) at 9 patellofemoral and tibiofemoral locations were scored using the knee OA scoring system. Symptomatic OA in the imaged knee was defined following the ACR criteria.
The relation between structural abnormalities on different locations within the joint was visualized by network graphs, constructed using R, by estimating a sparse inverse covariance matrix using a lasso penalty, based on the pooled variance-covariance matrix across the entire study population. Logistic ridge regression analyses using a double cross-validatory approach were used to investigate which MR abnormalities discriminate best between individuals with and without symptomatic OA, taking co-occurrence of all abnormalities into account. Higher

regression coefficients reflect better discrimination between presence or absence of symptomatic OA. Analyses were performed crude and adjusted for age, sex and BMI.
**Results:** In the sub-study (55% women, median age 56 years (IQR 50–61), BMI 30.0 kg/m$^2$ (27.9–33.0)) 177 participants had symptomatic knee OA.
All MR abnormalities except for subchondral cysts were highly frequent both in individuals with and without OA. The network graphs showed relations between osteophytes within all compartments of the knee and between cartilage defects on different locations. Within the same compartment, osteophytes and cartilage defects were related.
Baker's cysts showed the highest regression coefficient (0.293) for presence of symptomatic OA, followed by osteophytes and BMLs in the medial tibiofemoral compartment (0.185–0.279), osteophytes in the medial trochlear facet (0.262), and effusion (0.197). After adjustment for age, sex and BMI, the same abnormalities identified OA best. The area under the curve of the logistic ridge regression model including all assessed abnormalities was approximately 0.7. The figure illustrates which abnormalities best identify symptomatic OA (A: Baker's cyst, effusion, osteophyte in medial trochlear facet, B: osteophytes in medial femoral condyle and medial tibial plateau, C: BMLs in medial femoral condyle and medial tibial plateau).

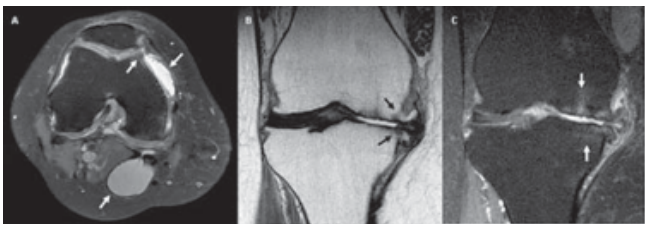


Figure 1

**Conclusions:** Baker's cysts discriminate best between individuals with and without symptomatic knee OA. Especially structural abnormalities as osteophytes and BMLs in the medial side of the tibiofemoral joint and effusion add further in discriminating symptomatic OA. Presence of Baker's cysts may present as a target for treatment.
**Disclosure of Interest:** None declared
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### AB0767 EFFECT OF CHONDROITIN SULFATE ON SOLUBLE BIOMARKERS OF OSTEOARTHRITIS: HOW TO ANALYZE AND INTERPRET THE RESULTS FROM AN OPEN-LABEL TRIAL IN UNILATERAL KNEE OSTEOARTHRITIS PATIENTS

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**Background:** Changes in the level of biomarkers specific of osteoarthritis (OA) could help not only for the diagnosis but also for the monitoring of the disease progression and efficacy of a therapeutic intervention.
**Objectives:** The aim of this study was to investigate the effects of chondroitin sulfate (CS) on the serum levels of biomarkers in patients with knee OA.
**Methods:** Seventy two patients with unilateral symptomatic knee OA were involved in a post-authorization open-label study. Patients treated with CS (800 mg/day) were evaluated 5 times from D-30 to 6-month. The primary outcome was the % relative change in serum biomarkers (Coll2–1, Coll2–1NO2, Fib3–2). Secondary outcomes were the evaluation of pain (VAS) and function (Lequesne's Index). Responders and non-responders were classified according to OMERACT-OARSI recommendations. Finally, an original cut-off method was applied to categorize patients and interpret variations in serum levels of Coll2–1.
**Results:** Patients from either ITT or PP populations showed no difference in the serum biomarkers levels at baseline. Most of the biomarkers levels decreased after 1 month of treatment but no significant differences were reported. However when considering responders and non-responders from the ITT population, a significant difference was found for Coll2–1 at 3 months (p=0.030) and 6 months (p=0.038) (ACA approach). A decrease in pain (VAS) and an improvement in function (LI) were recorded throughout the visits ($p<0.01$). The decrease in pain was significant at 1, 3 and 6 months in ITT and PP populations when compared to baseline. The improvement of function was shown to be significant after 6 months. Finally, an intra-batch cut-off of 22% was determined for Coll2–1 assay based on the variation of Coll2–1 between two blood collections in non-arthritic adult subjects. This value allowed the definition of metabolic responders as patients with variation of Coll2–1 by more than 22%.This means that a variation of 22% or less in the serum level of Coll2–1 consisted in a variation related to homeostasis. In contrast, a variation over this limit revealed either an increase or a decrease in cartilage catabolism. Considering these categories, CS decreased Coll2–1 serum levels between baseline and 1-month visit compared to the value of Coll2–1 before treatment (screening visit) which can be interpreted as a drastic reduction of the proportion of patients with an increase of Coll2–1 over 22% (reduction from 13% to 3). It also consisted in a more important proportion of patients with a decrease in Coll2–1.
**Conclusions:** CS was effective modulating the metabolic status of KOA patients trough the reduction of Coll2–1 levels in responders and the disease's symptoms. Biomarkers are important tools for the monitoring of OA disease and of treatment. The main goal in biomarker research is to qualify them as surrogate endpoints in clinical trials. This study proposes a new approach for the analysis and the interpretation of the variation in biomarker levels and introduces the notion of metabolic responders.
**Disclosure of Interest:** None declared
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## Osteoporosis

### AB0768 PREVALENCE OF LOW BONE MASS IN PATIENT WITH EARLY INFLAMMATORY ARTHRITIS PRESENTING TO EARLY ARTHRITIS CLINIC

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**Background:** Low Bone Mineral Density (BMD) was described in patients with inflammatory arthritis. The data on its occurrence at preliminary phase of arthritis onset is insufficient. This study looks into the prevalence of low BMD in patients with early inflammatory arthritis (EIA).
**Methods:** We reviewed the medical records and electronic files of all patients with synovitis who attended rheumatology clinic between 1st December 2012 and 1st June 2015. Cases with features of synovitis less than two years were only included in the study. The following data was captured; demographics, time of symptom's onset, results of Dual-energy X-ray absorptiometry (DEXA) scan, and 25-hydroxyvitamin D level (ng/ml). Data are presented as the median values and interquartile range (IQR). The prevalence was described as a fraction. Mann-Whitney test was used to compare those with low BMD and those with normal BMD.
**Results:** We identified 83 patients with inflammatory arthritis for less than two years only 31 (37.3%) patients underwent DEXA scan. 26 (83.8%) were Emirati's, 27 (87.0%) were females, and median age was 61 (IQR 57 -65 years). 9 (29%) patients had normal BMD (T-score $>$-1.0 S.D), 13 (41.9%) patients had osteopenia (T-score between -1.0 and -2.5 S.D), and 9 (29%) patients had osteoporosis (T-score$<$- 2.5 S.D). Among osteoporotic patients, 4 (12.9%) had osteoporosis at the lumbar spine only, 1 (3.2%) had osteoporosis at neck of the femur, and 4 (12.9%) patients had osteoporosis at both the lumbar spine and neck of the femur. Age was a significant predictor of low BMD in patients with EIA (Z-Score is 2.357, p-value less than 0.02). However, ethnicity, gender, time lag before the initiation of therapy, and vitamin D level did not predict the occurrence of low BMD.
**Conclusions:** Low BMD is a frequent manifestation in patients with EIA, especially in the elder age group. Prospective studies are required to evaluate the long term significance of low BMD in EIA.
**Disclosure of Interest:** None declared
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### AB0769 ASSESSMENT OF SEQUELS OF POLIOMYELITIS IN HIPS BY 3D-DXA

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**Background:** Polio is a devastating infectious disease that causes paralysis and severe muscular atrophy. When any of the legs is affected, a low aBMD at the corresponding hip is a common finding in DXA measurement.
**Objectives:** to study the influence of polio consequences on volumetric bone density and cortical thickness using the 3D-DXA technology.
**Methods:** 22 patients of both sexes suffering post-polio syndromes (mean age 57±uffering pos were scanned using a GE iDXA system and both proximal femurs were reconstructed using the 3D-DXA technology. 3D-DXA is based on the registration of a 3D statistical model of the femoral shape and density onto the 2D DXA image and provides measurements of volumetric BMD (vBMD) and BMCof the trabecular and cortical bone as well as a quantification of the cortical thickness. The measurements at the leg affected by polio were compared by t-test with those at the non-affected leg.
**Results:** Trabecular BMC was 22% lower (-1.8 g, $p<0.01$) and cortical BMC 19% lower (-2.9 g, $p<0.01$) at the polio leg (total hip region). Similar findings were observed for the vBMD: 18% decrease (-0.020 g/cm$^3$, $p<0.01$) at the trabecular region and a 2.3% decrease for the cortical bone (-0.024 g/cm$^3$, $p<0.01$). The proximal femur volume was also inferior (-12%, -9 cm$^3$, $p<0.01$). The cortical thickness was thinner at the polio leg (-12%, -0.2 mm, $p<0.01$).
**Conclusions:** A long period of decreased of mechanical charges, low muscle strength, postural imbalance has dramatic consequences on bone development. The analyses performed using the 3D-DXA technology indicates an overall

impairment of cortical and trabecular BMD and a significant decrease of the cortical thickness.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5914

## AB0770 SERUM CALCIDIOL, DUAL-ENERGY X-RAY ABSORPTIOMETRY AND LUNG RESPIRATORY TESTS IN PATIENTS WITH INTERSTITIAL LUNG DISEASES

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**Background:** Vitamin D plays an essential paper in the regulation of the bone metabolism. Its role in the modulation of the autoimmune system is better known every day as well as its involvement in the pathogenesis of the autoimmune diseases. Some studies have shown a possible implication of the vitamin D in the development of lung diseases, as the interstitial lung diseases (ILD) through the inhibition of the fibroblasts' profibrotic phenotype. Likewise, it's been described a possible association between serum calcidiol levels and a decreased pulmonary function.
**Objectives:** Analyze the prevalence of vitamin D insufficiency. Evaluate a possible relationship between calcidiol levels and lung respiratory tests. Asses the prevalence of low bone mineral density (BMD) and its correlation with risk factors.
**Methods:** Retrospective study of a cohort of patients with ILD referred from the pulmonary consultation. We analyzed demographic and analytics aspects, dual-energy x-ray absorptiometry (DXA), spinal column radiographies, and lung respiratory tests. The statistical study was performed with SPSS.
**Results:** 44 patients were recruited, 68% women with median age 66 years. 45.5% presented an idiopathic ILD (Usual Interstitial Pneumonia (UIP), Nonspecific IP and Cryptogenic Organizing Pneumonia) and 40.1% sarcoidosis. The 20% left was composed by patients with ANCA-Vasculitis (2), Extrinsic Allergic Alveolitis (6) and ILD related to connective tissue diseases (3 Rheumatoid Arthritis). 79.5% had received corticosteroids with a median dose of 5 grams.
The prevalence of vitamin D insufficiency (<30ng/dl) was 81.3%, 42.9% presented calcidiol levels under 20 ng/dl and 6.80% <10ng/dl. The creatinine clearance rate, age and ESR were correlated with calcidiol levels. Upon the studied factors, we found no statistically association between vitamin D levels and lung respiratory tests and neither with the DLCO. By contrast, we did find an indirect association between FVC and trochanteric BMD which was removed by adjustment for sex, age and smoking status.
About the bone density measures, 33.3% presented a normal BMD, 47.6% osteopenia and 19% osteoporosis. BMD was related to the renal function in total hip, wards triangle, trochanter and intertrochanteric region. We established an inverse association between BMD and ESR too. In the subgroup analysis, we found a younger population in the sarcoidosis group with a greater BMD in total hip, trochanter and intertrochanteric region as well as a smaller FRAX index. There were no statistically significant differences in the prevalence of osteoporosis or osteopenia and the subtype of pneumopathy, middle levels of calcidiol and the other bone metabolism parameters.
**Conclusions:** In our patients with ILD, we found a high prevalence of vitamin D insufficiency. Nonetheless, there was no association between calcidiol levels and a worse obstructive pattern as it has been described in other chronic lung diseases. It is especially interesting the indirect correlation established between BMD and ESR, concluding the own disease activity can play a determinant role in the regulation of the bone metabolism.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6038

## AB0771 OSTEOPOROSIS AS A PROGNOSTIC FACTOR FOR SURGERY TREATMENT FAILURE IN HIP FRACTURE PATIENTS TREATED WITH INTERNAL SCREW FIXATION

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**Background:** Arthroplasty has become the method of choice for the treatment of displaced femoral neck fractures. This because the previous treatment standard using internal fixation had an unacceptable failure rate ranging from 33–45%. One explanation may have been the presence of osteoporosis which is highly prevalent in elderly patients with hip fracture. Less is known about how osteoporosis influences bone healing and the risk of treatment failure in hip fracture patients treated internal screw fixation.
**Objectives:** The aim of this study was to investigate whether osteoporosis may predict failure of displaced femoral neck fractures treated with internal fixation.
**Methods:** Individuals over 60 years of age with a displaced fracture of the femoral neck (Garden 3 and 4) in 2004 and 2005 were retrospectively identified at the Department of Orthopedics, Hospital of Southern Norway Trust in Kristiansand. All patients were operated with two cannulated screws. All patients assessed in the present study had participated in a cross sectional study on hip fracture in southern Norway in 2004 and 2005 (1). The bone mineral density of the non-fractured femoral neck as well as the bone mineral density of the lumbar spine was measured within three days post-operatively by dual-energy x-ray absorptiometry (DEXA). Osteoporosis was defined according to the WHO definition (T-score <-2.5 SD at hip and/or lumbar spine). Potential predictors of hip fracture mortality were tested using univariate and multivariate logistic regression analysis.
**Results:** 145 patients were identified (100 females, 45 males) with a mean age of 80.9 years (females 80.5 years, males 81.6 years). 63 patients (43.4%) suffered of internal fixation failure, 51 (81.0%) of them had osteoporosis. The univariate and multivariate logistic regression analysis including gender, osteoporosis and age groups and the dependent variable of the study (internal fixation failure) are presented in the table 1.

| | Univariate model | | Multivariate model | |
|---|---|---|---|---|
| | OR (95% CI) | P values | OR (95% CI) | P values |
| Gender (ref. male) | 2.46 (1.16–5.23) | 0.02 | 2.27 (1.04–4.92) | 0.04 |
| Osteoporosis (ref no) | 3.01 (1.40–6,48) | <0.01 | 2.79 (1.26–6.15) | 0.01 |
| Age group (ref ≤80 years) | 1.35 (0.68–2.67) | 0.40 | 1.09 (0.52–2.24) | 0.82 |

OR: odds ratio, CI: confidence interval, ref.: reference.

**Conclusions:** Osteoporosis appears to be strongly associated with increased risk of treatment failure in hip fracture patients treated with internal screw fixation. In adjusted analysis, only gender and osteoporosis but not age was associated with treatment failure. Thus, patients suffering of osteoporosis should not be offered internal fixation after a hip fracture. Our results should be confirmed in a large scale prospective study.
**References:**
[1] Diamantopoulos AP, Rohde G, Johnsrud I, Skoie IM, Johnsen V, Hochberg M, et al. Incidence rates of fragility hip fracture in middle-aged and elderly men and women in southern Norway. Age and ageing. 2012;41(1):86–92.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4444

## AB0772 PREVELANCE OF OSTEOPOROSIS IN ADULT HOMOCYSTINURIA PATIENTS

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**Background:** Homocystinuria is an inborn error of metabolism associated with elevated plasma and urine homocysteine levels. Osteoporosis is a recognised feature of the disease and is thought to be related to defective collagen cross-linkage. Limited data exists, however, concerning levels of bone health in unselected patients with homocystinuria.
**Objectives:** The aim of this analysis was to determine the prevalence of osteoporosis in a cohort of adult homocystinuria patients.
**Methods:** 46 adult homocystinuria patients, mean age 36.9 years, (Standard deviation [SD]=12.9) attending a specialist metabolic medicine clinic at Salford Royal Hospital NHS Trust (Salford, United Kingdom) were identified and retrospective analysis of their medical records performed. Information obtained included data on previous medications, and bone mineral density (BMD) scans which had been performed using Dual energy x-ray absorptiometry (DEXA). Also, when available information about plasma homocysteine levels was obtained.
**Results:** 78% of patients (n=36) had had at least one DEXA scan. The mean lumbar spine BMD Z-score was -0.51 (SD=1.20) and for the total hip site, mean Z-score was -0.36 (SD=1.40). Mean level of plasma homocysteine was 96.6 μmol/Litre (normal range: <16μmol/Litre), (SD=69.7). Using the International Society of Clinical Densitometry (ISCD) criteria (Z-score < -2.0), five (10.9%) patients had evidence of osteoporosis; while using the World Health Organisation (WHO) criteria (T-score < -2.5), only three (6.5%) patients had evidence of osteoporosis. There was no association between either total hip or lumbar spine BMD Z-score and levels of plasma homocysteine.
**Conclusions:** In this cohort of patients with homocystinuria attending hospital clinics, the prevalence of osteoporosis was relatively low.
**References:**
[1] Ortop Traumatol Rehabil. 2007 Jul-Aug; 9(4): 337–56.
[2] J Clin Densitom. 2014; 17: 219–224.
**Acknowledgement:** Ms.Azita Rajai, Statistician, Manchester Biomedical Centre, Central Manchester NHS Foundation Trust, Manchester, United Kingdom
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2989

## AB0773 THE TREATMENT WITH DENOSUMAB PLUS BIOLOGIC DMARDS IN PATIENTS WITH RHEUMATIC CHRONIC DISEASES SHOWED EFFICACY AND SAFETY. A CASE SERIES

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**Background:** The T2T strategy of treatment in severe inflammatory rheumatic diseases includes the use of biologic DMARDs (bDMARDs). However, the combination of two or more bDMARDs is not recommended due to toxicity, mainly infections. These patients had high risk of osteoporosis (OP) and its treatment is at least as important as the rheumatic disease. For this, the use of the combination of denosumab (DNS) plus bDMARD is increasing.
**Objectives:** To know the prevalence of patients in treatment with DNS + bDMARD. To describe the inflammatory rheumatic disease and the OP. To know the frequency of severe adverse events of the combination.
**Methods:** Design: An observational, retrospective, case series in common clinical practice.
Methods: Nine rheumatologists were trained about design, protocol and data management. They reviewed all the clinical charts of patients with bDMARDs and identified those with at least one prescription of DNS. Of each case 53 variables were filled in a database, and the database was re-reviewed in order to verify the data. The statistical analysis was done with descriptive statistic. The incidence density rate for adverse events was calculated.
**Results:** 1,540 clinical charts were reviewed (569 of the HUVM and 971 of the HUVR), 38 cases of patients with DNS+bDMARD were found. The prevalence was 2.46%. They were female (36, 95%), with RA (28, 74%), SLE (2, 5%), and APs (2, 5%) and others. The mean (p25-p75) age at the rheumatic disease diagnostic was 49 (35–62) years old; the mean age at the OP diagnostic was 61 (54 - 68). The bDMARD were ETN (16, 42%), RTX (9, 24%), ADA (4, 10%), INF (3, 8%), ABA (3, 8%), TCZ (2, 5%) y GOLI (1, 3%) and the duration of the bDMARD treatment was of 60 (25–120) months. In addition, the most common synthetic DMARD used was MTX in 15 (40%) cases, and the dose was 15 mg/week (7.5 – 20). In 26 (67%) cases corticosteroids were used and the dose was 5 mg/day (5–10). Most of them had a mixed OP (glucocorticoid related and postmenopausal), n=26, 72% and in 5 cases the OP was postmenopausal. Fragility fractures (FF) previous to DNS were found in 9 cases (23%). The FF were peripheral (5, 13%); 2 (5%) vertebral FF and 2 (5%) with both of them. The patients received a mean of 3 (2–6) doses of DNS, with a duration of DNS treatment of 14.7 (6 – 37.9) months. The baseline FRAX score calculated without BMD for major osteoporotic FF was 13 (5.6 – 31) and for hip FF was 3.8 (0.7 – 16). The BMD showed T-score of femoral neck of -2.5 (-1.3 - -3.1) and total lumbar of -2.4 (-1 - -3.5). There were three cases of incident FF (5.07 FF x 100 patient/year). The adverse events were three urinary tract infections, and one of soft tissue. The infections were mild and treated with PO antibiotics. The rate was 6,75x 100 patients/year. There were not severe infections, admissions to the emergency room, neither deaths.
**Conclusions:** The frequency of the combination of DNS + bDMARD is low. This combination is used in patients with inflammatory rheumatic disease of a major length, damage and long treatment with steroids. The efficacy of DNS was the expected with no increased in toxicity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4982

## AB0774 THE EFFECT OF 1 YEAR ORAL IBANDRONATE ON BONE MINERAL DENSITY AND HR QOL – AN OUTPATIENT STUDY IN A SPECIALITY CLINIC IN ALBANIA

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**Background:** Biphosphonate use is expected to increase Bone Mineral Density (BMD) and reduce the risk of vertebral and non-vertebral fractures. This may also lead to an improvement of Health Related Quality of Life (HR QoL) in the treated patients.
**Objectives:** To confirm the efficacy and safety of 1 year oral Ibandronate, 150 mg monthly. To analyze its effect on patients' quality of life.
**Methods:** 140 postmenopausal patients (average age 65.2 yrs, avg age of menopause 46.8 yrs, avg years from menopause 18.3yrs) diagnosed with osteoporosis (T-score $<$2.5 SD) during 2014 – 2015, were given 150mg of oral Ibandronic Acid monthly and supplements of Calcium and Vitamin D daily. BMD was measured with DXA HOLOGIC at baseline and after 1 year of treatment. HR QoL was assessed through EQ – VAS at baseline and after 1 year.
**Results:** 132 patients completed the study. 5 patients (3.5%) withdrew from the study because of G-I complications, 3 patients (2.1%) did not repeat the DXA. A statistically significant increase of BMD was noted in the lumbar spine, (4.7%, $p<0.001$) and in the hip region (2.9%, $p<0.001$). Patients' perceived health also improved on a Visual Analogue Scale. Median 74 IR 60: 89 compared to median 70 IR 51:86 at the beginning of the study.
**Conclusions:** Oral Ibandronate is safe and effective in increasing BMD in both Hip and lumbar spine. Apart from reducing the risk of fractures, it helps to improve the patients' perceived Health Related Quality of Life.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4856

## AB0775 EFFECTIVENESS OF THE USE OF TRANSDERMAL BUPRENORPHINE THERAPY IN AXIAL PAIN RELATED TO NON-ACUTE VERTEBRAL FRACTURE IN COMPARISON TO OTHER PHARMACOLOGICAL MANAGEMENTS: A RETROSPECTIVE ROUTINE PRACTICE-BASED STUDY IN TERMS OF REDUCTION OF URGENT RECIDIVISM

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**Background:** Previous studies demonstrated that lumbar and dorsal pain episodes are two to three times more frequent in patients of the same age when a documented vertebral fracture is present. Many treatments have been tested in musculoskeletal pain with different results. There are no studies conducted to compare different therapeutic strategies in back pain treatment related to non-acute vertebral fractures in terms of recidivism in an urgency enviroment.
**Objectives:** To compare the effectivenes of buprenorphine transermal therapy with other level of OMS pain control therapies in terms of urgency recidivism.
**Methods:** A retrospective observational study was conducted. Data was retrieved from the database of registries of A&E department of our hospital and the follow up registries of the rheumatologic and musculoskeletal urgencies unit. No identity data was gathered. Registries included had the following criteria: (1) Al least 60 years old, (2) Radiological demonstration of a previous known vertebral fracture/collapse since at least 3 months, and (3) chief complain related to dorsal or back pain. Patients were grouped according to the treatment at discharge: First scale of the WHO pain treatment ladder (Group I), second scale (Group II) and Transdermal buprenorphine (Group III). Main outcome variable was the time until the need of a further urgent assessment (Kaplan-Meier curve).
**Results:** 180 registries were analyzed. Group I, II and III contained 39, 74 and 67 cases. No demographic statistically significant differences were founded between groups. Group I consisted by patients who underwent treatment with metamizol, paracetamol or both (24), NSAID alone or associated with metamizol or paracetamol (15). Group II consisted by patients who underwent treatment with an average dose of 155mg/day of tramadol (range 37.5–300mg/day) and patients treated with codein (2). Group III consisted by patients treated with 35 mcg/72h of transdermal buprenorphine, 50 mcg/72h (2) and 70 mcg/72h (1). 50% of patients of group III had to be assessed after the 50th day since the first urgent visit (ICR 41–60), while same proportion of patients from group I and II consulted at the 28th (ICR 21–53)and 19th (ICR 10–37) day, respectively. Patients from group I drugs increase their re-assessment rate 4.19 fold (CI95% 2.57–6.80; $P<0.001$) while patients from group II have a 1.91 fold re-assessment rate (CI95% 1.22–2.99, $P=0.005$) compared with group III patients. 3/39, 10/74 and 1/67 patient from groups I, II and III, respectively requested a new urgent assessment due to what was finally interpreted as a prescription side effect. Tramadol users (Group II) had a significantly higher proportion of side effects than transdermal buprenorphine by the first month ($P=0.01$). There were no statistically significant differences between proportions of side effects in patients from group I compared to group III ($P=0.14$)
**Conclusions:** Treatment with transdermal buprenorphine in patients with non-acute vertebral fracture seems to reduce the ratio of further need of urgent re-assessments compared to tramadol or first scale drugs of the WHO-pain treatment ladder.
**Disclosure of Interest:** None declared
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## AB0776 IMPROVING ADHERENCE TO OSTEOPOROSIS TREATMENT BY PROMOTING PATIENT INVOLVEMENT IN PHYSICIAN/PHARMACISTS COOPERATION

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**Background:** The management of osteoporosis requires multi-years drug treatment and lifestyle changes: maintenance of adapted physical activity, adequate dietary calcium intake, maintaining balance on the ground. It is admitted that adherence to medication does not exceed 50% at one year
**Objectives:** To improve patients follow-up, we have created cooperation between their family doctor and the City pharmacist initiated by the patient himself.
**Methods:** We proposed participation to therapeutic session education to each osteoporotic patient at the end of which we give him a logbook that contains 6 doctor questionnaires and 6 pharmacist questionnaires. The patient remains the owner of the diary, he transmit it to his doctors and his pharmacist twice a year over 3 years. The doctor questionnaire covers the changes in lifestyle; the pharmacist questionnaire covers the medication. Once a year, doctors and pharmacists meet to develop the protocol and addressing diagnostic and therapeutic innovations. The inclusions began in January 2013. We have been able to study the results of the questionnaires one (2014) and two (2015). A nurse and a secretaress call many time ech patient to remain them the project. We conducted a semi led interview with 10 doctors and 10 pharmacists to detect the brakes and levers of successful interprofessional cooperation.
**Results:** Cooperation physicians/pharmacists: the patient initiates cooperation

doctors/pharmacists by providing logbook at regular intervals to both health professionals. Patients play a role in the initiation and continuation of their collaboration. We undertook an exploration work with the anthropological laboratory to investigate the change in the perception of its role by the patient over program. We included 48 patients in 2013. 36/48 continue their treatment at 2 years. Only 1 patient has stopped his treatment without medical reason.
4 patients discontinued treatment for dental care side, 2 for intolerance to any treatment. 9 continue their treatment althougt their physician or pharmacist don't full the questionnaire. 5 don't give any news about them.
The analysis of 73 questionnaires received at one year and 32 questionnaires received at 2 years shows sufficient dietary calcium intake at 2 years to 81% against 84% at one year and a satisfactory for ground balance 75% against 90% at one year. All patients knew at one year the name of their treatment and 96% meet the conditions of the drug taken. 69% do not forget their treatment at two years against 86% at one year thank pharmacist intervention. Only 6% wanted to stop the treatment at 2 years because of side effects, of excessive stresses, lack of noticeable effect, against 17% at 1 year, but they have not stopped after consulting the doctor and/or pharmacist. 25% improved their level of physical activity at 2 years against 14% at one year, 69% were held against 76% at one year.
**Conclusions:** 75% patients continue their treatment at 2 years: the cooperation between doctor and pharmacist induced by the patient has a positive effect on adherence.
**Disclosure of Interest:** None declared
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## AB0777 BONE METABOLISM AND OSTEOPOROSIS RISK FACTORS ANALYSIS IN SPINAL CORD INJURY PATIENTS

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**Background:** It is noticed that spinal cord injury (SPI) is a difficult process associated to patient immobilization which leads to bone mass decrease, osteoporosis risk and high risk of bone fracture. In these patients a low bone mass and bone resorption is observed, even in the six months after SPI, and this situation stabilizes over the next 22–26 months after injury. Moreover there is an increased bone fracture risk due to the high risk of osteoporosis.
**Objectives:** To assess bone metabolism and bone fracture incidence in SPI patients.
**Methods:** Prospective study of SPI patients from the Spinal Cord Injury Unit of La Fe Hospital. In all cases lower backs and hips densitometry, spinal cord plain x-ray image, bone metabolism biomarkers and clinical evaluation have been performed. Statistical techniques was carried out using R software 3.2.3.
**Results:** We studied 37 patients with SCI, 46% of them women, with a mean age at SPI of 54.38±24.77 years. The 58.9% of patients showed thoracic injuries, 48.6% paraparesis and 46.7% presented level C in Asia scale. Results from biochemical markers of bone turnover and densitometry are showed in the table.

| | Mean (SD) | | Mean (SD) |
|---|---|---|---|
| Calcium | 9.06 (0.48) | Body-mass index (BMI) | 27.22 (4.2) |
| Phosphorus | 3.84 (0.62) | Lumbar spine DXA (g/cm$^2$) | 2.04 (0.29) |
| Alkaline phosphatase | 202.89 (68.34) | Lumbar spine t-score | –0.39 (2.72) |
| 25-OHVitamin-D | 26.6 (20) | Femoral neck DXA (g/cm$^2$) | 0.82 (0.26) |
| PTH | 34.93 (22.52) | Femoral neck t-score | –0.79 (2.33) |
| P1NP | 70.5 (74.75) | Hip bone DXA (g/cm$^2$) | 0.88 (0.29) |
| bCTX | 0.89 (0.42) | Hip bone t-score | –0.82 (2.33) |

We observed a statistically association between decreased vitamin D values and increased values of bCTX (P=0.002) and PTH (P=0.03). In addition, altered PTH and vit D values are associated with thoracic location of the SCI (P=0.03), total loss of mobility (P=0.02) and high levels in Asia Scale (P=0.004). Also, classic osteoporosis risk factors were evaluated, and they were significantly and inversely related to alcohol consumption (P=0,022), frequent falls in the last year (P=0.02), long-term use of anticoagulants (P=0.006), and altered values of PTH and vitamin D.
**Conclusions:** A high proportion of our SCI patients showed serum vitamin D deficit, associated to high levels of bCTX and PTH. Moreover, patients with the lowest vitamin D levels were more likely to have higher limitation of movement and higher Asia Scale levels.
**Disclosure of Interest:** None declared
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## AB0778 TRABECULAR BONE SCORE IS SEVERELY AFFECTED IN MALE PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**Background:** Patients with chronic obstructive pulmonary disease (COPD) have a high risk of osteoporosis and fractures. We reported 27% of vertebral fractures in COPD male patients with normal bone mineral density (BMD)[1]. TBS has been described as an index of bone microarquitecture, and could be a new assessment tool to detect bone quality impairment.
**Objectives:** Analysis of TBS in a sub-cohort of male patients with COPD and its possible association with BMD,corticoid use, COPD severity or vertebral fractures.
**Methods:** Male patients, older than 50 years, with COPD were included.Exclusion criteria: Other concomitant pulmonary disease, rheumatologic and/or vertebral disease that may lead to missinterpretation of BMD by DXA.
Exclusion criteria: Other concomitant pulmonary disease,rheumatologic and/or vertebral disease that may lead to missinterpretation of BMD by DXA. BMD wasdetermined by dual-energy X-ray absorptiometry (DXA) at lumbar spine and proximal femur. Vertebralfractures were assessed by thoracic and lumbar X-ray. Corticosteroid use in the previous five years andnumber of hospitalizations were recorded in all patients.
**Results:** We included 98 patients. Mean age 67.8±7.5 years. 38% patients had a mild pulmonar disease, 39% moderate and 23% had a severe disease ((FEV1/FVC<30%). 29 patients (30%) had morphometric vertebral fractures. Mean BMD T-score at lumbar spine -1.67±1.55, at femoral neck -1.81±1.04, and al total hip -1.31±1.14. Mean TBS was 1.035±0,135 (T-score -2.85±1.18). TBS was lower in fractured patients (T -2.59±1.16 vs -2.34±1.22; p=NS). According to COPD severity TBS was lower in patients with modereate disease (T-2.57±1.34) and severe disease (T -2.54±1.34) than in patients with mild disease (T -2.19±1.32), although without reaching significant differences. We didn't find any significant assotiation between TBS and corticosteroid use.
98 patients were included. Mean age 67.8±7.5 years. 41% of patients had mild lung disease and 22% had severe disease (FEV1/FVC <30%). 58% of patients had received corticosteroid therapy in the past 5 years. 29 patients (30%) presented morphometric vertebral fractures. BMD values were: lumbar spine T-score -1.67±1.55, femoral neck T-score -1.81± 1.04, total hip T-score -1.31±1.14. 91% of patients had a degraded or very degraded microarchitecture according to TBS, with a mean value of 1.035±0.135 (T-score -2.85±1.18). Microarchitecture (TBS) was more deteriorated in fractured patients (2.59±1.16 vs T - 2.34 ±1.22; p = NS). TBS was lower in patients with moderate pulmonary disease (2.57±1.34 T) and severe disease (T -2.54±1.34) than in patients with mild disease (T -2.19±1.32, p<0.05). Both, use of corticosteroids and high cumulative dose were associated with lower TBS (p=0.002 and p=0.015 respectively).
**Conclusions:** TBS is severely impaired in male patients with chronic obstructive pulmonary disease, especially in patients with moderate and severe pulmonary disease and those who have received corticosteroids. Although patients with vertebral fractures have a lower value of TBS, this technique does not detect many cases with fracture.
**References:**
[1] Casado E, et al. JBMR 2007; 22 (S1): S202
**Disclosure of Interest:** None declared
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## AB0779 MULTIDISCIPLINARY OUT-PATIENT CLINIC (REUMATOLOGY-ENDOCRINOLOGY) FOR PATIENTS WITH COMPLEX METABOLIC BONE DISEASE: 2 YEARS EXPERIENCE

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**Background:** Osteoporosis (OP) is a highly prevalent metabolic bone disease and may be secondary to endocrine diseases. In these cases the assessment of a rheumatologist and an endocrinologist may be complementary and beneficial for both the patient and the hospital.
**Objectives:** To describe the experience of two years of a multidisciplinary out-patient consultation Rheumatology-Endocrinology in the care of patients with metabolic bone diseases.
**Methods:** A multidisciplinary outpatient clinic Rheumatology-Endocrinology was set in December 2013 to assess patients coming from one or another specialty with some metabolic bone disease that could benefit from both a rheumatologist and an endocrinologist. The consultation takes place between 12–14h, on a monthly basis. Demographic characteristics, department of origin, diagnosis, complementary tests, and implemented changes in both the diagnosis and treatment were recorded. Data collected during the years 2014 and 2015 are presented.
**Results:** In these 2 years there have been 20 consultation sessions (10 per year), with a total of 103 visits. 54 patients (43 women and 11 men) were treated as first visit. Age 57±15 years (range 29–88). There have been 27 successive visits (ratio first/successive 2/1) and in 22 cases the patients did not attend the appointment. 63% of patients (34) came from Endocrinology and 31% (17) from Rheumatology.

Three patients came from other services (Internal Medicine, Primary Care and Physical Therapy).
Pathologies in order of frequency derived from Endocrinology were OP in the context of primary hyperparathyroidism (29%), hypogonadism (26%), bariatric surgery (15%) and glucocorticoid induced OP (6%). In 6 patients the inquiry was not related to bone metabolism and the diagnoses were: gout, psoriatic arthritis, osteoarthritis, fibromyalgia, among others. The pathologies most frequently derived from Rheumatology were primary hyperparathyroidism (41%), hypogonadism (18%) and adrenal insufficiency in patients with chronic corticosteroid therapy (12%). In 62% of patients referred from Endocrinology and in 65% of patients from Rheumatology underwent some change, either diagnosis or treatment.
**Conclusions:** A multidisciplinary consultation Rheumatology-Endocrinology improves communication between the two specialties and facilitates the standardization of diagnostic and therapeutic criteria. It also represents a convenience for the patient and savings for the hospital, as the number of visits and complementary tests are reduced.
**Disclosure of Interest:** None declared
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## AB0780 THE INFLUENCE OF DXA INACCURACIES ON THE EVALUATION OF A NEW ULTRASOUND METHOD FOR PROXIMAL FEMUR DENSITOMETRY

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**Background:** According to the operational definition provided by the World Health Organization, osteoporosis is diagnosed when bone mineral density (BMD) measured at lumbar spine or proximal femur is at least 2.5 standard deviations lower than the young adult mean. Currently, dual X-ray absorptiometry (DXA) is the most widely adopted method for osteoporosis diagnosis, since it is considered the gold standard for BMD measurements. Therefore, DXA outcomes are often used as the ground truth reference to assess the diagnostic performance of novel alternative approaches that are undergoing clinical validation. However, very recent literature [1] documented that high percentages of clinical routine DXA investigations are typically affected by specific errors altering the final measurement result. This may also have significant effects on the comparative evaluation of the effectiveness of the innovative diagnostic methods under validation.
**Objectives:** To assess the actual diagnostic performance of the Osteoporosis Score (OS), a recently introduced ultrasound (US) parameter for osteoporosis diagnosis on the femoral neck, through a retrospective analysis of the DXA reports of the enrolled patients.
**Methods:** In a previous study [2], we directly assumed the outcome of DXA investigations as the gold standard reference to assess the OS performance for osteoporosis diagnosis on the femoral neck in a population of 170 patients aged in 55–80 years, obtaining an overall accuracy of 84.7% in patient classification (osteoporotic, osteopenic, or healthy) coupled with a good correlation between DXA-measured BMD and corresponding OS-derived values ($r$ =0.71, $p<0.001$). In the present work, we performed a retrospective check of the 170 DXA reports, excluding all those cases presenting a typical DXA error as identified by recent literature (e.g., incorrect patient positioning, presence of artefacts, improper image segmentation, etc.) [1] and re-assessing the actual diagnostic accuracy of our US approach by considering only those patients having a reliable DXA report.
**Results:** 57 patients out of the initial 170 (33.5%) were excluded because of clear DXA inaccuracies. The overall agreement between DXA and OS-based diagnoses on the remaining 113 patients was 93.8% ($r$ =0.79, $p<0.001$), ranging from a minimum of 85.7% ($r$ =0.79, $p<0.001$) to a maximum of 95.6% ($r$ =0.82, $p<0.001$) when single 5-year age intervals were considered. Therefore, undetected DXA errors had resulted in a significant underestimation of OS accuracy in our previous study.
**Conclusions:** The actual potential of the OS-based approach for osteoporosis diagnosis on the femoral neck was previously underestimated. The adopted method for retrospective analysis of DXA reports could be also used to re-assess the performance of different US methods that assumed routine DXA investigations as the gold standard reference.
**References:**
[1] Messina et al, Eur Radiol 2015;25:1504–11.
[2] Muratore et al, Osteoporos Int 2015;26(Suppl 1):P530.
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## AB0781 EFFECTS OF TERIPARATIDE FOR BONE LOSS AND PAIN-RELATED BEHAVIOR IN THE HIND LIMB-UNLOADED MOUSE MODEL OF DISUSE OSTEOPOROSIS

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**Background:** Factors of chronic pain due to hemiplegia or prolonged immobility are varied, there is osteoporosis (a rarefaction due to bone atrophy) as the cause. Osteoporotic patients with no evidence of fractures sometimes experience vague lower back pain. However, there have been few reports regarding the correlation between osteoporosis and pain-related behavior. Our previous studies have indicated that hindlimb-unloading induced bone loss and mechanical hyperalgesia in hindlimb of mice. We investigated the effects of teriparatide (PTH) on bone mass and pain-related behaviors in osteoporosis model mice with hindlimb unloading.
**Objectives:** The objective of the current study was to investigate the effect of PTH on bone mass and pain-related behaviors in hindlimb-unloaded mice model of disuse osteoporosis.
**Methods:** Male ddY mice (8 weeks old) were tail-suspended for 2 weeks and assigned to 3 groups; hindlimb-loaded mice treated with vehicle (control), hindlimb-unloaded mice treated with vehicle (HU), hindlimb-unloaded mice treated with PTH (HU-PTH)
(n=8/group). Starting immediately after tail-suspension, vehicle or 40μg/kg PTH was injected subcutaneously twice a week for 2 weeks. The bilateral distal femoral metaphyses and proximal tibial metaphyses were analyzed three-dimensionally by micro-computed tomography (μCT) 2 weeks after tail-suspension. Mechanical sensitivity was also tested using von Frey filaments 2 week after the tail suspension. The withdrawal threshold, the 50% withdrawal threshold and the frequency of the withdrawal response to the application of von Frey filaments to the plantar surface of the hind paws was examined. Measurement of pain-related behavior with von Frey filaments was interpreted as indicative of mechanical allodynia.
**Results:** μCT analysis of the distal femoral metaphysis and the proximal tibial metaphysis showed that significantly decreased bone volume/tissue volume (BV/TV) and trabecular thickness (Tb.Th) in HU compared with HL was significantly increased by PTH treatment. (Fig.1) Similarly, decreased trabecular number (Tb.N) in HU compared with HL was increased, and increased trabecular separation (Tb.Sp) in HU compared with HL was decreased by PTH treatment, but not significant. The paw withdrawal threshold and the 50% paw withdrawal threshold were significantly lower in the HU than in the control, whereas it was significantly higher in the HU-PTH than in the HU group. (Fig.2) The paw withdrawal frequency stimulated by von Frey filaments with strength of 0.4–2.0 g was significantly higher in the HU than in the control. Whereas it was significantly lower in the HU-PTH than in the HU.
**Conclusions:** In this study, treatment of PTH prevented bone loss and mechanical hyperalgesia in disuse osteoporotic animal models by hindlimb-unloading. The results suggest that low bone volume itself is one of the causes of osteoporotic pain.
**Disclosure of Interest:** None declared
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## AB0782 TWO-YEAR STUDY OF BONE METABOLISM IN LIVER TRANSPLANT PATIENTS. INFLUENCE OF ANTIRESORPTIVE TREATMENT AND EVALUATIONS BEFORE SURGERY

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**Background:** Osteoporosis is a frequent complication in patients with chronic liver disease, especially in end-stage and when there is a history or evidence of chronic cholestasis. But even more important is that liver transplant patients, in the first few months after the transplant there may be an accelerated loss of bone mass, which also means greater osteopenia and osteoporosis incidence and fracture risk.
**Objectives:** To study the effect in bone metabolism of antiresorptive treatments in patients undergoing liver transplantation (LT), as well as an evaluation prior to transplant to decrease the risk of osteoporosis.
**Methods:** We collected patients undergoing LT, where data is available at transplant (month 0) and 6–12–18–24 month follow-up after surgery. We collected data of bone metabolism biomarkers, densitometric and antiosteoporotic treatment. Statistical analysis was carried out using R software 3.2.3.
**Results:** We selected 172 patients with LT, and 56 of them had completed the 24 months follow-up. Of the total cohort, 89.7% are men, with a mean age at transplantation of 57.7±6.7 years. The 89% of patients were supplemented with 25-OHVitamin-D after surgery and during follow-up, the 6.4% initiated treatment with bisphosphonates and 2.3% with denosumab.

Improved vitamin D levels and normalization of the values of PTH, beta-CTX and P1NP were observed. The t-score densitometric value for the first 12 months of follow-up dropped slightly, to increase again at 24 months of follow-up. This situation is still more pronounced in lumbar spine (t-score -1.49±1.29 after surgery and -1.29±1.1 at 24 months of follow-up).
Statistical analysis yield a significant influence of antiresorptive treatment ($P<0.0001$) on the normalization densitometric values, as well as on the normalization of vitD (P=0.003), bCTX (P=0.03) and P1NP (P=0.02). In contrast, obesity correlates with altered densitometric (P=0.003). Finally, there is a clear difference in bone metabolism biomarkers between LT patients evaluated and treated before surgery and those evaluated after surgery ($P<0.0001$).
**Conclusions:** In general, there is a normalization of serum vitamin D levels and biomarkers of bone metabolism in two years after surgery. The use of antiresorptive treatment is crucial to reach with stage, as well as to establish an evaluation before surgery and treat the patient if is required.
**Disclosure of Interest:** None declared
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## AB0783 OSTEOPOROTIC FRACTURE AS THE MAIN RISK FACTOR IN THE DETECTION OF OSTEOPOROSIS IN MEN UNDER 70 YEARS

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**Background:** Osteoporosis (OP) in male under 70 years is less common than postmenopausal and senile OP, but causes important social and health costs associated with morbidity and mortality from fractures. It's common in patients with inflammatory rheumatic diseases, enteric and endocrine diseases, also in COPD patients and in those undergoing chronic corticosteroid therapy.
Sometimes clinical risk factors of male OP go unnoticed, so the diagnosis is done when one or more low energy mechanism fractures have already occurred (failure in early detection).
Bone Metabolism Unit at Basurto University Hospital values from years ago male patients referred from different specialties with suspected OP.
**Objectives:** To describe main demographic and clinical characteristics of men aged 70 years or less, visited in our monographic OP consultation, with previous to 2013 protocols established with Primary Care (PC) and rheumatology (derivation according to risk factors).
**Methods:** Retrospective descriptive study based on a review of medical records and database of these patients. We analyze origin of derivation, risk factors, presence of fractures at moment of diagnosis, primary diagnoses and occurrence of refractures.
The analysis was performed using statistical system SPSSv22.
**Results:** 127 patients, mean aged 58.17 years (18–70), up to 74% of the total derived from PC (47), and general rheumatology (47); 10 patients (7.9%) from traumatology; 8 from endocrinology (6.3%); 7 from gastroenterology (5.5%).
55.9% were smokers or former smokers, 22% kept drinking habit. 19.7% had received prednisone doses $\geq$7.5 mg for more than 3 months.
9 patients had family history of fracture (6.3%), and 46 themselves presented with one or more fractures (36.2%): 36 with one or more vertebral fractures, 4 hip fracture and 12 wrist fracture. 64 patients were diagnosed of OP with treatment indication by bone agent.
61% have secondary OP, the main cause (19%) enteric disorders (malabsorption syndromes and inflammatory bowel disease); 13% endocrine disorders and rheumatic inflammatory diseases by 13%. No primary cause was found in 39% of cases.
The presence of fractures was associated with decreased DXA lumbar spine (p=0.027) and DXA hip (p=0.004). A very weak correlation between higher fracture FRAX and number of risk factors was detected, on the other hand a moderate correlation was observed with the number of fractures (Spearman Rho =0.472; $p<0.001$). So does to the hip FRAX (Spearman Rho =0.417; $p<0.001$).
Of the 46 patients with previous fractures, only 12 (26%) had received prior treatment with bone agent. Only 5 patients suffered refracture after starting treatment and during follow-up (94.06 months) (25–129).
**Conclusions:** Almost 1/3 of men were referred for fractures caused by low energy impact, what means a late diagnose of male OP.
It's important to establish protocols with other medical specialties for men at risk to be identified and referred, in order to make an early diagnose.
It highlights the lack of patients derived from pneumologists, although vertebral fractures in chronic respiratory patients worsen their functional status and mean a frequent cause of hospitalization in this group.
**Disclosure of Interest:** None declared
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## AB0784 A STUDY OF SERUM ELECTROLYTE LEVELS AFTER DENOSUMAB ADMINISTRATION

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**Background:** Denosumab is a fully human monoclonal antibody that targets the receptor activator of nuclear factor kappa B ligand (RANKL) and blocks its binding to RANK, preventing osteoclasts from resorbing bone mass and significantly reducing the risk of vertebral, non-vertebral, and proximal femoral fractures. One of the major and critical adverse events of denosumab injection is hypocalcemia, which is most often observed in the one-week period following administration. Examination of albumin-adjusted calcium (Ca) level after one week is recommended to exclude the presence of hypocalcemia. Although hypophosphatemia has been reported to be an adverse event with a frequency of more than 1% in patients subcutaneously administered 120mg of denosumab for tumor treatment, there have been no reported data regarding its frequency in patients administered 60mg for osteoporosis. The purpose of the present study was to evaluate the occurrence of denosumab adverse events, focusing on serum electrolyte levels soon after administration, as well as to confirm its efficacy.
**Objectives:** Thirty-one women between the ages of 55 and 91 years with post-menopausal osteoporosis were enrolled and treated with a 60mg subcutaneous injection of denosumab and an oral calcium tablet combined with native vitamin D and magnesium.
**Methods:** Serum Ca and phosphorus (P) were measured at baseline and at 1,2,3,and 4 weeks after administration. The bone resorption marker intact serum procollagen type 1 N-terminal propeptide (P1NP) and bone formation marker tartrate-resistant acid phosphatase-5b (TRAP-5b) were also evaluated at baseline and 4 weeks after administration. Laboratory investigations after a second injection were performed in three patients in the same manner. Bone mineral density (BMD) was measured at baseline and 6 months after administration.
**Results:** Both serum Ca and P electrolyte levels significantly decreased soon after administration. Hypocalcemia was detected in 2 patients: one patient 1 week after administration, and the other 2 weeks after. Hypophosphatemia was observed in 7 patients: 5 patients 1 week after administration and 2 patients after 2 weeks. Hypocalcemia was observed 1 week after the second administration in 1 of the 3 patients. Patients with hypocalcemia and/or hypophosphatemia tended to have a body mass index (BMI) of less than 22.There were no patients who discontinued the treatment due to adverse events in the present study. All serum electrolyte levels recovered within 4 weeks of each administration. At 4 weeks, P1NP level was decreased by 31.7% and TRAP-5b was decreased by 71.3%. At 6 months, BMD of the lumbar spine was increased by 2.0%, the femur by 1.5%, and the distal radius by 0.6%.
**Conclusions:** Hypocalcemia and hypophosphatemia were observed within 1 or 2 weeks after the first and/or second administration of denosumab. Therefore, measuring serum electrolyte levels of Ca and P within in 1 or 2 weeks is strongly recommended for the detection of hypocalcemia and hypophosphatemia. Adverse events were not observed clinically throughout the duration of the study period. However, denosumab administration to individuals with a BMI less than 22 may carry a risk of hypocalcemia and /or hypophosphatemia. Furthermore, denosumab administration resulted in a low bone remodeling ratio reflected by decreases in both P1NP and TRAP5b levels, and increase in BMD, which may reduce fracture risk.
**Disclosure of Interest:** None declared
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## AB0785 RELATIONSHIP BETWEEN METABOLIC SYNDROME AND ITS COMPONENTS WITH BONE DENSITY IN MENOPAUSE WOMEN

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**Background:** Prevention of osteoporosis and bone fracture and the relationship between metabolic syndrome and bone density are controversial issues.
**Objectives:** The present study aimed to investigate metabolic syndrome and its components and the association with bone mineral density in post menopausal women referring for bone mineral density (BMD) test.
**Methods:** A total of 143 postmenopausal women with at least one year of menopause experience participated in this cross-sectional study. Demographic and anthropometric characteristics for all participants were collected. Biochemical parameters including fasting blood sugar, Cholesterol (HDL and LDL), triglyceride were also measured prior to BMD test. Afterwards, association between the components of metabolic syndrome and bone densitometry were analyzed using statistical methods.
**Results:** In this study, 72% of participants did not have metabolic syndrome. Among them, 43.4% and 28.7% had osteoporosis and normal density, respectively. Of the remaining28% with metabolic syndrome 12.6% had osteoporosis and 15.4% had normal density. Among the metabolic syndrome components, waist circumference, HDL cholesterol, and waist to hip ratio were found to be significantly associated with bone mass ($P<0.05$). Osteoporotic women had lower waist circumference and waist to hip ratio and higher HDL than women without osteoporosis. In contrast, women with metabolic syndrome did not have significant differences with women without metabolic syndrome in terms of lumbar and femoral neck densitometry ($P>0.05$).
**Conclusions:** Results from this study showed that metabolic syndrome and its components did not induce bone mass loss. Due to discrepancies of the studies in this area, it seems that more studies are needed so as to make it possible to take some preventive measures in large scale.

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## AB0786 ARE WE MANAGING MALE OSTEOPOROSIS ADEQUATELY?

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**Background:** Osteoporosis is becoming increasingly recognized as an important public health problem in men, with one in four men over the age of 50 years developing at least one osteoporosis-related fracture in their lifetime.[1]
**Objectives:** The primary aim of our project was to evaluate whether male patients with osteopenia or osteoporosis are being investigated and managed according to the Endocrine Society Guidelines[2] published in June 2012. We also assessed the indications for bone mineral density (BMD) measurements in our cohort.
**Methods:** Patients who had a BMD measurement done at Mater Dei Hospital, Malta, between September and December 2012 were recruited in this study. Information on patient demographics, indication for BMD measurement and other investigations carried out were obtained from the patients' medical notes and iSoft Clinical Manager®.
**Results:** A total of 116 patients had a BMD scan done during the study period. Mean age was 56 years (SD ±15.28). 75.86% (n=88) had at least one documented risk factor for osteoporosis and therefore an indication for BMD measurement. The commonest risk factors were smoking (34.5%), history of long-term corticosteroid use (33.6%) and age above 70 years (18.1%).
49.1% (n=57) had their BMD result recorded in their medical notes. Of these, 24.6% (n=14) were osteoporotic at the hip, and 14.0% (n=8) at the spine. From the cohort of patients with osteoporosis or osteopenia, 40.9% (n=18) had testosterone levels, 27.3% (n=12) had Vitamin D levels, and none had 24-hour urinary calcium levels checked. All patients had a full blood count, calcium, phosphate, renal and liver function tests checked.
77% (n=34) were prescribed calcium supplements and 75% (n=33) also received Vitamin D supplementation. Advice on weight bearing exercise was documented in 22.7% (n=10), whilst advice on smoking cessation was only documented for 12.5% of smoking patients.
Of all cases where bisphosphonate therapy was indicated, 55.6% (n=15) were on treatment. 46.7% (n=7) of patients had a dental assessment prior to starting treatment.
**Conclusions:** Our study has identified that a high proportion of BMD scans are being requested in concordance with guidelines. However, a significant number of patients with osteoporosis remain untreated. This stresses the need of increasing awareness amongst clinicians of current guidelines together with improving our patients' education on lifestyle measures and smoking cessation, in order to avoid potential complications which can result in significant morbidity and also mortality.
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## AB0787 SCALES ELDERLY PATIENT GLOBAL ASSESSMENT APPLIED TO ELDERLY PATIENTS WITH HIP FRACTURE

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**Objectives:** Analyze the potential relationship between the risk of hip fracture and the results of the scales Elderly Patient Global Rating geriatric patients.
**Methods:** Retrospective and descriptive study of a random series of 120 patients over 75 years attending emergencies in the University Hospital of Vigo in the year 2013 with a diagnosis of hip fracture. Data collected from medical records that refer to the functional, mental and social value at the time of the event are analyzed.
**Results:** Of the 120 patients analyzed in the study, 92 were women (76.6%) and 28 males (23.3%) with a mean age of 84.53 years. Considering the Elderly Patient Global Assessment in the functional area, according to the scale of disability of the Red Cross in terms of ambulation is concerned, we classified our patients in 6 degrees: grade 0 (normal walking) on 30.83% of patients; Group 1 (wanders with some difficulty) 27.5%; Grade 2 (roams using cane or similar) 17.5%; Grade 3 (roams helped at least one person) 10.83%; Grade 4 (roams helped with extreme difficulty, two people) 6.67%; and grade 5 (immobilization in bed or chair) 6.67%). Regarding the mental sphere in 75% of our patients any cognitive decline is not evidence. Only 10% of them were institutionalized at the time of the fracture.
**Conclusions:** In this series of 120 elderly patients a direct relationship between hip fracture by low-impact crash, and functional, mental and social situation is evident; being at greatest percentage of fractures, those elderly who have difficulty walking or in need of a single support, without any cognitive impairment and who live in residence.
**Disclosure of Interest:** None declared
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## AB0788 PREDICTORS OF FRACTURES IN EXCESSIVE CONSUMPTION OF ALCOHOL: AN OBSERVATIONAL STUDY

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**Background:** High alcohol intake is a known risk factor for fractures.[1] This association is mediated by a combination of factors including muscle atrophy, unsteadiness and loss of bone mineral density (BMD). Chronic alcohol consumption is common, and predictors of fractures in these patients have not been the object of many studies.
**Objectives:** We used data from a large observational cohort to determine predictors of fractures among chronic heavy drinkers.
**Methods:** A dual X-ray absorptiometry (DEXA) database from a district general hospital in Northwest England was used to identify patients drinking more than the maximum recommended amount of alcohol. Patient demographics, presence of other risk factors and bone mineral density (BMD) at the femoral neck, total proximal femur and L1-L4 lumbar vertebrae were recorded. Univariate logistic regression models predicting fracture risk were fitted using traditional FRAX risk factors for osteoporosis. These include age at scan, female gender, total hip BMD (left and right), femoral neck BMD (left and right), L1-L4 BMD, presence or absence of smoking, rheumatoid arthritis, family history of fracture, steroid exposure and body mass index (BMI). Subsequently a multivariate model was fitted with a cut off value of $p<0.05$ for individual variables.
**Results:** 1794 patients were referred between 2004–2014; of these, 737 (41.1%) had sustained a fracture. Median age at scan was 59.6 years, and 1221 (68.1%) were female. Results of univariate analysis are shown in Table 1.

| Risk factor | Odds ratio | 95% CI |
|---|---|---|
| Age at scan (years) | 1.02 | 1.01, 1.03* |
| Female gender | 1.06 | 0.87, 1.30 |
| Femoral neck BMD (right) | 0.036 | 0.016, 0.079* |
| Femoral neck BMD (left) | 0.046 | 0.022, 0.095* |
| Total hip BMD (right) | 0.036 | 0.017, 0.074* |
| Total hip BMD (left) | 0.035 | 0.017, 0.070* |
| Lumbar spine BMD | 0.094 | 0.054, 0.16* |
| Body mass index (kg/m$^2$) | 0.99 | 0.97, 1.01 |
| Smoker | 1.24 | 1.01, 1.48* |
| Rheumatoid arthritis | 0.71 | 0.40, 1.21 |
| Family history of fracture | 0.85 | 0.65, 1.09 |
| Steroid exposure | 0.58 | 0.46, 0.74 |

In the multivariate model, age at scan, total hip BMD (left), lumbar spine BMD, BMI and steroid exposure were predictors of risk. As in the univariate model, steroid exposure in this cohort appears to reduce the risk of fractures.
**Conclusions:** In the univariate analyses, bone mineral density measured at any site, age and smoking status were predictors. In the multivariate model, the strongest predictors were lumbar spine BMD, BMI and steroid exposure ($p<0.001$), with age and total left hip BMD also significant. In this population, lumbar spine BMD may be a better predictor than hip BMD used in the FRAX risk assessment tool. There may well be an as yet undetermined role of unmeasured confounders, and further research is needed to guide the development of a more accurate risk assessment tool in this population.
Steroid exposure reduces the risk of fractures in both models, which is difficult to explain. Steroid exposure indicates engagement with medical care, which may be less likely amongst the heaviest drinkers, thus creating confounding. Our data does not quantify alcohol consumed, and it is possible that those with significant steroid exposure consume less alcohol overall. Further work is needed to clarify the role of steroid exposure in fracture risk prediction in chronic drinkers.
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**Disclosure of Interest:** None declared
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## AB0789 BMD CHANGE AROUND PROSTHESIS AFTER UNCEMENTED TOTAL HIP ARTHROPLASTY IN RA PATIENTS: 15-YEAR FOLLOW UP

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**Background:** In previous studies we noted that maximum bone loss around total hip prosthesis occurs in first six months after surgery. After six months bone loss becomes slower and in some cases BMD even can increase.
**Objectives:** To study the 15-year follow up changes of BMD in patients with RA.
**Methods:** 282 RA patients were examined at the baseline. At the end of investigation we analyzed 43 patients. DEXA was used for BMD assessment around stem (7 ROIs) and cup (3 ROIs) of prosthesis. First examination was conducted 2 weeks after the operation and repeated at 3, 5, 10 and 15 year after surgery.
**Results:** 3 years after decrease of BMD was -5,8% and -4,9% around stem and cup respectively ($p<0,01$). By 5 and 10 year the bone loss was not significant (-6,1% and -5,5%; -7,1% and -6,3% around stem and cup respectively). 15 years after surgery we observed significant increase of bone loss (-18,9% and -22,7% around stem and cup respectively ($p<0,01$))
**Conclusions:** These data supports our opinion of stress remodeling of bone around hip prosthesis. This phenomenon doesn't stop after 1 year but keep on even 15 years after surgery. This means that all RA patients after THA need to use medication to normalize bone remodeling
**Disclosure of Interest:** None declared
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## AB0790 DESCRIPTIVE STUDY OF ZOLEDRONIC ACID TREATMENT IN A HOSPITAL OF THIRD LEVEL. OUR EXPERIENCE

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**Background:** The zoledronate is a bisphosphonate widely used in the treatment of bone pathologies such as the Paget's disease and the osteoporosis, due to its convenient dosage (annual infusion), its rate of therapeutic compliance and its excellent safety profile.
**Objectives:** Our objective in this study is to describe the clinical and demographic features of the patients treated with zoledronate in our hospital over the past five years, according to the different therapeutic indications.
**Methods:** This is a retrospective observational study that has included 186 patients treated with zoledronate at the University Health Care Complex of Leon since January 1st, 2011 to December 31st, 2015. Two of the main therapeutic indications of the drug have included in the study: osteoporosis and Paget's disease of bone. Clinical and analytical data have been obtained from the information reported in the medical record.
**Results:** 186 patients were included, 76.9% female and 23.1% male, with a mean age at the moment of the first infusion of 73,77±10,451 |43–97|. Forty-six of the treatments were indicated for active Paget's disease of bone (26.3%), 136 for osteoporosis (76.1%) and one for osteogenesis imperfecta.
Among the patients treated for Paget's disease of bone, 51% were male and 49% female, presenting the 48% of them monostotic fibrous dysplasia and the 52% of them polyostotic fibrous dysplasia. The mean Alkaline Phosphatase levels (ALP) at baseline was 444.82±292.85 IU/L, receiving an average dose of infusions of 1.12 with SD 0.389. The ALP levels after the infusion of zoledronate decreased to an average value of 91.98±41.94 IU/L within a year. Two of the patients needed reinfusion 4 years after the first infusion. 2% of them had flu-like symptoms and only one patient had post-infusion pathological fracture as complication.
In the group treated for osteoporosis, 18 patients were men and 118 women. 59.1% of the patients required infusion due to abnormal DXA results with -2.5 SD or less, 31.4% of the patients required it due to previous fractures and 7% due to a concomitant use of high dosage of oral steroids (prednisone>10mg/day). The mean dose of infusion in these patients was 2,63±1,38 with a mean bone mass density at the beginning of the treatment of 0,804±0,116 in the lumbar spine and of 0,73±0,128gr/cm$^2$ in the hip. The mean bone mass density after 2 years of treatment was of 0,831±0,114 in the lumbar spine and of 0,767±0,141 in the hip. 54.8% of all patients included in the study had not received prior treatment with oral bisphosphonates, while the remaining 45.2% did receive it (33.3% for <5 years and 11.8% for>5 years).
7 patients had side effects after infusion: 4 mild adverse reactions and 2 severe reactions. Therefore, these patients required the discontinuation of the treatment due to uncomplicated osteonecrosis of the jaw and due to severe hypocalcaemia. Other causes for suspension of treatment were post-infusion fractures in the 2.2% of the cases and no improvement of bone mass density according to the DXA in the 1.1% of the patients.
**Conclusions:** Zoledronic acid has been shown to improve the levels of ALP in the Paget's disease with a single dose, and in the bone mineral density of both the lumbar spine and the hip, presenting few complications and being a good therapeutic option.
**Disclosure of Interest:** None declared
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## AB0791 A COMPARISON BETWEEN COMBINATION TREATMENT WITH ALENDRONATE AND VITAMIN K AND ALENDRONATE ALONE ON BONE MINERAL DENSITY IN PATIENTS WITH POSTMENOPAUSAL OSTEOPOROSIS? THE RESULTS OF A PILOT STUDY

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**Background:** Osteoporosis is the most common metabolic bone disease. It affects a significant number of postmenopausal women and elderly people. Standard treatment of osteoporosis is the use of oral calcium and vitamin D in combination with one of the following drugs: bisphosphonates, raloxifene, parathyroid hormone, calcitonin, denosumab and strontium ralenate [1]. Numerous studies have investigated the effects of vitamin K in bone health. These studies have shown conflicting results [2]. There isn't any human study about adding of vitamin k to alendronate to treat osteoporosis.
**Objectives:** The purpose of the present study was to compare the vitamin K and alenddronte versus alendronate alon on the bone mineral denity in postmenopausal osteoporosis.
**Methods:** Forty - seven patients were introduced to the study from our Rheumatology Clinics. All patients had postmenopausal osteoporosis ($T\leq$ -2.5). The patients were randomly assigned into two groups: one group (n=23) received calcium pills (500 mg twice daily), vitamin D pills (400 IU daily) and alendronate pills (70 mg weekly). The other group (n=24) received the same combination plus vitamin K1 pills (10 mg daily). The duration of treatment was one year in both groups. At the enrollment and the end of the study, bone mineral density was measure for all patients by the same scanner. Data were analyzed using SPSS software.
**Results:** There was no significant difference in the baseline characteristics between the two groups. In the Vitamin K+ Alendronate group, the mean bone mineral density (BMD) of femoral neck before and after the intervention was 0.56±0.08 mg/cm$^2$, that the difference was not significant (P=0.93). The mean BMD of femoral neck in the alendronate group before and after treatment were 0.61±0.09 mg/cm$^2$ and 0.58±0.09 mg/cm$^2$, that the difference was not significant (P=0.93). There was no significant difference between two groups regarding to the mean change of BMD of femoral neck before and after treatment (P=0.31). In the Vitamin K+ Alendronate group, the mean BMD of lumbar spine before and after the intervention were 0.76±0.11 mg/cm$^2$ and 0.76±0.12 mg/cm$^2$ and there was not significant change. In the alendronate group, the mean BMD of lumbar spine before and after were 0.71±0.06 mg/cm$^2$ and 0.76±0.04 mg/cm$^2$, that the change was significant (P=0.009). There was also no significant difference between two groups regarding to the mean change of BMD of lumbar spine before and after treatment (P=0.24). There was not any osteoporotic fracture in two groups.
**Conclusions:** Adding vitamin K pills (10 mg daily) to Alendronate, calcium and vitamin D regime had no more effect on the increasing of BMD in patients with postmenopausal osteoporosis.
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**Disclosure of Interest:** None declared
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## AB0792 KNOWLEDGE ABOUT OSTEOPOROSIS AND IT'S RISK FACTORS AMONG ELDERLY PARTICIPANTS OF HEALTHY AGING ACADEMY

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**Background:** Osteoporosis and osteoporotic fractures are among the major problems of elderly population. Although deaths related to bone disease usually have indirect causes it is assessed that approximately 20% patients dies due to complications within first year after hip fracture and another 30% need permanent care. Some of the risk factors of osteoporotic fracture can be modified by lifestyle (diet, habits, exercise) intervention. To introduce this modifications elderly people need to be aware of the burden, risk factors and preventive measures of osteoporosis. Healthy Aging Academy is an initiative of Healthy Aging Research Center at Medical University of Lodz, which one of the aims is to educate local community of elderly people.
**Objectives:** The aim of the study was to assess the knowledge of elderly patients

about osteoporosis, its risk factors, prevention measures and available treatment.
**Methods:** The study group included 177 students (34 men and 143 women, mean age 69±10 years old) of Healthy Aging Academy. Students were asked to answer 22 questions grouped in 4 domains: questions regarding symptoms and burden of osteoporosis (6 questions), risk factors (8 questions), preventive measures (5 questions) and treatment (3 questions).
**Results:** In total 177 participants filled questionnaire. The mean percentage of correct answers was 63±13% (range from 31% to 82%). The mean percentage of correct answers in the group of questions on symptoms and burden of osteoporosis was 54±14±13%. The mean percentage of correct answers on risk factors, preventive measures and treatment was 84±22%, 63±18% and 53±25% respectively. It has to be noticed that only 1/3 patients were aware about prevalence of osteoporosis and were convinced that bone pain is a symptom of osteoporosis preceding fracture. The sources of vitamin D and calcium were correctly identified only by 62% and 70% of students.
**Conclusions:** Despite fact that our questionnaire was filled by group of relatively well educated and active elderly a significant proportion of subjects did not present adequate knowledge on treatment and preventive measures in osteoporosis.
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**Disclosure of Interest:** None declared
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## AB0793 RHEUMATIC DISEASES WITH EMPHASIS IN OSTEOPOROSIS IN A COHORT OF PATIENTS WITH BREAST ADENOCARCINOMA

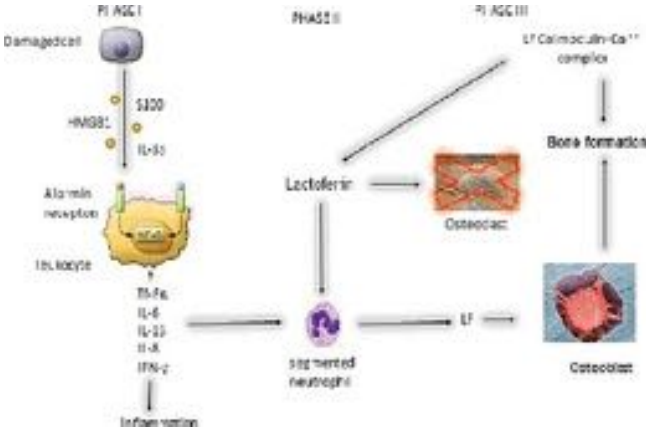
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**Background:** The osteoporosis (OP) and the breast cancer (BC) are diseases with increasing prevalence. The BC treatment includes total and early castration. In addition to surgical treatment and chemotherapy, they had lower levels of 25-OH-D vitamin, reduced physical activity and sun exposure, with effects in the bone health.
**Objectives:** To know the prevalence of rheumatic diseases in a cohort of patients with BC attended in clinical practice in two hospitals. To identify the characteristics of the OP and their treatment.
**Methods:** Setting: The Oncology Services and OP Unit of the Rheumatology Departments of the Hospital Virgen del Rocío (HUVR) and the Hospital Virgen Macarena (HUVM) in Seville, Spain. A prospective case series was design. Consecutive patients with BC who attended the Oncology Service (September to December of 2014) were evaluated. The patients were reviewed by 5 rheumatologists, previously trained about design, variables, data management, and the study protocol in order to collected 152 clinical variables. Descriptive statistics and univariate and multivariate statistics were done. The work was conducted in according to GPC and approved for the local ethical committee.
**Results:** 151 patients were included, all them women. The mean age (p25-p75) was 64.3 years (40.0 – 81.2). The menopausal was at 48 (34–56) years; in 44% it was before than 45 years. There were 11% smokers; 34% with regular sun exposure; 5% on corticosteroids and 2% drinkers. The rheumatic diseases were: OP in 103 (68%), chronic musculoskeletal pain 16%, osteoarthritis 16%, fibromyalgia 9%. The most frequent comorbidities were depression (16%), hypothyroidism (9%), Secondary hyperparathyroidism 9%, and Diabetes (8%). The comorbidity Index (Charlson) was 2 (2–5). The mean OP duration was 3.3 (0.19 – 9.8) years. The OP diagnostic was done with FF in 26 (23%) cases, 7 of them without OP by BMD. The FF were vertebral in 15 (10%), peripheral in 10 (7%) and one case with both. The baseline FRAX was 5.1 (1.4 -26) for major FF and 1.3 (0.1 – 10) for hip FF. The OP was diagnosed with BDM of femoral neck in 31 (24%) and in total lumbar column in 57 (45%), and in both in 15 (12%). The patients were treated with Calcium plus 25-OH-VitD 89%, PO bisphosphonates 51%, denosumab 26%, IV bisphosphonates 11%, teriparatide 3%, and 36% received 25-OHVitD. None of the multiple regression models was able to predict FF. In the best of cases the models predicted 20% of the FF ($R^2$). The model with the FRAX as predictor of major FF was poor: $R^2$ 0,15, $p<0,0001$; OR 1.15 (1.06 – 1.2). The FF were best predicted by the comorbidity index, SLE, RA or drinker; but with significant collinearity, and was impossible calculate statistics.
**Conclusions:** Patients with BC had an elevated prevalence of rheumatic diseases and comorbidity. The OP was severe with a high prevalence of FF. The classical risk variables of FF cannot predicted it. In this group of patients, the FRAX was not a good tool of prediction.
**Disclosure of Interest:** None declared
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## AB0794 POSSIBLE MOLECULAR MECHANISM OF LACTOFERRIN ACTION ON BONE FORMATION

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**Background:** Lactoferrin (LF) is a multifunctional protein, for which several biological activities were determined, among which the main are antimicrobial, antiviral, antifungal, anti-inflammatory and antioxidant effects. LF takes an active part in stimulation of tissue regeneration processes. LF's active role in the stimulation of tissue regeneration processes was established. In the last decade LF has also been shown to play the role in bone formation.
**Objectives:** In experiments carried out in different countries, it was found that the ovariectomized experimental animals, when giving LF per os, achieved relief of symptoms of osteoporosis, occurring at similar postmenstrual osteoporosis in women and human aging. Accumulating facts are showing a decrease in physiological serum LF in patients under pathological conditions of bone formation. In molecular genetic studies the identical mechanisms, resulting in reduced expression of LF and the emergence of bone desorption were determined.
**Methods:** We present a possible model of bone formation under the LF influence (Fig).
**Results:** According to our conception in osteoporosis, various injuries, or surgical impacts associated with the bones, the involvement of LF in the regenerative processes of the bone formation, apparently, is implemented as follows: as a result of damage of different tissues are released risk molecules – alarmins (high-mobility group protein B1 (HMGB1), S100 protein, IL-α, IL-33), which are necessary to repair damaged tissues, including bone. They interact with alarmins receptors on the surface of leukocytes, thus there is a release of proinflammatory cytokines (TNFα, IL-6, IL-1β, IL-8, INFγ) (Fig. Phase I). Further, under the action of IL-8, which is a chemotactic factor for neutrophils in the bone defect area segmented leukocytes migrate from granules which stands LF (Fig. Phase II). Then LF immerses in osteoblasts (OB), activating them, and osteoclasts (OC), inhibiting their activity (Fig. Phase III).



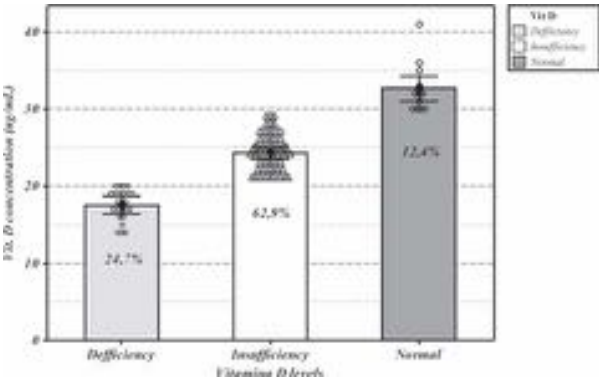

**Conclusions:** According to the presented model, the LF is simultaneously a factor of implementing the calcium transfer. The ability of LF to bind calcium is well known. The transfer of calcium in the bone tissue due to the complex LF-Calmodulin-Ca ++ (Fig.).
It is possible that the expansion of research of the role of LF in bone formation will help create new and effective drugs to combat osteoporosis.
**Disclosure of Interest:** None declared
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## AB0795 HYPOVITAMINOSIS D AND CALCIUM INTAKE OF ADULT POPULATION IN BOGOTA (DICAVITD)

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**Background:** The calcium intake on the diet below normal daily requirements is related with low levels of vitamin D. The available scientific evidence supports a key role of calcium and vitamin D in skeletal health. We analyzed this relationship in healthy colombian population and describe this association.
**Objectives:** The main objetive is to Assess the prevalence of hypovitaminosis D and the relationship with the daily calcium intake in a healthy Colombian population. Furthermore it is crucial to estimate the impact of key mineral elements such as Calcium and Vitamin D in bone health.
**Methods:** In a prospective cohort of general population we measure the prevalence of hypovitaminosis D and the calcium intake, (mg/dl) following demographic, antropomethric, biochemical characteristics and sun exposure of the population evaluated. We used a model of multiple regresion to predict the

levels of vitamin D regarding the factors analysed. We excluded patients with secondary conditions that affect the absorption of calcium and vitamin D.
**Results:** We included 97 patients, average age 23 yrs, 61% women, average weight 65 kg, Height 165 cm, average BMI 22.8. The calcium intake was 393,7 mg/d, levels of vitamin D were 23.71. We identified hypovitaminosis D in 87% of the patients, 24.7% had vitamin D defficiency and 63% had insufficiency (Figure 1, Levels of Vitamin D in the population study).
The concentration of Vitamin D was calculated in quadratic function, for the relationship between sex, sun exposure and habitual calcium intake. (R:>90%).




**Conclusions:** We found a strong relationship between low calcium intake and hypovitaminosis D in the study group. In a healthy colombian population we saw an important low intake of calcium on the diet and high prevalence of Hypovitaminosis D. These findings have enormous impact on public health policy in our country. Effective and imperative strategies are required to prevent future complications such as Osteoporosis and secondary fractures.
**References:**
[1] Catharine-Ross A., et al. The 2011 report on dietary references intake for calcium and vitamin D from the Institute of Medicine. What clinicians need to know. JCEM 2011;96:53–58
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3330

## AB0796 THE PREDICTORS OF FRACTURE IN PATIENTS WITH HYPERPARATHYROIDISM: AN OBSERVATIONAL STUDY

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**Background:** Hyperparathyroidism and other endocrine disorders have been associated with a low bone mineral density. The FRAX ™ tool uses the femoral neck to predict fractures on a population basis and ignores the lumbar spine.
**Objectives:** We set out to determine the predictors of fragility fractures in a large cross sectional study of 508 patients diagnosed with Hyperparathyroidism.
**Methods:** Patients referred for bone mineral density (BMD) estimation in a scanner in the North West of England with a history of Hyperparathyroidism were identified from a dual X-ray absorptiometry (DEXA) database. Demographics and other risk factors were recorded as well as fragility fractures. Initially, Univariate logistic regression models were modelled predicting fractures in the data set and a multivariate model was subsequently fitted. Variables included age at scan, gender, body mass index (BMI), family history of fracture, alcohol intake, smoking, glucocorticoid exposure, rheumatoid arthritis, in addition to BMD in the lumbar spine and femoral neck.
**Results:** 508 patients were scanned in the referral period. Mean age at scan was 65.0 (SD 12.4). 411 (80.9%) of the patients were female and 97 were male. Results of the univariate analysis (adjusted for age and gender) are shown in table 1. Significant predictors are denoted with an asterisk.

Table 1

| Predictor | Odds ratio | 95% CI |
|---|---|---|
| Lumbar spine BMD | 0.18 | 0.31, 1.04* |
| Femoral neck BMD | 0.70 | 0.72, 6.80 |
| Rheumatoid arthritis | 0.65 | 0.73, 5.77 |
| Smoking | 0.84 | 0.50, 1.42 |
| Excess alcohol | 1.30 | 0.34, 5.00 |
| Family history of fracture | 1.43 | 0.57, 3.64 |
| Steroid exposure | 1.55 | 0.82, 2.93 |
| Body mass index kg/m$^2$ | 1.04 | 0.99, 1.09 |

In the multivariate model, the only variable that predicted fractures in this cohort was Lumbar spine BMD OR 0.18 (95% CI 0.31,1.04)
**Conclusions:** In the univariate analysis, many risk factors are associated with fracture. However in the multivariate analysis conducted, the best predictor was Lumbar Spine BMD. This is not included in the FRAX ™ tool and would make estimating the fracture risk in this cohort difficult. Further modelling in other cohorts is needed to validate this finding.
**Disclosure of Interest:** None declared
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## AB0797 ANKLE FRACTURES AND ITS RELATIONSHIP BETWEEN OSTEOPOROSIS, DIABETES AND OBESITY

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**Background:** Osteoporosis is a major health problem worldwide and leads to several million fractures every year. Diabetes mellitus (DM) and obesity are an increasing threat for global health. While the pathophysiology of diabetic bone disease is unknown, some recent studies have demonstrated an increased fracture risk related to type 2 DM. Type 1 DM has also been associated with a decreased bone mineral density (BMD).
**Objectives:** To investigate the relationship between DM and obesity, and their relation to osteoporosis and ankle fractures.
**Methods:** Retrospective study 2008–2014. Center: tertiary academic hospital with a referral area of 850,000 inhabitants. The medical charts, dual-energy X-ray absorptiometry (DXA), radiographs and electronic data bases were retrospectively reviewed of patients seen for ankle fractures. Patients were classified in 4 groups: obesity (IMC>30), non-obesity, diabetic and non-diabetic. We compared demographic data (age, gender), mechanism of injury (high or low energy trauma), pattern of fracture (single malleolus, bimaleollar and trimalleolar), treatment of the fracture, presence of new fracture (in other localizations) and osteoporosis treatment
**Results:** We compared a total of 65 diabetic patients (32.3% male and 67.7% female, mean age 61.8 years [DS 17.6]) with 234 non-diabetic patients (52.9% male, 47.1 female, mean age 31.5 [DS 41.7]) and 40 obese patients (37.5% male and 34.7% female, mean age 42 years [DS 21.2]) with 76 non obese patients (38.2% male, 61.8% female). The main characteristics of the study groups are presented in Table 1. There were no differences in fracture pattern, mechanism of injury, BMD and fracture treatment among all groups. Bimaleolar fracture was the most common pattern in all groups. Diabetic group had higher frequency of a low energy trauma, osteoporosis and new fracture. New fracture was reported in 12 patients, between 3 and 48 months (after the ankle fracture). There was 5 Colles'fracture, 3 hip, 2 in other localization. One patient had two fractures (Colles and vertebral) Obese group had higher frequency of osteopenia compared with non obese.

Table 1

| | Diabetic (%) | Non diabetic (%) | p | Obese (%) | Non obese (%) | p |
|---|---|---|---|---|---|---|
| Female | 53 | 67.7 | 0.03 | 61.8 | 62.5 | 0.9 |
| Bimaleolar | 61.5 | 51.7 | 0.4 | 52.6 | 52.5 | 0.8 |
| Trimaleolar | 10.8 | 17.5 | 0.4 | 20 | 17.1 | 0.8 |
| Low energy trauma | 52.3 | 43.2 | 0.3 | 47.5 | 56.6 | 0.6 |
| Conservative treatment | 13.8 | 11.1 | 0.5 | 7.5 | 7.9 | 0.9 |
| Osteopenia | 25 | 62.5 | 0.2 | 60 | 42.9 | 0.2 |
| Osteoporosis | 50 | 37.5 | 0.2 | 20 | 57.1 | 0.2 |
| New fracture | 18.5 | 15 | 0.4 | 15 | 19.7 | 0.5 |

**Conclusions:** We did not found statistical differences between diabetic and obese compared with non diabetic or non obese patients. Ankle fracture in diabetic group could have features of osteoporotic injury including the high frequency of new fracture.
**Disclosure of Interest:** None declared
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## AB0798 CAN ANTI-OSTEOPOROTIC THERAPY REDUCE ADJACENT FRACTURE IN MAGNETIC RESONANCE IMAGING-PROVEN ACUTE OSTEOPOROTIC VERTEBRAL FRACTURES?

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**Background:** Adjacent fracture of the cemented vertebrae may result from unfilled space left during the procedure or from crushed fragile trabeculae underneath the cement during follow-up, suggesting impaired bone marrow integrity of the injured vertebrae. Anti-osteoporotic therapy is reported to increase spinal, total hip, and femoral neck bone mineral density[1]. If treating osteoporosis does have a positive impact on adjacent fracture among patients who have undergone vertebroplasty, there will be several important potential implications for managing skeletal health specifically and for the health care of the elderly in general.
**Objectives:** This study aimed to determine if anti-osteoporotic therapy can decrease the risk of adjacent fracture in patients with acute vertebral fracture after vertebroplasty.
**Methods:** This retrospective study reviewed of cases of osteoporosis patients with magnetic resonance imaging (MRI)-proven acute vertebral fractures between 2001 and 2007. Osteoporotic patients were investigated as determined by pre-operative MRI with subsequent adjacent fracture of the cemented vertebrae and for the possibility of anti-osteoporotic therapy decreasing the progression of collapse after a minimum of 6 months follow-up. All associated co-morbidities were

recorded, as well as the use of anti-osteoporotic drugs (i.e., alendronate, raloxifen, calcitonin, and teriparatide). Cox regression analysis was also performed.
**Results:** The 192 patients with acute vertebral fractures who underwent vertebroplasty and anti-osteoporotic therapy had a mean age of 74.40±6.41. The basic characteristics of patients with and without adjacent fracture differed in age, body mass index, rheumatoid arthritis, and use of glucocorticoids and anti-osteoporotic drugs (Table 1). Using the Kaplan-Meier curve, anti-osteoporotic therapy after vertebroplasty had a significant effect on adjacent fracture ($p$=0.037, by log rank text). After adjusting for potential confounders, patients with anti-osteoporotic therapy still had a lower adjacent fracture rate than patients without anti-osteoporotic therapy ($p$=0.006; HR: 2.137, 95% CI: 1.1238–3.690). The adjacent fracture rate also increased in old age ($p$=0.019; HR: 1.049; 95% CI:1.008–1.039) and among smokers ($p$=0.026; HR: 3.891; 95% CI: 1.175–12.890).

Table 1. Multivariable Cox regression analysis of the hazard ratios for adjacent fracture

| Variables | Regression coefficient | p value | HR (95% CI) |
|---|---|---|---|
| Age | 0.048 | 0.019 | 1.049 (1.008–1.093) |
| Body mass index (kg/m$^2$) | –0.055 | 0.126 | 0.946 (0.882–1.016) |
| Sex | –0.595 | 0.248 | 0.551 (0.201–1.513) |
| Smoking | 1.359 | 0.026 | 3.891 (1.175–12.890) |
| Glucocorticoid use | –0.304 | 0.492 | 0.737 (0.310–1.756) |
| Anti-osteoporotic therapy | 0.759 | 0.006 | 2.137 (1.238–3.690) |

Abbreviations: HR, hazard ratio; SE, standard error.

**Conclusions:** In this study, adjacent fracture of cemented vertebrae is inevitable after vertebroplasty but can be mitigated by anti-osteoporotic therapy to increase bone mass.
**References:**
[1] Center JR, et al. J Clin Endocrinol Metab. 2011;96(4):1006–14.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5601

## Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

### AB0799 GOUT MANAGEMENT: AUDIT FOR BEST PRACTICE IN GOUT

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**Background:** Gout is well known old disease, with still increasing prevalence. We are not in short of well-established clear guidelines for its management. However, it is still not well managed even in developed countries.
**Objectives:** We share our experience of auditing the gout management in our out-patient clinic with the completion of our audit cycle. The aim is to improve gout service in line with 2006 EULAR guidelines, using the ethos of treat-to-target approach.
**Methods:** We audited randomly selected 101 patients seen in our well established gout clinic. All patients should be in that clinic for a minimum of 6 months, ensuring sufficient time for prophylactic therapy to take effect. Records from patients attending the gout clinic between 07/07/2014 and 29/06/2015 were accessed & information was collected on serum urate and the treating medications, gouty attacks & presence of tophi. Patients' comorbidities were recorded. Recent serum uric acid levels were specifically scrutinized against both BSR and EULAR targets of $\leq$300 and $\leq$360 mmol/L respectively
**Results:** Female (27%), males (73%). Average age: 64. Acute attack management: NSAID (42%), Colchicine: (82%), Oral Steroid (10%), IA Steroid (27%).
42% and 69% of patients acieved the BSR & EULAR s. uric acid target as compared with 9.3% for BSR target in 2010 and 29% & 60% for 2012 audit respectively. 64% of patients were under the BSR target reported no acute gout episodes since their last appointment, which is almost the same (66%) of patients achieving EULAR target.
70%, 20% & 10% of patients in the sample were on allopurinol, Febuxostat and Benzbromarone respectively. For Allopurinol treated patients 36.6% & 67.6% were under BSR and EULAR targets respectively. For Febuxostat these figures were much better at: 61.9% and 85.7% and for Benzbromarone 54.5% achieved EULAR & BSR target. Patients on Febuxostat had a significantly lower average urate (290) than allopurinol (351) (P=0.015). Patients prescribed Febuxostat if they had experienced side-effects to allopurinol (in concordance with NICE guidelines) or if allopurinol found it to be ineffective (31%).
However, for patient with tophi s. uric acid target of $<$300 (BSR) was achieved in 33.3% and of $<$360 (EULAR) in 59.3%.
100% of patients received lifestyle advice on diet, exercise & alcohol (NICE recommendation) as compared to only 9% in 2010. In CHD patients, 71% reduced their Cholesterol/HDL ratio to $<$5.0. In hypertensive patients, 60% reduced systolic blood pressure to $<$160 & in obese patients 7.84% were able to significantly reduce their weight ($>$5 kg).
**Conclusions:** The proportion of patients achieving BSR & EULAR targets, in comparison to 2010 and 2012 were increased significantly on adapting gout speciality clinic. A greater proportion of patients on Febuxostat reached their targets compared to other urate lowering agents. No significant benefit (in terms of stopping further acute attacks with the meeting of the BSR target of $<$300 over the EULAR target of $<$360 were seen. Tophaceous gout has not been treated well when compared to the rest of the cohort. The impact of the clinic on improving and managing other co-morbidities associated with gout has much improved. We recommend that all gout patients should be treated with target to treat stratigy & this will be best achieved in specialized gout clinic
**Disclosure of Interest:** None declared
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### AB0800 NEUTROPHIL: LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME IN PATIENTS WITH GOUT

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**Background:** Gout is a clinical syndrome with increased uric acid concentration, which is caused by inflammatory response against mono sodium urate (MSU) crystals. In gout, neutrophils are involved in inflammatory response and neutrophil activation is dependent to local cytokine production. Mean platelet volume (MPV) and neutrophil:lymphocyte ratio (NLR) are considered as inflammatory markers in several diseases and it is reported that they may have prognostic significance.
**Objectives:** According to current literature, there is no study evaluating MPV and NLR in gout. In this retrospective study, we investigated role of MPV and NLR in determination of inflammation in gout disease.
**Methods:** In this retrospective study, 106 patients with gout (91 men and 15 women) meeting inclusion criteria by patients records and 148 age- and sex-matched healthy controls (128 men and 20 women) were included. Laboratory data during attacks (group I) and intercritical period (group II) were collected in the patient group.
**Results:** Mean age was 59.46±12.93 years in the patient group whereas 59.00±11.33 years in the control group. Age at first attack was 52.00±12.77 years and mean time interval between first 2 attacks was 6.00±5.52 months. There was tophus in 9 patients (8.5%) and family history of gout in 17 patients (16.0%). Compared to group 2 (intercritical period) and control, no significant difference in MPV levels was found in the group 1 (during attack). MPV was similar among three groups. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were found to be significantly higher in the group I compared to group II. There was significant difference in NLR among three groups. When classified according to presence of tophus, it was seen that MPV and NLR were similar in both groups.

Table 1. Parameters evaluated in the groups

| Parametre | Group I (during attack period) n=106 | Group II (during intercritical period) n=106 | Control n=148 | p |
|---|---|---|---|---|
| MPV (f/L) | 8.1 (5.9–10.7) | 8.2 (5.4–12) | 8.3 (6.7–12.9) | 0.054 |
| NLR | 2.88 (1.21–21.16) | 2.19 (0.69–21.82) | 1.72 (0.78–11.25) | **<0.001**† |
| ESR (mm/h) | 36 (24–65) | 12.5 (2–30) | – | **<0.001** |
| CRP (mg/dL) | 35 (19–60) | 3.2 (1.6–4.7) | – | **<0.001** |

CRP: C-reactive protein, Normal reference range: 0–10 mg/dL. ESR: erythrocyte sedimentation rate, MPV: mean platelet volume; NLR: neutrophil:lymphocyte ratio; †There are statistically significant differences in all groups.

**Conclusions:** The finding of increased NLR during attacks and intercritical period shows that patients with gout are subjected to chronic inflammation. Thus, NLR can be simple, inexpensive and useful diagnostic marker in gout. Studies comparing cytokine levels with NLR will be helpful in elucidating this topic.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2232

### AB0801 OSTEOPOROSIS FREQUENCY AND THE ASSOCIATION OF RANK, RANKL, OSTEOPROTEGERIN GENE POLYMORPHISMS WITH OSTEOPOROSIS IN GOUT PATIENTS

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**Background:** Gout is a disease characterized by acute arthritis as a result of increased serum uric acid concentration and deposition of monosodium urate crystals into tissues. In recent times the significant role of RANK- RANKL- OPG network in bone remodeling and osteoclastogenesis was proven. In patients with osteoporosis and in rheumatoid arthritis patients, genetic variations in the genes encoding RANK, RANKL and OPG was investigated and conflicting results were obtained. Also the role of these genes in the pathogenesis of psoriasis, psoriatic arthritis and ankylosing spondylitis has been researched. There is not any study that evaluates RANK, RANKL, Osteoprotegerin gene polymorphisms and their

association with the susceptibility to osteoporosis in gout patients. To the best of our knowledge, this is the first study to investigate this subject.
**Methods:** 69 gout patients, 50 RA patients and 51 healthy controls were recruited for this study. BMD of lumbar spine and femoral sites were measured using DEXA. After acquisition of the BMD T- score, the patients and controls divided into normal, osteopenic and osteoporotic groups according to WHO criteria. We studied 7 SNP in the genes of RANK gene (2 SNP: rs1805034, rs35211496), OPG gene (2 SNP: rs3102735, rs 2073618) and RANKL gene (3 SNP: rs9533156, rs1054016, rs2277438) using real time PCR.
**Results:** There was no significant difference for BMD scores between three groups. The 7 SNP genotypes showed no significant difference between three groups. The 7 SNP allel frequencies showed no significant difference between three groups. Gout patients with rs1805034 wild genotype had lower incidence of osteoporosis at the femoral sites. Gout patients with rs1805034 heterozygous genotype had higher incidence of normal BMD scores at the femoral sites than other gout patients. Controls with rs2277238 wild genotype, had lower incidence of osteoporosis and those with mutant genotype had higher incidence of osteoporosis at any sites than other controls. Controls with normal BMD at lumbar spine, frequency of rs35211496 wild genotype was higher than other controls.
**Conclusions:** As a result it is seen that the C allel of the RANK SNP rs1805034 is protective against osteoporosis at femoral site in gout patients. The A allel of the RANKL SNP rs2277438 is protective against osteoporosis at either femoral sites or lumbar spine in healthy people. BMD in patients with Gout, RA and healthy population unexpectedly is not different from each other which may be related to low number of cases. Genotype distribution and genetic diversity varies between ethnic groups. There is a need for more studies with larger patient populations to explain the subject.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2551

## AB0802 EFFECT OF ALLOPURINOL AND FEBUXOSTAT IN PROLONGING THE FLARE-FREE TIME IN GOUTY PATIENTS WITH OR WITHOUT PROPHYLACTIC TREATMENT WITH COLCHICINE: A RETROSPECTIVE KAPLAN-MEIER ANALYSIS

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**Background:** Among inflammatory joint diseases, gout is a main cause of recidivism in urgency departments due to insufficient pain control or development of arthritis flares. This burden produces time and resources consumption and time of work off. New and old hypouricemic treatments are not only intended to control uric acid level below 6mg/dL but to reduce the number of flares per year. It is well known that their activity removing uric deposits could trigger new flares so prophylactic treatment is always recommended when those treatments are initiated. There are many studies conducted to compare hypouricemic effectiveness with those treatments, however, their impact in flare-free survival is a topic not previously studied.
**Objectives:** To compare the effectiveness of Allopurinol and febuxostat in terms of recidivism in patients with gout flares.
**Methods:** A descriptive retrospective study was performed. Electronic registries of patients diagnosed by gout and treated with Allopurinol (100–200mg/d and 300–600mg/d) and febuxostat (80mg/d and 120mg/d) with at least a gout flare were included. Prophylaxis treatment was considered as positive in patients on treatment with colchicine 0.5–1mg/día or NSAIDs according to the 2012 ACR Guidelines for management of gout (Khanna et al. Arthritis Care & Research, 2012: 64 (10); 1447–61). Follow up period was 2013–2015. Only patients with flares were included. Kaplan Meier curves were built considered censored any flare which took place after 6 months since the treatment started. Data recovered from electronic registries were: demographic and clinical data, number of consultations and work off time where appropriated. Comparisons were made according to hypouricemic treatment and colchicine prophylaxis treatment. No data about treatment compliance were considered.
**Results:** 90 registries of different patients were identified: 18 were under treatment with febuxostat (14 on 80mg/day and 3 on 120mg/day) and 72 under treatment with allopurinol (22 on 100–200mg/day, 50 on 300–600mg/day). Difference on average of age, proportion of males and proportion of tophus were not statistically significant between both groups. Mean of time until the first flare after starting treatment with allopurinol was 132.4 SD 6.8 days (CI95% 119.0–145.8) and 142.6 SD 11.63 (CI95% 119.8–165.4) with febuxostat (Chi-squared 0.304; *P*=0.581, Hazard ratio 0.806; 95%CI 0.3935–1.654). Excluding patients without prophylaxis treatment (2 on febuxostat and 26 on allopurinol), the mean of time until the first flare was 116.4 SD 8.0 days (CI95% 100.7–132.1) in the group on allopurinol and 153.8 SD 9.9 days (CI95% 134.3–173.3) in the group on febuxostat (Chi-squared 5.984; *P*=0.0144, Hazard ratio 0.356 (CI95% 0.183–0.692). No differences statistically significant were observed when Kaplan Meier curves were built groping patients according to the doses of Allopurinol or febuxostat.
**Conclusions:** Our observations point that there is a tendency to higher surveillance without flares in gouty patients on febuxostat than on allopurinol. This tendency becomes statistically significant when only patients on colchicine treatment were compared, so it seems that prophylaxis treatment benefits specially this group of patients prolonging the period of time free of flares.
**Disclosure of Interest:** None declared
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## AB0803 CHRONIC KIDNEY DISEASE DOES NOT AFFECT THE NUMBER OF THE ATTACKS AND THE ATTACK DURATIONS IN GOUT PATIENTS

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**Background:** Gout is one of the most severe and frequent rheumatic diseases. Clinical manifestations of gout arise from uric acid crystal deposition in the musculoskeletal tissue. Many patients with gout have co-morbidities, including hypertension and chronic kidney disease (CKD).
**Objectives:** The goals when treating gout are no different in these patients, but the choice and dosage of drugs may need to be modified. In this study, we aimed to determine whether the chronic kidney disease affects or not the number of the gout attacks.
**Methods:** Consecutively 31 gout patients with CKD (group 1, n=31) and 46 gout patients without CKD (group 2, n=46) were enrolled in the study. The gout attack durations and the number of the gout attack in the last one year were compared among groups.
**Results:** The clinical, demographical and anthropometric variables were presented on table 1. There were no statistical differences in body mass index, use of diuretics and history of nephrolithiasis between two groups ($p>0.05$ for all). Compared to group 2, group 1 had statistically similar levels of the gout attack durations and the number of the gout attacks in the last one year (both $p>0.05$). In Bivariate Pearson correlation analysis; gout attack durations and the number of the gout attacks in the last one year were not correlated in any parameters in group 1 ($p>0.05$ for all).

Table 1. Comparison of the demographic and anthropometric and biochemical characteristics of all patients

| Variables | Group 1 (n=31) | Group 2 (n=46) | *p* |
|---|---|---|---|
| Gender, male/female | 20/11 | 42/4 | 0.004 |
| Age, years | 62.64±12.75 | 53.00±12.40 | 0.002 |
| BMI, kg/m$^2$ | 29.89±5.18 | 29.99±4.20 | 0.925 |
| Creatinine, mg/dL | 1.55±1.08 | 0.97±0.17 | 0.001 |
| GFR, ml/min | 64.96±24.05 | 112.59±30.26 | <0.001 |
| Uric acid, mg/dL | 8.43±1.80 | 7.69±1.42 | 0.064 |
| Use of diuretics, +/– | 11/20 | 11/35 | 0.310 |
| History of nephrolithiasis, +/– | 12/19 | 12/34 | 0.317 |
| Disease duration, months | 72.00±100.25 | 74.08±106.97 | 0.931 |
| Number of the attacks, in the last one year | 2.38±2.10 | 2.78±2.24 | 0.434 |
| Attack durations, days | 8.54±7.64 | 14.30±16.56 | 0.075 |

**Conclusions:** The present study revealed that CKD does not affect the number of the attacks and the attack durations in gout patients. Future large scale multicenter randomized controlled studies are needed and warranted to clarify our results.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4962

## AB0804 THE EFFICACY AND TOLERABILITY OF FEBUXOSTAT IN HYPERURICEMIC PATIENTS UNDERGOING DIALYSIS

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**Background:** Febuxostat is metabolized mainly in the liver and is excreted through both urine and feces, suggesting that it may be an alternative choice for the treatment of hyperuricemia and gout in chronic kidney disease (CKD) patients. However, there are insufficient data on the use of febuxostat in patients undergoing dialysis.
**Objectives:** The aims of our study were to investigate the efficacy and tolerability of febuxostat in hyperuricemic patients on dialysis.
**Methods:** We retrospectively reviewed clinical and laboratory data from two tertiary referral centers from January 2012 to December 2015. We included 49 patients with underlying CKD on dialysis who started febuxostat treatment in the two hospitals.
**Results:** The mean age of the study patients was 54.4±12.5 year and follow-up duration was 12.7±10.2 months (Table 1). Among 41 patients who were treated with febuxostat for over 3 months, the mean serum uric acid level at 3 months after treatment (4.97±1.84 mg/dL) was significantly reduced compared with the pretreatment level (9.61± 2.18 mg/dL) ($p<0.001$). And the serum uric acid level stayed significantly lower for 12 months without deterioration in eGFR. Of the 49 patients, only 2 stopped the medication due to adverse event. The two patients who stopped taking febuxostat were on peritoneal dialysis.

Table 1. Baseline characteristics of the study patients at the time of febuxostat initiation

| Characteristic | Dialysis patients (n=49) |
|---|---|
| Age, years | 54.4±12.5 |
| Sex, male (%) | 41 (83.7) |
| Follow-up duration, months | 12.7±10.2 |
| Renal disease | |
| Diabetic nephropathy (%) | 8 (16.4) |
| IgA nephropathy (%) | 8 (16.4) |
| Primary glomerulonephritis (%) | 6 (12.2) |
| Polycystic kidney (%) | 5 (10.2) |
| Lupus nephritis (%) | 1 (2.0) |
| Others (%) | 21 (42.8) |
| Comorbidity | |
| Hypertension (%) | 35 (71.4) |
| Gout (%) | 36 (73.5) |
| Diabetes (%) | 9 (18.4) |
| Malignancy (%) | 4 (8.2) |
| Initial dose of febuxostat | |
| 40 mg/day (%) | 38 (77.6) |
| 80 mg/day (%) | 11 (22.4) |

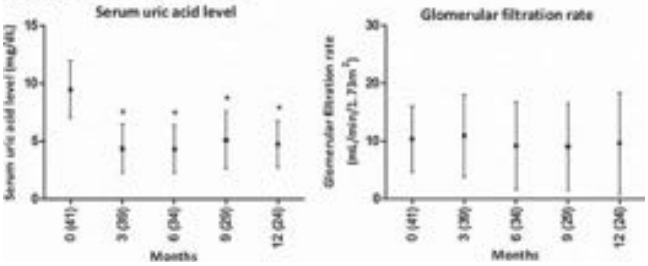



**Figure 1** Changes in serum uric acid levels and eGFR during the 12-month period after febuxostat initiation (number in parentheses indicates number of patients). Data are shown as mean ± SD. * $p<0.05$ versus month 0 (paired *t* test).

**Conclusions:** Febuxostat is efficacious and well tolerated in hyperuricemic patients undergoing dialysis. Close observation for adverse events might be needed for patients on peritoneal dialysis.
**Disclosure of Interest:** None declared
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## AB0805 CONCORDANCE BETWEEN CLINICAL FINDINGS AND ULTRASOUND IN GOUT

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**Background:** Ultrasound (US) evidence of double contour (DC) sign has been incorporated to new ACR/ EULAR gout classification criteria. Other specific US symptoms like tophus (T) and unspecific features like synovial hypertrophy (SH), synovial effusion (SE) are still under investigation. Which joints should be investigated – only symptomatic or more - still a matter of debate [1]. The US studies with rheumatoid arthritis showed that US adds information to clinical findings [2]. The concordance between clinical symptoms and ultrasound in gout still needs to be investigated.
**Objectives:** to evaluate concordance between clinical examination, patient reported gout symptoms and ultrasound findings in gout patients.
**Methods:** observational, prospective, controlled single centre study has been performed. 50 crystal proven gout patients with different disease duration, activity and treatment and 36 healthy controlls has been included. 36 joints were systematically investigated by experienced rheumatologist, blinded to patients clinical data and complaints. The concordance between clinical signs, such as tender joints and swollen joints defined by other rheumatologist, joints with previous gout flares, reported by the patient and presence of ultrasonographic SE, SH, DC and T was assessed by computing the kappa coefficient.
**Results:** the concordance between patient reported gout flare (PRGF) and SH, SE was poor with kappa 0,125 (95% CI 0,070–0,179) and 0,136 (95%CI 0,082–0,190) accordingly. The concordance between (PRGF) and T, DC and combination of T plus DC was fair – kappa 0,325; 0,275 and 0,376 accordingly. There was negative kappa (-0,053) between reported joint flare in I MTF and DC sign, poor concordance between knee, ankle PRGF and DC sign. Negative kappa (-0,005) between PRGF and T in wrist joints. The concordance between US T and DC and patient reported flare stayed fair in untreated (33) group. The strongest concordance between PRGF and T, considered as moderate (kappa 0,420; 95% CI 0,296- 0,544) was found in early gout group (16 patients), with fair agreement according DC sign in this subgroup. Poor agreemant was found between SE, SH, T and DK and objectively found tender and swollen joints, ultrasound was found to be much more sensitive - SH in 92% (195/211) cases, T in 93% (211/228) of cases and DC in 92% (268/290) of cases was found in non swollen joints. The overall specificity of DC, T and SH according controls was 86% ($p<0,0001$), 81% ($p<0,0001$) and 64% ($p<0,0001$).
**Conclusions:** The concordance between patient reported gout flare in the joint and US tophus or double contour sign was poor to fair in total gout group and moderate in early gout according tophus. We found no agreement according clinics and tophus sign in wrist and double contour sign in I MTF. Ultrasound added information to clinical examination with good specificity for tophus and double contour sign.
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**Disclosure of Interest:** None declared
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## AB0806 HOW OFTEN DO GOUT PATIENTS REACH TARGET IN A RHEUMATOLOGY PRACTICE?

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**Background:** Achieving the target serum urate has been repeatedly emphasized in published guidelines as a key determinant of successful gout management. Success rates are low in general practice and community audits but few studies have assessed results in a gout-orientated rheumatology practice
**Objectives:** To determine the frequency of achieving target urate levels and the drugs required.
**Methods:** Consecutive patients with gout who attended the private rooms between Jan 2010 and Sept 2014, in whom rheumatologist (NMcG) and patient agreed that urate-lowering therapy (ULT) was indicated and who commenced therapy were included. Serum urate targets: no tophus $\leq$0.36mmol/L; tophi $\leq$0.30mmol/L. Allopurinol was used initially. Due to limited access to febuxostat, for allopurinol intolerant patients with adequate renal function, probenecid was used next, then febuxostat.
**Results:** Of 168 patients (148 male), 123 (83.1%) achieved target. The average;standard dev;range of serum creatinine were 98;31.9;21–231. Of patients able to tolerate allopurinol, 103/145 (71.0%) achieved target with an average dose of 393mg/day. Included in the 103 patients were 40 who did not achieve target on allopurinol 300mg/day, but did achieve target with a higher dose (400–900mg/day). For the remaining 42 of 145 patients, 35 were deemed to be non-compliant (did not attempt $>$3 dose increases or a change to another medication and failed to achieve target). For 7/145 patients, allopurinol was ineffective. 3/7 reached target on combination of allopurinol and probenecid. 2 did not increase beyond allopurinol 400mg/day and failed to reach target, 1 increased to allopurinol 900mg/day but failed to reach target, 1 changed to febuxostat 80mg/day without reaching target. 23/168 (13.7%) were unable to use allopurinol (due to concurrent azathioprine or intolerance). Of the 23, 8 reached target on probenecid, 1 on benzbromarone, 8 on febuxostat and 1 on combination of probenecid and febuxostat. 5 did not reach target (4 increased only to febuxostat 40mg/day, 1 attempted probenecid without reaching target and was unable to attempt febuxostat due to supply difficulties).
Of 18 patients on probenecid (12 due to inability to use allopurinol), target was achieved by probenecid alone (7) or in combination with allopurinol (4) or with febuxostat (1). 2 attempted probenecid unsuccessfully, but then reached target on a retrial of allopurinol (1) or benzbromarone (1).
Of 19 patients on febuxostat, target was reached on febuxostat alone (10) or on a combination of febuxostat and probenecid (1). 1 reached target on a re-trial of allopurinol, and 7 did not reach target. Of those 7, only 1 failed febuxostat 80mg daily, with 2 non-compliant and the others on febuxostat 40mg/day by end of the study period.
In total (considering any ULT), 37/168 (22.0%) were non-compliant. No patient was intolerant or allergic to all ULTs.
**Conclusions:** Even in a gout-oriented rheumatology practice, non-compliance was by far the commonest reason for not achieving the serum urate target. For compliant patients able to tolerate allopurinol, failure to achieve target was uncommon (4.8%). Although potent newer ULTs are of benefit in specific patients, if advances in ULT availability are going to have a major impact on overall treatment success, they will need to be associated with improved compliance.
**Disclosure of Interest:** None declared
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## AB0807 GOUT IN RURAL AREA IN SUB-SAHARAN AFRICA: A COMPARISON BETWEEN PATIENTS COMING FROM RURAL AND URBAN AREAS, IN AN URBAN TERTIARY HEALTHCARE CENTER IN CAMEROON

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**Background:** Gout, the disease of kings is seen today in both urban and rural areas. However, few data are available on the characteristics of gout in the rural area, especially in sub-Saharan Africa.
**Objectives:** To evaluate the differences between gouty patients in rural and urban areas in Cameroon, Central Africa.
**Methods:** We performed a cross-sectional study in all 511 patients (96 women and 415 men) seen at General Hospital, Douala, Cameroon, between January 2004 and December 2013. The main demographic and clinical features of gouty patients living in rural and urban were compared. A $p< 0.05$ was considered statistically significant.
**Results:** The baseline characteristics of patients are presented in Table 1. Patients living in rural areas were older, had an oligoarticular clinical presentation, more hyperuricemia and higher serum uric acid levels and a more frequent chronic inflammation compared to patients living in urban areas.
Chronic kidney disease and dyslipidemia were more frequent in rural areas while obesity and hypertension were more frequent in urban areas.

Table 1. Main baseline characteristics of patients

| Variables | | Rural area (n=49) | Urban area (n=462) | *p* |
|---|---|---|---|---|
| Age (years), mean ± SD | | 60±12.05 | 56±10.63 | 0.001 |
| Sex | Men | 34 | 381 | <0.001 |
| | Women | 15 | 81 | |
| Obesity | | 24 | 297 | 0.01 |
| Arthritis | | 16 | 182 | 0.001 |
| Tophi | | 9 | 183 | 0.01 |
| Presentation at diagnosis | Acute gout | 25 | 230 | <0.001 |
| | Chronic gout | 24 | 232 | <0.001 |
| Clinical presentation, n | Monoarticular | 25 | 230 | <0.001 |
| | Oligoarticular | 22 | 173 | <0.001 |
| | Polyarticular | 2 | 59 | 0.12 |
| Fever, n | | 2 | 19 | 0.21 |
| Elevated uric acid levels, n | | 26 | 231 | <0.001 |
| Serum uric acid, mean ± SD, mg/dL (μmol/L) | | 84.68±3.22 | 82.21±1.07 | <0.001 |
| MSU cristal (synovial fluid)†, n | | 2 | 20 | 0.21 |
| Acute phase reactants, n | Elevated CRP | 13 | 151 | <0.001 |
| | Elevated ESR | 28 | 223 | <0.001 |
| Urate arthropathies, n‡ | | 6 | 62 | <0.001 |

**Conclusions:** Gout is characterized in patients living in rural area by a late age at onset and hyperuricemia higher compared to patients living in urban area. Cardiovascular risk factors are common. Further studies are needed to evaluate lifestyle changes in rural area.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2481

## AB0808 COMORBIDITIES ASSOCIATED WITH GOUT ARE ALSO COMMON IN SUB-SAHARAN AFRICA THAN IN DEVELOPED COUNTRIES: A CROSS-SECTIONAL STUDY IN CAMEROON

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**Background:** Comorbidities associated with gout are frequently described in developed countries. Data are scarce in sub-Saharan Africa.
**Objectives:** To identify the main comorbidities associated with gout in Cameroon, Central Africa.
**Methods:** We performed a cross-sectional study on patients seen in the Rheumatology department of the Douala General Hospital, Douala, Cameroon, between January 2004 and December 2013. We have included the records of patients with diagnosis of gout according to ACR criteria 1977. The main comorbidities of gouty patients were recorded. A $p<0.05$ was considered statistically significant.
**Results:** We included 511 patients (415 men and 96 women). The mean age was 55.9±10.8 years. The main comorbidities associated with gout in our study are summarized in Table 1.
Metabolic syndrome was present in 101 patients (19.7%). Chronic kidney disease and dyslipidemia were more frequent in rural areas while the obesity and hypertension were more frequent in urban areas ($p<0.05$) [Table 2]. The association between gout and components of metabolic syndrome were all significant ($p<0.001$), particularly for obesity and dyslipidemia in men and hypertension and diabetes in women.

Table 1. Main comorbidities associated with gout

| Comorbidities | n (%) |
|---|---|
| Obesity | 256 (52.2%) |
| Hypertension | 208 (40.7%) |
| Osteoarthritis | 111 (21.7%) |
| Dyslipidemia | 80 (15.9%) |
| Digestive diseases (epigastralgia, gastroduodenal ulcer, upper gastrointestinal haemorrhages) | 74 (14.5%) |
| Diabetes | 52 (10.2%) |
| Chronic kidney diseases | 42 (8.2%) |
| Heart failure | 16 (3.1%) |
| HIV infection | 10 (2%) |
| Others | 13 (2.6%) |

**Conclusions:** Comorbidities are common in Cameroonians with gout like in developed countries. These data should encourage seeking and treating gastrointestinal adverse events and cardiovascular risk factors in gouty patients to reduce morbidity and mortality linked to gout.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3161

## AB0809 EFFICACY AND SAFETY OF A PERSONALIZED NUTRITIONAL DIET IN GOUTY PATIENTS IN CAMEROON: A PILOT STUDY

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**Background:** Many guidelines from different parts of the world mention the impact of diet on gout (1). However, data are scarce in sub-Saharan Africa.
**Objectives:** To evaluate the efficacy and safety of a gouty apurinic personalized diet based on ethnic origin, dietary habits and patient comorbidities.
**Methods:** Gout (177 ACR preliminary criteria) patients with serum urate levels >70g/dL were recruited. Patients were randomized to receive a standard diet apurinic gout or a personalized diet. At 1 month, all patients in the standard diet group were put under the personalized diet.
The primary endpoint was the reduction of serum uric acid at 1 month (M1) and 3 months (M3). Secondary outcomes were the number of gout attacks and changes in anthropometric measures at M1 and M3. A $p<0.05$ was considered statistically significant.
**Results:** Of the 30 patients randomized, 12 patients have not respected their diet. Only 18 were retained in the final analysis: 10 patients on personalized diet group and 8 on standard diet group. The baseline characteristics of both groups were similar at baseline ($p>0.05$). At M1, we have observed a significant decrease in serum uric acid in the personalized diet group compared to the standard diet group (p=0.0001). We have observed 5 acute gout attacks in the standard diet group against 2 acute gout attacks in the personalized diet group (p=0.03). A trend of decrease was observed for all other parameters without significance ($p>0.05$) [Table 1].
At M3, all patients received personalized diet. Initial efficacy was maintained in all the patients of the personalized diet group. For patients of the standard diet group, we observed a significant decrease in serum uric acid (p=0.02). There was no difference in the number of acute gout attacks (p=0.08). A trend of decrease was also observed for all other parameters without significance (Table 1).

**Abstract AB0809** – Table 1. Comparison of personalized diet group and standard diet group at baseline and at 1 month

| | | Baseline | Month 1 | *p** | Month 3** | *p**** |
|---|---|---|---|---|---|---|
| Weight | Standard diet | 90.12±16.72 | 89.37±16.31 | 0.46 | 88.02±52.31 | 0.31 |
| | Personalized diet | 89.30±24.66 | 87.40±23.35 | 0.33 | 86.76±53.46 | 0.06 |
| BMI | Standard diet | 32.63±5.11 | 32.35±8.52 | 0.45 | 30.95±8.23 | 0.12 |
| | Personalized diet | 31.49±8.52 | 30.88±8.25 | 0.43 | 28.74±6.21 | 0.08 |
| Waist-to-hip ratio | Standard diet | 0.89±0.14 | 0.88±0.10 | 0.63 | 0.87±0.21 | 0.09 |
| | Personalized diet | 0.90±0.17 | 0.89±0.13 | 0.44 | 0.88±0.15 | 0.08 |
| Uricemia | Standard diet | 87.37±8.68 | 88.30±12.68 | 0.57 | 75.56±5.97 | 0.02 |
| | Personalized diet | 89±19.21 | 65.32±41.19 | 0.0001 | 59.05±17.13 | 0.0001 |
| Uricemia without urate-lowering therapy | Standard diet | 87.37±8.68 | 88.30±12.68 | 0.57 | 88.30±12.68 | 0.03 |
| | Personalized diet | 89.02±19.21 | 61.15±12.36 | 0.004 | 57.88±12.13 | 0.0001 |
| Uricemia with urate-lowering therapy | Standard diet | 87.37±8.68 | – | – | – | – |
| | Personalized diet | 105.50±10.81 | 75.90±11.85 | 0.0001 | 63.79±15.32 | 0.0001 |
| Acute gout attacks | Standard diet | – | 5 | 0.04 | 0 | 0.08 |
| | Personalized diet | – | 2 | | 1 | |

**p*: baseline vs. Month 1. **Only 7 patients of Standard diet group and 9 patients of Personalized diet group ended the study. ***p*: baseline vs. Month 3.

No adverse events related to both diet group were observed.
**Conclusions:** This study shows that the diet should be personalized in gouty patients according to socio-cultural environment, lifestyle, and comorbidities of each patients. Efforts should be made to improve compliance to diet like other non-pharmacological and pharmacological treatment.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6157

## AB0810 MACROPHAGE MIGRATION INHIBITORY FACTOR IN GOUTY ARTHRITIS

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**Background:** Macrophage migration inhibitory factor (MIF) is proinflammatory, angiogenic and tissue degrading cytokine.
**Objectives:** This study aimed to determine monosodium urate (MSU)-induced MIF production and the role of MIF in gouty arthritis.
**Methods:** Peripheral blood and clinical data were obtained from 98 patients (31 patients with acute gouty arthritis and 67 patients with intercritical gout). Synovial fluid (SF) was obtained from patients with acute gouty arthritis and SF white blood cells and neutrophils were counted. SF and serum levels of MIF, interleukin (IL)-1, IL-8 and leukotriene B4, were measure using enzyme-linked immunosorbent assay (ELISA) and their relationship was analyzed. Peripheral blood mononuclear cells (PBMC) were isolated and cultured with MSU crystal, the production of MIF was determined.
**Results:** SF MIF level was higher in acute gouty arthritis than osteoarthritis. Serum MIF was higher in patients with intercritical gout than patients with acute gouty arthritis or healthy volunteers. SF MIF level was positively correlated with SF WBC and neutrophil counts, IL-1b and IL-8 levels in acute gouty arthritis. Serum MIF level was correlated with IL-1b and IL-8 levels in patients with intercritical gout. MSU crystal induced MIF production in PBMC with maximal effect at 100mg/ml.
**Conclusions:** MIF was highly produced in gouty arthritis and MSU induced MIF production. MIF could be involved in early inflammatory process in acute gouty arthritis.
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**Disclosure of Interest:** None declared
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## AB0811 MTHFR C677T POLYMORPHISM IS ASSOCIATED WITH INCREASE IN HOMOCYSTEINE BUT NOT WITH URIC ACID

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**Background:** Serum homocysteine (sHcy) is currently well recognized as an independent risk factor for cardiovascular and cerebrovascular diseases. Hyperhomocysteinemia is reportedly associated with high serum uric acid (sUA) levels. MTHFR C677T polymorphism is associated with increase in sHcy. Some studies have suggested a positive correlation between MTHFR C677T polymorphism and sUA, but it remains unclear.
**Objectives:** We aimed to evaluate the association between sHcy and sUA as well as MTHFR C677T polymorphism and sUA.
**Methods:** Patients with memory impairment who visited neurology outpatient clinic were enrolled excluding those who were taking medication for the control of hyperuricemia. Hyperuricemia was defined as $>7.0$ mg/dl for male and $>5.6$ mg/dl for female. Hyperhomocysteinemia was defined as $>15$ μmol/l. Clinical laboratory examinations and genotyping for MTHFR C677T polymorphism was performed. Statistical analyses were performed using chi-square, Pearson's correlation coefficients, and ANOVA.
**Results:** Data from 861 subjects (264 male and 597 female) were analyzed. The mean age was 73.2±11.3 years in male and 75.3±10.3 years in female. Male showed significantly higher smoking, alcohol intake, LDL cholesterol, sUA, and sHcy levels, whereas HDL cholesterol, vitamin B12, folic acid were significantly lower compared to female. The prevalence of hyperhomocysteinemia was 38.6% (n=102) in male and 21.4% (n=128) in female. Hyperuricemia was also more common in male with prevalence of 13.3% (n=35) compared to 18.8% (n=112) in female and the mean sUA level was significantly higher in male (5.7±1.4 mg/dl vs 4.6±1.3 mg/dl, $p<0.001$).
sHcy was significantly associated with both folic acid ($r=-0.307$, $p<0.001$) and vitamin B12 ($r=-0.197$ $p<0.001$). Subjects with elevated sHcy levels had an odds ratio (OR) of 2.7 (95% CI 1.4–5.4) in male and 2.0 (95% CI 1.4–3.1, $p=0.001$) in female for hyperuricemia. The genotype frequency of MTHFR C677T was 32.8% (n=282) for CC, 49.8% (n=429) for CT, and 17.4% (n=150) for TT. TT genotype showed association with hyperhomocysteinemia when both gender were analyzed. In male, TT genotype ($r=0.399$, $p=0.007$) was associated with positive correlation between hyperhomocysteineima and hyperuricemia. In female, CT ($r=0.289$, $p<0.001$) and CC ($r=0.240$, $p<0.001$) was associated with positive correlation between hyperhomocysteineima and hyperuricemia. MTHFR C677T polymorphism was not associated with hyperuricemia.
**Conclusions:** Low serum folic acid and vitamin B12 are significant risk factors for hyperhomocysteinema, which reflects the influence of alcohol consumption and vitamin deficiencies on sHcy level. TT genotype of the MTHFR C677T was associated with hyperhomocysteinemia.
A positive association was observed between sHcy levels and sUA levels for both males and females which is in agreement with previous studies. Male having the TT genotype and female having the CT and CC genotype with hyperhomocysteinemia are likely to have higher sUA level.
MTHFR C677T polymorphism is not associated with sUA level, which is inconsistent with recent studies.
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## AB0812 AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA: REVIEW OF 63 CASES

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**Background:** Multiple myeloma is a malignant disorder in which plasma cells accumulate in the bone marrow and produce an entire immunoglobulin (usually IgG or IgA) or only immunoglobulin light chains (kappa or lambda). Multiple myeloma accounts for approximately 10% of hematologic cancers and 1% of all cancers. In recent years there is huge improvement in treatment of patients with multiple myeloma. The milestone of these improvement is the Autologous hematopoietic stem cell transplantation
**Methods:** We analyzed results of 63 consecutive patients (16 male and 47 female) of MM who underwent Autologous hematopoietic stem cell transplantation (ASCT).
**Results:** A review of 63 cases of multiple myeloma seen from 2006 through 2015 revealed that The median age was 59,1 years (range: 38–80) and that 25% of them were male. Inital findings were bone pain in 73,8% of patients, anemia in 14%, renal insufficiency in 11% and hypercalcemia in 34,9%. Proteinuria was noted in 10% and Bence Jones proteinuria was identified in 5,2%. Skeletal roentgenographic abnormalities were seen in 78%. Serum proteinelectrophoresis showed a spike in 83% and hypogammaglobulinemia in 17%. Immunoelectrophoresis of the serum revealed a monoclonal heavy chain in 80% and a monoclonal light chain in the serum, in 5.2% (Bence Jones proteinemia). ASCT was performed in 15 patient (age <65ans); Post ASCT 47,1% of patients achieved complete reponse, 24,2% had very good partial response (VGPR), and 38.7% had partial response (PR).
**Conclusions:** Multiple myeloma is still an incurable disease with pattern of regression and remission followed by multiple relapses raising from the residual myeloma cells surviving even in the patients who achieve complete clinical response to treatment.
**Disclosure of Interest:** None declared
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## AB0813 HIGH PREVALENCE OF UROLITHIASIS DUE TO EXCESS URINARY URIC ACID CONCENTRATION AND CALCIUM EXCRETION IN SOUTH CHINESE GOUT PATIENTS

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**Background:** Urolithiasis greatly impact urate lowering therapy in Chinese gout patients. Benzbromarone is contraindicated and Chinese is high risk of allopurinol hypersensitivity syndrome. Febuxostat is too expensive for many patients. Few study about urolithiasis in Chinese gout patients are presented.
**Objectives:** To investigate the prevalence and risk factors of urolithiasis in south Chinese gout patients.
**Methods:** Patients with primary gout were recruited in the present cross-section study. Urolithiasis was defined as positive stone history and/or ultrasonography. All inpatients with estimated glomerular filtration rate (eGFR) over 30 ml/min/1.73 $m^2$ underwent 24 hours urinary chemistry assay including uric acid (UA), UA concentration, clearance of UA, Cr, calcium, phosphorus, potassium, sodium and chloride. Logistic regression were performed to examine association of urolithiasis with independent variables including age, gender, duration of gout, sUA, previous urate lowering therapy, serum creatinine, eGFR, body mass index, urine pH and 24 hours urinary chemistry assay.
**Results:** (1) Two hundred and nighty-four patients were recruited. Mean age of male (N=255) and female (N=39) were 54.4±16.4 and 67.2±15.3, respectively. Average serum UA was 9.0±2.5mg/dl and 25.9% of patients presented tophi.

Allopurinol, benzbromarone, or a combination of these two drugs had been prescribed in 97 patients (33.0%), 18 patients (6.1%) and 36 patients (12.2%), respectively. The rest 143 patients (48.6%) had not received urate lowering therapy before. (2) One hundred and eleven gout patients (37.8%) complicated with urolithiasis and urolithiasis was observed in 69 of them (62.1%) on ultrasonography. Compared with non urolithiasis group, urolithiasis group had significant higher serum creatinine (1.6±0.6 VS 1.3±0.3 mg/dl], lower eGFR (56.3±18.0 VS 64.1±18.4 ml/min/1.73m$^2$) and higher alcohol overuse (38.7% VS 26.2%) (P<0.05). (3) Among 102 patients performed 24 hours urinary chemical assay, 45 patients complicated with urolithiasis. Urolithiasis group had significantly higher 24 hours urine UA concentration than non-urolithiasis group (30.4±13.1 VS 23.9±11.9 mg/dl, P=0.01). There were no significant difference of other variables between two groups. Prevalence of urolithiasis increased significantly across increasing quartiles of urinary UA concentration (P=0.012, Table 1). (4) Logistic regression suggested that risk factors of urolithiasis were urinary UA concentration grouped by quartile (P=0.05) and urinary calcium excretion [OR 1.26 (1.01, 1.57), P=0.04]. Urinary UA concentration over 24.4mg/dl was associated with increasing risk of urolithiasis (Table 1).

Table 1. Prevalence of urolithiasis among quartiles of urinary UA concentration

| | Quartiles of urinary UA concentration (mg/dl) | | | |
|---|---|---|---|---|
| | I (<17.6) | II (17.6–24.3) | III (24.4–34.9) | IV (≥35.0) |
| Median (mg/dl) | 12.8 | 20.8 | 30.0 | 42.5 |
| Prevalence* | 13.3% (6) | 22.2% (10) | 33.3% (15) | 31.1% (14) |
| Adjusted OR# | 1 | 2.47 (0.66, 9.24) | 5.5 (1.50, 20.72) | 4.58 (1.24, 16.92) |
| P# | – | 0.18 | 0.01 | 0.02 |

*Test for a linear trend P=0.012. #By logistic regression.

**Conclusions:** Prevalence of urolithiasis in Chinese gout patients were high and predicted by excess urinary UA concentration and urinary calcium excretion.
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## AB0814 ONLINE PATIENT INFORMATION RESOURCES ON GOUT PROVIDE INADEQUATE INFORMATION AND MINIMAL EMPHASIS ON POTENTIALLY CURATIVE URATE LOWERING TREATMENT

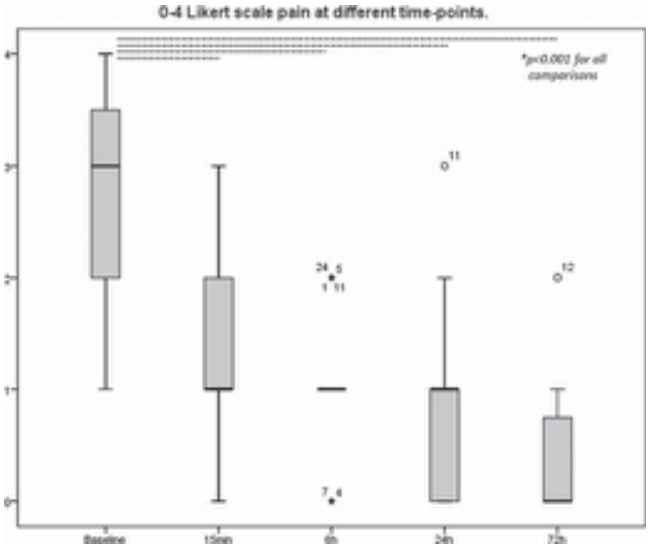
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**Background:** Nowadays patients use the internet to find more about their disease and its management. The accuracy of online gout patient information resources has not been examined before.
**Objectives:** To assess the content, accuracy and readability of freely available online patient information resources against the current understanding of gout.
**Methods:** An internet search was carried out to identify online gout patient information resources from the United States of America (USA), United Kingdom (UK), Australia and Canada in October 2015. Websites aimed at healthcare professionals, those requiring a paid subscription, or focussed on a specific aspect of gout were excluded. Information provided in the websites was compared against 15 key points. If information on a key point was regarded as present, it was classified on a 1–3 Likert Scale (1-inaccurate, 2-acceptable information with some inaccuracy and 3-acurate). Readability was assessed using Flesch-Kincaid Reading Ease score. Fifteen randomly selected websites were reviewed by a binder second reviewer.
**Results:** Eighty-five websites (30 provided by a medical and/or healthcare organisation were selected). Information was provided for a mean (SD) 7.73 (2.85) of 15 key points overall. The websites were more likely to contain information on risk-factors than on treatment of gout (p<0.001). More than 50% provided no information, or had inaccuracies regarding the pathogenesis of gout and over 75% of websites had no or inaccurate information on the role of ULT. Most websites highlighted information on dietary and lifestyle modifications for treating gout and did not emphasise ULT and its potential for cure. The two raters agreed in 80% of occasions on whether information on a particular question was present or not (*k* 0.60). The majority of websites were difficult to read, with information in 68% websites rated as at least fairly difficult.
**Conclusions:** Most of the patient information on gout available online is inaccurate and commonly over emphasises the use of dietary and lifestyle changes as a way of managing gout. The importance of ULT in managing gout and the potential for gout being curable with long-term ULT are not explained well. Moreover, most websites were difficult to read and most on-line resources had inaccuracies regarding the pathogenesis and treatment of gout.
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## AB0815 INTRAARTICULAR TRIAMCINOLONE PLUS MEPIVACAINE PROVIDES A RAPID AND SUSTAINED RELIEF FOR ACUTE GOUTY ARTHRITIS

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**Background:** Gout attacks are often considered as especially painful. Effective treatments for gout attacks - colchicine, NSAIDs, systemic or intra-articular corticosteroids, IL-1 blockers -result in a rapid subsidence of the attacks, but it usually requires 1–3 days (1–3) to relieve the symptoms. Our standard procedure in clinics is to add 2% mepivacaine to intra-articular triamcinolone, as we have repeatedly observed a very rapid and persistent subsidence of pain. Here we aimed to document this outcome in a prospective way.
**Methods:** Consecutive patients with crystal-proven gout and an acute, monoarticular attack were recruited. All cases were treated with an intra-articular injection of triamcinolone plus 2% mepivacaine, according to our clinical practice. Joint pain was registered using a 0–4 Likert semiquantitative scale (0=absent; 4=severe) at baseline and 15min, 6h, 24h, and 72h after the injection. Presence of joint swelling and erythema was also collected at baseline and after 72h. Treatment response after 72h was evaluated by both the physician and the patient on a 0–4 Likert scale (0=no effect; 4=complete resolution). Between-after comparisons were analyzed using Wilcoxon signed-rank test.
**Results:** A total of 24 patients were recruited, median (±SD) aged 64.8 years (±12.7), 22 males. Involved joints were 16 first metatarsophalangeal (1MTP), 5 knees, 2 wrists, and one ankle. Triamcinolone doses ranged from 10mg (1MTP) to 20–40mg (others). Median (p25–75) pain at baseline was 3 (2–3.8), joint swelling was present in all cases, and in 13 cases (54.2%) erythema was observed. After the intra-articular injection, a significant pain reduction was observed at all time-points, even at 15min after the injection, as shown in the Figure. No symptoms rebounds between time-points were reported. Treatment was effective as assessed by both patients and rheumatologists (3 (3–4) and 3.5 (3–4), respectively).




**Conclusions:** This small study confirms a rapid relief of gout attacks with adding mepivacaine to intra-articular corticosteroids, with a significant response even at 15min after the injection. Large, controlled studies should confirm these results.
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**Disclosure of Interest:** M. Andrés Speakers bureau: Menarini, A. Begazo: None declared, F. Sivera: None declared, P. Vela: None declared, E. Pascual: None declared
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## AB0816 GOUTY FLARES AND ATHEROGENIC SERUM LIPID PROFILE IN PATIENTS WITH GOUT

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**Background:** Atherogenic serum lipid profile is prevalent in gouty patients.Recently conducted *in vitro,in vivo and clinical studies* of gout have evidenced proinflammatory effects of LDL-C and antiinflammatory properties of HDL-C (1–3).

**Objectives:** To investigate if atherogenic serum lipid profile in gouty patients predicts gout activity.
**Methods:** A total number of 69 patients (97,1% male) were divided into two groups with regard to the frequency of their gouty flares: group 1 (up to 1 flare per year) and group 2 (2 or more flares per year, with the maximum flare number of 20). Logistic regression model was used to identify the set of metabolic items able to predict frequent flares in gout. The following variables were included in the model: total cholesterol level (border set up at 5,2 mmol/L), HDL cholesterol level (1,03 mmol/L for men and 1,3 mmol/L for women), LDL cholesterol level (3,37 mmol/L) triglicerydes (1,68 mmol/L) and serum uric acid (359 mmol/L). The fit of the selected model to the actual outcome was determined with a set of goodness of fit tests. All analyses were carried out using statistical program SPSS 20.0.
**Results:** Logistic model was acceptable, by showing 74% of correctly predicted cases in a classification table with a cut off value of p=0.5. Hosmer and Lemeshow goodness of fit test was found to be nonsignificant (p=0,881), suggesting that model fit to data well. Two additional goodness-of-fit tests which confirmed those results were Cox and Snell $R^2$ (p=0,195) and Nagelkerke $R^2$ (p=0,275). According to the logistic regression model, the only significant predictor of the gouty flares frequency in patients with gout was the high LDL cholesterol level (p=0,008).
**Conclusions:** More frequent flares in patients with gout were predicted by the higher LDL cholesterol level only. Surprisingly, gouty flares were not predicted by serum uric acid level, as it was commonly thought. HDL cholesterol level, total cholesterol level and level of triglycerides were not found to be the predictors of the frequent gout attacks.
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## AB0817 ANALYSIS OF INTERLEUKIN-1β INHIBITOR (CANAKINUMAB) IMPACT ON ENDOTHELIAL DYSFUNCTION

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**Background:** It is supposed that IL-1β inhibition may be associated with cardiovascular risk reduction [1, 2], but it isn't known what effect of it is on endothelial function.
**Objectives:** To assess canakinumab effects on structural and functional parameters of vasculature.
**Methods:** Open-label prospective study of 20 pts (17 (85%) males and 3 (15%) females) with chronic gout was performed in 2014–2015 y. at the V. A. Nasonova Research Institute of Rheumatology. All patients received one dose of canakinumab 150 mg subcutaneously. Lab parameters (uric acid, cholesterol, triglycerides, hsCRP and interleukin-6 (IL-6) levels), 24 hour BP monitoring, comprehensive Echo-CG, duplex scanning of carotid arteries the intima-media thickness (TIM) measurements of near and far wall were taken from both common carotid arteries (CCA), vascular wall stiffness was evaluated before injection of canakinumab and on days 14 and 120 after. The quantification of serum hsCRP levels was done with highly sensitive immune turbidimetric test, serum IL-6 levels was detected using of "xMAP" technology (Human Grp I Cytokine 27-plex panel) and on the analyzer "BioPlex-200" (Bio-Rad, the USA). Lipid-lowering and antihypertensive therapy was not modified during the study. Statistical analysis was performed using the application package STATISTICA 10.0 (StatSoft.Inc., USA). Differences were considered significant at $p<0.05$.
**Results:** Baseline TIM in the CCA was 0,83 [0.71; 0.94] mm, while by the end of the study it dropped to 0,74 [0.69; 0.84] mm (p=0.022). Median baseline pulse wave velocity (PWV) in the aorta was 14,12 [10; 17] m/s, dropping during the study to 13,1 [11; 14] (p=0,79). Falling down of baseline arterial stiffness index was documented in 13 (65%) pts, and by the end of the study in 7 out of them not a single joint was tender or swollen, hsCRP levels >5 mg/l was in 5 out of 13 pts, who was statistically significantly more rare as compared to pts without positive changes of this index (in 6 out of 7 pts (86%)) ($p$=0.043). Median of serum hsCRP level and IL-6 level in pts who had reduction of PWV was significantly smaller then in others pts at 120 days (respectively, hsCRP level – 2.7 [2.3; 7.7] mg/dl vs 11.5 [6.9; 17.7] mg/dl (p=0.0084) and IL-6 level – 5,9 [3,9; 7.7] pg/ml vs 12,6 [10,8; 22,4] pg/ml) (p=0,44). Based on BP monitoring data no changes from baseline BP measured before injection of Canakinumab, and on Day 14 or Day 120, occurred. Mean levels of cholesterol and triglycerides didn't change as well
**Conclusions:** IL-1β inhibitor Canakinumab may have positive effect on TIM parameters. Effects of Canakinumab on arterial stiffness parameters depend on the potency of anti-inflammatory effect.
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## AB0818 ULTRASONOGRAPHY SIGNS OF MSU URATE DEPOSITION IN PATIENTS WITH HYPERURICEMIA AND EARLY DIAGNOSIS OF GOUT

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**Background:** The role of ultrasonography (US) in diagnosis of gout is not clearly established [1].
**Objectives:** The detection of monosodium urate (MSU) crystals depositions in pts with asymptomatic hyperuricemia (ASHU) and in pts with gout by US examination for early diagnostics of gout.
**Methods:** The study included 84 pts with either ASHU (n=34), or gout (n=50), 72 males and 12 females. The diagnosis corresponded all pts with gout to the criteria developed by S.L. Wallace, and were subjected to joint puncture (1st metatarsophalangeal joint (MTPJ), knee, elbow, ankle) with further synovial fluid analysis under polarized microscopy. Mean age of gout pts was 48,1±12,6 y., disease duration <1 years was established in 12 out of 50 pts (24%); mean age of ASHU pts was 47,21±11,57 y., with mean level of uric acid – 473,71±73,7μmol/l. All pts were subjected to 1st MTPJ US examination with linear 7–17 MHz multi-frequency ultrasonic transducer. Statistica 10.0 package and Biostatistics were used for statistical processing of data. *P* values <0.05 were considered statistically significant.
**Results:** Based on US examination data the "double contour" (DC) sign in the 1st MTPJ was found in 36 (72%) out of 50 gout pts, intra-articular or soft tissue gouty tophi – in 27 (54%) pts, both signs – in 24 (48%) pts. MSU were found in 45 (90%) gout pts by synovial fluid analysis. 1st MTPJ arthritis was established in past medical history in 41 gout pts. In subjects with disease duration <1 years DC sign was found more frequently as compared to pts with disease duration ≥1 years, respectively in 30 (79%), and 6 (50%) ($p$=0,045), same refers to the presence of US tophus signs: in 22 (58%), and 5 (42%) pts ($p$=0,33) respectively; one of the two signs - in 36 (95%), and 6 (50%) pts, respectively ($p$=0,0002). In 4 out of 50 gout pts with only one attack of arthritis in past medical history the DC sign was found in 1 patient, as well as intra-articular or soft tissue tophus - also in 1 patient. The US DC sign in ASHU subgroup was found in 12 (35%) pts, US tophus sign – in 5 (15%) pts, both sings – in 2 (6%) pts. In 17 pts with UA level >420 μmol/l and ≤480 μmol/l the US DC sign was found in 4 (24%) pts. In 12 pts with UA level >480 μmol/l and ≤540 μmol/l the DC sign was found in 5 (42%) pts, and both signs – US DC and US tophus were present in 2 (17%) pts. Elevated uric acid levels >540 μmol/l were detected in 5 pts, the US DC sign was found in 3 out of them, while both signs – in 2 pts. Energy Doppler scanning identified synovitis in 15 (44%) out of 34 ASHU pts.
**Conclusions:** Serum UA levels may predefine US detection of MSU deposition in ASHU pts and in 44% of cases US signs of MSU depositions are combined with subtle signs of inflammation, detected with energy Doppler scanning. Detection rates of US gout signs grow in parallel with disease duration.
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## AB0819 INDIRECT COMPARISON OF URATE-LOWERING THERAPIES FOR HYPERURICEMIC PATIENTS WITH OR WITHOUT GOUT: META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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**Background:** Hyperuricemia is the most significant risk factor for the development of gout, defined as a serum concentration of uric acid at 6.8 mg/dl or greater. Long-term maintenance of serum urate levels below its saturation threshold can reduce the frequency of acute gout flares and resolve the existing tophi.
**Objectives:** To assess the urate-lowering efficacy and safety of febuxostat, allopurinol and benzbromarone in hyperuricemic patients with or without gout.
**Methods:** We included all the randomized controlled trials (RCTs) that compared any urate-lowering medication with placebo or head to head. The efficacy outcomes included the proportions of achieving the target urate level (<6.0 mg/dl) at final visit or last 3 visits and the percentage of gout flares during the first 8 weeks. The safety outcomes included total adverse events (AEs), withdrawals due to AEs and serious AEs. A Bayesian network model was used to compare all interventions simultaneously.

**Results:** Sixteen RCTs (6645 patients) were included in the analysis. All urate-lowering therapies were more likely to achieve the target urate level at final visit and last 3 visits than placebo, but had an inconclusive higher risk of gout flares. Furthermore, all of the febuxostat doses (40, 80, 120, 240 mg/day) had a higher proportion of achieving the target urate level at final visit than allopurinol. With febuxostat dosages increased, more patients achieved the target urate level. Febuxostat 240 mg/day was the most effective drug for serum urate normalization. Regarding safety, there were no significant differences among urate-lowering therapies and placebo for total AEs, withdrawals due to AEs and serious AEs, except that allopurinol had a higher risk of total AEs than febuxostat 120mg/day.

**Conclusions:** Compared to placebo, all urate-lowering therapies are effective in achieving the target urate level for hyperuricemic patients. Febuxostat is more efficacious than allopurinol for serum urate normalization.

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**Disclosure of Interest:** None declared

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## AB0820 CALCIUM PYROPHOSPHATE DIHYDRATE AND HYDROXYAPATITE CRYSTAL INDUCED METABOLIC DISEASES – SAME OR DIFFERENT?

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**Background:** Arthropathy induced by calcium pyrophosphate dihydrate [$Ca_2P_2O_7.2H_2O$] (CPPD) crystals (chondrocalcinosis, pseudogout, pyrophosphate arthropathy) and arthropathy induced by hydroxyapatite [$Ca_5(PO_4)_3(OH)$] (HA) crystals (apatite rheumatism, Milwaukee syndrome) are regarded as distinct clinical entities [1–3].

This distinction is justifiable clinically by the different localization and symptoms of CPPD and HA crystal depositions, and is supported by the observation of the crystals in conventional hematoxylin-eosin (H-E) stained histological sections. In H-E stained sections viewed under polarized light in case of chondrocalcinosis the CPPD crystals are detectable, while the more soluble HA crystals in case of apatite rheumatism are not.

The probability of identifying crystals is much higher in unstained sections viewed under polarized light, than in H-E stained ones [4,5].

**Objectives:** The aim of this study was to detect and compare the prevalence of CPPD and HA crystals in H-E stained and unstained sections in clinically diagnosed chondrocalcinosis and apatite rheumatism.

**Methods:** Eighteen (18) tissue samples of 10 patients with clinically diagnosed chondrocalcinosis, and ten (10) tissue samples of 3 patients with clinically diagnosed apatite rheumatism were studied in serially cut histologic sections of formalin fixed and paraffin embedded tissue blocks. The sections stained with H-E and unstained sections were viewed under polarized light with an Olympus BX51 polarization microscope.

**Results:** The H-E stained sections were examined under polarized light; CPPD crystals were detected in all 10 patients with clinically diagnosed chondrocalcinosis, and HA crystals were detected in 1 of 3 patients with clinically diagnosed apatite rheumatism.

In unstained sections viewed under polarized light CPPD and HA crystals were present in all 13 patients with different prevalence (dominance).

| Clinical diagnosis | Stained with HE | | Unstained | |
|---|---|---|---|---|
| | CPPD | HA | CPPD | HA |
| Chondrocalcinosis n=10 | 10 | 0 | 10 | 10 |
| Apatit rheumatism n=3 | 0 | 1 | 3 | 3 |
| Total n=13 | 10 | 1 | 13 | 13 |

In unstained sections CPPD dominated the crystal deposits in 6 of 13 patients (with sporadic presence of HA). The presence of HA crystals was absolutely dominant in crystal deposits in 4 of 13 patients (with sporadic presence of CPPD). The presence of CPPD and HA crystals was equal in 3 of 13 patients.

**Conclusions:** There is a difference in the shape, size, and intensity of birefringence of CPPD and HA crystals, furthermore in their solubility in conventional fixatives (formalin) and other aqueous solutions (e.g. dyes).

The presence of CPPD and the absence of HA crystals in H-E stained histologic sections supports the distinction between chondrocalcinosis and apatite rheumatism.

In unstained histologic sections variable amounts of CPPD and HA crystals were demonstrated in clinically diagnosed cases. Based on these findings the chondrocalcinosis and apatite rheumatism may represent different clinical manifestations and symptoms of the same metabolic disorder.

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## AB0821 EVOLUTION OF THE VALUES OF ALKALINE PHOSPHATASE (ALP) IN PATIENTS TREATED WITH ZOLEDRONIC ACID AND DIAGNOSED WITH THE PAGET'S DISEASE OF BONE

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**Background:** The indication or use of zoledronic acid on the Paget's disease of bone was approved in 2005. Recent studies point out the administration of a single intravenous dose of this medicine as the first therapeutic option.

**Objectives:** The aim of this study is to determine whether there is improvement in the ALP values among the patients with Paget's disease of bone after the administration of the zoledronic acid and to analyze whether this improvement is greater in the group previously treated with oral bisphosphonates or in the group who have not received prior treatment.

**Methods:** This is a retrospective study which included 49 patients with Paget's disease of bone that were examined by the rheumatology department and that have been registered in a retrospective database since 2010.

The independent variables included were age, gender, smoking habits, presence of diabetes mellitus, date of first treatment, doses received, corticosteroid therapy, presence of concomitant inflammatory disease, complications after treatment, fractures after the administration of the drug and pretreatment with oral bisphosphonates.

**Results:** The mean age of patients was 75±9,84 years [53–97]. 25 patients (51%) were male and 24 (49%) were female. 29 patients (59.2%) non-smokers, 10 (20.4%) former smokers, and 10 (20.4%) current smokers. 9 patients (18.4%) were diabetic. 26 patients had not received prior treatment with oral bisphosphonates, while 23 had been previously treated. 2 patients were treated with corticosteroids. 7 patients had active cancer, one patient had rheumatoid arthritis and one patient had another type of inflammatory disease. One patient developed fever as a post-infusion complication; however, this side effect did not require the discontinuation of therapy. Two patients required reinfusion due to the resurgence of the Paget and due to the high levels of ALP after the first dose. The mean dose received was 1.12± 0.389. One patient had a fracture after the administration of the drug.

There is a statistically significant difference between the average ALP prior to the initiation of treatment with zoledronic acid and after the treatment in both groups of patients. Nevertheless, when comparing both subgroups of patients (treated or not previously with bisphosphonates), there is a greater difference in the subgroup of patients who had not received prior treatment compared to those that had been treated with oral bisphosphonates.

**Conclusions:** * Zoledronic acid treatment is effective in reducing the ALP levels in patients with Paget's disease of bone.

* The difference in ALP levels after the zoledronic acid administration with respect to the previous ones is higher in the group of patients not previously treated with oral bisphosphonates.

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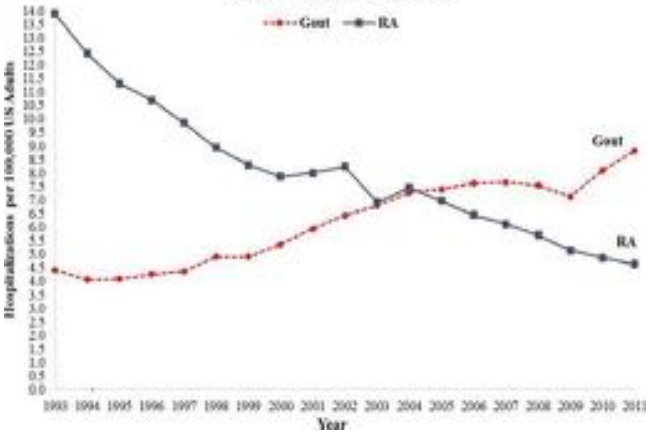
## AB0822 HOSPITALIZATION TRENDS OF GOUT AND RHEUMATOID ARTHRITIS IN THE UNITED STATES: A TALE OF TWO ARTHRITIDES

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**Background:** Gout and rheumatoid arthritis (RA) are the two most common

inflammatory *arthritides*. As hospitalizations for these conditions are known to incur substantial resource use, hospitalization trends and associated costs provide key benchmarks of disease burden. Varying levels of perceived success in their care and changing epidemiology (mainly for gout) may have made a substantial impact over recent years; however, relevant data are scarce.
**Objectives:** To examine hospitalization trends of gout and rheumatoid arthritis in the US.
**Methods:** We examined trends in the annual hospitalization rate of gout and RA using the US Nationwide Inpatient Sample (1993–2011).
**Results:** From 1993 to 2011, the annual hospitalization rate for patients with a principal diagnosis of RA declined by 67% from 13.9 to 4.6 per 100,000 US adults ($p<0.001$), whereas that for gout doubled from 4.4 to 8.8 per 100,000 US adults ($p<0.001$), reversing the hospitalization rates between the two conditions over the past two decades. These trends persisted among subgroups by age, sex, race, and geographic region (all p-values $<0.001$). Approximately 60% of RA admissions and 2% of gout admissions were associated with total joint replacement or other major joint surgeries; the frequency trend of these surgeries paralleled the declining trend in RA hospitalizations (all p-values $<0.001$). The hospital costs also reflected the hospitalization trends, resulting in $58,003 (2011 USD) per 100,000 US adults for gout and $55,988 per 100,000 US adults for RA in 2011.

Figure 1. Annual Rate of Hospitalization for Patients with a Principal Diagnosis of Gout and Rheumatoid Arthritis




**Conclusions:** These nationally representative inpatient data indicate that both primary hospitalization rates and the inpatient economic burden for gout have increased substantially over the past two decades, whereas those for RA have declined considerably. These trends reflect both suboptimal gout care in addition to its increasing prevalence; these data also provide a key reassuring benchmark for the perceived improvement in RA care, thereby preventing joint replacements. These data support the critical need to improve gout prevention and care.
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## AB0823 HOW CURABLE IS GOUT? EXPERIENCES FROM A RHEUMATOLOGY CLINIC

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**Background:** In spite of good treatment options results in surveys of gout have been disappointing. In general practice only 50% of gout pt.s are put on urate lowering treatment (ULT) and of these less than 50% reach the curative treatment target (TT)(p-Urate $<0.36$ mmol/l) rendering many pt.s prone to experience continuous disease activity or repeating flares. In order to improve gout treatment EULAR and ACR have elaborated guidelines based on the treat to target concept with gradually intensified ULT combined with flare prophylaxis.
**Objectives:** To evaluate the eligibility and effectiveness of the EULAR/ACR guidelines in clinical practice.
**Methods:** 100 consecutive pt.s diagnosed with crystal proven gout were offered personal disease information and a standardized treatment regime. ULT was started with allopurinol (ALL) 100 mgs daily and the dose was gradually increased at follow up visits typically every 6 weeks until TT was reached. Pt.s with known or new incident ALL intolerance were treated with/changed to febuxostat (FEB) or benzbromaron (BEN). All pt.s were unless contraindicated offered flare prophylaxis with colchicine (COL) 0.5 mgs bid as long as they had clinical symptoms or were dose escalated in ULT. The pt.s were offered to be followed until their reached "Clinical Remission" defined as TT reached for 3 months and no flares and no flare prophylaxis for the last month.
**Results:** 88 males (62,1±13,6 (SD) yr) and 12 females (74,1±6,9 yr) were included. Mean disease duration was 8,6±6,9 years. 18 had mon-, 37 oligo-, 25 polyarticular, and 20 had tophaceous gout. Recently affected joints included MTPs: 63%, midfoot/ankles: 57%, knees: 57%, hands/wrists/elbows: 47%. Most patients had comorbidity in the form of CVD: 36%, Hypertension: 80%, DM2: 28%, and nephropathy: 29%. 72% had Metabolic Syndrome. At entry 15 pt.s were on ALL treatment. P-urate was initially 0.53±0.11 mmol/l in untreated pt.s and 0.46±0.10 mmol/l in ALL treated pt.s.
93 pt.s started/continued ULT (ALL: 86, FEB: 12, BEN: 7). 85% reached TT after mean 4.7±3.9 months. 40% reached p-Urate $<0.40$ mmol/l. Median ALL dose was 300 mgs daily, 17% and 11% needed 450 and 600 mgs respectively. 90% received COL prophylaxis with mean treatment duration of 7.6±5,8 months. "Clinical Remission" was reached in 82 of 100 gout pt.s after mean treatment duration of 10.4±5.6 months. The mean number of visits were 5.5±2.4 and follow up timewas11.1±5.6months. The 18 patients who did not reach "Clinical Remission" either did not want any treatment (n=3), did not want ULT due to previous experience with flares (n=4), had bad compliance (n=6), could not reach TT due to co-morbidity with nephropathy (n=2), or were due to AEs satisfied with insufficient ULT and continuous COL treatment (n=3).
**Conclusions:** Reaching a good treatment result in gout still is challenging due to extensive morbidity and co-morbidity. This study shows that a good clinical response can be achieved in the majority of patients when given personalized disease information and long term follow up with long term flare prophylaxis in compliance with the EULAR/ACR guidelines. It is suggested that rheumatologists assume the role of following gout patients until they have reached TT and clinical remission and subsequently can be followed in general practice.
**Disclosure of Interest:** None declared
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## AB0824 SYNOVIAL FLUID ANALYSIS IN A RHEUMATOLOGY DEPARTMENT. PAST AND PRESENT

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**Background:** For decades the Departments of Rheumatology have used synovial fluid analysis for the differential diagnosis of various arthropathies, especially microcrystalline diseases. However, it is possible that access to new diagnostic techniques and new treatments has changed the frequency and characteristics of synovial fluid analysis.
**Objectives:** To compare the frequency and findings in synovial fluid analyses in two periods 10 years apart.
**Methods:** Retrospective cross-sectional study evaluating the synovial fluid analysis reports from a Rheumatology Department (including outpatient, inpatient and emergency departments) carried out for a 4-year period (2012- 2015). The results were compared with those obtained in a previous study conducted between 1998–2005.
**Results:** During the last 4 years we have analyzed a total of 440 samples of synovial fluid, with an average of 110±24.8 samples per year (range: 135–78), while in the previous study (1998–2005) 1,881 synovial fluid samples were analyzed, with an average of 235±54.8 samples per year (range: 326–162), decreasing the number of fluid analysis evaluations by 53%. In 31.8% of the current samples and in 18.8% of samples of the previous study microcrystals were detected. The identification of monosodium urate crystals (MSU) were observed in 50% and 49.1% of the current vs. the previous analysis of the samples, respectively, whereas calcium pyrophosphate dihydrate crystals (CPPD) were present in 44.2% and 47.4%, respectively. The identification of both crystals in the same sample (UMS + CPPD) was reported in 6% and 1% of the analyses in the current and previous study, respectively. In both studies, MSU crystals were more frequent in males (83% vs. 89% in the current and previous study), whereas in women CPPD crystals were observed in 48% and 64% of current and previous analyses, respectively.
**Conclusions:** In recent years a decrease in the number of synovial fluid analysis is observed. Although the proportion of synovial fluid analyses from pathologies other than crystal-induced arthritis has decreased, the proportion of detectable UMS and CPPD crystals has not changed.
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**Disclosure of Interest:** None declared
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## AB0825 SURVEY ON MANAGEMENT OF GOUT AND HYPERURICEMIA AMONG THAI PHYSICIANS

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**Background:** Gout is the most common inflammatory arthritis in men. Suboptimal treatment of gout has been reported[1]. To improve quality of care, it is essential to identify problems.

**Objectives:** To assess management of gout among physicians in Thailand.
**Methods:** A cross-sectional survey was conducted among physicians in Thailand. A questionnaire designed to evaluate knowledge regarding management of hyperuricemia and gout was sent to 3,916 doctors between December 1, 2011 and January 1, 2012. Only doctors having experience in taking care patients with hyperuricemia and gout were included in this study.
**Results:** A total of 742 (19.1%) questionnaires were returned. Six hundreds and seven (81.8%) participants had experience of hyperuricemia and gout management. Of total, 271 (44.6%) advised patients on non-pharmacologic management of hyperuricemia, as follows: stop alcohol drinking, 262 (43.2%); weight reduction, 223 (36.7%); stop entrails and gut, 216 (35.6%); stop purine rich vegetables, 198 (32.6%); and stop poultry, 196 (32.3%).
Regarding treating acute gout, colchicine was the most frequently used, 582 (95.9%) and 157 (27.0%) managed with high dose regimen, followed by non-steroidal anti-inflammatory drugs (NSAIDs) (88.8%), corticosteroid (47.1%), physiotherapy (33.9%), and topical NSAIDs (25.3%). Five hundreds and ten (84.0%) physicians used colchicine as the first medication for arthritis prophylaxis while only 36 (5.9%) doctors chose NSAIDs.
Three hundred and sixty nine (67%) of 575 respondents set the target of SUA of urate lowering therapy (ULT) less than 6 mg/dl. Among uric lowering agent, allopurinol was the most well-known, 592 (97.5%), followed by probenecid, 426 (70.2%), benzbromarone 244 (40.3%), and sulfinpyrazone, 140 (23.1%). Four hundred and eighty eight (80.4%) of respondents would hold or stop allopurinol sometimes along the course of allopurinol treatment. Ninety five (15.7%) and 58 (9.6%) held allopurinol when having gouty attack and acute illness, respectively. Reasons for stopping allopurinol were, as follows: normal serum uric acid for 5 years, 324 (53.4%); no tophi for 5 years, 206 (33.9%); no symptoms for 5 years, 224 (36.9%); no arthritis, no tophi, and normal serum uric acid for 5 years, 86 (14.2%); and no arthritis and normal serum uric acid for 5 years, 55 (9.1%).
**Conclusions:** In Thailand, physicians gave patient education less than 50%, and some of advice was not correct as evidence-based studies. Colchicine was commonly used to control acute gout; however, some of doctors still used a high dose regimen which may result in more toxicity. Approximately 30% of physicians did not keep the target of SUA when treating with ULR as the general accepted target. To improve overall quality of care for gout and hyperuricemia patients, education should focus on specific problems.
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**Acknowledgement:** The authors gratefully acknowledge the physicians of Thailand who generously participated in this study.
**Disclosure of Interest:** None declared
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## AB0826 DEVELOPMENT AND PILOT TESTING OF AN ONLINE GOUT EDUCATION TOOL – MYGOUTCARE®

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**Background:** Recent management guidelines for gout have identified unmet educational needs in patients with gout. Qualitative studies have documented that there is a paucity of patient-focused materials to facilitate ongoing patient-physician communication.
**Objectives:** To develop and test a web-based interactive educational resource for patients with gout tailored to improve their knowledge. This electronic platform has the potential to educate patients about gout and help facilitate communication with their physician to improve long term outcomes.
**Methods:** The website was developed in four phases. 1. Two advisory panels - 30 gout patients and 10 gout experts iteratively reviewed pre-identified content areas of modifiable gaps in pathogenesis, natural history and treatment goals from previously conducted focus groups[1]. They evaluated the design (graphics and lay out) of the website and provided written input. 2. Incorporation of a validated knowledge questionnaire[2] on gout and a 5-minute post-survey to assess knowledge about critical take-home messages and satisfaction with their physician's care. 3. With a team of web designer and health informatics expert content areas were tailored in the website so the patient could walk through their own journey to learn various aspects of gout including triggers of flares, comorbidities, pharmacologic and non-pharmacologic treatment, healthy gout diet, and lifestyle choices. 4. Beta testing by patients with gout in clinics for clarity and usability. The website is called MyGoutCare® and in the pilot study, the patient completes a baseline survey of demographics and gout knowledge, reviews the website and generates a list of customized questions (Mygoutreport®) to discuss at the upcoming visit with their physician. They next complete a post-survey within two weeks of the physician visit. Data was analyzed using a paired t-test and presented as mean change in scores between post and baseline surveys.
**Results:** 10 patients beta-tested the website for clarity, format, and flow. In the ongoing pilot study 22 subjects (mean age of 57 years, disease duration of 9.5 years, and 3–5 flares per year) were recruited from general medicine, podiatry, and rheumatology clinics and have completed MyGoutCare®. They were extremely receptive of an e-learning tool that was accessible 24/7. Pre-survey scores (0–10) on knowledge questions improved significantly (20%) when compared to post-survey scores with mean (SD) at -1.95 (1.76), $p<0.001$. All subjects reported satisfaction with the discussion on the natural history of disease and treatment choices. Most importantly they reported actionable changes moving forward, such as decision to continue lifelong urate-lowering therapy, compliance with monitoring serum urate, and dietary changes to achieve flare-free status.
**Conclusions:** Our preliminary data suggests web-based patient-focused materials can serve as a practical tool to positively impact ongoing educational needs of patients in busy clinical practice. It remains to be seen if this will lead to better long term outcomes and improve patient-physician interactions.
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**Disclosure of Interest:** P. Khanna Grant/research support from: research supported by investigator initiated grant to University of Michigan by AstraZeneca, A. Rankin: None declared, L. An: None declared, D. Khanna: None declared
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## AB0827 HIGH PREVALENCE OF HALLUX VALGUS IN GOUTY PATIENTS REQUIRING URATE LOWERING THERAPY

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**Background:** Hallux valgus (HV) is a common pathology leading to pain and deformation of the first metatarsophalangeal joint (MTP1). Gout preferentially affects MTP1 joint and gives disability and pain. It was suggested that gouty patients could have more severe hallux valgus.
**Objectives:** We aimed to determine: 1) the prevalence of HV in gouty patient starting urate lowering therapy (ULT) and 2) the potential factors associated with HV.
**Methods:** In this transversal single center study, we included patient with proven gout (presence of monosodic urate crystal in synovial fluid) requiring ULT. All patients underwent ultrasonography of MTP1s and radiography of the feet. Demographic and clinical characteristics were collected for each patient. Serum uric-acid (SUA) level was assessed at baseline. One trained ultrasonographer, blinded to radiographic measure, assessed at the MTP1 joints, US-evidenced urate deposits (double contour [DC] sign and/or tophi) before starting ULT. HV was analyzed, blinded to clinical and US data, according to the radiographic measure of hallux abductus (HA) angle, and the intermetatarsal (IM) angle. HV was defined by HA angle $\geq 20°$ and/or IM angle $\geq 10°$. Correlation between US findings and different HV angles was estimated by the Spearman coefficient of correlation.
**Results:** A total of 43 patients (93% of male patients) with untreated proven gouty patients were studied. The median age was 63.0 [IQR 57.0–73.0] years old. Median disease duration was 3.0 [1.0–6.0] years. Clinical tophi were found in 24% of patients. The median MDRD creatinin clearance and serum uric acid level were 63.0 [IQR 39.8–78.0] ml/mn/1.73m$^2$ and 507 [IQR 446–601] $\mu$mol/l, respectively. Ultrasound assessment of MTP1 joints revealed a DC sign and tophus in 59.3% and 69.8% of joints, respectively. The median size of US tophi were 11.7 [IQR 9.4–13.7] mm. Radiography found HV in 61.9% of feets (72% of patients). The median IM and HA angles were 8.9 [IQR 7.0–10.0] mm and 20.5 [IQR 15.1–26.0] mm, respectively. The percentage of MTP1 joints with US tophus or DC sign was not significantly higher in patients with HV. No correlation was found between the size of US tophus and HA angle ($P$=0.54). However, IM angle tended to be correlated with the size of US tophus ($P$=0.08). We did not observe any correlation between age, gender, SUA levels, presence of clinical tophus, creatinine clearance, disease duration, number of attacks and presence of HV.
**Conclusions:** Our results suggest a high prevalence of HV in gouty patients requiring ULT. Despite a tendency to have an association between US tophus size and IM angle, we did not observed any correlation between size of tophus and presence of HV. Our patients having a long disease duration, we might hypothesize that a sooner treatment could prevent the apparition of HV in these patients.
**Disclosure of Interest:** None declared
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## AB0828 CHANGING TRENDS IN RADIOLOGICAL PREVALENCE OF PAGET'S DISEASE OF THE BONE IN LANCASHIRE, UK

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**Background:** It is widely recognised that the United Kingdom has a very high prevalence of Paget's disease of the bone (PDB) alongside Western Europe, Australia and New Zealand.
In 1980, Barker et al (1), concluded from a meta-analysis of surveys done throughout 31 towns in Britain, that Lancashire showed to be a remarkably localised area of high prevalence of PDB. In 2006, Cooper et al (2) updated the prevalence of PDB in certain British centres and found prevalence rates had fallen by 50%.
**Objectives:** As there have been no further studies around the Lancashire area since, we aim to build on the current literature and present the prevalence of PDB in some local towns within Lancashire, 20 years later.

**Methods:** We began with Southport and Ormskirk the NHS trust whose patients are geographically located within the county of Lancashire. A computer generated random sample was listed for all plain x-rays that include entire lumbar vertebrae, pelvis, sacrum and femoral heads in those aged over 55. We identified 1000 patients whose unique hospital numbers were entered into the PACS system to view each x-ray.
**Results:** Out of 1000 patient x-rays only four were found to have definite evidence of PDB, all confirmed with radiological report. This gives a prevalence rate of 0.4%. Of these, 50% were female and the age ranged from 72–88 years.
**Conclusions:** Southport and Ormskirk towns lie just on the verge of the Lancashire focus (Lancaster, Preston, Bolton, Wigan, Burnley and Blackburn) therefore using the methodology, it was assumed that prevalence rates would be as high (4–8%) as other Lancashire's towns. (1). Consideration to the high socioeconomic status of many –albeit an older population- that live in the studied area and perhaps other environmental factors might explain the low prevalence (0.4%) of PDB. The influence of genetic factors seems less evident.
Additionally, the overall downward trend of prevalence rates in the UK, as hypothesised by Cooper et al (2), could also explain our findings.
This is an area that would be useful to investigate in further studies. An initial plan to re-study a high focus area such as Lancaster town, using the same methodology, might be extremely valuable.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3222

## AB0829 2012 AMERICAN GUIDELINES FOR THE MANAGEMENT OF GOUT AS SEEN BY FAMILY DOCTORS IN FRANCE

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**Background:** Gout is a common and potentially serious rheumatological disease. Its management in France remains inadequate, with target serum uric acid (SUA) levels being reached in 20% of cases. American guidelines for the management of gout were released in 2012.
**Objectives:** Our aim was to assess whether family doctors in Auvergne, France, agreed with the 14 recommendations for managing gout by mailing them a questionnaire.
**Methods:** An anonymous questionnaire was mailed to all the family doctors in our region in November 2014.
**Results:** The response rate was 40% (n=505/1263). Of the 505 family doctor respondents (FDRs), 60% had been in practice for more than 20 years. Some 56.2% were in practice in rural areas, and 53.6% followed on average 5 to 20 gout patients.
Management of acute gout: 90.7% of FDRs agreed with pharmacological management within 24 hours of the attack; 95% of FDRs agreed with using colchicine, 72% short-course nonsteroidal anti-inflammatory drugs, and 16.6% corticosteroids; 81% approved of continuing hypouricemic therapy during the attack.
Management of chronic gout: 61.6% agreed with not treating asymptomatic hyperuricemia. Allopurinol or febuxostat are used as the first-line therapies according to 88.7%. Half of respondents lowered target SUA when gout was tophaceous.
**Conclusions:** The guidelines generally met with the approval of family doctors in Auvergne (72% agreement). They were also confirmed on a European level in 2014. Their use should be disseminated with, however, some additional clarifications, particularly for the management of chronic gout.
**Disclosure of Interest:** None declared
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## AB0830 IRON METABOLISM: ASSOCIATION OF FERRITIN WITH SERUM URATE AND GOUT

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**Background:** Iron homeostasis is a tightly regulated set of biochemical processes. Transferrin and its cell-surface receptor regulate iron uptake and ferritin sequesters free iron and acts as a store for excess iron from intra- and extra-cellular pools. Ferritin has been positively associated with serum urate in the National Health and Nutrition Examination Survey III (NHANES III) [1]. There have been observational and interventional studies suggesting a role for iron as a trigger for gout flares, which may be due to a number of pro-inflammatory activities associated with iron [2, 3]. Consistent with this, genetic variation in the transferrin receptor is associated with gout and with an increased likelihood of self-report of an iron-rich food as a trigger of flares [2].
Genetic variation in the transferrin receptor is associated with gout and with an increased likelihood of self-report of an iron-rich food as a trigger of flares [2].
**Objectives:** To replicate the association of ferritin with serum urate and to test for association of ferritin with gout.
**Methods:** For the serum urate association analysis, African-American subjects from the publicly available Jackson Heart Study were included (693 females and 567 males). Subjects who self-reported taking diuretic or urate-lowering medication/s, or who had kidney disease or gout, were excluded. For the gout analysis 93 individuals were included, comprising 60 controls (all males) and 33 gout cases (4 females and 29 males). Linear regression analysis using R 3.2.0 and adjusting for age and body mass index was done to test for association between ferritin and serum urate. An unpaired *t* test was used to test for association between gout and plasma ferritin.
**Results:** A positive association of serum ferritin and urate was found in both males ($\beta$=1.02E-04 pmol/L, $P$=9.6E-03) and females ($\beta$=1.95E-04pmol/L, $P$=7.1E-04) in the Jackson Heart Study. Plasma concentrations of ferritin were elevated in gout cases (Mean±SD; 320.6±167.1 ng/mL) compared to controls (69.45±63.41 ng/mL) ($P<1x10^{-4}$).
**Conclusions:** The associations between ferritin and both serum urate and gout implicate iron metabolism in gout. While it is not possible to assign causality from this observational study, the previously reported association of the transferrin receptor with gout [1] is consistent with iron metabolism having a causal role in gout.
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## AB0831 LOW EDUCATION LEVEL AS A PREDICTOR OF GOUT IN WESTERN SWEDEN

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**Background:** Gout was previously regarded a disease of the affluent. Knowledge about the association between gout and socioeconomic status in modern times is limited.
**Objectives:** To investigate the association between gout and socioeconomic factors in a population based register study in a large region in Sweden.
**Methods:** All patients receiving ≥2 diagnoses of gout on at least two separate occasions in primary or secondary care or 1 diagnosis by a specialist in Rheumatology in Västra Götaland in the years 2007–2012 were identified by ICD10 codes in a regional database of health-care utilization. 3189 such patients were identified. The date of the first diagnosis was defined as the index date. A previous validation study of cases identified in this manner confirmed that this case definition is highly consistent with a diagnosis of gout as defined by established criteria (PPV >80%)(1).
For each case, up to 5 controls matched for age, gender and place of residence at the time of the first gout diagnosis were chosen by the Statistics Sweden agency (SCB) (N=14946).
Common comorbidities known to be associated with gout (ischemic heart disease, heart failure, atrial fibrillation, hypertension, hyperlipidemia, diabetes and renal failure) prior to the index date were retrieved from the regional database of health-care utilization based on ICD10-codes.
Data on education level and income at the index year was collected from the Longitudinal Integration Database for health Insurance and Labor market studies (LISA). The database holds annual registers since 1990 on all individuals above 16 years of age registered in Sweden.
**Results:** Data on education level and income was analyzed for cases and controls belonging to the working-age population as defined in Sweden (aged 15–74 years). Shorter education, <12 years, was significantly more common among cases. Yearly income was lower among cases irrespective of educational length (Table 1). Cases had significantly more pre-index comorbidities compared to the controls. In a subgroup analysis of 1084 cases and 6117 controls of working age without any cardiovascular- or renal comorbidity, educational level and income was still significantly lower among cases (data not shown).

Table 1. Education and income for individuals aged 15–74 years

| Educational length in years | | | | Mean yearly income in EUR | | |
|---|---|---|---|---|---|---|
| | Cases, N (%) | Controls, N (%) | p-value | Cases | Controls | p-value |
| ≥12 | 406 (20) | 2730 (28) | <0.001 | 22830 | 26230 | 0.037 |
| <12 | 1598 (79) | 6961 (71) | | 11850 | 12930 | 0.021 |

*1% of cases and controls had missing info on educational length.

**Conclusions:** Low education level and income are predictors for gout in the working age population. The effects of education do not seem to be largely/only mediated via cardiovascular- or renal comorbidity, supporting that other factors

possibly related to lifestyle or occupational exposures are of importance for gout development.

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**Disclosure of Interest:** None declared

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## AB0832 INCREASED SERUM URIC ACID (SUA) LEVELS ARE A COMMON FINDING IN PATIENTS WITH HIGH BLOOD PRESSURE, INSULIN RESISTANCE, OBESITY AND CARDIOVASCULAR (CV) DISEASE

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**Objectives:** To evaluate the connection between SUA and severity of coronary heart disease (CHD) assessed by angiography in patients with CHD.

**Methods:** 198 patients (75.8% men) undergoing cardiovascular rehabilitation at the Institute "Niska Banja" from October 1, 2014, to January 31, 2015, were evaluated. Mean (SD) patient age (62.1±10.4), prevalence of patients with 3-vessel coronary artery disease with stenosis >70% (31.3%), coronary artery bypass grafting (CABG) (37.4%), percutaneus coronary intervention (PCI) (38.9%), primary PCI (32.8%), mean ejection fraction (50% ±11). Prevalence of hyperuricemia (>386 μmol/l) 33.3%, hypertension 85.9%, hypelipoproteinemia 81.8%, diabetes mellitus 24%, family history of CHD (47%) and mean number risk factors 2.65. Patients were separated into a normal SUA group (n=132, with SUA <386 μmol/L) and a high SUA group (n=66, with SUA ≥386 μmol/L).

**Results:** Patients with high SUA had significantly higher 3-vessel coronary artery disease with stenosis >70% (40.9% vs. 26.5%; P=0.04), low ejection fraction (EF<34%)(19.7% vs. 8.3%; p=0.021), obesity (27% vs. 14.4; P=0.03), significantly higher triglycerides (2.38±1.7 vs. 1.88±1.44; P=0.028) and serum creatinine (111.5±46 vs. 90±21; p<0.001).

**Conclusions:** SUA levels were independently associated with EF in patients with CHD. Hyperuricemia is associated with severity of CAD- 3-vessel coronary artery disease with stenosis >70%.

**Disclosure of Interest:** None declared

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## AB0833 INVESTIGATION ON ALLELE FREQUENCY OF RS9263726 IN SOUTH CHINA

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**Background:** Gout is caused by chronic elevation of serum uric acid levels above the saturation point for monosodium urate crystal formation. Allopurinol, which can inhibit xanthine oxidase and decrease the formation of uric acid, is widely used as a primary therapy for the treatment chronic gout and hyperuricemia in China. However, some patients may develop allopurinol-induced life-threating severe cutaneous adverse reaction (SCAR). Hung and colleagues [1] in Taiwan reported a strong association between HLA-B*5801 and allopurinol-induced SCAR, and replicated by following studies in different areas and countries, including China [2]. Previously, Tohkin and colleagues [3] in Japan carried out a genome wide association study (GWAS) and indicates that rs9263726 in PSORS1C1, also significantly associated with allopurinol-related SCAR, is in absolute linkage disequilibrium (LD) with HLA-B*5801. Rs9263726 is expected to substitute HLA-B*5801 genotyping in clinical application for predicting the onset of allopurinol-induced SCAR.

**Objectives:** To investigate the allele frequency of rs9263726 in patients with gout or hyperuricemia as well as healthy volunteers from South China. Compare clinical characteristics between different genotype of rs9263726.

**Methods:** We enrolled 171 patients with gout or hyperuricemia which was diagnosed by clinicians. And 191 healthy volunteers with age and sex match were taken as controls in this study. Blood samples were collected and DNA samples were extracted. A pair of specific primers were employed to perform PCR amplification. All PCR products were carried out a Sanger sequencing.

**Results:** Genotype frequencies for rs9263726 polymorphism observed were G/G (88.89%), G/A (9.36%), A/A (1.75%) in patients with gout or hyperuricemis. Rs9263726 A allele was observed in 11.11% of patients, whereas the allele frequency was 6.43%. While in healthy volunteers group, 12.57% was carried rs9263726 A allele, whereas the allele frequency was 7.07%. There was no significant differences between the two groups when compared with the carried rate of rs9263726A allele. Patients were divided into two groups based on whether they carried rs9263726A allele or not. The mean uric acid level is (435.89±129.80)μmol/L in rs9263726A allele group and (419.84±139.45) μmol/L in rs9263726G allele. No significant difference was observed when compared the age, genders as well as uric acid level.

**Conclusions:** The frequency of rs9263726 A allele is relatively high in South China. There is no evidence that the frequency of rs9263726A allele is different in patients with gout or hyperuricemis and healthy volunteers. Further studies should carried out to explore the relationship between rs9263726A allele and allopurinol-related SCAR as well as HLA-B*5801.

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## AB0834 ACUTE CALCIUM PYROPHOSPHATE CRYSTAL ARTHRITIS AS A CAUSE OF SUDDEN ONSET OF FEVER AND ARTHRITIS IN GERIATRIC PATIENTS

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**Background:** Calcium pyrophosphate (CPP) deposition may give rise to clinical presentations that mimic septic arthritis, polyarticular inflammatory arthritis or osteoarthritis. Of 4 different presentations[1)], acute CPP crystal arthritis crystal arthritis, also known as pseudogout, is characterized by sudden attacks of arthritis frequently with systemic inflammatory features such as fever.

**Objectives:** To determine clinical findings of patients with acute CPP crystal arthritis who was hospitalized due to fever of unknown origin or developed during hospitalization from 2011 to 2015.

**Methods:** Patients were diagnosed as having acute CPP crystal arthritis according to the diagnostic criteria proposed by McCarty DJ[2)] and classification of clinical presentations proposed by EULAR recommendation[1)].

**Results:** We enrolled 26 patients with acute CPP crystal arthritis who were classified as described above, including 9 males and 17 females. All patients presented acute attacks of arthritis. Eight patients were hospitalized due to high fever; and others were for infections in 8 patients, strokes in 6, malignancies in 2 and other medial illnesses in 4, followed by arthritis or fever. The median age at diagnosis was 83.5 years (range 69–102). Fever (>37.5℃) developed in 17 patients and the mean CRP level (± SD) was 14.6±7.2 mg/dL (2.08 - 28.88; n=23). Ten patients were polyarticular or oligoarticular while 16 patients were monoarticular; and affected joints included knee joints in 18 patients, wrist in 6, ankle in 6, elbow in 3, shoulder in 2, cervical in 2, and finger in 2. CPP crystals were demonstrated in synovial fluids in 12 of 15 patients with arthrocentesis. The presence of CPPD deposition-related arthropathy including chondrocalcinosis was found in 24 patients by radiographic studies. All patients responded well to treatment including non-steroidal anti-inflammatory drugs (n=16), joint aspiration and rest (n=5), oral colchicine (n=3), intraarticular injection of glucocorticoids (n=3) and parenteral glucocorticoids (n=2; prednisolone 30 mg/day).

**Conclusions:** The results indicates that acute CPP crystal arthritis develops in not rarely the geriatric population over 75 years of age, often leading to sudden onset of fever and disability. It should be noted that these attacks are often provoked by severe medical diseases such as infections and strokes.

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**Disclosure of Interest:** None declared

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# Infection-related rheumatic diseases

## AB0835 REACTIVE ARTHRITIS: DIAGNOSTIC DIFFICULTIES AND CAUSES OF MISDIAGNOSIS

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**Background:** Timely diagnostics of inflammatory rheumatic diseases, particularly of Reactive Arthritis (ReA), and the development of reasonable management methods for their course are of a high importance in practice rheumatology, which are needed for early ethiotropic and pathogenetic treatment.

**Objectives:** Study course features of the urogenital ReA and causes of its misdiagnosis.

**Methods:** We have conducted 86 patients being admitted to the rheumatologic department of the 1st Clinic of Tashkent Medical Academy with directional

diagnosis of ReA. 86 patients were divided into 48 men and 38 women aged 19 to 49 years old, with the disease duration of 1 month to 5 years. Acute course was observed in 17 patients, subacute course in 44, and chronic course of the disease in 25 patients. Disease progression after urogenital infection of the urinary tract was established in 58 cases, enterocolitic form in 18 cases, mixed form of ReA in 10 cases. To detect the urogenital chlamydial infection, we used a method of the indirect immunofluorescence of urethral or endocervical smear, and method of DNA diagnostics, when necessary. Patients with enterocolitic form of ReA were conducted with bacteriological stool test.
**Results:** The classic disease presentation, including arthritis, eyes and genital tract impairment was established in 47 of 58 cases. Among them, all 14 patients suffered from acute, 30 of 33 from subacute, 11 of 14 from chronic form of ReA. As to the misdiagnoses at onset of the disease, 1 patient was diagnosed with gout, 3 with rheumatoid arthritis, and 1 patient over 35 years old was diagnosed with osteoarthritis. All patients had involvement of the lower limbs joints in the pathological process. The oligoarthritis prevailed in acute and sub-acute ReA (80% and 92.8% of cases respectively). Monoarthritis was observed only in 20% cases with acute form of the disease. In the chronic disease course, polyarthritis prevailed with symmetric and asymmetric forms, which were observed in 62.8%; and the oligoarthritis in 37.2% cases. All patients during hospitalization or in history mentioned eyes impairment, which, according to our observations, was course independent.
**Conclusions:** Thus, timely diagnosis and adequate management requires distinctive knowledge of ReA clinical presentation and taking into account the course of the disease, and use of existing diagnostic criteria. Difficult diagnostic situations should be extended with case follow-up.
**Disclosure of Interest:** None declared
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### AB0836 IMPACT OF EPIDEMIOCLINICAL PATIENTS CHARACTERISTICS ON GERM IDENTIFICATION DURING SEPTIC ARTHRITIS

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**Background:** Septic arthritis may cause damage and inflammation in short period of time. The germ determination must be the first objective to allow targeted treatment. Bacteriological tests remain negative in 7–35% of cases of septic arthritis.
**Objectives:** Our objective is to determine the impact of epidemioclinical patients profile on germ determination during septic arthritis.
**Methods:** This a retrospective study which included medical records of patients treated for septic arthritis during the seventeen past years. Epidemiologic, clinical, biologic, bacteriologic and therapeutic data were recorded and analysed. We made a comparison between patients who had a germ identified with whom who hadn't.
**Results:** Fifty nine cases of septic arthritis were treated during the study period with mean age about 54.6±19 years [range 15 to 95]. The germ was identified in 27 cases (45.77%). The patients with no identified microorganism had a female predominance (sex-ratio M/F=0.77). When germ was identified, there was no sex predominance (sex ratio =1.07) with no differences between the 2 groups (p=0.385). The two groups had same mean age (54.1 and 54.8 years). The maximum of frequency of the disease was for patients aged between 70 and 79 years when germ identified and between 40 and 59 years if not. The percentage of patients with risk factors of septic arthritis was higher if the germ was not identified but with no significant difference (p=0.893). Anorexia, weight loss and lameness were more frequently seen if germ wasn't identified. It was the same ascertainment with fever and inflammatory signs. There was no significant difference between the two groups as regards the arthritis localization and the number of joints involved.
**Conclusions:** This study showed that female sex was the only epidemio-clinical character associated with low chance to identify the germ during septic arthritis.
**Disclosure of Interest:** None declared
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## Fibromyalgia

### AB0837 EFFECTS OF VITAMIN D THERAPY ON QUALITY OF LIFE IN PATIENTS WITH FIBROMYALGIA

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**Background:** The role of vitamin D in the etiopathogenesis of fibromyalgia and non-specific musculoskeletal pain is controversial.
**Objectives:** In our study, we aimed to investigate the effect of vitamin D therapy on quality of life in patients with fibromyalgia.
**Methods:** 70 patients diagnosed with fibromyalgia and 65 age-sex match controls were included in the study. Patients were grouped as deficiency (<20 ng/mL), inadequacy (20–30 ng/mL) and sufficient (>30 ng/mL) according to the levels of vitamin D. Vitamin D replacement was performed for patients with deficiencies and inadequacies. Before and after vitamin D therapy, patients filled in the assessment tools.
**Results:** Vitamin D deficiencies and inadequacies were observed in 60% of the patients (n=42). Social function, mental health and vitality areas in patients' quality of life forms were significantly lower in normal vitamin D group compared with low vitamin D group. In scales examined after Vitamin D replacement therapy, statistically significant differences were observed in the fibromyalgia impact questionnaire, Beck depression inventory, VAS and SF-36 compared to pre-treatment.

Table 1. Baseline and post-treatment scores of Fibromyalgia Impact Questionnaire, Beck depression inventory, VAS, ASEX, sleep VAS

| | Pts with low vit. D (n=42) | Pts with normal vit. D ( n=28) | After vit. D treatment (n=42) | P value |
|---|---|---|---|---|
| Fibromyalgia Impact Questionnaire | 61.2±13.5 | 61.9±15 | 59.7±13.6 | 0.001* |
| Beck Depression Inventory | 15.6±10 | 18.7±11 | 14.8±9.9 | 0.001* |
| VAS | 84.4±12.3 | 85±13 | 79.9±12.7 | 0.001* |
| Arizona Sexual Experience Scale | 18.2±5.2 | 18.7±6 | 17.9±5.2 | 0.176 |
| Sleep Scale (VAS) | 4.9±2 | 5.1±1.6 | 4.7±2 | 0.317 |

Table 2. Baseline and post-treatment scores of SF-36

| SF-36 | Pts with low vit. D (n=42) | Pts with normal vit. D ( n=28) | After vit. D treatment (n=42) | P value |
|---|---|---|---|---|
| 1. Physical Function | 19.7±3.9 | 20.5±4.4 | 20.8±4 | 0.001* |
| 2. Role Physical | 5±1.3 | 4.9±1.1 | 5.5±1.4 | 0.001* |
| 3. Role Emotional | 3.7±1 | 3.6±0.9 | 4.2±1.1 | 0.001* |
| 4. Bodily Pain | 5.2±1.3 | 5.3±1.3 | 6±1.4 | 0.861 |
| 5. Social Function | 6.7±2.2 | 5.9±1.5 | 7.4±2.5 | 0.001* |
| 6. Mental Health | 19.2±5 | 17.7±4.8 | 20.2±4.9 | 0.001* |
| 7. Vitality | 13.1±3.2 | 12.4±3.9 | 13.6±3.8 | 0.003* |
| 8. General Health | 11.3±4 | 11.2±4.1 | 12.5±4.5 | 0.001* |

**Conclusions:** Since, vitamin D deficiency seems to be linked to the pathogenesis of FMS, serum vitamin D levels should be checked routinely as a general health problem and patients should be supplemented.
**Disclosure of Interest:** None declared
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### AB0838 A MICRORNA SIGNATURE IN LIQUID BIOPSIES FOR THE DIAGNOSIS OF FIBROMYALGIA

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**Background:** Fibromyalgia (FM) is a syndrome characterized by chronic widespread pain that affects about 2–8% of the general population, especially female gender [1].The pathogenesis of FM is not completely understood and diagnosis is clinical.MicroRNAs, a class of small non-coding RNAs of ~22–24 nucleotides, are involved in different post-transcriptional processes and have been identified as important biomarkers in many diseases [2]. Recently, it has been hypothesized that the modulation of protein expression, potentially mediated by miRNAs, is one of the main characteristic of the central and peripheral sensitization, which is a basic process to development and maintenance of chronic pain, as in FM [3].
**Objectives:** The aim of this study was to analyze the expression of circulating miRNAs in liquid biopsies (i.e. serum and saliva) of a group of selected FM patients.
**Methods:** Consecutive adults FM patients, according to both ACR criteria [4,5], and healthy donors were enrolled. Patients complaining of pain VAS more than 6 (0–10), with positivity of at least 14 tender points at clinical examination and free from drugs at the time of evaluation, were included in the study.Patients and controls completed the following questionnaires: Fibromyalgia Impact Questionnaire, Fibromyalgia Assessment Status, Health Assessment Questionnaire, Zung Self-Rating Anxiety and Depression Scale. After obtaining informed consent, samples from patients and controls were collected.Circulating miRNAs were extracted using miRCURY RNA Isolation Kit-Biofluids (Exiqon) and profiled using the Serum/Plasma Focus microRNA PCR Panel (Exiqon) following the manufacturer's instructions.Data were analyzed by SPSS software.
**Results:** The study population consisted of 14 female patients, without diagnosis of autoimmune diseases, psychiatric or neurological disorders and neuromuscular diseases, and 14 healthy controls matched for sex and age.The exploratory profiling of circulating miRNAs in serum revealed that six miRNAs (miR-23a-3p, miR-1, miR-133a, miR-346, miR-139–5p and miR-320b) were significantly ($p<0.05$) and differentially regulated in FM patients compared to controls, whereas some of these miRNAs were expressed but not significantly modulated in saliva.We found a significant negative correlation ($r=-0.608$; $p<0.05$) between

miR-320b and the score of depression scale.ROC curves for each miRNAs displayed a AUC greater than ~0.7 and the best generalized linear model that can be employed to discriminate FM patients from healthy controls was obtained by taking into account only 5 miRNAs: miR-23a-3p, miR-1, miR-133a, miR-346 and miR-320b (AUC=0.954, sensitivity=100%, specificity=83.3%).
**Conclusions:** Our preliminary work outlines the importance of using circulating miRNAs in liquid biopsies as a powerful diagnostic signature for the diagnosis of FM.Although the expression and the modulation of miRNAs seem to be site specific, we suggested a panel of serum miRNAs that can be used in the future as potential predictors of FM.A wider cohort of patients will be necessary to integrate the results that we obtained in this work and to suggest a more robust predictive model to exploit as an additional diagnostic tool for FM patients.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4274

## AB0839 FIBROMYALGIA SYNDROME IN PREGNANT WOMEN; THE EFFECTS ON PHYSICAL FUNCTIONING AND PSYCHOLOGICAL STATUS

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**Background:** There are many unexplored issues related to the presence of fibromyalgia syndrome (FS) in pregnancy such as prevalence of FS, most common symptoms, the impact of FS on physical functioning, psychological status, and treatment of a fibromyalgic pregnant
**Objectives:** To investigate the frequency and most common symptoms of FS among pregnant woman and determine the impacts of FS on physical functioning and psychological status in those patients.
**Methods:** A total of 360 pregnants in the third trimester of pregnancy were included in the study. The pregnants were split into two groups in terms of having or not having FS. Group 1 was consisted of 136 pregnant women with FS. 224 pregnant women without FS were formed control group (group 2). The presence of fibromyalgia was investigated via 2010 ACR classification criteria. Widespread pain index and symptom severity scores of the patients were recorded. The impact of FS on physical functions was evaluated using fibromyalgia impact questionnaire. Psychological status of the patients were evaluated using state-trait anxiety inventory, the Wijma delivery expectancy/experience questionnaire and Beck depression inventory.
**Results:** 136 of 360 pregnants (37.7%) had FS. Mean ages of the 136 pregnants with FS was 27 years and of the 224 without FS was 26.5 years ($p>0.05$). Low back pain is the most common complaint and fatique is the most common symptom in pregnants group with FS. Compared with the pregnants group without FS, pregnants group with FS had higher values of pain severity and higher levels of physical disability ($p<0.001$). Pregnants group with FS had also higher values of anxiety, fear of childbirth and depression ($p<0.001$, for all values). Symptom severity score and physical impairment score were found to be significantly correlated with increased levels of pain, depression, anxiety, fear of childbirth, fatique, increased scores of waking unrefreshed, cognitive symptoms and increased rate of low back pain ($p<0.001$ for all values).
**Conclusions:** FS is common among pregnant women and the existence of FS in pregnancy is a severe factor for maternal stres, anxiety and depression. If we desire a healthy pregnancy and a good child outcome, we need to get therapeutic measures for fibromyalgia syndrome.
**Disclosure of Interest:** None declared
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## AB0840 ASSOCIATION BETWEEN CATECHOL-O-METHYL TRANSFERASE GENE POLYMORPHISMS AND FIBROMYALGIA IN A KOREAN POPULATION: A CASE-CONTROL STUDY

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**Objectives:** Although polymorphisms of the catechol-O-methyl transferase (COMT) gene have been implicated in altered pain sensitivity, results concerning the association between COMT gene polymorphisms and FM are equivocal. We assessed the associations between COMT single-nucleotide polymorphisms (SNP) and FM risk and symptom severity.
**Methods:** In total, 409 FM patients and 423 controls were enrolled. Alleles and genotypes at five positions [rs6269 (A>G), rs4633 (C>T), rs4818 (C>G), rs4680 (C>G) and rs165599 (A>G)] in the COMT gene were genotyped from peripheral blood DNA.
**Results:** Alleles and genotypes of the rs4818 COMT gene polymorphism were significantly associated with increased susceptibility to FM. The rs4818 GG genotype was more strongly associated with FM compared to the CC genotype (OR =1.680, 95% CI: 1.057, 2.672, P=0.027). Although allele and genotype frequencies did not differ among groups, the rs4633 CT genotype was not associated with the presence of FM following adjustment for age and sex (OR =0.745; 95% CI: 0.558, 0.995; P=0.046). However, no association was observed between clinical measures and individual COMT SNPs. In haplotype analysis, there was a significant association between ACG haplotype and FM susceptibility sex (OR =2.960, 95% CI: 1.447, 6.056, P=0.003) and the number of tender points (P=0.046).
**Conclusions:** This large-scale study suggests that polymorphisms of the COMT gene may be associated with FM risk and pain sensitivity in Korean FM patients. However, our results differed to those of previous studies, suggesting ethnic variation in COMT gene polymorphisms in FM.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1948

## AB0841 PERFECTIONISM IN CHRONIC PAIN: ARE THERE DIFFERENCES BETWEEN FIBROMYALGIA, RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS?

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**Background:** Perfectionism has been associated with a plethora of medical conditions and psychopathological symptoms/disorders.[1] However, the potential impact of perfectionism in different chronic pain conditions is scarcely explored.
**Objectives:** Compare patients with fibromyalgia (FM), rheumatoid arthritis (RA) and pain-free controls regarding mean scores of perfectionism dimensions and cognitions; and test if perfectionism dimensions are significantly associated with the disease group.
**Methods:** Participants were recruited among consecutive attendees with FM, RA and pain-free controls at rheumatology and gynecology practices in Coimbra. Patients with FM and RA satisfied currently accepted classification criteria.[2,3] The absence of chronic pain in healthy controls (HC) was established by a score of zero in the London Fibromyalgia Epidemiological Study Screening[4]. All participants completed the Portuguese versions of the Frost and of the Hewitt and Flett Multidimensional Perfectionism Scales (MPS) and the Multidimensional Perfectionism Cognitions Inventory. To achieve our aims, descriptive analyses, one-way independent ANOVA (followed by *post hoc* tests) and linear multiple regression (LMR) were performed.
**Results:** The total sample comprised 302 participants [103 FM (34.11%), 98 RA (32.45%) and 101 HC (33.44%)]. Differences between samples were found regarding age ($F=30.598$; $p<.001$) and education years ($F=25.883$; $p<.001$).
Results revealed significant differences between the samples regarding: parental criticism (PC), organization (O), Frost-MPS total score, perfectionism cognitions related with concern over mistakes (CoM) and pursuit of perfection (PP). *Post hoc* comparisons indicated that FM patients exhibited higher levels than RA patients and HC in all of these variables (except for PP that did not significantly differ between FM and HC). No significant differences were found between RA and HC, except for PC and O, with RA patients scoring higher. Regarding LMR, the model was significant ($F(8,245)=5,203$; $p<.001$), with PC ($\beta=-.372$; $t=-5.014$; $p<.001$) and O ($\beta=-.161$; $t=-2.567$; $p=.011$) significantly predicting the type of sample.
**Conclusions:** FM patients seem to be noticeably more perfectionistic than RA patients and HC, which in turn, do not differ significantly, in the majority of the perfectionism traits and cognitions. PC and O appear to be the most discriminative perfectionism dimensions. Perfectionism seems a variable of utmost importance, especially in FM, and may deserve consideration as a target for interventions.
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### AB0842 RELATIONSHIP OF FIBROMYALGIA SYNDROME, DIFFUSE PAIN, AND SMALL FIBER PERIPHERAL NEUROPATHY

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**Background:** The pathophysiology of fibromyalgia syndrome (FMS) remains unclear, but the current predominant hypothesis is that FMS arises from centralized hypersensitivity to pain. Recently, some studies have suggested that a subset of FMS patients may have underlying small fiber peripheral neuropathy (SFPN), a selective degeneration of the cold/pressure and nociceptive nerve fibers (Oaklander et al., 2013). This discovery has challenged the completeness of the "central hypersensitivity" hypothesis.
**Objectives:** Here, we describe a cohort of FMS and/or diffuse unexplained pain patients who have undergone skin biopsy as part of their workup. Our goal was to identify whether these patients have underlying SFPN, and if so, whether the SFPN is idiopathic or secondary to another predisposing condition.
**Methods:** This study is a retrospective review of patients from our medical center. Patients were diagnosed using the 2011 American College of Rheumatology FMS diagnostic criteria. Additionally, a number of patients presented with diffuse, unexplained pain which carried many of the qualities of FMS, but were not formally diagnosed with the disorder. 172 patients have a diagnosis of either FMS or diffuse pain. Of these, 66 had tingling, burning, or numbness for which they underwent skin biopsy.
These patients underwent workup for etiologies of neuropathic pain including fasting glucose, hemoglobin A1C, thyroid-stimulating hormone, vitamin D level, serum protein electrophoresis, hepatitis C, human immunodeficiency virus (HIV), and obstructive sleep apnea (OSA). Additionally, they underwent assessment to search for other conditions which might explain their pain. Patients were referred for skin biopsy whenever possible. Biopsies were analyzed using protein gene product 9.5 (PGP 9.5) immunostaining to determine the epidermal nerve fiber density (EFND). Compared to an internal set of normal controls, the bottom 5 percentile of EFND was reported as diagnostic of SFPN.
**Results:** Overall, 43 patients (65%) had the diagnosis of FMS, while 23 patients (35%) had the diagnosis of diffuse pain. 13 patients were found to have no predisposing condition – their pain syndrome was considered to be idiopathic. 53 were found to have at least one predisposing disease.
Within the group undergoing skin biopsy that did not have predisposing factors for SFPN, 62% were found to have SFPN. Within the group of patients with an identifiable predisposing condition, 72% were found to have SFPN. Overall prevalence of SFPN was 70%. The average age at symptom onset was 35 years old (range 9 to 64 years), and the cohort was 94% female, 6% male. Prevalence of SFPN-predisposing conditions is listed on the table below.

| | |
|---|---|
| Hypovitaminosis D | 40% |
| Connective tissue disease | 32% |
| OSA | 25% |
| Ehler Danlos syndrome 3 | 23% |
| Impaired fasting glucose/diabetes mellitus | 23% |
| Hypothyroidism | 13% |
| Monoclonal gammopathy | 4% |
| Neurotoxic drug exposure | 2% |
| Other inflammatory disease | 2% |
| Other infectious | 2% |
| Hepatitis C | 0% |

**Conclusions:** In our experience, SFPN is highly prevalent among patients who were diagnosed with FMS or diffuse unexplained pain.
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## Back pain, mechanical musculoskeletal problems, local soft tissue disorders

### AB0843 TRAMADOL'S RESPIRATORY EFFECTS IN SUBJECTS WITH CHRONIC NON-SPECIFIC LOW BACK PAIN: A RANDOMISED CONTROLLED TRIAL

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**Background:** Chronic non-specific low back pain (CNSLBP) is defined as back pain localised at inferior portion of the rachis, without radiating anywhere else, lasting for more than 12 weeks, and whose etiology cannot be assigned to a specific injury, nerve compression, infection, tumor. This is the case in about 90% of all low back pain subjects. Nowadays physicians are aware that altered breathing patterns may be present in a proportion of individuals with CNSLBP. Researchers suggest that breathing patterns should also be evaluated in the presence of low back pain. Guidelines recommend therapeutic physical exercise as a first line treatment option in CNSLBP. That may be because pain itself contributes to loss of functioning, limits the subject's participation to activities of daily living and produces disability among these subjects. As medication, WHO guideline suggests the use of weak opioids. Tramadol is a centrally acting analgesic, which produces its effect by binding to the μ-opioid receptors, and by inhibiting the release of noradrenaline and serotonine. Studies suggest that, despite its part-opioid mechanism of action, tramadol doesn't produce respiratory depression as opioids do.
**Objectives:** Our study goal was to assess tramadol effects on respiratory markers in human subjects with CNSLBP.
**Methods:** A number of 30 subjects with CNSLBP joined this study for a period of 7 days. They were randomised in two groups: control (15 subjects, received placebo capsules twice a day), tramadol (15 subject, received tramadol 50 mg capsules twice a day). All subjects underwent cardio-pulmonary exercise testing using cycle-ergometer with progressive increasing work-rate at baseline and after 7 days of medication. We investigated peak oxygen uptake ($VO_2max$), respiratory reserve (RR), and exercise tolerance expressed as dioxide carbon ventilatory equivalent. All these parameters were investigated in the first and 7th day of study.
**Results:** Peak oxygen uptake significantly raised for tramadol group on last day of the study (p=0.001). RR improved for both groups but the statistical difference came up for tramadol group (p=0.005). Exercise tolerance was better for both groups but it was significantly higher for tramadol group ($p=0.98x10^{-5}$).
**Conclusions:** Tramadol administration to subjects with CNSLBP improved respiratory markers and exercise tolerance.
**References:**
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**Disclosure of Interest:** None declared
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### AB0844 COMPARING OF THE EFFECTIVENESS OF BOTILINUM TOXIN TYPE-A AND PRILOCAINE INJECTIONS CLINICALLY IN THE TREATMENT OF MYOFASCIAL PAIN SYNDROME

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**Objectives:** The objective of this study was to compare the effects of botulinum toxin-A (BTX-A) injection and prilocaine injection in the treatment of myofascial pain syndrome (MAS).
**Methods:** Thirty eight patients, having trigger points in the muscles diagnosed as MAS were analyzed in this randomized, single blind, comparative study.
*Setting:* Patients were randomized into two treatment groups namely BTX-A injection group and prilocaine group. Each group consisted of 19 patients.
*Intervention:* In BTX-A injection group, 10 U of BTX was injected to each trigger point. In the prilocaine group 2ml prilocaine was injected to each trigger point. All the patients were asked to do stretching exercises at home.
*Main outcome measure:* Treatment efficacy was evaluated clinically before and 2 and 6 weeks after treatment. Evaluation parameters were during function visual analog scale (VAS), pain score (PS), pain pressure threshold (PPT), general well-being by short form-36 (SF-36) and Beck Depression Inventory (BDI).
**Results:** Statistically significant improvements were observed during function VAS, PS, PPT, SF36 and BDI in both treatment group. Improvement in VAS and PPT at 2 weeks was more significant in the BTX-A group. Improvement in VAS, PPT, PS at 6 weeks was more significant in BTX-A group. There is no difference between two groups in BDI. Borderline improvement was observed in BTX-A group at 6 weeks.
**Conclusions:** BTX-A injections and prilocain injections are the beneficial treatment choices in this syndrome. But we observed the progressive cumulative effect of BTX-A in the course of time. Although cost effectivity limitation we suggest that patients with chronic persistant myofascial trigger points can be convenient candidates for BTX-A injections. Adjuvant appropriate exercises program should be included in primary treatment modality for optimal success.
**Disclosure of Interest:** None declared
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## AB0845 A RARE CAUSE OF ANTERIOR KNEE PAIN AND LIMITATION OF KNEE EXTENSION: SYMPTOMATIC INFRAPATELLAR PLICA

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**Background:** The synovial plica of the knee is recognized as a structure that represents remnants of synovial membranes in embryonic development of knee. Infrapatellar plica (IP) known as the ligamentum mucosum, arises from the anterior part of intercondylar notch of femur, widens as it descends anteriorly, and runs parallel to and above the anterior cruciate ligament and attaches to the infrapatellar fat.
**Objectives:** In this report, two cases of symptomatic infrapatellar plica which caused anterior knee pain and knee extension limitation were presented. The first case was 23 years old construction worker who admitted with complains of the left anterior knee pain and limitation of knee motion. The second case was a 21 years old amateur footballer with the complaints of knee movement limitation and anterior knee pain while crouching.
**Methods:** Although we detected infrapatellar plica on MR images of the first patient (Fig. 1a and 1b), the second patient showed no evidence of infrapatellar plica on MR sequences. Arthroscopic surgery planned for the patients and plica excision applied.
**Results:** Physical therapy started just right after surgery and there were no pain or knee motion limitation at routine inspection of patients at 1,5–3-6–12 months.




**Conclusions:** These cases demonstrate a potential role for the infrapatellar plica as a cause of anterior knee pain and movement limitation.We emphasize that with the patients who suffer from anterior knee pain and knee motion limitation, one should need to keep in mind the symptomatic infrapatellar plica.
**Disclosure of Interest:** None declared
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## AB0846 DOES DIABETES MELLITUS CAUSE PROBLEMS IN HAND FUNCTIONS AND QUALITY OF LIFE?

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**Background:** Diabetes mellitus (DM) is a chronic condition which can effect different systems of the body
**Objectives:** In this study we aimed to determine the impairments in hand and upper extremity functions, pain and quality of life in diabetic patients.
**Methods:** Fifty diabetic patients who attended to physical medicine and rehabilitation outpatient clinics were evaluated. The patients fasting blood glucose levels, hemoglobin A1 C levels, body mass indexes were detected; existing hand deformities were noted; evaluations of hand strength was made by hand grip strength, hand pain by VAS, hand skills by purdue pegboard test and nerve involvement by semmes weinstein monofilaments (SWM). For upper extremity functions Disabilities of Arm Shoulder and Hand scores (DASH) and for quality of life Nottingham Health profile (NHP) test were selected.
**Results:** The mean age of the patients were 62,76±10,99 years. Among our DM patients only 4 patients had normal weight, 14 were over weight, 29 were obese and 4 had morbid obesity. The mean valueof fasting blood gucose was 145,2 and that of HbA1 c was 7,64. In hand evaluations we found trigger finger and dupuytren contracture in 10,6%, restricted hand mobility in 3,4%,crepitation of hand tendons in 55,3% and carpal tunnel syndrome in 38,3%. SWM median nerve mean values were 3,64±0,68 and that of ulnar nerve was 3,77±0,83.In correlation analysis we found hand pain by VAS correlated all evaluation parameters except purdue pegboard test. SWM scores correlated with all subgroups of NHP, purdue pegboard test and hand pain by VAS. DASH scores correlated with HbA1 c levels, abdominal circumference, grip strength and SWM evaluations.
**Conclusions:** In our diabetic patients we found nearly all patients were obese or overweight; had problems both in hand functions and median - ulnar nerves. Involvement of the nerves leads to problems in quality of life and fine skills of hands. Additional upper extremity impairments increase their pain and disability. As a result we suggest the patients to have a strict glucose control for a better life standard.
**Disclosure of Interest:** None declared
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## AB0847 NON-SPECIFIC CHRONIC LOW BACK PAIN IS COMMON IN SUB-SAHARAN AFRICA: A HOSPITAL-BASED STUDY IN CAMEROON

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**Background:** Low back pain is the most frequent cause of rheumatic diseases in Africa (1). However the studies are scarce, especially in sub-Saharan Africa.
**Objectives:** To determine the main characteristics of non-specific chronic low back pain in Cameroon, Central Africa.
**Methods:** We performed a cross-sectional study in all 6804 patients seen in Rheumatology department in a tertiary healthcare centre, the General Hospital of Douala, Cameroon, between January 2004 and December 2013. All patients followed for low back pain (pain experienced in all the lumbar region of the spine) were screened. Patients were classified into acute low back pain (<3 weeks), subacute low back pain (3 weeks - 3 months) and chronic low back pain (>3 months).
Patients with specific low back pain (infection, tumor, fracture, inflammation, ...) were excluded from this study. A $p<0.05$ was considered statistically significant.
**Results:** During the study period, 3008 patients were seen for low back pain. Of these, 220 patients (7.3%) had specific low back pain and 2788 (92.7%) had non-specific low back pain, including 1302 with chronic low back pain. Chronic low back pain were more common than acute and subacute low back pain (p=0.001) without statistical difference in mean age and sex ratio ($p>0.05$) (Table 1).

Table 1. Distribution of patients according to the low back pain duration

| N=2788 | n (%) | Mean age, years [interquartile range] | Sex ratio (F/H) |
|---|---|---|---|
| Acute low back pain | 980 (35.2) | 51.71 (16–90) | 1.14 |
| Subacute low back pain | 506 (18.1) | 52.32 (16–87) | 1.20 |
| Chronic low back pain | 1302 (46.7) | 52.38 (20–81) | 1.67 |

Table 2 shows the distribution of patients according to the radiographic lesions found. The disc disease, particularly the degenerative disc disease were the most common radiographic lesions, found in more than half of the patients.

Table 2. Radiographics findings

| | N (%) | Mean age ± standard deviation | Sex (women/men) |
|---|---|---|---|
| Degenerative disc disease | 1542 (55) | 55.74±14.21 | 985/565 |
| Disc herniation | 383 (13) | 52.46±14.29 | 225/158 |
| Lumbar osteoarthritis | 247 (9) | 52.68±13.94 | 156/76 |
| Facet joint osteoarthritis | 139 (5) | 52.38±14.28 | 105/32 |
| Spinal stenosis | 93 (3) | 61.13±11.99 | 55/37 |
| Spondylolisthesis | 88 (3) | 53.04±13.63 | 68/18 |
| Transitional abnormalities | 116 (4) | 53.32±13.37 | 59/57 |
| Combination of several lesions | 323 (12) | 52.45±14.21 | 230/93 |
| No lesions | 173 (6) | 52.37±14.30 | 105/68 |

**Conclusions:** Non-specific chronic low back pain is the most prevalent musculoskeletal condition in Cameroon. It concerns almost half of the patients seen in Rheumatology department. The degenerative disc disease are the most common radiographic lesions.
The hospital-based study would explain the marked prevalence of chronic low back pain on acute and subacute low back pain. These latter would probably be more often seen in peripheral hospitals by general practitioners.
**References:**
[1] Louw QA et al. BMC Musculoskelet Disord 2007;8:105.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2587

## AB0848 SPINAL PAIN IS THE MAIN COMPLAINT OF OUTPATIENTS SEEN IN RHEUMATOLOGY IN CAMEROON, SUB-SAHARAN AFRICA

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**Background:** The prevalence of spinal pain or back pain among Africans may be comparable to that reported in research undertaken in developed nations. However, studies evaluating the epidemiological characteristics of spinal pain are rare in sub-Saharan Africa (1).
**Objectives:** To determine the main epidemiological characteristics of spinal pain in a tertiary healthcare center in Cameroon, sub-Saharan Africa;
To describe the profile of specific spinal pain found in Cameroon.
**Methods:** We performed a cross-sectional study among outpatients seen in Rheumatology consultation at Douala General Hospital, Cameroon, between January 2004 and December 2013. All patients followed for spinal pain (pain experienced in all the regions of the spine) were screened.
**Results:** During the study period, 7024 patients were seen in Rheumatology Department but only 6804 cases (4433 women and 2371 men) were selected for analysis because it had a clearly defined rheumatic disease. The mean age of patients was 52.3±14.3 years. The mean body mass index was 29.3 kg/m$^2$±5.1, with 5194 patients with overweight and obesity.
The main reason for consultation concerned the peripheral skeleton in 3230

Table 1. Distribution of patients according to the affected anatomical region

| | Anatomic region | n (%) |
|---|---|---|
| Axial skeleton, n=3574 (52.5%) | Cervical spine | 449 (12.5) |
| | Dorsal spine | 114 (3.2) |
| | Lombar spine | 3011 (84.2) |
| | Sacro-iliac joints | 3 (0.1) |

Table 2. Distribution of patients with specific back pain

| | n (%) |
|---|---|
| Infectious spondylodiscitis | 64 (0.9) |
| Osteoporosis | 59 (0.8) |
| Axial spondyloarthritis | 40 (0.6) |
| Cancer | 36 (0.5) |
| Others | 21 (0.3) |

patients (47.5%) and 3574 (52.5%) in the axial skeleton. The pain was present in all patients with axial involvement and was localized in the lumbar spine in 3008 patients (84.2%) [Table 1].
Most cases are nonspecific, but in 223 (6.2%) of cases a specific cause was suspected, especially of infectious origin (Table 2). Indeed, 64 cases of infectious spondylodiscitis were collected. Tuberculosis was suspected in the majority of patients, but only one case had been documented.
**Conclusions:** Spinal pain, especially in the lumbar region of the spine is the main location of pain in Rheumatology in Cameroon. The infectious and inflammatory etiologies are rare.
**References:**
[1] Louw QA et al. BMC Musculoskelet Disord 2007;8:105.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3074

## AB0849 SPINAL BRUCELLOSIS: A STUDY OF 40 CASES IN A TUNISIAN HOSPITAL

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**Background:** Brucellosis is a major health problem in Mediterranean countries, including Tunisia. The clinical presentation of this zoonosis varies considerably, but osteoarticular involvement and spinal brucellosis particularly, is the commonest complication.
**Methods:** This study was carried out between 2006 and 2013. Forty patients with infectious spondylodiscitis hospitalized in the department of Rheumatology were analyzed. All patients were thoroughly interrogated, subjected to a rigorous clinical examination and a battery of investigations including: complete blood count, urine analysis, blood culture, erythrocyte sedimentation rate, C-reactive protein (CRP) and serology for brucellosis. The imaging ordered including: plain X-ray of the lumbosacral spine, bone scan and magnetic resonance imaging (MRI) with contrast enhancement of the spine.
**Results:** Ten of the forty patients (25%) proved to have spinal brucellosis. The mean age of this patients was 51 years (range 15 – 68 years) and female/male ratio: 1,5. The mean delay of diagnosis was 7 months. The following symptoms were observed: fever in 9 patients and back pain in all patients. Other symptoms were less frequently observed, such as splenomegaly (one patient), peripheral adenopathy (two patients) and diarrhoea (one patient). Laboratory exams showed elevated erythrocyte sedimentation rate in most of them (8 patients), high levels of CRP in all patients and leukocytosis in 7 cases. Wright serology was positive in all of them. Brucella melitensis was isolated in blood cultures in 2 cases. Standard X-rays were performed in all patients; they showed signs of spondylodiscitis in the lumbar spine in 5 cases, cervical in one case and dorsal in two cases. CT-scan and MRI confirms the diagnosis and showed associated epiduritis (3cases) or abscess (4 cases). Bone biopsy and histopathological examination were performed in three cases. A combination of cycline and rifampicin was given to all patients. The duration of therapy was between 6 and 8 weeks.
**Conclusions:** Brucellosis is present with various clinical signs in endemic areas and may simulate many diseases. The need for prompt diagnosis and treatment of spinal brucellosis is of the utmost importance to prevent serious bone destruction and severe neurologic sequelae.
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## AB0850 PREVALENCE OF MUSCULOSKELETAL DISORDERS IN FIREFIGHTERS AND ITS ASSOCIATION WITH INSOMNIA

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**Background:** Musculoskeletal disorders (MSDs) are among the main underlying reasons for decreased productivity at workplace. Awkward working posture, forceful movements, and unexpected events are main reasons for high prevalence of MSDs in firefighters. According to previous research, there is a significant contribution between MSDs and other co-morbidities such as insomnia.
**Objectives:** The present study aimed to evaluate the prevalence of MSDs in firefighters and its relation with severity of insomnia.
**Methods:** A cross sectional study was conducted on firefighters in Qazvin. Demographic information was collected for the participants. A self-administered questionnaire including Nordic question, body map, and insomnia severity index were completed by the firefighters. Descriptive statistics, student t-test, and Chi-square were used for data analysis.
**Results:** Prevalence of MSDs was 54.2% amongst the firefighters, and low back pain was the most common complaint with 30.5%. The highest intensity of pain was in the middle of lumbar region. 20.3% of firefighters had subclinical insomnia, and 30% of them had moderate to severe insomnia. Severity of insomnia was significantly more in subjects with MSDs (12.4±7.9) compared to those without MSDs (7.1±6.6) ($P<0.05$). Among different parts of body, significant association was solely found between back pain and severity of insomnia.
**Conclusions:** The results showed that MSDs, especially around the lumbar region is associated with the severity of insomnia in firefighters. In addition, the prevalence of MSDs and insomnia was significantly higher in firefighters compared to similar studies in general population which calls for preventive activities.
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## AB0851 IMPROVEMENT OF WORK CAPACITY IS DEPENDENT OF A DECREASE IN THE KINESIOPHOBIA

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**Background:** The avoidances of movement is a key structure in the chronic pain patient. In this situation the kinesiophobia has a great importance. It could be evaluated using different questionnaires (Tampa, TSK, but also the Fabq).According to Vlayen, the kinesiophobia is the most important prognostic factor when evaluating the return to work.
**Objectives:** In this situation, we wanted to evaluate the evolution of the kniesiophobia before and after a functional restoration program, and its relationship to the work capacity in a group of chronic lumbar back pain patients.
**Methods:** We included 702 patients who had followed an outpatient program of functional restoration during 3 weeks. The program was composed of physical exercices, occupational therapy and psychologcial follow. The patientes were followed on questionnaires (Tampa (3), Fabq, Pact (2) -subective work capacity-) their work capacity and their physical performances (using different tests as Shirado, Biering-Sörensen, Bruce, lumbar mobility)
**Results:** There were a clear relationship between a decrease in kinesiophobia and an increase of work capacity. In fact in patient were the Tampa score decreased with more than 10 points, there were a still staying increased work capaciry. On the other side, none of he physical characteristics were associated with an increase or decrease of work capacity.
**Conclusions:** We have confirmed the observation of Vlayen from 1996, saying that the kinesiophobia is an important prognostic factor for work capacity. This observation is important in functional restoration programs.
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## AB0852 RESIDUAL PAIN IN THE INFECTIOUS SPONDYLODISCITIS, WHEN TO EXPECT IT?

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**Background:** Residual pain after Infectious spondylodiscitis can result in a major handicap in social and professional life. The aim of the present work was to describe predictive factors of Residual pain after Infectious Spondylodiscitis according to the experience of an internal medicine department in Tunisia.
**Methods:** Patients with SDI either confirmed or presumed and hospitalized in the internal medicine department of The Principle Military Hospital Of Tunis, Tunisia have been included in the Study. Factors correlated with later pain are gathered in this study.
**Results:** See Table 1.

Table 1

| | | Residual pain | | P |
|---|---|---|---|---|
| | | yes | No | |
| Pain at initial examination (ie) | Yes | 4 | 8 | **0.026** |
| | No | 20 | 67 | |
| Neurological compression signs (ie) | Yes | 7 | 9 | **0.049** |
| | No | 17 | 5 | |
| Cutaneous infection | Yes | 10 | 7 | **0.03** |
| | No | 9 | 0 | |
| Germ identified | Yes | 1 | 7 | **0.008** |
| | No | 23 | 7 | |
| SD group | SDT | 9 | 12 | **0.003** |
| | SDP | 15 | 2 | |
| MRI signs of compression | yes | 11 | 13 | **0.048** |
| | no | 5 | 1 | |

Fourty-four patients met the inclusion criteria. They have been gathered over 20 years-period. They were 24 men and 20 women with an average age at 52.5 years. The diagnosis was a Tuberculous Spondylodiscitis in 22 cases (50%): among them 10 patients had a concomitant extra spinal TB. The diagnostic delay was 231 days for TB SDI and 40.5 days for SDP.
Treatment duration was 13 months for SDT and 18 weeks for SDP. The outcome was favorabl Regular monitoring was observed in 38 patients (17 SDP, SDT 21) with an average duration of 20 months (5–48 months).
**Conclusions:** Neurological signs at first examination and MRI are main factors of residual pain in SDI.
**Disclosure of Interest:** None declared
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## AB0853 ELECTROACUPUNCTURE TREATMENT OF MERALGIA PARAESTHETICA

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**Background:** Meralgia Paraesthetica (MP) (meros = thigh, algos = pain) is an under diagnosed fairly condition caused by entrapment of the lateral femoral cutaneous nerve. Paraesthesiae, numbness or burning typically affect the thigh. I noticed that acupuncture produced a rapid improvement and invited referrals from rheumatology consultants.
**Objectives:** I had treated several rheumatology patients [1] and decided to do a case series of MP, using a series of tender and traditional Chinese acupuncture points. I found that all patients were tender over GB31 acupuncture point on the affected lateral thigh (7 inches proximal to the popliteal crease).
**Methods:** A series of 10 patients, including two who had refused surgery (excluding those with significant lumbar spine problems), were treated. Xray/MRI scans were taken if relevant. Acupuncture points used were UB25, GB30, GB34, Ex21 lumbar facet trigger points, GB31+ “Ah chi” tender buttock and Chinese points using an infra-red lamp. Electro-acupuncture (using a dense-disperse mode), was used after the first treatment if significant benefit was not obtained. VAS pain scores were collected weekly from patients prior to treatment by a nurse or receptionist Analgesic intake was recorded.
**Results:** Without exception patients were tender over GB31 point on the thigh.
The pain scores improved for all 10 patients by at least 50% with an average of 3–4 treatments. At follow up (3–36 months), improvement was nearly 100%. They were all able to reduce or stop their medication
**Conclusions:** A series of 10 patients all improved, including a patient with a 20 year history. Two patients had refused surgery and three were misdiagnosed. The patients had no signs of radiculopathy. Nerve conduction studies were considered to be non feasible. Electroacupuncture appears to be a good treatment for this debilitating condition.
A Cochrane review in 2008 found observational studies only, not RCTs [1]. Many patients appear to improve spontaneously but 10–15% may need local steroid/anaesthetic injections. Decompression or resection of the nerve may be necessary [2]. In this series 50% of patients needed surgery. I found one paper only discussing two case reports of the treatment of MP with acupuncture [1]. Acupuncture is a safe non-invasive treatment for this debilitating condition. Tenderness of GB31 acupuncture point on the lateral side of the thigh was consistently present, which may aid diagnosis.
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**Disclosure of Interest:** None declared
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## AB0854 BODY ADIPOSITY MEASURES AND THEIR ASSOCIATION WITH LOW BACK PAIN: RESULT FROM A PROSPECTIVE COHORT STUDY

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**Background:** Although obesity is associated with low back pain (LBP) prevalence in adults, the mechanism how obesity causes LBP remained unexplored. Since, our current understanding on how obesity causes other joint pain i.e. pain in hand joints suggest that, there must be additional systemic effect of obesity in the pathogenesis of LBP. Thus, clarifying the role of body composition on the risk of LBP is important as it will help in the understanding of likely pathological mechanisms.
**Objectives:** To examine the relationship between adiposity measures and LBP intensity and disability in community based population.
**Methods:** 5,058 participants (44% men) of the Australian Diabetes, Obesity and Lifestyle Study recruited at 1999–2000 were included. Their body mass index (BMI), waist circumference, and waist-to-hip ratio were obtained from direct anthropometric measurements. The fat mass and percentage fat were estimated from bioelectrical impedance analysis. LBP intensity and disability assessed in 2013–2014 using the Chronic Pain Grade Questionnaire.
**Results:** All the adiposity measures were associated with LBP intensity, independent of fat free mass, for both men and women. The odd ratios (OR) of men for high intensity LBP were BMI OR 1.41 (95% CI 1.17–1.70), waist OR 1.25 (95% CI 1.07–1.46), waist-to-hip ratio OR 1.33 (95% CI 1.03–1.71), percent fat OR 1.45 (95% CI 1.19–1.77), fat mass OR 1.23 (95% CI 1.05–1.44). For women the ORs were - BMI OR 1.39 (95% CI 1.22–1.59), waist OR 1.36 (95% CI 1.22–1.52), waist-to-hip ratio OR 1.49 (95% CI 1.21–1.84), percent fat (10%) OR 1.39 (95% CI 1.22–1.57), fat mass OR 1.27 (95% CI 1.15–1.40). Similarly all adiposity measures were associated with LBP disability. The risk of LBP intensity and disability increased in a linear manner in sex-specific quartiles of all adiposity measures such that the individuals in the highest quartile had the highest risk of developing LBP.
**Conclusions:** All adiposity measures were significantly associated with LBP intensity and disability. This suggests a role for metabolic mechanisms associated with adiposity contribute to the risk of LBP. The rise in the obesity epidemic throughout the world is likely to increase the burden of LBP, as such understanding the mechanism of action will be important in effective prevention of the disease.
**Disclosure of Interest:** None declared
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# Paediatric rheumatology

## AB0855 FOOT INVOLVEMENT IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS AND ITS EFFECT ON FUNCTIONAL STATUS AND QUALITY OF LIFE

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children that often results in persistent and disabling foot impairments (1). Foot and ankle problems are common but relatively neglected manifestations of JIA (2). Ultrasound examination is beneficial for detecting subclinical disease, especially in foot and ankle, which are otherwise difficult to examine in children (3). Therefore, in this study, we evaluated the involvement of foot and ankle in JIA patients using both ultrasonography and physical examination.
**Objectives:** The aim of the study was to investigate the foot and ankle involvement in JIA patients and determine the relationship between this involvement and disease activity, functional status, and quality of life.
**Methods:** We evaluated those children who attended the Pediatric Rheumatology Department between December 2014 and April 2015. Thirty two JIA patients, aged between 6–16 years, participated in this study. Along with the demographic characteristics, the Disease Activity Score-28 (DAS-28), Childhood Health Assessment Questionnaire (CHAQ), and Pediatric Quality of Life (PEDsQoL) scores were recorded for the measurement of disease activity, physical functional status, and quality of life, respectively. The involvement of foot and ankle was investigated by both physical examination (tenderness, swelling and deformities) and detailed gray-scale ultrasonographic evaluation.
**Results:** Of the total included JIA patients, 17 patients (53%) showed foot and ankle involvement. Foot or ankle tenderness was detected in eight patients, swelling in four patients, pes planus in four patients, calcaneal valgus in four patients, limited ankle joint range in two patients, and hallux valgus was detected in three patients. The ultrasonographic investigation revealed tenosynovitis in five patients, ankle joint effusion in four patients, synovial hypertrophy in one patient, bursitis in one patient, and plantar fasciitis in one patient. There was no difference between the group with foot and ankle involvement and the group with no such involvement in terms of demographical data or disease activity ($p>0.05$).

A lower physical functional state was detected in the patients of the foot and ankle involvement group compared to the patients who had no such sign ($p<0.05$). However, this difference was not reflected in the quality of life of the patients ($p>0.05$).

**Conclusions:** This study showed that foot and ankle disorders are not rare in children with JIA. Appropriate evaluation and management of the foot and ankle are important for better functional status of JIA patients.

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## AB0856 EVALUATION OF CARDIAC CAPACITY PARAMETERS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Children with juvenile idiopathic arthritis (JIA) are believed to have a lower cardiopulmonary capacity and functional ability. This means that they face more problems in performing daily activities compared with healthy children (1). Anaerobic capacity is important because most daily activities performed by children are anaerobic in nature (2). The association between anaerobic physical fitness and functional ability emphasized the importance of anaerobic physical fitness in children with JIA (3).

**Objectives:** The purpose of this study is to examine whether children with JIA have lower cardiac capacity compared to healthy children and determine the clinical features that might be related to low aerobic capacity in children with JIA.

**Methods:** 32 JIA patients and 11 healthy children aged between 6–16 years old participated in this study. The age, sex, height, weight, body mass index, disease duration, disease subtype, and medications of the participants were noted. Disease activity, functional disability and quality of life were measured with Disease Activity Score-28, Childhood Health Assessment Questionnaire and Pediatric Quality of Life scores, respectively. Knee or hip involvement in the patients was detected with physical examination. The ergospirometry stress test with bicycle was applied to all the participants to determine their cardiac capacity. The participants began the test with a load of half of their weight and a speed of 100 rpm (rapid per minute) and continued with a load that increased by 1 watt per 3 minutes. They were asked to pass the anaerobic threshold (respiratory exchange ratio). The VO2peak (the maximum volume of the oxygen consumed per minute) values were recorded to assess the aerobic capacity. The time passed after the thresholds (anaerobic capacity) and the total test time were also recorded to measure the whole (aerobic and anaerobic) cardiac capacity.

**Results:** The averages of the cardiac capacity parameters (VO2peak level for the aerobic capacity and the total test time for the cardiac capacity) of the JIA group were significantly lower than those of the control group (p=0.00, p=0.00). There was no significant difference between the JIA (5.88 ±4.13 min) and the control groups (10.50±5.40 min) in terms of the time passed after the threshold (p=0.15). The investigations of the parameters that affect the VO2peak level revealed that women had a lower VO2peak level (p=0.02) compared to men and the participants with knee or hip involvement had a lower VO2peak level (p=0.01) compared to the ones who had no such a sign. Sex and CHAQ were identified as the most determinant factors on VO2peak level when the other probable risk factors were corrected (p=0.00, p=0.04).

**Conclusions:** This study shows that JIA patients have lower aerobic capacities. In JIA treatment, the lower limb involvement, physical functional state, and sex should be considered when targeting to increase the cardiopulmonary capacity of the patients In addition, customized treatment programs should be designed for the JIA patients.

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## AB0857 SPONTANEOUS REGRESSION OF EBV-ASSOCIATED LYMPHOPROLIFERATIVE DISORDER IN A JUVENILE IDIOPATHIC ARTHRITIS PATIENT AFTER DISCONTINUATION OF METHOTREXATE AND ETANERCEPT

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**Background:** The risk for malignancies especially lymphoma seems higher for JIA patients. So far, treatment with TNF-inhibitors, especially with Etanercept has not been described to further enhance the malignancy rate. The association of EBV induced lymphoproliferation/lymphoma has been described in adult patients with rheumatoid arthritis upon treatment with several immunosuppressive drugs including Methotrexate and may not be related to Etanercept.

**Results:** A case of a 16-year-old female patient with polyarticular JIA since the age of 4 years is reported. The patient also suffers from a complex congenital cardiac and several other congenital abnormalities including mental retardation, sensoneurinal hearing loss, growth retardation and pubertas tarda. Microdeletion 22q was ruled out and a microarray assay in search of an underlying genetic disorder was normal. When diagnosed with JIA at the age of 4 years treatment with methotrexate was started but discontinued due to elevated liver enzymes 10 months later. At the age of 13 years, JIA relapsed with multiple joint involvement and treatment with methotrexate and Etanercept was initiated leading to acceptable clinical condition, with functional impairment due to restricted joint movements. Complete remission of JIA was not reached.

After 3 years on combination treatment, the patient reported multiple subcutaneous nodules on the lower extremities. On palpation such nodules were 0.5 to 2.0 cm of size and the largest one was slightly tender. No overlying skin changes such as erythema were noted. Laboratory analysis revealed normal blood counts, normal CRP, but elevated lactate dehydrogenase and uric acid. Ultrasound investigation showed several round lesions with a maximum diameter of 1.7 cm with enhanced signal of capsules and in some of the lesions hypoechoic centers. Thoracic CT detected a mediastinal lesion suggestive of a mediastinal lymphoma.

Biopsy of the largest nodule revealed diffuse large B-cell lymphoma (DLBCL). EBV-RNA (EBER-in-situ-hybridization) could be detected in the nuclei of the blasts. While IgG antibodies to EBV VCA and EBNA were positive, EBV VCA IgM was negative and in the patient's peripheral blood EBV DNA PCR gave negative results. The patient was classified as clinical stage IIIA due to a mediastinal lesion. Immunosuppressive treatment was discontinued immediately, which led to regression of remaining nodules, mediastinal lymphoma and normalization of lactate dehydrogenase. So far, no recurrence of DLBCL or JIA could be detected, 9 months after discontinutation of immunosuppressive treatment.

**Conclusions:** The clinical course with spontaneous regression of the lymphoproliferative lesions and normalization of LDH after discontinuation of antirheumatic treatment lead to the assessment of the neoplasm as lymphoproliferative disorder (LDP) associated with iatrogenic immunosuppression rather than manifest lymphoma. The patient was considered to have iatrogenic lymphoproliferative disorder classified as "other iatrogenic immunodeficiency-associated lymphoproliferative disorders" by the WHO. This is the first case-report of a JIA patient with EBV-positive DLBCL following administration of Etanercept and Methotrexate showing spontaneous regression of lymphoproliferation after discontinuation of antirheumatic treatment.

**Disclosure of Interest:** None declared
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## AB0858 RARE NOD2 VARIANTS IN PATIENTS WITH GRANULOMATOUS UVEITIS

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**Background:** Blau Syndrome is a rare autosomal dominant inflammatory disease characterized by early-onset granulomatous arthritis, dermatitis and recurrent uveitis (1). Mutations in the nucleotide-binding domain (NBD) of *CARD15/NOD2* gene (mainly R334W, R334Q and L469F) have been identified in Blau syndrome (2). Polymorphisms in the leucine-rich repeats (LRR) of *CARD15* are associated with Crohn's Disease, and mutations in the NBD domain are observed in Blau syndrome (3).

**Objectives:** We describe two patients with granulomatous uveitis carrying rare genetic variants of NOD2.

**Methods:** The analysis of the coding exons of the *NOD2/CARD15* gene was performed in our two patients because they had a granulomatous uveitis.

**Results:** The first patient, a 14 years old boy, had an isolated bilateral granulomatous uveitis since he was 10 years old. He was treated by steroids and methotrexate. He carried the A725G variant of *NOD2* (rs5743278 MAF 0.018). The second patient, a 15 years old girl had an isolated bilateral granulomatous panuveitis since she was 5 years old. She was treated by azathioprine and steroids. She carried two other rare genetic variants of *NOD2:* H287Y and L682F (MAF=0.0002).

**Conclusions:** NOD2 is composed of three domains: a C-terminal LRR domain involved in ligand recognition, a central NBD and an N-terminal CARD domain.

Our two patients carried a rare genetic variant located between the LRR and the NBD domains (A725G and L682F). The A725G variant has been previously described in patients with Crohn disease's (CD) phenotype by Hugot et al (3) but our first patient had no clinical symptom related to CD. The second patient carried another rare variant located in the NBD domain (H287Y), compatible with the diagnosis of Blau syndrome. According to these observations, genetic variations located between the LRR and the NBD domains of NOD2 might be associated with the occurrence of granulomatous uveitis. It should be thus recommended to screen NOD2 mutations in patients with isolated granulomatous uveitis.

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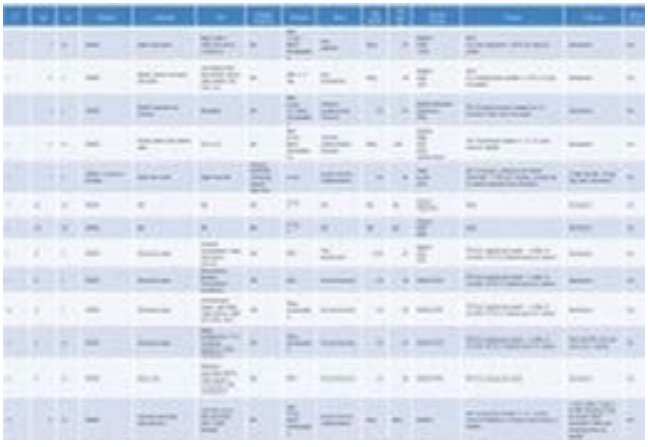
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## AB0859 EFFICACY AND SAFETY OF ANTI-TNFα THERAPIES IN CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO): AN EXTENSIVE REVIEW OF THE LITERATURE

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**Background:** CRMO is an autoinflammatory disease characterized by relapsing and remitting episodes of pain related to the presence of foci of sterile bone inflammation [1]. TNFα levels are elevated in the serum of patients affected by CRMO and in bone-biopsy specimens [2]. NSAIDs and steroid afford symptomatic relief of pain and swelling in approximately 80% of patients [1]. Some recent reports have shown that anti-TNFα agents lead to clinical and radiological improvement in refractory cases of CRMO.
**Objectives:** We provide a review of the literature concerning the efficacy and safety of anti-TNFα in CRMO.
**Methods:** We searched the MEDLINE database and selected articles published in the English language with the headings "CRMO" and "anti-TNFα". We only included unambiguous CRMO cases. We added a patient from our cohort.
**Results:** A total of 13 patients met our inclusion criteria (see Table 1). Etanercept (ETN) was the anti-TNFα most commonly used (7 pts). In 6 cases ETN was used at a dosage of 0.8 mg/kg/week. In 5 cases the dosage was modified after 6 months to 0.8 mg/kg every 2 weeks. In 1 case the drug was used at a dosage of 0.4 mg/kg twice a week. In 2 cases MTX was added to ETN. Infliximab (IFX) was used in 4 pts. It was administered at a dose of 5 mg/kg in 3 pts. In 2 cases a loading dose similar to the one recommended for the treatment of RA was used. In our case, due to the recurrence of bone pain after 4 years with IFX 5 mg/kg every 8 weeks, we reduced the administration interval to 6 weeks. In another patient with worsening bone pain after an initial administration of IFX at a dosage of 5 mg/kg every 8 weeks, a loading dose of 6.7 mg/kg was used for three times every 2 weeks. The patient was then treated with an IFX 6.7 mg/kg every 4 weeks. In 1 pt, an initial regimen of IFX every 4 weeks was modified after 1 year to an 8-weeks regimen. 1 pt was instead treated with IFX at a dosage of 3 mg/kg every 8 weeks. IFX was used as a monotherapy in all cases. Adalimumab (ADA) was used in 2 pts. No data about ADA dose or administration interval were recorded in the published article. Of note, all patients underwent remission after starting an anti-TNFα therapy. In 3 cases a disease flare occurred during the anti-TNFα treatment. In 1 case the flare occurred after increasing the administration interval of ETA from one to two weeks. In the 2 remaining cases the disease flare occurred without any previous therapy modification. In all cases increasing the anti-TNFα agent dosage allowed to achieve remission of CRMO. No adverse events were recorded during the anti-TNFα therapy. No pt required a switch to a different anti-TNFα agent. Attempts to discontinue etanercept therapy were performed in 4 pts, but were followed by disease relapses within a month in 3 cases; in the remaining case, ETA was successfully discontinued after 4.5 years of treatment.
**Conclusions:** Our experience and the review of the literature indicate that anti-TNFα agents represent an effective and possibly safe option in the treatment of refractory CRMO.



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## AB0860 JIA ASSOCIATED UVEITIS IN GREEK ADULT PATIENTS: PROFILE AND LONG-TERM OUTCOME

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**Background:** JIA-associated uveitis is an important cause of ocular morbidity overtime.
**Objectives:** To evaluate the risk factors of uveitis development and describe its characteristics and outcome in a cohort of Greek adult patients with JIA. No relevant Greek data have been published so far.
**Methods:** Medical charts were reviewed in terms of gender, current age, ILAR category, age and ANA titer at disease onset. For patients with an established uveitis, the type of uveitis, date of diagnosis, uveitis complications (synechiae, cataract, glaucoma) were also recorded. The final ocular outcome was the Best Corrected Visual Acuity (BCVA) at the last follow up visit and was ranked in 3 levels: a) good visual acuity: BCVA $\geq$20/40, b) impaired visual acuity: BCVA 20/50–20/100, c) legal blindness: BCVA $\leq$20/200.
**Results:** A total of 102 (72 females) patients were enrolled with a disease age of onset (mean ±SD) 7.7±4 years, a disease course 17.2±6.7 years and patients' current age 25±5.9 years. The JIA subtypes were systemic (12.7%), oligoarthritis (29.4%), polyarthritis (29.4%, 10.8% RF positive), psoriatic (8.8%), enthesitis-related arthritis (17.6%) and unclassified arthritis (1.9%). Uveitis developed in 11 patients (10.8%), mainly in females (10/11 females, p=0.224). In 90.9% of the patients, uveitis was diagnosed within the first 3.5 years of the disease (mean time 2.2, range 0–13 years). In none of these patients uveitis was diagnosed prior to JIA, while in only one, concurrently. Uveitis was mainly bilateral than unilateral (81.8% vs 18.2%). Patients with oligoarticular type of onset had the highest rate of uveitis (9/30, 30%). Patients with uveitis were significantly younger at onset than those free of uveitis ($p<0.001$) and had a higher rate of ANA positivity (81.8% vs 27.3%, p=0.001). Five of these 11 patients (45.5%, 4.9% of the cohort) developed at least one ophthalmologic complication. Cataract was detected in 4/11 patients (36.3%), synechiae in 4/11 (36.3%) and glaucoma in 4/11 patients (36.3%). Three of the 11 (27.3%) developed all the aforementioned complications. The visual outcome at the study visit revealed unilateral legal blindness in 18.2% and the rest (81.8%) had a bilateral good visual acuity. Predictors of uveitis development were early disease onset [OR (95%) 0.562 (0.381, 0.829), p=0.004] and ANA positivity at onset [OR (95%) 10.703 (1.821, 62.899), p=0.009]. Oligoarticular onset was positively associated with uveitis development only in the univariate analysis (p=0.01).
**Conclusions:** The majority of adults with JIA-associated uveitis had a good visual bilateral acuity after a -17 year disease onset. ANA positivity and younger age at disease presentation have been proved to be independent risk factors for uveitis development in Greek patients, too.

**References:**

[1] Saurenmann et al (2007). Arthritis Rheum. 56:647–57.

**Disclosure of Interest:** None declared
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## AB0861 PROGNOSTIC VALUE OF ANA POSITIVITY IN GREEK ADULT JIA PATIENTS

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**Background:** Antinuclear antibodies (ANA), one of the biomarkers of ILAR JIA classification, has been proposed to be associated with a protracted disease course overtime, regardless of JIA subtype. However, their role in the disease outcome is still debated.
**Objectives:** To investigate the impact of ANA positivity in the long-term outcome of JIA patients.

**Methods:** Patients ≥18 years with an established JIA, a minimal disease duration of 5 years and no history of a >6–month care from external rheumatologists, were enrolled in the study. Data were retrieved from the patients' charts, including ANA titers at onset (2 measurements, 3 months apart). The ANA were measured by indirect immunofluorescence (cut-off value ≥1:160). Clinical, laboratory -including ANA- and radiographic assessment were performed at the last follow-up visit, 17.2 years post-diagnosis. The outcome variables defined were: radiographic damage assessed by the total modified Sharp/van der Heijde Score (TmSvdHS), articular and extra-articular damage by Juvenile Arthritis Damage Index (JADI-A and JADI-E), physical ability by the Health Assessment Questionnaire-Disability Index (HAQ-DI) and the cumulative % times spent in a state of disease activity and of clinical remission off medication (CR).
**Results:** Hundred two patients (72 females) were enrolled. The disease age of onset (mean ±SD) was 7.7±4 years, the interval from onset to last visit 17.2±6.7 years and the patients' current age 25±5.9 years. Thirty three (32.4%) patients were ANA positive at onset. At the last follow-up, there was no significant difference between ANA positive and ANA negative patients in terms of TmSvdHS (p=0.982), JADI-A (p=0.699), JADI-E (p=0.235), HAQ-DI (p=0.234), cumulative % time spent in disease activity (p=0.583) or CR (p=0.175). There was no statistical gender difference among ANA positive patients (F:M 36.6%:25%, p=0.385), but they had an earlier disease onset (p=0.038), mostly oligoarticular (p=0.004) and were more prone to uveitis development (p=0.001). In the multivariate analysis ANA positivity was found to be the single independent risk factor for uveitis development [OR (95%) 10.703 (1.821, 62.899), p=0.009].
**Conclusions:** Patients with ANA positive had predominantly an earlier and oligoarticular disease onset and a higher risk of uveitis development. However, ANA positivity was not found to influence the final disease outcome in terms of articular and extra articular degree of damage, radiographic abnormalities, physical disability and cumulative % time spent in disease activity or CR.
**References:**
[1] Martini et al.(2010). Ann Rheum Dis. 69:1260–3,
[2] Ravelli et al.(2011) Arthritis Rheum. 63:267–75.
**Disclosure of Interest:** None declared
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## AB0862 ARTICULAR AND EXTRA-ARTICULAR DAMAGE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Objectives:** The objective of this study was to asses the damage present in patients with JIA using the JADI-A and JADI-E scores, as well as their correlation to various clinical, lab and functional parameters.
**Methods:** The study was prospective and it took place between 2009 and 2014, involving 45 Romanian patients with JIA:15 patients with the systemic form, 15 patients with the polyarticular form and 15 patients with the oligoarticular form, in which the clinical, lab and radiological factors at the onset of the disease were assessed. The reevaluation of the patients was done 3 years later, following a special protocol that included the assessment of the general state, the disease activity score (DAS 28), joint involvement, radiological modifications (according to the Dale scoring system), CHAQ, the JADI-A and JADI-E scores. The correlation between the JADI scores and other parameters was made with the help of Spearman's correlation coefficient.
**Results:** The articular damage highlighted by the JADI-A score was present in 15 patients (33.33%). Extra-articular damage was present in 24 patients (53.33%) and the most affected form was the systemic one – 12 patients (80%). The most frequent extra-articular impairment was growth hypotrophy, which was present in 15 patients (33.33%). In the entire subject group of patients with JIA, the JADI-A score is correlated ($p<0.01$) with the articular score (0.62), CHAQ (0.41), and the parents (0.56) and physician (0.52) visual analogue scale. The JADI-E score is positively correlated ($p<0.01$) with the Steinbrocker classification (0.56), the DAS 28 score (0.53), ESR (0.3) and CHAQ (0.52).
**Conclusions:** The articular and extra-articular damage JADI scores can represent a useful instrument for the monitoring of damage in children with JIA.
**Disclosure of Interest:** None declared
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## AB0863 HIGH FREQUENCY OF CAPS AND TRAPS IN RUSSIAN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** The main clinical manifestations of monogenic autoinflammatory syndromes and polygenic Systemic juvenile idiopathic arthritis (sJIA) are similar and presented with fever, migratory erythematous rash, arthritis/arthralgia and eye manifestations. The right diagnosis is reached using gene analysis and prognosis depends on correct personified therapy.
**Objectives:** To evaluate frequency of CAPS and TRAPS in Russian systemic JIA pts.
**Methods:** 170 pts (61 boys, 109 girls) at the age from 1 to 17y. (6.9 (3.9;9.4) followed with a diagnosis of sJIA were selected according to the clinical manifestations, with subsequent obligatory genetic counseling in the Department of Rheumatology of the Scientific Center for Children's Health. The median age of disease onset was 2.9 (1.2;6.0)y., disease duration – 4.0 (2.6;5.4)y. The commonest features were fever (100%), arthritis/arthragia (100%), rash (163 pts/96%), hepato- and splenomegaly (160/94%), lymphadenopathy (136/80%), headache (88/52%), abdominal pain (98/58%) and eye manifestations (42/25%). Patients' DNA was sequenced in all coding exons and intronic flanks of the TNFRSF1A and NLRP3 genes.
**Results:** In 18/130 (10.6%) pts genetic autoinflammatory syndrome was established. In 12 pts we found mutations in TNFRSF1A: In 9/12 pts - the most frequent mutations c.362G>A (p.R92Q) located in exon 4 and associated with the mild progression of TRAPS. One pt revealed a TNFRSF1A mutation c.374G>A (C96Y). Two pts identified mutations which were not previously described in the databases. They had TNFRSF1A deletion c.337_339del (p.Glu113del) and frameshift mutation c.792delT (p.Lys265Serfs*87) located in exons 04 and 09 of TNFRSF1A gene, respectively. The median age of disease onset was 5.3 y. Pts had a median 85 symptomatic days per year, attacks were recurrent in 78%. A family history was present in 3 pts: 2 girls with R92Q and one – with C96Y mutation. Four pts identified mutations in NLRP3 gene. One pt had mutation c.598G>A (p.Val200Met). Three pts had mutations which were not previously described in the databases. One pt had a mutation c.796C>T (p.Leu266Phe) in exon 04 of NLRP3 gene. Two other pts had mutations c.2861C>T and c.2173C>A, respectively. Pts with c.2173C>A and c.796C>T mutations have CINCA/NOMID phenotype and dramatic effect of canacinumab.
2 pts presented changes in both genes. They had R92Q mutation in TNFRSF1A and polymorphism Q705K in NLRP3 gene.
In 15 (7.6%) pts we identified NLRP3 gene polymorphism Q705K associated with elevated levels of IL1.
**Conclusions:** Our results suggests for a relatively frequent incidence of CAPS and TRAPS in Russian systemic JIA pts. The number of genetically confirmed pts with periodic fever syndromes in Russia is very low. It is important to establish a network for genetic testing of periodic fever syndromes.
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## AB0864 PEDIATRIC ACUTE-ONSET NEUROPSYCHIATRIC SYNDROME (PANS): CLINICAL EVALUATION IN A GROUP OF ITALIAN CHILDREN. A DIFFERENT ENTITY FROM PANDAS?

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**Background:** PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcal Infections) identifies a subgroup of pts with unusually abrupt and dramatic TIC/OCD onset GAS infection related. PANS "Pediatric acute-onset neuropsychiatric syndrome" is a term proposed to describe a clinically distinct presentation of OCD/TIC with post infectious origin. Differently from PANDAS, in PANS other agents may trigger the disease, including *Mycoplasma pneumonia*, Influenza viruses, Epstein Barr virus, *Borrelia Burgdorferi*, Herpes simplex and Varicella viruses. Clinical presentation is characterized by an abrupt dramatic onset of OCD and additional neuropsychiatric symptoms nor explained by known neurologic or medical disorders[1].
**Objectives:** To describe clinical features of 23 Italian children with OCD/TIC diagnosed as PANS in comparison to our PANDAS group.
**Methods:** Between May 2009 through January 2016 we recruited 23 pts (13 M, 10 F) with OCD/TIC starting before puberty. The mean age at onset 77 mnths±35.6SD.
**Results:** 19 (86.4%) were full-term born, 3 (13.6%) from Caesarean section (no information in 1 adopted child). 8/21 (38.1%) had familiars with OCD/tics or other neurologic diseases (2 pts without data). At onset, clinical signs were OCD in 3 (13%), OCD and motor tics in 7 (30.4%), motor tics in 5 (21.7%), vocal tics in 1 (4.3%), motor/vocal tics in 5 (21.7%), motor/vocal tics and OCD in 2 (8.7%), Mean age at diagnosis 106.8 months±36.9 SD. Antistreptolysin O and antiDNaseB titers were negative in all pts. In all *EBV*, *Mycoplasma pneumoniae*, *CMV*, *Borrelia Burgdorferi* were tested: 2 pts had history of tick bite and *Borrelia Burgorferi* Ab+, 6 pts Mycoplasma pneumoniae Ab+, 1 EBV Ab+; in 2 pts a VZV infectionAb+ was found. In 1 child Rotavirus infection was suspected and 12 had a viral pharyngitis before OCD/Tics onset. All underwent neuropsychiatric evaluation, none had deficit of psychological development; in all autoimmunity (ANA; antiDNA and ENA Ab) was negative as well as cerebral MR and EEG. All received antibiotic therapy according to the specific infection: pts with *Mycoplasma* macrolide, pts with *VZV* antiviral, pts with *Borrelia* amoxicillina. All showed benefit during and after the treatment. Pts, with no specific agent, received amoxicillina and benzathine benzylpenicillin with benefit after a more prolonged period than PANDAS pts.

**Conclusions:** Our data show that PANS as PANDAS prediliges males with higher familiar predisposition in PANS. The age at onset is comparable to PANDAS, while OCD are more common and severe than in PANDAS. All pts had an infectious event, as PANDAS pts, but the trigger agent was different from GAS, and all responded to the specific therapy. PANDAS and PANS mainly differs from the trigger agent. The knowledge of PANS and PANDAS is mandatory to early recognize children at the disease onset avoiding to delay the diagnosis and the beginning of therapy.

**Acknowledgement:** [1]Chang K et al. Clinical evaluation of Youth with pediatric acute onset neuropsychiatric syndrome (PANS): recommendations from the 2013 PANS Consensus Conference. J Child Adolescent Psychopharmacology 2015:25:3–13

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## AB0865 VITAMIN D RECEPTOR POLYMORPHISMS ARE NOT ASSOCIATED WITH THE RISK OF KAWASAKI DISEASE (KD) IN A GROUP OF ITALIAN CHILDREN

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**Background:** Kawasaki disease (KD) is an acute multisystemic vasculitis, affecting primarily infants and children, and it is the most common cause of acquired heart disease in Western countries. The exact pathogenesis of KD has not been clearly identified, but infections caused by one or more pathogens are strongly suspected as major cause of the disease. Our previous study demonstrated that KD patients have highly reduced 25(OH)-vitamin D levels in comparison with healthy controls and also with other immunological disorders, suggesting a hypothetical role of vitamin D deficiency in the development of coronary artery damage in KD, and low vitamin D levels might contribute to the severity of chronic vascular abnormalities. Specific polymorphisms of vitamin D receptor (*VDR*) gene have recently been associated with different biologic response to vitamin D itself.

**Objectives:** 1.To analyze the possible associations of these polymorphisms in a series of Italian children affected by KD. 2. To evaluate a possible influence of VDR polymorphism in enhancing the risk of the disease.

**Methods:** We recruited 50 Italian infants and children affected by typical KD (38 males, 12 females), age ranging from 2 through to 62 months.

Genomic DNA was extracted from peripheral blood leukocytes to analyze *VDR* polymorphisms by PCR-based sequencing (*CDX2* in the promoter region) and PCR-based enzymatic digestions (*FokI* in exon 2, *BsmI* and *ApaI* in intron 8, and *TaqI* in exon 9).

An Italian population of 2221 unrelated individuals without KD or other immunological disorders was used as healthy controls. The distribution of polymorphism genotypes and alleles was evaluated in patients vs healthy controls.

**Results:** The distribution of all Cdx2, *FokI, BsmI, ApaI*, and *TaqI* polymorphisms (both as genotypes or alleles) did not show significant differences between affected subjects and healthy controls.

**Conclusions:** In conclusion, this pilot study evidence that *VDR* polymorphisms seem not to have any influence in determining the risk of KD. Anyway, future larger studies are needed to unravel the exact relationship between *VDR* genotype and KD development and/or clinical characteristics.

**Disclosure of Interest:** None declared

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## AB0866 CROSS-SECTIONAL EVALUATION OF VITAMIN D LEVELS IN A LARGE COHORT OF PATIENTS WITH PEDIATRIC AUTOIMMUNE NEUROPSYCHIATRIC DISORDERS ASSOCIATED WITH STREPTOCOCCAL INFECTIONS (PANDAS)

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**Background:** Vitamin D (vitD) is known for its essential role in calcium homeostasis and bone health. It is now considered as a potent neurosteroid hormone, with a pivotal role on the brain development and normal brain function. VitD ligand-receptor, a receptor that mediates the majority of vitamin D biological actions, has been found throughout the body including the central nervous system (CNS). Vitamin D deficiency is commonly observed in patients with severe mental illness such as schizophrenia. PANDAS is an autoimmune disorder characterized by obsessive-compulsive symptoms and/or tics triggered by group-A beta-hemolytic Streptococcus infections with relapsing/remitting course due to recurrence of infections itself. Despite the action of 25-hydroxyvitamin D [25(OH)D] on immune and CNS system, to our knowledge, no studies have been performed in patients with PANDAS.

**Objectives:** To evaluate 25(OH)D levels in a large cohort of children and adolescents with PANDAS 2. To compare the results with a healthy control group.

**Methods:** We measured plasma 25(OH)D levels in one hundred seventy-nine patients with PANDAS (49 females, 132 males, mean age at diagnosis 101.4 ±30.1 months) and an age, sex, and body mass index-matched control group of 179 subjects.

**Results:** Patients with PANDAS showed a higher percentage of reduced 25(OH)-vitamin D levels ($<$30 ng/mL) in comparison with controls (94.6% *vs.* 82.5%; $p<0.005$). In addition, PANDAS patients have lower levels of 25(OH) D than controls (20.4±6.9 *vs.* 24.8±7.3 ng/mL, $p<0.0001$). This difference has been confirmed also considering the winter (13.7±3.25 vs. 21.4±5.9) and summer (21.8±6.5 *vs.* 32.5±8.7) period. Yet, serum 25(OH)-vitamin D levels correlated with the number of streptococcal infections before the diagnosis ($p<0.005$) and with their recurrences ($p<0.005$).

**Conclusions:** PANDAS patients have reduced 25(OH)D values that seem to be associated with streptococcal infections, and the probability of its recurrences. So, reduced 25(OH)D levels may be a cause significantly important in PANDAS etiopathogenesis. A regular supplementation of VitD in PANDAS patients is recommended as it should improve the course of the disease and prevent or reduce the recurrences of infections and the relapses of neurological symptoms. This hypothesis should be further explored in future studies.

**Disclosure of Interest:** None declared

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## AB0867 EXPERIENCE OF ETANERCEPT USE IN TREATMENT OF JUVENILE IDIOPATHIC ATRTRITIS IN CHELYABINSK REGIONAL CHILDREN HOSPITAL

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**Background:** Recently due to application of genetically engineered biologic drugs (GEBD) prognosis for juvenile idiopathic arthritis (JIA) has significantly improved. 558 children with JIA are under monitoring in Chelyabinsk region. If basic therapy with Methotrexane is inefficient Etanercept is the drug of choice for JIA treatment. Etanercept is registered within the Russian Federation for use in children older than 2 years. In Chelyabinsk regional children hospital Etanercept has been used during 5 years.

**Methods:** 23 children aged from 2 to 17 (mean age 9.2 years) diagnosed with JIA were under monitoring (10 boys, 13 girls). Disease duration was from 6 months to 14 years (mean duration 4.5 years). JIA was diagnosed based on ILAR diagnostic criteria. Oligo arthritis was diagnosed in 8 children, sero-negative polyarthritis was diagnosed in 8 children. Five patients had systemic JIA (without active systemic presentations), two children had enthesitic JIA. X-ray stage 1–2 was observed in 22 children and stage 3 in one. Enhancement antigens HLA B 27 were found in 7 children. In all children Methotrexate was ineffective in dose of 15 mg/m$^2$ during 6–12 months. Etanercept was introduced in dose of 0.4 mg s/c biweekly, or 0.8 mg QW. Therapy duration was from 3 months to 5 years (mean duration 17 months). Assessment of disease activity and therapy efficiency was conducted in accordance with ACR pedi criteria. Nonparametric statistical methods were used to compare results.

**Results:** Prior to etanercept use high disease activity was observed in all children. Mean number of joints with active arthritis was 6 [3, 8] (Me [25; 75%]). Mean number of joints with functional impairments – 4 [2, 8]. Mean ESR (according to Panchenkov) – 31 [18.40] mm/h, CRP 19.7 [8.37] g/L. Assessment of functional activity according to CHAQ questionnaire- 1 [0.75; 2]. Activity assessment according to VAS by doctor – 70 [70,80]. Assessment of parents/patients according to VAS 80 [65,90]. No active systemic presentations and eye lesions were found in children under monitoring.

On the background of eternacept therapy a decrease in disease activity was observed in 21 patients. Mean number of joints with active arthritis was 0 [0, 1] (Me [25; 75%]) (P=0.0004). Mean number of joints with functional impairments – 1 [0.2] (P=0.0006). Mean ESR was 4 [3.7] mm/h (P=0.00008), CRP 3 [1; 4.1] g/L (P=0.0001). Assessment of functional activity according to CHAQ questionnaire was 0.25 [0; 0.5] (P=0.0004). Activity assessment according to VAS by doctor – 10 [10, 30] (P=0.0004). Assessment of parents according to VAS 20 [10, 30] (P=0.0004).

Clinical disease remission (according to ACR pedi criteria– $\geq$90%) was observed in 11 patients after 6–12 months of treatment. Remission duration up to now is from 3 months to 4 years. Efficiency according to ACR pedi criteria is 70% in 8 children, 50% in 1, 30% in 2.

The drug was well-tolerated. Drug was cancelled only in 2 patients due to change in disease presentations: one patient developed bilateral uveitis, the other one experienced recurrence with expressed systemic presentations.

**Conclusions:** Etanercept therapy was highly effective and safe in patients with JIA. Clinical remission was achieved in 47.8% children. Decrease in disease activity was observed in 91.3% of children. No serious undesirable effects were reported.

**Disclosure of Interest:** None declared

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## AB0868 A DESCRIPTIVE RETROSPECTIVE STUDY OF JUVENILE IDIOPATHIC ARTHRITIS PATIENTS WITH TREATED BIOLOGICAL

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**Background:** Biologic drugs are a mainstay in the treatment of juvenile idiopathic arthritis (JIA). The early use of these drugs allows controlling disease activity avoiding its consequences and improving the quality of life of patients. We know the main characteristics of our cohort of JIA patients treated with biologics.
**Objectives:** To describe the main characteristics of patients and biological treatments received during the last 5 years (2010–2015) in a pediatric unit of a children's hospital.
**Methods:** Retrospective descriptive analytical study of patients diagnosed with JIA (as proposed by ILAR nomenclature) receiving biological treatment from 1 January 2010 to 30 June 2015. Data from medical records collected from patients who biological treatment received. Statistical analysis performed on SPSS.19.0 program.
**Results:** Total 105 patients treated with biological drugs in the last 5 years, 2/3 female (67 girls, 64%), 1/3 male (38 boys, 36%), mean age at diagnosis 5.3 years (DE ±3.95años). The distribution of JIA: Oligoarticular arthritis 40% (42 patients). Polyarticular RF negative arthritis 22.9% (24 patients). Enthesitis-Related arthritis 15.2% (16 patients). Systemic 14.3% (15 patients). Polyarticular RF positive arthritis 3.8% (4 patients). Psoriatic arthritis 3.8% (4 patients).
Patients with positive antinuclear antibodies (ANA) 24.8% (26 of 105 patients).
Of the patients 32.2% (34 patients), i.e. 1/3 had uveitis, of these 41% (14 patients) had positive ANA.
Initial treatment with methotrexate 78.1% (82 patients), methotrexate maintained 56.2 (59 patients), with adalimumab 37.1% (39 patients), etanercept 16.2% (17 patients), tocilizumab 2.9% (3 patients).
Total received 123 biological treatments: adalimumab 49 (39.8%), etanercept 47 (39.2%), tocilizumab 16 (13%), anakinra 8 (3.5%) and canakinumab 3 (2.4%). Overall median time of monitoring 33.3 months (SD ±22.4 months). Continue with the drug 54 (43.9%), decrement regimen 50 (40.7%), replaced by inefficiency 15 (12.2%) (adalimumab 3, etanercept 4, anakinra 3, tocilizumab 5), suspended for toxicity 4 (3.3%) (anakinra 3, adalimumab 1). No deaths recorded.
**Conclusions:** The clinical features in this cohort of JIA patients treated with biologics are similar to those described in other "general series" that do not distinguish the type of treatment.
The biological treatments used most often are etanercept and adalimumab, both with similar percentages (mainly in non-systemic JIA). The most commonly used drugs in systemic JIA are anakinra, tocilizumab and canakinumab.
The biological treatments appear to be safe based on what has been described: few drugs had to be replaced by toxicity, and was not recorded death by the treatment or the disease itself.
**Disclosure of Interest:** None declared
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## AB0869 THE CONTENT OF ADIPONECTIN IN THE BLOOD OF CHILDREN WITH RHEUMATIC DISEASES

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**Background:** The hormone adiponectin is an indispensable component in the regulation of energy homeostasis and maintaining optimal lipid profile. It was found that low levels of adiponectin may be regarded as a predictor of metabolic syndrome. Despite the fact that adiponectin has an effect on energy homeostasis and is an anti-inflammatory agent, its main role is antiatherogenic effect and influence on the lipid profile body.
**Objectives:** to study the contents of adiponectin in the blood of children with rheumatic diseases.
**Methods:** Indicators serum lipid spectrum (total cholesterol, triglycerides, and HDL cholesterol) were studied at a biochemical analyzer. The concentration of adiponectin and serum CRP levels determined by ELISA.
Statistical analysis was performed using the software package Statistica 8.0 ("StatSoft, Inc.", USA).
**Results:** The study involved 54 children with juvenile idiopathic arthritis (JIA), 18 children with systemic lupus erythematosus (SLE) and 24 children with juvenile scleroderma (JS). Most of the children receiving long-term glucocorticoid and immunosuppressive therapy. 28 children with JIA, 9 children with SLE and 11 children with JS were overweight. Obesity is defined in 13 children with JIA, 8 children with SLE and 5 children with JS. When comparing the average concentrations of adiponectin according to the body mass index (BMI) found that with an increase in this index decreased adiponectin content in blood. Adiponectin level was significantly lower in obese children (10,8±4,6 mg/ml) compared with children with overweight (13,2±5,3 mg/ml) and children with normal body weight (16,4±4,1 mg/ml). In healthy children adiponectin content was 21,3±5,7 mg/ml. There was a significant negative correlation of adiponectin with body mass index (r=-0,36), glucose concentrations (r=-0,29), C-reactive protein (r=-0,31), the levels of blood pressure (r=-0.34) and positive to the level of high density lipoprotein (r=0.26).
**Conclusions:** The negative correlation between the level of adiponectin blood concentration of C-reactive protein and a positive correlation with the level of HDL indicates the probable anti-inflammatory properties of adiponectin and its protective effect against the development of atherosclerosis in children with rheumatic diseases.
**Acknowledgement:** This study would not have been possible without the collaboration of numerous Belarusian pediatric rheumatologists, patients and their parents.
**Disclosure of Interest:** None declared
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## AB0870 LIPID DISORDERS IN CHILDREN WITH RHEUMATIC DISEASES

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**Background:** Lipid metabolism disorders is one of the most studied problems in adult patients with rheumatic diseases in the world of rheumatology in connection with proven dyslipidemia in these patients, and raises the question of the genesis of atherosclerosis in the background of autoimmune disease.
**Objectives:** To examine the state of lipid metabolism in children with rheumatic diseases.
**Methods:** The survey included: the collection of family history, anthropometry, instrumental and laboratory examination, including the study of lipid profile (total lipids, total cholesterol, triglycerides, HDL, LDL, apolipoproteins: ApoA, ApoB, ApoE).
**Results:** The study involved 96 children, suffering from rheumatic diseases - 54 children with juvenile idiopathic arthritis (JIA), 18 children with systemic lupus erythematosus (SLE) and 24 children with juvenile scleroderma (JS). Additionally it was examined 50 healthy children. Children with SLE found a significant increase in the content of total lipids, total cholesterol and triglycerides when compared with the control group ($P<0.001$). Children with JIA, there was a significant increase in total lipids and triglycerides ($P<0.001$) when compared with the control group. In children with JS found a significant increase in serum total lipids ($P<0.05$), as well as the reduction of HDL cholesterol ($P<0.05$) when compared with the control group. Increased levels of total lipids in serum>7.0 g/l are set at 61.1% of children with SLE, in 44.4% of patients with JIA and in 62.5% of JS. Elevated triglycerides >1.4 mmol/l were detected in 50% of children with SLE, 20.4% of patients with JIA and 25% of patients with JS. Elevated levels of total cholesterol >5.2 mmol/l is set at 16.7% of children with JIA, and reduced levels of HDL cholesterol <0.96 mmol/l was found in 29.6% of patients with JIA and in 25% of children with JS.
During the correlation analysis established a direct correlation between the level of total cholesterol in blood serum and disease duration ($r_s$=0,71; $P<0.01$), as well as between the degree of disease activity and the content of total lipids ($r_s$=0,63; $P<0$ 01).
Apolipoprotein A is the major protein component of HDL. The significant (P 0.05) decrease in the concentration of ApoA patients clinical groups compared with the control group.
ApoA1 ratio and ApoB is a valuable indicator for assessing the atherogenic shift and the risk of cardiovascular disease. Normally ApoA1/ApoB >1 and is seen as a low atherogenic risk factor. Among children with rheumatic diseases indicator ApoA1/ApoB <1 is set at 16.7% of patients with SLE, in 14.8 patients with JIA and in 12.5% of patients with JS. An inverse correlation between the ratio ApoA1/ApoB and the concentration of serum cholesterol ($r_s$=-0,31; $P<0.01$).
Apolipoprotein E (ApoE) is a part of the fat particles of chylomicrons and very low density lipoproteins, initiating their capture and removal of blood by interacting with specific cell surface receptor on the liver. The study established an elevated level of ApoE in the serum of children with rheumatic diseases compared to the control group. Established correlation ($r_s$=0,37; $P<0.05$) between the content of ApoE and total cholesterol in the blood serum.
**Conclusions:** For children suffering from rheumatic diseases characterized by atherogenic disorders of lipid metabolism.
**Disclosure of Interest:** None declared
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## AB0871 IMPACT OF FAMILIAL MEDITERRANEAN FEVER, MKD/HIDS, AND TRAPS ON PATIENTS AND FAMILIES, DATA FROM PATIENT INTERVIEWS

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**Background:** Patients with the rare autoinflammatory diseases of Familial

Mediterranean Fever (FMF), mevalonate kinase deficiency (MKD)/Hyperimmunoglobulin D syndrome (HIDS), and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) often have long diagnostic journeys. Patient and family experiences along this path to diagnosis are poorly understood.
**Objectives:** To understand the experiences of patients and families with autoinflammatory diseases through diagnosis and treatment.
**Methods:** We employed 90-minute semi-structured qualitative interviews and 5-day written/video diaries of patients and families with autoinflammatory diseases.
**Results:** Twelve US families participated in the fall of 2015 including 4 TRAPS patients, 5 MKD/HIDS patients, and 5 FMF patients. The patients' ages ranged from 1–28 years. Caregivers reported an insidious onset of symptoms, but were initially reassured by their healthcare providers (HCPs) that symptoms were related to normal childhood illnesses. Most parents in this study (86%) realized that something was seriously wrong only after medical crises and hospitalizations. The diagnostic path began in earnest then, including many specialist visits (often with long waits for appointments), extensive testing, and many misdiagnoses including Lyme disease, meningitis, H1N1 influenza, systemic lupus erythematosus, systemic juvenile idiopathic arthritis, atypical Kawasaki's disease, leukemia, lymphoma, bone cancer, and Crohn's disease. Most parents (92%) lost faith in the medical system's ability to find an answer to their children's symptoms, while they also struggled with unsupportive school officials and dismissive friends and relatives. Parents and patients frequently felt a loss of self-confidence and increasing alienation in the face of criticism and disbelief. Patients and caregivers report holding onto a memory of what normal life was like prior to the onset of symptoms, and mourning their subsequent loss of normalcy. Receiving the diagnosis of an autoinflammatory disease provided vindication and relief, as well as a focus for further education and treatment. Even after diagnosis, patients and caregivers reported continuing confusion about what to expect in the future. Many (64%) reported disease symptoms between flares that were rarely recognized as such by their HCPs. Uncertainties about their diseases led patients and caregivers to seek online support communities, but struggled finding patients whose symptoms mirrored their own.
**Conclusions:** Patients with autoinflammatory diseases often encounter long diagnostic delays, causing significant stress and confusion for the patient and their families. Distrust of the medical establishment may persist even after diagnosis. Loss of normalcy is a core tragedy for many families. Confusion and uncertainty continue to mark these families' lives, even after diagnosis. Initiatives that improve the speed and accuracy of diagnosis, provide more comprehensive patient education, and support patients and their families through their illness have the potential to greatly improve the lives of patients with autoinflammatory diseases.
**Disclosure of Interest:** J. Hausmann Consultant for: Novartis, K. Lomax Employee of: Novartis, A. Shapiro Consultant for: Novartis, K. Durrant: None declared
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## AB0872 SWITCHING OF BIOLOGIC TREATMENT IN ONE PAEDIATRIC RHEUMATOLOGY CENTRE. RETROSPECTIVE REVIEW

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**Background:** The treatment of children with rheumatic and musculoskeletal diseases (RMD) have changed significantly with biologic treatment.
**Objectives:** To look at reasons for switching from one biologic to another.
**Methods:** Patients with confirmed RMD identified in our centre using The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), from 1st January 2011 to 31st December 2015. Retrospective review of electronic records and paper case notes of patients presented to the centre reviewed using pre-specified Clinical Research Form (CRF).
**Results:** We identified 181 paediatric patients on continuous follow up. The distribution as follows; juvenile Idiopathic Arthritis (JIA) 78, Systemic Lupus (JSLE) 19, Juvenile Scleroderma (Scl) 5, vasculitis 7, Juvenile Dermatomyositis (JDM) 6, Familial Mediterranean Fever (FMF) 9, Macrophage Activation Syndrome (MAS) 3 and Uveitis only in 2. Other diagnoses of non-inflammatory nature 52 including juvenile osteoporosis, mechanical pain syndromes and vitamin D deficiency.
The total number of patients on biological therapy is 35 patients including 33 JIA and 2 JSLE. The number of patients still on the same biologic agent is 25.
The following are the biologics with numbers of patients still on the same therapy (25): Etanercept 7 (JIA), Infliximab 3 (JIA), Adalimumab 1 (Uveitis), Abatacept 1 (JIA), Tocilizumab 7 (JIA), Anakina 4 (JIA 3, FMF 1), Rituximab 2 (JSLE).
The number of patients who switched their treatment to a second or third agent is 10. The reason for switching biological treatment was lack of efficacy in 7 out of the 10 patients and side effects in the other 3 patients (table 1). Average follow up on current treatment of 36.6 months (range 0.5 to 81 months).
**Conclusions:** The percentage of patients who switched biological treatment is 28.6% although numbers are small. Reasons for switching biologic treatment in our experience in children with RMD is:
-lack of efficacy with persistent inflammation in 7 out of 10.
-Side effects of treatment in 3 out of the 10 (Uveitis while on etanercept (2) and one developed MAS twice on canakinumab.
**Acknowledgement:** To all the children and their families for allowing us to use their data.
**Disclosure of Interest:** None declared
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**Abstract AB0872** – Table 1

| Case Number | Diagnosis | 1st biologic | 2nd Biologic | 3rd Biologic | Reason for switching |
|---|---|---|---|---|---|
| 1 | Oligo JIA + Uveitis | Adalimumab | Infliximab | | Persistent eye inflammation |
| 2 | Extended JIA | Etanercept | Tocilizumab | | Persistent joint inflammation |
| 3 | Polyarticular JIA | Adalimumab | Abatacept | | Persistent joint inflammation |
| 4 | Polyarticular JIA | Adalimumab | Tocilizumab | Abatacept | Persistent joint inflammation in 2nd and 3rd |
| 5 | Polyarticular JIA | Etanercept | Adalimumab | | Uveitis with etanercept |
| 6 | Extended Oligo JIA | Abatacept | Tocilizumab | | Persistent inflammation |
| 7 | Systemic JIA | Tocilizumab | Canakinumab | Anakinra | Persistent inflammation with 1st biologic MAS twice on Canakinumab |
| 8 | Enthesitis Related JIA | Etanercept | Adalimumab | | Uveitis on Etanercept |
| 9 | Poly JIA | Adalimumab | Tocilizumab | | Persistent joint inflammation |
| 10 | Systemic JIA | Etanercept | Tocilizumab | | Persistent inflammation |

## AB0873 COMPREHENSIVE MEDICAL AND PSYCHOSOCIAL CARE TO REDUCE THE BURDEN OF CHRONIC RHEUMATIC DISEASES IN CHILDREN: TWO-YEAR EXPERIENCE OF THE FRENCH NETWORK RESRIP

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**Background:** Chronic rheumatic diseases (CRD) in children are associated with significant morbidity and disability, poor quality of life and impact on families. In the region of Paris (France), CRD affect around 2000 children. Management of CRD involves different physicians and health professionals, in a multidisciplinary approach that is particularly valuable in paediatric patients. The RESRIP (Réseau pour les Rhumatismes Inflammatoires Pédiatriques) network has been created to improve coordination between health professionals and personalize patient care for paediatric patients affected by CRD
**Objectives:** To describe demographics, socioeconomic features and diseases characteristics of patients enrolled in the RESRIP network in a 2-year period
**Methods:** Retrospective study involving patients included in the network (September 2013-December 2015). Inclusion criteria were $\geq$2 of the following: disease severity (defined as a disease impacting on $\geq$1 of the following: physical/psychological status, school attendance, growth/development; complexity of treatment); association of $\geq$2 diseases; necessity of $\geq$3 different health professionals; socioeconomic frailty; demand of support expressed by the patient/parents; transition to adult health care; patient followed in a peripheral hospital
**Results:** 147 patients (103F, 44M, median age at disease onset 4.2 y (0.42–15.2) were included. Median time to diagnosis was 4 months (0–134). Median disease duration at enrolment in the network was 14 months (1–172). Main diseases were: juvenile idiopathic arthritis (JIA) (49.7%) (polyarticular 38%, oligoarticular 29%, enthesitis-related arthritis 18%, psoriatic arthritis 11%, systemic arthritis 4%); connective tissue diseases (CTDs) (19%) (overlap-syndrome: 43%, systemic lupus erythematosus: 32%, dermatomyositis 21%, systemic sclerosis 4%) and auto-inflammatory diseases (AIDs) (14.3%) (FMF 52%, Mevalonate Kinase deficiency 4.8%, PFAPA 4.8%, CRMO 28%, other 9.5%). Inclusion criteria were: disease severity (82%), necessity of $\geq$3 different health professionals (80%), demand of support expressed by the patient or the parents (28%), socioeconomic frailty (24%), association of $\geq$2 diseases (20%), patient followed in a peripheral hospital (8%), transition to adult healthcare (7%). Inclusion criteria differed according to the disease: for JIA, it was the necessity of several health professionals (96%), mostly physiotherapists and nurses, while disease severity was the main criterion for CTDs (100%) and for AIDs (72%). For AIDs, the demand of support by patient/parents was a frequent reason for enrolment (53%)
**Conclusions:** RESRIP enrolled mostly patients with JIA, CTDs and AIDs. Disease severity and the necessity of multiple health professionals were the main identified reasons to be followed in the network. These data confirm that CRD patients and their families are in need of support for everyday care. Health networks can provide help by improving care coordination and treatment adherence
**Disclosure of Interest:** None declared
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## AB0874 JUVENILE IDIOPATHIC ARTHRITIS. FOLLOW-UP IN ADULTHOOD: A DESCRIPTIVE STUDY

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**Background:** Juvenile Idiopathic Arthritis (JIA) is the most prevalent clinical entity between childhood rheumatic diseases. Treatment and follow-up in adulthood of patients diagnosed with JIA is not well defined, it is therefore important to define the clinical features and complications during adulthood of these patients, and thus achieve better management of the disease.
**Objectives:** To describe the clinical features and complications in adult patients diagnosed with JIA.
**Methods:** Cross-sectional descriptive study where the evolution of 44 patients older than 18 years diagnosed with JIA in current monitoring Services Rheumatology two tertiary hospitals is determined.
**Results:** The current average age of the patients is 31.06 years (18–64); sex: 34 woman,10 men; average age of diagnosis was 9.9 years (1–16); mean duration of disease 21.2 years (4–53). The patient characteritics and their complications are specified in Table 1.
During follow-up the number of relevant infections occurred in 9 patients (20.5%): 4 polyarticular JIA (community-acquired pneumonia, pyelonephritis E. coli, catheter-related sepsis and repeat UTI), 2 in JIA Oligoarticular 2 with systemic JIA and another in psoriatic way; and they have required hospitalization at some point in the evolution of his illness 80% of systemic JIA, 71.4% of polyarticular JIA and 66.6% of oligoarticular JIA. Orthopedic surgery was performed in 14 patients (32%); JIA subtypes with higher number of surgeries were systemic and polyarticular RF positive. The most common surgeries: total knee and hip prosthesis. All patients have been treated with FAME (especially LFN and MTX), except for one patient with psoriatic JIA and 2 ERA B27+. Biological treatment has been used in 23 patients (52.3%): polyarticular JIA (47.6%), systemic onset JIA (100%), oligoarticular JIA (50%), arthritis-entesistis (50%). 25% received a biological; 16% received two biological and 10% three or more biological.
**Conclusions:** Despite the small number of patients in our series, we have determined the following:1)The most frequent form of JIA on follow-up in adulthood is polyarticular (47.7%). 2)93.2% of patients received FAME treatment. 3) More than half of patients (52.3%) received treatment with biologics. 4) Relevant infections occurred in 20.5% of patients, especially in subtype polyarticular JIA. 5)The vast majority of orthopedic surgeries were performed in the pre-biological age. JIA subtypes that needed more systemic way were systemic JIA and polyarticular RF positive, the most common surgeries total hip and knee prosthesis.
**References:**
[1] Cohorte de adultos jóvenes diagnosticados con enfermedad reumática crónica infantil. López Robledillo, J.C. Sociedad Española de Reumatología.
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## AB0875 ANALYSIS OF JOINT FUNCTION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS AGAINST THE BACKGROUND OF STANDARD THERAPY

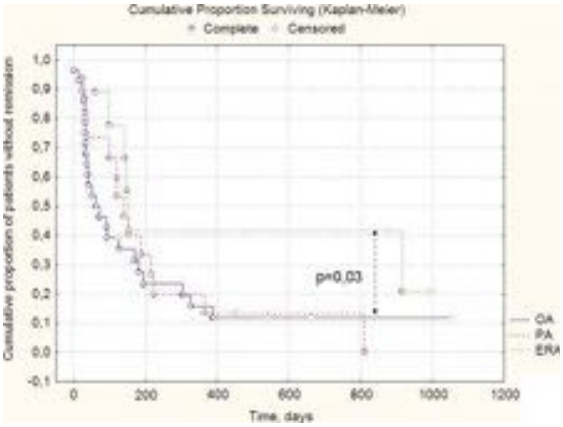
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**Background:** Juvenile idiopathic arthritis (JIA) is a chronic and socially significant disease as it leads to quick disability in childhood despite treatment
**Objectives:** To study the development of joint dysfunction in patients with JIA against the background of standard therapy with methotrexate
**Methods:** The study involved 83 children within 2–18 years with JIA: oligoarthritis in 39,6%, polyarticular form – 37,7%, systemic form – 20,8%, enthesitis-related arthritis – 1,9%. Changes in the joints were assessed depending on the duration of disease: 1–2 years (25 patients), 3–5 years (23 patients), 5–10 years (35 patients). There were 51 females, 33 males. Criteria of decreased function of joints include: amplitude of motion of hands less then 110°; elbows, knees, ankles and wrists – less then 50°, shoulder and hip joints - less than 70°. For the statistic processing of the material, Stagraphics 3.0 was used.
**Results:** With an increase in the duration of the disease despite standard care, the joint tenderness according to Ritchie index and joint pain according to *Visual Analogue Scale* were decreased, especially after 5 years of illness ($p<0,0\ 5$). The most significant signs of joint determination were limitation of motion and function of articular apparatus. It was found that frequency limited to function of joints among our patients was 77.11%, which was a prerequisite of patients' disability. With an increase in duration of disease, frequency of limited function of joints constantly grew and probably greater in comparison with the initial stages of the disease ($p<0.05$). The most common joints, which lost motion, were knee, radio-wrist, ankle and hip. In stages over three years of course of JIA, limited motion were found in all of the affected joints. Cervical spine lesion was determined in 33.3% of patients typically after 2 years of duration of JIA. In term from one to two years despite treatment in 50% of patients, affection of hip joints were presented. It was determined during the first two years, the changes that correspond to 0 (27,3%) and I stage of the disease by Steinbrocker (72,7%), from 3 year in 45,5% of children II stage was found, from 4th year 15,4% - III, after 6th year 14,7% persons had IV stage. The main stage of deterioration of the radiological changes is the term disease for more than 5 years, when significantly the frequency of the III stage in comparison with the previous period is increased ($p<0,01$) and the IV stage is appeared.
**Conclusions:** It reflected steadily progressive destructive changes of the musculoskeletal system with limited motion of joints function despite therapy with methotrexate and independent of activity of disease and symptom load.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2197

## AB0876 ACHIEVEMENT REMISSION IN DIFFERENT JUVENILE IDIOPATHIC ARTHRITIS CATEGORIES DURING ADALIMUMAB THERAPY: DATA OF RETROSPECTIVE ANALYSIS

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**Background:** Juvenile idiopathic arthritis (JIA) is a chronic rheumatic disease with onset before 16 years. According ILAR classification there are several categories based on number of joints, clinical and laboratorial features. Patients with JIA without systemic features who fall or not tolerated to methotrexate (MTX) or sulfasalasine (SSZ) usually treated by biologics, especially TNFα-inhibitors. Currently only 2 TNFα-inhibitors approved in JIA: etanercept and adalimumab (ADA).
**Objectives:** The aim of study was to evaluate the efficacy of ADA in children with JIA without systemic features and ability to induce remission.
**Methods:** In the retrospective observation study were included 53 children (67.9% girls) with active JIA without systemic features, who were resistant to previous therapy with MTX alone (or SSZ in enthesytis-related arthritis) or with combination with other non-biologic DMARDs and were treated with subcutaneous ADA injections every 2 weeks. The onset age was 3.9 (1.7–7.8) years, the interval between onset of JIA and start of ADA was 4.2 (0.3–15.2). Uveitis was detected in 32 (60.3%) patients. According number of active joints and clinical features all patients were divided into 3 groups: oligoarthicular course (OA) – 4 active joints or less, polyarthricular course (PA) – 5 active joints or more and enthesitis-related arthritis (ERA) with any active joints. We evaluated routine clinical and laboratorial test for JIA and ability and time to achieve inactive disease, according to C. Wallace criteria (2004).




**Abstract AB0874** – Table 1

| Subtype of JIA | Number of patients (n=44) | Sex | Time evolution (mean in years) | ANA | Uveitis | MAS | Infections | Ortopedic Surgery | Synovectomy/synoviorthesis |
|---|---|---|---|---|---|---|---|---|---|
| Sistemic-onset | 5 (11.3%) | 3♀: 2♂ | 24.8 | ND | No | 2/5 | 2/5 | 4/5 | No |
| Oligoarticular | 12 (27.3%) | 10♀: 2♂ | 21.7 | 10+/2– | 7/12 | No | 2/12 | 2/12 | 3/12 |
| Poliarticular | 21 (47.7%) | 17♀: 4♂ | 23.9 | 10+/11– | 1 (ANA–) | No | 4/21 | 7/21 | 3/21 |
| FR+ | 9 (42.9%) | | | | | | 3/9 | 4/9 | 2/9 |
| FR– | 12 (57.1%) | | | | | | 1/12 | 3/12 | 1/12 |
| Psoriatic | 2 (4.5%) | 2♀ | 7 | ND | No | No | 1/2 | 1/2 | No |
| ERA B27+ | 4 (9.1%) | 2♀: 2♂ | 14,2 | ND | No | No | No | No | No |

**Results:** Number of active joints (NAJ) and erythrocyte sedimentation rates significantly decreased, while levels of C-reactive protein, WBC, Hb and platelets still unchanged. In 12 months after start of ADA median of NAJ was equal 0. During the trial 44 (84.6%) patients reached the status of inactive disease (ID) according the C. Wallace criteria in median time 122.0 (36.5–220.0). We have not found any significant differences of initial JIA parameters between patients who achieved and not achieved status of ID. We have found differences in JIA groups in achievement ID: patients with OA similar to PA faster and frequently get into remission than patients with ERA (p=0.03, Log-Rank test, OA vs ERA). During the trial 26 (50.0%) have experienced the flare throw the median time 551.0 (317.0–809.0) days after 1st ADA injection. Patients with flare had less NAJ [1.0 (0,0; 2,0) vs 4.0 (1,0; 8,0), p=0.007]. The main predictors of JIA flare during the ADA trial were calculated with Cox-regression models: JIA duration ≥4 years before start of ADA (HR=2.4, p=0.055), presence of concomitant uveitis (HR=4.8, p=0.0008) and discontinuation of MTX (HR=3.2, p=0.19). During the trial 1 SAE was detected: disseminated tuberculosis in patient who received ADA near 3 years (unrecognized family contact).
**Conclusions:** In our study the efficacy of ADA was shown. Further trials required for evaluation long-term outcomes.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5654

## AB0877 DYNAMICS OF PARAMETERS CHANGES OF ANTIOXIDANT DEFENSE AND LIPID PEROXIDATION IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** The dependence of intensity of carbonyl stress and its correlation with the pathogenic inflammatory and erosive process of joint tissue were determined in adults with rheumatoid arthritis. These issues in patients with juvenile idiopathic arthritis (JIA) were not studied.
**Objectives:** It was to determine the role of content in the blood of carbonylated proteins (CP), the intensity of induced lipid peroxidation (LPO), the activity of superoxidedismutase (SOD), glutathioneperoxidase (GPO) and the correlations between them and the early immunological markers of the disease, such as anti-cyclic citrullinated peptide antibodies (a-CCP) and *modified* citrullinated *vimentin antibody (a-MCV),* at different stages of the disease development in patients with JIA.
**Methods:** The study included 29 patients with oligoarticular and polyarticular forms of JIA within 2 – 18 years old. 12 healthy children of identical age and gender with the studying patients were present in the control group. For the statistic processing of the material Stagraphics 3.0 was used.
**Results:** Investigated group included 21 female and 8 - male. Patients under 10 years predominated. In children with JIA increase of the intensity of induced LPO in comparison with persons of control group was presented ($p<0.001$) and did not depend on the duration of JIA, number of affected joints and inflammatory activity. Patients with oligoarthritis had higher values of induced LPO than with polyarthritis ($p<0.05$). The level of CB had a significant decrease in patients with JIA in comparison with persons of control group ($p<0.05$). It is presented in the first 6 months of the onset of the disease, mostly by patients with III degree of inflammatory activity. Variations of GPO activity in patients and the children of control group were not different, and did not depend on the form of arthritis, duration of disease, inflammatory activity. Rate of activity of SOD was lower in children with JIA in comparison with persons of control group ($p<0.05$). Among patients with positive a-CCP in comparison with children with positive a-MCV decrease of SOD activity was determined ($p<0.05$). A similar pattern was typical for JIA in the first 6 months of illness, during 6–12 months of pathological process development it was marked increase in SOD activity ($p<0.05$), and the longer history of the disease level of SOD activity was not different in comparison with control group. Level of SOD activity was authentically lower among patients with polyarthritis and with high degree of activity ($p<0.05$).
**Conclusions:** Increasing of level of induced LPO was presented at early stage of JIA, with increasing duration of the disease it was also increased. For the first 6 months of JRA development level of CB in serum was decreased, especially in patients with high (III) degree of disease activity. Decreasing of SOD activity was determined in the first year of the disease's development, mainly in patients with polyarthritis, with II-III degree of inflammatory activity and positive titers of a-CCP. Activity of GPO was not different between patients and persons of control group. Reasonability and methods of correction of above-noted changes of parameters of antioxidant defense and lipid peroxidation in patients with juvenile idiopathic arthritis should be investigated further.
**Disclosure of Interest:** None declared
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## AB0878 LIVER CONDITION AND SIGNS OF THE FIBROSIS FORMATION IN SLE IN ADOLESCENTS

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**Background:** The liver damage in SLE usually occurs in 60% of cases. Histological investigation shows plethora, blood stagnation in the vessels, fat infiltration and necrosis in the portal system. The data on the liver pathology in SLE in children and adolescents are quite poor. Clinical and laboratory instrumental signs of the liver damage lack both in diagnostic criteria of SLE and in SLICC/ACR damage index. Together with that, liver is a hidden target organ, the pathological changes in which can be registered at the fibrosis formation stage.
**Objectives:** To determine the liver function tests and determination of the stage of fibrosis in the adolescents with SLE at the onset of disease.
**Methods:** The study involved 48 patients with SLE (mostly female (90,00%). The mean age of the patients was 14,4 years (172,9±4,72 months). The diagnosis was based on SLICC, 2012 criteria. The functional state of liver was examined with a complex of clinical laboratory, biochemical and instrumental methods (objective examination, ultrasound investigation of liver and gallbladder, the levels of bilirubin and its fractions, general cholesterol, the activities of alanine transferase (ALT), aspartate transferase (AST), alkaline phosphatase (AP). De Ritis's coefficient (AST/ALT) and APRI index (Aspartate-aminotransferase-to-Platelet Radio Index) have been estimated.
**Results:** At the onset of SLE an increase in size and an increase in transaminase activity were registered in 11 of 48 patients (22,9%). The SLE onset age in this group was 14,1 years (169,09±5,91 months), the mean SLE duration was 4,63±1,90 months, 54,5% of the patients had subacute onset and 63,6% had an increased activity of pathological process. 81,1% had liver cytolysis manifestations (increase in ALT (115,66±5,42 IU/l), AST (60,6±3,47 IU/l), decrease in De Ritis's coefficient (down to 0,79 with its normal values 1,3–1,4). 37,4% of the patients of this group had De Ritis's coefficient higher than 1,0 (AST prevailing) that is more typical for "cardiac" cytolysis. 63,6% of the patients of this group had De Ritis's coefficient lower than 1,0 (ALT prevailing) that is an evidence of liver changes. Activity of AP and pigment metabolism did not have changes. The level of cholesterol in the serum was decreased in 30,0%. USI data showed an increase in the size of liver in 81,81% of the patients, an increase in parenchyma echogenicity and fading of ultrasound signal in deep layers. AST positively correlated with CRP ($r=0,67$, $p<0,05$), sialic acids ($r=0,66$, $p<0,05$), glycoproteins ($r=0,62$, $p<0,05$); ALT positively correlated with the level of circulating immune complexes ($r=0,81$, $p<0,001$). Tests for fibrosis showed an increased risk of its formation in 27,3% of patients at the onset of SLE, and its reliable probability in 9,1% (APRI index 1,1).
**Conclusions:** Liver is involved in SLE, with high occurrence of liver damage manifested as cytolisis, a decrease in synthetic activity, signs of fibrogenesis activation and the presence of the initial stage of fibrosis in some patients at adolescent age. The degree of changes depends on SLE activity and the presence of cardiac and renal syndromes. The examination of the patients should take into account the markers of functional state of liver, including inflammatory activity and fibrosis formation. A timely discovery of such changes can benefit the therapy able to decrease their progress.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4541

## AB0879 PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF TOFACITINIB IN PAEDIATRIC PATIENTS FROM TWO TO LESS THAN EIGHTEEN YEARS OF AGE WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).
**Objectives:** Report the pharmacokinetics (PK), safety and taste acceptability of tofacitinib following multiple oral doses in patients (pts) 2-<18 years (yrs) old with active juvenile idiopathic arthritis (JIA).
**Methods:** Data were obtained from an open-label, non-randomised, multicentre, Phase I study (NCT01513902) where JIA pts were given 5 mg adult equivalent (based on body weight) of tofacitinib (tablet or solution) twice daily (BID) for 5 days (Table). There were 3 cohorts (COH) based on pt age, COH1: 12-<18 yrs, COH2: 6-<12 yrs, and COH3: 2-<6 yrs, with a target enrolment per group of ≥8 JIA pts for N=≥24 evaluable pts completing the study. Pts were enrolled in a step-wise approach beginning with the older age COH first. Subsequent younger age COH were enrolled following confirmation of safety and PK from the previous COH. PK parameters of tofacitinib were calculated using non-compartmental analysis of plasma concentration (conc)-time data. Taste acceptability of the solution formulation was listed and categorically summarised (frequency and %).

**Results:** 26 pts (COH1 [N=8], COH2 [N=9] and COH3 [N=9]) were included in this analysis. Pts' age ranged from 2–17 years; all were white race except for one; there were 17 females and 9 males. Baseline disease characteristics were similar across all COH. All exposure metrics including geometric mean (GM) area under the conc-time curves ($AUC_{tau}$), maximum ($C_{max}$), minimum ($C_{min}$) and predose ($C_{trough}$) conc were lower in COH2 relative to those in COH1; however, due to higher doses in COH3 (modified after interim analysis of COH1 and 2), the mean $AUC_{tau}$ in COH3 was comparable to COH1. GM apparent volume of distribution ($V_z$/F) decreased with age (COH1=104.9L, COH2=71.0L, COH3=51.4L). Average terminal half-life ($t_{1/2}$) were COH1=2.62h, COH2=1.95h and COH3=1.77h. GM tofacitinib CL/F were 53%, 39% and 11% higher in COH1, COH2 and COH3 pts, respectively, vs adult RA pts (18.4L/h) receiving tofacitinib 5 mg BID. GM CL/F and V/F parameters were similar between males and females. Tofacitinib, administered over 5 days as multiple dose tablets or solution formulation, was well tolerated and taste for the solution formulation was found acceptable in children with active JIA. No serious adverse events or new safety signals were identified.

| Body Weight (kg) | Tofacitinib Dose BID (mg) | Volume (mL) |
|---|---|---|
| Dosing Scheme for Age 6 to <18 years | | |
| 5-11 | 1 | 1 |
| 12-18 | 1.5 | 1.5 |
| 19-24 | 2 | 2 |
| 25-31 | 2.5 | 2.5 |
| 32-39 | 3 | 3 |
| ≥40 | 5 | 5 |
| Dosing Scheme for Age 2 to <6 years | | |
| 5-6 | 1 | 1 |
| 7-9 | 1.5 | 1.5 |
| 10-12 | 2 | 2 |
| 13-15 | 2.5 | 2.5 |
| 16-19 | 3 | 3 |
| 20-22 | 3.5 | 3.5 |
| 23-26 | 4 | 4 |
| 27-29 | 4.5 | 4.5 |
| ≥30 | 5 | 5 |

BID, twice daily

**Conclusions:** PK results from this study established dosing regimens for pts aged ≥2 years to be used in the upcoming efficacy and safety studies of tofacitinib in JIA pts. Tofacitinib was well tolerated in this study in JIA pts. Overall, pts found the taste of the tofacitinib solution formulation to be acceptable.

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## AB0880 MACROPHAGE ACTIVATION SYNDROME – AN INDIAN EXPERIENCE

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**Background:** Macrophage activation syndrome is a deadly complication of systemic rheumatic disease namely Systemic Juvenile Idiopathic arthritis (SJIA). But many other rheumatic diseases like SLE and Kawasaki disease (KD) can be complicated by MAS due to immune deregulation and extreme hypercytokinemia. Here we present a series of 24 cases of MAS that we have encountered in last 7 and half years.

**Objectives:** 1.To evaluate the clinical and laboratory characteristics of MAS
2.To assess the treatment responsiveness to different therapies
3. To identify the poor prognostic factors

**Methods:** Children fulfilled the recent 2014 diagnostic criteria of MAS that has been admitted in the time period of July 2008 to November 2015 has been included in the study. The details of clinical features, laboratory results and outcome were noted down.

**Results:** The total number of patient was 24 among them, Systemic JIA was 18, SLE was 5 and rest one had KD as a primary illness. The male: female ratio was 17:7 and the mean age at presentation was:7.9 years. CNS, cardiac and respiratory involvement were present respectively in 78, 52 and 35% of cases. 20 patients needed ICU admission, 10 needed mechanical ventilation. 16 survived and 7 expired with a mortality rate of around 30%. All of them received Pulse Methylprednisolne (30mg/kg) for 5–7 days +/– Intravenous immunoglobulin. 12 needed Cyclosporine.

**Conclusions:** 1. MAS is a deadly complication of pediatric rheumatological diseases with a high mortality rate of 30% in our series.
2. Features of acute liver failure along with CNS and cardiac involvement with extreme hyperferritenemia (ferritin >50,000ng/ml) was associated with bad prognosis.
3. The effectiveness of IV pulse methylprednisolone was only 40%.

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## AB0881 ANTI-ADALIMUMAB ANTIBODIES IN JUVENIL IDIOPATHIC ARTHRITIS AND LOSS OF RESPONSE. PRELIMINARY STUDY

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**Background:** The longterm use of adalimumab (ADL) is limited by the formation of neutralizing antibodies. To the best of our knowledge, immunogenicity in juvenile idiopathic arthritis (JIA) has not been investigates in depth.

**Objectives:** Our main objective was to evaluate the prevalence of adalimumab immunogenicity in JIA and the association of anti-adalimumab antibodies (AAA) with response to treatment. Secondary objectives were to assess the association between AAA and ADL treatment time, and the influence of use of concomitant immunosuppressive therapy in the formation of AAA.

**Methods:** Twenty consecutive patients with JIA treated with ADL >6 month participated in our cross-sectional study. The demographic and clinical characteristics, disease activity and use of methotrexate (MTX) were collected. Until now, were evaluated drugs levels (ELISA) and AAA (Brindgind ELISA) in ten of these patients, before the next injection. Serum samples with ADL concentrations >2mg/L were not analysed for AAA.

**Results:** A total of 10 patients with JIA were recruited, with a mean age of 12.2 years (range 8.15–18.76 yrs), 50% women. 60% of the patients were concomitantly treated with MTX. Altogether, 70% of the patients demonstrated therapeutic drug levels. Of the 10 patients studied, 3 (30%) had AAA coinciding with the relapse of the disease despite treatment. Also, these 3 patients had undetectable levels of drug. Note that 2 patients (66.6%) who have developed AAA and 4 patients (57.14%) who have not developed AAA also received MTX, there were no significant differences. The duration of JIA was 6.6 years (range 2.54–13.04 yrs) and half time ADL treatment was 2.6 years (range 0.95.5.79 yrs). Half time to ADL treatment before AAA development was 3.62 years (range 1.6–5.44 yrs) and in patients who do not develop AAA was 2.19 years (0.95–5.79 yrs), there were no significant differences.

**Conclusions:** - Significant levels of AAA were present in up to 30% of patients with JIA treated with ADL.
- In our patients, the formation of AAA during treatment with ADL is associated with a loss of clinical response.
- In our preliminary study, the development of AAA was not associated with ADL treatment time.
- In principle, not appear to be significant using combination therapy with MTX and the development of antibodies.
- To consider that this is a preliminary study with a sample size too small, so these results should be confirmed once the study is completed.

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**Disclosure of Interest:** None declared
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## AB0882 ACUTE RHEUMATIC FEVER: A EVER PRESENT DISEASE IN THE WESTERN WORLD WITH POSSIBLE INSIDIOUS INVALIDATING HEART INVOLVEMENT

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**Background:** Rheumatic Fever (RF) is a systemic inflammatory disease following pharyngeal infection by goup A beta–hemolytic Streptococcus (GAS).
**Objectives:** to describe the characteristics of rheumatic Fever in a pediatric population of Verona between the 2005–2015.
**Methods:** Clinical presentation of 44 patients with diagnosis of Rheumatic Fever was investigated. Patient age, sex, age at diagnosis as well as Jones criteria fulfilled were reported. The presence/absence of familiarity of Rheumatic Fever, therapy prescibed, pophylaxis' adhesion and primary cardiac involvement with it's evolution after therapy were evaluated.
**Results:**
Incidence of RF in Verona is increasing according to our data Age at diagnosis ranged from 2 to 17 years old (mean age 9-+4 years). Among Jones criteria carditis is most frequently encountered and its severity is not correlated with the values of antistreptolysin o titer (ASO). Heart murmur Was present in 57% of cases at diagnosis. 2 cases had a grade 1 AV blockade and two children underwent pacemaker implantation due to complete not reversibile AV blockade; no case of pericarditis was diagnosed and valvular involment (according to WHF classification) included mitral rigugitation (46,5%), aortic rigurgitation (7%) and bivalvular aortic-mitral rigurgitation (46.5%).
**Conclusions:** RF has not disappeared in the western world; cardiac involvement, which is not correlated with the absolute value of ASO, is the most worrysome clinical condition due to its possible severe sequaela; regular cardiac US and EKG togetherwith thorough physical examination should always be performed in order to identify subclincal cases. While prompt high dose steroids and NSAIDS administration prevent severe evolutions, antibiotics rappresent the main instrument in the primary and secondary prevention of the chronic reumatic Heart disease.Individual susceptabilty is a point of concern for the outbrake of RF as well as the need to identify "rheumatic" streptococci in order to elaborate a specific vaccination.
**Disclosure of Interest:** None declared
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## AB0883 CRYOPYRINOPATHY DETECTED IN 10 FAMILY MEMBERS OF 4 GENERATIONS: IMPORTANCE OF INTERDISCIPLINARY COLLABORATION

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**Background:** Cryopyrin-associated periodic syndromes (CAPS)are autoinflammatory disorders with autosomal dominant inheritance. Although Muckle-Wells Syndrome (MWS) stands in the middle of theCAPS severity spectrum, it is associated with the high risk of severe late complications that include hearing loss, vision impairment and AA amyloidosis affecting about 26% of individuals. Early diagnosis and appropriate treatment with interleukin-1 (IL-1)blockade may prevent their development
**Objectives:** Analysis of a single paediatric patient trajectory leading to the revelation of multiple members of his family suffering with MWS, description of evolving disease phenotype in patients from different generations. To stress an importance of disease awareness as well as interdisciplinary collaboration in detecting familiar conditions affecting both children and adults.
**Methods:** Multiple-case study.
**Results:** A 3-years old Caucasian boy was referred to the allergologyclinic by his primary care paediatrician for recurrent flares of non-pruritic urticarial rash from about 4 months of age. There were no other symptoms of note. Detailed family history suggested presence of rash in other family members.Working together, paediatric and adult rheumatologist detected additional 9 individuals suffering with variable combinations of fever episodes with rash (all), episodic arthritis, eye inflammation, hearing loss, headache and proteinuria (Graph 1, Table 1). Patient's great grandmother died in 52 years of age from renal failure. Although renal biopsy was not performed at the time, presence of other symptoms as reported by her children made clinical diagnosis of MWS and amyloidosis very likely.
Genetic analysis of exon 3 of NLRP3 gene in affected individuals revealed heterozygous mutation c.1322C>T causing change of amino acids p.Ala441Val and prompted referral to the autoinflammatory disease centre for biologic therapy.

| Patient | Age (yrs) | Onset (yrs) | Fever | Rash | Eyes | Arthritis | Hearing loss | Headache | Proteinuria |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 3 | 0.3 | – | + | – | – | – | – | – |
| 2a | 31 | 2 | + | + | + | + | – | + | – |
| 2b | 31 | 3 | + | + | + | + | – | – | ? |
| 2c | 27 | 7 | + | + | + | + | – | – | – |
| 2d | 24 | ? | + | + | + | + | – | – | – |
| 2e | 21 | 6 | + | + | + | + | – | – | – |
| 3a | 51 | 2 | + | + | + | + | + | + | + |
| 3b | 52 | 4 | + | + | + | + | + | – | + |
| 3c | 43 | ? | – | + | + | – | ? | ? | ? |
| 4a | 52 | ? | ? | + | + | + | + | ? | + |

**Conclusions:** In this family medical care was not primarily seeked by adults who have got used to their long-term and relatively mild symptoms. The diagnostic procedure was initiated by the paediatric referral. Detailed analysis of the symptoms suggests presence of the high risk of severe complications. Hearing loss and/or proteinuria have only been noticed in individuals older than 50 years of age. Importantly, younger members below 30 years have not yet developed any of these symptoms which may now be prevented with long-term biologict herapy. This multi-case report illustrates importance of the high degree of suspicion as well as close collaboration between paediatric and adult specialists in order to establish timely diagnosis and initiate appropriate investigations and treatment.
**Disclosure of Interest:** None declared
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## AB0884 DIAGNOSTIC VALUE OF PROCALCITONIN FOR DIFFERENTIATION BETWEEN BACTERIAL INFECTION AND NON INFECTIOUS INFLAMMATION IN FEBRILE CHILDREN WITH SYSTEMIC AUTOIMMUNE DISEASE

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**Background:** Systemic autoimmune disease children presents with fever during disease flare and systemic infection. It is very difficult for clinician to decide the diagnosis clinically, acute phase reactants helps in this situation. Hence we decided to determine the diagnostic value of procalcitonin to differentiate bacterial infection and non infectious inflammation.
**Objectives:** To determine the clinical value of procalcitonin (PCT) in differentiating bacterial infection from disease activity in children with systemic autoimmune disease.
**Methods:** This was a cross-sectional study of children with systemic autoimmune disease presented with fever recruited over 9 months. Baseline demographic variables were recorded and measurements of PCT, CRP, ESR and blood cultures were done. The disease activity for SLE was determined by SLEDAI score and for JIA by Wallace criteria. During the study period, 24 children with systemic autoimmune disease were recruited and analysed. Children were divided in 2 groups: Fever due to disease flare and due to infections.
**Results:** Out of 24 children recruited as per inclusion criteria, 16 had SLE (11 in disease flare group and 5 in infection group) and 8 had disease flare of Systemic JIA. 2 children in SLE infection group died. As for infections, serum PCT concentration (cut-off value >1.2 ng/ml) gave a sensitivity of 83% (95% CI 43.6 - 0.97), a specificity of 72% (95% CI 49.1–87.5), a positive predictive value of 50% (95% CI 23.6- 76.3) and a negative predictive value of 93% (95% CI 68.5 - 98.7).To achieve the same sensitivity (as of PCT) of 83%, the cut off value for CRP was 34 mg/dl and ESR was 76 mm/hr. Mean PCT was 92.2 ng/ml in SLE infectious group and 3.50 ng/ml in SLE flare group which was statistically significant (p=0.009). But mean CRP was 98 mg/dl in SLE infectious group and 52 mg/dl in SLE flare group which was not statistically significant (p=0.25). Similarly mean ESR level (38 mm/hr) in SLE infectious group and in SLE flare group (66 mm/hr) was not statistically significant (p=0.35).
**Conclusions:** Our results suggested that the procalcitonin level was the most discriminatory parameter, followed by CRP in children with SLE presenting with fever between disease flare and infection. Procalcitonin levels>1.2 ng/ml in febrile SLE patients should point to bacterial infection, whereas procalcitonin levels less than <1.2 ng/ml might indicate non-infectious inflammation that could reduce unnecessary antibiotic use.
**Disclosure of Interest:** None declared
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## AB0885 CHILDHOOD-ONSET EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: A RARE CHILDHOOD VASCULITIS MIMICKING ANTHRAX AND EOSINOPHILIC LEUKEMIA

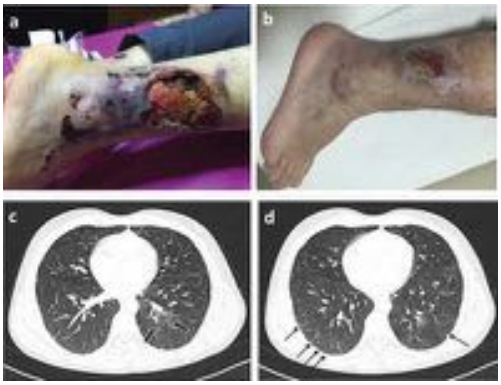
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**Background:** Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare small-vessel vasculitis most commonly presents in adults with the average age of diagnosis is being 50 years. After the long-standing prodromal phase (asthma,

allergic rhinitis, nasal polyposis) patients progress to eosinophilic phase which is marked by eosinophilia and pulmonary infiltrates and then to the vasculitic phase (1,2).

**Objectives:** Herein, we present a child in the vasculitic phase of EGPA with a severe skin involvement, who was initially diagnosed and treated for cutaneous anthrax.

**Results:** A 14-year-old male previously misdiagnosed as cutaneous anthrax was referred with a 2-month history of multiple wide and deep ulceronecrotic lesions in lower extremities, started after contact with animals (1a). Complete blood count (CBC) revealed anemia (hemoglobin: 8.5 g/dl, hematocrit: 26.9%), eosinophilia (4100/$mm^3$) and thrombocytopenia (34000/$mm^3$). Peripheral blood smear also revealed marked eosinophilia (42%). Infectious etiologies such as cutaneous anthrax, leishmaniosis, aspergillosis and nonspecific agents were excluded by gram staining, wound-blood-bone marrow cultures and serological investigations. Bone marrow aspiration was performed owing to the prominent eosinophilia, anemia and thrombocytopenia. However, the result was also pointing out eosinophilia without signs of eosinophilic leukemia. Although ANCAs were negative, the robust clinical manifestations concordant with EGPA (e.g. eosinophilia, increased Ig E level, history of asthma, vasculitic lesions) had led us to repeat the skin biopsy and search for lung involvement. Pulmonary high resolution computed tomography (HRCT) demonstrated bilateral ground glass opacity (figure 1c) and millimetric subpleural nodules (figure 1d). Skin biopsy revealed necrotizing inflammation without apparent granulomas and marked eosinophilic infiltrations in the extravascular areas. On the second day of hospitalization he developed deep vein thrombosis (DVT). A diagnosis of EGPA was established and intravenous methylprednisolone with low–molecular weight heparin were administered. Patient showed remarkable improvement of cutaneous lesions and DVT (Figure 1b).



**Conclusions:** Lack of awareness for EGPA among paediatricians as a consequence of limited childhood cases, results with diagnostic delay. Diagnosis of EGPA is challenging in the vasculitic phase and necessitates a detailed history that specifically questions the patient for asthma history. Coexistence of vasculitic lesions and eosinophilia associated with a prior history of asthma should lead to the consideration of EGPA in differential diagnosis.

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## AB0886 A QUALITY OF LIFE (QOL) STUDY OF 100 CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) FROM NORTHERN INDIA

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**Background:** JIA affects many domains of a child's life. The patient with JIA has a lot to cope with: Physical pain, medicine intake (both parenteral and oral), clinic appointments, phlebotomy, exclusion from school and social activities during disease flares and anxiety about disease.JIA has an impact on the child's physical, mental and psychosocial health. There is a lacuna in the assessment of Pediatric QoL in these children from our country,we thus undertook this study.

**Objectives:** 1) To assess the QoL score of JIA patients using i) Pediatric rheumatology quality of life (PRQL) score [1] and ii) Pediatric quality of life 3.0 rheumatology module(PedsQL) score [2]. 2) To assess the clinical and socioeconomic factors that may impact the QoL. 3) To correlate PRQL and PedsQL

**Methods:** 100 consecutive children with JIA, 2–18 yr,attending Ped rheumatology unit during a 8 week period were evaluated for QoL. PRQL (parent & child version) PedsQL (parent & child version) & CHAQ (Childhood Health Assessment Questionaire) [3] were completed. Entry criteria was JIA patients with at least 6 months of disease.

**Results:** 46 girls & 54 boys with a median age of 11 yrs (2–18 yrs). Median age:6.2 yrs at disease onset,7.62yrs at diagnosis. 28 children had clinically active disease on the day of QoL assessment. Age:2–4 yr:8, 5–7 yr.:18, 8–12 yr.:35 and 13–18 yr.:39.Diagnosis: SOJIA: 31,ERA: 42,PJIA:14,OJIA:13.Socio economic indicators: Mother's literacy status: Unlettered 4,primary schooling 10,High school 12,Senior school 7,Graduates 37,Post graduates 30.Stay at home mothers:85,working 15. 19 children belonged to lower socioeconomic strata. Children with clinically active disease had poorer QoL as compared to clinically inactive group (Mann-Whitney test: $p<0.00$).QoL indicators and CHAQ had no statistical correlation. PRQL and PedsQL were in agreement with each other (Spearman's rho,r=0.72) and both parent and child versions were in concordance.

**Conclusions:** Both PRQL and PedsQL are appropriate tools to assess QOL in JIA. Clinical disease activity status impacts QoL adversely.There was no difference in QoL of children from various socioeconomic strata, nor did the parental education or professional status impact it.

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## AB0887 DYNAMICS OF GROWTH IN CHILDREN WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH TOCILIZUMAB

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**Background:** systemic juvenile idiopathic arthritis (sJIA) is an arthritis with systemic manifestations (fever, rash, lymphadenopathy, hepatosplenomegaly) in children up to 16 years. In juvenile arthritis often occur growth disorders. Prior to the widespread use of biologic agents in 10–20% of children with sJIA was noted growth retardation. Currently it is of importance to investigate the influence of biologic agents on growth.

**Objectives:** To evaluate the effect of tocilizumab (TCZ) the growth of children with sJIA.

**Methods:** the study included 25 children with sJIA, all children with high clinical and laboratory activity. All patients received active anti-rheumatic therapy, including therapy with glucocorticoids (GC): all patients (100%) – pulse therapy; oral - 12 children (48%). The age of the onset was 6,2±2,4years (from 9 months to 13,6years). 9 children (36%) before tocilizumab received anti-rheumatic therapy, 5 (20%) children – another biological agent. The duration of such therapy was 2,9±2,9 years (1 month to 12 years), 11 children (44%) began receiving tocilizumab during the year from the onset of the disease. The average age of initiation: 9,4±3,4 years (4 to 14 years old). The study evaluated growth SDS, growth rate and growth rate SDS prior of the therapy with tocilizumab after 6 months, after 1 year and after 2 years of therapy.

**Results:** In 22 children (88%) with sJIA prior TCZ growth SDS was normal: -0,03±1,2 (-1,4 to 2,6). In 3 patients (12%) identified growth retardation: growth SDS from -2,6 to -6,0. These children were transferred tocilizumab via 7,6±3,0 years from the onset of the disease.

After 6 months of TCZ therapy in all children the average rate of growth amounted to 5,0±2,4 cm/yr, growth rate SDS was -0.2±2,4 (from -4,8 to 6,4). After 1 year growth rate was 6,5±3,2cm/yr, growth rate SDS was 2,5±2,8 (6,61 to -2.9). After

**Abstract AB0886** – Table 1. QoL in JIA patients

| Domain | No. of patients | Range | Result |
|---|---|---|---|
| Clinically active disease | 100 | – | 28 |
| MD global score (median IQR) | 100 | 0–100 | 0 (IQR 0–10) |
| Patient global score (median IQR) | 100 | 0–100 | 0 (IQR 0–10) |
| CHAQ (median IQR) | 100 | 0–3 | 0 (IQR 0–0.25) |
| PRQL – Parent (median IQR) | 100 | 0–30 (higher scores indicating poorer QoL) | 0 (IQR 0–3) |
| PRQL – Child (median IQR) | 92 (not assessable in 8 very young children) | 0–30 (higher score indicating poorer QoL) | 0 (IQR 0–2) |
| PedsQL 3.0 Rheumatology module – Parent (median IQR) | 100 | 0–100% (higher scores indicate better QoL) | 98.25 (IQR 86.6–100) |
| PedsQL 3.0 Rheumatology module – Child) (median IQR) | 92 (not assessable in 2–4 years old) | 0–100% (higher scores indicate better QoL) | 100 (IQR 89.7–100) |

2 years of therapy growth rate amounted 6,5±2,5 cm/yr. Growth rate SDS on the 2nd year amounted to 2,8±2,8 (6,4 to -2,1).
In children previously treated with anti-rheumatic therapy and other biological agent, the average rate of growth prior to the TCZ initiation was 4,3±2,3 cm/year, growth rate SDS was -2,3±2,3 (-5,5 to 0,06). After 6 months of TCZ therapy growth rate was 5,9±2,8cm/year, growth rate SDS was 0,9±1,9 (-2,2 to 3,9). After 2 years of therapy growth rate was 6,1±3,1cm/year, growth rate SDS was 2.9±2,7 (from 1,7 to 6,2). Growth rate SDS was significantly higher than the previous one as after 6 months as after 2 years of TCZ therapy.
Growth SDS in all children after 2 years of TCZ therapy was -0,1±1,5 (-4,3 to 2,3). In children with growth retardation growth SDS has improved significantly -2,6 up to -1,7, -3,5 to -3,2, and -6,0 to -4,2 respectively.
**Conclusions:** Treatment with tocilizumab increases growth rate not only in the first year, but in the subsequent period of treatment. Timely therapy sJIA with TCZ prevents growth retardation in children with normal growth and reduces existing growth retardation.
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**Acknowledgement:** The staff of rheumatologic department of Pediatric Clinic of 1st Medical state University named after Sechenov
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## AB0888 CHILDHOOD ARTHRITIS AS THE FIRST MANIFESTATION OF INFLAMMATORY BOWEL DISEASE

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**Background:** Joint involvement is the most common extraintestinal manifestation in children with inflammatory bowel disease and it may appear years before its diagnosis.
**Objectives:** To describe the characteristics of arthritis associated with inflammatory bowel disease (IBD) in children.
**Methods:** A retrospective, cross sectional, descriptive study was performed including patients of two Pediatric Rheumatology Units from tertiary hospitals with arthritis as the first manifestation of an inflammatory bowel disease.
**Results:** Data for all JIA patients controlled in 2 tertiary centers were analyzed. 14 patients met the inclusion criteria (10 females/4 males). Median age of onset of joint manifestation was 7 years (3–14.3 years). Median age of onset of gastrointestinal symptoms was 17.1 years (8.8–29.8 years). Musculoskeletal manifestations preceded the intestinal manifestations about 12 years (0.3–21.8 years). Most frequent JIA subtype was extended/persistent oligoarticular form (36% of all cases). Polyarticular type of JIA was present in 3 patient, enthesitis related arthritis in 2 patients and undifferentiated JIA in 2 patients. One patient had reactive arthritis. The most common type of IBD was Crohn's disease (60%). The most frequently affected joint was the knee (57%). In 2 patients the initial affected joint was the hip. ANA were positive in 6 children (40%) and 3 had HLA B27 positive (20%). Fecal calprotectin was normal in 10 patients studied. All patients have received systemic corticosteroids and 70% needed articular infiltration. 85% of patients required biological treatment to control the articular symptoms and/or gastrointestinal (mostly adalimumab) associated with DMARDs in a high percentage.
**Conclusions:** It isn't common that the joint involvement precede the digestive symptoms in IBD. In our series the most frequent category was the oligoarticular form with negative ANA and this presented later than usual. They present an evolution with difficult control of the flares. A large number of patients needed biological treatment to control the articular manifestations. These results support the need for new biomarkers that could detect subclinical intestinal disease in children.
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## AB0889 TRANSITIONAL CARE UNIT FOR PATIENTS WITH PEDIATRIC-ONSET RHEUMATIC DISEASES: 4 YEARS EXPERIENCE IN A SPANISH TERTIARY HOSPITAL

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**Background:** The transition of patients with childhood-onset rheumatic diseases from pediatric to adult rheumatology care providers requires a gradual and effective approachment given the chronic and complex nature of these disorders. The transition units play an important role to facilitate this step. Several models have been proposed to manage this process in a multidisciplinary way, but there is no consensus on which is the best model.
**Objectives:** To describe the epidemiological and clinical characteristics of patients treated in a transition care unit for pediatric-onset rheumatic diseases in a Spanish tertiary center.
**Methods:** We performed a descriptive and retrospective study of patients seen in the transition unit of our center between January 2011 and December 2014. All patients with age range 16–24 years (target population of the unit) were included. Demographics, diagnosis and treatment data were collected through review of their medical records. The consultation of the transition unit is carried out once a week and has a continuous model in which the pediatric rheumatologist is the same responsible of the transition consultation and coordinates the multidisciplinary team, attending patients of our own center as well as other patients referred to the unit.
**Results:** During the period studied a total of 109 patients were attended, the majority of them women (62.4%) with a mean age at beginning of follow-up by the unit of 17 years. The origin of the patients was the pediatric rheumatology consultation of our center in 47%, primary care 13%, the department of Pediatrics of our center 4%, departments of pediatric rheumatology of other centers 4%, other non-pediatric rheumatologists 8% and pediatric orthopedics 5%. The patients came from the area assigned to the hospital in 54%, other areas 32% and other regions in 14%. The most frequent diagnoses were juvenile idiopathic arthritis (JIA) in 32.7%, juvenile systemic lupus erythematosus 13.1%, juvenile dermatomyositis 2.8%, juvenile systemic sclerosis 2.8%, primary Raynaud's phenomenon 5%, Behcet's disease 2.8%, Scheuermann's disease 2.8% and mechanical low back pain 2.8%. The management of the patients required participation of other medical specialties in 53%. At the end period studied 62% of patients were still in follow-up, 22% were discharged, 15% lost follow-up and 1% died. With regard to treatment 43% of patients received DMARDs (methotrexate, sulfasalazine, hydroxychloroquine), 13.7% immunosuppressants (azathioprine, cyclosporine, mycophenolate mofetil, cyclophosphamide) and 21% biologic drugs (anti-TNF 14, tocilizumab 4, rituximab 3, anakinra 3, belimumab 1).
**Conclusions:** The diseases most frequently treated in the transition unit of our center were JIA and systemic autoimmune diseases and more than half of the cases require a multidisciplinary management with involvement of other departments. A high percentage of patients were still active at the end of follow-up by the unity and required treatment with DMARDs and biologic drugs. Due to the characteristics of the population treated at our center, the current operating model of the unit allows the continuity of proper management of these patients.
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## AB0890 NEUROPSYCHIATRIC MANIFESTATIONS IN PEDIATRIC-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: EXPERIENCE OF A SPANISH TERTIARY CENTER

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**Background:** The neuropsychiatric (NP) manifestations are an important cause of morbidity and mortality in patients with pediatric-onset systemic lupus erythematosus (pSLE). The prevalence of these manifestations ranges from 29% to 44% in different series, but data in the spanish pediatric population are scarce.
**Objectives:** To analyze the clinical and immunological features of patients with pSLE and NP followed in a Spanish tertiary center.
**Methods:** We performed a retrospective study of 49 patients with pSLE diagnosed between 1985 and 2005 in our center. The ACR NPSLE case definitions were used for classification. Demographic, clinical and immunological data were obtained through review of their medical charts.
**Results:** Twenty six patients (53%) developed NP manifestations. Mean age was 13.6 years and female:male ratio was 2.7:1. NP manifestations were present at the beginning of the disease in 7 cases (26.9%) and the mean time to

Table 1. Comparison of clinical and immunological features in patients with and without NPSLE

| | Total | NPSLE | Non-NPSLE | p-value |
|---|---|---|---|---|
| Number of patients | 49 (100%) | 26 (53%) | 23 (47%) | – |
| Females:males | 42:7 | 19:7 | 23:0 | 0.0072* |
| Age at diagnosis (years) | 13.2±3.1 (2–18) | 13.6±3.3 (2–18) | 12.9±2.9 (7–17) | 0.4179 |
| Disease duration (months) | 19.6±10.8 | 18.9±11.8 | 20.2±9.6 | 0.5287 |
| Secondary antiphospholipid syndrome | 8 (16.3%) | 5 (19%) | 2 (8.6%) | 0.0557 |
| ANA $\geq$1/1280 | 10/40 (25%) | 8/21 (38.1%) | 2/19 (48.6%) | 0.0443* |
| Anti-DNA antibodies (IU/mL) | 117.1 | 196.2 | 49.9 | 0.0042* |
| Anti-Ro/SSA antibodies | 14/46 | 10/23 | 4/23 | 0.0545 |
| Antiphospholipid antibodies | 11/40 | 6/20 | 5/20 | 0.7233 |
| Anti-cardiolipin antibodies | 4/40 | 3/20 | 1/20 | 0.2918 |
| Anti-$\beta_2$GPI antibodies | 5/40 | 5/20 | 0/20 | 0.0168* |
| Lupus anticoagulant | 11/39 | 6/20 | 5/19 | 0.7982 |
| Cryoglobulins | 6/18 | 6/12 | 0/6 | 0.0339* |
| ESR (mm/h) | 23.2 | 25.1 | 13.5 | 0.0108* |
| C reactive protein (mg/L) | 3.5 | 5 | 2.6 | 0.2077 |
| C3 (mg/dL) | 66.1 | 54.4 | 75.7 | 0.0042* |
| Low C3 ($<$80 mg/dL) | 32/46 | 20/23 | 12/23 | 0.0104* |
| C4 (mg/dL) | 11.7 | 7.2 | 15.4 | 0.0037* |
| Low C4 ($<$16 mg/dL) | 14/46 | 20/23 | 11/23 | 0.0046* |

develop them was 30.5 months. The most common presentations of NPSLE were seizures (50%), headache (26.9%), mood disorder/depression (26.9%), psychosis (19.2%), cerebrovascular disease (15.3%) and aseptic meningitis (15.3%). There was more than one NP manifestation in 15 cases (57.7%), with an average of 2.4 manifestations/patient. The comparison of patients with and without NPSLE demonstrated significant diffences ($p<0.05$) in the number of males, titers of antinuclear antibodies (ANA) and anti-DNA antibodies, positivity for anti-$\beta_2$-glicoprotein I ($\beta_2$GPI) and cryoglobulins, high erythrosedimentation rate (ESR) and low complement (C3, C4) (Table 1). There were 2 cases of mortality in NPSLE (7.7%) during follow-up period, one as a result of infection of the central nervous system and another due to sepsis associated with intestinal thrombosis.

**Conclusions:** In our series >50% of patients had NPSLE manifestations and frequently occurred early during the course of the disease. The clinical spectrum of NPSLE was wide in our cases and most of them had more than one manifestation. Patients with NPSLE showed a higher disease activity as measured by levels of autoantibodies, increased acute-phase reactants and low complement. Although NPSLE has been associated with antiphospholipid antibodies in other series, specifically anticardiolipin antibodies and lupus anticoagulant, we only found significant association with anti-$\beta_2$GPI antibodies. Mortality in patients with NPSLE was high.

**Disclosure of Interest:** None declared

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## AB0891 DYNAMICS OF PARAMETERS OF CONNECTIVE TISSUE METABOLISM IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS BY THE FOLLOW-UP STUDY

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**Background:** Juvenile idiopathic arthritis (JIA) is a chronic and socially significant disease as it leads to quick disability in childhood. Metabolic processes of connective tissue are important part of pathogenesis of JIA.

**Objectives:** It was to study dynamics of parameters of connective tissue metabolism in children with JIA against the background of standard therapy with methotrexate by the follow-up study.

**Methods:** The study involved 65 children within 2–18 years with JIA: oligoarthritis in 39,6%, polyarticular form - 37,7%, systemic form - 20,8%, enthesitis-related arthritis – 1,9%. In serum the total level of glucosaminoglycans (GAG) and chondroitinsulfate (CS), level of chondroitin-6-sulfate as I fraction of GAG, level of chondroitin-4-sulfate as II fraction of GAG, level of heparansulfate as III fraction of GAG, calcium, phosphorus and in urine level of oxyproline, uronic acid, calcium, phosphorus were determined. Parameters were assessed depending on the duration of disease: till 1 years (19 patients), 1–2 years (17 patients), 2–3 years (29 patients). They had being evaluated over the following 3 years.

**Results:** 77.78% of patients had decreased level of GAG in the serum. Decrease of I fraction of GAG was determined in 11.11% of patients, of II fraction of GAG -92.59% and III fraction of GAG – 96.3% of patients. Increased level of I fraction of GAG was presented in 48.15% of children. Mean general level of GAG was not difference in comparison with persons of control group and did not depend on duration of disease. Mean level of I and II fractions of GAG in patients with JIA was higher in comparison with persons of control group, beginning from 1st year of diseases development and for next 3 years ($p<0.001$). Mean level of III fraction of GAG was not difference in comparison with persons of control group and did not depend on duration of disease. 51.85% of patients had increased level of CS. Mean level of CS in patients with JIA was higher in comparison with persons of control group, beginning from 1st year of diseases development and for next 3 years ($p<0.001$). 59.26% of children with JIA had increased urinary excretion of oxyproline. The mean levels of oxyproline, uronic acid, phosphorus in urine in patients with JIA were not different in comparison with children of control group and did not depend on duration of disease. The level of serum calcium in the majority of patients (96.3%) was within the limits of norm, in urine – in 74.07% of patients was increased. The average level of calcium in urine was reliably below, than at group of the control ($p <0, 01$), irrespective of duration of disease.

**Conclusions:** Changes in the exchange of connective tissue metabolism are occurred already during the first year of JIA development and presented in subsequent years, despite treatment.

**Disclosure of Interest:** None declared

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# Other orphan diseases

## AB0892 THE FEATURES OF CHRONIC RHEUMATIC HEART DISEASE IN SAINT-PETERSBURG

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**Background:** Chronic rheumatic heart disease (CRHD) is a pathology characterized by valve anomaly formed after acute rheumatic fever. The adequate management of CRHD is important for prognosis, necessity of surgical intervention, and life quality of patients.

**Objectives:** The purpose of the study was to analyze the patterns of CRHD in adults with different valve anomalies together with the role of tonsillectomy and secondary prevention.

**Methods:** 150 patients (16 males, 134 females) were examined. The age was 19–80. The anamnesis (the age of disease manifestation, number of rheumatic fevers, the age of heart failure manifestation, the period from the disease manifestation to the first symptoms of heart failure, the age of permanent atrial fibrillation manifestation, the period from disease manifestation to permanent atrial fibrillation, cardiac operation, tonsillectomy, bicillin secondary prevention, chorea), examination, ECG, echocardiography was assessed.

**Results:** The period from disease manifestation to the first symptoms of heart failure and the first symptoms outbreak period of heart failure were more in the group of non operated patients ($P<0.01$). There were no differences in functional class (NYHA) between operated and non operated patients ($P=0.06$). The operated patients had higher level of pulmonary hypertension ($P<0.001$). Chorea was observed more often in the group of non operated patients. In the non operated group the age of permanent atrial fibrillation manifestation and the period from disease manifestation to permanent atrial fibrillation was observed more than in operated group ($P<0.01$). The permanent atrial fibrillation was seen more often in operated group ($P<0.001$). Operated patients had more damaged valves ($P<0.001$). There were no differences in age of disease manifestation in operated and non operated groups.

There were no differences between the group which had 1–2 rheumatic fevers and the group that had 3–5 rheumatic fevers in the period from disease manifestation to the first symptoms of heart failure, the age of permanent atrial fibrillation manifestation and the period from disease manifestation to permanent atrial fibrillation and in functional class (NYHA).

The patients with the history of chorea had a smaller number of damaged valves and the longer period from disease manifestation to the first symptoms of heart failure outbreak.

There were also no differences in the group which had secondary prevention in comparison with other patients in the period from disease manifestation to the first symptoms of heart failure outbreak, in functional class (NYHA), the age of permanent atrial fibrillation manifestation and the period from disease manifestation to permanent atrial fibrillation, number of damaged valves.

There were also no differences in patients with tonsillectomy and without it on the same signs.

The age of first symptoms of heart failure was more in the group without secondary prevention.

**Conclusions:** The operation was performed in patients with more severe variant of CRHD. The operated patients have acceptable quality of life in comparison with the other patients. The quantity of rheumatic fevers does not affect the rate of progression and severity of the disease in future. Tonsillectomy and secondary prevention do not affect the rate of progression and severity of CRHD, which requires to be analyzed more.

**Disclosure of Interest:** None declared

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## AB0893 COMPARISON OF ANTI-INFLAMMATORY EFFECTS OF THE GEL INCLUDED DICLOFENAC SODIUM AND THE MIXTURE OF ZINGIBER OFFICINALE, HYPERRICUM PERFORATUM, EUGENIA CARYOPHYLLATA AND LAURUS NOBILIS OIL IN COLLAGEN-INDUCED ARTHRITIS MODEL IN RATS

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**Background:** Phytotherapy is a therapeutic option which aims to prevent and treat diseases with using the herbal preparations prepared by the whole or some parts of plants.

**Objectives:** We aimed to investigate the anti-inflammatory effect of Herbal cream on experimentally induced arthritis model in rats.

**Methods:** 60 Wistar-albino rats were divided into 5 groups as Control, Freund's Complete Adjuvant (FCA), Arthritis, Arthritis + Diclofenac gel, Arthritis + Herbal cream. A single dose of saline 300 $\mu$L for Control group, a single dose of FCA + acetic acid 300 $\mu$L for FCA group, a single dose of collagen Type II + CFA emulsion for other 3 groups injected to induce arthritis intradermally to 5–6 separate sites around the tail. Treatments (diclofenac gel or herbal cream) were given as b.i.d. after day 14, for five consecutive days. Blood samples were collected from all animals at the end of the experiment by cardiac puncture. IL-1$\beta$, IL-6, TNF-$\alpha$, COX-1, COX-2 and hsCRP levels were measured by an ELISA method.

**Results:** HsCRP levels was found significantly elevated in the Arthritis group when compared to Control group ($p<0,0001$). In comparison between Arthritis group and Arthritis + Herbal cream groups, there was no significant differences between them according to the levels of hsCRP.In the model of collagen induced arthritis and FCA groups the levels of IL-6 were significantly higher then Control group ($p<0,0001$). When we compared the Arthritis group to the Arthritis +

Diclofenac group IL-6 level was found significantly lower in the latter ($p<0,0001$). In comparison between Arthritis group and Arthritis + Herbal cream group, significantly lower concentration of IL-6 was found also in Arthritis + Herbal cream group ($p<0,0001$). Despite COX-1 and COX-2 levels were both significantly lower in Arthritis + Diclofenac group, only COX-2 levels were found significantly low in Arthritis + Herbal cream group. However, no significant difference was found between each group in IL-1β and TNF-α levels.
**Conclusions:** In our study, we concluded that topical herbal cream has a weak antiinflammatory efficacy via lovering IL-6 but not hsCRP and this efficacy is formed by COX-2 inhibition. However, designing new studies in the future would be valuable to determine the effective dose and mixture to achieve evident improvement.
**Disclosure of Interest:** None declared
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## AB0894 THE SIGNIFICANCE OF URINARY BETA-2 MICROGLOBULIN LEVEL FOR DIFFERENTIAL DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER AND ACUTE APPENDICITIS

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**Background:** The clinical and laboratory parameters widely used are not specific to discriminate the abdominal pain due to FMF attack from that of acute appendicitis.
**Objectives:** The present study aims to investigate the urinary beta-2 microglobulin (U-$\beta_2$M) level as a potential parameter to identify these two diseases mimicking each other.
**Methods:** A total of 51 patients with established FMF diagnosis due to Tel Hashomer criteria on colchicine treatment (1–1.5mg/day), 15 patients with acute appendicitis who had appropriate clinical picture and were also supported pathologically after the surgery, and 20 healthy controls were enrolled in the study. Of the 51 patients with FMF, 25 were at an attack period, while remaining 26 were not. For the diagnosis of acute attack, as well as physical examination, laboratory tests including white blood cell count, C-reactive protein, and erythrocyte sedimentation rate were performed. From urine specimens urinary Beta-2 Microglobulin, microalbumin, and N-acetyl glucosaminidase (U-NAG) were measured.
**Results:** U-$\beta_2$M levels were significantly higher in acute appendicitis group compared to FMF group during attack period, FMF group during attack free period, and control groups ($p<0.001$, $p<0.001$, and $p<0.001$ respectively). U-NAG and microalbuminuria were significantly higher in acute appendicitis, FMF group during attack period, and FMF group during attack free period compared to controls (U-NAG $p<0.001$, $p=0.016$, $p=0.004$, microalbuminuria $p<0.001$, $p<0.001$, $p<0.001$ respectively). Microalbuminuria was significantly higher in acute appendicitis group compared to the FMF group during attack period ($p=0.004$).
**Conclusions:** Determination of U-$\beta_2$M levels may be helpful for differential diagnosis of peritonitis attacks of FMF patients on colchicine treatment, and acute appendicitis. However, this finding should be substantiated with other studies.
**Disclosure of Interest:** None declared
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## AB0895 EFFECTS OF COLCHICINE ON NEUTROPHIL APOPTOSIS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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**Background:** Familial mediterranean fever (FMF) is an autoinflammatory disease associated with a self-limiting attacks of fever and serositis.
**Objectives:** We aimed to investigate the assessment of apoptosis during acute attack and the effect of colchicine on apoptosis in patients with familial mediterranean fever (FMF).
**Methods:** This study was performed on 7 FMF patients during acute attack period and 7 age-sex matched healthy persons. Caspase 3 and caspase 9 were studied as the markers of apoptosis. Caspase 3–9 were studied again after neutrophils were incubated with colchicine in cell culture.
**Results:** Apoptosis level (0.21±0.009 versus 0.17±0.009, $p<0.05$) and markers of apoptosis (caspase 3 and 9) was significantly higher in FMF group during attack period than the control group ($p<0.001$). After the incubation with colchicine, apoptosis markers were found to provide a significantly decrease in comparison with attack period ($p<0.001$).

Table 1. Apoptosis, caspase 3 and caspase 9 levels in between groups

| Parameters | FMF (n=7) | Control (n=7) | P |
|---|---|---|---|
| Apoptosis | 0.21±0.009 | 0.17±0.009 | <0.05 |
| Caspase 3 | 14.33±0.69 | 8.01±0.18 | <0.001 |
| Caspase 9 | 12.54±1.57 | 6.17±0.83 | <0.001 |
| | FMF (n=7) | FMF + Colchicine (n=7) | P |
| Apoptosis | 0.21±0.009 | 0.15±0.014 | <0.01 |
| Caspase 3 | 14.33±0.69 | 9.16±1.99 | <0.001 |
| Caspase 9 | 12.54±1.57 | 7.11±1.99 | <0.001 |

**Conclusions:** Changing the structure of pyrin after mutation can cause failure in the regulation of inflammation and apoptosis. We suggest that defects in the regulation of apoptosis may play a role in the pathogenesis of FMF. Colchicine may reduces apoptosis as well as other mechanisms of action. More studies are needed to clarify the pathogenetic mechanisms of apoptosis in FMF.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2804

## AB0896 COGAN SYNDROME: DIFFERENTIAL RESPONSE TO BIOLOGIC AGENTS AND ROLE OF PET-CT IN THE INCREASED DIAGNOSIS OF AORTITIS

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**Background:** Cogan syndrome (CS) is a rare inflammatory disorder typically characterized by interstitial keratitis and audiovestibular symptoms. Patients may also develop other inflammatory ocular symptoms, progressive sensorineural hearing loss and systemic manifestations including aortitis, aortic insufficiency, and cerebral vascular manifestations. It has been classified as “variable vessel vasculitis”, and autoantibodies against inner ear and endothelial antigens has been claimed in its pathogenesis. There is no diagnostic test, and classification of patients as CS is still problematic due to variability of clinical findings. Glucocorticoids are the mainstay of CS treatment. Also, azathioprine, methotrexate, and biological agents including TNF and IL-6 inhibitors have been tried in the treatment of CS.
**Objectives:** We herein report the diagnostic and therapeutic findings of eight patients diagnosed with CS or CS-like illness with an aim of characterisation of the spectrum of CS.
**Methods:** We retrospectively reviewed the charts of the eight patients diagnosed with CS or CS-like illness according to their clinical manifestations. All of the clinical findings, laboratory and imaging results and treatment responses were recorded using a standard form. Because of the sample size, no statistical analysis was carried out. Results are summarized as descriptive findings.
**Results:** The mean age of the patients diagnosed with CS was 36 years, and the mean follow-up duration was 5.6 years. Demographic and clinical characteristics of CS patients are summarized in Table 1. Sensorineural hearing loss and intraocular findings were present in all patients. We observed variability in ocular findings, which included typical interstitial keratitis in three, scleritis in four patients, and occlusive retinal vasculopathy in one patient. Although aortitis has rarely been reported previously, diagnostic work-up included PET-CT imaging in three patients, and it revealed positive findings compatible with aortitis. One of our patients needed aortic valve replacement due to severe aortic regurgitation. All patients responded well to high dose corticosteroids initially. Partial or complete remission could be achieved in three patients with a mild disease course with azathioprine or methotrexate. Remaining 5 patients required biologic agents to control inflammatory activity. One patient with polyarthritis responded adalimumab and methotrexate combination. However, no response or even exacerbation of findings were observed with anti-TNF agents in two patients. In four patients, a partial, near-complete, or complete remission could be achieved with IL-1 blockade.




**Conclusions:** Patients with CS comprise a heterogeneous group, which may include some yet undiagnosed hereditary autoinflammatory conditions. Aortic involvement has rarely been reported in CS patients, but PET-CT imaging may help diagnosing asymptomatic patients with inflammatory imaging findings in

aorta. Early and effective treatment may prevent organ damage, and a differential response to IL-1 blocking biologic agents requires further investigation for both understanding its pathogenesis and better management of refractory patients.
**Disclosure of Interest:** None declared
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## AB0897 EVALUATION OF CLINICAL FACTORS AFFECTING THE DIAGNOSIS TIME IN FAMILIAL MEDITERRANEAN FEVER

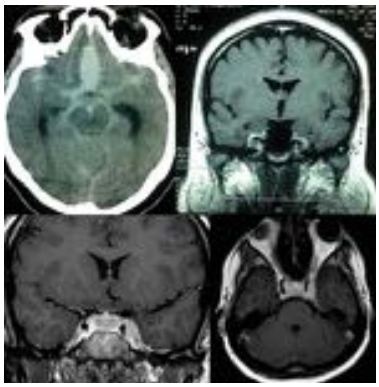
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**Background:** Familial Mediterranean fever (FMF) is the most frequent periodic febrile syndrome among the autoinflammatory disease, characterized by recurrent, self-limiting episodes of fever and serositis. FMF is a common disease in mediterranean countries although the diagnosis may be delayed due to especially patients-related reasons.
**Objectives:** In this study, we aimed to investigate the relationship between the diagnosis time and clinical features in patients with FMF.
**Methods:** Consecutively 44 patients diagnosed with FMF were recruited for this cohort study. The diagnosis time, clinical features, genetic mutations of MEFV genes and disease severity calculated with the Tel-Hashomer Severity Score were recorded retrospectively. The period from disease onset to diagnosis was named as undiagnosed time (UT). Correlation coefficients and significance were calculated by Pearson's test to assess the differences between groups. For all the tests, a two-tailed p value of $<0.05$ was considered statistically significant. Statistical analysis were performed using the software package SPSS 17 running on Windows NT.
**Results:** The mean age was 27.25±5.83 years, (59% female). The mean disease severity score was 6.25±2.06. Patient's clinical features included fever (79.5%), peritonitis (95.4%), arthralgia and/or arthritis (36.6%), pleuritis (13.6%), and erysipelas-like erythema (13.6%). Genetic analysis of 44 patients revealed that M694V was the most frequent mutation (63.6%). The mean UT was found 12.72±7.08 years. Amyloidosis was diagnosed in 3 (6.8%) patients with UT of up to 27 years. There was a negative correlation between UT and disease severity ($p<0.05$).
**Conclusions:** Our study, although a small patient group, suggested that the time from disease onset to diagnosis may still be longer in FMF. Disease severity is seen as an important factor for diagnosis time. Mild attacks or the lack of any symptom in the attack intervals may be reasons for late admission to physician. We have considered that emphasizing of patient education is substantial especially in countries which have high FMF prevalence.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2566

## AB0898 IDIOPATHIC HYPERTROPHIC PACHYMENINGITIS: CLINICO-RADIOLOGICAL FEATURES AND OUTCOME IN MEXICAN PATIENTS

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**Background:** Idiopathic hypertrophic pachymeningitis (IHP) is a rare chronic inflammatory disease characterized by fibrous thickening of the cerebral and/or spinal dura matter, with a clinical presentation depending on the topography of the dural thickening. Prevalence of IHP is not known due to its rarity. Case series come mainly from Asian countries and only a handful of case reports from Latin American countries can be found in the literature.
**Objectives:** We aimed to elucidate the clinical, laboratory, and radiological features, treatment and outcome of a cohort of Mexican patients with IHP.
**Methods:** Consecutive patients with the final diagnosis of IHP seen between November 2002 and January 2016 at *Hospital Civil de Guadalajara "Fray Antonio Alcalde",* a tertiary referral center in western Mexico, were included. Known causes of secondary hypertrophic pachymeningitis were ruled out. All patients gave informed consent to be included in this study. We analyzed demographic, clinical, laboratory, neuroimaging and therapeutic data.
**Results:** Five patients were included (1 male and 4 female). Mean age of beginning of symptoms was 32.2 years (range: 13–59); mean age at diagnosis of IHP was 36.8 years (range: 20–63); mean duration of symptoms before diagnosis was 55.4 months (range 2–132). All patients presented with headache and visual complaints. One presented with ataxia and 2 with encephalopathy. Main cranial nerve (CN) affected was CN II (4/5, 80%), followed by CN IV, CN VI and CN VII (3/5, 60% each). Multiple cranial neuropathy was the presentation in 4 patients (4/5, 80%). One patient presented with bilateral proptosis and one patient with the Tolosa-Hunt syndrome. Mean C-reactive protein (CRP) level of 4.05 mg/dl ($N=<0.80$) (range: 0.78–6.63). Mean erythrocyte sedimentation rate (ESR) was 77 mm/hr ($N=<10$) (range: 35–109). Mean CSF cell count was 58 cells/ml (range: 2–169) and mean CSF protein was 98 mg/dl (range: 25–254). Contrast-enhanced brain MRI showed diffuse dural thickening in 4 patients and focal in one; other MRI findings were: cavernous sinus involvement (1), hypophysitis (1), orbital pseudotumor (1), pansinusitis (1), cerebral edema (3), involvement of internal auditory canals and optic canals (1). Biopsy of orbital pseudotumor was performed in one patient showing non-specific chronic inflammation. Corticosteroids were used in 4 patients. Other immunosuppressants were used as corticosteroid-sparing agents, mainly methotrexate (MTX) (4/5 patients). Mean duration of follow-up was 18.4 months (range: 2–38). Mean pre-treatment clinical score was 8.2 (range: 5–10) and mean post-treatment clinical score was 2.6 (range: 0–5).



**Conclusions:** IHP in Mexican patients seem to occur more commonly in female patients and at a younger age compare to other populations. Main symptoms were headache and multiple cranial neuropathies and main CN affected was CN II, consistent with other series. Corticosteroids and MTX were used successfully as first line treatment with an evident decline in the HP clinical score. IHP should be consider in the differential diagnosis of headache associated with visual complaints, even in younger patients.
**Acknowledgement:** No acknowledgements to report.
**Disclosure of Interest:** None declared
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## AB0899 SERUM LEVELS OF CALPROTECTIN IN ACTIVE NON INFECTIOUS ENDOGENOUS UVEITIS. COMPARISON WITH HEALTHY CONTROLS

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**Background:** Calprotectin is a highly immunogenic molecule principally expressed in the cytosol of granulocytes and monocytes. Serum calprotectin levels are increased in different inflammatory conditions such as bacterial infections, inflammatory joint diseases and cystic fibrosis.
It has been suggested that measurement of serum calprotectin levels may be a sensitive indicator of disease activity in patients with endogenous posterior uveitis and that this molecule could play a role in the clearance of inflammatory cells at the late phase of uveitis.
**Objectives:** *Main objective:*To determine serum calprotectin levels in patients with active non infectious endogenous uveitis.
*Secondary objectives:* To compare serum calprotectin levels with those of a control cohort of healthy volunteers.
**Methods:** Study type: transversal study.
Patients: Uveitis cohort: patients with active non infectious endogenous uveitis. Control cohort: healthy volunteers.
Stadistic analysis: Proportions for categorical variables and average ± SD (or median if appropiate) for continuous variables were calculated. Categorical variables were compared by chi-square test (applying continuity correction if necessary). T-test (or Kruskal-Wallis if appropiate) was used to compare averages. Spearman coefficient was calculated in order to stablish correlation between continous and ordinal variables.
**Results:** 22 uveitis patients and 8 healthy volunteers were included.
From 22 patients with uveitis, 14 were diagnosed with anterior uveitis, 1 with intermediate uveitis, 5 with posterior uveitis and 2 with panuveitis. 17 patients had received corticosteriods (topical, systemic or periocular) previously to the serological determination. 9 were diagnosed with another inflammatory disease: spondyloarthritis (4), Crohn's disease (2), pulmonary sarcoidosis (1), psoriasis (1), systemic sclerosis (1).
No statistically significant differences were observed between both cohorts regarding age (p=0.156) and gender (p=0.554).
The median of calprotectin levels was higher in the uveitis cohort than in the control cohort (637.5 vs 396 mg/kg), although the difference didn't reached statistically significance (p=0.174).
No statistically significant differences were found between patients who were diagnosed with another inflammatory disease and those who weren't (p=0.548).

Taking into account anterior uveitis, a moderate-good correlation was observed between Tyndall degree and serum calprotectin levels (Spearman $\rho$=0.627, p=0.016).
**Conclusions:** In our study, serum calprotectin levels were higher in patients with active non infectious endogenous uveitis than in healthy volunteers, although this difference didn't reach statistical significance. A moderate-good correlation was observed between Tyndall degree and serum calprotectin levels.
This work is limited by the small sample size. Results are probably influenced by previous use of corticosteroids in the most part of patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3731

## AB0900 EVOLUTION AND OUTCOMES OF PREGNANCIES IN PATIENTS WITH SYSTEMIC INFLAMMATORY RHEUMATIC DISEASES

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**Background:** Rheumatic diseases are prevalent in women of childbearing age who want to have offspring. Hormonal and immunologic changes during pregnancy may influence the course of the inflammatory disease and could carry maternal or fetal complications.
**Objectives:** To describe the characteristics of a cohort of pregnant patients with rheumatic diseases being controlled in a specific consultation of pregnancy.
**Methods:** Descriptive observational study. All patients controlled in this consultation from 2011 to 2015 were included. The following data were collected: age at the conception, diagnosis, treatment during pregnancy, weeks of gestation, type of birth, breastfeeding, complications affecting the mother and the fetus, and autoantibodies profile (antinuclear antibodies (ANA), anti-Ro, anti-La and antiphospholipid antibodies [aPL]). Statistical analysis was done using SPSS 17.0.
**Results:** Twenty-five patients having Rheumatoid Arthritis [RA] (4), Psoriatic arthritis [PsA] (2), Ankylosing spondylitis [AS] (4) (two associated with Crohn's disease [CD]), Palindromic rheumatism (1), chronic oligoarthritis (1), Systemic Lupus Erythematosus [SLE] (6) (2 having antiphospholipid syndrome (APS) and 1 showing anti-Ro and aPL), APS (1), Behcet's disease [BD] (2); Systemic Sclerosis [SSc] (1); Sjögren's Syndrome [SS] (1); Mixed connective tissue disease [MCTD] (1) and psoriasis [Ps] plus ANA, anti-Ro and anti-La antibodies (1) were studied. All the patients were in remission or low disease activity.
The mean age of the patients was 33.32±3.7 years, mean pregnancy duration was 38.5±2.2 weeks and 24% of the patients had two pregnancies during the follow-up period. Thirty-one pregnancies were recorded. 93.6% were term pregnancies (75.9% vaginal delivery, 24.1% caesarean). Two patients had a miscarriage at 8 weeks. Regarding previous abortions, 2 were reported in APS, 2 in BD, 1 in MCTD, 7 in CD-AS and 2 in RA patients. 64.5% of the patients chose breastfeeding. No hypertension, eclampsia, pre-eclampsia or thrombosis were observed as maternal complications. As for fetal complications, intrauterine growth restriction (16.1%) and fetal distress (12.9%) occurred in mothers with anti-Ro antibodies and in one RA patient. A patient having Ps and anti-Ro antibodies reported a case of fetal heart block in their 1st pregnancy, but she had a second pregnancy with no complications. A case of neonatal lupus without cardiac affection was recorded in a SS patient.
No treatment was needed during pregnancy in 22.6% of the patients. Patients having SLE, SS and MCTD had antimalarial drugs (along with salicylic acid and heparin in case of APS). Sulfasalazine and antimalarials were used in patients with inflammatory arthritis. Adalimumab and azathioprine (AZA) were maintained until week 30th in a CD-AS patient. AZA was also used in a BD patient. 25.8% needed low-dose corticosteroids.
**Conclusions:** Our results confirm that optimal treatment of diseases, before conception and during pregnancy, minimize complications during and after pregnancy. Patients having anti-Ro and aPL have higher frequency of complications. Better results can be achieved by means of the creation of specific pregnancy consultations.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4684

## AB0901 THE ROLE OF ALCOHOL RELATED FACIAL FLUSHING RESPONSE ON THE RELATIONSHIP BETWEEN RISK OF HYPERURICEMIA AND ALCOHOL CONSUMPTION

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**Background:** Alcohol is known to be associated with the occurrence of hyperuricemia. Facial flushing responses to drinking appears to be due to the intelerance to alcohol. This study assessed the role of the facial flushing response in the relationship between alcohol consumption and hyperuricemia.
**Objectives:** The subjects were 845 Korean adult males (463 non-flushers, 382 flushers) who had undergone a health check-up at an university hospital.
**Methods:** Data were collected from the subjects' medical records. After Adjusted for high density lipoprotein cholesterol, hypertension, diabetes, log-transformed triglyceride, log-transformed estimated glomerular filtration rate, body mass index, a logistic regression analysis was used to calculate the risk of hyperuricemia with drinks per week as compared with non-drinkers of each group.
**Results:** In non-flushing group, the risk of hypeuricemia was significantly increased when non-flushers consumed more than 8 drinks per week (odds ratio [OR], 2.61; 95% confidence interval [CI] 1.05–6.51). In contrast, a higher risk of hyperuricemia was associated with flushers who consumed even <2 drinks (OR, 3.33; 95% CI, 1.01–10.98) per week.
**Conclusions:** These findings suggest that the amount of drinking associated with the risk of hyperuricemia in flushers was lower than in non-flushers.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1117

## AB0902 GENETIC CHARACTERIZATION OF HEREDITARY PERIODIC FEVER SYNDROMES: A RETROSPECTIVE COHORT OF 25 PATIENTS

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**Background:** This is a descriptive study of the epidemiological, clinical and genetic characteristics of a cohort of adult patients of a health area of 975,000 inhabitants in the south of Spain, diagnosed with hereditary periodic fever syndrome features. We contrast the mutations found in the genetic study of these with previously published data.
**Objectives:** A retrospective analysis of medical records of patients was performed. Sex, age, ethnicity, family history, clinical manifestations, time of evolution, genetic testing, final diagnosis, treatment and therapeutic response: the following information was collected. For the diagnosis of FMF clinical criteria such Hashomer (TH) and Livneh (ACR) was choosen, besides the usual genetic study.
**Methods:**
A total of 25 patients, 13 women and 12 men, of whom 21 had altered marenostrin gene (MEFV) (11 women and 10 men) and 4 TRAPS (2 women and 2 men) were studied.
Regarding the FMF; 8 patients had mutations associated with familial Mediterranean fever (6 women and 2 men); while 13 patients (8 males, 5 females) showed mutations in MEFV protein polymorphisms considered by high high frequency in healthy population.
The mean age at diagnosis was 30 years and 8 patients (38%) debuted with less than 20 years. All patients met clinical criteria.
A total of 25 patients, 13 women and 12 men, of whom 21 had altered marenostrin gene (MEFV) (11 women and 10 men) and 4 TRAPS (2 women and 2 men) were studied.
Regarding the FMF; 8 patients had mutations associated with familial Mediterranean fever (6 women and 2 men); while 13 patients (8 males, 5 females) showed mutations in MEFV protein polymorphisms considered by high high frequency in healthy population.
Two of the patients are ethnic predisposing (an Armenian Jew and a citizen of the Middle East). Genetic testing was performed in all patients. Exons 1 to 10 of MEVF gene (marenostrin) were sequenced. Total 15 patients (71%) of patients had received sometime in the course of the disease treatment with colchicine, with good response in most cases.
In the case of TRAPS, 4 patients (2 men and 2 women) were diagnosed by clinic. The genetic study was performed in all patients. Exons 2, 3 and 4, encoding the extracellular domains of TNF receptor I, being the pR92Q mutation in exon 4 in 3 patients, and pP46L homozygous mutation in exon 3 in the fourth patient were sequenced, who turn pR202Q had homozygous mutation in the gene MEVF.
**Results:** In 8 patients (38%) recurrent mutations (M694V, E148Q and I591T, I640 M), in previous publications associated with FMF found. However, the most frequent mutation was the pR202Q detected in more than half of patients. This mutation is often associated with the pE148, but only 1 of the patients had both. Because of its high prevalence in the population (>1%) is considered a polymorphism.
Regarding TRAPS, both mutations found (pR92Q and p46L) are common, but with low penetrance and a controversial clinical significance, and are thought to TNFRSF1A gene variants, although not directly responsible for the syndrome.
**Conclusions:** Genetic studies in patients with a clinical diagnosis of FMF reveal heterogeneity. This may be due to the existence of genes at present unknown. They are generated by mutating genes similar to that seen in the FMF clinical phenotype, but in some cases, as with mutations pR202Q, pR92Q and p46L are considered polymorphisms.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5124

## AB0903 BEHCET'S DISEASE IN THE MIDWEST REGION OF IRELAND: PATIENT ACCESS AND RESPONSE TO ANTI-TNF BIOLOGICS

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**Background:** Current literature shows promising data for efficacy of anti-tumor necrosis factor (anti-TNF) biological therapy in Behcet's disease (BD) patients.
**Objectives:** The aim was to investigate a cohort of BD patients in Midwest Region of Ireland, current prescription practice for anti TNF biologics in this cohort, patient response & the risk of serious infections or other serious side effects.
**Methods:** All BD patients attending our rheumatology service & satisfying the ISGBD or ICBD criteria were included in the study. Response was evaluated on patient's new/worsening clinical features & improvement/resolution of clinical symptoms. Management was benchmarked against current European League Against Rheumatism (EULAR) guidelines published in 2009. Serious infection was defined as the requirement for intravenous antimicrobial therapy and hospitalization.
**Results:** From a cohort of 22 patients, 18 (81.9%) received anti-TNF (6 males, 12 females) with mean age 38.9 years. 14 patients (77.8%) achieved complete remission & 4 patients (22.2%) achieved low disease activity on anti-TNF. Among this 3 patients (16.7%) were successfully switched to a different agent due to secondary failure, 6 patients (33.3%) needed 3 different anti-TNFs and one patient required a fourth anti-TNF therapy to achieve remission. Indications to start anti-TNF among our cohort include severe mucocutaneous lesions with significant impact to quality of life (15/18), ocular manifestations (7/18), destructive laryngeal disease (5/18), vascular manifestations (3/18) & resistance or intolerance to conventional treatments (8/18). Anti-TNF was extremely effective in suppressing the mucocutaneous oral & laryngeal manifestations, significantly improving patient's quality of life. However resistant genital ulcers was often a difficult symptom to control with 3 patients achieving partial remission.5 allergic reactions were encountered, all with administration of infliximab. 5 serious infections were documented involving 3 patients (16.7%) and all in patients aged 50 years or above. No other serious side effects were noted.

Table I– Clinical manifestations of BD patients and the anti-TNFs used (n=22)

| No | G | Age | AOU | GU | OL | CL | PP | VI | GI | ENT | B1 | B2 | B3 | B4 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 23 | + | + | - | + | - | - | - | + | IFX | ADA | - | - |
| 2 | M | 69 | + | - | + | + | - | - | - | + | IFX | GOL | ADA | - |
| 3 | F | 33 | + | + | - | + | - | - | - | + | IFX | - | - | - |
| 4 | M | 51 | + | + | + | + | + | - | + | + | IFX | GOL | - | - |
| 5 | F | 38 | + | + | - | + | - | - | - | + | IFX | ETA | - | - |
| 6 | F | 22 | + | + | - | + | - | - | - | + | IFX | ADA | GOL | - |
| 7 | F | 17 | + | + | + | + | - | - | - | - | IFX | - | - | - |
| 8 | M | 49 | + | + | + | + | - | + | - | - | IFX | - | - | - |
| 9 | M | 55 | + | - | + | + | - | - | - | + | IFX | ADA | IFX-r | - |
| 10 | F | 35 | + | + | - | + | - | - | - | - | IFX | CER | - | - |
| 11 | F | 37 | + | + | - | + | - | - | - | - | IFX | ADA | GOL | - |
| 12 | F | 37 | + | + | - | - | + | - | - | - | - | - | - | - |
| 13 | M | 34 | + | + | - | + | - | - | - | - | ETA | - | - | - |
| 14 | F | 31 | + | + | - | + | - | - | - | - | - | - | - | - |
| 15 | F | 51 | + | + | - | + | - | + | - | - | IFX | ADA | GOL | IFX-r |
| 16 | F | 80 | + | + | + | + | - | - | - | - | IFX | - | - | - |
| 17 | F | 68 | + | + | - | + | - | - | + | - | - | - | - | - |
| 18 | M | 45 | + | + | - | - | - | + | - | - | IFX | ETA | - | - |
| 19 | F | 38 | + | + | - | + | - | - | - | - | - | - | - | - |
| 20 | F | 21 | + | + | + | + | - | - | - | - | IFX | ADA | GOL | CER |
| 21 | F | 20 | + | + | - | + | - | - | - | - | IFX | ADA | ETA | - |
| 22 | F | 24 | + | + | - | + | - | - | - | - | ETA | - | - | - |

**AOU**: Recurrent aphthous oral ulcers; **GU**: Genital ulcers; **OL**: Ocular lesions **CL**: Cutaneous lesions; **PP**: Positive pathergy test; **VI**: vascular involvement; **GI**: GI involvement; **ENT**: ENT manifestations; **B**: Anti-TNF Biologics; **IFX**: Infliximab; **IFX-r**: revital with infliximab **ADA**: Adalimumab; **ETA**: Etanercept; **GOL**: Golimumab; **CER**: Certolizumab

**Conclusions:** Anti TNF-α biological therapy is an important alternative option for first line therapy in severe BD as many conventional treatments failed to maintain clinical remission and prevention of life-threatening complications. Response rates to anti-TNF-α therapy were excellent and treatment was well tolerated but should be used with caution in patients age 50 or above. BD patients who fail one anti TNF-α due to intolerance, ineffectiveness or secondary failure may still benefit from switching to another drug from this group or even re-trial of a previously administered anti-TNF.
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## AB0904 PERICARDITIS AS A POSSIBLE PREDICTOR FOR BIOLOGICAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS NEED IN ADULT ONSET STILL'S DISEASE

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**Background:** Adult onset Still's disease (AOSD) is a rare systemic inflammatory disorder of unknown aetiology, which is considered to be similar to systemic-onset juvenile idiopathic arthritis (SOJIA). Peculiar clinical and laboratory features of SOJIA and AOSD led some authors to propose that these diseases should be included among the family of autoinflammatory diseases related to abnormalities in innate immune system. The optimal treatment strategy of AOSD is difficult to determine because of the absence of large-scale prospective studies. Predictive factors of outcome would be useful to draw guidelines for patient management.
**Objectives:** To look for clinical or serological markers able to predict the use of biological disease modifying anti-rheumatic drugs (bDMARDs) in patients with AOSD. To evaluate the efficacy and safety of bDMARDs in AOSD.
**Methods:** In a single-center retrospective study, 42 patients with AOSD were divided into two groups according to whether they were ever treated with bDMARDs (n:20) or not (n:22). Literature was searched for articles dealing with possible predictors of the use of bDMARDs in AOSD.
**Results:** Among 20 AOSD patients who received at least one bDMARDs, the prevalence of pericarditis was higher than in the other patients (8/20 vs 1/22; p:0.008; OR, 14.0, 95% CI 1.56 to 126). Literature search retrieved another paper dealing with predictors of bDMARDs need in AOSD (1): the analysis pooling data from our series and literature confirmed pericarditis at disease onset as a predictor of bDMARDs need (p:0.018; OR, 3.81, 95% CI 1.31 to 11.1). A complete remission was observed in 17 out of 18 evaluable patients treated with bDMARDs, allowing withdrawal or tapering of corticosteroid therapy ($p<0.001$), but, because of inefficacy or adverse events, some patients received more than one bDMARD during the course of the disease, and 33 different trials of bDMARDs were needed.
**Conclusions:** Pericarditis is a possible marker of the auto-inflammatory process that may underlie the pathogenesis of AOSD. Pericarditis at disease onset may be a predictor of bDMARDs need. Biological DMARDs have a good efficacy and safety profile in AOSD, and should be considered for patients not responding to conventional therapy.
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**Disclosure of Interest:** None declared
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## AB0905 THE EXPANDING SPECTRUM OF INFLAMMATORY DISEASES ASSOCIATED WITH MEFV GENE MUTATIONS

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**Background:** Familial Mediterranean fever is an autoinflammatory disease with recurrent inflammatory attacks. The genetic cause of FMF is the mutations in the MEFV gene coding pyrin, which has role in the activation of inflammasome, acitvation of caspase 1 and production of IL-1B. The impaired function of MEFV gen results increased systemic inflammation. It is shown that MEFV mutations can have effect on some other inflammatory diseases as contributing the disease development or increased inflammation or severe disease duration.
**Objectives:** It is reported several articles about the association between MEFV mutations and different inflammatory diseases. We aimed in this study to analyse the MEFV gene associated diseases with a systematic review.
**Methods:** We searched databases for articles about MEFV gene mutations

Table 1. MEFV gene associated diseases

| Disease | Number of articles | Increased frequency | Disease modulating effect |
|---|---|---|---|
| IBD | 12 | 5 | 4 |
| BD | 11 | 7 | 3 |
| HSP | 8 | 7 | 5 |
| AS | 7 | 5 | 3 |
| PFAPA | 6 | 4 | 4 |
| JIA | 4 | 4 | 2 |
| RA | 3 | 0 | 3 |
| AOSD | 3 | 1 | 0 |
| SLE | 3 | 0 | 3 |
| Ischemic heart disease | 2 | 2 | 1 |
| SNA | 2 | 2 | NA |
| Fibromiyalgia | 2 | 2 | 1 |
| Dismenorrhea | 2 | 1 | NA |
| Hematolymphoid malignancies | MM (2), AML (2), MDS (2), PV (1), ALL (2) | 2 | NA |
| Seizure | 2 | 2 | NA |
| PAN | 1 | 1 | NA |
| ROA | 1 | 1 | NA |
| Chronic renal failure | 1 | 1 | NA |

(MEFVm). We excluded the articles including FMF patients. 92 research articles were included our study which analysed the MEFV gene mutations in inflammatory diseases except FMF.
**Results:** Inflammatory bowel disease (IBD), Behçet's disease (BD), HSP, ankylosing spondylitis (AS), PFAPA, JIA, ischemic heart disease (IHD) were disorders which are associated increased MEFV gene mutation rate and it is shown in these diseases that MEFVm have disease modifying effect. Rheumatoid arthritis and SLE studies have shown no significant difference in MEFVm rates, but MEFVm are related with some clinical findings. The MEFVm carrier frequency was increased in seronegative arthritis, adult onset Still disease (AOSD), fibromiyalgia, dismenorrhea, chronic renal failure, hematolymphoid neoplasms (ALL, MM, MDS, PV). The study design of these disorders doesn't include to investigate the relationship of MEFVm with the disease activity. It was found any association with MEFVm in gouty arthritis, rheumatic heart disease, uveitis,idiopatic pericarditis, tip I Diabetes Mellitus and osteoarthritis. The detailed data is shown in Table-1.
**Conclusions:** MEFV mutations may have effect in the develeopment of inflammatory diseases and may modify the clinical findings. This modifying effect may be important especially in countries with high MEFVm mutation carrier rate.
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## AB0906 ANTI-INTERLEUKIN-1 THERAPY IN FAMILIAL MEDITERRANEAN FEVER AMYLOIDOSIS: A SINGLE CENTER EXPERIENCE

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**Background:** Recently there is increasing number of reports pointing out the efficacy of anti-interleukin 1 (anti-IL1) therapy to control AA amyloidosis secondary to autoinflammatory diseases.
**Objectives:** Here we report our experience in IL-1 blockade in patients with AA amyloidosis secondary to Familial Mediterranean fever (FMF)
**Methods:** Eighteen FMF patients with histologically proven secondary AA amyloidosis treated with anti-IL1 agents (canacinumab and anakinra). Creatinine, creatine clearance, 24-hour urine protein, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) parameters were measured before and throughout the treatment period in order to evaluate the response. Patients were closely monitored and adverse events were also reported.
**Results:** Eighteen (8 female, 10 male) patients with AA amyloidosis secondary to FMF who were also on colchicine (mean dose: 1.4±0.7 mg/day) were started on anti-IL1 agents (8 on canakinumab, 13 on anakinra, 3 on both). The mean age was 41.9±11.4 years, while the mean duration of FMF was 21.5±8.9 years. The mean follow-up period on anti-IL1 was 16.5±11.7 months (10.9±7.3 months on anakinra; 18.8±10.7 months on canakinumab).
Ten patients are still on anti-IL-1 therapy (7 on anakinra, 3 on canakinumab). Renal functions remained stable after therapy for 5 out of 10 patients (creatinine from 1.2±0.6 mg/dl to 1.1±0.6 mg/dl; creatine clearance from 82.3±49.5 ml/min to 87.7±53.2 ml/min; 24-hour urine protein from 1094.2±995.4 mg/dl to 885.0±725.0 mg/dl), while CRP (from 15.7±9.5 mg/L to 1.3±0.9 mg/L) and ESR (from 41.8±15.5 mm/h to 15.5±3.7 mm/h) decreased. Renal functions and acute phase reactants improved with therapy (creatinine from 0.7±0.7 mg/dl to 0.7±0.7 mg/dl; creatine clearance from 81.9±79.4 ml/min to 93.3±65.9 ml/min; 24-hour urine protein from 6963.9±7514.0 mg/dl to 304.8±81.5 mg/dl; CRP from 29.6±18.1 mg/L to 28.0±46.8 mg/L; ESR from 63.8±45.7 mm/h to 32.3±44.7 mm/h) for four patients. Renal functions deteriorated after anakinra and it was switched to other biological agents for the remaining patient. However since he progressed to end stage renal disease and started hemodialysis, anakinra was re-introduced to take control over attacks. Global patient assessment score of the whole group decreased significantly (from 8.6±1.6 to 1.2±1.8) with IL-1 blockade.
Anti-IL-1 therapy was discontinued in 8 patients, 3 of them were on anakinra (due to unresponsiveness in 2 and allergic reaction in 1), 5 were on canakinumab (due to increase in proteinuria during the course of treatment in 3, lichen plans in 1 and one was lost to follow up although showed improvement during the follow-up period, then the treatment was terminated since he developed lung adenocarcinoma). Anakinra was switched to canakinumab due to allergic reaction in one and unresponsiveness in two patients
**Conclusions:** Anti-IL1 therapy can improve renal functions and stabilize patients with AA amyloidosis secondary to FMF. The efficacy and safety of anti-IL1 therapy in this group of patients are needed to be verified by further researched.
**Disclosure of Interest:** None declared
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## AB0907 NECK PAIN MAKES NO ODDS ON CERVICAL ALIGNMENT IN PATIENTS WITH TEMPOROMANDIBULAR DISORDERS

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**Background:** Despite the extensive research on the possible link between cervical posture and temporomandibular disorders (TMDs), it still remains as a highly controversial issue. The inconclusive results derived from the previous studies, might be in part due to the ignorance of neck pain, which usually accompanies TMDs.
**Objectives:** In the present study, we aimed to elucidate the impact of neck pain-if any-on cervical alignment in patients with TMDs.
**Methods:** °Patients diagnosed with TMDs according to the research diagnostic criteria for TMDs (RDC/TMD) between November 2013-November 2015 were included in the study. All subjects underwent lateral cervical x-ray evaluation and were asked to complete the RDC/TMD Axis II Biobehavioral Questionnaire for TMDs. Pain, disability and depression scores for TMD were calculated. Computerized measurement of the cervical lordosis angle was performed according to the C2-C7 cobb method. Additionally, disability score for neck pain was measured through Neck Disability Index (NDI) in patients with concomitant neck pain. The study sample was divided into two groups according to the presence of neck pain and a comparative analysis for cervical lordosis angle was carried out between groups. The relation of cervical malalignment with neck disability, TMD-associated pain, depression and disability was evaluated via Pearson's correlation analysis.
**Results:** The study sample was consisted of 60 patients with a mean age of 31.2±10.8 years. The mean value for cervical lordosis angle in the whole group was 10.9±12.7°, which was consistent with hypolordosis. Cervical lordosis angle did not differ between patients with (n=28) and without (n=32) neck pain (12.2±12.8° versus 9.8±12.7°, respectively; p=0.46). Cervical alignment was correlated with neither neck disability nor TMD-related variables including pain intensity, depression and disability.
**Conclusions:** Patients with TMDs have hypolordotic cervical malalignment regardless of neck pain. The presence of neck pain makes no odds on patients' cervical alignment.
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## AB0908 A NOVEL MUTATION IN PROTEOGLYCAN-4 UNDERLIES CAMPTODACTYLY-ARTHROPATHY-COXA-VARA-PERICARDITIS SYNDROME IN A CHINESE FAMILY

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**Background:** Camptodactyly-arthropathy-coxa-vara-pericarditis (CACP) syndrome is an autosomal recessive condition characterized by the association of congenital or early onset camptodactyly and noninflammatory arthropathy, it can also affect the pericardium. CACP syndrome is caused by mutations in proteoglycan 4 (PRG4), a chondroitin sulfate proteoglycan that acts as a lubricant for the cartilage surface. Several cases were described in the literature from ethnically different populations including Caucasian, Egyptian, Saudi Arabian, Pakistani, Indian and Korean.
**Objectives:** We undertook this study to genetically screen a Chinese family segregating CACP in an autosomal recessive manner.
**Methods:** To screen for mutation in PRG4 gene, all coding exons and exon-intron junctions were sequenced using ABI prism 3730 automated DNA sequencer.
**Results:** Sequence analysis of PRG4 gene in affected individual of the family presented here revealed one base insertion (exon 9, c.3755_3756insT) predicting a frame shift mutation (p.Lys1253fs*1). Sequencing of PRG4 exon 9 in the parents showed that the father was a heterozygous carrier of the c.3755_3756insT mutation, but the mother did not have this alteration. To our knowledge, this is probably the first mutation identified in PRG4 gene in Chinese population.
**Conclusions:** We described a novel insertion mutation in PRG4 gene in a Chinese family with CACP.
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## AB0909 EFFECTS OF COMBINED THERAPY WITH PREDNISONE AND METHOTREXATE ON B CELL SUBPOPULATIONS IN PATIENTS WITH IGG4-RELATED DISEASE

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**Background:** IgG4-Related Disease (IgG4-RD) is a systemic fibro-inflammatory condition characterized by oligoclonal expansion of IgG4+ class-switched plasmablasts (PBs) (1). PBs swiftly decline together with clinical improvement after rituximab, suggesting a role for B cells in the pathogenesis of IgG4-RD (2). Studies with alternative effective non B-cell depleting therapies (3) are needed in order to confirm the pathogenic importance of PBs and their utility as disease biomarkers.
**Objectives:** To assess the impact of combined therapy with prednisone (PDN) and methotrexate (MTX) on B cell subpopulations in patients with IgG4-RD.
**Methods:** Five patients with active biopsy proven IgG4-RD were treated with PDN (0.6–1 mg/kg) and MTX (10–20 mg per week). PDN was gradually tapered and withdrawn in 6 months. Disease activity, partial (PR) and complete response (CR) were assessed through the IgG4-RD Responder Index (IgG4-RD RI) (4). Serological, immunological and radiological studies were performed according to the clinical presentation. Flow cytometry was used to measure PBs (CD19+CD20-CD27+CD38+bright cells), naïve (CD19+CD20+CD27-CD38+ cells), and memory (CD19+CD20+CD27+CD38- cells) B cells at baseline, after 3 and 6 months of therapy. Nine age and sex matched subjects were used as healthy controls (HC).
**Results:** At disease onset, the median IgG4-RD RI was 9 (normal $<3$). The median serum IgG4 level was 534 mg/dl (normal $<135$mg/dL). Circulating PBs were increased (median 7000 cells/mL) compared to HC (median 605 cells/mL; $p<0.004$). PBs showed a positive correlation with the number of organs involved ($r=0.77$), with serum IgG4 level ($r=0.87$), and with disease activity ($r=0.73$). The number of circulating memory B cells was comparable between IgG4-RD patients and HC ($p=0.57$). Naïve B cells were significantly lower in IgG4-RD patients compared to HC ($p<0.05$). After 6 months of therapy 4 patients achieved CR (IgG4-RD RI $<3$) and 1 PR. Serum IgG4 level decreased in all patients but normalized only in one patient at 6 months. Circulating PBs declined to levels comparable to HC (median 230 cells/mL, $p=0.3$). Memory B cells were unaffected by the therapy, while naïve B cells showed a declining trend, yet not statistically significant compared to baseline levels ($p>0.05$)
**Conclusions:** PBs and naïve B cells are expanded and reduced, respectively, in patients with active IgG4-RD compared to HC. Combined therapy with PDN and MTX leads to clinical improvement and to normalization of circulating PBs. Naïve B cells slightly decrease, while memory B cells are not affected by immunosuppressive treatment

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## AB0910 INVESTIGATION OF THE ARTERIAL STIFFNESS AND RELATED FACTORS IN PATIENTS WITH ACROCYANOSIS

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**Background:** Acrocyanosis is a disorder of the peripheral circulation and often arises due to cold, and describes the situation with diffuse blue-purplish discoloration of the hands and feet. Although its etiology is unknown, infections, malignancies, hematological disorders, neurological, psychiatric, autoimmune and metabolic status have all been suggested to contribute. It is more frequent in women and usually starts during the third decade. Unless there is another underlying disease, there is no data regarding whether these patients have increased risk of mortality and morbidity or not, compared to a healthy people. Arterial stiffness measurements have long-term high predictive value, accessibility, cost-effectiveness and repeatability for representing cardiovascular risk.
**Objectives:** To investigate long-term cardiovascular risk, determine factors that may play a role in the etiology and measure arterial stiffness in patients with acrocyanosis.
**Methods:** The study included 23 consecutive patients who were diagnosed as acrocyanosis and agreed to participate in the study (F/M: 1/22) and 17 healthy controls (F/M: 1/16) were included. Tensiomed Arteriograph device used for measuring arterial stiffness of the cases. T he demographic and clinical features, blood counts and routine laboratory tests were recorded and their relationships with arterial stiffness measurements were investigated. Correlation and regression analysis were used for the evaluation of the data.
**Results:** The mean age of the patient and control groups were similar (22.83±4.7 and 25.0±0.5 years, respectively, $p=0.066$). The average body mass indexes of the patient and control groups were also similar (21.6±2.6 and 22.7±1.3 kg/m 2). The average pulse wave velocity measurements were lower in acrocyanosis patients compared to controls, but the difference did not reach statistical significance (6.87 ±1.11 and 7.15±1.37 m/s, $p=0.508$). Pulse wave velocity measurements were associated with erythrocyte sedimentation rate ($r=0.551$, $p=0.012$). Ankle-brachial index (ABI) was associated with serum glucose levels ($r=0.896$, $p<0.001$). Serum calcium levels were associated with aortic and brachial augmentation indexes ($r=0.477$ and 0.474; $p=0.045$ and 0.047, respectively). Patient and control groups had similar aortic and brachial augmentation indexes, and there was no significant difference between the groups in terms of central aortic pressures.
**Conclusions:** According to our study, arterial stiffness indexes representing cardiovascular risk were similar in patients with acrocyanosis compared to healthy population of the same age. However, the lower average pulse wave velocity measurements in acrocyanosis, need to be further investigated in a larger group.

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## AB0911 SARCOPENIA ASSESSMENT IN CHRONIC KIDNEY DISEASE PATIENTS

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**Background:** Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death. Uremic sarcopenia causes a high morbidity and mortality and consequently a high priority for muscle wasting prevention and treatment in these patients.
**Objectives:** To assess sarcopenia (muscle state and power) in CKD patients with & without hemodialysis.
**Methods:** In this study there were three studied groups: Group I: 20 CKD patients on regular hemodialysis. Group II: 20 CKD patients on conservative treatment. Group III: 20 normal persons. After informed consent all patients recruited from dialysis unit, inpatient and outpatient clinics of Internal Medicine Department at Ain Shams University Hospital. Diabetic, patients with hemoglobin $\leq$10 g/dl, aged $\geq$50 years or have chronic diseases that may cause secondary sarcopenia had been excluded from the study. All subjected to full medical history and clinical examination. The muscle power assessed using the hand grip dynamometer[1], physical performance through using 4 Meter Walk Gait Speed Test[2]. CBC, serum creatinine, BUN, serum electrolytes & PTH. Dual-energy X-ray absorptiometry (DEXA)[3] was used to assess bone loss and total body mass loss (lean mass, fat mass, BMD). Assessment of nutritional status by using subjective global assessment (SGA) score[4].
**Results:** There is high significant positive correlation between age and 4 meter walk test. Group I & II had a higher mean time of 4 meter walk test & weaker hand grip strength compared to the control. There is positive correlation between 4 meter walk test and SGA score & clinical symptoms of sarcopenia (asthenia, easy fatigability, weakness & muscle cramps), negative correlation with hand grip strength. Also there is positive correlation between hand grip strength with lean mass & BMD and negative correlation with clinical symptoms of sarcopenia, fat mass & SGA score. There is negative correlation between SGA score with lean mass, fat mass & BMD. 4 meter walk test is the most specific & sensitive test to diagnose sarcopenia in CKD patients.
**Conclusions:** Sarcopenia was present in CKD patients with hemodialysis more than without hemodialysis than normal people. Asthenia, weakness, easy fatigability & cramps are warning symptoms for sarcopenia. 4 meter walk test was the most specific & sensitive test to assess sarcopenia in CKD patients.

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## AB0912 REVISITING THE DIFFERENTIAL DIAGNOSIS OF PANNICULITIS

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**Background:** Panniculitis (Pn) is a group of heterogeneous inflammatory diseases characterized by involvement of the subcutaneous fat (SF), locomotor system and viscera. Challenges in identification of Pn are associated with multiplicity of clinical and pathomorphological types alongside with the absence of specific Pn markers.
**Objectives:** to identify and analyze the diagnostic features of lipodermatosclerosis (LDS) as one of lobular Pn (LPn) varieties.
**Methods:** 550 patients with referral diagnosis of "erythema nodosum" (EN), "panniculitis", or "vasculitis" were thoroughly evaluated according to the in-house diagnostic algorithm.
**Results:** LPn was verified in 132 patients after through examination. LDS with disease duration 18,97±7,4 mo was found in 53 (9,6%) out of them (M-3, F–50, age 18- 80 y.). 32 patients were overweight with average body mass 91.5±21.8 kg. Inflammation in predominantly lower inner leg subcutaneous fat was documented in 37 pts (54,7%) resulting in the inverted coke bottle appearance of the lower leg (79,2%) ($p$=.00556). All main types of Pn clinical course were present: acute (up to 3 mo), subacute (3 to 6 mo) and chronic (>6 mo). Acute disease was diagnosed in 20 pts (37,7%) aged 51,8±15,7 y., with indurated non-demarcated pink nodules existing for 1,47±0,3 mo.($p$=.001). Subacute disease was found in 12 pts (22,6%) aged 57,50±12,1 y. with average disease duration 4,7±1,3 mo., dark red nodules and inverted coke bottle appearance of the lower leg in 91,67% cases. Chronic Pn with disease duration 43,3±24,0 mo was documented in 21 pts (39,6%) aged 56,1±11,9 y, with demarcated red-brownish nodules and inverted coke bottle appearance of the lower leg in 17 cases (80,95%). The risk of lower leg deformity was increased 2,3-fold in pts with chronic disease vs acute (95%, CI 1,2–4,4,$p$=.003). Asymmetric pattern of nodules was present in 70% of acute and subacute disease, symmetric pattern was found in 50% of chronic cases ($p$=.003). ROC-analysis showed with 86% sensitivity and 58% specificity that palpatory evaluation of pain in LDS using VAS corresponded with 40 mm cut-off value. In 46% of cases skin lesions were accompanied by polyarthralgia (in 15 pts), and myalgia (in 12 pts) with insignificant increase of inflammation activity markers. Chronic venous insufficiency lasting for 10,2±1,3 years and verified by US Doppler scanning of the lower extremities veins was found in 28 pts (including 19 with chronic LDS) ($p$<0,05). Pathomorphological examination of skin and subcutaneous fat biopsy samples in 7 pts confirmed lobular Pn-LDS with sclerosis of borderline fatty tissue and of small arteries in hypoderma.
**Conclusions:** LDS is a variation of LPn. Identified predisposing factors include female gender, middle age, increased body mass and chronic venous failure in lower extremities. Asymmetric nodules of specific color on the inner leg and inverted coke bottle appearance of the lower leg are established diagnostic criteria for LDS. Successful diagnosis is possible with detailed history case, adequate evaluation of clinical, laboratory and instrumental modalities.
**Disclosure of Interest:** None declared
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## AB0913 CLINICAL UTILITY OF MBDA PANEL VECTRA-DA IN THE MANAGEMENT OF ADULT ONSET STILL'S DISEASE

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**Background:** Adult Onset Still's disease (AOSD) is an inflammatory disorder with an expansive and heterogeneous presentation that can often be mistaken for infectious or malignant etiology. The diagnosis is largely based on clinical manifestations with corroborating laboratory features, such as elevated acute inflammatory markers, ferritin, and leukocytosis. The long-term management of AOSD can be difficult due to the limited amount of reliable biomarkers used to predict and manage disease activity.
**Objectives:** We present two cases with the diagnosis of AOSD and the use of Vectra DA to track clinical progression and response to therapy wit a goal to assess clinical utility of MBDA pannel *Vectra DA* in the management of Adult Onset Still's Disease
**Results:** *Case One:* 68-year-old male with history of hypothyroidism was evaluated for fever of unknown origin associated with generalized malaise, fatigue, and a maculopapular rash in bilateral upper extremities for 3 weeks. The patient was pan-CT scanned with results only remarkable for bladder thickening. He denied any familial history of rheumatological disorders, and was found to have negative ANA and RF. Further infectious and malignant work-up inpatient was negative. Patient was found to have ferritin level of 15,599 ng/mL, ESR 82 mm/hr, and CRP 18 mg/dL; and was diagnosed with Adult-Onset Still's Disease (AOSD). Vectra DA score was 77 at time of diagnosis. He was started on pulsed steroid and then discharged home to complete a tapered steroid regimen with the addition of Rilonacept with a good response; repeat Vectra DA score at three-month follow-up was 15. Delta of Vectra correlated with normalized CRP <0.9 and ESR 6.
*Case Two:* 25 year-old female with history of JIA that achieved remission for the past 14 years presented with recurrent fevers, sore throat, generalized malaise, arthralgias, and a new-onset maculopapular rash of the inner forearms and thighs bilaterally for one-month duration. Her blood work revealed WBC 20.8 k/uL but further infectious work-up was negative. She was found to have negative RF, ANA but elevated ferritin level of 321 mg/mL, ESR 75 mm/hr, CRP 138 mg/dL. Patient was diagnosed with AOSD, and started on pulsed oral steroid with methotrexate but failed treatment. Her Vectra DA score was 72 at the peak of her symptoms. Eventually received pulsed IV corticosteroids and started on Rilonasept with symptomatic improvement. A repeat Vectra DA score at three-month follow-up was 17. Delta of Vectra correlated with normalized CRP <0.1 and ESR 2.
**Conclusions:** Vectra DA is a 12-biomarker disease activity pannel commonly employed in the management of rheumatoid arthritis (RA). Vectra DA is not routinely employed in the management of AOSD and, here, we have illustrated two examples demonstrating the clinical utility of Vectra DA as an assessment tool in the diagnosis and management of AOSD. As such, this should prompt to reconsider the value of Vectra DA as a diagnostic tool in AOSD and other inflammatory disorders where there are limited biomarkers utilized to reliably track disease progression.
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## AB0914 HEMARTHROSIS AS GRAFT VERSUS HOST DISEASE IN A PATIENT AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION FOR CHRONIC MYELOGENOUS LEUKEMIA (CASE REPORT)

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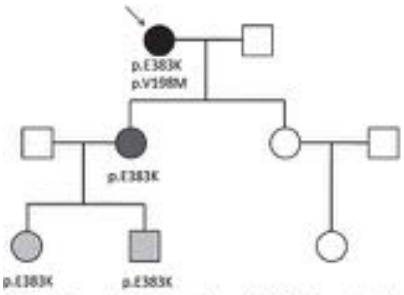
**Background:** The following manifestations of graft-versus-host disease damaging the musculoskeletal system were described: fasciitis, stiffness, myositis, arthralgia and arthritis. But we did not find any descriptions of the hemarthrosis.
**Objectives:** We present a case report.
**Results:** A 43-year-old man presents in June 2015 with pain in his left knee and left hip, swelling of left knee, subfebrile temperature.
Chronic myelogenous leukemia (CML) was diagnosed in July 2014, Imatinib therapy started. In 12.19.2014 an allogeneic bone marrow transplantation was made, and then the patient receives calcineurin blockers (cyclosporine A), and prednisone. In the early postoperative period cytopenia (the lowest level of white blood cell was 0,9 × 103/μL, platelets was 27 × 103/μL,) and diarrhea were recorded. In February 2015 appeared the pain in the joints, first they were weakly expressed, but to May 2015 pain had reached 70–80 mm by VAS.
Hematologist assumed the reactive arthritis, amoxicillin/clavulanate (14 days) and metamizol were given. The treatment was ineffective, and the patient referred to rheumatologist.
On examination, his temperature was 37.2 ℃. Skin and mucosa were pale with no rash. Mucosa is wet. Physical examination confirmed swelling in the knee, as well as tenderness in the areas, left knee flexion was limited to 110°. Also there was a significant movement limitation of the left hip joint. His lungs are clear to auscultation. His cardiac is unremarkable. He has palpable hepatomegaly but no splenomegaly. There is no clinical evidence of ascites
Initially we excluded septic arthritis especially tuberculosis. The initial laboratory analysis reveals white blood cell count of 9.06 × 103/μL, platelets of 30 × 103/μL, hemoglobin of 7,6 g/dL Procalcitonin serum <0.5 ng/ml (normal level). Blood cultures twice - negative result. Results of the left hip MRI were alarming. There were established the thickening of the synovial membrane, increased number of non-uniform fluid in the joint and cartilage plates damages which should have been differentiated between the previous osteoarthritis and secondary lesions on the background of a septic (tuberculosis) process. MRI results of the left knee: synovium cover thickening with areas of hemorrhagic impregnation. Synovitis.
Enzyme immunoassay serum to M.tuberculosis, also as QuantiFERON test - negative.
The synovial fluid tests show: white blood cell count of 4625 cells/ml, polymorphonuclear leukocyte 74%, erythrocytes of 50–70 in sight, crystals and culture isolation were not found.
**Conclusions:** Thus, we excluded septic genesis of arthritis. Considering hemorrhagic content (date of MRI and synovial fluid), and in our opinion the platelet count has not reached critical level for the development of hemarthrosis, we have assumed the existence of graft-versus-host desease. During the further observation for 3 months with continued cyclosporine A and prednisolone therapy, CML did not relapse, and joint complaints completely regressed.
This is one of the first cases which describe hemarthrosis as graft versus host desease.

**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1147

## AB0915 A LOW-PENETRANCE NLRP3 VARIANT IN A NOD2 CARRIER POSSIBLY WORSENS THE PHENOTYPE OF BLAU SYNDROME

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**Background:** Blau syndrome (BS) is a rare autosomal dominant autoinflammatory syndrome that primarily affects skin, joints, and eyes, with varying severity of inflammation, and results from mutations in the *NOD2* gene[1]. NOD2 bears highly conserved residues and structural similarities to the NLRP3 protein, a key component of the inflammasome which mutations underlie some autoinflammatory disorders, named cryopyrinopathies.
**Objectives:** This study assessed the potential contribution of *NLRP3* mutations to the inflammatory BS phenotype in an Italian affected family carrying p.E383K *NOD2* mutation (Fig. 1).
**Methods:** Genomic DNA was isolated from blood samples of the four affected family members and sequence analyses of *NLRP3* were performed by an ABI 3730XL DNA sequencer (Applied Biosystems). A genotype/phenotype correlation of the carriers of *NLRP3* variations was also assessed.
To explain the differences in inflammatory phenotype severity, peripheral blood mononuclear cells (PBMC) were isolated from patients and healthy subjects and their ability to activate NF-κB and inflammasome pathways was measured by an array-based assay (reverse phase protein array).
**Results:** A heterozygous genetic variant of *NLRP3* was found only in the proband's sample. The p.V198M mutation was known in literature as a low-penetrance mutation associated with cryopyrinopathies in symptomatic patients (Infevers database data). The proband with combined mutations presented the worsened BS phenotype (severe chronic bilateral uveitis with glaucoma, cataracts and visual impairment), whereas the three subjects with only p.E383K variant had a much milder disease.
Concerning the activation of NF-κB pathway, all BS patients have raised levels of signalling key molecules (phosphorylated NF-κB $p<0.05$; phosphorylated IkB-α $p<0.05$) compared to the controls. However, the components of inflammasome pathway presented a pattern of activation related to individual patients rather than to the whole disease. Enhanced level of cleaved caspase-1, the key component of inflammasome, was noticed only in proband PBMCs (p=0.03), potentially promoted by the additional presence of p.V198M *NLRP3* mutation.




Blau syndrome family carrying p.E383K BS-associated mutation.
The proband (arrowed) with the most severe phenotypes (black circle), inherited both *NOD2* (p.E383K) and *NLRP3* (p.V198M) mutations. The other three subjects with only *NOD2* variant, have milder symptomatology, even if proband's daughter have more severe phenotype than her children.

**Conclusions:** Our data strongly suggest that severe phenotype in BS may result from co-existence with mutations in genes associated with other autoinflammatory diseases, and are consistent with recently reported findings in hereditary periodic fever syndromes[2]. The synergistic effect of dual mutations can also explain the differential activation of the inflammatory pathways and may lead to appropriate targeted drug development.
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[2] Touitou I, J Med Genet. 2013
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2351

## AB0916 ADULT-ONSET STILL'S DISEASE-EXPERIENCE OVER LAST FIVE YEARS

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**Background:** Adult onset still's disease (AOSD) is a rare systemic inflammatory disorder of unknown etiology seen by a rheumatologist. There is limited data about this disease especially from our country.
**Objectives:** To study the clinical profile of AOSD patients in a tertiary care hospital.
**Methods:** A 5 year (2009–2014) retrospective analysis was done of patients with AOSD (Diagnosed using the Yamaguchi criteria). Their clinical features, laboratory findings at presentation, disease course, treatment and outcomes were analyzed.
**Results:** 14 patients with AOSD according to Yamaguchi criteria were enrolled. The mean age at disease onset was 43.57±16.91 years and the male to female ratio was 4:3. The mean duration of symptoms prior to diagnosis was 2.2 months (range 1–6 months). The most common clinical manifestations were fever (n=14), articular symptoms (n=14), rash (n=7), weight loss (n=7), sore throat (n=4), Lymphadenopathy (n=8), hepatomegaly (n=5), splenomegaly (n=3) and serositis (n=4). Most common joints involved were knee (n=9) followed by wrist (n=7).Neutrophilic leucocytosis was seen in 13, thrombocytosis was seen in 4 patients. Elevated ESR and Ferritin levels were present in all, with a mean of 70±35.18 mm/hr and 3966.35±2988 ng/ml respectively. Hepatic enzymes were elevated in 6. The mean duration of follow up was 18.71±16.99 months. Prednisolone was used in all while methotrexate was used in 12 patients; one patient each required sulfasalazine and cyclosporine. Tender joint and swollen joint counts displayed a progressive reduction on follow up. During treatment, we observed a resolution of fever in all patients. On first follow up mean ferritin levels decreased from 3966.35±2988 to 3018±699 ng/ml. Course of the disease was monophasic in 7 intermittent in 4 and chronic in 3 patients.
**Conclusions:** 1.Fever and joint symptoms were the most common presenting symptom.
2.Steroids and methotrexate was most commonly used for treatment.
3.Majority of patients had clinical improvement with resolution of systemic and joint symptoms.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2927

## AB0917 PULMONARY MANIFESTATIONS IN PATIENTS WITH IGG4-RELATED DISEASE AT A TERTIARY CARE INSTITUTE

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**Background:** IgG4-Related Disease (IgG4 RD) is a rare immune-mediated disease with multi-organ involvement.
**Objectives:** To describe pulmonary manifestations of patients with IgG4-RD.
**Methods:** Chart review was performed of consecutive patients diagnosed with IgG4 RD between 2009–2014 at the PD Hinduja National Hospital, Mumbai. Included patients fulfilled diagnostic criteria of Japanese Ministry of Health, Labour and Welfare guidelines, 2011.Their clinical features, laboratory findings were noted down.
**Results:** 8 of 11 patients with IgG4 RD had pulmonary manifestations. Ages of presentation ranged from 15–73 years.6 patients were female. Average delay in diagnosis was 9 months. Prior to diagnosis, 3 patients received empiric antituberculous drugs and bronchoalveolar lavage performed in 3 patients was non-diagnostic. The right mainstem bronchus was found to be narrowed in 1 patient. The serum IgG4 levels were elevated in all patients. Median IgG4 level was 4.76 mg/dl (IQR 3.26, 6.1).Presenting symptoms, thoracic CT and histopathological findings are summarized below

Table 1. Feature (number of patients)

| | |
|---|---|
| Symptoms | Fever (6), Cough (5), Shortness of breath (5), Weight loss (4), Stridor (1) |
| Thoracic CT findings (8 of 8 pts) | Multiple small nodules <1cm with an upper lobe predominance (5), ill-defined patchy areas of consolidation (4), cervical and mediastinal homogeneously enhancing lymphadenopathy (4), ground glass opacities (3,) peribronchial wall thickening (2), interlobular septal thickening (2), subglottic stenosis (2), mass-like lesion (1), bronchial stenosis (1). |
| Histopathological findings (4 of 8 pts) | Subglottic biopsy (2) – non-diagnostic. Transbronchial lung biopsy (1) – minimal interstitial fibrosis. Lymph node biopsy (1), – minimal inflammation and mild fibrosis. |

**Conclusions:** Pulmonary involvement in IgG4 RD is common and should be sought for in patients diagnosed with the disease.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4692

## AB0918 PREVALENCE OF PREVIOUS PFAPA SYNDROME IN BEHCET'S DISEASE

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**Background:** Marshall's syndrome or PFAPA (periodic fever, aphtous stomatitis, pharyngitis, cervical adenitis) is a pediatric diseases characterized by recurrent febrile episodes associtaed with head and neck symptoms, improved or cured after tonsillectomy. Differential diagnosis includes infectious angina, Behcet's disease, cyclic neutropenia, TRAPS syndrome and other autoinflammatory syndromes. However, part of the patients with Behcet's disease may have PFAPA as part of their disease onset.
**Objectives:** We aimed to investigate the reported prevalence of PFAPA symptoms in patients with Behcet's disease.
**Methods:** The patients in the evidence of the Rheumatology Dept, a tertiary referral unit, with confirmed Behcet's syndrome (according to ISSG) presenting in the last year, were taken into the cross-sectional study, after informed consent. A questionnaire (AMAB) was developed and employed, with regard to the presence of diagnostic Marshall/ PFAPA features (Thomas 1998), familial history, tonsillectomy, fever presence and pattern and other possible features of BD appearing in childhood. Cyclic neutropenia was ruled out as part of clinical investigations, and data regarded the pathergy, eye examination and thrombotic events were obtained from the medical records.
**Results:** We enrolled 21 patients (11 F, 12 M), average age 47.6 yrs, that agreed to answer the questionnaire. In the whole responder BD group, fever was present in 38.1%. We found that 23% of the responder BD patients reported symptoms compatible with a PFAPA diagnosis, with a medium age of onset of 8.2 years. BD was diagnosed at 40±12.8 yrs (15–56), but in the patients with PFAPA symptoms the onset was earlier (28±12.3 yrs). In the 3 patients with tonsillectomy, the symptoms improved for several years, only to reappear milder after adolescence, along with other features of BD. Most patients (76.19%) recalled ulcers since childhood, and isolated oral ulcers generally remained as such until occurrence of other diagnostic BD features. We found no differences in the severity of the disease, eye involvement or thrombosis prevalence in the patients with or without PFAPA features.
**Conclusions:** PFAPA may co-exist as an associated disease in BD and is not necessarily an exclusion diagnosis. Although many patients with BD suffer from oral ulcers since childhood, BD symptoms appear in most after adolescence.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.6025

## AB0919 H-FERRITIN AND CD68+/H-FERRITIN+ CELLS ARE INCREASED IN THE SKIN OF ADULT ONSET STILL'S DISEASE PATIENTS AND CORRELATE WITH THE DISEASE ACTIVITY

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**Background:** Adult onset Still's disease (AOSD) is an inflammatory disease, characterized by high spiking fevers, arthritis, salmon-pink erythema and multi-visceral involvement [1]. During AOSD, exceptionally high serum levels of ferritin may be observed and they might contribute to production of proinflammatory molecules [2]. Ferritin is composed by 24 subunits, heavy (H) subunits and light (L) subunits. The ferritin enriched in L subunits (L-ferritin) and the ferritin enriched in H subunits (H-ferritin) may be recognized in different tissues [3].
**Objectives:** To investigate the skin tissue expression of both H-and L-ferritin and the number of macrophages expressing these molecules, in the inflammatory cutaneous infiltrate from 10 AOSD patients with persistent (more than 24–36 hours) cutaneous lesions. In addition, we performed statistical analysis to evaluate whether these results might correlate with the severity of the disease.
**Methods:** We obtained skin samples from 10 consecutive patients with active AOSD with persistent cutaneous lesions and 10 healthy controls (HC). An immunofluorescence analysis was performed evaluating the tissue expression of both H- and L-ferritin and the number of macrophages expressing these moleculkes. Serum levels of ferritin, ESR, CRP, Pouchot's score were also recorded.
**Results:** We observed an increased H-ferritin expression in the skin samples of AOSD patients, when compared with HC ($p<0.001$). On the contrary, no differences were observed for L-ferritin when compared to HC. Furthermore, a significant increase of H-ferritin was detected when compared with L-ferritin in AOSD patients ($p<0.001$) and when compared with both H-ferritin and L-ferritin in HC ($p<0.001$; $p<0.001$). Furthermore, a positive correlation between H-ferritin and the Pouchot's score was observed ($p<0.01$). We also reported a positive correlation among the tissue expression of H-ferritin and both serum ferritin ($p<0.05$) and CRP ($p<0.05$). The double staining between the H-ferritin and CD68 showed an increased presence of macrophages expressing H-ferritin in the inflammatory infiltrate when compared with HC ($p<0.001$). In the same samples, we did not observe any co-localization between CD68 and L-ferritin. However, our analysis failed to show any positive correlation among the number of CD68+/H-ferritin+ in the skin and disease activity, serum ferritin and inflammatory markers.
**Conclusions:** Our data show an imbalance between the production of L- and H-ferritin in the skin of AOSD patients, associated with a strong infiltrate of CD68+/H-ferritin+ cells in the same samples suggesting a possible pathogenic role. Furthermore, a correlation between the levels of H-ferritin in the skin of these patients and the disease activity was observed.
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**Disclosure of Interest:** None declared
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## AB0920 ANY PREDICTIVE FACTORS OF THERAPEUTIC RESPONSE IN INFECTIOUS SPONDYLITIS?

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**Background:** The aim of the present work was to describe predictive factors of good or bad outcome Infectious Spondylodiscitis according to the experience of an internal medicine department in Tunisia.
**Methods:** Patients with SDI either confirmed or presumed and hospitalized in the internal medicine department of The Principle Military Hospital Of Tunis, Tunisia have been included in the Study.
**Results:** Fourty-four patients met the inclusion criteria. They have been gathered over 20 years-period. They were 24 men and 20 women with an average age at 52.5 years. The diagnosis was a Tuberculous Spondylodiscitis in 22 cases (50%): among them 10 patients had a concomitant extra spinal TB. The diagnostic delay was 231 days for TB SDI and 40.5 days for SDP.
Length of hospital stay was 48.6 days (6–225 days): with a mean of 48.9 days in SDT and 45.3 days in SDP.
Regular monitoring was observed in 38 patients (17 SDP, SDT 21) with an average duration of 20 months (5–48 months). Three were lost views and three died. Evolution was considered positive if there was a clinical and biological improvement and no recurrence or death.
The analytical study objectified that existence of a immunosuppression, a longer diagnosis period, or hospitalization period and the follow-up duration were associated with a longer duration of treatment ($p=0.038$, $p<0.001$).
The absence of orthopedic complications initially or during the evolution and treatment duration were the only factors associated with good favorable change ($p<0.001$, $p=0.004$), the existence of bacteriological evidence of multifocal involvement, the presence of epidural or spinal compression showed no significant association.
**Conclusions:** Earlier treatment with effective duration and follow up are predictive factors of favorable outcome in SDI either due to TB or regular germs.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5696

## AB0921 INFECTIOUS SPONDYLODISCITIS FEATURES: ABOUT 44 CASES

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**Background:** Spinal infections can be described aetiologically as pyogenic, granulomatous (tuberculous, brucellar, fungal) and parasitic. Its early diagnosis is crucial to the establishment of adequate treatment in order to get favorable outcomes.
The aim of the present work was to describe clinical, diagnostic and therapeutic aspects of Infectious Spondylodiscitis according to the experience of an internal medicine department in Tunisia.
**Methods:** Patients with SDI either confirmed or presumed and hospitalized in the internal medicine department of The Principle Military Hospital Of Tunis, Tunisia have been included in the Study.
**Results:** Fourty-four patients met the inclusion criteria. They have been gathered over 20 years-period. They were 24 men and 20 women with an average age at 52.5 years. The diagnosis was a Tuberculous Spondylodiscitis in 22 cases (50%): among them 10 patients had a concomitant extra spinal TB. The diagnostic delay was 231 days for TB SDI and 40.5 days for SDP.

Revealing symptoms were dominated by pain:, often mixed (61%). Radicular pain was noted in 15 cases. Fever was found in 17 cases. On examination: spinal syndrom was present in 65.9% of cases, spinal cord compression signs were found in 8 patients. MRI was contributive in all cases showing a disc enhancement in 50% (SDP in 67%, TSDI in 33%), epiduritis in 63.5% (SDP 60%, TSDI 67%). The disc biopsy was contributive in 71% of cases. The diagnosis was certain in 15 cases, highly probable in 18 cases and presumptive in 11 cases.
Treatment duration was 13 months for SDT and 18 weeks for SDP. The outcome was favorable in 30 cases (SDP 13, TSDI 17).
**Conclusions:** Infectious sondylodiscitis remains a diagnostic and therapeutic problem in our country. Only an early care can enhance its prognosis.
**Disclosure of Interest:** None declared
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## AB0922 FDG-PET/CT IS A VALUABLE TOOL FOR RELAPSING POLYCHONDRITIS

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**Background:** Relapsing polychondritis (RP) is a comparatively rare inflammatory disorder t in which recurrent episodes of inflammation occur in the external ear, nose, and joints. Although the pathogenesis of RP is unclear, it is believed to involve autoimmune mechanism such as autoantibody to type II collagen. Clinically, diagnosis in early stages of RP is difficult because of few typical physical findings. Furthermore, airway involvement is the most important complication of RP, and is associated with significant morbidity and mortality. Therefore it is important to diagnosis and treat RP in early stages. On the other hand, fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) has been an established in a field of oncology. Recently, FDG-PET/CT is used as diagnostic tool for inflammatory disorder such as infection or collagen vascular disease.
**Objectives:** We investigate the features and the usefulness of FDG-PET/CT in the diagnosis of RP.
**Methods:** We enrolled the five RP patients (M/F: 1/4) who fulfilled the RP criteria by Damiani and Levine, and treated in our facility between 2005 and 2015. All patients had undergone FDG-PET/CT before treatment. Inflammatory lesion was evaluated by using the maximum standardized uptake value (SUV max). Furthermore, we performed follow-up FDG-PET/CT due to evaluate the efficacy of treatment for RP.
**Results:** FDG-PET/CT findings revealed abnormal FDG accumulation in the cartilages for all five patients. The lesions of abnormal FDG accumulation were tracheal/bronchial in 3 cases, auricular cartilage in 2 cases. The mean SUV max in tracheal/bronchial was 4.84 and in auricular cartilage was 2.53. All RP patients received glucocorticoid (GC) treatment. 3 patients were performed methylprednisolone-pulse therapy. All RP patients had well responce to initial GC treatment. However three patients were refractory for GC treatment. In these patients, one treated with methotrexate combined with GC and another 2 cases cyclophosphamide. The follow-up FDG-PET/CT was undergone in 2 patients. These findings revealed that FDG accumulation was significantly decreased or disappeared.
**Conclusions:** In RP patients, FDG-PET/CT is useful for the early diagnosis. Additionally, we suggest that FDG-PET/CT is valuable for monitoring response to treatment.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4030

## AB0923 PREVALENCE OF RHEUMATOLOGIC SYMPTOMS AND SPECIFIC RHEUMATIC DISEASES IN PATIENTS WITH HISTORY OF BREAST IMPLANTS

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**Background:** The Autoimmune Syndrome Induced by Adjuvant (ASIA) includes several clinical conditions as siliconosis, gulf war syndrome, miofasciitis macrophagic syndrome and post vaccination phenomenon. Acting as an adjuvant the Breast implants (BI) could be potentially linked with several autoimmune diseases.
**Objectives:** The purpose of this study was to describe the rheumatological characteristics of a group of patients with the history of previous BI, that assisted to a rheumatologist, and to compare them with age matched controls.
**Methods:** A retrospective, descriptive study was designed. Patients with the history of BI, that assisted to a rheumatologist, where included. The data was collected from clinical registries, including socio-demographic data and comorbidities, kind and duration of symptoms, development of a specific rheumatologic syndrome/disease, fulfilment of ASIA proposed criteria and type of clinical evolution. All the patients and their controls attended private practice rheumatology outpatient clinics.
For each case, 2 controls were randomly selected from clinical registries if they had: ±2 years of age compared with the cases at the first visit, had no history of BI or pre-existing rheumatological disease and had attended at least 2 followup visits.
Statistical Analysis – Categorical data were expressed in frequency and percentage, continuous data in median and interquartile range (IQR). Chi$^2$ and Fisher test were used to analyse categorical data and Student T test or Mann-Whitney for continuous data based in its distribution. A p value $<0.05$ was considered as significative.
**Results:** Twenty-two female patients with history of BI (all met ASIA classification criteria) and 44 female controls were included. Median age was 44.5 years (IQR 38–53), without difference between groups (44.3 vs 44.9, p=0.8). The median time between the BI and the beginning of the rheumatologic symptoms was 4 years (IQR 1–10) since all the patients developed the symptoms after the BI surgery. The cases had significantly more frequency of arthritis (31.8% vs 11.4%, p=0.042), less myalgias (18.2% vs 75%, $p<0.0001$) and less fatigue (18.2% vs 47.7%, p=0.03) than the controls. Though it was not statistically significative, the group of patients had more frequency of specific rheumatic diseases (36.4% vs 19%, p=0.1), with more rheumatoid arthritis (13.6% vs 4.5%, p=0.1) and fibromyalgia (13.6% vs 9.1%, p=0.5) than controls. Overall, the frequency of any specific rheumatic disease (including fibromyalgia) was higher in patients than in controls (50% vs 29.5%, p=0.1).
**Conclusions:** In our group of patients with history of BI we found more prevalence of arthritis, and less of myalgia and fatigue. Maybe arthritis could be a characteristic symptom of ASIA. The weaknesses of this study relies in its retrospective design and the small sample size. Prospective studies could be helpful to answer the question of the possible link between BI and rheumatic diseases.
**Disclosure of Interest:** None declared
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## AB0924 SERUM ADIPOKINES LEVELS IN PATIENTS WITH SARCOIDOSIS

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**Background:** Adipokines are different proteins synthesized by adipose tissue who have an influence on angiogenesis, hemostasis, lipid metabolism and immune system regulation. Sarcoidosis is a chronic inflammatory disease characterized by non-caseating granuloma which etiology is unknown yet. Adipokines may play an important role in the pathogenesis of sarcoidosis.
**Objectives:** To determine the serum adipokines levels in patients with sarcoidosis and to determine a possible correlation with clinical and laboratory signs of disease.
**Methods:** Forty-four biopsy proven sarcoidosis patients followed at a single center and age and sex matched 41 healthy volunteers were included in the study. Demographic, clinical, laboratory and radiological data were recorded and body mass index (BMI) was calculated in all patients. Routine laboratory tests (blood glucose, liver and kidney function test) were measured. Serum adiponectin and leptin levels were measured by ELISA method.
**Results:** Among 44sarcoidosis patients 13 (29.5%) were male and 31 (70.5%) were female. Twenty-one (47.7%) patients had erythema nodosum, three (6.8%) had uveitis, 40 (90.9%) had arthralgia, 23 (52.3%) had ankle arthritis, 15 (34.1%) had enthesitis. Laboratory evaluation showed increased serum ACE level in 24 (54.5%) patients, increased serum calcium level in 11 (25%) patients, increased serum D3 level in 5 (11.4%) patients, increased ESR and CRP levels in 22 (50%) and 23 (52.3%) patients, respectively. Compared with the control group serum adiponectin levels were significantly higher in patients with sarcoidosis (p=0.007). Serum adiponectin level were associated with arthralgia and ankle arthritis (p=0.007, p=0.006 respectively). Serum leptin levels were similar in sarcoidosis patients and controls (p=0.327). There was no relationship between serum leptin level and disease features ($p>0.05$).
**Conclusions:** In this study, high serum adiponectin level was detected in patients with sarcoidosis while serum leptin level were similar in the sarcoidosis and control group. Adiponectin, an anti-inflammatory protein may play an important role in the pathogenesis of sarcoidosis. Studies are needed to shed light on this topic.
**Disclosure of Interest:** None declared
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## AB0925 SERUM GALECTIN-3 AND TGF-BETA LEVELS IN PATIENTS WITH SARCOIDOSIS

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**Background:** Sarcoidosis is a chronic granulomatous disease characterized by non-caseating granuloma formation. Galectin-3 is a multifunctional protein involved in many biological processes such as fibrosis, angiogenesis and immune activation.
**Objectives:** To determine the serum galectin-3 and transforming growth factor-beta (TGF-beta) levels in patients with sarcoidosis and to determine a possible correlation with clinical findings.

**Methods:** Forty-four biopsy proven sarcoidosis patients followed at a single center and age and sex matched 41 healthy volunteers were included in the study. Demographic, clinical, laboratory and radiological data were recorded in all patients. Serum galectin-3 and TGF-beta levels were measured by ELISA method.
**Results:** Among 44sarcoidosis patients 13 (29.5%) were male and 31 (70.5%) were female. Average patient age was 47.4 years, mean disease duration was 3.2year. Twenty-one (47.7%) patients had erythema nodosum, three (6.8%) had uveitis, 40 (90.9%) had arthralgia, 23 (52.3%) had ankle arthritis, 15 (34.1%) had enthesitis. Laboratory evaluation showed increased serum ACE level in 24 (54.5%) patients, increased serum calcium level in 11 (25%) patients, increased serum D3 level in 5 (11.4%) patients, increased ESR and CRP levels in 22 (50%) and 23 (52.3%) patients, respectively. Serum galectin-3 level were similar in the sarcoidosis patients and the control group (p=0.977). No relationship were found between serum galectin-3 level and clinical and laboratory findings ($p>0.05$). Serum TGF-beta level were higher in patients with sarcoidosis compared with the control group (p=0.005). Serum TGF-beta level was associated only with enthesitis and arthralgia (p=0.006,p=0.02), while no correlation were detected with other disease features ($p>0.05$).
**Conclusions:** We found high level of serum TGF-beta, but normal level of galectin-3 in patients with sarcoidosis. These findings suggest that TGF-beta play an important role in the pathogenesis of sarcoidosis. to, there is a need for new Multicenter prospective studies are needed to illuminate the possible relationship between serum galectin-3 and sarcoidosis.
**Disclosure of Interest:** None declared
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## AB0926 INCREASED CIRCULATING INTERLEUKIN-23 IN PATIENTS WITH SARCOIDOSIS

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**Background:** Sarcoidosis is Th1-mediated chronic granulomatous disease characterized by non-caseating granulomas formation. Interleukin-23 (IL-23) is a protein encoded by the IL-23 gene in humans and is produced by dendritic cells and macrophages. IL-23 and IL-12 share a common p40 subunit and are important proinflammatory cytokines.
**Objectives:** This study aim to determine the serum IL-23 level as well as serum IL-6, IL-12, IL-17 levels in patients with sarcoidosis, and to determine a possible correlation with clinical and laboratory findings of the disease.
**Methods:** Forty-four biopsy proven sarcoidosis patients followed at a single center and 41 healthy volunteers were included in the study. Demographic, clinical, laboratory and radiological data of all patients were recorded. Serum samples from all the patients and the control group were taken and IL-6, IL-12, IL-17, IL-23 were measured by ELISA method.
**Results:** Among 44sarcoidosis patients 13 (29.5%) were male and 31 (70.5%) were female. Average patient age was 47.4 years, mean disease duration was 3.2year. Twenty-one (47.7%) patients had erythema nodosum, three (6.8%) had uveitis, 40 (90.9%) had arthralgia, 23 (52.3%) had ankle arthritis, 15 (34.1%) had enthesitis. Laboratory evaluation showed increased serum ACE level in 24 (54.5%) patients, increased serum calcium level in 11 (25%) patients, increased serum D3 level in 5 (11.4%) patients, increased ESR and CRP levels in 22 (50%) and 23 (52.3%) patients, respectively. Compared with the control group higher serum IL-23 level were found in patients with sarcoidosis (p=0.01). Serum IL-23 were associated with ankle arthritis (p=0.02). Serum IL-6, IL-12 and IL-17 levels were similar in sarcoidosis patients and control group (p=0.128, p=0.212, p=0.521 respectively).
**Conclusions:** In our study we found increased serum IL-23 in patients with sarcoidosis, while serum IL-6, IL-12 and IL-17 were detected as normal. Despite our results are somewhat contradictory to other studies in literature, sarcoidosis still should be discussed if is Th1/Th17 disease or not? Multicenter studies are needed in this regard.
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## AB0927 BIOLOGICAL DRUGS USE IN PRIMARY IMMUNODEFICIENCIES

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**Background:** Many patients with primary immunodeficiencies develop immune-mediated diseases that require biological treatment. For some time it has been denied the use of biological treatment to patients with immunodeficiencies, because of the theoretical risk of serious infections.
**Objectives:** To analyze our experience in the use of biological agents in patients with primary immunodeficiency.
**Methods:** Retrospective analysis of 8 patients over 18 years, diagnosed with primary imunodeficiency, by WHO classification, that have received biological treatment. Demographic data, type of immune-mediated disease, biological treatment used, response to treatment and rate of infection were record.
**Results:** We present 8 patients that have received biological drugs. The mean age was 23 years, all of whom were male,except one woman. The time evolution of the priamry immunodeficiency was on average 10.2 years. Five patients have a common variable immunodeficiency, two chronic granulomatous disease and one of them agammaglobulinemia-X. Patients with chronic granulomatous disease and agammaglobulinemia received anti-TNF, for the treatment of inflammatory bowel disease. While patients with common variable immunodeficiency received rituximab; two of them for immune-mediated thrombocytopenia, two for lymphoid interstitial pneumonitis and another by transverse myelitis. Agammaglobulinemia-X and one patient with chronic granulomatous disease precised the use of various anti-TNF (infliximab, adalimumab, certolizumab). All patients had disease improvement in which biological treatment was indicated. The rate of infection was lower along the use of biological drugs (median follow up 1.2 years) than along the treatment with other immunosuppressants. There was only one episode of serious infection that required hospitalization, a patient with agammaglobulinemia-X who presented a herpes zoster, while being trated with steroids and certolizumab for inflammatory bowel disease. The perceived quality of life was better when using biological agents than previously to it.
**Conclusions:** Our experience could open the prudent use of biological drugs for patients with primary immunodeficiencies, always under close monitoring and appropriate prescription.
**Disclosure of Interest:** None declared
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## AB0928 SOME GENETIC MARKERS IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE IN COMPARISON WITH SYSTEMIC LUPUS ERYTHEMATOSUS, SYSTEMIC SCLEROSIS AND RHEUMATOID ARTHRITIS PATIENTS

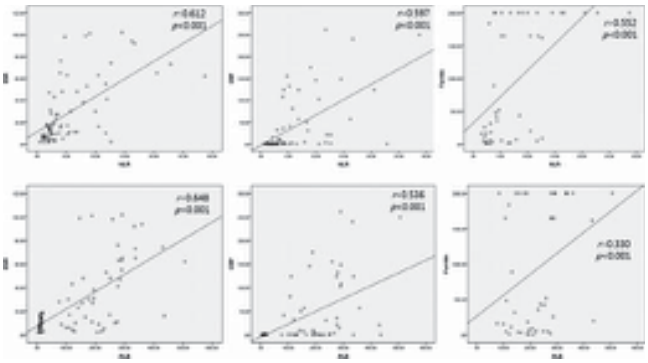
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**Background:** Mixed connective tissue disease or Sharp syndrome (MCTD) was described in 1972 [1] as a connective tissue inflammatory syndrome with overlapping features of systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), polymyositis/dermatomyositis (PM/DM) and systemic sclerosis (SS) associated with antibodies to U1 small ribonuclear protein (U1 RNP). The long-term follow-up studies revealed a tendency for MCTD to evolve into SLE or SS over time [2].
**Objectives:** To reveal genetic markers associated with MCTD and to estimate their discriminating and prognostic value.
**Methods:** For the twenty-five year period (1980–2005) MCTD was diagnosed in 29 patients (25 women and 4 men) observed at Byelorussian Republican Rheumatologic Center. There were 17 cases of overlapping SLE and RA, 7 patients had features of SLE and SS, and combination of SS and RA was revealed in 5 patients. A number of some genetic markers as HLA-A; (8 loci) and HLA-B (17 loci) antigens, AB0 and Rhesus ($Rh_0^+$, $Rh_0^-$) blood groups and haptoglobin phenotype ($Hp_{1-1}$, $Hp_{2-1}$, $Hp_{2-2}$) were investigated in patients with MCTD as well as in patients with RA (n=260), SLE (n=182), SS (n=52) and healthy individuals of the control group (n=120) for the comparison. All the patients fulfilled the ACR criteria for the corresponding diseases.
**Results:** The least differences in A and B loci were revealed between patients with MCTD and SLE (locus A: $\chi^2$=5.3, df=8, p=0.725; locus B: $\chi^2$=10.9, df=16, p=0.813) and the greatest differences – between patients with MCTD and healthy individuals of the control group (locus A: $\chi^2$=11.7, df=8, p=0.165; locus B: $\chi^2$=15.5, df=17, p=0.557). The differences in pairs MCTD vs RA and MCTD vs SS had the intermediate significance level of $\chi^2$ criterion. HLA-$A_1$ antigen was determined in patients with MCTD more often than in the control group (40.9% vs 18.3%, $p_{2\text{-}t}$=0.0231, two-way Fisher's exact test) as well as HLA-$B_8$ (31.8% vs 10.8%, $p_{2\text{-}t}$=0.017) and phenotype $A_1B_8$ (27.3% vs 8.3%, $p_{2\text{-}t}$=0.0198). The same significant differences of HLA phenotype were revealed between MCTD patients and RA and SS patients in contrast to the SLE patients, characterized by the HLA profile similar to MCTD patients. The following frequency of erythrocyte antigens and haptoglobin phenotypes in MCTD patients was determined: I(0) 41.7%; II(A) 16.7%; III(B) 33.3%; IV(AB) 8.3%; $Rh_0^+$ 100.0%; $Hp_{1-1}$ 22.2%; $Hp_{2-1}$ 44.5%; $Hp_{2-2}$ 33.3%. II (A) blood group was determined rarer in MCTD than in RA (40.1%), SLE (42.0%) and SS (50.8%) and in the control group (37.2%). The only significant difference of erythrocyte antigens was between MCTD and SS patients (p=0.043, one-way Fisher's exact test, and $p_{2\text{-}t}$=0,073).
**Conclusions:** HLA-$A_1$, HLA-$B_8$ and phenotype $A_1B_8$ were associated with MCTD. The findings agree with recently published data identified HLA-B8 as risk allele for MCTD [3] and highlight the genetic and clinical similarity between MCTD and SLE in Byelorussian MCTD cohort.
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**Disclosure of Interest:** None declared
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AB0929 **NEUTROPHIL/LYMPHOCYTE RATIO (NLR), PLATELET/LYMPHOCYTE RATIO (PLR) WERE USEFUL MARKERS IN ASSESSMENT OF INFLAMMATORY RESPONSE IN AOSD PATIENTS**

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**Background:** Both neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte (PLR) are reported to be increased in various inflammatory diseases, but there clinical significance in adult onset still disease (AOSD) remains unclear.
**Objectives:** The aim of the present study was to evaluate NLR and PLR as a inflammatory marker in AOSD.
**Methods:** The medical records of 23 AOSD patients and age, sex-matched 25 healthy individuals were retrospectively reviewed. NLR, PLR between AOSD patients and healthy controls were compared, and correlation between these indexes and clinical characteristics were analyzed. Exclusion criteria included active infection and/or the presence of any hematological, cardiovascular or metabolic disorder.
**Results:** The NLR and PLR were found to be significantly higher in AOSD patients when compared to the healthy control (NLR: 10.67± 6.73 vs 2.05±1.07, $p<0.001$, PLR: 255.78±107.22 vs 128.10 ±42.60, $p<0.001$). The NLR and PLR were decreased significantly after treatment (4.67±3.22, 196.84±78.54). NLR was positively correlated with erythrocyte sedimentation rate (ESR)($r=0.612$, $p<0.001$), C-reaction protein (CRP)($r=0.597$, $p<0.001$) and ferritin ($r=0.552$, $p<0.001$). PLR was positively correlated with ESR ($r=0.648$, $p<0.001$), CRP ($r=0.536$, $p<0.001$) except ferritin ($r=0.33$, $p=0.025$).



**Conclusions:** NLR, PLR, together with other serum inflammatory markers, were proving as significant clinical tools which could be used as biomarkers for inflammatory response of disease activity in AOSD patients.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1563

## Diagnostics and imaging procedures

AB0930 **QUANTITATIVE CHEST CT IN ILD-SSC PATIENTS WITH DIVERGENT RISKS OF MORTALITY**

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**Background:** Quantitative analysis of chest CT (QCT) is increasingly applied to characterization of Interstitial Lung Disease (ILD) associated to Systemic Sclerosis (SSc). However, there is no prognostic evidence for QCT in predicting lung detrimental evolution or death. Many Authors proposed composite clinical indexes to predict 1-year mortality. Recently the ILD-GAP index and du Bois index were proven to stratify ILD-SSc patients in outcome-related subgroups.
**Objectives:** The main aim of this study was to compare QCT assessment of SSc-ILD and composite clinical indexes in the selection of patients with high risk of mortality.
**Methods:** Chest CT, anamnestic data and pulmonary function test of 146 patients with SSc were retrospectively collected and ILD-GAP and DuBois score were calculated. Each chest CT underwent a quantitative assessment. Correlation between clinical prediction models and QCT parameters was tested. $p<0,05$ was considered statistically significant.
**Results:** All QCT parameters had a statistically different distribution in patients with diverging mortality risk according to both clinical prediction models. The cut-off of QCT parameters were calculated by ROC curve analysis, with statistically significant value as compared to clinical prediction models (AUC $>0.7$, $p<0.0001$).
**Conclusions:** QCT assessment of SSc-ILD can distinguish between different mortality risk categories, therefore it yields prognostic value. These findings, together with the operator-independence, strengthen the accuracy of QCT for assessment of SSc-ILD.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2995

AB0931 **QUANTITATIVE CT IN ILD-SSC: FEASIBILITY OF AN OPERATOR INDEPENDENT METHOD BASED ON FREE OPEN SOURCE DICOM VIEWER**

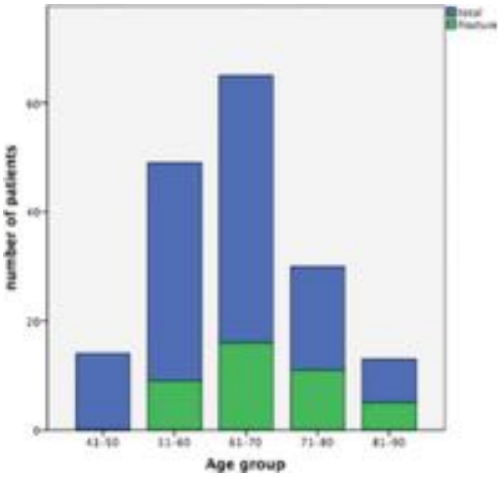
A. Ariani[1], M. Ronconi[1], M. Matucci-Cerinic[2], D.E. Furst[3]. *[1]Dipartimento di Medicina, Unità di Medicina Interna e Reumatologia, Azienda Ospedaliero Universitaria di Parma, Parma; [2]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Florence, Italy; [3]David Geffen School of Medicine, University of California, Los Angeles, United States*

**Background:** Quantitative chest CT (QCT) is a promising procedure to assess the extent and severity of interstitial lung disease (ILD) in systemic sclerosis (SSc) patients. OsiriX and its 64-bit version, Horos, are two free open source software that make it possible to put to use a CT post-processing procedure that is definitely operator independent.
**Objectives:** The main aim of this study is to investigate the feasibility of the operator independent method based on OsiriX/Horos as described by Ariani et al. [1] and hereafter abbreviated as ARIANI.
**Methods:** To explore the feasibility, we address the following areas of focus: a) Demand ("Can ARIANI fill a gap in the field of ILD-SSc studies?"); b) Implementation ("Can ARIANI improve the current way to evaluate ILD-SSc?"); c) Acceptability ("Can ARIANI be used by a newbie after a one-hour training?"); d) Practicality ("How long does ARIANI take to give the QCT of a patient's ILD-SSc?"); e) Dissemination ("Does ARIANI require special equipment? Is it expensive and/or barely available?"). All the answers were extracted from the most current literature (only Pubmed and Academia.edu indexed papers or abstracts about ARIANI were reviewed) and from our own practice-based experience.
**Results:** We selected four papers and five abstracts. Also taking into account our four year experience in performing QCT with ARIANI, we answered to all focus areas chosen. In summary, ARIANI can be extremely useful because the current ways to assess ILD-SSc are not completely satisfying for their inter/intra-observer variability (Demand). Conversely, an operator independent algorithm can represent a starting point to develop a new standard evaluation (Implementation). All the rheumatologists (two) and medical students (two) that were trained, learned how to successfully complete the QCT assessment without requiring any other explanation even after three years (Acceptability). ARIANI requires 1.8 min (range from 0.5 to 3.2 min); this time interval is mainly influenced by the computer configuration (Practicality). The use of Apple (R) computers (which are quite widespread hardware) is mandatory because of the OsiriX/Horos software architecture running only on MacOs X. ARIANI performance is virtually possible on every Mac now available for sale and on the majority of those built in the last seven years (Dissemination).
**Conclusions:** Taking into account the previous close examination, the use of OsiriX/Horos with ARIANI appears potentially useful in ILS-SSc assessment and limited only in those few centers in which there is no availability of the required equipment (i.e. computed tomographies and Mac computers). Thus, ARIANI feasibility seems to be good and ready for a world-wide spread.
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**Disclosure of Interest:** None declared
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## AB0932 FREQUENCY OF VERTEBRAL FRACTURE ON LATERAL VERTEBRAL ASSESSMENT IN PATIENTS WITH OSTEOPENIA UNDERGOING DXA SCANNING

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**Background:** Previous low trauma fracture is a strong predictor of future fracture. Lateral Vertebral Assessment (LVA) is useful to screen for preexisting but undiagnosed vertebral fracture. It is however commonly not performed at the time of DXA scanning. Anti resorptive therapy is frequently withheld in patients with Osteopenia on DXA as fracture risk is perceived not to be high. This perception might change if LVA performed at the time of DXA scanning demonstrated previous fracture.
**Objectives:** The aim of this study was to measure the frequency of vertebral fracture on LVA in patients found to have Osteopenia on DXA.
**Methods:** DXA scans from 170 female patients from two centers in Ireland (Connolly Hospital/Clane Hospital) performed in 2013/2014 were analyzed retrospectively. Patients ranged in age from 40 to 90 years. All patients had T-score between -1.0 and -2.5. They underwent Lateral Vertebral Assessment at the same session following BMD measurement.
All patients are scanned by the same certified densitometry technologist at both centers, using quantitive (vertebral morphometry) and semiquantitative (visual assessment). The scans were reported by a consultant Rheumatologist and Rheumatology registrar. A vertebral fracture was diagnosed if identified by all 3 reviewers.
**Results:** 41 out of 170 Osteopenic patients i.e 24% had vertebral fractures seen on LVA. 51 fractures in total were identified, involving 32 thoracic and 19 lumbar vertebrae. They all occurred in those above 50 years of age, and the frequency of fractures increased with age. 43 of the fractures were classified as mild, 3 as moderate and 5 as severe fractures according to Genant et al. [4].

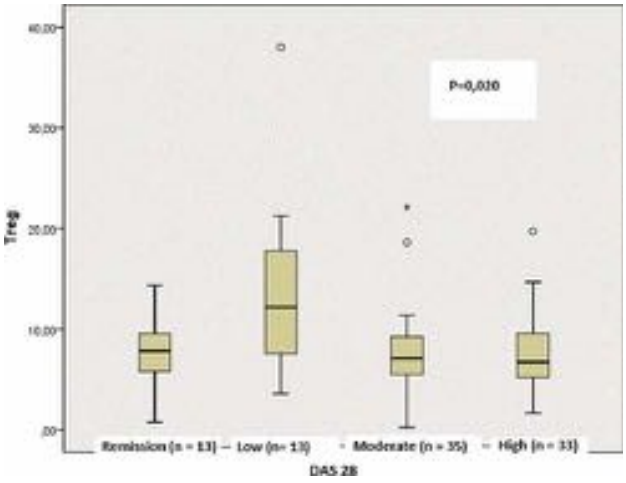



**Conclusions:** Our study emphasizes the importance of LVA in identifying vertebral fractures in osteopenic patients. In view of its advantages, we suggest that any patient undergoing DXA assessment should have an LVA performed regardless of age.
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## AB0933 TREG/TH17 CELLS AND HIGH RESOLUTION ULTRASOUND INFLAMMATORY FINDINGS IN ESTABLISHED RHEUMATOID ARTHRITIS: A CROSS SECTIONAL STUDY

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**Background:** Imbalance and disfuntion in regulatory T-cells (Tregs) and IL-17 producer lymphocytes (Th17) have been implicated in the pathogenesis of rheumatoid arthritis (RA). Gray scale synovial proliferation (GS), power Doppler signal (pD) and bone erosions seen on high resolution muskuloskeletal ultrasound (MSUS) are hallmarks of destructive articular disease.
**Objectives:** The present study was undertaken to evaluate the association of peripheral Tregs and Th17 with MSUS findings in RA.
**Methods:** 90 RA patients (1987 ACR criteria) treated with disease-modifying antirheumatic drugs (DMARDs) were included in this prospective cross-sectional study. A blood sample was taken just before clinical and ultrasonographic evaluation. Lymphocytes were isolated and immunophenotyped by flow cytometry to investigate regulatory FoxP3+ T cells and IL-17+ cells. MSUS (MyLab 60, Esaote, Genova, Italy, linear probe 6–18 MHz) was performed consecutively by two ultrassound-trained rheumatologists on the wrists, 2th and 3th metacarpophalangeal and 2th and 3th proximal interphalangeal joints of both hands. GS and pD were searched using a semi-quantitative scale (0–3). Bone erosions were classified as present or absent. The sum of the individual joint scores for GS and pD (score 10) was calculated and used to correlate with clinical and laboratory data. Disease acitivity and disability were measured using Disease Activity Score in 28 joints (DAS28) and Health Assessment Questionnaire (HAQ), respectively. Mann-Whitney test, Kruskal-Wallis test and Spearman correlation coefficient ($r_S$) were used for statistical analysis. Inter-rater agreement was tested using the weighted *kappa* statistic (WKS) and intraclass correlation (ICC).
**Results:** Clinical and demographic features were: mean age, 55.8 ±11 years; female gender, 79%; Caucasians, 84%; positive rheumatoid factor by nephelometry, 63%; median (interquartile range) disease duration 6 (2–13) years; mean ± SD DAS28, 4.28±1.64; mean ± SD HAQ score, 1.11±0.85. WKS for erosions was 1, and ICC for GS- and pD-score10 were 0.964 (95%CI 0.899 to 0.986) and 0.859 (0.646 to 0.941), respectively. There was no significant association of bone erosions, GS- and pD-score10 with peripheral Tregs and Th17 cells ($P>0.25$ for all tests). Tregs but not Th17 cells were significantly associated with DAS28 level of disease activity (figure 1).




**Conclusions:** In this first study addressing MSUS features and lymphocytes subtypes in established RA, data did not support an association of circulating Tregs and Th17 lymphocytes with inflammatory and structural damage findings on MSUS.
**Disclosure of Interest:** None declared
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## AB0934 BLOOD PRESSURE IS NOT CHANGED BY TOPICAL NSAID – A PILOT CONTINUOUS AUTOMATED BLOOD PRESSURE MONITOR STUDY

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**Background:** Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used by rheumatic patients for both acute and chronic conditions. A certain increase

in blood pressure of 3–5 mmHg seems to be a NSAID class effect. Although the effect appears from the beginning of the treatment, due to his"modest" amplitude, it was largely ignored both by patients and physicians. However, new epidemiological data suggest that such a small increase in BP could produces in USA about 21.000 deaths per year (higher than in case of gastrointestinal deaths produced by the unprotected usage of nonselective NSAID). For the time being we do know that topical and systemic NSAID have similar therapeutic effect on superficial exposed joints (e.g. knee, wrists, elbows etc).
**Objectives:** The aim of the study was to evaluate whether or not the use of topical NSAIDs in rheumatic patients affects blood pressure or pulse rate values.
**Methods:** This was a prospective study which included patients diagnosed with various rheumatic diseases using a continuous Automated BP Monitoring (ABPM): both BP and pulse rate have been continuously recorded for 48 hours at baseline (24 hours without topical NSAID use) and day1 (24 hours with topical NSAID use). Same NSAID (namely Aceclofenac) in same dose was used in all cases. Subjects that changed their concomitant medication have been excluded from the analyses. Daytime (0700–2200), nighttime (2201–0659) and all-day (24h) systolic and diastolic BP along with pulse rate values have been analyzed. Difference between Baseline and Day1 have been tested by using ANOVA and Fisher exact test; a $p<0.05$ was considered significant.
**Results:** 15 subjects have been evaluated between October 2015 to January 2016. The meanSystolic BP varied between 101.75 and 147.9 in Baseline respectively between 103.9 and 132.25 during D1. The mean diastolic BP varied between 55.5 – 88.1 in Baseline and respectively between 56.4–82.5 during D1. Pulse varied between 60.2 and 95.9 in Baseline and respectively 59.3 and 90.2 during Day1. No difference between baseline and Day1 have been identified for Systolic or DiastolicBP, cardiac pulse; same results have been obtained for all-day, nighttime and daytime subanalysis.
**Conclusions:** Although this study has certain limitations our data suggest no significant change in BP or cardiac pulse associated to topic use of NSAID (in our case Aceclofenac). Larger studies should be made to confirm the conclusion of this pilot study.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4626

## AB0935 RHEUMATOLOGISTS AND MUSCULOSKELETAL ULTRASOUND: DISCREPANCY BETWEEN ATTITUDES, DESIRE AND REALITY IN ROUTINE PRACTICE IN SOUTH EAST ENGLAND

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**Background:** The use of musculoskeletal ultrasound (MSK US) in routine care is expanding. The number of rheumatologists using or seeking to learn the technique is also increasing, though it is unclear how US is being incorporated into routine work practices (RWP).
**Objectives:** This survey sought to gain an insight into the use of MSK US in a region of Southern England.
**Methods:** A questionnaire was designed by the authors to collect information on training, access & service delivery, indications and attitudes towards use of MSK US in RWP. All rheumatology consultants (RC), trainees (RT) and specialist nurses (SN) working in 19 Hospitals (Hs) (4 Medical School Universities, 15 District General) in London South, Kent, Surrey and Sussex regions of England were invited to complete the survey. Data were analysed using simple descriptive and summary statistics.
**Results:** A total of 70 questionnaires (51%) were returned (RC 61%, RT 27%, SN 12%) with at least one response from all 19 Hs.
*Training:* Of the 70 responders (Rs), 42% report having had formal training in the use of US, however only 12% had support for this and 10% have a formal MSK US certificate.
*Access & service delivery:* MSK US scans are most usually performed by radiologists (64%). In 11 Hs there are also US machines in the rheumatology department, of which 8/11 are currently used for routine care. The routine waiting time for a MSK US is up to 6 weeks.
10 of the 29 Rs who have had training (34%) perform US scans themselves. They report greatest confidence scanning the hands (90%), followed by feet (70%) and 20% are confident to scan all joints. US guided injections are given by 50% and US guided synovial biopsies performed by 20%.
The maximum number of joints scanned in one session varies from 5 – 40 joints, taking an average time of 20 minutes per scan.
*Indications:* MSK US are requested for diagnostic purposes by 92%, guided injection by 80%, assessment of treatment response by 52%, research purposes by 8% and 75% request a scan at least 1 – 5 times a week. The proportion of Rs requesting MSK US per disease groups is: Inflammatory Arthritis (IA) >85% and soft tissue 63%.
*Attitudes:* More than 60% of the Rs report that MSK US results often lead to a change in their management plans and that it enhances patients' satisfaction. 82% think it appropriate that RC should perform MSK US scans as part of their RWP. 50% of the RC and 72% of the RT think that proficiency in use of US should be a mandatory part of the rheumatology training curriculum. 51% of the Rs indicated a willingness to learn the technique.
Free text responses revealed concerns about available time and proper training but others commented that MSK US is beneficial in an early IA setting.
**Conclusions:** This cross-sectional, observational, multicentre survey demonstrates widespread use of MSK US by rheumatologists in routine care in the South East Coast region of England. 82% of Rs think it appropriate that RC should perform MSK US in RWP and 57% believe training in this should be a mandatory part of the curriculum. In contrast 42% of Rs have had formal training, but only 14% of them have incorporated MSK US into RWP, the majority relying on radiology colleagues to do the scans. This illustrates a discrepancy between attitudes, desire and reality of MSK US use in routine rheumatological practice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5790

## AB0936 USEFULNESS OF SALIVARY GLANDS ULTRASONOGRAPHY IN THE DIAGNOSIS OF SJÖGREN SYNDROME

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**Background:** Sjögren syndrome (SS) is a chronic autoimmune disease characterized by lymphocytic infiltration of the lacrimal and salivary glands resulting in clinical symptoms of keratoconjunctivitis sicca and xerostomia. Recent studies have shown that salivary gland ultrasonography (SGUS) is a valid tool to evaluate the involvement of major salivary glands in SS.
**Objectives:** To assess the utility and accuracy of the USGS for diagnosis of SS.
**Methods:** Single-center experimental study in a cohort of patients with suspected SS in whom a salivary gland biopsy (SGB) would be performed as requested by their usual physician.
SGUS examination of the parotid and submandibular salivary glands was preformed prior to the realization of minor salivary gland biopsy. Changes in the echostructure of the glands were scored according to the scoring system of de Vita et al., which mostly focuses on the inhomogeneity of gland tissue with scores ranging from 0 to 3 (0: homogenous glands, 1: isolated hypoechoic areas, 2: scattered hypoechoic areas with variable size, not uniformly distributed, and/or to multiple punctate or linear non-shadowing densities and 3: large round or confluent hypoechoic areas, and/or to linear densities, and/or to multiple cysts or multiple calcifications). The SGB was considered as Gold standard. The definitive diagnosis of SS was made according to the AECG criteria.
**Results:** From a sample of 24 patients with suspected SS, SGUS was performed in 20 patients before the SGB. All the patients were women with a mean age of 58±14. Eleven patients (46%) fulfilled AECG criteria, 4 (17%) did not met criteria and in 9 of them (37%) was not possible to classify because of insufficient data (at least two unregistered criteria). Eleven patients (55%) had a normal SGUS while 9 (45%) had some degree of changes in the gland's echostructure.
In the group of patients who met AECG criteria, four (36%) had a negative biopsy, four (36%) positive biopsy and 3 (28%) had nonspecific biopsy. Of the 9 patients with an uncertain diagnosis for lack of data, 7 (78%) had a nonspecific biopsy. 5 patients (56%) with changes in the SGUS met AECG criteria. Of the 6 patients with positive biopsy for SS, 4 (67%) had ultrasound abnormalities. Of the 7 patients with pathological salivary scintigraphy, 5 (71%) had alterations in USGS. Taking biopsy as the gold standard, the sensitivity of the SGUS was 100%, specificity was 68.75%, PPV 44.4% and NPV of 100%; the sensitivity of scintigraphy was 80%, specificity was 44%, PPV 44% and NPV 44%. Considering the scintigraphy as the gold standard, sensitivity of ultrasound was 71.4%, specificity was 100%, PPV 100% and NPV 60%. As limitations of this study is important to remark that these are preliminary results from a small sample in early stages of the disease.
**Conclusions:** Our findings suggest the potential of SGUS as a diagnostic tool for distinguishing SS. Although data is preliminary we found high sensitivity and NPV of SGUS compared to biopsy and high specificity of SGUS compared to scintigraphy.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5499

## AB0937 THE COMPARISON OF SYNOVIAL DEGREE INFLAMMATION BETWEEN SYSTEMIC SCLEROSIS AND RHEUMATOID ARTHRITIS BY MAGNETIC RESONANCE IMAGING OF HANDS

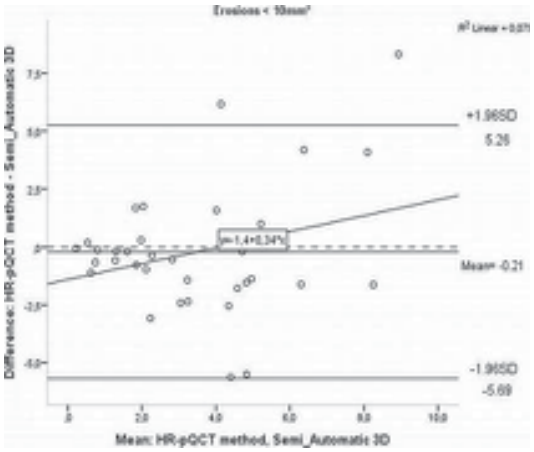
B.N. Stamenkovic[1], A.M. Stankovic[2], J.M. Nedovic[1], S.K. Stojanovic[1], V. Zivkovic[1], S.B. Milenkovic[1], I. Aleksic[1], N. Damjanov[3]. *[1]Rheumatology, Institute for treatment and rehabilitation Niska Banja, Medical Faculty of Nis, Serbia; [2]Rheumatology, Intermedica, Nis; [3]Rheumatology, Institute of Rheumatology, Medical Faculty of Belgrade, Belgrade, Serbia*

**Background:** MRI is a usefull tool for assessing subclinical synovial inflammation and joint damage in rheumatic diseases. There are no references clarifying the problem of distinguishing arthritis in systemic sclerosis (SSc) and rheumatoid arthritis (RA) so far
**Objectives:** The aim of our investigation is to compare the degree of inflamatory changes of the hand (bone edema, synovitis, bone erosion and tenosynovitis) in SSc and RA.
**Methods:** 82 SSc pts, mean age 54,5y and 35 RA pts (EULAR/ACR 2010 criteria), mean age 54,3y underwent low field MRI with gadolinium at the dominant hand including wrist and MCP joints 2–5. Assessment of bone marrow edema, synovitis, bone erosions and tenosynovitis was performed by the OMERACT RA MRI scoring system. Images were evaluated independently by two blinded readers. The mean scores of the two readers were analyzed.
**Results:** Anti-citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF) were found in 89% and 74,3% of RA pts and 13,4% and 14,6% of SSc pts. Synovitis was more frequently detected on MRI with significantly higher score in RA compared to SSc (wrist:4,37±1,31 vs 2,69±2,29,p<0,001; MCP joints:5,26±2,09 vs 3,15±2,95, p<0, 001). MRI erosion score in the wrist and MCP was significantly higher in RA compared to SSc (wrist:20,57±10,23 vs 6,58±10,89,p<0,001; MCP joints:10,51±7,90 vs 3,99±9,82, p<0,001). MRI bone edema score was also significantly higher in RA compared to SSc (wrist:18,60±5,01 vs 6,84±7,43, p<0,001; MCP joints:9,09±4,27 vs 4,04±4,76, p<0,001).
**Conclusions:** The present data suggest great frequency of inflammatory changes on the hands in SSc and RA using MRI. Inflammation scores were significantly higher in RA compared to SSc. MRI may be helpful in differentiating arthritis in RA and SSc, specially in subclinical inflammation.
**Disclosure of Interest:** None declared
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## AB0938 A COMPARISON OF TWO METHODS TO SEGMENT BONE EROSIONS IN THE METACARPOPHALANGEAL JOINTS OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Bone erosions are a central feature of rheumatoid arthritis (RA). In particular small erosions not yet detectable on radiographs or even MRI, but already well depicted in high-resolution quantitative computed tomography (HR-pQCT) are a sign for early RA and may guide intervention before major bone destruction and functional impairment.
**Objectives:** To compare standard segmentation tools implemented on the HR-pQCT scanner (XCT) with MIAF (Medical Image Analysis Framework) software in their ability to quantify erosion shape and size in metacarpophalangeal (MCP) joints. MIAF runs on external PCs and requires DICOM export of XtremeCT images.
**Methods:** 2D threshold based contouring of bone is a standard feature of the XtremeCT software to segment the distal radius and tibia. These contouring algorithms along with the manual editing options were applied to segment erosions of MCP joints. In contrast MIAF uses more sophisticated 3D algorithms to separately segment periosteal bone surface and erosions. In particular the cortical break and (for larger erosions) the border between bone marrow and erosion can be better defined. HR-pQCT scans of the 2nd and 3rd MCP joints of ACPA positive RA patients, which represent a homogeneous subgroup with high level structural damage, were analyzed. Based on volume, erosions were categorized into 2 groups: $<10mm^3$ (MIAF measurement) and $>10mm^3$. Based on their shape, they also were visually classified into “regular” or “Irregular”. This classification was compared with sphericity (0–1), which can be obtained with MIAF but not with XCT.
**Results:** 76 erosions of 65 (46F; 19M) patients were analyzed. Irregular erosions were larger ($>10mm^3$) than regular erosions ($\chi(1)^2$=20.52, p<0.001). Irregular erosions had lower sphericity (0.53±0.08); than regular ones (0.63±0.09, $t_{(74)}$= -4.645, p<0.001). Irregular erosions were considered smaller in MIAF than XCT (49.9±70.7 vs. 52.2±79.4; p=0.013), while regular erosions were larger than for XCT (7.0±9.4 vs. 4.0±4.5; p=0.002). There was a 47% absolute difference in size between MIAF and XCT. The differences could be largely explained over-segmentation of irregular erosions and under-segmentation of regular erosions in the XCT. The main reason was the under-segmentation of the cortical break.




**Conclusions:** Standard tools implemented on XtremeCT scanners can be applied for measurement of erosion size but compared to MIAF the segmentation of the cortical break is less accurate resulting in differences in the determination of erosion volume. MIAF performs a separate bone and erosion segmentation, avoiding under/overestimating volume. The visual classification of erosions according to their shape could be useful to infer the amount of bone damage in RA patients but an operator independent quantitative parameter such as sphericity may be preferable as precision will likely increase.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5335

## AB0939 SHOULDER PAIN ACCORDING TO TIME OF ONSET OF SYMPTOMS: AN ULTRASONOGRAPHIC FEATURES COMPARISON

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**Background:** Ultrasonographic features in shoulder pain have been extensively described in many series. Most epidemiological studies have focused on ultrasonographic findings without considering time of onset of symptoms. In our experience with patients with shoulder pain of recent onset (less than a week) we find ultrasonographic features which proportions are discordant with global epidemiological data especially in terms of prevalence of subacromial bursitis and supraspinatus tendinosis.
**Objectives:** To describe and compare ultrasonographic findings on patients with shoulder pain who consulted to our emergency department and underwent an ultrasonographic shoulder assessment.
**Methods:** The registries of the musculoskeletal and rheumatologic urgencies unit of our A&E department, from 2013 to 2015 were consulted. The known ratio of ultrasonographic assessment of our unit is close to 95% of all shoulder pain cases. Two rheumatologists with full ultrasonographic training and at least 3 years of experience performed the studies following Eular shoulder ultrasonographic definitions. Findings were grouped according to time of onset of symptoms using an arbitrary definition of hyperacute (<7 days), acute (1 to 6 weeks) and chronic (>6 weeks) of shoulder pain.
**Results:** 474 registries of shoulder ultrasonographic assessments were reviewed. Average age of patients was 59 SD 17 years old. Male proportion was 67%. Global findings showed that supraspinatus tendon was affected in 86.7% of all records, while subscapularis tendon in 26.8% and biceps tendon in 11.8%. 67, 47 and 20 registries were classified as hyperacute, acute and chronic shoulder pain, respectively. 38.6% of all supraspinatus tendinosis was present in hyperacute, 25.1% in acute and 36.3% in chronic shoulder pain. 50% of all subacromial bursitis detected were present in hyperacute shoulders, 35.1% in acute and 14.9% in chronic shoulder pain. 34.2% of all supraspinatus tears were present in hyperacute shoulders, 47.4% in acute and 18.4% in chronic

| Ultrasonographic shoulder findings | Time since onset of symptoms: Less than a week | | 1 to 6 weeks | | More than 6 weeks | |
|---|---|---|---|---|---|---|
| | N | Row N % | N | Row N % | N | Row N % |
| Subacromial bursitis | 67 | 50.0 | 47 | 35.1 | 20 | 14.9 |
| Supraspinatus tendinosis[a] | 103 | 38.6 | 67 | 25.1 | 97 | 36.3 |
| Supraspinatus tear | 52 | 34.2 | 72 | 47.4 | 28 | 18.4 |
| Supraspinatus calcification | 8 | 12.7 | 20 | 31.7 | 35 | 55.6 |
| Subscapularis tendinosis[b] | 28 | 70.0 | 12 | 30 | - | - |
| Subscapularis tear | 8 | 66.7 | 4 | 33.3 | - | - |
| Bicipital tendinosis | 8 | 22.2 | 16 | 44.4 | 12 | 33.3 |
| Bicipital synovitis | 8 | 40.0 | 4 | 20.0 | 8 | 40.0 |
| Bicipital tear | 4 | 50.0 | 4 | 50.0 | - | - |

[a] Excluding calcificant tendinosis.
[b] Including a single case of calcificant tendinosis.

shoulder pain. 70% of all subscapularis tendinosis were present in hyperacute and 30% in acute shoulders. 12.7% of all subscapularis calcifications were present in hyperacute shoulders, 31.7% in acute and 55.6% in chronic shoulders. All of these distributions had differences statistically significant. Supraspinatus calcification distribution was not statistically different in the three groups.
**Conclusions:** Subacromial bursitis and subscapularis tendinosis seems to be the most frequent finding in patients with hyperacute shoulder pain. Our results, in patients with less than a week of symptoms, do not agree with most epidemiological ultrasonographic studies of the shoulder. It is possible that differences could be explained by the fact that most studies have not been performed in patients with hyperacute shoulder pain. In our opinion, a better comprehension of shoulder ultrasonographic features in shoulder pain should be linked to the time of onset of symptoms.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4291

## AB0940 COMPARISON OF US7 AND US10 RISK SCORES IN EARLY INFLAMMATORY ARTHRITIS (EIA)

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**Background:** Ultrasound (US) can anticipate joint damage better than DAS28 [1], correlates well with MRI [2] and can be of value determining persistence of EIA [3].
US scoring systems aim to standardise risk assessment. US10 risk score showed clinical utility in predicting benefit from early biologic therapy [4]. The US7 score reflects arthritis therapeutic response [5]. No study has directly compared these US scores.
**Objectives:** Compare measurement performance of US7 and US10 scores in assessing EIA.
**Methods:** 32 EIA patients were examined by 2 trained musculoskeletal US Rheumatologists. 52 DAS28 scores and US7/US10 risk assessments were completed. Inter-observer variability was assessed by intraclass correlation coefficient (ICC). Criterion validity assessed by Pearson correlation with DAS28.
**Results:** Mean age 57 (SD=14), 24/32 (75%) female, 28/32 (87.5%) anti-CCP positive, 27/32 (84%) RF positive. Inter-observer variability (ICC) for US10 and US7 were 0.57 ($P<0.0001$) and 0.73 ($P<0.0001$) respectively. DAS28 correlation with US7 (r=0.335, P=0.018) and US10 (r=0.095, P=0.514). US7 and US10 correlated with swollen joint count (r=0.499, P=0.000) and (r=0.368, P=0.006). The addition of wrist US improved DAS28 correlation with US10 (r=0.255, p=0.077).

Table 1. Correlation coefficient between US7/US10 and DAS28

| Risk score | P value | Correlation coefficient with DAS28 |
|---|---|---|
| US7 | 0.018 | 0.335 |
| US10 | 0.514 | 0.095 |
| US10 with wrist | 0.077 | 0.255 |

**Conclusions:** Inter-observer variability is moderate to good with US7 and US10. US7 and US10 correlates with SJC. US7 score in comparison with US10, correlates with the DAS28. Addition of wrist US score to US10 improved correlation with DAS28. This could be a more time effective method to stratify patients if feet assessment is not feasible.
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[5] Arthritis & Rheumatism (Arthritis Care & Research) Vol. 61, No. 9, September 15, 2009, pp 1194–1201 DOI 10.1002/art.24646 Evaluation of a Novel 7-Joint Ultrasound Score in Daily Rheumatologic Practice: A Pilot Project M. Backhous, S. Ohrndorf, H. Kellner, J. Strunk, T. M. Backhaus, W. Hartung, H. Sattler, K. Albrecht, J. Kaufmann, K. Becker, H. Sörensen, L. Meier, G. R. Burmester, and W. A. Schmidt.
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## AB0941 SYSTEMATIC LITERATURE REVIEW OF ULTRASOUND IN LARGE VESSEL VASCULITIS FOR ESTABLISHING OMERACT DEFINITIONS

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**Background:** Ultrasound (US) is increasingly used for the diagnosis of large vessel vasculitis (LVV), as this imaging technique enables the visualization of the inflammatory vessel wall swelling. A consensus about the definition of US lesions for diagnosis of LVV has not yet been accomplished.
**Objectives:** 1) To identify definitions of US lesions in LVV; 2) to evaluate the role of US in monitoring disease response; and 3) to assess the value of identified US lesions for diagnosis of LVV.
**Methods:** A systematic literature search was conducted in PubMed, Embase and the Cochrane Library (till 23rd November 2014). Research articles enrolling at least 20 patients with suspected cranial giant cell arteritis (GCA) or large-vessel GCA (LV-GCA), Takayasu arteritis (TAK), published in English or German were selected. The study design, subjects, methods, imaging protocols and diagnostic values were evaluated, as well as the US definitions of vasculitis. The quality of the included studies was assessed by the QUADAS2 tool.
**Results:** Of 2960 articles identified, 34 studies were included in the review for the extraction of definitions of vasculitis in US. Thirty-two reports addressed the role of US in diagnosis of cranial GCA, whereas only 6 studies evaluated US in the settings of LV-GCA. The role of US in disease monitoring was evaluated in 11 articles on cranial GCA and in 2 articles on LV-GCA. No studies assessing the role of US in TAK fulfilled the inclusion criteria. Most studies investigated the value of the "halo sign" (32 articles), whereas "compression sign", "stenosis", "occlusion" or "decreased vessel wall pulsation" as signs of vasculitis were addressed in 1, 22, 19, and 1 paper(s), respectively.
**Conclusions:** US is a valuable diagnostic tool in patients with suspected GCA. In this systematic literature review we identified "halo sign", "stenosis", "occlusion", "compression sign" and a "decreased vessel wall pulsation" as possible key US lesions for vasculitis. Based on these results future research on the role of US in LVV is now being performed by the OMERACT US group.
**Disclosure of Interest:** None declared
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## AB0942 DIAGNOSTIC VALUE OF ANTI-RA33 ANTIBODY IN COMPARISON WITH ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES AND RHEUMATOID FACTOR IN PATIENTS WITH EARLY ARTHRITIS AND INDIVIDUALS WITH FIRST-DEGREE RELATIVES OF PATIENTS WITH RA

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**Background:** Rheumatoid Arthritis (RA) is an inflammatory autoimmune disease characterized by joint involvement, pain and inflammation with or without extra-articular joint commitment. Serological markers can guide early diagnosis before that clinical activity takes place, optimizing early diagnosis, less activity and functional disability. RA 33 is considered a diagnosis-marker in RA patients related to prognosis and therapeutic response compared with conventional markers. RA 33 is common in patients with negative conventional markers and with few clinical symptoms.
**Objectives:** Evaluated the frecuency of RA33 in individuals with first-degree relatives of patients with RA and patients diagnosed with early rheumatoid arthritis as a good prognosis marker
**Methods:** A transversal study was conducted evaluated rheumatologic and periodontal condition of 112 individuals with first-degree relatives of patients with RA and 46 patients diagnosed with early rheumatoid arthritis, according to classification criteria for RA (ACR-EULAR 2010). In addition, 47 healthy individuals were included. RA patients and control group were matched for age and gender. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor RF, ACPAs, and RA 33 were performed. VAS Pain Scale, SDAI Index, HAQ and DAS28 were evaluated. *Porphyromona gingivalis (Pg)* by CRP, IgG1, and IgG2 were determined. The data included in the study were analyzed using STATA 11.1. Associations were determined by the statistical test Chi 2, and Comparisons between groups of rheumatologic diagnosis and median values for continuous variables was performed using Mann-Whitney Test. Approved by the Ethics Committee of the Institution.
**Results:** 112 healthy individuals with first-degree relatives of patients with RA were assessed. Of them 78.3% has periodontal disease, presence of painful joints (30.63%). 36.94% patients had *Pg* in subgingival plaque samples. In the control

group the presence of periodontal disease was 71.74%, tender joints (19.57%), swollen joints (6.52%). Disease activity measures were not representative. Only a woman in the group of family related RA patients was positive for RA 33 (49 years old, without treatment, painful and swollen joints and the presence of periodontal disease and *Pg*, ESR and CRP positives but RF and ACPAs negative). No patient with RA of less than two years of diagnosis was positive for RA 33.

**Conclusions:** The diagnostic value of anti RA33 was low in this population, with regard of worst prognosis markers and higher disease severity. Ra33 should be more follow-up clinical and paraclinical to subjects with risk factors who could have positive markers, without symptoms.

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## AB0943 RELIABILITY OF MUSCULOSKELETAL ULTRASOUND TO DETECT ELEMENTARY LESIONS IN JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Clinical evaluation has limitations to detect inflammation in JIA. Musculoskeletal ultrasonography (MSKUS) is a useful tool to detect inflammation in various arthropathies, but in children has not been validated for detection of elementary lesions such as synovitis [effusion (SE) and synovial hypertrophy (SH)], erosions, tenosynovitis (TNS) and cartilage damage.

**Objectives:** To evaluate the reliability of MSKUS to detect carpal and metacarpal joint synovitis in patients with JIA.

**Methods:** Seven patients with JIA diagnose according to ILAR criteria were included; they were evaluated by MSKUS for 5 ultrasonographers to evaluate synovitis, erosions, TNS and cartilage in the carpal joint, 2nd and 3rd metacarpophalangeal joints bilaterally; in 2 rounds in one day. Intra- and interobserver variability was established with Cohen's kappa, according to Landis and Koch classification.

**Results:** The mean age of the children was 9 years old; disease duration of 5 years. The inter-observer DS, HS, TNS and erosions agreement was good to excellent (k=.88 0.5889–1.0 95%, p=0.0000) and moderate for cartilage (k=0.43, 95% CI 0.0545 to 0.8964, p=0). The intra-observer variability was good (0.71, IC95% from 0.591 to 0.8498, p=0.0000).

**Conclusions:** The US is reliable for assessing the presence of synovitis, tenosynovitis, erosion and cartilage in hands, in patients with JIA.

**Disclosure of Interest:** None declared

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## AB0944 AUTOMATING EVALUATION OF SALIVARY GLAND ULTRASOUND IMAGES IN PSS PATIENTS USING THE SCATTERED TRANSFORM ALGORITHM – A PILOT STUDY

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**Background:** Primary Sjögren's syndrome (pSS) is an autoimmune inflammatory disease predominantly affecting the salivary and lacrimal glands. The main symptoms are dryness of the mouth and eyes. The diagnosis of pSS is based on 6 items according to the American-European consensus group (AECG) classification criteria. Interest regarding ultrasonography (US) as a diagnostic tool for pSS has increased over the last years. However, the applied scoring-systems vary and as of yet international consensus on how to perform the evaluation are lacking. Consequently, the examination and evaluation depends on the examiners skill and experience. In both clinical work and a scientific setting there is a need to use objective methods with as little inter- and intra-examiner variation as possible.

**Objectives:** The aim of this study was to develop a software able to analyze changes in digitally stored US images of the major salivary glands.

**Methods:** Digitally stored US images of glandula parotis (n=94) were blindly evaluated and scored as "normal" or "SS-like" by three independent clinical researchers. At least 2/3 evaluations had to be in agreement to classify the image. All images were from patients fulfilling the AECG criteria. Images had been obtained by six clinical investigators using similar protocols on different US machines. For the analysis, images were divided into databases of SS-like changes and normal-appearing morphology. The image classification and analysis was performed using the ScatNet (v.02) algorithm (Ref: http://www.di.ens.fr/data/software/) for MatLab, which is an algorithm for advanced pattern recognition. Images from the databases were randomly selected to be used as either "training" images or "test" images. Each database of "training" images was analysed, and features of pathological and non-pathological morphology were identified by the software. For the software test, the algorithm analyses which of the databases of training images are most similar to the test images and decides in which group the test images belong. This selection was then compared to the manual scoring.

**Results:** Out of the 94 images evaluated, 40 were classified as normal-appearing and 54 as corresponding to SS-like pathological changes. In the preliminary simulations we have used the following training: test ratios 84:10 (90%), 70:24 (75%) and 47:47 (50%), to respectively train the classification algorithm, and then test the algorithm. The best result with 9/10 correctly classified (92% accuracy) was obtained using 90% of the images to train the software and 10% to test the software. Using 75% or 50% of the images to train the software, the accuracy was reduced to 21/24 (88%) and 25/36 (78%), respectively.

**Conclusions:** Preliminary results indicate that the success rate of the algorithm is closely dependent on the number of images used to train the algorithm. The results are promising and indicate possible clinical use in the evaluation of SGUS images. We will further focus on expanding the image database to achieve more precise results.

**Disclosure of Interest:** None declared

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## AB0945 AN ATLAS BASED AUTOMATIC SEGMENTATION OF THE HUMAN THIGH MUSCLES: A PROMISING APPROACH FOR MUSCLE VOLUME QUANTIFICATION IN LONGITUDINAL STUDIES

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**Background:** Atlas segmentation is a powerful method for automatic structural segmentation of several sub-structures in many organs. However, so far, very few studies have assessed this method for skeletal muscle segmentation.

**Objectives:** In this study, we present an atlas-based pipeline we have developed for segmentation of quadriceps muscles from magnetic resonance images obtained in twenty five young healthy males and illustrate the potential of this approach for a longitudinal follow-up in a group of 7 subjects.

**Methods:** T1-weighted axial MR images from the thigh were recorded once in a group of 25 subjects (G1) and twice (a few days apart) in another group of 7 subjects (G2). The multi-atlas library was built from G1. In order to do so, MR images were initially automatically segmented for bone, muscle and fat tissues and each muscle of the thigh anterior compartment was manually delineated. The same process was applied to G2 in order to obtain the ground-truth set of images. Then each MRI dataset from G1 was registered to each MRI dataset of G2 using a non-linear registration process. An optimal fusion method was then used applied in order to obtain the highest DICE index, a similarity index between the atlas-based manual segmentation and the ground-truth set of images. A single-atlas version of the pipeline was used without the fusion process and a similar validation was performed for a longitudinal follow-up study.

**Results:** In control subjects, the results for each quadriceps muscle show a mean DICE similarity coefficient higher than 0.85. While the multi-atlas pipeline did not provide sensitive enough for muscle volume quantification, the single-atlas version proved to be far better.

**Conclusions:** In the present study we reported two segmentation pipelines based on atlases. The examples provided in a control population demonstrated a robust method which could be useful for muscle quantification in the fields of neuromuscular disorders, sports medicine and rehabilitation.

**Disclosure of Interest:** None declared

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## AB0946 S100A8 BUT NOT S100A9 LEVEL IS RELATED TO THE EXTENT OF EROSIVE BONE DAMAGE IN PSORIATIC ARTHRITIS PATIENTS

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**Background:** Psoriasis and psoriasis arthritis are associated with bone damage [1–3]. However, little is known about markers associated with structural bone damage in patients with psoriasis (PsO) and psoriasis arthritis (PsA). C-reactive protein is of limited use in PsO and PsA and therefore development of new markers is needed to identify patients with higher level structural bone damage. The calcium-binding proteins S100A8 and S100A9, which are predominantly produced by myeloid cells and elevated in certain forms of inflammatory diseases are interesting candidates.
**Objectives:** To analyse whether S100A8 and S100A9 serum levels are related to structural bone damage in patients with PsO and PsA.
**Methods:** Both PsO and PsA patients (according to the CASPAR criteria) were analysed. Demographic and disease-specific variables were recorded. Bone architecture was assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT, XtremeCT, Scanco, Switzerland) of the metacarpal heads 2 and 3. Number and size of bone erosions were quantified as described previously [1]. Levels of S100A8 and S100A9 were measured by enzyme-linked immunosorbent test. Serum markers were correlated to the extent (volume) of bone erosions, respectively using Spearmans correlation.
**Results:** 94 patients were included into this combined imaging and serum analysis, 42 of them had PsO (18 female, mean age 48.4±12.8 years) and 52 had PsA (29 female, age 48.3±14.8 years). Duration of skin disease was 14.7±16.1 years in PsO and 13.3±13.6 years in PsA. Duration of joint disease in PsA was 4.6±5.9 years. Mean time between blood collection and HR-pQCT measurement was 0.3±1.7 days (maximum 10 days). Mean±SD S100A8 level was 11.8±15.3 ng/ml in PsO patients and 12.8±13.8 ng/ml in PsA, while mean ±SD S100A9 level was 66.8±51.1 ng/ml in PsO and 75.9±58.3 ng/ml in PsA. Mean±SD erosion volume was 0.7±1.8 $mm^3$ in PsO patients and as high as 2.2±3.6 $mm^3$ in PsA. Serum levels of S100A8 were significantly correlated to erosion volumes ($\rho$=0.327 (p=0.019)) in PsA but not in PSO. No significant correlation for S100A9 was found.
**Conclusions:** S100A8 but not S100A9 level is significantly correlated to the extent of structural bone damage in patients with PsA. Hence, S100A8 may emerge as an interesting biomarker for determining the severity of psoriatic disease, especially the extent of structural bone damage.
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## AB0947 THE ROLE OF MUSCULOSKELETAL ULTRASOUND IN MANAGING SYSTEMIC LUPUS ERYTHEMATOSOUS AND SJOGREN'S SYNDROME IN A REAL LIFE CLINIC

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**Background:** Musculoskeletal Ultrasound Assessment (US) is increasingly used as a valid and reliable tool for guiding the management of inflammatory arthritides. However its use in Systemic Lupus Erythematosous (SLE) and Sjogren's Syndrome (SS) in clinical practice remains limited[1], thus potentially missing an opportunity to appreciate severity of joint involvement and optimise management[2].
**Objectives:** To analyse a real life cohort of SLE and SS patients referred for US assessment on clinical grounds, to review their characteristics and whether US assessment led to a change in treatment.
**Methods:** Retrospective analysis of real life data from a dedicated rheumatology US clinic at a tertiary referral hospital. The OMERACT scoring system was used for the US examination of 22 hand joints in every patient (wrists, metacarpophalangeal and proximal interphalangeal (PIP) joints bilaterally).
**Results:** Over a 2 year period (01/2014–12/2015) a total of 604 patients were scanned including 19 with SLE and 17 with SS. Patient characteristics and differences between their US outcomes are shown in table 1. US assessment prompted treatment change in 84% of SLE patients and 82% of SS cohort. ESR showed a better association with swollen joint count in SS (r=0.29) than SLE (r=0.17), however this did not reach statistical significance. A subanalysis of the SLE cohort showed poor correlation of the MSK BILAG items scores with active joint disease defined as PD presence on US (r=0.189, p=0.5).

Table 1. Patient characteristics and US features

| Patients characteristics and US features | | SJögren | SLE | Significance |
|---|---|---|---|---|
| Age at scan | | 56 | 47 | p=0.03** |
| Gender | Male/female | 0/17 | 0/19 | NS |
| Duration of symptoms (years) | | 12.5 | 14.6 | NS |
| ANAs | | 29.4% | 76.5% | p=0.006** |
| dsDNA | | 11.8% | 33.3% | NS |
| ENAs | | 70.6% | 70.6% | NS |
| ESR (mm/h) | | 22.47 | 29.29 | NS |
| CRP (mg/L) | | 3.7 | 3.5 | NS |
| Mean number of joints with power Doppler (PD) | | 0.18 | 2.06 | p=0.013** |
| Mean number of joint with synovial hypertrophy | (Grade 2) | 0.47 | 4.32 | p=0.002** |
| Mean number of joints with erosions | | 2.18 | 3.44 | NS |
| Mean number of joints with effusions | | 0.47 | 1.06 | NS |
| Mean number of joints with osteophytes | | 2.24 | 3.11 | NS |
| Swollen Joint Count | PD negative | 1.75 | 2.14 | NS |
| | PD positive | 1.41 | 4.29 | NS |
| PIP involvement | | 5.9% | 52.6% | p=0.02** |
| Tendon abnormalities | | 5,9% | 15,8% | NS |
| Treatment | HCQ | 47.1% | 68.4% | NS |
| | Prednisolone | 5.9% | 52.6% | p=0.003** |

NS = non-significant.

**Conclusions:** US assessment led to significant change in management for both cohorts. The SLE group had more active disease on US than SS, despite similar swollen joint count and increased prednisolone. There was poor correlation of US disease activity and MSK BILAG in SLE patients, suggesting that US can provide additional information in identifying active joint disease. US proves a useful and reliable tool to monitor musculoskeletal features and therapeutic outcomes in both SLE and SS patients that can be used routinely in real life clinical practice.
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## AB0948 SIGNAL PEPTIDE-CUB-EGF DOMAIN-CONTAINING PROTEIN (SCUBE); A NOVEL MARKER IN RELATION WITH ANJIOGENESIS IN RHEUMATOID ARTHRITIS?

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**Background:** Rheumatoid Arthritis (RA) is a multifactorial, systemic, progressive, inflammatory disease which is characterized with bone and cartilage destruction. Synovial angiogenesis is important at the etiopathology. Recently with the better understanding of RA pathogenesis, the target specific treatment approaches come up with better results.
**Objectives:** The purpose is to study levels of newly identified plasma signal peptide-CUP-EGF domain containing protein (SCUBE) 1and 3 in RA patients. Moreover, to determine whether there exists any correlation between these proteins, other angiogenesis parameters and disease activities
**Methods:** This study covers 106 patients diagnosed with RA associated with 2010 American Collage of Rheumatology (ACR) diagnosis criteria matched with healthy controllers who are equivalent of RA patients in terms of age and gender. All necessary data such as age, gender and body mass index of all participants were recorded. Detailed background information and examination of the patients are recorded and disease activity scores (DAS28) were figured out. The levels of SCUBE 1–3, Vascular Endotedial Growth Factor (VEGF), Matrix metaloproteinaz-9 (MM-9), Interlökin-6 (IL-6), CD40L are evaluated with the method of Enzyme-Linked Immuno-Sorbent Assay (ELISA) in both patients and control group
**Results:** This study covers 201 individuals 106 of whom were diagnosed with RA (82 women, 24 men) and 95 of them were healthy controllers (64 women, 31 men). Age, body mass index (BMI) and gender distribution of both groups were very similar to one another. Significant differences were observed between RA patients and healthy controller groups in terms of SCUBE 1 (respectively1.28±1.41ng/mL, 0.94±0.67ng/mL p=0.002) and CD40L MMP-9 levels ($p<0.001$, p=0.012). Any significant difference was not detected between disease activity and SCUBE 1–3 and other angiogenesis markers. Any significant correlation was not determined between disease activities, SCUBE 1–3 and other parameters.
**Conclusions:** Levels of SCUBE might be considered as a significant marker in the disease pathogenesis independent from other parameters in the RA diagnosed patients.
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## AB0949 ENTHESITIS IN RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS: AN ULTRASOUND STUDY

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**Background:** Enthesitis is a common clinical feature of spondyloarthritis (SpA) that could be evaluated by ultrasound (US). Some studies suggested that US assessment of enthesitis might be sensitive and specific of SpA diagnosis. However, others studies found similar prevalence of US enthesitis in rheumatoid arthtitis (RA) and SpA (1) or that US assessment of heels could not differentiate SpA to controls (2).
**Objectives:** We aimed to determine the prevalence of US enthesitis in SpA and RA patient.
**Methods:** In this transversal single center study, we included patient with RA (ACR/EULAR 2010 criteria) and SpA (ASAS criteria). All patients underwent clinical and ultrasonographic evaluation of both upper and lower limbs at seven sites (quadriceps tendon enthesis, proximal and distal patellar tendon enthesis, Achilles tendon enthesis, plantar aponeurosis enthesis, triceps tendon enthesis, lateral epicondyle enthesis). Two US scores were calculated for each patient using the Glasgow Ultrasound Enthesitis Scoring System (GUESS) and the Madrid Sonographic Enthesitis Index (MASEI). US assessment of tendon thickness and structure, bone erosion, bursitis, power Doppler, calcifications and enthesophytes was performed for all patients by a sonographer blinded to clinical data. Demographic and clinical characteristics were collected for each patient.
**Results:** A total of 30 RA (mean age: 45.3±15.4 years old, 17% of male patients, mean disease duration: 10.5±7.9 years) and 41 SpA (mean age: 55.7±14.8 years old, 68% of male patients, mean disease duration: 9.2±8.7 years) patients were analyzed. In SpA patients, 67% of them were HLAB27 positive. ACPA and rheumatoid factor were found in 93% and 83% of RA patients, respectively. Clinical examination found painful enthesis in 98 (17%) of 574 examined sites in SpA patients and in 59 (14%) of 420 sites in RA ($P$=0.2). SpA and RA patients had 2.4 and 1.96 painful enthesis sites per patients, respectively ($P$=0.81). The mean MASEI score was 8.5±7.3 in RA and 7.8±6.5 in SpA patients ($P$=0.87). A MASEI score $\geq$18 was found in 6 (20%) RA patients and in 4 (10%) of SpA patients ($P$=0.22). The mean GUESS score was 5.8±3.1 in RA and 6.3±3.9 in SpA patients ($P$=0.67). At least one enthesis abnormality was found by US in 264 (46%) of 574 sites in SpA patients and in 200 (48%) of 420 sites in RA ($P$=0.61).
**Conclusions:** Our results suggest that entheseal abnormalities are frequent in RA and SpA without difference in the population. We could hypothesize that the US assessed entheseal features have low specificity in inflammatory conditions affecting joints and enthesis as SpA and RA.
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## AB0950 LEUCINE-RICH ALPHA-2 GLYCOPROTEIN (LRG) AS A POSSIBLE URINARY MARKER FOR LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE). Its accurate evaluation is dependent on renal biopsy. A search for other non-invasive methods such as urinalysis is warranted. Recently, we identified a novel acute phase protein, LRG[1,2] whose expression is induced at the site of inflammation by various inflammatory cytokines.
**Objectives:** To investigate whether LRG can be a new urinary biomarker of LN.
**Methods:** We determined LRG levels in serum and urine of SLE patients (n=46, M:F=3:43, age: 37.1 (22–66)) with or without LN by ELISA. We divided SLE patients into four groups according to the results of renal biopsy (group 1: no LN [n =19], group 2: LN class 5 [n =3], group 3: LN class 1 or 2 [n =4], group 4: LN class 3 or 4 [n =20] (ISN/RPS)), and analyzed the relationship between urinary LRG levels and renal pathology. Also, we analyzed NZ B/W F1 mice, a lupus model, to study the mechanism of LRG expression in LN. Mouse urinary LRG levels were determined by western blot. Also, we evaluated the expression of LRG and several cytokines in kidney by real-time PCR, immunohistochemistry (IHC) and immunofluorescence (IF). In vitro, we investigated the expression and secretion of LRG in primary tubular epithelial cells (PTEC) obtained from NZ B/W F1.
**Results:** Urinary LRG levels were significantly higher in group 4 patients, and tend to be high in group 2 and 3 patients compared with group 1. In kidney of NZ B/W F1 mice with LN-like alteration, mRNA expression of LRG and IL-1 beta was significantly up-regulated, compared with NZ B/W F1 mice without LN-like alteration and B6 mice. By IHC and IF analysis, LRG protein was detected in renal tubular epithelia of NZ B/W F1 mice with nephritis. Additionally, macrophage infiltration and IL-1beta production was detectable around of the LRG-positive tubules in NZ B/W F1 mice. In vitro, LRG expression and secretion was induced by IL-1beta in PTEC of NZ B/W F1 mice.
**Conclusions:** Urinary LRG may be a useful biomarker which reflects the active inflammation of LN.
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## AB0951 ULTRASONOGRAPHIC DIFFERENTIATION BETWEEN PSA AND RA BASED ON FINGER FLEXOR TENDON PULLEY ENTHESEAL COMPLEX

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**Background:** Both RA and PsA are associated with hand involvement including synovitis and tenosynovitis. Differentiation between RA and PsA can sometimes be impossible using existing serological, genetic and imaging biomarkers.
At the micro anatomical level PsA is strongly linked to disease localisation to entheses and other sites of high mechanical stressing. Recently high resolution MRI has shown prominent abnormalities at the mini-entheses of the flexor tendon pulleys may be common (1).
**Objectives:** This study tested the hypothesis that that mini-entheses disease of the hand including the A1,3, and 5 pulleys and flexor tendon insertion could be used to differentiate between RA and PsA.
**Methods:** 46 cases of seropositive RA and 37 PsA patients were consecutively recruted. Cases were matched for disease duration, age and BMI with the majority being under therapy with conventional DMARDs (table1). Patients underwent completely rheumatological examination (AM, MC) and CRP and ESR determination. US examination was done with ESAOTE MyLabClass equiped with 18–6 linear probe. The 2nd to 4th dominant finger were scanned both on the dorsal and palmar surface. The sonograraphers (IT, PM) were blinded to the clinical details. The following changes were recorded as present (1) or absent (0): tendon flexor tenosynovitis, flexor pseudotensynovitis (peritendinous oedema), bone formation and the DIP flexor tendon insertion enthesophyte or calcifcations. A1, 3 and 5 pulley tendon thickness was measured at the level of maximal thickness in longitudinal or transverse way. The ecogenicity of the pulley was recorded as normal (if anecogen) or abnormal (no complete anecogenicity).
**Results:** Flexor tenosynovitis was evident in 25/108 digits in PsA versus 8/135 in RA ($p<0.001$). Peritendinous oedema was evident in 23/108 PsA digit compared to only 8/135 RA digit ($p<0.001$) despite the fact that the magnitude of tenosynovitis was the same in RA and PsA. The A1, A3 and A5 pulleys were *not* significantly thicker in PsA compared to RA. Flexor tendon enthesopathy as determined by intra tendinous new bone was evident in 78/108 PsA cases, 21/135 RA and 2/30 health control ($p<0.001$ for both comparisons.

Table 1

| | PsA (n=37) | RA (n=46) | HC (n=10) |
|---|---|---|---|
| Age, mean±SD years | 59.2±9.7 | 60.1±11.8 | 55.9±16.9 |
| Women, number (%) | 22 (60) | 33 (72) | 6 (60) |
| BMI, mean, kg/m$^2$ (SD) | 25.0±3.6 | 24.4±3.5 | 23.8±1.7 |
| DAS 28 CRP | 2.9±0.6 | 3.2±0.9 | nd |

**Conclusions:** This study suggests that PsA cases have a much higher burden of abnormalities in the min-entheses of the hand flexor tendons. With the improving resolution and capabilities of MKUS these findings may be relevant for defining the phenotype of joint swelling as RA (synovial centric) or SpA (entheseal like).
**References:**
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shows flexor tendon pulley and sheath-related enthesitis.Ann Rheum Dis. 2015 Jan;74(1):185–9.
**Disclosure of Interest:** None declared
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## AB0952 SERUM VISFATIN AND RESISTIN, BUT NOT ADIPONECTIN OR LEPTIN, ARE ASSOCIATED WITH ULTRASOUND SYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Adipocytokines are soluble mediators secreted by adipose tissue and immune cells with potent immune regulatory functions. Some adipocytokines have been previously associated with disease activity and radiographic progression in patients with rheumatoid arthritis (RA)[1].
**Objectives:** To investigate associations between adipocytokines, clinical and traditional laboratory markers as well as with ultrasound synovitis in patients with RA.
**Methods:** A total of 82 patients with RA (62 females, median disease duration 4.2 years) were enrolled into this study. All patients underwent clinical examination (swollen joint count - SJC, tender joint count – TJC, Disease activity score - DAS28-ESR and DAS28-CRP, Clinical disease activity index - CDAI, Simplified disease activity index - SDAI). Moreover, ultrasound examination of 7 selected joints mostly affected in RA (wrist, second and third metacarpophalangeal and proximal interphalangeal, and second and fifth metatarsophalangeal joints) was performed to measure synovial hypertrophy in Grey Scale (GS) and pathological neovascularization in Power Doppler (PD) using semi-quantitative grading 0–3[3]. Blood samples were taken at the same day as clinical and ultrasound assessments. Serum concentrations of adiponectin, resistin, visfatin, leptin and CRP were measured. Clinical and laboratory measures were correlated with ultrasound findings using Spearman's correlation coefficient.
**Results:** Serum visfatin and resistin levels were associated with the disease activity (Figure 1) and correlated significantly with DAS28-ESR ($r=0.473$, $p<0.001$; $r=0.363$, $p<0.001$, resp.), DAS28-CRP ($r=0.443$, $p<0.001$; $r=0.348$, $p<0.005$, resp.), SDAI ($r=0.431$, $p<0.001$; $r=0.344$, $p<0.005$, resp.), CDAI ($r=0.419$, $p<0.001$, $r=0.344$, $p<0.005$, resp.) and with CRP levels ($r=0.456$, $p<0.001$; $r=0.364$, $p<0.001$, resp.). Moreover, visfatin and resistin levels significantly correlated with GS ($r=0.430$, $p<0.001$, $r=0.273$, $p<0.05$, resp.) and PD synovitis scores ($r=0.309$, $p<0.01$, $r=0.283$, $p=0.01$, resp.). Neither leptin nor adiponectin correlated with parameters of disease activity in patients with RA.

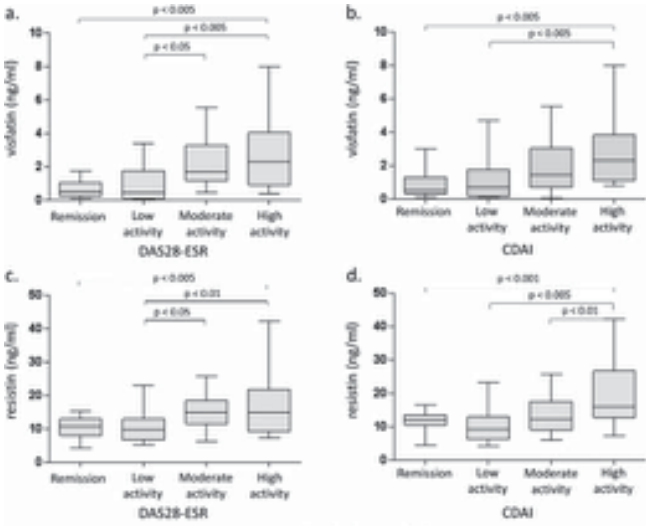


Figure 1. Box plots showing associations between visfatin (a,b), resistin (c,d) and DAS28-ESR and CDAI, respectively

**Conclusions:** Our study supports circulating visfatin and resistin as promising serum pro-inflammatory biomarkers reflecting clinical, laboratory as well as ultrasound parameters of synovial inflammation in RA.
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## AB0953 CONTRIBUTION OF ULTRASONOGRAPHY TO ASSESS DISEASE ACTIVITY IN PATIENTS WITH INFLAMMATORY MYOPATHIES

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**Background:** Inflammatory myopathies (IM) comprise a group of rare and heterogeneous diseases, challenging to diagnose, treat and follow-up. Monitoring patients with IM is difficult as there is a lack of precise measures for assessing disease activity. Ultrasonography (US) is a non-invasive, relatively inexpensive technique that is increasingly being used to evaluate muscular system.
**Objectives:** To assess the utility of US evaluation in the monitoring of patients with IM.
**Methods:** Patients diagnosed of IM from 2005 to 2015 followed up at a Rheumatology Department were included. Fourteen patients (11 female) with a mean age of 50.1±21.4 years and mean disease duration of 4.8±3.2 years were evaluated. The different diagnosis were as follows: 6 dermatomyositis (DM), 3 polymyositis (PM), 2 myositis associated with Systemic Lupus Erythematosus, 1 inclusion body myositis (IBM), 1 recurrent focal myositis (RFM) and 1 undifferentiated IM. Physical examination, including muscle strength tests, laboratorial tests (comprising levels of serum muscle enzymes) and a selective muscle US assessment were performed to each patient. For US evaluation a General Electric LOGIQ S8 equipment with a 6–15 MHz linear transducer was used. Muscles were subjectively evaluated for echogenicity (determined by gray-scale) and muscle morphology. Power Doppler (PD) was used to assess vascularity.
**Results:** Nine of the 14 patients evaluated were on clinical remission, with absence of symptoms or signs of disease, preserved muscle strength, normal muscle enzyme levels and conserved muscle pattern on US assessment. One female with DM presented with an acute exacerbation of disease, with proximal muscular weakness of the upper limb and US findings of increased muscle echogenicity of biceps revealing a muscle oedema pattern. The patient with IBM also experienced a flare which was associated with proximal muscle weakness and asthenia; US assessment showed focal oedema through right biceps muscle but also proximal lower limb muscle atrophy characterized by increased echogenicity with diminished volume of the quadriceps compartment and change of normal architecture of tibialis anterior muscle of both legs. These findings are consistent with a long term disease with acute flare. Another patient with longstanding PM in remission revealed no signs or symptoms of active disease, normal muscle strength but low creatine phosphokinase levels and symmetrical proximal muscle atrophy pattern in US evaluation. On the other hand, the patient with shorter duration of disease, recently diagnosed as myositis (undifferentiated IM), revealed proximal weakness and elevated serum muscle enzymes; in this case, US assessment showed diffuse increased echogenicity of proximal muscle compartment and increased PD signal. Finally, the patient with RFM presented with left arm swelling and weakness and US evaluation showed enlargement and diffuse increased echogenicity within the left carpal extensor compartment.
**Conclusions:** US findings in patients with IM seem to correlate well with disease activity suggested by clinical and laboratory data. As a result, US imaging may be a useful tool to assess disease activity and damage in these patients as well as to monitor disease progression.
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**Disclosure of Interest:** None declared
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## AB0954 A NEW ULTRASONOGRAPHY PROTOCOL FOR THE ASSESSMENT OF PRIMARY KNEE OSTEOARTHRITIS

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**Background:** There is a lack of adequate outcome measures of treatment response in Knee Osteoarthritis (KOA). The role of Ultrasonography (US) in the management of inflammatory articular and periarticular diseases is well established, but it has been less extensively used in OA.
**Objectives:** To develop a new high-resolution US protocol for the assessment of structural and inflammatory changes in primary KOA and to evaluate its inter-observer reliability.

**Methods:** A scanning protocol was developed by consensus among 3 senior Rheumatologists with similar high levels of experience in musculoskeletal US. The protocol includes both inflammatory elementary lesions (synovitis, power Doppler, Baker's cyst) and structural damage lesions (medial collateral ligament bulging, meniscal lesions and osteophytes) measured as dichotomous variables (present/absent). Cartilage thickness (in millimeters) is assessed at the notch and 10mm towards the lateral and medial condyles (mean value of 3 measurements). The OMERACT definitions for elementary lesions were used whenever available. In addition, global scores were calculated for joint inflammation (range: 0–3) and structural damage (range 0–11). Patients with primary KOA according to the American College of Rheumatology classification criteria underwent Knee US assessment in the same day by the 3 experts using the same device. For dichotomous parameters, Inter-observer agreement was estimated by the free-marginal multirater Kappa and the proportion of agreement (Agt). For continuous parameters two-way mixed effects models were used and absolute-agreement Intraclass Correlation Coefficients (ICC) was measured between individual ratings and global scores.
**Results:** In total, 7 patients were included (14 knees), corresponding to 42 US assessments by the 3 readers. Patients were 6 females and 1 male, with a mean age of 58.6 years. Concerning inflammatory lesions, agreement was good for synovitis $\kappa$=0.714; Agt=85.7%) and Baker cyst $\kappa$=0.714;Agt=85.7%). All power Doppler analysis were negative, thus achieving excellent agreement $\kappa$=1; Agt=100%). As a result, agreement was good for the inflammatory score (ICC: 0.774; 95% CI). Results were not as homogenous for structural damage lesions. In one hand, agreement was excellent for medial meniscus cyst $\kappa$=0.810; Agt=90.5%), good for lateral and medial femoral osteophytes [$\kappa$=0.619; Agt=80.9%) and $\kappa$=0.714; Agt=85.7%) respectively] and for lateral meniscus extrusion and cyst $\kappa$=0.619 and 0.619; Agt=81.0%). On the other hand, it was poor for lateral meniscus fracture $\kappa$=0.143; Agt=57.1%). For cartilage thickness, agreement was good for notch and medial condyle (ICC=0.652 and 0.619). Finally, the overall structural score agreement was moderate (ICC: 0.484).
**Conclusions:** The proposed protocol has shown to be reliable in patients with KOA, therefore a promising tool to be used both in clinical practice and for research purposes. Long-term reproducibility and responsiveness to change is needed to become a valid outcome measure, thus filling in an important gap in OA assessment.
**Disclosure of Interest:** None declared
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## AB0956 ATYPICAL PATTERNS OF ANTINUCLEAR ANTIBODIES IN COLOMBIAN GENERAL POPULATION

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**Background:** Since more common patterns of antinuclear antibodies (ANAs) such as homogeneous or nucleolar patterns are well recognized, the prevalence of uncommon or atypical pattern is not well described
**Objectives:** Our aim was to describe the prevalence of atypical ANAs patterns in a big cohort of ANA measurements in general Colombian population.
**Methods:** We included all ANAS determinations done during 2 consecutive years (2013 and 2014) from Dinamica IPS in 8 different cities in Colombia. We defined such as uncommon patters the following: anti MSA-2 (mitotic spindle apparatus), cytoplasmatic fibers, lysosomal, Golgi, multiple dots, NuMA1 (MSA-1), anti MSA-3, PCNA, centrosome and nuclear envelope. All patient sera submitted for ANAs testing were tested by conventional indirect immunofluorescence using Hep-2 cells (AESKU.DIAGNOSTICS, Wendelsheim, Germany). We use 3 images for sample and in some cases several dilutions were needed. Parametric test were used for comparison among groups.
**Results:** The overall sample included 113,491 consecutive samples for ANAs, being positive in 62,501 (55%) cases. 912 (1.45%) samples in 838 patients were classified as atypical pattern. Mean age for atypical positive pattern patients was 47±16.8 years and 80% of patients were female. The most common atypical patterns are summarized in Table. We did not find any difference among sex according atypical patterns. In subgroup analysis, centrosome pattern was more common in younger patients ($<$18 years) than in older than 18 years (27.84% vs 11.5%; Chi2, p=0.001), anti MSA-2 pattern was significantly more common in patients $>$18 years than in $\leq$18 years (23.6% vs 11.3%; Chi2, p=0.038), and cytoplasmic fibers was more prevalent in patients older than 55 years (14.7 vs 9%, p=0.013).

Table 1. More common atypical ANA patterns in Colombian population

| | N=843 | % |
|---|---|---|
| NuMA | 294 | 35.0 |
| Midbody (MSA-2) | 190 | 22.5 |
| Centriosome | 106 | 12.5 |
| Cytoplasmatic fibers | 93 | 11.0 |
| Multiple dots | 82 | 9.7 |
| Lysosomal | 28 | 3.3 |
| Golgi | 21 | 2.5 |
| PCNA | 19 | 2.3 |
| MSA-3 | 8 | 1.0 |
| Nuclear envelope | 2 | 0.2 |

**Conclusions:** In this large cohort of almost 130.000 samples of ANAs from a Colombian general population, the prevalence of atypical ANAs was around 1.5%. That prevalence is in concordance with some other series (1). Anti NuMa and MSA-2 patterns were the most common atypical ANAS. Anti centrosome were more common in young people, anti MSA in middle age patients and anti cytoplasmic fibers in elderly population.
**References:**
[1] Vermeersch P et al. Autoimmunity Rev 2013;12:998–1003
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3763

## AB0957 ULTRASOUND MEASURES OF SYNOVITIS ARE INDEPENDENT OF CLINICAL PARAMETERS IN THE SETTING OF RHEUMATOID ARTHRITIS REMISSION: A CROSS-SECTIONAL ANALYSIS

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**Background:** Musculoskeletal ultrasound (MSUS) is a useful tool for the diagnosis of rheumatoid arthritis (RA), and can be used to help guide treatment escalation in patients with active disease. At the opposite end of the spectrum however, the relationship between clinical and ultrasound measures of remission remains poorly understood.
**Objectives:** To define the relationships between clinical and ultrasound parameters in the setting of RA low disease activity and remission.
**Methods:** Patients with a clinical diagnosis of established RA were recruited as part of an ongoing study of RA clinical remission. Patients who were taking biological therapies or who had received corticosteroids within the past 3 months were excluded. At the baseline visit, a 7-joint ultrasound scan (US-7 scan) was performed blinded to the clinical disease activity assessment. All scans were performed by the same trained operator (KB) using the same ultrasound machine. Greyscale (GS) and power Doppler (PD) synovitis was scored on a 4-point semi-quantitative scale (0–3); erosions were scored as either present (1) or absent (0). MSUS images were then re-scored in a blinded fashion by KB and BT, with intra- and inter-observer reliability assessed by Cohen's Kappa statistic with linear weighting. Multivariate ordinal logistic regression was used to analyse the significance of relationships between total GS, PD and erosion scores with age, sex, disease duration, seropositivity for rheumatoid factor (RhF) and/or anti-citrullinated peptide antibody (ACPA), smoking history, and clinical remission as defined by the 2011 ACR/EULAR Boolean criteria.
**Results:** 29 patients were assessed in this preliminary cross-sectional analysis (19 [66%] female, 22 [76%] RhF and 20 [69%] ACPA positive) of median (IQR) age 67 (53–72) years and 6 (4–13) years following RA diagnosis. Methotrexate, sulfasalazine and hydroxychloroquine were prescribed to 25 (86%), 8 (28%) and 5 (17%) patients respectively. The median (IQR) DAS28-CRP score was 1.18 (0.97–1.81) and 16 (55%) patients satisfied ACR/EULAR remission. Median (range) total GS, PD and erosion MSUS scores were 5 (1–10), 0 (0–2) and 0 (0–8) respectively. Intra- and inter-observer MSUS score agreement ranged from good to excellent; intra/inter $\kappa$: GS 0.72/0.43, PD 0.92/0.83, erosions 0.70/0.65. In multivariate analyses, disease duration ($p<0.001$) and male sex (p=0.038) were independent predictors of a higher total erosion score only. Patients who were seropositive for either RhF and/or ACPA tended to have higher GS and PD scores though this was not statistically significant (p=0.053 and p=0.063 respectively).
**Conclusions:** Joint erosions were more frequently seen in male patients with a longer duration of disease, the latter in keeping with increased cumulative inflammatory joint damage. Substantial levels of synovitis, particularly GS, were visualised by MSUS despite low clinical measures of disease activity. Whether such ultrasound findings provide added value in predicting subsequent disease course following the withdrawal of DMARD therapy is an important focus of our ongoing prospective study.
**References:**
[1] Backhaus et al. (2009) Arthritis Rheum; 61: 1194–201.
**Disclosure of Interest:** None declared
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## AB0958 SERONEGATIVE EARLY ARTHRITIS. MAY POWER DOPPLER ULTRASONOGRAPHY PREDICT PROGRESSION TO RHEUMATOID ARTHRITIS?

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**Background:** The presence of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) are classic risk factors used for the diagnosis and classification of rheumatoid arthritis (RA) patients. Seropositive patients are at higher risk of developing RA, although in early arthritis RF/ACPA may be within the range of normality.
**Objectives:** To assess if the presence of basal Power Doppler (PD) signal in patients with negative baseline status for RF and ACPA may predict the risk of final diagnosis of RA according ACR criteria 1987, at 12 months of follow up.

**Methods:** We included 48 patients remited to an early arthritis consulting with at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes with <12 months of duration of the symptoms and negative for RF and ACPA, not previously treated with esteroides or DMARDs, without previous diagnose of RA or other inflammatory chronic articular disease. The presence of ultrasonographic Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, knees) and 44 joints (28 joints and in addition hips, tarsus, ankles and MTPs), was studied with an ultrasound equipment GE L5 by an expert rheumatologist. Presence of basal CRP and ESR and basal erosions (score ≥2 in at least one joint by modified Sharp method) for each patient were registered (only 44 patients with complete radiology sets available) by and independent trained radiologist. The patients who met criteria for RA according 1987 ACR during first 12 months of follow-up and did not have any exclusion criteria were classified as definite rheumatoid arhtritis. Statistical study: Chi-square, Fisher exact test, p univariant, Odds Ratio and Post-Test Probability calculation.
**Results:** The presence of basal power doppler signal in ≥1 joints of 44 (PD44) at baseline shows statistically significant association with the RA diagnosis at 12 months by ACR 1987 classification criteria, with p=0.002, OR=19,46 (2,25–168,27) but the presence of at least one joint with power doppler signal of 28 joints (PD28) did not (p=0.111). Presence of basal radiographic erosions (RXERb) were associated to RA with p<0.0005 and OR 12,04 (2,87–50,45) as well as high CRP p=0.019, OR 4,20 (1,23–14,36). Elevated ESR was not associated to RA diagnosis. The presence of PD44 and RXERb together is greater in patients with final diagnose of RA, p<0.0005 OR 45,71 (5,08–410,92). The combined presence of PD28 and RXERb is also associated to RA diagnose p<0.0005, OR 31,11 (3,53–274,11). Post-test probability of RA (considering a given pretest probability of 10% for seronegative patients obtained in our study) was 61% (19,1–91,8) for PD44+RXERb, 58% (16,9–90,8) for PD28+RXERb and 30% (15–51.8%) for RXERb.

| Basal variables n=48 | | AR (ACR 1987) YES | p (univariant) | OR | 95% CI |
|---|---|---|---|---|---|
| PD28 | yes | 20/34 (58,8%) | NS | - | - |
| | NO | 4/14 (28,6%) | 0,111 | | |
| PD44 | yes | 23/36 (63,9%) | 0,002 | 19,46 | (2,25-168,27) |
| | NO | 1/12 (8,3%) | | | |
| PD28+EROS BASAL n=44 | yes | 14/15 (94,1%) | < 0,0005 | 31,11 | (3,53-274,11) |
| | NO | 9/29 (31%) | | | |
| PD44+EROS BASAL n=44 | yes | 16/17 (94,1%) | <0,0005 | 45,71 | (5,08-410,92) |
| | NO | 7/27 (25,9%) | | | |
| EROSION BASAL n=44 | yes | 17/21 (81 %) | <0,0005 | 12,04 | (2,87-50,45) |
| | NO | 6/23 (26,1%) | | | |
| CRP | yes | 18/28(64,3%) | 0,019 | 4,20 | (1,23-14,36) |
| | NO | 6/20(30%) | | | |

**Conclusions:** The presence of at least one joint with power doppler signal on 44 joints (PD44) at baseline may help to predict progression to RA at 12 months according to ACR 1987 criteria in seronegative patients. Combined presence of PD44 or PD28 associated to basal radiographic erosions was able to select seronegative patients with higher risk of progression to RA at 12 months according to ACR 1987 criteria.
**Disclosure of Interest:** None declared
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## AB0959 THE AUTOMATED SOFTWARE-GUIDED ULTRASOUND ASSESSMENT OF BILATERAL COMMON CAROTIDS INTIMA-MEDIA THICKNESS FOR INVESTIGATION OF CARDIOVASCULAR RISK: COMPARISON BETWEEN PSORIATIC AND RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Recent studies have shown the relationship between psoriatic and rheumatoid arthritis and subclinical atherosclerosis. Currently, a new automated ultrasound software, based on radio frequency, called RF-QIMT technology, proved to be a useful method for assessing subclinical atherosclerosis with the measurement of the intima-media thickness (IMT) in carotid arteries.
**Objectives:** To compare the carotid IMT in patients with ordinary psoriatic arthritis (PsA) and rheumatoid arthritis (RA) through the RF-QIMT.
**Methods:** Total of 28 patients with APs (n=14) and RA (n=14) were enrolled in this case-control study. Patients with diabetes mellittus, dyslipidemia and previous cardiovascular events excluded. We evaluated the body mass index (BMI) and disease activity, including DAS28 score. The patients underwent a US assessment of the IMT of the posterior wall of common carotids using a My Lab 60 (Esaote SpA, Genoa, Italy) equipped with a 4–13 MHz linear probe adopting an automatic software-guided technique (named RF-QIMT technology).
**Results:** Mean age was 42.5. ±7.7 years and 46,6± 11.6 years in patients with APs and RA with no statistical difference between the groups (p>0.05). The mean disease duration was 14.1±9,5 and 6.17±4.4 years (p<0.05) in patients with APs and RA, respectively, with a predominance of men in those with APs (50% vs. 0%) (p<0.05). In addition, there was no statistical difference (p>0.05) between the groups regarding BMI (26.3±5.7 vs. 26.6±4.5 kg/m$^2$) and DAS28 score (3.93±0.7 vs. 2.8±0.63). There was no statistical difference (p>0.05) in relation to the average values of IMT (0.744± 0.244 in APs vs. 0.626 mm ±0.113mm in RA), the standard deviation (SD) of the six average values indicated by the system, were ranging from 12,7μm to 21μm, respectively. In addition, it was found that 64.3% of the patients with APs and 78.6% of those AR had higher IMT measurement than expected (p>0.05). There was no statistically significant correlation between IMT and the DAS28 score. However, there was a moderate statistically significant correlation (r =0.51; p<0.05) between the higher IMT measurement than expected and the DAS28 score.
**Conclusions:** The results show that patients with APs and AR have high rates of subclinical atherosclerosis, which can be measured by the new adopting an automatic software (called RF-QIMT) of evaluating the IMT, moreover there was correlation and validation with disease activty score.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3782

## AB0960 RELIABILITY OF ULTRASOUND TO DETECT GOUT ELEMENTARY LESIONS

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**Background:** The double contour (DC) seen by ultrasonography (US) was recently included in the classification criteria of gout, but this injury and other ones like tophi, hyperechoic aggregates Intra -articular and/or intra-tendinous, and bone erosions have not been validated.
**Objectives:** To evaluate the reliability of US to detect gout elementary lesions
**Methods:** Nine patients with Gout were included; diagnosis established by demonstration of monosodium urate crystals; patients were evaluated by 5 ultrasonographers in 2 rounds to detect tophi, hyperechoic aggregates, DC and bone erosions according to OMERACT definitions (1) in knee joint recesses and 1st metatarsophalangeal (MTP) joint, quadriceps, patellar and Achilles tendons bilaterally. Cohen's Kappa was used to establish Intra and inter-observer variability; the Kappa values were assigned as follows: poor (below 0.2), just (0.21 to 0.40), moderate (0.41 to 0.60), good (0.61 to 0.80) and excellent (0.81 to 1).
**Results:** Patients were 48+10 years old and 10+6 years of disease evolution. The inter-observer Kappa was good for DC in the knee and 1st MTP joint (0.87, 95% CI 0577–1170, p=0.000), good for hyperechoic aggregates in parapatellar recess, quadriceps and patellar tendon (distal insertion) and 1st MTP joint (0.71, -1064 to 2834, 95%, p=0.0001), moderate to proximal insertion of patellar tendon (0.46, 95% CI NA-NA, p=0.168), excellent for tophi in all tendons and in 1st MTP joint (0.82, 95% CI 0366–1270, p=0.000) and the same for erosion in 1st MTP joint (0.83, 95% CI 0349–1000, p=.0003). The intra-observer reliability was good (K=0.80; 95% CI 0758–0852, p=0.0000)
**Conclusions:** The US is reliable for detecting gout elementary lesions in the knee and the 1st MTP joint.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1726

## AB0961 COMPARISON BETWEEN ULTRASOUND B-FLOW, COLOUR DOPPLER AND MAGNETIC RESONANCE IMAGING FOR ASSESSMENT OF TENOSYNOVITIS IN THE HAND OF RHEUMATOID ARTHRITIS PATIENTS - A PILOT STUDY

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**Background:** Ultrasound (US) B-flow imaging (BFI) is a new technique for vascular imaging, based on US grey scale physics [1]. Therefore, Doppler artefacts such as aliasing, blooming and reverberations are not seen. Whether it is an alternative to Doppler for depicting inflammatory flow in the tendon sheath in rheumatoid arthritis patients (RA) is unknown.

**Objectives:** To evaluate US BFI for assessment of inflammatory activity in the tendon sheath compared to grey scale (GS), colour Doppler (CD) US and magnetic resonance imaging (MRI).
**Methods:** Ten RA patients with US-verified tenosynovitis were included. GS, CD and BFI assessment were performed using a GE Logiq E9 US unit with a high frequency linear 6–15 ML probe. BFI settings were adjusted to maximum sensitivity of 50, frequency at 12 MHz and dynamic range at 66. GS frequency was 15 MHz and CD settings according to published recommendations (ref). All settings were identical in all examinations. Axial T1-weighted pre- and post-contrast fat-saturated MR image sets (0.8mm slice thickness) were obtained using a Philips 1T MRI scanner (figure 1). One tendon sheath per patient was scored, in either the wrist or at the metacarpophalangeal joint level. CD, GS and MR images were scored for tenosynovitis 0–3 as proposed by the OMERACT US group and the OMERACT MRI in arthritis working group. BFI was scored peritendiniously as: 0: No flow, 1: Focal flow, 2: Multifocal flow, 3: Diffuse flow. Descriptive statistics were used for comparison of BFI, GS, CD and MRI scores.
**Results:** The mean (SD) score for the patients were 0.89 (0.74), 2.10 (0.74), 2.20 (0.92) and 2.30 (0.95) for BFI, GS, CD, and MRI, respectively. The difference between CD vs GS and MRI was never larger than ±1. The difference between CD and BFI was 1 in 5 patients and ≥2 in 3 patients (table 1).

Table 1. Baseline scores (0–3) and Δ scores with CD as reference, for BFI imaging, CD, GS and MRI

| Patient No. | Tendon sheath | BFI | GS | CD | MRI | ΔCD; BFI | ΔCD; GS | ΔCD; MRI |
|---|---|---|---|---|---|---|---|---|
| 1 | Extensor carpi ulnaris | 1 | 3 | 3 | 3 | 2 | 0 | 0 |
| 2 | Flexor carpi radialis | 1 | 2 | 2 | 3 | 1 | 0 | –1 |
| 3 | Flexor tendon of the 4th digit | 2 | 2 | 3 | 3 | 1 | 1 | 0 |
| 4 | Flexor tendons of the 5th digit | 0 | 2 | 3 | 3 | 3 | 1 | 0 |
| 5 | Flexor tendon of the 2nd digit | 1 | 2 | 2 | 1 | 1 | 0 | 1 |
| 6 | Extensor carpi ulnaris | 2 | 3 | 3 | 3 | 1 | 0 | 0 |
| 7 | Extensor carpi ulnaris | 0 | 1 | 0 | 1 | 0 | –1 | –1 |
| 8 | Extensor carpis radialis brevis/longus | 0 | 1 | 2 | 2 | 2 | 1 | 0 |
| 9 | Extensor pollicis longus | 1 | 2 | 2 | 1 | 1 | 0 | 1 |
| 10 | Extensor digitorum communis/ indicis proprius | 1 | 3 | 2 | 3 | 1 | –1 | –1 |

Note: Number (n), B-flow imaging (BFI), grey scale (GS), colour Doppler (CD), magnetic resonance imaging (MRI).

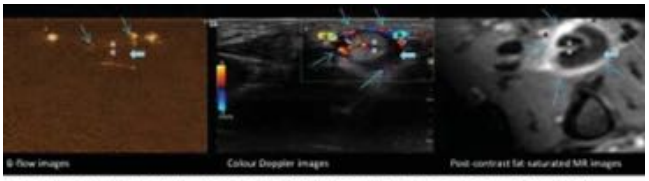



**Figure 1.** Tenosynovitis at the *flexor tendons (**) of the 4th finger* in 3 imaging modalities; BFI, CD and MRI, respectively. The pathological flow/enhancement is marked with thin *arrows and a peritendinous effusion is marked with a thick arrow. Interdigital arteries are marked with one (*) asterisk.*

**Conclusions:** BFI is a new imaging modality for visualization of perfusion. However, the presented results indicate that BFI is less sensitive to detect inflammation in the tendon sheath than CD, GS and MRI in RA patients. Further studies are required, in order to increase image optimization and flow sensitivity, but also to evaluate further use of BFI in diagnosis of inflammatory conditions.
**References:**
[1] Weskott HP. [B-flow–a new method for detecting blood flow]. Ultraschall in der Medizin (Stuttgart, Germany: 1980) 2000;21(2):59–65.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2335

## AB0962 VALIDITY AND SENSITIVITY TO CHANGE OF THE SEMI-QUANTITATIVE OMERACT ULTRASOUND SCORING SYSTEM FOR TENOSYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRIT

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**Background:** Tenosynovitis is frequent in rheumatoid arthritis (RA) patients. In 2012 the Outcome Measures in Rheumatology (OMERACT) US group proposed a new tenosynovitis scoring system with a good inter-observer reliability. However, its interreader agreement longitudinally and the sensitivity to change during treatment have not been tested.
**Objectives:** In a 6-months follow-up study of RA patients with US tenosynovitis, initiating treatment intensification with synthetic and/or biological disease-modifying anti-rheumatic drug (DMARD), to validate the semi-quantitative OMERACT US-scoring system of tenosynovitis by testing its interreader reliability, sensitivity to change, and comparison to clinical evaluation.
**Methods:** US (by grey-scale (GS) and color Doppler (CD)) and clinical assessment of the flexor and extensor tendon sheaths of the clinically most affected hand and foot was performed at baseline and after 3 and 6 months. Tenosynovitis was assessed using the semi-quantitative scoring system (0–3) proposed by the OMERACT US group for GS and CD calculating a sum score (0–39 for the hand and 0–21 for the foot) for each patient. In 20 patients, US was done independently by 2 physicians at baseline and 6 months, to assess the inter-observer agreement. A GE Logiq E9 with a linear 6–15 ML probe was used. CD frequency was 7.5 MHz, a pulse repetition frequency =0.4 and gain just below the noise limit. The same Doppler settings were used for all examinations. A binary score for clinical tendon involvement (0–1) was also performed at the same locations as the US score, with reference to published recommendations (3), calculating a sum score (0–13 for the hand and 0–7 for the foot)
**Results:** Fifty-one RA patients, planned for treatment intensification, were included: 43 women (age: mean 55.6; standard deviation (SD) 13.1) and 8 men (mean 49.1; SD 9.34). Thirty-four patients were anti-rheumatoid factor positive and 30 had early RA (duration <1 year). The interreader agreement, as assessed by the intra-class correlation coefficient (ICC) was very good at baseline and for change for GS sum scores (ICC Baseline=0.89; Change=0.89) and CD (ICC Baseline=0.95; Change=0.90) tenosynovitis. The smallest detectable change for change in scores was 0.97 for GS and 0.93 for CD. Tenosynovitis scores had decreased significantly at months 3 and 6 (Table 1 and figure 2). The sensitivity to change, as expressed by the standardized response mean from month 0–6, was high for GS and CD tenosynovitis (0.90 and 0.76, respectively), and moderate (0.59) for the clinical score (Table 1).

**Table 1** Changes in ultrasound and clinical evaluation sum score over 6 month and standardized response mean (SRM) for each score

| | | Baseline | 3 months | 6 months | Δ 0-3 months | Δ 1-6 months | Δ 0-6 months | SRM 0-3 months | SRM 3-6 months | SRM 0-6 months |
|---|---|---|---|---|---|---|---|---|---|---|
| Grey scale | Mean (Std Dev) | 3.5 (2.6) | 2.1 (1.6) | 1.4 (1.4) | -1.4 (2.2) | -0.7 (1.3) | -2.1 (2.4) | 0.6 | 0.5 | 0.9 |
| | Median (25;75 pctl) | 3.0 (2;4) | 2.0 (1;3) | 1.0 (0;2) | 1.0 (-2;0) | 0.0 (-1;0) | -2.0 (-3;-1) | | | |
| | p | | | | P<0.0001 | P=0.0001 | P<0.0001 | | | |
| Colour Doppler | Mean (Std Dev) | 3.4 (3.5) | 1.4 (1.9) | 0.8 (1.7) | -2.0 (3.3) | -0.6 (1.7) | -2.8 (3.4) | 0.6 | 0.3 | 0.8 |
| | Median (25;75 pctl) | 3.0 (1;4) | 1.0 (0;2) | 0.0 (0;1) | -1.0 (-3;0) | 0.0 (-1;0) | -2.0 (-3;0) | | | |
| | p | | | | P<0.0001 | P=0.0211 | P<0.0001 | | | |
| Clinical | Mean (Std Dev) | 2.4 (1.8) | 1.8 (1.6) | 0.9 (1.4) | -0.6 (1.8) | -0.6 (1.6) | -1.4 (2.4) | 0.4 | 0.3 | 0.6 |
| | Median (25;75 pctl) | 2.0 (1;3) | 1.0 (0;3) | 0.0 (0;1) | 0.0 (-2;0) | 0.0 (-1;0) | -1.0 (-3;0) | | | |
| | p | | | | P=0.0043 | P=0.0181 | P<0.0001 | | | |

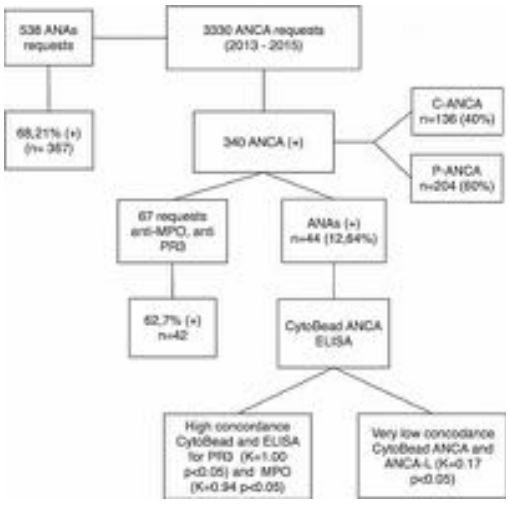
Note - P = Wilcoxon Pratt tests

**Conclusions:** The present study demonstrated an excellent interreader agreement for the OMERACT US scoring system for tenosynovitis and a high ability to detect changes over time. The high reproducibility and responsiveness of both GS and CD scores indicate that the OMERACT US scoring system is useful for diagnosing and monitoring of tenosynovitis in RA clinical trials and practice
**Disclosure of Interest:** None declared
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## AB0963 INTEFERENCE OF ANAS IN ANCA ANALYSIS AND COMPARISON TO CLINICAL OUTCOME OF VASCULITIS

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**Background:** Anti-neutrophil cytoplasmic antibodies (ANCAs) are directed against the primary granules of neutrophils and monocytes and are essential in the diagnosis of vasculitis pauciimmune. The positivity of anti nuclear antibodies (ANAs) interferes with the interpretation of ANCAs leading to false positives.
**Objectives:** Evaluate the interference of ANAs in the interpretation of ANCAs in a population with manifestations of autoimmune disease
**Methods:** 3330 patient data involving ANCA requests between 2013 and 2015 were analyzed. Indirect immunofluorescence (IIF) was used to determine whether the samples had interference with ANAs through the L-ANCA system



(Inmmunoconcepts®). Results were evaluated by the Generic assay kit ELISA® and CytoBead® ANCA (Generic Assays) to confirm positivity to MPO and/or PR3.The technical performance was evaluated by correlation analysis with Kappa values for data in which ANCAs was assessed at least by two techniques. Subsequently positivity of ANCAs was determined in a small sample of patients with clinical manifestations of autoimmune disease

**Results:** Positive ANCAS were found in 10.21% (340/3330) of the data, 40% (136/340) were C-ANCA and 60% (204/340) P-ANCA. Only 67 requests included specific anti-MPO and anti-PR3 assays, and 62.7% of these (42/67) were positive for ANCAs. ANAs were requested in 538 data resulting positive in 68.21% (367), predominantly homogeneous pattern. 12,64% of ANCAs positive data were also positive for ANAs, with P-ANCA in 83.72% of cases. The technique comparison included 44 samples positive for ANCAs evaluated by L-ANCA, CytoBead ANCA and ELISA. The correlation analysis showed high concordance between *CytoBead* and ELISA for PR3 (K=1.00 $p<0.05$) and MPO (K=0.94 $p<0.05$). However, in the evaluation between *CytoBead* ANCA and ANCA-L, a very low concordance (K=0.17 $p<0.05$) was observed

**Conclusions:** The results suggest there is interference of ANAs in the positive P-ANCA results. IIF is an excellent technique for screening the presence of ANCAs while other methods such as anti-PR3 and anti- MPO by ELISA or microparticles assays are required for confirmation

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.5195

## AB0964 SYNOVIAL INFLAMMATION ANALYSED BY 3 TESLA MAGNETIC RESONANCE IMAGING IN ETANERCEPT-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS INDICATES PERSISTENT DISEASE ACTIVITY DESPITE OF CLINICAL REMISSION

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**Background:** Treatment efficacy of conventional disease-modifying anti-rheumatic drugs (DMARDs) is insufficient in some patients with rheumatoid arthritis (RA). These patients require TNF-a antagonists that demonstrate excellent remission rates confirmed by clinical scores and conventional radiographs. Magnetic resonance imaging (MRI) is a more detailed diagnostic tool and furthermore, the 3 Tesla technique provides a higher spatial resolution compared to 1.5 Tesla. Especially early and thus prognostically relevant subchondral bone lesions might be detected more precisely using 3 Tesla MRI.[1]

**Objectives:** The aim of this study was to evaluate a reduction of joint inflammation in RA patients treated with DMARDs as compared to etanercept (ETA) over a period of 12 months.

**Methods:** This epidemiologic clinical pilot MRI study examined 10 ACR/EULAR-positive RA patients with inadequate response to two DMARDs with an indication for ETA using the RA MRI system (RAMRIS). The control group consisted of 10 patients adequately responding to DMARDs. 3 Tesla MRI (PDSPAIR; T1 with and without contrast agent) using a multi-channel hand coil was performed at baseline, four (only ETA) and 12 months following initiation of ETA. RAMRIS scoring included analysis of synovitis, effusion, subchondral erosion, and also bone marrow edema. Additional analysis consisted of the visual analogue scale (VAS) and the Disease Activity Score 28-joint count (DAS28) at baseline and after 12 months in DMARD patients and at baseline, four and 12 months in ETA-patients.

**Results:** In DMARD-patients, the VAS averaged 21.0±11.3 and 20.2±24.6 (p=0.9). In ETA-patients, the VAS decreased from 46.3±7.9 (baseline) to 23.9±7.1 (p=0.04) and 24.0±6.3 (p=0.04). In DMARD-patients, the DAS28 remained at 2.1±0.6 and 2.9±1.0 (p=0.06). In ETA-patients, however, it decreased from 3.8±0.4 (baseline) to 2.8±0.3 (p=0.08) and then significantly to 2.5±0.3 (p=0.01). In DMARD-patients, the RAMRIS did not change between baseline and 12 months (11.0±2.3 vs. 11.8±2.8, respectively, p=0.8). Similarly, in ETA-patients, the RAMRIS did not change significantly (28.9±5.0 vs. 25.8±4.7, p=0.7 and 24.6±4.5, p=0.5). In contrast, the RAMRIS was significantly higher at baseline in ETA-patients as compared to DMARD-patients (28.9±5.0 vs. 11.0±2.3 p=0.005) and after 12 months (24.6±4.5 vs. 11.8±2.8, p=0.03). Separate analysis of synovitis, erosion and bone marrow edema did not change after 12 months.

**Conclusions:** The data show a significant higher RAMRIS and thus more actively diseased patients prior to ETA treatment as compared to DMARD-patients at baseline and after 12 months despite of adequate DAS28 remission ($<2.6$). Persistence of 3 Tesla MRI synovial inflammation and DAS28 remission are thus separate entities. MRI scoring before starting a treatment may indicate the requirement for anti-TNF-a agents.

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## AB0966 COLOUR DOPPLER ULTRASONOGRAPHY IS SPECIFIC BUT NOT SENSITIVE IN DIAGNOSIS OF CARPAL TUNNEL SYNDROME

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**Background:** Carpal tunnel syndrome (CTS) is the most common form of peripheral entrapment neuropathies. Ultrasonography (US) has been used to diagnose CTS with a good sensitivity and specificity.There is no consensus about the role of colour Doppler US in diagnosis of CTS (1).

**Objectives:** To assess the diagnostic role of color Doppler ultrasonography in idiopathic CTS.

**Methods:** This study included 2 groups. The first group included 35females middle aged (32.1±4.8) patients with idiopathic CTS. The second group included 35 healthy middle aged (40.1±7.6) females. The diagnosis of CTS was done clinically and by nerve conduction studies.Ultrasonography of the median nerve was performed to find colour Doppler signals, wrist cross sectional area, forearm cross sectional area, flattening ratio, flexor retinaculum bowing and pronator quadratus ratio by use of high frequency (5–12MHz) linear probe diagnostic ultrasound.

**Results:** There was a statistical highly significant difference between control group and patients with CTS regarding colour Doppler signal (p=0.00).the specificity of CDUS in diagnosis of CTS was excellent (100%) but its sensitivity was poor (22.9%) with an accuracy of 61.4%. As regards the other US parameters, flattening ratio was the most accurate method (86.4%) with a senstivity (88.7%) and a specificity of (83.3%).There was a statistical highly significant positive correlation between nerve conduction study grading and Color Doppler ultrasonography (p=0.005).

**Conclusions:** CDUS is a highly specific test in evaluation of idiopathic CTS. It represents a useful confirmatory tool in diagnosis. Flattening ratio is the most accurate grey scale US parameter and highly correlated with CT severity.

**References:**

[1] Akcar N, et al. (2010).Korean Journal of Radiology; 11 (6): 632–639.

**Disclosure of Interest:** None declared

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## AB0967 ULTRASONOGRAPHIC FEATURES OF NEUROPATHIC (CHARCOT) ARTHROPATHY OF ANKLE JOINT

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**Background:** neuropathic osteoarthropathy (Charcot arthropathy) is a progressive condition that is characterized by joint dislocations, pathologic fractures, and debilitating deformities. It occurs most commonly in the lower extremity, at the foot and ankle. Although magnetic resonance imaging (MRI) is the modality of choice to examine patients with suspected neuropathic osteoarthropathy, for its ability to depict bone and soft tissues changes, ultrasonography (US) may be able to identify pathological changes in cases of Charcot arthropathy.

Up to the best of our knowledge this the first study of ultrasonographic feature of neuropathic ankle joint.

**Objectives:** Our aim was to characterize the ultrasonographic features of patients with neuropathic (Charcot) arthropathy of ankle joint.

**Methods:** In this retrospective study, all 26 patients between January 2013 and December 2015 with neuropathic (Charcot) arthropathy of ankle joint proved by X ray and/or MRI were enrolled. We collected and analyzed 26 patients, on whom high-resolution (5–15 MHz) muculoskeletal US of ankle and small joints of the affected feet had been carried out.

**Results:** Ages of our patients ranged from 38 to 67years (57.3± 6.4). Most of our patients (25 patients) 96.2% had diabetes mellitus and all of our patients had peripheral neuropathy. According to the modified Eichenholtz classification system; 3 patients (11.5%) were in grade 0, 11 patients (42.3%) were in grade 1, 10 patients (38.5%) were in grade 2, and 2 patients (7.7%) were in grade 3.

Ultrasonographic findings were: Effusion/synovitis of ankle joints (100%), High Doppler activity (grade 2 or 3) in ankle joint was present in 92.3% of our patients, bone irregularities in distal fibula 73.1%, bone irregularities in distal tibia were found in 34.6%, tendonitis of tibialis posterior 65.4%, proneal tendonitis were found in 50%. Double contour sign were present in 2 ankle joints (7.7%). Arthritis (effusion/synovitis) in mid tarsal joints were found in 92.3% of patients with high Doppler activity in 65.4% and bone irregularities in57.7%.

**Conclusions:** The main US features of neuropathic (Charcot) arthropathy of ankle joint are: effusion, synovitis, high grade Doppler activity, bone irregularities of the distal fibula and involvement of mid tarsal joints (synovitis, high Doppler activity and bone irregularities).

**Disclosure of Interest:** None declared
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## AB0968 HIGH-FRAME RATE POWER DOPPLER IMAGING IS MORE SENSITIVE THAN CONVENTIONAL POWER DOPPLER IN DETECTING LOW BLOOD FLOWS IN A FLOW-PHANTOM AND IN HEALTHY VOLUNTEERS

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**Background:** Early detection of inflammation at diagnosis of rheumatoid arthritis (RA) or in remission of RA is important to optimise treatment in order to prevent joint damage and disability. Recent studies in ultrasound (US) indicate that US, especially power Doppler (PD), is more sensitive to detect inflammation than physical examination. Early diagnosis and treatment monitoring could be achieved by a more sensitive power Doppler (PD) method to detect early increased vascularisation. Inspired by recent breakthrough work in high-frame rate Doppler US imaging that was shown to be more sensitive to low flows associated with vascularisation [1], we systemically explored this method for its application in diagnosing and monitoring RA.
**Objectives:** (i) To compare the minimal flow velocity that can be detected with the high-frame rate Doppler US technique and a conventional clinical US machine using a flow phantom. (ii) To show visual differences between high-frame rate PDUS and conventional PDUS in healthy volunteers assuming that high-frame rate PDUS would detect more vascularisation in MCP2 joints.
**Methods:** In a flow phantom filled with tissue mimicking material [2] and a vessel diameter of 700 μm, we tested the PDUS performance of conventional PDUS (Esaote MyLab60) and a custom high-frame rate PD imaging technique (Verasonics Vantage). Settings for both methods were optimised to detect lowest flows (continuous PDUS signal) by adjusting pulse repetition frequency (PRF), velocity range, wall filters, frequency and gain. Subsequently we included six healthy volunteers and we performed conventional PDUS and high-frame rate PDUS of the MCP2 joint. The US images were graded on power Doppler (PD; 0–3) according to a semi-quantitatively scoring system of Naredo et al.
**Results:** In the flow phantom we could detect a flow velocity of 2.5 mm/s with the conventional PDUS. With the high-frame rate PDUS the lowest detectable flow was 0.5 mm/s. Results in healthy volunteers (n=6) showed no PD signal in MCP2 joints using conventional PDUS (Figure 1A). With high-frame rate PDUS (Figure 1B) the median PD grade was 2 (IQR: 2 - 2).

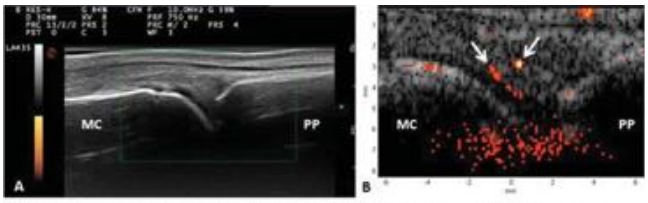



Figure 1. Power Doppler ultrasound (PDUS) of a MCP2 joint of a healthy volunteer; A) Conventional PDUS; B) High-frame rate PDUS (arrows: positive PD signal); MC: metacarpal; PP: proximal phalanx

**Conclusions:** In a flow phantom we could detect five times lower flows with the high-frame rate PDUS technique than with conventional PDUS. Contrary to conventional PDUS, we detected a positive PD signal in all healthy volunteers with high-frame rate PDUS. Therefore, high-frame rate PDUS is more sensitive to vascularisation. Further evaluation whether this will facilitate early diagnosis and monitoring in RA is needed.
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**Disclosure of Interest:** None declared
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## AB0969 THE ROLE OF HIGH RESOLUTION CT SCANNING IN THE ASSESSMENT OF PATIENTS WITH INFLAMMATORY JOINT DISEASE (IJD) ON BIOLOGICS

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**Background:** Biologic therapy (BT) in the treatment of IJD is now well established. The risks and potential complications of this modality of the treatment including infections and interstitial lung pathology have been described previously including in reports from several national registry databases such as the BSRBR. Furthermore the prevalence of lung disease in rheumatoid IJD is estimated at 5%. HRCT scanning for lung disease is therefore an important but under-utilized means of objective assessment of patients with IJD particularly in later stages of disease and when medical treatment is escalated to include immunomodulatory and biologic therapies.
**Objectives:** Our data examines the role of HRCT in the assessment of IJD patients before and after introduction of biologic therapies to consider the merits of this investigation in the intermediate and long term surveillance of IJD and biologic therapies.
**Methods:** Hospital records of patients with IJD under the care of one rheumatologist (MN) submitted for assessment for biologics were assessed. Specific diagnosis, treatment regimens and progression to biologic therapy were documented along with a record of submission for HRCT. Outcome and changes in treatment over time as well as follow up scan results were documented and analysed.
**Results:** Of the 130 patients assessed for BT in the 5 year period up to 2015, 106 (82%) had HRCT prior to commencing BT. 92 (71%) had normal scans. A total of 116 patients were submitted for BT (93 anti TNF and 23 other) of these 70 (60%) were also on MTX. Thus 10 patients had BT without HRCT. 14 (11%) had abnormal scans (including ground glass change, bronchiectasis, COPD) and were not commenced on anti TNF, Rituximab or other BT. Of the 130 patients 87 (67%) had RA of which 71 (81.6%) were seropositive. Of the 14 with abnormal scans, 8 were seropositive and 8 were on MTX. Of the 93 patients started on Anti TNF, 35 (37.6%) were discontinued/switched to another BT for a variety of reasons including inefficacy and side effects. Of the anti-TNF start-ups, 29 (31%) had progressive changes on repeat HRCT within 0 to 12 months. Of these 14 were switched to Rituximab with no further change in HRCT. Repeat HRCT scan data is available in only 5 of 15 patients switched to a second anti TNF, in three of which progression of lung changes was noted.
**Conclusions:** These preliminary data reveal the importance of HRCT scanning in the pre-assessment and monitoring of patients requiring BT for IJD. Progression of lung disease was seen in 31% patients on anti TNF. We recommend early repeat scans if any adverse effects are experienced or a change in BT planned due to lack or loss of efficacy. As lung disease is now recognised as the main non-infective cause of mortality in IJD, consideration should be given to routine review HRCT at 12 months after introduction of BT and then at regular (no longer than 3 year) intervals to monitor change even in asymptomatic patients controlled on biologics.
**Disclosure of Interest:** None declared
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## AB0970 ULTRASONOGRAPHY IN DIAGNOSIS AND MANAGEMENT OF ILIOLUMBAR SYNDROME: CASE SERIES

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**Background:** The iliolumbar ligament may be an important cause of acute and chronic Low Back Pain (LBP). The diagnosis of iliolumbar ligament inflammation is based on clinical history and physical examination which lack sufficient specificity. The treatment consisted of the standard care used in common LBP. Nowadays, ultrasonography (US) is used in routine practice in rheumatology for diagnostic purposes and to guide local injections but this technique is generally confined to assess peripheral joints and peri-articular structures.
**Objectives:** To describe the role of ultrasonography in the diagnosis and treatment of LBP related to an inflammation of the iliolumbar ligament.
**Methods:** From December 2012 till December 2015, all patients with clinically suspected iliolumbar syndrome were included in this study. Patients underwent an ultrasonography to confirm the diagnosis. For this technique, the patient is in the prone position and the probe is positioned almost horizontally for L5 and in slightly oblique direction for L4. To confirm the diagnosis, we should have a swollen hypoechoic iliolumbar ligament with reproduction of the usual back pain during the passage of the probe above the ligament[1]. Also, the thickness of the inflamed ligament should be higher than 1mm. The US was always performed bilaterally so we can compare both sides. Patients who failed standard treatment were injected under US-guidance or in clinic with 80mg of methyl-Prednisolone and 5cc of local xylocaïne. The patient's assessment of usual LBP was recorded 20mn after the injection of xylocaïne.
**Results:** 30 consecutive patients with clinically suspected iliolumbar syndrome (LBP with presence of tenderness on palpation of the posterior/ medial aspect of the iliac crest) were evaluated by US. Patients included in this study were relatively young with a mean age 38.87 years (22–65 years). The sex ratio is 5/1 (female/male). As suspected, X-ray and/or MRI of the lumbar spine and pelvis, when performed, were normal in most cases. Few cases of mild degenerative disc disease are noted. US showed, in all patients, an inflammation of the iliolumbar ligament (fig.1). In four patients, the iliolumbar ligament was inflamed at both sides. The mean thickness of the ligament was 2.64 mm (1.5–6mm). There was an associated tendonitis of the gluteus medius muscle in 5 patients, diagnosed also on US. The patients received a treatment with NSAIDs and a 12-session course of physical therapy, but this standard therapy was insufficient in 67% of cases. Twenty one (70%) patients received injection of 80 mg of methyl-Prednisolone and 5cc of local xylocaïne, 11 patients under US-guidance and 10 in clinic. All

patients noted the disappearance of the usual LBP 20mn after the injection (effect of local anesthesia).



*Fig 1. Ultrasound image of iliolumbar ligament. Note the thickened hypoechoic iliolumbar ligament at right (2.2mm) versus a small thickening of this ligament at left without an hypoechoic area. SC= subcutaneous tissue, IL= iliolumbar ligament, IC= iliac crest, PM= paravertebral muscle.*

**Conclusions:** Ultrasonography allows the diagnosis of iliolumbar syndrome in patients with LBP. It is a useful tool to guide infiltrations of corticoids as an effective therapy for this pathology. Prospective randomized trials are needed to confirm our conclusions.

**References:**

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**Acknowledgement:** None declared

**Disclosure of Interest:** None declared

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## AB0971 CHANGE IN SONOGRAPHIC CARTILAGE THICKNESS CORRELATES WITH CHANGE IN RADIOGRAPHIC JOINT SPACE NARROWING IN THE METACARPHALANGEAL JOINTS OF PATIENTS WITH RHEUMATOID ARTHRITIS

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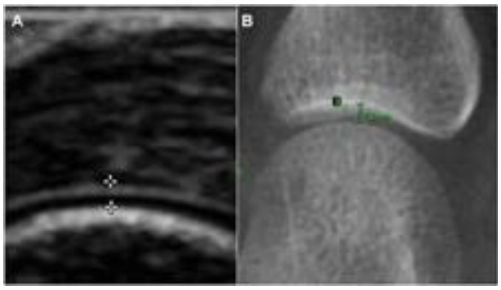
**Background:** It was previosly shown that metacarpal cartilage thickness (MCT) as assessed by ultrasound (US) correlates with both radiographic joint space width (JSW) and joint space narrowing (JSN) in the metacarpophalangeal joints (MCP) of patients with rheumatoid arthritis (RA).

**Objectives:** To correlate change in MCT with change in radiographic JSW and JSN in a longitudinal study of patients with RA.

**Methods:** We performed US examination of 19 consecutive outpatients with RA fulfilling the 2010 ACR/EULAR classification criteria with recent hand X-rays. Metacarpal cartilage of MCP 2–5 was assessed bilaterally by US at baseline and after 3 years in mm with an integrated caliper on static images (Figure 1A). JSN was evaluated on X-rays taken $<1$ year before the sonographic assessment as well as within 6 months of the second sonographic assessment by the van der Heijde modified Sharp method (vdHS). In addition, JSW was measured on the very same hand X-rays using an integrated calliper (Figure 1B). The relationship between sonographic and radiographic measures was investigated by Spearman correlation.

**Results:** Over the study period of 3 years a mean change of MCT of 0.00±0.01mm, was paralleled by a mean change of JSW of -0.08±0.20mm and a change of 0.12±0.37 in the JSN component of the vdHS. Change in MCT correlated with change in JSW (r: 0.37; p:$<$0.001) as well as with change in JSN (r:-0.26; p:$<$0.001). We could also demonstrate correlation between the two radiographic measures (r: 0.33; p:$<$0.001). Change in erosion did not correlate with either sonographic MCT or with the radiographic measures.

**Conclusions:** Change in sonographic cartilage thickness correlates with radiographic measures of joint space narrowing in the MCP joints of RA patients over time. Thus, ultrasound may be a valid tool for the longitudinal assessment of metacarpal cartilage in RA patients, but also the radiographic assessments appear to reflect "true" cartilage dimensions.




**Disclosure of Interest:** None declared

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## AB0972 UTILITY OF THE ULTRASOUND FOR THE EVALUATION OF ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REMISSION OR LOW CLINICAL ACTIVITY IN TREATMENT WITH BIOLOGICAL IN OPTIMIZATION PHASE

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**Background:** In rheumatoid arthritis (RA), the activity is correlated with radiological damage. Our therapeutic goal is clinical remission. The concept of clinical remission may be insufficient due to persistent subclinical inflammation, which can be determined by ultrasound.

**Objectives:** Our goal is to determine the frequency of subclinical synovitis by ultrasonography in patients with RA in low activity or remission of the disease measured by CDAI, in biological treatment optimization phase.

**Methods:** Transversal and longitudinal study describing the ultrasonographic changes in gray scale and Doppler in parallel with blind clinical evaluation. We included 23 patients (16 women and 7 men) with RA according to ACR criteria/EULAR under low activity/remission measured by CDAI, under biological treatment and optimized at least for 6 months. They were sent by their usual clinician, making a random selection. They were evaluated in the same day by a rheumatologist and blind sonographer. VAS, VGP, VGM, HAQ, number joints painful, joints swelling, ESR, CRP and CDAI were evaluated. Regarding the ultrasound, were evaluated; Synovitis and Doppler in 12 joints (wrists, second to fifth MCF and fifth bilateral MTF).

**Results:** All patients were in low activity/remission in accordance with their rheumatologist. The baseline characteristics and different variables are described in Table 1B, 1B. After the blind rheumatologist evaluation, the percentage of patients in remission/low activity was lower, 65.2% (15 patients, 2 in remission, 13 in low activity), p$<$0.005 compared to regular clinician. 8 patients had CDAI $>$10. The presence of subclinical synovitis in ultrasound was 69.6% (16 patients) with an average of 2.02± 1.9 of joints and 15 patients with Doppler. Therefore, only the 47.8% (11) of patients in remission/low activity was classified, compared to 100% and 65.2% of the regular and blind clinical respectively. 14 of the 23 patients were under optimization dose for 6–8 months, while 9 of them exceeded the 8 months. No differences were observed in the clinical status of both groups.

Table 1

| | Total (n=23 patients) |
|---|---|
| **A. Basal characteristics** | |
| Average age ± DE (years) | 57.7±9.7 |
| Average time of disease progression (years) | 11.57±5.86 |
| Immunology | |
| RF positive/CCP positive (%) | 87 |
| RF positive/CCP negative (%) | 4.3 |
| RF negative/CCP negative (%) | 8.7 |
| Treatment with DMARDs (%) | 60.9 (methotrexate 65.2%) |
| Biological treatment (optimization) (%) | 100 |
| Optimization average time (months) | 9.6±4.26 |
| **B. Clinical and functional characteristics** | |
| VAS | 48.26±24.80 |
| VGM | 18.48±15.62 |
| VGP | 45.22±24.65 |
| Joints painfull (number) | 2.62±2.85 |
| Joints swelling (number) | 2.65±2.82 |
| ESR | 10.74±6.78 |
| CRP | 3.37±7.32 |
| HAQ | 1.184±0.682 |
| CDAI usual rheumatologist | 3.2±3.04 |
| CDAI blind rheumatologist | 11.56±8.11 |

**Conclusions:** Our study shows how the exploration performed by a rheumatologist blind to the patient's clinical situation brings a lower percentage of remission compared to outpatient valuation. As well, with the ultrasound we can observe a greater sensitivity for the detection of the disease than with physical examination. The detection of subclinical joint damage is often undertreated, showing ultrasound as a noninvasive technique of great help reducing joint damage.

**Disclosure of Interest:** R. Martínez Pérez Grant/research support from: Abbvie, Phizer, Roche, E. Rubio Grant/research support from: Abbvie, Phizer, Roche, M. D. Fernández Alba Grant/research support from: Abbvie, Phizer, Roche, B. Hernández: None declared, R. Menor: None declared, J. Povedano: None declared

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## AB0973 THE 8-JOINT ULTRASOUND SCORE IS USEFUL FOR MONITORING RESPONSE TO TREATMENT FOR RHEUMATOID ARTHRITIS

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**Background:** Musculoskeletal ultrasonography (US) is one of the standard tools for the diagnosis and monitoring of rheumatoid arthritis (RA). Although we and other groups have proposed several sets of US assessment procedures in arbitrary combinations of selected joints,[1–3] there is still no consensus in defining the joints to evaluate.
**Objectives:** To investigate whether US assessment in the selected 8 joints which we advocate as a routine assessment is useful for monitoring response to treatment for RA.
**Methods:** Power Doppler (PD) US was performed in 24 joints, including all PIP, MCP, bilateral wrist and knee joints, as comprehensive evaluation in 15 RA patients treated with certolizumab pegol (CZP). Before and after treatment with CZP, PD signals were scored semiquantitatively from 0 to 3 in each joint, and total PD oscore-24 and total PD score-8 were calculated by summing up PD scores of the 24 joints and the selected 8 joints (bilateral second and third MCP, wrist, and knee joints), respectively.[1]
**Results:** Amount of change of total PD score-24 by treatment with CZP correlated highly with the changes of disease activity indices, SDAI ($r_s$ =0.91, $p$ <0.01) and DAS28-CRP ($r_s$ =0.86, $p$ <0.01). Although it correlated well with the changes of some components of disease activity indices, including swollen joint count ($r_s$ =0.74, $p$ <0.01), tender joint count ($r_s$ =0.86, $p$ <0.01), CRP ($r_s$ =0.85, $p$ <0.01) and ESR ($r_s$ =0.62, $p$ <0.01), there were no significant correlations between the changes of total PD score-24 and the changes of patient's global assessment ($r_s$ =0.42, $p$ >0.05) and evaluator's global assessment ($r_s$ =0.27, $p$ >0.05). Amount of change of total PD score-8 exhibited stronger correlations with the changes of SDAI ($r_s$ =0.92, $p$ <0.01) and DAS28-CRP ($r_s$ =0.89, $p$ <0.01) as compared to that of total PD score-24 (Figure 1). The change of total PD score-8 correlated more highly with the changes of swollen joint count ($r_s$ =0.81, $p$ <0.01) and tender joint count ($r_s$ =0.91, $p$ <0.01), while it showed lower correlation coefficients with the changes of patient's global assessment ($r_s$ =0.39, $p$ >0.05) and evaluator's global assessment ($r_s$ =0.22, $p$ >0.05) as compared to that of total PD score-24.

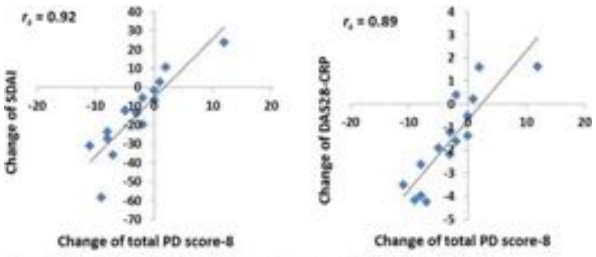



Figure 1 Correlation diagrams between the change of total PD score-8 and the change of disease activity indices.

**Conclusions:** This study suggests that total PD score-8 is useful for monitoring response to treatment in RA patients.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4533

## AB0974 HIGH-FIELD MRI: INFRA-RADIOLOGICAL STRUCTURAL ABNORMALITIES DETECTION IN WRIST OF PATIENTS WITH SPONDYLOARTHRITIS AND EARLY RHEUMATOID ARTHRITIS

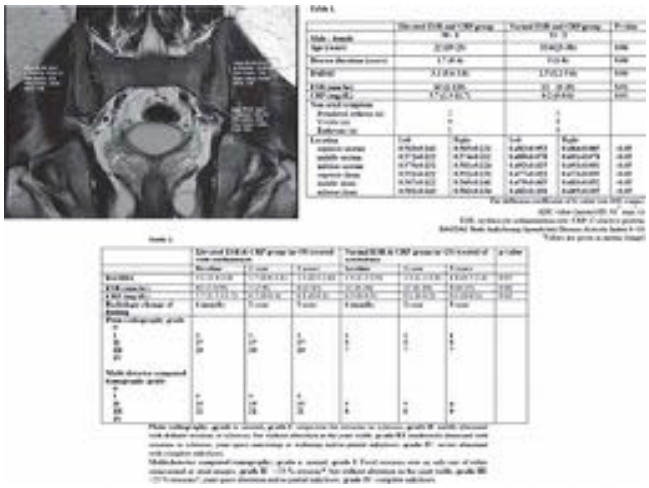
S. Guis[1], P. Souteyrand[2], D. Militianu[3], C. Chagnaud[2], Y. Le Fur[4], J.-P. Mattei[5], M. Rozenbaum[6], I. Rosner[6], H. Boudinet[1], M. Bernard[4], D. Bendahan[4]. *[1]Department of Rheumatology, Aix-Marseille University, AP-HM; [2]Radiology, AP-HM, Conception, Aix Marseille University, Marseille, France; [3]Musculo-Skeletal MRI, Rambam Health Care Campus, Haifa, Israel; [4]CRMBM/CEMEREM UMR CNRS 7339, CNRS, Aix Marseille University; [5]Department of Rheumatology, Aix-Marseille University, AP-HM, Marseille, France; [6]Department of Rheumatology, Bnai Zion Medical Center, Haifa, Israel*

**Background:** Previous studies have showed that structural abnormalities such as erosions and geodes could be detected in wrist of patients with Rheumatoid Arthritis (RA) using high-field MRI whereas corresponding anomalies were invisible using conventional 1.5 T MRI. Similar observations have not been reported so far for patients with either an early form of RA or patients with axial and peripheral forms of spondyloarthritis (SpA).
**Objectives:** In the present study, we compared wrist MRI investigations performed at 1.5 and 3 T in SpA and early RA patients (less than one-year disease evolution). We aimed at determining whether synovitis, geodes and erosions are similarly observed in both cases.
**Methods:** The study was conducted in the wrist of 9 SpA patients (6 with ankylosing spondyloarthritis (AS) and 3 with psoriatic arthritis) and in 7 early RA patients. Age in the RA group ranged from 35 to 54 (6 females, 1 male) while it ranged between 22 and 64 in the SpA group (7 females, 2 males). All the patients provided their written informed consent before their inclusion in the protocol which was approved by the local ethics committee.
MRI investigations were performed at 1.5T (Philips Achieva) using a Flex-M coil and at 3T (Siemens Verio) using a 4-channel flexible coil. In both cases, subjects were asked to lie down in the supine position inside the scanner and wrist was scanned at 1.5T using a T1-SE and a PD-FS-SE and at 3T using both a VIBE and a DESS sequences. MR images were analyzed by one senior radiologist (CC).
**Results:** In the RA group, we identified more abnormalities at 3T as compared to 1.5T for 1 patient while for 5 patients the number of abnormalities was identical in both cases. 1 patient did show no abnormality. Similarly, in the SpA group, more abnormalities were observed at 3T as compared to 1.5T for 2 patients. In those cases, more erosions were identified whereas geodes, synovitis and oedema were similar. These two patients had AS with peripheral and axial pain without psoriasis. For 1 patient with structural abnormalities, the results at both fields were similar. In 6 patients, (including 2 patients with psoriatic arthritis), we did not detect any structural abnormality.
**Conclusions:** In the present study, we illustrated that for both RA and SpA patients, MRI investigations performed at high-field can detect wrist abnormalities which were not detectable at 1.5T.
**Disclosure of Interest:** None declared
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## AB0975 DIFFUSION WEIGHT MAGNETIC RESONANCE IMAGING MAY PREDICT A TREATMENT RESPONSE IN ANKYLOSING SPONDYLITIS

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**Background:** With the today's advanced magnetic resonance imaging (MRI) techniques, the pathologic features of ankylosing spondylitis (AS) can be detected early and promptly treatment.
**Objectives:** This study aimed to determine the value of diffusion-weighted MR imaging (DWI) in determined of AS treatment strategy and assess the role of quantitative MRI in the evaluation of AS treatment outcome.
**Methods:** 52 patients with the diagnosis of early AS were included in this study. Disease activity was measured according to clinical instruments and laboratory tests. For each patient, both inflamed sacroiliac (S-I) joint lesion was checked quantitatively at first diagnosis by diffusion-weighted MR imaging (DWI) and measured the apparent diffusion coefficient (ADC). Based on ADC value, low ADC value group were treated with conventional NSAIDs and high ADC value group were treated with TNF-α inhibitor. all subjects were revaluated continuously by pelvis multi-directional computer tomography (MDCT) for bone change in sacroiliac joint, after treatment.
**Results:** The high ADC value patient had higher BASDIA score, ESR and CRP than low ADC value patients relatively. The clinical parameters diminished significantly with regression of the inflammatory activity after treated with TNF-α



inhibitor or NSAIDs. But paradoxically, one patient who was low ADC value and treated with NSAID had radiologic change of S-I joint and no change of ADC value in follow up MRI.
**Conclusions:** The ADC value measured by DWI maybe predicted treatment response.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2211

## AB0976 ACHILLES TENDON INJURY AND COMPLEX PATELLAR FOR OVERUSE IN SOCCER PLAYERS: ULTRASOUND INVESTIGATION BEFORE AND AFTER THE MATCH

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**Background:** Football is one of the most popular sports in the world. Many players are suffering from disease of the Achilles tendon and the complex of the patellar tendon during periods of intense training with characteristics painful conditions of the tendons. Football players use their tendons to the limit because of the 'intensity of your workouts and frequent games. They participate in tournaments with echographic signs of underlying disease, and most of them play with a certain degree of pain.
**Objectives:** To investigate the changes in the players ultrasound at baseline and after participating in a youth football tournament.
**Methods:** 72 players were interviewed. 64 of the respondents underwent ultrasound examination before the game. 45 of the 64 players (70%) were scanned again at follow-up after the match. The interviews were conducted by the same person and all scans were done by the same doctor. The players were chosen randomly among those controlled interview Scanning was performed with a 15 MHz linear transducer. E 'was performed a careful examination grayscale and Doppler of the Achilles tendon and patellar complex. Ultimate goal was to determine the amount and distribution of activities Doppler with a score of 0–4.
**Results:** Sixty-two players (86%) had severe damage to tendons 80 over the past three years. 45 (50%) covered the whole patellar and 34 (37%) the Achilles tendon. In 60% of the problems they had started slowly and the mean duration of symptoms was 4 months (0–36). The '86% accepted the pain, 21% took painkillers, especially NSAIDs, to be able to play.
At baseline, the Doppler activity was evaluated in most players. After the match, these changes were not significantly changed in most investigated regions. However, a very significant increase was observed in the tendons on the non-dominant side: quadriceps (Willcoxon $p<0.001$), patellar tendon ($p<0.05$), and Achilles tendon central portion ($p<0.05$).
**Conclusions:** Doppler activity was found in all the tendons of soccer players examined to indicate a high degree of tension of these tendons. An increase in the fraction of color Doppler was significant only at the non-dominant leg. This can be explained by the fact that players load more frequently on this side. Changes Doppler correspond to the highest number of accidents on this side and a possible prognostic value of Doppler information is to be tested in a prospective study.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5839

## AB0977 ULTRASONOGRAPHY-DETECTED SUBCLINICAL INFLAMMATION IN PATIENTS WITH HAND OSTEOARTHRITIS AND ESTABLISHED RHEUMATOID ARTHRITIS: EVALUATION OF DIFFERENT ULTRASOUND HAND JOINT SCORES

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**Background:** Despite the interest in validating ultrasound (US) as an outcome measure in rheumatology, progress has been achieved only in defining the pathological US abnormalities associated with rheumatoid arthritis (RA). A recent review of US studies in osteoarthritis (OA) showed very limited data about hand OA (1). Patients with OA have been previously described as having synovial thickening (SH), erosions, osteophytes and rarely positive Power Doppler (PD) signal on US examination (2). These findings suggest a possible overlap between US features of hand OA and RA.
**Objectives:** This study aimed to investigate the usefulness of a standardised US examination protocol for hand joints in differentiating subclinical RA from OA, in patients with equivocal clinical examination. In addition, we explored which simplified hand US scores perform better for every disease taken separately.
**Methods:** A retrospective, observational study was conducted in patients with inflammatory hand joint pains referred to the US clinic with suspected subclinical inflammation. We compared patients with established RA (n=224) and hand OA (n=73), with respect of several demographic, clinical, laboratory and US parameters. We used a 22 hand joint US examination protocol (wrists, metacarpophalangeal and proximal interphalangeal joints bilaterally - OMERACT scoring system) for all patients, and compared it with a range of smaller, pre-defined US joint scores.
**Results:** Significant statistical differences were found for age at the time of scan, US parameters and clinical examination between the two groups. Subclinical joint inflammation in the context of equivocal clinical examination was found in 9.6% OA patients compared to 46.4% in RA ($p<0.05$). The comparison between several joint scores in OA patients suggested that for detecting subclinical inflammation, multiple finger joints should be examined (20 joint score, comprising MCPs and PIPs was significantly more informative than the 12, 10 and 4 joint scores, ($p<0.05$)), whereas in RA, the 4 joint scores (assessing wrists and MCP 5 or MCP 2 and 3 bilaterally) detected inflammation just as well as the 22 joint score ($p<0.05$).
**Conclusions:** Our study findings reflected differences between the incidence and characteristics of subclinical inflammation in patients with RA and OA. The attractiveness of using US scores assessing a smaller number of joints may pose limitations, despite being of benefit in a time-constrained clinical setting. Our study assessed comparatively the utility of several US hand scores, however, further research is need to validate their use in practice.
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## AB0978 THE ASSOCIATION OF POWER DOPPLER SIGNAL GRADES WITH THE SERUM INFLAMMATORY MARKER LEVEL

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**Background:** Power Doppler can show the degree of hyperemia in inflamed synovium. Serum inflammatory markers also reflect the arthritic activity in various rheumatic disease including rheumatoid arthritis. However, no report has been published regarding an association between them.
**Objectives:** We investigated an association between power Doppler semiquantitative signal grade and all the 5 serum inflammatory markers of white blood cell (WBC), hemoglobin (Hb) and platelet (PLT) count which possibly can be used in the practical field as well as commonly used ESR and CRP.
**Methods:** Rheumatic disease patients initially presenting with objective joint tenderness or swelling were evaluated with ultrasound and blood test was done to determine serum inflammatory marker level. A total of 827 ultrasound examined joints (112 metacarpophalangeal, 85 metatarsophalangeal, 82 proximal interphalangeal, 13 knee, 46 tendons, 136 ankle, 53 elbow, 15 hip, 255 wrist, 29 shoulder) from 2009 to 2014 were analyzed in this study. According to rheumatic disease classification, rheumatoid arthritis was most common and undifferentiated arthritis, ankylosing spondylitis and gout followed. ANOVA, two sample T-test, Spearman correlation test, multiple linear regression and logistic regression analysis were performed for statistics using SAS 9.2 version. $p<0.05$ were considered as significant.
**Results:** The presence of positive Doppler signal itself was associated with elevated ESR, CRP and PLT number but not Hb level at the time of ultrasound examination (ESR, CRP: $p<0.0001$, WBC: $p=0.0116$, platelet: $p=0.0246$). Spearman correlation coefficients showed positive linear association between power Doppler grade and serum levels inflammatory markers (ESR: $r=0.21$, CRP: $r=0.30$, WBC: $r=0.13$, platelet: 0.11, p-value $<0.05$) except Hb level. However, multiple linear regression test after adjusting confounding variables showed that only the CRP level among the 5 variables showed a positive relationship with power Doppler grade ($p=0.0022$). Furthermore, logistic regression test showed one step increase of Doppler grade resulted in 1.3 mg/dL increase of serum CRP level. Post hoc (Scheffe) analysis showed rheumatoid arthritis was the most correlated disease among the rheumatic diseases we included.
**Conclusions:** In a patient with presenting objective joint tenderness or swelling, if there is a positive power Doppler signal, it is associated with elevated serum markers of inflammation. Especially, the CRP is the only marker that have positive correlation with the Doppler signal semi-quantitative grade. One grade up of Power Doppler signal is expected to elevate CRP as amount of 1.3 mg/dL. Rheumatoid arthritis is the most associated disease that can be applied this result.
**Disclosure of Interest:** None declared
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## AB0979 A COMPARISON OF PHYSICAL AND JOINT ULTRASONOGRAPHY FINDINGS OF THE MTP JOINT IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) causes a variety of foot lesions, but the feet and ankles are not included in disease activity indices such as the Disease Activity Score (DAS). The spread and usefulness of joint ultrasonography in RA diagnosis and treatment have recently been reported. Many disease activity indices use tender (painful) joints and swollen joints, but few reports have examined the association between synovitis on joint ultrasonography and physical findings. This study evaluated joint ultrasonography of the metatarsophalangeal (MTP) joint in RA patients and examined the results in conjunction with physical findings.
**Objectives:** This study evaluated joint ultrasonography of the metatarsophalangeal (MTP) joint in RA patients and examined the results in conjunction with physical findings.
**Methods:** The subjects were 65 RA patients (82 feet) visiting our department on an outpatient basis. Surgical patients were excluded. Their mean age was 64.1 (27–84) years, and the disease stage was Stage I in 19 subjects, II in 11 subjects, III in 10 subjects, and IV in 25 subjects. The degree of functional disability according to the Steinbrocker classification was Class I in 45 subjects, Class II in 16 subjects, and Class III in four subjects. Disease activity according to the DAS28-ESR was complete response in 16 subjects, low disease activity (LDA) in 27 subjects, moderate disease activity in 14 subjects, and high disease activity in 7 subjects. Twenty-two subjects were taking a combination of biological agents. After interviewing subjects about any foot-related complaints, pain and swelling were evaluated, and joint ultrasonography was performed. The same examiner examined all subjects in the same room using the same diagnostic equipment. Grade 1 or higher on power Doppler ultrasonography was defined as synovitis.
**Results:** The detection rates of pain, swelling, and synovitis in all 410 toes were 33.9%, 14.1%, and 13.4%, respectively. Forefoot-related complaints were cited in 13 feet, and pain was observed in all subjects. However, synovitis was only detected in 38.5%, and many cases had asymptomatic synovitis. The detection rates of synovitis in subjects taking biological agents and subjects not taking biological agents were 11.0% and 24.4%, respectively, with no significant difference (Pearson's chi-squared test). When examined according to disease activity, synovitis was observed in 27.9% of those with LDA or less, which was the treatment objective. During the evaluations, joint swelling had to be differentiated from edema in a large number of cases.
**Conclusions:** Out of pain, swelling, and synovitis, the detection rate was highest for pain. This was likely due to the inclusion of pain other than that from arthritis, such as from subluxation and dislocation of the MTP joint and plantar calluses. There was a high prevalence of asymptomatic synovitis, suggesting the utility of evaluating synovitis by joint ultrasonography.
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## AB0980 VALUE OF ULTRASOUND IN THE FOLLOW-UP OF PATIENTS AFTER NEEDLING AND LAVAGE OF CALCIFIC TENDINOPATHY

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**Background:** Calcific tendinopathy is a frequent cause of shoulder pain. Needling and lavage of the calcification is considered as the first line treatment after failure of NSAID or physiotherapy. X-ray remains the best imaging modality to diagnose and follow-up calcification changes after treatment. Ultrasound (US) has also shown its interest in the diagnosis of calcific tendinopathy and to guide the needling. It allows an evaluation of the calcification aspect and size. However, the value of US to follow-up calcification changes after needling is currently unknown.
**Objectives:** The goal of our study was to evaluate the value of US in the follow-up of patients after needling and lavage of shoulder calcifications.
**Methods:** Patients undergoing a needling and lavage of a shoulder calcific deposit were followed prospectively. Calcification size was measured on X-Ray and their aspect classified according to the French Arthroscopy Association (type A (sharp contours and a homogeneous structure); type B (sharp contours and a nonhomogeneous structure). Measurements were performed at the same time with US and calcifications were classified according to their echogenicity (arc-shaped; fragmented with or without shadowing, nodular). Changes in the X-ray and US at 3 months were studied.
**Results:** Thirty patients were included, 20 female (66%), mean age 50 years (±11). On X-ray, calcifications were type A in 11 patients (36%) and type B in 19 patients (64%). Calcific deposits were mostly in the supraspinatus tendon (96%). Mean length, width and height of the calcific deposit were 15 mm (±6), 12 mm (±5.7) and 5.2 mm (±1.9) respectively. On US, calcification were arc shaped in 12 cases (40%), fragmented with shadowing in 15 (50%), without shadowing in one case and nodular in 2 cases (6.7%). Type A calcification on X-Ray were mainly arc shaped on US (80%) whereas type B on X-ray were fragmented or nodular on US in 79% of the cases. Bursitis was associated in 12 patients (40%). A significant correlation was found between the size of the calcification recorded on US and X-Ray (length (r=0.78), width (r=0.65) and height (r=0.59); $p<0.01$). A 3 months, 12 calcifications (40%) had completely disappeared on X-Ray, 3 (10%) were reduced between 50 and 90%, 9 (30%) reduced by less than 50% and (20%) had not changed. In contrast, only two patients had a complete disappearance of their calcific deposit on US. Calcifications became most of the time fragmented with (9; 30%) or without (12; 40%) acoustic shadowing. Calcific deposit remained arc shaped in only 2 patients. Bursitis was still present in 12 patients at 3 month.
**Conclusions:** US seems a good imaging modality to follow-up patients with calcific tendonitis. Indeed, we found a good correlation between the sizes of the calcification assessed by US and X-ray as well as their radiological and US pattern. Three months after needling and lavage of the calcification, US was able to depict changes in morphology of the calcific deposit and could still detect calcifications even in patients with a complete disappearance of the calcification on X-Ray. In view of the lack of radiation for the physician and the patients, US could be of value in the follow-up of patients after treatment of a calcific tendinopathy.
**Disclosure of Interest:** None declared
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## AB0981 HAND JOINT INFLAMMATION IN EARLY RA: CLINICAL ULTRASOUND AND FLUORESCENCE OPTICAL IMAGING DIAGNOSTICS

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**Background:** Altered microcirculation (abnormal perfusion/capillary leakage) of synovial tissue can be detected early using Fluorescence Optical Imaging (FOI). FOI utilizes an intravenous fluorophore[1,2] that displays high-resolution hand images that can be analyzed visually (FOI-v) in real-time, or by using digital Disease ACTivity (DACT) scoring methods. We previously reported FOI's sensitivity and specificity in detecting silent synovitis in various rheumatic diseases[1].
**Objectives:** Here, we test the diagnostic performance of FOI-DACT in detecting subtle hand joint inflammation in early rheumatoid arthritis (eRA), as compared to clinical evaluation and MusculoSkeletal UltraSound (MSUS).
**Methods:** Fingers and wrists of patients with eRA were assessed by clinical examination, MSUS and FOI-DACT imaging. Inflammation was defined as having synovial hypertrophy/effusions and intra-articular Doppler signaling on MSUS, and as increased optical intensities on FOI-v. Scores of DACT$\geq$1 were considered indicative of disease activity.
**Results:** 1326 joints of 39 eRA patients [72% females, 56% previous/current smokers, 54% RF(+) and 69% ACPA(+)] were studied. The incidence and mean number ±SD of joints inflamed by clinical, MSUS and FOI-v were 23% (7.8±8.1), 29% (9.7±7.7) and 30% (10.3±7.2), respectively. Using MSUS as a reference, FOI-DACT was 95% (35/37) accurate in identifying patients with active disease, 24% (9/37) of whom had erosive RA. High correlations and agreements emerged between MSUS and FOI-v (r=0.803, $p<0.001$; kappa±SE:0.70±0.02 [95% CI 0.67–0.75]), clinical and FOI-v (r=0.732, $p<0.001$; kappa±SE:0.56±0.03 [95% CI 0.51–0.61]) and MSUS and clinical (r=0.793, $p<0.001$; kappa±SE:0.59±0.03 [95% CI 0.54–0.64]). The sensitivity, specificity, NPV and PPV of inflammation



by FOI-v was 81% (308/380), 90% (854/946), 61%, and 96% respectively. Of the clinically negative but MSUS positive (145/1023) joints, 68% (Subclinical: 98/145) were also FOI positive. Remarkably, one patient had 15 joints that were FOI-DACT positive and MSUS negative, but a month later, the same joints became MSUS positive. Although the wrists and MCPs were frequently inflamed, DIP joint inflammation was noted in 12 patients by FOI-DACT and MSUS. Nine of these patients had osteoarthritis by conventional radiography.

**Conclusions:** In early RA, Fluorescence Optical Imaging (FOI) coupled with digital Disease ACTivity (DACT) scoring correlates well with MSUS, and has a high positive predictive value. FOI-DACT emerges as a useful automated quantitative scoring method for synovial inflammation, and may be used in monitoring the effects of therapy.

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## AB0982 DICHOTOMOUS SCORING OF RA ULTRASOUND INFLAMMATION DEMONSTRATES GOOD RESPONSIVENESS COMPARED TO SEMI-QUANTITATIVE SCORING WHEN USING NOVEL JOINT SELECTION METHODS

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**Background:** Novel joint selection methods using semi-quantitative scoring (SQS) of ultrasound (US) joint inflammation (power Doppler (PD) vascularity and grey-scale synovial hypertrophy (GSSH)) have shown good sensitivity to change versus existing methods and DAS28 in RA (1). However SQS may have more variability than dichotomous scoring (DS) as SQS requires grading across multiple categories.

**Objectives:** Compare responsiveness of DS of US joint inflammation versus SQS using 2 novel and 2 existing joint selection methods.

**Methods:** Novel methods were Individualized US [IUS], which selects up to 7 or 12 most inflamed joints on US and Individualized Composite-US [ICUS], which additionally considers joint symptoms. Existing methods were a pre-defined 7-joint count and a 12-joint count derived from an US data reduction method. PD vascularity and GSSH at the joints were scored via a DS system [USDSS] as Y/N or via a SQS system [USSQS] on a 0–3 severity scale. Both systems scored tenosynovitis (PD and GS changes), tender and swollen joints as Y/N. Joint pain was scored as Y/N (with USDSS) or using a 0–3 severity scale (with USSQS). Responsiveness at 3 months was measured using the standardized response mean (SRM). Relative gains in SRM magnitude (SRM-Gains) were reported comparing novel to existing methods.

**Results:** 20 RA subjects (mean DAS28 at baseline and 3-months =4.68 and 4.19, respectively) starting/escalating on DMARDs and corticosteroid therapy were followed for 3 months. SRMs using existing methods were modest for both USDSS and USSQS (ranged from 0.30 to 0.49). SRMs ranged from 0.94 to 1.06 using novel methods with both systems. There were substantial SRM-Gains (ranged from 1.94 to 3.47) for both systems using ICUS and IUS with the 7 or 12 joint approaches.

Table 1. Results of USDSS and USSQS

| Approach | 7-joint | | 12-joint | |
|---|---|---|---|---|
| | USDSS | USSQS | USDSS | USSQS |
| ICUS[#] | | | | |
| Baseline TIS* | 2.30 (0.79) | 1.87 (0.82) | 3.16 (1.18) | 2.46 (1.11) |
| 3 month TIS | 1.62 (0.71) | 1.25 (0.68) | 2.04 (0.94) | 1.67 (0.87) |
| SRM (95% CI) | 0.94 (0.40, 1.46) | 1.05 (0.49, 1.59) | 1.06 (0.50, 1.60) | 0.96 (0.42, 1.48) |
| SRM-Gain | 3.13 | 2.92 | 3.31 | 1.96 |
| IUS[†] | | | | |
| Baseline TIS | 2.83 (1.32) | 1.81 (1.08) | 3.59 (1.88) | 2.24 (1.47) |
| 3 month TIS | 1.89 (0.95) | 1.22 (0.69) | 2.44 (1.26) | 1.49 (0.88) |
| SRM (95% CI) | 1.04 (0.48, 1.58) | 0.98 (0.43, 1.50) | 1.02 (0.47, 1.55) | 0.95 (0.41, 1.47) |
| SRM-Gain | 3.47 | 2.72 | 3.19 | 1.94 |
| Existing[†] | | | | |
| Baseline TIS | 0.62 (0.39) | 0.43 (0.29) | 1.97 (1.12) | 1.17 (0.76) |
| 3 month TIS | 0.51 (0.39) | 0.35 (0.28) | 1.78 (1.07) | 1.02 (0.67) |
| SRM (95% CI) | 0.30 (–0.15, 0.75) | 0.36 (–0.09, 0.81) | 0.32 (–0.13, 0.77) | 0.49 (0.02, 0.95) |

*TIS: Total inflammatory score reported as mean (SD). [†]TIS of IUS and existing methods = sum of individual joint scores (IJSs) derived from US subscores from relevant joints per patient. [#]TIS of ICUS = sum of IJSs derived from clinical and US subscores from relevant joints per patient.

**Conclusions:** Results of this small study suggest USDSS may be as responsive as USSQS (both had substantial SRM-Gains) using novel joint selection methods.

**References:**

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# Epidemiology, health services and outcome research

## AB0983 WHAT IS THE FASTEST ROUTE FOR PATIENTS WITH INFLAMMATORY ARTHRITIS TO EARLY ARTHRITIS CLINIC

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**Background:** Patient self-referral to a rheumatologist, without any former visit to the general practitioner (GP), was shown to be a significant contributing factor in delivering the optimal care for patients with early arthritis [1]. The literature has limited data on the referral of patients with early arthritis by secondary care specialities to rheumatologists. This abstract compares the time required for patients with inflammatory arthritis to access the rheumatology clinic when referred by different specialities.

**Methods:** We reviewed the medical records and electronic files of all patients with synovitis who attended our rheumatology clinic between 1st June 2012 and 1st June 2015. The following data was captured; demographics, time lag between onset of symptoms and the first rheumatologist consultation, date of referral, and the speciality of the referring physician. We stratified the patients according to the source of referral into two groups; GP referral and specialist referral. Data are presented as the median values and interquartile range (IQR). Mann-Whitney test was used to compare the two groups.

**Results:** We identified 173 patients with inflammatory arthritis. 134 (77.5%) were Emirati's, 137 (79.2%) were females, and median age was 41 (IQR 34–52 years). 91 (52.6%) patients were referred by a GP. The median delay from the onset of symptoms to assessment by a rheumatologist for patients referred by GP was 214 days (IQR 59–722). Whereas, for those referred by secondary care specialities was 95 days (IQR 31–372). This difference was statistically significant (Z-Score =2.4655, p-value $<0.01$). The fastest referral was through accident and emergency department 63 days (IQR 5–185).

**Conclusions:** In our population, patients with early arthritis were referred faster to the rheumatology clinic by a secondary care specialist rather than the GP.

**References:**

[1] Fautrel B, et al. Rheumatology 2010; 49:1 47–155.

**Disclosure of Interest:** None declared

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## AB0984 HERPES ZOSTER VACCINATION, SHOULD OUR PATIENTS WITH RHEUMATOLOGICAL DISORDERS BE PRIORITIZED?

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**Background:** Herpes Zoster infection is a common and painful condition with potential for serious complications. The overall life time risk is one in three but the risk is much higher in immunosuppressed patients and in our patients with rheumatological diseases. For example in patients with rheumatoid arthritis alone the risk is 2 fold higher compared to the age and sex matched controls.

The risk also increases with age and more than 50% of Herpes infection occurs in those aged over 60.

The Herpes Zoster vaccination has been approved by FDA for people aged 50 years and older and CDC recommends it in those aged 60 and above.

In United Kingdom this vaccination has recently been started, last year only people who were 70 and 79 years old were being offered the vaccine and this year those aged 71 and 78 are being vaccinated. Current guidelines do not recommend vaccination on biologic treatment, high dose steroid or other significant immunosuppression.

**Objectives:** This is a small study to look into Herpes infection in our rheumatology patients and whether we need a more pro-active approach towards vaccinating our patients particularly those who are about to start biologic therapies.

**Methods:** We looked at the self-reported incidence of Herpes Zoster infection in our cohort of rheumatology patients. We sent out a questionnaire to all patients on our biologics database asking if they had ever suffered from shingles and whether they had it before or after their respective rheumatological diagnosis and if they were on a biologic or non-biologic DMARD at the time of shingles.

Of 512 sent, 160 replied. Mean Age was (65) and main rheumatological diagnoses were: Rheumatoid Arthritis 96/160 (60%), Psoriatic Arthritis 29/160 (18%), and

Ankylosing spondylitis 21/160 (13%), the rest were other conditions treated with biologics.
**Results:** 38 of 160 (23.75%) had previous shingles and 6 of these 38 patients (15.7%) had suffered more than one episode. 24 of 38 (63.1%) patients had shingles post rheumatologic diagnosis and out of these 24; 6 (25.0%) had shingles whilst on biologic treatment; 6 (25.0%) had it whilst on combination DMARDs plus biologics; 9 (37.5%) on small molecule DMARDS; 3 patients could not tell their drugs at the time of shingles.
The mean age for those who had shingles was 61.8 years.
**Conclusions:** Nearly one quarter of patients on our biologic database reported one or more episodes of shingles. Out of them 63% had it post their rheumatological diagnosis, and most patients had it whilst on Biologic or Non-Biologic DMARDs.
The mean age of those who had shingles was 61.8 years which is much less than the current cut off for vaccination in UK.
This is a small study but serves as a reminder for us to consider a more proactive approach towards shingles vaccination in our rheumatology patients, particularly before starting Biologics, in older patients who do not qualify for routine government funded Vaccination.
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**Disclosure of Interest:** None declared
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## AB0985 CLINICAL CHARACTERISTICS AND MORTALITY OF OUR PATIENTS ADMITTED TO ICU

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**Objectives:** To determine the characteristics and mortality of patients with inflammatory rheumatic diseases admitted to intensive care unit (ICU).
**Methods:** We present a retrospective observational study including all patients with inflammatory rheumatic diseases admitted to the ICU of a tertiary hospital in Madrid from January 2004 to December 2014. We excluded all those with stay of less than 24 hours in this unit. Patients who were readmitted to ICU during the same hospital admission were considered as a single entry. We retrospectively collected several characteristics of the diseases, including biological activity, and also treatments received for the three months before admission to the ICU. Statistical analysis was performed using Stata 12.1.
**Results:** A total population of 56 patients required 62 income in ICU (6 of them required 2 consecutive admissions). The mean age was 58.6 ±14 years. 55% were women. 41% of patients (23) had systemic vasculitis, 7 of them ANCA positive. 28.5% (16) suffered connective tissue disease: 10 spondylitis, 3 rheumatoid arthritis and 4 other different processes. The average from diagnosis until their first ICU admission was 127± 176 months. 67% of patients had previously been treated with glucocorticoids for an average of 13 months at a dose of 7 mg (p50) prednisone/day. 14% of patients had received boluses of glucocorticoids, 20% biologic therapies and 18% cyclophosphamide. 63% showed signs of disease activity at the time of entering the ICU.
At ICU admission APACHE II severity index was p50: 20 (p25-p75: 13.5–26) and p50 SAPSII: 34.5 (p25-p75: 24–43). The most common causes were respiratory failure (58% of episodes) and septic shock (14.5%). During their stay in ICU 79% of patients required glucocorticoids, 35% received boluses of glucocorticoids, 20% cyclophosphamide and 11% plasmapheresis. 41 patients (68%) required mechanical ventilation, being invasive in 38. The mean ICU stay was 15.8 ±14 days. 28.5% (16) patients died during their stay in this unit, and 11% (7 patients) died in the hospital after leaving the ICU. Deaths was significantly associated with age (OR: 1.09 annually), elderly (OR: 7.52 for patients $>70$ compared to those $<45$) female sex (OR 3.7), APACHE II (OR: 1.15 per unit increased) and iv administration of gamma globulins in ICU (OR: 16.6) in multivariate analysis.
**Conclusions:** Vasculitis and connective tissue diseases are the main inflammatory rheumatic diseases that require our patients to ICU admission. At the time of these they have high rates of disease gravity. Mortality was associated with advanced age, elderly, female sex, severity measured by APACHE II and also with the need of gamma globulin iv administration.
**Disclosure of Interest:** None declared
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## AB0986 A SYSTEMATIC SCREENING OF COMORBIDITIES BY THE RHEUMATOLOGIST IN INFLAMMATORY RHEUMATISMS IMPACTS CHRONIC DISEASE CARE

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**Background:** In chronic inflammatory rheumatic diseases, comorbidities such as cardiovascular disease and infections are sub-optimally managed. EULAR recently developed points to consider to collect and report comorbidities and up-dated recommendation on cardiovascular disease evaluation.
**Objectives:** We developed a systematic screening of comorbidities in out-patient daily clinic of the Rheumatology department in Montpellier University Hospital. Our objective was to evaluate the impact of such a screening.
**Methods:** The assessment included rheumatism evaluation, cardiovascular risk factors and diseases, osteoporosis, chronic respiratory disease screenings, check-up of vaccine calendar and recommended neoplasia screenings. This was a medical and paramedics evaluation (physicians, nurses and physiotherapists) including anthropometric and blood pressure measures, blood tests, vessel ultrasound, echocardiography, self-questionnaires, spirometry and bone mineral density. Therapeutic changes for rheumatism and osteoporosis were performed during hospitalization whereas those related to cardiovascular and lung diseases were addressed to the general practitioner. Three months later, patients were called and the application of recommendation evaluated.
**Results:** 200 patients had a systematic chronic disease screening with 78.5% (n=157) of RA, 18.5% (n=37) of spondyloarthritis, and 3% (n=6) of other diseases. The mean rheumatism duration was 14±9 years, the mean age was 59±11 years. Unknown or uncontrolled hypertension was diagnosed in 20.5% (n=41); LDL above the recommended target in 63% (n=126); unknown diabetes in 3.5% (n=7) of the patients and uncontrolled diabetes in 4 of the diabetic patients (23.5%). Moreover, 7 patients had low systolic pression index (3.5%), 10 had a significant supra-aortic vessel stenosis of more than 50% (5%) and 18 had significant abnormalities in echocardiography (9%). An obstructive respiratory syndrome was found in 20 patients (10%) and sleep apnea syndrome in 78 patients (39%). An anti-osteoporosis drug was prescribed in 11% (n=22) patients. The update of the vaccinations and the neoplasia screenings were proposed for 52.5% (n=105) and 39% (n=79) patients respectively. 144 patients received physiotherapy or occupational therapy advice for the management of their rheumatologic disease (72%). At 3 months, patients declared to have followed the recommendations in 50 to 75% of the cases, the items related to rheumatology being more often applied.
**Conclusions:** A daily hospitalisation for comorbidities screening seems profitable with many abnormalities discovered in patients yet monitored regularly at hospital. The effective implementation of the proposed or prescribed measures is being assessed.
**Disclosure of Interest:** None declared
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## AB0987 RECURRENCE OF NSAID - INDUCED ULCERS: HAS THE SITUATION CHANGED IN RECENT YEARS?

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**Background:** Gastric or duodenal ulcers are one of the most common side effects of NSAIDs. These lesions are important as a cause of of life-threatening complications, such as GI-bleeding. Therefore, patients who had NSAIDs-induced ulcers in history require special control for the prophylaxis of GI-complications if they need to continue to use NSAIDs.
**Objectives:** To compare the frequency of relapses of NSAIDs-induced ulcers in patients with rheumatic diseases who had long-term use of NSAIDs during the periods of 1996–2006 and 2011–2013.
**Methods:** Group 1 (1996–2006): 407 pts (85.3% females, 52.1±13.6 y.o.), with gastric or duodenal ulcers, which developed during NSAIDs treatment; and 1640 pts (83.1% females, aged 50.1±14.6 y.o.), who didn't develop ulcer during NSAIDs intake. Group 2 (2011–2013): 82 pts (80.6% females, 58.3±12.7) with NSAIDs-induced gastric or duodenal ulcers, and 206 pts (85.1% females, 51.7±15.2 y.o.), without GI lesions during NSAIDs therapy. Patients from Group 1 used selective COX-2 inhibitors (coxibs) less in comparison to pts from Group – 4.9% vs 15.7%, as well as proton pump inhibitors (PPIs) – 14.6% vs 47.6% ($p$=0.000). All pts continued to use NSAIDs at least for one year after the first upper gastrointestinal endoscopy (UGE). All patients underwent repeated UGE after 12 months.
**Results:** Relapse of NSAID-induced ulcers were documented in 40.7% pts from Group 1, and in 28.0% pts from Group 2. Another situation was observed in patients of group 1 and 2 who did not have NSAID-induced GI lesions according data of first UGE. All of them continued to use NSAIDs $\geq$12 month and only 6.5% and 2.4% had developed ulcers according data of second UGE, respectively. PPI use significantly reduced the risk of relapsing NSAIDs-induced ulcers in Group 1 and 2: odds ratio (OR) 0.51 (95% CI 0.28–0.67) and OR 0.47 (95% CI 0.11–0.74).
**Conclusions:** Relapses of NSAID-induced ulcers still remain a serious problem. Pts with NSAID-induced ulcers in history should be protected with PPIs if they require continuation of using NSAIDs. Patients, who have not observed the development of NSAID-gastropathy with short-term NSAID therapy, have a lower risk of developing these lesions by continuing to use them for a long time.

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## AB0988 CONSUMER PERCEIVED NEEDS FOR NON-HEALTH CARE SERVICES RELATED TO OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) is a common condition worldwide, resulting in significant morbidity but with limited effective disease-modifying therapies. The challenges and disability of patients living with OA may not poorly recognised.
**Objectives:** We conducted a systematic search to identify consumer perceived needs for other services (not related to the provision of health information or health services) related to OA.
**Methods:** Medline, PsychINFO, Embase and CINAHL were searched electronically from 1990–2015 using a combination of MeSH terms and key words to capture consumer perceived needs in adults related to "other services" and "osteoarthritis". Articles were identified from the comprehensive search, with reference lists of reviews also examined. From relevant manuscripts, pertinent themes were identified and evidentiary data extracted to provide a systematic review of the current literature.
**Results:** 931 papers were identified, of which 5 investigated consumer perceived needs for other services amongst people with OA using qualitative methods (semi-structured interviews and focus groups). Participants were predominantly female 49.6–65 years, recruited from the outpatient setting. Joints involved were knee or hand.
Six key areas of perceived need emerged, identified in at least 2 manuscripts, including;
1) assistance for activities of daily living: consumers' ability to perform daily activities was limited by pain, thus requiring reliance on others and support from partners, use of gadgets and assistive devices to improve function;
2) assistance to perform exercise/leisure activities: consumers identified an inability to continue activities due to pain, becoming more sedentary;
3) facilitation of social participation: consumers identified barriers that could be overcome to improve this, including limited transport options, lack of understanding from families and community and poor profile of OA in the media;
4) financial security: cost of health-seeking behaviour and impact of reduced work;
5) occupational needs: the requirement for flexibility of scheduling and the work environment;
6) transport: was noted to be limited relating to person transport, with hand OA limiting the ability to drive and also public transport due to poor mobility.



**Conclusions:** This demonstrates the breadth of impact that OA has on daily life. This work was limited as no studies focussed on the perceived need for services, but rather on problems experienced by participants. Thus perceived needs can only be extrapolated, as they have not been directly assessed. This highlights the dearth of data pertaining to knowledge of consumer perceived needs relating to other needs required to combat difficulty in performing daily tasks and social functioning, which may often be overlooked by the health care system. A better understanding of consumer perceived needs of other services is required for the health care system and support groups to better meet consumers' needs relating to OA.
**Acknowledgement:** This work was supported by arthritis and osteoporosis Victoria. AE Wluka is the recipient of an Nhmrc career development fellowship (clinical level 2).
**Disclosure of Interest:** None declared
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## AB0989 A REVIEW OF PNEUMOCYSTIS PNEUMONIA IN RHEUMATOLOGY PATIENTS IN THE NORTHERN HEALTH & SOCIAL CARE TRUST

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**Background:** Formerly known as pneumocystis carinii and more recently pneumocystis jiroveci, pneumoncystis pneumonia is a potentially life threatening opportunistic infection that occurs in immunocompromised patients. In rheumatology our patients are immunocompromised both due to their underlying condition and drug treatments required. With advancements in available drug treatments we are becoming more aware of the need for prohalaxis and early recognition of opportunistic infection.
**Objectives:** To determine the Incidence of Pneumocystis in Rheumatology Patients within our Trust
**Methods:** A Retrospective analysis of all positive virology samples for pneumocystis in the Northern Health and Social Care Trust between February 2011-September 2015.
**Results:** 2498 samples were received from the Trust in total. 90 of these were positive for pneumocystis pneumonia. 38 were paediatric patients and 52 adults. 1 adult was not identifiable and therefore excluded, resulting in 51 positive adults. Of these 9 were primary rheumatology patients (17.6%). 6 patients had rheumatoid arthritis (4 seropositive, 1 seronegative, 1 unknown). The remaining patients had psoriatic arthritis, polymyalgia rheumatica and dermatomyositis. At the time of diagnosis all but one of the patients were on immunosuppressive medications. None of the patients had received biologic treatments. 7 of the patients were receiving oral Prednisolone or had received intra-muscular depomedrone within 4 weeks of diagnosis. 6 of the patients were receiving Prednisolone plus a DMARD (5 Methotrexate, 1 Salazaparin). One patient was receiving Methotrexate mono therapy (dose 15mg) and one patient had no active rheumatology treatment for 6 months prior to diagnosis due to recurrent infections (previously having received Leflunomide for several years). The minimum dose of oral prednisolone at time of diagnosis was 7mg, with the maximum dose being 25mg. The minimum dose of Methotrexate was 15mg with maximum dose being 22.5mg. Mortality rate for rheumatology patients was 44.4% compared to overall mortality rate of 43% for all positive patients.
**Conclusions:** Rheumatology patients are at risk of opportunistic infections and accounted for 17.6% of Pneumocystis pneumonia within our Trust. The mortality rate is high and was higher in our group of patients than the general population affected. There are currently no guidelines available to advise on prevention or prohalaxis of pneumocystis. Biologics had not been used in our cohort of patients however there is concern that with the increased availability and usage of biologics we may see an increase in incidence of opportunistic infections. This study highlights the need for more investigation and guidance on pneumocystis prohalaxis in rheumatology patients
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3737

## AB0990 RITUXIMAB IN CHRONIC AUTOIMMUNE RHEUMATIC DISEASES: SAFETY AND CLINICAL PROFILE AFTER 12 AND 24 MONTHS OF FOLLOW-UP

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**Background:** Rituximab (RTX) is a chimeric monoclonal anti-CD20 antibody. Several studies have proved its safety when used in different autoimmune chronic rheumatic diseases (ACRD). However, the real conditions of daily practice are not comparable to the ideal frame of a clinical trial.
**Objectives:** The aim of this study is to describe the profile of safety of RTX in patients with ACRD 12 and 24 months after the administration of the first cycle.
**Methods:** It is an observational retrospective study of patients diagnosed with ACRD who received treatment with RTX. Data were collected on demographic, clinical and biochemical profiles right before the first infusion, 12 and 24 months later. Other parameters were concomitant medication, prednisone dose, previous biologic treatment, accumulated RTX dose, infusion and anaphylactic reactions, infections, tumor relapses.Comparison was done using Wilcoxon non parametric test.
**Results:** Data were collected from 50 patients that received RTX. 24 months after treatment no major cytopenias or hypogammaglobulinemia were found. Hepatic and lipid profile did not show any alterations and complement levels did not experiment relevant changes. The average dose of prednisone was reduced significantly 1 year after the treatment. A decline in levels of acute phase reactants and antibodies was observed. This effect was maintained in every parameter with the exception of the rheumatoid factor; which continued presenting a downwards trend after 24 months. Concerning the infections, 3 patients were hospitalised (because of severe infections): two of them suffered from pneumonia and the other one required a surgical intervention in order to replace an infected prosthetic knee. 14 mild infections were registered: 8 mucocutaneous, 2 gastrointestinal, 2 respiratory and 2 genitourinary. There were no cases of primoinfection, reactivation of hepatic viruses or mycobacteria.

No tumoral relapses, new diagnosis of tumors or demyelinising diseases were observed. 5 patients experimented mild infusion reactions but none of them had an anaphylactic reaction or died.

| ITEMS | N=50 (%) | | |
|---|---|---|---|
| Total average dose of prednisone (Grs) ±SD (Range) | 4± 2,4 (1-8) | | |
| Infusion reactions | 5 (10) | | |
| Mild-moderate infections | 14 (28%) | | |
| Severe infections | 3 (6%) | | |
| | Basal Average ±SD | 12 Months Average ±SD | 24 Months Average ±SD |
| Leucocytes (10E3/µL) | 7,8± 3,7 | 7,0±1,8 | 7,2±2,2 |
| Hemoglobin (g/dL) | 13,1±1,7 | 13,5±1,4 | 13,5±1,6 |
| Platelets (10E3/µL) | 248,1±94,4 | 238,6±56,9 | 237,1±60,2 |
| ESR (mm/1ªhora) | 20,4±19,1 | 11,7±12,6 * | 12,8±16,7 * |
| CRP (mg/dL) | 1,3±1,7 | 1,1±3,6 * | 0,9±1,5 * |
| ALT (U/L) | 37,5±81 | 22,6±28,9 | 20,6±10,6 |
| Total Cholesterol (mg/dL) | 193,9±38,8 | 196,1±36,9 | 194,4±36,2 |
| Rheumatoid Factor (UI/mL) | 1203,3±455,1 | 1114±423,4 | 135,3±477,9 * |
| ACPA RA♥ (UI/mL) | 772,1±939,4 | 400,9±516,4 * | 539,5±781,5 * |
| AntiDNA♥ (UI/mL) | 96,8±130,9 | 30±26,8 | 90±173,7 |
| IgG (mg/dL) | 1203,3±455,1 | 1114,5±423,4 * | 1184,5±440,0 * |
| IgM (mg/dL) | 172,7±138,7 | 111,5±72,9 * | 110,7±83,1 * |
| IgA (mg/dL) | 283,9±154,2 | 269,2±148,6 * | 259,8±151,5 * |
| C3 (mg/dL) | 100,1±26,5 | 101,5±20,2 | 98,8±21,1 |
| C4 (mg/dL) | 17,3±6,7 | 21,9±19,6 | 20,1±8,9 |
| Prednisone (mg/día) | 6,7±7,5 | 3,6±3,3 * | 3,8±3,6 * |

**Conclusions:** RTX has reduced the average maintenance dose of prednisone and also lowered the levels of serum immunoglobulins (including antibodies) without inducing hypogammaglobulinemia. It has proved to be a relatively safe treatment that does not cause hematic, hepatic toxicity or deep immunosuppresion after 12 and 24 months of follow up in patients with ACRD. Further studies are needed in order to evaluate long term safety of RTX.

**References:**

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**Disclosure of Interest:** None declared

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## AB0991 DO WE REALLY KNOW WHEN WE SHOULD SCREEN FOR HEPATITIS B & C BEFORE STARTING IMMUNOSUPPRESSIVE THERAPY?

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**Background:** Established guidelines from a variety of societies are vague and do not necessarily agree about recommendations for Hepatitis B & C (Hep B/C) screening prior to initiation of immuno suppresive medications (ISM)[1].

**Objectives:** This study was designed to better understand the existing practices for Hep B/C screening among rheumatologists. There were two primary aims: a) Determination of the *actual performance measures (PM)* (i.e. screening rates prior to ISM), as well as factors significantly associated with the likelihood of screening, among rheumatology patients and b) Determination of the *self-reported PM*'s among rheumatologists for each ISM and the associated factors.

**Methods:** For actual PM's, retrospective chart review study of 200 patients seen in the rheumatology clinic was done. Data collected included demographics, total number, name and dose of ISMs currently used, and if tests (and results) for Hep B/C were ordered prior to ISM initiation. ISM use was defined as current use of any ISM including corticosteroids. We defined Significant ISM (SISM) use as a) current use of prednisone ≥7.5 mg/day with hydroxy-chloroquine (HCQ), or (b) ISM use other than only HCQ. For self-reported PM's, a survey study was designed using Survey Monkey & e-mailed to 1200 rheumatologists. Data collected included demographics, board certification, number of years out of fellowship, setting of practice, number of patients seen in a month and hours of clinical care provided per week along with Hep B/C screening prior to each ISM. Options were scaled and included the following options: routinely screened or screened only if at high risk or did not routinely screen prior to starting ISM. Chi square test was used to compare discrete variables, while t tests were used to compare continuous variables.

**Results:** *Retrospective chart study:* A total of 200 patients were included, Mean age: 40 years, 85% female; 16% were on biologics and 82% were on SISM. Actual performance measures (PM) for Hep B/C screening ranged between 28–56% prior to ISM initiation. PM's for Hep B & C prior to ISM were as follows: biologics 72% & 69%; Anti-TNF 81% & 71% and SISM 62% & 57%, respectively. Age correlated negatively whereas number of ISMs correlated positively with Hep B/C screening. *Survey study:* Survey was mailed to 1200 rheumatologists, response rate: 20% (n=251), Nearly 60% were >15 years out of fellowship, 46% practicing academics, 43% saw >80 patients/week requiring ISM, and 74% spent >20 hours/week in clinical care. Self-reported PM's were varied for routine Hep B/C screening and ranged between 8–90% prior to ISM therapy. Age & years out of fellowship correlated inversely whereas number of patients seen per month correlated positively with screening.

**Conclusions:** Actual Hep B/C screening rates are low and range from 28–56% prior to initiating any ISM. In comparison, self-reported screening rates vary from 8–90% reflecting the varied physician screening practices with regards to various ISM. There is a clear need for consistent guidelines regarding screening for hep B/C in the presence of ISM therapy, and to improve awareness among rheumatologists regarding the risks of reactivation, and the need for screening and vaccination in at-risk patients.

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**Disclosure of Interest:** None declared

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## AB0992 "I NEVER HAD THE VERBIAGE": ENGAGING CLINIC STAFF TO ADAPT A TOBACCO CESSATION E-REFERRAL PROTOCOL FOR RHEUMATOLOGY CLINICS

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**Background:** Smoking increases the severity and cardiopulmonary complications of many rheumatologic conditions. Yet despite tobacco assessment in many rheumatology clinics, we reported that <10% of eligible notes documented cessation counselling. New models show increased efficacy with Ask-Advise-Connect approaches using non-physician staff protocols. Under protocols, front-line clinic staff assessing pre-visit vital signs and tobacco use are cued to recommend and refer patients electronically to telephone tobacco quit line support. Such approaches increased uptake of cessation support 13-fold in primary care studies but have not been adapted for rheumatology clinics.

**Objectives:** Our objective was to engage clinic staff in participatory work system redesign to develop and plan implementing an Ask-Advise-Connect tobacco protocol in rheumatology clinics. We report the results of this redesign study under the Systems Engineering In Patient Safety (SEIPS) model's five work system domains: people, organization, technology, environment, and tasks.

**Methods:** Our multidisciplinary team facilitated participatory work system redesign with medical assistants (MA) and nurses (RN) from three US academic rheumatology clinics. Staff participated in one of two hour-long focus groups. Trained facilitators used semi-structured interview questions informed by the SEIPS domains to appraise pre-visit assessment workflows, educational needs, proposed protocols, brochures, electronic health record (EHR) tools, and implementation plans.

**Results:** Over 80% (9 MAs, 5 RNs) of clinic nursing staff participated in focus groups. SEIPS domain questions facilitated discussions on intervention design, implementation, and sustainability planning (Table 1). The work system redesign included training (people); a protocol and workflows adapted to specialty care (organization, tasks); customized EHR alerts for assessing tobacco status and an EHR order set for e-referral to quit line services (technology); and physical cues like a desktop patient brochure linking rheumatologic conditions, tobacco use, and cardiovascular risk (environment).

Focus group participants reported routinely assessing tobacco use, but most had not asked about readiness to quit. A few had asked such questions, but noted low outcome expectancy and not knowing what to do next. One nurse said, "I'd ask, 'Are you ready to quit?' and they'd say 'No' and then I'd stop." Staff groups identified that education about links between tobacco use and rheumatologic diseases and stepwise support from our Ask-Advise-Connect protocol would help them overcome barriers to tobacco cessation counselling. They requested specific best-practice language in the EHR tools and appreciated rheumatology-specific brochures with printed conversational prompts.

Table 1. Results of Participatory Work System Redesign (n=16 MA and nurse participants)

| Work System Components | Before Redesign | Protocol Redesign Components |
|---|---|---|
| People | Staff uncomfortable with tobacco conversations | 1-hour education and rehearsal session with trained tobacco cessation experts |
| Organization | No tobacco care follow-up procedure | Standard protocol supported by clinic staff and leadership |
| Technology | No use of reminders to assess readiness to quit; no easy way to refer to quit line | EHR alert & order set with talking points for quit line referral and electronic transmittal to/from quit line |
| Environment | No physical cues for tobacco cessation conversations | Patient brochure on tobacco cessation tailored to rheumatology clinics discussing links with diseases |
| Tasks | Assessment of tobacco use only | **Ask** about tobacco use and 30-day readiness to quit, **Advise** quit line support, and **Connect** via e-referral to quit line who will call the patient within 48 hours |
| Staff Quotes: | *"I never had the verbiage to continue... I never asked [about tobacco cessation] because I didn't know where to go from there." Medical Assistant* | *"It doesn't seem like this [protocol] would be hard to do." Medical Assistant* |

**Conclusions:** We engaged rheumatology clinic staff in participatory work system redesign to plan implementing a tobacco cessation protocol. The

participatory redesign process resulted in a tailored implementation plan for a quasi-experimental trial of a tobacco cessation e-referral protocol in rheumatology clinics.
**Disclosure of Interest:** C. Bartels Grant/research support from: Independent Grants for Learning and Change (Pfizer), A. Gilmore: None declared, D. Panyard: None declared, C. Maxcy: None declared, R. Adsit: None declared, A. Skora: None declared, E. Ramly: None declared
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## AB0993 DEPRESSIVE SYMPTOMS IN PATIENTS CONSULTING FOR THE FIRST TIME A RHEUMATOLOGY SERVICE

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**Background:** Depression can easily go unnoticed in routine clinical care. The delay in the diagnosis may increase the risk of chronicity, the number of visits, health care costs and deteriorates the quality of life.[1–3]
**Objectives:** Estimate the prevalence of depressive symptoms in patients consulting for the first time and determine if patients with depression had different reasons for consultation and highest score in the visual analog scale (VAS) of pain than patients without depression.
**Methods:** A observational, prospective study was performed. We included patients who consulted for the first time in Rheumatology Service, excluding these with psychiatric treatments and rheumatic diseases. The PHQ-9 (Patient Health Questionnaire) evaluated the presence of depressive symptoms in the last two weeks. According to the score, they were classified in 4 categories: (1) major depressive syndrome, (2) other depressive disorders, (3) positive depressive symptoms and (4) negative depressive symptoms. To perform the analysis the patients were divided into those with a depressive disorder (1 and 2) and those who did not have it (3 and 4). T-test or Mann Whitney test was used as sample size distribution for continuous variables. Chi square or Fisher exact test was used as expected frequency distribution table for categorical variables. Multivariate logistic regression analysis taking depression as the dependent variable was performed.
**Results:** 121 patients were included in the study. 86% were women, mean age of 49±15 years. The most frequent reasons for consultations were polyarthralgia (35.5%) and back pain (13%). According PHQ-9, 37% of patients were classified in major depressive syndrome and 19% in other depressive disorders. No statistically significant differences between patients with and without a depressive disorder in terms of different reasons were found. However, patients with depressive disorders were more VAS pain (7, IQR 5–8) than patients without depression (5, IQR 4–6) and more days with pain in the week (7, IQR 5–7 vs 5, IQR 3–7), both with $p<0.01$. Increased frequency of self-medication (61% vs 39%) and sleep disorders (63% vs 37%) among patients with depressive disorders was observed, although these differences were not statistically significant. In the multivariate analysis, the only variable that was found associated with depression was independently VAS pain (OR 1.33, CI 1.13–1.56).
**Conclusions:** High percentage of patients had a depressive disorder with higher frequency and pain perception. So rheumatologists should be aware of this problem in order to make a proper diagnosis, optimize the application of complementary studies, and perform a multidisciplinary approach to the patient.
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## AB0994 DETERMINANTS OF FUNCTIONAL CAPACITY IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS – A CROSS-SECTIONAL STUDY

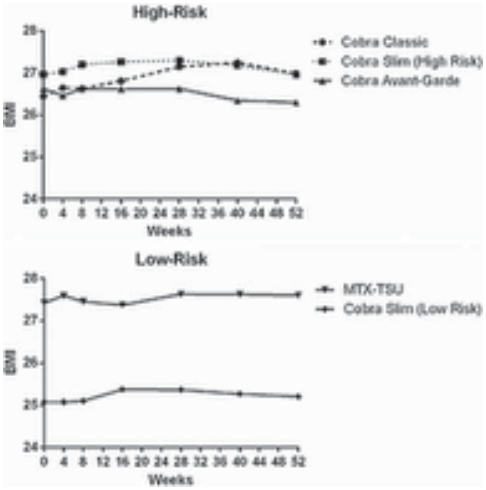
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**Background:** Impairment of functional capacity is a common problem for patients with rheumatoid arthritis (RA) with high costs for the patient and society in general. Therefore, it is important to explore its determinants.
**Objectives:** To find variables that can explain the functional capacity of patients with RA.
**Methods:** A cross-sectional study was conducted in 82 established RA patients under biological therapy from a university hospital of Portugal. The analyzed variables were: age, sex, age at disease onset, education level, disease duration, time under biological therapy, serology status, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tender and swollen joint count, DAS28, radiographs scored by the van der Heijde modified Sharp method (sSharp score), HAQ (functional capacity), EQ-5D, physical and mental health summary measure of SF36 (SF36-PSM and SF36-MSM) and pain and patient global assessment of disease activity by visual analog scale (P-VAS and PGA-VAS). Descriptive statistics were calculated for several demographic and clinical characteristics. Pearson or Spearman correlations were used for the assessment of the correlations between the different variables and the HAQ. Subsequently, multiple linear regression analysis (backward selection) was carried out using the HAQ as the dependent variable. As independent variables, were included variables that had a significant association with HAQ in the univariate analysis.
**Results:** Most of patients (87.8%) were women; mean (SD) age was 55 (±11) years. Mean age at diagnosis was 34 (±11) years with a disease duration of 21 (±9) years. Most of the patients (n=72, 86.7%) were positive for rheumatoid factor and/or anti–citrullinated protein antibodies. Mean time under biological therapy was 7 (±3) years. Mean of HAQ was 1.19 (±0.66), DAS28 3.29 (±1.13), total sSharp score 191 (±77), EQ5D median (min,max) was 0.69 (-0.35,1.00), PSM 34.93 (14.21,65.50) and MSM 52.18 (23.07,66.23). HAQ correlation coefficients (r) above 40% were observed with, in descending order, EQ5D, PSM, PGA-VAS, P-VAS, age, total sSharp, hands and total erosion scores; $p<0.001$ for all analysis. DAS28 score and age at disease onset had a weak correlation (r=0.30 and 0.34, respectively, $p<0.05$). Time under biological therapy, serology status, disease duration, joint count, ESR and CRP showed weak or no significant correlations. Multiple regression analysis identified age, sex, total sSharp score, EQ5D and PSM as determinants of physical function (r=0.73, $r^2=0.71$; $p<0.001$). Absence of collinearity among the variables included in the regression model was observed.
**Conclusions:** This study, showed that older age, female gender, quality of life and joint damage are the main determinants of functional capacity. Furthermore, our results suggest that in established disease, HAQ score measures mainly the degree of joint damage and not the disease activity.
**Disclosure of Interest:** None declared
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## AB0995 DOES BMI INCREASE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS WHEN TREATED WITH SHORT-TERM GLUCOCORTICOID REMISSION INDUCTION SCHEMES?

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**Background:** Glucocorticoids (GCs) can rapidly reduce disease activity in many chronic inflammatory diseases. Numerous adverse events have been attributed to GCs. One of the most commonly mentioned and feared side effects is an increase in weight and BMI, especially with chronic GC use. However, data remains scarce about the impact of short term glucocorticoid remission induction schemes on BMI in patients with Early RA (ERA).
**Objectives:** To explore the BMI evolution of patients with ERA treated with short term glucocorticoid remission induction schemes in the (Care in Early RA) CareRA trial.
**Methods:** The CareRA trial is a RCT comparing remission induction regimens in a treat-to-target approach. DMARD naïve ERA patients were stratified into a high- or low-risk arm based on classical prognostic markers. High-risk patients were randomized to COBRA Classic (Methotrexate (MTX) + Sulphasalazine + prednisone step-down from 60mg), COBRA Slim (MTX + prednisone step-down from 30mg) or COBRA Avant-Garde (MTX + Leflunomide + prednisone step-down from 30mg) scheme. Low-risk patients were randomized to MTX tight step-up (MTX-TSU) without oral GCs or COBRA Slim. Prednisone was tapered down over 6 weeks to 7.5mg in Classic and 5mg in the other COBRA arms. Oral GCs were discontinued from Week 28 and stopped at week 34. Demographics including BMI and disease parameters were routinely registered. For this analysis, only patients with all BMI parameters on all study visits during the first 52 treatment weeks were included. BMI change per group was tested with a paired t-test. Differences in BMI change between groups were tested with a student's t-test, Spearman's rho was used for correlation between variables of interest and BMI change. Finally, an adjusted linear regression model further explored the effect of treatment choice on BMI change.
**Results:** 281 Of 379 patients were included. Figure 1 describes the evolution of BMI over 52 weeks for the different treatment strategies. Only patients on Cobra Classic had an increase in BMI after 52 weeks ($p=0.003$). In the High-Risk arm, change in BMI over 52 treatment weeks was larger in Classic versus Slim (High-Risk) ($p<0.039$) and in Classic versus Avant-Garde ($p<0.001$). In the Low-Risk arm, no difference between groups was found. No correlations were detected between change in BMI and cumulative GC dose, DAS28(CRP) change nor HAQ change. In the High-Risk arm, linear regression revealed a statistically significant effect of treatment strategy on BMI change, even when corrected for age, gender, GC cumulative dose, DAS28(CRP) change and HAQ change ($p=0.014$). No effect of treatment strategy on BMI change was seen in the Low-risk group in a similar linear regression model.
**Conclusions:** In general, BMI changes were small with any treatment strategy. A statistically significant increase in BMI over 52 weeks was only seen with a remission induction scheme starting at a high GC dose in patients with poor prognosis ERA. No difference in BMI change over 52 weeks was seen between




a remission induction scheme starting at a moderate GC dose and a treatment strategy without oral GCs in patients with good prognosis ERA.
**Disclosure of Interest:** None declared
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## AB0996 TRANSLATION AND VALIDATION OF THE FLEMISH VERSION OF THE BRITISH DELAY QUESTIONNAIRE TO MEASURE HELP-SEEKING BEHAVIOUR IN PATIENTS WITH NEWLY ONSET RHEUMATOID ARTHRITIS

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**Background:** Delays in initiating therapy in patients with Rheumatoid Arthritis (RA) adversely affect treatment outcomes such as disease activity, functional capacity and radiographic progression. Delays can be attributed to the patient, healthcare professional and the healthcare system. In Belgium and the UK, patient-related delay was shown to contribute most to overall treatment delay. A standardized instrument for measuring patients' help-seeking behaviour after symptom onset could aid in a better understanding of patient-related delay in RA.
**Objectives:** To develop a Flemish version of the original DELAY (delays in evaluating arthritis early) questionnaire following guidelines for cross-cultural adaptation and validation in Flemish speaking patients with early RA.
**Methods:** Firstly, the British questionnaire was independently forward translated by three Flemish speaking biomedical researchers (DDC, AE, SS), all fluent in the source language. A first Flemish consensus version was drafted by these three forward-translators and a rheumatologist (PV), including adaptation to intercultural differences. Secondly, a backward translation was carried out by one independent Flemish native translator (FD), naive to RA research and with advanced English language skills. This backward translated version was compared to the original questionnaire and discrepancies were discussed with the backward-translator, a forward translator (DDC) and a rheumatologist (PV) before drafting a new Flemish consensus version. This second draft was evaluated for clarity and comprehensibility by a group of five expert patients with RA and by a group of 6 healthcare professionals of our RA team, resulting in a pre-final Flemish version. Subsequently, for internal validation of the pre-final version, we randomly selected five Flemish patients with RA from the University Hospitals Leuven. After having read the questionnaire, these patients were individually inquired by DDC, and their comments were addressed in a final Flemish version of the questionnaire. External validation was performed by doing a test re-test evaluation in a consecutive sample of Flemish patients with early RA. Internal consistency and reproducibility were measured by Cronbach's alpha and the intra-class correlation coefficient (ICC), respectively.
**Results:** For the external validation, 32 patients were invited to participate. The questionnaire was completed twice within 2 weeks by 26 patients. The Flemish DELAY questionnaire showed satisfactory internal consistency (Cronbach's alpha, 0.95). Also reproducibility was satisfactory (ICC, 0.86).
**Conclusions:** The standardized translation and validation process preserved the content, construct validity and reproducibility of the original DELAY questionnaire and resulted in a valid version for mapping patient-related delay in Flemish patients with early RA.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5484

## AB0997 DAY CARE HOSPITAL PATIENT ATTENDANCE CIRCUIT IN RHEUMATOLOGY: INTRODUCTION OF A NURSE CONSULTATION

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**Background:** Day care hospital (DCH) in rheumatology attends patients who need intravenous (IV) treatments, mainly biological therapy (BT), and other proceedings that cannot be made in the clinic but don't require hospitalization.The administration of BT demands a security monitoring prior to the administration that is made usually by the rheumatologist, which involves clinic overloading. The introduction of a protocolized nurse consultation (PNC)with the application of a security check-list would reduce the number of consultations without risks for the patient.
**Objectives:** To analyze the number of consultations and events registered after the introduction of a PNC in rheumatology DCH
**Methods:** Introduction of PNC in DCH with modification of the patient circuit from april 2015 in patients who receive BT as usual therapy (infliximab, abatacept, golimumab and tocilizumab). After the first consultation the patient is alternatively directed to the PNC (even consults) where the nurse applies the security check-list, provides the BT following the protocol, gives the activity questionnaires and records events, and the medical consultation (odds consults) where the rheumatologist carries out the anamnesis, physical examination, blood analysis and complementary tests review and treatment modifications. Retrospective review of patients, proceedings, consultations and events registered at DCH of Rheumatology over 2015 in a tertiary hospital after the introduction of a PNC in April 2015. Statistical analysis was made with SAS System for windows,v 9.2.
**Results:** Over 2015, 116 patients were attended in DCH: 49 rheumatoid arthritis (42,2%), 29 spondilytis (25,1%), 16 connective diseases (13,8%), 8 vasculitis (6,9%), 10 psoriastic arthritis (8,6%) and 4 juvenile arthritis (3,4%). Usual TB treatment received was: infliximab in 59, tocilizumab in 48, abatacept in 6 and golimumab in 3 patients. Over the period January- March/ April-December the following treatments were received: infliximab 72/ 214, tocilizumab 80/ 189, abatacept 8/ 36, and golimumab 3/ 21. 819 consultations were made: 610 medical (74,48%) (203 January-March and 407 April-December) and 209 nursery (25,52%) (April–December). 22 events were registered in the PNC (10,5%) that required telephone consultation with the rheumatologist: 6 common cold, 5 fever, 3 chills, 1 urinary disturbance, 2 dental removal, 2 arthritis, 1 skin eruption, 1 hypoglycemia, 1 peripheral edema), and five of them forced to the interruption of the treatment (2 urinary tract infections and 3 respiratory infections), giving the patient a new date in the medical consultation, without relevant secondary effects or complications for the patient.
**Conclusions:** The introduction of a Protocolized Nurse Consultation in Day Care Hospital in Rheumatology allows reduction in medical consultations number without relevant events in treatment administration or risks for the patient.
**Disclosure of Interest:** None declared
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## AB0998 EVALUATION OF THE EFFECTIVENESS OF JOINT STATUS SELF-ASSESSMENT BY PATIENTS WITH RHEUMATOID ARTHRITIS

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**Objectives:** The cooperation in the "doctor-patient" pair is necessary to implement the TREAT TO TARGET conception in the management of rheumatoid arthritis (RA). For greater adherence to treatment, self–control of the disease activity is important for a patient. We have created an original method of training RA patients to self-assess the count of swollen and tender joints correctly. The objective of the research was to study the effectiveness of the method of training patients to self-assess the RA activity.
**Methods:** The study included 96 patients with the definite diagnosis of RA, according to the ACR/EULAR 2010 diagnostic criteria (88 females; 8 males, mean age 58,1 (51,0; 65,0), the median duration of RA was 8,3 (2,0; 11,5). During the first visit patients were trained using the original method of Disease Activity Self-Assessment (the physician demonstrated the technique of self-assessment of swollen and tender joints and provided the patient with printed guidelines and photos). During the second and third visits with one-month interval, there was an independent control of swollen and tender joint count by a physician and a patient. Statistical significance was analyzed using the McNemar's test.
**Results:** Absolute coincidence of the number of tender joints as assessed in parallel by a physician and a patient was observed in 35 cases during the second visit and in 62 (p=0,01) cases during the third visit. Absolute coincidence of the number of swollen joints as assessed in parallel by a physician and a patient was observed in 43 cases during the second visit and in 65 (p=0,01) cases during the third visit.
**Conclusions:** Our original method of Disease Activity Self-Assessment allows training most patients with RA to assess swollen and tender joints. This is

important for self-control of the diseases activity and allows a patent to visit a physician for timely therapy correction.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3367

## AB0999 DEVELOPMENT OF AN ACTIVITY DISEASE SCORE IN PATIENTS WITH UVEITIS (UVEDAI)

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**Background:** Uveitis is defined as inflammation of the uvea. As standardized and validated outcome measures are lacking in uveitis management.
**Objectives:** To develop a disease activity score for patients with uveitis and determine its discriminating ability to classify patients based on the level of activity.
**Methods:** Multicenter cross-sectional observational study. The construct "uveitis inflammation activity" was defined as intraocular inflammation. Seven dimensions and 14 items were identified and were agreed upon by experts via a two-round Delphi technique. Patients diagnosed with uveitis, who were aged five years or older and who presented inflammatory activity at the time of their visit, were selected. An ordinal logistic regression model was built in which the dependent variable was uveitis inflammatory activity (mild, moderate, or severe). Modeling accuracy for patient classification was assessed by the Area Under the Curve (AUC). Two AUC measures were calculated: one for discriminating mild versus moderate and severe activity level of uveitis, and another for mild and moderate versus severe activity.
**Results:** 195 patients were included. The regression model revealed an associations between intraocular activity level and an elevated number of anterior chamber cells ($OR_{4\ cells\ vs\ 0\ cells}$ = 27.85; 95% CI: 3.42; 226.75), a high degree of vitreous haze ($OR_{severe\ vs\ null}$ = 3.95; 95% CI: 1.40; 11.16), macular edema over 315mm ($OR_{>315\ vs\ \leq 315}$ = 3.58; 95% CI: 1.56; 8.21), inflammatory vessel sheathing (OR=4.43; 95% CI: 1.71; 11.53), higher patient evaluation scores ($OR_{1\text{-}unit\ increase}$ = 1.23; 95% CI: 1.09; 1.39), the presence of papilitis (OR=4.05; 95% CI: 1.18; 13.92) and increased numbers of choroidal or retinal lesions ($OR_{>6\ vs\ 0}$ =4.99; 95% CI =1.08; 23.01). The discriminatory capacity of UVEDAI was 87% for differentiating patients with mild uveitis from those with moderate or severe uveitis, and 88% for discriminating patients with mild or moderate uveitis versus those with severe uveitis.
**Conclusions:** UVEDAI assesses and classifies patients depending on global ocular inflammatory activity with high discriminative capacity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2014

## AB1000 EVALUATION OF THE PRESENCE AND FREQUENCY OF NEUROPATHIC PAIN COMPONENT IN MYOFASCIAL PAIN SYNDROME

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**Background:** Neuropathic Pain Component in Myofascial Pain Syndrome is very imoprtant in the grups of aged between 20–50 years which is neck or upper back region. It was evalueyted by using specific diagnostic crtiteria, visual analog scale (VAS) and Neck Pain and Disability Index (NPDI)
**Objectives:** The aim of this study was to determine the presence and incidence of neuropathic pain in myofascial pain syndrome (MPS) and to detect factors that may be related to neuropathic pain
**Methods:** 112 patients with MPS in their neck or upper back region (aged between 20–50 years) and 62 age, gender and body mass index matched, healthy controls were included in the study. The existence of MPS was evaluated using specific diagnostic crtiteria. Pain assessment was made by visual analog scale (VAS). Neck Pain and Disability Index (NPDI) was used for the evaluation of the disability depends on neck and upper back pain. The existence of neuropathic pain component in both trigger point and referred pain regions was assessed with Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), painDETECT and Douleur Neuropathique 4 (DN4) questionnaires.
**Results:** Mean ages of the patients with MPS was 33.4±8.0 years and controls was 33.5±8.4 years ($p>0.05$). The mean VAS score for pain and the mean NPDI values were significantly higher in the patients group (5.9±1.0 and 35.7±28.3, respectively, $p<0.001$). Neuropathic pain component was identified at both trigger points and referred pain areas in the patients group. Neuropathic component in the trigger point area was detected in 19 of 112 patients (17%) using DN4, in 4 patients (3.6%) using LANSS and in 2 patients (1.8%) using painDETECT scales. On the other hand; DN4, LANSS and painDETECT scales showed positive results for neuropathic component at 33 (% 29.5), 14 (% 12.5) and 12 (%10.7) of 112 patients in referred pain areas, respectively. Significant correlations were found between the higher values of NPDI and VAS with DN4, LANSS and painDETECT values in patiens with MPS.
**Conclusions:** In this study, the existence of neuropathic component was determined in both trigger point and referred pain regions of patients with MPS. Neuropathic component was more prominent in the referred pain area. Central pain mechanisms may be responsible for this result. Further studies with more patients are needed to confirm our results. We think that, it is important to consider neuropathic component in the treatment of MPS.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5990

## AB1001 ONLINE CONSULTATION FOR CHINESE PATIENTS WITH RHEUMATIC DISEASES BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS: A STUDY OF MEDICAL ECONOMICS

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**Background:** China has no primary medical care and referral system. Patients can choose any hospitals or any doctors they like to seek medical care in China. As a result, most patients with rheumatic diseases rushed to a few large cities. Survey shows more than 40% of the rheumatic disease patients don't need to go to hospital and they only need advices from specialist.
Smart System of Disease Management (SSDM) is a series of applications for chronic diseases management, which develop the interaction between doctors and patients. The study shows that, after training, the RA patients can master the SSDM and perform self-management, including DAS28 and HAQ evaluations, as well as medication and lab test data entries.
**Objectives:** To evaluate the feasibility and benefit of the medical economics of online consultation based on SSDM by rheumatologist.
**Methods:** The rheumatologists implemented the education and training programs on using SSDM and assist the patients in downloading SSDM APP.
The SSDM includes doctors' application and patients' application. The patient application includes self-assessment (DAS28, HAQ), medication management, adverse events management and laboratory records. After data entry, patients can synchronize data to the authorized doctor. On the basis of understanding of the disease activities, medication and laboratory test results, the rheumatologists can accept consultation request from their patients, and practice consultation in the form of text or telephone call.
**Results:** Between February 14, 2015 and January 24, 2016, 11 rheumatologists supplied 76 patients with 58 times free and 45 paid consultations. Paid

Table 1: Detailed online consultation information with Smart System of Disease Management (SSDM).

| Doctors | Numbers of patients | Numbers of consultation | Actual payment (¥) | Projected direct cost (¥) | Projected indirect cost (¥) | Total projected cost (¥) | Saved (¥) | Saved (%) |
|---|---|---|---|---|---|---|---|---|
| Doctor FC Zhang | 18 | 29 | 9,300 | 9,300 | 46,700 | 56,000 | 46,700 | 83.39 |
| Doctor XY Liu | 23 | 24 | 800 | 4,800 | 34,100 | 38,900 | 38,100 | 97.94 |
| Doctor H Wei | 2 | 5 | 1,000 | 1,000 | 5,500 | 6,500 | 5,500 | 84.62 |
| Doctor HQ Zhou | 6 | 6 | 300 | 1,300 | 8,400 | 9,700 | 9,400 | 96.91 |
| Doctor MZ Wang | 1 | 2 | 200 | 200 | 1,300 | 1,500 | 1,300 | 86.67 |
| Doctor YH Jiang | 1 | 2 | 150 | 150 | 2,800 | 2,950 | 2,800 | 94.92 |
| Doctor R Mu | 1 | 1 | 300 | 300 | 2,800 | 3,100 | 2,800 | 90.32 |
| Doctor Y Zhang | 1 | 1 | 200 | 200 | 1,300 | 1,500 | 1,300 | 86.70 |
| Doctor ZJ Li | 18 | 26 | 0 | 5,200 | 25,800 | 31,000 | 31,000 | 100.00 |
| Doctor YH Huang | 4 | 6 | 0 | 1,800 | 7,000 | 8,800 | 8,800 | 100.00 |
| Doctor Y Wang | 1 | 1 | 0 | 200 | 300 | 500 | 500 | 100.00 |
| Totally | 76 | 103 | 12,250 | 24,450 | 136,000 | 160,450 | 148,200 | 92.37 |

consultations included 34 times text Q&A and 11 telephone consultations. The consulting fee ranged from RMB 50 to 500 yuan (EUR: RMB =1:7.1) each in average of 272.22 ±90.40 yuan, which is approximate to the registration fee in hospital. The total amount of consultation fee was 12,250 yuan.
87% patients receiving online consultation lived in different city with the rheumatologists. If patients seek medical care in hospital, in addition to the registration fees and medical expenses, the mean cost of transportation, accommodation, meals and lost wages was 1320.39±456.10 (300 - 2,800) yuan. The total of cost for all patients would have been 160,450 yuan, which is 13.10 times compared with the cost of online. Through the SSDM system for online consultations, patients can save 92.37% of the cost. Table 1 shows detailed information. Survey shows all patients were satisfied and 64.86% of them were "very satisfied" with the consultations.
**Conclusions:** Using SSDM system to obtain online consultation, Chinese patients with rheumatic disease can enjoy reduced cost with high satisfaction. In the era lack of primary care system in China, SSDM may serve as a complimentary platform to control medical care cost, as well as relieve the tensions between health care professionals and patients.
**Disclosure of Interest:** None declared
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## AB1002 DETERMINANTS OF QUALITY OF LIFE, LABOR-MARKET STATUS AND HEALTHCARE UTILIZATION IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Ankylosing Spondylitis (AS) typically affects young people, leading to progressive deterioration of physical function and quality of life (QoL) with higher use of healthcare services. Work disability and early retirement is also higher in AS patients than in the general population, with a remarkable negative impact on productivity and social costs.
**Objectives:** The objectives of this study were to assess the gradient of AS severity, measured by several well-established scores, for QoL, labour-market status and healthcare services demand, in a group of AS patients.
**Methods:** We collected cross-sectional data in patients under 65 years, concerning demographic characteristics, disease duration, time to diagnosis, BASDAI, BASFI, BASMI, SF-36, ASQoL, EQ-5D and evaluated the ASDAS. The number of appointments and emergency room visits during the year before and working status in active ages people, were also collected. To measure the gradient of AS on QoL scores, healthcare use and working status, regression models, with application of stepwise procedure for removal of statistically non-significant effects, were performed.
**Results:** A total of 369 patients were included (62.3% men and 37.1% women), with a mean age of 45.4±13.2 years (range 20–79 years). For SF-36 and ASQoL, only BASDAI and BASFI scores matter and both mean higher value associated with lower health and it seems that a one point increase in one score is roughly equal to one point increase in the other score. The same conclusion holds for EQ5D. The only difference lies with the group of patients with 7–12 years of schooling, who have higher utility score than the others. The probability of being employed is negatively related to age and to BASMI. Only the BASFI is positively associated with the number of medical appointments. Age and ASDAS are the only determinants of emergency rooms visits.
**Conclusions:** BASDAI and BASFAI, which are modifiable scores, are negatively associated with utility/ QoL scores. Age and BASMI (no modifiable scores) are negatively associated with being employed. In addition, earlier or later disease detection, have no influence on these gradients. Accuracy of therapy intervention has a pivotal role on impacts, more than a precise time in detection.
**Disclosure of Interest:** None declared
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## AB1003 VALIDATION OF LAY DESCRIPTIONS OF LEVELS OF SEVERITY OF KNEE AND HIP OA IN THE KHOALA COHORT STUDY

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**Background:** Estimating the proportion of the population with severe OA is of use in health service planning. To calculate the proportion of the population with mild, moderate or severe OA, the Global Burden of Disease 2010 Study (GBD2010) used published WOMAC scores. From this, the proportion of the population in high income countries with mild OA was estimated as 71%, moderate 27% and severe 2%.
Lay descriptions of levels of severity of OA were developed for GBD2010. If these are accurate measures of disease severity, these descriptions would be useful additions to population-based health questionnaires or brief assessments in clinical practice.
**Objectives:** To validate lay descriptions of mild, moderate and severe OA and determine the proportion of a cohort within each category.
**Methods:** Descriptions were presented to the KHOALA cohort comprising 878 OA knee and hip prevalent cases recruited as a representative sample of French patients with clinical and radiographic OA. Participants were asked to indicate which description they felt best described their condition. An additional level of "No pain or disability" was added for this cohort.
Mild OA was described as "Has pain in the leg, which causes some difficulty running, walking long distances, and getting up and down"
Moderate OA: "Has moderate pain in the leg, which makes the person limp, and causes some difficulty walking, standing, lifting and carrying heavy things, getting up and down and sleeping"
Severe OA: "Has severe pain in the leg, which makes the person limp and causes a lot of difficulty walking, standing, lifting and carrying heavy things, getting up and down, and sleeping"
Participants also completed WOMAC, EQ5D, EUROQOL VAS and walking times.
**Results:** Currently, 307 participants have completed the questionnaire with results shown below.

Table 1

| | No pain/ Difficulty Mean (sd) | Mild Mean (sd) | Moderate Mean (sd) | Severe Mean (sd) | P value |
|---|---|---|---|---|---|
| n | 49 | 135 | 80 | 43 | |
| % of total | 16.0 | 44.0 | 26.1 | 14.0 | |
| Age | 63.3 (7.1) | 60.5 (8.1) | 62.1 (8.7) | 61.3 (8.0) | |
| WOMAC Pain [0–20] | 3.0 (2.3) | 5.2 (2.6) | 7.5 (2.9) | 11.0 (2.9) | <0.0001 |
| WOMAC Function [0–68] | 11.4 (8.8) | 16.8 (9.4) | 25.1 (12.3) | 36.9 (9.3) | <0.0001 |
| EQ5D [0,1] | 0.9 (0.1) | 0.8 (0.2) | 0.7 (0.2) | 0.4 (0.3) | <0.0001 |
| EUROQOL VAS [0,100] | 76.2 (12.1) | 72.8 (15.1) | 63.8 (15.0) | 52.7 (14.9) | <0.0001 |
| Walking time | 90.9 (53.3) | 95.7 (84.9) | 55.5 (47.7) | 19.1 (12.1) | <0.0001 |

There was a significant trend for the WOMAC, EQ5D, EUROQOL and Maximal walking time to decline as self-reported level of severity moved from none through mild and moderate to severe. The lay descriptions show significant convergent and divergent validity with the standardized measures used.
**Conclusions:** These preliminary results suggest that the lay descriptions are understandable by participants in this cohort. Those who rated their condition as consistent with the severe description also scored worse on the measures of pain and function.
14% classified themselves as having severe OA, in contrast to GBD2010, where only 2% were classified as having severe OA. The burden of OA may in fact be greater than reported in GBD2010 as the proportion of the population living with more severe disease may have been underestimated.
Further assessment is being undertaken with a larger sample of the KHOALA cohort. These lay descriptions may be useful as a brief starting point for discussions in clinical care, or a contribution to the assessment of severity of OA.
**Disclosure of Interest:** None declared
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## AB1004 SOURCES OF INFORMATION USED BY PATIENTS WITH RHEUMATIC DISEASES TREATED WITH SUBCUTANEOUS BIOLOGICAL THERAPY. RHEU-LIFE SURVEY

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**Background:** Adequate information to patients on disease and therapies is important to improve lifestyle, adherence to treatments and outcomes.
**Objectives:** To describe which are the main sources of information for patients with rheumatic diseases treated with subcutaneous (SC) biological drugs, which ones they consider relevant, and their satisfaction with the information received from the clinical team.
**Methods:** RHEU-LIFE was a survey to patients >18 years with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis treated with SC biological drugs, from 50 rheumatology outpatient clinics from Spain. The patients completed the survey anonymously at home. They selected from a list: 1) their sources of general information on disease (multiple choice), 2) the most important (one option), 3) who had informed them about the treatment alternatives (multiple choice) and 4) about the SC biological drug (multiple choice).
**Results:** The survey was given to 1000 patients, 592 responded (59.2%, mean age 51.7 years [SD 13.2], 42.4% men, 57.6% women). The main source of general information on disease was the rheumatologist (92.3%). Other sources mentioned were the primary care physician (21.7%), nurses (19.3%), medical websites (19.8%) or health related blogs (5.6%), brochures for patients (11.5%), friends or relatives (6.3%), patient associations (4.4%) or other patients (3.1%) and pharmacists (3.4%). Information about treatment options and the SC biological drug came mainly from the rheumatologist (>90%) and infrequently

from nurses or hospital pharmacists (Table). 46.1% mentioned having received only oral information, 6.0% only written and 45.2% both ways. Some 44.5% and 42.6% reported to be "very satisfied" and "satisfied" with the information received respectively, 10.6% "neither satisfied nor dissatisfied" and 2.1% and 0.2% "dissatisfied" or "very dissatisfied". 45.2% alleged to search for information about the biological treatment in sources other than the hospital clinical staff.

Sources of information mentioned by patients (multiple choice)

| | General info about treatment (%) | Specific info about the biologic drug (%) |
|---|---|---|
| Rheumatologist | 91.9 | 91.0 |
| Nurses | 10.2 | 17.9 |
| Hospital pharmacy | 3.2 | 11.5 |
| Others | 5.3 | 3.6 |
| Does not remember | 1.2 | 0.8 |
| No information received | 0.8 | 1.7 |

**Conclusions:** The rheumatologist is the main source of information for patients on SC biological drugs. Nurses and hospital pharmacists are seldom mentioned, even though being very often visited for drug dispensing. Satisfaction with the information received is high, however nearly half said to have searched for information on the biological drug in alternative sources.
**Acknowledgement:** This survey was financed by Merck Sharp & Dohme of Spain and endorsed by the patient's association ConArtritis (Arthritis National Coordinator).
**Disclosure of Interest:** None declared
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## AB1005 MULTIPLE MODELING METHODS OF ADMINISTRATIVE DATA YIELD CONSISTENT RESULTS BUT LIMITED ABILITY TO PREDICT RHEUMATOID ARTHRITIS DISEASE ACTIVITY IN US VETERANS

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**Background:** Epidemiologic research would be significantly enhanced if accurate and reliable methods were available to assess rheumatoid arthritis (RA) disease activity using administrative data. The VA rheumatoid arthritis (VARA) registry is a prospective observational cohort that collects RA disease activity including the 28 joint count disease activity score (DAS28) and clinical disease activity index (CDAI). VA administrative data are available and can be employed to develop models to estimate RA disease activity measured by DAS28 and CDAI.
**Objectives:** 1. Use administrative data to develop models that predict disease activity.
2. Assess the accuracy of the model under different conditions including defining administrative variables as continuous (CON) and/or categorical (CAT) and stratifying by different disease durations.
3. Describe the accuracy of the models for predicting disease activity for both DAS28 and CDAI.
**Methods:** US Veterans with RA enrolled in the VARA registry without cancer, organ transplantation, or other autoimmune diseases were included in the model if they were enrolled in VA with one year of administrative data available before the first DAS28. We identified 1,275 administrative data elements with suspected association with disease activity for prediction modeling. The least absolute shrinkage and selection operator (LASSO) was used for variable selection and model development. A series of LASSO models were developed that varied the input variables. Variables were required to have $\geq$1% prevalence in the cohort to be included in model selection. Sub-analysis was also performed in patients with $\leq$2 years and $\leq$5 years of disease duration.
**Results:** There were 1,582 US Veterans with RA who fulfilled enrollment criteria. The average age was 62.7±11.0 years, 91% male, with a disease duration 13.7±12.1 years with 78% and 74% seropositive for rheumatoid factor and anti-CCP antibodies respectively. The adjusted r-square for the six models tested ranged from 0.20–0.24 for DAS28 and 0.17 to 0.24 for CDAI. When stratified by disease duration, the r-square associations for patients with and without $\leq$2 and $\leq$5 years of RA duration were 0.29–0.31 versus 0.22–0.27 for DAS28 and CDAI respectively.
**Conclusions:** The multiple models tested yielded very similar results with limited association of predicted disease activity with actual measured disease activity by DAS28 and CDAI in VARA. The use of CON versus CAT variables, multiple definitions for disease activity, and limitation of disease duration to early RA did drastically affect prediction accuracy. Future research should investigate additional strategies to collect components of disease activity measures directly from medical records.
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## AB1006 ANTI-CITRULLINATED PEPTIDE ANTIBODIES AND RHEUMATOID FACTOR TESTING PATTERNS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN THE US

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**Background:** Serological markers have been investigated for the identification of RA. Current diagnostic criteria recommend conducting tests for anti-citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF) prior to reaching the RA diagnosis. However, there is a lack of information about how these tests are utilized in a managed care setting.
**Objectives:** To describe the frequency of ACPA/RF tests at the time of RA diagnosis and at follow-up, as well as to compare baseline characteristics between patients who received ACPA/RF tests and those who did not.
**Methods:** A cohort study was conducted using adult patients newly diagnosed with RA within a US integrated healthcare delivery system from 1 January 2007 to 31 December 2014. Individuals were followed from their first RA diagnosis (index date) until 30 June 2015. Patients were required to have two ICD-9 codes of 714.x, treatment with a DMARD, and continuous eligibility for 12 months prior to the index date (baseline period). At baseline, data were collected on co-morbid conditions, laboratory test results and dispensed medications. Descriptive statistics and multivariable logistic regression analyses were conducted to describe ACPA/RF testing patterns and to investigate baseline patient characteristics associated with ACPA/RF testing.
**Results:** A total of 7444 patients with newly diagnosed RA were identified. Mean (SD) age was 55.6 (15.0) years, 75% were female, 69% of patients received corticosteroid treatment and 22% had other autoimmune diseases at baseline. Overall, 83% had both ACPA and RF tests at baseline while 10% and 2% had only an RF or an ACPA test, respectively. Baseline ACPA and RF testing rates were increased over time ($p<0.001$) and both ACPA and RF testing rates were >90% from 2012 onwards (Table). At baseline, 34% of patients had positive ACPA and RF test results, 30% had negative ACPA and RF results, 6% had only ACPA-positive and 21% had only RF-positive results. During follow-up, 20% of patients repeated their ACPA tests; 11% had a repeat test within 1 year of baseline. Patients with a higher Elixhauser index (odds ratio [OR]=0.72, 95% CI 0.62, 0.95) were less likely to receive ACPA tests at baseline, whereas patients receiving NSAIDs (OR=1.45, 95% CI 1.25, 1.69) or corticosteroids (OR=1.23, 95% CI 1.07, 1.43) were more likely to receive baseline ACPA tests. Patients who had other autoimmune conditions were more likely to repeat their ACPA tests during follow-up.

Table 1. Baseline ACPA and RF testing rates by index year

| Index year | New RA patients, total N | Baseline ACPA test, N (%) | Baseline RF test, N (%) |
|---|---|---|---|
| 2007 | 1095 | 740 (67.6) | 919 (83.9) |
| 2008 | 926 | 703 (75.9) | 856 (92.4) |
| 2009 | 921 | 782 (84.9) | 870 (94.4) |
| 2010 | 914 | 796 (87.1) | 870 (95.2) |
| 2011 | 885 | 812 (91.8) | 856 (96.7) |
| 2012 | 921 | 847 (92.0) | 880 (95.5) |
| 2013 | 919 | 841 (91.5) | 876 (95.3) |
| 2014 | 863 | 829 (96.1) | 833 (96.5) |
| Total | 7444 | 6350 (85.3) | 6960 (93.5) |

**Conclusions:** ACPA and RF testing rates in patients with RA have increased over time, with 96% of patients with newly diagnosed RA receiving both tests at the time of RA diagnosis in 2014. However, there may be still discrepancies in testing based on co-morbidities and medications. The reasons why RF or ACPA tests were not conducted in some patients with RA remain to be identified.

**Abstract AB1005** – Table 1

| Variables included in the model | | DAS 28 (n=1,582) Numbers of variables | | | Adjusted r-square | CDAI (n=1,563) Numbers of variables | | | Adjusted r-square |
|---|---|---|---|---|---|---|---|---|---|
| | | Total | >1% prevalence | Final inclusion | | Total | >1% prevalence | Final inclusion | |
| All variables | CON + CAT | 1275 | 567 | 45 | 0.22 | 1275 | 565 | 54 | 0.21 |
| | CON only | 966 | 420 | 30 | 0.20 | 966 | 418 | 21 | 0.17 |
| | CAT only | 966 | 420 | 39 | 0.22 | 966 | 418 | 56 | 0.22 |
| Only clinical variables | CON + CAT | 253 | 175 | 32 | 0.22 | 253 | 173 | 71 | 0.24 |
| | CON only | 217 | 149 | 27 | 0.22 | 217 | 147 | 65 | 0.24 |
| | CAT only | 217 | 149 | 27 | 0.22 | 217 | 147 | 66 | 0.23 |

CON = continuous, CAT = categorical.

**References:**
[1] Aletaha D, et al. Ann Rheum Dis 2010;69:1580–8.
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## AB1007 RECURRENT INFECTION AFTER BIOLOGICALS IN AUTOIMMUNE DISEASE: PRELIMINARY RESULTS WITH MUCOSAL VACCINES RECURRENT INFECTION AFTER BIOLOGICALS IN AUTOIMMUNE DISEASE: PRELIMINARY RESULTS WITH MUCOSAL VACCINES

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**Background:** Over a decade has passed since the introduction of biologic therapies for autoimmune diseases.
The use of biologic therapies as an adjuvant to disease-modifying anti-rheumatic drugs (DMARDs) for the treatment of systemic autoimmune diseases is rapidly expanding, due the efficacy and safety profiles of these drugs, and the better understanding of the targets of altered immune regulation. However, infections complications after biologicals are major concerns in their use.
**Objectives:** The aim of this study is to evaluate the clinical benefit of new personalized polybacterial sublingual vaccines in patients with systemic autoimmune disease and recurrent infections.
**Methods:** An observational study in a cohort of patients with systemic autoimmune disease and recurrent respiratory tract infections (RRTI) (3 or more episodes of upper respiratory tract infection or at least 1 pneumonia episode per year) and recurrent urinary tract infections (RUTI) (3 or more UTIs per year) was carried out. All patients underwent immunization with sublingual polyvalent preparation (Bactek®, ImmunoteK S.L. Madrid, Spain) for RRTI (*Staphylococcus spp., S. pneumoniae, K. pneumoniae, B. catarrhalis, H. influenzae*) and RUTI (*K. pneumonia, E. coli, E. faecalis, P. vulgaris*). Immunological evaluation was performed at baseline and at 6- and 12-mo., including serum immunoglobulins, IgG subclasses, specific antibodies production and B and T cell subsets counts.
**Results:** Twenty-three patients (mean age, 55.52±15.69, 21 women and 2 men) were studied: rheumatoid arthritis (RA) (n=11, 47%), SLE (n=5, 22%), MCTD (n=3, 13%), psoriatic arthritis (n=1, 4.%), SLE/RA (n=1, 4%), DLE/Sjögren (n=1, 4%), cryoglobulinemia II (n=1, 4%) and Sjögren syndrome (n=1, 4%). All patients presented a decrease in RRTI and RUTI frequency at 6-mo of vaccine: RRTI decreased from 4.81±2.04 to 0.75±1.29 and RUTI from 4.56±1.59 to 0.22±0.44. An episode of pneumonia in two patients. Nine out of 23 patients (39%) showed alterations of the humoral immune response at baseline: hypogammaglobulinemia (n=6, 26%) and IgG2 subclass deficiency (n=3, 13%). Eleven of 23 (47%) disclosed a defect on specific antibody production to polysaccharide and protein stimuli, 7 (30%) with normal Ig serum levels and 5 (21%) with hypogammaglobulinemia. At baseline, 21 were on DMARDs (metotrexate in 12, 52%). The most used biologicals were anti-TNF-α monoclonal antibodies (n=9, 39%) followed by anti-CD20 (n=8, 34%) and tocilizumab (n=4, 17%).
**Conclusions:** Vaccination in immunosuppressed patients with systemic autoimmune disease and recurrent infections is a commonly missed opportunity. There is an urgent need to develop alternative strategies to prevent the overuse of antibiotics in what is called the post-antibiotic era. Our preliminary results seem to be promising in these patients, reducing the infections rates, avoiding chronic use of antibiotics and subsequent resistance and adverse effects.
**Disclosure of Interest:** None declared
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## AB1008 PREVALENCE OF FIBROMYALGIA IN INFLAMMATORY RHEUMATIC DISEASE. SINGLE-CENTER CROSS-SECTIONAL STUDY IN 691 PATIENTS

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**Background:** Fibromyalgia (FM) is a prevalent syndrome in patients with inflammatory rheumatic disease.
**Objectives:** The purpose of this study was to evaluate and compare the prevalence of FM in various inflammatory rheumatic diseases.
**Methods:** This single-center cross-sectional study was conducted between September 2014 and April 2015. We screened for clinical signs of fibromyalgia in all patients presenting for rheumatoid arthritis (RA), spondyloarthritis (SpA), and connective tissue disease (Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), scleroderma (Scl), myositis). Diagnosis of FM was based on ACR–90 classification criteria (to minimize interfering overlap between rheumatic disease-related pain and FM-related pain) and expert opinion.
**Results:** In total, 691 patients were included in the study: 325 RA, 298 SpA (59 psoriatic arthritis, 137 radiographic axial SpA, 64 non-radiographic axial SpA, 38 peripheral SpA), 28 SLE, 27 SS, 14 Scl, and 6 myositis. The population counted 451 women (65.3%) and 240 men (34.7%). Mean all-population age was 55.8±15.5 years. Median disease duration was 11 years [IQR 5–20]. In the total population, 55 patients (8%) met the ACR–90 criteria, and 97 patients (14%) were given a diagnosis of FM by the expert doctor. Prevalence of FM meeting ACR–90 criteria was 4.9% in RA, 11.1% in SpA, and 11.3% in connective tissue disease, and was significantly higher in the SpA group than in the RA group ($p$=0.05). The expert settled on a diagnosis of FM for 7.7% of patients with RA, 17.5% of patients with SpA, and 28.2% of patients with connective tissue disease. The expert diagnosed significantly more FM in SpA ($p$=0.003) and connective tissue disease ($p$=0.001) than in RA.
**Conclusions:** Concomitant fibromyalgia is prevalent in inflammatory rheumatic disease, especially in spondyloarthritis and connective tissue disease. The expert doctor makes the diagnosis of fibromyalgia more often than ACR–90 criteria.
**Disclosure of Interest:** None declared
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## AB1009 AN EPIDEMIOLOGICAL STUDY OF THE PREVALENCE RATE OF IBP AND AXIAL SPA IN THE UNIVERSITY IN THE SOUTH OF CHINA

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**Background:** In China, there is little research supply the data of the prevalence rate of IBP and axial spondyloarthritis (axial SpA). However, IBP and axial spondyloarthritis were common in China, so it is important to get the data about them.
**Objectives:** Inflammatory back pain (IBP) is an important clinical features for ankylosing spondylitis and axial spondyloarthritis. We conducted an epidemiological study in a university detect prevalence rate of IBP and axial SpA.
**Methods:** 3770 students from South China Agricultural University were enrolled in our study. We investigate the patients information by questionnaires face to face. We collected patients' parameters including the parameters for diagnosis of IBP criteria (ASAS), which include onset age, insidious onset, improvement with exercise, no improvement with rest and pain at night. We also collected the parameters for diagnosis of axial spondyloarthritis criteria (ASAS). To assess prevalence rate of IBP and axial spondyloarthritis.
**Results:** (1) Data of the 3770 students enrolled were shown as follows: mean age was 19.48±2.80 years; female to male ratio was 1.45:1 (2229/1541). (1) 731 students (19.39%) had back pain. In these students, female to male ratio was 1.97:1 (485/246). (2) In patients who had the back pain, 111 (15.18%) students had IBP. In other word, in all students who involved in, 2.94% of them had Inflammatory back pain IBP. (3) After investigation, we found 333 students had received the HLA-B27 examination. 19 (5.71%) students were positive. And 13 students (3.90%) of them who had result of HLA-B27 were diagnosed as axial SpA. Based on the data, the prevalence rate of back pain and IBP was 19.39% and 2.94%, respectively. The prevalence rate of axial SpA were 3.90%. (4) Although more female students than male ones had back pain, more male than female ones were diagnosed as axial SpA (Back pain: Female/Male: 485/246, Axial SpA:Female/Male:4/9; P=0.014).

Table 1. The number of students with back pain, IBP and axial SpA in this study

| | Back pain | IBP | axial SpA |
|---|---|---|---|
| Female n (%) | 485 (66.35) | 61 (54.95) | 4 (30.77) |
| Male n (%) | 246 (33.65) | 50 (45.05) | 9 (69.23) |
| Totle | 731 | 111 | 13 |

**Conclusions:** In the south of China, the prevalence rate of back pain and IBP was 19.39% and 2.94% in university respectively, and the prevalence rate of axial SpA were 3.90%. Although more female students than male ones had back pain, male ones were more likely to suffer from axial SpA.
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## AB1010 ACHIEVEMENT OF NICE QUALITY STANDARDS FOR PATIENTS WITH NEW PRESENTATION OF INFLAMMATORY ARTHRITIS: RESULTS FROM THE UK NATIONAL CLINICAL AUDIT FOR RHEUMATOID AND EARLY INFLAMMATORY ARTHRITIS

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**Background:** The national audit office reported variation in the quality of services for patients with Inflammatory Arthritis (IA) in the UK in 2009. The Health Quality Improvement Partnership funded a national audit to explore this further.
**Objectives:** We set out to assesses whether trusts in England & Wales are achieving the 7 quality standards (QS) published by the National Institute for Health & Care Excellence (NICE).
**Methods:** All individuals >16 years presenting to specialist rheumatology services in England & Wales with suspected new onset IA were recruited. Clinician & patient derived data were collected against all NICE QS over the 1st 3 months of specialist care.
**Results:** 6,354 patients were recruited nationally from 1 February 2014 to 31 January 2015. 94% of trusts/health submitted data. Patients were predominantly female (66%); white British (79%); and of working age (70%). At recruitment 46% had a diagnosis of Rheumatoid Arthritis (RA); 16% undifferentiated inflammatory arthritis (EIA).
Only 17% of patients were referred by their general practitioner (GP) within 3 days of first presentation (QS1); median time interval 34 days. Over 25% waited >3 months. 12% of referrals had no indication that EIA was suspected.
Specialist assessment occurred <3 weeks of referral for 38% (QS2). The median time interval was 4 weeks, >25% of patients waited >7 weeks. Higher staffing levels (>1 consultant/100,000 population) & the presence of EIA clinics were associated with shorter waiting times (odds ratio (95%CI) 1.3 (1.1–1.4) & 1.6 (1.4–1.7) respectively).
Disease modifying anti-rheumatic drug (DMARD) initiation within 6 weeks of referral (QS3) was achieved in 53% of RA patients; 36% were treated with combination DMARDs & 82% with steroids.
Clinicians reported that 59% of patients received structured education (QS4). Treat to target plans were set for 91% of patients. These targets were achieved in only 27% (QS5). Almost all trusts reported access to urgent advice (QS6) & incorporated annual review services (QS7).
**Conclusions:** This audit has enabled English & Welsh rheumatology services to measure their performance against NICE QS for the early management of IA & RA, benchmarked to regional & national comparators for the first time. The findings clearly demonstrate where improvement is needed. Delays in referral from primary care as well as delays in offering a first appointment in secondary care have been identified as key barriers to effective early arthritis care.
**Disclosure of Interest:** None declared
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## AB1011 VITAMIN D STATUS – A TRANSVERSAL EVALUATION IN RHEUMATIC PATIENTS

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**Background:** Vitamin D deficiency is a condition reported both in young adults and in elderly and institutionalized patients. It has been increasingly recognized and, although conflicting data subsists, hypovitaminosis D has been related to a variety of rheumatic conditions from osteoporosis (OP) to inflammatory diseases and generalized pain syndromes.
**Objectives:** To assess vitamin D status in a rheumatic outpatient setting.
**Methods:** Observational, transversal, retrospective study encompassing rheumatic outpatients with at least one 25-hidroxyvitamin D determination since 2014. Data ascertained included gender, age, parathyroid hormone (PTH) and vitamin D levels, rheumatic conditions (<3/patient), co morbidities and therapeutics. Bone mineral density was assessed by densitometry (DXA) and results classified as normal (Tscore >-1), osteopenia (-2.5<Tscore<-1) and osteoporosis (Tscore<-2.5). Statistics: Mann-Whitney, Kruskal-Wallis, ANOVA and Chi-Squared tests and Pearson's correlation; $p<0.05$. Software: SPSS 17.
**Results:** 370 patients included, 87.3% female, mean age 64.9±13.9 years (y), 151 patients <65y. Most prevalent rheumatic conditions: osteoarthritis (OA; 47.8%), OP (43.5% - 33.5% of which with reported fractures), fibromyalgia (FM; 14.6%) and rheumatoid arthritis (RA; 13.2%); 43.9% patients had inflammatory diseases. Most common co morbidities: arterial hypertension (38.6%), dyslipidemia (32.4%) and depression (22.9%). 38.4% were on synthetic Disease Modifying Anti-Rheumatic Drugs (DMARD); 34.1% on corticosteroids (CTC), 49.2% on bisphosphonates (BF) and 69.5% on calcium/vitamin D (Ca/D) supplements. As for patients with available DXA, 41.4% were classified as having osteopenia and 43.6% as having osteoporosis. Mean vitamin D was 29.7±24.5μg/L; 65.4% patients had vitamin D levels <30μg/L. Mean PTH was 56.6±31.3ng/L and alkaline phosphatase (ALP) was 73.8±31.8U/L. In the group >65y, mean PTH was higher than in the <65y group (61.3±33.6 vs 49.7±26.1, p=0.015); 70.9% of the patients <65y and 61.6% of the patients >65y had vitamin D<30 – not significant. We compared vitamin D in OP vs OP with fractures vs OA vs associated OP/OA and found lower vitamin D levels in patients with isolated OA (38.7±32.5 vs 38.1±33.9 vs 25.9±23.3 vs 30.6±20.7, p=0.012); 76.6% with isolated OA had vitamin D<30. 55.7% of the patients on BF >5y, 61.2% on BF <5y and 72.3% without BF had vitamin D<30 (p=0.013). 68.7% in the group with inflammatory conditions and 62.9% in the group with non-inflammatory conditions had vitamin D <30 – not significant. We further compared vitamin D levels in OA vs AR, AR vs FM and OA vs FM, DMARD and CTC use and Ca/D supplementation and found no difference. There was a positive correlation between age and vitamin D (r=0.111, p=0.033), age and PTH (r=0.208, p=0.010) and vitamin D and ALP levels (r=0.311, p<0.0001).
**Conclusions:** In this study, vitamin D levels <30μg/L were found in nearly 2/3 of patients, across disease groups. There was a tendency for higher vitamin D levels in elderly patients, in the group with OP comparing with OA and in the group on BF, which may be related to previous supplementation. A potential bias is the fact rheumatologists request vitamin D dosing in patients with risk factors/clinical features of hypovitaminosis.
**Disclosure of Interest:** None declared
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## AB1012 KNOWLEDGE AND USE OF DERIVATION PATHWAYS FROM PRIMARY HEALTH CARE TO ONSET ARTHRITIS OUTPATIENT CLINICS. IMPROVEMENT STRATEGIES

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**Background:** Among the factors that allow early diagnosis of recent-onset arthritis, there is the implementation of preferential derivation pathways from Primary Health Care (PHC). For 18 months, the Rheumatology unit from Health Area North of Cadiz (HANC) provides these routes (WEB/FAX) with criteria agreed with PHC. We analyze the opinion of primary care physicians on the need for early diagnosis of arthritis, degree of knowledge and use of these tools by PHC and collect proposals for improving the accessibility of these patients to our unit.
**Objectives:** To analyze the level of knowledge and use of the preferential derivation pathways from primary care physicians to onset arthritis outpatient clinics; assess the satisfaction of the response received from the doctor and the importance of early diagnosis of rheumatoid arthritis for primary care physicians and collect proposals for improvement.
**Methods:** Sharing a survey to primary care physicians from HANC serving 411,000 habitants. Demographics of respondents, uptime in the public health system, number of patients seen per day, % estimated of musculoeskeletal pathology patients treated per day, importance of early diagnosis of rheumatoid arthritis and motives, level of knowledge of preferential derivation pathways collected by FAX/WEB, degree of utilization of these pathways, assessment and utility response received and proposals for improvement. A descriptive analysis of the sample is performed.
**Results:** A total of 77 surveys from 13 Health Centers from HANC were analyzed. The 62.34% were men and 66.1% older than 50 years; 62% of respondents has worked in the public health system over 20 years. 88.3% (68) professionals attend over 40 patients/day and 40.2% (31) of respondents reported that 20–30% of consultations were musculoskeletal cause. 96.1% (74) of respondents gave importance to the early detection of arthritis, the main reason to avoid joint damage and improvement in quality of life (84.4%) and the establishment of an early treatment (79.2%). 87.01% (67) was unaware of the preferential derivation pathways through the web and 38.9% (30) knew via FAX. Only 19 doctors (24.6%) respondents acknowledged having used the pathway in the past 6 months; 17 of them (22.08%) considered appropriate response received. 97.4% of respondents considered helpful the existence of these preferential derivation pathways. Between strategies for improvement, 81.2% (63) propose conducting training and outreach campaigns, 88.31% (68) raises the need for training sessions and 79.2% (61) considered necessary conducting face consultations in health centers.
**Conclusions:** A high percentage of primary care physicians surveyed recognize the importance of early diagnosis of recent-onset arthritis. Despite having preferential derivation pathways, there is a high degree of ignorance and low utilization of them. However, professionals who use them regard the response perceived as adequate. Most respondents believe that conducting training, outreach and onsite consulting and improvement strategies for early diagnosis of arthritis onset are necessary.
**Disclosure of Interest:** None declared
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## AB1013 SYSTEMATIC REVIEW OF PATIENT PERCEIVED HEALTH SERVICE NEEDS IN INFLAMMATORY ARTHRITIS

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**Background:** The inflammatory arthritides (IA) are a heterogeneous group of diseases which cause significant morbidity and mortality. Optimising patient engagement to provide patient-centred care are important in improving outcomes in IA. Although individual aspects of patient preferences and satisfaction relating to health services have been previously examined, few studies have directly investigated people with IAs perceived needs of health service needs.
**Objectives:** The aim of this review was to systematically identify the existing literature relating to patient perceived health service needs related to IA, including use of allied health (AH) and complementary and alternative medicines (CAM).
**Methods:** A systematic literature review of MEDLINE, EMBASE, CINAHL and PsycINFO was conducted (1990 – May 2015). Using a comprehensive search strategy, studies examining patient perceived needs relating to health service needs relating to inflammatory arthritis was performed. Data regarding study design and methodology were extracted. Needs were identified and collated to show the current knowledge of this issue.
**Results:** The search strategy returned 1778 papers of which 24 articles were identified as relevant (figure 1): 14 used qualitative methods, 9 used quantitative methods and 1 used mixed methods. 16 studies included only patients with rheumatoid arthritis (RA). The quality of the included literature was variable.
The main areas of need, identified in at least 2 studies, related to
1) Communication needs: consumers wanted clear, empathic communication and to be involved with decision making. Positive relationships with health care providers with an holistic approach were prized.
2) Characteristics of ongoing care: adequate consultation length with continuity and timely care were valued.
3) Factors influencing care seeking behaviour: an individual's attitude towards health care, and disease activity and severity affected care seeking behaviour. Financial factors and family expectations, influence and beliefs were also seen to impact on the perception of need.
4) AH and CAM were perceived as useful by many. CAM was seen as an adjunct to conventional therapy, especially where pain control was inadequate. The reporting of CAM use to their doctors was variable, with several factors related for under-reporting.




**Conclusions:** Within the existing literature that has infrequently targeted patient perceived health services needs, this review identified factors that patients with IA perceive to be important in their management. It also identified gaps in this area of knowledge, such as patient preferences for alternative methods of health care delivery, information from non-European and North American countries and information about patients with IA other than RA. Increasing knowledge regarding patient perceived needs in this area has the potential to inform novel methods of health care provision which could improve patient satisfaction whilst optimising outcomes for both the patient and health care system.
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## AB1014 COMPARISON BETWEEN ARASHI SCORE AND MODIFIED TOTAL SHARP SCORE IN THE EVALUATION OF LARGE JOINTS DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER DISEASE CONTROL OF BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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**Background:** Treatment of rheumatoid arthritis (RA) has improved over the past decade with the modification of treatment strategy and recent application of biologic agents (Bio). It has been revealed that the treatment by Bio achieved not only improvement of clinical symptom, but also inhibition of the progression of joint destruction in small joints of hand and foot. However, there are little evidences of inhibition of the progression of the large joint destruction with the treatment by Bio.
ARASHI score, is composed of ARASHI Status Score (ASS) and ARASHI Change Score (ACS), and have been newly developed to evaluate the progression of the large joint destruction as well as remodeling[1)]
**Objectives:** We aimed to investigate the correlation among the ARASHI score, modified total sharp score (mTSS), and other clinical parameters, and to clarify the patients' parameters leading to large joint destructions in patients with RA under disease control by Bio.
**Methods:** 75 patients with RA under disease control by Bio were available for the current study. Average patients' age, disease duration, and follow-up periods were 62.6 (years old), 11.7 (year), and 21.8 (month), respectively. They were examined for serum level of C-reactive protein (CRP), mHAQ, DAS28-CRP, SDAI, CDAI, mTSS, and ASS at the beginning of the study. The amount of change of CRP, mHAQ, DAS28-CRP, SDAI, CDAI, and mTSS at the final follow-up were defined as ΔCRP, ΔmHAQ, ΔDAS28-CRP, ΔSDAI, ΔCDAI, and ΔmTSS, respectively. Statistical analysis was performed by Spearman's correlation co-efficient.
**Results:** Average ΔCRP, ΔmHAQ, ΔDAS28-CRP, ΔSDAI, ΔCDAI, ΔmTSS, and ACS were 0.01, -0.02, -0.28, -2.62, -2.64, and 0.03, respectively. There was no significant correlation between the ACS and ΔmTSS. There were no significant correlations between ΔmTSS and other clinical parameters, whereas ACS was significantly correlated with ΔCRP (r=0.39), ΔmHAQ (r=0.28), ΔDAS28-CRP (r=0.39), ΔSDAI (r=0.35), and ΔCDAI (r=0.32).
**Conclusions:** The correlation between the destruction of small joints of hands and feet and the disease activity was not seen among the current patients group with long-standing disease. In contrast, our results suggested that sufficient suppression of the disease activity is important to prevent the progression of large joint destruction among long-standing RA patients under control by Bio.
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**Disclosure of Interest:** None declared
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## AB1015 MORTALITY RATE ACCORDING TO CAUSE IN PATIENTS WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: A META-ANALYSIS

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**Background:** Hemophagocytic lymphohistiocytosis (HLH) is a rare syndrome of excessive immune activation associated with high mortality. Early diagnosis and treatment can reduce mortality among these patients.
**Objectives:** To determine the rate of mortality independently and according to the cause in patients with HLH.
**Methods:** Pubmed database with the MeSH terms ("lymphohistiocytosis, hemophagocytic" [MeSH Terms] OR ("lymphohistiocytosis" [All Fields] AND "hemophagocytic" [All Fields]) OR "hemophagocytic lymphohistiocytosis" [All Fields] OR ("hemophagocytic" [All Fields] AND "lymphohistiocytosis" [All Fields])) AND cases [All Fields] were queried which yielded 466 results. Case series referenced from these studies were also studied. 74 studies were identified out of which the studies with a sample size smaller than 10 were excluded. 48 studies were kept with a total of 1983 patients. Meta analysis was performed to combine the mortality rates of all studies and studies of patients with the same cause. The results were presented in a Forest plot. Prior to the meta analysis, the heterogeneity test on mortalities was conducted to choose a fixed or random effects model. $I^2$, a common heterogeneity measure, was reported with 25%, 50%, 75% suggesting low, moderate, and high heterogeneity.
**Results:** The combined mortality rate for all studies was 41.99% [95% confidence interval (CI) 36%>49%]. In studies of patients with EBV infection (n=4), the combined mortality rate was 44% (95% CI 18%>74%) whereas the mortality rate in studies with other infections (n=4) was 46% (95% CI 13–83%). The

mortality rate in patients with hematological malignancy (n=8) was higher at 60% (95% CI 44%>74%]. For studies of patients with autoimmune diseases (n=2) and in transplant (n=4) patients, the combined mortality rate was 11% (95% CI 5%>21%) in patients with autoimmune disease and 38% (95% CI 27%>51%) in transplant patients. $I^2$ for the mortalities of all studies and each cause was presented as follows: $I^2$=0% (p=0.764) for autoimmune disease, $I^2$=94.8% [89.6%; 97.4%] (p<0.0001) for EBV infection, $I^2$=75.2% [50%; 87.7%] (p=0.0002) for hematological malignancy, $I^2$=75.2% [50%; 87.7%] (p=0.0002) for infection malignancy, $I^2$=89.2% [75.1%; 95.3%] (p<0.0001) for other infection, and $I^2$=0% [0%; 52.1%] (p=0.811) for transplant. The heterogeneity test result remained significant but for the causes of autoimmune disease and transplant.
**Conclusions:** Based on our results, mortality is higher in patients with hematological malignancy compared to patients with other causes, whereas it is lower in patients with autoimmune disease.
**Disclosure of Interest:** None declared
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## AB1016 THE CHANGE OF PREVALENCE OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS IN KOREA BETWEEN 2011 AND 2014

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**Background:** Rheumatoid arthritis (RA) and Osteoarthritis (OA) are common arthritis in adults, and leading causes of disability. Estimating the prevalence of RA and OA is important for planning health care and public health systems. In South Korea, the Korean National Health Insurance (NHI) database has the medial and prescription claims data for most of Korean people. We evaluated the change of prevalence of RA and OA using NHI database between 2011 and 2014.
**Objectives:** The purpose of this study is to evaluate the prevalence and annual direct medical costs of rheumatoid arthritis and osteoarthritis in Korea.
**Methods:** We used data provided by Korean Health Insurance Research and Assessment agency. Identification of patients with RA and OA was based by main diagnostic code in database. The prevalence of RA and OA was evaluated in adults aged 20 years or older from 2011 to 2014. Annual direct medical costs per patient were also calculated.
**Results:** The prevalence of RA was decreased from 0.74% at 2011 to 0.68% at 2014. On the other hand, that of OA was increased from 7.96% at 2011 to 8.75% at 2014. Annual direct medical costs per patient tended to increase in both RA and OA, but rate of increase was greater in RA. In OA, annual direct medical costs were $226.86 at 2011, and increased up to $239.95 (105.8%). In RA, those were $209.95 at 2011, and increased up to $319.19 (152.0%).

Table 1. The change of prevalence and annual direct medical cost per patient of rheumatoid arthritis and osteoarthritis

| | | 2011 | 2012 | 2013 | 2014 |
|---|---|---|---|---|---|
| Prevalence (%) | RA | 0.74 | 0.72 | 0.69 | 0.68 |
| | OA | 7.96 | 8.31 | 8.33 | 8.75 |
| Annual direct medical cost per patient (USD) | RA | 209.95 | 238.69 | 277.26 | 319.19 |
| | OA | 226.86 | 232.92 | 235.35 | 239.95 |

**Conclusions:** The prevalence of RA was decreased, but that of OA was increased in Korea between 2011 and 2014. Annual direct medical costs per patient increased in both RA and OA, but rate of increase was greater in RA.
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## AB1017 RHEUMATOID ARTHRITIS IN GREECE: PATIENT JOURNEY, ACCESS TO TREATMENT BARRIERS AND THEIR IMPACT TO ADHERENCE

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**Background:** Early active treatment of rheumatoid arthritis (RA) by a rheumatologist and adherence to the prescribed drugs are crucial factors for inducing remission and preventing irreversible joint damage[1,2]. However, Greece's fiscal situation has inevitably impacted the healthcare sector by raising barriers to patient access to treatment and medication and limits to patient and doctor education[3]. Hence, identifying obstacles/adherence issues and attempting to overcome them is essential to improving RA care.
**Objectives:** The objectives of this national patient study were to record: a) the patient journey from the 1st symptom until official diagnosis and the physician specialties that were visited, b) the potential barriers in access to treatment and medicines and c) the possible adherence issues for patients suffering from RA in Greece.
**Methods:** An innovative research method was followed, using a structured questionnaire. Using a stratified sampling methodology, 1,030,000 randomly selected households were contacted over the telephone, via an Interactive Voice Response (IVR) system asking them to participate in the survey concerning auto-immune diseases. Eventually, 1,422 households agreed to do so and were subsequently interviewed by a telephone researcher. The achieved response rate is well above previous studies and scientifically accepted standrads[4].
**Results:** 557 RA patients were identified (90% women, median age 56–65 years), making RA the most prevalent rheumatic autoimmune disease (44% of sample). The average time needed from the 1st symptom until an official diagnosis is 23.3 months. Only 31% of RA patients visited a rheumatologist first and 10% have to make 3 or more visits until they are officially diagnosed. 43% of them did not receive any medicine and of those receiving, 34% were non-adherent during the last six months (at least 1 day late to take the medicine or skipping at least 1 dose). 28% of biological treatment patients were non-adherent. The physician's visit cost was the main barrier to treatment access (31%), followed by the need to use someone else to pick the medicine due to patients' inability (18%) and by the difficulty of booking an appointment with a specialist (15%). For SSF pharmacies the distance from the patient's home (31%) plus a long waiting time (17%) were additional barriers. $\chi^2$ tests revealed that most barriers exerted a statistically significant influence on adherence (p<0.05).
**Conclusions:** Appropriately educating the public and the doctors about RA's symptoms and to visit the appropriate physician, and removing the barriers to treatment and medication access will massively benefit RA patients and consequently society.
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**Disclosure of Interest:** None declared
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## AB1018 DOES FATIGUE IMPROVE IN A SIMILAR MANNER TO PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH A BIOLOGIC? A REANALYSIS OF RANDOMIZED CONTROLLED TRIALS OF ABATACEPT IN 1536 PATIENTS WITH ACTIVE RA

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**Background:** Fatigue is a major issue for patients (pts) with RA. Biologic DMARDs including abatacept (ABA) have shown efficacy in improving fatigue in randomized controlled trials (RCTs),[1–3] but questions remain.
**Objectives:** We explored the effects of ABA on fatigue versus on pain in RA.
**Methods:** This was a *post hoc* analysis of 3 RCTs of ABA in RA: AIM[1] and ATTAIN[2] in established RA, and AGREE3 in early RA. Pts were randomized to ABA versus placebo (pbo), with concomitant MTX in both treatment arms in most cases. Fatigue and pain were assessed by visual analogue scales (VAS, 0–10 cm) at baseline (BL), Days 29, 85 and 169; mean changes from BL were analysed using an ANCOVA model with treatment as a factor and BL value as a covariate. Associations between fatigue VAS score and pain score were evaluated using Pearson correlation coefficients at BL and Days 29, 85 and 169. Agreement of reporting minimum clinically important differences (MCID; improvement of ≥10 mm from BL to 169 day) for fatigue and pain was evaluated using Kappa coefficients, MCID was cross-tabulated for fatigue and pain. Data from each trial were analysed separately.

**Results:** Data were available for 1536 pts (women: 78–79%, mean age: 50–53 years across RCTs). Mean disease duration was 8.5–12.2 years (AIM and ATTAIN) and 6.2–6.7 months (AGREE). ABA was efficacious relieving fatigue, with mean relative decreases from BL to day 169 of 30–44%. Benefit on fatigue was reported early, decreasing by 18–24% at Day 29, indicating that ~50% of the mean decrease in fatigue was already achieved by this time point. Results were consistent across RCTs, although the effect of ABA on fatigue was greater in pts with shorter versus longer disease duration. ABA also significantly reduced pain: mean decreases were 29–49% across trials. There was an association between treatment effects on fatigue and pain: Pearson correlation coefficients were 0.69–0.72 at Day 169. Agreement between MCID improvements in pain and fatigue were, however, moderate: kappas ranged from 0.30–0.51 across RCTs and time points. Cross-tabulation indicated most pts who reported improvements ≥MCID in fatigue also did so in pain (795/903 pts; 88.0%), and vice versa (795/1004 pts; 79.2%) at Day 169.

**Conclusions:** ABA led to a rapid improvement in both fatigue and pain in pts with active RA. However, agreement between clinically meaningful improvements in these outcomes was only moderate, suggesting that the pathways of fatigue and pain in RA represent different domains of response. Fatigue should be further studied in RA.

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**Disclosure of Interest:** L. Gossec Grant/research support from: UCB France, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer, Roche, UCB, S. Ahdjoudj Employee of: Bristol-Myers Squibb, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, V. Strand Consultant for: AbbVie, Alder, Amgen Corporation, AstraZeneca, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Crescendo/Myriad Genetics, EMD Serono, Genentech/Roche, GlaxoSmithKline, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, UCB

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## AB1019 IS THE SELF-ASSESSMENT OF DISEASE ACTIVITY (AUTO-DAS28) BY PATIENTS A FEASIBLE AND ACCEPTABLE MEASURE OVER THE LONG TERM IN RHEUMATOID ARTHRITIS (RA)? THREE-YEAR FOLLOW-UP OF A NURSE-LED PROGRAM IN 771 PATIENTS WITH ESTABLISHED RA

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**Background:** Patients with RA can be trained in self-assessment of disease activity by a self-assessment of their joints and calculation of the Disease activity Score 28 (DAS28) [1].

**Objectives:** To assess if such an auto-DAS assessment is a feasible measure over the long-term (i.e., do patients adhere to such an assessment) and to determine the characteristics of patients related to adherence to auto-DAS.

**Methods:** This was an open long term (2–4 years) extension of the 6 month randomized controlled COMEDRA trial of patients with definite, stable RA. Patients were trained to perform auto-DAS by a nurse, using a video and teaching of self-assessment of joints (the training took approximately 30 minutes) and nurses provided the advice to perform the auto-DAS regularly in a dedicated booklet. 2–4 years after the end of the trial, patients were seen in a face-to-face interview with a nurse and the frequency of auto-DAS was assessed through the auto-DAS booklet and if unavailable, from patient questioning. Adherence to auto-DAS was defined as the performance of at least one auto-DAS more than 6 months after the end of the trial. Characteristics of adherent versus non adherent patients were compared by univariate and multivariate logistic regression analyses and included demographic and disease activity variables as well as the centre (high versus low inclusion rate, based on the median).

**Results:** Of the 970 recruited patients, 771 (79.5%) were followed up at 3 years and had available data regarding auto-DAS: mean (±standard deviation) age 61 (±11) years, median [IQR] disease duration 15 [9 - 23] years; 615 (80%) were women and 82% had received a biologic. The mean (±sd) baseline and 3-year DAS28 scores were respectively 3.1±1.3 and 2.8±1.4.

After 3 years, 354 (46%) patients were adherent to auto-DAS (i.e., had at least one auto-DAS completed more than 6 months after the end of the trial). For adherent patients the median [IQR] number of auto-DAS performed was 5.4 [1.7 – 12.8] overall, i.e. 2.3 [0.8 – 5.9] per year. However among the adherent population, the number of patients who completed their autoDAS booklet at least once per year decreased over time, with 351 (99%), 162 (46%) and 118 (33%) patients respectively for 2012, 2013 and 2014 ($p<0.0001$).

In the multivariate analysis, only larger inclusion centres were significantly associated to an adherent behaviour (OR [95% CI] 2.9 [2.0 – 4.1], $p<0.0001$).

**Conclusions:** After a short training, many of these long-standing, moderately active RA patients continued to perform an auto-DAS, though the performance of auto-DAS decreased over time in this cohort where patients did not receive any ongoing positive feedback on their auto-DAS. In the larger inclusions centres, autoDAS adherence was higher, perhaps related to more patient/physician interaction around autoDAS results.

Self-assessment of disease activity is feasible in RA but positive reinforcement appears necessary. Further studies should analyse if outcomes are better for patients who self-assess.

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**Disclosure of Interest:** None declared

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## AB1020 HIGH PREVALENCE OF BF% OBESITY IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

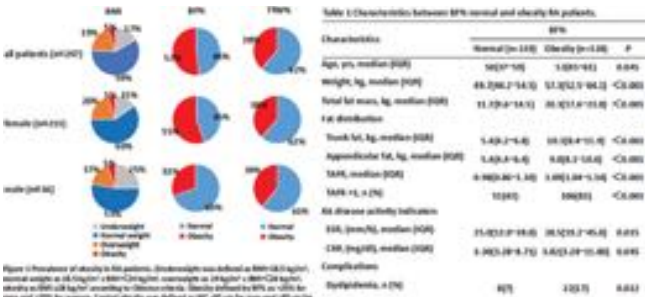
J.-Z. Lin[1], Y.-B. Chen[2], X.-T. Lin[2], J.-D. Ma[1], Y.-Q. Mo[1], X.-Y. Wang[1], L. Dai[1].
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**Background:** There is about 14%–19% lipid of weight in normal people and most of the lipid stores in fat cells that can secrete adipokines to promote inflammation, which may exacerbate rheumatoid arthritis (RA) synovial inflammation, rise severity of clinical feature, disable functional capacity and reduce quality of life. A worldwide study in 15 countries (mainly in Europe and the United States) identified 18% of RA patients as obese defined by body mass index (BMI ≥30 kg/m$^2$), while higher prevalence of 25% in a USA-based study and 31% in a UK–based study were reported. However, little is known about the prevalence of obesity in Chinese RA patients.

**Objectives:** To investigate the prevalence and character of obesity in Chinese RA patients.

**Methods:** Two hundred and forty–seven consecutive RA patients were assessed BMI, waist circumference (WC), waist–to–hip ratio (WHR) and waist–to–height ratio (WHtR). Clinical data including RA disease activity, physical function and complications were collected. Body fat percentage (BF%) was assessed by bioelectric impedance and obesity by BF% was defined as >25% for men and >30% for women.

**Results:** (1) According to Chinese criteria of BMI, there were 19% patients with overweight and 5% with obesity. According to BF%, there was 52% patients with obesity and female RA patients had significantly higher prevalence of obesity than male patients (55% vs 31%, P=0.006, Figure 1). (2) Weight, total fat mass and trunk–to–appendicular fat ratio (TAFR) were significantly higher in BF% obesity patients than normal ones (all $P<0.05$). The percentages of patients whose fat distributed mainly in trunk rather than appendicular extremities (TAFR >1) was also higher in BF% obesity patients than normal ones (83% vs 43%, $P<0.001$, Table 1). (3) According to WC, WHR and WHtR, there were 33%, 41% and 42% patients with central obesity respectively. The trunk-fat-to-weight percentage (TfW%) was significantly higher in central obesity patients (according to WC in Chinese criteria) than that in normal WC patients (female: 18.7% (16.6%–19.8%) vs 13.6% (11.0%–15.7%); male: 15.0% (12.4%–18.3%) vs 7.4% (3.8%–10.6%), both $P<0.001$). ROC curve analysis showed that the cut–off value of the TfW% for diagnosing central obesity was 11.8% in men with sensitivity 91.7% and specificity 87.5% and 16.3% in women with sensitivity 81.2% and specificity 83.1% (male: AUC=0.941, 95%CI: 0.868–1.0; female: AUC=0.865, 95%CI: 0.811–0.919, both $P<0.001$). There were 95 (38%) patients with central obesity according to the cut–off value of the TfW% (female 38% and male 39%, Figure 1). (4) Comparing with normal BF% patients, BF% obesity patients were older with higher disease activity indicators (ESR and CRP) and had more complications such as dyslipidemia and fat liver (all $P<0.05$, Table 1).



**Conclusions:** This cross–sectional study suggests that high prevalence of BF% obesity in Chinese RA patients especially in female patients which might be associated with disease activity.

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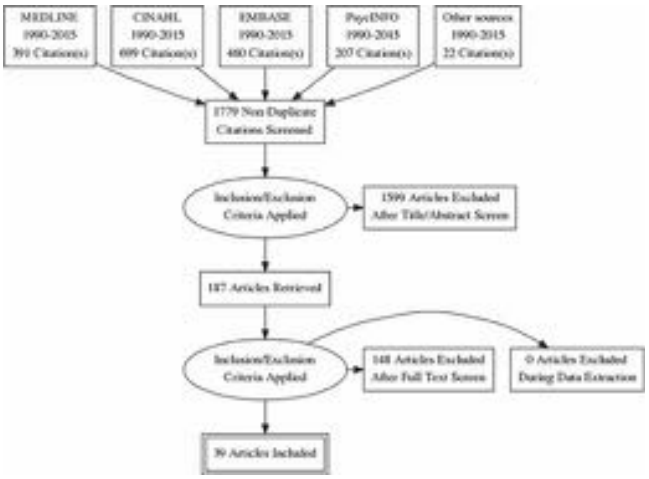
**Disclosure of Interest:** None declared

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## AB1021 SYSTEMATIC REVIEW OF LOW BACK PAIN CONSUMERS' PERCEIVED NEEDS OF ALLIED HEALTH AND COMPLEMENTARY AND ALTERNATIVE THERAPIES

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**Background:** Low back pain (LBP), a major public health problem, is the leading cause of disability worldwide (1). Current management recommendations include medical, psychological and physical treatments, complementary and alternative medicines (2,3). Initiatives to improve the management of LBP have been largely based on outcomes determined by health professionals. The relative success and requirement for health care interventions may differ from the patient's perspective.
**Objectives:** To systematically review the literature about consumer perceived needs of allied health and complementary and alternative therapies (CAM) relating to LBP.
**Methods:** A comprehensive systematic review of MEDLINE, EMBASE, CINAHL and PsycINFO was conducted to identify studies examining consumer perceived needs relating to allied health and CAM services in managing LBP (1990 - May 2015). Data regarding study design and methods were extracted. Emergent themes were identified and aggregated to provide a systematic review of the current literature.
**Results:** 1779 manuscripts were identified, of which 39 were found to be relevant (figure 1). Of these, 25 used qualitative, 14 used quantitative and 1 used mixed methods. The quality of the literature was variable. Few studies directly addressed the review question. Many results were consistent, with the following main themes emerging from at least 2 studies:
1) CAM elicited conflicting views from consumers, with some willing to try CAM, believing it to be beneficial and CAM practitioners perceived to be more empathetic and understanding. Other consumers questioned the legitimacy of CAM and believed it offered only transitory benefits.
2) Chiropractic therapy was perceived to be effective by some consumers, but not others, who had concerns about side effects and were disappointed with the temporary effects.
3) Physiotherapy and exercise therapy were often preferred by patients for LBP. Consumers believed these to help with pain relief, prevent worsening of back pain and to improve mobility and function. Consumers strongly preferred physiotherapy to be individually tailored to their health needs and abilities.
This review identified a paucity of data examining LBP consumers' perceived needs of allied health and CAM in males, geriatric populations and patients from developing countries or non-English speaking backgrounds.




**Conclusions:** Consumers with LBP perceive a role for physiotherapy but have inconsistent beliefs regarding CAM and chiropractic therapy. This review has highlighted significant gaps in the literature relating to consumers' needs of allied health and CAM for LBP. Health care practitioners need to understand consumers' beliefs regarding the multiple modes of therapy used by consumers to manage their LBP, to better align care provision. Incorporating this into care has the potential to improve outcomes for both consumers and the health system.
**References:**
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**Acknowledgement:** This work was supported by Arthritis and Osteoporosis Victoria. D Urqhuart and A Wluka are recipients of an NHMRC Career Development Fellowship (Clinical level 2).
**Disclosure of Interest:** None declared
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## AB1022 ASSOCIATION BETWEEN PSORIASIS AND INCIDENT DIABETES MELLITUS: A POPULATION-BASED STUDY IN TAIWAN

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**Background:** Psoriasis is a known risk factor of cardiovascular disorders in addition to traditional risk factors such as diabetes mellitus (DM). However, the association between psoriasis and DM is unclear.
**Objectives:** To quantify the risk by comparing the incidence of DM between patients with psoriasis and the general population in Taiwan.
**Methods:** The study cohort consisted of two populations. The first population is the whole patients first diagnosed with psoriasis in 2000 in Taiwan, and the second population is a nationally representative cohort of 1,000,000 individuals from the Longitudinal Health Research Database in 2000. Those who younger than age of 10 or had DM before 2000 were excluded from analysis. They were followed from 2000 until the occurrence of DM, death or 31 December 2012. Incidence rates of DM were calculated. Poisson regression was used to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for DM, adjusted for age, gender and pre-existing comorbidity.
**Results:** The study cohort comprised 756,333 subjects with a mean follow-up of 11.27 years; among them 15,099 patients with incident psoriasis were identified. Patients with psoriasis had a higher comorbidity of renal disease (1.48%), congestive heart failure (0.91%), cardiac dysrhythmia (1.82%), cerebrovascular disease (2.74%) and peripheral vascular disease (0.94%) than the general population. The incidence rate for DM was 2.04 (95% CI, 2.01–2.08) per 100 person-years for psoriasis patients comparing to 1.10 (95% CI 1.03–1.16) per 100 person-year in the general population. The adjusted IRR of incident DM was 1.34 (95% CI 1.29–1.38) for patients with psoriasis.
**Conclusions:** Patients with psoriasis has an increased risk for DM. A vigilant monitoring for DM in patients with incident psoriasis is warranted to reduce long-term cardiovascular risks.
**Disclosure of Interest:** None declared
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## AB1023 RHEUMA SPACE: STANDARD PRACTICE AIMING CLINICAL EXCELLENCE IN RHEUMATOLOGY

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**Background:** The evaluation of the quality of medical practice and the implementation of corresponding measures to improve it are crucial steps for the development of Rheumatology in Europe. Herein we describe the implementation of a national program, Rheuma Space, aiming at quality improvement in the field of Rheumatology.
**Objectives:** To develop standards for the quality of care accepted by most of the rheumatology services in Portugal.
**Methods:** Quality indicators were obtained through a four-step RAND-modified Delphi methodology. The first step involved a literature search for international benchmarking of quality of care initiatives and indicators, followed by a pre-selection of a initial set of criteria by a task force. The final steps, aiming at defining a smaller set of criteria that could best analyze rheumatology quality of care, encompassed an online Delphi round with all Portuguese rheumatologists and a consensus meeting with a panel of invited experts representing all the Portuguese Rheumatology Departments of the National Health Service.
**Results:** A total of 412 different indicators were collected throughout the first project phase and the final set of 26 quality indicators was defined, within the three Donabedian dimensions of healthcare quality: nine "*structure*", eleven "*processes*" and seven "*outcome*" indicators. These criteria cover eleven domains of quality of care: personnel and organizational structure, training and research, facilities, equipment and IT, budgeting and financial resources, access to care, clinical records, patient communication, multidisciplinary management, clinical outcomes, and patient and personnel satisfaction.
**Conclusions:** The 26 quality indicators set constitutes the basis for a quality management tool, which is now being implemented in all the Portuguese Rheumatology Departments of the National Health Service. Direct surveys derived from the 26 quality indicators are being applied to health professionals and patients allowing to benchmark departments and to identify strengths and weakness for future improvement. This initiative is deemed to improve the process of care for Portuguese rheumatic patients, thereby ensuring quality standards of structure and process criteria, for a patient-oriented clinical practice, favouring desirable continuous quality improvement on health outcomes.
**Acknowledgement:** Portuguese Rheumatology participating in the online Delphi and all the participants in the expert consensus meeting
**Disclosure of Interest:** None declared

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## AB1024 HEALTH-RELATED QUALITY OF LIFE IN DIFFERENT MUSCULOSKELETAL DISORDERS: A COMPARISON AMONG THE CONDITIONS AND WITH A SELECTED SAMPLE OF HEALTHY INDIVIDUALS USING SF-36 QUESTIONNAIRE, EQ-5D AND SF-6D UTILITY VALUES

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**Background:** Given the high prevalence of musculoskeletal (MSK) disorders, there is a need to determine which conditions have the greatest impact on health-related quality of life (HRQoL).
**Objectives:** To compare the HRQoL scores of the Medical Outcomes Study Short-Form 36 Health Survey (SF-36) and of the two widely used indirect utility instruments, the EuroQol Five Dimensions questionnaire (EQ-5D) and the Short-Form Six Dimensions questionnaire (SF-6D) among 14 different MSK disorders and to compare them with the results of a selecting sample of healthy controls.
**Methods:** 2,633 patients participated to this study. MSK disorders were classified into five diagnostic groups: inflammatory rheumatic diseases (IRD), connective tissue disorders (CTD), symptomatic peripheral osteoarthritis (SPOA), soft tissue disorders (STD) and osteoporosis (OP). IRD were further classified into 3 subgroups: rheumatoid arthritis (RA) (n=572), peripheral psoriatic arthritis (PsA) (n=150) and ankylosing spondylitis (AS) (n=251). CTD were classified into sistemic sclerosis (SSc) (n=75), sistemic lupus erythematosus (SLE) (n=83) and Sjogren sindrome (SS) (n=50). SPOA included symptomatic knee (n=176), hip (n=136 patients), and hand OA (n=87). The STD group included fibromyalgia (FM) (n=226 patients), low back pain (n=141) and shoulder tendinitis/adhesive capsulitis (n=112 patients). The OP group included 172 women who had vertebral fractures due to osteoporosis, and a group of 402 asymptomatic osteoporotic women without vertebral fractures. For comparison were used 649 healthy controls. The HRQoL was evaluated with the SF-36, using physical (PCS) and mental (MCS) component scales and EQ-5D. The SF-6D utility values were calculated from SF-36 by using a definite scoring function.
**Results:** The five major rheumatic disease groups, compared to healthy people, significantly impaired all eight health concepts of the SF-36 ($p<0.0001$). Similar results were found for EQ-5D, EQ-VAS and SF-6D. The patients with IRD have poorer self-reported health status than those without arthritis in all domains of living, but particularly with respect to scales measuring aspects of physical functioning or mobility, role limitation due to physical health problems and usual activities, and bodily pain. RA had the largest negative impact on HRQoL at the individual level, followed by FM, vertebral fractures due to OP, OA of the hip, and SSc.
**Conclusions:** Our results indicates that MSK conditions have a clearly detrimental effect on the HRQoL, and physical domain is more impaired than mental and social ones. These findings may help clinical decision making and priority setting for management of individuals with MSK diseases.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2946

## AB1025 GLYCEMIA AND SYSTEMIC BLOOD PRESSURE IN PATIENTS WHO RECEIVE CORTICOSTEROID PULSE THERAPY

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**Background:** Supra-pharmacological doses of corticosteroids (pulse therapy) are used in various autoimmune disorders. Methylprednisolone and dexamethasone pulse therapy have demonstrated similar efficacy for some diseases;[1] therefore, differences in their adverse effects can help the selection of any of them.
**Objectives:** To evaluate changes in glycemia and blood pressure in patients who received pulse therapy with dexamethasone or methylprednisolone.
**Methods:** We evaluated the charts of patients who received corticosteroid pulse therapy with dexamethasone (200 mg/day) or methylprednisolone (1000 mg/day). We included patients who received at least three days of pulse therapy and who had records of glycemia and blood pressure four times at day. We evaluated the blood pressure and glycemia measurements before the first pulse therapy and the next three-day measurements each six hours. We evaluated through linear mixed models the factors associated with an increase in glycemia or blood pressure (systolic or diastolic) in the program R 3.0.2. For the glycemia analysis we excluded patients with diabetes history and patients having glycemia $>180$ before the pulse therapy.
**Results:** We included 117 patients, 83 received pulse therapy with methylprednisolone and 34 with dexamethasone. Multivariate mixed models showed a statistically significant increase in glycemia and blood pressure (systolic and diastolic) from the first measurement after the initial dose of pulse therapy (Figure 1);

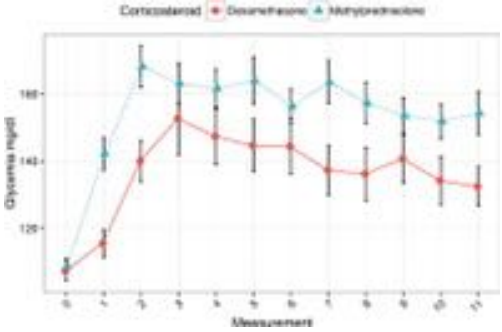



Figure 1. Mean and standard error of glycemia according each measurement.

factors associated with hyperglycemia (adjusted for creatinine levels, sex and units of insulin received) were higher glycemia before the pulse therapy ($p=0.0016$) and the use of methylprednisolone ($p=0.0098$). Factors associated with an increase of systolic or diastolic blood pressure were: higher blood pressure before the first pulse therapy ($p<0.0001$) and higher creatinine levels ($p=0.0099$ and $0.0031$) but not the type of corticosteroid (dexamethasone or methylprednisolone).
**Conclusions:** Pulse therapy with methylprednisolone showed a higher increase in glycemia than dexamethasone. Susceptible patients to an increase of glycemia are who have initial hyperglycemia; patients susceptible to an increase in blood pressure are who have elevated serum creatinine levels and who have initial hypertension.
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**Disclosure of Interest:** None declared
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## AB1026 ACHIEVING MINIMAL DISEASE ACTIVITY AND REMISSION IN PSORIATIC ARTHRITIS PATIENTS TREATED CONTINUOUSLY WITH TNF INHIBITORS FOR 2 YEARS IN THE REAL LIFE

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy commonly associated with psoriasis. Minimal disease activity (MDA) and remission represent treatment targets. However, their assessment is to date an unmet need in PsA patients.
**Objectives:** Aim of the study was to prospectively evaluate MDA and remission in PsA patients who were treated with subcutaneous TNF inhibitors (iTNF), every 3/6 months for 2 years.
**Methods:** Clinical and laboratory data from 221 PsA patients were analyzed (F:M=1.3, age 55±13 years, disease duration 12.3±6.1 years) at baseline (T0), after 22 (T22), 54 (T54) and 104 (T104) weeks from the beginning of TNFi (adalimumab n=94; etanercept n=84; golimumab n=43). Values of DAS28-CRP, CPDAI, and DAPSA were calculated, and MDA/remission were assessed at the all the time points. MDA was defined as the occurrence of 5/7 criteria, while remission was assessed as DAS28-CRP$<2.6$, DAPSA$\leq3.3$, and CPDAI$<2$. Occurrences of comorbidities such as cardio-vascular, renal, respiratory, infectious, metabolic, neuropsychiatric and thyroid diseases were registered. Concomitant therapies (steroids and csDMARDs) and predictive factors of remission were analyzed in accordance with the above-mentioned scores. The Chi-square test was used to compare the remission rate at the follow-up and to analyze the predictive factors. Cohen's kappa analysis was performed to measure the concordance between clinimetric scores: kappa $\geq0.6$ was considered as a good agreement and kappa $\geq0.8$ was considered as an excellent agreement.
**Results:** Prevalence of patients on DAS28 and DAPSA remission was significantly higher at T104 comparing to T0, T22 and T54 while patients on MDA and CPDAI remission were more frequent at T104 compared with T0 and T22 (Figure1A). At all the time points, a good concordance between MDA and DAS28$<2.6$ occurred (k=0.63) and an excellent concordance was obtained between MDA, CPDAI$<2$ and DAPSA$\leq3.3$ (k=0.81). At T22, patients with thyreopathies achieved the CPDAI remission in a lower percentage compared to patients without thyreopathies (P=0.02, OR=3.3) (Figure 1B). At T104, the female sex was

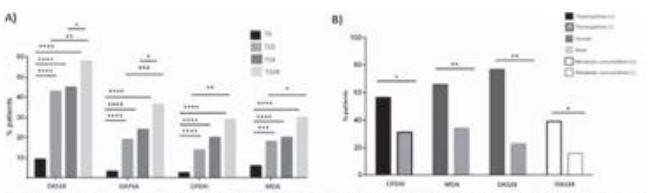



**Figure 1. Panel A:** Patients (as a percentage) on DAS28, DAPSA, CPDAI remission and MDA at T0, T22, T54, T104. **Panel B:** Patients (as a percentage) who were not on CPDAI remission at T22 in accordance with the presence of thyreopathies, and MDA/DAS remission at T104 according to female sex and metabolic comorbidities. *P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.

associated with a lower prevalence of patients on DAS28 remission (P=0.005, OR=2.3) and MDA (P=0.01, OR=2.7) while a lower percentage of patients with metabolic comorbidities was on DAS28 remission with the respect to patients without them (P=0.02, OR=3.3) (Figure1B). Patients on concomitant steroid therapy were fewer at T22/54/104 with the respect to T0 ($P<0.0001$ for all the comparisons) while the rate of patients on csDMARDs was lower at T104 compared with T0 ($P<0.01$).

**Conclusions:** In clinical practice, MDA and remission were achieved in a high prevalence of PsA patients during TNFi treatment with a rate that increased from 22 to 104 weeks. Tapering of the concomitant treatment was thus allowed. Predictors as thyreopathies, female sex, and metabolic comorbidities were associated with a lower probability to achieve clinical remission.

**Disclosure of Interest:** None declared

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## AB1027 USE OF BIOLOGIC DMARDS IN RUSSIAN PATIENTS WITH RHEUMATIC DISEASES: ANALYSIS OF THE 6 YEAR-EXPERIENCE OF THE MOSCOW REGIONAL RESEARCH AND CLINICAL INSTITUTE

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**Background:** Biologic disease-modifying antirheumatic drugs (bDMARDs) are increasingly used for treating patients with different rheumatic diseases. The safety and effectiveness of using biologics therefore become important issues of the rheumatologists' practice.

**Objectives:** To analyze the data, gathered over the 6 year-experience of using bDMARDs in Moscow Regional Research and Clinical Institute ("MONIKI"), including safety issues, reasons for biologic switch and its frequency.

**Methods:** A retrospective open cohort study was conducted. 159 patients (female – 89; 56%; men – 70; 44%), that were followed up at the rheumatology department of "MONIKI" for more than 0,5 year during the period from the 01 Sept 2009 until the 01 Nov 2015, and taking bDMARDs, were randomly included, regardless of the diagnosis or the biologic agent. To the undesirable events during the treatment with bDMARDs applied: cases of infections (latent or active tuberculosis, active herpes zoster infection, candidiasis, urinary infection, unusually frequent acute respiratory infections, pneumonia) and elevated liver enzymes.

**Results:** The median age of patients was 46 years. The median duration of the disease – 12 years. The diagnoses were ankylosing spondylitis (n=83; 52,2%), rheumatoid arthritis (n=58; 36,48%), psoriatic arthritis (n=15; 9,4%), systemic lupus erythematosus (n=2; 1,3%), Takayasu arteritis (n=1; 0,6%). The used bDMARDS were infliximab (n=63; 39,62%), adalimumab (n=42; 26,42%), etanercept (n=18; 11,32%), rituximab (n=16; 10,1%), abatacept (n=7; 4,4%), golimumab (n=6; 3,77%), tocilizumab (n=3; 1,89%), belimumab (n=2; 1,26%), certolizumab pegol (n=2; 1,26%). In 45 patients (28,3%) the biologic was switched, in 13 – two or more times. In 17 patients (37,8% of all switches) the underlying cause was an ineffectiveness of the bDMARD; in 14 (31,1%) the reason for the switch were adverse events or infusion reactions. Most frequently were switched for the reason of ineffectiveness etanercept (14,8%) and infliximab (14%). The incidence of the undesirable events among all the agents was 8,344 per 100 patient years. 8,18 per 100 patient years in rituximab; 5,34 in etanercept; 10,11 in infliximab and 6,14 in adalimumab patients. One adverse event was registered on abatacept patient. The median period of adverse events appearance was 12 months. Infusion reactions were most common in patients taking rituximab (n=7; 43,8%; $p<0,01$) and none were present in patients on etanercept. Ten cases of tuberculosis were registered during the treatment with infliximab, including 1 lethal case, therefore one or none cases were registered in patients taking other bDMARDs.

**Conclusions:** In our department, ankylosing spondylitis was the most frequent reason for treatment with biologics. For the reason of ineffectiveness almost one third of patients have required a biologic switch and a large part even more than once. Another one third of switches was made due to undesirable events or infusion reactions. Infliximab is widely used for the treatment of patients with rheumatic diseases, although we registered an increased frequency of undesirable events during the treatment with infliximab, including tuberculosis, and a high frequency of the switch for the reason of ineffectiveness.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4105

## AB1028 DEVELOPMENT AND VALIDATION OF A PATIENT QUESTIONNAIRE ON RHEUMATOID ARTHRITIS DISEASE RELATED KNOWLEDGE IN THE TREAT TO TARGET ERA: PRELIMINARY RESULTS

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**Background:** Patient involvement and personalisation of healthcare has become increasingly important in managing chronic diseases. Knowledge about their disease and its treatment is an important precondition for patients to be able to be involved in their own care.[1] Hence, EULAR recommends education to be an integral and continuous element of Rheumatoid Arthritis (RA) management, so that patient can be involved in their RA care.

An instrument to assess patients' knowledge about their disease and its treatment can provide insight into the effectiveness of healthcare professionals' education efforts. Moreover, it can be used as an instrument to personalize education based on individual patients' knowledge gaps. Currently available patient knowledge questionnaires were developed before the introduction of biologicals as well as treat to target strategies in rheumatoid arthritis (RA). Therefore we started the development and validation of an RA knowledge questionnaire for patients.

**Objectives:** To propose an instrument to measure factual disease related knowledge in RA patients with additional focus on knowledge related to modern treatment methods.

**Methods:** Content to be covered by the instrument was adopted from existing questionnaires. Consensus was reached on relevant content by a RAND modified Delphi scoring procedure by six rheumatology nurses and six rheumatologists, and a subsequent consensus meeting among six rheumatology nurses and four rheumatologists. Six rheumatology nurses and five rheumatologists provided written feedback on a preliminary pool of items written to assess the identified content domains. Subsequently, a focus group among nine patients was organised to identify additional content areas that might have been omitted from the item pool. Readability, feasibility and comprehensiveness of the resulting pool of 63 items were rated by eight patients from the focus group.

**Results:** Cross-sectional data of 340 patients recruited from Bernhoven rheumatology department were used to evaluate psychometric properties. Preliminary analysis suggests that 21 (27%) items should be discarded based on an item total point biserial correlation $<0.30$. Confirmatory factor analysis with weighted least squares estimation on the polychoric correlation matrix suggested acceptable fit for a unidimensional measurement model for the remaining 45 items (CFI =0.95, TLI=0.95, RMSEA=0.02, WRMR=0.95). Internal consistency was also high for 45 items, with Cronbach's $\alpha$=0.92.

**Conclusions:** These preliminary results suggest that the questionnaire is a valid and reliable measure for assessing factual disease related knowledge in RA patients. Further validation efforts based on modern item response theory based approaches are ongoing as well as work directed at developing a calibrated item bank, tailored short-forms and a computerized adaptive testing algorithm.

**References:**

[1] Joseph-Williams N, Elwyn G, Edwards A. Knowledge is not power for patients: a systematic review and thematic synthesis of patient-reported barriers and facilitators to shared decision making. Patient education and counseling. 2014;94(3):291–309.

**Acknowledgement:** We thank all rheumatology nurses, rheumatologists and patients who have helped in the development or validation of the questionnaire.

**Disclosure of Interest:** M. de Jonge Grant/research support from: Dutch Arthritis Foundation (Reumafonds), M. Oude Voshaar: None declared, A. Huis: None declared, M. van de Laar: None declared, M. Hulscher: None declared, P. van Riel: None declared

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## AB1029 COSTS OF BIOLOGICAL AGENTS AND PATTERNS OF BIOLOGICAL THERAPY IN ROUTINE TREATMENT FOR RHEUMATOID ARTHRITIS

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**Background:** Biological agents, introduced in the late 1990s, had significant impact on treatment for rheumatoid arthritis and patient outcomes. However, this treatment is costly, and increases in healthcare payment are of concern.

**Objectives:** This study examined the costs and patterns of biological therapy in routine treatment provided at our hospital.

**Methods:** Subjects were 206 rheumatoid arthritis patients who received etanercept, infliximab, adalimumab, tocilizumab, or abatacept between January 2005 and December 2014. Cumulative costs of each agent administered to a patient over a period of 1, 2, and 3 years were calculated using the current prices of biological agents listed by the National Health Insurance program. Therapy continuation rates and relative dose intensities (RDI) were calculated, and reasons for treatment withdrawal were investigated to ascertain patterns of biological therapy.

**Results:** There were a total of 360 cases of biological agent treatment (174 etanercept cases, 44 infliximab cases, 27 adalimumab cases, 49 tocilizumab cases, and 66 abatacept cases) in 206 rheumatoid arthritis patients, among which 60 etanercept, 9 infliximab, 9 adalimumab, 9 tocilizumab, and 12 abatacept cases were continued for at least 3 years without disruption. When exchanging 1 euro with 127 yen, cumulative costs of one-year and three-year treatment with 25 mg/week etanercept (53 cases) were approximately 6,160 euro and 17,490 euro per patient, respectively, while costs with 50 mg/week etanercept (7 cases) were approximately 11,450 euro and 32,240 euro per patient, respectively. Costs of 1- and 3-year treatment with infliximab were approximately 11,910 euro and 32,430

euro per patient, respectively; those with adalimumab were approximately 13,450 euro and 38,590 euro per patient, respectively; those with tocilizumab were approximately 8,690 euro and 24,730 euro per patient, respectively; and those with abatacept were approximately 13,460 euro and 34,140 euro per patient, respectively. Withdrawal from therapy with any biological agent was due mainly to insufficient therapeutic effect (50% of withdrawals), adverse effects (35.5%), patients' circumstances (9.2%), and remission (5.3%). Therapy continuation rates for etanercept, infliximab, adalimumab, tocilizumab, and abatacept at the end of 3 years were 57.7%, 24.7%, 42%, 25%, and 39.3%, respectively (Kaplan-Meier method). The continuation rate of etanercept therapy was significantly higher than the rates of therapy with any of the other 4 biological agents (log-rank test, $P<0.05$). Mean RDI values (95% CI) for 3 years were calculated for etanercept 25 mg/week (0.93; 0.81–1.04), etanercept 50 mg/week (0.86; 0.64–1.07), infliximab (1.10; 1.002–1.19), adalimumab (0.95; 0.89–1.01), tocilizumab (0.84; 0.78–0.89), and abatacept (0.85; 0.75–0.94). Decreases in tocilizumab and abatacept dosage were confirmed, and longer dosing intervals were speculated. Furthermore, the dose intensity of infliximab was increased by 10%, indicating increases in dosage and shortened dosing intervals. Significant changes in dosage were not confirmed for etanercept and adalimumab therapy.

**Conclusions:** Etanercept therapy had a high continuation rate. In particular, a 25 mg/week regimen was rarely changed to a 50 mg/week regimen, suggesting that the use of 25 mg/week etanercept therapy may be able to reduce medical costs.

**Disclosure of Interest:** None declared

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## AB1030 EFFECTS OF CONDUCTING DIRECTLY OBSERVED TREATMENT, SHORT-COURSE (DOTS) STRATEGY AND CONFERENCES ON LATENT TUBERCULOSIS INFECTION IN RHEUMATOID ARTHRITIS PATIENTS UNDERGOING IMMUNOSUPPRESSIVE THERAPY

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**Background:** As our hospital lacks a pulmonologist, screening for respiratory infections in the treatment of rheumatoid arthritis (RA) is carried out through collaboration with a pulmonary medicine specialist outside of our facility. Patients in whom latent tuberculosis infection (LTBI) is detected by screening are prescribed isoniazid (INH). At the Fuji Public Health Center, which has jurisdiction over our hospital, directly observed treatment, short-course (DOTS) is implemented for all tuberculosis patients, including the LTBI cases registered. In our practice, we have held DOTS conferences (DOTS-C) with the health center regularly since 2013 to ensure proper patient education and thorough patient management.

**Objectives:** We investigated the status of the respiratory infection screening conducted in our hospital and studied the impact of DOTS-C on treatment outcomes in LTBI and the treatment of RA.

**Methods:** For 250 patients who underwent screening for respiratory infections between 2010 and 2014, we retrospectively examined data in regard to the items associated with LTBI and RA treatment.

**Results:** There were 58 patients diagnosed with LTBI and prescribed INH. As of October 31, 2015, immunosuppressive drugs used in the 58 patients were methotrexate in 37 patients at doses of 7.57±2.28 mg/week (mean ± standard deviation), prednisolone in 6 patients at doses of 2.17±0.85 mg/day, and biological preparations in 45 patients. In all cases, the scheduled duration of INH therapy was 270 days. DOTS-C was conducted in 23 patients. The number of patients who completed the entire treatment course was 19 (82.6%) in the DOTS-C group and 11 (31.4%) in the non-DOTS-C group. The number of patients hospitalized and treated for infections and other complications developing during RA treatment was 1 (4.3%) in the DOTS-C group and 8 (22.9%) in the non-DOTS-C group.

**Conclusions:** In our medical institution, despite not having a pulmonologist, it was possible to complete the entire course of LTBI treatment through collaboration with an associated public health center. Our findings indicate that DOTS-C is useful for achieving both the completion of LTBI treatment and patient education to prevent complications.

**Disclosure of Interest:** None declared

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## AB1031 RHEUMATOID ARTHRITIS, A SINGLE-CENTER EGYPTIAN EXPERIENCE

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**Background:** The Epidemiology of Rheumatoid Arthritis (RA) is changing over time provided by several studies showing an increase in frequency and change in joint presentation.(1) Moreover, the characteristics of the disease may differ among different ethnicities and populations that necessitate studying each population to define its own pattern of RA.

**Objectives:** Our aim was to define disease characteristics in a cohort of Egyptian RA patients by retrospective analysis of their medical records through a period of 20 years.

**Methods:** Medical records of all cases who fulfilled the ACR 1987 criteria for diagnosis of RA starting from January 1995 till July 2015 were reviewed (n=3219). All patients were receiving medical follow–up at the Rheumatology outpatient clinic, Kasr AlAiny Hospital. Demographic data and disease characteristics were documented and statistically analyzed.

**Results:**

A total of 3219 patients fulfilling the ACR 1987 criteria of RA were identified in the duration (1995–2015), 84% were females with mean age 48.8±13.8 that was not significantly lower than that of males 49.1±15.7 (p-value=0.62).The mean age of onset was 36.1±13.4 years and the mean disease duration was 12.9±7.9 years.

Rheumatoid factor (RF) was detected in 49.9% of cases; erosions were found at diagnosis in 19.6% of patients.77.1% of RA cases presented with polyarticular and 22.9% with oligoarticular patterns.

There was a significant increase by 0.12% in newly diagnosed cases annually (P-value=0.01) throughout the period studied (20y) (Fig. 1), however there was a significant decrement by 0.4% annually in females (p-value=0.02). On the other hand there was a significant steady increase in the mean age of onset by 0.2 year annually (P-value<0.001). While, there was a steady decline in erosions by 0.5% annually (p-value=0.01)

Females were more prone to have erosions although this was not found to be statistically significant; on the other hand RF was significantly higher in the erosive group (32.6%). Similarly the mean age at disease onset and age at diagnosis were statistically significantly higher in the erosive group (p-value=0.002 and p-value<0.001 respectively).

Regarding Extra-articular manifestations at the time of diagnosis, there was a significant decline in the presence of subcutaneous nodules and Sicca symptoms by0.4% & 0.5% annually respectively (P-value=0.03).

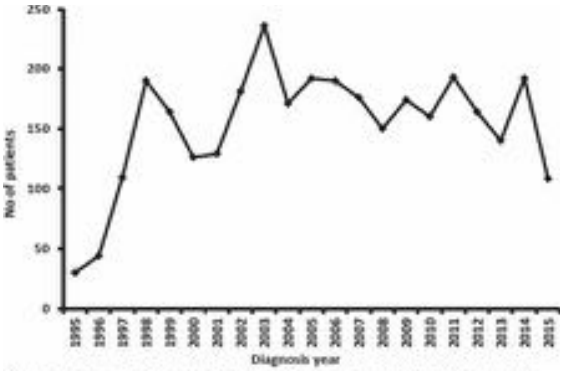



Figure one showing increase in newly diagnosed cases by 0.12% annually

**Conclusions:** The present study describes the demographic and disease characteristics of RA in the largest retrospective study as regards Egyptian RA patients.

**References:**

[1] Gibofsky, A. (2012). Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. The American journal of managed care, 18(13 Suppl), S295–302.

**Disclosure of Interest:** None declared

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## AB1032 PROFILES OF PATIENTS AGED OVER 80 YEARS WITH RHEUMATOID ARTHRITIS IN AORA REGISTRY

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**Background:** The proportion of the aging population is increasing worldwide. Currently, the population of aging individuals is the highest in Japan; the percentage of 65-year-old people is 26.7%, indicating an aged society. Furthermore, the proportion of elderly people over 65 years of age is the highest (33.6%) in Akita prefecture, Japan.

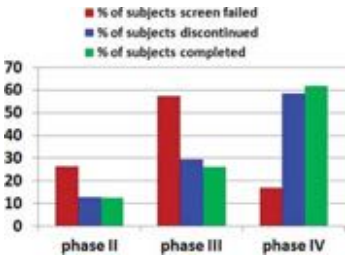
**Objectives:** We investigated the data of patients with rheumatoid arthritis (RA) in various medical centers where in the orthopedic surgeons belonged to Akita

Orthopedic Group on RA (AORA) in Akita. We think that Akita registry is the future vision for RA treatment.
**Methods:** In this cohort study, we examined 324 of 2021 cases of patients aged ≥80 years (16.0%) from AORA registry in 2015 (average age, 66 years).
**Results:** The average age of our cohort was 84 years (range, 80–99 years); of the 324 patients, 59 were men and 265 were women, and the average disease period was 14 years (range, 2 months–66 years). Two-hundred sixty eight (83.0%) cases were of elderly-onset RA (EORA). According to the Steinbrocker classification criteria, 82 cases were stage I; 69, stage II; 80 stage III; and 87, stage IV. Further, 77cases were cass 1; 128 class 2; 89 class 3; and 22, class 4. The past medical history of the patients was as follows: 176 cases of hypertension, 59 cases of respiratory diseases, 56 cases of heart diseases, and 38 cases of diabetes. MTX (average, 5.5 mg per week; range, 1–14 mg per week) was administered to 101 patients. Prednisolone (average, 3.8 mg/d; range, 1–12.5 mg/d) was administered to 170 patients. A combination of conventional systemic disease-modifying antirheumatic drugs was administered as follows: bucillamine to 97, salazosulfapyridine to 84, tacrolimus to 21, mizoribine to 8, gold sodium isothiomalate to 7, actarit to 5, iguratimod to3, and auranofin to 1 patient. Biologics were administered to 33 patients (10.2%); etanercept was administered to 15, abatacept to 6, adalimumab to 4, tocilizumab to 4, infliximab to 3, golimumab to 1, and certolizumab pegol 1 patient. DAS28CRP remission was observed in 149 patients. The disease activity was low, moderate, and high in 53, 74, and 4 patients, respectively. In our study, a few patients showed high disease activity and an increase in the extent of functional disorder. These results may be attributed to the limited number of patients visiting the orthopedic department and the quality of the patients.
**Conclusions:** The study showed the low using ratio of MTX and high using ratio of PSL as much as previous reports. Sixty two percent of RA patients over 80 years of age showed rather low disease activity. Conventional therapy, without the use of bDMARDs, was used to treat 89.8% of the elderly patients with RA.
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[1] Miyamoto S, Sugimura Y, Kashiwagura T, Urayama M, Kobayashi M, et al; Evaluation for treatment of rheumatoid arthritis patients in AORA cohort. The Japanese Society for Clinical Rheumatology and Related Reserch 2015, 27: 135–45.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1567

## AB1033 CHALLENGES IN RECRUITMENT AND RETENTION OF SUBJECTS IN CONDUCTING CLINICAL DRUG TRIALS IN A DEVELOPING COUNTRY

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**Background:** Increasing enrollment and retention rates is important for clinical trials and healthcare advancements. Barriers in conducting clinical trials are physician-related, protocol-related or patient-related. Some of the factors that may hinder successful completion of a clinical drug trial are screen failures, adverse events leading to withdrawals and dropout of subjects. Inability to achieve adequate sample size for the trial may make the data insufficient to conclude objectives of a clinical drug trial and also increase overall cost and duration.
**Objectives:** To study the factors such as subject recruitment and retention that may impede the successful conduct of clinical drug trials in India.
**Methods:** Sixteen clinical drug trials conducted at a tertiary care for rheumatological disorders in Hyderabad, India were analyzed. The study period was during 2006–2015. Thirteen trials were pertained to rheumatoid arthritis (RA) and 3 to osteoarthritis (OA). Three trials were of phase II, 8 in phase III and 5 in phase IV. Ethics committee approval was obtained for each trial. After obtaining the informed consent, subjects were screened to evaluate study specific inclusion/exclusion criteria; those not fulfilling the criteria were not included into the trials. While conducting the trials the number of subjects withdrawn or dropped out was duly noted. Factors relating to subjects recruitment and retention were analyzed.
**Results:** Among 228 screened subjects (mean age 47.3±11 years) women were 201 (88%). A total of 42 (18.4%) subjects were screen failed; 19 (45.3%) due to infection (latent tuberculosis) and 23 (54.7%) due to other reasons. One hundred and eighty six (81.6%) subjects were enrolled into the trials after fulfilling study specific inclusion and exclusion criteria. Screen failures were more in phase II (26.2%) and phase III (57.1%) trials; nearly half of them were due to latent tuberculosis.




Among 186 subjects enrolled, 162 (87%) completed the trials and 24 (13%) discontinued. Half of the subjects discontinued (n=12) were withdrawn in view of adverse events. Two (8.3%) withdrew consent from the trials and 10 (41.7%) were lost to follow up. Maximum number of subjects discontinued was in phase IV (figure).
**Conclusions:** Screen failures have an impact on recruitment of the subjects. Number of screen failure was more in phase III. Number of screen failure was least and number of discontinuation was most in phase IV. In the present study nearly half of the subjects screen failed due to latent tuberculosis peculiar to endemic countries like India. Subject retention is also important in conducting successful clinical trials. In this study 40% of subjects dropped out due to unknown reasons. Further studies are required to analyze the factors related to subject recruitment and retention from the clinical trials conducted at other centers in developing countries like India.
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[1] Peter Bower et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. Trials 2014; 15:399
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3383

## AB1034 THE EPIDEMIOLOGY OF THE RHEUMATIC MANIFESTATIONS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE: THE PRELIMINARY DATA FROM A HOSPITAL-BASED COHORT STUDY IN ISTANBUL

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**Background:** Rheumatic manifestations are the most common frequent extra-intestinal manifestations (EIM) of inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), and affected 6–46% of patients[1].
Despite the common manifestations, data on the various ethnic populations are limited so far. Therefore, the cohort study seems a more useful tool to learn more about epidemiology and possible risk factors in the different geographical and racial groups[2].
**Objectives:** We conducted this survey to estimate the prevalences of some rheumatic manifestations associated with IBD and to study epidemiological factors of IBD in Istanbul, Turkey.
**Methods:** The patients were enrolled from the Gastroenterological Out-patient Clinics at two Hospitals. The diagnosis was made by gastroenterologists using endoscopy and histological studies. All patients with established diagnosis of CD and UC were evaluated byr heumatolgogists for EIM. Inflammatory back pain (IBP) was defined according to Calin's criteria. The modified New York criteria were used to define ankylosing spondylitis (AS) and the European Spondyloarthropathy Study Group criteria for spondyloarthropathy (SpA).
**Results:** A total of 223 patients diagnosed as IBD.115 ulcerative colltis (UC) and 108 Crohn'sdisease (CD).We estmated the prevalence of IBP as 21%; AS: 2.7%; sacroiliitis (SA): 5.4%; psoriasis: 1.3%; psoriatic arthritis (PsA): 0.9%; pustulosis: 0.9%; uveitis: 1.8%; polyarticular arthritis: 6%; oligoarticular arthritis: 9%; arthralgia: 27%; erythema nodosum (EN): 2.2%; recurrent oral aphthous (ROU): 18.4% (Table 1).

Table 1. Demographic and clinical features of patients with IBD

| | Total, n (%) | UC | CD |
|---|---|---|---|
| IBD no. | 223 | 115 | 108 |
| Age | 41.8±12.6 | 43.5±12.6 | 39.8±11.9 |
| Arthralgia | 60 (27%) | 27 | 33 |
| Polyarticular arthritis | 14 (6%) | 6 | 8 |
| Oligoarticular arthritis | 20 (9%) | 10 | 10 |
| IBP | 46 (21%) | 27 | 19 |
| Heel pain | 16 (7%) | 11 | 5 |
| AS | 6 (2.7%) | 5 | 1 |
| SA | 12 (5.4%) | 6 | 6 |
| SpA | 4 (1.8%) | 2 | 2 |
| Psoriasis | 3 (1.3%) | 2 | 1 |
| PsA | 2 (0.9%) | 0 | 2 |
| Uveitis | 4 (1.8%) | 1 | 3 |
| E. nodosum | 5 (2.2%) | 3 | 2 |
| Pustulosis | 2 (0.9%) | 1 | 1 |
| ROU | 41 (18.4%) | 19 | 22 |

MN: manifestations, IBD: inflammatory bowel disease, AS: ankylosing spondylitis, IBP: inflammatory back pain, SpA: spondyloarthropathy, PsA: psoriatic arthritis, UC: ulcerative colitis, CD: Crohn's disease, ROU: recurrent oral aphthous, SA: sacroiliitis.

**Conclusions:** We concluded that AS occurs more frequently in IBD, and more often than the prevalence of AS found in the general population. There is a high prevalence of IBP in IBD. The prevalence of ROU significantly higher than in the health population[3].
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## AB1035 RHEUMATOID ARTHRITIS AND JUVENILE IDIOPATHIC ARTHRITIS REGISTRIES: A QUALITATIVE ANALYSIS OF DATA IN CLINICALTRIALS.GOV

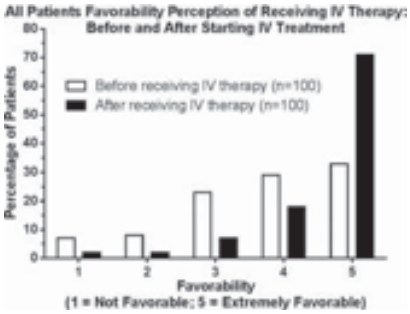
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**Background:** Efforts to standardize and catalog outcome measures for registries are important to improve our understanding of conclusions drawn both intra- and inter-registry(ies). A generic framework, the Outcome Measures Framework Model (OMFM),[1] has been developed to use across all registries with the aim to identify the major categories of outcome measures. A condition specific framework exists for rheumatology clinical trials defined by the Outcome Measures in Rheumatology group (OMERACT),[2] and may be applied to observational studies.
**Objectives:** We undertook a qualitative evaluation of various rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) registries to evaluate the types and details of the outcome measures reported as a mechanism to refine the existing frameworks to guide registry data collection.
**Methods:** Active RA and JIA registries within ClinicalTrials.gov (CT.gov) were identified using a cutoff date of 23 June 2015. The 10 largest registries based on anticipated enrollment were selected for evaluation and supplemented by additional registries, not necessarily in CT.gov but considered important for inclusion by the project team and external stakeholders. Two reviewers, an epidemiologist and rheumatologist, evaluated the registry reported outcome measure details, terminology, and variations qualitatively.
**Results:** Twenty-one registries were evaluated, 11 in common by both reviewers. Registries included populations from the US, the EU, Asia and Latin America and were run by various government, industry, or non-profit organizations. Key findings were that the outcome measures utilized and the time points of their assessment were often not clearly defined in CT.gov. Both the OMERACT framework and OMFM were missing various outcome measures and their definitions to properly categorize all the identified outcomes. Registries varied with respect to detailing how results would be analyzed, e.g., prospective or post hoc analyses. Diagnostic criteria used for inclusion were frequently vague, e.g., investigator judgement vs available classification criteria vs not specified. Published data from earlier investigations were typically not cited, results to date not reported, and links to registry websites not provided. Data not available in CT.gov were often available in publications or websites regarding analytical methods, but these external resources were not always easily located.
**Conclusions:** Current CT.gov registry postings often are missing key details to ensure a clear understanding regarding the populations enrolled, outcomes data to be collected and analyzed, and opportunities to combine data amongst registries. This preliminary work also identified instances to improve the OMERACT framework and OMFM as well as expand the OMERACT outcome measures to address the needs of observational studies beyond clinical trials.
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**Disclosure of Interest:** N. Goel Employee of: Quintiles Inc., F. Eisenberg Consultant for: Quintiles Inc., M. Barboza Employee of: Quintiles Inc., D. Campion Employee of: Quintiles Inc., K. Bibeau Employee of: Quintiles Inc.
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## AB1036 UPDATED RESULTS FROM THE PRO ASSESSMENT OF INFLAMMATORY ARTHRITIS PATIENTS' EXPERIENCE WITH IV ADMINISTERED BIOLOGIC THERAPY

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**Background:** Pt-reported outcomes (PRO) are used to assess pt-related benefit in clinical trials. Inflammatory arthritis (IA) pts are equally receptive to intravenous (IV) or subcutaneous (SC) biologic treatment[1].
**Objectives:** We obtained PRO data to understand characteristics of pts who receive IV biologic agents for IA.
**Methods:** This was a questionnaire-based study conducted at a rheumatology practice with extensive clinical trial experience. A total of 100 pts enrolled & are included in this final analysis. Inclusion criteria: a diagnosis of IA with IV biologic use for ≥3 mo; ≥18 yrs age; able to read, write & speak English, willing to complete the questionnaire & a signed informed consent form. IV biologic treatment was per clinical practice; there were no treatment assignments & study drug was not supplied. The questionnaire had 30 questions which pts completed prior to receiving a regularly scheduled dose of IV biologic.
**Results:** Mean (±SD) age of pts was 58.35 (±14.64) yrs with mean disease duration of 10.1 (±8.13) yrs (range 0.7–45 years). Pts were Caucasian (38%), African American (28%), Latino/Hispanic (22%), Asian/Pacific Islander (1%) & 11% not identified. IV biologics used were infliximab [IFX](71%), rituximab [RTX](12%), tocilizumab [TCZ](10%), abatacept [ABT](6%) & golimumab [GLM](1%). The mean duration of current IV therapy was 4.07 (±3.27) yrs (range 0.1 to 16.0 yrs). Pts' favorability perception of IV therapy BEFORE & AFTER starting IV therapy is shown in the Figure. Amongst all pts, "Extremely favorable" increased ($p<0.05$) from 33% to 71% after receiving IV therapy; the increase in "Extremely favorable" was evident in pts with or without previous SC biologic therapy. Of the 33% of pts reporting an "Extremely favorable" rating BEFORE starting IV therapy, 6% changed their opinion to a lesser rating AFTER starting therapy, whereas 44% of patients reporting "Extremely favorable" AFTER starting IV therapy had indicated a lesser rating BEFORE starting IV therapy.




**Conclusions:** These results suggest that among IA pts receiving IV biologic therapy for treatment of IA, there is a high degree of pt satisfaction, including a similar favorability perception of IV therapy among pts who switched from a SC to an IV biologic. Our results support the concept that when there is a shared decision making discussion with pts regarding biologic treatments, the option of IV therapy should be an essential part of that discussion & that the IA pts' perspective should be given meaningful consideration.
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## AB1037 EFFECTIVENESS OF CONVENTIONAL DMARD THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SUCCEEDING COST-SAVINGS FOR A HEALTH SYSTEM BY DIMINISHING USE OF BIOLOGICAL THERAPY

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**Background:** Biological therapy is useful to prevent clinical and radiological progression in patients with rheumatoid arthritis (RA) but is associated with high costs and has impacted budget in Colombian health system. Consequently, it is important to develop strategies to achieve positive outcomes in RA patients and at the same time to obtain cost-savings for health system.
**Objectives:** We describe effectiveness of conventional DMARD therapy in RA patients with moderate-severe disease activity, usefulness of Treat to Target (T2T) strategy with a multidisciplinary care team (MCT) model and subsequently cost-savings obtained.
**Methods:** We conducted a real-world, retrospective, cross-sectional study. We included patients who had moderate-severe disease activity; these patients were potential candidates for biologic therapy because were using conventional treatment; they were followed-up and treated according to T2T and MCT model. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1); therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it. The aim of the study was to evaluate patients who were in moderate-severe disease activity and reached low disease activity or remission impacting on health costs. Descriptive epidemiology was done, the medians were analyzed using t-Student by performing a normality test for DAS28 distribution; the disease activity was analyzed using Pearson's statistics.

**Results:** 526 patients were included, mean age 63.5±11.8, 424 (80%) female and 102 (20%) male. These patients had a DAS28 on average 4.5±1 at beginning and after 24 months 410 patients (78%) got remission/low disease activity status with a mean DAS28 2.57±1. The costs of biological therapy in Colombia finishing 2015 on average were $7,725 US dollars/year/patient, and taking into account that 410 patients in moderate-severe disease activity who were candidates to biologic treatment and reached at least low disease activity, the amount in costs-savings projected for health system by preventing early use of biologics was approximately $3,167,551million dollars/year, ranging between the cheapest biological and the most expensive ($4,878 and $12,774 US dollars/year respectively).
**Conclusions:** This study showed that it is possible to decrease disease activity and obtain a significant cost-reduction in treatment of RA by using conventional DMARDs in a model with therapeutic goals like T2T and optimizing a multidisciplinary approach.
**Disclosure of Interest:** None declared
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## AB1038 HIGH COSTS FOR HEALTH SYSTEM OF MISDIAGNOSING OSTEOARTHRITIS AS RHEUMATOID ARTHRITIS

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**Background:** There are an important number of patients with osteoarthritis (OA) that are misdiagnosed as rheumatoid arthritis (RA) in general practice in Colombia. They are treated as such with disease modifying anti-rheumatic drugs (DMARDs), leading to higher economic costs for health system.
**Objectives:** The aim of this study was to calculate the possible direct economic costs of the care of OA patients misdiagnosed as RA in a 48 month period in a cohort of patients derived to a specialized RA center in Colombia.
**Methods:** A descriptive cross sectional study was performed. Patients derived during a 48 month period to a RA specialized center with presumptive diagnosis of this disease and found finally diagnosed with OA were included in analysis. Each patient was evaluated to confirm or rule-out diagnosis of RA as follows: a rheumatologist fulfilled a complete medical record, including joint counts; it was assessed rheumatoid factor and anti-citrullinated antibodies, and other laboratories depending on each case. Also were made x-rays of hands and feet, and in some cases of persistent doubt about the diagnosis was requested comparative MRI of hands or/and feet. Then we described the direct costs of care in Colombian pesos (COP) of these false-positive RA patients assuming an average of 4 visits/year to general practitioner (8.400 COP/medical appointment), 2 visits/year for physiatrist and orthopedics (33.995 COP/ medical appointment) and 4 set/year of conventional laboratories (92.161 COP/set). Cost of medication doses were calculated for an average use of methotrexate, sulfasalazine, chloroquine and prednisolone (200.840 COP/monthly). Indirect costs were not calculated.
**Results:** We found 2930 OA patients misdiagnosed as RA in a period of 48 months. For each patient we calculated 33.600 COP/year for general practitioner visits, 135.980 COP/year for specialized medicine visits, 368.644 COP/year for laboratory sets and 2.431.248 COP/year for medications. This leads to a total cost of 2.969.472 COP/year per patient. Given a total of 2930 misdiagnosed patients cost rise to 8.700.552 million COP/year ($2,900,184 US dollars/year).
**Conclusions:** There is an important economic implication of the misdiagnosis of OA as RA, being this the most frequent mistake in the diagnosis of this disease. The implementation of educational programs for health care primary physicians and specialized RA centers where a process of screening diagnosis is made could save this amount of money for the health system in Colombia.
**Disclosure of Interest:** None declared
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## AB1039 BETTER OUTCOMES OF DISEASE ACTIVITY IN A LARGE COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS

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**Background:** Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA). This strategy is being used last years in Colombia. On the other hand a multidisciplinary care team (MCT) model was generated in order to improve outcomes.
**Objectives:** The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 24-month period in a large cohort of patients from a Colombian specialized in RA center with a MCT model.
**Methods:** A descriptive retrospective study was performed. Records of patients from specialized in RA center were reviewed; those patients were followed-up under T2T standards. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 $>$5.1), every 7–9 weeks (DAS28 $\geq$3.1 and $\leq$5.1), and every 11–13 weeks (DAS28 $<$3.1). Therapy had to be adjusted with DAS28 $>$3.2 unless patient's conditions don't permit it. A MCT model means that a patient should be seen by other specialties such as physiatrist, physical and occupational therapy, nutritionist and psychologist at least 3 times a year. We divided patients in three groups: low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission (REM). Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson's statistics.
**Results:** 1147 patients were included in this study, 934 (81%) women and 213 (19%) men. Mean was 62±10 years. In regard to treatment it was found that 370 (33%) patients were treated with biologics, and 767 (67%) patients with conventional therapy. It was found a global increase in the percentage of patients in LDA/REM and decrease in moderate and severe disease activity groups. The mean of DAS28 was 4.1±1.1 at the beginning and 24 months after was 2.8±0.61. At 24 months was observed an increase in percentage of patients in remission or LDA (up to 80%) and a decrease in percentage of patients in MDA/SDA disease activity statistically significant. The difference of medians for each variable showed improvement with statistical significance ($p<0.00$). Although there was a slight decrease in HAQ, this was not statistically significant.

| ACTIVITY LEVEL | TIME 0 n (%) | 6 MONTHS n (%) | 12 MONTHS n (%) | 24 MONTHS n (%) |
|---|---|---|---|---|
| REM | - | 305 (26) | 541 (47) | 562 (49) |
| LDA | 269 (23) | 350(30) | 278 (24) | 362 (31) |
| MDA | 635 (55) | 436 (38) | 305 (26) | 217 (19) |
| SDA | 243 (21) | 56 (5) | 24 (3) | 6(1) |

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**Conclusions:** This study shows improvement of DAS28 and level of disease activity in a cohort of RA patients from a specialized center in Colombia treated under recommendations of T2T strategy and based on a MCT model. This revision shows the importance of T2T follow-up and treatment for this disease.
**Disclosure of Interest:** None declared
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## AB1040 COMPARISON OF ADHERENCE AND DOSING INTERVAL OF SUBCUTANEOUS ANTI-TNF BIOLOGICS IN INFLAMMATORY ARTHRITIS FROM A CANADIAN ADMINISTRATIVE DATABASE

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**Objectives:** Subcutaneous (SC) anti-TNF agents such as Golimumab (GLM) Adalimumab (ADA), Etanercept (ETA) and Certolizumab pegol (CZP) have been used for many years for the treatment of inflammatory arthritis. It is known that across diseases, and especially with chronic diseases, adherence to therapy is an important modifiable factor that may compromise treatment outcomes. The aim of this analysis was to compare adherence and dosing interval of SC anti-TNF in the treatment of inflammatory arthritis.
**Methods:** We used the IMS Brogan database which combined both private (PDP) and public drug plan databases of the provinces of Ontario (OPDP) and Quebec (RAMQ). Target drugs included SC anti-TNF biologics for indication of rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis combined. The Index period was from January 1, 2010 - June 30, 2012 and patients were followed for 24 months through June 30, 2014. Patient selection criteria were adult patients newly prescribed a target biologic drug with at least three prescriptions and retained on therapy at 24 months.
Recommended dose regimens as per the Canadian product monographs were used to compare actual vs. expected drug utilization. The compliance rate (MPR) was calculated as the estimated days' supply in the defined period divided by the number of days in the defined period. Patients who scored $>$80% were considered adherent. For dose-interval analysis, the average days between units was estimated by taking the total days on therapy and dividing by the number of units the patient received. A unit is a syringe or vial; the total amount of drugs dispensed (in mg) were standardized at units as per the following: GLM: 50 mg; ADA: 40 mg; ETA: 50 mg; CZP: 200 mg. P-value obtained from Chi-square and Pair-wise comparison tests for statistical differences on the proportion of adherent patients; p-value $<0.05$ is considered to be statistically significantly different.
**Results:** There were 4,035 new patients on target biologic drugs with at least three prescriptions and retained on therapy at 24 months. The number of patients for each biologic drug used was 683, 1400, 1765 and 187 for GLM, ADA, ETA and CZP, respectively. The data source was as follow: PDP national (N=2509), RAMQ (N=634) and OPDP (N=892). In 24 months-retained patients, there was a greater proportion of GLM-treated adherent patients (n=595/683, 87%, $p<0.0001$) compared to ADA- (n=1044/1400, 75%), ETA- (n=1285/1765, 73%) or CZP-treated patients (132/187, 71%). We also investigated the number of patients receiving biologic drug at a shorter dosing interval. That proportion was

similar between groups and was 5%, 6%, 12% and 4% in GLM- (≤26 days), ADA- (≤12 days), ETA- (≤6 days) and CZP-treated patients (≤12 days), respectively.
**Conclusions:** In this real life Canadian administrative database, GLM has better adherence compared to other SC biologics. The reason for this difference and impact on long-term outcomes are currently under investigation.
**Disclosure of Interest:** P. Bhoi Employee of: Janssen Inc., L. Bessette: None declared, M. Bell: None declared, C. Tkaczyk Employee of: Janssen Inc., F. Nantel Employee of: Janssen Inc., K. Maslova Employee of: Janssen Inc.
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## AB1041 HOUSEHOLD ERGONOMICS: DEVELOPMENT AND VALIDATION OF A NOVEL TOOL TO ASSESS PHYSICAL EXPOSURES CONTRIBUTING TO HOUSEHOLD WORK RELATED LOW BACK PAIN

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**Background:** Household ergonomic risks-especially physical exposures straining the low back during manual household work can contribute to low back pain in housewives. To date, there are no screening tools to identify physical exposures that cause household work related low back pain.
**Objectives:** To develop and validate "Physical Exposure Check-Household work related low back pain (PEC-HLBP)", a tool to assess physical exposures contributing to household work related low back pain.
**Methods:** Items for PEC-HLBP were generated based on a theoretical framework developed through review of literature, qualitative observations and expert opinion. Item reduction was by a panel of 10 experts based on a scoring system. The draft PEC-HLBP was developed into an interviewer-administered questionnaire with responses in a Likert scale to facilitate responses on the gradient of the physical exposure and the scoring system adopted reflected the gradient of exposure. PEC-HLBP was designed to be answered based on household work activities routinely being performed by the respondent.
Exploratory factor analysis using principal component analysis was performed on a sample of 250, 20–50 year old eligible housewives to further reduce items and to assess construct validity. Internal consistency and test retest assessed the reliability.
**Results:** The initial PEC-HLBP contained 36 items. Ten items which scored an average score less than 2 by the panel of experts (score based on the importance as a physical exposure on a 1–5 scale) were eliminated. Exploratory factor analysis of draft PEC-HLBP with 26 items showed 9 factors (Eigen values 1.008–5.163) explaining 64.18% of total variance. All 26 items in draft tool showed factor loadings above 0.4 not requiring further reduction of items. Two factors with items of similar loadings were amalgamated based on the theoretical framework. Finalized PEC-HLBP contained 26 items in eight domains which were assigned names to depict the items they contained (figure 1). Experiencing the physical exposures or not were determined based on a predetermined cut off score for each domain.
The mean duration to complete the questionnaire was 16 (±4) minutes. Cronbach's Alpha was 0.789 (95% CI 0.725–0.825).The test-retest reliability was good (Spearman's coefficient above 0.77) for all domains. Response rate among housewives was 83.3% and the response rate for each question was 100% with no missing data.
**Conclusions:** PEC-HLBP is a valid, reliable and acceptable tool to assess physical exposures contributing to household work related low back pain among housewives
**Acknowledgement:** Medical Research Institute, Sri Lanka
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2850



Figure 1: Final structure of PEC-HLBP indicating domain names and the items that are assigned to each domain

## AB1042 PATIENT BELIEFS REGARDING ASSOCIATIONS BETWEEN WEATHER AND PAIN; AN ANALYSIS OF ENROLMENT QUESTIONNAIRES WITHIN "CLOUDY WITH A CHANCE OF PAIN"

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**Background:** The association between the weather and chronic pain is complex and largely undetermined. More than 80% of patients believe in an association between weather and pain. However, beliefs vary about which weather variable (e.g. temperature, atmospheric pressure) influences pain, with possible differences across pain disorders.
**Objectives:** To describe participants' beliefs about an association between weather and pain at the time of enrolment to a national smartphone study entitled "Cloudy with a Chance of Pain", stratified by self-reported diagnosis.
**Methods:** Participants in the UK aged 17 years or older, with access to a smartphone and who had arthritis or other chronic pain for at least 3 months were recruited to "Cloudy with a Chance of Pain". Participants completed an 8 point enrolment questionnaire which included two questions about their beliefs: 1) Belief strength: On a scale of 0–10, how likely do you think weather is associated with pain? 2) Belief type: If you think there is a possible association, which weather condition(s) affect your pain the most? Both questions offered categorical response options. In question 2, participants were permitted to select multiple categories and a "free text" option was also offered. We present a descriptive analysis of the categorical data and sub-analyses of differential beliefs by age (above/below 50yrs), gender and self-reported diagnosis. Results are reported as median (IQR) or number (%). Mann-Whitney U-Test and Fisher's exact test were used for statistical analysis. Within Table 1, significant associations ($p<0.05$) are denoted by bold text.
**Results:** 5,282 enrolment questionnaires were included in analysis. Median belief strength was 7 (5–9). 8% reported a belief strength of 4 or less. Participants most commonly believed that "damp/rain" affected their symptoms (72%). When compared to the total study population, those with fibromyalgia, chronic headache and neuropathic pain more frequently believed that changes in temperature and pressure correlated with pain. Indeed, participants with fibromyalgia and neuropathic pain more commonly reported belief in an association between all aspects of weather and pain when compared to the total study population. Table 1 summarises belief strength and belief type by gender, age and underlying diagnosis.

| | | Belief strength | Belief type | | | | |
|---|---|---|---|---|---|---|---|
| | | (0–10) | Temp change | Damp/ rain | Pressure change | Hot | Cold |
| | All (n=5282) | 7 (5–9) | 28% | 72% | 30% | 15% | 67% |
| Sex | Male (n=1667) | 7 (5–8) | 27% | **70%** | 31% | **11%** | **67%** |
| | Female (n=4115) | 7 (6–9) | 28% | **73%** | 29% | **16%** | **63%** |
| Age | <50 (n=2538) | 7 (6–9) | **34%** | **71%** | 29% | **17%** | **72%** |
| | ≥50 (n=2466) | 7 (5–8) | **22%** | **75%** | 31% | **12%** | **61%** |
| Diagnosis | Arthritis (other) (n=2425) | 7 (6–9) | 26% | **78%** | 30% | **13%** | 68% |
| | Fibromyalgia (n=1102) | 8 (6–9) | **44%** | **78%** | **40%** | **24%** | **77%** |
| | RA (n=1052) | 7 (5–9) | 27% | 70% | 29% | 17% | 62% |
| | Neuropathic pain (n=626) | 8 (6–9) | **38%** | **77%** | **40%** | **21%** | **73%** |
| | Spondyloarthropathy (n=493) | 7 (6–9) | 30% | 73% | 33% | 16% | 65% |
| | Chronic headache (n=337) | 8 (6–10) | **43%** | 70% | **49%** | **22%** | 67% |
| | Crystal arthritis (n=215) | 7 (5–9) | **34%** | **64%** | 33% | 20% | **56%** |

**Conclusions:** Most participants strongly believed in an association between weather and pain. Participants most commonly believed that damp/rain affected their pain. Specific beliefs vary between participants and between diagnostic groups, perhaps reflecting different causal pathways in these conditions.
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**Disclosure of Interest:** None declared
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## AB1043 THE RELATIONSHIP AMONG PAIN SLEEP DISORDERS AND SMOKE IN PATIENTS WHO ACCESS FOR THE FIRST TIME IN A RHEUMATOLOGY UNIT

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**Background:** Pain is the most frequent manifestation of musculoskeletal conditions. Sleep disorders are common in a variety of rheumatologic diseases (1). The cigarette smoking is associated with exacerbated pain intensity and related symptoms (2,3).
**Objectives:** This study aimed to investigate the relationship between pain,sleep disorders and current smoker status in an Italian population sample who suffered by muscoloskeletal conditions.
**Methods:** A total of 978 patients were consecutively included from december 2014 to december 2015.Partecipants were assessed by Visual Analogic Scale (VAS) for pain intensity and by questions about sleep duration for sleep disorders (<6 h short sleeper;6–9 h normal sleeper, >9 h long sleeper) Smoker o non smoker current status was determinate by using one question. We considered patients without pain as controls.
**Results:** The mean age of partecipants was 52,7 years in wich most of them (86%) was female. Strong correlation (p=0.0058) was found between high pain, current smoker and short sleeper status. A correlation (p=0,085) was found between high pain, no current smoker and short sleeper status.High pain was strongly associated with short sleeper satus.(p=0,0078)
**Conclusions:** Short sleeper status is very prevalent in patients suffered by a musculoskeletal condition with high pain.Current smoker status is an independent variable.
**References:**
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[2] Ditre JW. Pain as a motivator of smoking:effect of pain induction on smoking urge and behavior. J Abnorm Psychol 2008 May;117(2): 467–47
[3] BA Stipelman et al. J Behave Med (2013)36:539–548
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5653

## AB1044 PAIN AND PSYCHOLOGICAL HEALTH MAY BE ASSOCIATED TO RISK FACTORS FOR CARDIOVASCULAR DISEASE IN PATIENTS WITH RHEUMATIC JOINT DISEASE

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**Background:** Patients with rheumatological joint diseases (RJD) have an increased risk of cardiovascular disease (CVD). There is a lack of knowledge concerning the impact of health status on CVD risk. Augmentation index (AIx) and reactive hyperemia index (RHI) are two markers of CVD risk. High values of AIx, and low values of RHI signify an increased risk of CVD.
**Objectives:** To investigate whether pain and self-reported health status are associated with CVD risk in patients with RJD.
**Methods:** 895 patients with RJD were included. 425 patients with self-reported osteoarthritis (OA), 159 patients with ankylosing spondylitis (AS) and 148 patients with rheumatoid arthritis (RA).
Variables of demography, co-morbidities, self-reported pain, health related quality of life (EuroQOL (EQ-5D) (AS and OA)) and health status (Short form 36 (SF-36)) were collected on questionnaires. Clinical examinations were performed by a study nurse and the 28-tender joint count recorded (28-TJC) (RA and OA). AIx (Sphygmocor apparatua (Atcor®)) and RHI (Itamar®) were measured. Cross-sectional linear regression analyses were performed with AIx and RHI as dependent variables in separate models. The associations between pain, health status and CVD risk (AIx and RHI as dependent variables) were examined in cross-sectional models adjusted for type of RJD, age and sex. (AIx was also adjusted for height). Possible confounders were identified from previous literature and plotted in directed acyclic graphs[1]. Relevant variables were entered into multivariate models.
**Results:** 895 patients with RJD were included, mean age was 61.3 (range 28–85), (64.7%) females. AIx was available in 143 patients with RA, 130 with AS, and 424 with OA. RHI was available in 143 patients with RA and 42 with AS. The results from the linear regression models are presented in the table. The multivariate models were adjusted for body mass index and disease activity (DAS ≥2.6 or ASDAS ≥1.3 = active disease).
**Conclusions:** Pain and psychological health are related to markers of CVD risk in RJD, after adjustments for disease activity. These novel findings require confirmation in longitudinal studies.
**References:**
[1] Williamson EJ. Respirology 2014.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3320

**Abstract AB1044** – Table 1

| | AIx n=697 | | RHI n=185 | |
|---|---|---|---|---|
| | Age and sex adjusted model | Fully adjusted model* | Age and sex adjusted model | Fully adjusted model |
| 28-TJC | –0.03 (–0.23, 0.17) | –0.05 (–0.25, 0.15) | –0.05 (–0.09,-0.00)* | –0.03 (–0.08, 0.01) |
| SF35 vitailty | –0.05 (–0.08, –0.02)** | –0.05 (–0.08, –0.02)** | 0.01 (0.00, 0.01)* | 0.01 (0.00, 0.01)* |
| SF36 bodily pain | –0.05 (–0.07, –0.02)** | –0.04 (–0.07, –0.01)** | 0.01 (0.00, 0.01)* | 0.00 (–0.00, 0.01) |
| SF36 social functioning | –0.03 (–0.05, –0.00)* | –0.03 (–0.05, –0.00)* | 0.01 (0.00, 0.01)* | 0.00 (0.00, 0.01) |
| SF36 mental health | –0.04 (–0.08, –0.01)* | –0.04 (–0.08, –0.00)* | 0.01 (–0.00, 0.02) | 0.01 (–0.01, 0.02) |
| EQ-5D-pain | 1.46 (0.04, 2.88)* | 1.59 (0.25, 2.93)* | –0.12 (–0.74, 0.50) | –0.18 (–0.82, 0.46) |
| EQ-5D-anxiety | 1.99 (0.74, 3.23)* | 2.04 (0.79, 3.29)* | –0.15 (–0.60, 0.31) | –0.21 (–0.68, 0.27) |

*p<0.05 *p<0.001.

## AB1045 EFFICACY OF ETANERCEPT ON RADIOGRAPHIC PROGRESSION IN ADULT PATIENTS WITH RHEUMATOID ARTHRITIS OR PSORIATIC ARTHRITIS: RESULTS FROM THE SECOND INTERIM ANALYSIS OF A GERMAN NON-INTERVENTIONAL, PROSPECTIVE, MULTI-CENTER STUDY

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**Background:** Several clinical trials have shown that etanercept (ETN) is highly effective in reducing clinical disease activity and reaching remission while it may also decrease and even reverse radiographic progression in rheumatoid arthritis (RA) and in psoriatic arthritis (PsA). However, the proportion of patients with RA or PsA achieving remission and radiographic non-progression in routine everyday practice is not known.
**Objectives:** To assess radiographic change and clinical disease activity in RA and PsA patients during long-term routine use of ETN under real-world conditions in a non-interventional trial. This is an interim analysis of the data after 52–78 weeks of observation per patient.
**Methods:** 1,600 adult RA and 400 PsA patients will be included into the study. Radiographs of hands and feet taken at baseline (±3 months start of ETN treatment), after 12 to 18 and 36 months follow up and 12 to 36 months before baseline ("historic"), if available, are scored by 2 blinded readers with random time order by the "van der Heijde modified Sharp score"[1] ($mTSS^{RA}$) for RA patients and the "van der Heijde modified Sharp score adapted"[2] ($mTSS^{PsA}$) for PsA patients. Additional parameters such as disease activity score (DAS28) and (serious) adverse events are recorded regularly.
**Results:** 282 RA and 87 PsA patients (77% vs. 51% females) were evaluated for this interim analysis. The median disease duration at baseline was 5.3 (range: 0;46) years (RA) and 4.3 (0;37) years (PsA). At baseline, mean $mTSS^{RA}$ was 22.1±33.2 (n=136), mean $mTSS^{PsA}$ was 21.6±30.6 (n=34). X-rays after 52–78 weeks were available for 131 RA (32 PsA) patients with a mean annualized radiographic progression of 1.4±6.4 (-0.9±4.2) under ETN therapy. During ETN treatment, 29.8% RA (28.1% PsA) patients experienced no change (-0.5 to 0.5) and 30.5% RA (43.8% PsA) an improvement (<-0.5) in mTSS. In total, numerically more PsA than RA patients were considered to be in radiographic non-progression (60.3% RA vs. 71.9% PsA, change in $mTSS^{RA/PsA}$ ≤0.5 from baseline). 65 RA (16 PsA) patients had a historic (i.e. 12–48 months prior to baseline) and a baseline x-ray with a mean annualized radiographic progression of 3.7±21.3 (2.1±3.5). Comparison between the annualized radiographic progression under ETN therapy with prior disease progression (before baseline x-ray) revealed less annual radiographic progression under therapy with ETN in both treated groups (RA: n=61; -3.6±22.1; p=0.205, PsA: n=14; -3.5±6.1; p=0.049). In RA (PsA) patients, the DAS28 decreased from a mean baseline value of 4.6±1.3 (4.2±1.0) to 2.9±1.2 (2.4±1.0) at week 78 indicating an important decrease of disease activity under ETN treatment. At week 78 fewer RA than PsA patients reached remission (DAS28<2.6) (44.6% RA vs. 60.7% PsA). Treatment with ETN was well tolerated and no new safety signals were observed.
**Conclusions:** The results of this interim analysis suggest that treatment with ETN slows radiographic progression and reduces disease activity in RA and PsA patients in routine clinical care.
**References:**
[1] J Rheumatol 2000; 27: 261–63;
[2] Ann Rheum Dis 2005; 64: (Suppl II):ii61-ii64
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**Disclosure of Interest:** S. Wassenberg Consultant for: Chugai, Janssen, Novartis, Pfizer, Speakers bureau: Abbvie, Chugai, Janssen, MSD, Pfizer, Roche, R. Rau: None declared, T. Klopsch Shareholder of: Abbvie, Amgen, Gilead, Novartis,

Roche, Consultant for: Abbvie, BMS, Pfizer, Roche, UCB, M. Buecheler Employee of: Pfizer Pharma GmbH, T. Meng Employee of: Pfizer Pharma GmbH, P.-A. Loeschmann Employee of: Pfizer Pharma GmbH
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## AB1046 THE IMPACT OF BIOLOGIC THERAPY ON WORKING CAPACITY IN SERBIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic progressive disease that can have profound influence on working capacity of affected people. It has been highlighted that reduced productivity is one of the major issue in RA and represents a significant economic burden on the patients, their families, and society.
**Objectives:** The objective of this study was to estimate the impact of biologic therapy on self-reported working capacity in Serbian patients with RA.
**Methods:** During the period from November 1 to December 15, 2015, 315 consecutive RA patients who were treated in one of three randomly chosen Serbian clinics were enrolled in a cross-sectional study. The inclusion criteria were: age $\geq$18 years, diagnosis of RA of at least 6 months, current MTX use for at least 1 month (with or without concomitant usage of biologic therapy), and written informed consent. The severity of pain is estimated by visual analogue scale (VAS). The differences between groups were assessed using the Mann-Whitney U-test. The relationships between the biologic therapy-related changes in productivity and the indicated parameters were evaluated using the Spearman rank correlation.
**Results:** Distribution of study sample regarding the employment status showed that 26.3% of the responders were employed, 23.5% were unemployed, while 50.2% were retired. The analysis of self-reported working ability demonstrated that 25.4% of the RA patients stated full work capacity, 38.1% partial work capacity, while 36.5% of the participants reported inability to work. Work incapacity was statistically significantly correlated with following variables: duration of RA ($\rho$=0,136; p=0,016), duration of MTX treatment ($\rho$=0,179; p=0,001) and the use of biologic therapy ($\rho$=-0,134; p=0,017). More than half (51.7%) of RA patients used biologic therapy. The average value of VAS score in the group currently receiving biologic therapy was 48.6±28.8 mm, while in the group that was not receiving a biological therapy was 61.3±25.1 mm, with statistically significant difference between these two groups (Z =-3.948; p$<$0.001). The majority of the participants (82.2%) who used biologic drug reported an improvement of working capacity following the introduction of this therapy. Also, more than half of these patients (53.4%) stated that the increase of working capacity occurred after 4 weeks of biologic therapy initiation.
**Conclusions:** The results of our study suggested that biologic therapy deeply and rapidly improved working capacity in patients with RA. Keeping in mind the fact that the loss of working ability is a significant outcome of RA, the effectiveness of treatment strategies should be evaluated not only using traditional clinical, functional, and radiographic measures, but also by establishing the possible influence of these treatments on working ability in this group of patients.
**Disclosure of Interest:** S. Zivojinovic: None declared, S. Stojanovic: None declared, M. Lazarevic: None declared, S. Mamula Masic Grant/research support from: The research was sponsored by Roche d.o.o., Employee of: Roche d.o.o., N. Damjanov: None declared
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## AB1048 THE TRANSFORMATION OF INPATIENT RHEUMATOLOGY SERVICES IN A POST-BIOLOGICS ERA

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**Background:** Over the last 15 years the rapid development of an armoury of biological drugs has revolutionised the management of inflammatory arthritis and other rheumatological conditions[1]. In the past Rheumatology inpatient wards were largely occupied with patients with difficult rheumatoid arthritis and associated extra-articular disease, with little option bar synthetic DMARDS, corticosteroid, respite and physiotherapy.
**Objectives:** In 1996 we audited inpatient services for the month of February within the Belfast Rheumatology Unit and a report was issued as a result of this to help plan service development. Twenty years later we repeated the audit.
**Methods:** We audited the inpatient admissions between 5th October 2015 and 5th November 2015. Data was collected contemporaneously by reviewing the medical notes whilst the patients remained on the ward and any omissions filled in retrospectively using our local database NIECR. Information collected included age, gender, method of admission, diagnosis on discharge, duration of admission, procedures carried out, allied health professionals inputting, radiology services required and onward referral as inpatient to other specialities. We compared this to the audit report from 1995.
**Results:** The audit discovered that there was some similarities between the two eras including:
1) Inpatients remain predominantly female – 77% in February 1996 compared with 88% in October 2015.
2) Emergency admissions remain in the minority – 17% in February 1996 compared with 25% in October 2015.
3) 59 patients were admitted to the ward in February 1996 compared with 44 in October 2015.
4) The mean age of our inpatients was 56 years. The commonest age interval in 1996 in both males and females was 45–64.
Conversely there are a few notable differences including;
1) In 1996 there were 44 beds in the department compared with 16 beds currently.
2) In 2015 21/44 patients were elective admissions to the ward for administration of Iloprost or Flolan. Other common reasons for admission included multiple joint injections (5/44) and flares of inflammatory arthritis (4/44). In 1996, 23/49 patients were admitted for the management of flares of inflammatory arthritis. This represents a 38% reduction in admissions for disease flares.
3) Less patients required access to the multidisciplinary team (MDT). In 1996 85% of patients were reported to access inpatient physiotherapy, compared with 52% in 2015. 80% of patients in 1996 were said to access OT, but it was 18% in 2015.
4) The mean length of stay in 1996 was 11.8 days, compared with 7.1 days in 2015.
**Conclusions:** Our ward serves a comparable number of patients nowadays, as it did in 1996. However the inpatient population has certainly evolved. Better treatments for inflammatory arthritis have reduced the number of admissions to manage flares. Those patients that are admitted, stay for a shorter time and require less MDT input, perhaps due to less acquired disability.
**References:**
[1] Katherine S. Upchurch and Jonathan Kay. Evolution of treatment for rheumatoid arthritis Rheumatology 2012;51:vi28-vi36
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4658

## AB1049 MUSCULOSKELETAL MANIFESTATIONS IN RENAL HEMODIALYSIS PATIENTS

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**Background:** Pain is a significant problem in more than 50% of hemodialysis patients and is not being effectively managed[1]. In patients on regular dialysis, musculoskeletal pain was identified as the most disturbing pain and the majority reported that pain limited their daily life activities[2]
**Objectives:** The aim of the study is to detect and describe the incidence of musculoskeletal manifestations, comorbidities and gender differences in renal failure patients on regular hemodialysis
**Methods:** Forty-nine patients with renal failure and on regular dialysis were included in the present study. The patients were subjected to full history taking and clinical examination. Blood samples were collected before the mid-week session for laboratory investigations. The bone mineral density (BMD) was assessed by dual energy X-ray absorptiometry (DXA) in all patients. Kt/V was used as a marker of dialysis adequacy
**Results:** The 49 patients mean age was 54.41±15.9 years. They were 28 males and 21 females. The dialysis duration was 3±2.31 years. Comorbidities were present as diabetes (45%), hypertension (96%), cardiovascular (33%), cerebrovascular stroke (6%), hyperuricemia (37%), hepatitis C (16%) and amyloidosis (8%). The following musculoskeletal findings were present in descending frequency: fibromyalgia syndrome (51%), myalgias (37%), arthralgia (37%), flexor tenosynovitis (29%), cramps (29%), ectopic calcifications (25%), flexion deformity of the elbow (16%), carpal tunnel syndrome (14%), and destructive spondyloarthritis (8%). Vasculitis was present in 2. Positive anti-CCP was present in 1 female and rheumatoid factor in 4 females and 1 male. Otherwise, there was a tendency to a higher frequency of musculoskeletal findings in males. Vitamin D insufficiency (25.1±14.6ng/ml) and reduced bone mineral density were present. The DXA t-score at lumbosacral spine was -1.51±1.77, hip (-1.65±1.59) and forearm (-1.89±1.9).
**Conclusions:** Musculoskeletal manifestations and comorbidities are frequent and overlooked in hemodialysis patients especially males and the associated chronic pain may affect their quality of life.
**References:**
[1] Davison SN. Pain in hemodialysis patients: prevalence, cause, severity, and management. Am J Kidney Dis. 2003;42(6):1239–47.
[2] Gamondi C, Galli N, Schönholzer C, Marone C, Zwahlen H, Gabutti L, et al. Frequency and severity of pain and symptom distress among patients with chronic kidney disease receiving dialysis. Swiss Med Wkly. 2013;143:w13750
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1569

## AB1050 FACTORS OF WORK DISABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a progressive disease which leads to early work disability.
**Objectives:** To determine the factors of work disability in patients with RA.
**Methods:** The study included 283 patients with RA in the Special Hospital for Rheumatic Diseases Novi Sad in the period of one year. Patients average age was 51.5 years (range 30–68), mean disease duration 11 years (range 2–37 years). All patients were treated with conventional DMARD's and 38% got prednisolone,too. They were determined with disease activity-DAS28, HAQ-DI Health Assessment Questionnaire for Rheumatoid Arthritis and made a X-ray of hands and feet. All patients filled out a questionnaire that included questions related to education, qualifications, type of work, conditions of the workplace, motivisanos to work, distance and way of coming to work, the existence of some of the categories of disability and time of its creation, and the existence of other diseases.
**Results:** After 2 years of the disease, 99% of patients were able to work. After 5 years in 30% was required retraining, 10% had part-time work, while 9% of patients were permanently disabled for work. After 10 years of the disease in 50% of patients was required retraining, 10% had part-time work, while 40% was permanently work disabled. After 15 years, 61% of patients were permanently unable to work. After 23 years there was no working abled patients. The most common cause of work disability 32% was the weight of work that has been associated with a low level of education ($p<0.001$) -without a professional education 50%, 42% high school education, 28% had high disease activity that is correlated with high values of HAQ-DI ($p<0.001$). Poor working conditions as risk factors were present in 17%, the presence of concomitant diseases in 10% (57% cardio vascular diseases), lack of motivation to work in 8%, distance from work in 5%.
**Conclusions:** The lower level of education, heavier physical labor and poor working conditions in patients with high disease activity and low functional ability led to early work disability. Early and aggressive treatment of RA with conventional DMAR and biological medications, also as raising the level of education and the improvement of working conditions can affect the reduction of work disability after years of disease duration.
**References:**
[1] Ann Rheum Dis 2013;72:875–875.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5203

## AB1051 EPIDEMIOLOGY OF EARLY RHEUMATOID ARTHRITIS: RESULTS FROM AN EARLY ARTHRITIS RESEARCH CENTER FROM ROMANIA

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**Background:** The early phase of rheumatoid arthritis (RA), known as "window of opportunity" was considered to be represented by the first years of evolution, but nowadays this period is considered to be very short and therapeutic intervention at this point is very important for better long-term outcomes (1).
**Objectives:** The aim of this study is to describe the epidemiology of early RA (ERA) in a population of Romanian patients from an Early Arthritis Research Center (EARC).
**Methods:** We have evaluated the data obtained from patients diagnosed with ERA in the EARC of "Dr. I. Cantacuzino" Hospital. Only data form patients who fulfilled EULAR/ACR 2010 criteria for RA (2) and had symptom duration less than 12 months were analyzed.
**Results:** 217 patients were referred to the EARC between 2010 and 2015, among whom only 47 patients fulfilled the EULAR/ACR criteria for RA and had a duration of symptoms for less than 12 months. There was a clear predominance of women (61.7%). The mean age was 55.17±14.62 years and the difference wasn't statistically significant between sexes (p=0.311). 17 patients (36.2%) were smokers and they presented higher values of ACPA but the difference wasn't significant between smokers and non-smokers (p=0.466). The mean duration of symptoms was 3.48±3.32 months and 36 patients (76.59%) had a duration of symptoms less or equal to 3 months which classifies them as very ERA (VERA). Patient positives for RF and ACPA were 87.2% and 82.1%, respectively. The vast majority of patients (74.5%) presented with polyarticular involvement. 68.1% of patients administered treatment with NSAIDs, while 23.4% didn't receive any treatment and no patient was treated with DMARDs previously. Patients with no previous treatment had higher values of disease activity indices than those who had administered NSAIDs, but the difference assessed by Wilcoxon test wasn't significant ($p>0.05$ for all disease activity indices). The median value and interquartile range for lab tests and for disease activity indices are shown in Table 1.

Table 1. Lab tests and disease activity indices results

| Lab test | Median (Interquartile range) |
|---|---|
| CRP (mg/l) | 8.63 (2.63–18.44) |
| ESR (mm/h) | 27 (11–44) |
| RF (IU/ml) | 34.00 (10.08–79.30) |
| ACPA (IU/ml) | 34.50 (5.00–134.77) |
| DAS28 | 4.75 (3.63–5.35) |
| CDAI | 22.80 (14.70–29.55) |
| SDAI | 26.12 (14.94–32.13) |

The level of acute phase reactants didn't correlate with the level of RF or ACPA ($p>0.05$ for each Spearman correlation). CDAI and SDAI identified more patients with high disease activity than DAS28.
**Conclusions:** There are large variations in epidemiologic parameters of different populations with early RA and knowing the particularities of the population treated is important to improve clinical practice. Although the majority of patients presented very early in the course of the disease, they had polyarticular involvement and very active disease. NSAIDs were administered by the majority of patients before the first presentation and this can lead to a decrease in disease activity parameters. This is an ongoing study and we have to see if this results are maintained on larger numbers of patients.
**References:**
[1] van Nies JAB et al. Ann Rheum Dis. 2015;74:806–812
[2] Aletaha D et al. Arthritis Rheum. 2010;62:2569–2581
**Acknowledgement:** None
**Disclosure of Interest:** None declared
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## AB1052 JOINT DAMAGE IN RHEUMATOID ARTHRITIS APPEARS AS SEVERE AS INFLAMMATION IN CONTEMPARY CARE AT ONE SITE, WHICH MAY EXPLAIN IN PART LIMITATIONS TO TREAT-TO-TARGET

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**Background:** "Treat-to-target" should guide treatment of patients with rheumatoid arthritis (RA), with intensification of therapy if an index indicates moderate/high disease activity. However, low activity or remission are unusual in even 50% of patients. One study suggests a partial explanation, as about 20% of patients with high index scores whose therapy is not intensified had clinically important joint damage[1]. However, a quantitative estimate of the extent of joint damage is not included in quantitaive assessments of patients with RA.
**Objectives:** To analyze quantitative physician estimates on visual analog scales (VAS) for inflammation and damage in routine care of patients with RA for the proportions of clinical management decisions which are attributable to either inflammation and/or damage.
**Methods:** All patients seen at a one academic site complete an MDHAQ/RAPID3 at each visit, and rheumatologists complete a RheuMetric physician checklist, which includes four 0–10 VAS, for overall global estimate, inflammation or reversible disease, damage or irreversible disease, and distress or fibromyalgia, etc., explained by neither inflammation nor damage. Physicians also estimate the proportion of decisions concerning management that is attributable to inflammation, damage, or distress, totaling 100%. Cross-tabulations here were performed to analyze the proportion of clinical decisions attributable to inflammation and/or damage (not including distress), classified as low (<20%), moderate (20–60%), and severe (>60%), using chi square tests for statistical significance.
**Results:** 110 RA patients were studied. Mean age was 56.2 (SD=17.5); 84.4% were female. Mean estimate of the physician VAS for inflammation was 2.3 (SD=2.2) and for damage was 3.1 (SD=2.2). Among the 110 patients, 29 (26%) were estimated to have clinical decisions based on high inflammation, while 39 (35%) were estimated to have high damage (Table). A high level of inflammation and low level of damage was estimated in 19 patients (22% of all patients), while a high level of damage and low level of inflammation was estimated in 27 patients (35% of all patients).

Proportion of clinical decision in 110 RA patients based on inflammation vs damage*

| % Based on damage (total=100%) | % Based on inflammation (total=100%) | | | |
|---|---|---|---|---|
| | Low (<20%) | Moderate (20–60%) | High (>60%) | Total |
| Low (<20%) | 3 (3%) | 0 (0)% | 19 (17%) | 22 (20%) |
| Moderate (20–60%) | 9 (8%) | 37 (34%) | 10 (9%) | 56 (51%) |
| High (>60%) | 27 (25%) | 5 (5%) | 0 (0%) | 32 (29%) |
| Total | 39 (35%) | 42 (38%) | 24 (26%) | 110 |

*All percentages (%) shown are of total of 110 RA patients, $p<0.001$.

**Conclusions:** Damage appears to impact clinical decisions in current treatment of patients with RA as much as inflammation. Structural damage is unlikely to be ameliorated by aggressive medical therapy, and these data may explain in part why clinical trials of established patients indicate only 60% ACR20 responses with all 10 approved biological agents for RA. Moreover, the data may explain in part why fewer patients are in remission than might be expected using a "treat-to-target" strategy. Estimates of inflammation, damage and distress are feasibly completed by rheumatologists in busy clinical settings, and may help clarify and document decisions concerning therapies and outcomes.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5843

## AB1053 THE NATIONWIDE DANISH RHEUMATOLOGIC BIOBANK – PAVING THE ROAD TO PERSONALIZED TREATMENT OF PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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**Background:** The medical treatment of inflammatory rheumatic diseases has improved during the last decades. However, many patients experience treatment failure due to lack of effectiveness or serious adverse events. Biomarkers are promising future tools to predict treatment outcome on the patient level (personalized treatment), but these biomarkers still remain to be identified. The newly started nationwide Danish Rheumatologic Biobank (DRB) provides the infrastructure needed to promote research within this field. The protocol "Identification of biomarkers that improve diagnostics, predict treatment responses, adverse events or prognosis among patients with inflammatory rheumatic disease followed in the Danish nationwide DANBIO registry" (approvals: H-2–2014–086 and GLO-2015–6) is the first national study within DRB. DRB is built on the infrastructure of the Danish CancerBiobank [1] and is funded by The Danish Rheumatism Association and the hospital owners (Danish Regions).
**Objectives:** The aim of DRB is to promote the identification of new biomarkers for personalised treatment of patients with inflammatory rheumatic diseases. We here present the first protocol in DRB.
**Methods:** DRB is established through the collaboration between Depts. of Rheumatology and Depts. Clinical Biochemistry at hospitals in all regions of Denmark. Currently, 9 hospitals participate. Patients are included after having signed an informed consent. Blood samples are collected 1) cross-sectionally (i.e. patients provide one blood sample); 2) longitudinally (i.e. patients are enrolled when they start a new disease-modifying anti-rheumatic drug (DMARD, biologic or conventional synthetic) and provide blood samples at 0, 3, 6, 12, 24, 36, 48 and 60 months and at time of treatment withdrawal. Synovial fluid, tissue and urine may also be collected. Samples are collected, handled and stored (at minus $80^0$C) according to nationally approved Standard Operating Procedures (SOPs) and all data regarding the samples are registered in the nationwide database, the Biobank of Danish Regions. Sample-associated high-quality clinical data are registered prospectively in the nationwide quality and research registry, DANBIO, e.g. patient demographics and patient-reported outcomes, previous and current treatment (DMARDs) including reasons for withdrawal, and physician-reported outcomes (clinical characteristics, treatment response, imaging) [2].
**Results:** From May 2015 to January 2016, 840 patients with rheumatoid arthritis (67%), axial spondyloarthritis (22%), psoriatic arthritis (9%) and other diagnoses (2%) had been included in the study, and had contributed 1,239 blood sample packages stored at minus $80^0$C, each including whole blood (1x1.5 ml), buffy coat (1x1.5 ml), EDTA plasma (2x2 ml), serum (4x2 ml) and whole blood in PAXgene RNA tubes (2x2.5 ml).
**Conclusions:** The establishing of DRB has been successful with >1,200 samples collected. Sampling from patients included in the first biomarker protocol continues and the first scientific results are expected in 2016. DRB is unique due to the nationwide and parallel collection of clinical data and biological material from patients with inflammatory rheumatic diseases.
**References:**
[1] www.cancerbiobank.dk
[2] Rheumatology (Oxford). 2011 Jan;50(1):69–77
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2666

## AB1054 THE BURDEN OF SYSTEMIC LUPUS ERYTHEMATOSUS ON PATIENT'S OCCUPATIONAL ACTIVITIES

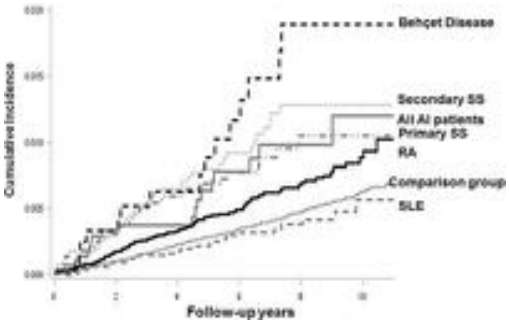
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**Objectives:** To determine the burden on systemic lupus erythematosus (SLE) on patient's occupational activities
**Methods:** We conducted a cross-sectional study of SLE patients, fulfilling SLICC/ACR 2012 classification criteria. All patients were assessed for disease activity by SLEDAI, damage index by SLICC/ACR DI, general assessments by PGA and MGDA. We collected data on work activity using the Work Productivity Activity Impairment (WPAI) questionnaire for lupus patients. All patients completed the SF-8 questionnaire, estimating physical and mental component summaries (PCS and MCS) of the quality of life (QoL).
**Results:** The study included 102 SLE patients, 94,1% females, mean age ±SD 42,4±13,3 (range 20–73) years, mean disease duration±SD 93,9±77,1 (range 0,1–228) months. A proportion of 34,3% of the patients had high university education. The employment history in our cohort included: 23,5% of subjects were working full time and 3,9% part time. Meantime, 58,8% of patients had disability for SLE and 6,9% - disability for other disease than SLE; 3,9% of the subjects were studying and 2% were not employed at the moment of the questionning. The results of WPAI questionnaire confirmed a dicrease of all work domains, by absenteism (10%) and presenteism (63.4%). To be noticed that 20 from 28 working subjects were missing from their work during last 12 months during 15,3 days (range 5–40 days) for SLE problems. The analysis of the QoL showed a dicrease of both components, PCS and MCS were 43,2±9,6 and 46,9±13,4 points, respectively. According to the results, the level of the QoL and the disease activity were predictors for impaired work productivity ($R^2$=0.21 and $R^2$=0.5, $p<0.05$).
**Conclusions:** Systemic lupus erythematosus had a substantial burden on patient's occupational activities, high disease activity and low indices of the quality of life were predictors for impaired work productivity.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2048

## AB1055 THE RISK OF OBSTRUCTIVE SLEEP APNEA IN 52994 PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES IN TAIWAN: A NATIONWIDE POPULATION-BASED STUDY

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**Background:** Several pathological mechanisiums may underlies an association between sleep apnea and autoimmune diseases. There are few evidances of increasing risk of OSA in patients with rheumatoid arthritis, ankylosing spondylitis. The risk of OSA in RA or Sjogren syndrome (SS)was thought to be attributed to upper airway dryness with a resulting in a colappsibility or temporomandibular joint involvement (1,2). The association between asystemic autoimmune disease nd obstructive sleep apnea were not clear in Asian. We hypothesized that autoimmune diseases would predispose patients to the occurance of OSA.
**Objectives:** To explore the association between the obstructive sleep apnea (OSA) and autoimmune diseases
**Methods:** 52994 adult patients with systemic autoimmune diseases diagnoses recorded in the Taiwan National Health Insurance Research Database between 2002 and 2011, after excluding those with antecedent obstructive sleep apnea. A comparison cohort of 211976 participants was formed by age-, gender-matched controls. Multivariable Cox regression was performed on the two cohorts to compute the risk of OSA during follow-up period.
**Results:** In patients with systemic autoimmune diseases, the overall risk for incident OSA was significantly higher than in controls (adjusted hazard ratio [HR] =1.58, 95% confidence interval [CI] =1.38–1.82). Risk of OSA in individual autoimmune diseases, including rheumatoid arthritis (RA), Sjögren's syndrome (SS) and Behçet disease, was also significantly higher than in controls (HR [95% CI] for RA, primary SS, secondary SS and Behçet disease were 1.36 [1.12–1.63], 2.28 [1.68–3.10], 2.88 [2.14–3.87] and 2.39 [1.43–4.01], respectively). Increased risk for systemic lupus erythematosus did not reach statistical significance (HR: 0.79 [0.49–1.28]).




**Conclusions:** Patients with systemic autoimmune diseases including of RA, primary or secondary SS and Behçet disease were associated with a higher risk for developing OSA.
**References:**
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2221

AB1056 **PSYCHOMETRIC TESTING OF THE DUTCH EVALUATION OF DAILY ACTIVITIES QUESTIONNAIRE IN RHEUMATOID ARTHRITIS**

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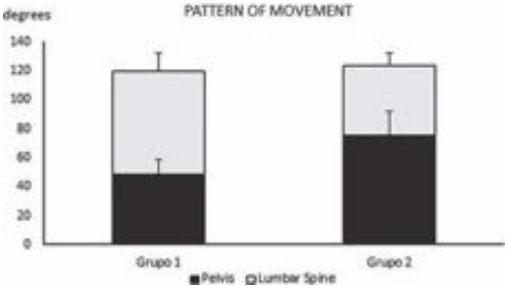
**Background:** The Evaluation of Daily Activity Questionnaire (EDAQ) is a patient reported measure of activity limitations in Rheumatoid Arthritis (RA) and other musculoskeletal conditions, for which there is a Swedish (1) and an updated English version (2–4). The English version was translated into Dutch, and linguistically validated, with phrasing changes made following cognitive debriefing interviews with six Dutch people with RA. The Dutch EDAQ includes 138 items in 14 "domains" (Eating/ Drinking; Personal Care; Dressing; Bathing; Cooking; Moving Indoors; House Cleaning; Laundry; Moving and Transfers; Moving Outdoors; Gardening/Household Maintenance; Caring; and Leisure/ Social Activities). Each domain is split into two sections: one (A) scores whether activities can be performed without aids, alternate methods or help; and another (B) which scores whether the activities can be performed with aids or alternate methods. All items are scored on a 0–3 scale (no difficulty to unable to do).
**Objectives:** To test the reliability and validity of the Dutch version of the EDAQ in people with RA in the Netherlands.
**Methods:** Participants from an out-patient Rheumatology clinic (Reinier de Graaf Hospital, Delft) completed postal questionnaires of demographic questions, the EDAQ, HAQ, SF36v2, RAQOL, a hand pain numeric rating scale (NRS) and a current condition severity scale. Three weeks later, the EDAQ was mailed again. Test-retest reliability of domain scores was evaluated using nonparametric correlations. Internal consistency was tested using Cronbach's alpha. Validity of the 14 domains of the EDAQ against the other measures was assessed with non-parametric correlations.
**Results:** 252 people participated: 155 women and 93 men; age =65.16 (SD 13.45) years; RA duration =11.75 years (SD 9.93). 68 (27%) were employed; 20 had children <18y at home. Average pain score =3 (IQR 1–6) and fatigue =4 (IQR 2–7).
155 (62%) completed Test 2 and test-retest reliability of total domain scores was excellent for nine domains ($r_s$=0.81 -0.88) and moderate-substantial for five ($r_s$=0.56–0.78). Internal consistency was high in all domains: Cronbach's alpha=0.79–0.92 for Section A.
All domains of the EDAQ correlated significantly ($p<0.001$) with: HAQ $r_s$=0.51-0.88; SF36v2 (Physical Function) $r_s$= -0.55 to -0.87; SF36v2 Bodily Pain $r_s$=0.44–0.67; SF36v2 (Vitality) $r_s$= -0.35 to -0.62; RAQOL $r_s$=0.50–0.83; and hand pain $r_s$=0.46–0.64. An exception was the "Caring" domain as many did not have childcare responsibilities, and thus validity was lower compared to the above variables, although still significant ($p<0.01$; $r_s$=0.16 to 0.31).
**Conclusions:** The Dutch version of the EDAQ is a valid and reliable measure of daily activity in people with RA. It can be used in both clinical practice and research.
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[3] Hammond et al (2015) Rheumatology 54:1605–1615.
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**Acknowledgement:** This research was funded by a EULAR Health Professionals Research Grant.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2517

## Rehabilitation

AB1057 **RISK FACTORS ASSOCIATED WITH DIFFERENT LUMBOPELVIC PATTERNS OF MOVEMENT**

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**Background:** Rapid flexion movement increases the loading on the spine and it increases the risk of injuries[1]. In asymptomatic subjects lumbar-dominant and pelvis-dominant patterns of movement during trunk flexion have been observed[2,3]. However, little information about lumbar spine kinematics has been provided.
**Objectives:** To find out whether exhibiting different lumbopelvic patterns of movement during trunk flexion affects the kinematics of the lumbar spine in terms of velocity of motion.
**Methods:** Differential lumbar spine and pelvis angular displacement during the time course of a standardised sagittal trunk flexion from an upright position was recorded with an electromagnetic tracking device in 32 asymptomatic females (22.65±3.5 years). Range of motion (ROM) (degrees) for the lumbar spine, pelvis and average angular velocity (degrees/sec) for the entire movement were calculated. Subjects were divided into groups according to moving more in the lumbar spine than in pelvis, group1 (n=17) and vice-versa moving more in the pelvis (at the hip joint) than in lumbar spine, group2 (n=15). The one-way MANOVA followed by F test showed significant differences in lumbar spine velocity between groups.
**Results:** The lumbopelvic pattern of movement is shown for both groups in the figure. Average angular velocity (degrees/sec) for the spine was significantly ($p<0.01$) greater in group 1 (18.7±3.8) than in 2 (13.1±2.4).




**Conclusions:** Changes in the lumbopelvic pattern of movement bring about differences in lumbar spine velocity of motion. Consequently, the risk of injury for the spine may be different for both groups and clinical implications may be different as well.
**References:**
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[2] Nakayama T, Yamamoto I, Fujiwara T, Yamada T. Sagittal Kinematics and Muscular Activities of Torso and Hip During Trunk Flexion and extension. J.Phys.Ther.Sci.2006;18:165–173.
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**Acknowledgement:** This study has been supported by the following grants:Ref. FIS2001–0070–01, Ref. TIC2001–2786-C02–02, Ref. AP2001–376
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4929

AB1058 **THE NEW JOINT WEIGHTED SCORING SYSTEM WHICH PREDICTS THE MODIFIED HEALTH ASSESSMENT QUESTIONNAIRES SCORES IN RHEUMATOID ARTHRITIS PATIENTS: A VALIDATION STUDY USING THE NATIONAL DATABASE OF RHEUMATIC DISEASES BY IR-NET IN JAPAN**

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**Background:** We reported the impact of each joint disease on the MHAQ (Modified Health Questionnaire) by using 2011 NinJa (the National Database of Rheumatic Diseases by iR-net in Japan) data in the past study. The odds ratio of physical impairment according to the MHAQ using multivariable logistic regression models for bilateral and unilateral joints, respectively, were: shoulder, 4.0 and 1.8; elbow, 2.6 and 1.8; wrist, 1.9 and 1.5; hip, 1.7 and 3.0; knee, 2.6 and 1.9; ankle, 2.3 and 2.0; finger, 1.4 and 1.2; and toe, 1.0 and 1.1. The MHAQ score was significantly affected by shoulder, elbow, wrist, knee, and ankle joint disease, and bilateral disease tended to have a greater effect on physical impairment than unilateral disease. We also developed a joint weighted scoring system from the results of the odds ratio. An integer score was assigned to each identified bilateral and unilateral joint disease, respectively, as follows: shoulder, 4 and 2; elbow, 3 and 2; wrist, 2 and 2; hip, 0 and 3; knee, 3 and 2; ankle, 2 and 2; finger, 1 and 1. We acquired 3 points as the cut-off value of this scoring system through statistical analysis (Modern Rheumatology, 2015, Epub ahead of print).
**Objectives:** To validate this scoring system by applying to NinJa in 2014.
**Methods:** A total of 13,459 subjects (2,586 men, 10,873 female) from NinJa in 2014 were analyzed. The presence or absence of disease in each joint (swelling and/or tenderness were considered as disease) and whether the disease was unilateral or bilateral were investigated. ROC curve analysis was performed to each patient with total score calculated according to the scoring system.
**Results:** The patients' mean age and disease duration was 64.1 and 13.0 years, respectively. The Disease Activity Score-28CRP was 2.4. ROC analysis'

results were as follows: cut-off value, 3 points; AUC, 0.68; sensitivity, 53.4%; and specificity, 75.0%.
**Conclusions:** This joint weighted scoring system was validated and suggested to be useful to predict of functional disability of RA patients in a daily practice.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4505

## AB1059 CLINICAL AND ELECTROPHYSIOLOGICAL EVALUATION OF THE EFFECTIVENESS OF LOCAL INSULIN INJECTION IN MANAGEMENT OF IDIOPATHIC CARPAL TUNNEL SYNDROME (PROSPECTIVE STUDY)

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**Background:** Carpal tunnel syndrome (CTS) is the most common type of peripheral nerves entrapment; It has a great socioeconomic impact. CTS may be idiopathic or secondary to many causes, especially diabetes mellitus. Insulin has anti-inflammatory effects[1] and the effectiveness of local insulin Injection in diabetic patients with CTS has been previously evaluated [2]. Local insulin Injection in idiopathic CTS has not been studied.
**Objectives:** To evaluate the effectiveness of local insulin injection as a therapeutic tool in management of idiopathic CTS.
**Methods:** Twenty eight consecutive hands of mild & moderate idiopathic CTS (diagnosed clinically & electrophysiologically and classified according to American association of neuromuscular diagnostic medicine monograph) received two local injections of 10 IU NPH insulin into the affected carpal tunnel 2 weeks intervals after informed consent. Patients with severe or secondary type of CTS were excluded from this study. Evaluation of the patients at baseline, then at 1 & 3 months after 2nd insulin injection was done clinically [by measuring visual analogue scale (VAS), paraesthesia, Phallen and compression tests] and electrophysiologically (by measuring motor and sensory nerve conduction studies of the median and ulnar nerves using a standardized technique).
**Results:** Clinically; there was statistically significant improvement in VAS, paraesthesis, Phallen and compression tests at 1 & 3 months after 2nd insulin injection ($p<0.01$). Electrophysiologically; there was statistically significant improvement in distal motor latency (DML) and distal sensory velocity of median nerve 1 and 3 months after treatment ($p<0.01$), but the improvement was not statistically significant as regards median distal motor and sensory amplitudes ($p>0.05$).

| | Before injection | 1 month after injection | 3 months after injection |
|---|---|---|---|
| VAS | 7.57±0.95 | 4.678±1.41 | 3.285± 2.07 |
| Paraesthesia | 100% | 39.2%, | 25% |
| Positive Phallen test | 100% | 53.5% | 28.6% |
| Positive Compression test | 92.8% | 60.7% | 32.1% |
| DML | 4.52±0.83 msec | 4.25±0.38 msec | 4.15±0.47 msec |
| Distal median sensory velocity | 34.41±4.89m/s | 36.76±4.96m/s | 39.01±3.41m/s |
| Median distal motor amplitude | 3.756±0.96 mv | 3.603±1.046 mv | 3.626±0.91 mv |
| Median distal sensory amplitude | 12.56+7.19 μv | 14.62+7.185 μv | 15.93+7.21 μv |

**Conclusions:** Local insulin injection is a promising effective treatment for idiopathic CTS. This is the first study to detect the effect of local insulin injection in idiopathic CTS.
**References:**
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**Acknowledgement:** Thanks a lot to Dr. Samar Abd Alhamed for her great efforts in completing statistical analysis in this study.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1035

## AB1060 QUADRICEPS MUSCLE ENDURANCE IN KNEE OSTEOARTHRITIS

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**Background:** Current rehabilitation programs place a significant emphasis on strength training, with minimal attention paid to specifically developing muscle endurance. Yet resistance to fatigue may be of importance, as the successful performance of many functional activities requires individuals to sustain muscle activity over long periods. To date, there has been limited research into the fatigue characteristics of the quadriceps in those with OA and findings are contrasting.
**Objectives:** The objective of this study was to investigate differences in the fatigue resistance of the vastus medialis quadriceps muscle of subjects with and without knee joint osteoarthritis. Endurance characteristics were investigated during a sub-maximal (50%) isometric contraction with a high-spatial resolution surface electromyography technique.
**Methods:** Twenty-six subjects with unilateral knee osteoarthritis, and seventeen subjects with no known knee pathology were evaluated. All subjects performed initial tests to evaluate maximum voluntary contraction (MVC), voluntary activation levels, and true maximum force (TMF). Endurance time was assessed during an isometric quadriceps contraction at 50% of the true maximum force with the knee at 90 degrees flexion while sitting. Surface electromyography (sEMG) data was collected from the vastus medialis muscle of the quadriceps group during the endurance test with a Laplacian high spatial resolution electrode. The variables of interest were median frequency (MDF); mean power frequency (MPF); root mean square (RMS); muscle fibre conduction velocity (CV); the relative slopes of each sEMG parameter calculated over the initial thirty seconds ($T_{30}$), and the percentage change in each parameter over the entire endurance test.
**Results:** MVC tests showed that the affected leg of the group with osteoarthritis was significantly weaker ($p<0.05$) than the unaffected leg. Voluntary activation data showed that subjects with osteoarthritis presented with significant bilateral deficits ($p<0.05$). TMF data showed a significantly lower ($p<0.05$) true potential for force generation in the affected compared to the unaffected leg of the osteoarthritis group.
No significant differences were observed between the endurance times of the groups: affected legs mean: 83 sec, SD: 31; unaffected legs mean: 79 sec, SD: 33; control legs 67s, SD: 23. Irrespective of group, all parameters were significantly different at the beginning of the contraction compared to the end of the test. MDF, MPF and CV decreased with time, while RMS increased with time. In comparison to the unaffected leg, the affected leg showed significantly lower ($p<0.05$) initial values for MDF, MPF and CV. No significant differences were seen between the initial values of the unaffected legs and controls. From initial to end values, across groups, a significant difference ($p<0.05$) was detected in the conduction velocity between the affected (-14.3%) and un-affected (-28.3%) legs of the group with osteoarthritis.
**Conclusions:** The endurance times and the behaviour of the EMG signals indicate an improvement in the relative fatigue resistance of the affected leg in relation to the unaffected leg of the group with knee osteoarthritis. Such findings are consistent with other literature showing increased resistance to fatigue during isometric contractions in muscles with low proportions of type-2 muscle fibres, as well as studies indicating improved relative fatigue resistance following knee injury.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3060

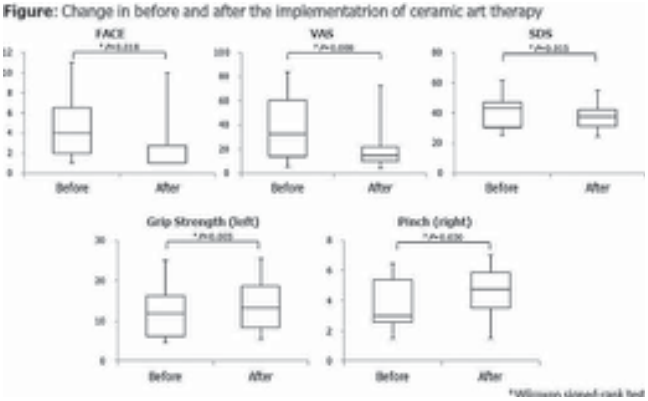
## AB1061 IS CERAMIC ART USEFUL IN TREATMENT OF RHEUMATOID ARTHRITIS?

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**Background:** A published study demonstrating that listening to Rakugo (a comic story) alleviated the pain experienced by patients with rheumatoid arthritis (RA), accompanied by reduction in serum IL-6 and cortisol levels [1]. Overall physical condition improvement and pain alleviation with music therapy have also been reported [2]. However, only few studies have assessed the efficacy of occupational therapy (particularly handcraft work) in outpatients with RA.
**Objectives:** The present study evaluated the usefulness of handcraft work (particularly ceramic art) for both physical and mental rehabilitation for outpatients with RA.
**Methods:** The study involved 10 outpatients with RA managed at our hospital (all females, all right-handed persons, mean age 63.1 years, the average duration of disease was 10.7 years). For physical and mental evaluation, grip, pinching power, VAS score for systemic pain, 20-level FACE scale score, self-rating depression scale (SDS) score were measured before and after participation in ceramic art craft and compared. In addition, a questionnaire survey was administered to assess patient perception of ceramic art.
**Results:** The range of annual changes among the participants was 0.4±0.3 for Modified Health Assessment Questionnaire (m-HAQ) and 0.9±1.6 for C-reactive protein (CRP).
Right hand grip was 14.3±7.2 kgw before participation and 14.8 ±7.1 after participation in ceramic art craft. Left hand grip was 12.1±7.1 and 13.4±7.1 before and after participation, respectively.
Right pinching power was 8.2±4.1 and 10.8±4.0 and left pinching power was 8.7±4.0 and 10.8±3.8 before and after participation, respectively.
VAS score for systemic pain was 38.0±29.2 and 22.4±21.5, and FACE scale scores was 4.7±3.6 and 2.9±3.3 before and after participation, respectively.
SDS score was 41.2±11.8 and 37.1±9.4 before and after participation, respectively.
Thus, all parameters except right hand grip and left pinching power differed significantly between the pre-participation and post-participation periods.
In the questionnaire survey, many patients answered “having pleasure/joy in creation and use of ceramic products.” This indicates that ceramic art can serve as a continued activity for patients with RA, useful not only during treatment but also during daily living. In addition, ceramic art was shown to be useful in

functional training, e.g., in “maintaining and reinforcing grip and finger function” and “maintaining and checking skilled movements.” These results suggest that ceramic art is an activity effective as a means of rehabilitation, with both physical and mental effects perceptible to the patients.

**Figure:** Change in before and after the implementatrion of ceramic art therapy




**Conclusions:** Ceramic art is an activity capable of improving the physical condition and mental state (alleviation of depression, etc.) of patients with RA and improving physical functions such as grip of opposite hand and dominant pinching power. It is useful in the treatment of RA, similar to listening to Rakugo and music therapy.

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**Disclosure of Interest:** None declared

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## AB1062 INVESTIGATION OF INTERACTION BETWEEN HAND DEXTERITY AND PARENTAL ATTITUDE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** There was a gap in the literature about the reason of high prevalence of hand- and wrist-related symptoms in children with juvenile idiopathic arthritis (1).

**Objectives:** This study was planned for investigate hand dexterity and the relationship between children’s hand dexterity and parental attitude in children with Juvenil Idiopathic Arthritis (JIA).

**Methods:** 34 children with JIA (according to International League Aganist Rheumatism (ILAR) Classification) and 38 healthy children that matched according to age, sex and hand dominance. 9 Hole Peg Test (9PHT) and Functional Dexterity Test (FDT) were used to evaluate hand dexterity for both groups (2,3). Childhood Health Assessment Questionnaire (CHAQ) was applied for assessing daily living activities (4). Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and State and Trait Anxiety Inventory (STAI) were applied to investigate parental attitude.

**Results:** There was no difference between hand dexterity values of two groups ($p>0.05$). There was no relationship between Hand Dexterity Scores and CHAQ, BDI, BAI, STAI.

**Conclusions:** Consequently, the result of the tests we used have shown that hand dexterity was not affected by parental attitude.

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# Education

## AB1063 A SURVEY OF MUSCULOSKELETAL ULTRASOUND (MSUS) TRAINING AMONGST RHEUMATOLOGISTS AND TRAINEES ACROSS WALES

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**Background:** Although MSUS is routinely used in rheumatology practice, expertise in performing MSUS and training opportunities vary considerably across UK and Europe. [1, 2, 3] There is a growing consensus to include MSUS in the UK Rheumatology curriculum. The All Wales Rheumatology Ultrasound group (AWRUG) conducted a preliminary survey of rheumatologists across Wales in 2013 and based on this survey, developed a modular MSUS training programme to improve training facilities and access to mentorship.[4] In August 2015, AWRUG re-surveyed rheumatologists across Wales, seeking their feedback and views on MSUS training. This 2 year follow on survey depicts the current state of Rheumatology MSUS training and expertise in Wales.

**Objectives:** 1. To ascertain the level of MSUS expertise and interest following the modular MSUS training programme.

2. To ascertain the opinion of rheumatology consultants and trainees as to whether MSUS training should be part of the Rheumatology curriculum in the UK.

**Methods:** An online survey link was sent to all rheumatologists in Wales by email in August 2015, asking for their feedback on the AWRUG delivered MSUS training and about their expertise in MSUS.

**Results:** Out of 32 respondents including 9 trainees and 21 consultants, 14 (44%) had access to US mentorship and training facilities. 11 (34%) respondents had no MSUS training and 2 (6%) were expert/ trainers. 13 (41%) could identify synovitis/ erosions on MSUS. 18 (56%) attended an AWRUG MSUS masterclass (with 11 finding it useful and 7 very useful). 17 (53%) were using MSUS routinely in their clinical practice, mostly requesting scans for synovitis or shoulder pathology.

27 (85%) felt that MSUS should be included in the rheumatology curriculum; however 3 (33%) trainees and 2 (9%) consultants felt that it should not be included. 13 (41%) felt that theoretical knowledge of MSUS plus scanning for synovitis should be mandatory. Regarding service provision, 20 (62%) felt that Routine MSUS should be provided by radiology department whereas 11 (34%) felt that rheumatologists should also offer this. Most respondents felt that MSUS for synovitis should be provided by rheumatologists wholly 9 (28%) or in collaboration with radiology 15 (47%).

**Conclusions:** 1. All respondents who attended the AWRUG Masterclasses, found them useful, confirming the need for an ongoing regional training programme.

2. Most rheumatology consultants and two thirds of rheumatology trainees in Wales feel that MSUS training should be included in the rheumatology curriculum.

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## AB1064 EVALUATION OF SAFETY SKILLS OF BIOTHERAPIES IN TUNISIA

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**Background:** Biotherapies have become common practice in Tunisia, however, they present specific risks that patients must know and learn to manage. So far, patients’ security skills have not been studied in our country.

**Objectives:** The present work aims to assess the skills level of patients using biotherapies, in order to improve them.

**Methods:** Patients with chronic arthritis were recuited. we have established a questionnaire with practical situations in which the patient is confronted, based on the biosecure questionnaire. the main items were the leading symptoms to consult, vaccination, contraception, and situations excluding biotherapy.

**Results:** Thirty nine patients were recuited for the study, 77% with SA and 23% with RA. The mean age was 52, and 54% were female. 48% of patients have high education level. Etanercep was used in 15 cases, adalimumab in 12 cases, infleximab in 9 cases and one patient used tocilizumab. The mean duration of biotherapy was four years. 38% were in clinical remission. 69% had already

received therapeutic education session about security of biotherapy use, by a doctor in 77% of cases. The median score of the questionnaire was 71,4% (58,8–100%). skills on symptoms must lead to consult and contraception are the least mastered.

**Conclusions:** This work showed that all patients didn't master all situations concerning biotherpy. However, it is important for patients to have a basic control, to minimize the incidence of severe and avoidable side effects such as severe infections.

**Disclosure of Interest:** None declared

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## AB1065 DEVELOPMENT OF THE FIRST SKILL FRAMEWORK IN JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** In the " list of healthcare treatments and interventions-JIA " of 2009, HAS recalls that " therapeutic education must ensure involvement of the patient and his parents: understandability of the disease, mastering of the technical skills, and adaptation of the lifestyle. The main aim of the ETP of the child, the adolescent, and his relatives is to take care of and prevent complications and to learn the skills involved in care. "

**Objectives:** In this context, we have decided to develop a framework of the necessary skills needed for children suffering from JIA (REAJI) in order to improve their quality of life (knowledge, know-how, know-how-to-be).

**Methods:** The steering committee is composed of health professionals involved in paediatric rheumatology and patients' associations.

Different stages are scheduled:

1. Literature review
2. Setup of four focus groups (FG) with different facilitation methods: 2 patient FGs (8–12 year olds and adolescents), 1 parent FG, 1 health professional (HP)
3. Analysis by the steering committee et production of a first skills list.
4. Submission of the list to a panel of patients and to the national JIA competence centres for further information.
5. Submission of the completed list to the same participants for ranking (primary and secondary objectives).
6. Validation of the final list by the committee.

**Results:** The steering committee is made up of two rheumatologists, two paediatricians, and two patients associations, ANDAR (association of patients suffering from RA) and KOURIR (association of parents whose children suffer from JIA).

The press review highlights a number of works, mainly on adolescents and outside the French territory.

The HP FG is composed of 1 rehabilitation doctor, 1 rheumatologist, 1 paediatrician, 1 psychologist, 1 occupational therapist, 1 nurse and 1 pain nurse. The parent FG is composed of 10 people (6 mothers, 1 aunt, 3 fathers).

The 8–12 year olds FG had 3 children and the adolescents FG 4 teenagers.

The committee gathers to establish the initial skills list and then proposes to complete it via an online questionnaire to a selection of HPs from the 38 French centres listed by the Francophone Society of Rheumatology And Internal Paediatric Medicine (SOFREMIP) and an equal number of patients/ parents.

This expanded list is sent back to participants using the same method in order to rank it and lastly to be validated in its final version by the committee.

**Conclusions:** The collectively-developed REAJI framework is a consensus-based support tool that anyone will be able to call upon: not only individual families but in particular teams working on educational projects. This mutidisciplinary participative, national effort is an example of health democracy, the results of which will be made available to all.

**Disclosure of Interest:** None declared

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## AB1066 ASSESSING AWARENESS OF THE EFFECTS OF SMOKING IN A RHEUMATOLOGICAL OUTPATIENT SETTING

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**Background:** Tobacco smoking is an important modifiable environmental risk factor in the development and disease activity of autoimmune rheumatic disease including rheumatoid arthritis (RA), systemic lupus erythematous, systemic sclerosis and antiphospholipid syndrome. In RA the risk is two-fold in ever vs never smokers[1], appears to be dose related[2] and correlated to severe extra-articular disease[3]. Response to disease-modifying antirheumatic drugs and tumour necrosis factor inhibitors is also decreased in smokers[4].

**Objectives:** This pilot study is to assess awareness of the negative impact of smoking on rheumatic disease and establish the methods by which previous smokers achieved long-term abstinence.

**Methods:** 100 patients (median age 55 years) in a rheumatology outpatient setting were asked to complete a questionnaire relating to smoking history. Surveys were distributed over a two month period. Rheumatological diagnosis, comprehensive smoking history and awareness of the negative impact of smoking on rheumatic disease was established. Ever-smokers (those having smoked >100 cigarettes or equivalent over their lifetime) were specifically questioned whether they had received information regarding smoking and rheumatological disease burden, or cessation advice directly from healthcare professionals. Methods to achieve smoking abstinence was also established.

**Results:** 34/49 individuals completing the questionnaire met inclusion criteria. 17/34 (50%) identified themselves as current or former smokers and of this population only 8/17 (47%) were aware of the negative association of smoking and rheumatological disease. All current smokers said they would like to stop, with the majority 4/7 (57%) stating health reasons as the impetus to do this. Of ever-smokers 7/17 (41%) had received cessation advice from a healthcare professional, 3/17 (18%) stated this was from a rheumatologist. The majority of former smokers 8/10 (80%) abstained without pharmaco- or behavioural therapies and 9/10 (90%) felt they would be unlikely or very unlikely to restart. Of current smokers 3/7 (43%) had previously tried to stop, 2/7 (29%) had attempted on 10 or more occasions using 3 or more therapies. Only e-cigarettes were deemed a beneficial adjuvant in smoking cessation.

**Conclusions:** This survey highlights the need for enhanced patient education regarding the risks of smoking in rheumatalogical disease.

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## AB1067 QUANTITY AND QUALITY OF FEEDBACK ON CLERKING OBTAINED BY 4TH YEAR MANCHESTER MEDICAL STUDENTS DURING RHEUMATOLOGY AND ORTHOPAEDICS

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**Background:** Feedback is the cornerstone of effective clinical teaching [1] allowing students to improve by reinforcing good practice and improving poor practice. The ability to take a clinical history is a key skill required to practise effectively as a doctor. The four week Rheumatology and Orthopaedic placement for the University of Manchester medical students requires them to take a minimum of 12 case histories, at least four of which must be presented to clinicians to obtain feedback.

**Objectives:** To review quantity and quality of feedback on clerking obtained by 4th year Manchester Medical students as a part of Rheumatology and Orthopaedic placement.

**Methods:** A questionnaire survey of 4th year medical students studying Rheumatology and Orthopaedics at the University Hospital of South Manchester was performed to review clinical history taking and feedback during this module. It consisted of 13 questions designed around the four levels of training evaluation described by Kirkpatrick's evaluation framework [2]. It was given to three cohorts of students on the day that they completed their Rheumatology and Orthopaedics block.

**Results:** 43/64 (67.2%) of students responded to the questionnaire, of which 21 students (48.8%) either agreed or strongly agreed that it was easy to find patients from whom to take clinical histories during the placement. However, 18.6% of students reported not achieving the minimum of 12 case histories required. 32.6% of students agreed that it was easy to identify staff from which feedback could be sought, and 44.2% received feedback for at least four clinical histories. The majority of the students (81.4%) agreed that feedback was useful. The content of the feedback that was evaluated in the first two cohorts of students varied greatly, with very few students received feedback covering positive and negative comments as well as ways to improve (Orthopaedics 19.2%; Rheumatology 31.7%). Feedback varied in length of time with 58.1%taking less than five minutes, 25.6% lasting 5–10 minutes and 11.6% lasting 11–15 minutes.

**Conclusions:** Our survey demonstrates that there are some issues with the current system for facilitating student history taking, and obtaining feedback on this. The vast majority of feedback received is perceived as useful. Over half of students are not achieving the amount of feedback that they should receive, hence students are potentially missing out on an important opportunity to improve their clinical performance. Considering the results of this survey the authors plan to develop an intervention to try to increase the quality and quantity of feedback given, similar to the feedback postcard project being piloted in Edinburgh [3],

which seems on track to improve both the quality and quantity of feedback during clinical placements.

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## AB1068 SPECIFIC DIET FOR GOUT - CAN GENERAL PRACTICIONER EDUCATE THEIR PATIENTS?

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**Background:** Gout is a chronic disease that occurs with joint crises. Almost 50% of patients with gout are treated by general practitioners (GPs). Nonpharmacological treatment - proper diet and lifestyle, are held parallel with medication throughout life (1).
**Objectives:** The aim of the study was to analyze the training of GPs on gout diet and the opportunities for educating patients with gout in general practice.
**Methods:** A direct anonymous questionnaire among 37 GPs was performed. Seven (7) close questions with possible answers "yes" or "no" were included. Collected data were processed by alternative analysis.
**Results and discussion:** Unfavorable relationship between alcohol (beer, spirits, wine) noted 37 of all 37 respondents (100%). Regarding the increased intake of coffee and the worsening of gout information had 19 of the 37 GPs (51.35%). Nine of 37 respondents (2.43%) believe that black tea has unfavorable effect on gout. Traditionally recommended milk and yoghurt in gout noted as useful 33 of 37 (85.19%) of GPs. About the relationship between low-fat yogurt and worsening the in serum levels of uric acid 7 of 37 respondents (18.92%) are informed. Eleven (11) of 37 GPs (29,73%) are aware on the positive effect of vit.C supplementation on the relative frequency of joint crisis, as well as 5 of 35 (13,51%) noted the beneficial effects of vitamin D supplementation in gout.
Regularly updated recommendations and guidelines for patients with gout are very helpful in their everyday life (2). New data about this disease known since the time of Hippocrates, are accumulated in recent years especially on gout diet (3,4).
**Conclusions:** Good medical practice requires constant upgrading of knowledge. The survey data has shown need to extend education programs for GPs about gout, focusing on diet as an essential part of the treatment.

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## AB1069 THE EDUCATIONAL NEEDS OF PEOPLE WITH SPONDYLOARTHROPATHIES (AS AND PSA): A CROSS-SECTIONAL STUDY

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**Background:** Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) have significant impact on patients' lives and patient education is integral to the management of the diseases.
**Objectives:** To assess the self-reported educational needs of patients with AS and PsA, and test differences across gender, age, disease duration and educational background.
**Methods:** In this cross-sectional study, patients completed the Portuguese version of the Educational Needs Assessment Tool (PortENAT). Data was then Rasch-transformed to obtain interval-level measures of their educational needs which were summarized descriptively. Univariable analyses were used to determine differences between patient subgroups.
**Results:** The study included 121 AS and 132 PsA patients (mean age =47.3 and 53.8 years; disease duration =15.6 and 14.4 years, respectively). Overall, patients with AS had higher educational needs than those with PsA (Table 1). On the domains' scores, age, gender and educational background had different effects in the disease groups; gender affected all domains, except treatments and support systems, with women expressing higher educational needs. Educational background had the strongest effect on overall score – higher education being related to higher educational needs.
**Conclusions:** The educational needs vary by disease and demographic characteristics. Assessing individual patient education needs with tools such as the PortENAT may help target individual patient education.

**Disclosure of Interest:** None declared
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## AB1070 COULD ENHANCED PATIENT EDUCATION IMPROVE THE OUTCOME OF CLINICAL TRIALS IN RHEUMATOID ARTHRITIS?

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**Background:** Patient education is considered to be a highly cost-effective way to limit disability in rheumatic diseases as well as to achieve an improvement in quality of life. Since 1997 our team has carried out a variety of educational programs for RA patients [1]. Since the year 2000 several clinical trials have been carried out on RA patients at Revita Clinic.
**Objectives:** Internationally, medical teams involved in clinical trials work according to the "gold standard" (ICH-GCP) based on regular training and international guidelines. It is suggested that apart from the known and obvious prerequisites for clinical trials, individual sites could add to the process of developing a new molecular entity by enhancing the education of recruited patients thereby improving compliance and reducing the failure rate of investigational products used in such trials.
**Methods:** Data and statistical analyses from 16 RA studies on biologics & JAK inhibitors from the last 5 years involving 185 patients are presented of which 144 were involved in customized educational programs utilizing an educational DVD, and 6-week courses involving meetings with other patients, doctors, and physiotherapists. Compliance measured using standard and site-specific questionnaires were compared with meta-analyses of international studies. Efficacy measures a) withdrawal risk [2]; b) HAQ; c) DAS28; d) GAD VAS; e) Physician Assessment, were analyzed and compared with meta-analyses of international studies.
**Results:** The mean withdrawal risk of Revita Clinic patients was found to be

**Abstract AB1069** – Table 1. Educational needs by age, gender, disease duration, educational background and disease[§]

| Domain (score range) | Patients | Disease | Age | | Gender | | Disease duration | | Educational background | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Older | Younger | Male | Female | Longer | Shorter | Lower | Higher |
| Managing pain (0–24) | AS | 14.3±5.3 | 14.3±4.5 | 14.6±5.9 | 13.3±4.8* | 15.6±5.5* | 14.3±5.6 | 13.9±4.1 | 13.6±3.9 | 14.5±5.9 |
| | PsA | 13.3±6.4 | 12.3±7.0 | 14.2±5.5 | 12.3±6.5 | 14.0±6.1 | 13.0±6.7 | 14.4±5.3 | 11.9±6.9 | 15.7±5.7 |
| Movement (0–20) | AS | 10.6±3.9 | 10.9±3.4 | 10.4±4.3 | 9.7±3.6* | 11.8±3.9* | 10.9±3.9 | 9.5±3.3 | 11.0±3.3* | 8.6±3.7* |
| | PsA | 10.5±4.8 | 9.9±4.6 | 11.1±4.9 | 10.0±4.8 | 10.8±4.6 | 10.1±4.8 | 11.4±4.8 | 9.7±5.0 | 12.4±4.3 |
| Feelings (0–16) | AS | 9.6±3.8 | 9.5±3.4 | 9.5±4.0 | 8.6±3.8* | 10.9±3.3* | 9.8±3.6 | 9.0±4.2 | 10.6±3.1* | 8.0±4.2* |
| | PsA | 9.5±3.5 | 9.0±3.6 | 11.1±4.9 | 8.3±3.3* | 10.6±3.3* | 9.3±3.3 | 10.2±3.9 | 9.0±3.6* | 11.4±4.8* |
| Disease process (0–28) | AS | 18.2±5.6 | 17.7±5.5 | 18.9±5.4 | 17.6±5.6 | 19.1±5.5 | 18.3±5.7 | 19.0±5.3 | 17.6±5.6 | 17.8±5.2 |
| | PsA | 17.6±6.2 | 17.0±6.8 | 18.3±5.7 | 16.5±6.1* | 18.6±6.0* | 17.0±6.0* | 19.8±6.3* | 17.2±6.6 | 17.0±6.1 |
| Treatments (0–28) | AS | 14.6±5.2 | 14.0±4.3 | 14.9±5.9 | 14.0±5.1 | 15.4±5.2 | 14.4±5.3 | 15.0±5.1 | 15.5±3.9 | 12.9±6.5 |
| | PsA | 12.9±5.2 | 12.4±5.0 | 13.4±5.5 | 12.8±5.3 | 13.0±5.2 | 12.6±5.0 | 13.3±6.0 | 12.5±5.4 | 14.0±7.2 |
| Self-help measures (0–24) | AS | 14.8±5.3[#] | 13.5±5.2* | 16.1±5.3* | 14.0±5.2* | 16.0±5.3* | 14.8±5.2 | 14.9±5.7 | 13.2±4.6 | 14.4±6.2 |
| | PsA | 12.8±6.1[#] | 11.9±6.7 | 13.9±5.5 | 11.5±6.3* | 14.0±5.5* | 12.6±6.0 | 14.3±6.1 | 11.7±6.3* | 16.8±6.1* |
| Support systems (0–16) | AS | 9.3±3.6[#] | 9.0±3.3 | 9.7±3.7 | 8.8±3.6 | 10.1±3.5 | 9.6±3.4 | 8.8±3.6 | 9.6±3.2 | 8.2±3.1 |
| | PsA | 7.3±3.8[#] | 7.3±4.3 | 7.5±3.5 | 6.6±3.5 | 7.9±3.9 | 7.4±3.8 | 7.5±3.5 | 7.3±4.3 | 6.7±3.4 |
| Total ENAT score (0–156) | AS | 88.6±23.2[#] | 84.9±18.5 | 91.9±26.4 | 83.4±23.1* | 96.0±21.5* | 88.8±24.2 | 88.3±21.1 | 89.6±18.4 | 82.2±26.5 |
| | PsA | 79.7±26.5[#] | 73.8±26.7* | 85.3±25.5* | 75.8±28.6 | 83.7±23.6 | 77.2±26.1 | 87.8±26.0 | 73.6±26.7* | 93.9±32.9* |

[§]Values are mean ± standard desviation; age subgroups based on median split; disease duration categories based on split at 25th percentile. *Significant p-value (<0.05) for that parameter within disease, [#]Significant p-value (<0.05) for difference between diseases groups.

| | Withdrawal (%) | DAS28 | HAQ | GAD | Physician Assessment |
|---|---|---|---|---|---|
| Revita | 4.2 ±1.8 | -2.23 ±1.68 | -0.39 ±0.54 | -26 | -30 |
| Global mean | 9.3 ±0.6 | -1.17 ±0.67 | -0.28 ±0.12 | | |
| | p=0.05 | p<0.0001 | p<0.0001 | | |

significantly lower compared to global data [2] ($p<0.05$). The mean DAS28 value change is -2.23±1.68, significantly higher than the global average of -1.17±0.67 [3] ($p<0.0001$). The mean HAQ value change is -0.39±0.54, significantly higher than the global average: -0.28±0.12 [3] ($p<0.0001$). The mean GAD VAS and Physician Assessment, changes are -26 and -30, respectively.

**Conclusions:** The overall goal is to increase participation, reduce costs, and accelerate the time factor in clinical trials. The high failure rate of investigational products in such trials, especially in the later stages of development, is a significant contributor to the costs and time associated with bringing new molecular entities to market. Enhanced patient education might well help to overcome the present shortcomings thereby increasing the cost-effectiveness of clinical trials.

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**Disclosure of Interest:** None declared
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## AB1071 HOW MUCH IS THE AWARENESS ABOUT RHEUMATOLOGY? SURVEY AMONG MEDICAL STUDENTS (YR 3) IN VELAMMAL MEDICAL COLLEGE, MADURAI, TAMILNADU, INDIA

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**Background:** Rheumatology is a fascinating medical subspeciality. Over 200 syndromes and diagnosis have been described in rheumatology and recently lot of thrust has been given to improve the Rheumatology both in government and private sectors in health care in India. Rheumatology as super specialty in India is slowly gaining prominence, however public awareness still needs to improve.
**Objectives:** 1. To assess the awareness of rheumatology and musculoskeletal health among the medical students (year 3). 2. To gain insight in to their knowledge about this medical subspecialty, in order to improve their educational tools and sessions, which inturn will shape up the changes in their curriculum.(MBBS)
**Methods:** This survey was conducted as anonymised questionnaire. All 3rd yr medical students were requested to express their opinion while answering on a scale of 1 to 10.
**Results:** 118 students participated in this survey and answered 10 questions:

| All ratings were scored from 1 to 10, 1 being low and 10 being high | Mean score |
|---|---|
| 1. How much are you aware about Rheumatology as medical sub speciality? | 5.59 |
| 2. How complex are rheumatological diseases? | 6.44 |
| 3. Are you aware that most rheumatological diseases are multi system disease? | 6.9 |
| 4. Do you think the musculoskeletal problems will top the list of chronic diseases | 5.49 |
| 5. Do you think rheumatological diseases in India are comparable to Europe? | 4.49 |
| 6. How likely you would be interested to take up Rheumatology as career option? | 4.58 |
| 7. How much you are aware that Research and Rheumatology are interlinked? | 4.85 |
| 8. How much do you know about EULAR or BSR as Europe's Rheumatology leagues? | 3.09 |
| 9. Can you rate your current rheumatology knowledge against your curriculum? | 4.26 |
| 10. Do you feel that non governmental agencies and charities need more support? | 6.48 |

**Conclusions:** Although this is the first of its kind, young medical students have insights in to the rheumatology around the world. They are aware about the multisystem nature of the diseases, research benefits and support to the charities. We are aware about their interests.
We need to improve the access to rheumatology education and help our patients. There has been increasing awareness about the EULAR/BSR/ACR/APLAR-the four big leagues around the world, which guide the patients and medical professionals in Rheumatology

**Acknowledgement:** Special acknowledgement to all the year 3 medical students.
**Disclosure of Interest:** None declared
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## AB1072 GENERAL PRACTITIONER PERCEPTIONS OF METHOTREXATE AND ANTI-TNF TREATMENTS: A QUALITATIVE STUDY

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**Background:** The objective of rheumatic disease management is to achieve remission. Methotrexate (MTX) is the first-line treatment choice and tumor necrosis factor alpha antagonists (anti-TNFs) are used in case of MTX failure or intolerance. While these treatments are initially prescribed then renewed by rheumatologists, general practitioners (GPs) are often confronted with them during routine patient follow-up.
**Objectives:** We sought to study the perceptions of GPs from Auvergne (a region of France) regarding MTX and anti-TNFs treatments in common daily practice.
**Methods:** A qualitative study was carried out among 14 GPs following up patients receiving methotrexate and anti-TNFs. The semi-structured interviews were conducted between May and October, 2014. Thematic transversal analyses of the data were conducted by both the interviewer and an independent researcher. Each difference detected between them was discussed, then resolved by consensus.
**Results:** Of the 285 physicians who completed a preliminary questionnaire, 31 consented to participate in the qualitative. A total of 14 interviews, sufficient to obtain data saturation, *i.e.,* until no new data emerged, were conducted, lasting between 8 minutes and 1 hour, with a mean duration of 23 minutes 30 seconds. In total, 57% of the physicians interviewed were female and 42% of all practiced within 15km of a rheumatologist. The participating physicians were either young doctors (14%) or had over 20 years of experience (78%).
Four principal themes were recognized in the analysis: the GP's role with regard to the patients, their experience and difficulties concerning these treatments, their opinions of therapeutic education programs, as well as the need for improvements in clinical practices. The physician's role consisted in renewing methotrexate prescription (10/14) and managing comorbidities *via* vaccination, for example (7/14). The GPs reported good tolerance (10/14) and efficacy (8/14) with the treatments. However, there was still concern over the immunosuppression and increased infection risk associated with these treatments, causing them to hesitate in using them. The difficulties especially concerned drug interactions and managing anti-TNF discontinuation in the event of infection (5/14), especially for rural-based practices with less easy access to specialists. All the physicians expressed a desire for a practical tool to be implemented aiding them to manage these treatments (10/14).
**Conclusions:** All the physicians reported difficulties in their daily management of these treatments. Close collaboration between GPs and specialists thus appears essential for this management. GP training is also to be encouraged.

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## AB1073 EXPLORATION OF THE DIFFICULTIES ENCOUNTERED BY GENERAL PRACTITIONERS WITH METHOTREXATE AND TNF-INHIBITOR TREATMENT IN COMMON PRACTICE

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**Background:** Rheumatic diseases are frequently occurring pathologies (approximately 1% of the population exhibits rheumatoid arthritis), causing pain, articular destruction, and functional handicaps. Early diagnosis and regular disease monitoring are required in order to avoid such complications. The therapy's objective is to attain remission, which entails optimal use of long-term treatments, such as methotrexate (MTX) or TNF-alpha inhibitors (anti-TNF alpha). These treatments are then increasingly prescribed. General practitioners (GPs) therefore must be able to manage such treatments, along with their potential side-effects.
**Objectives:** Our study's aim was to explore the potential difficulties of GPs from the Auvergne region of France with regard to using anti-TNF alpha and MTX in their common practice.
**Methods:** A questionnaire collecting the GPs' characteristics, difficulties in daily clinical practice, and expectations designed to ease the management of MTX and anti-TNF alpha treatments was mailed to 1,190 GPs in our region.
**Results:** The response rate was 24.9%, equating to 296 responses. The analysis covered 285 responses, since 11 doctors did not wish to participate. The majority of doctor respondents was men (57%) and was in group practice settings (55%). No respondents had practices situated at more than 100 km from a rheumatologist. Of the 230 GPs treating patients on MTX (81%: 230/285), 113 reported difficulties in managing therapy, such as infectious problems (30%) and the occurrence of side-effects (23%). Overall, 31% were troubled by potential drug interactions. GPs practicing for less than 10 years had more difficulties than the others ($p=0.002$). No significant differences were observed based on practice location, type of practice, or distance from the rheumatologist. In total, 22% of doctors surveyed (n=41) were prepared to initiate MTX therapy.
Of the 189 respondents (66%) managing patients on TNF inhibitors, 127 encountered similar difficulties, yet with a higher frequency (infectious problems: 53%; side-effects: 29%, and drug interactions: 39%). No differences were observed based on GPs characteristics. Overall, 57.2% of the GPs (163/285) felt that TNF-inhibitor therapies displayed a favorable benefit/risk ratio. Amongst the respondents, 80% (228/285) desired further training.
**Conclusions:** In our study, more than half of the GPs managing patients on MTX- or TNF-inhibitor therapy reported difficulties with the treatment.

**Disclosure of Interest:** None declared
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# Health Professionals in Rheumatology Abstracts

# Poster Presentations

## Miscellaneous forms of clinical care

### THU0639-HPR A NEW ELECTROMECHANICAL PLATFORM FOR SUBCUTANEOUS DRUG DELIVERY: RESULTS FROM AN EU USABILITY STUDY

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**Background:** UCB Pharma have designed and developed an innovative electromechanical, universal injection platform for subcutaneous drug delivery (eDevice), providing full electronic management of the injection process via an interactive graphical user interface (GUI). Here, the eDevice was tested for use with certolizumab pegol (CZP).
**Objectives:** To validate that patients (pts) can self-inject safely and effectively using the eDevice, and that healthcare professionals (HCPs) are able to configure the eDevice and demonstrate its operation by performing a simulated injection, in the expected scenarios and environments, using the instructions for use (IFU), eDevice GUI and training cassette.
**Methods:** The study took place in Stockport and London, UK, with 15 pts with moderate to severe rheumatoid arthritis (RA), and 15 HCPs. An injection test scenario was performed in a room simulating a home (pts) or office (HCPs). Pts/HCPs were supplied with the eDevice, IFU, training cassette and a CZP cassette containing sorbitol, mimicking CZP viscosity. Using an artificial skin pad attached to the intended injection site (abdomen/thigh), pts were asked to perform 2 simulated self-injections of CZP loading dose (LD; 2 x 200mg) and determine the next scheduled injection date. HCPs were asked to configure CZP LD (2 x 200mg Q2W at Wks 0, 2, 4) and 2 maintenance regimens (200mg Q2W, 2 x 200mg Q4W), and perform 2 simulated pt injections. No training was provided; pts/HCPs could use only the IFU, GUI and training cassette for guidance.
An independent human factors researcher scored pts and HCPs against 18 and 22 predefined critical tasks, respectively. Pts/HCPs had 3 attempts for each task. Critical tasks were those required to safely and effectively use the eDevice, scored on the final attempt as pass, pass with difficulty, or fail. Pts/HCPs were then interviewed for 120 mins to identify root causes (RC) of difficulties/failures. RC analyses were reported as perception failure (misreading GUI/IFU), cognition failure (misinterpreting GUI/IFU), action failure (participant understood task but performed incorrectly), prior experience (assumed eDevice was same as other injection devices), test artefact (if pt said "I did not do X as it is not a real situation") or medical condition (symptoms caused use error).
**Results:** All 15 pts and 15 HCPs were able to inject the full simulated CZP LD. 330 critical tasks were assessed for HCPs, and 270 for pts. 4 task failures were recorded for HCPs and 8 for pts (Table). The 1 HCP failure to correctly configure the eDevice was due to poor English understanding, not device design (post-study interview RC analysis). 14 pt and 26 HCP critical tasks were passed with difficulty (Table); the most common reason being an inability to find information within IFU (RC analysis). There were no needle stick injuries or unexpected user errors.

**Table:** Scores for critical tasks completed with difficulty/failed during the injection simulation

| | RA patients | | | HCPs | | | RCA of failed tasks |
|---|---|---|---|---|---|---|---|
| | n | Difficulty | Fail | n | Difficulty | Fail | |
| Configure eDevice for Q2W | N/A | N/A | N/A | 15 | 6 | 1 | Cognition failure |
| Configure eDevice for Q4W | N/A | N/A | N/A | 14 | 5 | 0 | |
| Configure eDevice to maintenance dose 1 | N/A | N/A | N/A | 14 | 2 | 0 | |
| Configure eDevice to maintenance dose 2 | N/A | N/A | N/A | 14 | 2 | 0 | |
| Prepare 1 or 2 cassettes | 15 | 1 | 0 | 15 | 0 | 0 | |
| Inspect cassette window for visible defects | 15 | 0 | 1 | 15 | 0 | 1 | Perception failure (patient and HCP) |
| Insert cassette into eDevice | 15 | 1 | 0 | 15 | 0 | 0 | |
| Remove needle cap | 15 | 2 | 0 | 15 | 1 | 0 | |
| Position eDevice | 15 | 2 | 0 | 15 | 1 | 0 | |
| Re-cap cassette | 15 | 0 | 0 | 15 | 3 | 0 | |
| Dispose of used cassette correctly | 15 | 0 | 5 | 15 | 0 | 2 | Test artefact (patients and HCPs) |
| Clean eDevice | 15 | 3 | 2 | N/A | 0 | 0 | Perception failure |
| Respond to high and medium priority alarms correctly | 15 | 5 | 0 | 15 | 6 | 0 | |

n: number of study subjects. HCPs: healthcare professional; N/A: not applicable; RCA: root cause analysis.

**Conclusions:** All study participants could perform a simulated injection and administer a full CZP LD safely and effectively. There were no incidences of potential over or under dosing, either by self-injection or incorrectly reading the next treatment date on the GUI. All HCPs able to read the instructions could configure the eDevice.
Most difficulties encountered by pts/HCPs could be rectified by improving the IFU design.
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### THU0640-HPR PROVISION OF CARE SERVICES FOR RHEUMATIC AND MUSCULOSKELETAL DISEASES-RELATED FOOT AND ANKLE PROBLEMS: A SURVEY FROM SIXTEEN EUROPEAN COUNTRIES

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**Background:** The increased prevalence of foot and ankle pathologies in Rheumatic and Musculoskeletal diseases (RMDs) is well documented[1], however the provision of foot & ankle (F&A) healthcare services for people with RMDs in Europe has not been evaluated.
**Objectives:** To assess the current healthcare systems for providing foot & ankle healthcare services for people with RMDs in Europe.
**Methods:** A survey was undertaken to evaluate current provision of F&A health care services for people with RMDs across Europe. A questionnaire was distributed to all 22 country presidents representing HP associations within EULAR. The questionnaire used was developed and piloted (in 7 countries) by the EULAR F&A Study Group, and structured to capture the provision and type of F&A services for people with RMDs. When the HP presidents felt unable to answer specific questions they were encouraged to consult a colleague who may be better placed to provide the answers.
**Results:** Sixteen questionnaires were completed (Norway, Ireland, Sweden, Hungary, Netherlands, UK, Denmark, Portugal, Italy, Switzerland, Austria, France, Czech Republic, Spain, Belgium, Malta). Of the 16, 13 respondents indicated provision of F&A health care services in their country, but only three countries had services specialising in RMD-related F&A problems (Netherlands, UK, Malta). The professions providing the care for patients with RMD-related F&A problems were different depending on the pathology and the country (Table1). Podiatrists provided care for F&A pain and deformity problems in 11 countries, but provided F&A ulcer care in only 8 countries.

Table 1. Number of countries reporting which professions are involved in providing the health services specialising in RMD-related F&A problems. Only professions that were present in ≥10 countries were included

| Professions | Foot problems | | |
|---|---|---|---|
| | F&A pain No. Countries (N=16) | F&A deformity No. Countries (N=16) | F&A ulcers No. Countries (N=16) |
| General Practitioner | 14 | 7 | 10 |
| Rheumatologist | 15 | 11 | 10 |
| Rehabilitation Medical Dr | 11 | 10 | 5 |
| Nurses | 9 | 5 | 14 |
| Podiatrist | 11 | 11 | 8 |
| Physiotherapist | 14 | 11 | 3 |
| Orthotist/prosthetist | 14 | 14 | 8 |
| Orthopaedic surgeon | 12 | 14 | 7 |

**Conclusions:** Only 3 countries have F&A health care services specialised to the needs of people with RMDs. The professions providing the care varied between countries, and also depended on the F&A pathology. Interestingly, F&A healthcare services were provided by professions that do not solely specialised in F&A care. Further research is needed to assess the variation of F&A healthcare services

between and within European countries and the impact on healthcare of various F&A healthcare service designs.

**References:**
[1] Woodburn, J. & Helliwell, P. Foot problems in rheumatology. Rheumatology 36, 932–934 (1997).

**Disclosure of Interest:** None declared

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## THU0641-HPR THE CHALLENGE OF PET THERAPY IN RHEUMATOLOGY: EVIDENCE FOR THE IMPROVEMENT OF PATIENTS COMPLIANCE IN SYSTEMIC SCLEROSIS

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**Background:** "Pet Therapy", better defined as Animal-assisted Intervention (AAI), is based on the interaction between animal and human being and is a tool which may complement and support traditional therapies. It can be used on patients affected by different diseases, improving their quality of life from behavioral, physical and psychosocial point of view.

**Objectives:** The aim of our study was to evaluate the effect of AAI in improving quality of life and compliance to standard pharmacological treatment in a cohort of Systemic Sclerosis (SSc) patients.

**Methods:** 42 SSc patients attending at Scleroderma Unit and undergoing iloprost intravenous infusion were divided in three groups: 1) 14 SSc patients (mean age 60.4±8.6 yrs) submitted to 20 AAI sessions with a professional team (doctor, nurse, couple of animal-handler); 2)control (C1) 14 SSc patients (mean age 63.4±5.3 yrs) engaged in alternative social activity as create a cookbook; 3)control (C0) 14 SSc patients (mean age 62.3±6.8 yrs) without any alternative activity. All patients underwent psychological evaluation at baseline (t0) and at the end of project of AAI (t1); moreover the following test (italian standardized version) was performed at the beginning (s0) and at the end (s1) of each single session: General Anxiety State-Trait Anxiety Inventory (STAI-T), Beck Depression Inventory (BDI), Social Interaction Anxiety Scale (SIAS), Eysenck Personality Questionnaire-Revised (EPQ-R), the Social Phobia Scale (SPS), the Toronto Alexythymia Scale (TAS-20), the Thought Control Questionnaire (TCQ), the Visual Analog Scale (VAS), the State-anxiety (STAI-S).

**Results:** At the end of each session, AAI group showed a decrease of the anxiety state level while it was higher in the two control groups ($p_s<0.001$). VAS scale resulted lower both in AAI group ($p<0.001$) and in C1 group ($p<0.01$). Moreover, STAI-T and TAS scores were significantly reduced in AAI group at t1 compared to t0 and to both control groups ($p_s<0.001$). No significant differences were found for depression in the BDI scores at the end of all sessions. TCQ scale showed that patients treated with AAI, compared to control group C0, had greater capacity to avoid unpleasant and unwanted thoughts by using positive distraction strategies ($p<0.05$).The EPQ-R test (used for analyze personality traits, such as extraversion/introversion) revealed in AAI group an enhancement of extroversion trait compared to both C1 and C0 ($p<0.05$).

**Conclusions:** In agreement with literature [1], our work showed that AAI might be a crucial tool to support the traditional therapies thanks to the creation of a different relationship between patient and doctor. This may allow a better compliance to the therapy in a chronic disease like SSc, where patient's compliance is usually low.

**References:**
[1] Matuszek S. Animal-facilitated therapy in various patient populations: systematic literature review. Holist Nurs Pract. 2010 Jul-Aug;24(4):187–203.

**Disclosure of Interest:** None declared

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## THU0642-HPR BETTER ARTHRITIS CARE: WHAT TRAINING DO COMMUNITY BASED HEALTH PROFESSIONALS NEED TO BETTER CARE FOR PEOPLE WITH ARTHRITIS?

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**Background:** It has been shown that arthritis management in primary care does not always meet guidelines (Goodwin 2010) and that insufficient knowledge of Rheumatoid Arthritis (RA) and Osteoarthritis (OA) can lead to a lack of ability to educate and inform patients. To ensure people with arthritis receive the care they need and consistent self-management and life style messages it is important that all health professionals (HPs) they may have contact with are familiar with arthritis, its impact, diagnosis and management. There is very little evidence on the education community based HPs need in order to fulfil these requirements (Fletcher 2012, Lillie 2012, Mann 2012).

**Objectives:** To identify what education community based nurses and allied health professionals (AHPs) need to enable them to appropriately assess, care for and manage arthritis.

**Methods:** The study used a Delphi survey technique with an Expert Panel of 43 rheumatology specialists and expert patients was established to identify the competencies needed by community based nurses and AHPs (occupational therapists, physiotherapists, podiatrists and community pharmacists) to enable them to care for people with arthritis. Focus groups were held with a total of 25 women and men with inflammatory arthritis (IA) and OA and with 26 community based nurses and AHPs to elicit their views on what nurses and AHPs need to know to enable them to appropriately and effectively care for people with arthritis.

**Results:** Frameworks for the core competencies in arthritis care for community based HPs and for profession specific training were developed. The key goals identified were to increase HPs understanding of arthritis, and its impact on patients' lives and to increase their ability to help patients self-manage their condition and access all the means of support available to them. Competencies include a basic understanding of the pathology underlying inflammatory and non-inflammatory arthritis, the ability to distinguish between the two and to recognise early warning signs with emphasis on OA, RA, gout and septic arthritis. Essential competencies included the ability to engage in shared decision making, goal setting, signposting, to provide patients with education and information and to make appropriate referrals.

**Conclusions:** Health professionals (HPs) working in the community commonly encounter arthritis as a presenting problem or as co-morbidity. Care quality to people with IA and OA is currently highly variable and sub-optimal and could be significantly improved (Goodwin et al 2010). This study identifies the core competencies that all community based nurses and AHPs should have in relation to OA and IA.

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## THU0643-HPR PREVALENCE OF FOOT PROBLEMS IN PEOPLE WITH INFLAMMATORY ARTHRITIS IN SINGAPORE

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**Background:** Foot problems are highly prevalent in people with inflammatory arthritis [1]. Podiatry intervention can significantly reduce foot pain and disability [2]. Most knowledge of the epidemiology of foot involvement is based on studies from the UK, Europe and New Zealand [1,3,4] with limited evidence relating to the podiatric need of people with inflammatory arthritis in Singapore.

**Objectives:** To evaluate the prevalence of foot problems in people with inflammatory arthritis in Singapore.

**Methods:** People with inflammatory arthritis were recruited from the rheumatology outpatient clinic of a large public hospital in Singapore. Disease and clinical characteristics included age, sex, disease duration, BMI, current disease modifying anti-rheumatic drug (DMARD) medications, ESR and CRP. Foot pain was measured using a 10cm visual analogue scale. The Leeds Foot Impact Scale (LFIS) [5] was used to evaluate foot impairment and disability and the Modified Health Assessment Questionnaire (MHAQ) was used to assess global function [6]. Foot assessments were conducted and prevalence of foot deformity was ascertained.

**Results:** We recruited 101 people with inflammatory arthritis, of which 50% were female. The mean of age was 52±15 years, and the mean disease duration was 9.3±0.3 years. The most commonly reported inflammatory arthritis conditions were rheumatoid arthritis (46%), spondyloarthritis (18%) and gout (15%). Most (61%) were overweight with a mean BMI of 27.2±5.4 kg/m$^2$. 42% of all participants were on a current prescription of methotrexate and 52% were receiving a combination DMARD therapy. Only 4% were receiving biologic therapy. The mean ESR was 31.6±21.2mg/hr and mean CRP was 27.4±32.2mm/L. The mean of the total LFIS was 17±13 indicating moderate to severe levels of foot impairment and activity limitation. The mean MHAQ score was 0.25±0.36. Over 80% of participants experienced foot problems during the course of their condition, and 48% reported current foot pain. The mean pain score was 5.0±2.3. Despite the high prevalence of foot problems (81%), only 21 participants (21%) had been referred to a podiatrist.

**Conclusions:** This is the first study to investigate the prevalence of foot problems in people with inflammatory arthritis in Singapore. The majority of the participants reported foot problems, but had not been referred to a podiatry service. Findings

from this study will be used to improve referral rates, service provision and quality of patient care.

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## THU0644-HPR E-LEARNING: AN EFFECTIVE METHOD TO IMPROVE DISEASE KNOWLEDGE AND SELF-EFFICACY FOR PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** There is a growing body of evidence to support the effectiveness of education programs for patients with arthritis. However, there has been little investigation into education strategies for patients with axial spondyloarthritis (axSpA). A number of studies examining education strategies for patients with arthritis have involved an interdisciplinary approach and found positive impact on disease activity, function and overall health (1). Furthermore, the use of electronic formats for education are preferred over other formats for patients with axSpA (2). As such, the Toronto Western Hospital Spondylitis Program developed a novel e-Learning education module for patients with axSpA with input from patients and an interdisciplinary team of health care professionals. The module consists of an interactive web-based platform covering evidence-based topics including diagnosis, treatment and self-management for axSpA.
**Objectives:** To measure the effect of the axSpA e-Learning patient education module with respect to: 1) chronic disease self-efficacy; 2) knowledge of axSpA, and 3) exercise behaviour.
**Methods:** Fifty-four adult patients with axSpA attending a tertiary academic spondylitis clinic were randomly assigned to one of two groups: 1) e-Learning intervention, where patients were emailed a link to the web-based patient education module and were asked to complete the module at their leisure; or, 2) usual care. All patients completed baseline and follow-up questionnaires that included: the Ankylosing Spondylitis (AS): "what do you know" knowledge questionnaire; Stanford Chronic Disease Self-Efficacy Scale (CDSE), and, the Stanford questionnaire for Exercise Behaviours.
**Results:** Twenty-one patients with axSpA completed the e-Learning module and 33 patients continued with usual care. Overall, mean (SD) age was 42.6 (13.2) years, 70% were male, mean (SD) disease duration was 19.3 (10.1) years and 85% had a post-secondary education. There were no statistically significant differences in the above outcome measures between the two groups at baseline or follow-up. However there was significant improvement from baseline to follow-up in patients that completed the e-Learning module with respect to their AS knowledge mean score (SD) 19.0 (4.1) vs 19.9 (5.0) (p=0.0002) and CDSE sub-scale "manage disease in general" mean score (SD) regarding when to visit a doctor and ability to manage health condition 7.5 (1.8) vs. 7.9 (1.9) (p=0.02) and 7.3 (1.8) vs. 7.9 (2.1) (p=0.02) respectively.
**Conclusions:** The above demonstrates an increase in overall disease knowledge and improved self-efficacy through the implementation of a novel e-Learning patient education module. This e-Learning module has the potential to provide benefit to patients with axSpA who have limited access to specialized care, ultimately optimizing outcomes in this patient population.

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## THU0645-HPR PERCEIVED BARRIERS AND FACILITATORS FOR BDMARD DOSE OPTIMIZATION: A QUALITATIVE STUDY INTO RA PATIENTS' PERSPECTIVES

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**Background:** Although bDMARDs are effective in treating RA, they are associated with high costs and (rare) dose-dependent side effects. It is therefore desirable to find and use the lowest effective dose in individual patients. Several studies have shown that dose reduction or interval lengthening of bDMARDs using the tight control principle can be successful in RA patients while preserving stable low disease activity.[1] Unfortunately, bDMARD dose optimization is still limited in clinical practice.[2] The successful implementation of bDMARD dose optimization could, among other factors, be influenced by patient's attitudes and beliefs. Insight into RA patients' barriers and facilitators to bDMARD dose optimization might help to improve implementation.
**Objectives:** To investigate the self-reported barriers and facilitators for bDMARD dose optimization in RA patients.
**Methods:** We performed semi-structured interviews with RA patients who used or had used a bDMARD. Patients were recruited at the Sint Maartenskliniek through purposive sampling. Patients with varying characteristics were included, looking at type of bDMARD, treating rheumatologist and experience with tapering/stopping. The interviews were performed by one researcher (18 by telephone, 4 face-to-face), audio-recorded and transcribed verbatim. Two researchers analyzed the transcriptions by inductive thematic analysis using the qualitative data analysis software MAXQDA.
**Results:** 22 RA patients were interviewed (68.2% female; age: 61.8±7.6 years; disease duration: 13.2±9.4 years; 90.9% current bDMARD user). RA patients' overall attitude towards bDMARD optimization was positive. Nine main themes emerged from the interviews: disease activity, functioning/pain, adverse effects, practical use of bDMARDs, attitude towards medication, previous experiences with tapering/stopping, social aspects, organizational aspects and costs. Within these themes, a total of 43 barriers and facilitators were identified. These include affective factors (e.g. fear), cognitive factors (e.g. beliefs) and practical factors (e.g. organization of care, costs).
**Conclusions:** RA patients perceive several barriers and facilitators that influence their willingness to attempt tapering or stopping their bDMARD treatment. The results of this study could be used to target strategies aiming at implementation of bDMARD optimization in clinical practice.

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**DOI:** 10.1136/annrheumdis-2016-eular.2179

## THU0646-HPR EXPERIENCES OF LIFE WITH BIOLOGIC DRUG THERAPY: "I'M DOING MORE THAN I THOUGHT POSSIBLE 3-4 YEARS AGO!"

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**Background:** With significant advancements in new treatment modalities for rheumatoid arthritis with biological therapies, the literature has largely focused on quantifying improvements. However from an extensive review of the literature very little evidence is available relative to experiences of mobility in this group after commencing biologic drug therapy. A challenge exists in informing services of what patients truely experience with changes to their pharmacological management. Furthermore if they notice changes, how do they value them. Three key qualitative publications were identified. Marshall et al (2004) reported improvements in physical function, pain and well-being. Arkell et al (2013) found that participants were very positive about being on anti-TNFα as it was described to make dramatic changes in their physical symptoms. Linden and Bjorklund (2010) concluded that with successful anti-TNFα treatment most participants experienced dramatic changesincluding a return to leisure interests. However Linden & Bjorklund (2011) also suggested that such dramatic changes may risk overuse and consequent strain. The aim of this study was to use a qualitative method to explore the understanding and experiences of People with Rheumatoid Arthritis (PwRA) who are receiving biological therapy treatment, relative to their physical function and lower limb mobility levels.
**Methods:** An interpretative phenomenological analysis (IPA) approach was used to explore the understanding and experience of PwRA when receiving biologics. A purposive selection of a small sample of PwRA was adopted and in-depth semi structured interviews were used. Interviews were conducted in the homes of participants and then later transcribed verbatim. Thematic analysis was employed for identifying meanings, analysing and reporting patterns within data.
**Results:** Five PwRA participated in the study. The mean duration of their RA disease was 20.2 years (range 6 -32 years) and all were being treated with biologic therapies. Four key themes emerged from the interviews: 1) Life before biologic treatment. 2) Life with biologic treatment. 3) Sense of self. 4) Podiatric implications.
**Conclusions:** The findings from this study reinforce those known such as improved physical function. The dramatic, postive change experienced by participants and a sense of appreciation was linked with physical improvements and a return to activity. However there are consequences to these improvements. Regardless of improvements in physical ability and reduced pain, it emerges that lower limb complications are an ongoing experience for people receiving biologics. Importantly an ongoing need for foot health advice and management involving the multidisciplinary team in this patient group is warranted.

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**Disclosure of Interest:** None declared
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## THU0647-HPR IMPROVING ACCESS TO A BETTER MODEL OF CARE FOR PEOPLE WITH KNEE AND HIP PAIN IN PRIMARY CARE - THE OSTEOARTHRITIS ADVISOR

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**Background:** Primary care management of osteoarthritis (OA)is often sub-optimal[1] because physicians feel overwhelmed by patient numbers and don't have time or skills to deliver lifestyle advice effectively – information, self-management, physical activity, weight control[2]. Allied healthcare professionals (AHPs) are better skilled in delivering lifestyle coaching. Although AHP-led care is common in many chronic conditions, it is still uncommon in primary care management of OA.
**Objectives:** We placed an AHP in the primary care pathway to improve access of more people, and to assess if AHP-led primary care was feasible, safe, effective and valued.
**Methods:** In February 2015 a physiotherapist began running clinics for people with knee/hip OA in a primary care surgery.
At an initial assessment (~30 minutes) the *Advisor;*
– assessed their pain and function, physical activity level, waist circumference, body mass
– taught the effective self-management strategies - weight control, exercise, pain management
– used behavioural change techniques - motivational interviewing, set SMART goals, action/coping plans, monitoring, feedback
– help construct personalised care plans
– identified people's physical activity preferences (swimming, walking) and identified local availability
– referred to relevant agencies (dietician) if necessary
Patients were invited to return for review (30 mins) 6 weeks later when the *Advisor*;
– repeated the outcome measures
– feedback progress and success
– reinforced health messages
– offered on-going support, reassurance and encouragement
Qualitative interviews assessed people's opinions of the effectiveness and value.
**Results:** 117 patients were recruited.
Initially people were not receiving recommended advice and support. Between the initial assessment and the 6-week follow-up improvements were seen across *all* outcomes:
- Knee/Hip Osteoarthritis Outcome Score improved - pain 16%; function 17%; quality of life 15%
– waist circumference decreased by 1.8cm
– weight decreased by 0.8kg
– physical activity increased by 2.1 days walking 20min per week
– patients were able to do on average 5.6 more "sit-to-stands" in 30 seconds
Patient satisfaction was very high. they valued advice tailored to their individual needs, appreciated easier access to care, the convenience and familiarity of the service being in their local GP surgery. This translated into self-reported improvements;
*"...it worked...I got a big improvement..."*
*"...from February to April I wasn't walking, now I can..."*
*"...I was 10 stone and went down to 9 stone..."*
Staff satisfaction was also very positive and interest from neighbouring practices meant the role was adopted by 4 other surgeries.
**Conclusions:** AHP-led care of people with knee/hip OA is feasible, safe, quickly accepted and implements evidence-based guidelines care management recommendations that improves important clinical outcomes. Patients, GPs and other practice staff liked and wanted the service.
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**Acknowledgement:** The project was funded by the Health Innovation Network South London.
**Disclosure of Interest:** None declared
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## THU0648-HPR INCREASING ACCESS TO COMMUNITY-BASED REHABILITATION FOR OSTEOARTHRITIS

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**Background:** *Enabling Self-management and Coping with Arthritic Pain using Exercise, ESCAPE-pain,* is a rehabilitation programme for people with knee and/or hip osteoarthritis (OA). It delivers guideline core recommendations (information, self-management advice, exercise) that reduce pain, improve function, is cheaper and more cost-effective than usual care[1,2] and participants value its benefits[3].
The programme is usually delivered in physiotherapy departments. However, financial and logistical constraints limit the number of people able to access the programme. Delivering *ESCAPE-pain* in community centres would increase accessibility, "reach" and provide better on-going support, and many more people would benefit.
**Objectives:** This study wanted to establish if delivering *ESCAPE-pain* in community leisure centres was feasible, effective, acceptable and sustainable.
**Methods:** The programme (described in detail at http://www.escape-pain.org/) was supervised by 2 physiotherapists in 3 Inner London leisure centres. Briefly, participants attended 12 sessions (2 sessions/week for 6 weeks) each comprised of a 25-minute education component and 45-minute exercise component. The education is a supervisor-guided theme discussions giving information, self-management and coping advice and incorporates behavioural change techniques. The exercise is an individualised, progressive regimen circuit that helps participants come to appreciate exercise is a safe, effective self-management strategy that reduces the impact of OA.
Pain, function and quality of life (Knee Osteoarthritis Outcome Score), anxiety and depression (Hospital Anxiety and Depression Scale) were measured before and after the programme. Participant experiences were evaluated using semi-structured interviews.
**Results:** 136 people with knee OA were recruited, mean age 63 years old.
Before (n-136) After (n=117)
KOOS-pain 46 (±20) 54 (±18; $p<0.0001$)
KOOS-ADL 48 (±22) 56 (±20; $p<0.0001$)
KOOS-QoL 31 (±23) 39 (±21; $p<0.0001$)
HADS-depression 7.5 (±4.1) 6.2 (±4.3; $p<0.016$)
HADS-anxiety 8.3 (±4.5) 7.0 (±4.5; $p<0.016$)
Attendance was good 64% of people attended ≥9 sessions. Participant were very satisfied with the programme and its outcomes, not only describing improvements in knowledge and symptoms, but also their confidence and attitude to exercise and understanding of the role of exercise in the management of OA. A large majority (80%) planned to continue exercising at leisure centres after completing the programme. The leisure centres decided to run the programme permanently.
*"...I now have more movement and less pain..."*
*"...it has helped me get back into regular exercise..."*
*"...I have gained more confidence and knowledge about my arthritis..."*
**Conclusions:** Delivering *ESCAPE-pain* in community settings is feasible, safe, improves clinical outcomes, acceptable, sustainable and nurtures an exercise habit. It is a community-based programme capable of caring for the large and rapidly increasing number of people with chronic joint pain.
**References:**
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**Acknowledgement:** Fusion Lifestyle hosted the programme.
**Disclosure of Interest:** None declared
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## THU0649-HPR VARIATION IN THE PROVISION AND COMPOSITION OF MULTIDISCIPLINARY TEAMS IN RHEUMATOLOGY SERVICES ACROSS THE UK: A CROSS-SECTIONAL STUDY

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**Background:** Care by the multidisciplinary team (MDT) is recommended by the current treatment guidelines in the UK and elsewhere in Europe. In rheumatology the evidence to support the effectiveness of multidisciplinary working is limited.[1,2] Furthermore, the availability of all members of the MDT in rheumatology teams across the UK is unclear.
**Objectives:** To describe the national provision of MDT care within Rheumatology services across the UK.
**Methods:** This was a "service" survey conducted in all rheumatology departments within the UK. In England, the survey was a part of a broader national audit for rheumatoid and early inflammatory arthritis commissioned by Healthcare Quality Improvement Partnership (HQIP). The approval to undertake this sub-analysis was gained from HQIP and supported by the British Society for Rheumatology research committee and British Health Professionals in Rheumatology. Scotland

and Northern Ireland were not included in the national audit therefore a separate, but identical, survey was conducted.
The design of the service survey content was agreed in consultation with the BHPR committee, which is formed of health professionals with clinical and research experience in rheumatology. The survey collected organisation data regarding the specific inclusion of, or direct access to, medical, nursing, physiotherapy, podiatry and occupational therapy practitioners as part of the MDT. Detail regarding the whole time equivalent (WTE) availability of each named speciality was recorded and summarised by region.
**Results:** The survey response rate was 98% (164/167). Table 1 shows the overall rheumatology staffing levels measured in WTE between professional groups. All departments reported having medical staff present and almost all had a nurse but the inclusion of physiotherapists, occupational therapists and podiatrists in the MDT was variable. Only 48% of the teams surveyed had access to a podiatrist.
There was a high degree of regional variation in the provision of health professionals and only 28 (17%) of the surveyed teams had all the named professional groups represented in their multidisciplinary teams.

Table 1. Overall rheumatology MDT staffing levels between professional groups

| Profession | Adjusted mean* WTE | SD | Range | Represented within MDT Y/N (%) |
|---|---|---|---|---|
| Medical | 1.05 | 0.62 | 0.70–3.09 | 164 (100) |
| Medical trainee | 0.32 | 0.08 | 0.22–0.54 | 132 (80) |
| Nursing | 0.99 | 0.34 | 0.51–1.55 | 162 (99) |
| Physiotherapy | 0.30 | 0.14 | 0.00- 0.60 | 120 (73) |
| Occupational therapy | 0.28 | 0.11 | 0.15–0.52 | 123 (75) |
| Podiatry | 0.11 | 0.06 | 0.00–0.20 | 79 (48) |

*Adjusted to per 100,000 population.

**Conclusions:** There is a high degree of regional variation in the composition and staffing levels of the Rheumatology MDT across the UK. Further research is required determine the most efficient configuration of the MDT in rheumatology services.
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**Disclosure of Interest:** None declared
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## THU0650-HPR PHYSICAL ACTIVITY AND AEROBIC CAPACITY ASSESSMENT - A SURVEY AMONG HEALTH PROFESSIONALS IN SWEDEN, IRELAND AND DENMARK

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**Background:** Regular physical activity (PA) is associated with improvements in health outcomes, such as quality of life, aerobic fitness, and disease-related characteristics, including pain, stiffness and inflammation, in people with inflammatory arthritis. Current practice in the management of patients with inflammatory arthritis emphasises the importance of Health Professionals (HP's) in assessing PA and aerobic capacity. To ensure baseline knowledge on PA and aerobic capacity assessment among HP's, it is important to identify if knowledge and training gaps exist.
**Objectives:** Investigate the awareness and use of objective and subjective measures of PA and aerobic capacity and to identify barriers for implementation of such methods in Health Professionals (Physiotherapist; Occupational Therapist; Nurse) working in the field of rheumatology in Sweden, Ireland and Denmark.
**Methods:** Health Professional's in Rheumatology were invited to participate in a cross-sectional, descriptive, observational study using an online survey methodology. Separate ethics approval was received in each country. Descriptive statistics and chi-square tests were used to analyse the data using SPSS v22.
**Results:** One hundred and forty four (144) HP's responded (50 Denmark, 28 Ireland and 66 Sweden), with 93% being female. Results found the mean number of years qualified to be 20.08 (SD 9.37) and years working in Rheumatology to be 12.29 (SD 8.27), with 61% reporting half of their workload coming from people who have inflammatory arthritis. The majority of respondents (96%) believe it is important to measure PA. Moderate levels of confidence were reported in using a simple body-worn sensor (mean 6.15/10; SD 3.63) and paper questionnaire (6.85/10; SD 3.62) as ways in monitoring PA, with lower levels of confidence in using a complex body-worn sensor (3.80/10; SD 3.55) and digital diary (4.22/10; SD 3.67). There was no statistically significant association between longer years qualified, more years working with people with inflammatory arthritis, age or gender in relation to the importance in measuring PA. When assessing aerobic capacity 58% were very familiar/somewhat familiar using a bicycle ergometer, 44% a treadmill and 56% other aerobic capacity tests. Low levels of confidence were reported in instructing their patients in performing aerobic capacity tests (4.54/10; SD 3.74) and in interpreting the results (4.79/10; SD 3.58). A large majority would be interested in further education around measuring PA (83%) and aerobic capacity measurement (74%), with an online module favoured for both.
**Conclusions:** The majority of Health Professionals surveyed believe it is important to measure PA however, levels of confidence are moderate to low when using various devices/ways. Regarding aerobic capacity tests low levels of familiarity were reported for both performing and interpreting results. There is strong interest in further education around measuring PA and aerobic capacity measurement highlighting a need to develop education and training for HP's in this area.
**Disclosure of Interest:** None declared
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## THU0651-HPR STRUCTURE, PROCESS AND OUTCOME OF PRIMARY CARE RHEUMATOLOGY NETWORKS FOR PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES IN THE NETHERLANDS

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**Background:** Primary care networks of health professionals (HPs) are instituted to improve the quality of care for patients with rheumatic and musculoskeletal diseases (RMDs). So far, research into their organization and outcomes is limited.
**Objectives:** To describe the characteristics of primary care rheumatology networks in the Netherlands, and satisfaction of patients with RMDs treated by network members.
**Methods:** Through the Internet and personal communication, existing primary care rheumatology networks were identified. Data on network characteristics were collected by interviewing network coordinators, and an online questionnaire for all network members (organizational aspects, education, patient load, and satisfaction). Members were asked to invite max. 4 patients to complete an online satisfaction questionnaire (Consumer Quality Index (CQ) subscales: Information, Attitude of HPs, Cooperation and Self-management (range 1–4)), and grading satisfaction (range 1–10). Satisfaction scores of patients treated within the networks were compared with aggregated data from a national dataset of 1648 patients treated in 45 physiotherapy (PT) practices using unpaired Students' T-tests.
**Results:** 19 rheumatology networks were identified, with 5 having an organizational structure, 17 networks set membership criteria, in 7 a fee was imposed. In 10 networks patients were involved, and 17 collaborated with a hospital rheumatology department. There were 479 network members (median 18 per network, range 7–106), with 15 including only PTs, 18 organized network meetings for professionals and 11 for patients. Communication within the network and with referring rheumatologists was scored as insufficient by 7 and 6 network coordinators, respectively, whereas all expressed the need for central support regarding network organization and activities. 214 network members returned the online survey, 38% had taken part in accredited postgraduate education on RMDs, 21% had seen no patients with Rheumatoid Arthritis, Osteoarthritis or Spondylarthropathy in the past year. Standardization of postgraduate education and organizational requirements for networks was desired by 70–80% of the members. 149 patients returned the survey. Compared to the reference set the patients treated in the rheumatology networks were significantly more satisfied



concerning CQ information (3.6 (SD 0.4) vs 3.8 (SD 0.3); CQ attitude of health professionals (3.8 (SD 0.3) vs 3.9 (SD 0.3); CQ cooperation and self-management (3.3 (SD 0.6) vs 3.5 (SD 0.5); and overall satisfaction (8.7 (SD 0.8) vs 8.4 (SD 1.1) (all $p<0.001$).

**Conclusions:** There is a large variety concerning the structure and process of primary care networks focusing on the management of patients with RMDs in the Netherlands. Although their added value with respect to patient satisfaction is plausible, there is a need for standardization of postgraduate education and the organization of such networks on the national level.

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## Physiotherapy & miscellaneous forms of clinical care

### FRI0610-HPR COMPARATIVE STUDY OF THE FUNCTIONAL MEASUREMENTS OF THE RHEUMATIC FOOT

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**Background:** During rheumatoid arthritis the structure of the foot as well as the plantar pressure surfaces are changing due to the disease. The examinations carried out with the help of machines serve as an overview of the objective state of the foot during function, whereas the functional surveys cumulate the subjective opinion of the patients during the everyday usage of the foot.

**Objectives:** In the study research methods were used which help the work of the physiotherapists, have lack of tool demand and make the diagnosis more accurate.

**Methods:** The study was carried out from 2015 September onwards among the patients of the National Institute of Rheumatology and Physiotherapy with rheumatoid arthritis (RA) and osteoarthritis (OA). The survey was based on the Foot Functional Index (FFI), the Leed's Foot Impact Scale (LFIS) and Health Assessment Questionnaire (HAQ). The function of the foot during walking was examined by the Zebris-FDM Treadmill system (7 zones e.x. Forefoot Medial, Lateral, Heel Medial, Lateral). To examine the structural deviations and deformities the Foot Posture Index (FPI) was used. The percentage values of time maximum force measured by the Zebris FDM-T system compared with FPI values. The examination consisted of two groups, patients with RA (n=23, age mean=61,47±11,13 years) and OA (n=22, age mean=59,54±13,73 years) as control group. For statistical analysis Statsoft Statistica v. 7.0 61.0 EN program was used and the Pearson correlation was calculated. The results were defined with $p<0,05$ statistical margin.

**Results:** In the values of the questionnaire based examination, there were significant correlations between FFI and $LFIS_{IF}$ (r=0,606; p=0,002), FFI and LFIS (r=0,511; p=0,013), $LFIS_{AP}$ and HAQ (r=0,537; p=0,008) in RA. In the control group there were significant correlations between FFI and $LFIS_{IF}$ (r=0,430; p=0,046), FFI and $LFIS_{AP}$ (r=0,727; p=0,000), FFI and LFIS (r=0,680; p=0,000), FFI and HAQ (r=0,794; p=0,000), HAQ and $LFIS_{AP}$ (r=0,635; p=0,001), HAQ and LFIS (r=0,575; p=0,005).

In the results of the dynamic and static measurement methods, there was a significant tendency between FPI and Forefoot Lateral (p=0,085) and there was a negative correlation between FPI and Heel Medial (r=-0,922; p=0,026) in RA group (FPI>5). In the OA group there were significant tendencies between FFI and Forefoot Medial (r= -376; p=0,084) and between FFI and Heel Medial (r=-0,395; p=0,068).

**Conclusions:** Our study is the first comparison of the physical examination, gait analysis and questionnaires in case of rheumatic foot.

In the light of the results it is recommended in the clinical practice that both static and dynamic examinations should be executed.

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### FRI0612-HPR THE DEVELOPMENT OF PHYSIOTHERAPY-LED MUSCULOSKELETAL TRIAGE SERVICES IN IRELAND

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**Background:** In 2012, funding was approved for twenty-four Advanced Practice Physiotherapy (APP) posts in Ireland through the Clinical Strategy and Programmes Directorate of the HSE. These posts were to provide orthopaedic and rheumatology triage clinics across 16 hospitals throughout the country.

**Objectives:** The aims of these clinics were to reduce the waiting time for outpatient consultation for orthopaedic and rheumatology patients; to establish a diagnosis and triage patients along the most appropriate care pathway according to their diagnosis.

**Methods:** Initially 18 APPs were recruited in 2012 and currently there are 22.5 in post nationally. Guidelines regarding inclusion for attendance at these clinics were disseminated to APPs recruited to posts. Clinical governance for APP clinics is provided by either a consultant orthopaedic surgeon or a consultant rheumatologist who provide support with clinical diagnosis; with the ordering of investigations and with management of patients as appropriate.

**Results:** From January 2012 to May 2015 48,279 patients have been removed from orthopaedic and rheumatology waiting lists nationally. In orthopaedic clinics APPs reviewed 33,092 new patients and discharged 25,917 (78%); in rheumatology clinics APP's reviewed 7,550 new patients and of this 5,417 (72%) were discharged following their review.

**Conclusions:** Advanced Practice Physiotherapist's can assist in the management of orthopaedic and rheumatology waiting lists. These services provide patients with early access for a specialist opinion and management and therefore prevent chronicity of symptoms. It can be hypothesized that prevention of chronicity would result in a reduction in the use of health care resources by this subgroup of patients.

**Disclosure of Interest:** None declared

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### FRI0613-HPR DO PHYSIOTHERAPISTS DOCUMENT WEIGHT AND DISCUSS THE INFLUENCE OF WEIGHT ON PATHOLOGY IN PATIENTS WITH OSTEOARTHRITIS?

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**Background:** There is a strong association between increased body weight and osteoarthritis (OA). The NICE (2014) and ACR (2012) guidelines strongly recommend that patients with OA consider weight loss if overweight.

**Objectives:** The aim of this audit was to investigate if physiotherapists treating patients with knee and lumbar-spine OA: i) Documented patients weight; ii) Discussed the role of increased weight on OA

**Methods:** An audit of seventy physiotherapy charts of patients attending physiotherapy in 2013 found that 15percent (knee) and 11percent (lumbar-spine) had their weight documented. The role of increased weight was discussed with 15percent (knee) and 11percent (lumbar-spine). A "BMI station" was set up to use with patients. A lifestyle education class was established. In 2015 a re-audit was carried out on patients who attended for physiotherapy in 2014.

**Results:** Seventy physiotherapy charts were randomly selected and included. The median age was 64years (knee) and 53years (lumbar-spine). Of these 7 were male and 23 female (knee), 17 were male and 19 female (lumbar-spine). Of these, 38percent (knee) and 31percent (lumbar-spine) had their weight documented. The role of increased weight was discussed with 19percent (n=7) (knee) and 22percent (n=8) (lumbar-spine).

**Conclusions:** Physiotherapists have improved in relation to documenting weight and discussing the role of increased weight on OA since the previous audit. However, it is evident that they do not regularly document weight in patients with knee and lumbar-spine OA or document if they advised patients regarding the role of weight management for the treatment of OA. Further strategies to address this are necessary.

**Disclosure of Interest:** None declared

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### FRI0614-HPR DELAYED DIAGNOSIS, PAIN AND LOSS OF FUNCTION ARE SOME OF THE CONSEQUENCES OF SPONTANEOUS FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS – A QUALITATIVE ANALYSIS OF PATIENTS' EXPERIENCE

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**Background:** Spontaneous fractures in patients with rheumatoid arthritis (RA) have only occasionally been reported in the literature[1,2]. However, rheumatologists

at Vendsyssel Hospital have noticed several cases where new onset knee or ankle pain was misdiagnosed as arthritis activity but was later shown to be spontaneous fractures. An x-ray examination did not reveal the fracture, but it was identified on an MRI examination. The fractures are at risk of being overlooked, and this fact may lead to a delay in diagnosis and a risk of ineffective treatment with e.g. steroid injections.

**Objectives:** The study was carried out in the Physio- and Occupational Therapist unit in Vendsyssel Hospital. The included patients were diagnosed with RA and spontaneous fractures. Fifteen patients, all women, were identified. Ten patients in the age of 57–88 years participated in the study. They had an average disease duration of 14.2 years and a MRI was performed at a median of eight months.

**Methods:** The patients were divided into two age specific groups: 57–69 and 70–88 years. The focus groups data were subjected to thematic analysis to provide a sense of the important themes. Categorizing, coding and analysing the data from the focus groups identified the themes.

**Results:** All patients identified the missing diagnosis as a significant burden. The patients were experiencing pain, but did not receive a diagnosis or an explanation for their symptoms. "I've never been as happy as when I was told my leg was broken ..." Most of the patients experienced more pain than usual for their RA: *"You suddenly have a lot more pain, but you just don't know where it comes from".* All patients noticed a significant loss of function before the diagnosis was made and during immobilisation: *"I was so unhappy about not being able to do anything ... even just getting up at night to go to the toilet ...".* When the patients were immobilised they were offered crutches, but they were not able to use standard crutches due to their RA: *"I can't use crutches because I don't have enough strength to lift myself..."*

**Conclusions:** Patients with RA with spontaneous fractures experience the delayed diagnosis as a burden, and it is stressful for them to wait for an explanation for their pain. Due to the patients missing ability to use crutches or use a wheelchair, it is important to find other aids that patients with RA and spontaneous fractures can use. When the patients were immobilised they experienced loss of function. This calls for the need to focus on the diagnosis and guidance of these patients in relation to daily activities and aids.

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**Disclosure of Interest:** None declared

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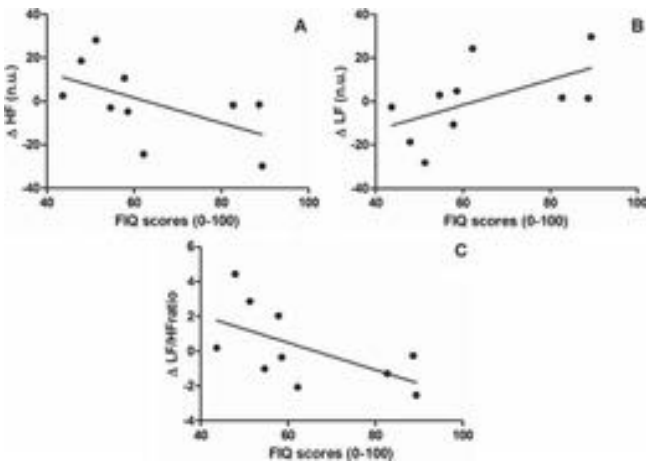
## FRI0615-HPR BLUNTED CARDIAC AUTONOMIC RESPONSE TO THE ACTIVE STANDING IS RELATED TO THE IMPACT OF FIBROMYALGIA ON QUALITY OF LIFE

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**Background:** Several studies have shown that autonomic dysfunction plays an important role in the fibromyalgia syndrome (FMS).[1–3] Recent studies have used the active standing test to assess the cardiovascular autonomic control responses to the orthostatic stimulus in several disorders, including FMS.[4] However, there are few studies correlating symptoms and clinical factors with cardiovascular autonomic dysfunction.

**Objectives:** To assess the relationship between the impact of fibromyalgia on quality of life and cardiac autonomic control response to the active standing test.

**Methods:** Ten women (47.9±7.3 years old) with clinical diagnosis of FMS took part in the study. Diagnosis followed the criteria established by the American College of Rheumatology.[5] All participants answered the fibromyalgia impact questionnaire (FIQ)[6] and underwent the recording of RR intervals (RRi) using a transmitter belt. The RRi were recorded for 15 min in resting supine position and during 15 min in an orthostatic position reached by active standing. The cardiac autonomic control was assessed by indices computed via spectral analysis of RRi in low frequency (LF, 0.04–0.15 Hz) and high frequency bands (HF, 0.15–0.4 Hz). To quantify the magnitude of cardiac autonomic response to the orthostatic stimulus, the delta between values obtained in supine and standing positions was calculated for all variables. Changes induced by the orthostatic stimulus were evaluated by Wilcoxon test. Spearman's coefficient was used to assess the association between the delta of the HRV indices and the FIQ scores. $\alpha$ =5%.




**Results:** There were no significant differences between the supine and standing positions in any of the spectral indices. Positive correlation was found between FIQ scores and HF (n.u.) (r =0.67; p=0.03). Negative correlations were observed between the FIQ scores and LF (n.u.) index (r = -0.67; p=0.03, Figure 1B) and LF/HF ratio (r = -0.73; p=0.016, Figure 1C).

**Conclusions:** The results showed that the larger the magnitude of the cardiac autonomic adjustments to the gravitational stimulus, the smaller the impact of FMS on quality of life.

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## FRI0616-HPR CARDIAC AUTONOMIC RESPONSE TO OSTHOSTATIC CHANGES IN FIBROMYALGIA SINDROME

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**Background:** Patients with fibromyalgia syndrome (FMS) have autonomic nervous system (ANS) related disorder[1]. The orthostatic stimulus is an important method for the assessment of neurocardiac integrity[2]. However, little is known about the cardiac autonomic response to the active standing test in women with FMS.

**Objectives:** To evaluate the cardiac autonomic control response to the active standing test in women with FMS.

**Methods:** Ten women with FMS (FMSG n=10) and ten healthy women (HG n=10) took part in the study. The volunteers were submitted to the recording of RR intervals (RRi) during 15 min in supine and 15 min in orthostatic (active standing) positions. RRi were recorded by a heart rate monitor. The parameters of the frequency domain were determined by the heart rate variability (HRV) spectral analysis, obtained in low frequency (LF, 0.04–0.15 Hz) and high frequency bands (HF, 0.15–0.4 Hz) in normalized units (n.u.) and LF/HF ratio[3].

**Results:** The results are shown in table 1. There were significant group x posture interaction for LF (n.u.) and HF (n.u.). Post hoc analysis revealed that the HG increased LF (n.u.) and decreased the HF (n.u.) during active standing, compared to the supine position. On the other hand, the FMSG presented no significant differences between supine and orthostatic position. Regarding between group comparisons, FMSG presented higher LF (n.u.) and lower HF (n.u.) at supine position.

Table 1. Power Spectral Analysis in the HRV of FMSG and HG from supine position to orthostatic (active standing)

| | HG (n=10) | | FMSG (n=10) | | P-value | | |
|---|---|---|---|---|---|---|---|
| | Supine | Orthostatic | Supine | Orthostatic | Posture | Groups | Interaction |
| LF (n.u.) | 50.11±10.28*† | 71.03±8.54 | 72.13±11.00 | 71.62±14.58 | 0.006 | 0.009 | 0.004 |
| HF (n.u.) | 49.89±10.28*† | 28.97±8.54 | 27.87±11.00 | 28.37±14.58 | 0.006 | 0.009 | 0.004 |
| LF/HF | 1.09±0.46*† | 2.82±1.45 | 3.26±2.13 | 4.82±2.20 | 0.03 | 0.04 | 0.08 |

Data are expressed as mean± SD. LF = low frequency component of RR intervals; HF = high frequency component of RR intervals; n.u. = normalized units. Two-way mixed ANOVA with Bonferroni's post hoc test. *p<0,05 GS supine posture vs FMSG supine posture. †p<0,05 GS supine posture vs GS orthostatic posture.

**Conclusions:** FMSG showed cardiac autonomic dysfunction at supine position, characterized by higher sympathetic and lower parasympathetic cardiac autonomic

modulation. In addition, FMSG present a blunted cardiac autonomic control response to the active standing, characterized by a lack of cardiac sympathetic modulation increase and parasympathetic decrease. Therefore, the neurocardiac integrity seems to be compromised in the FMSG.

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## FRI0617-HPR AN AUDIT OF THE ROLE OF A CLINICAL SPECIALIST PHYSIOTHERAPIST IN RHEUMATOLOGY TRIAGE

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**Background:** Clinical Specialist Physiotherapy roles were developed in Ireland in 2012 as part of the National clinical care programs. A Rheumatology triage post was assigned to the South /South West group. The Musculoskeletal Assessment Clinic (MAC) runs across two sites the South Infirmary Victoria University Hospital (SIVUH) and Cork University Hospital (CUH). Triage by physiotherapists has been running in other parts of the world for a number of years with favourable outcomes in terms of patient experiences, GP satisfaction and diagnostic accuracy (1). Patients are triaged to the MAC by the Rheumatology consultant based on information supplied in the GP referral letter indicating non inflammatory conditions. These include mechanical neck and back pain, OA and soft tissue rheumatism suitable for injection therapy.
**Objectives:** The objective of this of this audit was to establish (1) the number of patients seen at MAC (b) number of referrals onwards to the Rheumatology consultant led clinics from MAC, (c) to assess the appropriateness of these onward referrals (d) the rate of re-referral to the rheumatology service of patients assessed at the MAC Rheum and discharged.
**Methods:** A retrospective audit of GP referrals to the Rheumatology service triaged to MAC between July 2012 and October 2015 was undertaken.
**Results:** 1,297 new patients were assessed at the MAC between July 2012 and October 2015. 92% were managed by the triage physiotherapist without seeing the Rheumatology team although in some cases the physiotherapist did consult with the Rheumatology consultant at initial assessment. 8% (98 Patients) were referred to a Rheumatology consultant led clinic for assessment. Of these 49% (48) were confirmed as having an inflammatory arthritis, 39% (38 patients had a variety of other diagnoses requiring medical review including SLE,CREST, Paget's, new vertebral fracture and CPPD. The remaining 12% (12 patients) were diagnosed as OA on review and discharged. At the time of audit 4% (55 patients) had been re-referred to the service. 2% (1 patient) was assessed by the Rheumatology consultant and diagnosed as having an inflammatory arthritis. 25% (14 patients) were reviewed at MAC and discharged, 22% (12 patients) were reviewed by consultant and discharged. 4% (2 patients) DNA follow up appointment. 47% (26) were still awaiting routine review with consultant.
**Conclusions:** 92% of patients triaged to the MAC were assessed and managed by the triage physiotherapist without the need for review by the Rheumatology team. The low rate of onward referral (8%) from MAC to Rheumatology and of re-referral (4%) to the Rheumatology service would appear to indicate the patients triaged to the MAC are appropriate for that pathway. Of the patients referred on to the consultant clinic 88% required input by the Rheumatology team. This initiative helps reduce OPD waiting times for specialist services by reducing the time spent by the Rheumatology team on non inflammatory mechanical disorders. GP satisfaction and patient experience surveys are currently being undertaken and the results will be included in the presentation.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2149

## FRI0618-HPR THE SHORT-TIME EFFECTS OF KINESIOTAPING ON HALLUX VALGUS DEGREE, PAIN INTENSITY AND PLANTAR PRESSURE DISTRIBUTION IN RHEUMATOID FOOT: A PILOT STUDY

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**Background:** Hallux valgus is one of the most common deformities of rheumatoid arthritis.[1] The foot deformities as hallux valgus that causes consequent antalgic gait often result in unusual forces on bones and soft tissues of the plantar surface.[2] Accordingly, elevated plantar pressures while walking are thought to cause mechanical damage to the rheumatoid foot.[3] A recent study showed that 10-day kinesiotape implementation improved the pain and joint alignment in patients with hallux valgus.[4] There is no study that investigates the implementation effects of kinesiotaping in rheumatoid foot.
**Objectives:** The aim of this study is to investigate the effects of kinesiotaping on hallux valgus angle, pain intensity and plantar pressure distribution in individuals with rheumatoid arthritis.
**Methods:** A total of 6 rheumatoid arthritis patients (age:50.00±10.71 years, HAQ: 18.66±3.82) diagnosed with hallux valgus in total of 12 feet were recruited in our study.A toe goniometer was used to determine the angle of hallux valgus, Visual Analog Scale (VAS) was used for pain assessment, Foot Posture Index (FPI) was used to determine foot posture and Emed-50/D pedobarographic system was used to analyze peak pressure under 10 foot regions. Kinesiotaping was implemented after the first assessment and renewed in days 3 and 7 by a qualified physiotherapist with 5-year experience. After the big toe was aligned to its estimated correct with a moderate to high tension, first Y-shaped kinesiotape was implemented through the first ray. The second Y-shaped tape was placed over metatarsophalangeal joints with a mechanical correction technique on hallux.[4] The evaluations were renewed in days 3, 7, and 10. Friedman test was used to compare to differences among repeated assessments.
**Results:** All of the feet were determined as normal foot posture according to FPI. There was a significant reduction in hallux valgus angle ($\chi^2$=27.94, $p<0.001$). There was significant reductions for the assessment of days of 3, 7, and 10 compared to initial assessment of VAS scores ($p<0,05$). There was no significant differences at peak pressure data under 10 foot regions among all repeated assessments ($p>0,05$).



**Conclusions:** Pain and hallux valgus angle were decreased after a 10-day kinesiotape implementation in patients with RA. Our results of plantar pressure distribution couldn't show statistically change which might arise by low number of patients. Further studies should be carried out by increasing the number of cases in the future. Also radiographic changes of foot should be investigated in long term.

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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5065

## FRI0619-HPR INVESTIGATING THE EFFECTS OF A MULTIDIMENSIONAL EXERCISE PROGRAM ON SYMPTOMS AND ANTIINFLAMMATORY STATUS IN OA PATIENTS OF THE KNEE

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**Background:** Effects of exercise on pain, physical function, daily living activities

and cytokines have been investigated in osteoarthritis (OA) patients (1). However there is no reported multidimensional approach including all these parameters at once in OA patients. On the other hand, the cognitive exercise therapy approach (BETY: Bilişsel Egzersiz Terapi Yaklaşımı) was used as a multidimensional exercise model including effects of improvements on symptoms and anti-inflammatory status in ankylosing spondylitis patients (2).

**Objectives:** The purpose of this study is to investigate the effects of a multidimensional (BETY) exercise program on symptoms and anti-inflammatory status in OA patients of the knee.

**Methods:** Forty patients with knee osteoarthritis defined as Kellgren-Lawrence (K-L) grade1 and 2, were included in this study, and divided randomly into two groups (BETY group and control). Health Assessment Questionnaire (HAQ), The Western Ontario and McMaster Universities Arthritis Index (WOMAC) was used for functional evaluation and IL-6 were analyzed for anti-inflammatory status in both groups. Control group did not get any exercise intervention. However, BETY group were participated to exercise sessions 3 times a week for 10 weeks. All measurements were repeated after 10 weeks in both groups.

**Results:** WOMAC pain, physical function and WOMAC total score values were decreased significantly ($p<0.05$) in exercise group. However HAQ, WOMAC stiffness score were remained stable according to pretreatment values in this group ($p>0.05$). Although any significant change in IL-6 in both groups were not observed, IL-6 decreased in BETY group. Moreover, TNF-a showed significant increase in control group ($p<0.05$). No change was observed for other values between pre- and post-treatment in control group ($p>0.05$). There was no difference between two groups after 10 weeks ($p>0.05$).

Table.1. Comparison of the all scores

| | BETY group (n=19) | | | Control group (n=21) | | | P intergroups |
|---|---|---|---|---|---|---|---|
| | X ± SD | | p | X ± SD | | p | |
| | Before | After | | Before | After | | |
| WOMAC $_{pain}$ | 3.94±2.20 | 3.44±2.00 | 0.019 | 3.09±1.49 | 2.87±1.78 | 0.531 | 0.373 |
| WOMAC $_{function}$ | 4.30±1.91 | 3.24±1.81 | 0.013 | 3.40±1.56 | 3.01±2.37 | 0.045 | 0.610 |
| WOMAC $_{stiffness}$ | 0.46±0.22 | 0.41±0.23 | 0.223 | 0.35±0.24 | 0.34±0.23 | 0.832 | 0.419 |
| WOMAC $_{total}$ | 8.71±4.16 | 7.09±3.72 | 0.015 | 7.00±3.14 | 6.23±4.14 | 0.099 | 0.452 |
| HAQ | 11.88±8.50 | 9.29±9.06 | 0.224 | 8.38±6.29 | 6.42±5.45 | 0.171 | 0.490 |
| IL-6 | 5.21±6.12 | 2.96±1.77 | 0.053 | 2.68±0.76 | 2.45±1.14 | 0.195 | 0.524 |
| TNF-a | 4.45±2.00 | 4.65±2.47 | 0.753 | 3.44±2.10 | 4.27±2.09 | 0.047 | 0.641 |

**Conclusions:** This study is an original study in terms of analyzing exercise-induced TNF-a and IL-6 relationship in OA patients of the knee. We concluded that BETY program did not cause negative effects in OA patients. BETY should be taken into consideration as a multidimensional exercise program for OA patients.

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**Disclosure of Interest:** None declared

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## FRI0620-HPR EFFICACY OF LOCAL INFILTRATION ANALGESIA IN TOTAL KNEE ARTHROPLASTY: A RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND TRIAL

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**Background:** Total knee arthroplasty (TKA) is a common surgical procedure in patients with end-stage osteoarthritis to reduce pain and improve locomotor function. However, TKA may result in severe postoperative pain, usually requiring hospitalization from 5 to 10 days to provide effective analgesia (1). Local infiltration analgesia (LIA) is a simple technique for the treatment of postoperative pain after TKA. However, the specific efficacy of LIA has been confounded by frequent limitations in study design (2).

**Objectives:** To investigate the efficacy of LIA in patients with TKA.

**Methods:** The study was designed as a *randomized double blind placebo control* trial. A total of 63 patients with primary total knee arthroplasty were randomized either to receive a periarticular local infiltration analgesia or to receive placebo injection (63 patients: 57 knee in LIA group, 44 knee in placebo group). Pain intensity, active range of motion, knee function score [Hospital for Special Surgery (HSS) score] and length of hospital stay (LOS) were evaluated. Functional activities were evaluated using the Iowa Level of Assistance Scale, and walking speed was evaluated using the Iowa Ambulation Velocity Scale. The dates of ability to perform straight leg raise actively and to reach 70° of knee flexion were recorded. Patients and investigator were blinded the groups.

**Results:** There were no significant differences between the groups for demographic characteristic. Lower pain scores were recorded on postoperative day 1 and postoperative day 2 after the operation in Group LIA ($p<.0001$ and $p=0.022$, respectively). Higher range of motion of knee flexion and extension postoperative day 1 and postoperative day 2 in Group LIA (Flexion:$p=0.004$ and $p=0.020$, respectively; extension: $p=0.028$ and $p=0.022$ respectively). There were also a significant differences in terms of the date of 70° knee flexion reach ($p=0.034$) and ability to perform straight leg raise actively in favour of Group LIA ($p=0.034$). There was no significant difference between the groups in the HSS score, Iowa Level of Assistance Scale, Iowa Ambulation Velocity Scale and LOS.

**Conclusions:** Andersen and Kehlet reported that LIA significantly reduced pain intensity, specifically during standing and walking up to 48 h after operation. Our results suggest that LIA significantly reduced pain intensity in early postoperative day. This results are corroborate with Andersen and Kehlet's study (2). We also have found a better recovery of knee flexion immediately after operation. Possible mechanisms of better recovery of knee flexion could be lower pain scores. Patients with lower pain scores can also perform earlier straight leg raise. However, LIA technique did not provide additional impact on LOS because LOS depends on many other factors. In conclusion, LIA significantly reduced pain intensity, improve recovery of active range of motion but did not provide additional impact on LOS compared with placebo injection in patients with TKA.

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## FRI0621-HPR REFERENCE VALUES FOR THE MODIFIED FUNCTIONAL REACH TEST IN YOUNGER AND MIDDLE-AGED TURKISH POPULATION

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**Background:** Modified Functional Reach Test (MFRT) is reliable, precise, and less time-consuming for detecting dynamic sitting balance (1). Normative data for this measurement tool have been reported in Indian and American population (1,2). Reference values for MFRT are not available in Turkish population.

**Objectives:** Our aim was to establish reference values for the MFRT to examine the effect of gender and various anthropometric measurements on MFRT in healthy younger and middle-aged Turkish population

**Methods:** Ethics approval for this study was obtained from the Ethics Committee of Celal Bayar University. Informed consent was obtained from all participants in accordance with the Declaration of Helsinki before participation.

Participants (employee and academic staff) were recruited from Celal Bayar University campus. Permission was obtained from authorities of the University to carry out the study. Therefore, 462 participants within the age range of 20 to 59 years successfully included to the study and completed all necessary process. Based on the literature, these participants were stratified into 2 age groups; younger age group (ages 20–39 years) and middle age group (ages 40–59 years). There were 278 people in the younger age group and 184 people in the middle-aged group.

Prior to testing, the participants were screened based on inclusion criteria: both gender without balance problems, healthy subjects and 120 of shoulder flexion and abduction range of motion to perform the reach tests. Participants were excluded based on following criteria: any neurological disorder, balance disorder and any treatment for an ear infection within the past 6 weeks.

**Results:** For younger age group, the reference value of forward reach was 41.8±11.9 cm and reference values for lateral right and left reach were 30.9 ± 9.5 cm and 30.5 ± 9.5 cm, respectively. For middle-aged group, the reference values of forward, lateral right and left reach were 46.3± 12.4 cm, 33.1±10.5 cm and 32.9±10.8 cm, respectively. There is no significant differences between male and female in terms of all scores in each group. Anthropometric characteristics were similar in both age groups.

**Conclusions:** Although these reference values are similar with American populations, the mean MFRT scores for younger and middle aged Turkish population are higher than same age Indian population, especially reference values of lateral reaches. These normative data will be also useful to researchers and clinicians in the sitting balance assessment in the Turkish population.

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**Disclosure of Interest:** None declared

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FRI0622-HPR **A NEW PATIENT REPORTED TOOL IN THE ASSESSMENT OF PHYSIOTHERAPY FOR PATIENTS WITH KNEE OSTEOARTHRITIS**

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**Background:** Symptoms in patients with knee osteoarthritis (KOA) reflect many factors including lifestyle, fitness, weight, extent of damage and altered biomechanics etc. Our patients with KOA attend an education session followed by 4 weekly exercise sessions. The aim of the program is to improve knowledge and understanding and self-management techniques. Activity modification and exercises help symptoms in the short term and provide motivation in the long term. A new user-friendly patient reported outcome measure has been developed to easily and reliably assess patient perspectives of well-being and symptoms in musculoskeletal conditions. The application of this tool in KOA is explored
**Objectives:** To use a new patient reported outcome tool to assess the value of the components of a specific package of physiotherapy for KOA
**Methods:** 49 consecutive patients referred from rheumatology clinics with a diagnosis of KOA completed the assessment tool at their first physiotherapy session.
The tool consists of 12 statements each defining a separate domain - communication, relationships, knowledge, anxiety, fatigue, pain, movement, strength, independence, mobility, work and social aspects. These are domains assessed independently or in three clusters broadly addressing emotional, physical and functional status of the patient at a time point.
The patients score each of the 12 statements on a visual analogue scale (0–10) reflecting their perceived status in that domain at the time of assessment. The measure is repeated with the patient blinded to original scores after their final exercise session in the KOA program.
The change in domain scores is documented on a database allowing multi-variate analysis within individual domains and the three composite clusters
**Results:** Overall improvement with the treatment program was reported by 41 (84%) of patients with improvement ranging from 30% in 9 (18%) to 10% in 27 (55%) of patients. Thus only 8 patients reported a decline after the treatment program. In patients with decline in average scores, this is domain specific and not global. Overall cohort analysis shows on average all 12 domains improved but to varying degrees with the largest VAS change ($\geq$2.0) in two domains, ability to communicate and knowledge of their condition. In three domains (relationships, independence and social activities) change was marginal with average VAS improvement score less than 1.0. In the other 7 domains improvement was moderate ranging between 1.0 and 2.0 on the VAS.
**Conclusions:** The new tool is effective and efficient in a time limited, busy clinical setting. It is easily understood and quickly completed by patients allowing for accurate reflection of their domain specific perspective at a specific time.
Through the successful application of this assessment tool the value of this specific physiotherapy package of care has been demonstrated. This validation of practice is of value to patients, the clinical team involved and managers. The tool allows the assessment of positive and negative response to the treatment package to be analysed within domains. KOA patients improve in physical and functional clusters but show only marginal change in the emotional cluster of domains. Our new patient assessment tool will allow for appropriate and informed modifications of the treatment package to further improve patient outcome.
**Disclosure of Interest:** None declared
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FRI0623-HPR **KINESIOPHOBIA AFFECTS RANGE OF KNEE FLEXION AT EARLY STAGE FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION**

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**Background:** One of the most common complications following anterior cruciate ligament (ACL) reconstruction in sport rehabilitation is loss of knee motion (1). A fear of re-injury of ACL may contribute limitations of knee functions in terms of range of motions during rehabilitation process (2). Some athletes are not able to return to their pre-injury level due to loss of knee function and fear of motion in other words kinesiophobia.
**Objectives:** To investigate the relationship between range of motion (ROM) of the knee which is an important target in rehabilitation and kinesiophobia degree following ACL reconstruction in professional athletes.
**Methods:** The study was carried out with 14 certified athletes (8 male and 6 female, mean age: 21.5±5.86 years; mean body weight: 68.7±15.2 kg; mean height: 177.5±10.3 cm) who had unilateral ACL reconstruction and started post-op physiotherapy treatment participated in the study. All assessments were performed at 15th day following reconstruction. Kinesiophobia degrees of the athletes were assessed with Tampa Kinesiophobia Scale. A high score obtained from the scale indicates a high degree of kinesiophobia. Active and passive flexion degrees of knee joint were measured by using goniometer in accordance with Kendall-McCreary's criteria. All ROM measurements were performed 3 times and mean values of 3 measurements were saved for data analysis. The relationships between kinesiophobia degrees and active & passive flexion of the knee joint were analyzed by using Spearman's Correlation test.
**Results:** There was a strong negative relationship between the kinesiophobia degrees and active ($r=-0.881$, $p<0.001$) & passive ($r=-0.887$, $p<0.001$) ROM degrees of knee flexion.
**Conclusions:** One of the important aims of the treatment following ACL reconstruction is regaining functional level before injury and providing an early return to sports without any movement limitation. The results of this study revealed that presence of kinesiophobia at early stage influenced active and passive range of motion of knee joint negatively. Assessment of the kinesiophobia at early stage in ACL reconstructions could make a significant contribution to rehabilitation process in terms of achieving projected ranges of motions sooner in clinical settings.
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FRI0624-HPR **THE RELATION BETWEEN FOOT POSTURE AND CHRONIC LOW BACK PAIN INTENSITY**

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**Background:** The link between foot structure and low back pain (LBP) has been investigated recently because of biomechanical abnormalities are widely believed to be the likely causes of LBP (1, 2). Back and spine impairments were more common in women (3) and women slightly more often reported some kind of consequences due to spinal pain (4). Despite of detected gender differences arising from spinal pain, there has been no study that investigates the effect of foot posture on LBP among men and women separately.
**Objectives:** The aim of this study to investigate the gender differences in foot posture and back pain intensity and to explore relation between foot posture and level of pain in men and women suffering from chronic LBP.
**Methods:** 50 subjects of age 51.02±12.41years who admitted with chronic LBP to Physiotherapy Clinics between December 2014-March 2015 participated in this study. Foot posture of dominant side was determined by using Foot Posture Index (FPI). Higher positive FPI scores indicates a pronated foot posture, negative scores indicates a supinated foot posture (5). Visual Analog Scale (VAS) and Oswestry back pain scale was used for pain assessment. Mann Whitney U test was used to compare FPI scores and pain intensity according to VAS and Oswestry back pain scale. Spearman correlation test was used to determine the relationship between foot posture scores and level of LBP for men and women separately.
**Results:** There was no statistically difference between men and women for FPI scores ($p=0.552$) and LBP pain intensity according to VAS ($p=0.579$) and Oswestry back pain scale ($p=0.890$). While there was no statistically correlation between FPI scores and LBP pain intensity among men ($p>0.05$), a positively moderate correlation was detected between FPI scores and LBP pain intensity according to VAS among women ($r=-0.393$, $p=0.019$).
**Conclusions:** In the literature, excessive pronation of foot was detected more frequently in individuals with LBP (6). Similarly in this study, women with pronated foot posture have higher level of LBP, not men. Therefore, clinicians should be interpreted the link between foot posture and LBP by considering gender.
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FRI0625-HPR **LEARNING TO GUIDE PEOPLE WITH RHEUMATOID ARTHRITIS TO HEALTH-ENHANCING PHYSICAL ACTIVITY BEHAVIOR: PHYSIOTHERAPISTS' KNOWLEDGE, BELIEFS AND BEHAVIOR**

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**Background:** Physiotherapists (PTs) are raised in a biomedical tradition. They promote health-enhancing physical activity (HEPA) in persons with RA mainly by providing information, instructions and follow-up of prescribed exercises. To facilitate maintained HEPA behavior, PTs in rheumatology need to integrate their knowledge on RA and exercise physiology with use of evidence-based behavior change techniques (BCTs). Detailed, theory-based studies of how PTs can integrate these competencies are scarce. To gain more knowledge on PTs learning in this aspect, we performed the present study as a substudy in a HEPA intervention in the Physical Activity in RA (PARA 2010) program.
**Objectives:** To describe changes in PTs' knowledge, beliefs and behaviours assessed before, during and after a theory-based skills training course preparing them to guide persons with RA to HEPA within a one-year intervention trial.
**Methods:** This was a longitudinal case study performed within a one-year HEPA intervention for persons with RA, including circuit training at public gyms twice a week and 30 minutes daily free-living physical activity of moderate intensity, framed by 20 bi-weekly support group sessions led by a PT. Our participants were ten registered PTs leading 10 support groups with 5–10 persons each. To prepare the PTs for their task we gave a course based on Social Cognitive Theory (SCT) principles and structured use of BCTs, see Figure 1. Data were collected by questionnaire at five occasions; at baseline, three times during the course and once after the course, assessing knowledge on physical activity in RA (score 0–6), knowledge on BCTs (score 0–18), fear-avoidance beliefs about physical activity in RA (score 8–48), and self-efficacy to guide in behaviour change (score 9–54). The questionnaire had good face validity and good test-retest reliability with ICC 0.88–0.98 for the four variables. Data were also collected by a log book for self-reported use of BCTs during group sessions, dichotomised as adherence to the support group session protocol or not.
**Results:** PTs' knowledge on BCTs and their self-efficacy to guide in behaviour change increased significantly (Friedman's test, $p<0.05$) from baseline to post-course from median 9 to 13 and from median 38 to 46.5, respectively. Their knowledge on physical activity in RA and their fear-avoidance beliefs were adequate at baseline and did not change. Two out of ten PTs fulfilled the pre-established criteria for adherence to the group session protocol for use of BCTs throughout the HEPA intervention.

Figure 1. Format, learning activities and targets of PT course in the PARA 2010 program.

| | Before the HEPA intervention | During the HEPA intervention |
|---|---|---|
| Format | 2 times 2 course days | 2 times 1 course day |
| Learning activities | • Lectures, workshops with role-play<br>• Home assignments between course days | • On-site visits with video recordings and feedback on performance during support group sessions<br>• Viewing video sequences from sessions to provide model examples |
| Targets | • Knowledge on HEPA in RA<br>• Knowledge on BCTs<br>• Fear-avoidance beliefs<br>• Self-efficacy in guiding to behaviour change<br>• Skills to use the following BCTs: goal-setting, action planning, self-monitoring, positive reinforcement, modeling, problem solving, review of goals and relapse prevention | |

**Conclusions:** A course for PTs based on SCT principles emphasizing skills training and feedback on performance seems useful to affect knowledge on BCTs and self-efficacy to guide in behaviour change. To improve adherence in PTs applying evidence-based BCTs to guide persons with RA to HEPA, closer monitoring and more frequent feedback on performance are suggested.
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FRI0626-HPR **PHYSIOTHERAPISTS' MANAGEMENT OF CHALLENGING SITUATIONS IN GUIDING PERSONS WITH RHEUMATOID ARTHRITIS TO HEALTH-ENHANCING PHYSICAL ACTIVITY**

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**Background:** Physical activity is crucial for the management of rheumatoid arthritis (RA). In the Physical Activity in RA 2010 (PARA 2010) program we evaluated a one-year health-enhancing physical activity (HEPA) intervention. It included circuit training at public gyms twice a week and daily free-living physical activity of moderate intensity, framed by 20 bi-weekly support group sessions led by a physiotherapist. The PTs were trained to facilitate HEPA behavior not only by instructing exercises and check exercise intensity, but by inviting participants to share their experiences and give social support as they strived to reach HEPA. Integrating these communication competencies may be challenging to PTs, traditionally providing expert advice on exercise and physiology.
**Objectives:** The aim was to explore strategies that PTs use to manage challenges when guiding persons with RA to HEPA behavior within a one-year intervention.
**Methods:** The study was exploratory and descriptive. Eleven PTs, all women, were included. To prepare the PTs for their group leader task, they participated in a six-day skills training course and received a written manual for the support group sessions. In addition, they received individual feedback on performance during group sessions twice during the HEPA intervention. Data were collected by video recordings during altogether 22 support group sessions ranging from 46 to 78 minutes in length (mean 57 minutes, 1433 minutes in total). The analysis procedure was performed by three researchers in three stages; a preliminary review, a substantive review and an analytic search according to Heath et al (2010).
**Results:** Analysis revealed three categories of challenging situations deemed to be of clinical relevance for PTs and other health professionals promoting HEPA in patients. The challenges occurred while the support group participants perceived barriers to performing physical activity, when they neglected using the diary for planning physical activity as intended in the program, and when they experienced a mix of negative and positive outcomes of physical activity. The analysis yielded eight strategies PTs used to manage these three challenges (Figure 1). The strategies either focused on provision of information or on involvement of group participants in discussions. The PTs switched back and forth between strategies, demonstrating that they adapted to different situations.

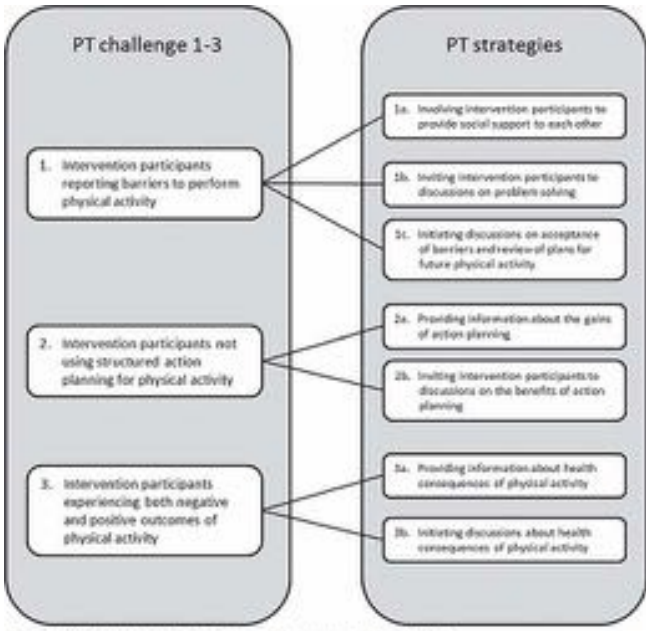


Figure 1. PT challenges and strategies in guiding persons with RA to HEPA.

**Conclusions:** Our results are promising for future initiatives to integrate PTs' traditional information-provision strategies with strategies facilitating participation by inviting group participants to interaction and discussion, potentially enhancing the uptake of HEPA interventions in group formats.
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FRI0627-HPR **IN PATIENTS WITH INFLAMMATORY MYOPATHY QUANTITATIVE MUSCLE TESTING HAS A HIGHER RELIABILITY THAN MANUAL MUSCLE TESTING**

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**Background:** Inflammatory myopathies (IMs) are systemic autoimmune diseases, characterized by reduced muscle strength and endurance. Although IMs are relatively rare, patients' disabilities in daily life are substantial. Thus, there is a need for appropriate and reliable assessments to quantify muscle weakness. Although the manual muscle test (MMT) and the quantitative muscle test (QMT), which employs a dynamometer, are commonly used tests to evaluate muscle strength, their psychometric properties (e.g. reliability) have not yet been sufficiently studied[1].
**Objectives:** To determine the reliability of the MMT8 and the QMT in patients with IM.
**Methods:** Twenty-four adult, German speaking patients with established diagnosis of IM were included. The majority of patients was female (83%), 57±12 years old with a mean disease duration of 28±29 months. The maximum isometric strength of eight muscle groups, which are most often affected, was evaluated with the MMT8 using the 10 point Kendall scale and the QMT indicating strength in Newton (N). For intra-rater reliability, one tester performed the MMT8 and the QMT twice and for inter-rater reliability, they were tested by a second independent tester. The Intraclass Correlation Coefficient (ICC) and the Standard Error of Measurement (SEM) were evaluated.
**Results:** The intra-rater reliability of the MMT8 yielded moderate to good ICCs (0.63–0.89) for all muscle groups and an excellent ICC (0.92) for the total score. Inter-rater reliability yielded moderate to good ICCs (0.54–0.84) for shoulder abductors, wrist and hip extensors, hip abductors, neck flexors and the total score, and low ICCs (0.08–0.34) for the remaining muscle groups (elbow flexors, knee and foot extensors). The SEM was smaller for the intra-rater (SEM 0.5/10 point of Kendall scale for muscle groups and 2/10 points for the total score) than for inter-rater reliability (SEM 0.5–1/10 point for muscle groups and 3/10 points for the total score). QMT presented moderate to excellent intra- and inter-rater reliability (ICCs 0.52–0.92) for all muscle groups. The intra-rater comparison for shoulder abductors was 10N, inter-rater comparison 13N and the intra-rater and inter-rater comparisons for the knee extensors were 28N and 35N, respectively. In contrast to the QMT, the MMT8 showed high ceiling effects between 18% and 77% for all but one muscle group (hip extensors).
**Conclusions:** In this study, the QMT showed a better reliability than the MMT8 because of missing ceiling effects and due to the good to excellent intra- and inter-rater reliability. Notably, the QMT seems to be more accurate to measure single muscle groups especially in patients with mild weakness as for example in early disease. If no hand-held dynamometer is available, the total score of MMT8 represents an appropriate alternative.
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FRI0628-HPR **ADVANCED PRACTICE MUSCULOSKELETAL PHYSIOTHERAPISTS IN RHEUMATOLOGY- A NATIONAL REPORT OF THE 2014 DATA**

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**Background:** Research studies have supported the role of Advanced Practice Physiotherapists (APP's) acting as first contact practitioners in the management of musculoskeletal (MSK) patients[1]. In 2012, funding was approved for 24 APP posts in Ireland through the Clinical Strategy and Care Programmes Directorate of the Health Service Executive (HSE) in Ireland. These posts were to provide orthopaedic and rheumatology triage clinics across 16 hospitals throughout the country as a waiting list initative for patients with MSK complaints.
**Objectives:** i)To present the data reported on the throughput of Rheumatology patients seen by the APPs nationally in 2014.
**Methods:** 13 sites provided MSK triage through rheumatology clinics nationally in 2014. While each post has a target of seeing 1,000 patients per year it has been reported that APP's see a ratio of 5:1 orthopaedic to rheumatology patients. Data was collected monthly from all sites and reported directly to the rheumatology clinical care programme. Descriptive data was analysed using a Microsoft® Excel package.
**Results:** 2,177 new and 530 return rheumatology patients were seen nationally in 2014. Regarding new patients the most common areas were shoulder (n=329, 15.1%) and lumbar spine (n=288, 13.2%), 35.2% (n=766) had multiple pain sites. Regarding waiting times 58.6% (n=1275) were seen within 6months of referral and 21% (n=457) had imaging ordered. 40.1% (n=873) were referred for physiotherapy within the hospital or primary care. 63.3% (n=1378) were discharged directly from the APP clinic and 15% (n=327) were referred on to another medical speciality.
**Conclusions:** APPs have been effective in triaging MSK referrals within a rheumatology setting. A large proportion of patients were discharged back to the referring source.
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**Acknowledgement:** The authors would like to acknowledge the work of the APP's nationally in the collection of the data.
**Disclosure of Interest:** None declared
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FRI0629-HPR **BACK TO ACTION: A GUIDE TO EXERCISING SAFELY IN THE GYM WITH ANKYLOSING SPONDYLITIS - BOOK AND APP USER PERSPECTIVES**

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**Background:** *Back to Action* (*B2A*) is a guide designed to help people with ankylosing spondylitis and axial spondyloarthritis (AS) exercise safely in the gym, produced by NASS in association with the Defence Medical Rehabilitation Centre at Headley Court. It was first published in print in 2010, and was published as a free iOS app in 2011 and in Android format in 2012. Two surveys were conducted from 1 November 2014 to 30 April 2015 to gather information on user satisfaction with the *B2A* book and app, and their impact on users. Key findings included; the structure and content of *B2A* was highly regarded, 67% now exercise more at home than previously, and 95% of respondents would recommend the guide to others with AS.
**Objectives:** The information and comments collected will help to shape the next phase of *B2A*'s development as well as help to review the current versions of the book and app to ensure that the needs of the user are met fully.
**Methods:** One survey dealt with the printed version of *B2A*, the other with the app. Apart from questions relating to format-specific topics, both surveys contained the same 17 questions designed to elicit both numerical ratings and qualitative comments, and were advertised via the NASS website, Facebook and Twitter. Additionally, the apps survey was sent to all users via a push notification update. The answers to both surveys were analysed together.
**Results:** Two hundred and five people completed the surveys. Sixty-five percent were in the 25–44 age range. Each section of *B2A* received an average rating of 4.10 or above out of a possible 5 for excellence, with the guide overall receiving an average rating of 4.23 out of 5. Ninety-five percent of those surveyed would recommend *B2A* to someone with AS. In terms of measuring *B2A*'s impact, 67% said that they exercise more at home since buying or downloading the guide. When asked to rate how significantly the guide has improved their general fitness (where 5 is very significantly), the average rating was 3.50. The average rating was 3.20 when respondents were asked to rate how significantly *B2A* had improved their AS. Suggestions for future development of *B2A* showed a strong desire for sections on the use of free weights (53%) and gym balls (33%). Other respondents asked for walking and cycling tips, and stretches for the swimming pool.
**Conclusions:** Although the structure and content of *B2A* were rated high, the impact of the guide on respondents' general fitness and AS symptoms did not rate as correspondingly high. However, the material never formally addressed how to measure general fitness and therefore the potential variability in interrupting this may explain the low score. More successfully, *B2A* seems to have had an effect on the numbers of users now exercising more at home, as well as encouraging others to join gyms, crucial to the management of AS. Compliance in exercising at home is low amongst people with AS despite awareness of the benefits of exercise [i] and so the book and app were successful in this area. Various areas for future development were also identified, which should increase the scope and impact of subsequent editions.
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[1] [i]Physical Activity and Exercise: Perspectives of Adults With Ankylosing Spondylitis, O'Dwyer T, McGowan E, O'Shea F, Wilson F, Journal of Physical Activity & Health, 28 October 2015
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## FRI0630-HPR THE IMPACT OF STRETCHING ON AXIAL SPONDYLOARTHRITIS (AXSPA): A LITERATURE REVIEW

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**Background:** AxSpA encompasses the conditions Axial Spondyloarthritis (AS) and non-radiographic axial spondyloarthritis. [1] AxSpA patients often present with symptoms such as inflammatory back pain, stiffness, fatigue and joint swelling. [2] To date, optimal management of axSpA has included a combination of medical and therapy interventions. [3] Regular exercise and stretching are fundamental parts of AS rehabilitation that has been used for many years.
The protein Tumour Necrosis Factor- alpha (TNF) is often overproduced in axSpA leading to inflammation which can damage connective tissue structures. In the last decade, anti-TNF agents (biologics) have been used more regularly in the treatment of AS. [4]
**Objectives:** To establish an evidence-base for a physiotherapy-led programme by:
– Clarifying the effect of stretching exercise therapy for patients with axSpA
– Determining whether exercise therapy is indicated in the management of axSpA patients receiving biologic therapy
**Methods:** The search databases used were AMED, EMBASE, HMIC, BNI, Medline, PsycInfo, CINAHL, and HEALTH BUSINESS ELITE. The "PICO" approach to literature searching was used.
"'P' Patient/ population: Ankylosing Spondylitis, Axial Spondyloarthritis
"I" Interaction: Stretch*, Active, Passive, Dynamic, Resistant, Yoga, Pilates, Proprioceptive neuromuscular facilitation
"C" Comparison: Not applicable
"O" Outcomes: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Functional Index (BASFI)
**Results:**
– Stretching with other modes of exercise improves BASDAI, BASMI, and BASFI measurement
– Individual specific stretching programs have better results than segmental stretching
– Stretching with strengthening is a favourable approach with a focus on movement control
– Possible decrease in inflammatory processes during stretching
– Possible decreased occurrence of tendinopathy/ enthesopathy which may lower risk of ossification and associated stiffness
**Conclusions:** There is evidence to support that exercise is beneficial for the axSpA patient, and research is beginning to study the components of such programs. Patients with axSpA on biologics should complete regular multi-modal exercise. Exercise works synergistically with Biologics to aid decrease of systemic inflammation. This review has shown that stretch is used as an integral part of patients' exercise programs. Only a few articles have looked specifically into the effects of stretching on axSpA, therefore it is difficult to give definitive recommendations regarding intensity and frequency. High quality studies are needed on axSpA patients completing specific postural stretches in a group setting, with further investigation into the impact on BASDAI, joint ROM and systemic inflammation. Different frequencies and intensities of stretching could then be studied.
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## FRI0631-HPR A NEW IMPULSE RESPONSE METHOD TO ASSESS EARLY KNEE OSTEOARTHRITIS DIFFERENCES BETWEEN YOUNG AND ELDERLY WOMEN

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**Background:** Decreased shock absorbing of the cartilage between the femur-tibia is assumed in patients with knee osteoarthritis (OA), and the impulse response method was considered to apply the evaluation of initial degeneration for cartilage.
**Objectives:** The purposes of the present study were 1) to establish the impulse response method deciding the appropriate location for input and output impulse to assess cartilage degeneration in the knee joint, and 2) to determine the differences between young and elderly women using this method.
**Methods:** 1) Ten young women (age: 20 ± 0 years) participated. Input value was measured by an input device attached to the distal end of the load cell. Output value was measured by a one-axis accelerometer. Input locations were the medial epicondyle and the medial condyle. Output points were distal 5 cm, 10 cm and 15 cm from the knee joint space. The input-output ratio of ten times was calculated to six combinations of input points and output points. The intraclass correlation coefficient (ICC) was calculated by re-measurement several days before.
2) Two groups of 26 elderly (age: 69 ± 6 years) and young (age: 21 ± 1 years) women each were recruited. The elderly group included those who matched the knee osteoarthritis classification criteria by clinical findings. The outcome measures were the input-output ratio (unit: $\times 9.8$ m/s$^2$/N) and the attenuation rate that was the ratio of a second amplitude for the first amplitude, the frequency, and the power spectrum. The power spectrum was obtained by Fast Fourier Transform and each 10 Hz ranging from 1 to 100 Hz was used as the final analysis [1,2].
**Results:** 1) ICCs of output location at 15 cm point with two input locations were greater than 0.9. The medial condyle (22.7±3.1 [N]) was significantly greater than compared to the medial epicondyle (18.4±2.8 [N], $p<0.001$).
2) The input-output ratio was 0.11 ± 0.03 in the young group and 0.11 ± 0.04 in the elderly group; there were no significant differences in the input-output ratio. The attenuation rates of the young and elderly groups were 0.38 ± 0.14, and 0.36 ± 0.19, respectively, and there were no significant differences in the attenuation rate of the two groups. The frequencies (unit: Hz) were 68.7 ± 13.1, and 77.2 ± 25.2, respectively, and there were no significant differences in the frequency of the two groups. The power spectrum (unit: $(\times 9.8$ m/s$^2)^2$) of the young group ($1.21\times10^{-4}\pm1.06\times10^{-8}$) was significantly greater than the value of the elderly group ($2.97\times10^{-4}\pm1.61\times10^{-7}$) at 21–30 Hz (p=0.036). Additionally, the power spectrum of 21–30 Hz was correlated to knee pain (r=0.39, p=0.049).
**Conclusions:** The location of the medial condyle was appropriate in the input point, and 15 cm point distal from the knee joint space was a suitable location as the output point based on the present findings.
In 21–30 Hz, the impulse absorbing by the cartilage in elderly women was less than compared to the values in young women. The impulse response method of the present study could be applied to assess early knee osteoarthritis.
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## FRI0632-HPR PATIENT EDUCATION EVENT: "WHY DOES MY BACK HURT?"

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**Background:** Back pain is common; 84% of people suffer with back pain at some point in their life.(1) 1.3%>5.3% of back pain sufferers have Axial Spondyloarthritis (AxSpA), a chronic inflammatory condition predominantly involving the spine and sacroiliac joints (SIJ).(1,2) With recent developments for the treatments of AxSpA, this condition can be treated much more effectively, reducing pain and improving quality of life. Differentiating between mechanical and inflammatory back pain remains a challenge. The mean delay in diagnosis is still 8.54 years in the UK.(3) A lot of work has been done to raising awareness with medics and Allied Health Professionals. Improving the understanding of back pain sufferers also has a role in reducing the time to diagnosis.
**Objectives:** To raise awareness of AxSpA, and ensure patients (pts) get referred correctly to receive appropriate investigations, diagnosis and treatment.
**Methods:** An event was organised with the objective of raising awareness of AxSpA and identifying those suffering with the condition. The event was advertised through local press, social media and East Kent Hospital University Trust (GP Practices, physiotherapists, osteopaths and chiropractors).
Attendees completed a back pain questionnaire before, immediately after and at 6 months after the event. The event consisted of 3 lectures: differentiating inflammatory and mechanical back pain, management on inflammatory back pain and 10 top tips for back pain. The National Ankylosing Spondylitis Society was also represented. An "Ask The Expert" session followed this, where pts had the opportunity to ask a panel consisting of therapists, rheumatologists and NASS representative questions.
**Results:** 104 people with undiagnosed back pain, attended the event. 87 questionnaires were completed the on the day; 54 described themselves as back pain sufferers and 33 were supporters of back pain sufferers. The response rate at 6 months was 28 (52%) As a result of the survey, 5 pts were diagnosed with AxSpA, with a further 9 undergoing further investigations in secondary care (Table).

| Outcome | No. of attendees | % |
|---|---|---|
| AxSpA | 5 | 2.7 |
| Red flag (prostate cancer, myeloma) | 2 | 1.08 |
| Undergoing investigations in secondary care | 9 | 4.86 |
| Referred to physiotherapy | 5 | 2.7 |
| Private physiotherapy/osteopathy | 3 | 1.62 |
| Offered spinal surgery after orthopaedic review | 1 | 0.54 |
| GP took no action | 3 | 1.62 |

These results not only highlight that, as a result of this event, 5 people were diagnosed with AxSpA, but also demonstrate that there is a substantial amount of "undiagnosed" back pain, needing different treatment pathways.
**Conclusions:** Educational events such as this can facilitate early diagnosis and treatment of pts with AxSpA. The high response rate at 6 months illustrates the event was well received and useful to the audience. Further education events would be useful both for pts and professionals to facilitate diagnosis and early treatment.
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## FRI0633-HPR "IT MIGHT HURT, BUT STILL IT'S GOOD": PEOPLE WITH RHEUMATOID ARTHRITIS BELIEFS AND EXPECTATIONS ABOUT PHYSICAL ACTIVITY INTERVENTIONS

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**Background:** People who have Rheumatoid Arthritis (RA) report low levels of physical activity despite the many health benefits of being physically active [1,2]. Involving key stakeholders is important when designing interventions which target behaviour change as it allows consideration of particular issues that may influence the delivery of complex interventions [3,4].
**Objectives:** This study aimed to explore the views of people who have RA on being physically active and the design of a future physical activity intervention.
**Methods:** A qualitative methodology using a constructivist approach was employed. Recruitment was through an outpatient rheumatology clinic in an urban hospital. Interviews were conducted by telephone, with an interview question guide being used by the interviewer. Interviews were transcribed and analysed using thematic analysis. Transcripts were read, notes made and ideas formulated to facilitate coding. The research team searched for patterns, analysed and coded the data, and generated sub-themes and themes. Themes were reviewed by the research team to check if the themes worked in relation to the coded extracts and the entire data set.
**Results:** Twelve females and five males participated in the study. Their mean age was 59.8 years (range 35–83, SD 12.5) and mean disease duration was 13.7 years (range 1–47, SD 15.3). Four main themes were generated: "*Being active*", "*Barriers and facilitators*", "*Information and advice*", and "*Supporting physical activity*". "*Being active*" encapsulated the participants' understanding of physical activity, their perceptions' that they could be active and their physical activity limits due to having RA. Beliefs and emotions were highlighted as both key barriers and facilitators to being active, e.g. fear about increasing disease activity by "overdoing it" whilst locating an intervention in a hospital setting was discussed as being negative. The need for accurate information about being physically active from a credible source was highlighted in "*Information and advice*", whilst goal setting, monitoring and social support were thought to be important to support physical activity.
**Conclusions:** There is a lack of information and knowledge about being physically active amongst people who have RA, which contributes to uncertainty about being active. Future interventions should consider delivery in a group, community setting and should incorporate methods which support and monitor behaviour. This study highlights the importance of involving key stakeholders when designing future physical activity interventions as such contributions can help to ensure that such interventions are successful.
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## FRI0634-HPR COMPLEX TREATEMENT OF PATIENTS WITH GOUTY ARTHRITIS

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**Background:** Gout is a type of arthritis caused by the formation of uric acid crystals within or around the joints. It is the most common type of inflammation arthritis for people over 40.
For some of the patients, the leading symptoms are pain and stiffness in the joints, while others develop heavy joint deformations and permanent disabilities. Applying a complex rehabilitation approach with rheumatologic aid and a physio-rehabilitation program significantly improves the condition of the patients with gouty arthritis, the strength of their symptoms diminishes, and becoming handicapped is avoided or significantly delayed.
**Objectives:** The aim of this study is to measure the effect of conducting a complex drug treatment combined with a physio-rehabilitation program in patients with gouty arthritis in an acute or chronic stage that heavily affects the musculoskeletal system.
**Methods:** Between 2013 and 2015, 39 patients with gouty arthritis were hospitalized and treated at the Rheumatology Ward at UMHAT "Dr. Georgi Stranski" – Pleven. 26 of them were male and 13 female, aged between 43 and 62 years old, in subacute or chronic stage (SUE $<$25 mm, fibrinogen and CRP at relevant values, AST and RF (–).
In addition to the drug therapy with analgesics, NSAIDs and chondoprotectors, uricoinhibitors and urikoeliminators during the non-paroxysmal period, the patients also undergo a complex physical and rehabilitation program consisting of: electrotherapy (magnetic field, mid-frequency currents and ultrasound therapy with NSAIDs, therapeutic massages, cryotherapy, active methods of kinesitherapy and occupational therapy.
Functional tests and measurements – VAS for the pain, a daily activities life test (DAL) and complex functional assessment test (CFA) – were made for the purpose of the study at the beginning and at the end of the observed period.
**Results:** An individual file was created for every patient where the results from the tests and measurements are stored in order to track the patient's condition over the course of treatment. The treatment consists of 3 stages: a period in the Rheumatology ward, treatment in the Medical Rehabilitation ward and ambulatory physio-rehabilitation courses.
Conducting physiotherapeutic treatment for patients with gouty arthritis in an acute or chronic stage complements the drug treatment and leads to faster relief of the symptoms during an acute stage, decreases the timeframe of the temporary inability to work, prevents any permanent damage to the affected joints and prevents the occurrence of permanent disabilities.
**Conclusions:** For patients with gouty arthritis in an acute or chronic stage that heavily affects the musculoskeletal system, the complex physio-rehabilitational and rheumathological treatment is effective and leads to a significant improvement in the quality of life of the patients.
**Disclosure of Interest:** None declared
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## FRI0635-HPR THE MYOSITIS ACTIVITY PROFILE – FIRST RESULTS OF CONTENT AND CONSTRUCT VALIDITY OF THE GERMAN VERSION

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**Background:** The Myositis Activity Profile (MAP), a questionnaire to assess limitations of activities of daily life in patients with inflammatory myopathy (IM), was developed and tested on psychometric properties in Sweden and later on translated and validated in English[1,2]. To the best of our knowledge, there is no validated version available for German speaking patients.
**Objectives:** To translate and cross-culturally adapt the MAP into German language and to determine content and construct validity.
**Methods:** A cross-cultural adaptation of the English version of the MAP into German was performed following international guidelines. To assess content validity of the new German version, patients rated difficulty and importance of items of the MAP using a visual analog scale (VAS range 0–10). For construct validity the correlation between the MAP and five functional tests (Short Physical Performance Battery, one leg stand, Grip Ability Test, upper and lower Progressive Isoinertial Lifting, and the 6 minute walk) were analyzed with the Spearman correlation coefficient. Additionally, for discriminative validity differences between patients and age and gender matched healthy controls were analyzed using the Mann-Whitney- U Test. Item fit within subscales was calculated by Cronbach's alpha.
**Results:** Twenty German speaking patients with a diagnosis of acute (20%),

subacute (25%) or chronic (55%) myositis were included. Participants were 56.5 ±10.13 years old and 75% of them were female. The median combined difficulty and importance of the 32 items of the MAP was 5.67 (range 5.3–6.5). Correlations between the total score of the MAP and the Short Physical Performance Battery (-0.52), Grip Ability Test (0.52), Progressive Isoinertial Lifting Evaluation (lumbal part: -0.62, cervical part -0.60) and the 6 minute walk test (-0.69) were moderate and the correlation with the one leg stand test was low (-0.26). Healthy participants had significant lower scores (single items, subscales and total score) than patients ($p \leq 0.05$). Cronbach's alpha coefficients for the four subscales varied between 0.85 and 0.92.

**Conclusions:** This initial validation of the German version of the MAP showed that the 32 items from the English version were also suitable for Swiss conditions. Cronbach's alpha coefficients were similar to those from the English version. As expected the MAP correlated moderately with functional tests, except with the one leg stand. Although balance may be important in patients with IM, the MAP does not cover balance ability. In summary, the MAP seems to be a valid and easy applicable methodology for assessing limitations of activity in daily life. However, further research is required to confirm these preliminary results and to test reliability.

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## FRI0636-HPR EFFECTS OF CLINICAL PILATES EXERCISES COMBINED WITH DANCETHERAPY ON MOOD IN PATIENTS WITH RHEUMATIC DISEASES

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**Background:** Clinical pilates exercises are described as mind-body exercise models which are also recommended on treatment of rheumatic diseases (1, 2). Since dancetherapy has positive effects on mood, it has been preferred in the rehabilitation of the chronic diseases in recent years (3,4). However, clinical pilates exercises combined with dancetherapy in rheumatic patients is not found in the literature.

**Objectives:** To investigate the effects of clinical pilates exercise combined with dancetherapy on mood in rheumatic patients.

**Methods:** 20 rheumatic patients aged 42.00±12.00 years were participated in this study. Mood status of the patients were assessed by Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale (HADS) and The Multidimensional Scale of Perceived Social Support (MSPSS). Patients performed supervised clinical pilates exercises in a period of one hour, 3 times a week for 10 weeks. Dancetherapy was added to only 12 of patients' program once a week, one hour, for 10 weeks.

**Results:** All scores improved in all patients' for the post-exercise assessments relevant to the pre-exercise assessments. However, statistically significant improvement were observed only in MSPSS scores for the patients participated to the dancetherapy sessions ($p<0.05$) (Table.1).

Table 1. Comparison of the all scores

| | Pilates and dencetherapy group (n=12) | | | Only pilates group (n=8) | | | P intergroups |
|---|---|---|---|---|---|---|---|
| | X ± SD | | p | X ± SD | | p | |
| | Before | After | | Before | After | | |
| MSPSS | 59.83±10.24 | 69.00±11.24 | 0.003 | 64.38±5.85 | 66.13±7.49 | 0.307 | 0.282 |
| HADS | 13.08±4.05 | 15.32±3.45 | 0.260 | 13.5±3.62 | 11.88±3.68 | 0.463 | 0.664 |
| BDI | 10.58±5.61 | 7.08±5.36 | 0.760 | 12.25±6.20 | 9.75±6.60 | 0.089 | 0.496 |

**Conclusions:** Clinical pilates exercises may provide improvement in mood characteristics in rheumatic patients. We concluded that these exercises enhance patients social support perceptions when combined with dancetherapy.

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**Disclosure of Interest:** None declared

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## FRI0637-HPR THE EFFECTS OF CLINICAL PILATES EXERCISES ON KINESTESIA AND POSITION SENSE IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

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**Background:** Proprioception is a deep perception which constitutes kinesthesia and position sense. In particular, it is extremely affected due to cartilage degeneration in patients with osteoarthritis (OA) of the knee (1–3). Although exercise treatment is suggested as an effective method in OA, there is no study that investigates the effects of clinical pilates exercises on proprioception in patients with OA of the knee.

**Objectives:** The aim of this study is to investigate the effects of clinical pilates exercises on kinesthesia and position sense in patients with knee OA.

**Methods:** 39 patients with knee osteoarthritis defined as Kellgren-Lawrence (K-L) grade1 and 2 at mean age 55.95± 5.54 years and disease duration 6.59± 3.15 years were participated in this study (Control group; 20 patients, Exercise group; 19 patients). Exercise group attended in clinical pilates exercises sessions for three times a week (one hour session) during ten weeks. Kinesthesia and position sense were assessed with PMS-1000 Proprioception Test, Sport Expert Proprioceptional Sports Tech. Instrument. All measurements were repeated after ten weeks.

**Results:** Although the kinesthesia perception of patients improved ($p<0.05$), position sense did not improve in exercise group ($p>0.05$). There were no improvements in control group according to pre- and post-treatment values.

Table 1

| | BETY group (n=19) | | | Control group (n=20) | | | P intergroups |
|---|---|---|---|---|---|---|---|
| | X ± SD | | p | X ± SD | | p | |
| | Before | After | | Before | After | | |
| Kinestesia | 3.04±2.84 | 2.33±1.74 | 0.050 | 1.87±1.47 | 2.18±2.23 | 0.938 | 0.672 |
| Position sense | 1.75±1.44 | 1.08±0.70 | 0.480 | 2.27±2.73 | 1.20±0.96 | 0.121 | 0.865 |

**Conclusions:** As a conclusion, clinical pilates exercises should be kept in mind in terms of kinesthesia in patients with OA of the knee. We recommended that in further OA-related-studies using clinical pilates exercises, position sense should be examined in more detail.

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**Disclosure of Interest:** None declared

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## FRI0638-HPR INVESTIGATING PLANTAR PRESSURE DURING WALKING IN PLANTAR FASCIITIS

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**Background:** Plantar fasciitis (PF) is an inflammation of the plantar fascia on the bottom of the foot, characterized by stiffness of medial arch and pain especially during the first steps. It can effect on daily living activities such as walking and a difference in the plantar pressures during walking can be expected (1). But, no studies were found in the literature related to this situation.

**Objectives:** The aim of this study was to investigate the dynamic plantar pressure during walking and compare the pedography measurements of the affected and unaffected feet of patients with plantar fasciitis during walking.

**Methods:** Forty patients (28 female, 12 male) with unilateral plantar fasciitis

were included in the study. Pain status and functionality was assessed with a visual analog scale (VAS) and Foot Function Index (FFI), respectively. EMED-m pedography platform (Novel GmbH, Germany) was used for dynamic foot plantar pressure measurements. Maximum force, contact area and contact time were measured for total object and hind foot in both affected and unaffected feet. These measures were recorded three times and average values were used in the analysis.The data were not distributed normally and as a result, non-parametric tests were used for interpreting the data.

**Results:** Average age, height and weight were 51.1 (min-max: 74–33), 165.7 (min-max: 150–190), 82.4 (min-max: 60–110), respectively. VAS was 7.5 (min-max: 6–8) FFI was 55.9 (min-max: 40–63). The results related to pedography measurements were given in Table 1. While, it was observed that hind foot maximum force and contact area were diminished in the affected foot, no differences were found in measures related to total object nor contact time of hind foot. Although a moderate relationship was found between pain status and functionality (rho: 0.57, $p<0.001$), none of these variables were correlated with pedoghraphy measures ($p>0.05$).

**Table 1. Pedography measurements**

| | Affected Foot Median (IQR 25/75) | Unaffected Foot Median (IQR 25/75) | p |
|---|---|---|---|
| Total Object Maximum Force (N) | 998.7 (886.0/1115.7) | 1011.1(897.5/1106.6) | 0.536 |
| Total Object Contact Area ($cm^2$) | 128.1 (118.3/142.2) | 131.2 (121.8/144.1) | 0.074 |
| Total Object Contact Time (ms) | 840.0 (780.0/899.2) | 853.3 (800.0/927.1) | 0.492 |
| Hindfoot maxium Force (N) | 500.6 (442.0/557.9) | 536.5 (460.5/619.5) | **0.044** |
| Hindfoot Contact Area ($cm^2$) | 31.6 (29.1/35.1) | 32.5 (30.1/36.3) | **0.010** |
| Hindfoot Contact Time (ms) | 550.0 (432.5/615.7) | 530.0 (485.4/598.7) | 0.812 |

N: Newton; ms: microseconds; IQR: Interquartile Range; $p<0.05$.

**Conclusions:** According to the results of this study, there was a difference in plantar pressures between affected and unaffected feet in plantar fasciitis patients. It seems that the difference is not related to pain status nor functionality. Treatment strategies aiming to resolve this difference might be beneficial to improve outcomes of the treatment. More studies are needed to understand the importance of the dynamic foot pressures during walking in this patient population.

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## FRI0639-HPR GENDER DIFFERENCES IN ACUTE INFLUENCE OF RESTRICTED ANKLE DORSIFLEXION ANGLE ON KNEE ADDUCTION MOMENT DURING GAIT

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**Background:** Ankle dorsiflexion (DF) is necessary during terminal stance of gait, and its restricted range leads to increased knee adduction moment (KAM) in a previous report. Females are found to have a greater decrease in DF than males across age groups (every 5 years from 55 to 85 years old). Female gender is one of the critical risk factors of advanced and symptomatic medial knee osteoarthritis (knee OA). From this point of view, restricting the ankle range of motion is thought to be more related to increase the risk of knee OA in female compared to the risk in male. However, it is not clear whether there are gender differences in the influence of restricted ankle dorsiflexion angle on KAM during gait.

**Objectives:** The purpose of the present study was to investigate gender differences in KAM during the terminal stance of gait between unrestricted and restricted ankle range of motion.

**Methods:** Forty-nine healthy volunteers (24 males, 25 females) walked with a custom-designed ankle brace that restricted ankle DF. Kinematics and kinetics were collected using a 7-camera motion analysis system and two force plates. Ankle DF was unrestricted and restricted to 0 degree. Ankle DF angle, knee extension angle and KAM were measured during terminal stance. The significant difference was set for both conditions of $p<0.05$ and above 0.50 effect size (ES) in the present study.

**Results:** Peak ankle DF angles for unrestricted and restricted by the brace were 13.9 ± 4.1° and 7.0 ± 5.4° in males, and 10.1 ± 5.6° and 2.8 ± 4.1° in females, and peak knee extension angles were –9.0 ± 4.8° and –4.0 ± 6.4° in males, and –3.2 ± 5.2° and 2.0 ± 5.7° in female, respectively. The peak KAMs were 0.38 ± 0.15 Nm/kg and 0.42 ± 0.15 Nm/kg in males ($p=0.018$, ES =0.27), and 0.37 ± 0.12 Nm/kg and 0.47 ± 0.12 Nm/kg in females ($p<0.001$, ES =0.83). KAM was significantly different between unrestricted and restricted ankle range of motion in females.

In both genders, significant correlations were observed between the changes with both conditions in KAM and changes in peak knee extension angle. A stronger relationship was observed between them in females than in males ($r=0.52$, $p=0.012$ in males, $r=0.64$, $p=0.001$ in females). Significant correlations were observed between changes in peak knee extension angle and changes in peak ankle DF angle in males ($r=-0.65$, $p=0.001$), but no relationship was observed in females.

**Conclusions:** KAM in females was more affected by restricted ankle DF during terminal stance of gait than KAM in males. Increased KAM was related to greater knee extension angle, which may be caused by restricted ankle DF. However, knee extension angle in female is assumed to be affected by the genu recurvatum observed during the restricted ankle range of motion condition and the ceiling effect shown in the relationship with changes in peak ankle DF angle.

**Disclosure of Interest:** None declared
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## FRI0640-HPR EFFECTS OF POSTURAL TAPING ON PAIN AND FUNCTION FOLLOWING OSTEOPOROTIC VERTEBRAL FRACTURES – A PILOT STUDY

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**Background:** Osteoporotic Vertebral Fractures (OVFs) are common and present a significant burden to patients and healthcare services. It is known that poor posture (such as forward flexion) can increase the pressure on vertebrae, increasing pain and the risk of further fracture. Postural taping may therefore act to reduce spinal loading and pain.

**Objectives:** To assess the effects of postural taping on pain and function when used for a 4-week period in addition to usual care. To decide if a fully-powered study is feasible.

**Methods:** *Recruitment:* Men and women with OVFs recruited from two local healthcare organisations. *Inclusion criteria:* At least one painful OVF; Fracture not immobilised; Independently mobile (with or without an aid); Able to apply taping device independently or with assistance. *Exclusion criteria:* Osteoporosis secondary to metabolic bone disorders or other disease (steroid-induced osteoporosis was *not* an exclusion); Fragile or broken skin; Known allergy to adhesive plasters; Vertebroplasty or kyphoplasty. Diagnosis was confirmed by a consultant rheumatologist. A mutually convenient appointment was agreed when participants gave formal consent and completed baseline questionnaires.

*Outcome measures:* Outcomes were assessed at baseline and at 4 weeks. *Pain:* Visual Analogue Scale (VAS) for pain on movement and at rest. *Function and Quality of Life:* Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO).

*Intervention:* Following baseline assessment, participants were randomly allocated to receive the taping device ("PosturePlast") for home use and received full instruction (including skin care) and a supply of devices. The taping device is like a large sticking plaster with a built-in flexible plastic "X". The manufacturer claims it controls back movement, reduces pain and improves posture. Those randomised to the control condition continued with usual care.

**Results:** 25 participants took part (taping n=13, control n=11). The groups were comparable in terms of age and time between assessments, although the control group contained more men (n=3 versus n=0) and scored slightly lower on most clinical scores.

Descriptive analysis showed fairly consistent improvements in outcomes in both groups. The mean difference favoured the taping group for most outcomes. Generally the observed standardised effect sizes were small to medium (see Table). The largest effects were evident for pain and physical function. As might be expected in a small study, the observed mean group differences were associated with large confidence intervals.

| | | Standardised effect size (Cohen's *d*) |
|---|---|---|
| VAS pain at rest | | 0.37 |
| VAS pain on movement | | 0.45 |
| QUALEFFO total score | | 0.66 |
| QUALEFFO subscales | Pain | 0.54 |
| | Physical function | 0.78 |
| | Social function | 0.06 |
| | General health perception | –0.29 |
| | Mental function | 0.35 |

**Conclusions:** The taping device has the potential to improve pain and function, which is notable for such a simple device. However the findings need to be replicated in an appropriately powered study. The study procedures were acceptable to most participants and it seems that a definitive trial is feasible.

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## FRI0641-HPR BENEFICAL EFFECT OF A GAIT MODIFICATION, "NANBA STYLE WALK," FOR DECREASED KNEE ADDUCTION MOMENT

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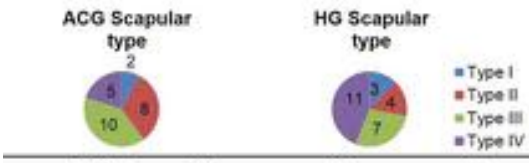
**Background:** The knee adduction moment (KAM) during gait was reported to affect knee osteoarthritis (OA) [1], and therefore a gait style with decreased KAM

is thought to be one way to prevent knee OA [2]. The Nanba style walk (N-walk) is a walking style with the step of the leg and swing of the arm at the same time as small trunk rotation [3], and the body's center of gravity is directly moved close to the center of the pressure. This gait modification is assumed to decrease the lever arm of the KAM, so that the KAM would be decreased due to the N-walk.
**Objectives:** The purpose of the study was to investigate the effect of the Nanba walk on KAM during gait in healthy adults as a preliminary study.
**Methods:** 28 healthy adults consisting of 16 men and 12 women (21.7 ± 0.4 years old) participated. All participants including those in the pilot study were informed as to the nature of the study, and their informed consent was obtained as approved by the Ethics Committee of Seijoh University. A three-dimensional analysis system (Venus 3D; Nobby Tech, Tokyo, Japan) with a 10-camera and a force plate (AccuGait; AMTI, MA, USA) were used to obtain the kinematics and kinetic data by inverse dynamic methods and global optimization. KAMs were normalized to body mass and leg length (no unit). The 1st and 2nd peak KAMs during stance phase and the lever arm length of the KAM (frontal plane) at both peak KAMs were measured to compare with free gait and N-walk. N-walk gait speed was controlled within ± 5% of a free gait. Subjects were asked to walk along a 6-m walkway, and three successful trials were recorded. Average data were used in final analysis. The EMG of the gluteus medius muscle, which was reported to relate to KAM [4], was measured, and Integral EMGs (iEMG) of the first and second half of the stance phase after full-wave EMG rectification were used to compare the two gait styles.
**Results:** The peak 1st and 2nd KAM of N-walk (4.9 ± 1.2 $\times 10^{-2}$ and 4.7 ± 1.5 $\times 10^{-2}$) were significantly decreased compared to the KAMs of free gait (5.6 ± 1.1 $\times 10^{-2}$ and 5.6 ± 1.6 $\times 10^{-2}$). The lever arm length at the peak 1st and 2nd KAM of N-walk (3.7 ± 1.1 and 3.3 ± 1.0 cm) were also significantly decreased compared to the lever arm length of free gait (3.9 ± 1.0 and 4.1 ± 1.0 cm). The iEMGs of gluteus medius muscle of the first and second half of the N-walk (2.8 ± 1.3 and 3.0 ± 1.4 Vs) were significantly increased compared to the iEMGs of the free gait (1.9 ± 0.9 and 2.1 ± 1.0 Vs, $p<0.05$).
**Conclusions:** The 1st and 2nd peak of KAM with N-walk were significantly decreased compared to the KAMs of free gait due to the lever arm length of KAMs with increased gluteus medius muscle activity. N-walk is one of the traditional Japanese walking styles when wearing a *kimono*. This gait modification is assumed to one of the indications of a walking style to help prevent medial knee osteoarthritis.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1267

## FRI0642-HPR SCAPULAR BIOMECHANICS IN PATIENTS WITH ADHESIVE CAPSULITIS

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**Background:** It is necessary that coordinated, synchronous motion of humerus, scapula and clavicula for full shoulder mobility and function. This motion may be impaired by adhesive capsulitis (AC) which is characterized by fibrosis and contracture of the glenohumeral joint capsule and ligaments.
**Objectives:** In this study we aimed to assess scapular biomechanics in patients with adhesive capsulitis and determine changes.




| LSST | ACG X±SS | HG X±SS | P |
|---|---|---|---|
| 0° abduction - T3 | 0.06 ±1.55 | -0.30±1.25 | 0.30 |
| 0° abduction - T7 | -0.28±1.01 | -0.28±1.63 | 0.52 |
| 45°abduction - T3 | -0.16±1.23 | 1.13±0.97 | 0.78 |
| 45°abduction - T7 | -0.31±1.34 | -0.22±1.48 | 0.82 |
| 90°abduction - T3 | -0.18±0.99 | 0.02±0.72 | 0.42 |
| 90°abduction - T7 | 1.16±0.79 | 0.08± 1.00 | **0.03** |

*Differences for HG derived by subtracting the measured side from the other side. Differences for subjects with AC derived by subtracting the injured side from the uninjured side. All measurements are expressed in centimeters. $p<0.05$

**Methods:** Twenty five patients with AC (21 female, 4 male; mean age 53±6 years; age range 44–67) and twenty five healthy people (21 female, 4 male; mean age 51±7; age range 39–65) were included in this study. Mean Body Mass Index (BMI) was 29.02±4.89 in AC group (ACG) and 28.40±4.67 in healthy group (HG). 11 dominant and 14 non-dominant shoulders in ACG and 12 dominant and 13 non-dominant shoulders in HG were measured. Kibler's observational classification system and lateral scapular slide test (LSST) were used for evaluating scapular position and mobility.
**Results:** There were 2 type I, 8 type II,10 type III and 5 symetric scapula in ACG and 3 type I, 4 type II,7 type III and 11 symetric scapula in HG. 80% of ACG and 56% of HG had scapular dyskinesia but it was not significant ($p>0.05$). There was significant difference between groups in LSST the distance between inferior angle of scapula and T7 at 90° abduction ($p<0.05$) (Table 1).
**Conclusions:** In this study, our results showed that scapular biomechanics were impaired in patients with AC. Especially the majority of type III scapula and the distance between inferior angle of scapula and T7 at 90° abduction demonstrate increase in scapular upward rotation in upper degrees of elevation.
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## FRI0643-HPR A MULTICENTRE FOCUS GROUP STUDY ON IMPORTANT OUTCOMES FOR PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a variable and complex inflammatory arthritis. Symptoms can arise from psoriasis, enthesitis, dactylitis, and arthritis, which can compromise physical function, cause disability, and accrue significant health costs. The PROMPT research programme includes a randomised controlled trial (RCT) to investigate the benefit of earlier diagnosis of PsA on long term outcomes. Before the RCT can begin, it is important to include patient reported outcomes (PROMs) that are meaningful to patients. The measures currently used in PsA trials cover some of these domains and occasionally include a combined instrument such as the Composite Psoriatic Disease Activity Index questionnaire (CPDAI). However, they have been developed largely by professionals, consequently it is not known whether they capture what is most important to patients.
**Objectives:** To identify the disease activity and impact outcomes that are important to patients with PsA.
**Methods:** Eight focus groups at 5 hospital sites. Focus groups were audio-recorded, transcribed, anonymised, and analysed using Inductive Thematic Analysis. The full data set was analysed by the lead researcher, and a subset by 3 other team members (including patient partners).
**Results:** Forty-one patients sampled for a range of phenotypes and domains of disease activity took part: men=20; mean age=58 years (range 28–75; SD 11.4); mean disease duration=9 years (range 0.5–39; SD 8.3); mean HAQ=1 (range 0.0–2.5; SD 0.7). Over 60 outcomes were identified and grouped into 5 main categories:
1. Symptoms: including pain (e.g. back, arms, hips); swelling (e.g. sausage digits; puffy hands); stiffness (e.g. feet, hands); fatigue (e.g. physically tired, mentally foggy); skin (e.g. red, itchy, flaky), and poor sleep.
2. Personal impact: including physical (e.g. loss of fitness, restricted mobility); emotional (e.g. low mood, anxiety, anger); and social (e.g. embarrassment; isolation; loss of work).
3. Negative outcomes from treatment: including experiences (e.g. side effects, nausea); fears (e.g. concerns about toxicity); and practical challenges (e.g. mode of administration; requirement of regular blood tests).
4. Effective outcomes of treatment: including alleviation of symptoms (e.g. pain, stiffness); better skin; life-changing/miraculous drugs; and able to lead a normal life.
5. Expectations of treatment: including able to do more; improve quality of life/wellbeing; halt long term joint damage and symptoms of PsA; maintain independence; gain greater disease control (e.g. fewer flares); and understand reasons for prescribed treatment.

**Conclusions:** Qualitative data captured varied outcomes important to patients, from specific physical symptoms to the psychological, social and emotional impact on wellbeing and daily life. As it is not feasible or acceptable to include measures for all the outcomes generated, patients will now prioritise them in nominal groups. These priorities will be compared to the existing core set and the CPDAI. If patients identify important outcomes not currently measured, validated PROMs to

capture these will be identified. This will lead to a set of measures capturing all relevant domains of PsA from the patient perspective.
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**Disclosure of Interest:** None declared
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## FRI0644-HPR PERCEIVED PHYSICAL ACTIVITY BENEFITS AND BARRIERS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is associated with an increased risk of osteoporosis and cardiovascular disease, a reduction in physical fitness, and consequently a reduction in quality of life. Scientific evidence now supports various forms of exercise as both safe and even beneficial for RA patients. In RA, physical activity appears to play a central role in the management of the disease, maintenance of muscular function, joint range of motion and the ability to perform activities of daily life.
**Objectives:** The present study aimed to examine the perceived exercise benefits and barriers in a cross-section of patients diagnosed with RA, with the hope to tailor physical activity interventions to this group of patients.
**Methods:** Utilising a cross sectional study design thirty-seven participants (age, 58 ± 13 yrs) completed a self-administered survey. Participants were convenience-sampled from patients diagnosed with RA, attending the day-case unit for regular biologic intravenous infusions. Exercise barriers and perceived benefits of exercise were assessed using the exercise benefits/barriers scale (EBBS), with added questions in a rheumatology specific subscale. Physical activity guidelines (PAG's) were assessed using the single question physical activity questionnaire. Data are presented as means ± SD. Statistically significant differences reported by those meeting, and those not meeting PAG's was assessed using independent samples *t*-tests.
**Results:** The greatest perceived benefit of exercise was the physical performance subscale (score, 3.0 ± 0.4), and the greatest perceived barrier was the physical exertion subscale (score, 3.0 ± 0.6).Within the rheumatology specific subscale, "Exercise keeps my joints moving" was the highest perceived benefit, whereas "Exercise causes pain" was the highest perceived barrier. Despite attending regular intravenous biologic drug infusion sessions, patients disagreed that they do not have enough time to exercise (score, 2.1 ± 0.6) as presented by the time expenditure subscale. Of 37 participants, 43.2% ($n$=16) do not meet current PAG's. Such patients reported significantly lower overall perceived benefits of exercise than those meeting PAG's (respective scores, 2.6 ± 0.3 vs. 3.0 ± 0.4, $P<0.05$), and significantly higher overall barriers (respective scores, 2.5 ± 0.4 vs. 2.1 ± 0.4, $P<0.05$). Of the various specific EBBS subscales, statistically significant ($P<0.05$) differences were reported across life enhancement, physical performance, psychological outlook and physical exertion subscales, between those meeting, and those not meeting PAG's. Furthermore, those not meeting PAG's reported significantly greater perceived barriers in the rheumatoid specific subscale (score,3.1± 0.5 vs. 2.4± 0.4, $P<0.001$).
**Conclusions:** Less than half of the sample currently meet PAG's, with significant differences in perceived benefits/barriers between who meet and those who do not meet guidelines. Fatigue related to exercise was the greatest perceived barrier overall, which is also regarded as an extra-articular symptom of the disease. Contrary to the traditional advice, exercise is an intervention targeted against fatigue and has a critical bearing on wellbeing and quality of life in RA patients. Patients attending for biologic drug infusions represent a key opportunity to promote physical activity in this population.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.1338

## FRI0645-HPR FREQUENTLY ASKED QUESTIONS OF PATIENTS WITH OSTEOARTHRITIS: A CONSENSUS EXERCISE

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**Background:** Providing unambiguous information about osteoarthritis (OA) and describing options for self-management help patients to become actively involved in their own care. The lack of consensus among clinicians and the heterogeneous terminology between involved disciplines may complicate effective communication. Therefore, we decided to develop an educational course based on a structured inventory of informational needs and on consensus-based information addressing those needs.
**Objectives:** 1) to make an inventory of the most frequently asked questions (FAQs) on OA, expressed by patients to their different health care providers, 2) to formulate answers based on consensus among health care providers in the area of Nijmegen.
**Methods:** To identify and formulate answers to FAQS the following steps were taken: 1) Orthopaedic surgeons, rheumatologists, nurse practitioners from 3 different hospitals, and general practitioners and physiotherapists participating in a local network, were invited to provide 5–10 FAQs, not covered by a website providing information on OA (ran by The Dutch College of General Practitioners). Additionally the Dutch Arthritis Foundation was asked to provide FAQs from their arthritis helpline. 2) After deleting overlapping FAQs, the remaining FAQs were categorized by two researchers. 3) Care providers who provided FAQs and patients (responding to a call on various websites of local patient organisations) were asked to indicate a top 5 of most important FAQs per category and divide 100 points among their top 5 per category. 4) Twenty most important FAQs were selected for answer formulation. Then, for each FAQ 3 care providers from 3 different disciplines were asked to formulate an answer. 5) Finally, in consensus meetings draft answers were combined into one final answer per FAQ.
**Results:** A total of 28 responders provided 192 FAQs. From these FAQs, 93 overlapping FAQs were deleted and remaining 99 FAQs were categorized into 9 categories of 7–14 FAQs each, namely: "OA; cause, symptoms and disease course", "diagnostics", "medication", "care providers", "lifestyle", "surgery", "work", "self-management", "other". Seventeen professionals and 29 patients responded to the subsequent round of prioritising. The overall top 5 FAQs were: 1."What are the newest treatment options?" 2. "What is the natural course of OA?" 3. "If medication does not work, what other treatment options do I have?" 4. "'What sports are suitable? At what frequency and intensity?" 5. "When am I eligible for a joint replacement?". In 3 meetings the project group reached consensus on answers of the Top-20 FAQs.
**Conclusions:** Our study shows that it is feasible to achieve consensus among disciplines on information on topics not covered by guidelines, which can help to overcome communication hazards between patient and professionals from different disciplines. Formulated answers have been used in the development of an OA educational self-management course for OA-patients. Future research is necessary to examine to what extent consistency of information can contribute to self-management.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2140

## FRI0646-HPR DOES PAINFUL HAND ARTHRITIS INFLUENCE MOTOR CORTEX EXCITABILITY AND MOTOR SKILL LEARNING?

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**Background:** Painful hand arthritis frequently leads to reduced quality of life [1] and impaired hand function [2]. This may be partially mediated by impaired motor control [3] and changes in primary motor cortex excitability [4]. Previous studies have shown that other chronic pain conditions are associated with reduced motor cortex inhibition [5], which is also associated with motor learning [6]. Therefore, impaired motor control and learning in arthritic pain populations is potentially due to changes in motor cortex excitability. Supporting this, previous studies have shown that motor learning may be influenced by acute experimental pain. However, no previous study has sought to establish whether chronic arthritic pain may influence motor learning and if this relates to changes in motor cortex excitability.
**Objectives:** To provide a thorough analysis of corticomotor and intracortical excitability in people with painful hand arthritis, and to examine the relationship between these measures and performance on a motor skill learning task.
**Methods:** Twenty three people with arthritic hand pain and 20 pain-free controls participated in a cross-sectional study. Hand pain and function were assessed using the AUSCAN osteoarthritis hand index. Transcranial magnetic stimulation was used to measure corticomotor and intracortical excitability of a finger muscle. Motor skill learning was assessed using a 30 minute training task involving the index finger of the same hand.
**Results:** Compared with controls, participants with hand arthritis showed evidence of reduced intracortical inhibition and enhanced facilitation ($p<0.05$). However, overall corticomotor excitability was normal. Participants with arthritis were initially poorer at the motor skill task, but over the total training time performance was equivalent between groups. There were no associations found between measures of intracortical or corticomotor excitability and motor skill learning or hand function.
**Conclusions:** This study provides novel evidence that hand arthritis is associated with reduced intracortical inhibition similar to other chronic pain populations. However, no relationship was observed between these cortical alterations and impaired function or skill learning.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.2216

FRI0647-HPR **PHYSICAL ACTIVITY AND AEROBIC CAPACITY ASSESSMENT - A SURVEY AMONG PATIENTS WITH RHEUMATIC DISEASE IN SWEDEN, IRELAND, AND DENMARK**

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**Background:** Despite its positive effects on health outcomes, insufficient levels of physical activity (PA) have been found in the arthritis population. In addition, lower aerobic capacity adds to the patient's risk for cardiovascular disease. Increasing PA is thus important for this group and the use of objective and self-reported measures of PA should be encouraged as self-monitoring and evaluation of PA support promotion of healthy PA behaviours.
**Objectives:** To investigate the familiarity with objective and self-reported PA and aerobic capacity assessments and to identify barriers for their implementation in patients with rheumatic disease in Sweden, Ireland and Denmark.
**Methods:** Patients with rheumatic disease were invited through each country's patient organisations to participate in a cross-sectional, observational study using online survey methodology.
**Results:** A total of 791 patients (87% female) responded (579 Danish, 90 Irish and 122 Swedish) with Rheumatoid Arthritis (42%), Ankylosing Spondylitis (14%), Psoriatic Arthritis (25%) as main diagnoses. 99% of the patients reported pain during the past week in hand (62%), leg (60%), arm (58%), foot (51%), back (49%) and/or neck (36%). A total of 25% reported large limitations in moderate daily activities and 24% in climbing stairs. Use of biological disease modifying anti rheumatic drugs (Bio-DMARDS) was reported by 28% and non-biological DMARDS by 47%. Two thirds found it important to measure PA and approximately half stated they do not receive information regarding the same. Moderate levels of familiarity with simple body-worn sensor (mean 5.47/10; SD 4.04) to measure PA was found. Familiarity was lower with paper questionnaires (4.09/10; SD 3.69), complex body-worn sensors (3.70/10; SD 3.87), digital diaries (3.07/10; SD 3.53), paper diaries (3.45/10; SD 3.64) and digital questionnaires (3.46/10; SD 3.67) to measure PA. There was no statistically significant association between diagnosis, physical limitation or localisation of pain in relation to the familiarity of the above measures of PA ($p>0.05$), however, patients on Bio-DMARDS were more familiar with simple ($p=0.016$) and complex sensors ($p=0.003$), digital questionnaires ($p=0.009$) and diaries ($p=0.006$). 34% reported that their aerobic capacity had been tested whilst 57% reported no testing. Barriers for patients with rheumatic disease for measuring PA were reported by 43% and access to device (25%), uncertainty of handling the results (14–17%) and cost of device (10%) were most common.
**Conclusions:** Although most patients with rheumatic diseases in our sample perceived measures of PA as important, familiarity and information of their use was largely lacking. Also, aerobic capacity assessment occurred infrequently. To motivate behavioural change towards a more physically active lifestyle and to support individuals' independence of health care, health professionals should facilitate awareness and knowledge of PA measures, encourage their patients to regularly self-monitor PA and more often offer PA and aerobic capacity testing to their patients.
**Disclosure of Interest:** None declared
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FRI0648-HPR **GOAL SETTING IN REHABILITATION; A SYSTEMATIC SYNTHESIS OF CLINICAL PRACTICE DESCRIBED IN RANDOMIZED CONTROLLED TRIALS**

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**Background:** Person-centred goal setting and shared decision-making are emphasised as essential parts of effective team work and good clinical practice in rehabilitation.
**Objectives:** To explore the practice of collaborative goal setting in rehabilitation for adults with rheumatic and musculoskeletal diseases (RMDs), as described in published randomized controlled trials (RCTs).
**Methods:** A comprehensive, systematic literature search was undertaken to identify RCTs evaluating the effect of rehabilitation involving health professionals from at least two disciplines. We included trials from the period 1997–2012. Participants in the trials had a RMD with duration of more than three months.
Following a deductive approach, four categories and nine keywords were developed from existing theory (1) and prior research about goal setting. The categories were i) goal negotiation, ii) specific goal setting, iii) goal-directed planning, iv) goal evaluation. Keywords were goal, aim, expect, need, tailor, objective, target, plan and outcome. The categories and keywords were used to identify text units in the articles, which were analyzed using a directive and summative content analysis.
**Results:** 21 RCTs were included, of which 12 included participants with chronic low back pain and 9 included participants with inflammatory arthropathies, connective tissue diseases or fibromyalgia. The intervention was inpatient or outpatient rehabilitation, and involved group and/or individual sessions. The multidisciplinary teams consisted of 3 to 7 professions. A total of 430 text units were identified, of which 18 (4%) contained descriptions of patients as active participants in the goal setting process. These units came from 8 papers. Goal negotiation was described in 7 of these 8 papers, and specific goal setting in all 8 papers. Goal-directed planning was described in 6 papers, and patient-centred goal evaluation in 3 papers. No papers described a specific instrument or a formal method of goal setting. The remaining text units (96%) did not describe any collaboration in the goal setting process between patients and health professionals. However, content related to predefined treatment goals was identified in 19 papers. These treatment goals were set by health professionals without patient involvement.
**Conclusions:** In articles reporting results from RCTs examining the effect of rehabilitation, the occurrence of patients as active participants in collaborative goal setting in general was low, and lower than the occurrence of predefined treatment goals set by health professionals alone. The results indicate that there is a gap between the emphasis on goal setting in rehabilitation theory and its implementation in clinical practice and research.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.3509

FRI0649-HPR **INNOVATION IN HEALTH CARE – LABORATORY VALIDITY AND RELIABILITY OF A NEW SENSOR DEVELOPED TO MEASURE CERVICAL ROTATION**

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**Background:** For patients with axial spondyloarthritis (axSpA) it is recommended to monitor spinal mobility regularly. Cervical rotation (CR) is usually measured with goniometer or myrinometer, but might give imprecise results. Technological innovation provides opportunities to develop and improve measurement methods for use in clinical practice.
**Objectives:** To evaluate validity and reliability of a sensor developed to measure rotation around the vertical axis in a laboratory setting.
**Methods:** A sensor was developed by engineers in close collaboration with health professionals and patients with axSpA. It was tested in a laboratory setting and the data collected was compared with Cybex 6000 simulation data as gold standard. The sensor was mounted to the cybex with a bracket in six different positions, 1) straight up 2) straight down 3) up, tilted 30°around the frontal axis 4) down, tilted 30°around the frontal axis 5) up, tilted 30°around the frontal axis, 20° around the sagittal axis 6) down, tilted 30°around the frontal axis, 20° around the sagittal axis. Reference angles were set at approximately 10, 30, 60, 90 and 120 degrees. From a centre position the sensor was moved from left to right (one cycle) by manual force at the speed allowed (60°/second) until stop brackets were reached.
Criterion validity and reliability for single measures and for the mean of three trials (left, right or cycle) was evaluated with two ways mixed interclass correlation coefficient$_{agreement}$ (ICC). Limits of agreement (LoA) (Bland and Altman method), and smallest detectable change$_{agreement}$ (SDC$_{95\%}$) with 95%CI were calculated to evaluate the measurement error of the sensor.
**Results:** A total number of 261 cycles were performed. The ICC values were excellent for all measurement (ICC: 1.0; 95% CI 1.0, 1.0). One cycle of movement showed lower measure error (LoA) compared to single measures (left or right) (table 1). The measurement error was further improved by using the mean of 3 cycles (figure 1). The SDC$_{95}$ was 0.87 for one cycle and 0.80 for the mean of three cycles.

Table 1. Results from the reliability evaluation of a new sensor

| | | Mean diff (SD) | LoA | SDC$_{95\%}$ |
|---|---|---|---|---|
| Single | Left, ° | –0.06 (0.93) | –1.88–1.76 | 1.82 |
| | Right, ° | 0.28 (1.35) | –2.36–2.93 | 2.65 |
| | Cycle, ° | 0.11 (0.44) | –0.78–0.98 | 0.87 |
| Mean of three | Left, ° | –0.02 (0.82) | –1.59–1.61 | 1.61 |
| | Right, ° | 0.30 (1.25) | –2.15–2.75 | 2.44 |
| | Cycle, ° | 0.14 (0.40) | –0.65–0.93 | 0.80 |

**Conclusions:** The sensor showed excellent criterion validity and reliability for rotation around the vertical axis in the range of motion from 10 to 120 degrees, especially for cycles and mean of 3 cycles. When assessing a single cycle or the average of three cycles, a change of 1 degree is needed for real change beyond

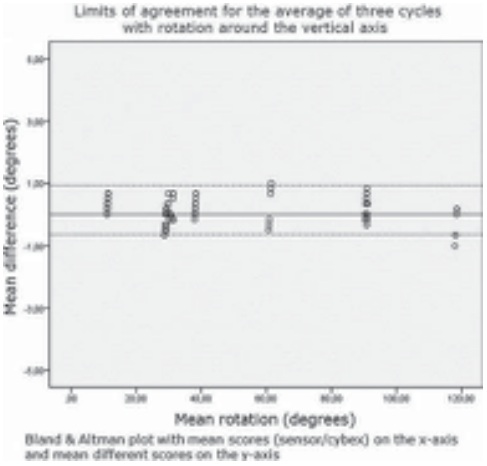



Figure 1

measurement error. Our findings justify proceeding with further evaluations of the sensor in patients with axSpA.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4002

## FRI0650-HPR COMPARISON OF THE EFFECTIVENESS OF FUNCTIONAL AND NIGHT SPLINT FOR RHIZARTHROSIS: A CONTROLLED, RANDOMIZED, BLINDED CLINICAL TRIAL

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**Background:** Rhizarthrosis is an inflammatory degenerative joint disease affecting the trapeziometacarpal joint of the thumb that impairs lateral pinching and movements of opposition and retroposition. The main symptom is pain, leading to difficulty with hand functions and reduced quality of life. Immobilization of the trapeziometacarpal joint of the thumb by splint has proved effective in reducing pain and improving hand function in patients suffering from the condition. Two randomized controlled trials found in the literature reported similar findings in terms of pain reduction and improved hand function with the use of a short orthosis for rhizarthrosis; one of the trials showed the benefits when the device was used for daytime function while the other showed the benefits when the orthosis was used during nighttime rest.
**Objectives:** To compare the effectiveness of functional (daytime) and night splint (Figure 1) in reducing pain and improving functionality in patients with rhizarthrosis.

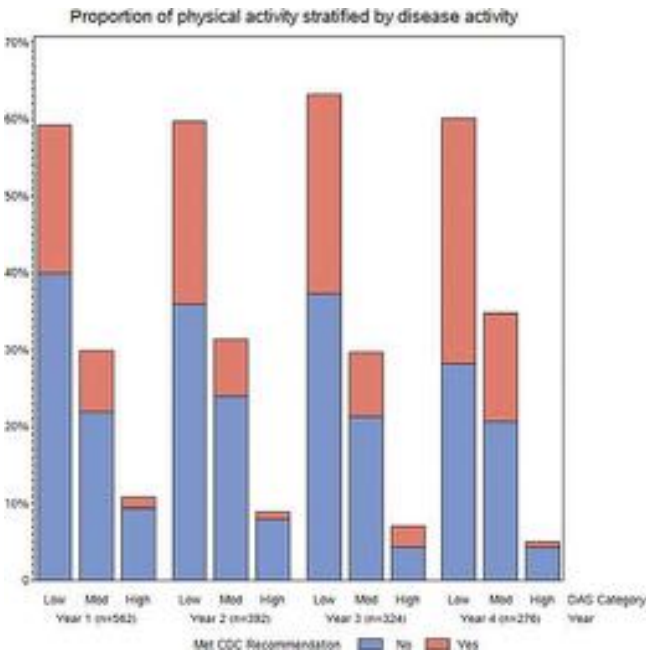



**Methods:** A controlled, randomized, blinded clinical trial with sixty patients diagnosed with rhizarthrosis. The patients were assessed by a blinded assessor at the beginning of the treatment and after 45, 90 and 180 days the following variables were evaluated: pain at the base of the thumb using a a numerical pain scale; thumb range of motion measured using a goniometer; grip strength evaluated by a hydraulic hand dynamometer; pinch strength using the pinch gage; hand dexterity evaluated with the pick-up test; function evaluated by the Brazilian version of the AUSCAN LK 3.01 Hand Osteoarthritis Index, the Cochin Hand Function Scale, the Michigan Hand Outcomes Questionnaire and a Likert-type scale. The Hand Outcomes Questionnaire, Cochin Scale and Michigan Questionnaire were used to assess hand function and patient satisfaction using a Likert scale.
**Results:** Most of the variables analyzed, including patient characteristics such as age, gender, disease duration and hand dominance, were homogeneous at the beginning of the study. In both groups there was a reduction in hand pain with time (intragroup analysis). Pain in the functional group, expressed as mean ± standard deviation, was 6.82±1.72 and 4.77±2.45 at the beginning and end of the treatment, respectively, and the corresponding figures for the nighttime group were 7.20±1.63 and 4.83±2.68. The p values for both groups were $p<0.001$. There were no statistically significant differences in the majority of the parameters assessed between the groups. The only domains with a statistically significant difference ($p<0.001$) between the two groups were: *activities of daily living* in the AUSCAN questionnaire and *satisfaction* in the Michigan questionnaire, for both of which the functional group had better scores
**Conclusions:** There was no statistically significant difference between functional and night splint in terms of pain, function or any of the other parameters assessed in rhizarthrosis patients.
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[2] Rannou F, Dimet J, Boutron I, et al. Splint for Base-of-Thumb Osteoarthritis. A randomized trial. Annals of Internal Medicine 2009;150(10):661–9;
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4293

## FRI0651-HPR THREE YEAR TRENDS IN PHYSICAL ACTIVITY IN ADULTS WITH RHEUMATOID ARTHRITIS

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**Background:** Adults with Rheumatoid Arthritis (RA) demonstrate low physical activity (PA) levels and excess cardiovascular risk. Most PA studies in RA are cross-sectional and PA interventions are often part of self-management programs of short-term duration ($\leq$1 year). Longitudinal examination of PA in RA may inform PA intervention design.
**Objectives:** To identify trends in PA in adults with RA over 3 years and to longitudinally characterize correlates of PA.
**Methods:** This 3-yr study included 573 RA registry patients with $\geq$1 annual visit and complete PA data. Baseline and annual measures were: demographics, medical history/meds, alcohol use, psychosocial support, self-efficacy, disease activity, quality of life, patient/physician global assessment, function, and PA defined as either meeting or not meeting the US Dept Health & Human Services (DHHS) recommendations of 150 min of moderate activity/wk or 90 min vigorous PA/week, at each interval. McNemar $\chi^2$ tests assessed the relationship between disease activity (DAS-CRP3 categories) and PA. A mixed model repeated measures analysis identified factors associated with PA, adjusting for disease activity over time.
**Results:** 94% of adults were Caucasian, 83% female with a mean age of 61 yrs (SD=12). Average RA duration was 19.5 yrs (SD=11.8). At baseline, 59.2% had low disease activity, 29.9% moderate and 10.9% highly active disease. 36% of subjects were sedentary and 29% met the PA recommendations. Over 3 years, PA was significantly negatively associated with disease activity ($\chi^2$, $p<0.001$). Factors associated with meeting PA recommendations, after adjusting for disease activity, were being Caucasian (OR=2.86; 95%CI 1.26–6.48), married/living with partner (OR=1.43; 95% CI 1.03,1.98), and alcohol use (OR=1.33; 95%CI 1.04,1.71). Older age (>53–62 OR=0.62; 95%CI 0.40,0.94; age >62–69 OR=0.64; 95%CI



0.42,0.96; age >69 OR=0.53; 95%CI 0.33,0.83) poor mental health (OR =0.58; 95%CI 0.38,0.87) and higher patient global assessment scores [10–20] OR=0.59; 95%CI 0.41,0.85; [>20–50] OR=0.61; 95%CI 0.39,0.96; [>50] OR=0.51; 95%CI 0.29,0.89) were associated with not meeting the PA threshold.

**Conclusions:** A small proportion of adults with RA met PA recommendations, despite well-controlled disease, and the proportion decreased over time. After controlling for disease activity, modifiable correlates of PA were linked to lifestyle, mental health and patient perceptions of disease, suggesting PA interventions target patient perspectives and lifestyles.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4358

## FRI0652-HPR SPINAL MOBILITY IN LONG STANDING ANKYLOSING SPONDYLITIS. APPLICATION OF NEWLY DEVELOPED REFERENCE INTERVALS ON CLINICAL DATA

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**Background:** A hallmark of ankylosing spondylitis (AS) is the progressive decline of spinal mobility. Recently published reference intervals (RI) for spinal mobility measurements in healthy individuals offer new possibilities to assess impairment during the course of the AS disease (1).

**Objectives:** To evaluate the development of subnormal spinal mobility among patients with AS with regards to disease duration.

**Methods:** The cohort comprised all patients born 1937 or later with a validated (modified NY criteria) AS diagnosis 1980–2015 at the Rheumatology department in Västerbotten, whom had one or more registered spinal mobility measurement (n=232). The first subnormal value (lower than the 2.5th percentile of healthy individuals) regarding 10 cm Schober test, lateral spinal flexion, chest expansion, and cervical rotation, respectively, using the age-, sex- and length specific reference intervals, was defined as outcome. The follow-up started at the first measurement and ended at the date of the outcome, the study end (June 30, 2015), death or the time point for the last visit + 2 years. The results were presented by Kaplan-Meier curves.

**Results:** The median (range) of the total disease duration during follow-up was 31 (5–61) years. 3706 examinations were evaluated, with a median of 24 examinations/patient, or median (range) 1.0 (0.1–2.8) examinations/year of follow-up. The proportion of patients with subnormal mobility increased by disease duration for all measurements. Lumbar mobility was most impaired, but after 15–20 years half of the patients still had mobility measurements within the normal range (Figure 1).

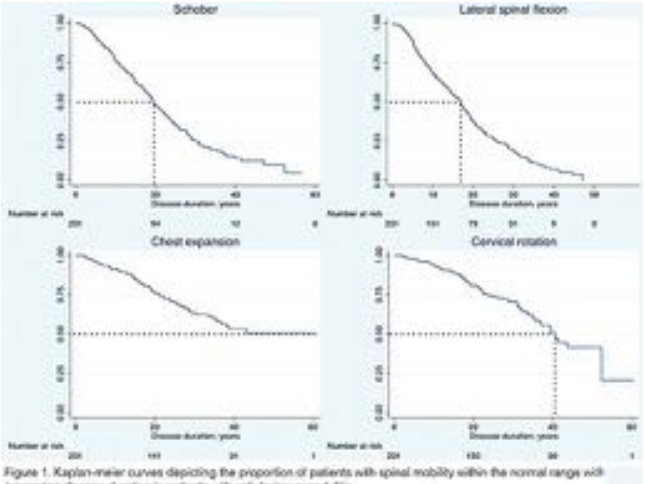



Figure 1. Kaplan-Meier curves depicting the proportion of patients with spinal mobility within the normal range with increasing disease duration in patients with ankylosing spondylitis.

**Conclusions:** Preserved spinal mobility is common in long-standing AS. However, the results indicated a continuous progression of spinal stiffness also after 20 years of AS disease.

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**Disclosure of Interest:** B. Sundström: None declared, L. Ljung Paid instructor for: Educational activities for BMS, Pfizer. Abbvie, S. Wållberg-Jonsson: None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4390

# Nursing

## SAT0627-HPR EDUCATIONAL NEEDS OF FRENCH RHEUMATOLOGY NURSES ARE NOT LIMITED TO INFLAMMATORY ARTHRITIS MANAGEMENT. RESULTS OF THE MULTICENTRIC "CAIRE" SURVEY

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**Background:** EULAR recommendations aim to promote the role of the nurse in the management of inflammatory arthritis (IA) (1). A survey among French nurses in 2014–2015 showed a gap between educational needs and reported competences of French nurses regarding IA management (2).

**Objectives:** The objective was to investigate competencies in other rheumatic and musculoskeletal conditions (RMD), patient education and research compared with those found in IA.

**Methods:** The list of potentially useful competencies for RN was validated by a multidisciplinary group (2). The survey was conducted through 3 on-line quesitionnaires in Dec 2014-Jan 2015 (2) then in Jan-May 2015, including 78, 72, 70 items. For each item, the RN were asked on a 4 point likert scale if they believed they had acquired the competency and considered it of importance.

**Results:** All RMD were adressed: rheumatoid arthritis RA, spondyloarthritis SpA, connective tissue diseases (CTD), other RMD e.g osteoarthritis, osteoporosis, low back pain. The cross-functional skills were pain management, patient-nurse communication, patient education, research. Respectively 104, 71 et 64 RN responded the 3 on-line investigations, 92% female, 70% worked full time, 70% in a university hospital; 30–29% declared qualifications in patient education, 9–20% in pain management, 6–17% in research. Reported competencies were very good in DMARDS, analgesics and NSAIDs, good in patient-nurse communication and patient education. In other fields, educational needs are high, particularly for non-pharmacological treatments, CTD, osteoarthritis, low back pain and research (table). Practical skills were less than cognitive skills.

| Competencies | "Very much or rather acquired" competencies % | | Competencies rated "rather important or essential"(%) | |
|---|---|---|---|---|
| | Cognitive | Know how | Cognitive | Know how |
| RA-SpA | 56 [8–94]* | 44 [6–94] | 96 [57–100]* | 91 [48–100] |
| – DMARDS | 79 [57–83] | 72 [50–76] | 100 [93–100] | 100 [86–100] |
| – Symptomatic treatments | 90 [87–94] | 87 [85–94] | 100 [100 – 100] | 100 [100–100] |
| – Non pharmacological treatments | 53 [28–64] | 41 [31–45] | 97 [9–98] | 95 [89–100] |
| – Co morbidités | 43 [36–50] | 37 [31–43] | 98 [98 – 98] | 91 [90–93] |
| CTD | 28 [21–40] | | 90 [86–98] | |
| Osteoporosis | 54 [19–83] | 27 [6–68] | 97 [67–99] | 90 [68–99] |
| Low back pain | 30 [3–72] | 19 [3–54] | 87 [65–96] | 84 [62–95] |
| Osteoarthritis | 31 [5–47] | 18 [3–47] | 87 [62–97] | 86 [58–99] |
| Pain management | 63 [25–81] | 39 [17–87] | 98 [75–100] | 98 [72–100] |
| Patient-nurse communication | 64 [29–84] | 54 [7–80] | 98 [90–100] | 98 [77–100] |
| Patient education | 63 [25–78] | 55 [32–68] | 96 [85–99] | 95 [85–99] |
| Research | 28 [10–35] | 26 [9–35] | 69 [52–82] | 66 [35–82] |

*Median, extreme values.

**Conclusions:** This multicentric survey provides accurate information on French RN educational needs. They are greater in the management of RMD other than RA and SpA. These results should be considered in elaborating a curriculum to improve RN competencies.

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**Acknowledgement:** Members of the committee for the French Rheumatology Nurse educational course

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2016-eular.4901

SAT0628-HPR **CARDIOVASCULAR RISK ASSESSMENT IN INFLAMMATORY ARTHRITIS PATIENTS IN A NURSE-LED CLINIC AND SUPPORTED BY ULTRASONOGRAPHY**

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**Background:** There is a wide range of evidence of increased risk of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) and other forms of inflammatory arthritis. Although people wiht RA have an increased number of the traditional risk factors for the development of CVD, it seems the presentation of a chronic inflammatory state is pivotal because of the accelerate atherogenesis as a result of endotelial dysfunction, leading to increased thickness and plaque formation in carotid arteries. EULAR recommendations for CV risk advised to assess CV risk in all patients with RA, and the patient's risk should be scored according to the SCORE system. Nurse-led care is a model of care, where nurses manage their own patient caseload, monitor patients' sign and symptoms, provide education and refer appropriately.
**Objectives:** The aim of this study was to assess CVD risk in patients with RA and other inflammatory arthritis, in a nurse-led clinic and, supported by a carotid ultrasonography (US).
**Methods:** Patients with inflammatory arthritis (RA, PsA, SpA, SLE) attends a nurse-led clinic for diseases activity measurement and based in a self-efficacy framework, lifestyle change support and, CV risk assessment. Those patients with smoking habits, blood pressure above the recommended level and total colesterol above 250 mg/dl were follow up closer with the nurse based in a motivational interview, treatment were prescribed by the rheumatologist and written leaflets concerning smoking cessation, low-lipid diet were offered. The CV assessment included: age, gender, blood pressure, glucose, triglycerides, total cholesterol, HDL, LDL cholesterol, smoking habits, height, weight and BMI were measured. Presence and type of diabetes were asked. Patient's risk SCORE was calculated. The risk SCORE was multiplied by 1.5 if the patient met certain criteria associated with higher CV risk. No multiplication was proposed for other arthritides. In those patients with intermediate risk SCORE (1–4%) a carotid ultrasonography was performed by a rheumatologist.
**Results:** 68 patients with inflammatory arthritis had an intermediate risk SCORE. 51 were RA, 13 SpA, 1 PsA, 3 SLE. Mean age: 60 years. 59% were women. Mean modified risk SCORE: 2,6%. Prior to performing US, 68 patients had intermediate risk SCORE. Media right IMT:0,77 mm, plaque was found in 19 patients (28%); media left IMT:0,82 and plaque was found in 27 patients (40%) Only 41% of our patients remained with intermediate riks SCORE after US. 43% patients had a very high risk SCORE after US and, 13% a high risk SCORE. Overall, a total of 48 patients (59%) had their CV risk upgraded after nurse and US assessment
**Conclusions:** Adding carotid US to nurse assessment in CVD risk stratification in patient wiht inflammatory arthritis and intermediate risk SCORE increases performance, being thus, a helpful technique for a CV tight control.
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**Disclosure of Interest:** None declared
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SAT0629-HPR **RAPID ACCESS TRIAGE CLINIC: A NURSING SERVICE THAT SHORTENS RHEUMATOLOGY CLINIC WAITING TIME AND FACILITATES EARLY TREATMENT**

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**Background:** The waiting time for newly referred patients to the rheumatology clinic is approximately 24 months. The Rheumatology Nurse Rapid Access Triage Clinic aims to shorten the waiting time of patients suspected to have rheumatoid arthritis (RA). It is hoped that patients with active RA can be fast-tracked to commence earlier treatment for better disease control.
**Objectives:** To validate if Rheumatology Nurses (RhN) can screen out patients with active RA for earlier treatment and to evaluate the level of agreement in RA diagnosis between RhN and rheumatologists.
**Methods:** Newly referred patients suspected to have RA were assessed by RhN from March 2012 to September 2015. Based on a protocol modelled upon the 2010 European League Against Rheumatism (EULAR)/American College of Rheumatologists (ACR) criteria for the classification of RA, RhN performed history taking, physical examination of joints, and ordered relevant blood and X-ray investigations. RhN then reviewed all results to discriminate between RA and non-RA. Paired t-tests and logistic regression were used to compare variables between RA and non-RA patients diagnosed by RhN. Correlation coefficient (CC) was used to compare the level of agreement between RhN's and rheumatologists' assessment.
**Results:** RhN assessed 102 patients (mean age =53.46 ± 12.59 years, 84.3% women). The group diagnosed to have RA by RhN had shortened waiting time for the rheumatology clinic when compared to the non-RA group. (11.5 vs 3.6 months; $p<0.001$) Agreement between RhN diagnosed RA and rheumatologist diagnosed RA was excellent (CC 90%; $P<0.001$). Comparing with the non-RA group, RhN diagnosed RA group also had greater chance of receiving disease modifying anti-rheumatic drugs (DMARDs) early (OR 43.08, $p<0.001$). The mean duration between onset of joint symptom and DMARDs commencement was 8.26 ± 11.52 months ranging from 3 to 52 months.
**Conclusions:** The Rheumatology Nurse Rapid Access Triage Clinic provides accurate diagnosis and shortens RA patient's waiting time. It also helps to screen out active patients to receive earlier treatment.
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**Disclosure of Interest:** None declared
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SAT0630-HPR **VARIABLES PREDICTIVE OF THE SLEEP DISORDERS IN PATIENTS WITH PSORIATIC ARTHRITIS AND SPONDYLARTHRITIS**

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**Background:** Since insomnia is a chronic problem in patients with chronic diseases, factors that are associated with it are varied.
**Objectives:** To study the variables associated with the severity of insomnia according to the questionnaire of Oviedo's dream (QOD) in patients with spondylarthritis (AE) and psoriatic arthritis (PsA), including the activity of the disease as measured by restriction, BASDAI and DAS28.
**Methods:** Design. Descriptive cross-sectional study. Patients: Were selected by sampling consecutive patients with AE or PsA in follow-up by our unit of biologic therapy. Inclusion criteria: adults ($\geq$16 years old) with AE (ASAS criteria) or PsA (CASPAR criteria) capable of understanding and willing to make the questionnaires. Exclusion criteria: other rheumatic diseases, age $<$16 years old. Protocol: arriving at the inquiry, he was offered participate in study, explained to him and gave the patient the battery of questionnaires; your doctor performed the evaluation of activity of disease and registration of comorbidities and current medication. Main outcomes: the 3 dimensions of QOD: subjective (1) satisfaction with sleep, insomnia (2) and (3) Hypersomnia. The QOD is a semi-structured interview help diagnose insomnia and Hypersomnia according to the diagnostic criteria of CIE-10 and DSM-IV. Other variables: current medication for the AE or PsA, comorbidities, medication use for sleep and/or CPAP according to QOD, disease activity questionnaire: AE (BASDAI) and PsA (DAS28), quality of life related to health (HRQOL) by means of EQ-5 d and SF-36, perception of pain (questionnaire Brief Pain Inventory BPI), AE (BASFI, BASDAI) and PsA (DAS28, HAQ) and fatigue by FACIT. Statistical analysis: descriptive and analysis of normality. Bivariate Chi-square, T-Student, Mann-Whitney or correlations, as appropriate. Multiple="Multiple" linear regression to 3 dependent variables (subjective satisfaction with sleep, insomnia and hypersomnia).
**Results:** 120 patients participated: 60 patients with ad (36.7% women, 45, 1±10, 6 years) and 60 patients with APs (58.6% women, 49, 9±9, 2 years). The most common comorbidities were: anxiety, depression, and disc disease. Women had more multimorbidity (p=0, 047) and osteoporosis ($p<0$, 001) than men. We found no correlation between disease activity and results in QOS. Also found correlation of variables COS with an HRQOL in SF-36 with EQ-5D, or physical function. There were no differences in treatment with biological and/or DMARs. Multiple linear regression analysis showed an inverse association between subjective satisfaction with sleep and the results of the FACIT and the middle pain. Insomnia showed an association with FACIT and interference of pain with daily life. And finally, hypersomnia partnered with FACIT and middle pain.
**Conclusions:** The insomnia and hypersomnia are 2 health problems strongly linked to pain and fatigue in patients with AE ans PsA but not with the activity of the disease. It would be necessary to work in nursing consultation the improvement in the management of sleep in these patients in a structured way to decrease the impact of insomnia and hypersomnia.
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SAT0631-HPR **CHRONIC DISEASE AND SELF-INJECTION: ETHNOGRAPHIC INVESTIGATIONS INTO THE PATIENT EXPERIENCE DURING TREATMENT**

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**Background:** Drug administration by self-injection is often an option to treat

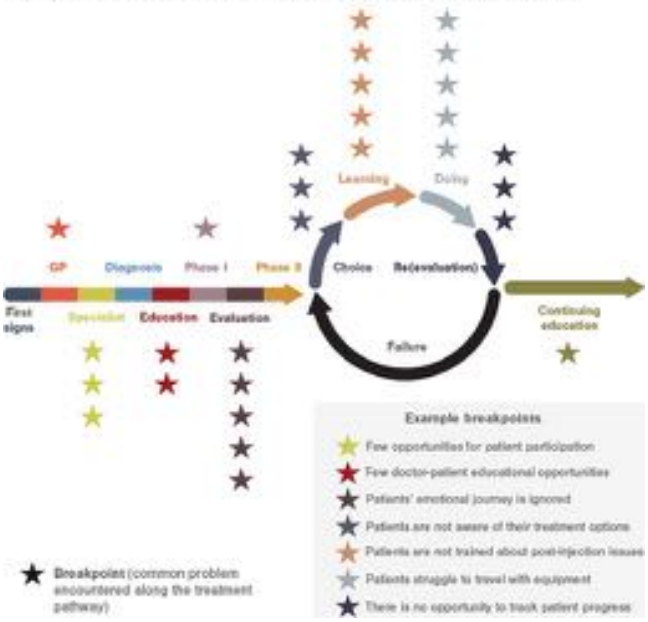
chronic diseases. This treatment option can be emotionally and physically demanding for patients (pts).[1]

**Objectives:** To use a holistic approach to identify common themes both along the treatment pathway (ie. from diagnosis and throughout treatment), and at the moment of self-injection that, if changed, have potential to improve pt experience and treatment outcomes.

**Methods:** Two ethnographic research projects were designed and conducted: Field Insights CODE (FI[CODE]) provided an overview of the treatment pathway and Injection Mission 2020 (IM2020) focused on the moment of self-injection. FI(CODE) consisted of individual and group interviews investigating the treatment process from a pt and healthcare professional (HCP) perspective. It used an open ethnographic approach (no set questions/discussion guides) to avoid restricting the feedback obtained. Interviews were conducted in San Francisco, Chicago, London and Manchester, with 10 HCPs and 58 pts (8 pts in-home and 50 pts over 12 focus groups). IM2020 consisted of a review of over 50 UCB Pharma injection device design internal information sources, and expert interviews aiming to understand how injection devices affect individuals. Interviews were conducted in San Francisco, London, Boston, Atlanta, New York, Toronto and Tokyo with 10 pts, 7 HCPs and 5 medical device design experts.

**Results:** FI(CODE) interviews identified common problems encountered along the treatment pathway that could increase treatment failure rates (Figure). Pts with more treatment options and greater disease understanding through education were less likely to struggle with the treatment process. Pt treatment choice was limited by the healthcare system (ie. institutional guidelines, reimbursement restrictions) and the method of device selection; specifically, pre-selection by doctors and nurses reduced the number of device options for the pt. By focusing closely on the moment of self-injection, IM2020 demonstrated that pts who developed an effective, personalized injection process had greater levels of success with self-injection. Five tightly linked components that influence the injection experience were identified: delivery process, emotional state, social perception, educational level and ritualized development. Pts who successfully mastered all 5 of these were more likely to succeed at self-injection.

**Figure:** Number of breakpoints identified at each step in the treatment pathway




**Conclusions:** By examining the pt treatment journey in a novel way, FI(CODE) and IM2020 identified common problems along the treatment pathway, advancing our understanding to help improve pt treatment experience. Small changes that improve pt education and increase choice at the start of the treatment process were identified as key to improving treatment success rates. Pt education should aim to help pts understand their disease and develop an optimum personalized self-injection process.

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## SAT0632-HPR THE EFFICACY OF BIOLOGICS ON HEALTH STATUS INCLUDING PSYCHOLOGICAL STATUS, SELF-EFFICACY AND PATIENT SATISFACTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Biologics are effective for improving disease activity in patients with rheumatoid arthritis (RA). We also reported the efficacy of biologicals on health status [1]. However, efficacy of biologics on psychological status, self-efficacy and patient satisfaction in RA patients is not well evaluated.

**Objectives:** We evaluated improvement of health status, psychological status, self-efficacy and patient satisfaction in patients with RA treated with biologics.

**Methods:** The patients with RA who were planning to be treated with the biologics (adalimumab (ADA), tocilizumab (TCZ) and abatacept (ABT)) were enrolled. Disease activity was evaluated using SJC, TJC, PGA and CDAI. Psychological status was examined using the Hospital Anxiety and Depression Scale-Depression (HADS-D) and Anxiety (HADS-A). Self-efficacy and health status including patient satisfaction were assessed using the General Self-Efficacy Scale (GSES) and the Arthritis Impact Measurement Scale 2 (AIMS-2), respectively. Comparison analysis was performed between the baseline and 24 weeks after biological therapy. To further investigate the items related to satisfaction, correlation analysis was performed between patient satisfaction and disease activity and health status including psychological status. Data analyses were performed utilizing Wilcoxon rank-sum test and Spearman correlation analysis.

**Results:** Twenty-six patients (male/female: 7/19) (ADA: 8, TCZ: 9, ABT: 9) were evaluated. Patients' characteristics were as follows: median (interquartile range) age of 57 (49.2 - 75.0) years and duration of 2.9 (0.8 - 5.5) years. SJC, TJC, PGA and CDAI showed statistically significant improvement at week 24 compared to the baseline ($p<0.0001$, for each of all items). In the components of AIMS-2, "physical", "symptom", "affect" and "role" improved significantly at week 24 compared to the baseline, while "social interaction" did not improve. Patient satisfaction and GSES also improved significantly at week 24 ($p<0.0001$, $p=0.0124$, respectively). As for psychological status, HADS-A and HADS-D improved significantly at week 24 compared to the baseline ($p=0.018$, $p=0.0143$, respectively).

Patient satisfaction showed statistically significant correlation with SJC ($r=0.686$, $p<0.0001$), TJC ($r=0.758$, $p<0.0001$), PGA ($r=0.586$, $p<0.0001$), HADS-A ($r=0.561$, $p<0.0001$) and HADS-D ($r=0.512$, $p=0.0001$). PGA and TJC were also correlated with HADS-A ($r=0.374$, $p=0.0062$, $r=0.325$, $p=0.018$, respectively) and HADS-D ($r=0.412$, $p=0.0024$, $r=0.392$, $p=0.0040$, respectively). Moreover, patient satisfaction was also statistically significantly correlated with "physical" ($r=0.804$, $p<0.0001$), "symptom" ($r=0.751$, $p<0.0001$), "affect" ($r=0.746$, $p<0.0001$) and "role" ($r=0.717$, $p<0.0001$), "social interaction" ($r=0.279$, $p=0.0476$) of AIMS-2.

**Conclusions:** Biologics were effective in improving psychological status, patient satisfaction and self-efficacy as well as disease activity and health status. For further improving patient satisfaction, psychological support and social assistance by health professionals' team in addition to appropriate treatment may be required.

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## SAT0633-HPR SOCIAL SUPPORT MAY BE IMPORTANT FOR IMPROVING PATIENT SATISFACTION AND HEALTH STATUS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS

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**Background:** The clinical benefits of biologics to patients with rheumatoid arthritis (RA) have been demonstrated in various clinical trials. However, patient satisfaction in patients treated with biologics is not well evaluated.

**Objectives:** We evaluated patient satisfaction and health status in patients with RA treated with biologics.

**Methods:** The patients with RA who were planning to be treated with IL-6 inhibitor (tocilizumab; TCZ) (IL-6 group) and TNF inhibitor (adalimumab: ADA, infliximab; IFX, etanercept; ETN) (TNF group) were enrolled. Disease activity was evaluated using swollen joint counts (SJC), tender joint counts (TJC) and patient global assessment (PGA), and Clinical Disease Activity Index (CDAI). Patient satisfaction was evaluated utilizing patient satisfaction scores of the Arthritis Impact Measurement Scale 2 (AIMS-2). Satisfaction was measured before and after 6-months of treatment with each of the biologics, and the results were compared. Statistical analysis was performed utilizing Wilcoxon rank-sum test and t-test.

**Results:** Patients with RA (n=85) were evaluated in this study. 48 patients were

treated with TCZ, and 47 patients were treated with anti-TNF agents (ADA: 17, IFX:17, ETN:13).Patients characteristics were as follows as follows: mean±SD of age (55.6±11.9 years old) and duration (7.29±8.83 years), male/female (16/79). Both at baseline and at 6 months after treatment, there was no statistically significant differences in SJC, TJC, PGA, EGA and CDAI between TCZ group and TNF group. All these evaluations showed statistically significant improvement after 6 months of treatment in each group.As for health status, all 5 components of AIMS-2 showed statistically significant improvement at 6 months compared to the baseline in TNF groups. In IL-6 group, "physical", "symptom", "affect" and "role" improved significantly at 6 months ($p<0.001$, for all items), while "social interaction" did not statistically improve compared to the baseline (p=0.114). Out of 12 satisfaction scores, all scores except "understanding and support for patients' problems by families or friends" (p=0.133) showed statistically significant improvement with 6 months of treatment in TNF group, while all 12 scores improved significantly at 6 months in IL-6 groups.

**Conclusions:** Patient satisfaction and health status except social interaction were improved by TNF inhibitor or IL-6 inhibitor. To solve the problems related to social function, understandings and social support for patients by health professionals may be required.

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## SAT0634-HPR TREAT TO TARGET ACCESS, CARE AND OUTCOME: A NURSE LED CARE INITIATIVE

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**Background:** Contributing factors to the acknowledged inefficient clinical pathway for patients with inflammatory arthritis (IA) in Ireland include the inadequate number of practicing rheumatologists and specialist nurses (0.7 per 100,000 and 0.5 per 135, 000 inhabitants, respectively). There is evidence that nurse led care (NLC) delivers quality care, improves access and delivers cost savings.

**Objectives:** To address lengthy waiting lists, inefficient use of physician time, reduced patient outcome, and deliver as standard care patient centred Treat to Target (T2T) in a cost neutral/cost effective manner through NLC.

**Methods:** The IRNF presented a business case to the Health Service Executive detailing how patient centred T2T could be realised nationally, through the implementation of 12 advanced nurse practitioner (ANP), and 29 clinical nurse specialist (CNS) posts, under the direction of consultant rheumatologists. Evidence to support this proposal as a cost neutral investment was compiled based on the secondary benefits of T2T, firstly as a NLC initiative and secondly, through improved medication optimisation/management.

**Results:** The non–inferiority of NLC versus rheumatologist led care, and superiority with respect to satisfaction and costs is proven. In Ireland an estimated 4,500 patients are diagnosed with IA annually, T2T requires each patient to have up to 6 reviews creating the demand for 27,000 out-patient reviews during year 1. NLC could provide the required access for 300–600 out-patient reviews per 100,000 head of population (≈13,500–27,000 per annum). Optimisation of methotrexate (MTX) dosing has demonstrated both efficacy and reduced requirements for more expensive treatments in specific patients. Through nurse led MTX optimisation 12 patients in 17 rheumatology departments saved from initiation of a biologic therapy (12 x 17 x €12,300) could provide €2.5 million savings annually. A potential national saving of €15 million through reduced biologic dosing in stable disease has already been demonstrated. Therefore, a 50% dose reduction of a biologic treatment in 10 patients could yield annual savings of €67,500 which exceeds the maximum ANP/CNS salary scale. This evidence demonstrates that the estimated required funds (€2.9 million) could be generated and a potential saving of €13m realised from the secondary benefits of T2T, namely a NLC initiative, and improved medication optimisation. A specially commissioned electronic patient record will ensure capture of agreed health care performance statistics to demonstrate the impact on improvements in service access and costs to the implementation, as well as on patient outcome, of these additional nursing posts.

**Conclusions:** This proposal demonstrates how this physician directed nurse led initiative to implement T2T can be realised in a cost neutral/cost effective manner. Estimated conservative and speculative benefits to the health service profit and loss account range from zero loss to circa €15 million savings, respectively. These savings will more than adequately fund the additional posts. Moreover, tighter disease management and control in early IA will lessen the requirement for more expensive treatments in the long term, and enhance patient outcome.

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## SAT0635-HPR EFFECTS AND COSTS OF A COMMUNITY-BASED SELF-MANAGEMENT SUPPORT PROGRAM FOR KOREAN MEDICAL AID BENEFICIARIES WITH OSTEOARTHRITIS: 12-MONTH FOLLOW-UP

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**Background:** Osteoarthritis (OA) is increasing in frequency and becoming a growing burden in terms of both illness and cost. Support for self-management may have a part to play in the effective disease management. However, the evidence for arthritis self-management support program is inconclusive, and economic evaluations in this field are relatively rare.

**Objectives:** The purpose of this study was to identify changes in over time and costs of a newly developed self-management support program for Korean medical aid beneficiaries with osteoarthritis

**Methods:** The research design was an open-label, randomized and controlled evaluation of a community-based self-management intervention. Medical aid beneficiaries with osteoarthritis were allocated to the intervention group (n=30) or the control group (n=30). The 8 week-intervention program which focused on patient-centered, tailored intervention was developed to support disease self-management. A trained case manager with cognitive-emotional-behavioral approaches and coaching strategy led the participants. Outcome measures included patient activation, joint flexibility, and health related quality of life. Data were collected at baseline, 8 weeks (post-intervention), 6 and 12-month follow-up using structured questionnaire, goniometer and tape. Data were analyzed using mixed-effects regression model. For economic evaluation, a cost-benefit analysis was done using the net benefit and benefit/cost ratio.

**Results:** As compared with the control group, the experimental group showed significantly greater improvement across the follow-ups on patient activation (Time x Group, $F=13.395$, $p<.0001$), joint flexibility, (Time x Group, Right Shoulder $F=7.550$, $p<.0001$; Left Shoulder $F=5.692$, $p=.001$; Right Knee $F=5.998$, $p=.0007$; Left Knee $F=3.395$, $p=.0195$) and health-related quality of life (Time x Group, $F=6.381$, $p=.0004$). The experimental group had large initial improvements in patient activation, joint flexibility, and health–related quality of life. These improvements declined over time, but still were better than at baseline except for joint flexibility. The result of cost-benefit analysis was found that the total cost was 72,096 Korean won per person and the net benefit was 167,904 Korean won per person, so the ratio of benefit versus cost was 2.33.

**Conclusions:** Findings indicate that this 8-week community-based self-management support program is effective for patient activation, joint flexibility and health-related quality and an efficient model of nursing care reducing healthcare costs for medical aid beneficiaries with osteoarthritis. This study has the potential to be a sustainable model for practice in the community.

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## SAT0636-HPR STARTING CARE AT THE PEEP OF RHEUMATOID ARTHRITIS- A PATIENT EDUCATION AND EMPOWERMENT PROGRAM

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**Background:** Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease which impacting on physical, psychosocial and economic aspects. Poor disease control will cause flare up and remission periodically and increase the risk of deformity. Various studies indicating that patient education on disease knowledge, treatment plan and self-management skill are all contributing factors for disease control and successful coping with long-term condition. However, barriers such as knowledge deficit on disease and related treatments are common in general public, a patient education and empowerment program (PEEP) was then designed and conducted for newly diagnosed RA patients in a regional hospital of Hong Kong.

**Objectives:** To evaluate the effectiveness of PEEP on improving disease control; patient's functional ability and self-management knowledge for newly diagnosed RA patients.

**Methods:** This was a retrospective and observational study, the data retrieved from January 2014 to December 2015. Patients with newly diagnosed RA were recruited into a health education and patient empowerment program (PEEP)

conducted by specialist nurse in rheumatology. The program included one-to-one interview in nurse-led clinic and telephone advice line (TAL) support. A health education checklist was designed to standardize the health education content and ensure essential information was delivered to participants. A disease knowledge assessment form to assess disease knowledge, medication management and self-management skill was designed to measure patient's understanding; and health assessment questionnaire (HAQ) was used to assess patient's functional ability and health outcome. Patient's knowledge score accompanied with disease activity score (DAS 28) and HAQ score were collected before and after the PEEP.
**Results:** Until the end of year 2015, totally 73 patients have been recruited into the program. 51 patients attended the program once and 22 patients attended twice. Age of participants between 17 and 79, majority (82.2%) was female. Mean knowledge assessment score was increased from 22.6% to 72% after PEEP, reflecting an average increase of 49.4% in the knowledge of disease, treatment and self-management skill. Mean DAS 28 score before PEEP was 4.44 (2.05 to 7.27) while post PEEP was 3.61 (1.55 to 7.0) which indicated improvement on arthritis control (mean difference -0.83; $P<0.0001$). Mean HAQ score of pre and post PEEP were 0.84 and 0.59 respectively indicated an improved functional and health outcome. During the study period, TAL support was sought for 41 times, in which 19 episodes were related to drug problems and 10 episodes were related to disease flare up.
**Conclusions:** Health education is an effective way to increase patient's disease knowledge, improve medication management and enhance self-management skill; which also contribute to better disease control and better functional ability. A structured and comprehensive patient education and self-management program should be promoted for all newly diagnosed RA patients.
**Disclosure of Interest:** None declared
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## Miscellaneous forms of clinical care

### SAT0637-HPR BIOSIMILARS: THE PERCEPTION AMONGST MALTESE CLINICIANS

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**Background:** The concept of biosimilar presents a myriad of issues such as patient safety, efficacy and financial aspects to clinicians, pharmacists and policy makers. The introduction of biosimilar infliximab, the first biosimilar on the local national health system in Malta, put clinicians at the forefront of these challenges.
**Objectives:** The objective of the study was to assess the perception and awareness of Maltese clinicians working within the National Health System on the concept of biosimilars.
**Methods:** The questionnaire developed by the Alliance for Safe Biologics Medicines and which was previously run in 5 European countries was shortlisted to be used in the study[1]. Permission from the Alliance for Safe Biologics Medicines was sought to use the questionnaire. The questionnaire was sent online to prescribing clinicians working within the Maltese National Health System. The clinicians were given one month to answer the questionnaire during which time three reminders were forwarded.
**Results:** A total of 132 prescribers participated in the study giving a 14% response rate. Approximately 34% prescribed biologics within their practice whereas 40% treated patients prescribed biologics by another specialist. Out of the total respondents 6% consider themselves very familiar with the concept of biosimilars, 35% had a basic understanding of biosimilars whereas 59% could not define biosimilars or had never heard of them. Less than half of the respondents (36%) believe that patients can safely receive either originator or biosimilar and expect the same result. Only 27% agree that patients can safely be switched between products during the course of treatment and 46% state that is is very important or critical for them to have the sole authority to decide whether to prescribed the biosimilar or originator. Around 27% answered that they prescribe by generic name irrespective of whether the drug is a biologic or not.
**Conclusions:** The awareness (6%) on biosimilars in Malta is much less than that achieved in 5 European countries where an average of 22% of prescribers considered themselves very familiar with the concept of biosimilars[1]. Although prescribing of biologic medicines is regulated by Subsidiary Legislation 458.59 "Prescribing and Dispensing requirement rules", Maltese prescribers are unaware that biosimilars should be prescribed by brand name. Switchability is an aspect where Maltese clinicians are not comfortable since only 27% believe that patients can be safely switched between products during treatment. This however correlates to results of the ASBM European survey where only 39% agree with switchability. Increased awareness on biosimilars together with more robust data on switchability will help Maltese clinicians adopt biosimilars in their practice without having concerns on patient safety and efficacy.
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## Psychology/Social sciences

### SAT0638-HPR DELAYS IN DIAGNOSING OF PATIENTS WITH RHEUMATIC DISEASES IN POLAND

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**Background:** According to the recommendations of EULAR 2007, every patient with persistent swelling of at least one joint should be referred to a rheumatologist and examined within 6 weeks from the onset of the first symptoms. Time from first symptoms to start of treatment on rheumatoid arthritis (RA) is only 12 weeks. Results of unique research conducted in Poland showed that diagnostic delay in RA is 35 weeks and it is one of the biggest in Europe. Early diagnosis has positive impact for effectiveness of treatment, cost economization and patient well-being.
**Objectives:** The aim of the study was to determine the time passed since the onset of the first symptoms of rheumatic disease to the first visit the doctor. Additional objective of the study was to identify factors of the delay and of speeding up the diagnostic process.
**Methods:** An anonymous questionnaire survey was carried out in the period from June 2014 to June of 2015 among patients treated in 6 rheumatological centers in different regions of Poland. The questionnaire consisted of 18 closed questions concerning: first symptoms of disease and actions taken by patient, absence in workplace/school, factors influencing patient's decision, path of patient from first contact with general practitioner (GP) to rheumatologist, diagnosed diseases and taking care of him/her own health. During the study 239 completed questionnaires were collected.
**Results:** The first symptoms connected with rheumatic disease before contact with physician declared by respondents were: pain of the joints (86%), morning stiffness (71%), swelling of the joints (70%) and tiredness (69%). The greatest impact on searching help with the doctor were: worsening of symptoms (86%), difficulties in everyday activities (83%), talks with relatives (65%) and a fear that there are symptoms of severe disease (64%). The most important causes of delay of contact with physician were: limited access to physician (68%), belief that symptoms will pass spontaneously (56%) and lack of time to visit a doctor (45%). Only 17% of patients visit a doctor up to 7 days from first onset of rheumatic diseases (from 7 to 30 days - 32%; during 2–3 months - 23%; later than 3 month from first symptoms 28%). Before first visit to rheumatologist 97% of patients were treated by general practitioner (GP), 56% by orthopaedist, 41% - by neurologist.
**Conclusions:** Patient's behaviour and the functioning of the health care system has an impact on delay of diagnosis of rheumatic diseases in Poland. One of the main problem identified by the study is GPs and other specialists low awareness of proper handling of a patient with early arthritis. As a result, the patient is treated in an inefficient way and referral to a rheumatologist as the disease is in the advanced stage.
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## Nursing

### SAT0639-HPR THE MOST FREQUENT INQUIRIES OF PATIENTS ON SUBCUTANEOUS ANTI -TNF ALPHA THERAPIES

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**Background:** Subcutaneous TNFα blockers enable patients with inflammatory arthritis to better control their disease and subsequently improve the quality of their daily functioning. At our Department of Rheumatology trained nurses provide education about proper subcutaneous (s.c.) administration techniques and telephone counseling about different issues asked by patients concerning their treatment. One of the key components of patient education and counseling is to explain when to postpone the biologic therapy in case of infection or planned surgical procedure.
**Objectives:** The aim of our study was to look at the most frequent questions raised by patients about their treatment. In addition we looked at a potential association between particular patient problem and specific subcutaneous TNFα blocker.
**Methods:** Data was collected between January 2013 and May 2014 and included

demographic data, prescribed anti-TNF drug, and description of the patient reported query regarding their s.c. anti-TNF treatment. Patient queries were grouped into six topics: skin reactions, infections, vaccinations, drug interactions, planned surgical procedures and other (Table 1). Appropriate statistical methods were used to analyze data.
**Results:** During the observation period 98 patients (23% males, mean (SD) age 56.1 (13.9) years) treated with subcutaneous TNFα blocker asked for help using a telephone call. Patients were treated with the following s.c. anti-TNF drugs: certolizumab (9%), etanercept (27%), adalimumab (41%), and golimumab (23%). The most common patient problems on subcutaneous TNFα inhibitors are presented in Table 1.

Table 1. The patient's inquiries grouped by topics

| Patients queries | % | Patients queries | % |
|---|---|---|---|
| Skin reactions | 20% | Drug interactions | 10% |
| Infection | 36% | Planned surgical procedures | 10% |
| Vaccinations | 2% | Other | 22% |

In 22% of cases patients seeked telephone advice for other different health problems (swollen joints, drug ineffectiveness, potential adverse effects).We did not find any significant difference concerning particular TNFα blocker and the pertinent patient problem.
**Conclusions:** Telephone assistance is valuable for patients. Patients request more information about their treatment and continuous patient education could improve outcomes in the management of inflammatory rheumatic diseases.
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## Miscellaneous forms of clinical care

### SAT0640-HPR UNDERSTANDING THE IMPORTANCE OF A PATIENT'S ROLE IN THE MANAGEMENT OF RA: PHYSICIAN- AND PATIENT-BASED SURVEY RESULTS DEVELOPED BY THE RA NARRATIVE ADVISORY PANEL

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**Background:** RA is a chronic, debilitating condition for which there is no cure.
**Objectives:** To identify and better understand the perspectives of both healthcare providers (HCPs) and patients (pts) regarding RA treatment and management, using data from an HCP- and a pt-based survey, developed by the RA NarRAtive global advisory panel.
**Methods:** The RA NarRAtive initiative comprises an advisory panel of 39 RA experts from 17 countries. An HCP-based (16 countries) and a pt-based survey (15 countries), designed by the working group, were fielded online between Aug-Oct 2015, and Sept 2014-Jan 2016, respectively. Results are presented from pts treated by a rheumatologist. All respondents are from the same 15 countries.
**Results:** 3987 pts responded (1653 were currently managed by a rheumatologist): mean age 51.5 years (yrs), 64% female, median time since diagnosis 7 yrs; respondents represented a wide spectrum of disease activity: moderate to severe (30%; 501) and severe (11%; 176). In the HCP survey, 90% of respondents were satisfied with their communications with pts but 68% acknowledged, "I wish my pts and I talked more about goals and treatment". In the pt survey, 53% of pts acknowledged that dialogue with the HCP would optimise the management of their RA. 61% of all respondents felt uncomfortable raising concerns or fears to their HCP. 93% of HCP respondents discuss quality of life (QoL) issues with their pts including impact of RA on ability to work, participation in activities and lifestyle goals. 86% discuss treatment-related issues including adherence to therapy, medication preferences and whether pts seek treatment from other HCPs. The most common topics that pts report worrying about (and HCPs believe their pts worry about) are similar but these factors were ranked differently between pts and HCPs: the number one factor for pts is the impact on QoL; the number one factor for HCPs is prescription side effects. HCPs and pts have similar views on what they would most like to change about currently available RA medications, ie severity and number of side effects, cost and efficacy. HCPs highlighted disease remission as a treatment goal; while pts more frequently referred to symptom reduction. Overall, 88% of HCPs agreed that pts involved in making treatment decisions tend to be more satisfied with their treatment experience; 74% felt that pts who are not involved are less likely to adhere to treatment. Setting treatment goals with pts and agreement on the treatment plan are considered important by 78% and 79% of HCPs, respectively, as is being able to have an open dialogue (86%).
**Conclusions:** Differences between treatment goals set by pts and HCPs were reported, highlighting the importance of an open pt-HCP dialogue in the successful management of RA. These findings could help improve adherence and pt satisfaction with their disease management.
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## Nursing

### SAT0641-HPR REASONS TO STOP DRINKING ALCOHOL AMONG PATIENTS WITH RHEUMATOID ARTHRITIS – A MIXED METHOD STUDY

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**Background:** Studies of alcohol use in patients with rheumatoid arthritis are sparse and studies of why patients choose to stop drinking alcohol in particular
**Objectives:** The aim of the current study was twofold: first to identify patients with RA who stopped drinking alcohol and compare those to patients drinking alcohol, and second, to explore reasons to stop drinking alcohol.
**Methods:** In 2010 a self-completion postal questionnaire was sent to all 2,102 prevalent patients in the Better anti-rheumatic farmacotherapy (BARFOT) study enquiring about disease severity, physical function (HAQ) and health related quality of life (EQ5D), pain, fatigue, patient global assessment (PatGA) and lifestyle factors e.g. alcohol. The questions assessing alcohol included the question "Have you stopped drinking alcohol?" and an open question "Why have you stopped drinking alcohol?" A mixed method design was used and 1512 patients had answered the alcohol questions and was included in the study of those 86 had stopped drinking alcohol. Seventy-one patients answered the open question and their answers were analyzed with qualitative content analysis (1).
**Results:** Comparing patient with RA using alcohol or not, the patients who stopped drinking alcohol was older median age (min-max) 69 (36–90) vs. 66 (23–95), p=0.011, more men 42% vs. 29%, p=0.015, had worse physical function, median HAQ (min-max) 0.50 (0–3.00) vs. 1.00 (0–2.75), p<0.001, worse health related quality of life, median EQ5D (min-max), 0.69 (-0.59–1.00) vs. 0.76 (-0.02–1.00), p<0.001, worse self-perceived health, median PatGA (min-max) 5 (0–10) vs. 3 (0–10), <0.001, more pain, median (min-max) 5 (0–10) vs. 3 (0–10), p<0.001, and more fatigue median (min-max) 6 (0–10) vs 4 (0–10), p<0.001. There were no differences between the groups regarding disease duration, swollen and tender joints. The qualitative content analysis resulted in five categories describing the reasons for patient with RA to stop drinking alcohol: disease and treatment, health and wellbeing, work and family, faith and belief and dependences and abuse
**Conclusions:** Patients with RA who stopped drinking alcohol have a lower physical function, health related quality of life, self-perceived health and more pain and fatigue comparing to patients with RA drinking alcohol. The reasons to stop drinking alcohol were of different nature such as medical, physical, mental, social and spiritual
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## Psychology/Social sciences

### SAT0642-HPR COLLABORATION OF PATIENTS AND HEALTH PROFESSIONALS IN DEVELOPMENT AND RESEARCH OF CARE-INTERVENTION: CASE EXAMPLE PRESENTED BY A PATIENT RESEARCH PARTNER

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**Background:** Patient participation in research and in development of interventions

has become a hot topic. Research on health beliefs of stakeholders shows that patients do have other views on health and well-being than health professionals without any experience of a chronic condition themselves (Ubel 2003, Huber 2014). Additionally, including the patients' perspective in research is a necessary condition for reaching patient-related-outcomes (De Wit 2014). Moreover, active involvement of patients is a critical factor for the actual use of an intervention in healthcare (Van Gemert-Pijnen 2011). Thus, including the patients' perspective has significant value. EULAR recommendations aim to stimulate the collaboration with patient (research) partners. Sharing examples may help both patients as health professionals to undertake these valued steps.
**Objectives:** To share experiences of the collaboration between patient research partners and health professionals in building an online self-management training, and in developing the framework and outcome measures of research on the efficacy of the intervention.
**Methods:** Patient partners and health professionals formed a research team who collaborated in all stages of development and research. The team conducted online focus groups among adult patients, a card sorting task and cluster analyses, all focusing on patients' needs and preferences. Results of this study were used to develop the content and structure of the online intervention.
**Results:** Throughout the process experiences and perspectives of patients were used to guide the development and research. Consequently, the results yielded in an online expert-patient guided intervention, tailored to the needs, life, disease stage, and goals of the patient. Hence, the framework of research is customized to these results. In sustaining constructive collaboration in development and research, we found it important to be clear about expectations and roles of all involved in the research team.
**Conclusions:** The involvement of patients had major influences on input, the details of the intervention, the framework of research including outcome measures customized to individual needs. To secure collaboration agreement about the roles and (load-taking) capacities of each research partner is essential. Concurrently, it is important to be clear about expectations, responsibilities, and ways of communication between all involved. Including patients in the development of interventions and research benefits all stakeholders and the product that results from the collaboration.
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## Miscellaneous forms of clinical care

### SAT0643-HPR POINTS TO CONSIDER FOR HEALTH PROFESSIONALS UNDERTAKING MUSCULOSKELETAL ULTRASOUND FOR RHEUMATIC AND MUSCULOSKELETAL DISEASES: PROGRESS OF A EULAR TASK FORCE

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**Background:** Musculoskeletal ultrasound (MSUS) has evolved into an important method for identifying musculoskeletal abnormalities, confirming the diagnosis in patients with suspected inflammatory arthritis, monitoring therapeutic response, influencing clinical decision making and guiding interventions. The role of the non-medical health professional has advanced with many health professionals undertaking training and using MSUS to extend their scope of practice. Guidelines to support training for rheumatologists have been identified but currently there are not any recommendations to support the education and training needs of non-medical health professionals using MSUS.
**Objectives:** The EULAR Task Force was established to reach a consensus on the role and education and training needs of non-medical health professionals undertaking MSUS for the management of patients with rheumatic and musculoskeletal diseases (RMDs).
**Methods:** The EULAR Task Force comprised an expert group from 11 European countries. The Task Force met twice and included rheumatologists, nurses, physiotherapists, a radiologist, radiographer and podiatrist with patient representation. In the first meeting the aims of the Task Force were defined and fourteen research questions were developed. This was followed by a comprehensive systematic search of the literature to identify publications on the role of health professionals using MSUS, their competency requirements and training undertaken. During the second meeting the Task Force were presented with the results of the literature review which supported the formulation and consensus of "points to consider". The level of agreement between task force members for each "point to consider" was determined after the second meeting.
**Results:** In total, seven "points to consider" were formulated. Two points covered the role and scope of health professionals using musculoskeletal ultrasound and one point addressed the application and feasibility in daily practice. Three "points to consider" focused on the training and competency required by health professionals and the final point addressed the added value in daily practice. The strength of the "points to consider" was D based on the category of evidence (3–4). A high level of agreement (range 9.0–9.7) was achieved between Task Force members. Additionally, the Task Force agreed upon eight topics for the future research agenda.
**Conclusions:** Seven "points to consider" for health professionals using MSUS for the management of patients with RMDs were developed using a combination of research-based evidence and expert consensus approach.
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## Nursing

### SAT0644-HPR BELIEFS, KNOWLEDGES AND REPRESENTATIONS OF PATIENTS WITH GOUT DISEASE FOLLOWED BY GENERAL HEALTHCARE AND HOSPITAL RHEUMATOLOGY: FROM DIONYSUS TO THE SWORD OF DAMOCLES

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**Background:** Gout disease is common and potentially serious due to its joint, renal and cardiovascular complications. It is well treated with multiple efficient treatments; however, we notice a lack in the medical care of this disease, especially due to a bad compliance with the treatment. This compliance depends of numerous factors as personal history of the patient, relation to the healthcare system, social and familial environment.
**Objectives:** To explore knowledge, beliefs and representations of gout with gout patients followed in general practice and hospital rheumatology
**Methods:** Qualitative study by semi directive interviews of gout patients followed by general practice. Population: 26 patients, with 14 patients followed in general practice (22 men) from 44 to 85 yo sampled for their familial situation, ethnical origin and comorbidities. The areas explored concerned the disease itself, the medical care, the family and professional environment, and the health care system. The interviews were recorded and then analyzed through the grounded theory model: encoding of the interviews as we go along until data saturation. The codes are combined into sets and then analyzed in order to deduct concepts with the Nvivo 10 software.
**Results:** Emerging concepts: shameful disease, traumatic disease on a physical level (painful and disabling), and on a psychic level (self-image damaged). Nevertheless, even if the disease is considered as trivial, it is for most of the patients like the sword of Damocles: permanent fear for the next attack. Each patient had its own physiopathological conception, a wrong one most of the time. For example, they believe the disease was directly link to a personal responsibility (bad food hygiene...) or linked to an external cause (professional diner, heredity...). Gout attack triggered by overeating was often reported, due to a trust relationship between patient and medical doctors. Most of the patients were counting on their wife or husband to manage treatment, diet and familial organization. The role of the diet was predominant for the medical care, much more than the hypo-uricemiant treatment. But it appeared that the diet was binding with questioning of the lifestyle, and was managed day by day. There was not much difference between the patients of general medicine and those of rheumatology.
Model of a relation between medical care – disease – patient: each patient develops its own gout under different influences: his life, returned image, information

received. All this creates a unique entity, with a particular physiopathology... And a proper medical care modeled by experience, family, doctor and information. Then there is a balance between benefits and barriers to observance.
**Conclusions:** The very personal and intimate vision of gout disease and its treatment by the patients should be taken into account in therapeutic education.
**Disclosure of Interest:** None declared
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## Psychology/Social sciences

### SAT0645-HPR RESULTS OF A GOAL MANAGEMENT INTERVENTION FOR PATIENTS WITH POLYARTHRITIS WITH MILD DEPRESSIVE SYMPTOMS

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**Background:** Persisting disease symptoms can threaten attainment of personal important goals for patients with polyarthritis, resulting in elevated levels of depression and anxiety[1]. Interventions that provide patients with the skills and techniques to live with and manage their disease in daily life are essential, as people have to manage a chronic disease most of the time outside of the health-care system. For this purpose participants practice four goal management competencies (goal maintenance, goal adjustment, goal disengagement and goal re-engagement) and the flexible use of these strategies during the self-management intervention "Right on Target".
**Objectives:** The purpose of this study was to establish whether an intervention aimed at increasing goal management capacities is effective in decreasing symptoms of depression and increasing adaptation in patients with polyarthritis with elevated levels of depressive symptoms.
**Methods:** In total, 85 persons with a diagnosis of polyarthritis and elevated levels of depression received the group-based goal management intervention *Right on Target* with measurements at baseline, post-intervention (after 2 months) and follow-up (6 months). A quasi-experimental design was applied in which the reference group consisted of 151 participants of a previously conducted observational study selected according to the inclusion criteria for the intervention group. Primary outcome was depression, secondary outcomes anxiety, purpose in life, positive affect and satisfaction with participation. Mediating variables were goal management strategies and arthritis self-efficacy. Linear mixed model procedure was applied to evaluate changes in outcomes. Proportions showing clinically relevant changes and possible mediators were analyzed.
**Results:** No improvement was found for depressive symptoms. Positive affect significantly improved in the intervention group mediated by an increase in goal adjustment. No changes were found for the other secondary outcomes, while goal maintenance decreased and self-efficacy for other symptoms than pain increased in the intervention group.
**Conclusions:** This study indicates the value of improving the management of personal threatened goals of people with polyarthritis and showed that especially facilitating goal adjustment and downgrading goal tenacity are potentially helpful. While more research is needed, the present study provides a small but promising direction towards greater wellbeing for patients with polyarthritis.
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### SAT0646-HPR WOMEN WITH PSORIATIC ARTHRITIS WHO ARE HOMEMAKERS OR OFFICE WORKERS DECLARE SIMILAR DIFFICULTIES DURING WORKING

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis. The differences between homemaker (HM) and working at paid work (PW) in women were not assessed.
**Objectives:** The aim of this study was to assess differences between being HM and working in PW in female patients with PsA related to clinical findings, quality of life and difficulties at working.
**Methods:** Female patients with PsA over the age of 18-year-old who met the CASPAR classification criteria were underwent clinical and laboratory evaluation by using standardized protocol and case report form, from three different universities outpatient's clinics. Female patients with PsA were divided into age matched two group as a HM or working in PW. Patients who were HM or PW were asked to mark their level of difficulty during household works or office works respectively, on a 0–10 Likert scale. 0, indicated no difficulty during household/office works; 10, unable to do household/office works because of PsA and high scores indicated more difficulty.
**Results:** A total of 115 female patients with PsA (mean age 41.9±11.9 year) were included. Mean symptom duration was 10.7±9.3 year. Out of 86 (74.8%) patients with PsA were HM and 29 (25.2%) were working at a regular PW. Homemaker had higher body mass index than PW (25.1±7.4 vs 29.7±6.6 p=0.012). Dactylitis (current or having history) were higher in PW (58.6 vs 31.4% p=0.014) whereas enthesitis (current or having history) were higher in HM (27.6 vs 52.3% p=0.021). Disease activity measures (acute phase reactants, BASDAI, DAS28, VAS-pain, physician's and patient's global assessment, tender and swollen joint count), functional status and health related quality of life assessments (BASFI, BASMI, Duruoz hand index, SF-36, Nottingham health profile, psoriatic arthritis quality of life, hospital anxiety and depression scale, fatigue severity scale) were similar between HM and PW patients with PsA ($p>0.05$). Level of difficulties in working at household works were 5.2±2.6 in HM and level of difficulties in office works were 5.3±2.3 (p=0.804) in PW. Depression risk (HAD-depression $\geq$7) was relatively higher in PW (59.3 vs 43.7%), but anxiety risk (HAD-anxiety $\geq$10) was relatively higher in HW (26.8 vs 22.2%) ($p>0.05$). Fatigue severity scale score$\geq$36 was associated with depression risk in all women with PsA by using univariate logistic regression analysis (OR: 5.1, 95% CI: 2.0–12.8 $p<0.0001$).

Table 1

| | Working at PW (n=29) | HM (n=86) | p |
|---|---|---|---|
| Age | 40.4±12.7 | 42.3±11.2 | 0.481 |
| Number of pregnancies | 3.6±3.6 | 4.4±2.6 | 0.354 |
| Difficulties in household/office work (0–10) | 5.3±2.3 | 5.2±2.6 | 0.804 |
| Dactilitis (current or having positive history) | 17 (58.6) | 27 (31.4) | 0.014 |
| Tenosynovitis (current or having positive history) | 8 (27.6) | 25 (29.1) | 0.887 |
| Enthesitis (current of having positive history) | 8 (27.6) | 45 (52.3) | 0.021 |
| BASDAI | 4.4±2.3 | 4.0±2.5 | 0.506 |
| DAS 28 | 4.0±1.4 | 4.0±1.7 | 0.992 |
| PsAQoL | 7.4±6.5 | 6.2±5.7 | 0.530 |
| HADS - - Depression | 6.8±3.7 | 6.8±4.0 | 0.945 |
| HADS – Anxiety | 5.9±4.9 | 6.6±4.3 | 0.529 |
| Fatigue severity scale | 3.9±1.5 | 3.9±1.0 | 0.561 |

**Conclusions:** Women with PsA who were homemakers or working in paid work do not differ from each other in terms of disease burden, health related quality of life, difficulties at homework or at office work.Furthermore, increased fatigue may be associated with depression risk in female patients with PsA.
**Disclosure of Interest:** None declared
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### SAT0647-HPR PATIENT PERSONALITY INFLUENCES THE PRESCRIPTION OF TREATMENT FOR RHEUMATOID ARTHRITIS

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**Background:** Individualized treatment of rheumatoid arthritis (RA) based on genetic and serologic factors is increasingly accepted. In addition, patients are more actively involved in the management of their disease. However, personality has received little attention with respect to perception of the need and adherence to treatment.
**Objectives:** Our objective was to evaluate the influence of personality on the intensity of RA treatment.
**Methods:** We performed a cross-sectional study in two hospitals with early arthritis clinics where sociodemographic, clinical, and therapeutic variables are systematically recorded. Patients completed Eysenck Personality Questionnaire, Multidimensional Health Locus of Control, Pain-Related Self-Statement Scale and Pain-Related Control Scale. Aggressive treatment was considered if patients received more than two DMARDs or biological agents during the first year of follow-up. Multivariate logistic regression analysis was performed to determine predictors of aggressive treatment.
**Results:** 176 RA patients were included (80% women, disease begin median age 55 years). Treatment was considered aggressive in 57.9% of the sample. Scores were high in extraversion in 50.8% of patients, neuroticism in 29.5%, and psychoticism in 14.7%.Neuroticism was the only factor associated with aggressive treatment, which was less probable (p=0.04, OR =0.40). Neuroticism also decreased the possibility of receiving a combination of biologics and DMARDs (p=0.04, OR =0.28).
**Conclusions:** Patients with high scores on neuroticism are more worried, obsessive and hypochondriac, leading them to reject more aggressive therapy. It is important educate patients about their disease so that they will accept more aggressive approaches in clear cases of poor outcome.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.4025

SAT0648-HPR **EXPLORING PHYSICIANS' PERCEPTIONS OF ILLNESS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS: A VIGNETTE-BASED STUDY**

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**Background:** Systemic Lupus Erythematosus (SLE) and Systemic Sclerosis (SSc) are complex chronic auto-immune diseases with a wide presentation of multi organ involvement, comorbidities and complications. This complexity implies that the management and treatment of SLE and SSc needs a multidisciplinary care team that exists of healthcare professionals from different professions, and physicians of different disciplines. Within this multidisciplinary approach, each physician might have certain ideas and beliefs about the disease of a particular patient with SLE and SSc. Differences in opinions and views can cause inconsistent advice, confusions and misinterpretations.
**Objectives:** The aim of this study was to cluster physicians based on their illness perceptions of patients with SLE and SSc.
**Methods:** A sample of 287 physicians from nine disciplines, working at three hospitals in Belgium was approached. The inclusion criteria were that physicians had to be certified in their specialism, and had experience with SLE or SSc patients. Participating physicians were asked to complete the Revised Illness Perception Questionnaire for Healthcare Professionals (IPQ-R HP) on the basis of four patient vignettes, i.e. 2 vignettes per disease (SLE-SSc). These vignettes were based on real-life patients followed at our outpatient clinic. The IPQ-R HP (38-items scored on a 5-point scale rated from 1 = strongly disagree to 5 = strongly agree) measures beliefs of the healthcare professional in relation to duration and cyclical nature of the patients' illness; perceived consequences; emotional impact; personal/treatment control; and understanding of the illness by the patient. Statistical analysis was performed using k-means cluster analysis for each disease separately.
**Results:** Fifty physicians (62% men, mean age 43 y (SD=11), mean working experience 13 y (SD=12)) were included. For each disease, three clusters of physicians with different illness perceptions were identified. For SLE, cluster 1 (42%) reported less severe consequences, less emotional impact and a clear picture of SLE by the patient. Cluster 2 (36%) perceived severe consequences for the patient and a chronic and cyclical time course. Cluster 3 (22%) reported less personal control and understanding of SLE by the patient. Three of the 5 rheumatologists were detected in cluster 2. For SSc, cluster 1 (22%) perceived less consequences and less emotional representations by the patient. Cluster 2 (42%) reported the cyclicity of SSc, emotional impact and severe consequences due to SSc. Cluster 3 (36%) perceived a non-cyclical time course and less personal/treatment control by the patient. Three of the 5 rheumatologists were present in cluster 2.
**Conclusions:** There is a lot of variability in illness perceptions between physicians of different disciplines and within physicians of the same discipline regarding SLE and SSc patients. Further studies should focus on the factors that determine these differences in perceptions and eventual consequences for patient care.
**Disclosure of Interest:** None declared
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## Occupational therapy

SAT0649-HPR **WOMEN WITH EARLY RA PREFER TO USE INTERACTION AND ADJUSTMENT STRATEGIES TO DEAL WITH THEIR EVERYDAY LIFE DILEMMAS: THE TIRA PROJECT)**

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**Background:** Due to advancements in medications and treatment, many patients with rheumatoid arthritis (RA) have high expectations of maintaining health, even though they still report participation restrictions in daily life. More women than men RA are affected and women have higher disease activity and more disability than men. Thereby there is a need for further exploration of women's perspective in order to provide tailored multi professional interventions.
**Objectives:** The aim of this study was to explore RA women's strategies for dealing with the dilemmas in everyday life.
**Methods:** The data collection was conducted with semi-structured interviews based on the Critical Incident Technique (CIT) [1]. The sample consists of women with early RA (n=35). The strategies for dealing with RA dilemmas of everyday life were analyzed and categorized using content analysis [2] and linked to the International classification of functioning, disability and health (ICF) domains [3]. This study is part of a longitudinal RA project approved by the Research Ethics Committee at Linkoping University (M168–05 T84–09).
**Results:** The women with early RA described four types of health strategies; interaction, adjustment, avoidance and acceptance. The interaction strategy was most frequently used, however often in combination with adjustment or avoidance strategies. The *interaction strategy* included to verbally express needs and wants and to interact with others. More easily said, to talk about the problem. In the *adjustment strategy* new behaviors and habits were developed to deal with the experienced participation restriction or the everyday life dilemma. The *avoidance strategy* included to deliberate avoid possible participation restrictions, and the *acceptance strategy* was identified by utterances that included descriptions of accepting the experienced situation or restriction. The everyday dilemmas experienced where related to several of ICF domains such as dressing, eating, drinking, driving, preparing meals, formal and informal relationships, interpersonal interactions and family relationships, employed work, and in leisure activities.
**Conclusions:** Women with early RA used combined health strategies to deal with everyday life dilemmas and participation restrictions. Especially the interaction strategy was preferred which could be argued to be an important facilitator for communication within health promotion initiatives and in rehabilitation. This highlights the importance of that health professionals, colleagues, family members and other persons in the social environment listen to women's articulations in order to support and decrease women's participation restrictions in early RA.
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# Abstracts Accepted for Publication

## Nursing

### AB1074-HPR INTERRUPTION OF BIOLOGICAL THERAPY: REASONS AND IMPACT ON DISEASE ACTIVITY

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**Background:** The development of biological therapies (BT) represented an important advancement in the treatment of patients with inflammatory arthritis. These treatments have proven to be effective in controlling disease activity, leading to clinical remission and avoiding disease progression, allowing a better prognosis of these patients.
**Objectives:** To describe the reasons of intra-venous BT interruption in a Rheumatology Day-Care Hospital. To evaluate whether this interruption of BT leads to an increased disease activity.
**Methods:** This is an observational, retrospective study performed in the Rheumatologic Day-Care Hospital of a UniversityHospital between June 2014 and December 2015. We included all patients treated with intra-venous BT [i.e. infliximab (IFX), tocilizumab (TCZ) and abatacept (ABA)] with a treatment interruption longer than 15 days. Demographics (i.e. gender, age), RA features (i.e. treatment, disease duration), clinical evaluation (i.e. tender joint count, swollen joint count, patient global pain intensity VAS) and laboratory tests (i.e. ESR, CRP) were recorded. Composite scores and indices (i.e. DAS28, CDAI, SDAI, ASAS, HAQ, BASDAI and BASFI) were calculated before and at BT re-starting.
**Results:** Out of 272 patients treated with BT, 55 (20.2%) had a temporary interruption of the treatment $\geq$15 days. Out of these patients, 56% were females, the mean (SD) age was 50 (32) years with a mean (SD) disease duration of 18.5 (18) years and a mean (SD) treatment duration of 8.1 (7.8) years. The diagnoses of these patients were as follows; 25 (45.4%) had rheumatoid arthritis (RA), 17 (30.9%) had spondyloarthritis (Sp), 8 (14.5%) had psoriatic arthritis (PsA), and 5 (9%) had other autoimmune disease. The BT received was as follows; 43 (78.1%) IFX, 8 (14.5%) TCZ and 4 (7.3%) ABA. Twenty two (40%) patients received also treatment with synthetic disease modifying drugs (sDMARDs) and 21 (38.1%) received also corticoid therapy with a mean dosage of 6.2 mg/day. The most frequent reasons for BT interruption were infections in 27 (49%) patients of which 11 required hospitalization (i.e. 8 pneumonias, 1 cholelithiasis, 1 lower urinary tract infection and 1 herpes zoster infection) and 16 didn't required hospitalization (i.e. 6 respiratory tract infections, 3 lower urinary tract infections, 1 herpes zoster infection, 1 cellulitis and 5 oral infections). The second reason for BT interruption was the performance of surgical procedures in 16 (29%) patients and the third reason was related to other situations such as the performance of diagnostic procedures for ruling out other diseases, work reasons or forgetfulness 12 (21.8%). In 3 patients the BT was interrupted because of a neoplasia (colon, lung and bladder adenocarcinoma) and 3 patients were pending to restart the treatment after ruling out cancer or infection. The mean (range) interruption duration was 72 (16–365) days. The disease activity before and after BT interruption is displayed in table 1.

| Clinical evaluation | | | |
|---|---|---|---|
| Variable | Basal | Restart | p-value |
| Patient global assessment by VAS | 4,12 | 6,14 | <0,001 |
| [redacted] | | | |
| Swollen joints | 2,17 | 1,89 | 0,029 |
| [redacted] | | | |
| DAS 28 ESR | 3,27 | 4,39 | 0,003 |
| [redacted] | | | |
| CDAI | 14,96 | 21,70 | 0,030 |
| [redacted] | | | |
| Back pain | 1,89 | 3,42 | 0,133 |
| [redacted] | | | |
| BASDAI | 2,58 | 3,82 | 0,076 |
| [redacted] | | | |
| ABDAS ESR | 1,52 | 2,11 | 0,059 |
| [redacted] | | | |
| ESR mm/h | 15,19 | 19,24 | 0,239 |

**Conclusions:** The most frequent reasons for BT interruption were infections, in particular respiratory tract infections and surgical procedures. BT interruption occurred in a wide age range. After BT reintroduction, we detected an increase in pain and disease activity as well as a decrease in the functional status.
**Disclosure of Interest:** None declared
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### AB1075-HPR A SURVEY OF IRISH RHEUMATOLOGY NURSES EXAMINING CLINICAL PRACTICE, PROFESSIONAL BEHAVIOUR AND EDUCATION NEEDS

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**Background:** Rheumatology nurses, as integral members of rheumatology teams, are instrumental in increasing treatment in response to clinical need to improve patient outcomes. Yet their specialist knowledge and skills are not always recognised or acknowledged with specialist or advanced practice titles (IRNF, 2014).
**Objectives:** The objectives of this online survey were to characterise rheumatology nursing role activities, assess confidence with these roles, and assess educational requirements to gain understanding about current rheumatology nursing practice in Ireland.
**Methods:** Approval was granted by Our Lady's Hospice & Care Services and the UK authors to use the tool. Following conversion from paper to online, it was emailed to all Irish Rheumatology Nursing Forum (IRNF) members (approx. 75 members at time of survey), with 2 further reminders. The UK survey was originally 38 questions with a mix of multiple choice and likert type questions analysing demographic information, patient-based and non-patient based clinical and professional activities, and self-assessment of competence in practice related clinical activities. Minor language changes were required within the tool to make it suitable to an Irish population. An additional component was added asking about postgraduate education to date, intention to study further and courses of interest. It took approx. 15–20 mins to complete.
**Results:** Response rate was approximately 45%, from rheumatology nurses. Respondents were working as specialist (51%), advanced (6%) or registered nurses (25%) or others (including management and research roles) (18%). Patient based clinical activities include high levels of confidence counselling patients on Methotrexate (73%), calculating a DAS score (68%) and to a lesser extent performing a joint count (54%) and least of all 19% supporting patients with chronic pain. Clinical activities included monitoring patients on DMARDs (62.5%) and Biologics (68%) as a major role although the majority were not qualified to prescribe medications (72%) or give joint/ soft tissue injections (68%). Providing psychological support was a major or significant role for all respondents. Non-patient based activities included majority of those surveyed taking part in activities such as clinical research (63%), teaching nursing students (58%), conducting audits (55%) with less writing business cases (26%) or giving talks outside their department (42%). 72% had undertaken rheumatology specific education while a third were considering further post graduate study.
**Conclusions:** The rheumatology nurses who completed the survey demonstrated advanced clinical knowledge and skills that are not reflected by their occupation title with many nurses not employed as specialist or advanced practitioners. Characterising the clinical practice of rheumatology nurses will inform the debate on nurses being acknowledged for the clinical skills they are delivering
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**Acknowledgement:** Thanks to Sarah Ryan and Jackie Hill for permission to use their survey tool
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### AB1076-HPR PROMOTING LOCAL RESEARCH THROUGH A POSTER CAMPAIGN: THE IMPORTANCE OF KNOWING YOUR AUDIENCE

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**Background:** Recruiting sufficient patients into studies is a perennial challenge for researchers. Increasing patient and carer awareness of local research

activity promotes recruitment through normalising the experience of research participation.
**Objectives:** To evaluate a programme promoting local research through a poster campaign in musculoskeletal clinic waiting areas. To measure differences in awareness of local research before and after the poster campaign.
**Methods:** 8 posters were developed collaboratively by clinical staff, research staff and patient representatives for display in musculoskeletal clinic waiting areas in a large UK teaching hospital. Each poster briefly describes the findings and potential impact of a study carried out locally. A questionnaire measuring awareness of local research was given to consecutive patients and relatives/friends/carers (aged 16+) entering the clinics on 6 dates and times before and 6 months after introduction of the posters. Responses were analysed adjusting for age and gender using ordinal logistic regression, with the SAS JMP Statistical Visualization System.
**Results:** The response rate was 92% (n=156/170). A majority of respondents were aged 50–69y (43%, n=56), with all other age groups (16–29, 30–49 and 70+) represented. 56% (n=88) of respondents were female and 74% (n=116) were patients. There were no significant differences in awareness of local research before and after the poster campaign ($p>0.20$ in all cases). 6 months after introduction of the posters, only 24% of people reported seeing the posters. There were, however, some differences in awareness of local research for those respondents who had seen the posters. This group were significantly more likely to agree with the statement 'Research is going on at this hospital to understand arthritis and develop new treatments' ($p<0.001$).
**Conclusions:** The poster campaign failed to increase awareness of local research amongst people using musculoskeletal clinic waiting areas. This was despite significant input to design and content by patient research partners and high approval of final drafts by this group. Few people reported seeing the posters, which may be due to the high volume of competing posters on display. This concurs with existing data that people fail to see and be influenced by posters in clinic waiting areas (1). Those people who had seen the posters were significantly more aware of local research, which may be due to the impact of the poster. Another explanation is that people already aware of local research disproportionately noticed and remembered the posters. To increase the success of a research awareness campaign, tools should be developed and tested with their target audience (i.e. patients not aware of or involved in research) in addition to patients already actively involved.
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**Acknowledgement:** This work was supported by Arthritis Research UK (20018) and the NIHR Biomedical Research Centre at Newcastle upon Tyne Hospitals NHS Trust and Newcastle University.
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## AB1077-HPR FIBROMYALGIA SYNDROME: NURSE CASE MANAGEMENT FOR A STRUCTURED PATIENT PATHWAY

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**Background:** Fibromyalgia Syndrome (FMS) is a common, potentially disabling, chronic disorder that is defined by widespread pain, often accompanied by fatigue and sleep disturbance, cognitive and somatic symptoms. Fibromyalgia continues to present a challenge for healthcare professionals (HCPs) because of the lack of a clear patient pathway. Nurses' role need to be better defined.
**Objectives:** Our aim is to investigate the presence of correlations between clinical and clinimetric parameters and Fibromyalgia Scale (FS) assessed by 2011 ACR criteria, in order to define which parameters should have priority in the construction of a care plan for FMS patients, as well as outline a role for nurses specifically designed for FMS patients.
**Methods:** 168 patients (155 women and 13 men; age MEAN±DS 54.50 ± 12.32) were evaluated for clinical and demographic parameters: age, sex, disease duration, year of diagnosis and latency of the disease. They were assessed by FS, which is divided into Wide Pain Index and Symptoms Score, and gives a total score of severity (FS with range 0–31 and cut off $\geq$13). They were also assessed for pain and sleep (Numeric Rating Scale Pain and NRS Sleep), Regional Pain Scale (RPS), disability (Fibromyalgia Impact Questionnaire and Health Assessment Questionnaire), mood disorders (Hospital Anxiety and Depression Scale), sleep quality (Numeric Rating Scale Sleep), fatigue (Functional Assessment of Chronic Illness Therapy- Fatigue) and quality of life (Short Form-36).
**Results:** FS is significantly and positively correlated with HADS-D for depression, HADS-A anxiety, NRS for pain, FIQ, HAQ and FACIT-F ($p<0.01$) and Tender-Points ($p<0.05$), it is also significantly and negatively correlated with the NRS for sleep quality, SF 36 all subscales, and ISF (p: $<0.05$) and ISM (p: $<0.01$). At linear regression model, FS is significantly and independently associated with RPS, FACIT-F and with SF_36_RE, that together explain the variability of FS in 96% (88.7%; 5.4%;1.9% respectively).
**Conclusions:** It would be desirable, therefore, the use of FS scale in everyday clinical practice, thus allowing nurses to assess FMS patients and plan their clinical and therapeutic pathway, together with the rheumatologist. Our results confirm that important aspects to be treated in FMS patients are quality of life, pain and fatigue, they are considered as independent predictors for FS. Thus, they explain 96% of FS score variability. In this context nurses' role is crucial since FMS most common symptoms seem to be adequately treated with a multimodal and holistic approach and with interventions tailored to the individual. Thus, we propose a Case Manager Nurse (CMN) that should set up and coordinate a multidisciplinary approach aiming at improving FMS patients' QoL and self-perceived health status.
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**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5585

## AB1078-HPR TELEPHONE FOLLOW-UP, STANDARDIZED TO THE INITIATION OF BIOLOGIC THERAPY OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN A SPECIFIC UNIT OF BIOLOGIC THERAPY. PILOT STUDY

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**Objectives:** To know the usefulness of follow-up call legalized at the beginning of biologic therapy and patient contact with consultation of nursing after the start of treatment.
**Methods:** Observational study cross.Patients: We collected 120 patients who began treatment with biologic therapy, intravenous or subcutaneous from December 2013 to November 2015. Protocol: Protocol is education for self-management of subcutaneous biological therapy at the beginning of the treatment. This Protocol includes a follow-up call from the consultation of nursing that matches the first administration of the treatment at home or within 3–5 days after the first infusion. This call is made in the case of the biological subcutaneous as per guideline: etanercept (7 days), adalimumab (14 days), golimumab (28 days), tocilizumab (7days), certolizumab (14 days), abatacept (7days) either guideline prescribed in case of dose reduction. Offers the possibility of contact (telephone and e-mail) with the consultation of nurses in case of doubt or incidence during treatment and is analytical control to the month of the beginning of nurse telephone consultation. Statistical analysis: a descriptive analysis of the main variables.
**Results:** 120 patients with RA initiated treatments were: etanercept 33,3% (n40), adalimumab 8,3% (10), tocilizumab sc 20% (24), abatacept sc 12,5% (15), golimumab 13,3% (16), rituximab 6,7% (8), certolizumab pegol 3,3% (4), biosimilar 2,5% (3). In terms of the associated FAME: none 38,3% (46), methotrexate 49,2% (59), Leflunomide 8.3% (10), sulfasalazine 1,7% (2), hydroxychloroquine 2,5% (3).They were detected in the Protocol call patients with incidences 14,16% (17): local reaction3.3% (4), pruritus 5.8% (7), upset general 0.8% (1), diarrhea 0.8% (1), constipation 0.8% (1), headache 1.7% (2). The patients called the nursing consultation to communicate incidences 10.83% (13): anemia 0.8% (1), hypertransaminasemia 1,7% (2), implant dental 0.8% (1), bruising 0,8% (1), inefficiency 6.7% (8). Also communicated to the consultation of nursing infections during 16.6% (20): urinary tract infection 5,8% (7), upper respiratory tract infection 1,7% (2), upper respiratory tract infection+herpes simplex 0,8% (1), lower respiratory tract infection 3,3% (4), surgical wound infection 0.8% (1), dental infection 0,8% (1), herpes simplex 0,8% (1), gastroenteritis 0,8% (1), not frightening infection 1,7% (2).Patients who started biologic therapy in the period studied only 8.3% (10) changed treatment.The emergence of new comorbidities were detected during treatment with biologic therapy 4,16% (5): hypertension 0,8% (1), hypertension + diabetes mellitus II 1,7% (2), nonspecific Interstitial pneumonia 0,8% (1), psoriasis 0,8% (1).
**Conclusions:** The follow-up call is a useful tool for the control of security of the new beginnings of biological agents. It could foster adherence to treatment monitoring at home and offering the possibility to communicate with the nursing.
**Disclosure of Interest:** None declared
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## AB1079-HPR ADAPTATION AND VALIDATION OF THE SYSTEMIC SCLEROSIS QUALITY OF LIFE QUESTIONNAIRE INTO POLISH: ITEM ANALYSIS USING RASCH MODELS

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**Background:** Systemic Sclerosis SSc is a multisystem autoimmune disease with serious effects on patients' Quality of Life (QoL). SScQoL questionnaire was developed in the in the UK to measure needs-based patient-reported quality of life in SSc.[1]
**Objectives:** The aim of this study was to adapt and validate the SScQoL for use in Poland.
**Methods:** This cross-sectional study involved the (i) adaptation phase and (ii) validation phase. In the adaptation phase, the SScQoL was translated into Polish using a standard process for adaptation of self-report quality of life measures.[2] In the validation phase, patients with SSc were recruited from 8 rheumatology centres in Poland and they were asked to complete the Polish version of the SScQoL. The data was then analysed using Rasch models to determine fit to the model, local dependency, internal consistency, unidimensionality and psychometric equivalence with other European versions of the SScQoL.
**Results:** The SScQoL translated well into Polish. The sample included 231 patients, 198 (86%) of whom were women. Their median age was 58 (IQR: 48 to 64) years, median disease duration, 6 (IQR: 3 to 12) years and the majority left school at age 19. The analysis of the 29 items revealed lack of fit to the Rasch model and suggested some multidimensionality (Table 1). Items were grouped into 5 subscales derived from components of the International Classification of Functioning, Disability and Health. Re-analysis of the 5-subscale SScQoL resulted into a valid, reliable and unidimensional scale (only 4.3% of independent t-tests were significant).[3] The scale was found to have measurement equivalence with five other European countries as described elsewhere.

Table 1. Summary statistics for the overall fit to Rasch model and unidimensionality

| Analyses | Item Fit Residual | | Person Residual | | Chi square Interaction | | PSI | N | Independent T-tests (95% CI)** |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Value (df) | p-value* | | | |
| 29-item SScQoL | −0.52 | 1.38 | −0.34 | 0.95 | 187.49 (116) | <0.001 | 0.90 | 224 | 0.10 (0.06 to 0.14) |
| 5-subscale SScQoL | −0.35 | 2.14 | −0.31 | 0.97 | 22.45 (15) | **0.097** | 0.84 | 221 | **0.04** (0.02 to 0.07) |

SD, Standard deviation; df, degrees of freedom; *P-value >0.05 suggest adequate fit to the model; PSI, Person separation index reliability (value >0.7 acceptable reliability); **Less than 5% significant independent t-tests suggests unidimensionality[3].

**Conclusions:** The Polish version of the SScQoL is a valid measure of needs-based quality of life in SSc. Transformed scores can be compared across five European countries.
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## AB1080-HPR THE ORGANIZATIONAL AND ENVIRONMENTAL FACTORS THAT AFFECT PATIENT SATISFACTION IN DAY CARE UNITS

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**Background:** Patients with inflammatory rheumatic disease, who are treated with biologics, often need a lifelong therapy and frequent examinations. Some of them receive biologics intravenously (i.v.) in a day care unit.Their satisfaction is an important indicator of quality in health care and is influenced by many yet undetermined nonclinical factors.
**Objectives:** The aim of our study was to determine the circumstances that have important influence on satisfaction of patients in our day care unit.
**Methods:** Patients treated in the day care unit of the Department of Rheumatology, University Medical Centre Ljubljana, Slovenia were enrolled from November 2014 to the end of January 2015. 130 questionnaires focusing on environmental adequacy of day care units, privacy during the treatments, organization of day care units, satisfaction with health care and access to phone advice were distributed. Data were analyzed using independent samples t-test when appropriate.
**Results:** One hundred and nineteen patients treated in our day care unit were included. Their average age was 57 ± 12, 6 years old, 73, 9% of them were women. The most frequently represented rheumatic disease was rheumatoid arthritis (77, 3%), the average disease duration was 14, 7 years. Most patients (41%) were being treated with biological therapy for 3–5 years. Most patients in our day care unit organised their own transport to the hospital (73, 9%), 49, 6% of patients commuted from places which are more than 25 km away. According to our questionnaire suitability of treatment rooms, have only marginal, t statistically unimportant, impact on patient satisfaction (p=0,050). The organization of work in daily hospital, the way of providing information about health condition, future treatment options, privacy during the treatment and possibility of obtaining information by phone all had important influence ob patient satisfaction (all $p<0.005$). Overcrowded rooms, high environmental temperatures in the summer, long waiting times for the treatment and the absence of the rheumatologist during the treatment in day-care unit all negatively affected patient satisfaction.
**Conclusions:** Our study shows important connections between the level of patient satisfaction and environmental as well as organizational aspects of day care unit treatment. This data provide new opportunities for our day care unit environmental improvements and organizational changes.
**Disclosure of Interest:** None declared
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## AB1081-HPR PHARMACOLOGICAL ADHERENCE TO CONVENTIONAL OR BIOLOGICAL THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A COLOMBIAN SPECIALIZED RHEUMATOLOGY CENTER

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**Background:** The lack of pharmacological adherence and consecutive therapeutic failure is a prevalent and relevant problem in clinical practice, especially in the treatment of chronic diseases such as rheumatoid arthritis (RA). In the context of chronic diseases, World Health Organization considers lack of adherence like a public health priority because represents negative consequences like: therapy failures, higher rates of hospitalization and increased costs of health care.
**Objectives:** The aim of this observational study was determine adherence to treatment in patients with RA, their demographic characteristics and clinical variables.
**Methods:** An observational, descriptive cross sectional study conducted in a non-probability sample of convenience in patients with RA who consult to rheumatology institution specialized in RA patients. Descriptive epidemiology was applied for continuous variables, measures of central tendency and dispersion for categorical and qualitative variables (averages/percentages); we used Pearson's chi-squared test ($\chi^2$) and T student test to evaluate bivariate correlation.
**Results:** 356 patients were included, 186 (52%) received DMARDs therapy and 170 (48%) biological therapy. 309 (86%) were female and 47 (43%) were male meanDAS28 was 2.5 ± 1 HAQ was 0.87 ± 1.3. The most frequent comorbidity was osteoporosis 145 (40%) and hypertension 135 (37%). 103 (28%) participants suspended the medication when they felt polimedicated. In the group using DMARDs 71 (38%) suspended the medication due to an adverse event and in the biological therapy group 55 (32%). 71 (38%) patients in the group with DMARDs referred administrative difficulties while in the group with biological therapy 56 (32%) referred the same issue. When we explored the adherence, regarding age the group where we found fewer adherence in the group between 40 and 60 years this correlation was not statistically significative. When patients suspended the medication when they felt medicated with many drugs mean DAS28–2.6 higher than who did not suspend medication mean DAS28–2.4. When the medication due to an adverse event was suspended mean DAS28–2.57 higher than those who did not suspend the medication (DAS28–2.46) and was statistically significative.
**Conclusions:** This study shows that most of patients (two thirds) are adherent to conventional or biological treatment; however a important number remains non-adherent with a higher DAS28 score with clinical and economical implications.
**Disclosure of Interest:** None declared
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## AB1082-HPR PROVIDING DRUG COUNSELLING ON METHOTREXATE IS ONE OCCASION ENOUGH?

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**Background:** Methotrexate is used in the treatment of patients with an active inflammatory arthritis. Patients routinely receive drug information on the commencement of treatment, often from the rheumatology nurse specialist, and can remain on Methotrexate for many years if it remains safe and effective. Despite the long duration of use of Methotrexate there is often no mechanism to reinforce information about continuing to take the medication safely.
**Objectives:** The aim of this survey was to establish what safety information patients recalled receiving about Methotrexate and whether patients would like to be updated with information about taking this medication.
**Methods:** A questionnaire was developed and distributed to patients attending

for their Methotrexate drug monitoring appointment in a rheumatology community hospital. The content of the questionnaire focused on:
a) The side effects patients had been asked to report.
b) When methotrexate could be safely taken (including pregnancy, alcohol intake, influenza vaccination and contraceptive precautions).
c) What action would be taken if a problem related to their Methotrexate occurred.
4) Whether patients would like to be updated with information about Methotrexate and if so how they would like to be updated and what information they would want to be included.
**Results:** The survey was completed by 100 patients on Methotrexate. The majority of the respondents (58%) were over 61 years and had been taking Methotrexate for longer than a year. Ony 35% of respondents recalled being asked to report shortness of breath and only 42% would report the presence of infection. Forty one per cent of respondents felt a small amount of alcohol was safe. Although all respondents stated that Methotrexate should not be taken in pregnancy, sixty seven percent of respondents did not know whether contraceptive precautions should be taken. Eighty eight percent of respondents would contact the rheumatology adviceline with a problem and 27% of respondents did not know whether it was safe to have the influenza vaccination. Eighty six per cent of respondents would like to be updated with information about Methotrexate with 83% requesting written information on any aspect that would enhance the safe taking of Methotrexate.
**Conclusions:** The majority of patients taking Methotrexate would not report shortness of breath or the presence of infection, both serious events that would require the Methotrexate to be stopped. It would appear that there is a need to update patients with safely information when they remain on Methotrexate for many years. Patients would welcome being updated with written information to enhance the safe taking of this medication. Further research would be required to identify if providing information at regualr intervals did improve the reporting of side effects and the safe administration of Methotrexate.
**Disclosure of Interest:** None declared
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## AB1083-HPR COMPUTERIZED NEUROPSYCHOLOGICAL PERFORMANCE IN PERSONS WITH RHEUMATOID ARTHRITIS

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**Background:** For persons with chronic diseases such as rheumatoid arthritis (RA), intact cognitive function is crucial for performing main daily activities and adhering to self-management regimens. Persons with impaired cognitive function have decreased functional independence, reduced quality of life, and increased risk of mortality. Although several mechanisms may influence cognitive function in RA, it has not been well-studied in this population.
**Objectives:** This study explored the prevalence of cognitive impairment in persons with RA using a set of computerized neurocognitive tests and the factors that were significantly correlated with cognitive impairment.
**Methods:** Individuals with RA were recruited by their rheumatologists during follow-up visits at one university hospital in Korea. After getting signed consents, a trained research nurse assessed participants with a range of physical, psychosocial, and biological metrics. Cognitive function was assessed using a set of 6 computerized neurocognitive tests yielding 18 indices covering a range of cognitive domains. Subjects were classified as "impaired" if they performed 1 *SD* below age-based population norms on each test [1]. The total cognitive impairment score was calculated by summing the transformed scores, ranging from 0 (no impairment) to 18 (worst impairment). Pearson correlation coefficient analyses were conducted to identify the variables that might be significantly associated with cognitive impairment.
**Results:** Twenty three subjects with a mean (±*SD*) age of 64.9 (±12.4) years were included in preliminary analyses. 87% were female, 87% were married, and mean educational level was 9.7 (±5.2) years. Mean DAS-28 level was 2.6 (±1.2) and mean disease duration was 116.5 (±85.4) months. Mean HAQ score was 0.6 (±0.8) and mean cardiovascular disease (CVD) risk factors were 3.1 (±1.5). 35% had depression and 70% had sleep problems. The proportion of persons who were classified as cognitively impaired on each test were 34% in Card Sorting Test (executive function), 68% in Trail Making Test (visuo-motor coordination), 78% in Visual Span Test (language memory), 83% in Verbal Learning Test (visuo-spatial memory), 83% in Visual Continuous Performance Test (continuous attention), and 91% in Word-Color Test (selective attention). Mean total cognitive impairment score was 11.0 (±4.2), and ranged from 2–17. 95% were classified as cognitively impaired on five or more test indices. Education (r=-514, $p<.05$), income (r=-.638, $p<.05$), and CVD risk factors (r=.434, $p<.05$) were significantly correlated with total cognitive impairment score.
**Conclusions:** A significant number of RA patients were cognitively impaired. Low educational levels, low income, and increased CVD risk factors may be potential risks of cognitive impairment in this population. These findings suggest that the burden of cognitive impairment in RA is significant, and future studies identifying specific etiological contributors to cognitive impairment are warranted.
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## AB1084-HPR LIGHT-MINDED FOLLOW UP OF OSTEOPOROSIS PROPHYLAXIS AT NURSE CONSULTATIONS IN GLUCOCORTICOID TREATED POLYMYALGIA RHEUMATICA LEADS TO HIGHER COMPLIANCE

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**Background:** Compliance to osteoporosis prophylaxis in postmenopausal women is described to be very poor [1]. The compliance to prophylactic osteoporosis medication in patients with inflammatory diseases treated with Glucocorticoids (GC) is higher [2], probably due to the risk of osteoporotic fractures as a side effect of GC treatment [3].
**Objectives:** To evaluate the adherence to osteoporosis prophylaxis in a group of patients suffering from polymyalgia rheumatica (PMR) treated with GC.
**Methods:** At our department patients with milder disease are seen at every second consultations by a nurse specialized in rheumatology. At all nurse consultations the patients are asked, in a friendly and understanding manner, if they remember to take the prescribed calcium and vitamin D, as well as the name of the medication and where they buy it. If Bisphosphonate is prescribed they will be questioned about this as well. The nurses also check the date of dual-energy x-ray absorptiometry (DEXA) scans. In this cross sectional study, all patients (138) diagnosed with PMR within 2013 were interviewed about their compliance toward osteoporosis prophylaxis using a standardized questionnaire.
**Results:** 138 patients were identified, 20 patients were excluded (diagnoses were changes (12), did not want to participate (2), unreachable (3), found dementia (3)). A total of 118 patients were included. Of these 117 were prescribed calcium and vitamin D. 88.9% of these took the medication as prescribed. The reasons for the non-compliance were given as: "Forgetfulness, did not want to eat so many pills and side-effects". Bisphosphonate was prescribed in patients (61) when the results of DEXA scan gave a T-score of less than -1. Of these patients 96.6% took the medication on a regular basis. Noncompliance to Bisphosphonate was in all cases due to gastrointestinal side effects.
**Conclusions:** Our results illustrate that it is possible to increase compliance considerably if the nurses at every consultation ask about the prophylactic medications, at least in this group of patients with a very painful disease. Furthermore we think that the friendly atmosphere, in which questions are given and the dialogue about the importance of the medication to avoid side effects of GC such as fractures, is very important. Our results should be confirmed in a randomized clinical trial, to rule out information bias.
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**Disclosure of Interest:** None declared
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## AB1085-HPR AUDIT OF NURSE-LED DGH RHEUMATOLOGY ADVICE LINE

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**Background:** We introduced a nurse led Rheumatology Advice Line in 2004 to offer telephone advice to patients with inflammatory arthritis (1). Since then there has been a year-on-year increase in the number and complexity of calls, putting unsustainable demand on service and staff. A service review in April 2014 demonstrated one third of calls were inappropriate, including calls about the Home delivery service, appointment times and general practice related problems. We therefore changed the recorded message with the expectation that the helpline be used for telephone consultations concerning: medication side effects and effectiveness; flares of arthritis; possible complications of biologics and DMARDs; results of blood and X-Ray tests to avoid outpatient appointments. We audited the use of the Advice Line.
**Methods:** We documented the number of calls to the Advice Line from 2004–2014. The recorded message for the Advice Line was altered in May 2014. We

audited the calls in April 2014 and compared with data from calls between May and December 2015. All calls were documented and categorised as: Patient calls leading to clinic appointment; Patient calls with advice give related to medication or inflammatory arthritis; GP or district nurse calls with advice given; Home delivery related; Inappropriate calls (including non rheumatological conditions, appointment time related, in-house calls). We also documented whether letters were generated and made a judgement about whether Consultant or GP consultation had been avoided

**Results:** The total annual number of calls increased from 438 in 2004; 2752 in 2006; 3074 in 2008; 2817 in 2010; 3857 in 2012; 3210 in 2014.

After the recorded message was changed, the number of inappropriate calls fell from 97/311 (31.2%) in April 2014 to 8/258 (3.1%) from April to December 2015. However the number of appropriate calls rose from 131/311 (42.1%) in April 2014 to 194/258 (75.2%). The complexity and time needed to deal with calls has also increased.

| Reason for call | April 2014 | April–December 2015 monthly mean (range) |
|---|---|---|
| Patient call – Appointments generated | 71 | 53 (37–55) |
| Patient call – Advice given | 131 | 182 (125–209) |
| GP/district nurse call – Advice given | 3 | 8 (3–11) |
| Home delivery related | 9 | 7 (2–12) |
| Inappropriate calls | 97 | 8 (4–12) |
| Total number of calls | 311 | 258 (224–282) |
| Number of letters generated | 60 | 59 (41–77) |
| Consultant/GP appointment saved | – | 117 (74–116) |

**Conclusions:** The Rheumatology Nurse Practitioner led Advice Line provides a valuable clinical service as an adjunct to face to face consultation. This audit suggests a saving over 100 face-to-face consultations per month. Changing the Advice Line message led to a fall in the number of inappropriate calls but the number and complexity of calls continues to increase. This will need to be reflected in future service evaluation.

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**Disclosure of Interest:** None declared

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## Psychology / Social sciences

### AB1086-HPR CULTURAL AND QUALITY OF LIFE CONSIDERATIONS WHEN ADMINISTERING CORTICOSTEROIDS AS A THERAPEUTIC STRATEGY FOR AFRICAN AMERICAN WOMEN LIVING WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** African American women with Systemic Lupus Erythematosus (SLE) disproportionately experience poor emotional and physical health, loss of self-esteem and earning potential compared to other women with the disease (Baker K, 2009) (Guillermo P, 2010) (Yuen H K, 2012) (Utset T, 2006). Despite ethic variations among African Americans, differences are rarely considered for SLE quality of life factors and therapeutic strategies such as corticosteroids.

**Objectives:** This study investigated the association among corticosteroids, emotional health, physical health, and work and regular daily activities among a racially- and ethnically-diverse sample of women with SLE (n=224) and controls (n=60).

**Methods:** A secondary analysis of data from the Medical University of South Carolina Lupus Database was conducted. Included in the sample were 57 Caucasian Americans, 141 Gullah African Americans, a subpopulation of African Americans from the Sea Islands of South Carolina and 86 non-Gullah African Americans. Linear regression analyses were performed to assess associations among corticosteroid use, emotional health, physical health and work and regular daily activities. Statistical models were also constructed to assess any moderating effects of ethnicity on emotional health and work and regular daily activities among women with SLE.

**Results:** Emotional health outcomes were better for women with SLE compared with controls. High emotional health scores may be influenced by cultural factors such as masking emotion, disease-coping mechanisms, religion and strong familial and social support. While a significant association was not detected for emotional health and work and regular daily activities, after adjusting for corticosteroid use, a significant association was detected. These findings suggest corticosteroid use does influence the strength of the association between emotional health and work and regular daily activities

**Conclusions:** These study findings highlight the importance of considering the impact of corticosteroids on emotional health among women with SLE. In particular, among African American women who disproportionately experience poor emotional health outcomes. Although this therapeutic strategy improves physical health, the emotional health implications should not be overlooked. Compounded poor emotional health can negatively influence health outcomes for women with SLE. Since SLE is such a debilitating chronic condition, researchers and practitioners must put equal emphasis on improving quality of life and decreasing mortality. However, these improvements in SLE outcomes can only be accomplished if racial and ethnic-sociocultural factors are examined in research and accounted for in the administering of corticosteroids and the development and implementation of interventions

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### AB1087-HPR NON-PHARMACOLOGICAL, NON-SURGICAL CARE IN HIP AND KNEE OSTEOARTHRITIS: THE VIEW OF HEALTHCARE PROVIDERS

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**Background:** Non-pharmacological, non-surgical treatment modalities are underused in the management of knee and hip osteoarthritis (OA)[1]. One possible explanation of this suboptimal use could be health care providers' lack of knowledge about non-pharmacological, non-surgical treatment modalities which might act as a barrier for referring patients to these treatment modalities[2].

**Objectives:** The objective of this qualitative study was to identify healthcare providers' view on non-pharmacological, non-surgical care of knee and hip OA.

**Methods:** Semi-structured in-depth interviews with 24 healthcare providers working in the field of OA were held (rheumatologists, orthopaedic surgeons, physiotherapists and GPs). Interviews were transcribed verbatim and analysed using a three-step thematic approach consisting of open, axial and selective coding. Two independent researchers continuously reflected upon, compared, discussed and adjusted the coding.

**Results:** Eight themes were identified: 1) patients' difficulties with weight reduction; 2) dieticians' capabilities in weight reduction management; 3) healthcare providers' responsibilities in weight reduction; 4) the importance of lifestyle advices; 5) (mis)trust in physiotherapy modalities; 6) the endorsement of non-pharmacological, non-surgical treatment to delay surgery; 7) dialogue between disciplines; 8) perceptions of healthcare providers' roles.

**Conclusions:** This study identified multiple factors affecting the suboptimal use of non-pharmacological, non-surgical treatment modalities in knee and hip OA from the perspective of the healthcare provider. The results of this study may be used to improve healthcare providers' knowledge and communication skills regarding weight reduction strategies. To enhance the cooperation between health care providers, opportunities should be created for easy referral to effective weight reduction programmes and to evidence-based physiotherapeutic interventions.

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**Disclosure of Interest:** None declared

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### AB1088-HPR INTENSE EMOTIONS AND MOOD STATES INFLUENCE THE DISEASE ACTIVITY AND QUALITY OF LIFE IN RHEUMATOID ARTHRITIS

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**Background:** Researchers began to unravel the complex interactions between mental and physical health. Some particular feelings (intense emotions) triggered

by a chronic disease as rheumatoid arthritis (RA) can induce different types of mood, such as generalized anxiety or stress with possible implications on disease activity and the quality of life HRQoL.

**Objectives:** The aims of the study were to investigate the associations of the intense positive and negative feelings, level of negative affect with aspects of HRQoL and disease activity in RA patients.

**Methods:** 50 patients with RA who met the 2010 ACR/EULAR classification criteria for RA but without an emotional disorder or mental health diagnosis were enrolled in this study. Disease activity was assessed with DAS 28-CRP, and visual analog scale (VAS) for pain. The study used: the Short Form-36 (SF-36), general questionnaire for assessment HRQoL, Depression, Anxiety and Stress Scale (DASS-21R) to measure the three related negative emotional states of depression, anxiety and stress. Both of them were Romanian validated versions of the original questionnaires[1,2]. Information about positive and negative feelings was collected by open- questions. Pearson correlations were used to verify associations between normally distributed variables, One Way Anova to compare means for different intense feelings and linear regression to identify the predictors for DAS 28-CRP, and components of HRQoL.

**Results:** The response rate was 74%. The study included 89% females, mean age 53.4 ± 13.3 years, mean duration of the disease 10.5 ± 7.1 years, DAS 28-CRP score 4.2 ± 1.1, mean pain score 4.9±2 cm. We found a moderate negative correlation between total DASS-21 scale and mental component score (MCS) of HRQoL (R=-0.428;p=0.007*). Intense feelings in the last month: positive, negative, positive and negative, without feelings are correlate with DAS28 CRP – F (3,35)=5.931, p=0.00. We identified that predictors for DAS 28 CRP are MCS with F(1,37)=13.176, p=0.00 with $R^2$=0.263, and PCS with F(1,37)=16.371, p=0.00 with $R^2$=0.306. The significant predictors for MCS were total DASS-21R score F(1,36)=8.062, p=0.00 with $R^2$=0,183, depression score F(1,37)=4.139, p=0.04 with $R^2$=0,317, anxiety score F(1,36)=6.961, p=0.01 with $R^2$=0,162 and stress score F(1,37)=4.928, p=0.03 with $R^2$=0,118. For PCS the only significant predictor we found was DAS-CRP F(1,37)=16,279, p=0.00 with $R^2$=0,306.

**Conclusions:** The negative affect doesn't impact the disease activity or pain in RA but it influences the mental health component of HRQoL. The experienced intense emotions (feelings) are very important for mental health and also for disease activity in RA and could represent a starting point for further research in orther to avoid bias in clinical trials.

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## AB1089-HPR PERCEPTIONS OF PATIENTS WITH RHEUMATOID ARTHRITIS ABOUT PREDICTIVE TESTING FOR TREATMENTS: A QUALITATIVE STUDY

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**Background:** Rheumatoid arthritis (RA) is a long term condition that requires early treatment to control symptoms and improve long-term outcomes.[1,2]. Identifying biomarkers predictive of treatment response offers an opportunity to improve clinical decisions about which treatment to recommend in patients[3]. For this, we should take into account patients' perspective of these tests and that requires an understanding of the range of effects that predictive testing can have on RA patients. This study explored the factors that might influence a patients' decision to agree to tests using a qualitative approach.

**Objectives:** To explore the factors that might influence a patients' decision to agree to tests.

**Methods:** A qualitative study was undertaken in which explorative focus groups were conducted with RA patients from Manchester, Birmingham and London, UK. Semi-structured interviews about their perceptions of the use of tests to predict response to treatments were performed. Interviews were audio-recorded, transcribed verbatim and analysed using thematic analysis.[4]

**Results:** Interviews were conducted with 16 patients. [13 female, age ranges: 26–80 years old, disease duration: 3–34 years]. Five interlinking themes influenced how RA patients would make decisions about predictive tests: [1] Perceptions surrounding the use of synovial biopsy and/or blood tests: [2] Perceptions surrounding the use of synovial biopsy vs blood test: [3] Utility of the test to manage expectations: [4] The stages of illness on decision making for predictive testing: [5] Understanding the predictive tests in clinic.

**Conclusions:** Besides supporting clinical decision making, the development of predictive testing in RA is supported by patients. Patients recommended that additional support should be offered to help them cope with results that might not accurately predict response. Developing strategies which communicate risk information about predictive testing effectively while reducing the psychological burden associated with this information is essential.

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## AB1090-HPR USE OF THEORY IN SELF-MANAGEMENT INTERVENTIONS FOR EXERCISE AND PHYSICAL ACTIVITY IN ADULTS WITH RHEUMATOID ARTHRITIS

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**Background:** The incorporation of behavioral theories into trials to promote self-management yields positive outcomes. Behavioral theories can inform study design, outcome measure selection and development and influence statistical analyses. However, the persuasiveness of behavioral theory application of exercise/physical activity (PA) trials in rheumatoid arthritis (RA) is limited.

**Objectives:** To identify the use of behavioral theories involving interventions that target exercise and physical activity, determine the most prevalent theories used, and describe how theory was used.

**Methods:** A literature review, searching articles published in English, between 01–01–1980 and 08–12–2015. MEDLINE, Cochrane Central Register of Controlled Trials and CINAHL were searched using the following terms "arthritis, rheumatoid" OR "rheumatoid arthritis" AND exercise [MESH] OR (exercise OR physical activity OR strengthening OR aerobic OR dynamic exercise OR isotonic OR static OR aquatic) AND (theory OR theories OR model OR models) in the title, abstract, or keywords. Inclusion criteria were: (1) published in international academic peer-reviewed journals; (2) evaluated an intervention designed to promote PA behavior; (3) had at least one PA behavior variable as the outcome (4) included adults (≥18 yrs) with RA. Study references and relevant review articles were also checked. Two investigators (ID, MDI) independently selected articles and extracted data using the Theory Coding Scheme (TCS), a standardized 19-item coding tool with good reliability that describes if and how theory informs intervention studies (Michie, 2010). Additional extracted data included: author, publication year, behavioral outcomes (PA and/or exercise), type and duration of intervention, and control group

**Results:** Of 245 articles identified, 45 were duplicates. 200 articles were screened as well as article references. A total of 29 full text articles met inclusion criteria and were reviewed. Of these, 17 were excluded (10 no theory mentioned, 5 were PA studies but were not intervention studies, 1 non-PA intervention and 1 health education evaluation, leaving 12 articles. These 12 studies included 1585 participants, of which 1209 (76%) women. Eleven studies (92%) were randomized controlled trials and 1 was a cohort study. Nine studies (82%) assessed self-management plus exercise and 2 (18%) exercise interventions. Program durations ranged from 5 wks–1 yr. Ten studies (83%) used a single theory. Social Cognitive /Social Learning Theory was the most prevalent theory; 7 studies (58%) linked at least 1 intervention technique to theory, 3 studies (25%) analyzed mediating effects of theoretical constructs, and in 6 studies (50%) results were discussed in relation to the theoretical model.

**Conclusions:** Most theory-based interventions to promote exercise were self-management programs. Social Cognitive/Social Learning Theory was most commonly used in interventions, focusing on self-efficacy, PA/exercise and self-regulation skills. However, only 50% of studies used theory to inform the intervention content and discuss results. We suggest expanding the use of theory throughout the design, evaluation and interpretation of results in intervention studies targeting physical activity in RA.

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AB1091-HPR **SEXUAL DISTURBANCES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND IT'S RELATION WITH DISEASE ACTIVITY**

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**Background:** Sexuality is an important dimension of personality and human body, therefore any involvement in this area should be considered as important. Sexual disturbances in rheumatoid arthritis (RA) patients are poorly described in literature.
**Objectives:** The aim of this study was to describe sexual disturbances using CIE-10 in population with RA and a possible correlation with disease activity.
**Methods:** A descriptive cross-sectional study was performed in a specialized clinic dedicated to care patients with RA. 1298 patients were included in the study, which were seen by the area of psychology, which information was collected through semi-structured interviews and non-probability sampling. Descriptive epidemiology was applied for continuous variables, using measures of central tendency and dispersion for categorical and qualitative variables by averages and percentages. We used chi2 test to stablish a relationship between disease activity severity and sexual disturbances.
**Results:** Total sample of patients was 1298, 1048 (80%) were women and 250 (19%) were men. Patients had a DAS28 2.6 in average ± 1.1; mean age was 55.1 ± 8.8 years; According to CIE-10 739 patients (57%) had psychological disorders, 279 patients (21%) had sexual and 373 (28%) had sleep disorders. Regarding entire cohort, 338 (26%) of the total of participants reported any sexual disturbances. *Regarding women*, 421 (40%) reported no sexual activity, while 627 (67%) reported sexual activity; from reporters of sexual activity 377 (60%) reported satisfactory sexual activity, while 101 (16%) reported no-satisfactory sexual activity, 49 (7%) reported lack or loss of sexual desire, 86 (13%) reported dyspareunia, and 14 (2.9%) orgasmic dysfunction. *Regarding men*, 77 (30%) of men reported no sexual activity, while 173 (69%) reported sexual activity; of these, 21 (12%) premature ejaculation, 85 (49%) reported satisfactory sexual activity, 23 (13%) reported no-satisfactory sexual activity, 10 (5%) reported lack or loss of sexual desire, 28 (16%) orgasmic dysfunction, 6 (3%) reported dyspareunia. When we analized these results with any factor that could precipitate any sexual disturbance (infidelity, wrong information about sexuality, insecurity in the sexual role, and biological or physical causes) we found that 117 of 338 patients with any sexual disturbance had insecurity in the sexual rol and this relationship was statistically significant ($p<0.00$). The relationship between having a sexual disturbance and disease activity severity was not statistically significant.
**Conclusions:** We found that patients with AR a high percentage reported not having any sexual activity and between patients with sexual activity there are many (one fourth) reporting any sexual disturbances. The level of disease activity has no relationship with having a sexual disturbance, but having any sexual disturbance had relationship with insecurity in the sexual role.
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AB1092-HPR **DEVELOPING AN ONLINE SELF-MANAGEMENT PROGRAM FOR RHEUMATOID ARTHRITIS PATIENTS, USING BEHAVIORAL CHANGE TECHNIQUES AND PATIENTS' INPUT**

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**Background:** To support individual behavioral change by self-management interventions, behavioral change techniques (BCT) may be helpful to induce behavior change [1]. Conditions for effectivity of BCT's are that they fit to experienced problems in self-management and that the conditions under which they work (parameters) are taken into account. So important steps in the development of self-management programs are 1) identifying the self-management behavioral problems and factors (determinants) affecting these problems in patients, 2) link BCT techniques to these behavioral problems and determinants, 3) identifying parameters of the BCT's and 4) implement BCT techniques into the intervention [2].
**Objectives:** Development of an online self-management program for Rheumatoid Arthritis (RA) patients.
**Methods:** A panel of 5 RA patients and 5 health professionals identified self-management behavioral problems and prioritized them. Determinants of these behavioral problems were identified in literature and confirmed by patients. Two independent researchers coded techniques from a list of BCT's linked to the determinants of the identified problems with the panel and discussed, which led to consensus [3]. Afterwards, parameters of BCT's where identified from literature. Lastly, RA patients' input during a meeting was used to implement the techniques into the intervention.
**Results:** In total 9 behavioral problems related to self-management were mentioned, namely: balancing rest and activity, setting boundaries in daily life, asking for help and supportuse of medicines, communication with health professionals, use of assistive devices, performing physical exercises, coping with worries, and coping with RA. Determinants of these problems were: knowledge, awareness, risk perception, social influence, attitude, self-efficacy, and habits. To change patients' self-management behavior, 15 BCT's were identified, for example persuasive communication, guided practice and self-monitoring. After identifying, the BCT's were linked to the determinants of behavioral problems and parameters where identified.An example of the BCT modeling, linked to a low self-efficacy an parameters, is presented in table 1.

**Table 1. Example of elaboration of a BCT, suited to the target group.**

| Behavioral problem | Behavioral goal | Identified BCT to change behavior | Parameters for the BCT modeling | Patients input to translate the BCT modeling into the program |
|---|---|---|---|---|
| Patients are not able to set their boundaries in daily life, for example in: - work situations - household chores - taking care of (grand)children | Setting boundaries in daily life | Modeling | There need to be similarities between the model and observer | RA patients mentioned the following similarities as important: age, gender, disease duration, and having problems in the same situations (at work, household chores, taking care of (grandchildren) |
| | | | The model must serve as a coping model | Model need to show that he/she has overcome the problems and demonstrate this with the specific techniques that he/she has used. |
| | | | The model must demonstrate successful skills | Model must demonstrate successful skills to learn to set boundaries in work situations, household chores, taking care of (grand)children |

**Conclusions:** Although the BCT taxonomy was helpful as a starting point to induce behavioral change in self-management, firstly the problems related to self-management and their determinants must be clear. Afterwards, the parameters of the BCTs and patients' preferences need to be taken into account when translating these techniques into the self-management program.
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## Physiotherapy

AB1093-HPR **INVESTIGATION OF HAND FUNCTIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune, chronic disease that may start with the involvements of small joints like hand and fingers in many patients. Hand problems can vary considerably from mild arthralgia to severe deformed hands. The most common problems are pain, stiffness, weakness, numbness and difficulty in daily living activities clinically. Inhibition in hand functions effects daily living activities and increases disability level.
**Objectives:** To investigate hand functions and disability level in women with SLE.
**Methods:** 27 women with SLE, 27 women with Rheumatoid Arthritis (RA) and 26 healthy controls were included in this study. Grip and pinch strength was assessed with dynamometer, dexterity was assessed with nine hole peg test (NHPT) and disability level was assessed with Turkish version of Disability Arm Shoulder and Hand Questionnaire (DASH). Differences between these measurements were analyzed.
**Results:** There were significant differences between patients with SLE and healthy controls ($p<0,05$) and also between patients with RA and healthy controls for all measurements. However, there were significant differences only in gross strength for both hands between patients with SLE and RA ($p<0,05$).
**Conclusions:** Hand functions and disability level were significantly different between patients with SLE and healthy controls although these measurements were generally similar between patients with SLE and RA. Hand involvement, disability and disfunction are known for patients with RA in literature. According to our results, hand disfunctions of patients with SLE are as prominent as patients with RA. So, in the treatment of SLE, hand functions should not be ignored and should be included in rehabilitation programme.
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## AB1094-HPR DEVELOPMENT OF A PATIENT REPORTED SELF-ASSESSMENT TOOL FOR RHEUMATOLOGY PATIENTS

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**Background:** Clinical outcome measures are required to define patient status and demonstrate the efficacy, quality and safety of clinical care to patients, clinicians and managers. Current assessments of the patient's perspective lack detail and clinical relevance and fail to reflect modern MDT care
**Objectives:** To develop a patient self-assessment tool that is clinically relevant, easy to administer, reproducible, practical and sensitive to change
**Methods:** Through a reiterative process at informal focus groups, patients described the facets of their lives affected by rheumatic illness. The transcripts were themed into 12 domains- communication, relationships, knowledge, anxiety, fatigue, pain, movement, strength, independence, mobility, work and social. These domains were clustered into 3 categories, emotional, physical and functional, each with 4 component statements defining that domain. The patients scored each of the 12 statements on a visual analogue scale (0–10) reflecting the patients' status in that domain at a time point.
Use of the assessment tool was repeated with the patient blinded to original scores, whenever required eg at a time when clinician and/or patient reported a change in disease status or to assess the result of some intervention, physical, therapeutic or both
**Results:** 212 patients have completed the paper based assessment tool each taking a maximum of five minutes on a minimum of two occasions at either physiotherapy clinic or day case attendance.

| Patient Cohort | 212 |
|---|---|
| Inflammatory Arthritis on DMARD | 70 |
| Inflammatory Arthritis on biologics | 31 |
| Osteoarthritis | 86 |
| Osteoporosis | 2 |
| CTD | 17 |
| Soft tissue | 6 |

Patient feedback on clarity of the tool and value was scored and documented on an EXCEL database as were diagnosis, disease status, medication group and work status for analysis and grouping purposes.
"Vertical" aggregated score of whole or part of patient cohort were analysed to:
- Define change in the 12 separate domains and 3 domain clusters.
- Indicate cumulative or disease/medication specific changes in domains with treatment or time.

"Horizontal" scores allowed 360 deg assessments of individual patients at a time point
- Showed changes for individual patients over time, indicative of patient outcome.

**Conclusions:** This self-reported assessment tool is easily understood and completed by patients. It accurately reflects their perception of their rheumatic health status and priorities at that time. When used with detailed history taking and examination, it conveys the impact of arthritis on their life and exposes particular problems to be addressed. It allows the clinician to confirm the findings of their assessment against the patient's perceptions. Joint goals can be established and expectations from planned interventions agreed thus enhancing the patient/clinician partnership.
The assessment can be repeated at any appropriate or agreed time point to gauge progress and response to treatment within the 12 domains individually or as a composite score. This tool provides a valuable and detailed patient perspective to compliment clinical examination and investigation, and inform decision making before treatment change is planned
**Disclosure of Interest:** None declared
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## AB1095-HPR EVALUATION OF THE STATIC FOOT FUNCTION IN PATIENTS WITH REDUCED MOBILITY IN THE COURSE OF RHEUMATIC DISEASES

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**Background:** Rheumatic diseases such as osteoarthritis (OA) and rheumatoid arthritis (RA), constitute the most frequent pathological states leading to the development of foot deformities, which reduce the quality of life and cause disability.
**Objectives:** The aim of the present study was to compare the results of plantoconturographic examination, obtained by means of a computer podoscope, in OA and RA patients. Special attention was paid to the differences in the values of each parameter determining the level of foot function.
**Methods:** The study was conducted on 94 female patients divided into two groups according to the type of disease. There were 54 patients with RA and 40 with OA. The control group consisted of 34 healthy women. The plantographic assessment of static foot structure was carried out by means of a device for computer-aided foot examination.
**Results:** A fallen transverse arch of the right foot was statistically much more frequent in the RA patients than in OA patients or the control group. Significant differences in the values of the Wejsflog index were observed between RA patients and the control group. Similarly, there were statistically significant differences in the values of the hallux valgus angle ($\alpha$) for the right foot between RA and OA patients vs. the control group, as well as between OA patients and the control group.
**Conclusions:** Rheumatic diseases predispose patients to the disturbances of static foot function. The obtained results highlight the importance of diagnosing foot statics disorders in the prevention of destructive changes affecting the functioning of OA and RA patients.
**Acknowledgement:** foot function, mobility, plantoconturography, RA patients, OA patients
**Disclosure of Interest:** None declared
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## AB1096-HPR USE OF PHYSIOTHERAPY AND EXERCISE PREFERENCES IN PEOPLE WITH ANKYLOSING SPONDYLITIS IN THE NETHERLANDS AND SWITZERLAND

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**Background:** Physiotherapy is a cornerstone in the management of ankylosing spondylitis (AS) [1]. Exercise interventions should be based on the available evidence as well as the patients' experiences and expectations.
**Objectives:** To survey the use of individual and group physiotherapy and exercise preferences in people with AS from the Netherlands (NL) and Switzerland (CH).
**Methods:** In NL, the questionnaires were sent by post-mail to 458 patients registered in hospitals in the Leiden area. In CH, an online survey was conducted. The link to the questionnaire was sent to 1742 German speaking members of the Swiss Ankylosing Spondylitis Association.
**Results:** Response rate was 45% (n=206) in NL and 29% in CH (n=507). Dutch and Swiss participants had a similar mean age (56 (SD±15) vs 53 (SD±13) years, but the Dutch sample consisted of less women (31% vs 48%), had a longer mean disease duration (23 [range 1–58] vs 14 [1–66]) and was less healthy according to ASAS health index (6 [1–16] vs 4 [1–16]).
44% and 84% of the Dutch and 28% and 54% of the Swiss have currently or had at least once in the past respectively, individual physiotherapy treatment. The major reason for stopping was "I could do the exercises at home myself" in both countries. 9% and 31% of the Dutch and 30% and 27% of the Swiss are currently, or were in the past respectively, participating in group physiotherapy. The major reasons to stop were "It was too heavy for me" in NL (28%) and "It consumed too much of my time" in CH (7%).
8% and 18% of the Dutch and 20% and 23% of the Swiss have currently or had at least once in the past respectively, participated in hydro-group physiotherapy. Reasons to stop were "I did not experience any positive effects" in NL (28%) and again "It consumed too much of my time" in CH (7%). When asked about preferences regarding exercising without supervision, 40% of the participants in NL and CH wanted "individually designed exercise programmes" and approximately 50% in NL and CH to exercise self-responsible regarding mode, intensity, and frequency.
When asked about their preferred type of supervised exercises, around a quarter of the answers in both countries supported each: "AS specific exercise groups", "fitness centers" and "individual physiotherapy", however the Swiss clearly preferred AS specific exercise groups (47%).
With respect to the supervision and physiotherapists specialized in AS as supervisors (38% NL vs 60% CH).
Their willingness to pay for a supervised group session was 8€ in NL and 25€ in CHF.
**Conclusions:** There are differences in the use of physiotherapy in both countries. But there are also similarities between the Dutch and Swiss AS patients regarding their preferences for exercises, except the financial valuation of group exercise classes. Findings may help to further develop patient-centred services in both countries. Especially, enabling people with AS to perform exercises independently would meet their needs and might enhance their daily physical activity.
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## AB1097-HPR A PAIN SCHOOL REHABILITATION PROGRAM FOR PATIENTS WITH CHRONIC WIDESPREAD PAIN – A QUALITATIVE INTERVIEW STUDY

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**Background:** The prevalence of chronic widespread pain is approximately 10–15% and it is a common problem in primary health care. Being female and older is associated with higher prevalence. Chronic pain is generally associated with low activity level, low work capability, and negative health consequences. Studies of education and exercise have shown effective results for patients with chronic pain. This pain school rehabilitation program "Knowledge for life" has been developed by professionals together with the Swedish Rheumatoid Association for use in primary health care, but is not previously evaluated.
**Objectives:** To evaluate the experience of participation in the pain school rehabilitation program Knowledge for life in patients with chronic widespread pain
**Methods:** 12 women (age 25–72 years) with chronic widespread pain were included in this qualitative interview study set in primary health care. Semi-structured interviews were held 10 weeks after participating in four weekly group sessions. Interviews were performed by two authors and transcribed verbatim. Data was analyzed through content analysis according to Graneheim and Lundman (1). Analyzes were performed by the first author, but was controlled by co-authors for agreement. Results are presented through themes and categories. Informed consent were signed by all participants.
**Results:** The preliminary results are based on four interviews. The analysis resulted in five themes, which are *the meaning of the group, positive experience of movement, change of relationship to self, change of relationship to pain, and external circumstances of change. The meaning of the group* reflects upon the shared experiences and a sense of belonging deriving from the group discussions. *Positive experience of movement* describes the participants' experiences of physical activity and exercise related to their body, group activities and change of habit and attitude towards movement in general. The participants described a *change of relationship to self* and *change of relationship to pain* related to increased knowledge, acceptance, and active strategies. *External circumstances to change* was also identified describing the leader and setting to be important factors in stimulating change.
**Conclusions:** Participation in a pain school rehabilitation program contributed to increased knowledge and awareness about pain and about the self for the patients with chronic widespread pain in the present study. They also reported positive experiences of group sessions and of physical activity and exercise. The program provides a structure of rehabilitation for patients with chronic widespread pain.
**References:**
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## AB1098-HPR COMPARISON BETWEEN KINESIOTAPING AND COLD THERAPY ON MUSCLE STRENGTH FUNCTIONAL PERFORMANCE OUTCOMES AFTER TOTAL KNEE ARTHROPLASTY: PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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**Background:** Total knee arthroplasty (TKA) are increasing steadily each year. Ninety percent of patients reported reduced pain, improved functional ability, and greater health related quality of life after TKA. Kinesiotaping (KT), a type of elastic tape that is being increasingly used for the management of pain and oedema after surgery (1). Cold therapy (CT) can also help relieve pain and swelling during early postoperative period (2). These two application may have impact on functional performance outcomes in patients with TKA. The number of studies that include KT in the rehabilitation process is increasing, but there isn't any study that compare KT application and CT after TKA.
**Objectives:** To compare the effectiveness of kinesiotaping and cold therapy on muscle strength and functional performance outcomes in patients with TKA during early postoperative period.
**Methods:** Fifteen patents with TKA randomly assigned to control, KT and CT groups (nC=nKT=nCT=5). KT group received KT for lymphatic correction and rectus femoris facilitation technique. CT group received CT immediately after operation and following postoperative days. After surgery, all patients received standard post-operative treatment. After operation, pain intensity, active range of motion and knee function score [Hospital for Special Surgery (HSS) score] and walking speed was evaluated using the Iowa Ambulation Velocity Scale. Isometric muscle strength measure of quadriceps femoris and hamstring muscles assessed by Hand-Held Dynamometer. All measurements evaluated at the discharge. One way *ANOVA* was used in statistical analysis.
**Results:** There was a significant group interaction in pain scores and active range of motion of knee (p=0.005). Following up this interaction, the KT group and CT group have lower pain score at discharge in comparison with control group (p=0.019). The KT group and CT group have higher range of motion of knee flexion at discharge (p=0.017). However, there was no significant differences between KT group and CT group ($p>0.05$). There was also significant group interaction in functional performance outcomes (p=0.033). KT group and CT group have better HSS score (p=0.010) and walking speed (p=0.013), but KT group and CT group *have no superiority* over each other in terms of functional performance outcomes ($p>0.05$). There was no significant in quadriceps femoris (QF) and hamstring muscles in groups.
**Conclusions:** Our preliminary results suggest that KT and CT reduce postoperative pain in patients with TKA in inpatient period. KT group and CT group have better knee functional score. Possible mechanisms of better functional performance in KT and CT group could be due to lower pain score. Functional activities may have limited by high level of pain after surgery. Both KT and CT are cost-effective to achieve sufficient pain relief following TKA. Sufficient pain relief may influence functional performance. However, both KT and CT have no impact on muscles strength. In conclusion, KT and CT can be used with standard post-operative treatment in patients with TKA, and they have no *s*uperiority over each other. However, future study on a larger sample of subjects is needed to attain more clear results.
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## AB1099-HPR COMPARISON OF THE EFFECT OF DAILY LIVING ACTIVITIES AND DEPRESSION ON QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS

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**Background:** Increasing activity and improving function are valuable parameters to prevent disability (1,2). The relationship between the functional impairment in depression and the activities of daily living was well known in terms of the quality of life in chronic diseases (3). However, studies comparing these effects on various rheumatic diseases were not sufficient.
**Objectives:** This study was conducted to compare the effects of depression and activities of daily living on quality of life for the patients with two different rheumatic diseases (Ankylosing Spondylitis (AS) and Rheumatoid Arthritis (RA)).
**Methods:** 265 patients with AS and 111 patients with RA were included in the study. The demographic data were collected for two groups. Mean age of the study group was 39.88±13.33. All patients were evaluated with disease-specific questionnaires according to their diseases. The patients with AS were asked to fill the Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) for quality of life, and the Rheumatoid Arthritis Quality of Life Questionnaire (RAQoL) were used for RA patients. Beck Depression Index (BDI) was used to assess depression levels of the subjects, and Health Assessment Questionnaire (HAQ) to assess activities of daily living in both groups.
**Results:** A mild and positive correlation was found between HAQ ($p<0.001$, r=0,564), BDI ($p<0.001$, r=0.477) and RAQoL scores. Similarly, a mild and positive correlation was found between HAQ ($p<0.001$, r=0.513), BDI ($p<0.001$, r=0.443) and ASQoL scores. In all patients, there was a fair-mild positive correlation between HAQ and BDI scores ($p<0.001$, r=0.350) (Table 1).

Table 1. Correlation between all variables

| | BDI | ASQoL | RAQoL |
|---|---|---|---|
| HAQ | r=0,350 | r=0,513 | r=0,564 |
| | $p<0.001$ | $p<0.001$ | $p<0.001$ |
| BDI | | r=0,443 | r=0,477 |
| | | $p<0.001$ | $p<0.001$ |

**Conclusions:** It is concluded that the depression level and the activities of daily living has similar effects on the quality of life for RA and AS patients. Also depression should be taken into consideration in both rheumatic diseases.
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## AB1100-HPR EFFECT OF RESISTANCE TRAINING IN WOMEN WITH JOINT HYPERMOBILITY – PRELIMINARY RESULTS OF A RANDOMISED CONTROLLED TRIAL

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**Background:** Little is known about the clinical management of persons with generalized joint hypermobility (GJH). Affected persons are often restricted in performing sports or leisure activities, as well as during work, due to pain and disability (1). Adequate muscle strength for movement control might be an important issue to overcome these restrictions. Resistance training has the possibility to improve muscle strength (2), but so far no study investigated how resistance training influences strength and muscle size in women with GJH.
**Objectives:** To evaluate the effects of a 12-week resistance training program on muscle properties of women with GJH.
**Methods:** This pragmatic randomised controlled trial included 51 hypermobile women (mean age 26.5, sd 4.5 years) with a Beighton-score of six or more (3). 27 women performed for 12 weeks a guided resistance training twice weekly and 24 women did not exercise. Before and after the 12 weeks maximum isometric strength of knee extensors and flexors was measured, which was the primary outcome. Additionally muscle cross-sectional-area (mCSA) of the thigh was measured at 33% above the knee, using peripheral quantitative computer tomography (pQCT). Data were analysed on an intention-to-treat basis. Differences between groups were tested with independent t-test at a significance level of p=0.05.
**Results:** The groups were comparable at baseline. Change of maximum strength of knee extensors in the training group was 6.3 N (sd 57.7, CI -16.5 to 29) and in the control group 8.3 N (sd 42.1, CI -9.4 to 26.1), with no significant difference between groups. Similar results were seen for knee flexors: change in training group was 8.0 N (sd 59.8, CI -15.6 to 31.7) and in control group 16.1 N (sd 42.8, CI -2.0 to 34.2). Muscle CSA of the thigh in the training group showed a significant increase (194 $mm^2$, CI 78 to 310 $mm^2$), compared to the control group (46 $mm^2$, CI -25 to 118 $mm^2$; p=0.031). Muscle mass at the thigh significantly increased 19.1 mg (sd 27.3, CI 8.3 to 29.9) in the training group, compared to the control group with 4.3 mg (sd 14.4, CI -1.8 to 10.33) mean change. Muscle density, however, showed no change in both groups.
**Conclusions:** The 12-week resistance training did not change isometric knee muscle strength, but led to a significant increase of mCSA of the thigh in women with GJH. However, this difference was only 2.4% and thus may not be clinically significant. In strength testing possibly no change was seen because the dynamic training could not be transformed to the isometric test condition and the intensity of the training might not have been high enough. The detailed analysis of the training protocols will provide further details concerning this issue. However, the small increase in muscle area may indicate that strength training is a possible option for these hypermobile women. Further analysis of the additional measurements in this trial, may give more insight into changes in pain or disability. Further research should investigate if the muscle increase could be optimized by a more intense or better supervised training.
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## AB1101-HPR QUALITY OF LIFE IN PATIENT WITH ESTABLISHED RHEUMATOID ARTHRITIS: A QUALITATIVE STUDY

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**Background:** Fatigue, pain, stiffness and impaired physical function are some of the most pronounced symptoms in rheumatoid arthritis (RA) that may affect quality of life. Quality of life is an individual experience composed of a wide range of factors, including physical health, psychological state, level of independence, social relationships, and the patients' relationship to salient features of their environment. There is a need to describe and assess quality of life in chronic diseases like established RA. Previous research has mainly focused on disease-specific instruments for assessing quality of life. A deeper understanding of patients' experience of quality of life in established RA is important in both clinical research and daily clinical practice.
**Objectives:** To describe variations in patients' experiences of quality of life in established RA
**Methods:** The study had a qualitative design with a phenomenographic approach, including 22 interviews with patients from the Swedish BARFOT (Better Anti-Rheumatic FarmacoTherapy) cohort, BARFOT, a long time follow up study of early RA. Patients were strategically selected by gender (14 women and 8 men), age (30 to 84 years old), disease duration (8–23 years), function as measured by HAQ (0–1.38), and quality of life as measured by EQ5D (0.52–1.00). The interviews were recorded, transcribed verbatim and coded into categories.
**Results:** Four categories emerged from the patients' experiences of quality of life in established RA: well-being, freedom, empowerment, and participation. Quality of life as well-being meant pleasure and being physical active. Quality of life as freedom meant dependence or independence in the ability to manage daily life activities. Quality of life as empowerment meant different coping strategies, such as positive thinking and resources to manage fatigue, pain and physical function. Quality of life as participation meant togetherness in different contexts with other people.
**Conclusions:** Quality of life in established RA could be understood by the patients in different ways. The patients experienced quality of life as well-being, freedom, empowerment, and participation. This is important knowledge when evaluating the concept of quality of life in RA research, and for health professionals when promoting quality of life in patients with RA.
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## AB1102-HPR "IF A JOINT IS HOT IT'S NOT THE TIME": HEALTH PROFESSIONALS' VIEWS ON DEVELOPING PHYSICAL ACTIVITY INTERVENTIONS FOR PEOPLE WHO HAVE RHEUMATOID ARTHRITIS

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**Background:** Although numerous physical activity interventions exist for people who have RA sustaining physical activity levels after an intervention is completed has been challenging. Involving key stakeholders is important when designing complex interventions which target behaviour change [1]. Health professionals (HPs) working in rheumatology can provide unique views on the design of interventions and can highlight potential challenges/facilitators to a proposed intervention for people who have RA [2–3].
**Objectives:** This study aimed to explore the views of HPs on physical activity in people who have RA, and the design of a behaviour change intervention to promote physical activity participation amongst people who have RA.
**Methods:** We used a qualitative methodology and constructivist approach. Interviews were conducted by phone, with the use of an interview guide. Interviews were transcribed and analysed using thematic analysis. The interview transcripts were read, notes made and ideas formulated to facilitate coding. The research team searched for patterns, analysed and coded the data, and generated sub-themes and themes. Themes were reviewed by the research team to check if the themes worked in relation to the coded extracts and the entire data set.
**Results:** 14 interviews were conducted (rheumatologists n=7, physiotherapists n=4 and clinical nurse specialists n=3). Mean clinical practice experience was 15 years (range 3–34 years, SD ±8.76 years). Three key themes were generated: "*Personal opinions", "Supporting physical activity*" and *'An ideal world'*. Although HPs viewed physical activity as important, recommending it was largely based on a persons' disease status rather than empirical evidence. There was also a strong feeling that physical activity should reduce during a disease flare-up. Supporting physical activity in clinical practice was discussed as being through the provision of information, goal setting and behaviour monitoring. Having contact with a HP was also thought to support physical activity. The "ideal world" was discussed with resources being highlighted as a key challenge to interventions in clinical practice, e.g. lack of time, staff numbers. Some participants felt that a group setting was most feasible in clinical practice whilst others preferred a 1:1.
**Conclusions:** HPs believe physical activity is important for people who have RA, although there is uncertainty regarding physical activity recommendations for this population. Thus there is scope to increase HPs' knowledge of recent evidence. Views varied on how an intervention to promote physical activity should be delivered but consideration of barriers to delivery in clinical practice is important.
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AB1103-HPR **RELATIONSHIP BETWEEN PHYSICAL AND MENTAL STATUS AND KINESIOPHOBIA IN PATIENTS WITH ARTHROPLASTY DURING INPATIENTS PERIOD**

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**Background:** Kinesiophobia is simply defined as a fear of movement and physical activity.It can be seen in patients as a result of any injury, which results in pain or a fear of injury recurrence. It leads to decreased motion and disuse that may result in a chronic pain syndrome and decreased physical function. Especially arthroplasty patients who suffer from osteoarthritis before the operation, physical and mental state of the patients affected due to pain and bigger incision areas (1). This situation can cause kinesiophobia, mental problems and a lower quality of life.
**Objectives:** The purpose of this study was to investigate the relationship between kinesiophobia, mental condition and quality of life in patients undergoing arthroplasty.
**Methods:** One hundred ninety one arthroplasty patients [76 total knee arthroplasty (TKA) and 115 total hip arthroplasty (THA)] were included in the study. Quality of life was evaluated with the *12-Item Short Form Health Survey* (SF-12) and European Quality of Life-5 Dimensions (EQ-5D), kinesiophobia was evaluated with the TAMPA Scale and anxiety-depression were evaluated with the Hospital Anxiety and Depression Scale (HADS) preoperatively and at discharge. The patients' daily health condition were evaluated with EQ-5D Visual Analogue Scale (EQ-5DVAS). All five components of EQ-5D (mobility, self-care, usual activities, pain and anxiety/depression), EQ-5DVAS and two components of SF-12 [physical component (PCS-12) and mental component (MCS-12], HADS, TAMPA Scale were used in the statistical analysis. Bivariate correlation and coefficient pearson were used in the analysis ($p<0.05$).
**Results:** Both gender and age parameters showed similarity between patients with THA and patients with TKA. There was a correlation between TAMPA and both pre-operative scores [TAMPA/SF-12 Total (r=0.204), TAMPA/EQ5D Total (r=0.226), TAMPA/HADS Anxiety (r=0.243), TAMPA/ HADS Depression (r=0.320)] and discharge scores [TAMPA/SF-12 Mental component (r=0.227), TAMPA/SF-12 Physical component (r=0.150), TAMPA/SF-12 Total (r=0.256), TAMPA/EQ5D Mobility (r=0.221), TAMPA/EQ5D Self-Care (r=0.129), TAMPA/EQ5D Usual Activities (r=0.143), TAMPA/EQ5D Pain/Discomfort (r=0.247), TAMPA/EQ5D Anxiety/Depression (r=0.268), TAMPA/HADS Anxiety (r=0.341), TAMPA/ HADS Depression (r=0.313)].
**Conclusions:** According to the results of this study, SF-12, EQ5-D and HADS have been found to correlate with TAMPA. This situation shows that the deterioration in quality of life is related to anxiety-depression and kinesiophobia. The reason of having a low score on TAMPA scale could be associated with high pain level. This high pain level limits the daily living activities such as walking. Daily living activity limitation in patients with THA and TKA due to pain, kinesiophobia could lead to more depression. Researchers considering this relationship might be beneficial to improve outcomes of the treatment.
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AB1104-HPR **ENGAGEMENT WITH PEOPLE WHO HAVE INFLAMMATORY ARTHRITIS, ON THEIR SLEEP QUALITY, SLEEP DISTURBANCES AND PHYSICAL ACTIVITY: A SURVEY OF IRISH HEALTH PROFESSIONALS IN RHEUMATOLOGY**

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**Background:** Sleep disturbance is common in people who have inflammatory arthritis and can contribute to disability, symptomatology, and increased healthcare use. Poor sleep quality and disturbances may exacerbate pain in this disease, which may further lead to reduced levels of physical activity. Little is known regarding the current practice of Health Professionals in Rheumatology on their engagement with patients in discussing their sleep quality and disturbances therefore, it is important to investigate if there are any educational needs in this important area of practice.
**Objectives:** To investigate the awareness of Irish Health Professionals in Rheumatology on their patients' engagement when discussing sleep quality, sleep disturbances and physical activity, among Irish people who have Inflammatory Arthritis.
**Methods:** Members from the Irish Rheumatology Health Professionals Society (IRHPS) (n=43) were invited to participate in a cross-sectional survey hosted on SurveyMonkey$^{(R)TM}$. Ethics approval was received through the University of Limerick. Descriptive statistics, Chi-square tests/Fisher's exact tests were used to analyse the data using SPSS v22.
**Results:** Twenty eight (65%) Health Professional's responded. Results found the mean number of years qualified to be 16.93 (SD 6.82), mean number of years working in Rheumatology to be 10.07 (SD 4.04) and 40% of respondents reporting half of their patient workload coming from people who have inflammatory arthritis. Just 52% discuss sleep with their patients with 46% mentioning fatigue as their main reason when enquiring. Of those who do discuss sleep, 100% of their patients mentioned "pain" and "waking up in the middle of the night or early morning" as disturbances when discussing their sleep, while 67% reported "taken prescribed or over the counter medication" to help with their sleep. There was no statistically significant association between longer years qualified, more years working with people with inflammatory arthritis or health profession, when discussing sleep. When using the SQUASH questionnaire, Health Professional's physical activity levels were 2,248 minutes per week, which exceeds the American College of Sports Medicine (ACSM) physical activity guidelines however, is low compared to other physical activity Health Professional surveys from European countries.
**Conclusions:** Only half of Irish Health Professional's discuss sleep with their patients, with fatigue as the main reason when enquiring. Health Professional's meet the physical activity guidelines however, are less active than their European peers. There is a need to develop education and training for physiotherapists in the importance of enquiring about their patients sleep quality and disturbances and the potential impact it has on their physical activity levels. In addition, the effects of physical activity interventions on poor sleep quality and disturbances needs to be examined so that Health Professional's are in a better position to promote health and well-being in people with Inflammatory Arthritis, in this important area of practice.
**Disclosure of Interest:** None declared
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AB1105-HPR **EVALUATING OF RHEUMATOLOGIC PATIENTS' VIEWS ON PHYSIOTHERAPY AND REHABILITATION PROGRAMS: A PILOT STUDY**

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**Background:** Rheumatologic diseases are one the state that causes loss of function, despite the use of very effective conservative and surgical approaches in treatment in recent years (1). In physiotherapy and rehabilitation of rheumatologic diseases, protecting the patients' functional status for the prevention of disability improves the quality of life of patients (2). Therefore, it is very important that practice of physiotherapy and rehabilitation starts and implements with medical treatment as early as possible (1,2).
**Objectives:** The aim of this study was to assess rheumatologic patients' knowledge, expectation and satisfaction about physiotherapy and rehabilitation programs.
**Methods:** In this study, 36 rheumatologic patients participated voluntarily who attended physiotherapy and rehabilitation programs in various health centers. The data on age, gender, economic status, diagnosis, habits of the participating individuals were recorded by researchers. For assessing the patients' views on physiotherapy and rehabilitation program, a questionarre was prepared by researchers which investigated patients' level of knowledge about their diseases, physiotherapists' duties, the aims of the applied treatment modalities. Also, the questionarre included the questions which examined patients' expectations, complaints and level of satisfaction for physiotherapy and rehabilitation program, changes in health quality and daily life after rehabilitation. The questionnaire was administered face to face to the volunteers.
**Results:** Of the 36 patients included, 20 (55.5%) were female and 16 (44.5%) were men. The mean age of individuals was 47.58 ± 11:23. 60% of rheumatologic patients expressed that physiotherapists did not define the therapists' duties and rehabilitation programme. 72% of rheumatologic patients expressed that physiotherapists did not explain the purpose of the treatment modalities. 46% of rheumatologic patients expressed that they did not know the importance of rehabilitation. A significant positive correlation was found between increasing of physiotherapists' explanations which were related to rehabilitation program and patients' satisfaction ($p<0.05$). It was determined that patients who graduated from university were more conscious about their diseases and attended therapy sessions more regularly. 78% of patients who began to work with physiotherapist in acute period stated that rehabilitation programme facilitated their daily life. 23% of patients who began to work with physiotherapist in chronic period stated that rehabilitation programme facilitated their daily life. A significant positive correlation was found between starting home exercise programme in acute period and reduction of patients' complaints ($p<0.05$). The common proposal of rheumatologic patients to physical therapists was that introducing and explaining of rehabilitation programme in all respects.
**Conclusions:** This study indicates that when rheumatologic patients start to work with physiotherapists in acute period and physiotherapists inform their patients about therapy in every respects, improvements of patients increase in daily life.
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## AB1106-HPR ALTERATION IN BODY POSTURE IS RELATED TO DECREASED FLEXIBILITY IN ADOLESCENTS WITH A HISTORY OF LOW BACK PAIN: A PILOT STUDY

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**Background:** Low back pain (LBP) is a significant public health problem among adolescent population. Postural alterations and decreased flexibility have been considered as possible risk factors for adolescent LBP. Thus, examination of posture and muscle flexibility is essential for determining any potential contributing factors (1–3). However, studies addressing the relationship between posture and flexibility in the adolescents with a history of LBP are limited.
**Objectives:** To examine whether the alteration in three-dimensional (3D) body posture is related to flexibility in adolescents with a history of LBP.
**Methods:** Fourteen adolescent students (9 female, 5 male, median age 14 years) participated in this study. For 3D evaluation of posture, internet-based postural assessment system was used. Thirteen reflective markers were placed on anatomical landmarks of subjects. Three digital photographs were obtained in upright stance (antero-posterior, left-right lateral) and were analyzed through the system. Postural displacements of head, rib cage, and pelvis were calculated as rotations in degrees and translations in millimeters. Alteration in body posture (head, rib cage, and pelvis) was evaluated using posture index which is total postural displacements score. In this system, total score is 96 points. The higher posture index score indicates more severely displaced posture. Flexibility was measured by a sit-and-reach test. Spearman's rank correlation coefficient (rho) was used to evaluate the association between the measured parameters. The significance level was set at $p<0.05$.
**Results:** As a result, 14.3% (n=2) of the adolescents had slight, 71.4% (n=10) had significant and 14.3% (n=2) had a moderate displacement in their posture according to posture index score. Participants had a median sit-and-reach score of 21 cm and a median posture index score of 17 points. Strong negative correlation was observed between posture index score and sit-and-reach test (rho=-0.610, p=0.020).



Table of Grades for Posture Index™

| Region | | | | | | Total Per Region |
|---|---|---|---|---|---|---|
| Head | 0 | 0 | 0 | 0 | 6 | 6 |
| Ribcage | 0 | 0 | 1 | 0 | 2 | 3 |
| Pelvis | 4 | 0 | N/A | 0 | 2 | 6 |
| Totals | 4 | 0 | 1 | 0 | 10 | 15 |
| Total Posture Index™ | P.I. = 15 , SIGNIFICANTLY DISPLACED | | | | | |

**Conclusions:** In conclusion, this pilot study suggests that alteration in body posture may be related to decreased flexibility in adolescents with a history of low back pain. Future studies should attempt to determine postural changes, flexibility evaluations and associations between these parameters more extensively.
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## AB1107-HPR LONG TERM EXERCISE TRAINING IMPROVES THE TOTAL HIP ARTHROPLASTYPATIENTS' ABILITY TO FORGET THEIR ARTIFICIAL JOINT

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**Background:** Total Hip Arthroplasty (THA) is among the most widely performed procedures in orthopedic practice and outcome studies consistently showed an overall satisfaction by both patients and physicians.The purpose of this study was to determine effect of exercise duration on the ability to forget the artificial joint, in hip osteoarthritis patients who underwent THA.
**Objectives:** Forty-two patients (female=26, male=16) who underwent unilateral THA were included in the study. Patients were divided into two groups either to do exercise for less than 6 months (Group I; short term exercise, n=24) or over 6 months (Group II; long term exercise, n=18). Mean age was 53.9± 15.1 years, mean Body Mass Index (BMI) was 27.2 ± 5.2 kg/m$^2$ in Group I and mean age was 57.5 ± 13.3 years, mean BMI was 27.2 ± 5.2 kg/m$^2$in Group II, respectively.
**Methods:** Forgotten Joint Score (FJS) was applied to detect the patients' ability to forget the artificial hip joint after THA surgery. Western Ontario and McMaster Osteoarthritis Index (WOMAC) pain, stiffness and activity of daily living (ADL) questionnaire were used to determine the functional status. Intensity of pain was measured with visual analog scale (VAS). Statistical analysis of the data was performed with Mann Whitney-U test.
**Results:** There were no differences in WOMAC stiffness scores (p=0.146) between groups. WOMAC pain scores (p=0.003), WOMAC ADL scores (p=0.019), VAS scores (p=0.000) were better in Group II. FJS scores (p=0.005) were in favor with Group II which the patients who were exercising more than 6 months.

| Variables | Group I (short term exe) Mean ±SD | Group II (long term exer) Mean± SD | p |
|---|---|---|---|
| Pain | 1 ± 1 | 3.2 ± 1.8 | p=0.000 |
| FJS | 53.2 ± 12.1 | 69.6 ± 22.2 | p= 0.005 |
| WOMAC pain | 3 ± 3.3 | 6.6 ± 3.9 | p=0.003 |
| WOMAC stiff | 1.3 ± 1.8 | 2.1 ± 1.8 | p=0.146 |
| WOMAC adl | 11.6 ± 8 | 19.7 ± 12 | p= 0.019 |

**Conclusions:** Exercise training over 6 months improves the THA patients' ability to forget their artificial joint.
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## AB1108-HPR AQUATIC EXERCISE FOR WOMEN WITH PERSISTENT KNEE PAIN. A PILOT RANDOMISED CONTROLLED TRIAL

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**Background:** Persistent Knee Pain (PKP) is a common cause of disability in Europe[1]. Therapeutic exercise, education and weight loss are central to the management of PKP[2]. Aquatic therapy (AT), (therapeutic exercise in water) is recommended but the optimal effective dosage is unknown.
**Objectives:** To investigate the acceptability and efficacy of six sessions of AT and self-management advice compared to self-management advice only on self-reported pain, function and general health in adults with PKP.
**Methods:** This two arm, single blinded, pilot, randomised controlled trial received ethical approval from the Joint UCL/UCLH Research Ethics Committee (08/H0715). A convenience sample of adults ≥50 years old with self reported knee pain of >12 weeks were recruited from an inner city physiotherapy department. They were randomly assigned to receive either 6 weekly sessions of group AT consisting of 30–40 minutes strengthening, stretching and balance exercises facilitated by a physiotherapist or a comparison group. All participants attended a single session of self-management advice and prescribed home exercises by a physiotherapist. Process outcomes: number of people willing to enter the study and adverse events were recorded by the researcher, attendance at AT sessions was recorded by treating physiotherapists. Clinical outcomes: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Pain visual analogue scale (0 -10cm VAS), SF12 and six minute walk distance (6MWD) were assessed at baseline and 6 weeks by a researcher blind to participant group allocation.
Process outcomes were evaluated using descriptive statistics. Clinical data were

analysed on an intention to treat basis and between group differences in mean change were investigated using Analysis of Covariance adjusted for baseline differences. Significance was accepted at $P<0.05$ level.
**Results:** 34 eligible patients were invited to participate in the study. 14 (41%) women (mean age 63 (7.46) years) were enrolled into the trial and 13 (93%) people completed the 6 week assessment. Compliance was 98% in the AT group. No adverse effects were reported. All clinical outcomes improved in the AT group in pre-post scores (mean change (95% CI)): WOMAC -17.7 (3.9, 31.6), VAS -3.4 (-.2, 7.0) SF12-Physical 4.3 (-16.2, 7.5), SF12-Mental 8.2 (-16.7, 0.4), 6WMD 48.6m (-102.3, 5.2) but not the comparison group: WOMAC 2.6 (-11.4, 6.3), VAS 0.5 (-1.5, 0.5), SF12-Physical 0.009 (-3.8, 3.7) and SF12-Mental 1.2 (-6.0, 3.7), 6MWD 22.9m (-62.6, 16.6). There were between group differences in change in WOMAC over 6 weeks (20.3 (-33.9, -1.0) p=0.039), the WOMAC pain subscale (5.4 (-8.6, -0.8) p=0.022) and SF12 mental subscale (6.982 (0.4, 13.2) p=0.04), but not other outcomes, favouring the AT group.
**Conclusions:** Whilst our study had a good recruitment rate, only women agreed to participate. Attendance at AT was high and no adverse events were reported. This study suggests that 6 sessions of AT improves PKP and function but not walking distance compared to self management only in women. Understanding the reasons why men did not wish to participate in the study warrants further investigation.
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### AB1109-HPR COMPARISON OF JOINT POSITION SENSE AT END RANGE AND MID RANGE IN FROZEN SHOULDER

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**Background:** Frozen shoulder (FS) is characterized by a painful, gradual loss of both active and passive glenohumeral motion resulting from progressive fibrosis and contracture of the glenohumeral joint capsule. Deformation of capsuloligamentous tissue is believed to stimulate mechanoreceptors in the tissue and provide the central nervous system with proprioceptive information. It was shown by studies that joint position sense acquity is good near the end of motion in healthy shoulders. There is not enough study about JPS in FS.
**Objectives:** The aim of this study is to compare the effect of mid or end range of motion on joint position sense (JPS) in patients with FS.
**Methods:** Twenty five patients with FS (21 female, 4 male; mean age 53±6 years; age range 44–67) were included in this study. Mean Body Mass Index (BMI) was 29.02±4.89. 11 dominant and 14 nondominant shoulders were measured. JPS was assessed with active repositioning process by inclinometer in flexion, elevation and rotations at mid range (MR) and end range (ER).
**Results:** Error scores at ER were lower than at MR in flexion (p=0.44), elevation (p=0.01) and internal (p=0.00) and external (p=0.19) rotations. There were significant difference in elevation and internal rotation ($p<0.05$) (Table 1).

Table 1. Joint position sense at mid range and end range

| | MR (X ± SD) | ER (X ± SD | p |
|---|---|---|---|
| Flexion | 4.90±2.99 | 4.37±2.73 | 0.44 |
| Elevation | 6.97±4.49 | 4.60±3.62 | 0.01 |
| Internal rotation | 6.70±3.96 | 3.70±2.15 | 0.00 |
| External rotation | 4.64±3.36 | 3.52±2.36 | 0.19 |

Measurements are expressed in degrees. X: mean, SD: standard deviation. $p<0.05$

**Conclusions:** Our study showed that JPS at ER is better than MR. Especially elevation and internal rotation that more affected motions in FS were more sensitive to JPS. It was thought that at end ranges capsuloligamentous structure is stimulated more than mid ranges.
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### AB1110-HPR INVESTIGATION OF FEAR AVOIDANCE BELIEFS IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Ankylosing Spondylitis is an chronic, inflamatory, systemic illness which effect on sacroiliac joints and spine. Chronic pain is an important problem in ankylosing Spondylitis patients (1). Catastrophic beliefs, which is developed by patients who experienced pain for along time, cause avoidance of use, defect and depression (2). As far as some studies there is a correlation between pain and psychological state (3). There is no study which investigate factors related with fear avoidance beliefs.
**Objectives:** The aim of this study was to investigate factors that association with fear avoidance beliefs in ankylosing spondylitis.
**Methods:** 51 patients with ankylosing spondylitis, who applied to Rheumatology Department of Trakya University Faculty of Medicine Hospital, were included in this study. Spinal mobility evaluated by Bath Ankylosing Spondylitis Metrology Index (BASMI), function evaluated by Bath Ankylosing Spondylitis Functional Index (BASFI); disease activity defined by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). To evaluate quality of life, Ankylosing Spondylitis Quality of Life (ASQoL) is used. The Fear Avoidance Beliefs Questionnaire (FABQ) is used to evaluate the fears, beliefs, and avoidance behaviors of patients with AS in relation to physical and work-related activities. Short Physical Performance Battery (SPPB) is used for evaluate the functions of mobility. C-reactive protein (CRP) and Erythrocytes sedimentation rate (ESR) were saved.
**Results:** Of the 51 patients included, 12 (23,52%) were female and 39 (76,47%) were male. There was no meaningful statistical difference in FABQ scores between active and inactive disease groups.Physical activity subscale score of FABQ was associated with age (r=0,355, p=0.014), ESR (r=-0.361 p=0.042), quality of life (r=0.428, p=0.0002), BASFI scores (r=0,287, p=0,041), intermalleolar distance,which is BASMI's subscale and assess hip mobility (r=-0,452, p=0,002) and SPPB (r=-0.303, p=0,041). Work subscale of FABQ was associated with age (r=0,353, p=0,015), ASQoL (r=0.461, p=0,001), intermalleolar distance (r=-0,457, p=0,002).
**Conclusions:** There is an association between fears, beliefs, and avoidance behaviors of patients with AS in relation to physical and work-related activities and mobility function, quality of life, hip mobility. So we think preserving and developing techniques of mobility function will play a role AS treatment plan. And also we think new researches which investigate factors about fear avoidance beliefs in AS should be done.
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## Occupational therapy

### AB1111-HPR VALIDITY OF CANADIAN OCCUPATIONAL PERFORMANCE MEASUREMENT IN PATIENTS WITH UPPER LIMB DISORDERS IN TURKEY

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**Background:** The Canadian Occupational Performance Measure (COPM)[1] was developed to identify and prioritize *patient-specific* occupational problems and evaluate changes in these problems. In literature on the COPM, consensus exists about the feasibility of the COPM as an instrument to identify a wide range of problems in daily activities.[2,3] There is only one research that investigate the validity of COPM with Disabilities of Shoulder arm Hand Questionnaire (DASH) in upper limb disorders.[4] This study did not showed the correlations between COPM and DASH, only reported the percentages.
**Objectives:** The aim of our study was to determine the construct validity of COPM by investigating the correlations with two different upper limb functional questionnaires in Turkish patients with upper limb problems. Second aim of our study was to determine the occupational performance problems specific to upper limb in Turkish culture.
**Methods:** Physical therapy outpatients (n=l02, 70% female, age 49.1±16.6) with upper limb disorders were consecutively recruited. All participants completed the the Upper Limb Functional Index Turkish (ULFI-Tk) and the DASH Turkish-version

(DASH-Tk) criterion. COPM was conducted by qualified therapist who has 5 year experience of using COPM. Pearson correlation analyses were done between COPM and DASH-Tk, ULFI-Tk.
**Results:** The COPM performance demonstrated statistically significant relationship with DASH-Tk disability scores (r=-0.217;p=0.02) and with ULFI-Tk (r=-0.290; p=0.003). There were also significant relationship between COPM satisfaction scores and DASH-Tk disability (r=-0.220;p=0.02), ULFI-Tk (r=-0.309; p=0.002). Totally 216 activity performance problems (self-care: 80, productivity:71, leisure: 65) determined with COPM.
**Conclusions:** The results of our study demonstrated that COPM is valid assessment in upper limb disorders. Our study was showed performance problems of patients with upper limb disorders that related with Turkish culture.
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**Disclosure of Interest:** None declared
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## AB1112-HPR SYSTEMIC SCLEROSIS TREATMENT: AN OCCUPATIONAL THERAPISTS' VIEW

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**Background:** SSc has a great impact on daily functioning [1]. People with SSc make regular use of allied health care, mainly physiotherapy and occupational therapy (OT), for guidance in coping with the many consequences of the disease. Little is known about the current practice of occupational therapy for people with SSc [2].
**Objectives:** The purpose of this qualitative pilot study was to map the experience of Dutch occupational therapists about their daily practice and vision on optimal SSc care through OTs.
**Methods:** Five female OTs, median age 38.6 years (range 25–46 years) from different work settings and regions with an average work experience of 8.6 years in SSc care, were recruited through the Dutch organisation of Health Professionals in rheumatology. A semi-structured interview was conducted with each participant and transcribed verbatim. Data were analysed by the three-step method of Boeije [3].
**Results:** OTs describe that in CURRENT PRACTICE patients report problems on a functional, activity and participation level, while the treatment is mostly aiming at functional level (including aids and compensations). They experience that their work is experience-based due to the lack of available evidence. The nature of interventions is significantly dependent on the phase of disease in which patients are. They experience a low number of referrals in a late state of the disease and suggest that this might be due to the lack of knowledge about occupational therapy.
In an OPTIMAL SITUATION OTs are involved earlier in the disease process and focus on training and patient needs. They would want to focus on prevention and education including the social environment of the patient. In order to offer optimal treatment they would want to work guideline-based and establish sustained treatment relationships. Earlier referral in the disease process would enable meaningful treatment. They express their need for a clear OT profile to be known by rheumatologists, to facilitate timely and appropriate referrals to OTs.
**Conclusions:** We found a distinct difference between current and ideal OT practice. The newly gained knowledge of this study can be used by OTs for a transition from treatment addressing compensation to a treatment targeting activity and participation. More attention should be paid to timely referrals with a transparent indication.
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## AB1113-HPR DESCRIPTION OF THE SPARE TIME UTILIZATION AND RELATIONSHIP BETWEEN FUNCTIONALITY AND DISEASE ACTIVITY IN A COLOMBIAN RHEUMATOID ARTHRITIS COHORT

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**Background:** Spare time utilization is defined as delectable and non-remunerated activities that a person realizes through its vital cycle. In rheumatoid arthritis (RA) patients this activities might be altered by multiple causes as functional deterioration, psychological problems and social exclusion.
**Objectives:** The aim of this study is to describe the spare time activities and possible relationship with disease activity and functionality of a RA patient's cohort.
**Methods:** A descriptive cross sectional study was realized. A revision of medical records of a cohort of RA patients was performed, including occupational therapy records. For all patients DAS28, HAQ, clinical evaluation and interests check list were made. Percentages, averages and Pearson's statistics were used for clinical and occupational variables.
**Results:** Total sample of patients was 1298, 1048 (80%) were women and 250 (19%) were men. Patients had a DAS28 2.6 in average ± 1.1; mean age was 55.1 ± 8.8 years; 846 (65%) were in remission, 205 (16%) were in low disease activity, 208 (16%) in moderate disease activity and 42 in severe disease activity (3%). Regarding education, 6% were illiterate, 44% had elementary school, 33% high school, 8% had a technical degree and only 7% had college level. In the spare time activities the most frequent were: mixed activities 26% housekeeping 24%, and intellectual activities 15% and handcrafting activities 12%. It was not established correlation between spare time use and disease activity or functionality.

| Occupations | n | % | HAQ (Mean) | | DAS 28 (Mean) | |
|---|---|---|---|---|---|---|
| | | | F | M | F | M |
| Sport and enjoying activities | 62 | 4.78 | 0.86 | 0.16 | 2.58 | 1.6 |
| Handcrafting activities | 158 | 12.17 | 1.06 | 0.36 | 2.66 | 2.55 |
| House keeping activities | 320 | 24.65 | 0.91 | 0.61 | 2.60 | 2.01 |
| Academic activities | 200 | 15.41 | 0.31 | 0.51 | 2.60 | 2.60 |
| Mixed activities | 341 | 26.27 | 0.49 | 0.48 | 2.70 | 2.4 |
| Not reported | 217 | 16.72 | 0.41 | 0.44 | 2.85 | 2.60 |

SPARE TIME USE. FUNCTIONALITY AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

**Conclusions:** Even we did not find a statically correlation between practicing spare activities or not practice and the disease activity, we found that practicing sports improves in men DAS score. Most patients in this cohort prefer mixed activities as their main spare time activity, and other main frequent activities were handcrafting or home activities; perhaps it's important to maintain in this cohort low activity disease and make more studies about this topic because study suggests that male who did only academic activities had more active disease.
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# Miscellaneous forms of clinical care

## AB1114-HPR BIOLOGIC DOSE TAPERING IMPROVES PATIENT CARE AND ADVANCES THE RHEUMATOLOGY SERVICE

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**Background:** Wye Valley NHS Trust has approximately 500 rheumatology patients on biologic therapy, with an annual growth rate of over 15%, increasing the clinical, administrative and financial burden to both the trust and commissioners. Evidence regarding the success of biologic dose tapering in rheumatoid arthritis (RA) patients in remission is emerging[1]. Savings generated by dose tapering can be shared between the provider and commissioner. We discuss the development of a dose tapering gain share which benefits the patient, provider and commissioner.
**Objectives:** The aim was to develop an evidence based protocol for tapering of biologic drugs and to embed the protocol in clinical practice, benefitting patients by reducing their biologic therapy without adversely affecting their arthritis. The savings generated would fund the project including a biologics pharmacist, co-ordinator, consultant time, IT support and ultrasound equipment. To achieve this, the Clinical Commissioning Group (CCG) was to be approached to establish a gain share agreement.
**Methods:** A gain share was agreed with the CCG. The initial savings would fund the cost of the project whilst the remainder would be split 50:50 in the first year, 60:40 in the second year and 70:30 in the subsequent three years, between the CCG and Trust respectively. A literature review was undertaken to devise an evidence-based dose tapering protocol for RA patients. The protocol also specified that ankylosing spondylitis (AS) and psoriatic arthritis (PsA) patients'

biologics could be tapered at the discretion of the clinician, as there is currently a lack of evidence in these diseases. Eligible patients were identified and their doses tapered according to the protocol. Outcomes were recorded on a database, from which we extracted clinical and financial information.
**Results:** After the first 8 months of dose tapering, 25 RA, 4 PsA and 3 AS patients' doses have been tapered. Only 2 RA patients (8%) so far have resumed their original doses due to disease flares. This indicates that we are likely to generate the savings required to fund the project. Importantly we have been able to reduce the medication burden of patients, hence reducing adverse effects whilst retaining disease control. There have also been fewer day case infusions, increasing the availability for day case treatments for other patients and reducing trust expenditure. In addition the project has enhanced the department's relationship with the CCG.
**Conclusions:** This innovative project in a district general hospital demonstrates that savings from a dose tapering gain share can enhance and support an expanding biologics service. Initial results suggest that biologic doses can be successfully tapered in the majority of patients, whilst maintaining remission, with original doses reinstated for small numbers thus far. Further studies are required to assess long term outcomes. The team working exhibited by the rheumatology department and the CCG was essential for the success of the project.
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**Disclosure of Interest:** None declared
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## AB1115-HPR DOSE REDUCTION OF BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS - THE PATIENT'S PERSPECTIVE

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**Background:** Although it is not possible to stop biological therapies for RA patients with established disease, it appears that dose reduction can be successful for some patients in remission or low disease activity. Dose reduction may reduce the risk of adverse events and produce economic benefits that allow greater numbers of patients to receive therapy. Negative consequences might include flares of disease, joint damage and immunogenicity. A vital component of developing dose reduction strategies is to include the patient perspectives. However, these have not been formally reported. Engagement of patients in shared decision-making about their management is vital to improving outcomes and a stated aim of many treatment guidelines.
**Objectives:** To develop a questionnaire, informed by patients and experts, that explores the views of patients with RA about biological therapies and dose reduction.
**Methods:** As a first step in developing a questionnaire we held a patient public involvement (PPI) qualitative focus group (9 patients, 8 female, mean age 49y, mean disease duration 17y) with RA. Eight were on a biological therapy with 2 on a reduced dose. Discussion was facilitated using an interview schedule by two PPI experts and a consultant rheumatologist and recorded. Participants (1) discussed biological therapy in general, (2) listed the top 10 concerns about biological therapy and (3) explored attitudes towards dose reduction. Statements describing the perceived benefits and concerns about dose reduction were separated into two lists and world clouds were generated for each list of statements. Respondent validation of the main themes identified and confirmed the findings.
**Results:** Common themes arising during discussion about biologics in general were: delays in accessing treatment, adverse effects, impact of disease on health, need for education about biologics, inefficacy of previous treatments, impact of disease on family and work and patient autonomy. When exploring attitudes towards dose reduction, the most common concerns were loss of disease control, delay in access to the previous dose and potential loss of efficacy of a previously successful treatment. Perceived benefits were a lower risk of adverse effects and reduced frequency of injection. The positive and negative aspects of dose reduction as cited by patients are shown in word clouds where the size of the word is proportional to the frequency of the word in the patients' statements (Fig 1). This work has led to the development of a questionnaire that will be given to a large population of patients receiving biological therapies to assess their views.

Figure 1. Word clouds demonstrating positive and negative aspects of biologic dose reduction according to patients




**Conclusions:** Patients were prepared to consider dose reduction but need reassurance about rapid access to higher doses should their disease flare. The data provide insight into patients' beliefs and attitudes towards biological therapies and dose reduction and have been used to generate a questionnaire to be distributed to a larger group of patients. The development of a questionnaire that is informed by patient experience and involvement, to explore the views of a wider population of patients, will be an important next step and will assist in the development of patient focussed strategies for dose reduction.
**Disclosure of Interest:** D. Wallis: None declared, C. Holroyd Speakers bureau: BMS, Abbvie, Chugai, Janssen, K. Sonpal: None declared, J. Zarroug: None declared, J. Adams: None declared, C. Edwards Speakers bureau: CE has attended advisory boards, provided consultancy or been part of a speakers bureau for Abbvie, Pfizer, Lilly, Celltrion, Mundipharma, Samsung, Anthera, UCB, Celgene, Roche, BMS, Janssen.
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## AB1116-HPR SHARED UNDERSTANDING AND HIGH INTENSITY – THE PATIENTS' PERSPECTIVES OF ATTENDING A REHABILITATION PROGRAM IN WARM CLIMATE SPECIALLY DESIGNED FOR YOUNG ADULTS

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**Background:** It has been a tradition in Norway to admit patients with rheumatic diseases (RMDs) to rehabilitation in a warm climate for periods of 3- 4 weeks. Young adults with RMDs have to deal with life challenges such as; relating to friends, family and partners, education, establish a family, adjusting to working life, and handling physical and emotional changes, in addition to coping with their RMD. Since young adults may have different challenges and needs than older adults, we developed a 17 day intensive rehabilitation programme aimed at this age group. Two pilot groups with a total of 15 young adults with RMDs age 18–35 participated. The main interventions were intensive exercise (2–3/day), individual physiotherapy (daily), individual treatment plans, group interventions (daily) and patient education (daily). Climatotherapy was also a part of the intervention.
**Objectives:** The aim of this study was to describe the perceptions and experiences of young patients with participating in a 17 day intensive warm climate rehabilitation program that was targeted, organized and adjusted to their age group.
**Methods:** In order to capture the patients' own experiences and perceptions of the rehabilitation program, a focus group interview was conducted six months after the end of the intervention (3 females, 2 men, age 27 - 35 years, disease duration 2 - 13 years, diagnosis: Juvenile Arthritis (1), Rheumatoid Arthritis (1) and Spondyloarthropathy (3)). The interview focused on topics related to the rehabilitation program, such as content and organization, confidence in the staffs' competence, possible effects on health and everyday life, significance of meeting other young adults, satisfaction/dissatisfaction with the programme and feasible negative aspects related to the intervention. Qualitative content analyses were used to make abstractions and categories.
**Results:** The identified themes were "shared understanding", "length of program", "changes in daily life routine", "high intensity" and "competence of healthcare providers'. Shared understanding of their life situation with the other group members was seen as an important component in the program. Sharing knowledge and personal experience with others who are in similar phases in life enhances learning was seen as a useful and positive way of providing self-management. Due to their phases of life, all the participants said that the length of the program was perfect. They could not have attended a traditionally four week program. The intensity of the exercise was higher than traditionally programs and suited the group. After the program they had made changes to their daily life routine both in exercise and diet, but they would like a form of organized follow up from a health care provider. All agreed that the physiotherapists provided an individual program with high intensity and adjusted programme suitable for the young group.
**Conclusions:** This qualitative study suggests that patients experience that their needs were met in this targeted rehabilitation program. The patients reported that the length and intensity of the program and being with others in the same phase of life seemed to enhance motivation and have positive effect on self-management. Further research is needed to document the long term effect of the program.
**Disclosure of Interest:** None declared
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## AB1117-HPR EVALUATION OF PATIENT REPORTED OUTCOME DATA FOLLOWING PERSISTENT MUSCULOSKELETAL PAIN SERVICE REDESIGN

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**Background:** Persistent musculoskeletal pain (lasting >3 months) is common

in the UK and Europe. Following an independent review of service provision, a person-centred, integrated pathway of bio-psychosocial care was commissioned in Oldham, UK. A stepped care model was introduced comprising a single point of access to multidisciplinary care including psychological medicine, prescribing advice and exercise classes.
**Objectives:** To evaluate improvements in pain reported by patient and clinicians discharged from the service and compliance with data capture in the first 6 months.
**Methods:** Outcome data was collected on all patients opting in between 1st June-30th November 2015 including Pain Self-Efficacy Questionnaire (PSEQ) and DoloTest scores on entry and discharge and Clinical Global Impression-Improvement scale (CGI-I) on discharge. PSEQ scores range from 0–60; lower scores reflect little/ no confidence in performing daily activities. DoloTest scores range from 0–800 with lower scores reflecting a lower impact on quality of life. CGI-I is a clinician assessment of patient improvement, scores range from 1–7, with low scores reflecting an improvement and high scores reflecting deterioration.
**Results:** 369 patients opted in throughout the 6 month period, of which 170 (46%) have been discharged. Mean PSEQ score on entry was 17.3 (n=163), which improved to 30.7 (n=50) on discharge. 86% had an improvement in their PSEQ scores with 60% benefiting from a clinically significant improvement. The mean improvement was a score of 17, the mean improvement of significantly improved patients was 22.2 points. Mean DoloTest score on entry was 546.5 and 431.3 on discharge. 70% had an improvement in their DoloTest results; mean improvement was 154 points. There is no available benchmark for a clinically significant improvement for DoloTest. 72% of patients assessed using CGI-I were scored as having very much or much improved.

Table 1

| | On entry | On discharge |
|---|---|---|
| PSEQ scores – mean; median (range) | | |
| All patients with complete data, n=50 | 17.4; 15 (0–60) | 30.7; 29 (4–58) |
| Improved patients, n=43 (86%) | 14.7; 12 (0–50) | 31.8; 29 (4–58) |
| No improvement, n=7 (14%) | 33.9; 30 (9–60) | 23.6; 17 (9–57) |
| Improvement ≥10 points | 12.8; 8 (0–35) | 35; 34 (18–58) |
| DoloTest scores – mean; median (range) | | |
| All patients with complete data, n=37 | 522.5: 526 (191–751) | 445.2; 427 (56–772) |
| Improved patients, n=26 (70%) | 538; 520 (191–751) | 384.1; 378 (56–725) |
| No improvement, n=11 (30%) | 485.7; 366 (242–538) | 589.5; 465 (266–772) |

59 patients (35%) had missing discharge data. Reasons included patients failing to attend follow ups or opting out (46%), stepping up care up to secondary care provision for patients with complex needs (25%), and missing data, unknown (29%). 13 (8%) patients were discharged at first appointment therefore no follow up assessments were completed.
**Conclusions:** In all assessments, the majority of patients improved throughout their treatment. A change in PSEQ score around 10 is considered clinically significant. Of 7 patients with no improvement in PSEQ score, 2 scored <20 indicating their focus on pain could influence their willingness to engage in activity. Of the remaining 5 patients, 3 had high initial scores (>40) thought to be incongruent with requiring a pain management programme. Missing data affected the evaluation and qualitative work is being undertaken to understand the reasons for this and to inform strategies to increase data capture.
**Disclosure of Interest:** None declared
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## AB1118-HPR HEALTH PROFESSIONALS' (HPS) PERSPECTIVES WHEN WORKING WITH PEOPLE WITH RHEUMATOLOGICAL & MUSCULOSKELETAL DISORDERS (RMDS) AND LOWER LEVELS OF HEALTH LITERACY: A QUALITATIVE FOCUS GROUP STUDY

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**Background:** The high prevalence of RMDs and the high proportion of time HPs spend on advising patients with RMDs means that implementing effective self-management strategies is important. Health literacy includes the cognitive and social skills which determine the motivation and ability of individuals to access, understand and use information to promote good health. People with lower health literacy levels have lower levels of activation for self-care and worse functional health outcomes than people with higher levels of health literacy.
**Objectives:** To explore HPs' patient education practice and perspectives when working with patients with RMDs and lower levels of health literacy.
**Methods:** Key contacts from clinics, community GP surgeries and groups identified interested HPs. They were eligible if they had supported patients in developing self-management skills. Participants completed a health literacy questionnaire prior to taking part in a focus group guided by an interview schedule. These were audio-recorded, transcribed and analysed thematically.
**Results:** Five focus group and 2 individual interviews (n=33) were conducted including a consultant rheumatologist; GPs, advance nurse practitioners, nurses, care assistants, occupational therapists, physiotherapists, a podiatrist, a patient advocate, health researchers, a project manager. Key themes included: *Experiencing low health literacy as a RMD service provider:* whilst HPs generally had not previously considered health literacy as an issue for their patients, most could identify indicators of low health literacy such as difficulty recalling information, adhering to exercises or medication and recurrent healthcare-seeking behaviour. *Working with lower health literacy and RMD patients:* HPs experienced that patients with lower health literacy had unrealistic expectations of a cure for their RMD pain. This could impact on patient perceptions about the need for ongoing self-management. *Delivering patient education:* HPs identified that person-centred advice, tailored to the needs of the individual constituted core practice. Time limitations, especially for GPs were the biggest challenge for delivering education. Several practical, educational strategies were in use and identified as relevant for patients with lower health literacy. *Strategies to support self-management:* different communication modes that did not rely on written material were in use alongside effective interpersonal techniques such as using analogies and metaphors to explain detail. The use of positive and encouraging language was recognised as important.
**Conclusions:** HPs did not have a clear way of identifying patients with low health literacy but used behaviour e.g. poor adherence and repeat appointments as indicators. Patients' perceived unrealistic expectations about a cure for their RMD and pain impacted negatively on their perceptions about self-management. There was evidence for health professionals utilising effective educational and inter-personal strategies as a means of supporting patients with lower health literacy.
**Acknowledgement:** Arthritis Research UK for full funding.
**Disclosure of Interest:** None declared
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## AB1119-HPR EVALUATION OF THE PODIATRIC NEED OF PEOPLE WITH INFLAMMATORY ARTHRITIS IN SINGAPORE

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**Background:** Foot problems are common in people with inflammatory arthritis [1]. International guidelines recommend referral to podiatry of all people with rheumatic disease and foot problems [2–4]. Areas covered in the guidelines include access to foot care, assessment and review, foot orthoses and footwear. It is known that access to podiatry services varies between, and even within, countries [5,6]. Such information relating to access and uptake to podiatry services in Singapore for people with inflammatory arthritis is not available.
**Objectives:** To assess the referral rate from a hospital rheumatology department to podiatry services, and the level of satisfaction of referred patients with their podiatry assessment and interventions.
**Methods:** People with inflammatory arthritis were recruited from the rheumatology outpatient clinic of a large public hospital in Singapore. Disease and clinical characteristics were recorded. Participants were asked questions relating to foot problems, access to podiatry services and their perceived usefulness of foot assessment and/or interventions in alleviating their foot symptoms. A footwear assessment was also conducted.
**Results:** 101 patients with inflammatory arthritis were recruited, of which 50% were female. The mean age was 52±15 years, and the mean disease duration was 9.3±0.3 years. The majority (86%, n=78) of participants with foot problems had discussed their foot symptoms with their rheumatologist, though only 21% of participants (n=21) were referred to a podiatrist. Of these, most (n=17, 81%) reported the foot assessments and the podiatric interventions as having been useful (n=15, 71%); 13 (62%) had been prescribed foot orthoses, of which only 9 reported finding them to be beneficial in reducing foot pain. Over 50% of all the study participants (n=51) reported problems with footwear. Only 32 people had correctly fitting footwear. No participants had been issued with therapeutic footwear.
**Conclusions:** Though the majority of people with inflammatory arthritis reported foot problems few received a referral to podiatry. This study is the first to identify an unmet need in Singapore in the podiatric treatment of foot problems in people with inflammatory arthritis, and the under utilization of podiatry service. The results provide a foundation for further study to identify and provide solutions to overcome barriers preventing the utilization of podiatry services.
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**Disclosure of Interest:** None declared
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## AB1120-HPR APPLICATION OF THE INNOVATIVE RHEUMATOID ARTHRITIS MEDICATION ASSEMENT TOOL WITHIN A PHARMACEUTICAL CARE MODEL

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**Background:** Pharmacists must adapt and evolve in order to face challenges and sustain the profession to continuously provide optimum personalised patient care to rheumatoid arthritis patients. Rheumatoid arthritis medication assessment tool, RhMAT is an innovative evidence-based instrument developed specifically to assess pharmacetherapy adherence to rheumatoid arthritis evidence-based guidelines and recommendations.
**Objectives:** The objective of the study was to use the RhMAT within an outpatient rheumatology clinic to identify pharmaceutical care issues and assess therapeutic management of rheumatoid arthritis patients.
**Methods:** Rheumatoid arthritis patients regularly attending the rheumatology clinic at Mater Dei Hospital eligible to participate in the study were offered a pharmaceutical care session. The pharmacist screened each patients' pharmacetherapy using the RhMAT at two time points, Phase 1 (time =0 months) and Phase 2 (time = approximately 12 months).The RhMAT adherence rate for each patient was calculated at both time points. A score of 50% of less was determined as low adherence, a score between 51% and 74% showed intermediate adherence and a score of 75% or more was determined as high adherence to the RhMAT.Gaps in non-adherence to the RhMAT which led to pharmaceutical care issues were documented and discussed with the clinician. Data analysis of the mean score at both phases was analysed using Wilcoxon signed rank test, SPSS verion 22.
**Results:** A total of 78 patients (52 females) participated in the study. The mean age was 64 years (SD 12).The majority of the patients (55%) were prescribed at least one traditional disease modifying anti-rheumatic drug (tDMARD) whereas 45% were on biologic disease modifying anti-rheumatic drug (bDMARD). The most common tDMARD prescribed was methotrexate (n=52 patients). The mean RhMAT adherence rate at phase 1 was 81.7%. Following the pharmacist's contribution whereby the identified gaps leading to non-adherence such as lack of appropriate monitoring or lack of drug therapy counselling, were discussed as necessary with the respective clinician and the patient, the mean RhMAT adherence rate at the follow up session at Phase 2 statistically significantly increased to 85.2% (Wilcoxon signed rank test p value $<0.05$).
**Conclusions:** The RhMAT is an innovative tool which aids pharmacists to identify adherence of prescribed pharmacotherapy in accordance to established guidelines. At the same time, the RhMAT allows pharmacists to identify gaps in individual patients care which lead to pharmaceutical care issues. Through the RhMAT, pharmacists further improve the quality of care offered to rheumatoid arthritis patients.
**Disclosure of Interest:** None declared
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## AB1121-HPR QUALITY OF LIFE AS A CRITERION OF EFFICIENCY IN TREATMENT OF PATIENTS WITH OSTEOARTHRITIS

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**Objectives:** To study the quality of life (QoL) of patients with osteoarthritis (OA), and how it changes depending on the clinical features of the disease and the psychological characteristics of the patients.
**Methods:** We examined 30 patients with OA prior and after treatment. For better comparisons, a control group was set up, which comprised of 30 residents of Volgograd city, in the same age range and sex and who did not suffer from serious somatic diseases. QoL was studied using the questionnaire "SF-36" (Ware JE, 1993).
**Results:** The QoL scores on all scales of the SF-36 questionnaire, in patients with OA were significantly lower than in the control group ($p<0.05$). This showed the lowest scores in QoL osteoarthritis patients ever had before treatment. The physical activity in patients with OA was considerably affected due to the physical ($p<0.001$) and role functioning (RF, RP) ($p<0.001$), as well as indicators of somatic pain (BP) ($p<0.01$). Factors that significantly impaired the physical component of QoL in patients with OA were: age of patients, stage of disease, the severity of joint pain on a visual analogue scale (VAS), and presence of clinically manifested anxiety ($p<0.05$). Factors that significantly impaired social and psychological component of quality of life in OA patients were: stage and duration of the disease and increased functional insufficiency of the joints ($p<0.05$). By improving the physical components of health (physical and role functioning, somatic pain) and psychological components (role emotional functioning, mental health) ($p<0.05$), therapeutic measures significantly had a positive impact on the basic parameters of QoL in patients with OA. Role physical (RP) and role emotional (RE) functioning significantly changed by more than 42% ($p<0.001$). The regularities were significantly associated with decreasing functional failure of the joints, decrease in the intensity of joint pain in VAS and decrease in ESR ($p<0.05$).
**Conclusions:** Thus, after treatment, patients with OA had a significant improvement in physical health, noted by a reduction in pain and physical limitations, and, as a consequence, improved performance. The effectiveness of therapy in the hospital environment contributed in the formation of a positive subjective assessment of the health status in patients with OA.
**Disclosure of Interest:** None declared
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## AB1122-HPR LOCUS OF CONTROL AND THE PHENOMENON OF ALEXITHYMIA IN ANKYLOSING SPONDYLITIS PATIENTS

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**Objectives:** To examine the role of locus of control and the phenomenon of alexithymia in the formation of psychosomatic personality traits in ankylosing spondylitis (AS) patients.
**Methods:** The group studied, comprised of 27 patients suffering from AS. The selection of patients for the study was conducted in accordance with the recommendations of the group of experts working on AS (ASAS, 2003). The patients were of an average age - 44, 94±13, 8 years and had an average duration of the disease - 3, 02 ± 3, 69 years. The main contingent of patients with AS was represented by males (89%). A study of locus of control was conducted by the method of "level of subjective control" (Bazhin E. F., et al. 1987). The study of alexithymia was conducted using the Toronto Alexithymia Scale (TAS) (G. J. Taylor et al., 1985).
**Results:** The study of locus of control in patients with AS showed a significant trend towards external locus of control in common sphere (3,81+1,387), as well as on the scale of failures (3,51+0,64), family relations (4,18+0,55), professional relations (2,74+0.98) and in relation to health (4,66+1,94). Trends towards internal locus of control were observed in the sphere of interpersonal interaction and achievements (5, 14+0, 71 and 5.0+1, 24 respectively). Correlation between the levels of locus of control with other clinical and psychological characteristics, such as age, activity, duration of disease and the level of neurotic disorders in patients has not been established.
A high level of alexithymia (77, 35±1.8 points) was also recorded in patients with AS. The level of alexithymia as such, did not depend on sex, age, character of duration and activity of the pathological process, but was inversely correlated with the level of education of the patients (r=-0.37 with p=0,028) and internality in relation to the disease (r=-0,64, p=0.031).
**Conclusions:** Thus, a certain correlation is formed between the development of the alexithymia phenomenon and some clinical and psychological characteristics in AS patients. This correlation is usually causal in nature, the understanding of which has implications for the organization of preventive measures, aimed at correction of alexithymia traits. Characteristics of locus of control in patients with AS can largely be predetermined by the peculiarities in the formation of personal relationships and the choice of certain strategies. These changes may hinder the effectiveness of therapeutic interventions and need for psychological adjustment in time.
**Disclosure of Interest:** None declared
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## AB1123-HPR THE ROLE OF PSYCHOLOGICAL DEFENSE MECHANISMS AND THE LEVEL OF SUBJECTIVE CONTROL IN THE DEVELOPMENT OF AFFECTIVE DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Objectives:** To examine the role of psychological defense mechanisms (PDM) and level of subjective control (LSC) in the development of affective disorders in patients with rheumatoid arthritis (RA).
**Methods:** We observed 28 patients with RA. The average age was 55, 59±8, 76 years and the average duration was – 7, 2±4,3years. The questionnaire "level of subjective control" (LSC) (Bazhin E. F., et al. 1993) was used in the study. Psychological defense mechanisms were studied according to the "index of lifestyle" inventory (IL) (E. B. Klubov et al., 1995). The study of affective disorders was conducted by the "neuroticism and psychopatization" psychological test (L. L. Dmitrieva, 1990).
**Results:** In women, a high intensity of PDM in the type of "Reactive formation" was seen. And in men, a higher tension in PDM in the type of "Displacement" and "Intellectualization" ($p<0.01$) was noted. RA patients with the third stage of activity had lowest indices related directly to defense "Denial" ($p<0.05$). Asthenia, depression, anxiety and hypochondria are directly correlated with the parameters of PDM "Reactive formations" (H). The level of asthenia and anxiety were directly correlated with intensity of "Regression" defense mechanism (r=0,316 and r=0,365; p=0.010 and p=0.003). The level of asthenia and depression were directly correlated with the defense "Projection" (r=0,399 and r=0,343; p=0.001 and p=0.005).
Patients with RA were mostly characterized by external locus of control in common

sphere (3,81+1,387), failures (3,51+0,64), family relations (4,18+0,55), industrial relations (2,74+0,98), health (4,66+1,94). The general internal locus of control in RA patients was significantly decreased (p=0.006) along with increasing stage of the disease. Significant negative correlations were established between the levels of asthenia, anxiety and hypochondria and internal locus of control (p=-0, 45; p=-0, 52; p=-0, 40, respectively, when r=0,005); and between level of anxiety and internality of failures (p=-0, 42, p=0.05).

**Conclusions:** The obtained data indicate the passiveness of RA patients fighting with the disease, and failure to appreciate the connection between their actions and important events of their lives; hence in this background, a choice more towards non-adaptive psychological defense mechanisms is made which in turn exacerbates the neurotic reactions in RA patients.

**Disclosure of Interest:** None declared

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## AB1124-HPR KEY ASPECTS OF HEALTH PROFESSIONALS REQUIRED TO BE EXPERTS IN RHEUMATIC DISEASES (REUMAPPA)

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**Background:** Spanish Rheumatology League (Liga Reumatológica Española, LIRE) is developing an application for mobile devices and web browsers that incorporates a map of resources for rheumatic patients and professionals who treat them (Reumappa). This app helps locate with ease professionals and specialized services in rheumatic pathologies in Spain. A focus group with rheumatic patients was conducted in a previous phase in order to identify which fields of health professionals are required to manage their disease. It was then considered interesting to know whether there are relevant aspects of these specialties that distinguish professionals who can provide better care for rheumatic patients.

**Objectives:** To identify key issues that health professionals should have to bring added value in the management of rheumatic patients.

**Methods:** Focus Group with health professionals selected by patients as useful for the management of their disease (occupational therapist, physiotherapist, podiatrist, nurse, nutritionist, dentist, psychologist, and 2 social workers), sex (4 male, 5 female), age (3 <45, 6>45), years of professional experience (3 <10, 6>10), sector (5 private, 4 public). Key question: "*What aspects do you think add value to the care your specialty provides to rheumatic patients?*".

**Results:** Table 1 shows the results of the focus group. N = nurse, SW = social worker, OT = occupational therapist, Nu = nutritionist, Po = podiatrist, Psi = psychologist, Phy = physiotherapist, D = dentist.

Table 1. Health professionals skills for optimal management of rheumatic diseases.

| | N | SW | OT | Nu | Po | Psi | Phy | D |
|---|---|---|---|---|---|---|---|---|
| General knowledge of rheumatic diseases (RD) | x | x | x | x | x* | x | x | x** |
| Knowledge of treatments | | | | | | | | |
| Pharmacological | x | | | x | | x | x | x |
| Specific exercises for RD | x | x | x | x | x | x | x | |
| Orthotics and prosthetics | x | x | x | | x | | x | x |
| Cognitive behavioral techniques | x | | x | | | x | x | |
| Dietary supplements | | | | x | | | | |
| Pain management (evaluation and treatment) | x | x | x | | x | x | x | |
| Specific exercises for RD | x | x | x | x | | x | x | |
| Knowledge of immunology | x | | | x | | x | x | |
| Occupational health | x | x | x | | | | | |
| Knowledge of local resources | x | x | | | | x | x | |

*Podiatrists only RA and osteoarthritis; **Dentists only Sjögren and osteoarthritis.

Imperative Required Advisable

**Conclusions:** All health professionals who treat rheumatic patients should have at least a general knowledge of rheumatic diseases. Most health professionals should have a knowledge of drug treatments and recommended exercises. Nurses, psychologists, and physiotherapists require greater specialization to treat these patients.

**Disclosure of Interest:** None declared

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## AB1125-HPR HEALTH- RELATED QUALITY OF LIFE IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHROPATHIES AND BIOLOGIC THERAPY

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**Background:** Chronic inflammatory arthropaties-CIA (RA-rheumatoid arthritis, PA-psoriatic arthritis, and AS-ankylosing spondylitis) cause functional disability and reduces health-related quality of life (HRQoL) of patients[1]

**Objectives:** To evaluate HRQoL in patients with CIA and biologic therapy (BT), as a measure of patient reported outcome.

**Methods:** Descriptive cross-sectional study (August 2014) in a tertiary hospital. Inclusion criteria:a)adult patients with RA, PA, SA and other CIA (O) attended at the Rheumatology Service and b)≥2 months of treatment with BT (sc/iv adalimumab-ADA, sc/iv etanercept-ETA, iv infliximab, sc golimumab, sc certolizumab, sc/iv abatacept, sc/iv tocilizumab or iv rituximab). Sociodemographic and clinical variables were obtained by structured interview and review of medical record.Degree of disease activity measures: DAS28 index (≤3.2:low activity; >3.2-≤5.1:moderate; >5.1:high) for RA and PA peripheral; BASDAI (<4:low activity ≥4:high activity) for AS and PA with predominant axial involvement. HRQoL was mesured by a self-administered questionnaire:EQ5D-5L[2]. It evaluates 5 dimensions:mobility (M), self-care, usual activities (UA)pain/discomfort (PD) and anxiety/depression. Each dimension has 5 levels of severity. A HRQoL score is obtained (EQ-index) from 0 (death) to 1 (full health). It also has a visual scale (EQ-VAS) of global health from 0 (the worst health) to 100 (the best health). Descriptive and multiple linear regression analysis (LRA) were performed to determine which variables contributed on HRQoL.

**Results:** A total of 382 patients were eligible for the study.314 patients agreed to answer the questionnaire (women:55.7%, average age (±SD): 55.2±13.9 years, average disease duration (±SD):13.05±8.1 years). Pathologies distribution: 44.3% RA, PA 26.1%, 21.3% AS, 8.3% O. BT: 51.9% ADA, 28.7% ETA and 19.4% others. 65.9% of patients had a first line of TB. 50% of patients had concomitant drug (corticosteroid/methotrexate/leflunomide). 71.7% of patients had low activity, with standard drug regimen (61.8%) and optimized regimen (37.6%). The EQ-index perceived was:0.73±0.22 and a global health EQ-VAS: 64.2±21.0 points. The worst rated questionnaire dimensions (severities 3–4-5) were P (33.7%), UA (29.9%) and M (26.7%).

LRA showed significance differences (p<0.001) for disease activity, disease duration and education. 0.4 and 9.05 EQ-VAS points were reduced for each year of evolution and each DAS28 point increase, respectively. Differences were not significant for age, sex, pathology, drug or line number.

**Conclusions:** Generally, patients evaluated have a good control of disease activity and an acceptable HRQoL perceived. Chronic P and loss of autonomy to perform UA are the worst rated dimensions

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## AB1126-HPR HOW PHYSICALLY ACTIVE ARE NORDIC PATIENTS WITH MODERATE TO SEVERE OSTEOARTHRITIS?

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**Background:** Osteoarthritis (OA) is one of the most frequent chronic rheumatic and musculoskeletal diseases (RMD), and one of the leading causes of pain and disability worldwide. Physical activity is a key lifestyle advice along with weight reduction if overweight. However, data on the amount of physical activity in patients with OA are limited.

**Objectives:** To examine physical activity in people referred to specialist care for their OA.

**Methods:** Patients with known OA with moderate to severe OA referred to a specialist clinic in Oslo, Norway were after informed consent mailed questionnaires on demographic data and physical activity before visiting the clinic. Of 391 people, 86% (n=338) were females with mean age (SD) 61.2 (7.8) years). Patients rated their weekly physical activity that included shortness of breath, based on experiences from the last two weeks. Other patient reported outcomes included pain, fatigue and stiffness on numeric rating scales, and body mass index (BMI). Through descriptive statistics and explorative analyses the group was described. Patients who fulfilled 3 hours of physical activity per week or more were slightly

Table 1. Patient characteristics (N=391)

| Variable | Value |
|---|---|
| Age (years), mean (SD) | 61.2 (7.8) |
| Gender women, n (%) | 338 (86%) |
| BMI (SD) | 25.6 (4.9) |
| Pain (NRS), mean (SD) | 5.3 (2.0) |
| Fatigue (NRS), mean (SD) | 4.1 (2.9) |
| Stiffness (NRS), mean (SD) | 5.2 (2.4) |

BMI = body mass index, NRS = numeric rating scales (11-point, range 0–10).

Table 2. Self-reported physical activity

| Weekly physical activity* | N (%) |
|---|---|
| 0 hours PA | 53 (13.6) |
| >1 hours PA | 56 (14.3) |
| 1–2 hours PA | 78 (19.9) |
| 2–3 hours PA | 81 (20.7) |
| 3–4 hours PA | 52 (13.3) |
| 4–5 hours PA | 28 (7.2) |
| 5< hours PA | 37 (9.5) |

*Self-reported physical activity.

leaner and had a numerically lower BMI than those who were less physically active (non-significant differences, data not shown) than those who were less physically active.
**Results:** See tables.
**Conclusions:** 29.9% (N=117/391) of OA patients fulfilled the recommended minimum of 3 hours of physical activity per week, while almost 14% reported not being physically active at all. To enhance recommended physical activity, emphasis on physical activity in OA is required during clinical care as well as easy access to programmes for health-enhancing physical activity. These interventions may decrease the burden of OA in the future.
**Disclosure of Interest:** None declared
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## AB1127-HPR CONSTRUCT VALIDITY TESTING OF RAST, A NEW RA STIFFNESS PATIENT REPORTED OUTCOME MEASURE (PROM)

S. Halls[1], E. Dures[1], J. Kirwan[2], J. Pollock[1], G. Baker[3], A. Edmunds[3], S. Hewlett[1]. *[1]Faculty of Health and Applied Sciences, The University of the West of England; [2]School of Clinical Sciences, University of Bristol; [3]Rheumatology Department, Bristol Royal Infirmary, Bristol, United Kingdom*

**Background:** Morning stiffness is a frequently used clinical and research outcome measure and is important to patients[1], but was omitted from the RA core set because of poor measurement properties[2]. Current stiffness assessment is inconsistent with patient's perspectives of the symptom[3,4] and has not been developed according to PROM development guidelines[5]. A new 21 item, 3-component Rheumatoid Arthritis Stiffness questionnaire (RAST) has been developed based on qualitative work[3] with RA patients and statistical assessment to enhance content validity and now requires testing for appropriate relationships with other measures of disease (construct validity).
**Objectives:** To perform construct validity testing of RAST.
**Methods:** The 21 item RAST was developed from 45 items assessing stiffness included in a questionnaire pack which was posted to patients with RA based in the South-West of England. The questionnaire pack also contained individual items capturing pain (VAS), fatigue (NRS), patient global assessment (PtG VAS), questionnaires capturing disability (MHAQ), and patient-reported disease activity (PDAS2[6], scores generated from an algorithm including PtG, swollen joint count (SJC), and MHAQ), and basic demographic information. The RAST was subjected to construct validity testing using a correlation matrix of Spearman's correlation coefficients (reported as explained variance ($R^2$).
**Results:** 277 patients (91 male) aged 23–97 years with disease durations 1–45 years participated in the study (42.9% response rate). The individual components and sum score of RAST demonstrated appropriate relationships with other measures of disease (pain $R^2$=45–72%; fatigue $R^2$=43–55%; PtG $R^2$=48–68%; MHAQ $R^2$=55–78%; PDAS2[6] $R^2$=56–78%). The shared variance indicated that while RAST (individual components and sum score) is related to other measures of disease, it is not measuring the same thing. Importantly, as identified by patients in earlier qualitative work[3], the variance explained by the RAST (individual components and sum score) and the (patient-reported) SJC included within the PDAS2[6] was between 31–41% indicating that RAST may capture something not currently included within disease activity assessment. The pattern of relationships between individual components and measures of disease also provided support for the 3-component structure. As expected, the "physical component" shared the most variance with disability ($R^2$=78%), the "severity component" shared the most variance with pain ($R^2$=72%) and PtG ($R^2$=68%), and the "psychosocial component" shared less variance with the above disease related measures.
**Conclusions:** During preliminary validity testing RAST, the new RA stiffness PROM, demonstrated promising construct validity. Further testing of RAST is now required in a fresh population to generate measurement property evidence of reliability and sensitivity to change to support its use.
**References:**
[1] Hewlett et al, 2005;
[2] Felson et al, 1993;
[3] Halls et al, 2014;
[4] Orbai et al, 2014;
[5] FDA, 2009;
[6] Choy et al, 2008; 2015
**Disclosure of Interest:** None declared
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## AB1128-HPR DEVELOPING A NEW RHEUMATOID ARTHRITIS (RA) STIFFNESS PATIENT REPORTED OUTCOME MEASURE (PROM)

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**Background:** Morning stiffness is a frequently used clinical and research outcome measure and is important to patients[1], but was omitted from the RA core set because of poor measurement properties[2]. Current stiffness assessment is inconsistent with patient's perspectives of the symptom[3,4] and has not been developed according to PROM development guidelines[5]. The appropriate content of a new RA stiffness PROM was previously explored and developed through qualitative interview[3] and focus group studies. Draft items were subsequently tested and refined with patients during cognitive interviews, resulting in 39 draft items for inclusion in a PROM. Here we report a quantitative assessment to create the smallest and most internally consistent set of items for a developmentally valid stiffness PROM.
**Objectives:** To develop the content and structure of a new RA stiffness PROM.
**Methods:** A postal questionnaire pack was sent to patients with RA based in the South-West of England. It contained 45 items assessing stiffness (39 draft items and 6 items currently used in stiffness assessment), individual items capturing pain (VAS), fatigue (NRS), patient global assessment (VAS), questionnaires capturing disability (MHAQ), and patient-reported disease activity (PDAS2[6]), and basic demographic information. Initial investigation identified items with poor response rates, distributions or correlations for removal. A series of principal component analyses were undertaken with the remaining items, balancing Cronbach's alpha for internal consistency, stability of the component structure (assessed by multiple analyses using random 50% samples of the respondents (bootstrapping)) and parsimony. Based on the statistical results and aided by expert judgement, the smallest number of informative items were retained.
**Results:** 277 patients (91 male) aged 23–97 years with disease durations 1–45 years participated in the study (42.9% response rate). Seven of the 45 items were removed during initial item investigation. The remaining 38 items demonstrated high Cronbach's alpha (>0.9). During successive rounds of analytical refinement, 17 items were removed. After round 5, a 3-component structure emerged which remained consistent for a further 13 rounds of testing item removal, demonstrating stability. These components captured "stiffness severity", "physical impact" and "psychosocial impact". The overall Cronbach's alpha of the final 21 items was 0.95 indicating a homogenous set of items and bootstrapping further demonstrated the stability of the structure.
**Conclusions:** A new 21 item, 3-component RA stiffness PROM has been developed based on qualitative work[3] with RA patients to enhance content validity. Further testing is now required to assess the validity, reliability and sensitivity to change of the new RA stiffness PROM.
**References:**
[1] Hewlett et al, 2005;
[2] Felson et al, 1993;
[3] Halls et al, 2014;
[4] Orbai et al, 2014;
[5] FDA, 2009;
[6] Choy et al, 2008; 2015
**Disclosure of Interest:** None declared
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## AB1129-HPR CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE PATIENT REPORTED OUTCOME MEASURES QUESTIONNAIRE FOR INFLAMMATORY ARTHRITIS FOR BULGARIAN-SPEAKING INDIVIDUALS

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**Background:** The PROMs-Arthritis questionnaire [1] was developed to evaluate the patient reported outcomes in individuals with inflammatory arthritis. Translation of the questionnaire to other languages will provide a standard outcome measure across populations.
**Objectives:** To translate the English version of the Patient Reported Outcome Measures for inflammatory arthritis (PROMs-Arthritis) to Bulgarian; and evaluate the psychometric properties of the Bulgarian version.
**Methods:** The PROMs-Arthritis questionnaire was cross-culturally adapted to Bulgarian, according to established guidelines. The validity and reliability of the Bulgarian version were assessed in 110 patients with rheumatoid arthritis (RA) as well as 44 healthy control. The questionnaire includes assessment for functional disability, quality of life, VAS for joint pain, patient global status, fatigue, duration of morning stiffness, assessment of co-morbidities, patient activation as well as self-reported joint pain.
**Results:** The expert committee and the participants considered the questionnaire to have good face and content validity. Dimensionality analysis revealed a 1-factor solution, explaining 97% of the total variance. Known group validity

was demonstrated by significant differences between patients compared with the asymptomatic group ($P<0.001$). An item analysis showed a high degree of internal consistency (Cronbach $\alpha$=0.805).The Bulgarian version exhibited excellent test-retest reliability (intraclass correlation coefficient =0.805 for the arthritis group). The questionnaire items correlated significantly ($p<0.01$) with clinical parameters of disease activity (DAS-28), physician global assessment, ESR and CRP levels. RA patient self-reported tender joints correlated significantly with the physicians' scores (0.893). Changes in functional disability, quality of life as well as Patient Activation scores showed significant ($p<0.01$) variation, with diseases activity status (DAS-28). The questionnaire showed also a high degree of comprehensibility (9.4).

**Conclusions:** Integrating patient reported outcome measures into standard clinical practice is feasible and applicable. The Bulgarian version, adapted from the original English PROMs-Arthritis questionnaire, shows a considerable validity and reliability, and its psychometric properties are comparable with the original version.

**References:**

[1] El Miedany Y et al. Clin Exp Rheumatol. 2010 Sep-Oct;28(5):734–44.

**Disclosure of Interest:** None declared

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## AB1130-HPR COGNITIVE THERAPY FOR REDUCING THE IMPACT OF RHEUMATOID ARTHRITIS FATIGUE: SUCESSFUL STRATEGIES FOR MEETING TARGETS IN A COMPLEX HEALTH CARE INTERVENTION

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**Background:** Complex interventions are widely used in modern health care practice and are defined as those having potentially interacting components. Evaluation can be challenging due to difficulties in logistics, standardisation, delivery, recruiting to time and target (particularly in multi-centre studies) and minimising attrition and data loss.

We report how the RAFT study (a 7-centre randomised controlled trial comparing a complex, group cognitive-behavioural intervention with standard care, for the reduction of fatigue impact in patients with rheumatoid arthritis) is implementing successful strategies to meet targets. The study requires patients to make a substantial commitment over a two year period and for the intervention to be delivered by routine clinical staff trained for this purpose.

**Objectives:** To recruit to time and target, ensure intervention delivery, minimise attrition and maximise retention.

**Methods:** Maximising recruitment: Funded research nurse time at all 7 sites, mailshot approach option, recruitment posters, flexible/pragmatic approach to session attendance, telephone, email and postal contact, newsletter and regular knowledge exchange between the central management team and sites, weekly recruitment review. Ensuring intervention delivery: Flexible course dates and times, regular discussions around foreseeable issues and preventative actions, provision of real-time clinical supervision and full-time telephone/email support. Minimising attrition and data loss: Primary outcome collected by telephone ensuring regular personal contact. Secondary data collected by postal questionnaire reducing the number of hospital visits. Telephone reminders, partial withdrawal options, personalised letters and thank you cards. Patient involvement: Acceptability and feasibility consultations with our 2 patient partners. Both have experience of attending the intervention, were co-applicants on the grant proposal and continue to provide the patient perspective as members of the trial management group.

**Results:** Recruitment: Target of 300 participants with no recent medication changes and a fatigue level of $\geq$6 (on a 1–10 scale where 10 is totally exhausted). During the 2 year recruitment phase 333 participants were randomised (11% over target). Intervention delivery: 28/28 programmes successfully delivered with 7/7 sites and 14/15 tutors remaining fully engaged with the study. Attrition and data loss: Retention at 6 months is currently 92.5% (sample size allows for 20% attrition). Data returned by those reaching the 6 month time point is 100% for the primary outcome and 97% for secondary outcomes.

**Conclusions:** Advanced planning and consistent application of these strategies has ensured success so far. A flexible and pragmatic approach, regular communication between local and central teams, personal contact with participants and extensive patient partner input are key components.

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# People with Arthritis and Rheumatism in Europe
# Abstracts

# Poster Presentations

## Patient information and education

### PARE0001 THE "SWEDISH YOUNG RHEUMATICS" PARTNERED UP WITH ANOTHER YOUNG IMID ASSOCIATION AND ABBVIE TO PRODUCE AN INFORMATIVE AND HOPE GIVING BOOK ON "STARTING A FAMILY". THE COLLABORATION RESULTED A HIGHLY INFORMATIVE BOOK THAT PROVIDES A WEALTH OF INFORMATION ON FAMILY PLANNING

M. Beermann. *Unga Reumatiker, Bandhagen, Sweden*

**Background:** For patients with an immune-mediated inflammatory disease (IMID), starting a family can seem like a daunting decision due to the lack of information and guidance around how IMID affects pregnancy. In addition to the normal concerns about pregnancy, living with a chronic illness raises complicated questions about the ability to conceive, caring for a young child or even whether patients should become parents given the potential for children to inherit the disease. As patients seek answers – and often find none – they can begin to lose hope, and some may forgo the decision to have a family altogether. The "Swedish Young Rheumatics" partnered up with another young IMID association, "Young with Psoriasis" and AbbVie to produce an informative and hope giving book. The collaboration resulted an informative book that provides a wealth of information on family planning for IMID patients

**Objectives:** We recognized that this was an issue that no one wanted to take on, but something very important in most young patient's life.

The purpose was to create a book that filled the void, something to start a discussion round and something to find comfort and support in for everybody involved.

The book also addresses questions regarding medication, adoption and IVF

**Methods:** In order to show the broadest and truest spectra of the topic, both "Swedish Young Rheumatics" and "Young with Psoriasis" searched through their channels, to find members who wanted to share their stories on the topic. The search was carried out through social media and their member magazines. Singles and couples were interviewed by an external party, finally 7 couples and 4 singles stories reached the book. The stories contain hope, longing, happiness, strength and a lot of questions is raised and answered. Everybody were interviewed in depth and their stories accompanied by beautiful pictures taken in their natural environment. All medical parts of the book were approved and checked by Prof of Dermatology Mona Ståhle and Prof of Rheumatology Lennart Jacobsson.

**Results:** The result is a highly informative photo-filled book that provides a wealth of information on family planning for IMID patients. "Starting a Family" captured a range of positive stories from young couples with IMID conditions who had been successful in starting a family, weaving a narrative of hope and providing definitive answers around family planning. The book has also led to initiated discussions with new target groups such as midwives, and the Associations have reached out with their messages in new channels, which have resulted in new valuable contacts and relationships. The book has been distributed for free to everybody who has got in contact with one of the associations and also to health care, both through the associations and the project partner AbbVie.

**Conclusions:** The Swedish Rheumatism Association believes in the importance of empowering the patients. By offering tools for self-help combined with personal advice from a professional health care worker we can support a general movement towards a healthier lifestyle.

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### PARE0002 A PHOTO-PROJECT ABOUT YOUNG PEOPLE SUFFERING FROM JUVENILE ARTHRITIS

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**Background:** "It is a vicious cycle. Early morning, you wake up. First thought: how much pain will I have today? Can I stand up? Can I move my joints? Can I go to school? Or can I go out later to play with my friends?"

These questions are normal for me, a twenty-five years old photojournalist; and all the other children in the world who suffer from juvenile idiopathic arthritis. Arthritis is a disease commonly considered by the general public to be an "old person's disease". The reality is that many young people live with this disease. The chronic progressive inflammation – primarily of the joints – appears for reasons unknown. It is one of the most common chronic diseases beginning in childhood.

So what does it mean for a child to suffer from this painful chronic disease so early?

**Objectives:** I am a photographer, or a "storyteller", but I am also affected by this disease; making the subject matter deeply personal. My goal is to share the voices of other young rheumatics and show how other young people deal with their arthritis individually. Through the means of photography and personal observations it is possible to create deeper insights into children's perspectives.

**Methods:** Driven by my personal ambitions of starting a professional career as a freelance photographer and living at the same time with a chronic disease, I started to follow young children and teenagers suffering from juvenile arthritis.

In 2014 the project began: for a couple of weeks I moved in with a family who had two arthritic children, in order to photograph their daily life. In 2015, I continued photographing more protagonist all over Germany. From there, the project became part of my final bachelor exam for my current University-level photographic studies. I spent weeks in hospitals in order to capture the realities that these young people are living within. I took part in support group events and weekends. In addition, I followed these subjects in their daily life and free time. My goal was to gain the closest possible relationship that I could with my protagonists.

**Results:** By spending such a considerable amount of time with these young people, I was not just a silent observer, I was part of their life. This helped me develop a deep understanding of their point of view and enabled me to tell their stories. The resulting photo-essay brings together all the different aspects of lives of children with rheumatism.

Juvenile arthritis is a disease which is often not visible. The pain can feel so different on a daily basis and is highly individual. My photographic series tries to approach this fact in an atmospheric way.

Young rheumatics have their ups and downs. One day they may wake up with a lot of pain and be unable to move, if their joints have stiffened. The next day they may feel fine; able to go out and live their lives as regular people. This creates the so called vicious cycle. These young people are obligated to accept these circumstances as continuously present hurdles and factors in their life.



**Conclusions:** The project is intended to be a sensitive example of how young people cope with such a disease. On one hand it is intended give courage to viewers who also have arthritis by showing them that they are not alone. On the other hand, the message is intended to introduce juvenile arthritis to a wider audience; the general public, whom are likely unaware of the realities of this disease.

**References:**

[1] Link to the photo-project: http://www.benediktziegler.com/index.php/eular2016

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### PARE0003 WHAT DO I WANT TO TALK ABOUT?

T. Bellerby, D. Stevens, L. Williamson. *Rheumatology, Great Western Hospital, Swindon, United Kingdom*

**Background:** Face to face appointment time between patient and clinician is precious. Patients can wait months between appointments, and usually allow clinicians to take the lead in their consultations. These may concentrate on disease related outcome measures and treatment targets. Patients may not feel able to raise other issues, or may forget to ask about them. Waiting time for appointments is almost inevitable, so to help patients make best use of their waiting time we decided to add a "What Do I Want to Talk About" area.

**Objectives:** To assess patient response to "What do I Want to Talk About".

**Methods:** In the centre of patient waiting area we put up an "What Do I Want To Talk About" A4 poster, encouraging patients to write down the questions important for them to discuss within their consultation. We provided A6 paper sheets and pens for patients to take into their consultations. We asked patients to provide feedback by anonymous questionnaire asking these questions:

Do you think this is a good idea? Yes/No; Have you used it? Yes/No.

Would you use it in future? Yes/No; Other comments?

**Results:** 26 patients completed the questionnaire. Of these, 25 patients (96%) thought it was a good idea. 3 (12%) said they had used these slips previously. 18 (69%) said they would use them on their next visit.

Comments: 'Good Idea thanks. I usually forget what I want to ask when I get in there and then remember on my way home'; "Why hasn't this been done before?"; "I always do notes before my appointments as it helps both doctor and patient"; "This is a really good idea, and thanks for the pen"
Clinician's comments: "Really helpful for consultations, patients seem better prepared "; "I used the same paper to respond to questions and as an aide-memoire for patients"
**Conclusions:** 'What do I Want to Talk About' is a very simple, universally applicable idea which uses minimal resources. It may help some patients better prepare for consultations, and ensure key issues important to patients are addressed during consultations.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2016-eular.5787

### PARE0004 TOOLS FOR A CUSTOMIZED HEALTHCARE PLAN FOR DUTCH PEOPLE WITH RHEUMATIC DISEASES

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**Background:** It is vital for people with rheumatic diseases to have a suitable healthcare plan in order to cover essential healthcare that is critical to maintain health and quality of life, to treat rheumatic diseases and to prevent high medical costs. Despite the urgency, finding a suitable healthcare plan is complicated: there are many options to choose and healthcare plans differ in coverage of rheumatic disease-specific healthcare (such as physical therapy, foot care and spa therapy), price, medical selection and provider network. Also the time to decide whether to change their healthcare insurer or plan is limited. Consequently, people may decide not to change their healthcare plan at all, at the risk of having an unsuitable healthcare plan in relation to the care they need and paying unnecessarily high medical costs. By developing tools and information, we tried to help people with rheumatic diseases finding a suitable healthcare plan in that short time limit.
**Objectives:** The purpose of this project was to make it less complicated for Dutch people with rheumatic diseases to find a personal healthcare plan which covers their personal needs for healthcare.
**Methods:** Through patient consultation (a survey) we got more insight in the needs, experiences and wishes among rheumatic disease-specific healthcare and healthcare plans. We analyzed the composition, price and conditions of individual healthcare plans concerning rheumatic disease-specific care. We analyzed the reimbursements of healthcare that is essential for patients with a rheumatic disease. In line with this we developed tools.
**Results:** The survey (n=1420) showed that people with rheumatic diseases want: 1. more information about reimbursement of rheumatic disease-specific healthcare, in particular physical therapy, medication and foot care. 2. more insight in personal health needs 3. an aid to compare healthcare plans and find a healthcare plan that fits personal health and budget *needs*.
Responding to these outcomes we developed three tools:
1. A "*checklist*" to make an overview of personal health and budget needs. People can fill in the checklist on their own or together with their care provider(s).
2. A "*healthcare plan comparison tool*" for comparing healthcare plans on rheumatic disease-specific care and finding a healthcare plan that matches with personal health and budget needs.
3. The *checklist* and the *healthcare plan comparison tool* are integrated in the "*Roadmap healthcare plans*". This roadmap guides people through the process of finding a suitable healthcare plan in 5 steps. In addition to these tools, we updated our online information about rheumatic disease-specific healthcare.

**Conclusions:** In response to the tools, we received positive reactions from people with rheumatic diseases. Local patient organizations paid attention to the tools as well. We think we made a step forward by launching interactive tools. With individual needs as a starting point, people can compare healthcare plans. Nevertheless, the Dutch system of healthcare plans is still complex and our information is still extensive. For the Dutch Arthritis Foundation it's important to keep paying attention to useful information and tools for people with rheumatic diseases.
**Disclosure of Interest:** None declared
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## Building patient led organisations

### PARE0005 BRIEF OVERVIEW OF ENCA (EUROPEAN NETWORK FOR CHILDREN WITH ARTHRITIS)

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**Background:** ENCA, the European Network for Children with Arthritis was founded in 2002 by parents representing national JIA (Juvenile Idiopathic Arthritis) associations from several European countries. ENCA is a broad based association that covers JIA and other orphan joint associated conditions. It is run on a voluntary basis by parents who wish to advance the quality of treatment their children receive through networking, communications and research. ENCA is associated with the Paediatric Rheumatology European Society (PReS) the European scientific society for healthcare professionals in the field of paediatric rheumatology.
ENCA is structured as an informal network between national JIA associations, and is open to all JIA associations.
**Objectives:** As an international networking group, ENCA's role is to gather and circulate information, knowledge, and expertise gathered by individual associations in order to promote knowledge and positive practices among all the associations. This knowledge, in turn, filters down through the national associations to medical systems, parents and sick children, thus upgrading the quality of care offered in each country.
ENCA has three strategic themes:
- Exchange information about the activities of each association
- Promote common projects at European level
- Set up information networks and regular exchanges between associations

**Methods:** Member associations are asked to send representatives to the yearly ENCA conference which takes place in conjunction with the PReS (every 4th year also as part of Eular). A website, closed Facebook group and a yahoo group allow members to have constant communication. International networking helps solve problems faced by all organizations on a national level and parents on an individual level. Pooling resources can help weaker countries acquire better treatment and social services by belonging to an International organization.
In addition ENCA collaborates with Doctor Organizations and research establishments to promote, initiate and facilitate research aimed to advance sick children's needs.
**Results:** Since its inception, ENCA has made advances in both fields: communication between the associations, and research with the medical establishment. Establishing communications between the associations has proven itself as an effective method for solving common problems faced by children in all countries, as well as an opportunity to bring information to the fore. In addition, ENCAs' cooperation with PReS and PRINTO have facilitated two important projects: The SHARE parents' survey initiated by PReS to collect information about the quality of care of JIA patients. The study was conducted through ENCA, allowing for a wider resource base and more accurate results. In addition, ENCA facilitated the translation of the new upgraded PRINTO (The European Union site for information on paediatric rheumatic diseases) site into national languages, thereby enabling access of up to date information to parents.
**Conclusions:** As parents of children with JIA, ENCA has greatly increased our knowledge within all areas of health and social care. It has given us a diverse network allowing us access to a broad source of expertise, knowledge and resources. Through pooled resources it has helped weaker organizations.
**Acknowledgement:** PReS, Share, Printo
**Disclosure of Interest:** None declared
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### PARE0006 IDENTIFICATION AND PRIORITIZATION OF RESOURCES FOR RHEUMATIC PATIENTS (REUMAPPA)

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**Background:** Spanish Rheumatology League (Liga Reumatológica Española, LIRE) is developing an application for mobile devices and web browsers that incorporates a map of resources for rheumatic patients and professionals who treat them (Reumappa). This app helps locate with ease professionals and specialized services in rheumatic pathologies in Spain.
**Objectives:** Identify and prioritize resources to be included in Reumappa.
**Methods:** Focus group with characteristic rheumatic diseases patients (Rheumatoid arthritis, Osteoporosis, Sjögren, Scleroderma, Spondylarthritis, Psoriatic Arthritis, Fibromyalgia, Behcet's disease, Lupus, and Osteoarthritis), sex (4 male, 6 female), age (3<45, 5 between 45 and 65, 2>65) and years of disease progression (4<10, 6>10). Key question for identification: "*If you could use an app to obtain information about professionals, services or useful things to cope better with your condition what would you expect to find in it?*" Prioritization was established by scoring from 0 = no relevance to 10 = maximum relevance.
**Results:** Resources that patients identified as important to help them with their disease and their appraisals according to their relevance (mean, SD) are in table 1 (see p. 1322).
**Conclusions:** There are a number of resources that can be helpful for rheumatic patients. Among professional resources most popular medical specialists are rheumatologists, ophthalmologists, pediatricians, gastroenterologists and dermatologists; nonmedical professionals that are considered most necessary are physiotherapists and psychologists. Services identified as most important are patient associations, units specialized in specific pathologies, orthopedics stores and gyms.
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| Table 1 | | APPRAISAL | |
|---|---|---|---|
| RESOURCES TO BE INCLUDED IN REUMAPPA | | Mean | SD |
| PATIENT ASSOCIATIONS | Local | 8,9 | 0,9 |
| | Provincial | 9,4 | 0,8 |
| | Autonomous Community | 8,9 | 0,9 |
| | National | 9,4 | 0,8 |
| | International | 6,7 | 1,5 |
| BUSINESSES | Orthopedics | 7,0 | 1,3 |
| | Drugstore | 5,3 | 1,6 |
| | Herbalist | 4,7 | 2,5 |
| LAWYERS | | 7,6 | 1,5 |
| PHYSICIANS | Rheumatologist | 9,9 | 0,4 |
| | Ophthalmologist | 8,6 | 1,5 |
| | Pediatrician | 8,4 | 1,8 |
| | Gastroenterologist | 8,3 | 0,8 |
| | Dermatologist | 8,1 | 1,7 |
| | Gynecologist | 8 | 1,4 |
| | Cardiologist | 7,7 | 1,5 |
| | Primary care | 7,1 | 3,3 |
| | Endocrinologist | 7 | 1,8 |
| | Internist | 6,7 | 4 |
| | Vascular | 6,7 | 3 |
| | Traumatologist | 6,7 | 1,7 |
| | Hematologist | 6,4 | 3,1 |
| | Psychiatrist | 6,1 | 2,6 |
| | Nephrologist | 6 | 3,4 |
| OTHER HEALTH PROFESSIONALS | Physiotherapist / Rehab technician | 8 | 1,6 |
| | Psychologist | 7,7 | 0,8 |
| | Social worker | 7,6 | 1,3 |
| | Nutritionist | 7,1 | 1,3 |
| | Nurse | 6,7 | 2,2 |
| | Dentist | 6,7 | 1,5 |
| | Occupational therapist | 5,9 | 2,2 |
| | Pharmacist | 5,3 | 2,6 |
| | Podiatrist | 4,7 | 3,1 |
| | Logopedist | 4,3 | 2,7 |
| TRAINING | Expert patient programs | 8,0 | 0,6 |
| | Training groups in health centers or hospitals | 8,3 | 0,5 |
| | Training for self-care | 8,3 | 1,0 |
| SPORTS FACILITIES | Gyms | 7,3 | 1,1 |
| | Pools | 6,7 | 1,6 |
| PATIENT REGISTRIES | | 7,9 | 1,6 |
| SPECIALTY UNITS | | 9,3 | 0,8 |

## Best practice campaigning

PARE0007 **A SUCCESFULL CAPS RECYCLING PROGECT "NOT SATIATE CAPS"**

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**Background:** The organization in the effort to implement the goal of social integration of people with RMDs and improve their self-service in order to feel independent and to have self-esteem, presented a need for providing free self-help tools to the members of the association. The need was created because of the economic crisis that exists in the country with all its consequences and, therefore, the high cost of living and reduced resources of people with Rheumatism.
**Objectives:** The main objective is to gain funds for the provision of self-help tools for everyday life and assessment and configuration of house and workplace, of people with Rheumatism. At the same time, the organization aims in The Raise Awareness of Rheumatism and The Raise of Volunteerism.
**Methods:** Use of recycling of caps in order to gain funds. As a result of the public interest, the organization decided to expand the campaign in the Junior and Kindergarten Schools because, children of this age are the best means to transfer the messages we want to convey to society. A collaboration with a Big Insurance Company started for this project, who sponsored the amount of 90000€. The Ministry of Education and Culture became an important supporter and the Media were involved too. Eventually, the recycling company agreed to enlarge their collecting program.
Through this program, we invite children to collect plastic caps from water containers, milk, and any other plastic caps, and place them in yellow plastic bins bought specifically for this purpose by the sponsor and placed in schools.
**Results:** More than 210 schools have declared their participation from the 2 bigger cities in the country. Leaflets have been prepared to share to all students in the schools for informing them and their families about the project, RMD's and organization.
A presentation has been also prepared to be shown to students by volunteers in the schools.
TV and radio advertisements have been prepared with the slogan "Not satiate caps".
A special website has been developed which a simple and understandable educational tool for children on recycling issues and rheumatic diseases as well as for the actions of the program.
A Press Conference has been made for the Campaign by the Organization together with the Ministry of Education and Culture, and the big Sponsor. A competition was launched between the schools participating in the program, with the first three schools from each district being awarded at a special ceremony to be held in May 2016, the total amount of 10,000€.
**Conclusions:** This campaign has successfully managed to: fund raise a big amount for help-self tools to be able to give them free to organization's members to Raise Awareness primarily for the RMD's and the Organization, and last but not least the Protection of the Environment and recycling and to Raise Volunteerism by building the next generation of volunteers.
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## Building patient led organisations

PARE0008 **SETTING UP A YOUTH GROUP: A CHALLENGE WORTH TACKLING – ANMAR'S STEP ZERO PROJECT**

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**Background:** EULAR PARE recommendations state that, by 2020, every European country member of the EULAR PARE network should have a youth group within its national association. Through EULAR's Knowledge Transfer Program, ANMAR – Italian national association for people with RMDs –, has made a start in this crucial direction. Before the Step Zero project, dedicated to the creation of Italy's first youth group, ANMAR hadn't promoted any activity specifically targeting young patients yet, counting very of them among its members. Thus, ANMAR was strongly willing to involve this rather invisible portion of RMDs patients and make space for their specific needs.
**Objectives:** ANMAR's Step Zero Project main aim was to identify, get in touch with and involve a first team of young Italian patients willing to be part of the first Italian Group for Young People with RMDs. By applying to EULAR's knowledge Transfer Program ANMAR aimed to share knowledge and learn best practices in creating a youth group by partnering with a country much more advanced than Italy in this field. The project had also an inspirational nature: by getting in direct touch with the young experts from our partner association, Youth-R-Well.com from the Netherlands, our young participants would begin to learn how an Italian youth group could be settled and nourished, this being a mid-term objective within the Step Zero Project.
**Methods:** starting from a real zero step, ANMAR – fruitfully synergic with other Italian associations working in the field of rheumatology (especially the parents' of children with RMDs' associations) – has in the first place collected and shared the existing contacts of young patients. Over three months, 15 young patients willing to be a part of this project have been reached. The Step Zero meeting has taken place in Milan on November 20th, 21st, 22nd 2015, registering the presence of 12 young patients, aged from 18 to 35, reaching Milan from 8 different Italian regions, and two guest speakers from the Netherlands. The meeting has focused firstly on mapping the unmet needs of Italian youth with RMDs, and secondly on thinking about solutions to effectively target those need
**Results:** This first group of participants is currently working on the development of a communication strategy aiming to reach and involve individuals under 35 suffering from RMDs across Italy. ANMAR's Youth Group is now transitioning from Step Zero to Step One, gradually engaging in advocating for better care and quality of life for Italian young rheumatic patients, as well as raising consciousness about the impact of rheumatic diseases on individuals under the age of 35.
**Conclusions:** Setting up a youth group is a very complex and challenging experience, and yet it is a challenge undoubtedly worth tackling. It is fundamental to be able to keep sharing those experiences within the European network EULAR YOUNG PARE, since empowering youth groups across Europe is crucial in order to improve health care for young rheumatic patients, involve them in the life of patients' associations and support their specific – and often still unmet – needs.
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## Best practice campaigning

PARE0009 **ESTONIAN YOUTH AWARENESS OF INVISIBLE CHRONIC DISEASES**

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**Background:** Chronic conditions affect people all over the world; over 100 million citizens or 40% of the population in Europe above the age of 15 is reported to have a chronic disease [1]. One of the main tasks of patient organisations is to raise awareness of them. So far, there have not been any studies conducted in Estonia that would show how successful they have been in raising awareness in the general population and among the youth in Estonia.
**Objectives:** The objective of the study was to find out how aware are 15–35 years

old Estonians of chronic diseases, and furthermore, through which channels they first learned about the diseases.
**Methods:** The study focused on the five most prevalent disease groups, out of which were selected specific diagnoses: juvenile idiopathic arthritis, diabetes mellitus, asthma, depression and chronic hypertension. The criteria for choosing the diagnoses were the following: diagnoses that have the most effect on young people are most prevalent or have the highest incidence rate. The data was collected via an online survey, which was spread on different social networks and among the pupils of two secondary schools.
**Results:** In total there were 191 responses from which 172 answers could be used. The average age of the respondents is 20 years. Most of them have heard about asthma (89.5%), diabetes mellitus (89.0%), chronic hypertension (78.0%) and depression (90.1%), but only 29.3% has heard about juvenile idiopathic arthritis. Most of the people, who answered, say that they first heard about the diseases from their family, friends or their acquaintances, 14.5% from television or radio and 13.4% from social media.
**Conclusions:** Although rheumatic and musculoskeletal diseases (RMDs) are one of the most common chronic conditions in Europe, from the results of the study it can be concluded that very few people in Estonia are aware of them. Since RMDs are not directly life-threatening like asthma or diabetes, it could be suggested that patients do not want to disclose their diagnosis to their acquaintances in fear of social stigma and discrimination. However, since this was a quantitative study, it is not possible to point out direct reasons and further qualitative research is needed. Additionally, from the results it can be concluded that the organisations for patients with RMDs should contribute more into raising awareness using the mediums of television, radio, and the internet.
**References:**
[1] European Union Health Policy Forum: Answer to DG SANCO consultation on chronic diseases. (2012).
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## Patient information and education

### PARE0010 INFLUENCE OF RMDS ON SEXUALITY AND COUPLE'S RELATIONSHIP: AN HARD PROBLEM FOR PATIENTS WHICH REMAINS UNSPOKEN

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**Background:** Over 50% of patients consider RMDs as a disabling illness which has a strong impact on sense of self, self-esteem and on the couple's wellbeing.
Many patients tend to deal with these issues independently, passively accepting them in the belief they are unsolvable.
As it is the task of an association to understand, to analyze and to find solutions to the problems of the people represented, ANMAR carried a survey into this problem on Italian patients.
**Objectives:** to evaluate frequency and importance of interferences on the relationship; to identify the main causes and the most useful tools to overcome the problem
**Methods:** inside a larger surveying program set by ONDA (National Observatory on Women's Health) we elaborate a 24 questions questionnaire about RMDs. For this analysis we mostly considered the answers to 10 questions, regarding how patients perceive their health, sense of self, self-esteem and the disease impact on sexuality.
**Results:** we evaluate answers from 719 patients - 2/3 with RA, 3/4 female – 56 years old in average, still working despite illness and pain and with a RA diagnosis over 10 years old in 50% of cases.
The disease is considered as disabling, has a strong impact on physical and mental wellbeing (50% defines their health "not good" or "fair" and refers many sacrifices in daily life due to illness) and on sense of self ad self-esteem: 50% of patients think that illness made him/her different and it has deeply undermined confidence in himself/herself and his own self-image.
Women will suffer more intensely the effects, appearing most suffering psychologically (they are angrier, they feel changed, they are liking less) and physically (they refer stronger pain, they have a more difficult relationship with the therapy and they are forced to more waivers, in home, children and partner care).
50% of those who have a love life says that their sexuality has suffered from the disease for loss of mobility (66%) or decreased sexual desire (50%); 74% did not share the problem with anyone and of these 66% would not want to do it, because they think it is unnecessary.
Males and females similarly perceive the impact of the disease on the intimacy of couples and equally share the problem with someone (25% for both genders), but choose to approach different figures: women their gynecologist (64%), men their partners (50%).
Men are more closed and resigned: only 16% of those who did not mention it, would like to do it, while the percentage rises up to 28% among women.
**Conclusions:** simple information, support and reassurance regarding the perception of self and the intimacy, but also practical tips and tricks to relieve pain or to facilitate mobility during sex, or simply offering communicative cues that lead us to reflect on the problem without aside it with resignation may be enough not to give up living with serenity the intimacy, in keeping with our body and with the limitations the disease imposes.
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### PARE0011 LIGAFLASH, BEYOND AN IMAGE. A PHOTOGRAPHIC EXHIBITION

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**Background:** The impact in the Spanish society of the rheumatic disease (RDs) is of 1 out of 5.
The rheumatic diseases are around 250 which affect all ages and can become chronic and be very invasive.
To raise awarness among or society about the social and emotional impact we decided to organize a exhibition of photography.
**Objectives:** Get rid off myths about rheumatic disease from a positive perspective.
**Methods:** The themes that were selected to be represented in the exhibition are the following:
1. Pregnancy and Maternity: On one hand some RDs increase the risk of miscarriage. On the other hand the need of medical treatment to control the disease makes more difficult to get pregnant.
2. Sexuality:Almost a third part of people with arthritis have difficulties in their sexual life because of the disease.
Pain, functional and articular impotence and the selfperception difficult secual relationships.
3. Work Life: RDs are the first cause of physical disability in the western world, according to the Health World Organization, and cause a big economic problem in our country, not because of the sick leaves or the disability pension but because it consumes a lot of sociosanitary resources.
This could be solved by making work policies more flexible with patient autocare.
**Childhood affected by rheumatic diseases:** In Spain, between 8,000 and 10,000 children are affected by RDs, so an specialized attention is needed, according to the President of the Spanish Rheumatic Society (SERPE), because generally this pathologies are associated with old age.
**Results:** Our organization elaborates this project with the intention of showing a new image of the person affected by the rheumatic disease, we leave morbidity behind and search beauty, symbology, sexuality, happiness and demonstrate that beyond illness there is another world, much richer and with variation in the life of a person with any type of disease.
For Galicia Rheumatic League, art is a therapeutical way of enriching the spirit that brings us happiness Therefore we give great importance to the performing arts, dance, painting, photography, cinema, theatre, etc. always with a double purpose: 1. raising awarness; 2. from a normalizing point of view.
All the people involved in this project overcame a personal challenge, the models where patients who where showing a very personal and sensitive part of their life in an image, the photographer trying to capture that important message with his camera, etc.
This exhibition was able to involve the patients family and their social environment as well as to catch the attention of politians and health professionals and is set to travel along the peninsula and abroad.



**Conclusions:** Raising awarness presenting the rheumatic diseases normalized and integrated in our society.
This exhibition has been in diferent cities within the Galician region breaking prejudices and building a different image of the rheumatic disease seeing in the images of the exhibition people who transcend happiness above pain, overcoming the limitation, etc.
**References:**
[1] Eular Congress Paris 2015
[2] www.ligaflash.com
**Disclosure of Interest:** None declared
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## Best practice campaigning

### PARE0012 REVMA CHALLENGE 2015 – GIVE A HELPING GLOVE AND SUPPORT A PATIENT WITH RHEUMATOID ARTHRITIS

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**Background:** Czech League Against Rheumatism plays an important role in promoting rheumatic patients in the Czech Republic. Its activity is aimed at raising awareness about rheumatic diseases, the struggle for full and equal life for people with rheumatic diseases and the establishment of regional clubs of Czech League Against Rheumatism.
**Objectives:** Create a campaign aimed to raise awareness about rheumatoid arthritis - a serious disease that destroys lives insidious way over 100,000 inhabitants of the Czech Republic. When most people understand the nature of rheumatoid arthritis, they can better help the patients manage their daily struggle with the disease.
**Methods:** Creating a campaign... "Give a helping glove and support a patient with rheumatoid arthritis" with the participation of experts from rheumatology and also the participation of personalities from the cultural and scientific life. Rheumatoid arthritis is most often manifested impairment of the joints of the hands. The symbol of the campaign thus became a special glove, developed by scientists from the Institute of Technology in the US, Georgia. These gloves can restrict the movement of the fingers and hand grip strength using metal plates - and faithfully simulate the symptoms of the disease. It can show a healthy people feeling in the shoes of people with rheumatoid arthritis. Creating a video with personalities who use gloves to perform daily activities and leisure activities.
**Results:** The main outcome of the campaign was the debate with an expert on the generation of positioning whitepaper document for timely treatment for patients with rheumatic disease. In response to the campaign has increased the number of members in Czech League Against Rheumatism, an increased number of visitors and fans of the Facebook page Czech League Against Rheumatism. It managed to raise awareness of rheumatic diseases among the general public.
**Conclusions:** This campaign seems to be very useful in influencing the professional and lay public. It is one of the ways how they can be involved in the functioning of the organization.
**References:**
[1] Czech PARE organization - Czech League Against Rheumatism
**Disclosure of Interest:** None declared
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## Patient information and education

### PARE0013 JUVENILE IDIOPATHIC ARTHRITIS: IT'S NOT JUST AN OLD PERSON'S DISEASE

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**Background:** Juvenile Idiopathic Arthritis (JIA) is a common form of chronic arthritis in children and young people (CYP), diagnosed under the age of 16 [1,2]. It is a long-term condition (LTC) that is poorly understood by the general public, and can severely impact patient quality of life [3,4]. Therefore, it is important to support CYP in self-managing their condition, particularly as they transition into adult health services. The need for interactive health communication applications (IHCAs) to improve knowledge and health behaviours of CYP with LTCs, supplementary to clinical advice, is well reported in the literature [5]; however, many existing resources are static and do not actively engage CYP in learning about their condition.
**Objectives:** Our research aims to improve the understanding of JIA amongst the general public, musculoskeletal researchers, and CYP living with JIA, using a variety of resources.
**Methods:** Four resources were developed to raise the understanding of JIA: two magazine articles, a presentation to musculoskeletal researchers, and the IHCA, translated from existing static resources produced by charities in the United Kingdom (UK). An expert advisory group (EAG) helped to design, distribute and evaluate the research. Distribution of the resource to CYP with JIA, aged 11 to 18, was achieved via JIA charities across the UK.
**Results:** The Biological Sciences Review article, aimed at young Biologists, focuses on the role of the immune system in JIA, highlighting the impact of the disease on quality of life. The New Scientist article discusses the pathophysiology of the disease, and novel therapies currently used. A presentation at The University of Manchester's Centre for Musculoskeletal Research's seminar adressed a diverse team of researchers, exposing them to JIA and the importance of patient involvement. The IHCA resource takes CYP on an interactive journey about JIA, the medicines that they take, and how they can be proactive in leading a healthy lifestyle.
**Conclusions:** The project helps to raise awareness of JIA. In addition, it is hoped that it will strengthen national and international relationships with regards to user involvement in research. Finally, this research will add to the wealth of literature on eHealth interventions, representing a "smart way of thinking", to improve efficiency in a modern healthcare delivery system, by optimising input from costly professional organisations, in a way that CYP find more accessible.
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[5] Swallow, V.M. et al. (2014). An interactive health communication application for supporting parents managing childhood long-term conditions: outcomes of a randomised controlled feasibility trial. JMIR Research Protocols. 3(4): e69.
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## Best practice campaigning

### PARE0014 PATIENT ADVOCACY FOR BETTER INFORMATION ON BIOSIMILARS AND SWITCHING

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**Background:** During the past ten years, treatments with biologics have proven added value for several inflammatory illnesses, such as rheumatoid arthritis, spondyloarthritis and juvenile arthritis. In 2015, the first biosimilars for infliximab were introduced in the Netherlands. They were welcomed for their financial benefits, but also some questions arose. The Dutch Arthritis Foundation was frequently asked to comment or advise on biosimilars. Yet, we found that clear and unbiased patient information was scarcely available, that opinions differed regarding switching existing patients, and lastly, that there were no recommendations available on switching practices, studies and monitoring.
**Objectives:** As several patents for widely-used biologics will expire the coming years, it was important to approach this development carefully and realistically. We wished to develop patient information and a view on biosimilars that would fit both new patients and existing arthritis patients. And it was clear to us that patients who worried about switching to biosimilars, wished for unbiased and reliable answers. Therefore, we contacted the Dutch Society for Rheumatology (NVR), who were updating their recommendations on biological treatments, and started working closely together with patient organisations, dealing with the same information challenges. And lastly, considering all the strong (financial) opinions around biosimilars, we wanted to raise awareness for the more practical issues and questions, arthritis patients had shared with us.
**Methods:** The Dutch Medicine Evaluation Board (MEB) published its stance in April 2015, permitting the exchange between biological medicines. However, the conditions for switching patients were interpreted differently, as we experienced in panel discussions and workshops with prescribing doctors, pharmacists, pharmaceutical companies and health insurers. Therefore, as patient organisations, we jointly asked MEB for guidance regarding patient information. In July 2015, MEB organised a meeting on biosimilars in the fields of IBD and arthritis, in which we expressed our concerns and asked for careful monitoring of patients and traceability of treatments. After this meeting, MEB started developing a patient information leaflet, involving several patient organisations. We analysed and collected all questions from arthritis patients on biosimilars and switching, and sent those to MEB.
**Results:** While biosimilars were being prescribed and administered, there was hardly any practical information available to patients in 2015, or patient organisations. Most information focused on the biochemistry and interchangeability of biosimilars, but did not answer practical questions on switching conditions, long-term (side) effects or health insurance issues. The MEB patient information leaflet will be ready in January 2016. And we will update our information for arthritis patients afterwards, closely cooperating with NVR.
**Conclusions:** It is interesting and important to learn from the introduction of infliximab biosimilars and the current switching studies. Also to prepare for the near future when biosimilars will be introduced for biological treatments that patients administer themselves. Patients ask for practical information instead of lessons in biochemistry. With suitable patient information, we can try to avoid concerns or prevent that adherence issues arise if medicines look slightly differently, or if the administration and packaging work slightly differently.
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## Innovations in arthritis health care

PARE0015 **PATIENT INVOLVEMENT IN THE DESIGN OF TECHNOLOGICALLY-ENHANCED CLOTHING TO HELP MANAGE MUSCULOSKELETAL CONDITIONS**

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**Background:** Patients with musculoskeletal conditions manage their symptoms on a daily basis. The physicality of dress demands movement and dexterity that this population often find difficult to perform due to pain and restricted joint mobility. Mainstream garments do not accommodate such concerns; as a result, patients have limited clothing choice and subsequently devise alternate methods of dress. Emerging technologies such as the 'Internet of Things'[1], wearables and biotechnology create the future potential for clothing to be used as a vehicle in the management of musculoskeletal conditions, by which to deliver topical medication and/or provide real time biofeedback to the patient's healthcare team (so their condition can be continuously monitored).
**Objectives:** 1) To design fashionable everyday garments which cater to the needs of patients with musculoskeletal conditions, and 2) to assess the acceptability of incorporating potential technological enhancements.
**Methods:** Four adult participants who met the inclusion criteria (diagnosis of a musculoskeletal condition and ability to communicate in English) were recruited from the Independent Patient Group, part of a London hospital rheumatology outpatient department, by the group's patient co-chairs (SdS and CS). Two males and two females (aged 37–68 years, 3 rheumatoid arthritis: 1 ankylosing spondylitis, disease duration 6–50 years and of diverse ethnic background) agreed to take part in four co-design workshops over a 4 month period in 2015. Workshops were conducted by a student fashion designer (AC). Garment prototypes were presented to patients and continually modified between workshops based on group feedback.
**Results:** Patients wanted a mode of dress to enable independence and provide comfort; whilst maintaining dignity and a sense of self-expression. It was important that the garments were easy to wear, versatile, made of a lightweight breathable fabric and looked like regular clothing (rather than a garment designed for those with additional physical needs). Patients requested minimum fuss with fastenings. The 5 resultant garments had three basic accommodative dress methods: entry from the bottom-up, side and a flip-over mechanism. Once the basic template designs were established, garments could be personalised to suit individual tastes. Patients were receptive to the potential future use of the clothing to deliver topical pain relief medication and would be happy for biofeedback data to be shared with their healthcare team, provided this data could be transmitted securely.
**Conclusions:** Garments can be instrumental in an individual's continued perception of normalcy, control and confidence over their lives. Technologically-enhanced clothing proposes a more personalised and empowering approach to healthcare delivery by way of connecting the interdisciplinary threads of fashion, medicine, new emerging technologies and user-focused design. Clothing is a big part of everyday life; its enhancement can play a welcome, unobtrusive role in the management of patients with musculoskeletal conditions.
**References:**
[1] Hoy MB. The "Internet of Things": What It Is and What It Means for Libraries. Med Ref Serv Q. 2015;34:353–8.
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## Arthritis research

PARE0016 **FAMILY PLANNING IN WOMEN WITH INFLAMMATORY ARTHRITIS: THE PATIENT'S PERSPECTIVE**

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**Background:** The inflammatory arthritis (IA) - rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and juvenile idiopathic arthritis (JIA) - affect a significant number of women of childbearing age. Epidemiological studies have shown that the number of births is lower in these patients compared with healthy controls, but the fertility rate is not always decreased. Personal choice of family planning in these patients is influenced by several factors, such as disease activity, use of potentially teratogenic drugs, functional impairment and information received.
**Objectives:** To assess the aspects related to the disease that have greater impact on family planning in women with IA and identify areas for improvement from the point of view of the patient.
**Methods:** We performed a cross-sectional study in women with IA (RA, AS, PsA and JIA) of childbearing age (17–47 years) during the period from June 2014 to July 2015. Two anonymous questionnaires were used for data collection, a questionnaire included clinical data and was completed by the physician and another questionnaire with demographic data, reproductive history and family planning was completed by the patient. Family planning assessment included 16 closed-ended questions about influence of disease activity, secondary concerns and fears, knowledge on diagnosis, treatment and its effects on pregnancy, and information provided by her rheumatologist. All patients signed an informed consent.
**Results:** A total number of 108 women were included. The mean age was 37.4±7.5 years and their diagnoses were: RA 43, AS 31, PsA 19 and JIA 16. The mean age at diagnosis was 27.7±10.2 years and 54% had children (0.82 children/woman). 33% of patients had been a mother before diagnosis and only 20% later (0.24 children/woman), although 40% had considered pregnancy during the disease. IA was considered a conditioning factor for family planning in 70% of cases, and the disease activity was chosen as the most influential factor followed by the treatment. Concerns about disease worsening was found in 64%, transmission of IA to their children in 48% and limitation for care them adequately due to functional impairment in 45%. Half of the patients reported having little knowledge about side effects of drugs on the mother or fetus and have received none or scarce information about pregnancy and breastfeeding from their rheumatologists in 52% and 68%, respectively. More than a third of the patients had considered a new pregnancy if they had received more information. There was no relationship with socio-demographic variables and no significant differences were found in the subgroup analysis (IA type, age, treatment).
**Conclusions:** Women with IA have a low birth rate. The factors with a greater impact in family planning were disease activity and treatment, but were also important the fear of worsening, disease transmission and not be able to care for children properly. Lack of knowledge and information needs to be detected in these patients and should be resolved since the diagnosis. A better understanding of their disease could help these patients to diminish their fears and facilitate family planning in those who wish it.
**Disclosure of Interest:** None declared
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## Patient information and education

PARE0017 **EULAR YOUNG PARE: THE VOICE OF YOUNG PEOPLE WITH RHEUMATIC DISEASES ACROSS EUROPE**

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**Background:** The group of Young Patients with Arthritis/Rheumatism in Europe (PARE) in EULAR, the European League Against Rheumatism, is a network of young people, from across Europe, living with a rheumatic or musculoskeletal disease (RMD) and working with a patient organisation in their country. They volunteer their time to represent young people with RMDs within EULAR PARE, advocating for better care, communication and quality of life for individuals, under 35, across Europe.
**Objectives:** When the group was established, objectives were designed to:
(1) establish and strengthen national RMD youth groups across Europe; (2) create and support the European network of RMD youth groups to exchange best practices; (3) empower youth leaders; and (4) ensure that the voice of young people with RMDs is heard on all levels in society.
**Methods:** EULAR Young PARE are actively involved in local, national and international activities to support young people with RMDs. Members of EULAR Young PARE developed an action plan to communicate and promote their work, embedding the youth perspective into and supporting all EULAR PARE activities.
**Results:** A strong voice of young people, especially at the Annual European Conference of PARE, has been established, with topics delivered and dedicated to the needs of young people. All PARE activities and projects now entail a young person living with an RMD, feeding back into the Young PARE working group. Furthermore, strengthening collaboration with the EMEUNET network is a leading example of how we learn together.
**Conclusions:** Young PARE have moved forward considerably over the last twelve months, gathering and sharing information about the ways that young people with RMDs are supported in European countries. Now, EULAR Young PARE is continuing to unite patient organisations across Europe, helping to raise awareness and make a difference to young people living with RMDs while challenges remain. It is important to keep the network sustainable, and EULAR Young PARE committed to working on this over the coming years.
**References:**
[1] EULAR Young PARE. Available from: http://www.youngpare.org [Accessed 13 December 2015].

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